# Acute Bacterial meningitis

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# OBJECTIVE

To KNOW at the end of the presentation

- Epidemiology of meningitis and The most common organisms leading to bacterial meningitis
- Pathogenesis and risk factors of ABM
- Clinical presentation at the different ages
- Diagnosis
- Principles of Antibiotic therapy
- Role of Adjunct therapy
- Complications
- Outcome
- Care for contacts
- Prevention of meningitis

# Epidemiology.

- 1.2 million cases/yr
- 135,000 deaths/yr one of the top ten, in developing countries
- Beyond the newborn period most important are three heavily encapsulated organisms
  - **Strep Pneumo**
  - **H Influenza b**
  - **Neisseria meningitides**
  - All have a polysacharide capsule which increases virulence and also confers immunity if anitbody to capsule is present
- Pneumo 38-17/100,000 population
- HIB 31-46/100,000
- Overall death rate 31-40/100,000

# Pathogenesis and risk factors

- Note that the CSF is protected and sterile
- The CSF lacks the defense mechanisms in the blood, no neutrophils, no immuneglobulins
- The integrity of the Blood brain barrier is one of the most protective mechanisms and any disruption of that may lead to meningitis
- In the newborn the BBB is poorly developed. Meningitis may be present in up to 20% of sepsis

**Table 4.** Bacterial Meningitis in the United States (% of Total Cases)

| Age | Organisms |
|---|---|
| 0-4 weeks | *Streptococcus agalactiae, Escherichia coli, Listeria monocytogenes, Klebsiella pneumoniae, Enterococcus* spp., *Salmonella* spp. |
| 4-12 weeks | *S. agalactiae, E. coli, L. monocytogenes, Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitidis* |
| 3 months to 18 years | *H. influenzae, S. pneumoniae, N. meningitidis* |

Adapted from Tunkel AR, 2000.

This is also applicable to our region

# Acute Bacterial Meningitis in special hosts

Post Head trauma

Strep Pneumo

H flu b.

Post Shunt, Neurosurgery

Staphylococcus epi/aureus, gram negatives

# Acute bacterial meningitis

## Bacterial pathogenetic factors

Polysaccharide capsule is common to all pathogens that cause ABM

HIB, Strep pneumo, Neisseria in older individuals

- In the newborn, E coli K1 antigen, Listeria monocytogenes and Gp b Strep all have capsules.
- Anticapsular antibodies=protection
- Colonization of the nasopharynx as well as the vagina in GBS also increases the risk because of increased exposure and invasion may occur

# Host factors that increase the risk for meningitis

- Extremes of Age, in the newborn exposure to maternal GBS
- Male sex
- Def of C5-8
- Def in IgM , IgG
- Asplenia, congenital or surgical
- Head trauma
- Chronic disease, Diabetes, Addison, Hypothyroid, CF
- Renal insufficiency
- Children with facial cellulitis, periorbital cellulitis, sinusitis, and septic arthritis have an increased risk of meningitis.
- Poverty
- Attendance at day care and Crowding
- Mass gatherings include the  Hajj which increase the risk of exposure and increase carraige

# Neonatal meningitis

- More common in the premature
- More common in complicated delivery and any condition that increases sepsis in the newborn
- 20% of sepsis cases may be associated with meningitis due to poor BBB in the newborn
- The newborn also has immature immune defense mechanisms
- Maternal colonization with GBS and other bacteria may be more likely to lead to sepsis and meningitis due to colonization in the newborn due to maternal exposure

# Epidemiology in neonatal meningitis

- GBS 50% of cases with risk being highest when mothers who are colonized with GBS.
- E Coli 20%
- Listeria 5-10% may be acquired transplacentally
- In developing countries ?? GNB
- HSV maybe acquired at birth, but may get sick in the second week of life leading to meningitis or encephalitis
- Enterobacter sakazakii was reported following ingestion of contaminated reconstituted formula In the newborn
- Enteroviruses may cause up to 3% of cases with sepsis and meningitis in the newborn

# Prognosis in the newborn

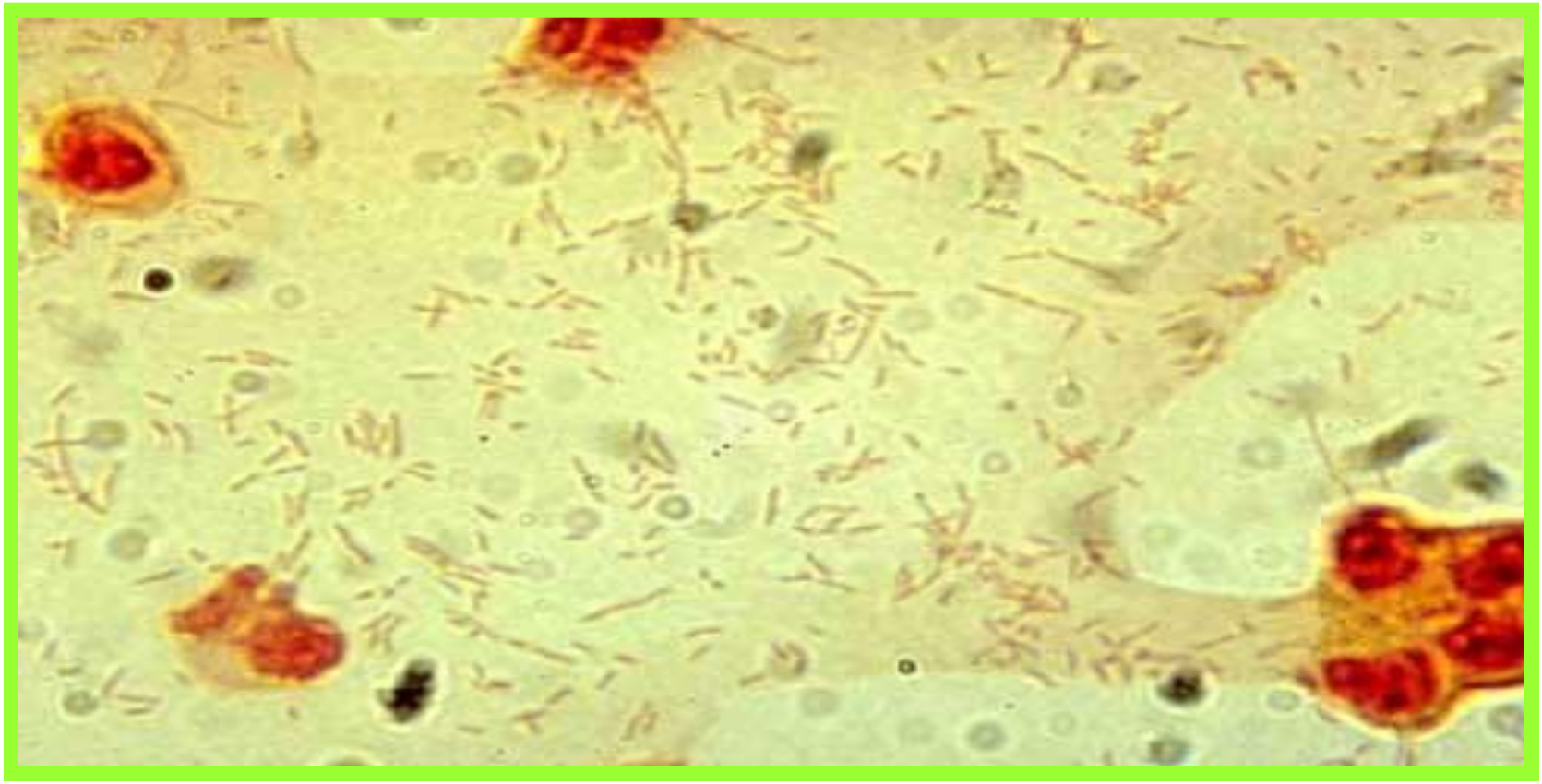
- Death 10% in bacterial meningitis and 15% in HSV
- HSV 1 and 2 same mortality
- Morbidity with increased CP,MR, Seizures,microcephaly
- 5-20% epilepsy
- 25-50% significant problems with language, motor function or cognition
- Poor indicators include LBW, significant leukopenia or neutropenia, High CSF protein
- Delayed sterilizaiton of the CSF and coma
- Seizures lasting longer than 72 hours or hypotension needing inotropes predict moderate to severe disability or death
- MRI must be done on all neonates following meningitis

# Acute Bacterial Meningitis

ABM beyond the newborn period

- HIB.
- Strep Pneumo
- Meningococcus

All have a polysaccharide capsule which is a major factor in invasiveness



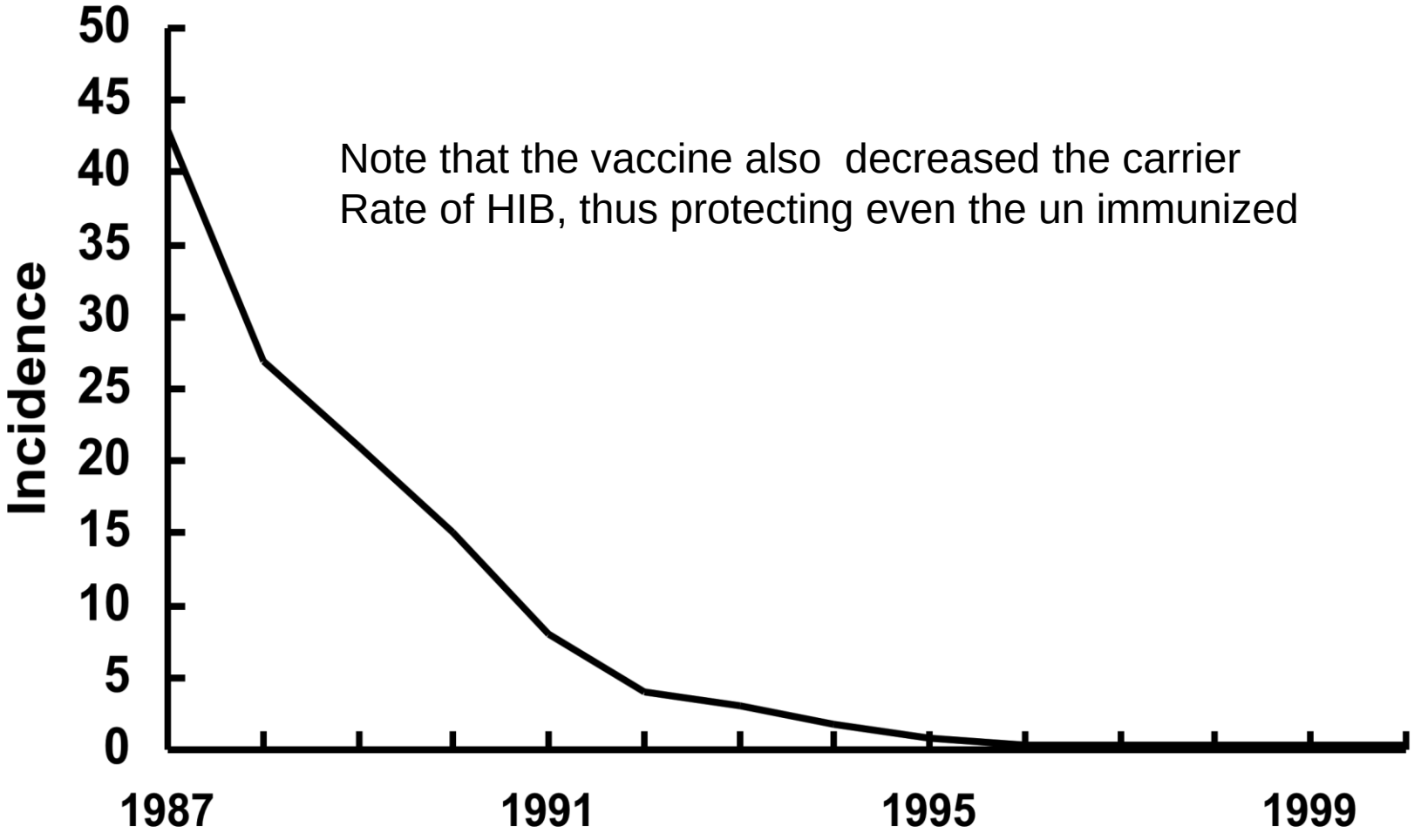
Hemophilus influenza b
Gram negative pleomorphic
Many shapes cocco bacillary

# Acute Bacterial Meningitis

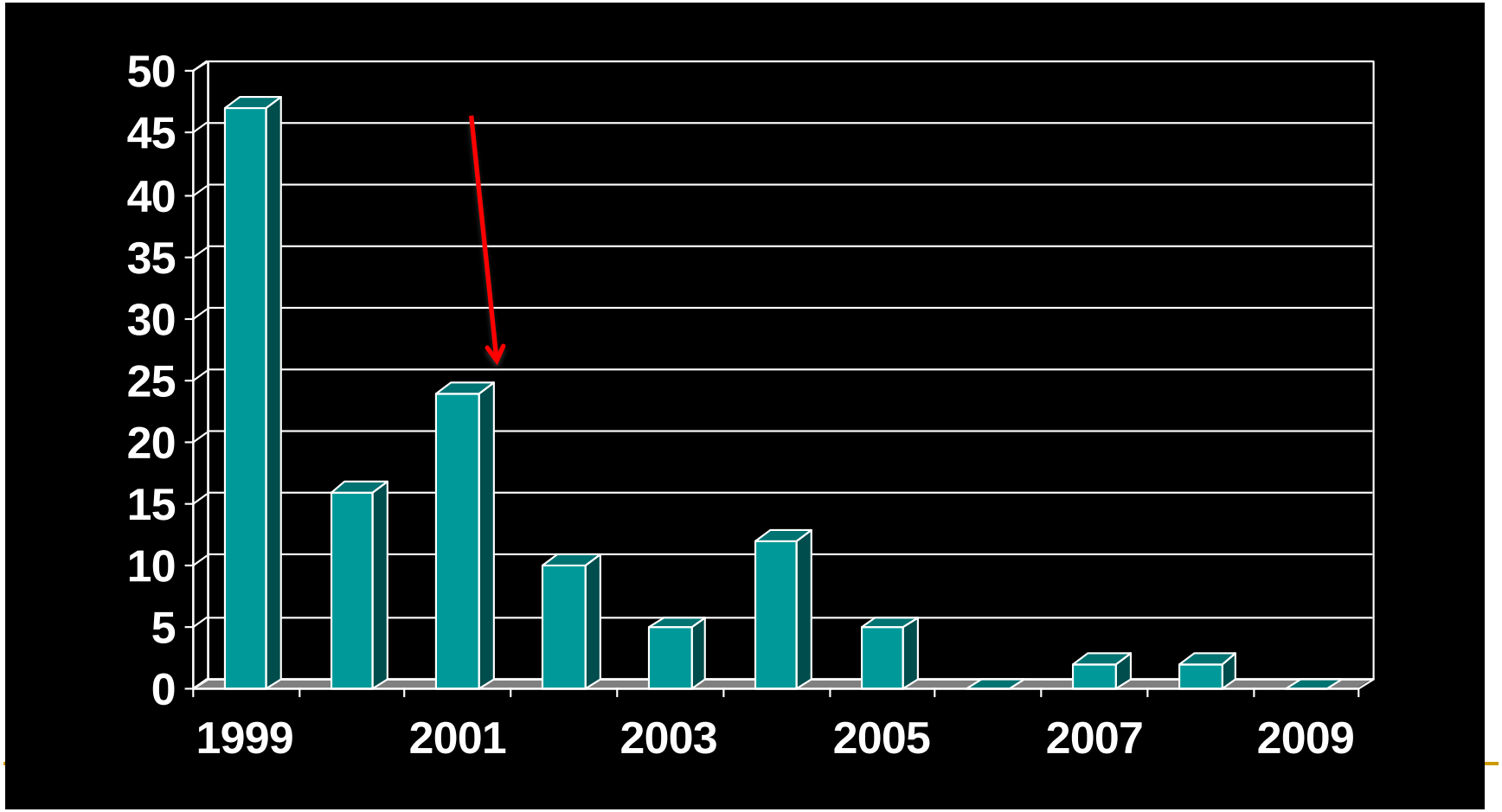
## H Flu B

- H influenza serotype a-f, gram negative pleomorphic bacterium
- Type b is the only one leading to invasive disease
- Polyshaccharide capsule determines serotype and
- pathogenecity, Anticapsular antibodies are protective
- Maternal antibodies protect the newborn for the first few months
- HIB vaccine is made of the conjugate polysaccharide and is given
- as a conjugated vaccine at 2 months of age
- Transmission of HIB is usually acquired by droplet by contact from
- others, NP HIB carriage is uncommon only 4%
- 2-3 months peak age of risk in <2 years, much less after 6 years of age even in the absence of vaccination since asymptomatic
- infection leads to antibodies

# Estimated Incidence* of Invasive Hib Disease, 1987-2000



# The impact of vaccination Hib meningitis 1999-2009 Jordan before and after vaccination



# Streptococcus pneumoniae

- 90 different serotypes
- Capsule is principle virulence factor
- Antibodies against capsule = protection
- Each serotype in vaccine = antibody
- Limited serotypes cause majority infections
- 14,6B,19F,18C,23F,4,9V = 80% infections
- PCV7 licensed in 2/2000
- 2,4,6 and 12 -15 mos, high risk 24 - 59 mos

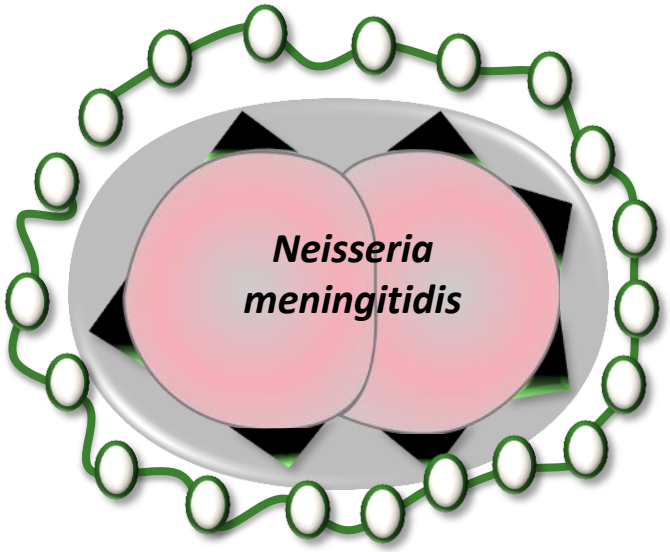
Most recent vaccine PCV 13 protects against 80% of types

# Strep pneumo

- Carrier state is common
- No increased risk to contacts
- Disease more common and severe in certain hosts
  - Sickle cell patients ( functional asplenia)
  - Nephrotic syndrome
  - Asplenia
  - IgG def
  - Properdin deficiency
  - Most common cause of meningitis with basal skull fracture

# *Neisseria meningitidis* (meningococcus

- Meningococci are diplococcal bacteria surrounded by a polysaccharide capsule[1]
  - The polysaccharide structure determines the pathogen's serogroup (SG)[1]
  - Six (A, B, C, Y, X, and W*) of 13 known SGs account for the majority of epidemics worldwide[3]




Polysaccharide capsule[1,4]

*W-135 has been replaced with W per new nomenclature.[5]

[1]**Pollard**. In: *Harrison's Principles of Internal Medicine*. 18th ed. 2012;chapter 143; [2]**Harrison**. *Clin Infect Dis*. 2010;50(Suppl 2)
[3]**WHO**. http://www.who.int/mediacentre/factsheets/fs141/en/; [4]Image adapted from **Criss**. *Nat Rev Microbiology*. 2012;10(3)
[5]**Harrison** et al. *Emerg Infect Dis.* 2013;19(4)

# Pathogenesis of meningococcal meningitis

- Colonization of the nasopharynx occurs with close contact with asymptomatic carriers.
- Usually around 3-5% are NP carriers but this increases with crowding up to 40%. Usually this occurs in the first few days of exposure
- Maximum risk of invasive disease occurs in the first few days after acquiring the carrier state.
- Disease is more common in patients with immune deficiency states and patients who have been splenectomized and also patients receiving certain drugs that interfere with complement such
- This risk for developing meningitis is higher in patients who have viral infection and in infants < 2 years of age
- Severe invasive disease occurs very fast and there is need to have antecedent antibody to protect from this infection which may lead to meningococcemia or meningitis

# Neisseria meningitides

Neisseria meningitides

- Serotypes, a,b,c,x,y,z,29E,W135
- Anticapsular antibody=protection
- A in Africa and the ME
- B,C in the USA, Europe
- Outbreaks Q 7-10 yrs
- Infants 6-12 months and adolescents are at high risk especially in dry season,and following URI
- Mass gathering including Hajj increase the risk of exposure and disease.

# Neisseria meningitides

- Carrier rate 1-15%.  Interepidemic 3%
- Family contacts 40-50%
- Risk of disease in contacts 1%
- Pts with C5-C8 def,  have very bad disease
- Early colonization with Neisseria lactamicus seems to be protective

# Listeria monocytogenes

- Most common in the newborn and older than 50 years of age
- Serotype 1a,1b and 1Vb most common
- May affect the immune compromised and pregnant women as well
- May be associated with consumption of raw milk and unpasteurized cheese.
- Signs and symptoms may be subtle and low grade, the diagnosis may be delayed.
- Misidentified as diphtheroid and alpha strep

# How do we diagnose meningitis

- Classically fever, headache, stiff neck and positive meningeal signs are present
- Clinical presentation depends on age and Classical signs may be absent at extremes of age,
- However changes in mental status expecially headache are present.
- In the infant paradoxical irritability may be present
- Bulged fontanelle is a late sign
- Must maintain a high sense of suspicion

**Table 1.** Common Presenting Symptoms and Signs in Children (<14 years old) with Bacterial Meningitis

| Symptom/Sign | Relative Frequency (%) |
|---|---|
| Fever | 85-99 |
| Irritability | 34-65 |
| Meningismus | 67-96 |
| Altered sensorium/comatose | 7-12 |
| Kernig's sign | N/A |
| Brudzinski's sign | N/A |
| Vomiting | 18-59 |
| Seizure | 11-30 |
| Focal findings | 7 |

Adapted from Kaplan SL, 1999.

# Diagnosis of ABM

- CSF examination is definitive
- Other tests are only adjunct BUT cannot be diagnostic
- However in patients who are very ill or if it is not possible to perform an LP it is acceptable to start treatment with antibiotics till that is possible
- The CSF will remain abnormal for several days afterwards and can make the diagnosis later. DO NOT WITHHOLD THERAPY.

# GUIDELINES FOR CT SCAN OF HEAD PRIOR TO LUMBAR PUNCTURE (B-II)

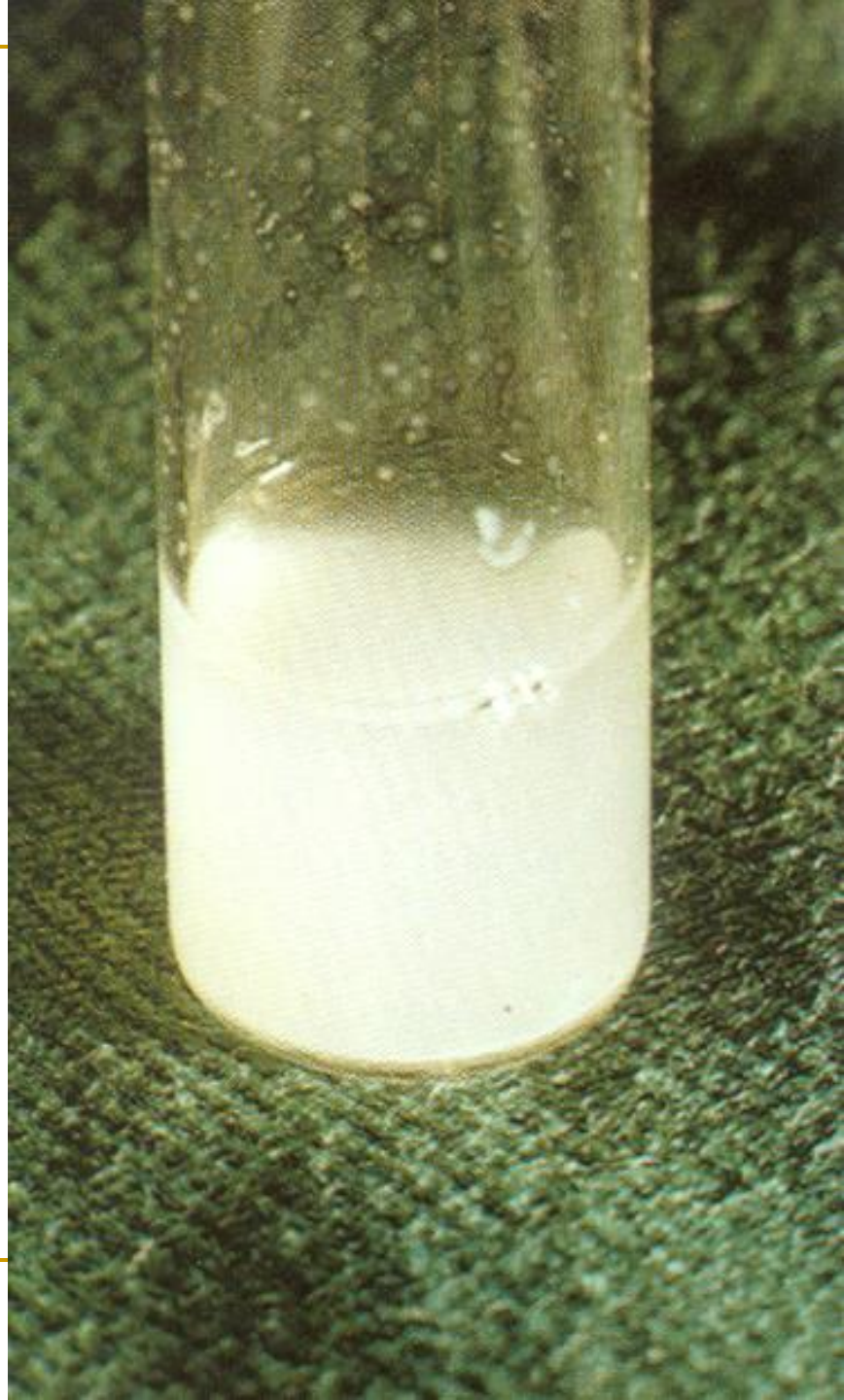
- DO NOT DELAY THERAPY DUE TO CT SCAN
- ALL Patients must have an eye examination for papilledema
- CT SCAN or MRI must be done if
  - Age is older than 60 years
  - Patient has Immunocompromised state
  - Patient has New onset seizure
  - Patient has Altered consciousness
  - Patient has Papilledema
  - Patient has Focal neurologic deficit

# Once assured of Safety obtain CSF

- Cell count and diff
- Glucose and Protein
- Culture and gm stain
- Other tests such as

PCR for bacteria and viruses are of help

But DO NOT DELAY empiric therapy while waiting for results



# CSF FINDINGS IN BACTERIAL MENINGITIS (

| CSF Parameter | Typical Findings |
|---|---|
| Opening pressure | 200-500 mm $H_2O$ |
| White blood cell count | 1000-5000/$mm^3$ |
| Percentage of neutrophils | $\geq$80% |
| Protein | 100-500 mg/dL |
| Glucose | <40 mg/dL |
| CSF:serum glucose | $\leq$0.4 |

# Note of caution

- The total WBC count cannot definitely distinguish between bacterial and other causes.
- At one time, it was generally believed that a predominance of polymorphonuclear leukocytes (PMNs) pointed to bacterial meningitis, but this has been an unreliable indicator; bacterial meningitis may also present with a lymphocytic predominance.
- Attempts to differentiate bacterial and aseptic meningitis on the basis of percentage and absolute number of premature neutrophils (ie, bands) have not yielded diagnostic results.[15]


  - Kanegaye JT, Nigrovic LE, Malley R, Cannavino CR, Schwab SH, Bennett JE, et al. Diagnostic value of immature neutrophils (bands) in the cerebrospinal fluid of children with cerebrospinal fluid pleocytosis. *Pediatrics*. Jun 2009;123(6):e967-71. [Medline].

# CSF analysis, important considerations A cautionary note, IDSA guidelines

- Both *N meningitidis* meningitis and *S pneumoniae* meningitis are known to give normal CSF results. In an evidence-based article, meningitis was found to exist in 10% of children who have normal CSF analysis.
- Several gram-negative bacteria and higher serotypes of *S pneumoniae* have capsular antigens that cross-react with *H influenzae* type b polyribophosphate.
- Capsular antigens of group B meningococcus cross-react with K1-containing *Escherichia coli*. Gram stains of CSF are more sensitive than these rapid diagnostic tests for the detection of *N meningitidis*.


The gram stain

# CSF GRAM'S STAIN

- Identifies causative microorganism in 60-90% of cases, with a specificity of ≥97%
- Likelihood of positive Gram's stain depends upon CSF concentration of microorganisms, specific bacterial pathogen, and prior antimicrobial therapy
- False-positive results may result from observer misinterpretation, reagent contamination, use of occluded lumbar needle (skin contamination)
- Rapid, inexpensive, highly specific (A-III)

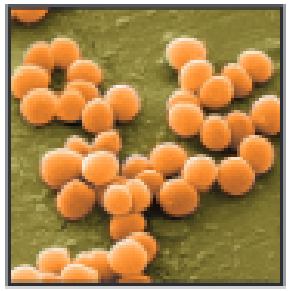
# CSF LATEX AGGLUTINATION IN CULTURE-PROVEN BACTERIAL MENINGITIS

## no need to perform not reliable

| **Microorganism** | **Sensitivity (%)** |
|---|---|
| *Haemophilus influenzae* type b | 78-100 |
| *Neisseria meningitidis* | 50-93 |
| *Streptococcus pneumoniae* | 67-100 |
| *Streptococcus agalactia* | 69-100 |

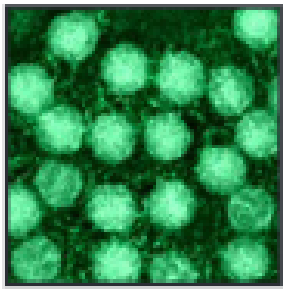
Gray LD, Fedorko DP. Clin Microbiol Rev 1992;5:130.

# 1 Test. 14 Targets. All in about an hour.



## Bacteria

*Escherichia coli* K1
*Haemophilus influenzae*
*Listeria monocytogenes*
*Neisseria meningitidis*
*Streptococcus agalactiae*
*Streptococcus pneumoniae*



## Viruses

Cytomegalovirus (CMV)
Enterovirus
Herpes simplex virus 1 (HSV-1)
Herpes simplex virus 2 (HSV-2)
Human herpesvirus 6 (HHV-6)
Human parechovirus
Varicella zoster virus (VZV)

PCR testing now available as multiplex

# Acute Bacterial Meningitis

Treatment of acute bacterial meningitis

# Principles of antibiotic therapy

- Choice of antibiotic is usually empiric and is dependent on epidemiologic considerations.
- Modify once results are back accordingly.
- Must give empiric antibiotic therapy immediately
- Must cover ALL possible pathogens no matter how small is the risk of infection
- Must choose a bactericidal agent
- Must choose an agent that crosses the CSF very well and have a good MIC against the organisms

# GUIDELINES FOR TIMING OF ANTIMICROBIAL ADMINISTRATION

- “time is brain”
- First dose no later than 2 hours of contact
- If taking care of patients in a remote location and cannot obtain CSF give antibiotics BEFORE transfer
- CSF abnormality will persist for a few days
- Prior antibiotics only interfere with culture
- Hence DO NOT DELAY giving antibiotics for referral of patients if meningitis is a possibility

# EMPIRIC ANTIMICROBIAL THERAPY OF PURULENT MENINGITIS (A-III)

| Age | Antimicrobial Therapy |
|---|---|
| <1 month | Ampicillin + cefotaxime; or ampicillin + an aminoglycoside |
| 1-23 months | Vancomycin + a third generation cephalosporin[a] |
| 2-50 years | Vancomycin + a third generation cephalosporin[a] |
| Older than 50 years | Vancomycin + ampicillin + a third generation cephalosporin[a] |

[a]cefotaxime or ceftriaxone  IDSA guidelines

# EMPIRIC ANTIMICROBIAL THERAPY OF PURULENT MENINGITIS (A-III)

| Predisposing Condition | Antimicrobial Therapy |
|---|---|
| Immunocompromise | Vancomycin + ampicillin + cefepime or ceftazidime |
| Basilar skull fracture | Vancomycin + a third generation ceph |
| Head trauma or after neurosurgery, or CSF shunt | Vancomycin + either ceftazidime, cefepime, or meropenem |

[a]cefotaxime or ceftriaxone

# TARGETED ANTIMICROBIAL THERAPY IN BACTERIAL MENINGITIS (A-III)

| **Microorganism** | **Antimicrobial Therapy** |
|---|---|
| *S. pneumoniae* | Vancomycin + a third generation cephalosporin[a,b] |
| *N. meningitidis* | Penicillin G, ampicillin, or a third generation ceph |
| *L. monocytogenes* | Ampicillin or penicillin G[c] |

[a]cefotaxime or ceftriaxone
[b]addition of rifampin may be considered
[c]addidion of an aminoglycoside may be considered

# ANTIMICROBIAL THERAPY IN BACTERIAL MENINGITIS (A-II, A-III)

| **Organism** | **Antimicrobial Therapy** |
|---|---|
| *Streptococcus pneumoniae* | |
| PCN MIC <0.1 μg/mL | Penicillin G or ampicillin |
| PCN MIC 0.1-1.0 μg/mL | Third generation cephalosporin[a] |
| PCN MIC ≥2.0 μg/mL | Vancomycin + a third generation cephalosporin[a] |
| CTX MIC ≥1.0 μg/mL | Vancomycin + a third generation cephalosporin[a] |

[a]cefotaxime or ceftriaxone

# ANTIMICROBIAL THERAPY IN BACTERIAL MENINGITIS (A-I, A-III)

| **Organism** | **Antimicrobial Therapy** |
|---|---|
| *Neisseria meningitidis* | |
| PCN MIC <0.1 μg/mL | Penicillin G or ampicillin |
| PCN MIC 0.1-1.0 μg/mL | Third generation ceph[a] |
| *Haemophilus influenzae* | |
| β-lactamase-negative | Ampicillin |
| β-lactamase-positive | Third generation ceph[a] |

[a]cefotaxime or ceftriaxone

# ANTIMICROBIAL THERAPY IN BACTERIAL MENINGITIS (A-II, A-III)

| Organism | Antimicrobial Therapy |
|---|---|
| Enterobacteriaceae | Third generation ceph[a], or meropenem |
| *Pseudomonas aeruginosa* | Ceftazidime[b], cefepime[b], or meropenem[b] |
| *Streptococcus agalactiae* | Ampicillin or penicillin G[b] |
| *Listeria monocytogenes* | Ampicillin or penicillin G[b] |
| *Staphylococcus aureus* | Nafcillin or oxacillin |
| MRSA or *S. epidermidis* | Vancomycin |

[b]addition of an aminoglycoside should be considered

# ADJUNCTIVE DEXAMETHASONE RATIONALE

- The subarchnoid space inflammatory response during bacterial meningitis is a major factor contributing to morbidity and mortality
- Attenuation of this inflammatory response may diminish many of the pathophysiologic consequences of bacterial meningitis (e.g., cerebral edema, increased intracranial pressure, altered cerebral blood flow, cerebral vasculitis, neuronal injury)

# The Guideline on ADJUNCTIVE DEXAMETHASONE IN BACTERIAL MENINGITIS

- Neonates (C-I) ( not proved)
- Infants and children with *Haemophilus influenzae* type b meningitis (A-I)
- Infants and children with pneumococcal meningitis (B-I)
- Adults with pneumococcal meningitis (A-I)
- Patients with pneumococcal meningitis caused by highly penicillin- or cephalosporin-resistant strains (B-III)
- Administer at 0.15 mg/kg every 6 hours for 2-4 days concomitant with or just before first antimicrobial dose

# Prognosis mortality

- Overall mortality for bacterial meningitis is 5-10%.
- In neonates, mortality is 15-20%, whereas in older children, it is 3-10%.
- *S pneumoniae* meningitis 26.3-30%;
- Hib meningitis 7.7-10.3%;
- *N meningitidis* has the lowest, at 3.5-10.3%.
- However meningococcemia is worse and may be associated with a very high rate unless identified in time

# Duration of antibiotic therapy

- *N meningitidis* 7 d
- *H influenzae* 7 d
- *S pneumoniae* 10-14 d
- *S agalactiae* (GBS) 14-21 d
- Aerobic gram-negative bacilli 21 days or
  2 wks beyond the first sterile culture
  (whichever is longer)
- *L monocytogenes* 21 d or longer

# End of therapy

- No need to repeat CSF if uncomplicated course
- Repeat CSF in the neonate and if complicated
- CT or MRI must be performed in the newborn at discharge to rule out abscess or hydrocephalous
- Brain stem evoked potential for hearing evaluation must be done for all individuals recovering from meningitis

# Prognostic factors, poor prognostic factors

- High Bacterial load> $10^{7}$/ml
- Age,  Neonatal mortality 15-20%, infants 2-5%
- Seizures after $4^{th}$ day of admission
- Focal neurological deficit
- Deteriorating level of consciousness
- Hypotension and coma at admission
- S pneumo has the  worst prognosis
- Inappropiate ADH release
- Delayed sterilization of the CSF, this should occur after 24 hours of therapy in children and < 4 days in the newborn
- Developing countries worse outcome

# Other Prognostic factors in ABM
# CFR ( Case fatality rate)

| | Developed countries | Underdeveloped |
|---|---|---|
| S pneumo | 20% | 50% |
| Sequelea | 30% | 60% |
| Older adults | 40% | |

# Care of contacts of meningococcal meningitis

- Prophylaxis should be given to contacts of cases of HIB and Meningococcal infections
- Prophylaxis for Meningococcal meningitis
  - Give to ALL household or very close contacts regardless of age
  - Risk of secondary case is 1%
  - Rifampicin, or ceftriaxone, or ciprofloxacin
  - PLUS meningococcal vaccine

# Complications of acute bacterial meningitis

- Death 3-5%
- Subdural effusion/empyema
- Hearing deficit 7-30%
- Decreased IQ 30-50%
- Seizures
- Hemiparesis,
- Other neurological deficit

# Secondary cases H flu b

- Risk of disease is age dependent
- Secondary disease in first month is 0.3%
- 600X that general population in young children

| | |
|---|---|
| <2years old | 3.7% |
| >6 yrs | 0 |
| Secondary cases | 64%in 1st wk |
| | 20% in 2nd wk, |
| | 16% in 3rd wk. |

# Prophylaxis for contacts of H flu b

- Rifampin 20mg/kg/dX4 d

  Give to ALL household contacts adults and children, if child <4 years of age and not vaccinated or if the child is less than one year of age

- Day care???

# Prevention of infection in the community

- Conjugate polysaccharide vaccines should be provided for these organisms
  - H flu b for children < 6 years of age
  - Strep pneumo
  - Meningococcal vaccines
  - These are conjugated to a protein antigen in order to be effective in children < 2years of age

# Recent trends in meningitis

- Decrease in HIB to almost nill after vaccination
- Decrease in pneumo after PCV 7 and 13 vaccines in countries that use them
- Note that conjugate vaccines also prevent NP carraige hence also decrease exposure and magnify benefit
- Decrease in GBS with antenatal screening and treatment. In our region ? Increase must institute the GBS screening and perinatal antibiotics to mothers
- Median age of cases is also increased
- No change in CFR however 15% in the adult

# Conclusions

- Acute bacterial meningitis remains a major cause of mortality and morbidity despite excellent antibiotics
- Epidemiologic factors depend on availability of vaccination, degree of development and crowding as well as availability of good health system
- Host factors play a major role in brain damage, need more drugs against this
- Dexamthasone adjunct therapy now recommended for children and adults

# Conclusions

- Outcome may be more guarded with subtle brain damage and decreased IQ
- Prevention is primary,  vaccines for all three pathogens are now present and we should try to give to at risk individuals
- In jordan we have only introduced N meningitides for the pilgrims and the military recruits and  HIB for all children
- Pneumo must be introduced soonest


2. 1. 1999

# Molecular pathogenesis

- Pili by meningococcus help attach to the mucosa
- Laminin receptor for the organisms does play a role. This is inducible on endothelial surfaces and allows organisms to bind to the endothelium and enter into the CNS
- Organisms that could not bind to the laminin receptor do not cause meningitis

# Pathogenesis continued

- Bacteria gain access to the CSF and CNS by the blood stream unless there is trauma and disruption of the anatomy
- Usually organisms enter the blood stream from the nasopharynx
- Colonization of the nasopharynx antidates bacteremia
- Viral infection of the upper respiratory tract may increase the risk of bacterial entry into the blood
- BBB plays a major role in protecting the CNS,

# Recent advances in pathogenesis

| Pathogenesis stage | Host defense | Pathogen strategies |
|---|---|---|
| Mucosal colonization and invasion | Secretary IgA<br>Ciliary activity | IgA protease<br>Adhesive Pili, neisseria |
| Blood stream survival | complement | Evasion of alternate complement pathway by polysacharide capsule, innate immunity |
| Cross blood brain barrier | Cerebral endothelium | Usurp laminin-R<br>Potential role of MIF, TNF |
| CSF survival | Poor opsonic activity | Bacterial replication |

# Neonatal meningitis common organisms at different time periods

- Early onset<3-7 days,
  - GBS,E Coli, Listeria, enteroviruses
- Late onset >7 days
  - GBS, E Coli, Other GNR, Listeria
  - Staph, Enterococcus, Candida, HSV, Enteroviruses

# Prevention of GBS sepsis and meningitis new Guidelines 2020

- The optimal window for antenatal GBS screening has been changed to 36 0/7 to 37 6/7 weeks' gestation instead of beginning at 35 0/7 weeks' gestation. The correlation between antenatal GBS colonization results and colonization status at the time of delivery decreases significantly when the culture-to-birth interval is longer than five weeks; therefore, moving antenatal culture timing to 36-37 weeks optimizes the value of the screening result up to 41 weeks' gestation.
- It is recommended that GBS IAP be administered to the following: all laboring women with GBS colonization detected by antenatal culture; those with GBS bacteriuria detected during the pregnancy; those who previously delivered a newborn with GBS disease; and women with unknown GBS status who present with preterm labor or preterm, prelabor rupture of membranes (ROM) prior to 37 weeks' gestation.
- Women who present at >37 weeks' gestation with unknown status should be administered GBS IAP if risk factors develop (duration of ROM 18 hours or intrapartum temperature of 100.4°F [38°C]. Additionally, women with known GBS colonization in a prior pregnancy may be offered IAP if status is unknown at >37 weeks' gestation given that such women have increased risk of colonization in the current pregnancy.
- Penicillin G remains the recommended antibiotic for GBS IAP; ampicillin is an acceptable alternative.

# Invasive Meningococcal Disease Is Difficult to Diagnose and Rapidly Lethal

- Flu-like nature of early symptoms makes a definitive diagnosis challenging[1]
- Rapid progression, with death in as little as 24 hours[1,2]

| 4–8 Hours[1,2] Nonspecific | 12–15 Hours[1,2] Characteristic | 15–~24 Hours[1,2] Late |
|---|---|---|
| Fever, irritability, nausea or vomiting, drowsiness, poor appetite, sore throat, coryza, general aches | Hemorrhagic rash, neck stiffness, photophobia | Confusion or delirium, seizure, unconsciousness; possible death |

**Hospital admission at median of ~19 hours[1]**

[1]Thompson et al. *Lancet*. 2006;367(9508); [2]Branco et al. *J Pediatr (Rio J)*. 2007;83(2 suppl)

# Time Is of the Essence

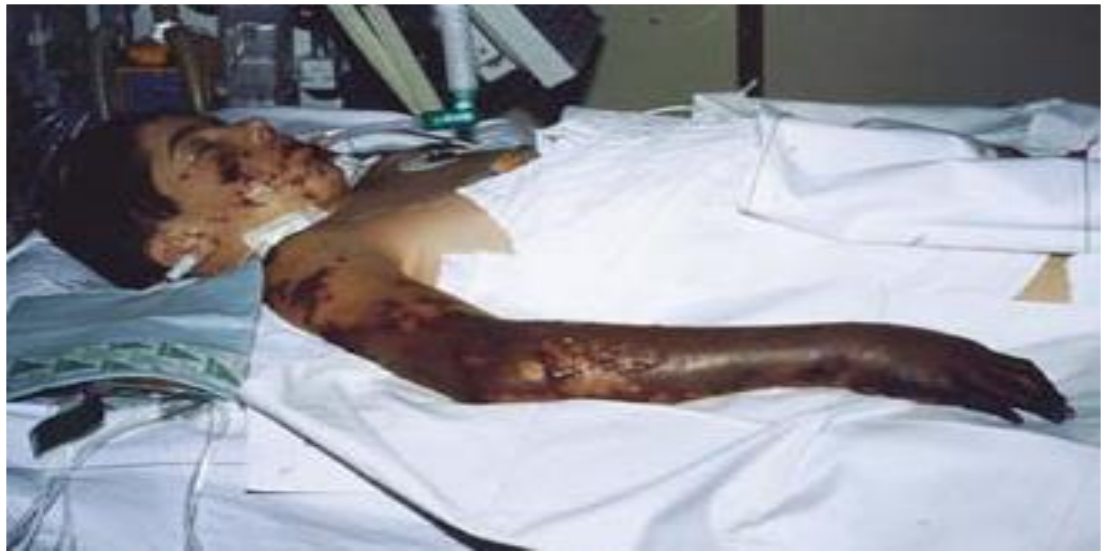
- Early symptoms are nonspecific
  - Fever, headache, nausea, vomiting, loss of appetite
  - Mimic symptoms of common viral illnesses
- Characteristic symptoms occur later
  - Hemorrhagic rash, neck stiffness, photophobia
  - Typically develop approximately 12-15 hours after symptoms begin[1] Rapid progression, De within 24 hours of symptom onset[1,2]
  - Fever and Petechia should be treated as if meningococcemia until proved otherwise

Getty Images/Creative Cro

**References:** **1.** Thompson MJ, et al. *Lancet*. 2006;367(9508):397-403. **2.** World Health Organition. http:// www.who.int/mediacentre/factsheets/fs141/en. Accessed March 1, 2017.

# Although Rare, Meningococcal Disease Is Mostly Sporadic, Affects All Ages, and Is Associated with Significant Morbidity and High Case Fatality Rates Inspite [1-4]

Treatment with antibiotics 10% die and 10-20% have sequelae



**Primary prevention is inhibiting the development of the disease before it occurs[1]**

[1]**Stephens** et al. *Lancet*. 2007;369(9580); [2]**Van** de Beek. *NEJM*, 2001;344(18); [3]**Keysserling**. Arch Pediatr Adolesc Med*, 2005;159(10)*