

MICROBIOLOGY

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Number

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Subject

Bacterial Meningitis

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Neuro-Science I

Bacterial Infections

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Bacterial Meningitis

■ Definition

Bacterial meningitis is an inflammatory response to bacterial infection of the pia-arachnoid and CSF of the subarachnoid space.

■ Common Causes:

- Viral Infection~ Mild, no treatment is necessary.
- Bacterial Infection~ Very serious, can be fatal.

- Suspected bacterial meningitis is a medical EMERGENCY
- Mortality up to 100% if not treated
- Mortality varies between 3-25%
- Poor prognostic factors:
 - ❖ Age above 60 Years
 - ❖ Obtundation on admission
 - ❖ Seizure within first 24 hours
 - ❖ Hypotension

■ Epidemiology

- Incidence is between 3-5 per 100,000
(Highest in the first month of life, Nearly 75% occur in children under 15)
- There are 1.2 million cases annually worldwide, approximately 135,000 deaths.
- Relative frequency of bacterial sp varies with age.
- Neonates (< 1 Month)
 - Gram negative bacilli, *E. coli*, *Kleb.spp* 50-60%
 - Gp B Strep. 20-40%
 - *Listeria* sp. 2-10%
 - *H. influenzae* 0-3%
 - *S. pneumoniae* 0-5%

- Infants and Children

- *H. influenzae* 40-60%

- Declining dramatically in many geographic regions

- *N. meningitidis* 25-40%

- *S. pneumoniae* 10-20%

- Adults (> 15 years)

- *S. pneumoniae* 30-50%

- *N. meningitidis* 10-35%

- Major cause in epidemics

- Gm (-) Bacilli 1-10%

- *S. aureus* 5-15%

- *H. influenzae* 1-3%

- >60 include *Listeria*, *E. coli*, *Pseudomonas*

■ Meningitis or intracranial abscesses associated with trauma, neurosurgery or intracranial foreign bodies: *Staphylococcus aureus*, *Staphylococcus epidermidis*, *S. pneumoniae*; anaerobic Gram-negative and Gram-positive bacteria; *Pseudomonas species*.

■ Intracranial abscesses not associated with trauma or surgery:

Microaerophilic or anaerobic streptococci, anaerobic Gram-negative bacteria.

■ Vaccination led to:

- Dramatic decline in the incidence of *Haemophilus influenzae meningitis*
- Smaller decline in *Neisseria meningitidis meningitis*

■ Transmission

- Humans are the only host
- Transmitted through “direct contact with large respiratory secretions” (coughing, kissing, sharing drinks, moving centrifuges).

■ Community-Acquired Meningitis

Etiology:

- *Streptococcus pneumoniae*-50%
- *N. Meningitidis*-25%
- *Group B streptococci*-15%
- *Listeria monocystogenes*-10%
- *H. Influenzae*- less than 10%

Pathophysiology

- Colonization of nasopharynx
- Bacteremia and infection of choroid plexus
- Invasion of the subarachnoid space and multiplication in CSF
- Induction of inflammatory reaction:
 - Release of inflammatory cytokines
 - Upregulation of adhesion molecules
 - Granulocyte penetration into CSF and further release of inflammatory mediators

- Increased vascular permeability causes vasogenic edema
- Toxins released by bacteria and granulocytes lead to cellular damage and loss of cellular homeostasis and worsen cerebral edema
- Obstruction of CSF leads to hydrocephalus
- Vasculitis and Thrombosis leads to infarction
- Cerebral herniation

■ Pathogenesis

- Majority of cases are hematogenous in origin
- Organisms have virulence factors that allow bypassing of normal defenses
 - Proteases
 - Polysaccharidases

- Sequential steps allow the pathogen into the CSF

- Nasopharyngeal colonization
- Nasopharyngeal epithelial cell invasion
- Bloodstream invasion
- Bacteremia with intravascular survival
- Crossing of the BBB and entry into the CSF
- Survival and replication in the subarachnoid space

- Hallmark

- Exudate in the subarachnoid space
- Accumulation of exudate in the dependent areas of the brain
- Large numbers of PMN's
- Within 2-3 days inflammation in the walls of the small and medium-sized blood vessels
- Blockage of normal CSF pathways and blockage of the normal absorption may lead to obstructive hydrocephalus

Clinical Presentation

■ Onset:

- Acute fulminant-few hours
- Subacute-over several days

■ Classic clinical triad: fever, headache and nuchal rigidity (stiff neck)-each more than 90%

■ Alteration in mental status: lethargy-coma-more than 75%

■ Nausea, vomiting and photophobia

■ Seizures: 20-40%

■ Focal or generalized

■ Focal seizures:

- Infarction
- Cortical venous thrombosis with hemorrhage
- Focal edema

■ Generalized: Anoxia, hyponatremia, drugs

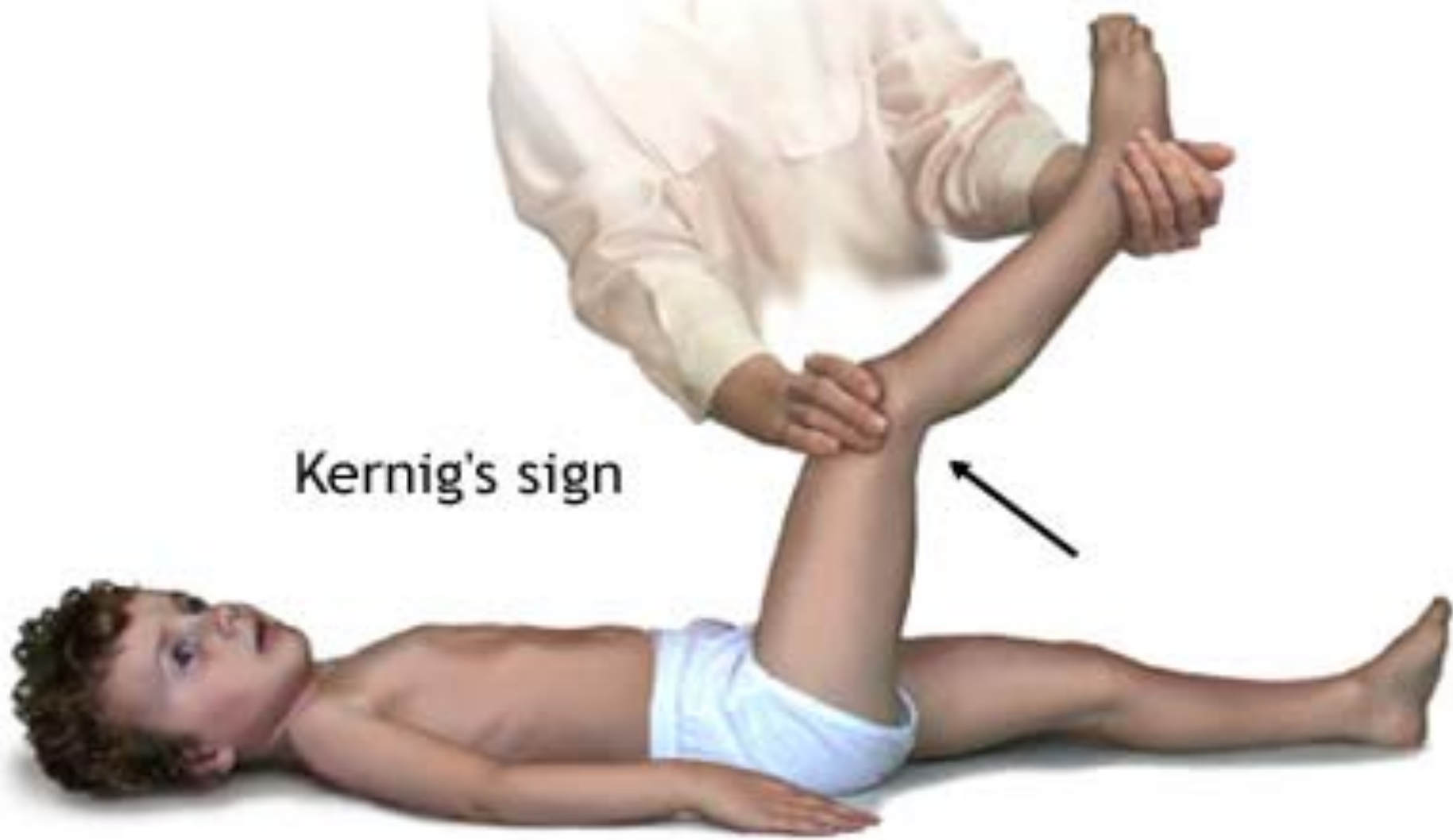
■ Petechial lesions in meningococcal meningitis.

CLINICAL ASPECTS

■ Manifestations – Nuchal rigidity

- Kernig's
 - Pt supine with flexed knee has increased pain with passive extension of the same leg
- Brudzinski's
 - Supine pt with neck flexed will raise knees to take pressure off of the meninges
 - Present in 50% of acute bacterial meningitis cases
- Cranial Nerve Palsies IV, VI, VII
- Seizures

Kernig's sign





Brudzinski's neck sign



■ Manifestations - Meningococemia

- Prominent rash
 - Diffuse purpuric lesions principally involving the extremities
- Fever, hypotension, DIC
- History of terminal complement deficiency
- Classic findings often absent
 - Neonates
 - Elderly





Diagnosis

■ When bacterial meningitis is suspected:

- Obtain blood culture
- Initiate empirical antimicrobial therapy

■ The diagnosis is made by examination of CSF

■ Neuroimaging is needed before LP:

- H/O head injury, Papilledema, altered level of consciousness and focal neurological signs

■ MRI: may demonstrate:

- Cerebral edema
- Ischemia
- Meningeal enhancement with gadolinium

■ Biopsy of petechial skin lesions:

- Gram stain may reveal meningococci

Typical CSF fluid findings in meningitis

■ Treatment

- Emergent empirical antimicrobial therapy
 - Based on age and underlying disease status
- Empiric antibiotic regimens
 - Neonates (<3 months)
 - Ampicillin plus a third generation cephalosporin
 - Children
 - Third generation cephalosporin (alternative -ampicillin and chloramphenicol)

■ Young adults

- Third generation cephalosporin (Ceftriaxone) + Vancomycin

■ Older adults

- Ampicillin in combination with third generation cephalosporins

■ Post neurosurgical Pt's

- Vancomycin plus ceftazidime until cultures are available

■ All antibiotics administered intravenously

- *H. Influenzae* & *N. meningitidis* - 7 days
- *S. pneumoniae* - 10-14 days
- Gm (-) bacilli for 3 weeks

■ Prognosis

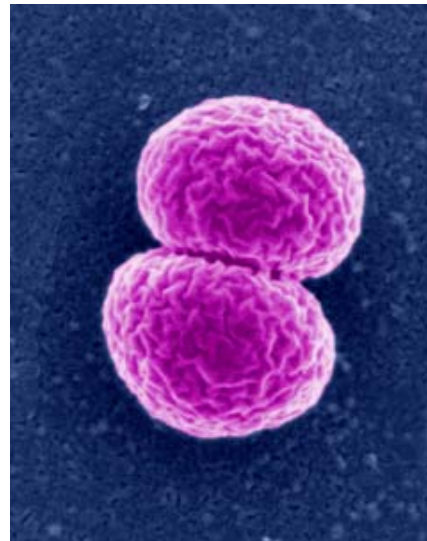
- Pneumococcal Meningitis
 - Associated with the highest mortality rate (20-30%)
 - Permanent neurologic sequelae
 - 1/3 of pts
 - Hearing loss
 - Mental retardation
 - Seizures
 - Cerebral Palsy

■ Vaccinations

- Asplenic pts should have had a pneumococcal vaccine prior to their splenectomy
- Vaccines available for *H. influenzae*
- Prophylaxis for *N. meningitidis* contacts
 - Rifampin

■ *Neisseria meningitidis*

- Most common cause of meningitis in U.S.
- Gram-negative diplococci (often referred to as “kissing kidney beans”)
- Facultative anaerobe
- Humans are only host of bacteria, it is present in the nasopharynx.
- 10-14% of cases are fatal

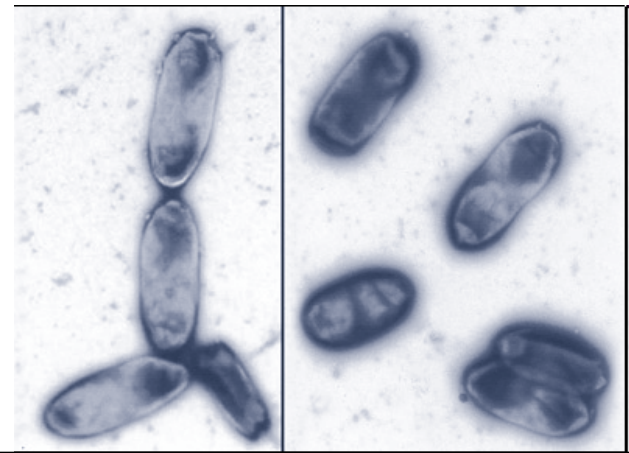


■ *Haemophilus influenzae* Serotype b (Hib)

- Often more severe
- Gram-negative coccobacillus
- Facultative anaerobe
- Affects about 13/1,000,000 children 3-4% are fatal.

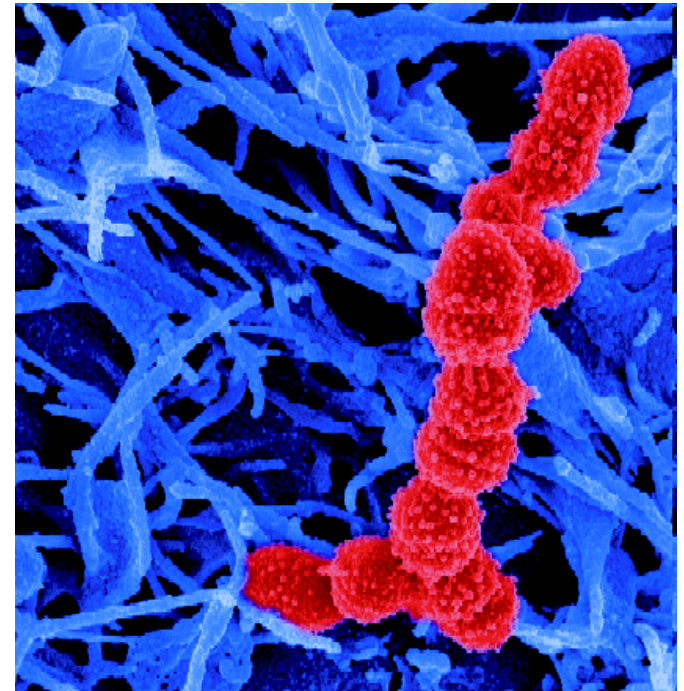
■ Infection has decreased drastically:

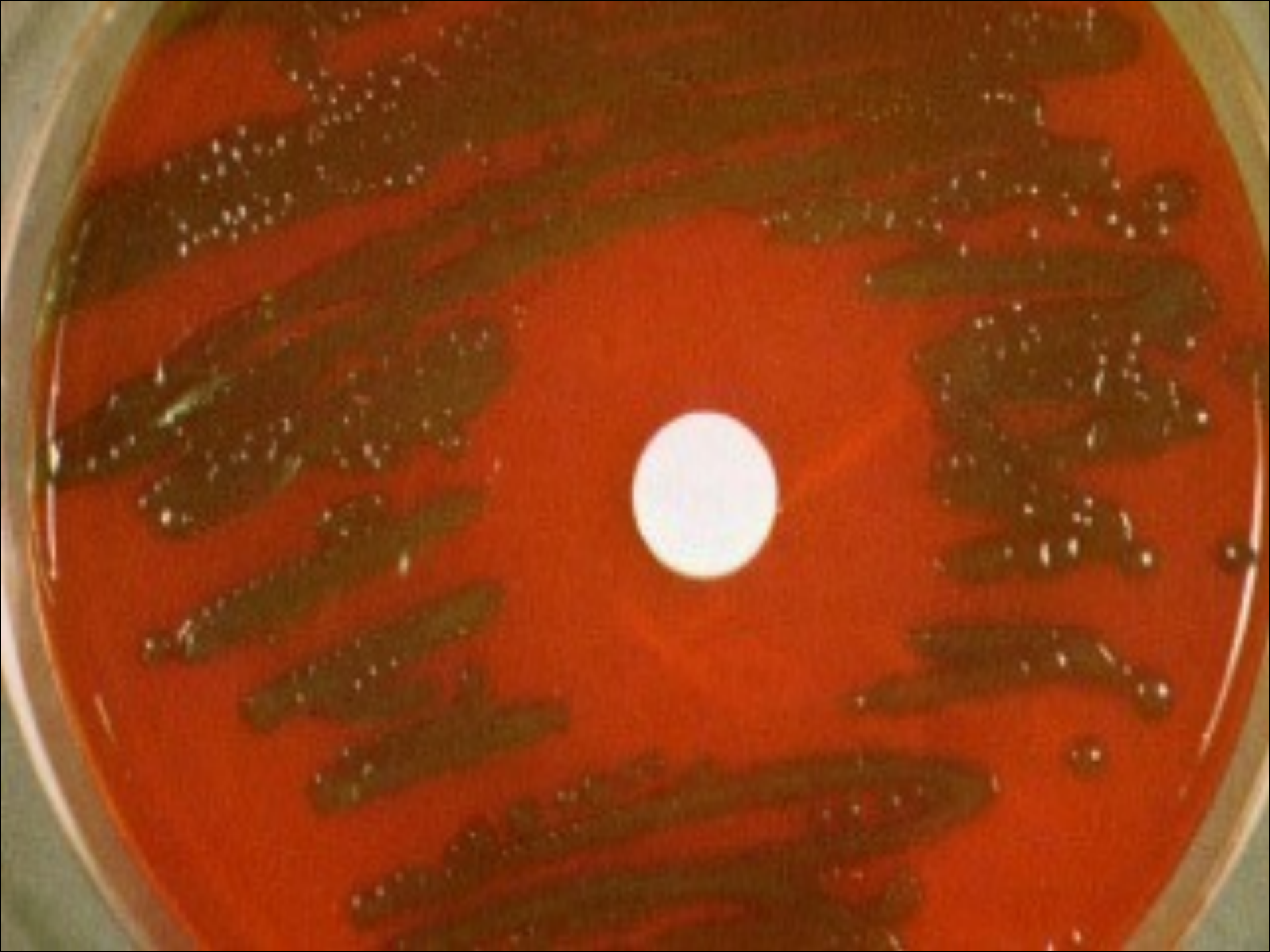
- From 4-10/10,000;
since routine use of the
Hib vaccine (since 1990)

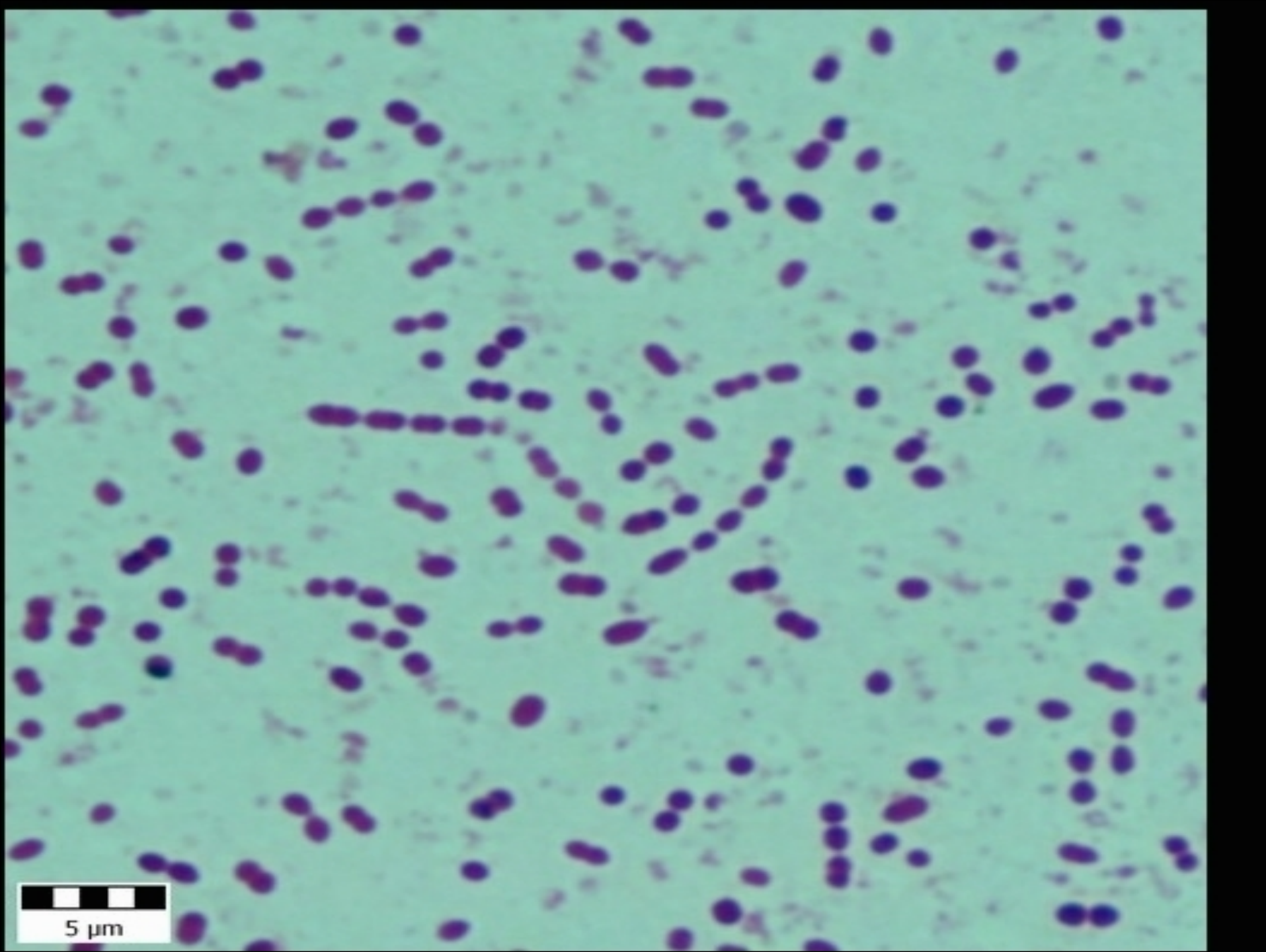


■ *Streptococcus pneumoniae*

- Gram-positive
- Diplococcal and streptococcal (chains of pairs)
- Facultative aerobe
- Infection rate in the U.S. has now decreased to 13/ 100,000, due to vaccination. (2002)
- Kills 14% of hospitalized adults with invasive disease.

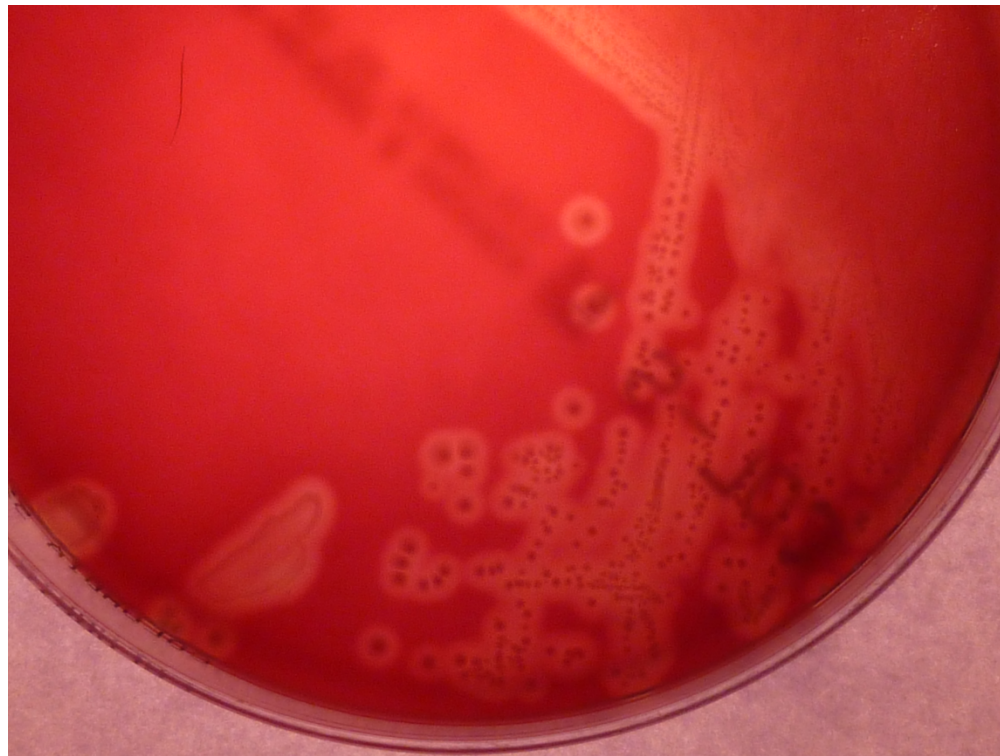


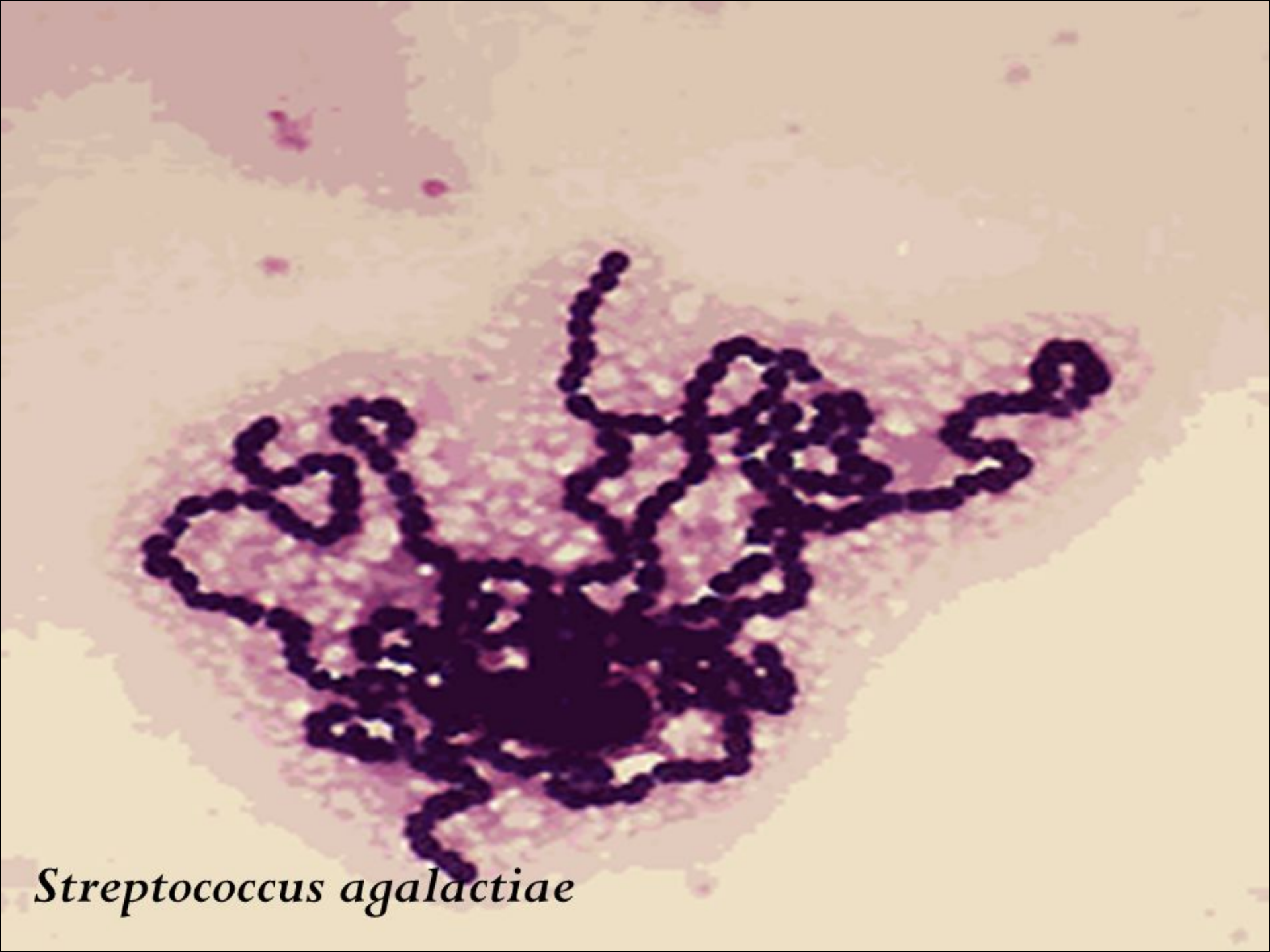




■ *Group B Streptococcus*

- Most common cause in newborns
- Gram-positive streptococci
- Aerobe





Streptococcus agalactiae