Chapter 19

Gram negative bacilli causing respiratory infection

There are **three medically important** Gram negative rods typically associated with **respiratory tract**:

Haemophilus influenzae

Bordetella pertussis

***Legionella pneumophila*.**

First two are found solely in humans, last one is found primarily in water.

Haemophilus

H. influenzae

-- ***H. influenzae*** used to be the **main cause of meningitis** in children but **use of highly successful conjugate vaccine** has reduced the incidence dramatically.

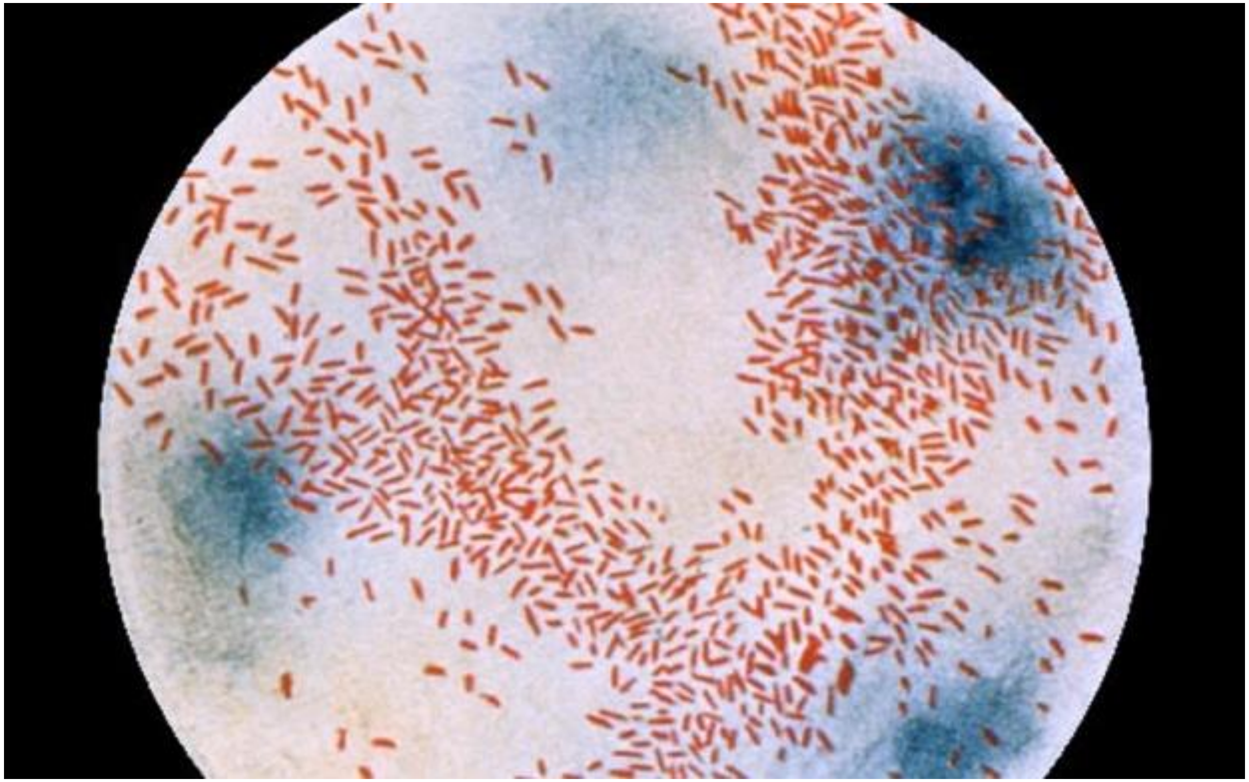
-- It is still an important pathogen in **upper respiratory tract infections** and **sepsis in children**.

-- It also causes **pneumonia in adults**, particularly in those with **chronic obstructive lung disease.**

H. ducreyi causes **chancroid**.

Important properties

H. influenzae is a small gram negative rod (**coccobacillus**) with a **polysaccharide capsule**.



-- Serological typing is based on the antigenicity of the **capsular polysaccharide**.

-- There are **six types** and **type b** is most invasive.

-- Its capsule is composed of **polyribotol phosphate**.

-- Strains without capsule can also cause disease but are usually not invasive.

-- Growth on laboratory media require addition of **heme (X factor)** and **NAD (factor V)** for adequate energy production.

Pathogenesis and Epidemiology

-- *H. influenzae* enters the body by **inhalation of airborne droplets** resulting in **asymptomatic colonization** or infections such as **otitis media, sinusitis,** or **pneumonia**.

-- It produces an **IgA protease** which help in colonization.

-- The organisms can **enter blood stream** and **infect meninges**.

-- **Meningitis is caused by type b in 95% cases.**

-- **Non capsulated strains** may be involved in **otitis media, sinusitis** and **pneumonia**.

-- Beside the capsule, **endotoxin** is a virulence factor.

-- There is **no exotoxin**.

-- Most infections occur in age group **6 months to 6 years**.

-- Up to two years the maternal IgG has gradually disappeared and child's own immune system is not fully developed.

Clinical findings

-- *H. influenzae* meningitis **cannot be distinguished from other bacterial meningitis.**

-- Rapid onset of **fever, headache,** and **stiff neck** along with **drowsiness** is typical.

-- **Sinusitis** and **otitis media** cause **pain** in the affected area, **opacification** of infected sinus, and **redness** with **bulging of tympanic membrane.**

-- Other serious infections include **septic arthritis, cellulitis** and **sepsis** which occur especially in splenectomized patients.

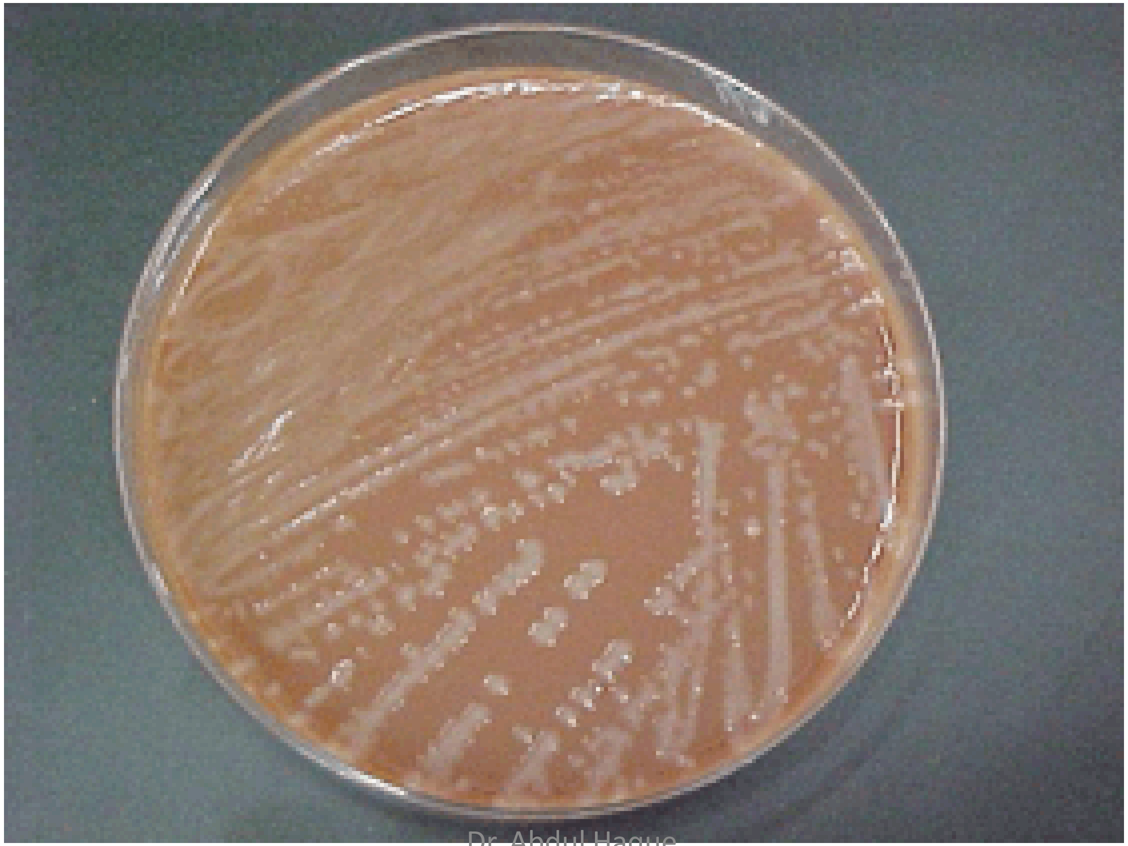
-- Rarely **epiglottitis** with swollen **“cherry red” epiglottis** is seen in children. It is a **life threatening disease**.

-- **Pneumonia in elderly people** may be caused by untypeable strains.

Laboratory diagnosis

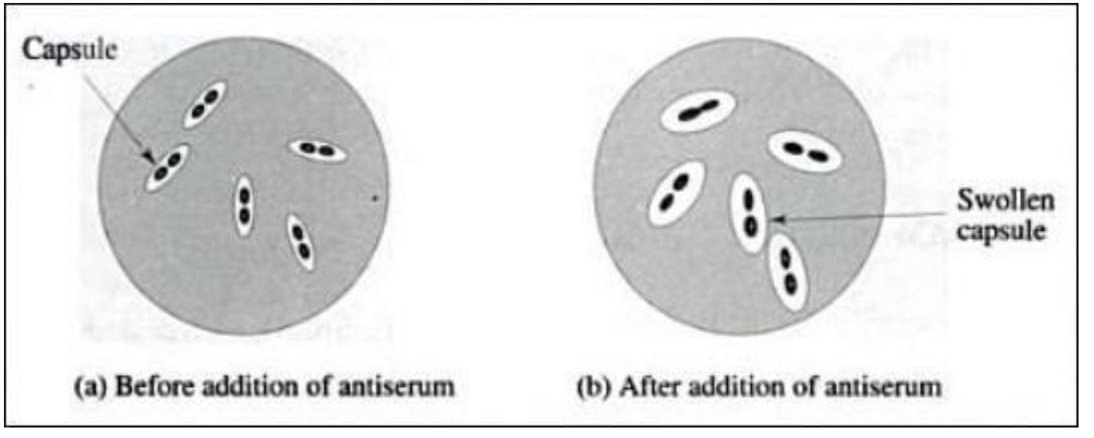
It depends on isolation on **chocolate agar enriched with factor X and V.**

Heating of blood inactivates nonspecific inhibitors.



-- **Other species of *Haemophilus* do not require X and V factors**.

-- Definitive identification is made by **biochemical tests** or Q**uellung reaction.**



-- **Fluorescent antibody** staining, **counterimmunoelectrophoresis** or **latex agglutination** may also be used.

Treatment

-- The choice antibiotic for ***H. influenzae*** infections is **ceftriaxone** because 20-30% isolates produce **β-lactamases** which destroy other β -lactam drugs.

-- If **antibiotic treatment is delayed** there are high chances of **neurologic sequelae**.

-- **Untreated meningitis has a fatality rate of 90%.**

-- Upper respiratory tract infections are treated with **amoxicillin-clavulanate** or **trimethoprim-sulfamethoxazole.**

Prevention

-- The **vaccine** contains the capsular polysaccharide of ***H. influenzae*** **type b conjugated to diphtheria toxoid or other carrier proteins.**

-- **Vaccination** is done between age of **2 and 15 months**.

-- It is **much more effective** than unconjugated vaccine and has reduced incidence of meningitis by **90%** in immunized children.

-- **Meningitis** in close contacts may be prevented by **rifampin**.

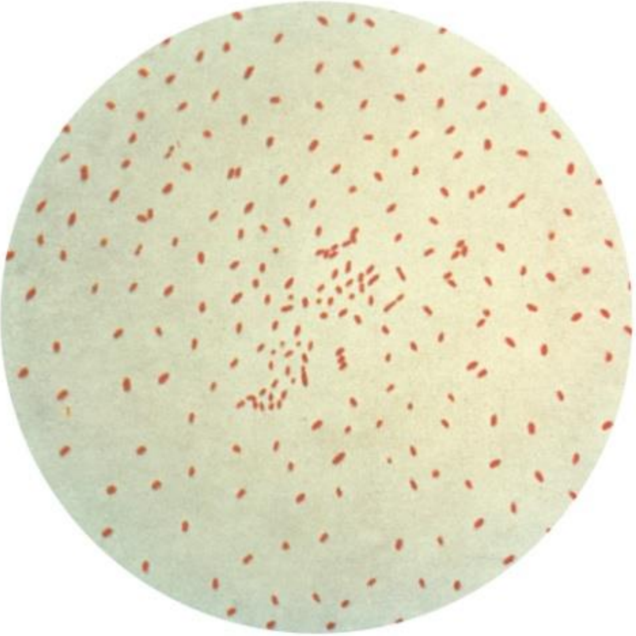
-- It is preferred to ampicillin because of **greater secretion in saliva**.

-- It reduces respiratory carriage and thereby transmission.

Bordetella

B. pertussis causes **whooping cough**.

It is a small, **coccobacillary, encapsulated**, Gram negative rod.



Pathogenesis and Epidemiology

-- It is a **human restricted pathogen** which is transmitted by **airborne droplets** produced during **severe coughing episodes**.

-- The organisms **attach to the ciliated epithelium** of the upper respiratory tract but **do not invade the underlying tissue**.

-- **Decreased cilia activity, followed by death of the ciliated epithelium, are important aspects of pathogenesis.**

-- **Pertussis is a highly contagious disease** primarily occurring in **infants and young children** with worldwide distribution.

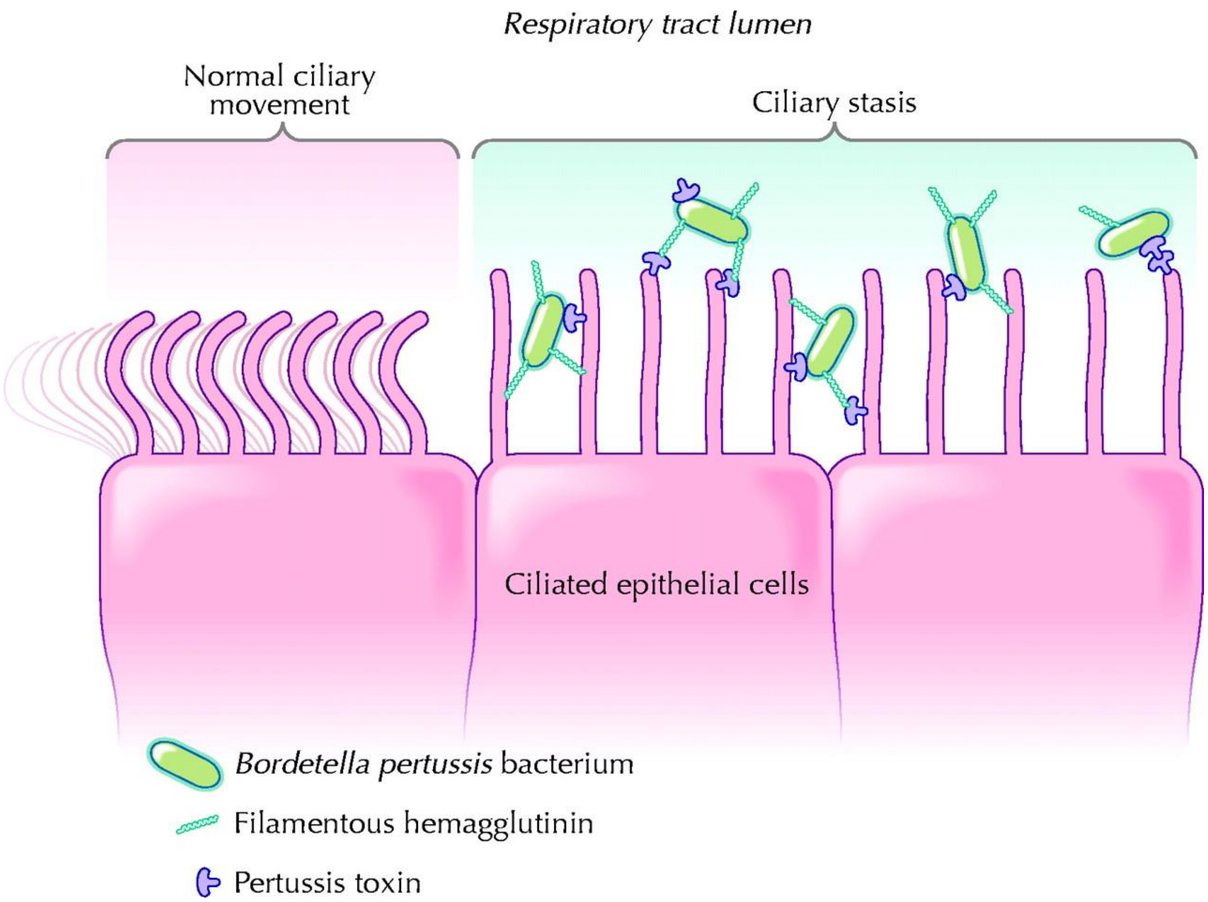
Following are the virulence factors:

1. The **pertussis toxin** stimulates adenylte cyclase by **ADP-ribosylation**.

   It is an **A-B subunit toxin** with a domain that mediates its binding to receptors on the surface of **respiratory tract epithelial cells**.

   This toxin also causes a **striking lymphocytosis** in the blood. **It inhibits signal transduction and lymphocytes cannot enter the lymph nodes and spleen.**

2. **Attachment of the organism to cilia** is facilitated by a protein on pili called **filamentous hemagglutinin**. Antibody against it inhibits attachment and protects against disease.



3. The organisms also synthesize and export **adenylate cyclase** which when taken up by **phagocytic cells** inhibit their activity.

   Mutants lacking this enzyme are **avirulent**.

4. **Tracheal cytotoxin** is a fragment of the bacterial peptidoglycan which acts in concert with endotoxin to induce nitric oxide which **kills the ciliated epithelial cells**.

Clinical findings

-- **Whooping cough** is an acute **tracheobronchitis** that begins with mild upper respiratory tract symptoms followed by a **severe paroxysmal cough** which lasts from 1-4 weeks.

-- The **paroxysmal pattern** is a series of **hacking coughs**, with production of **copious amounts of mucus** that end with inspiratory **“whoop”** as air rushes past the **narrowed glottis**.

-- Despite the severity of the symptoms, the organism is **restricted to the respiratory tract** and blood cultures are negative.

-- A pronounced **leukocytosis** with up to **70% lymphocytes** is seen.

-- Although **CNS anoxia** and **exhaustion** can occur as a result of severe coughing, **death is due mainly to pneumonia**.

-- The classic picture is seen in **young children**.

-- In **adults**, there is a **paroxysmal cough** of varying severity lasting for weeks.

-- **In adults, characteristic whoop is often absent.**

-- Patients with a **cough lasting several weeks** should be evaluated for ***B. pertussis*** infection.

Laboratory diagnosis

The organism can be isolated from **nasopharyngeal swabs** taken during the paroxysmal stage.

Bordet-Gengou medium used for this purpose contains **high % of blood (20-30%)** to inactivate inhibitors in agar.

-- Identification of isolated organism can be made by **agglutination** with specific antiserum or by **fluorescent antibody staining**.

-- Because organism **grows very slowly**, **direct fluorescent antibody staining** of nasopharyngeal specimens can be used for diagnosis.

-- **PCR-based test** are **highly specific and sensitive** and should be used if available.

-- Isolation of microbes in patients of prolonged cough is difficult so **serological tests** should be used.

Treatment

-- **Macrolides, erythromycin** or **azithromycin** are used.

-- These drugs can reduce number of organisms and **decrease chance of secondary complications.**

-- These have **no effect on course of disease** because toxins have already damaged the respiratory mucosa.

-- **Supportive care (e.g., oxygen therapy and suction of mucus) during the paroxysmal stage is important, especially in infants.**

Prevention

-- There are two vaccines: an **acellular vaccine** containing purified proteins from the organism and a **killed vaccine** containing inactivated ***B.pertussis*** organisms.

--- **The acellular vaccine has five proteins and main component is pertussis toxoid.**

-- The **toxoid** is made by eliminating ADP-ribosylation activity genetically.

-- Other components are **filamentous hemagglutinin, pertactin**, and **fimbriae types 2 and 3**.

-- Pertussis vaccine is usually given **combined with diphtheria and tetanus toxoid (DTaP)** beginning at 2 months of age.

-- A **booster at 12-15 months** and other at **school going age** is recommended.

-- A booster dose may be given between **10-18 years age** as well.

-- **Killed vaccine has side effects** so it is not commonly used.

-- **Erythromycin** is useful in prevention of disease in exposed, unimmunized individuals.

-- It should also be given to immunized children **younger than 4 years** because vaccine induced immunity is not fully protective.

Legionella

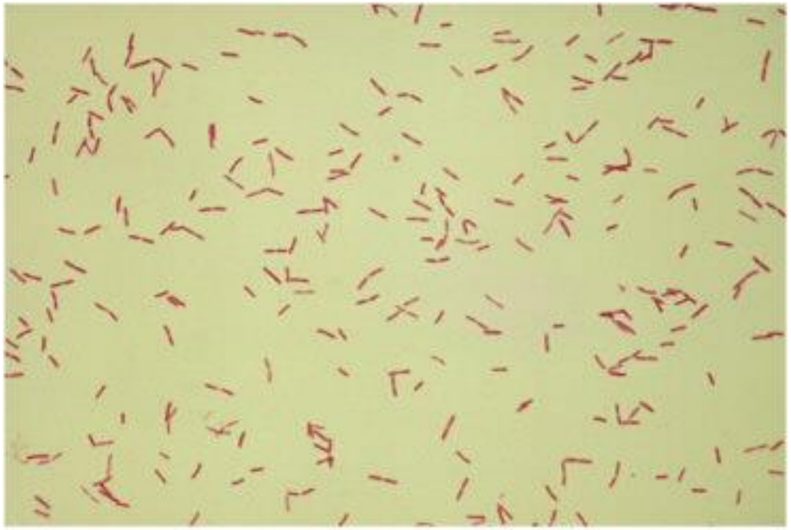
-- ***L. pneumophila*** (and other legionella) causes **pneumonia**, both in the community and in hospitalized immunocompromised patients.

-- ***L. pneumophila*** is the cause in **90% cases** of pneumonia by all legionella.

-- Although there are 30 species, two other important ones are ***L. micdadei*** and ***L. bozemanii***.

Important properties

These are Gram negative rods that **stain faintly** with the standard Gram stain.



They become more visible after **prolonged staining with safranin**.

In **lung biopsy** sections they **do not stain by standard H & E method** so special methods are used.

They grow **only in presence of high concentration of iron and cysteine**.

Growth on buffered charcoal yeast extract agar

Pathogenesis and Epidemiology

-- These are **chiefly associated with environmental water sources** such as air-conditioners and water cooling towers.

-- In **hospitals, infection** is attributed to **water taps, sinks** and **showers**.

-- Infection is **through respiratory tract** and mainly lung is affected.

-- In severe cases, **bacteremia may occur** leading to damage of vascular endothelium in multiple organs, esp. in brain and kidneys.

-- Major virulence factor is **lipopolysaccharide endotoxin**.

-- There is **no exotoxin**.

-- **Elderly people who smoke and drink** are most susceptible.

-- Patients with **AIDS, cancer** or **transplants** or those on **corticosteroid** treatment are also susceptible due to **lowered cell mediated immunity**.

-- **Person to person spread does not occur through air.**

Clinical findings

-- The clinical picture may vary from a **mild influenza** like illness to a **severe pneumonia** accompanied by mental confusion, non bloody diarrhea, proteinurea, and microscopic haematuria.

-- Although **cough is the prominent symptom**, sputum is scanty and nonpurulent.

-- **Hyponatremia** (serum sodium less than 130 mEq/L) is an important finding.

-- Healthy persons recover within 7-10 days, but it **can be fatal in older or immunocompromised persons**.

-- Legionellosis is an **atypical pneumonia** and must be distinguished from ***Mycoplasma*** and viral pneumonia, psittacosis and Q fever.

-- **Pontiac fever** is a mild, flulike form that does not result in pneumonia.

Laboratory Diagnosis

-- **Sputum Gram stain reveal many neutrophils but no bacteria.**

-- Organisms grow on **charcoal yeast agar** which is **supplemented with iron and cysteine.**

-- Diagnosis usually depend on **significant rise in antibody titer** in convalescent phase using indirect immunofluorescence assay.

-- **If antigens are detected in urine, it is rapid diagnosis.**

-- If tissue is available, the bacteria can also be detected in **infected lung**.

-- The **cold-agglutinin level** does not rise in ***Legionella*** pneumonia in contrast to pneumonia caused by ***Mycoplasma***.

Treatment

-- **Azithromycin** or **erythromycin** (with or without rifampin) is the treatment of choice.

-- **Fluoroquinolones** may also be used as they are effective against ***Mycoplasma*** and ***Streptococcus pneumonia*** as well.

-- Due to **β-lactamase production**, β -lactam drugs are less effective.

Prevention

-- Prevention involves **reducing cigarette and alcohol consumption**.

-- It also requires **eliminating aerosols** from water resources, and reducing the incidence in hospital water supplies by using **high temperatures** and **hyperchlorination**.

-- There is **no vaccine**.


Thank You!