

# Medically important Bacteria and Fungi

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# Bacteria

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## Gram positive

### Cocci

Staphylococcus aureus  
Streptococcus pneumonia  
Streptococcus pyogenes

### Rods

Bacillus anthracis  
Bacillus subtilis  
Clostridium tetani  
Clostridium botulinum

## Gram negative

### Cocci

Nesseria meningitis  
Nesseria ghonorrhea

### Rods

Salmonella typhimurium  
Pseudomonas aeruginosa  
Escherichia coli O157: H7

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# Gram Positive Cocci



# Staphylococcus spp

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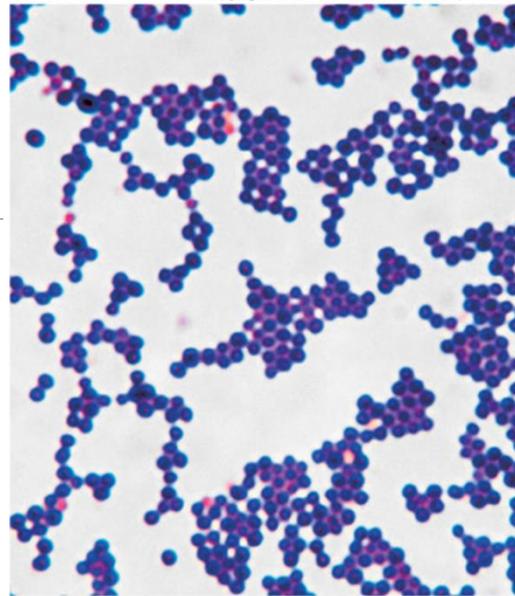
- ▶ Family: Micrococcaceae
- ▶ Genus:
  - A. Staphylococcus- derived from Greek “stapyle” (bunch of grapes)
- ▶ Include major human pathogen and skin commensals
- ▶ Staphylococcus divided into coagulase positive & coagulase negative categories
  
- ▶ Common spp:
  - ▶ S. aureus
  - ▶ S. epidermidis
  - ▶ S. saprophyticus
  
- B. Micrococcus- skin commensal
- ▶ Gram-positive spherical cells (0.5-1.5  $\mu$ m) in singles, pairs, and clusters
- ▶ Appear as “bunches of grapes”



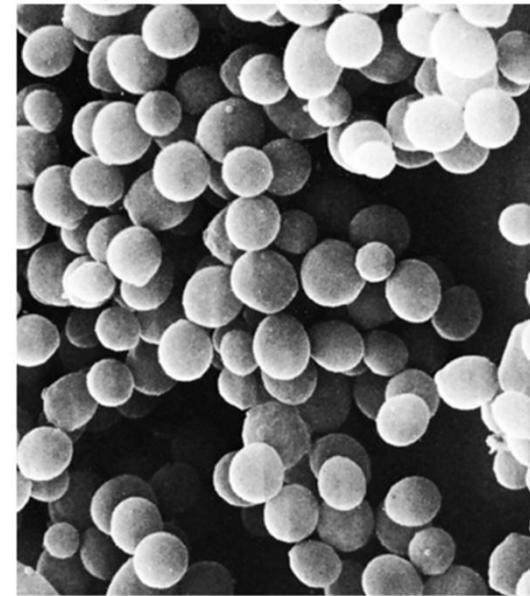
# S. aureus

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- ▶ Non motile
- ▶ Non-spore-forming
- ▶ Nonencapsulated
- ▶ Catalase-producing



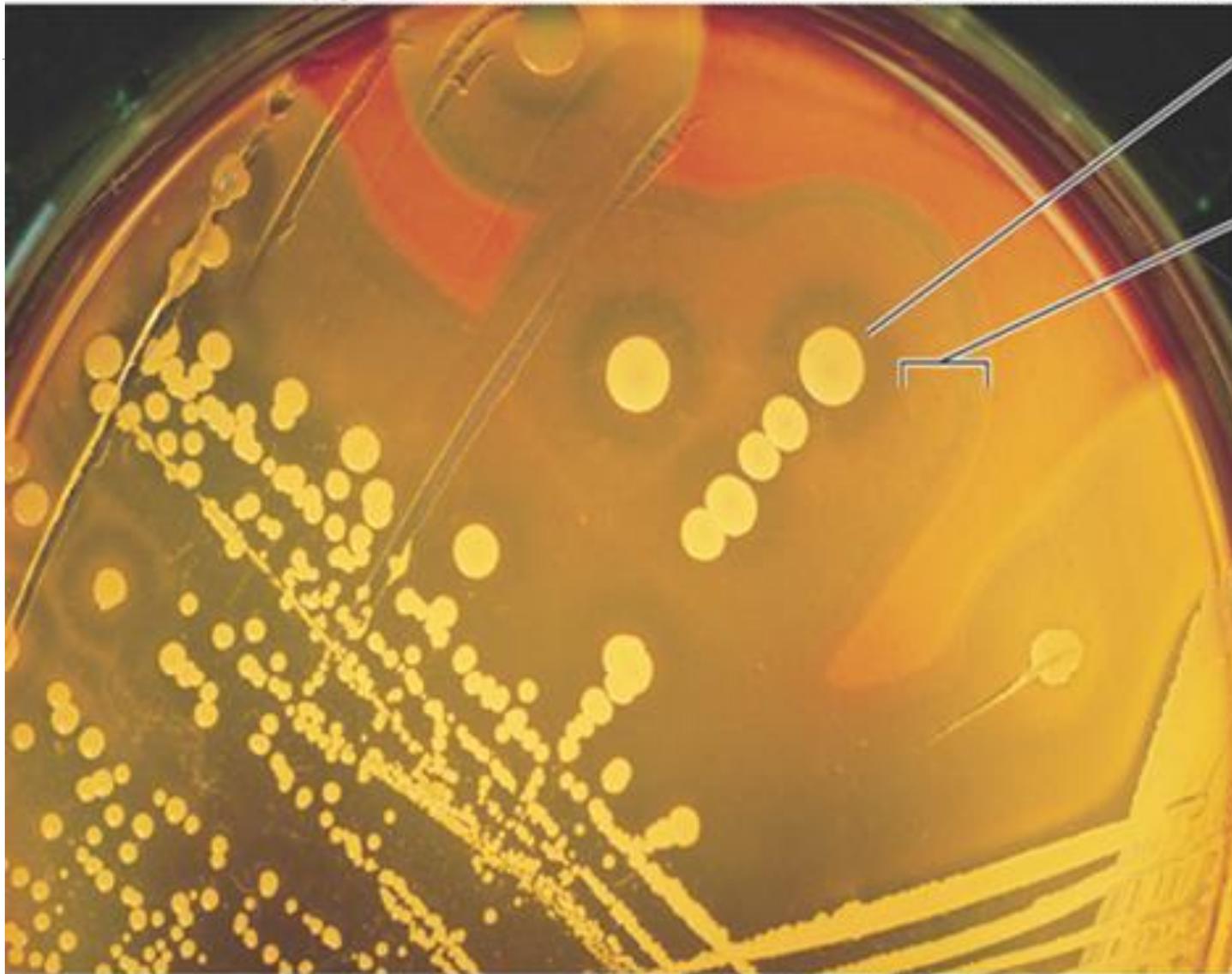
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- ▶ Primarily aerobic, some facultatively anaerobic
- ▶ Inhibited by high bile salt concentration
- ▶ S. aureus  $\beta$ -hemolytic
- ▶ Colony morphology:
  - ▶ buttery looking, cream or white colored





Beta-hemolysis  
caused by  
 $\alpha$ -toxin

Zone of  
hemolysis  
caused by  
 $\beta$ -toxin

# Virulence factors of *S. aureus*

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- ▶ Toxins:
- ▶ Hemolysins ( $\alpha$ ,  $\beta$ ,  $\gamma$ ,  $\delta$ ) – lyse red blood cells
- ▶ Leukocidin – lyses neutrophils and macrophages
- ▶ Enterotoxin – induce gastrointestinal distress
- ▶ Exfoliative toxin – separates the epidermis from the dermis
- ▶ Toxic shock syndrome toxin (TSST) - induces fever, vomiting, shock, systemic organ damage



# Epidemiology and pathogenesis

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- ▶ Present in most environments even humans
- ▶ Readily isolated from fomites
- ▶ Carriage is mostly in anterior nares, skin, nasopharynx, intestine.
- ▶ Predisposition to infection include: poor hygiene and nutrition, tissue injury, preexisting primary infection, diabetes, immunodeficiency.
- ▶ Increase in community acquired methicillin resistance - MRSA

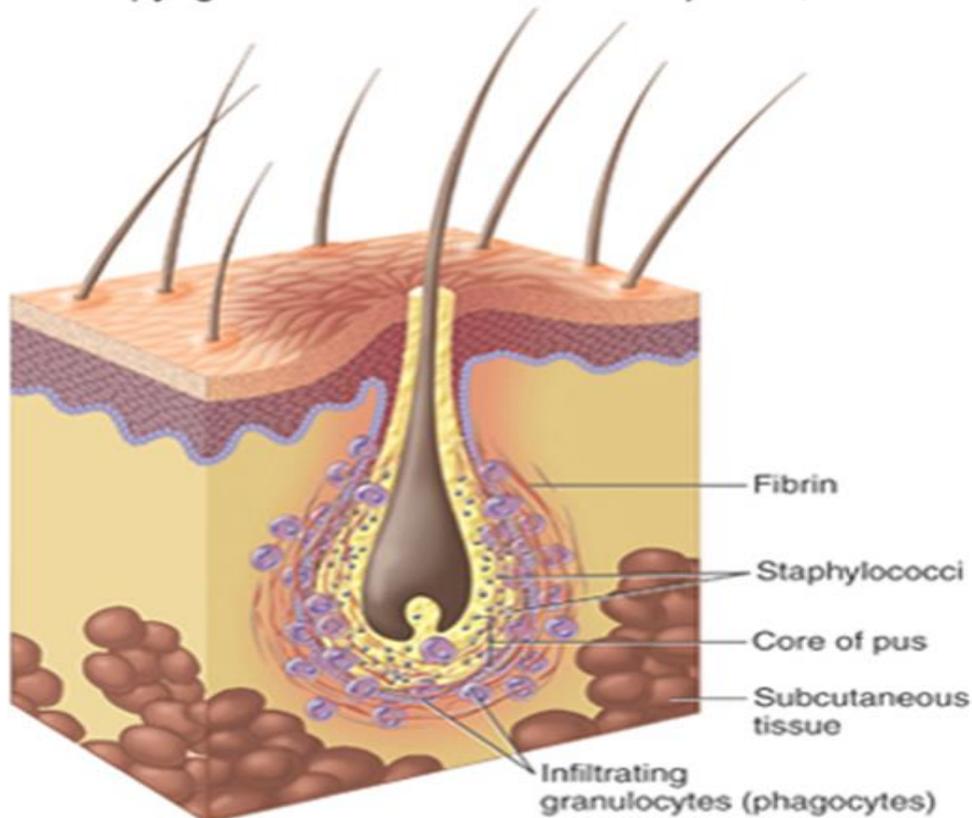


# Staphylococcal Disease

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- ▶ **Range from localized to systemic**
- ▶ 1. Localized cutaneous infections – invade skin through wounds, follicles, or glands
- ▶ 2. folliculitis – superficial inflammation of hair follicle; usually resolved with no complications but can progress
- ▶ 3. furuncle – boil; inflammation of hair follicle or sebaceous gland progresses into abscess or pustule
- ▶ 4. carbuncle – larger and deeper lesion created by aggregation and interconnection of a cluster of furuncles
- ▶ 5. impetigo – bubble-like swellings that can break and peel away; most common in newborns





(a) Sectional view of a boil or furuncle, a single pustule that develops in a hair follicle or gland and is the classic lesion of the species. The inflamed infection site becomes abscessed when masses of phagocytes, bacteria, and fluid are walled off by fibrin.



(b) A furuncle on the back of the hand. This lesion forms in a single follicle.

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(c) A carbuncle on the back of the neck. Carbuncles are massive deep lesions that result from multiple, interconnecting furuncles. Swelling and rupture into the surrounding tissues can be marked.

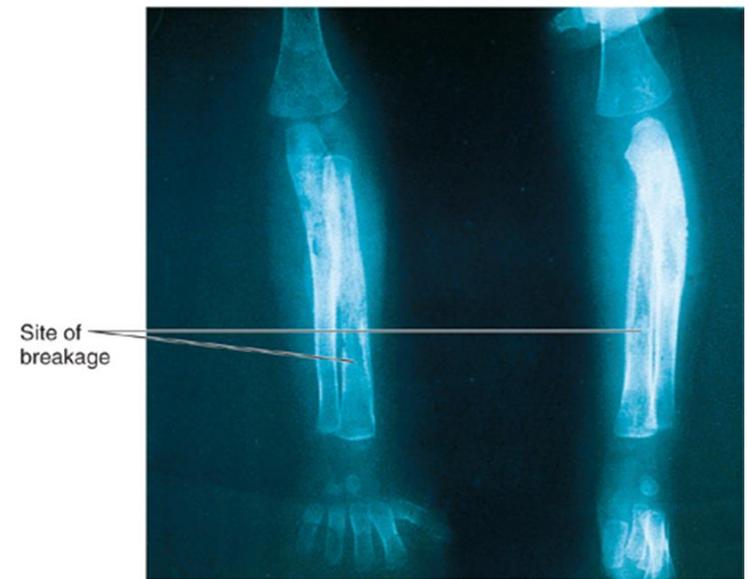
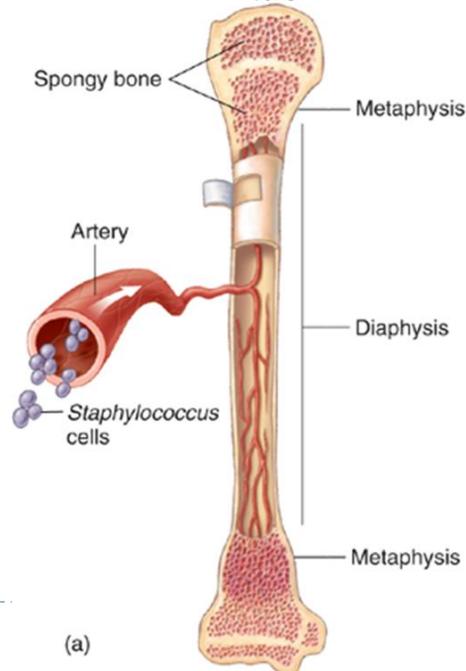
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# Continu----

## ▶ Systemic infections

- ▶ osteomyelitis – infection is established in the metaphysis; abscess forms
- ▶ bacteremia - primary origin is bacteria from another infected site or medical devices; endocarditis possible

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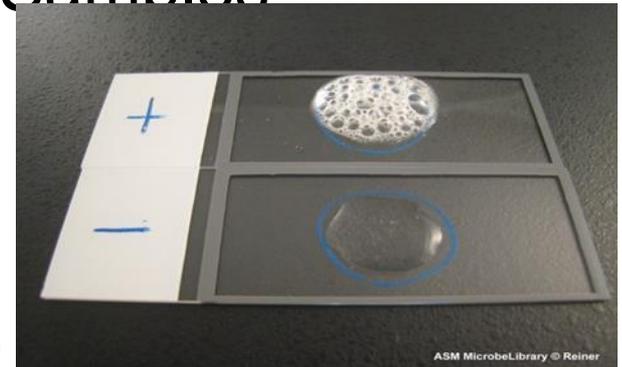
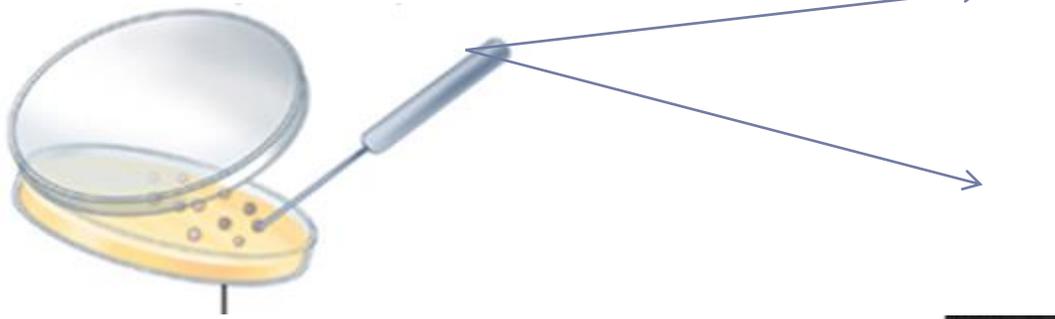
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- ▶ **Toxigenic disease**
- ▶ food intoxication – ingestion of heat stable enterotoxins; gastrointestinal distress
- ▶ staphylococcal scalded skin syndrome – toxin induces bright red flush, blisters, then desquamation of the epidermis
- ▶ toxic shock syndrome – toxemia leading to shock and organ failure



# Clinical detection

- ▶ Frequently isolated from pus, tissue exudates, sputum, urine, and blood
- ▶ Cultivation (MSA agar), catalase, biochemical testing, coagulase
- ▶ Identification of Staphylococcus in Samples



# Treatment

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- ▶ 95% have penicillinase and are resistant to penicillin and ampicillin.
- ▶ MRSA – methicillin-resistant *S. aureus* – carry multiple resistance
- ▶ Abscesses have to be surgically perforated.
- ▶ Systemic infections require intensive lengthy therapy.



# Other GPC

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- ▶ Catalase negative :
- ▶ Streptococcus pneumonia (pneumonia)
- ▶ streptococcus pyogenes (sore throat)
- ▶ Streptococcus mutans (tooth infection)
- ▶ Enterococcus faecalis (GIT + bacteremia)
- ▶





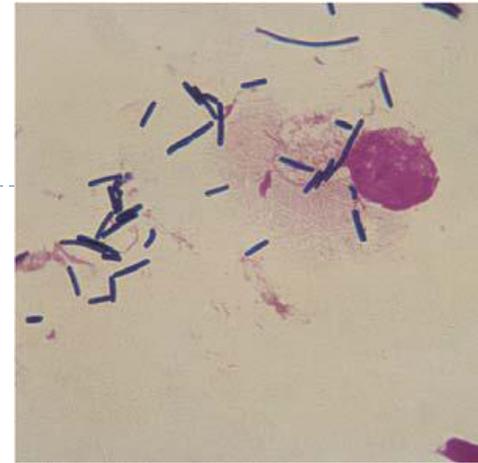
# Gram positive Rods



# Family: Clostridiaceae

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- ▶ 3–8 um long, thick, Gram-positive
- ▶ Spore forming, rod shaped bacteria
- ▶ Motile bacteria with flagella
- ▶ strictly obligate anaerobic to aerotolerant
- ▶ Occurrence → naturally inhabit the soil and the intestinal tracts of humans and animals.
- ▶ Common species:
  - ▶ *C. tetani* (tetanus, nervous system disorder)
  - ▶ *C. perfringens* (anaerobic cellulitis and gas gangrene)
  - ▶ *C. botulinum* (botulism, food poisoning)

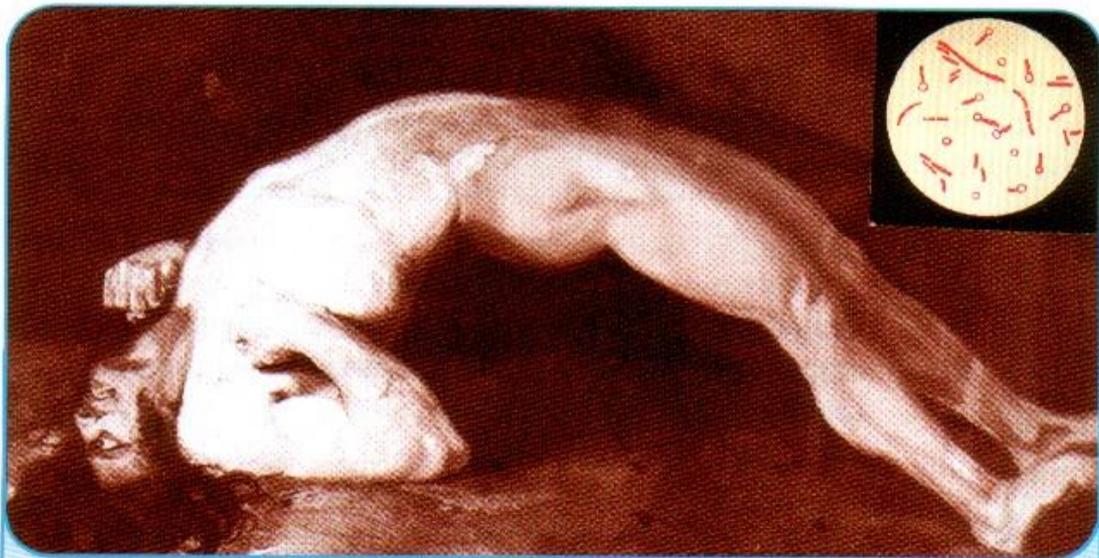


# C. tetani

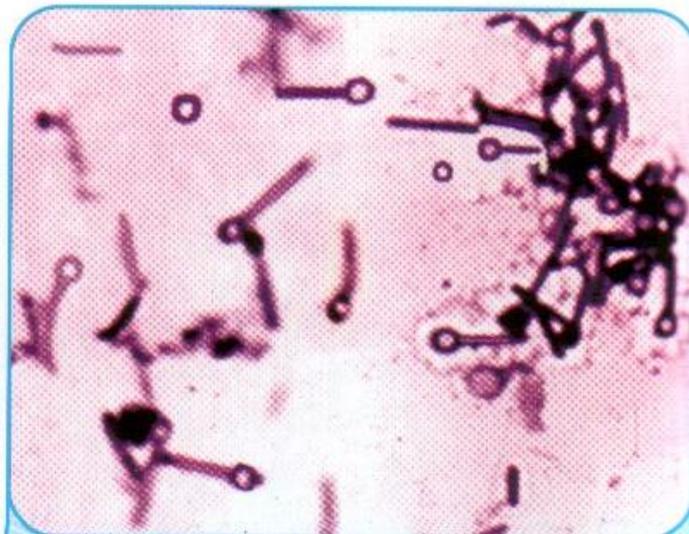
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- ▶ Tetanus (lockjaw) is an acute clostridial disease,
  - ▶ its clinical manifestations do not result directly from the invasive infection, but are rather caused by a strong neurotoxin.
  
  - ▶ **Pathogenesis and clinical picture.**
  
  - ▶ pathogens invade tissues via wounds/ injuries → anaerobic conditions → proliferate and produce the toxin (tetanospasmin) → reaches the anterior horns of the spinal cord or brain stem → spasms of muscles
  - ▶ ( incubation period : few days to several weeks)
  - ▶ **Toxin:**
  - ▶ Tetanospasmin consists of two polypeptide chains linked by a disulfide bridge. The heavy chain binds specifically to neuron receptors.
  - ▶ The light chain is a zinc-metalloprotease that is responsible for proteolysis of components of the neuroexocytosis apparatus in the synapses of the anterior horns of the spinal cord. This stops transmission of inhibitory efferent impulses from the cerebellum to the motor end plates.
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**Рис. 3.79.** Опистотонус



**Рис. 3.80.** Мазок из чистой культуры *C. tetani*.  
Окраска по Граму



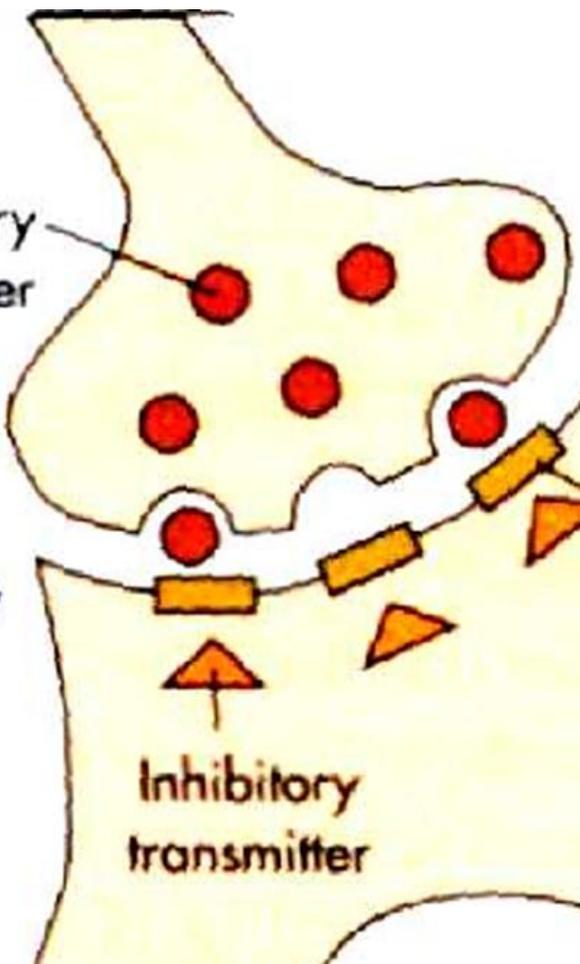
*C. tetani*



Tetanospasmin



Excitatory transmitter



Inhibitory transmitter

Continuous stimulation by excitatory transmitter



Inhibitory transmitter release blocked

# Vaccination & treatment

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- ▶ DPT (diphtheria, pertussis, tetanus)
- ▶ tetanus toxoid
- ▶ antigenic
- ▶ **TAT (tetnus antitoxin); Metronidazole (For more serious wounds)**





# Gram negative rods



# Enterobacteriaceae.

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- ▶ 41 genera with hundreds of species
- ▶ Gram-negative,
- ▶ usually motile (peritrichous flagellation or swarming movement)
- ▶ facultative anaerobic rod bacteria
- ▶ natural habitat is the intestinal tract of humans and animals
- ▶ Responsible for nosocomial diseases as well
- ▶ 0.5–1.5  $\mu\text{m}$  thick, and 2–4  $\mu\text{m}$  long
- ▶ Generation time in vitro is 20–30 minutes



## Several serovars

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- ▶ **O antigens.** Specific polysaccharide chains in the lipopolysaccharide complex of the outer membrane.
- ▶ **H antigens.** Flagellar antigens consisting of protein.
- ▶ **K antigens.** Linear polymers of the outer membrane built up of a repeated series of carbohydrate units (sometimes proteins as well). They can cover the cell densely.
- ▶ **F antigens.** Antigens of protein attachment fimbriae.



# Salmonella spp

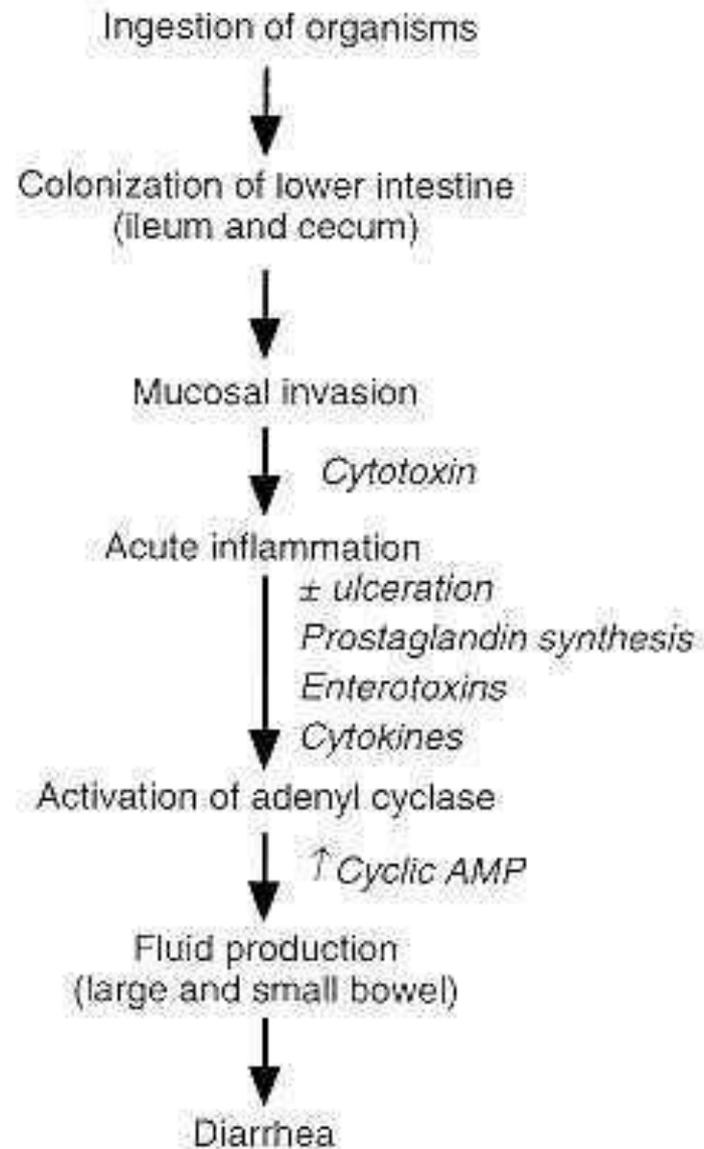
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- ▶ Salmonella enterica with seven subspecies.
- ▶ **Typhoid salmonellosis**: typhi and paratyphi A, B, and C
- ▶ Salmonellae are taken up orally and the invasion pathway is through the intestinal tract, from where they enter lymphatic tissue, first spreading lymphogenously, then hematogenously.
- ▶ 1-3 weeks
- ▶ Human carriers are the only source of infection
- ▶ **Enteric salmonellosis** : develop when pathogens are taken up with food. The primary infection source is usually livestock. These relatively frequent infections remain restricted to the gastrointestinal tract.
- ▶ 1–2 days

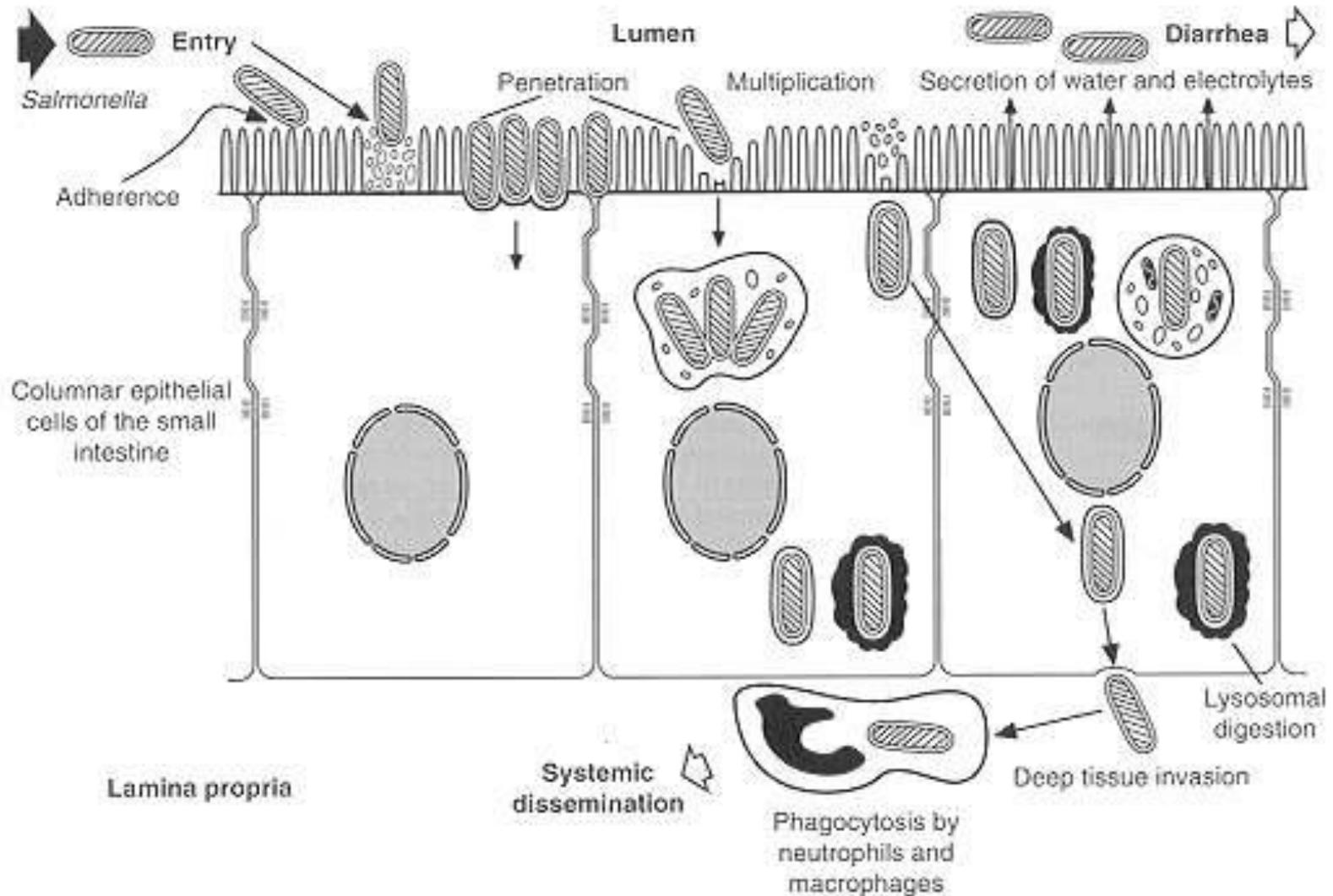


# Pathogenesis

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# Pathogenesis



# Diagnosis & Therapy.

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- ▶ Diagnosis by
  - ▶ stool culture
  - ▶ metabolic properties
- ▶ treated with anti-infective agents (antibiotics) e.g. aminopenicillins, 4-quinolones
- ▶ slowing down intestinal activity (e.g., with loperamide) and replacing fluid and electrolyte losses orally as required



# Control

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- ▶ providing training in hygienic practices for all food-handling personnel in slaughterhouses,
- ▶ food processing plants, and restaurants;
- ▶ cooking and refrigerating foods adequately in food processing plants, restaurants, and homes;
- ▶ and expanding of governmental enteric disease surveillance programs.



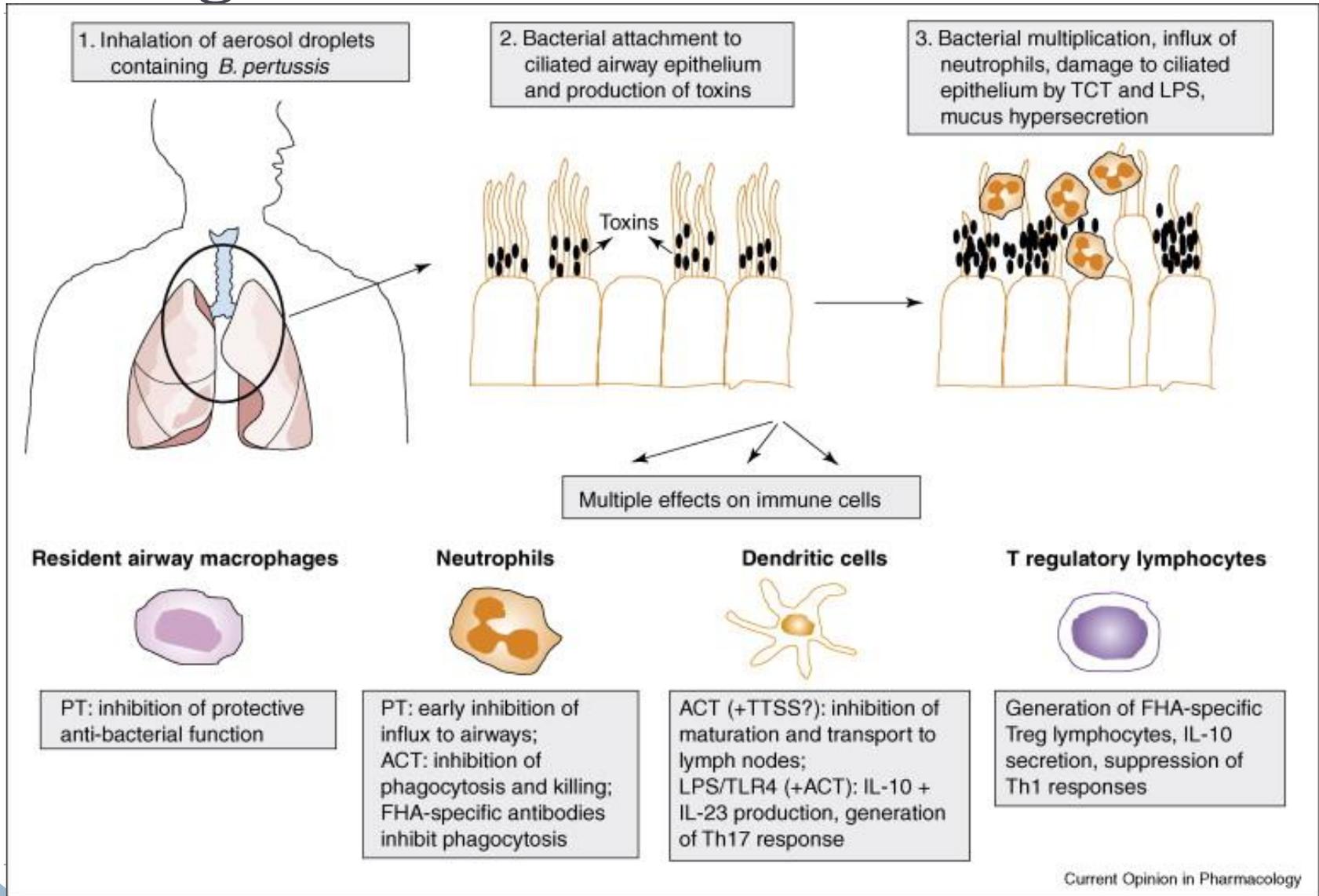
# Bordetella pertussis

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- ▶ Gram negative,
- ▶ aerobic,
- ▶ encapsulated coccobacillus
- ▶ the causative agent of pertussis or whooping cough.
- ▶ bacterium is spread by airborne droplets; its incubation period is 7–10 days on average (range 6–20 days)
- ▶ Humans are the only known reservoir for *B. pertussis*



# Pathogenesis



# Whooping cough (pertussis)

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- ▶ is a highly contagious respiratory tract infection. In many people, it's marked by a severe hacking cough followed by a high-pitched intake of breath that sounds like "whoop."
- ▶ **Symptoms**
- ▶ usually mild at first and resemble those of a common cold:
- ▶ Runny nose
- ▶ Nasal congestion
- ▶ Red, watery eyes
- ▶ Fever
- ▶ Cough
- ▶ After a week or two, signs and symptoms worsen. Thick mucus accumulates inside your airways, causing uncontrollable coughing. Severe and prolonged coughing attacks may:
- ▶ Provoke vomiting
- ▶ Result in a red or blue face
- ▶ Cause extreme fatigue
- ▶ End with a high-pitched "whoop" sound during the next breath of air



# Risk factors and prevention

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- ▶ infants who are younger than age 12 months who are unvaccinated or haven't received the full set of recommended vaccines have the highest risk for severe complications and death.
- ▶ the best way to prevent whooping cough is with the pertussis vaccine, which doctors often give in combination with vaccines against two other serious diseases — diphtheria and tetanus. Doctors recommend beginning vaccination during infancy.
- ▶ The vaccine consists of a series of five injections, typically given to children at these ages:
  - ▶ 2 months
  - ▶ 4 months
  - ▶ 6 months
  - ▶ 15 to 18 months
  - ▶ 4 to 6 years



# *Mycobacterium tuberculosis*

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- ▶ Over a century ago Robert Koch identified *Mycobacterium tuberculosis* as the causative agent of tuberculosis
- ▶ acid-fast rods, 0.4µm wide, and 3–4 µm long,
- ▶ Endospore forming
- ▶ non-motile.
- ▶ can be stained with special agents (Ziehl-Neelsen staining)
- ▶ *M. bovis* and *M. africanum* can also causes TB.
- ▶ obligate aerobes



## *Mycobacterium Tuberculosis*

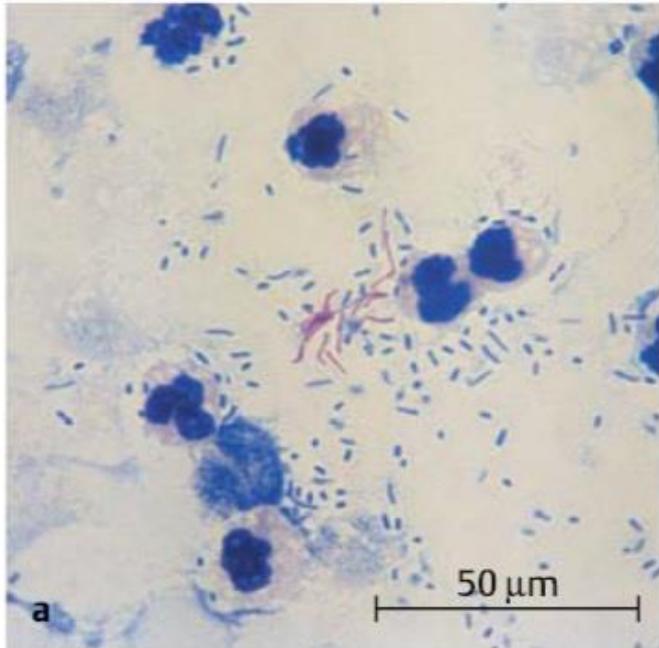
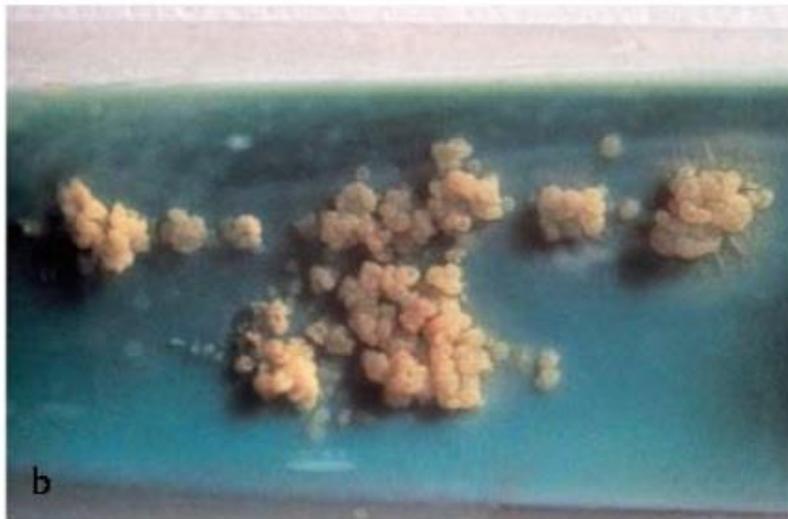


Fig.4.12 **a** Ziehl-Neelsen staining of a urine preparation: Fine, red, acid-fast rods, which tend to stick together. Clinical diagnosis: renal tuberculosis.

**b** Culture of *M. tuberculosis* on egg nutrient substrate according to Löwenstein-Jensen: after four weeks of incubation rough, yellowish, cauliflowerlike colonies.

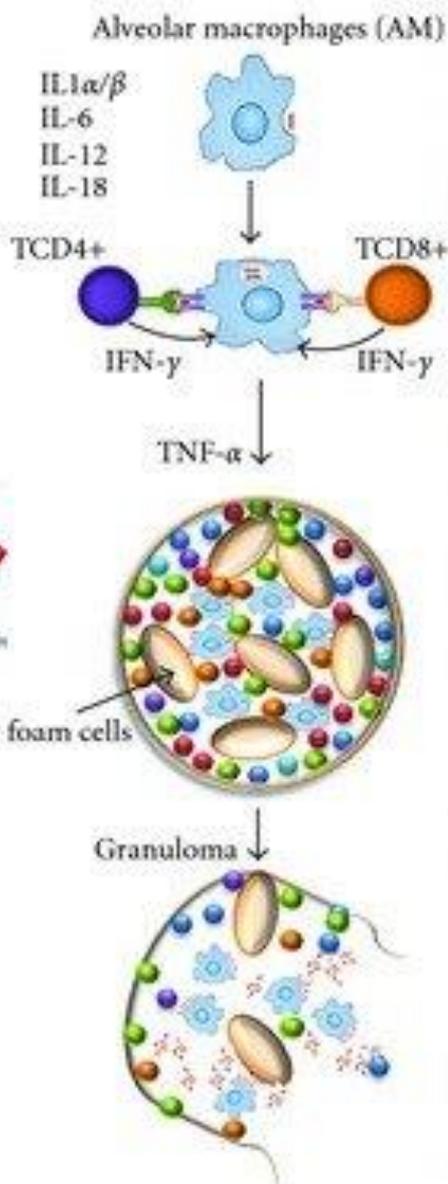
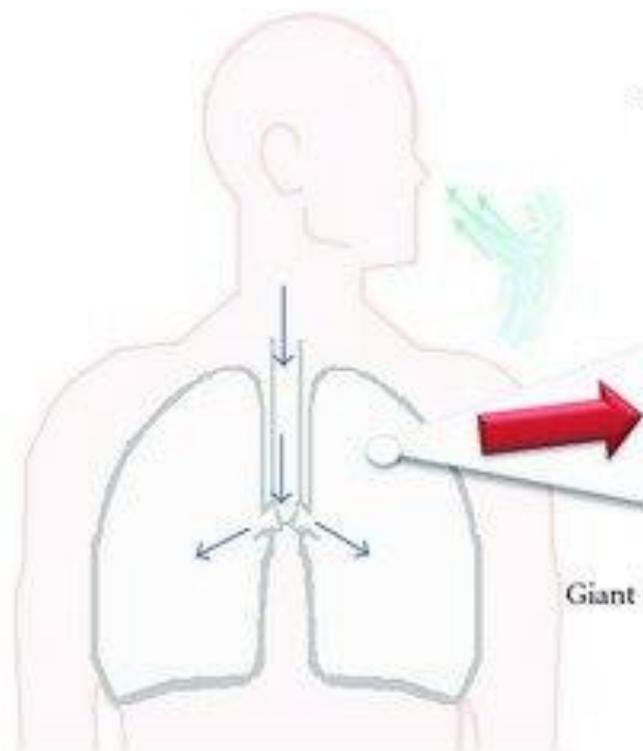


# Pathogenesis

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- ▶ Transmission: from other humans through droplet nuclei (1-5 micron in diameter) and the respiratory Route
- ▶ Transmission to humans from susceptible animal species and their products (e.g., milk) is also possible
- ▶ Depending on the environment, these tiny particles can remain suspended in the air for several hours.
  
- ▶ incubation period : about 4 to 12 weeks, and the disease develops slowly.
- ▶ symptoms : fever, fatigue, and weight loss.
  - ▶ A cough, which is characteristic of pulmonary involvement, may result in expectoration of bloody sputum.





#### Inhalation of Mtb

- Phagocytosis of bacilli

#### Inflammatory cell recruitment

- AM secreted IL-12 and IL-18
- IFN- $\gamma$  induce bacterial killing
- TNF- $\alpha$  is essential in the control of Mtb growth and granuloma formation

#### Control of mycobacteria growth

- Stops Mtb proliferation
- Chronic cytokine stimulation
- Granuloma is formed by several cells recruited to the lung. Inside, infected macrophages contain the Mtb preventing their spread.

#### Postprimary tuberculosis

- Mycobacteria persistence is associated to a failure in the immune-surveillance
- Disease may reactivate
- Damage of nearby bronchi
- Spreading of the Mtb to other areas of the lung

# Treatment and control

- ▶ chemotherapy and chemoprophylaxis are carried

Table 4.4 Scheme for Chemotherapy of Tuberculosis

	<b>Standard scheme</b>	<b>Months</b>	<b>Short scheme *</b>	<b>Months</b>
Initial phase	isoniazid (INH) rifampicin (RMP) ethambutol (EMB)	2	isoniazid rifampicin ethambutol pyrazinamide (PZA)	2
Continuation phase	isoniazid rifampicin	7	isoniazid rifampicin	4

- ▶ Recently, new multi-drug-resistant strains of tuberculosis (MDR-TB) have developed and are spreading
- ▶ infants and children, are vaccinated with bacille Calmette-Guérin (BCG) vaccine to prevent complications such as meningitis.

# Diagnosis

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- ▶ requires microscopic and cultural identification of the pathogen or pathogen-specific DNA
- ▶ generation time of TB is approximately 12–18 hours, so that cultures must be incubated for three to six or eight weeks at 37 °C until proliferation becomes macroscopically visible
- ▶ Tuberculin skin reaction



# Diagnosis

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- ▶ generation time of TB is approximately 12–18 hours, so that cultures must be incubated for three to six or eight weeks at 37 °C until proliferation becomes macroscopically visible
- ▶ Tuberculin reaction





# Gram negative Cocci



# Neisseriaceae

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- ▶ Gram-negative cocci often arranged in pairs (diplococci) with adjacent sides flattened (like coffee beans) a diameter of approximately 1  $\mu\text{m}$
  - ▶ Encapsulated
  - ▶ Non sporeforming
  - ▶ Aerobic
  - ▶ Nonmotile
  - ▶ Important human species
    - ▶ *Neisseria gonorrhoeae* → sexually transmitted pathogen (urethritis, cervicitis)
    - ▶ *Neisseria meningitides* (meningitis, meningococcal meningitis, arthritis,)
  - ▶ species normally colonize mucosal surfaces of oropharynx and nasopharynx and occasionally anogenital mucosal membranes
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***Neisseria gonorrhoeae* and *Neisseria meningitidis***

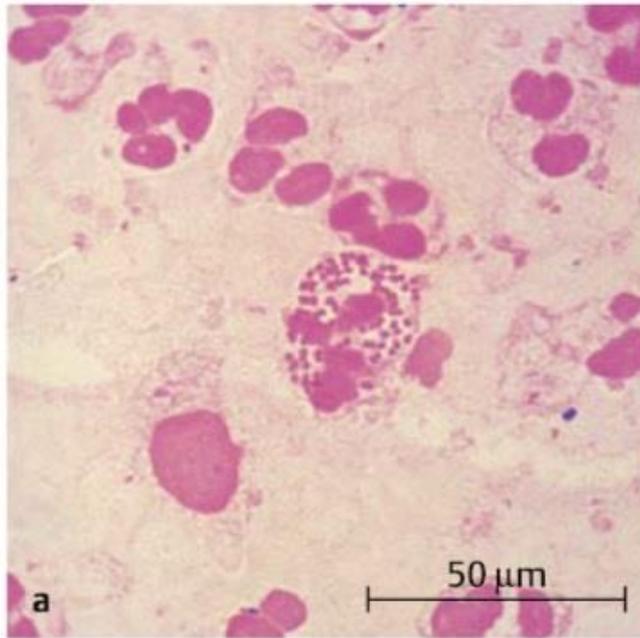
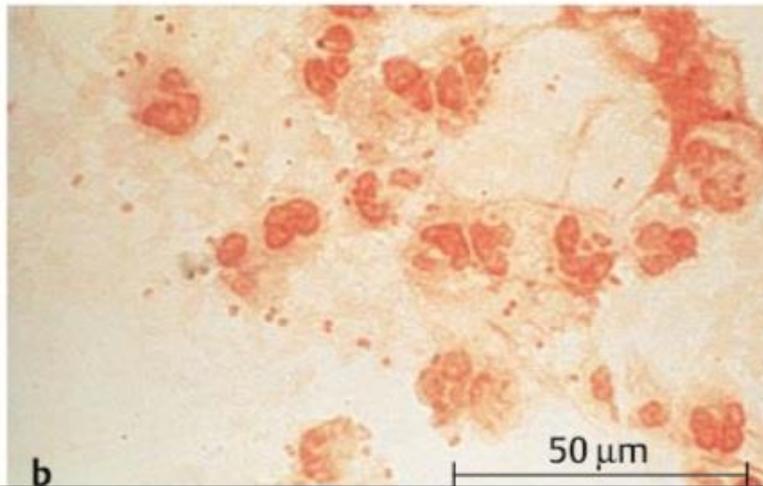


Fig. 4.16 **a** *N. gonorrhoeae*: gram staining of a preparation of urethral secretion: coffee-bean-shaped diplococci, grouped within a granulocyte. Clinical diagnosis: gonorrhoea. **b** *N. meningitidis*: gram staining of a preparation of cerebrospinal fluid sediment. Clinical diagnosis: acute purulent meningitis.



# Neisseria meningitides

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- ▶ Gram negative cocci shaped
- ▶ appears in kidney bean shape under the microscope .
- ▶ It requires anaerobic environment with 5% CO<sub>2</sub> and enriched media containing blood for growth
- ▶ oxidase and catalase positive.
- ▶ Serogroups A, B, C, D, etc. (a total of 12
- ▶ **Epidemiology:**
  - Humans only natural hosts
  - Person-to-person transmission by aerosolization of respiratory tract secretions in crowded conditions
  - Close contact with infectious person
  - Highest incidence in children younger than 5 years and particularly those younger than 1 year of age



# Pathogenesis

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- ▶ Pili-mediated receptor-specific colonization of nonciliated cells of nasopharynx



- ▶ Engulfed by phagocytes



- ▶ Antiphagocytic polysaccharide capsule does not allow phagolysosome activity



allows systemic spread i.e. to soft tissues

(brains n ligaments)



- ▶ Toxic effects mediated by hyperproduction of lipooligosaccharide
  - ▶ Causing meningitis, uteritis, arthritis etc.
- 



# Treatment

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- ▶ The antibiotic of choice is penicillin G.
- ▶ Therapy has been obtained with third-generation cephalosporins, e.g., cefotaxime or ceftriaxone.
- ▶ It is important to start treatment as quickly as possible to prevent delayed damage





# Mycoplasma

# Mycoplasmataceae

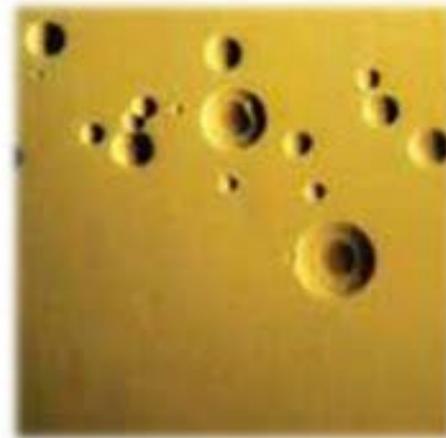
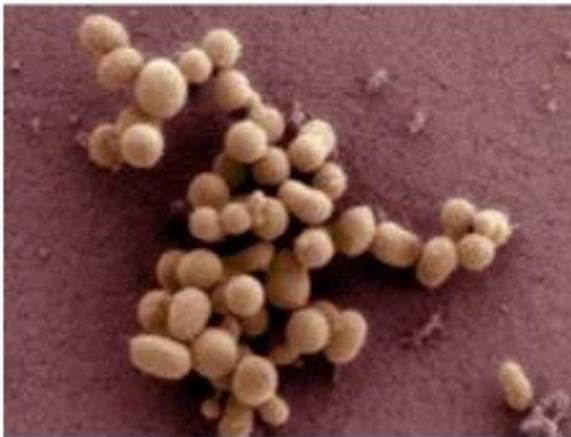
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- ▶ Do not possess rigid cell walls for lack of a murein layer
- ▶ Pleomorphic but most common form is coccoid cell with a diameter of 0.3–0.8  $\mu\text{m}$ .
- ▶ Long,
- ▶ fungi like filaments grown on culture mediums with high osmotic pressure levels.
- ▶ frequently causes pneumonias that run atypical courses, especially in young children.
- ▶ 10 -20% of pneumonias contracted outside of hospitals are caused by this pathogen
- ▶ Common species:
- ▶ *Mycoplasma pneumoniae*
- ▶ *Ureoplasma*
- ▶ Infections of the respiratory organs or urinary tract.



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# MYCOPLASMA



# Pathogenesis

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- ▶ transmitted by aerosol droplets → cells attach themselves to the epithelia of the trachea, bronchi, and bronchioles → destruction of the epithelial cells → infection develops into pneumonia with an inflammatory exudate in the lumens of the bronchi and bronchioles.
- ▶ The incubation period is 10–20 days.
- ▶ Symptoms : fever, headache, and a persistent cough.



# Treatment

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- ▶ The antibiotics of choice are tetracyclines and macrolides
- ▶ *M. pneumoniae* is found worldwide.
- ▶ Humans are the only source of infection. The pathogens are transmitted
- ▶ by droplet infection during close contact. Infections are frequently contracted
- ▶ in families, schools, homes for children, work camps, and military camps

