Introduction to Microbiology

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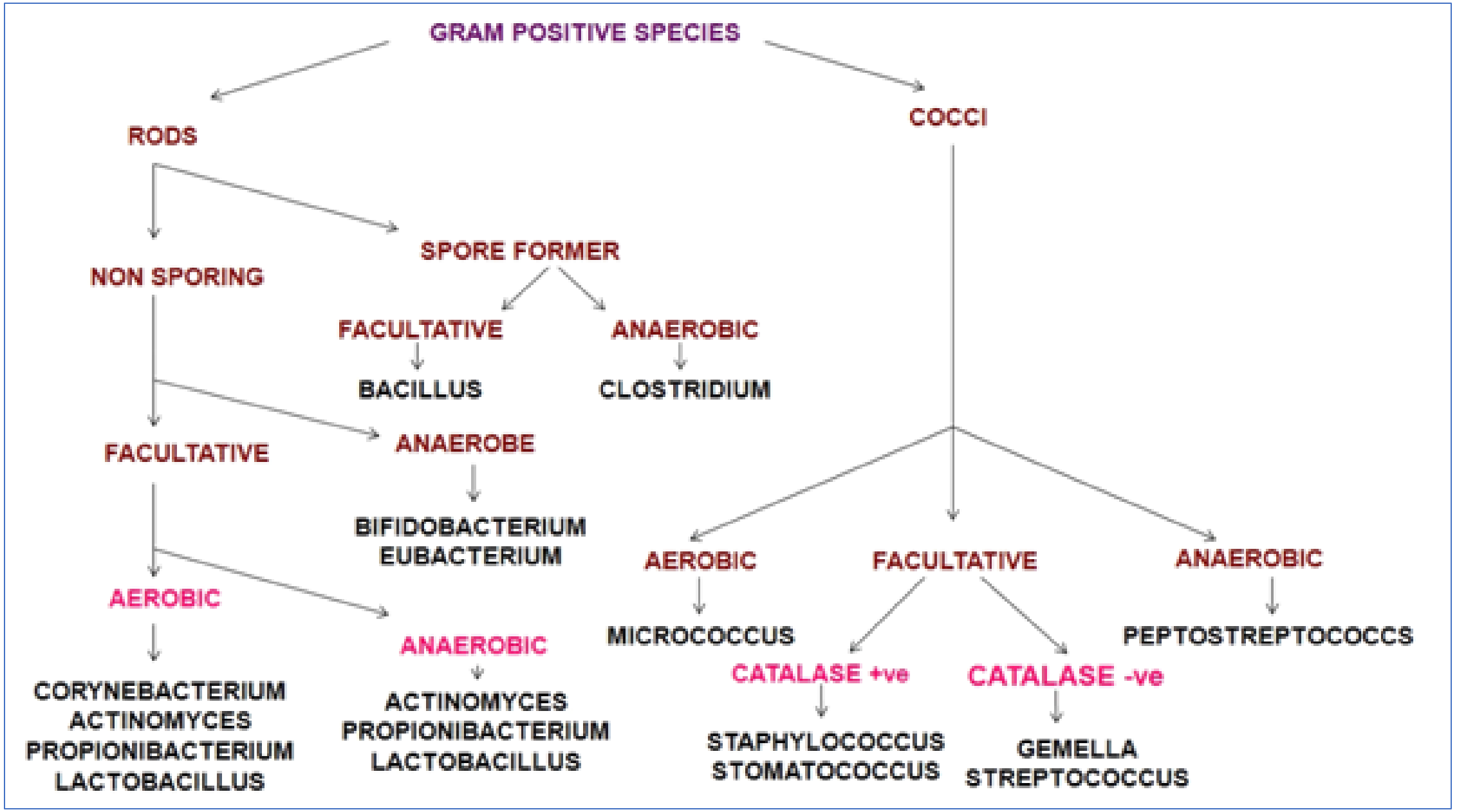
Lecture 20

Overview

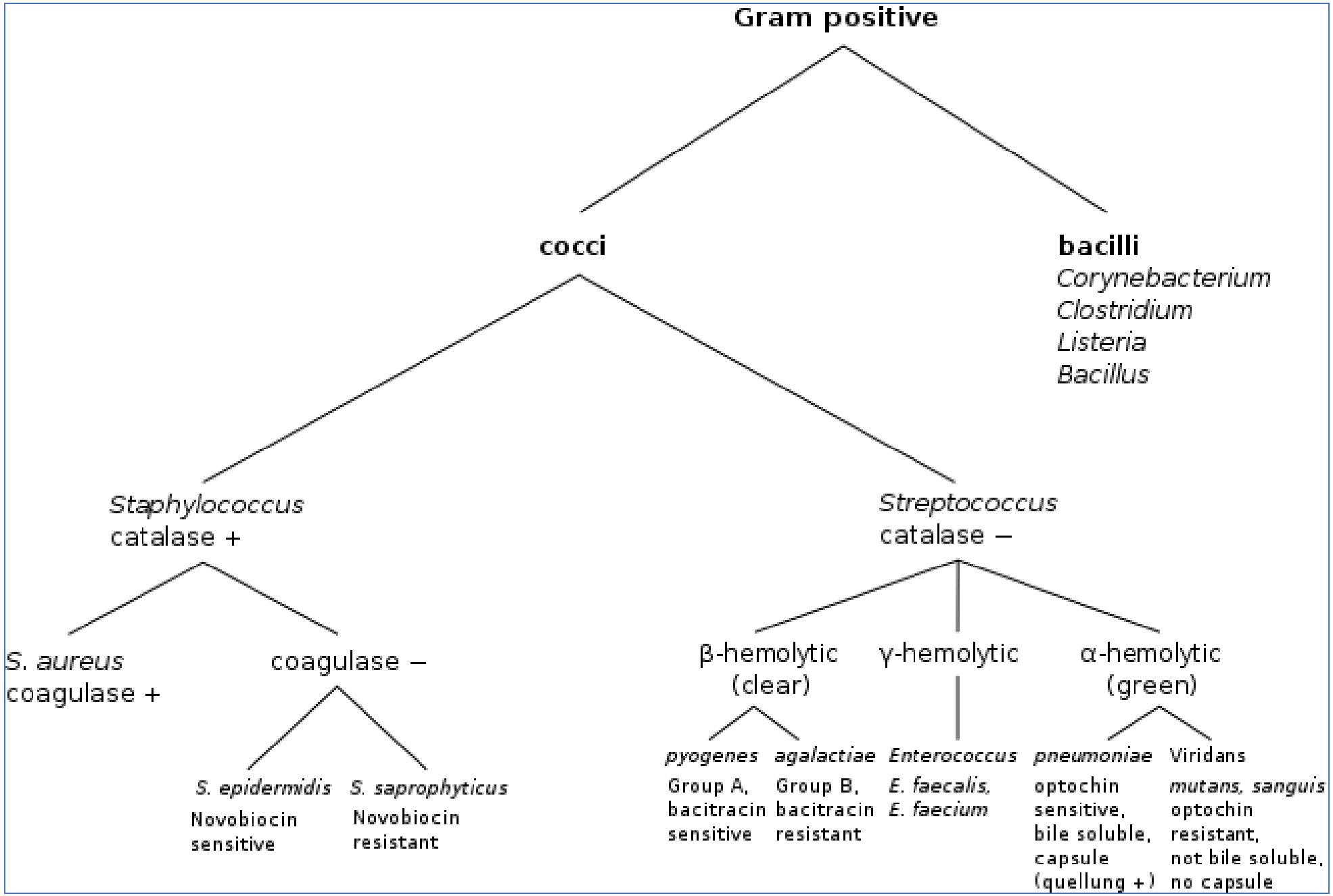
Pathogens that will be discussed this lecture are

- **Non-Spore-Forming Gram-Positive rods (aerobic and anaerobic),**
- **anerobic gram positive cocci,**

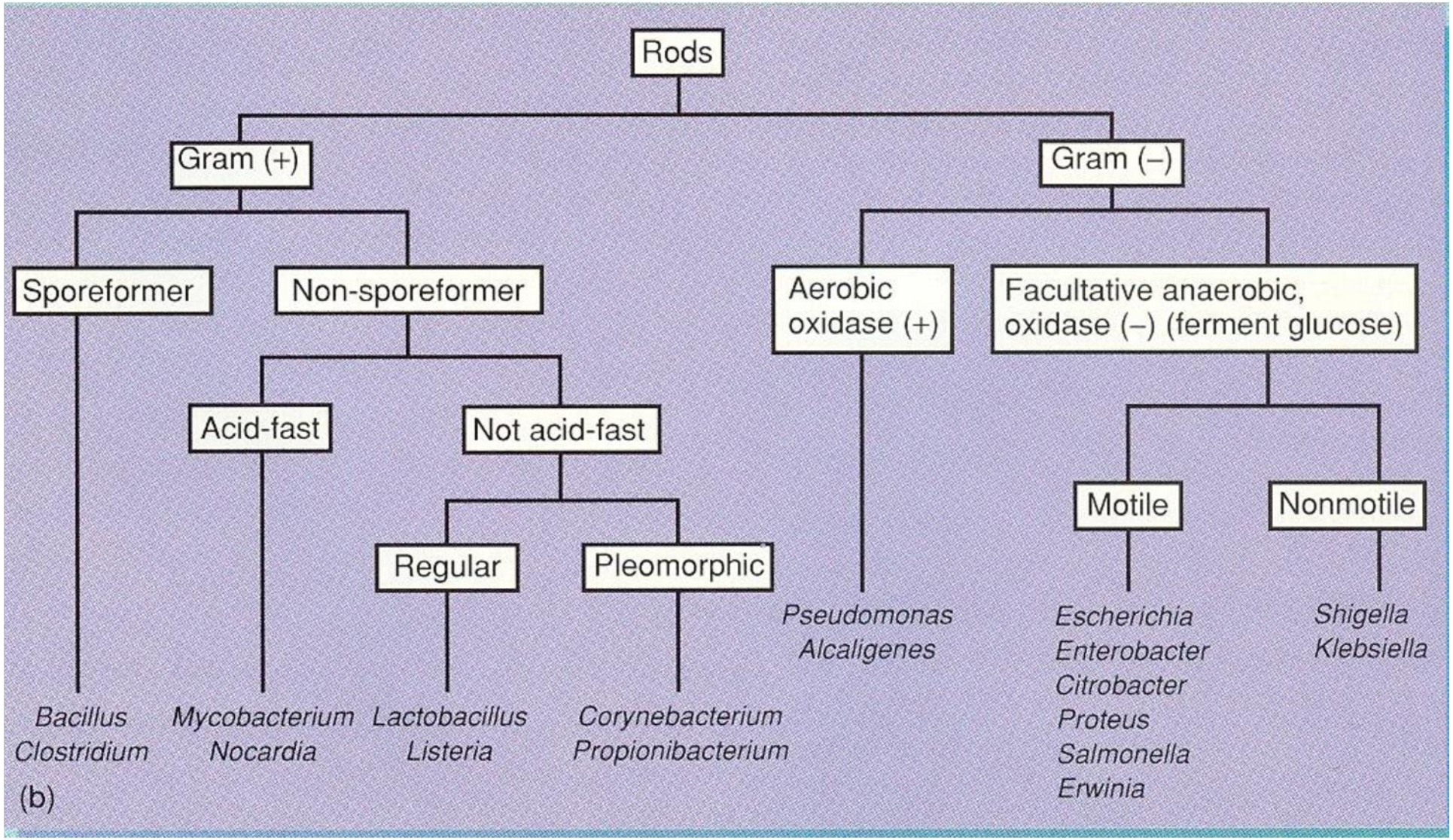
Overview


GRAM POSITIVE SPECIES
RODS
COCCI
NON SPORING
SPORE FORMER
FACULTATIVE
ANAEROBIC
BACILLUS
CLOSTRIDIUM
FACULTATIVE
ANAEROBE
BIFIDOBACTERIUM
EUBACTERIUM
AEROBIC
ANAEROBIC
CORYNEBACTERIUM
ACTINOMYCES
PROPIONIBACTERIUM
LACTOBACILLUS
ACTINOMYCES
PROPIONIBACTERIUM
LACTOBACILLUS
AEROBIC
FACULTATIVE
ANAEROBIC
MICROCOCCUS
CATALASE +ve
CATALASE -ve
PEPTOSTREPTOCOCCS
STAPHYLOCOCCUS
STOMATOCOCCUS
GEMELLA
STREPTOCOCCUS

Overview


Gram positive
cocci
bacilli
Corynebacterium
Clostridium
Listeria
Bacillus
Staphylococcus
catalase +
Streptococcus
catalase −
S. aureus
coagulase +
coagulase −
β-hemolytic
(clear)
γ-hemolytic
α-hemolytic
(green)
S. epidermidis
Novobiocin
sensitive
S. saprophyticus
Novobiocin
resistant
pyogenes
Group A,
bacitracin
sensitive
agalactiae
Group B,
bacitracin
resistant
Enterococcus
E. faecalis,
E. faecium
pneumoniae
optochin
sensitive,
bile soluble,
capsule
(quellung +)
Viridans
mutans, sanguis
optochin
resistant,
not bile soluble,
no capsule

Overview


Rods
Gram (+)
Gram (–)
Sporeformer
Non-sporeformer
Aerobic oxidase (+)
Facultative anaerobic, oxidase (–) (ferment glucose)
Acid-fast
Not acid-fast
Motile
Nonmotile
Regular
Pleomorphic
Pseudomonas
Alcaligenes
Escherichia
Enterobacter
Citrobacter
Proteus
Salmonella
Erwinia
Shigella
Klebsiella
Bacillus
Clostridium
Mycobacterium
Nocardia
Lactobacillus
Listeria
Corynebacterium
Propionibacterium
(b)

NON–SPORE-FORMING gram-positive rods

- **Anaerobic Gram-Positive Rods :** The non–spore-forming gram-positive rods are a diverse collection of facultatively anaerobic or strictly anaerobic bacteria that colonize the skin and mucosal surfaces.

- ***Actinomyces, Mobiluncus, Lactobacillus,* and *Propionibacterium*** are well-recognized opportunistic pathogens, whereas other genera such as *Bifidobacterium* and *Eubacterium* can be isolated in clinical specimens but rarely cause human disease.

Actinomyces

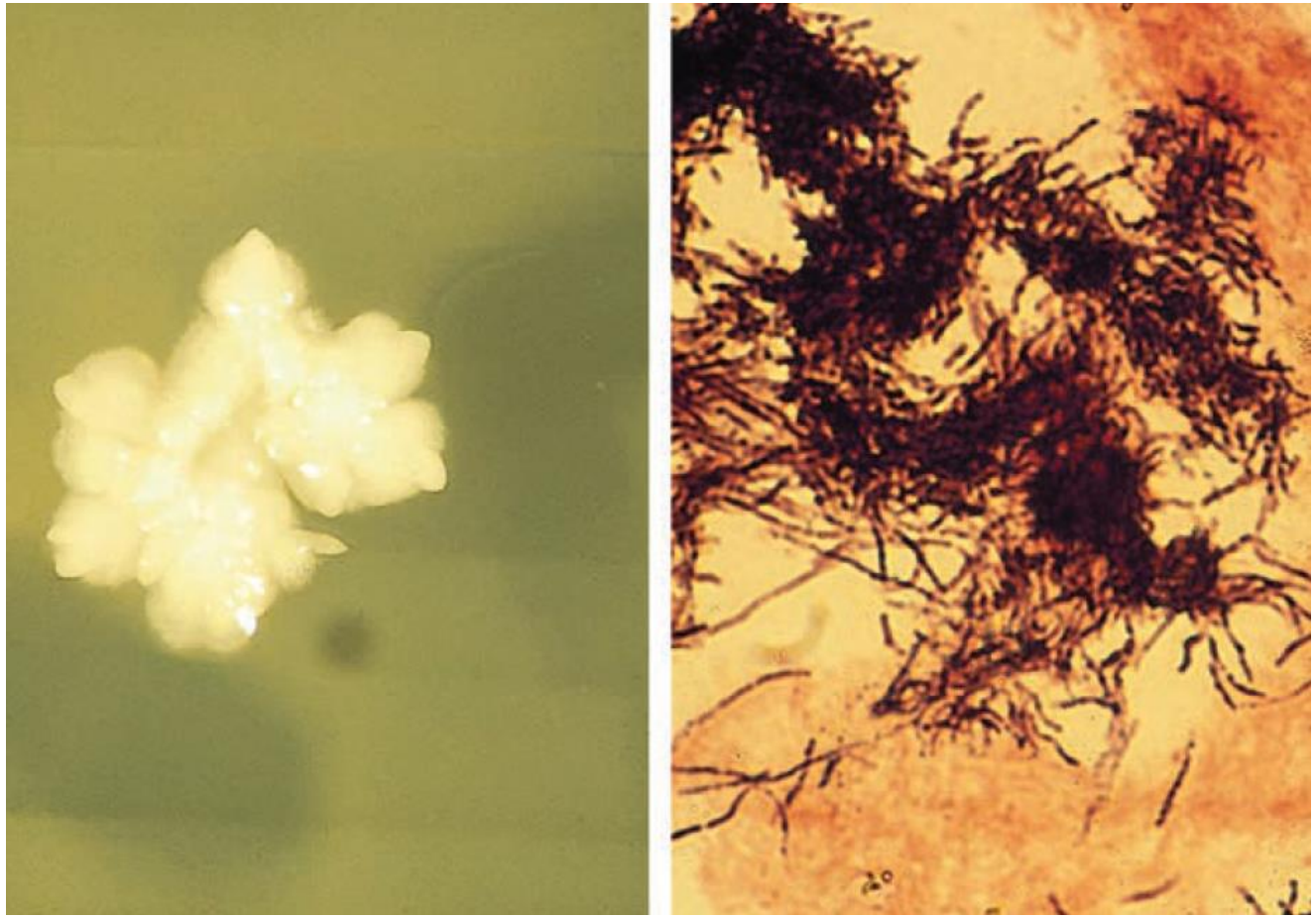
- *Actinomyces* organisms **are facultatively anaerobic or strictly anaerobic gram-positive rods**

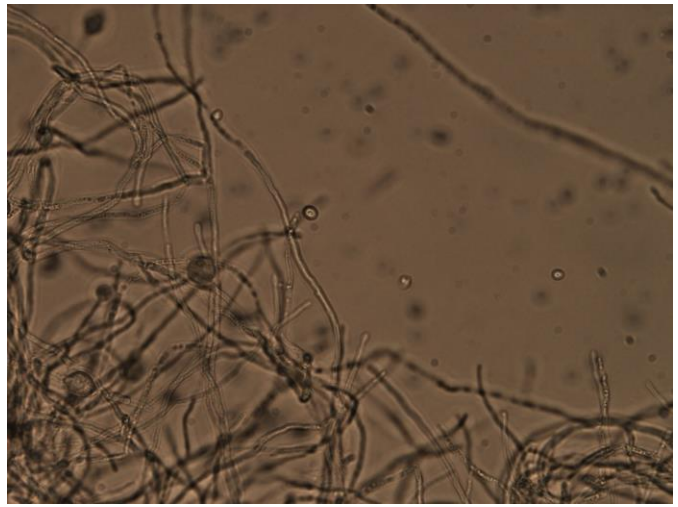
- they grow slowly in culture, and they tend to produce **chronic, slowly developing infections.**

- *Actinomyces* organisms colonize the upper respiratory, GI, and female genital tracts but are **not normally present** on the skin surface.

- Infections caused by actinomycetes are **endogenous,** with no evidence of person-to-person spread or disease originating from an exogenous source. (specimens can be contaminated with *Actinomyces* that are part of the normal bacterial population on mucosal surfaces).

Actinomyces





Fungal colonies and hyphae

They typically develop **delicate filamentous forms or hyphae** (resembling fungi) in clinical specimens or when isolated in culture, *Actinomyces* are **fastidious** and grow slowly under anaerobic conditions; it can take 2 weeks or more for the organisms to be isolated

Actinomyces

- Classic disease caused by *Actinomyces* is termed **actinomycosis. C**haracterized by the development of chronic granulomatous lesions that become suppurative and form abscesses connected by sinus tracts.

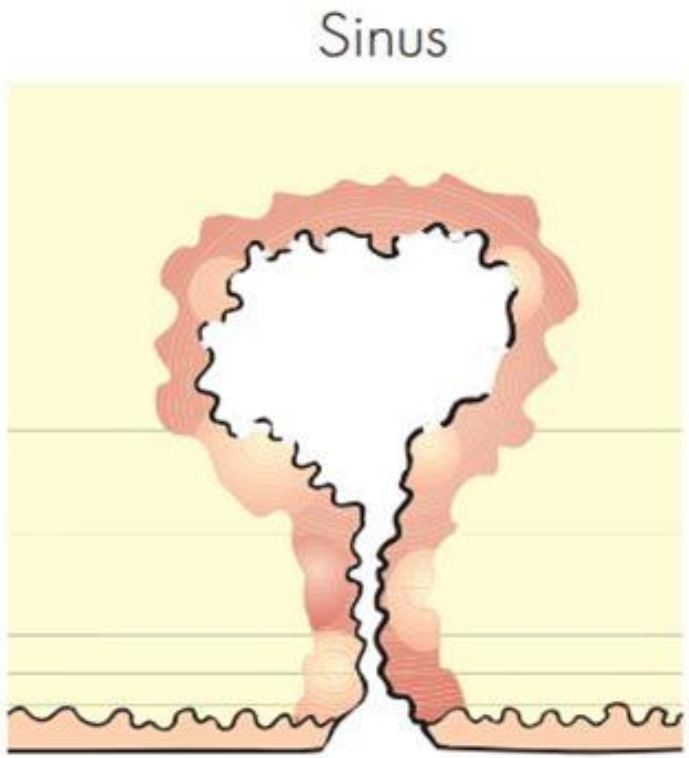
- Most actinomycetes infections are **cervicofacial (**following invasive dental procedure or oral trauma).

- The finding of tissue swelling with fibrosis and scarring, as well as **draining sinus** tracts along the angle of the jaw and neck, should alert the physician to the possibility of actinomycosis

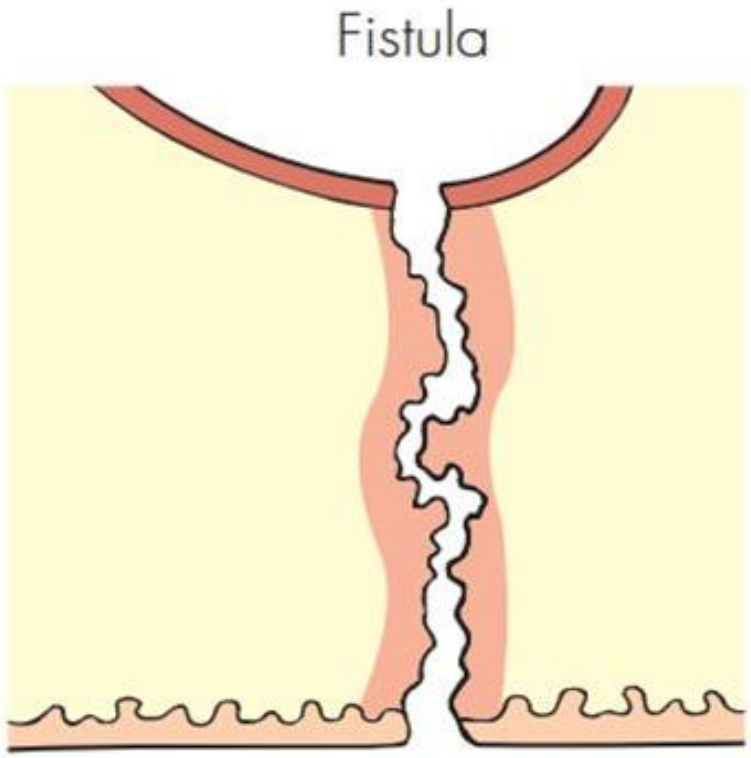
- The major sites of actinomycoses are cervicofacial, abdominopelvic, and thoracic

- Abdominal and pelvic infections are associated with abdominal surgery, tuboovarian abscess, ruptured appendicitis, and **intrauterine contraceptive devices (IUCD)**

- Treatment for actinomycosis involves the combination of drainage of a localized abscess or **surgical debridement** of the involved tissues, and **prolonged** administration of antibiotics.



A sinus is a connection between a cavity lined with granulation tissue and an epithelial surface.



A fistula is a connection between two epithelial-lined surfaces.

A **fistula** is an abnormal pathway between two anatomic spaces **or** a pathway that leads from an internal cavity **or** organ to the surface of the body.

A **sinus** tract is an abnormal channel that originates **or** ends in one opening.

FIGURE 31-4 Patient suffering from cervicofacial actinomycosis. Note the draining sinus tract *(arrow)*.

FIGURE 31-6 Molar tooth appearance of *Actinomyces israelii* after incubation for 1 week. This colonial morphology serves as a reminder that the bacteria are normally found in the mouth.

Nocardia (added here for similarity to actinomyces)

- Nocardiae are **strict aerobic rods** that form branched filaments in tissues and culture.

- *Nocardia* is described as **"weakly acid-fast";** that is, a weak decolorizing solution of hydrochloric acid must be used to demonstrate the acid-fast property of nocardiae. **This distinguish it from the similar Actinomyces.**

- Growth is slow, requiring 3 to 5 days of incubation before colonies may be observed on the culture plates.

- *Nocardia* infections are **exogenous** (i.e., caused by organisms not normally part of the normal human flora). The ubiquitous presence of the organism in soil rich with organic matter and the increasing numbers of immunocompromised individuals living in communities have led to dramatic increases in disease caused by this organism.

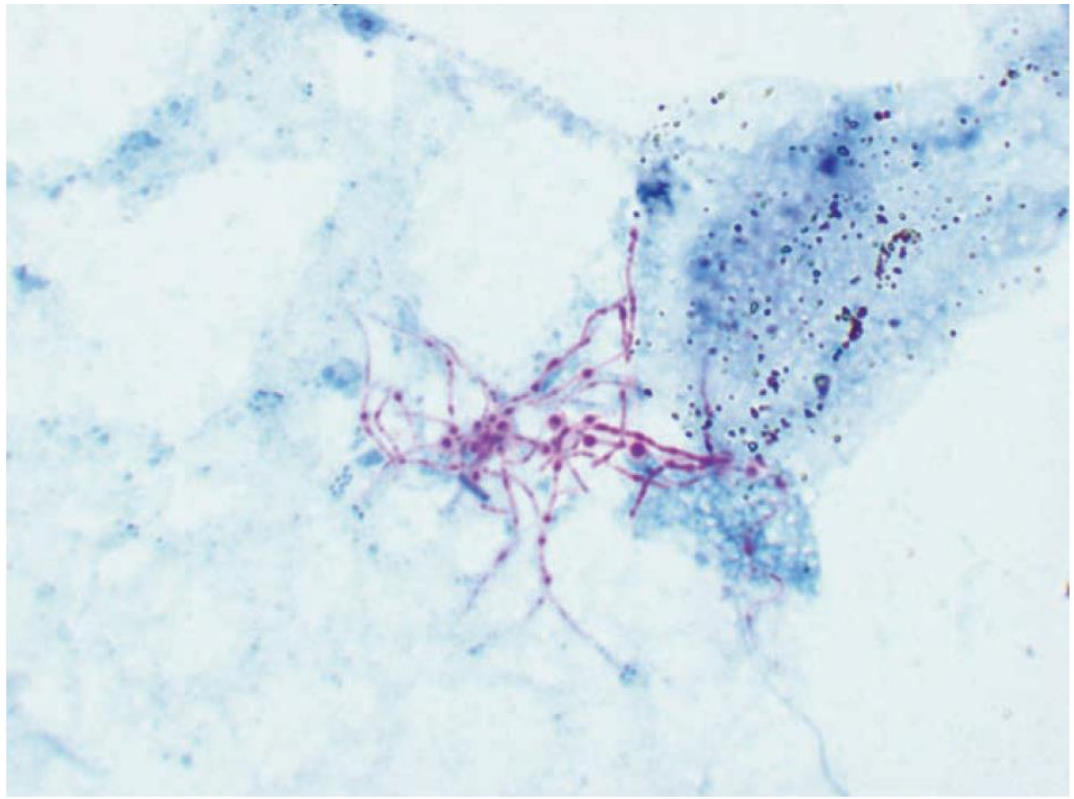


FIGURE 22-10 Acid-fast stain of *Nocardia* species in expectorated sputum. In contrast with the mycobacteria, members of the genus *Nocardia* do not uniformly retain the stain ("partially acid-fast").

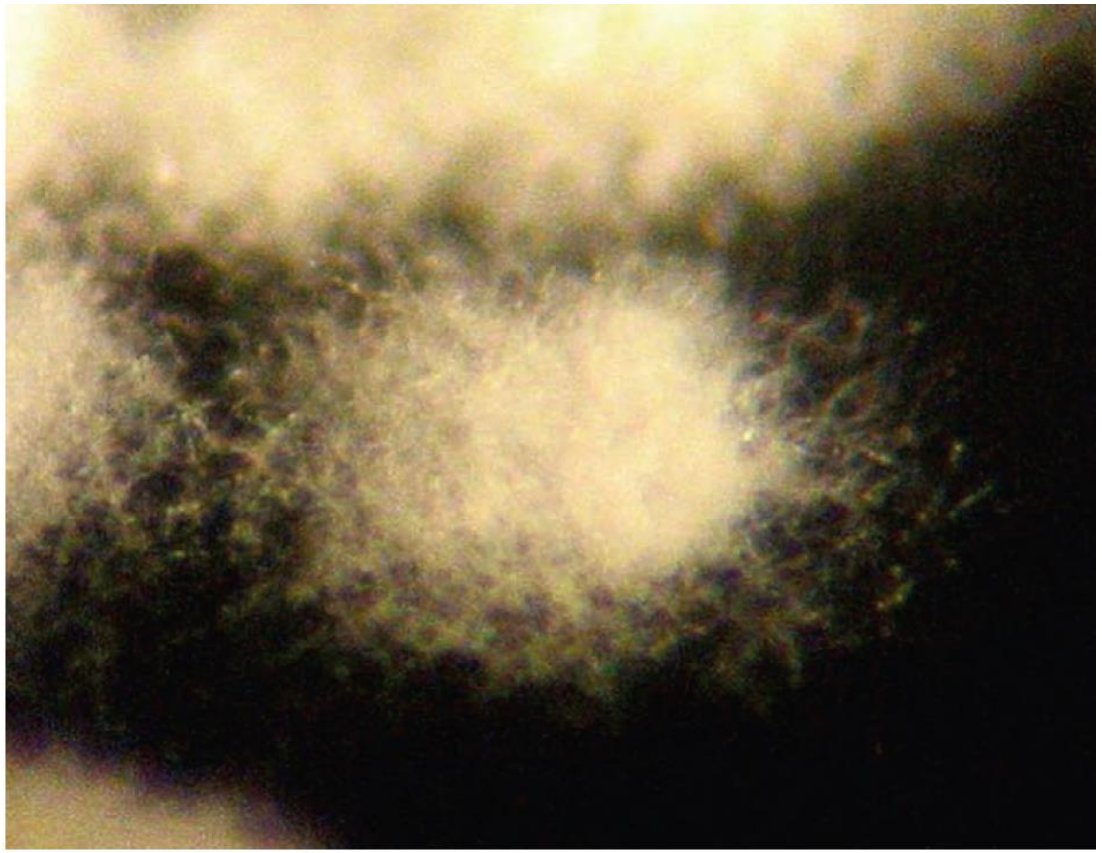


FIGURE 22-12 Aerial hyphae of *Nocardia*.

The combination of both **presence of aerial hyphae and acid-fastness is unique** to the genus *Nocardia* and can be used as a rapid test for identification of the genus

Nocardia

- It would appear that the primary factor associated with virulence is the ability of pathogenic strains to **avoid phagocytic killing.** Through :

Secretion of **catalase** and **superoxide dismutase** that counter **hydrogen peroxide and superoxide released by phagocytic cells,** preventing fusion of the phagosome-lysosome (mediated by **cord factor**) and preventing acidification of the phagosome.

- **Bronchopulmonary disease** develops after the initial colonization of the upper respiratory tract by inhalation and then aspiration of oral secretions into the lower airways, occurs **almost always in immunocompromised patients.**

- **Primary cutaneous nocardiosis** develops after traumatic introduction of organisms into subcutaneous tissues, can present in the form of ***Mycetoma*** is characterized by a triad of painless subcutaneous mass, multiple sinuses and discharge containing grains.

- As many as one third of all patients with *Nocardia* infections have dissemination to the brain, most commonly involving the formation of single or multiple **brain abscesses.**

Nocardia

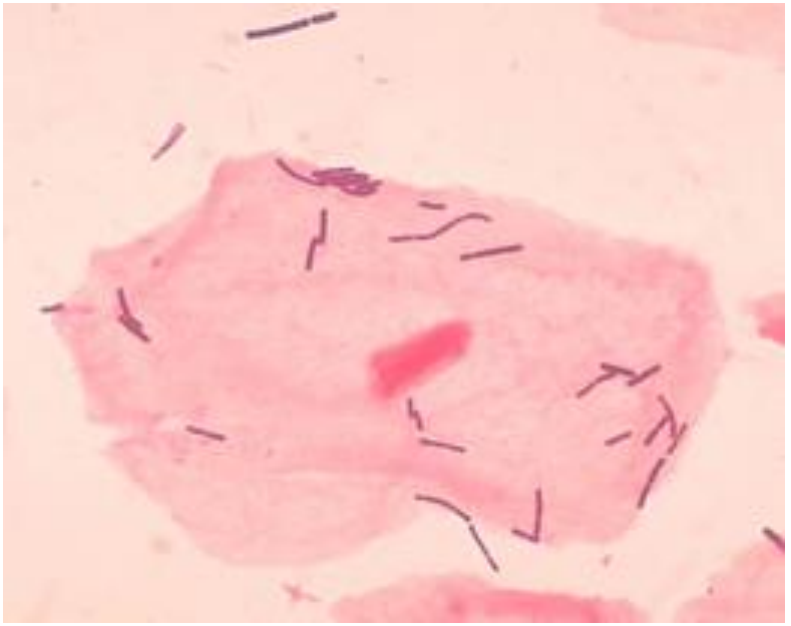
Mycetoma is a chronic suppurative disease of the skin and subcutaneous tissue, characterized by a symptomatic triad: tumor, fistulas and grains. It can be caused by fungi (eumycetoma) and bacteria (actinomycetoma), with similar clinical features.

Given its **slow progression, painless nature**, massive lack of health education and scarcity of medical and health facilities in endemic areas, many patients present late with advanced infection where amputation may be the only available treatment.

Lactobacillus

- *Lactobacillus* species are facultatively anaerobic or strictly anaerobic rods that **ferment to yield lactic acid**.

- They are found as part of the **normal flora** of the mouth, stomach, intestines, and genitourinary tract. In around 70% of women, a *Lactobacillus* species is dominant in the **female genital tract**.



- **Rarely cause infections**.

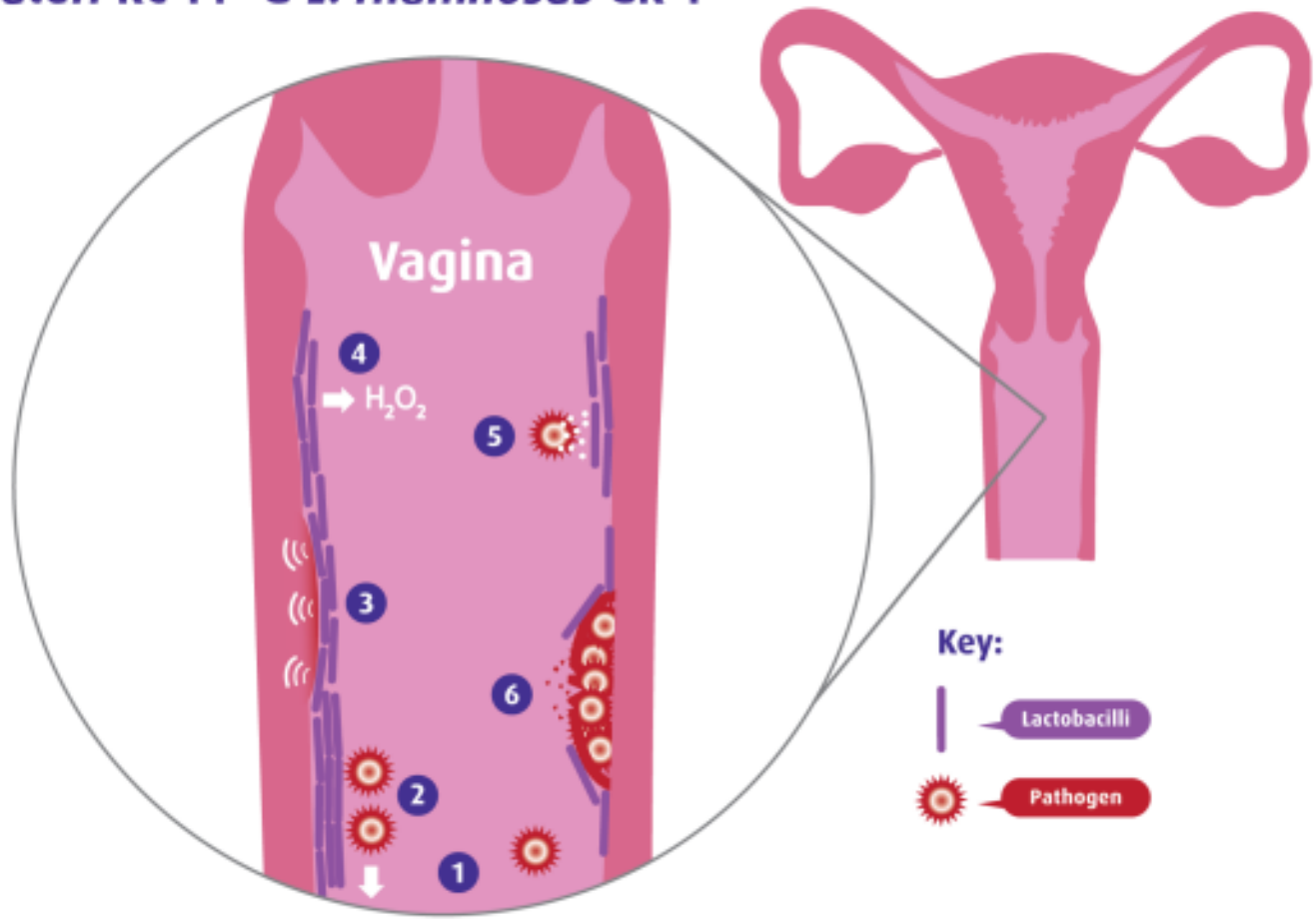
- Commonly found in **probiotics**.

- Some Lactobacillus species are used as starter cultures in **industry for controlled fermentation** in the production of yogurt, cheese, sauerkraut, pickles, beer, cider.

- Invasion into blood occurs in one of the following three settings: (1) **transient bacteremia** from a genitourinary source (e.g., after childbirth or a gynecologic procedure), (2) **endocarditis** and (3) **opportunistic septicemia** in an immunocompromised patient.

Mechanisms of action of *L. reuteri* RC-14® & *L. rhamnosus* GR-1®

1. Restores a healthy pH < 4.5
2. Competitive inhibition
3. Modulates cytokines to decrease inflammation
4. Produces H_2O_2 (kills pathogens and lowers pH)
5. Bacteriocin production (kills pathogens)
6. Produces biosurfactants, which breakdown pathogen biofilms



Taken from a website promoting probiotic therapy, proceed with caution!

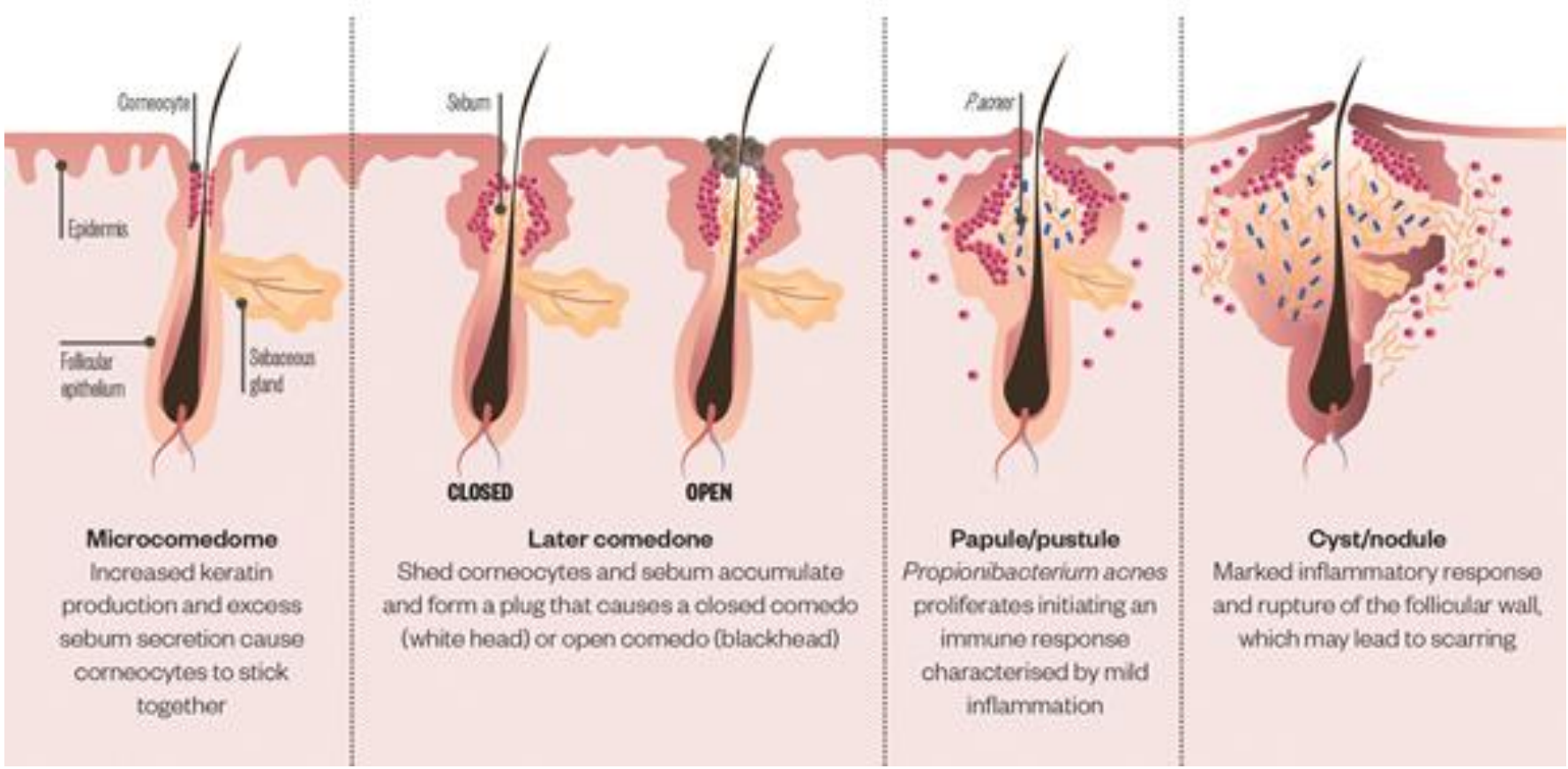
Propionibacterium

- Propionibacteria are small gram-positive rods often arranged in short chains or clumps, commonly **found on the skin** (in contrast with the *Actinomyces*), conjunctiva, and external ear, and in the oropharynx and female genital tract.

- The most commonly isolated species is ***Propionibacterium acnes***. *P. acnes* is responsible for two types of infections: (1) **acne vulgaris** in teenagers and young adults and (2) **opportunistic infections** in patients with prosthetic devices or intravascular lines.

- *P. acnes* apparently only triggers the disease (acne vulgaris) when it meets favorable dermatophysiological terrain; *P. acnes* colonization of the skin is therefore **necessary but not sufficient for the establishment of the pathology**.

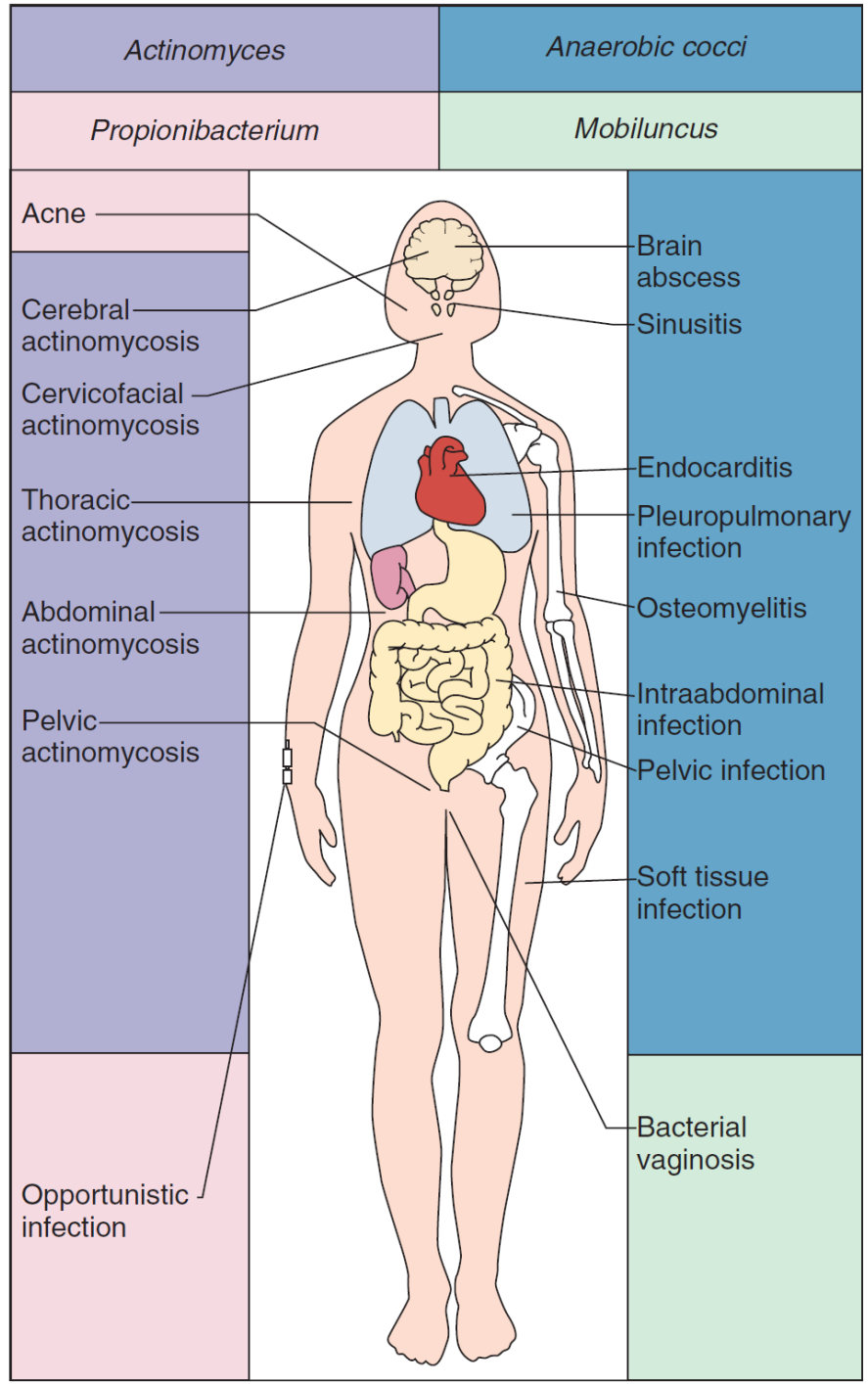
Propionibacterium



Other non–spore-forming anaerobic gram-positive rods

- ***Mobiluncus****:* Members of the genus *Mobiluncus* are obligate anaerobic, gram-variable or gram-negative, curved rods with tapered ends. ***But classified as gram positive****.* because they (1) have a gram-positive cell wall, (2) lack endotoxin, and (3) are susceptible to vancomycin, clindamycin, erythromycin, and ampicillin but resistant to colistin. ***M. curtisii*** is rarely found in the vaginas of healthy women but is abundant in women with **bacterial vaginosis.**

- ***Bifidobacterium*** **and** ***Eubacterium :*** commonly found in the oropharynx, large intestine, and vagina. Usually represent clinically insignificant contaminants


Actinomyces
Anaerobic cocci
Propionibacterium
Mobiluncus
Acne
Cerebral actinomycosis
Cervicofacial actinomycosis
Thoracic actinomycosis
Abdominal actinomycosis
Pelvic actinomycosis
Opportunistic infection
Brain abscess
Sinusitis
Endocarditis
Pleuropulmonary infection
Osteomyelitis
Intraabdominal infection
Pelvic infection
Soft tissue infection
Bacterial vaginosis

Overview

Non-spore forming Aerobic Gram-Positive Rods

- Heterogeneous group of bacteria.
- Some are well-recognized **human pathogens** (e.g., ***Listeria monocytogenes, Corynebacterium diphtheriae***);
- Others are **primarily animal pathogens** that can cause human disease (e.g., ***Erysipelothrix rhusiopathiae***);
- And some are opportunistic pathogens that typically infect hospitalized or immunocompromised patients (e.g., ***Corynebacterium jeikeium****)*

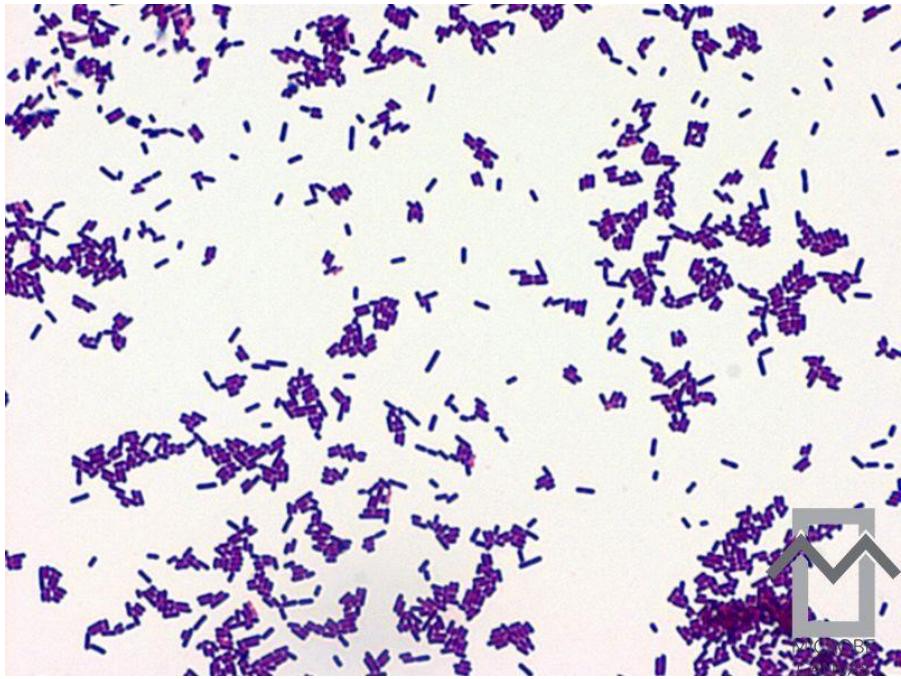
Listeria monocytogenes

- *L. monocytogenes* is a short (0.4 to 0.5 × 0.5 to 2 µm), nonbranching, gram-positive, **facultatively anaerobic rod**. The **short rods** appear singly, in pairs, or in short chains and can be mistaken for *Streptococcus pneumoniae*.

- The organisms are **motile** at room temperature but less so at 37° C, and they exhibit a characteristic end-over-end tumbling motion when a drop of broth is examined microscopically. exhibits **weak β-hemolysis** when grown on sheep blood agar plates.

- These differential characteristics (i.e., **Gram-stain morphology, motility, β-hemolysis**) are useful for the preliminary identification of *Listeria.*

- Although the bacteria are widely distributed in nature, human disease is uncommon and is restricted primarily to several well-defined populations: **neonates, the elderly, pregnant women, and patients with defective cellular immunity**



Listeria monocytogenes

Clinical Case 21-1 *Listeria* Meningitis in Immunocompromised Man

The following patient described by Bowie and associates (*Ann Pharmacother* 38:58–61, 2004) illustrates the clinical presentation of *Listeria* meningitis. A 73-year-old man with refractory rheumatoid arthritis was brought by his family to the local hospital because he had a decreased level of consciousness and a 3-day history of headache, nausea, and vomiting. His current medications were infliximab, methotrexate, and prednisone for his rheumatoid arthritis. On physical examination, the patient had a stiff neck and was febrile, had a pulse of 92 beats/min, and had a blood pressure of 179/72 mm Hg. Because meningitis was suspected, blood and cerebrospinal fluid (CSF) were collected for culture. The Gram stain of the CSF was negative, but *Listeria* grew from both blood and CSF cultures. The patient was treated with vancomycin, the infliximab was discontinued, and he made an uneventful recovery despite using less-than-optimal antimicrobial therapy. Infliximab has been associated with a dose-dependent monocytopenia. Because monocytes are key effectors for clearance of *Listeria,* this immunocompromised patient was specifically at risk for infection with this organism. Failure to detect *Listeria* in CSF by Gram stain is typical of this disease because the bacteria fail to multiply to detectable levels.

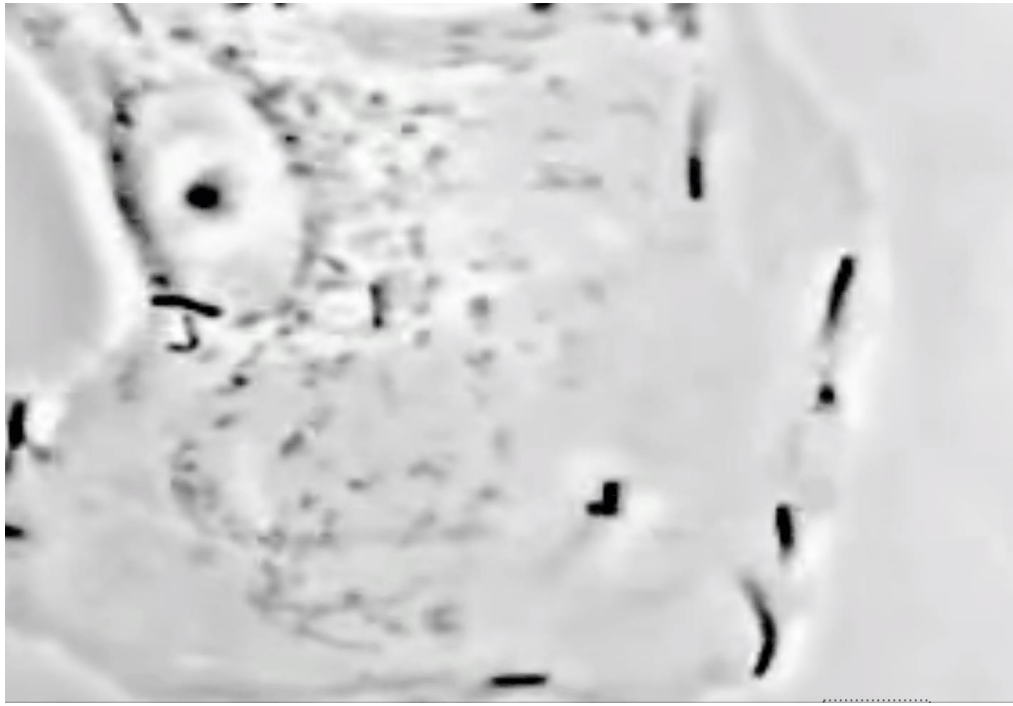
Listeria monocytogenes

- *L. monocytogenes* is a **facultative intracellular pathogen.** Following ingestion of contaminated food, *L. monocytogene* **adhere to host cells** via the interaction of proteins on the surface of the bacteria (**internalin A)** with glycoprotein receptors on the host cell surface (e.g., **epithelial cadherin)**

- After **penetration into the cells**, the acid pH of the phagolysosome that surrounds the bacteria activates a bacterial pore-forming cytolysin **(listeriolysin O)** and two different **phospholipase C** enzymes, leading to **release of the bacteria into the cell cytosol**.

- This movement is mediated by a bacterial protein, **ActA** that coordinates **assembly of actin.**

- These bacteria can replicate in **macrophages** and move within cells, thus avoiding antibody-mediated clearance. Patients with defects in **cellular immunity,** but not in humoral immunity, are particularly susceptible to severe infections



Listeria monocytogenes

- The primary source of infection with this organism **is consumption of contaminated food**; causing **Foodborne Listeriosis.**

- Human-to-human transmission can occur primarily from **mother to child in utero or at birth.**

- **Neonatal Disease** (1) **early-onset disease,** acquired **transplacentally** in utero, and (2) **late-onset disease,** acquired at or soon after birth. Early-onset disease can result in **abortion, stillbirth, or premature birth**. Late-onset disease occurs 2 to 3 weeks after birth in the form **of meningitis or meningoencephalitis** with **septicaemia.**

- Most infections in pregnant women occur during the third trimester when **cellular immunity is most impaired.**

- Disease in **Healthy Adults** is self limited and **asymptomatic** or in the form of a mild influenza-like illness.

Corynebacterium diphtheriae

- *C. diphtheriae* is an irregularly staining, pleomorphic rod (0.3 to 0.8 × 1.0 to 8.0 µm).

- Corynebacteria are **aerobic or facultatively anaerobic**, nonmotile, and catalase positive.

- Corynebacteria are **ubiquitous** in plants and animals, and they **normally colonize** the skin, upper respiratory tract, gastrointestinal tract, and urogenital tract in humans.

- The most famous of these is *C. diphtheriae,* the etiologic agent of **diphtheria**

- **Humans** are the **only known reservoir** for this organism. **Respiratory droplets or skin contact** transmits it from person to person.

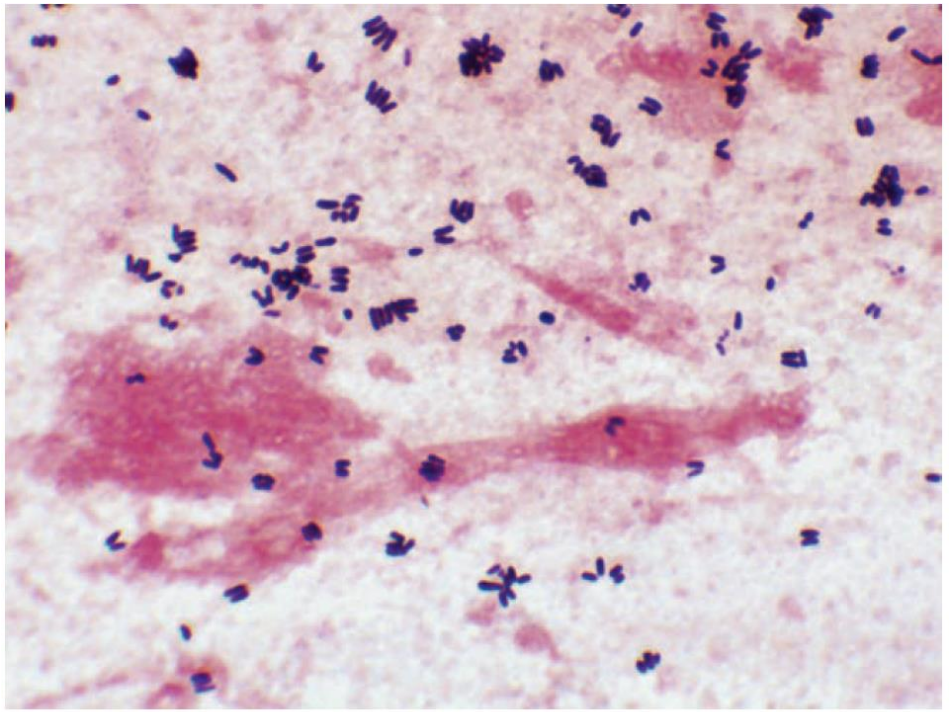


FIGURE 21-4 Gram stain of *Corynebacterium* species in sputum specimen.

Corynebacterium diphtheriae

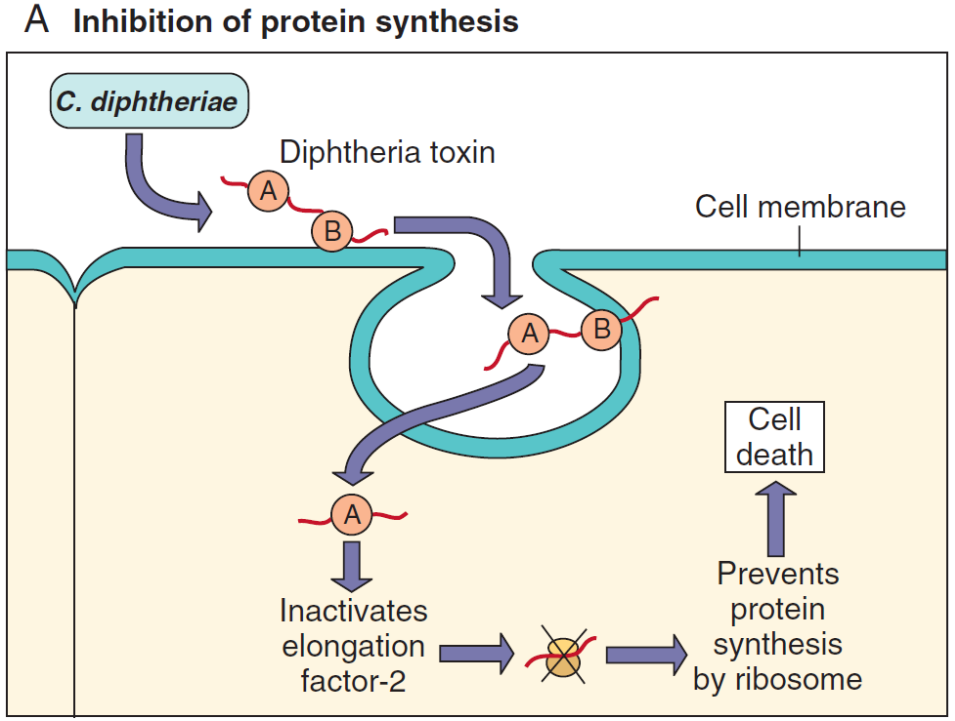
- **Diphtheria toxin** is the major virulence factor of *C. diphtheriae*. An example of the classic **A-B exotoxin.**

- A **catalytic region** on the **A subunit.**

And a **receptor-binding region** and a **translocation region** on the **B subunit.**

- The toxin binds to heparin-binding epidermal growth factor precursor (**HB-EGF**) present on many epithelial membranes. And is endocytosed by the cell. **A subunit** is translocated to the **cytosol**.

- A subunit ADP-ribosylates host eEF-2. **eEF-2** is required for **protein synthesis**; when it is inactivated by the toxin, the host cannot make protein and thus dies



Corynebacterium diphtheriae

Respiratory Diphtheria
The onset is sudden, with malaise, sore throat, **exudative pharyngitis,** and a low-grade fever. The exudate evolves into a thick **pseudomembrane** composed of bacteria, lymphocytes, plasma cells, fibrin, and dead cells that can cover the tonsils, uvula, and palate and can extend up into the nasopharynx or down into the larynx

Diphtheria has become **uncommon** in the United States because of an **active immunization program**, as shown by the fact that more than 200,000 cases were reported in 1921 but **no cases have been reported since 2003.**

FIGURE 21-5 Pharynx of a 39-year-old woman with bacteriologically confirmed diphtheria. The photograph was taken 4 days after the onset of fever, malaise, and sore throat. Hemorrhage caused by removal of the membrane by swabbing appears as a dark area on the left. (From Mandell G, Bennett J, Dolin R: *Principles and practice of infectious diseases,* ed 8, Philadelphia, 2015, Elsevier.)

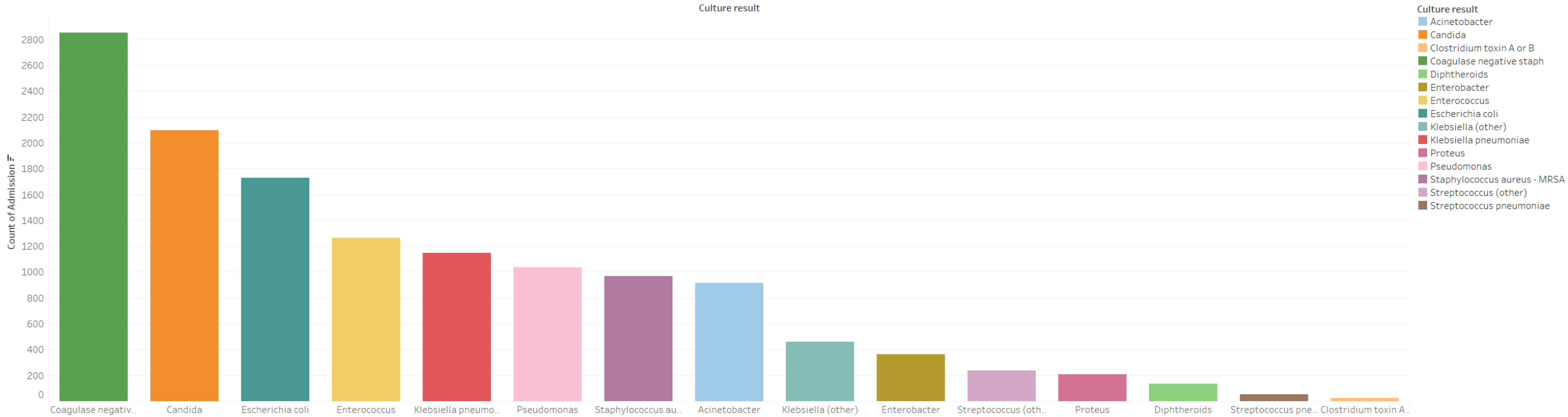
Anaerobic Gram-Positive Cocci

- **Anaerobic Gram-Positive Cocci**: The anaerobic gram-positive cocci normally colonize the oral cavity, gastrointestinal (GI) tract, genitourinary tract, and skin. They produce infections when they spread from these sites to normally sterile sites.

- Although anaerobic cocci can be isolated from infections at all body sites, a predisposition for certain sites has been observed.

- ***Peptostreptococcus*** species have been recovered more often **from subcutaneous and soft tissue abscesses and diabetes-related foot ulcers** than from intra-abdominal infections. *Peptostreptococcus* infections occur more often in **chronic infections**. Many infections caused by *peptostreptococcus* bacteria are **synergistic.**

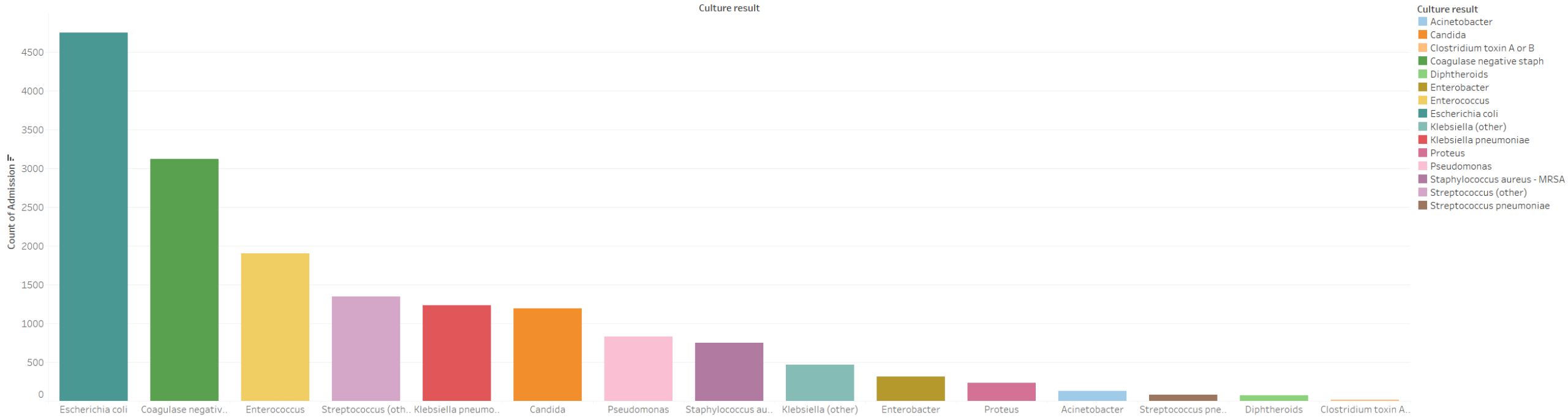
pathogen in vs out



Count of Admission for each Culture result. Colour shows details about Culture result.The data is filtered on Patient Type, which keeps in.The view is filtered on Culture result, which excludes Mixed,No bacterial growth - Normal - NegativeandNo culture result found.

Positive culture results for **inpatients** in the period June 2017 to June 2022

pathogen in vs out



Count of Admission for each Culture result. Colour shows details about Culture result.The data is filtered on Patient Type, which keeps out.The view is filtered on Culture result, which excludes Mixed,No bacterial growth - Normal - NegativeandNo culture result found.

Positive culture results for **outpatients** in the period June 2017 to June 2022

Further reading:

- Murray - Medical Microbiology 8th Edition
  Section 4: Bacteriology
  Chapter 21:
  Chapter 31: