16

# Microbiology

Doctor 2017 | Medicine | JU

◉Sheet ○Slides


**Done By**

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**Contributed in the Scientific Correction**

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**Contributed in the Grammatical Correction**

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**Doctor**

Dr.Anas

Today we will talk about non -spore forming bacteria

The majority of those are part of the microbiota but they can in some cases cause infections (opportunistic)

First a general concept that you need to know about that bacteria, they only cause disease if it enters a sterile tissue (a place where the bacteria is not common to be found in) and they cause disease in immunocompromised people.

The colonizers ability to cause disease depends on: **the host immune system**, **the virulence of the pathogen** and **where the pathogen is going to cause the disease**

## 1- non-spore forming Anaerobic Gram positive rods

it is a non-spore forming opportunistic pathogens

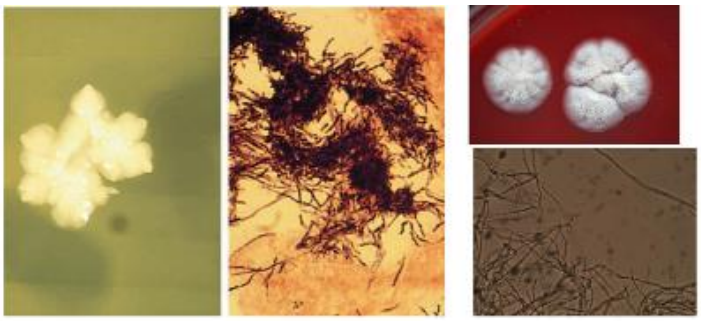
they are a diverse collection **of facultatively anaerobic or strictly anaerobic** bacteria that colonize the **skin** and **mucosal surface**

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

### 1-Actinomyces

Actinomyces organisms are facultatively anaerobic or strictly anaerobic gram-positive rods. A special characteristic of this bacteria that They typically develop delicate **filamentous** forms or **hyphae** (**resembling fungi**) in clinical specimens or when isolated in culture.

Actinomyces organisms colonize the upper respiratory, GI, and female genital tracts without causing any problems but are **not** normally present on the skin surface.



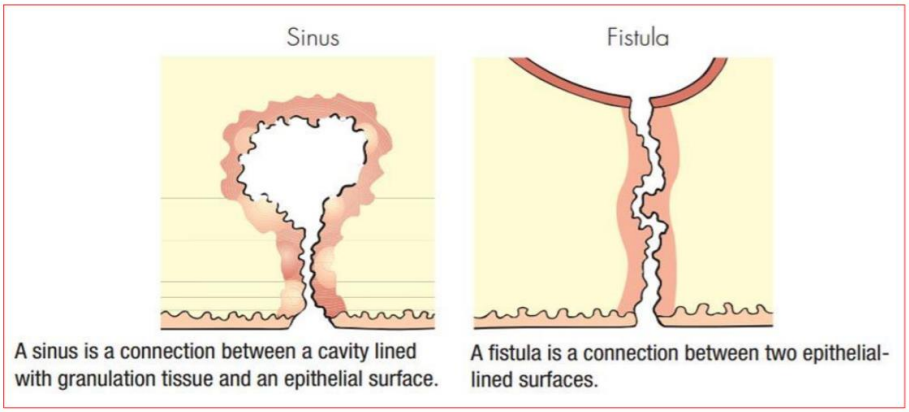
• Infections caused by actinomycetes are endogenous, with no evidence of person-to-person spread or disease originating from an exogenous source. (specimens can be contaminated with Actinomyces that are part of the normal bacterial population on mucosal surfaces).

they grow slowly in culture, and they tend to produce chronic, slowly developing infections.(In the cases where they do cause infection it will be a chronic and slowly developing infection similar to how they grow on agar actually ,they grow very slowly so it will take up to two weeks to see colonies growing on agar and for organism to be isolated and thus, Actinomyces are described as **fastidious (complex nutritional requirement)** this is why they grow slowly)

note: staph aureus is a non-fastidious that can grow on a variety of media and can grow quite fast in comparison to fastidious organisms

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

The Actinomyces are part of the normal flora of the mouth and usually does not cause infections but sometimes for example following an invasive **dental procedure** or oral trauma (tooth extraction or a dental manipulation within the mouth) Actinomyces can cause chronic and slowly developing infections and those infections will probably be in the form of abscess that is connected with sinuses that drain abscess into outside epithelial layer.




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.

**Sinus** connect s a cavity into another outside epithelium. Abscess here grows slowly and start forming the duct and this duct connects to outside epithelium. The whole structure is called a sinus and usually occurs with long standing infections, so when an infection is chronic and takes a long time a duct will start forming. The duct has epithelial layers that should not be there.

**fistula** is very similar but connects two epithelial lined structures.

Most actinomycetes infections are **cervicofacial** but that doesn't mean it is restricted to infection of cervicofacial area but it's the most common site. its major infection sites **cervicofacial**, thorax(**thoracic**), abdomen(**abdominopelvic**) (e.g. of causes in abdomen:

after abdominal surgery (manipulation) tuboovarian abscess, ruptured appendicitis, and intrauterine contraceptive devices (IUCD)

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

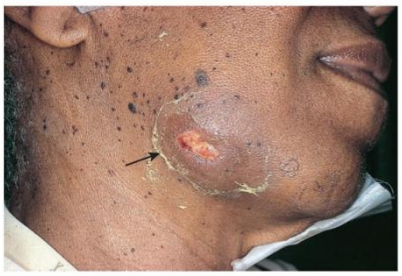


**FIGURE 31-4** Patient suffering from cervicofacial actinomycosis. Note the draining sinus tract *(arrow)*.

so this person probably has an abscess somewhere deeper maybe following a dental extraction or dental manipulation within the mouth and the sinus is draining to the outside

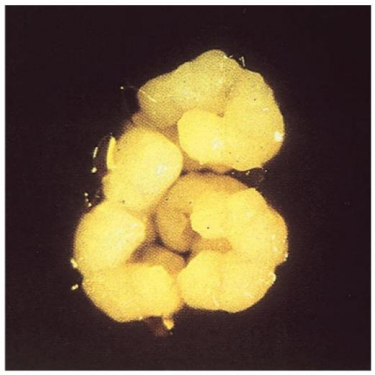


**FIGURE 31-6** Molar tooth appearance of *Actinomyces israelii* after incubation for 1 week. This colonial morphology serves as a reminder that the bacteria are normally found in the mouth.

and here is a colony form of actinomycin israelii which needed 1 week to grow (long time=fastidious) and they describe it as looking similar to a molar tooth ,that might help you remember that actinomycin infection that cause sinuses often happen in the cervicofacial area (within the neck and the face )

**slow abscess formation →sinus drains to the outside**

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

(its kind off repeated but further explanation by the doc):

for treatment of such infection, not only Actinomyces but any infection that causes sinus or fistula or a long standing abscess you need to do something called debridement, we already talked about it before when we talked about necrotizing fasciitis and gas gangrene, when there is necrotic tissue you debride it ( take it out ) and treat with antibiotics

**Nocardia (**added due to similarity to Actinomyces. It is another bacteria that also masquerades (false show) itself as a fungus)

Nocardia are strict **aerobic** (not like Actinomyces) rods that form branched **filaments** in tissues and culture also similar to Actinomyces, nocardia is a slow growing bacteria and can cause infections. Growth is slow, requiring 3 to 5 days of incubation before colonies may be observed on the culture plates.

and for a long time both nocardia and actinomyces where thought to be fungi and proof of that is that the infection caused by actinomyces is called actinomycosis, the suffix mycosis or mico in general refers to fungi but they retained the name actinomycosis due to historical reasons however actinomycosis is a bacterial infection not fungal one

nocardia although similar to actinomyces in shape is not anaerobic gram positive rod**. its actually an acid fast aerobic bacteria**.

acid fast bacteria are bacteria that retain dye even after washing it with **weak** acid. Strong acids cause decolorization.

This acid fast test helps us **differentiate** nocardia from Actinomyces, that is one of the main differential characteristics between actinomyces and nocardia.

unlike actinomyces infection caused by nocardia is **exogenous**. Nocardia is not part of the normal microbiota. It ubiquitous in the environment ,soil, plants

**immunocompetent** individual (healthy individual) does not develop infection by nocardia even if you get it from the environment but immunocompromised individual will develop infection.

**nocardia has three manifestations:**

1-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.

2-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.

so we expect to see 1-sinuses ,2-masses, and 3-discharge with cutaneous manifestation.

cutaneous manifestations are not very common in our societies where most people are immune competent but in places with poor access to health facilities and where there is more HIV patients or immune compromised patients you can commonly encounter such a disease. Lack of education and scarcity of health and medical facilities increase the disease caused by this organism.

3- 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.**

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## Immune evasion mechanisms

1-preventing fusion of phagosome and lysosome (mediated by cord factor) (one of the ways bacteria can evade the immune system after its engulfed in the phagosome it will prevent merger with lysosome and escape enzymes of lysosomes.

2-can secrete enzymes such as **catalase and superoxide dismutase**

how can these help bacteria evade immune system?

immune cells have a mechanism called oxidative burst ,in this mechanism oxygen radicles are formed and they are very harmful to bacteria (like h2o2 and superoxide ion that can be quite harmful to the bacteria )they form those oxygen radicles and try to attack bacteria with them but some bacteria have enzymes that will turn these ROS in to harmless end products (h20 and o2 )

Note to remember: **catalase** (to differentiates between streptococci and staphylococci+ **coagulase** to differentiate between pathogenic and nonpathogenic staphylococci )

3-Prevention of acidification of phagosome. Acidification means lowering the Ph.

Now that we are done with the two bacteria that masquerade as fungi

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## Lactobacilli

Lactobacillus species are facultatively anaerobic or strictly anaerobic rods that ferment to yield lactic acid. Gram positive rods.

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.**

Colonization of lactobasillus in females changes during different times of female's life (puberty, menopause ….) which results from change in microbial environment specially in the genital tract

It Rarely cause infections and if they do its immunocompromised patent (as all these anaerobic gram positive rods are opportunistic)

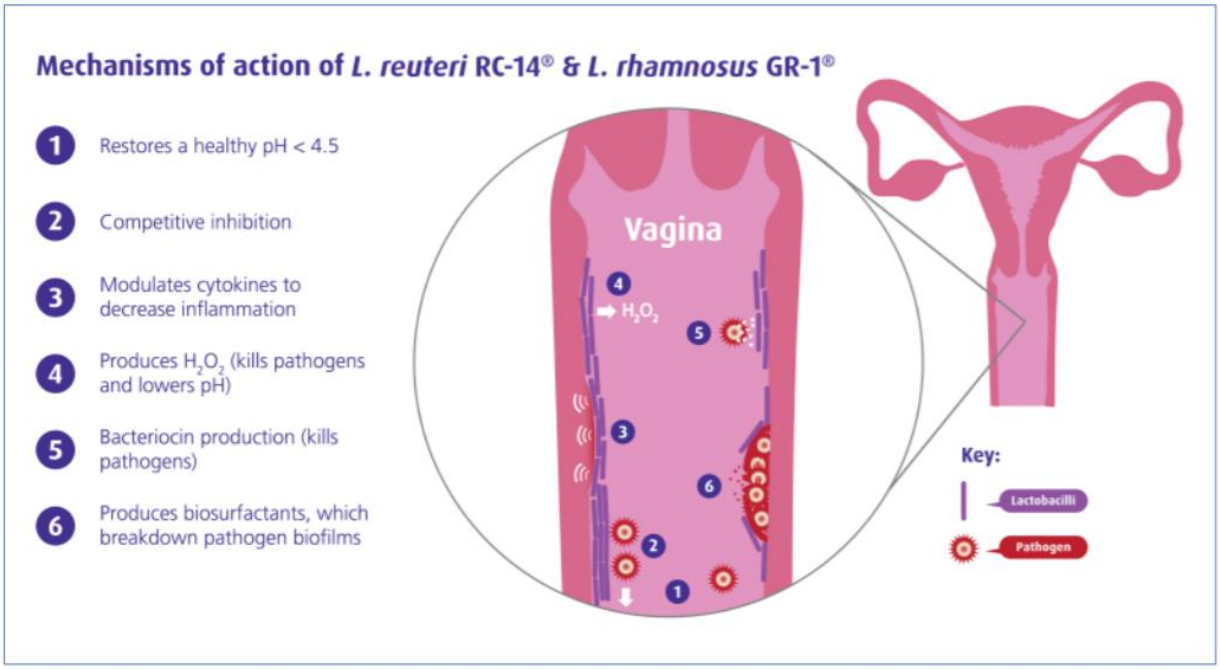
Invasion into blood occurs in one of the following three settings: (1) transient bacteremia from a genitourinary source (e.g., after childbirth or a gynecologic procedure), (2) endocarditis and (3) opportunistic septicemia in an immunocompromised patient

Its rather useful in industry to ferment yogurt and  because it turns carbs into lactic acids thus giving  taste to yogurt and cheese and so on

**Commonly found in probiotics. (giving the bacteria as a drug)**

pills containing millions of lactobacillus to be administered as a way of enhancing microbiota is still under investigation.

Lactobacillus can help in protection against the colonization of pathogenic bacteria in many ways:1- if environment changes occurs in vagina it will restore  acidic PH (healthy ph) ,2-compete over nutrition with pathogenic bacteria thus inhibiting them, 3-secrete molecules that are deadly to other bacteria so preventing colonization of pathogenic bacteria ,4-it can also regulate immune system



## Propionibacterium

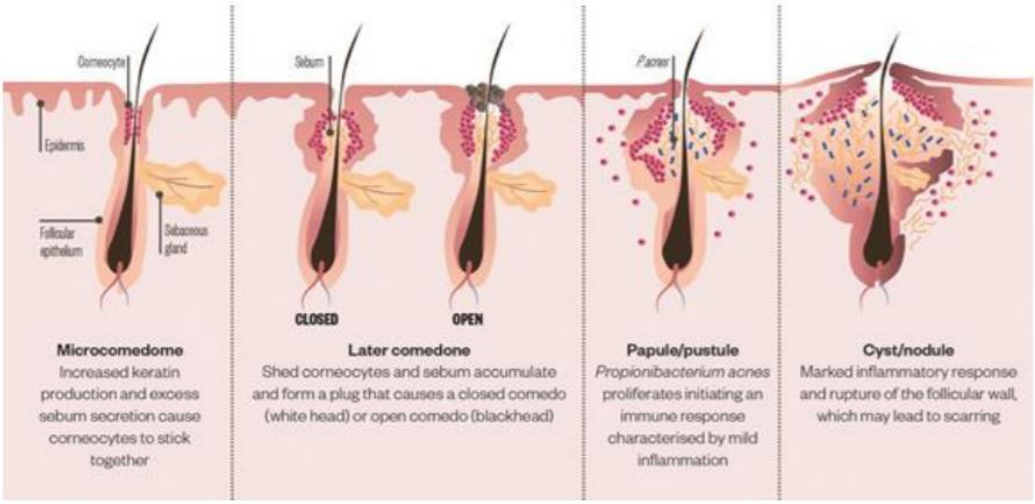
Propionibacteria are small gram-positive rods often arranged in short chains or clumps, **commonly found on the skin** (in contrast with the Actinomyces), conjunctiva, and external ear, and in the oropharynx and female genital tract.

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.

That means that you can have Propionibacterium acnes but have no problems with acne vulgaris ,But if you do have acne vulgaris then its most probably from Propionibacterium acne.

In the diagram there is a Hair follicle associated with sebaceous gland (secretions coming out )




Sometimes during puberty or due to other factors, these pores will be clogged by dead keratinocytes and thus decrease sebum secretions, the clogged pore causes a change in the environment the bacteria was living in ,this new environment (anaerobic) will be suitable for Propionibacterium acne to overpopulate the microbiome at that specific site and induce an inflammatory response ,manifesting as the pus found in the acne in the face .

## Mobillincus

Mobiluncus are obligate anaerobic, **gram-variable** or gram-negative, curved rods with tapered ends, M. curtisii is rarely found in the vaginas of healthy women but is abundant in women with **bacterial vaginosis**.

Gram variable: applying a gram stain test to some bacteria do not show exactly what the bacteria is but these bacteria however were classified as gram positive as **the cell wall is kind of similar to gram positive** (peptidoglycan is thick ,**lacks both endotoxin** and **LPS** and is also **susceptible to antibiotics that gram positives are usually sensitive to**: eg vancomycin, clindamycin, erythromycin, and ampicillin but resistant to colistin)

### Bifidobacterium and Eubacterium

Found within microbiota (commonly found in the oropharynx, large intestine, and vagina) and **rarely** cause disease and if you find them within a culture they are probably just a clinically insignificant contaminant

So if seen in a grown specimen it is probably due to contamination during specimen handling (collection or transportation)

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## 2-Non-spore forming Aerobic Gram-Positive Rod

Heterogeneous group of bacteria. There are 3 types : Human pathogen, animal pathogen and opportunistic pathogen.

**Human pathogens** (e.g., **Listeria monocytogenes** causing listeria infection, **Corynebacterium diphtheriae**, causing diphtheria)

**Animal pathogens** that can cause human disease (e.g., Erysipelothrix rhusiopathiae);

**opportunistic pathogens** that typically infect hospitalized or immunocompromised patients (e.g., Corynebacterium jeikeium)

### 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 Streptococci or staphylococci (as they are in the similar size range, around 1 micrometer)( confused with streptococci pneumonia because they are diplococci and listeria can also appear in pairs )

You can tell its listeria by its **motility** that can be viewed directly under the microscope, on slide with no fixing (you need bacteria alive and moving )and with no gram stain and you will see them moving in a tumbling motion called :end-over-end tumbling motion

It's quite motile, so if you see motility ,gram stain (+)and beta hemolysis you can preliminary tell that this is listeria

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

(the relation between pregnant women and neonates is present because if a pregnant women is infected it can cross placenta and go to the baby, with listeria in **the early onset** disease may lead to **abortion** ,or **stillbirth** ,or **premature birth**. Human-to-human transmission can occur primarily from mother to child in utero or at birth. Sometimes the listeria infection can happen **later on** with the baby two weeks after its born in the form of **meningitis or septicemia**

Reminder: Other bacteria that can cause meningitis and septicemia: group b streptococci (agalactia) and E.coli(of the extraintestinal manifestation we have UTI in females and vaginal tract E.coli colonization can be transferred to baby)

As a healthy adult (immunocompetent) ingestion of listeria is asymptomatic or sometimes go to mild forms of influenzas that will go away in few days

• Meningitis and bacteraemia usually happen in immunocompromised patients.

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

usually the part of immunity that is defective and allows infection to occur is the cellular immunity**. immunity in general is divided into**

1- humoral immunity found in tissues (tissue **fluid**) and blood (humor in Greek means water of fluid). Mainly composed of **opsonins** like **antibodies**, **complement system** and **antimicrobial peptides**

2- cellular immunity the immune response accounted by immune cells (neutrophils and lymphocytes and other WBC)

**Question**: Why a defect in cellular immunity and not in the humeral immunity causes an individual to be more susceptible to get infected with Listeria?

**Answer**: since they are quite mobile these bacteria can escape humoral immunity like antibodies and complement found in the fluid by going inside cells (they are thus called a facilitative intracellular pathogen which means they can survive both inside and outside the cell)

How does this process happen?

1- 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)

2- 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

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

4 - These bacteria can replicate in macrophages and move within cells, thus avoiding antibody mediated clearance.

## Corynebacterium diphtheriae

Gram stains of these bacteria reveal clumps and short chains of irregularly shaped **(club-shaped**) rods

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

**Corynebacterium diphtheria has only humans as a host**

Respiratory droplets or skin contact transmits it from person to person.

Diphtheria toxin is a classic **a-b exotoxin** made of two subunits (a +b) (B help in the **attachment** into epithelial surface(binding to surface protein :**heparin binding**

**epidermal growth factor precursor (HB-EGF)** and **endocytosis** of toxin into cell and within the endocytosed vesicle a **change in the ph** will release the A subunit and A subunit will then disturb protein synthesis by inactivating the elongation factor which is important in protein synthesis in the ribosome)

By inactivating this factor there is no protein synthesis and there is **cell death**

Diphtheria toxin is produced at the site of the infection and then **disseminates** through the **blood** to produce the **systemic** signs of diphtheria.

Respiratory Diphtheria, The symptoms of diphtheria involving the respiratory tract develop after a 2- to 4-day incubation period. Evidence of myocarditis can be detected in the majority of patients

In the case of respiratory diphtheria which is one of the most common forms The onset is sudden, with malaise, sore throat, **we will have exudative pharyngitis** (inflammation within pharynx) and pseudomembrane will form which is made of the exudate ,exudate contains bacteria,immune cells,fibrins(also called pus),if the exudate is very thick it can disturb breathing. Nowadays 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.due to immunization and vaccine.

Other manifestations include cutaneous diphtheria: A papule develops first and then evolves into a **chronic**, **nonhealing ulcer** and sometimes it can disseminate in the blood

Reminder: clinical manifestation of disease will always depend on

1-site of infection

2-immune status of patient

3-virulence of the organism

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## 3-Gram negative anaerobic rods:

Bacteroides:

part of normal microbiota

**Dominant bacteria in GI tract** (**overpopulates aerobic bacteria by 10 to a 1000 folds**)

Bacteroides fragilis is the one that most commonly causes disease

Characteristically, Bacteroides growth is **stimulated by bile.** Other anaerobic gram-negative rods are fastidious (need special growth requirements), also they are described as **pleomorphic** (come in different morphologies)

Most Bacteroides from colon and intestine will not cause disease unless they are introduced to other tissue, **how**?

**They spread by trauma or disease from the normally colonized mucosal surfaces to sterile tissues or fluids**

infections caused by Bacteroides are usually **polymicrobial** so as we said following surgery or trauma there is spill of bacteria in the sterile tissue (usually spread as a **group**)

LPS of Bacteroides is less virulent compared to other pathogenic gram negatives maybe that's why the immune system is tolerating them.

**Intraabdominal Infections,** Anaerobes are recovered in **virtually all** of these infections, with ***B. fragilis*** **the most common organism.**

Also similar to other anaerobic bacteria can cause cutaneous or subcutaneous infection if there is immune optimization eg .catheter insertion .

**For gram negative anaerobic rods refer to the slide if you want but the doctor didn't explain much about them that's why didn't add all the info about it**

**I'm sorry if the sheet isn't written as well as it should be**.