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Microbiology

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Sheet Slides

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This sheet discusses mainly Bacteria that is related to sexual transmitted disease (STD)

TREPONEMA

It is a SPIROCHETES (**thin and helica**l). It can't be stained with gram stain and can't be seen under the light microscope because it is too thin. However, it is classified as **gram negative** because the structural similarity of its wall with other **gram negative** bacteria.

Darkfield microscopy or (**immuno-fluorescent stains** which work by tagging the bacteria with antibodies(conjugated with flurochromes) that exhibit fluorescence under certain light) must be used for visualization and diagnosis.
The most important treponemal species that **causes human disease** is Treponema pallidum, the causative agent for **Syphilis** (the 3rd most common sexual transmitted disease after Chlamydia and Gonorrhea).

T. pallidum **has not been cultured** continuously or regularly in virto (outside the body)- they are quiet fastidious- for 2 main reasons:

1 - They are **dependent on host** cells for many metabolites (e.g. purines, pyrimidines, amino acids)

2 – They are extremely **sensitive to oxygen**, they are **anaerobic.**

Note: Information known about the bacteria have been obtained by isolating the pathogen from infectious lesions (take a swap from the discharge)**.**

SYPHILIS

Even with proper sexual education the incidence of newly acquired disease has been on the rise for the last 10 years and people have been more relaxed about the disease because of the presence of antibiotic.

It can be controlled only through the practice of **safe-sex** techniques and adequate treatment with **antibiotics**. The incidence is increasing because the symptoms may **subside** between different stages of the disease (discussed later) (practice of **non-safe-sex**.

Patients infected with syphilis are at **increased risk for transmitting and acquiring HIV** when genital lesions are present.

Route of spread : 1- Direct sexual contact (**the most common**).

2- congenital-vertical transmission-(from infected mother to her fetus)

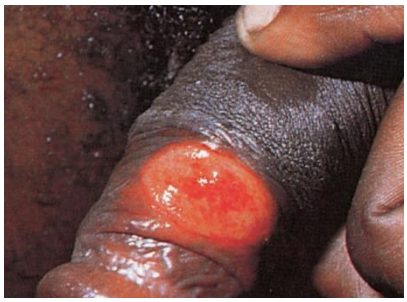
3- Transfusion with contaminated blood.

Note: Syphilis **cannot be spread through contact with inanimate objects** such as toilet seats (since the bacteria is very labile to drying and disinfectants).-In contrast to Gonorrhea that have a risk of being transmitted by using items of a gonorrhea patient-.
*Other resources were contradictory about gonorrhea transmission.

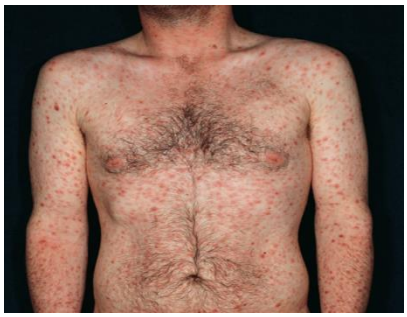
Diagnosis: since the bacteria cannot be seen under the microscope because it is too thin and it can't be cultured serology is the most important tool, a special test is used. ***Treponema pallidum* particle agglutination (TP-PA) test.**

This test depends on antigen-antibody reaction. If a person is infected with T.pallidum the body will synthesis antibody against the antigen found on the bacteria. Gelatin particles sensitized with T. pallidum **antigens** (not the bacteria since it is hard to culture it) are mixed with dilutions of the patient's **serum** (if the patient is infected, antibody will be found in the serum). If antibodies -against T. pallidum- are present, the particles agglutinate, indicating the patient has been infected.

THREE PHASES OF THE DISEAS:



Primary phase is characterized by skin lesions (**chancres**) at the site where the spirochete penetrated. It appears on penis and female genital tract (we can take a swap from these lesions).the lesion will subside after a while and maybe leave an ulcer behind. If the patient is not treated, he/she will develop a secondary phase.



In the **secondary phase**, the disease spread (disseminate) and more clinical systemic signs appear (e.g. **skin lesions over the entire body** as a rash, fever, headache, maybe a sore throat ((similar to flu)). Symptoms resolve (subside) within weeks.

If the patient is not treated, syphilis causes systemic devastating damage, leading to the tertiary phase (late syphilis). It may take years to reach that phase with no

symptoms (sort of). Many organs are severely damaged (e.g, **neurosyphilis**(brain is damaged), leading to various symptoms (e.g. **dementia** or **blindness**) cardiovascular syphilis(heart muscle is damaged).

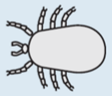
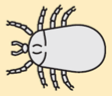
*nowadays with antibiotics it wouldn't commonly progress to the later stages the patient would present with the symptoms because mostly it is a symptomatic disease and can be treated with antibiotics.

BORRELIA

Spirochetes (it is not associated with STD but discussed here because it is a spirochetes) stain well with dyes such as Giemsa and stain poorly with gram stain, but have an outer membrane similar to **gram-negative bacteria.**

Members of the genus Borrelia cause two important human diseases: **Lyme disease** and **relapsing fever (both are ticks related disease, ticks are the vector of borrelia which is present in its saliva or feces).**

Diagnosis of diseases is done by serology for Lyme or microscopy for relapsing fever.

Infection	Reservoir	Vector
Relapsing fever epidemic (louse-borne)	Humans	Body louse 
Relapsing fever endemic (tick-borne)	Rodents, soft ticks	Soft tick 
Lyme disease	Rodents, deer, domestic pets, hard ticks	Hard tick 

Symptoms:

Many tick-borne diseases can have similar signs and symptoms such as, **sudden onset of fever/chills at varying degrees**, **Aches and pains** (headache, fatigue and muscle aches) and **Rash**.

These ticks are common in forests of north and South Africa, America and in Europe. We don't have that many ticks in this region.

Because of that similarity and culture might take a long time or might be unsuccessful identification might be problematic so the doctor should evaluate the following before choosing the appropriate treatment: **symptoms**, **geographic region**, **diagnostic tests**.

*sometimes the tick would still be present on the body.

N**ote**: <u>to start a treatment for Lyme disease, the following should be observed:</u>

Erythema Migrans(looks like a target sign) with a diameter more than 5 cm or at **least one of the late manifestations** (musculoskeletal, nervous system or cardiovascular

involvement.)in addition to laboratory confirmation of infection(serologic test where we use antibodies to detect the presence of bacteria).

*Approximately 60% of patients with untreated Lyme disease will develop **arthritis.**

CHLAMYDIA

This bacteria has characteristics that are **similar to viruses**, it is **very small** (0.3 micro in diameter**), obligate intracellular parasite** (they use host cell ATP for their energy requirement and metabolites (amino acid, pyrimidines and purines to build DNA ..)), and have a **unique life cycle**.

However, they are bacteria because they have the following characteristics:

1 - Possess inner and outer membranes similar to those of gram-negative bacteria.

2 - Contain both deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

3 - Possess prokaryotic ribosomes.

4 - Synthesize their own proteins, nucleic acids, and lipids.

5 – They are susceptible to numerous antibacterial antibiotics.

LIFE CYCLE

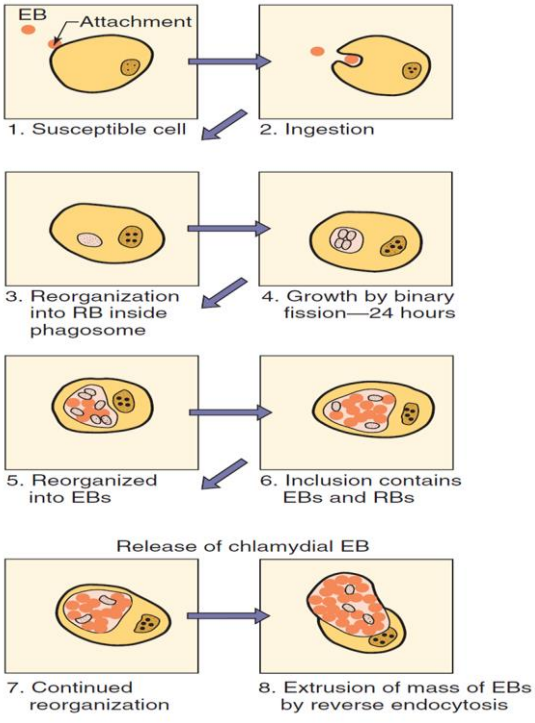
To understand the life cycle, you need to know that there are to forms of the bacteria.

1 – The **infectious** form: metabolically inactive (**cannot replicate**) = Elementary bodies

2 – The **noninfectious** form: metabolically active **(can replicate**) = Reticulate bodies

Stages of life cycle:

EB attach to surface of the cell (usually epithelial) →EB is ingested inside the cell be endocytosis →in order to replicate the EB must reorganize itself into RB inside the phagosome → replication occurs by binary fission (depending on the host energy and metabolite) → to be infectious, RBs must reorganize themselves into EBs again → the inclusion now contains both EBs and RBs → the mass of EBs get out of the cell by reverse endocytosis most probably



killing the cell in the process→ EBs go and infect other cells. THE SAME AS VIRUSES

From the life cycle, we can know that damage to the cell is caused by intracellular replication and destruction of infected cells upon release.

*most but not all diseases caused by chlamydia are sexually transmitted disease.

Tissues to be infected: Infects epithelial cells, which are found on the mucous membranes of the (urethra + endocervix + endometrium + fallopian tubes + anorectum = leading to **Urogenital infection),** respiratory tract leading to infant **pneumonia,** and conjunctivae (in the eye) leading to (**Trachoma, adult and neonatal conjunctivitis**)

Note: Chlamydia infections are the **most common bacterial sexually transmitted disease**s in humans and are **the leading cause of infectious blindness** worldwide.

The exact pathogen we are talking about is called C. trachomatis,it is very fastidious and hard to culture.

Diseases:

1– STD (chlamydia) and urogenital infections:

In women → asymptomatic (about 80%).

In men → symptomatic, only about 25% are asymptomatic.
* Asymptomatic person is considered the reservoir for the pathogen because they will not seek treatment.

*the infection will appear in the form of inflammation in the part that is affected (**urethritis** in men and women, and **cervicitis** in woman) accompanied by pain and discharge if it was symptomatic.

2 – **Trachoma**: is chronic and it is the leading **cause of preventable blindness** (if the person took antibiotics he/she will not become blind) in poor countries. Infections occur predominantly in **children**, who are the chief reservoir of C. trachomatis in endemic areas.

Eye-to-eye transmission of trachoma is by **droplet, hands, clothing contaminated with discharge**, and flies that transmit ocular discharges from the eyes of infected children to the eyes of uninfected children.

-it has a predisposition to respiratory epithelium where it can cause pneumonia.

Diagnosis: C. trachomatis infection can be diagnosed

(1) on the basis of cytologic, serologic, or **culture** findings.

(2) Through the direct **detection of antigen** in clinical specimens.

(3) Through the use of nucleic **acid–based tests** (we look for chlamydia DNA in lesion).

Neisseria

Neisseria species are aerobic **gram-negative bacteria**, arranged in pairs (**diplococci**), all species are **oxidase** positive and most produce **catalase.** These properties allow a rapid, presumptive **identification** of a clinical isolate.

Two species:

*strictly human pathogens.

1 - **Neisseria gonorrhoeae: its presence on clinical specimen is always considered significant** and indicates infection and disease. It is fastidious and only grows on enriched **chocolate agar** and other supplemented media (It can be hard to culture).

Gonorrhea:

Gonorrhea is **second** only to chlamydia as the most commonly reported sexually transmitted disease in the United States

Genital infection in men is primarily restricted to the **urethra and it's almost always symptomatic**. A purulent urethral discharge and dysuria develop after a 2- to 5-day incubation period. **Virtually all infected men have acute symptoms.**

As many as half of all infected women have mild or **asymptomatic infections.**

Gonococcemia : Disseminated infections with **septicemia** and **infection of skin and joints** occur in 1% to 3% of infected women and in a much lower percentage of infected men.

2 - **Neisseria meningitidis:** can colonize the nasopharynx of healthy people without producing disease. Antigenic differences in the **polysaccharide capsule** determine if an individual strain will cause disease or not.

When the disease occurs in the case of N.Meningitidis ?

In patients who **lack specific antibodies** directed against the polysaccharide capsule and other expressed bacterial antigens. Simply in patients whom immune system is weakened against that bacteria. This can occur in the following cases:

A - **Children younger than 2 years** who are not able to synthesis their own antibodies yet (antibodies transplacentally transferred from the mother are disappearing-during this period the child is at higher risk of many organisms).

B - **Patients with deficiencies in C5, C6, C7, or C8** of the complement system are estimated to be at a 6000-fold greater risk for meningococcal disease.

C - **Post-splenectomy patients.**

* in all cases above the individual will have an increased predisposition to acquiring infections caused by Neisseria meningitides, streptococcus pneumonia, haemophilus influenza because all 3 have a **capsule** as a major virulence factor.

How N.Meningitidis establish an infection?

In the cases above, the bacteria will penetrate the cells and multiply, and then pass through the cells into the sub epithelial space where infection is established. The bacteria can move from the nasopharynix into the blood (especially if it has a capsule and certain virulence factors or the individual is immunocompromised like mentioned before) causing **Meningococcemia** (bacteraemia with meningi cocci in the blood) it can disseminate around the body and cause skin lesions. with or without meningitis is a life-threatening disease.

N.Meningitidis can also reach the brain and cross the blood brain barrier (very strict barrier usually bacteria or other molecules cannot pass) with the help of its capsule and other pathogenic factors and cause **Meningitis (or inflammation in the brain).**

Symptoms of **Meningitis:**

The disease begins with headache, meningeal signs (photophobia -extreme sensitivity to light the patient is extremely uncomfortable looking into the light-and rigidity in the neck and fever.

If you see these symptoms in a less than 2 years of age child you should suspect

N.Meningitidis and if the sample shows gram-negative diplococci than it is for sure

N.Meningitidis.

However, very young children may have only nonspecific signs such as fever and vomiting.

Mortality approaches 100% in untreated patients.

Table 23-2 Virulence Factors in *Neisseria gonorrhoeae*

Virulence Factor	Biological Effect
Pilin	Protein that mediates initial attachment to nonciliated human cells (e.g., epithelium of vagina, fallopian tube, and buccal cavity); interferes with neutrophil killing
Por protein	Porin protein: promotes intracellular survival by preventing phagolysosome fusion in neutrophils
Opa protein	Opacity protein: mediates firm attachment to eukaryotic cells
Rmp protein	Reduction-modifiable protein: protects other surface antigens (Por protein, lipooligosaccharide) from bactericidal antibodies
Transferrin-, lactoferrin-, and hemoglobin-binding proteins	Mediate acquisition of iron for bacterial metabolism
LOS	Lipooligosaccharide: has endotoxin activity
IgA1 protease	Destroys immunoglobulin A1 (role in virulence is unknown)
β-Lactamase	Hydrolyzes the β-lactam ring in penicillin

Most of these factors have been discussed during the course. Just take a look at them and try to remember where they were mentioned