

Chlamydia group:

We will start by saying that it is the causative agent of respiratory tract infections, especially lower respiratory tract infections. It is a special group of microorganisms because this group of bacteria cannot be demonstrated by gram stain and it needs a special culture and method for diagnosis.

That is because:

1. It doesn't possess a complete cell wall (Chlamydia organisms have a cell wall similar to some extent to that of gram negative bacteria by the presence of lipopolysaccharides, but the amount of the lipopolysaccharides is less, resulting in thinner layers in the Chlamydia so it doesn't react in a similar way to the gram stain.)
2. The growth pattern of Chlamydia is intracellular replication instead of binary fission (this means it must replicate within the infected epithelial cells of the respiratory tract by the formation of inclusion bodies within the epithelial cells. Usually we have two forms of growth. **First one** is called elementary bodies; these elementary bodies are small cocci of different morphology - shape- that attach to the mucosa of the respiratory tract and penetrate the subcutaneous mucosa producing inclusions* within the infected tissue. Within these inclusions begins the reproduction process by the production of what we call inclusion bodies which is considered the **secondary stage** of growth. These inclusion bodies later can be later released from inclusions and spread as infectious elementary bodies.)

*inclusions are a form of cover (a sac like structure)

Because of the second point (mentioned above) we cannot grow this kind of bacteria on normal culture mediums like blood agar, chocolate agar, and other common types. That is why we have to use a special tissue culture called McCoy tissue culture that is usually obtained from the kidney or the liver. This culture has to be well controlled and it's not easily achieved because it requires a great deal of work and time (2 weeks). That's why chlamydia bacteria are

not cultured in clinical labs for diagnostic purposes. There is a simpler test called PCR test that looks for a specific gene (a plasma gene) that is associated with this organism.

~ Chlamydia group is widely distributed in nature with two main species related to humans and many species that are related to animals, especially birds. The animal infecting Chlamydia act in a similar way in animals as the human Chlamydia acts in humans which is producing pulmonary infections.

~We have two main types of human Chlamydia, Chlamydia trachomatis and Chlamydia pneumonia.

~Chlamydia Trachomatis.

The word trachomatis is associated with to the clinical infection of the eye which results in blindness due to the damaging of the cornea. The infection usually starts in the mucosa of the conjunctiva and later slowly damages the mucosa of the eye till it reaches the cornea and damages it causing trachoma. This specially occurs in children who are not treated because it's a slow progressive disease and the infected person should be treated as soon as possible with antimicrobial drug to prevent the progressive disease in children.

Chlamydia trachomatis is part of the genital tract flora and is associated with inflammatory reactions in the mucosa of the urethra and the uterus producing a type of disease called nonspecific urethritis. Chlamydia trachomatis is considered a sexually transmitted disease (like Neisseria gonorrhoeae) but there is a difference in the clinical features between these two bacteria. Chlamydia unlike gonorrhoeae does not induce a severe inflammatory reaction with slight irritations in the urethra and a possibility of few drops of discharge with few pus cells which can be recognized by the infected individual early in the morning. In most cases this infection is asymptomatic and this is the main issue with this bacteria. This problem arises in the case of pregnant women because the presence of this bacterium in pregnant women means that during delivery this bacteria will also infect the baby causing conjunctivitis and it might also reach the respiratory tract and cause pneumonia. These bacteria may cause

prostatitis (in men); vaginitis, cervicitis, and leading to infertility in women by damage in fallopian tube.

New born babies in the past used to be given (even if Chlamydia wasn't there) a kind of antiseptic reagent called silver nitrate (it had to be fresh to be able to function), but now the silver has been replaced by three types of antibiotics (tetracycline, sulfur, and chloramphenicol). One drop in each eye is enough to kill any Chlamydia and prevent trachoma. Despite this fact there are still at least 1 million cases of trachoma in the world reported by the WHO in underdeveloped countries.

~Chlamydia Pneumonia.

It is related to the respiratory tract of humans. It can be part of the respiratory tract flora but under certain conditions it might become activated and produce pulmonary infect; however, the infection caused by Chlamydia is not normal like the one caused by streptococcus pneumonia, staphylococcus aureus, or other organisms. It produces something called atypical pneumonia, what makes it atypical is that, unlike normal pneumonia, Chlamydia produces dry cough with no sputum, low persistent fever and muscle pain. In our country Chlamydia pneumonia is uncommon and it is found more often in countries with high humidity and high temperature.

Concerning diagnosis and treatment, in the past diagnosis has been done by using McCoy tissue culture and serological test with the demonstration of specific antibodies against chlamydia and this is not useful because the process of developing antibodies against Chlamydia is slow and may develop antibodies only after recovery. PCR is now used to identify the presence of chlamydia in samples of sputum. There are no vaccines available for both types of Chlamydia.

Mycoplasma Group:

The second group in relation to Chlamydia is the Mycoplasma group. The mycoplasma group is widely distributed between humans and animals; there are pathogenic and nonpathogenic species. In reality the Mycoplasma group is more important in animals than in humans especially in poultry and birds. The major groups that affect humans are Mycoplasma pneumonia, Mycoplasma genitalium, and Mycoplasma hominis.

~Mycoplasma pneumonia.

This pathogen is the smallest type of bacteria to be discovered so far. Mycoplasma doesn't have a cell wall; however, they have a special cell membrane which is composed of a lipid bilayer which to some extent protects the mycoplasma. Unlike Chlamydia, Mycoplasma can be grown on special culture media but it requires at least 2 weeks to recognize its growth. It can also be recognized by a special stain but as in the case with Chlamydia it's not an easy process to be used. Although both the culture and the staining can be done it's easier to recognize the Mycoplasma by using molecular technique. Mycoplasma pneumonia can be found as part of the normal respiratory tract flora but under certain conditions it may cause infections especially in young people (around our age) rather than in the elderly or young children. The optimum age to acquire this kind of infection is between the ages of 12-18. No one knows why this group is more susceptible but it is believed to have something with the surges of sexual hormones that occur at this age range. This infection is also correlated with winter season more than with summer season. Clinically it is associated with atypical pneumonia (dry cough and fever with an absence of sputum).

~Mycoplasma Hominis/ Mycoplasma Genitalium.

Mycoplasma hominis is found in the oral cavity as part of the oral flora (usually insignificant). Mycobacterium genitalium like Chlamydia trachomatis might be associated with unspecific urethritis, cervicitis...etc. Mycoplasma genitalium is not considered to be a true STD because they found that at least 20-30% of the population in certain countries to carry this bacterium without displaying any clinical feature. Thus it is believed that this bacterium in

association with other bacteria like *Neisseria gonorrhoeae* or syphilis might produce an effect causing specific urethritis.

Diagnosis methods like culture and staining as we said are not practical as they are time consuming. This bacterium's serological test is called cold agglutination test (all serological tests in the lab are usually done at 37°C in the incubator) this test is the only one in which labs use type A RBCs and place the serum, containing the antigen, in the refrigerator and if there is agglutination after 24 hrs. then this is a positive test. The process of developing antibodies for this bacterium is slow so we might not find antibodies during the acute infection stage. This means that this test is not useful because we don't get accurate results during the time the patient is in the hospital. PCR test on the other hand is very useful.

Note: "Some species such as *M. Hominis* can be recognized using cold agglutination."

There are no vaccines but antimicrobial drugs are available.

Legionella Pneumonia:

This organism in fact was discovered by accident in the United States in 1976. There was a meeting for war veterans in Philadelphia when suddenly hundreds of these veterans acquired a respiratory tract infection in the form of pulmonary infection. Following a full investigation they found that all of these soldiers had an organism that resembled gram negative bacilli to some extent. This organism was later found to be a usual inhabitant of water and often infect animals and fish and was rarely associated with humans.

This organism:

1. Grows in facultative anaerobic conditions
2. Is to some extent a gram negative coccobacilli
3. Can be cultured
4. Produces filaments

This organism was later named legionella in relation to Legionnaires (فيلق). It later became associated with air conditioning systems and in fact they found that the source of the

infection that occurred with these soldiers stemmed from the air conditioning system of the hotel. It had absorbed water that was contaminated with this organism and the organism was inhaled by the soldiers reaching their lungs producing a feature of pneumonia. This pneumonia was fatal at the time.

Fatality factors include:

1. Age
2. Presence of another disease in the lungs (many elderly people to some extent have fibrosis, up to 80% of people above 60 have fibrosis in their lungs)
3. Heavy smoking

Symptoms included dry cough, high fever, and had associations with **gastrointestinal symptoms (vomiting and diarrhea)** which are not usually seen in Chlamydia or mycoplasma except in children sometimes. The end result was a shortness of breath familiar of the respiratory tract and eventually death. In the outbreak that occurred in Philadelphia almost 30 soldiers died due to the infection. These fatalities occurred because nonspecific antimicrobial drugs were used. Chlamydia and Mycoplasma can be treated with tetracycline and fluoroquinolones and other drugs. Penicillin is **not adequate** for treatment. They found that the drug of choice to eliminate this organism is a macrolide like erythromycin.

A special culture can be done to isolate the organism and again we can demonstrate specific antibodies by serological means or we can use the molecular technique PCR. This type of bacteria manages to grow in a wide range of temperatures (0°-80°C). In our country this is an uncommon and nonfatal disease.

Spirochetes Group:

The spiral form of the bacteria is what gave them the name spirochetes. They have no cell wall; they only possess a special cell membrane. They can be as long as 10 µm and can be seen by a special stain or what we call contrast microscopy (**dark field microscopy**). They cannot be easily demonstrated .

Treponema is of two types: pathogenic and nonpathogenic. The nonpathogenic type usually resides in the oral cavity and the pathogenic is considered as a STD and is associated with the genital tract.

~Treponema Pallidum.

It is **very important STD** because throughout the ages this pathogen has killed maybe millions of people in Europe and Americas. Till now this species cannot be well-cultured. There are certain studies that state that this species can be cultured on special cultures but generally it's not easily cultured. You can remember the word pallidum by the Arabic word (بلید) because this organism is actually not very active and for that reason it causes a progressive disease. What's dangerous about this organism is that it shows the feature of syphilis. This feature doesn't cause an acute infection rather it is a progression of a previous infection and might extend for a few years. Like *Neisseria gonorrhoeae*, *Treponema pallidum* is only transferred by close sexual contact. The organism cannot survive in the outside environment for more than few minutes. Secondly this organism is able to penetrate any damage in the mucosa of the genital tract or the oral cavity and produce slow inflammatory reaction but this inflammatory reaction is often unrecognizable in the early stage; however, in later stages following antigen antibody reaction we might be able to recognize, after 2-3 weeks, lesions on the external genitalia in men or intra genitalia of women and these lesions are known as Chancre's lesions. This is the first stage of infection because syphilis usually has three stages of infection.

- 1st stage: acquiring of infection with mild lesions with few clinical symptoms like fever but it is often asymptomatic and can be discovered by examination.
- 2nd stage: more severe lesions and it may be associated with the CNS.
- 3rd stage: is associated with complications throughout the body whether internal organs, bones, or the CNS.

In short this organism has an incubation period for the infection 1st it's a few days- few weeks, 2nd the progress of the disease might extend for a few years; that's why it's highly

important to treat the patient in the first stage not in the 2nd or 3rd stage because their complications are usually irreversible.

The more dangerous disease is the congenital syphilis. If there is a pregnant woman infected with syphilis it might infect the fetus in the first trimester or second trimester. The organism might enter to the tissues and cells of the baby and in the long run (after birth in which the child will look normal at time of birth) the symptoms will start appearing in a year or two. Lesions on the skin of the baby and complications in the teeth, the bones, and the CNS of the baby will appear and the baby might not survive these complications. Untreated syphilis will eventually cause death or at least irreversible damage on the organs and the CNS of the infected individual.

The treatment is easy in the first stage. Penicillin is the drug of choice; a high dose of penicillin is enough to eradicate the organism in the first stage. But in later stages usage of antimicrobial drugs might not change the course of the disease. Diagnosis of syphilis is complicated and not easy in the second and third stages; however in the first stage it can be easily recognized in the external genitalia of men whereas in ladies it requires more investigation because the infection usually resides inside the vagina. In relation to the uterus we can use direct smear and by dark field microscopy we can see the spiral form. We can also use a serological test called a Screening test (nonspecific): only to indicate whether or not you have an antigen that is similar to syphilis that is also called VDRL test (venereal test). STDs are usually referred to as venereal disease (coming from the name Venus- the goddess of beauty)

VDRL test is a test to detect the nonspecific antigen of the spirochetes similar to Treponema. It's a simple test and can give you an idea whether or not the patient is infected by this organism; if it is positive you have to confirm your results by performing a more sophisticated test for example fluorescents Treponema technique (you have to take a serum to recognize and demonstrate the specific antibodies). Now they use the PCR test although its not accurate but it can be used to detect the organism. No culture method is available in most labs. Syphilis is typically diagnosed by clinical features in the first stage of infection and confirmed by serological means and by the demonstration of specific antibodies.

~ Borrelia Burgdorferi.

It's a type of spirochetes (related to animals) that can be transported to humans via insects called ticks. Ticks are typically associated with and found on animal skin. They can carry this bacterium by the absorption of an amount of blood from an infected animal and then transfer it to a human who is in close contact with animals or who lives in wild areas. These spirochetes are similar in morphology to Treponema but have different distal curvings and different genus name. The injection of these spirochetes into the skin of the individual results in lesions. These lesions can be small and associated with redness; they might persist for a few days before disappearing. The disappearance of these lesions doesn't necessary mean salvation from this pathogen because after the production of specific antibodies by the body some of the organisms may stay and proliferate in the tissues eventually causing what is called Lyme disease. Lyme disease affecting the internal organs is very serious with effects on the CNS, connective tissue, and may also form arthritis. It's a common disease in the US and is always asked in US clinical examinations but it is uncommon in our countries.

~Liptospiral diseases.

They are related to animals but can also infect humans when they come into contact with contaminated water or excretions from these animals. This organism produces a disease called Weils's disease which is basically a jaundice (inflammation of the liver), vasculitis (inflammation of the blood vessels), and it is also associated with bleeding in the oral cavity and the skin. This is not a common disease in Jordan.

Lyme disease and all other Liptospiral diseases can be easily diagnosed by serological means (the demonstration of specific antibodies) as well as by clinical means. Cultures are difficult and are not usually done in ordinary laboratories.

Good Luck 😊