

As you have seen from the first part we have concentrated on specific information. You should at least have basic knowledge about causative agents, virulence factors, and epidemiology of respiratory tract infections, especially in our country, it's not accepted to have no knowledge about these infections. You should know that there is no more diphtheria in our country, only imported cases from other countries.

## **Lower respiratory tract infections**

Here we are dealing again with certain opportunistic organisms, we have some which are considered part of our respiratory normal flora, and only under certain conditions they become active and can be associated directly with LRTI.

**\*\*Lower respiratory tract normally is free of microorganisms, rarely to be associated with few numbers of organisms, so the majority of infections are originated from upper respiratory tract; not only from larynx or throat but also might from oral cavity and sinuses, so some organisms can start from URT and then easily disseminate to LRT.**

-In order for any organism to cause infection in LRT, we have to consider the local immune defense of the respiratory tract, there are always number of people that might be susceptible more than others to acquire infections from organisms in the respiratory tract especially following viral infections, or following decreased immunity, or other clinical underlying diseases. Also, at least 20-30% of total **adult (not children)** population in any country might have some sort of chronic obstructive lung diseases, it can be very mild, related to allergic asthma or some fibrosis, and these people are more susceptible for developing LRTI in form of bronchitis or pneumonia.

-Infants and young children are highly susceptible for developing bacterial bronchitis or pneumonia following viral infections, where there is damage to respiratory mucosa.

**\*\*We always have to distinguish the age of the patient; infants, adults, or old patients. Old patients and infants normally have the same pattern of infection, while in adults the infection is related to other factors like consumption of alcohol or presence of other immunodeficiency conditions.**

**\*\*Nasal cavity, oral cavity and larynx might be a source of the majority of LRTI; because always they are associated with certain types of what we called opportunistic pathogens. In addition, we are always exposed to a large number of small particles that may carry one or more organisms.**

Hospitalized patients are more exposed to certain types of organisms especially those circulating in the environment of the hospitals in certain places where there are patients infected with RTI. This especially happens in intensive care units where most of the patients will have intubation, or ventilator to assist their respiratory functions, so they are exposed to gram negative multi resistant organisms.

### **Acute and Chronic bronchitis:**

#### **Acute bronchitis:**

It differs according to age. In children acute bronchitis is usually due to viral infection not bacterial infection, whereas in adults it could be mixed viral and bacterial or bacterial only according to age.

**\*\*Acute bronchitis in children is usually not related to bacterial infections; so we shouldn't use any type of antimicrobial drug.**

#### **Chronic bronchitis:**

More difficult to categorize because it might follow any continuous exposure to certain organism or due to presence of certain organisms in respiratory tract of either children or adults.

**\*\*Some organisms that might cause confusion in medical practice: Presence of bronchitis due to bordetella pertussis or parapertussis.**

In general, bordetella pertussis is not important organism in our community due to complete vaccination. It's rarely discovered in any infant except infants who are not immunized.

- Recently it was found that bordetella parapertussis might cause a form of bronchitis but not a form of true whooping cough. Our new pediatrics haven't seen any case of true whooping cough, so it's difficult for them to distinguish between parapertussis and true pertussis.

[[bordetella pertussis is the causative agent of pertussis, also known as whooping cough. Bordetella parapertussis causes a disease similar to it]

However, in both cases, if there is a true case of pertussis it must be associated with **two major clinical stages:**

- 1- Catarrhal stage: it is like any type of infection related to URT.
- 2- Paroxysmal cough stage: more dangerous. Severe cough lasts to 10-15 minutes or more. It is easily recognized by changing the color of the infected person which is associated with well-developed cyanosis and lack of O<sub>2</sub>.

These stages (in both pertussis or parapertussis) in fact are related to the release of two important cell wall antigens: endotoxin composed of lipopolysaccharide, and cytotoxin which is responsible for the invasion of macrophages of the lung and later development of fever and infection.

Despite that, bordetella pertussis or parapertussis is not an invasive organism, and rarely reaches the blood stream and causes sepsis.

**Diagnosis:**

Diagnosis of any case of pertussis which might give impression of bronchitis depends on clinical features more than isolation of the organism which is difficult and cannot be successfully done in most laboratories of the world. We might only use blood specimen to look for presence of specific antibodies, and this often cannot be developed before 4 to 6 weeks, so you don't have to wait and you have only one option which is to treat the patient with drugs. Early drugs are better.

You can detect antigens of true pertussis in urine but it's not easy to do also.

**Pneumonia:**

- The number of cases of pneumonia each year in different countries is not less than 1% of the total population, so we have millions of cases of pneumonia in all ages; infants, young children, adults, old age.

- Causative agents can manifest as mild pneumonia that requires no hospitalization, or severe form of pneumonia which might start as viral infection and end as bacterial infection.

[In children 90% start as viral and end as bacterial. While In adults 50% ].

So viral and bacterial organisms often are the causative agents of majority of cases of pneumonia.

**\*\*Severe pneumonia usually is related to bacterial causes, but recently they found some viruses like SARS that can cause severe pneumonia.**

In a study published recently they found that in addition to those viruses like coronaviruses they found bacterial agents, so most severe causes of pneumonia are viral and bacterial agents.

### **In relation to the causative agent there are two types of pneumonia:**

- 1- Community acquired: up to 90% associated with streptococcus pneumonia, less with staph, haemophilus and others.
- 2- Hospital acquired: especially in relation to ICU, mostly associated with gram negative multi drug resistant bacteria, like pseudomonas aeruginosa, Acinetobacter baumannii, Burkholderia cepacia, and klebsiella pneumonia which produce extended spectrum beta lactamase.

So hospital acquired pneumonia is more severe, and more associated with multidrug resistant bacteria, due to acquired infection from the hospital environment by using respiratory equipment and others.

\*\*H. Influenza type B and S. aureus are not truly associated with hospitalized patients in ICU, there is another new category of pneumonia which is health care acquired pneumonia. This new term is applied mainly to old persons who reside in nursing homes. It's not related to hospital acquired infections, but mainly related to the presence of these old persons in nursing homes. Normally these might suffer from H. influenza, streptococcus group A or C, or staph aureus, rarely associated with multidrug resistant organisms like hospital acquired pneumonia.

### **Streptococcus pneumonia:**

One of the most important causative agents of pneumonia is this gram positive bacteria which has 80 serotypes. According to many investigations; mostly between 10 to 20 serotypes account for capsular serotypes which produce pneumonia.

In addition, other types of strep pneumonia might cause mild forms and not so serious.

### **Three virulence factors associated with these serotypes:**

- 1- Large polysaccharide capsule.
- 2- Pneumolysin (type of hemolysin) which contributes to invasion and complications. It is released by majority of strep pneumonia in different amounts.
- 3- Specific proteases which affects mucosal IgA and allow the organism to produce severe inflammatory reaction in the mucosa and later to spread to the blood stream.

-In general Strep pneumonia starts with intrapulmonary tissues by producing mild to severe necrosis, later complicated with the organism reaching blood stream and causing sepsis.

-The source of infection is not necessarily to be directly from the throat for example, it might be from the sinuses or middle ear especially in children.

-In children if they develop strep pneumonia infection they will suffer from conjunctivitis, sinusitis, and otitis media at the same time.

-We have certain patients that are more susceptible to develop S. pneumonia infection especially in relation to immunodeficiency and sickle cell anemia. They are high risk persons and should be vaccinated according to their age and type of available vaccine. There is a vaccine for adults and vaccine for children.

-It's important to distinguish between viridans Strep and S. pneumonia by using specific laboratory tests like optochin test and gram stain.

-Lab diagnosis of S. pneumonia is easily accomplished within 24 hours. By gram stain and culture you will know the specific organism and have the serotyping which is important in relation to epidemiology.

**Treatment:**

We have a problem in our countries which is that at least 80% of the isolated bacteria are considered resistant to penicillin (so it's not a drug of choice in treatment of S.pneumonia infection). In western countries less than 5% resistant to penicillin. This can show that we overuse the antimicrobial drugs.

Drug of choice: macrolides or Fluoroquinolones like levofloxacin and ciprofloxacin.

In case of sepsis or meningitis we have to use vancomycin (still no resistance in) and 3<sup>rd</sup> generation cephalosporins; like cefotaxime and ceftriaxone.

**Prevention:**

All immunodeficient people whether children or adults should be protected by a specific type of vaccine. For adults pneumovax vaccine which is composed of 23 capsular serotypes, but it's not used for children because they might suffer from complications. For children we use Prevnar or Pneumococcal composed of 13 serotypes.

\*\* One single dose of Pneumococcal vaccine for children is not enough, must be 3 doses which results in at least 90% immune response for a long time. And the age should be not less than 2 years, where there is often no immune response for polysaccharide antigen in less than 2 years old children.

There is a study done in Ajloun that resulted in that they have reduced developing strep pneumonia infection in children up to 50%.

**Atypical pneumonia:**

Here we have a special group of organisms and they are associated with atypical pneumonia due to the fact that they cause a type of pneumonia that is not well characterized, which is called walking pneumonia, which is mostly not recognized and not well diagnosed and mostly doesn't require antimicrobial drug.

**Three types of bacteria cause atypical pneumonia:****Mycoplasma, chlamydia, legionella:**

-They have a defect in the cell wall so they don't have a complete gram negative cell wall, they have a small amount of polysaccharides, small amount of endotoxins, and cannot be easily cultured in vitro on culture media.

-Chlamydia cannot be cultured on artificial medium like blood agar or chocolate agar; it needs tissue agar because it is an intracellular organism. Mycoplasma and legionella can be cultured in fluid or solid medium with some experience.

-They are not demonstrated by gram stain, there are special stains that can be used for legionella, but not easily done. So gram stain has no value in diagnosis of these organisms.

There is only one type of stain which is silver stain which might demonstrate the organism in the biological biopsy but not directly from culture.

-The importance of these three organisms is that they might produce mild infection, not necessarily by presence of even fever. The most common feature is the presence of dry cough. Fever might be present or not, abdominal pain, vomiting, diarrhea might be found in relation to children, but a more important feature especially in legionella or legionnaire's disease is the presence of pain in the urinary tract during voiding of urine which indicates the presence of the antigen in the kidney, which may result later in kidney failure and complications.

-Other important feature is that some of these mycoplasma are only related to respiratory tract mucosa atypical pneumonia, and some related to urinary tract mucosa and produce non-specific urethritis.

-There are types of chlamydia that only cause RTI and other chlamydia only related to genital tract and cause nonspecific urethritis.

-Specific species of chlamydia might cause nonspecific urethritis and at the same time especially during delivery might reach the newborn baby and produce a form of chlamydia pneumonia, which means it produces both infections at the same time. This happens in chlamydia trachomatis with certain serotypes; L and K serotypes.

\*\*These serotypes could be dangerous, due to the fact that chlamydia trachomatis when it reaches the lungs of the new born baby it will not cause atypical pneumonia but it will cause acute pneumonia, which is so severe, so fatal, and associated with conjunctivitis and trachoma.

-Very important feature of chlamydia is that we can separate it from mycoplasma due to replication and growth, so chlamydia trachomatis and other types of chlamydia have a special replication process and this is the only type of organisms that have such cycle.

### **Chlamydia can be found in two forms:**

- 1- Infectious form: elementary bodies.
- 2- Reticulate bodies: found in inclusions inside the cytoplasm of infected cells where there will be division so the bacteria will replicate by binary fission and it they will be released from the infected epithelial cells and will produce infectious particles which easily can be dispersed in the atmosphere, inhaled, and then lodge in mucosa of the respiratory tract especially if the person has susceptibility to infections (this has no relation to immunodeficiency).

**In our country we have done 3 studies:** In children less than 2 years and children up to 12 years and in adults.

-One of these studies was in association with the American university with Doctor Najwa Khoury and they found no single case of chlamydia or mycoplasma pneumonia among our children who are less than 2 years. They found 2 cases of bordetella pertussis.

-In adults they found few cases and they have been detected by using blood agar or cold agglutination test for mycoplasma, and for chlamydia by PCR.

### **Diagnosis** of chlamydia, mycoplasma, legionella:

Not easily done by routine tissue culture. The most common way now is to use molecular techniques which are the only way which can confirm the presence or absence of these organisms. Often we hear that there are cases of pneumonia due to atypical organisms but in fact our country is not so associated with these organisms; because we don't have high humidity or big changes in temperatures in winter between day and night in contrast to Europe where they have more single cases and outbreaks.

**Treatment:** drug of choice: macrolides (no resistance), and tetracycline also is an excellent drug.

No vaccine available.

### **Legionella pneumophila:**

Special organism. Present in certain cases, we discovered in our country some persons who have some activities in relation to sport clubs, where there is a possibility to acquire infection due to this organism because it is the only organism that can survive in cold and hot temperatures (4-80C degrees) (except spore forming bacteria which can survive also), usually at 6 degrees u kill most of pathogens, but this pathogen also survives in clean water.

Also it is associated with air conditioning system because it can survive with a minimum amount of minerals.  
\*\*We are lucky that we haven't recognized any outbreaks of this organism, mostly single cases.

-Incubation period is 2-10 days (it might be extended to 1 or 2 months in some cases but let's stick to what is written in the slides).

-Difficult to diagnose in clinical practice because there is no productive cough, no fever usually only in old patients or patients having chronic obstructive disease or heavy smokers or alcoholics. It might result in certain complications: arthritis joint pain, kidney failure, even before we recognize the respiratory symptoms we directly see the complications.

**Diagnosis:**

-We might collect aspirated sputum or use pleural fluid, but usually blood can be used especially when using PCR. But more important is to look for presence of specific antigen in urine. Specific antibodies in blood might not be enough or are developed later, but specific antigens in urine are enough.

**Treatment:** Macrolides, quinolones.

-No vaccine.

---

~ اللهم إني أستودعك ما قرأت وما حفظت وما تعلمت فردّه إلي عند حاجتي إليه إنك على كل شيء قدير ~