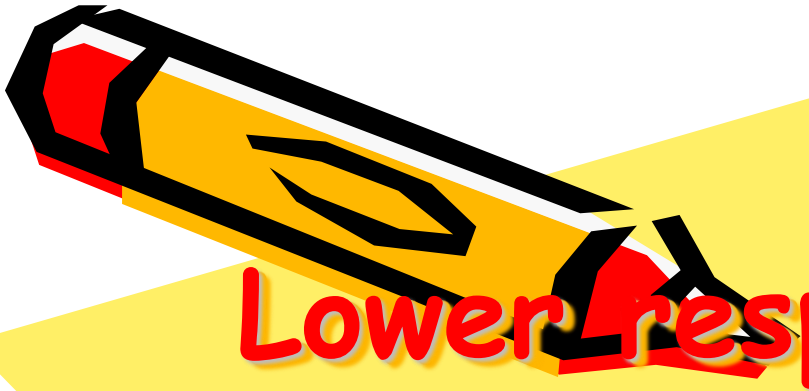
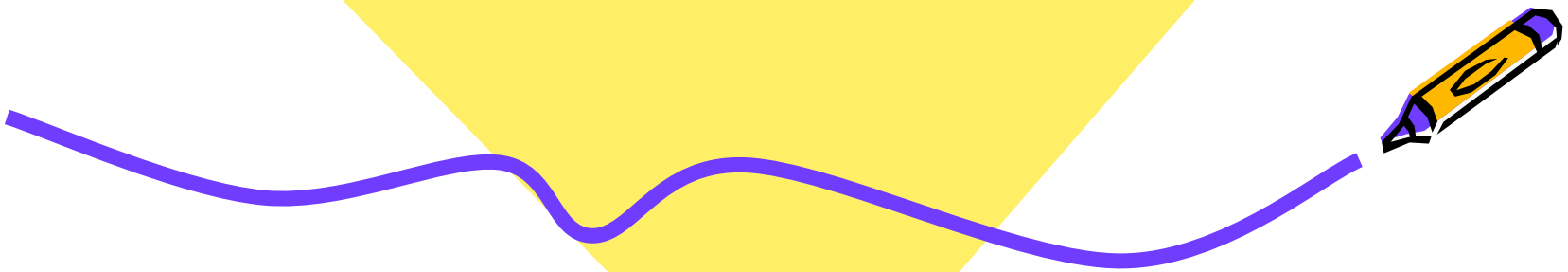
Lower respiratory tract infections





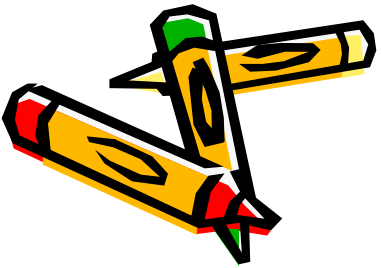
•The respiratory tract is continuous from nose to alveoli, but it is convenient to distinguish between infections of the upper and lower respiratory tract, even though the same microorganism may be implicated in infections throughout the continuum.

•The infections can be divided into acute and chronic.

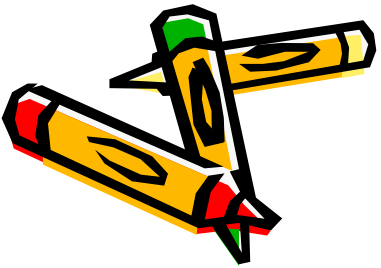
✓Among the **acute infections** four major syndromes can be ***identified:acute bronchitis, acute exacerbations of chronic bronchitis, bronchiolitis and pneumonia. Influenza*** is a specific infection which, if severe, may proceed to bronchitis or pneumonia. ***Whooping cough*** - considered as a serious and acute infection of the lower respiratory tract.

✓**Chronic infections** are including: ***tuberculosis and aspergillosis and conditions such as lung abscesses and empyema. Infections in cystic fibrosis*** patients are also covered in the section on chronic infections.

ACUTE INFECTIONS OF THE LOWER - RESPIRATORY TRACT



Whooping cough



Aetiology and pathogenesis

- Whooping cough or pertussis is a severe disease of child-hood caused by the bacterium ***Bordetella pertussis***.
- This species of *Bordetella is* confined to humans and is spread from person to person by airborne droplets. The organisms attach to and multiply in the ciliated respiratory mucosa, but do not invade deeper.
- Surface components such as filamentous ***haemagglutinin*** **and** ***fimbrial agglutinogens*** play an important role in specific attachment to respiratory epithelium.
- Several ***toxic factors*** have been identified, some of which affect inflammatory processes, while others damage ciliary epithelium.

- These are:
  - **Pertussis toxin** - this resembles diphtheria and other toxins in being a subunit toxin with an active (A) unit and a binding (B) unit. The A unit ***acts at the level of the host cell proteins***, with the disruption of signal transduction to the affected cell.
  - **Adenylate cyclase toxin** - this is a single peptide which can enter host cells and cause them to increase their cyclic AMPc levels. This results in an ***inhibition of defence functions: chemotaxis, phagocytosis and bactericidal killing***. This toxin may also be responsible for the haemolytic properties of *B. pertussis*,
  - **Tracheal cytotoxin** - a cell wall component derived from the peptidoglycan - which ***kills tracheal epithelial cells*** specifically;
  - **Endotoxin** - the structure of the ***cell wall LPS*** in *Bordetella* has functional similarities and may play a role in the pathogenesis of infection.

Clinical features

- After an **incubation period of 1-3 weeks**, infection is manifest first as a catarrhal illness with little to distinguish it from other upper respiratory tract infections.
- This is followed up to a week later by a dry, **non-productive cough** which becomes paroxysmal. A paroxysm is characterized by a series of short coughs productive of copious mucus, followed by a **`whoop';** a characteristic sound produced by an inspiratory gasp of air.
- Despite the severity of the cough, the symptoms are confined to the respiratory tract; lobar or segmental collapse of the lungs can occur.
- **Complications:** CNS-anoxia, exhaustion and secondary pneumonia due to invasion of other pathogens into the damaged respiratory tract.

Diagnosis, Treatment

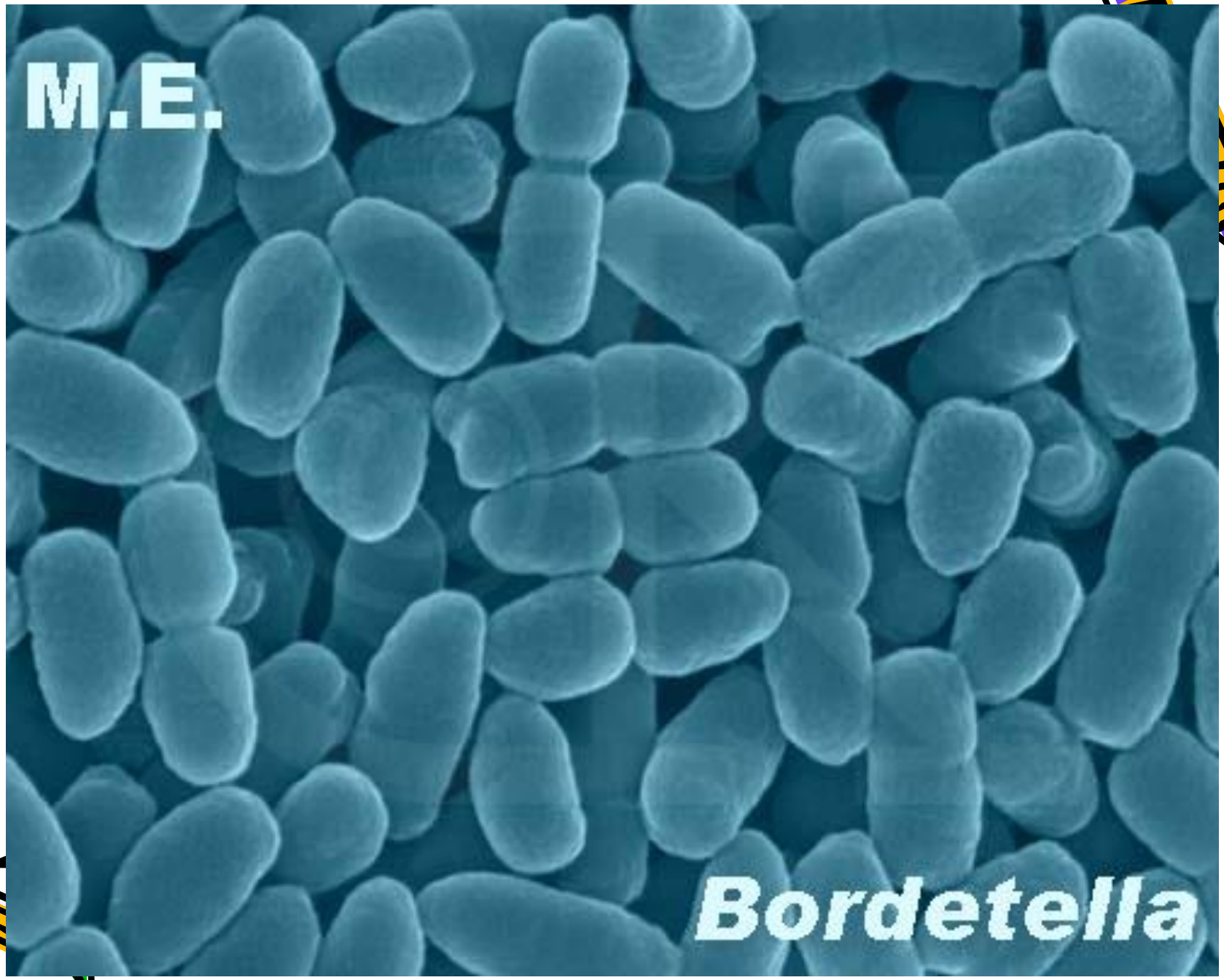
- The early clinical picture is non-specific and the true diagnosis may not be suspected until the paroxysmal phase.

- The organisms can be isolated on suitable media from throat swabs or on 'cough plates' but they are fastidious and do not survive well outside the host's environment.

- Supportive care for children under one year of age (with greatest risk of complications) and admission to hospital should be considered.

- For specific antibacterial treatment to be effective it must penetrate the respiratory mucosa and inhibit or kill the infecting organism. **Erythromycin** is the drug of choice. Although treatment is often not begun until the disease is recognized in the paroxysmal phase, it does appear to reduce the severity and duration. It also reduces the numbers of organisms in the throat and helps to reduce the number of secondary infections.

Erythromycin prophylaxis of close contacts of active cases is helpful in controlling the spread of infection.


M.E.
Bordetella

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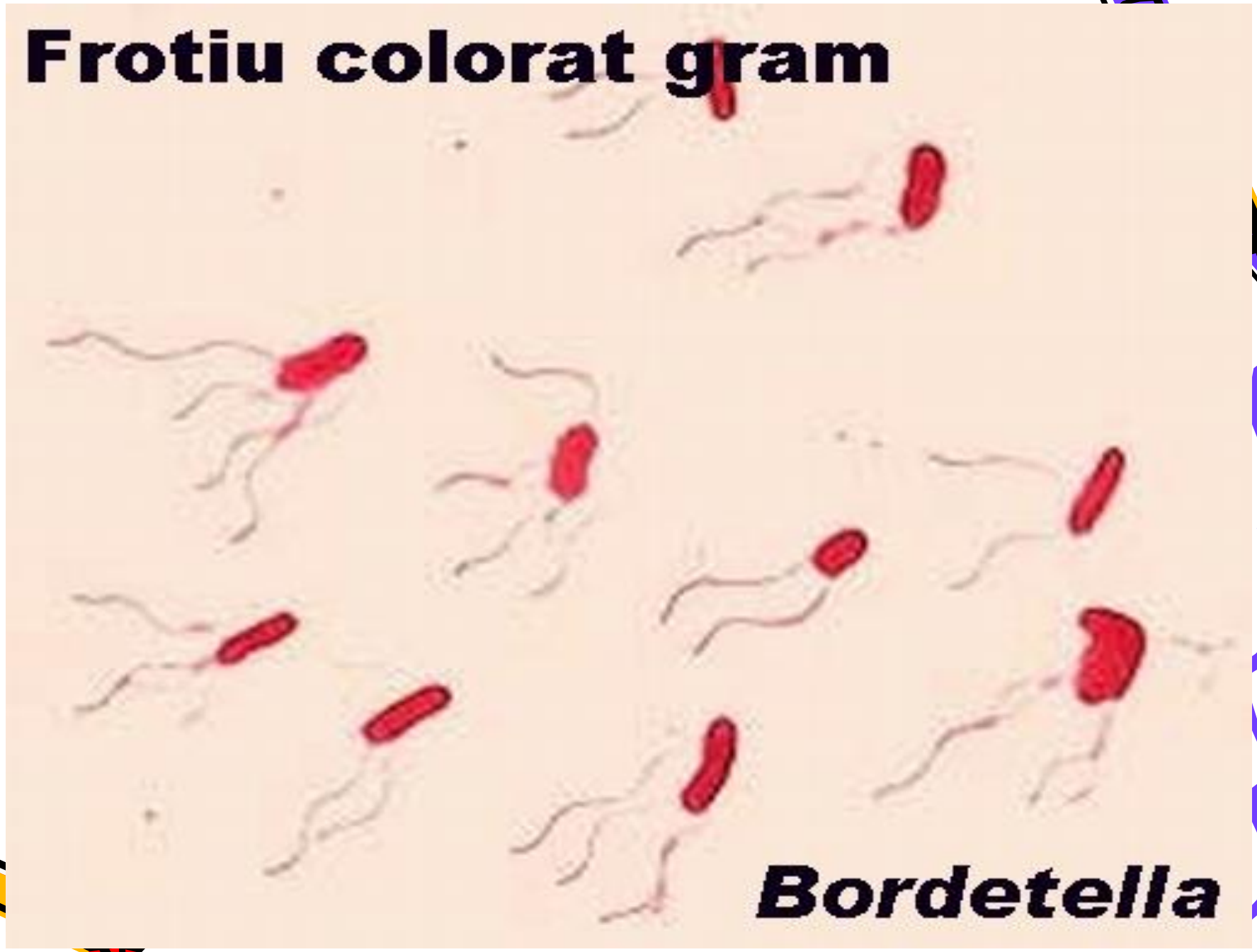

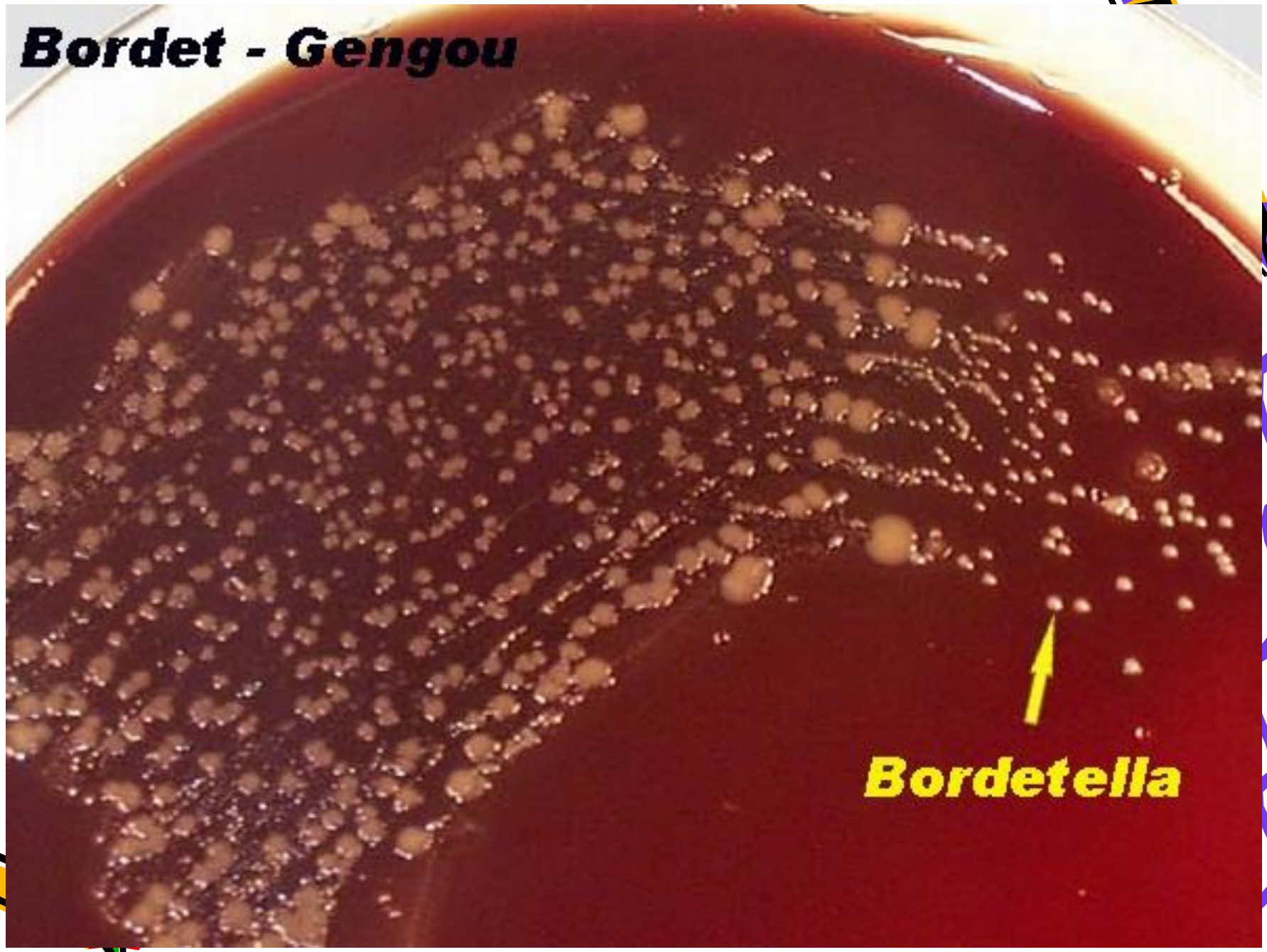
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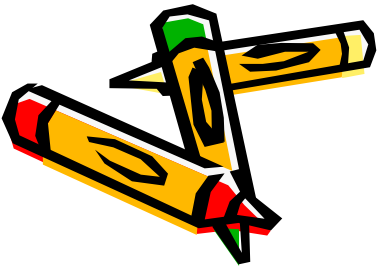
Bordetella

Prevention

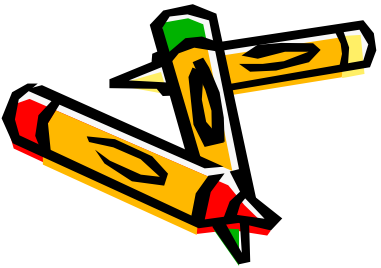
- Whooping cough can be prevented by active immunization. For many years a whole **cell vaccine comprising a killed suspension of B. *pertussis*** cells has been used. It is usually **combined with purified diphtheria and tetanus toxoids and administered as `DPT' or 'triple' vaccine**.
- The efficacy of pertussis vaccine is generally high but variable, and recent years have seen major concern about side effects:
  - (a) fever, malaise and pain at the site of administration, (in up to 20% of infants)
  - (b) convulsions, thought to be associated with the vaccine (in about 0.5% of vaccinees);
  - (c) encephalopathy and permanent neurologic sequelae associated with vaccination, with an estimated rate of 1 in 100 000 vaccinations (0.001%).

Acute bronchitis



- Causative agents include:
  - **viruses** (rhinoviruses, coronaviruses) which are also found infecting the upper respiratory tract, and lower tract pathogens such as influenza virus, adenoviruses, and bacteria (*M. pneumoniae).*
  - Secondary bacterial infection with ***S. pneumoniae and H.influenzae*** The degree of damage to the respiratory epithelium varies with the infecting agent;
  - ***A cough is the most prominent presentation and treatment is symptomatic***. The value of antibiotics is uncertain but they are usually recommended.

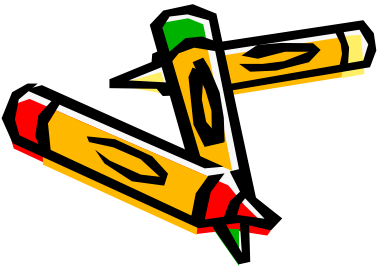
Acute exacerbations of chronic bronchitis

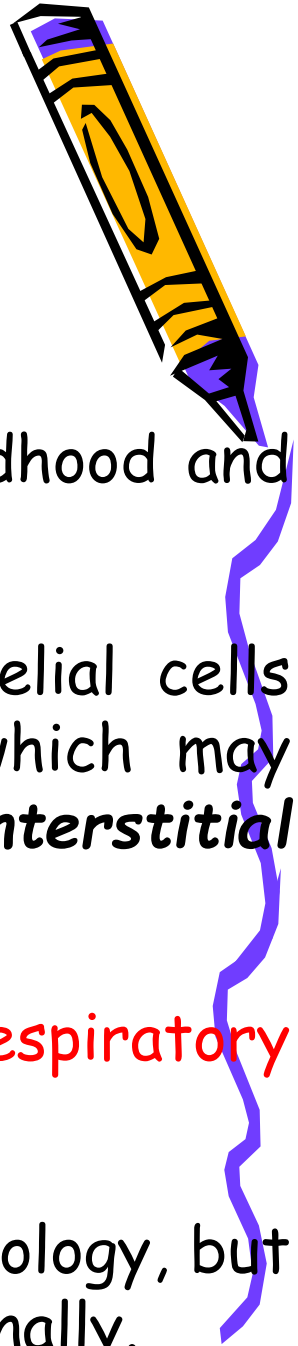


- Chronic bronchitis is a condition in which **cough** and **excessive secretion of mucus** are present in the tracheo-bronchial tree and are not attributable to specific diseases such as bronchiectasis, asthma, or tuberculosis.
- **Infection** appears to be only one component of the syndrome, the others being **cigarette smoking and inhalation of dust or fumes from the workplace.**
- Bacterial infection is probably significant in producing the characteristic acute exacerbations. ***S. pneumoniae*** and un-encapsulated strains of ***H. influenzae*** are the organisms most frequently isolated, but interpretation of their presence in sputum is difficult because they are also commonly found in the normal throat flora and thus can contaminate expectorated sputum.
- Other bacteria such as ***Staphylococcus aureus*** and ***Mycoplasma pneumoniae*** are less commonly associated with infection and exacerbation.

Viruses are frequent causes of acute infection. Antibiotic therapy may be helpful.

Bronchiolitis

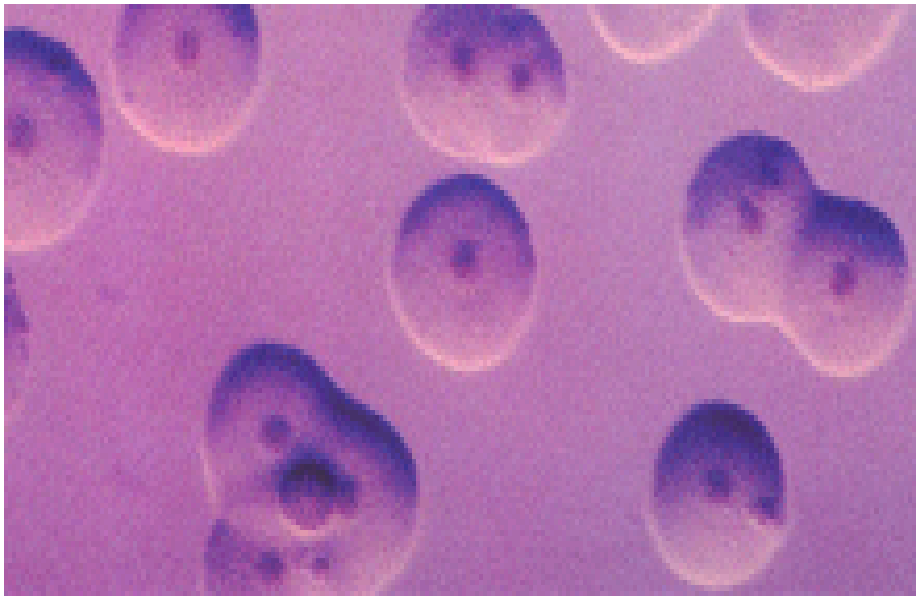




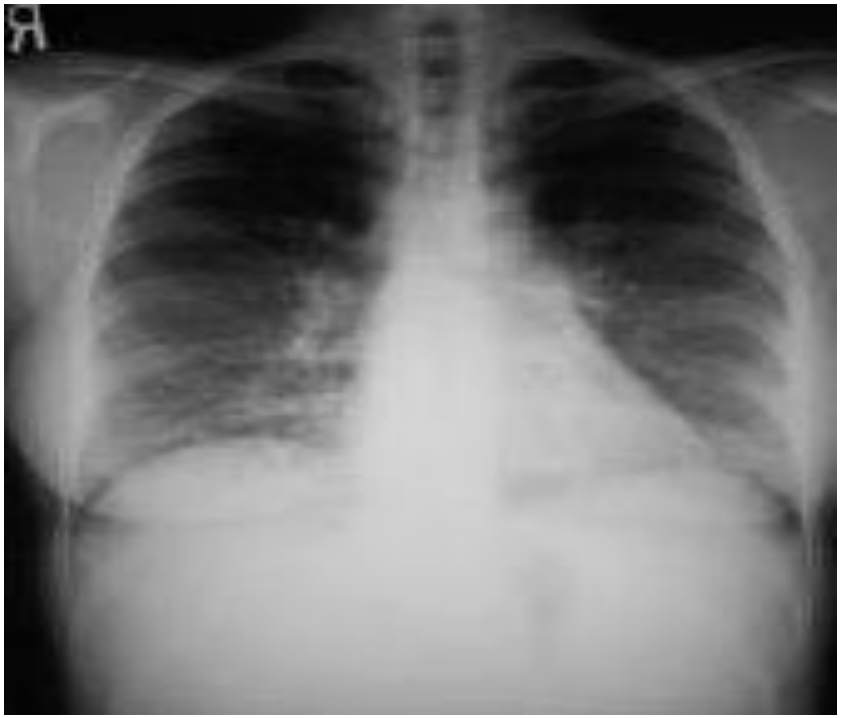
- Bronchiolitis is a disease restricted to childhood and usually to **children of less than 2 years**.
- Infection results in necrosis of the epithelial cells which leads to peribronchial infiltration which may spread into the lung fields to give an ***interstitial pneumonia***.
- 75% of these infections are caused by respiratory syncytial virus (RSV);

most of the remaining 25% are also viral aetiology, but *Mycoplasma pneumoniae* is implicated occasionally.

M.Pneumoniae



M.pneumoniae-Xrays



Respiratory syncytial virus infection

- Aetiology and transmission
  - This is a typical ***paramyxovirus*** and there is only one antigenic type. Its surface spikes are fusion proteins which fuse host cells to form 'syncytia'.
    - The infection is ***transmitted by droplets and to some extent via hands.*** RSV is the most important cause of bronchiolitis and pneumonia in infants, about one in a hundred cases requiring admission to hospital.
    - ***Outbreaks occur each winter***, and during the RSV season infection can spread in hospitals as well as in the community. Nearly all individuals have been infected by ***two years of age.***

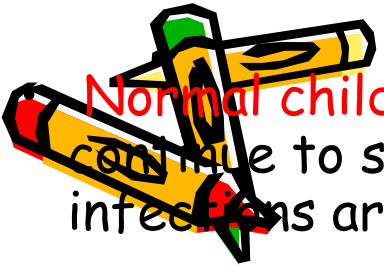
Clinical features and pathogenesis

- After inhalation the virus establishes infection in the nasopharynx and lower respiratory tract.

- **Clinical illness** appears after an ***incubation period of four to five days.*** The illness can be particularly severe in young infants (peak mortality at 3 months of age), the virus invading the lower respiratory tract by direct surface spread to cause bronchiolitis or pneumonia.

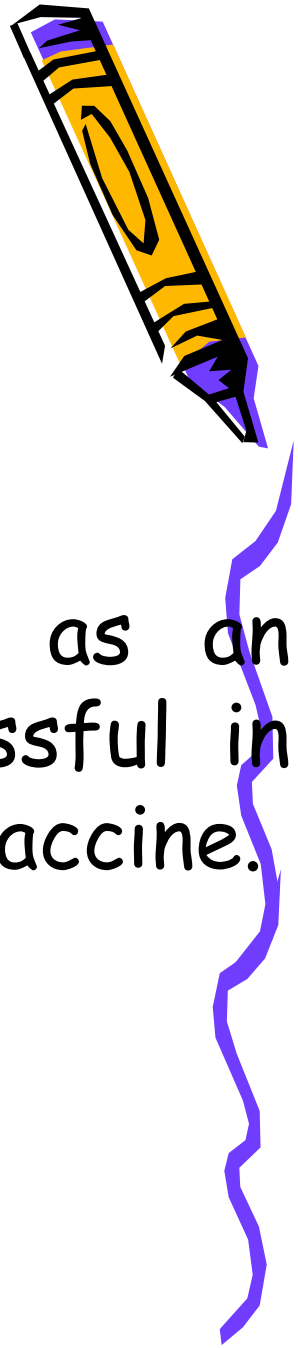
- In young children and adults, however, the virus is restricted to the upper respiratory tract, causing a ***less severe common cold-type illness***.

- Young infants ***develop a cough, rapid respiratory rate, and cyanosis. Otitis media is quite common.*** Secondary bacterial infection is rare and the disease appears to have an immunopathological basis.

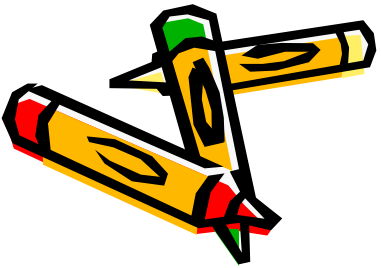


Normal children, even a year or two after apparent recovery, may continue to show ***depressed pulmonary function or wheezing***. Recurrent infections are common, but they are less severe.

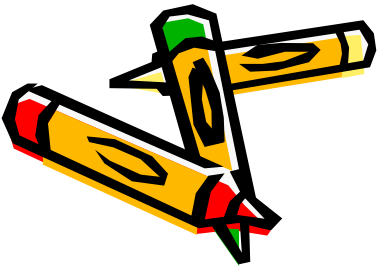
Treatment and prevention



- The antiviral agent ribavirin used as an aerosol has occasionally been successful in severe cases. At present there is no vaccine.



Pneumonia



- Pneumonia has long been known as `the old man's friend';
- it is caused by a ***wide range of microorganisms***. The challenge lies in the ***laboratory identification of the microbial cause***. In the absence of this, the choice of antimicrobial therapy may not be optimal.

- ***Pathogenesis:***

✓ Microorganisms gain access to the lower respiratory tract by inhalation of aerosolized material or by aspiration of the normal flora of the upper respiratory tract. The size of inhaled particles is important,**only those less than about 5μm diameter reaching the alveoli**. Less frequently, the lungs become seeded with organisms as a result of ***spread via the blood from other infected sites.***

✓ Perfectly healthy individuals are susceptible to infection possessing adhesins which allow them to attach to the respiratory epithelium.

•In addition, the ***host with impaired defences (immunocompromise, preceding viral damage, cystic fibrosis, etc.)*** may suffer infection with organisms which do not cause infections in the healthy person (e.g. *Pneumocystis carinii* - in AIDS patients).

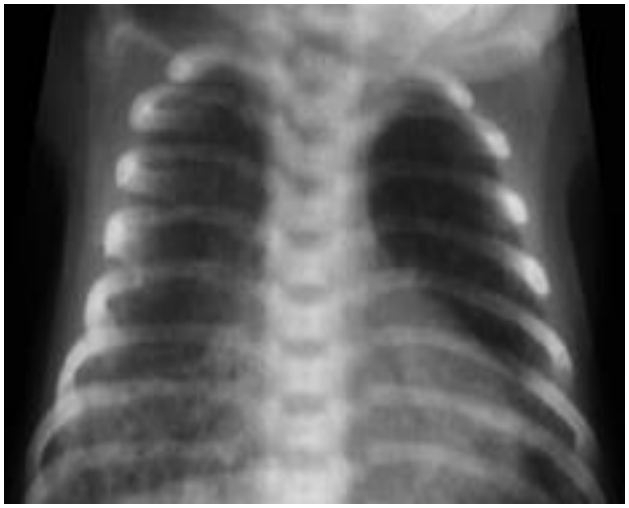
•However four descriptive terms are in common use :

- **Lobar pneumonia** refers to ***involvement of a distinct region of the lung***. The polymorphonuclear exudate is formed. Infection may spread to adjacent alveoli until constrained by anatomic barriers between segments or lobes of the lung. Thus one lobe may show complete consolidation;
- **Bronchopneumonia** refers to a ***more diffuse, patchy consolidation which may spread throughout the lung*** as a result of the original pathologic process in the small air-ways;
- **Interstitial pneumonia** involves ***invasion of the lung interstitium and is particularly characteristic of viral infections*** of the lungs;
- **Lung abscess**, sometimes referred to as necrotizing pneumonia, is a condition in which there is ***cavitation and destruction of the lung parenchyma.***

Causative organisms

- A very wide range of microorganisms is capable of causing pneumonia.
- Age is an important determinant.
  - **Neonates** born to mothers with genital *Chlamydia trachomatis* infection may develop a chlamydial interstitial pneumonitis resulting from colonization of the respiratory tract during birth.
  - In the absence of underlying abnormality such as cystic fibrosis, pneumonia is unusual in **older children**.
  - **Children and young adults** with cystic fibrosis are very prone to lower respiratory tract infection caused characteristically by *S. aureus, H. influenzae* and *Pseudomonas aeruginosa.*
  - The cause of pneumonia in **adults** depends on a number of risk factors such as **age, underlying disease and particular exposure to pathogens through occupation, travel or contact with animals.**
  - Pneumonia **acquired in hospital** tends to be caused by a different spectrum of organisms, particularly Gram-negative bacteria. Clinical and epidemiological clues help to suggest the likely cause, microbiological investigations are essential to confirm the diagnosis and ensure optimal antimicrobial therapy.

Chlamydia psittaci



Bacterial pneumonia

- The classic bacterial cause of acute, community-acquired pneumonia is ***S. pneumoniae*** (the `pneumococcus'). In the past, 50-90% of cases were caused by *S. pneumoniae* but in recent years the relative importance of this pathogen has decreased and it now causes only 25-60% of cases.
- ***Haemophilus influenzae*** is estimated to be the cause of 5-15% of cases but the true incidence is difficult to determine because this organism frequently colonizes the upper respiratory tract of bronchitic patients.
- When effective antibiotic treatment (**penicillin**) for the pneumococcus became widely available it was clear that a significant proportion of cases of pneumonia failed to respond to this treatment and were labelled `**primary atypical pneumonia**'. `

•“Primary” refers to pneumonia occurring as a new event, not secondary to influenza for example, and `atypical' because *S. pneumoniae* is not isolated from sputum from such patients, the symptoms are often general as well as respiratory, and because of failure to respond to penicillin or ampicillin therapy.

•The causes of atypical pneumonia include

- ***Mycoplasma pneumoniae,***
- ***Chlamydia pneumoniae* and C. *psittaci,***
- ***Legionella pneumophila*** *(*is acquired from contaminated environmental sources)
- **and *Coxiella burnetii.***
- ***Moraxella catarrhalis*** (previously *Branhamella catarrhalis) is* increasingly recognized as a cause of pneumonia, particularly ***in patients with carcinoma of the lung or other underlying lung disease.***

It is important to note that in as many as 35% of lower RTI a causative organism is not isolated.

Clinical features

- Patients usually present feeling unwell and with a **fever**. They may have signs and symptoms of a chest infection; **chest pain** (which may be pleuritic), a **cough** which may be **productive of sputum, shortness of breath and difficulty and pain on breathing.**
- Some infections result in **symptoms confined mainly to the chest**, whereas others e.g. Legionnaires disease (caused by ***Legionella pneumophila***) have **a much wider systemic involvement** and the patient may present with mental confusion, diarrhoea, and evidence of renal or liver derangement.

- **Chest examination** may reveal `rales' (abnormal crack-ling sounds) and evidence of consolidation even before changes become evident on x-ray.

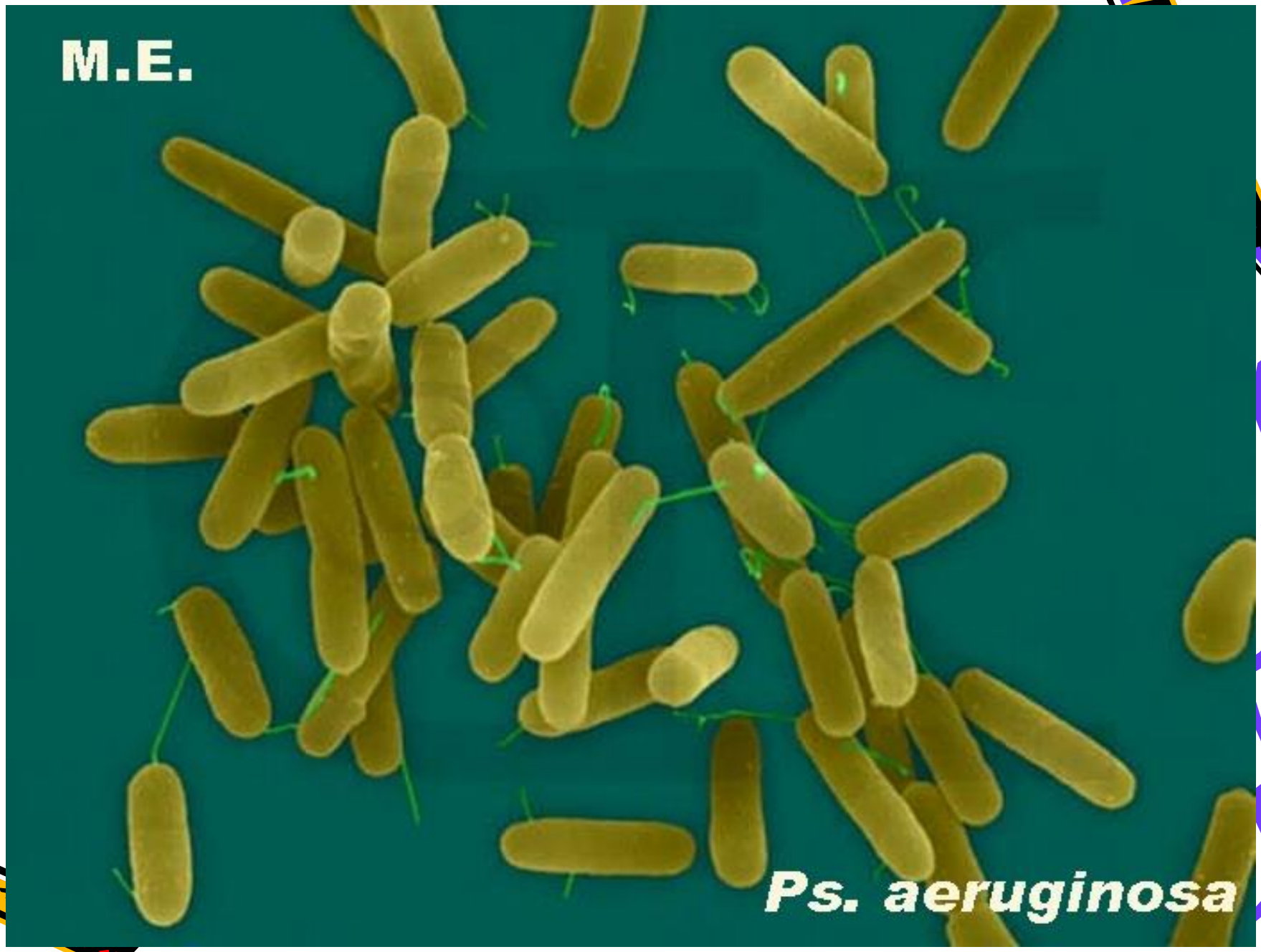
- The **chest x-ray** is an important adjunct to the clinical diagnosis. Patients with pneumonia usually have shadows in one or more areas of the lung indicating consolidation.

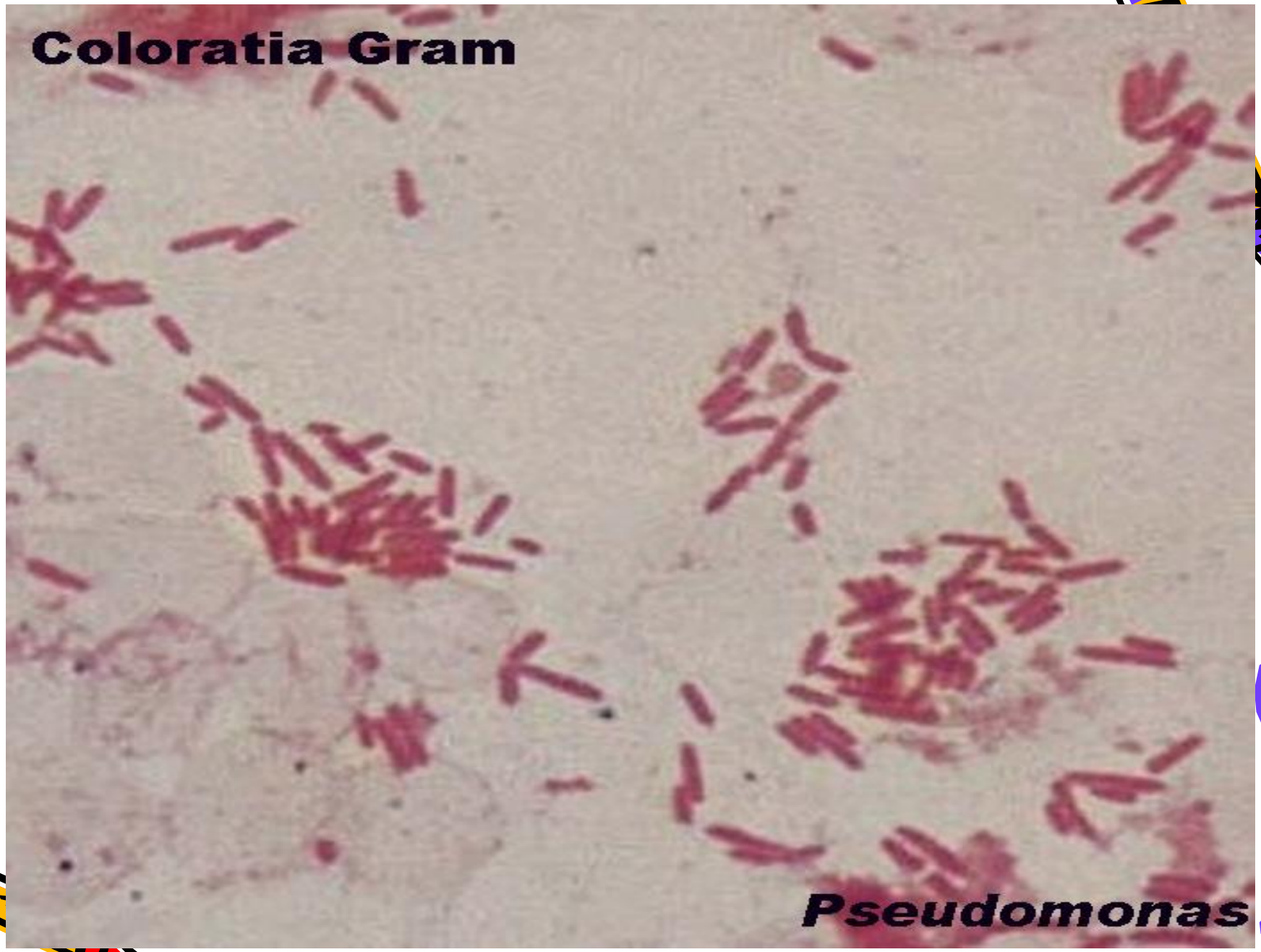
Complications

- Pneumonia is not only the most common **cause of death** from infection **in the elderly**, but it is also an important cause in the young and previously healthy.
- Complications of infection include spread of the infecting organisms directly to **extra-pulmonary sites** such as the **pleural space, giving rise to empyema, or indirectly via the bloodstream to other parts of the body**. For example, the majority of patients with pneumococcal pneumonia have positive blood cultures and pneumococcal meningitis not infrequently follows pneumonia in the elderly.

Laboratory diagnosis

- **Microscopic examination and culture** of expectorated sputum, transtracheal aspiration, bronchoscopy and bronchoalveolar lavage, and open lung biopsy, may yield more useful results.
- The causative agents of atypical pneumonia, with the exception of *L. pneumophila*, will not be seen in **Gram-stained smears**.
- **Standard culture** techniques will allow the growth of the bacterial pathogens such as *Strep. pneumoniae, Staph. aureus, H. influenzae* and *Klebsiella pneumoniae* and other non-fastidious Gram-negative rods.
- **Special media** or conditions are required for the causative agents of atypical pneumonia, including *Legionella pneumophila*.
- **Rapid non-cultural techniques** have been applied successfully to the diagnosis of pneumococcal pneumonia. Detection of pneumococcal antigen by agglutination of antibody-coated latex particles can be used both on sputum and urine specimens (antigen is excreted in the urine).


M.E.
Ps. aeruginosa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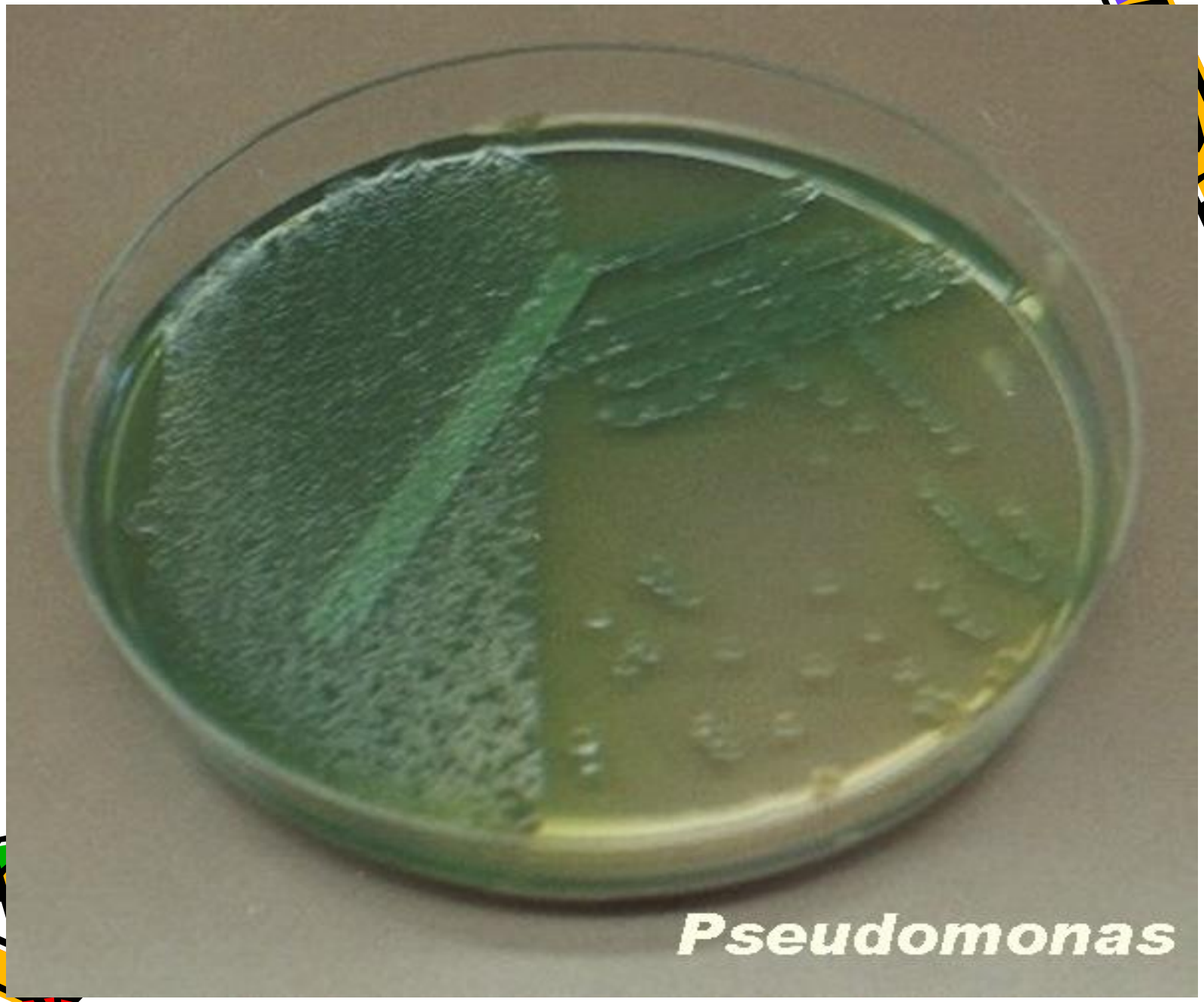
Pseudomonas


Pseudomonas


Pseudomonas

Treatment, Prevention

- **Treatment:** Once the cause of the infection has been identified, selection of **appropriate antimicrobial therapy** is important. The choice of treatment is more difficult when sputum is not produced or does not reveal the pathogen; so the importance of taking a **full history and employing invasive diagnostic techniques** - to improve the chances of establishing the cause.

- **Prevention:**

  -Respiratory infections are usually **transmitted by airborne droplets**, so that person-to-person spread is virtually **impossible to prevent**, although **less crowding and better ventilation** help to reduce the chances of acquisition of infection.

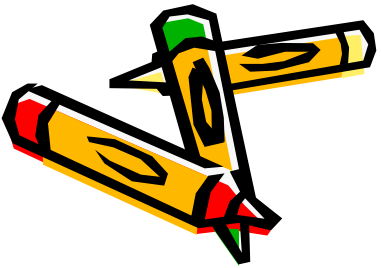
  -Infections acquired from sources other than humans may be prevented, e.g. by **avoiding contact with sick animals** (Q fever), or birds (psittacosis).

  -The **contamination of cooling systems and hot water supplies**

Viral pneumonia

- Viruses can invade the lung from the bloodstream as well as directly via the respiratory tract. Many viruses cause pneumonia and, as in the case of viruses in the upper respiratory tract, generally accomplish this in the face of normal host defences. **Perfectly healthy individuals are susceptible**, and most of these viruses have surface molecules that attach specifically to the respiratory epithelium.

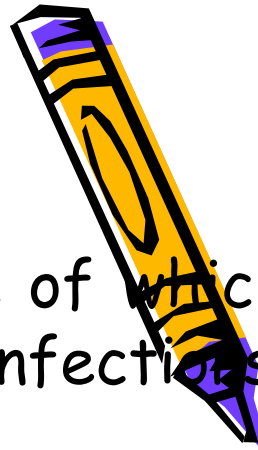
- Sometimes the virus fails to spread significantly to air spaces but **remains in interstitial tissues to cause interstitial pneumonia** (*e.g.* CMV in immunodeficient patients).
- Even when viruses of this group do not themselves cause pneumonia they may, by damaging respiratory defences, **lay the ground for secondary bacterial pneumonia.**



Parainfluenza virus infection

- These viruses are more likely to cause lower respiratory tract disease (croup and pneumonia) in children.
- **Aetiology and pathogenesis**.
- There are ***four types of parainfluenza viruses***, differing in their clinical effects as well as in their antigens. After infection by respiratory droplets these viruses spread locally on respiratory epithelium.
- **Clinical features.**
  - **Parainfluenza viruses 1 and 2** cause pharyngitis, and croup is seen in children under five years of age, consisting of acute laryngo-tracheobronchitis, with harsh cough and hoarseness.
  - Parainfluenza virus 3 infection is often subclinical.
  - Parainfluenza virus usually gives rise to a common cold-type illness.
- **Diagnosis, treatment and prevention**. Virus-specific antigens can often be detected in cells in respiratory washings. The virus can be isolated, and rises in antibody titre demonstrated. Neither antivirals nor vaccines are available.

Adenovirus infection



- There are 41 antigenic types of adenovirus, some of which cause upper and lower respiratory tract infections. (Pharyngoconjunctival fever, sore throat, etc.)
- Adenoviruses cause about five per cent of acute respiratory tract illness, generally with ***nonspecific symptoms*** under the age of five.
- As maternal antibody fades, lower respiratory tract illnesses become more frequent, especially with adenovirus 7.
- **Types 3, 4 and 7** have caused ***outbreaks of respiratory illness ranging from pharyngitis to atypical pneumonia*** in military recruits, with crowding and stress as possible factors.

Influenza virus infection

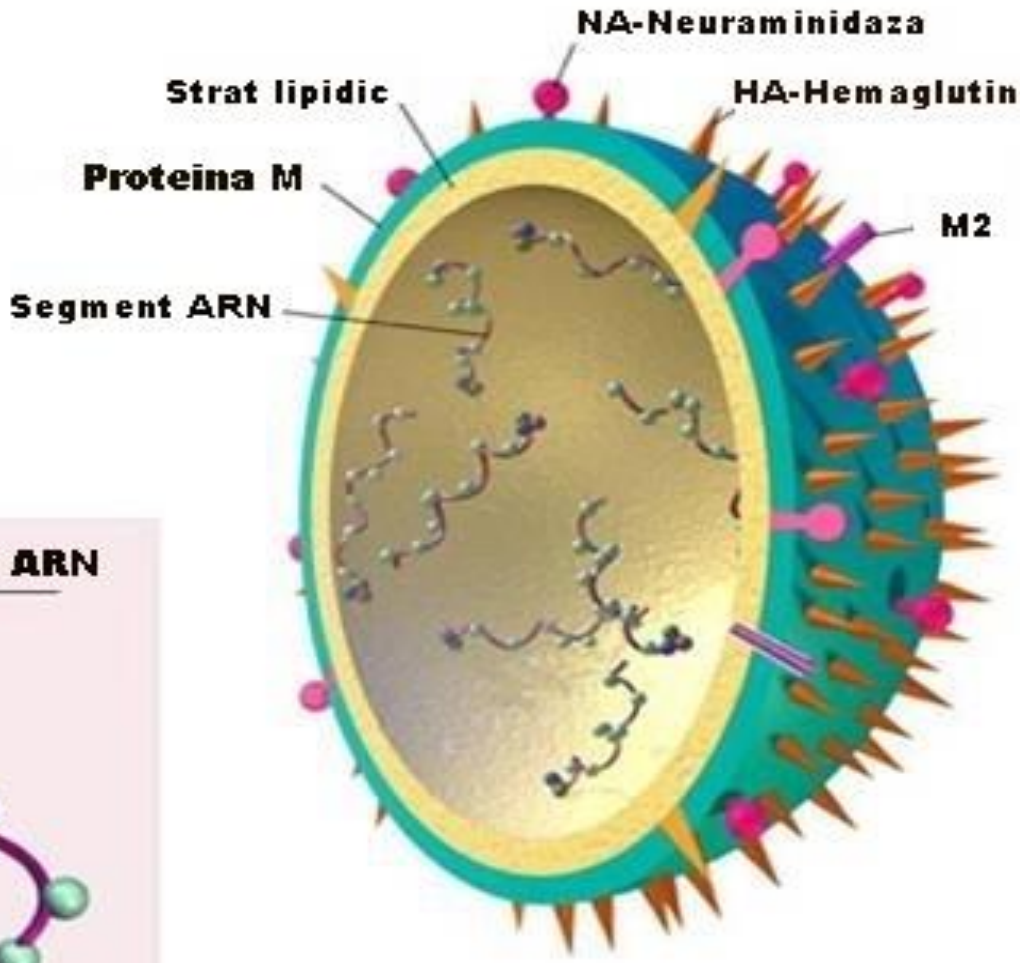
» These are classic respiratory viruses, causes of endemic, epidemic and pandemic influenza.

- **Aetiology and pathogenesis.**
- **Influenza A viruses cause epidemics**, occasionally pandemics, and there is an animal reservoir, notably in birds.
- **Influenza B viruses cause only epidemics** and do not involve animal hosts,
- while **influenza C viruses do not cause epidemics and give rise to only minor respiratory illness**.
- **The viral envelope has haemagglutinin (H) and neuraminidase (N) spikes.** In the case of influenza A, the H and N are type-specific antigens and are used to characterize different strains of influenza A virus . Current strains are H3N2 and HIN1.

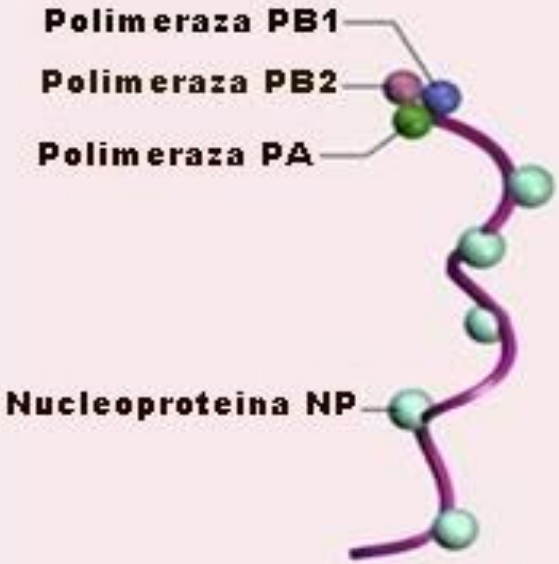
•Influenza viruses undergo genetic change as they spread through the host species. These changes are of two types:

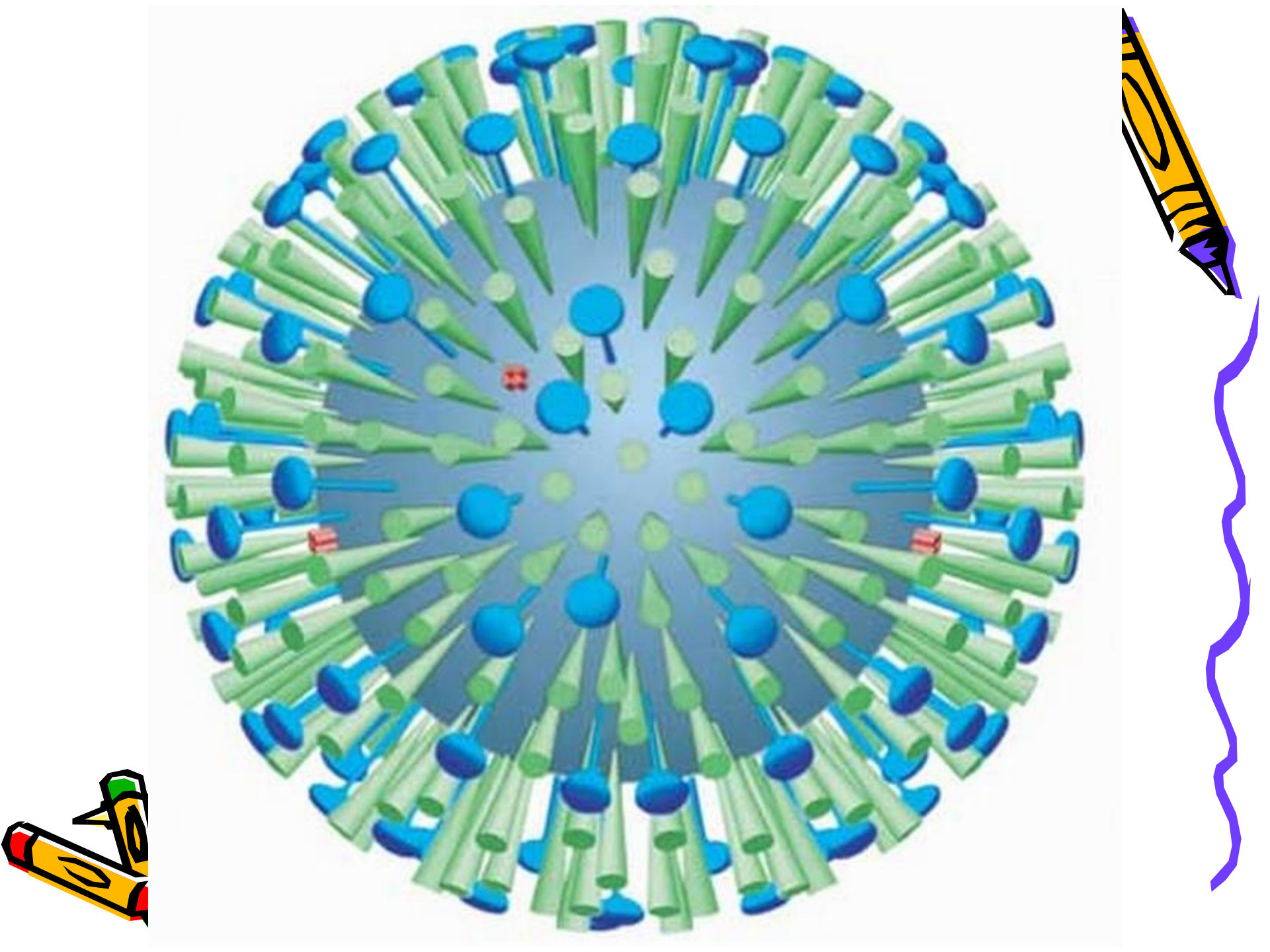
- ***Antigenic drift***. Small mutations, affecting the H and N antigens are constantly occurring., then the new subtype can reinfect the community. Antigenic drift is seen with all types of influenza.
- ***Antigenic shift***. Less commonly, and only with influenza A, there is a sudden major change (shift) in antigenicity of the H or N antigens. This is based on recombination between different virus strains when they infect the same cell. The major change in H or N means that the new strain can spread through population immune to pre-existing strains and the stage is set for a new pandemic.

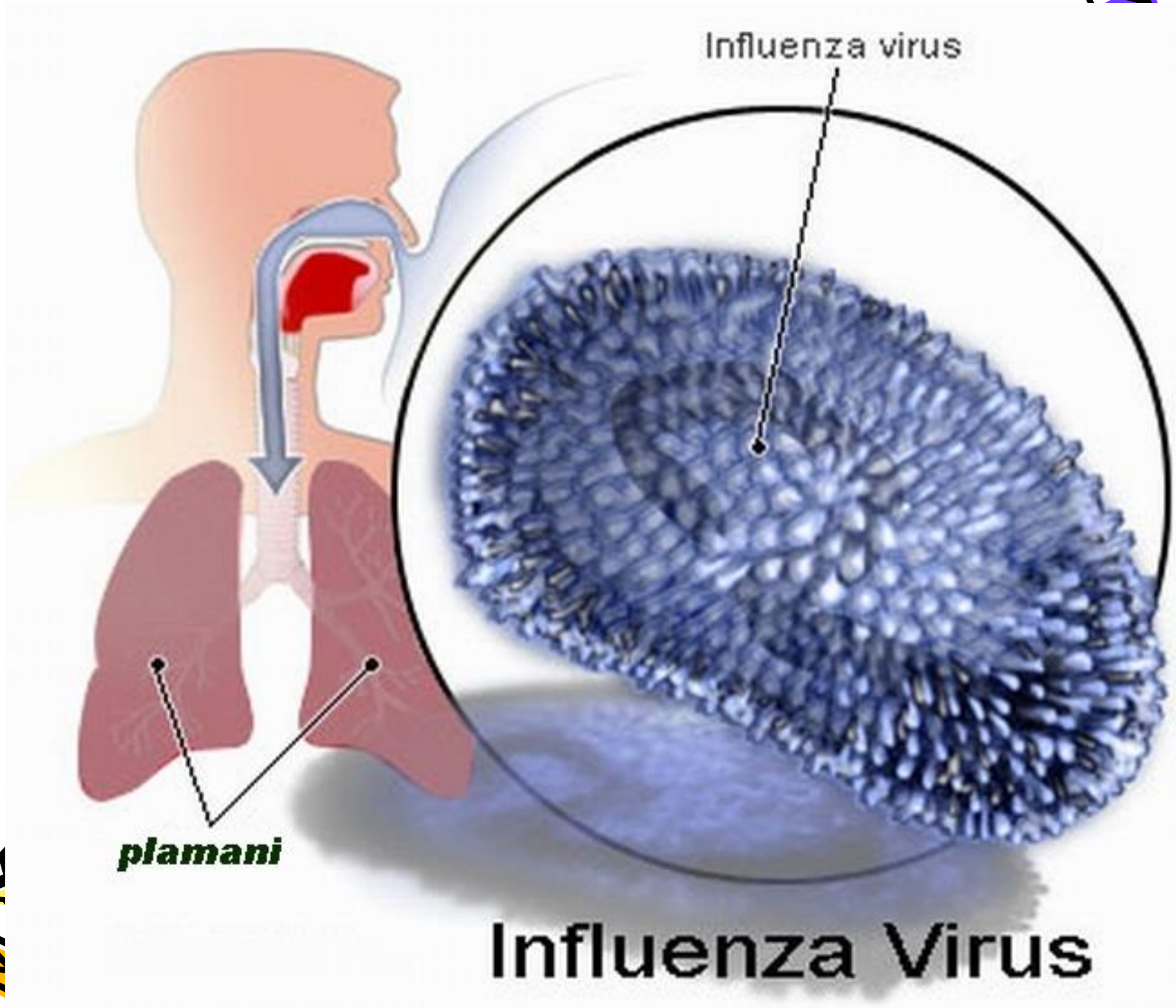
•Damage to the respiratory epithelium also gives opportunities to **secondary bacterial invaders**, especially staphylococci, pneumococci, and *H. influenzae*.



Detaliile segmentului ARN






Influenza virus
plamani
Influenza Virus

Complications

- Mortality due to **secondary bacterial pneumonia** higher in apparently normal individuals over the age of 60 years, and in those with impaired resistance due to chronic **cardiorespiratory disease** (emphysema, etc.) renal disease and so on.
- **Pregnant women are also more susceptible.**
- **CNS complications** occur rarely and include encephalomyelitis, polyneuritis (Guillain-Barre syndrome, GBS). These appear to be indirect immuno-pathological complications, rather then due to CNS invasion by the virus.

Diagnosis

- During epidemics a clinical diagnosis can generally be made.
- Influenza-infected cells are seen after **fluorescent antibody or immunoperoxidase staining** of cells obtained from nasal aspirates.
- A rise in specific anti-bodies can be detected (by **haemagglutination inhibition**, complement fixation or **ELISA**) in paired serum samples taken within a few days of illness and 7 to 10 days later.
- The virus can also be isolated from throat washings taken within a day or two of onset, after **inoculation into eggs or into certain cell cultures**. This takes several days and is more important for public health authorities following infection with new virus strains rather than for diagnosis in individual patients.

Treatment and prevention.

- Amantidine inhibits the replication of influenza virus. It can reduce the severity of the infection, but only if given within 1 to 2 days of disease onset and is more valuable when used for prophylaxis.
- **Vaccines.** The vaccines are given by parenteral injection, and provide protection against disease in up to 70% of individuals.
- Vaccination of **high risk individuals, especially those over 65 years of age and those with chronic cardiopulmonary disease, is recommended.**
- It might be expected that the respiratory route would be a better way of inducing respiratory immunity, and trials with live attenuated virus vaccines administered intranasally are in progress.

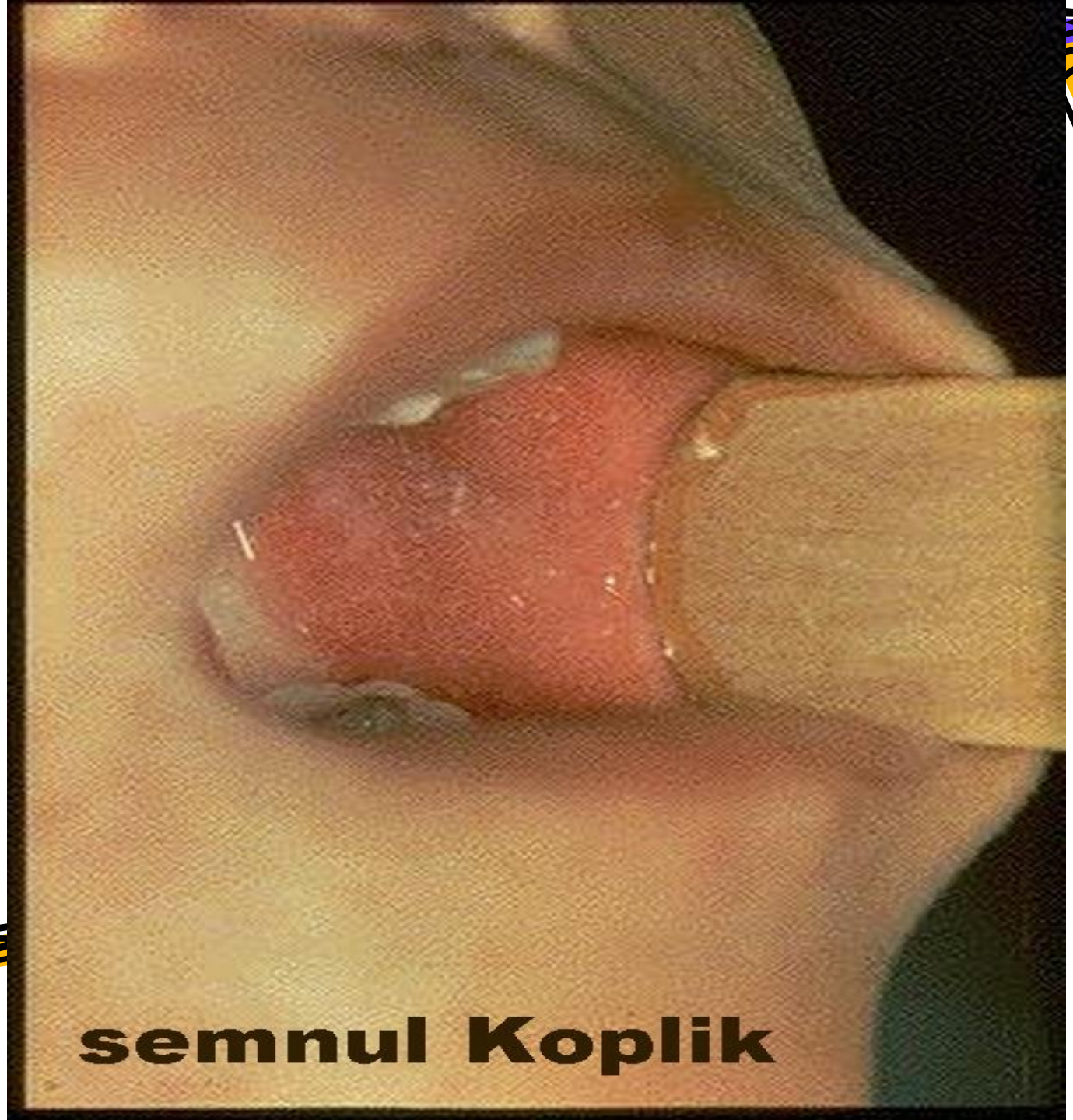
Measles

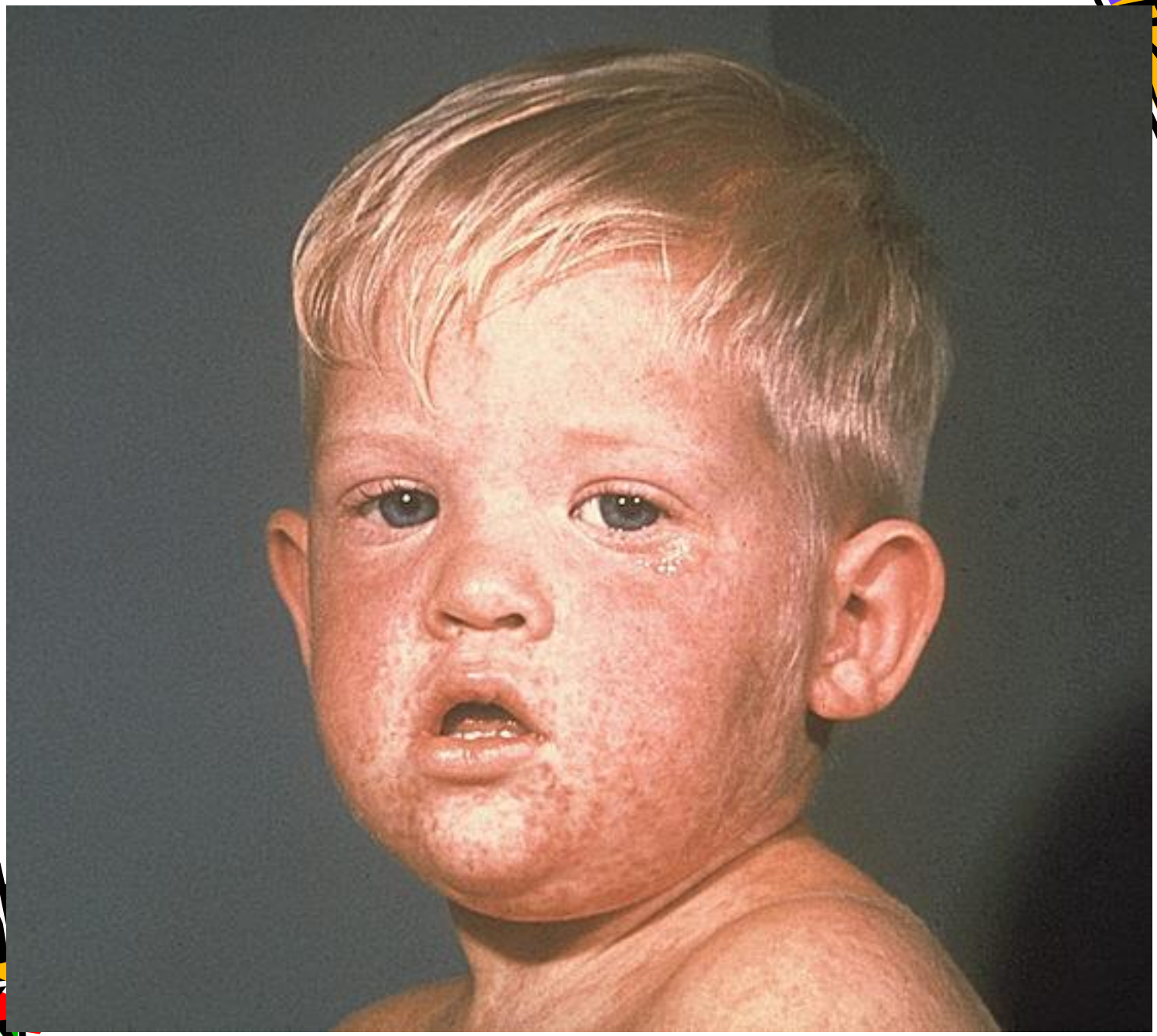
» **Aetiology and pathogenesis**.

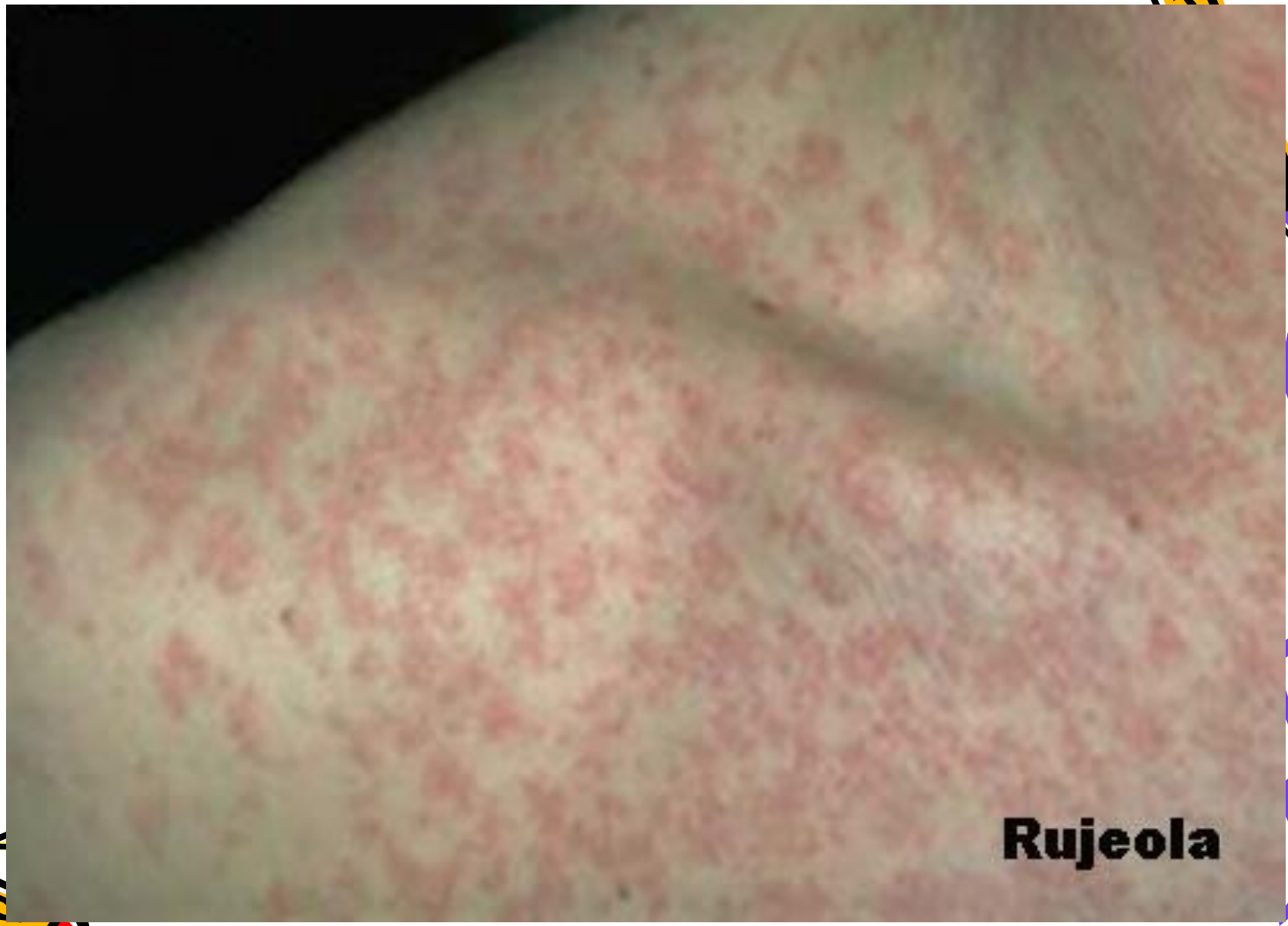
- It is mentioned here because
  - 1) it can cause `**giant cell' pneumonia in those with impaired immune responses,**
  - 2) the virus **replicates in the lower respiratory tract** and, under certain circumstances, causes enough damage to lead to **secondary bacterial pneumonia**. This is now uncommon in developed countries.
- However, in children in developing countries secondary bacterial pneumonia is a frequent complication, and measles remains a major cause of death in childhood.
- **Complications:**
  - depressed immune responsiveness,
  - inadequate vaccination programmes,
  - malnutrition and poor medical care

Clinical features,diagnosis, treatment and prevention

- **After an incubation period of 10 to 14 days, there is fever, a runny nose, conjunctivitis and cough. Koplik's spots and then the characteristic rash appear a day or two later.**
- The virus replicates in the epithelium of the nasopharynx, middle ear and lung, interfering with host defences and enabling bacteria such as pneumococci, staphylococci and meningococci to establish infection.
- Pneumonia , otitis media are also common. In children with severely impaired cell-mediated immune defences virus replication continues unchecked to give a giant cell pneumonia - a rare and usually fatal manifestation..
- The **diagnosis is made on clinical grounds**.
- **No antiviral treatment is available**, but antibiotics are needed for secondary bacterial complications.
- The disease is prevented by a **highly effective, live, attenuated vaccine, given with mumps and rubella (MMR).**


semnul Koplik



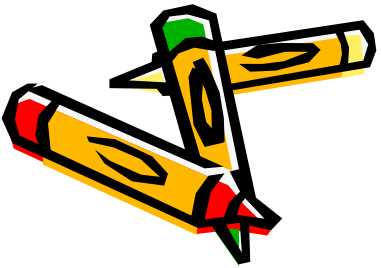

Rujeola


Rujeola

Cytomegalovirus infection

- The virus does not normally replicate on respiratory epithelium or cause respiratory illness, but **in immunocompromised patients** (bone marrow transplant recipients, AIDS patients) it can give rise to an **interstitial pneumonia**.
- In AIDS, for instance, pneumonia is associated with reactivation of persistent CMV infection. Virus can be isolated and characteristic inclusions demonstrated in lung tissue, but *Pneumocystis carinii* is also commonly present, contributing to the pathological picture.

CHRONIC INFECTIONS OF THE LOWER RESPIRATORY TRACT



Tuberculosis

- Tuberculosis is one of the most serious infectious diseases of the developing world and wherever poverty, malnutrition and poor housing prevail.
- It affects the apparently healthy as well as being a serious disease of the immunocompromised. Tuberculosis is primarily a disease of the lungs but may spread to other sites or proceed to a generalized infection (`miliary' tuberculosis).
- **Aetiology and transmission**
  - Tuberculosis is caused by *Mycobacterium tuberculosis* but other species of mycobacteria also cause infection in the lungs. These are called the `atypical' mycobacteria, `mycobacteria other than tuberculosis' (MOTT) or `non-tuberculous mycobacteria' (NTM).
  - Infection is acquired by ***inhalation of M. tuberculosis*** in aerosols and dust. Airborne transmission of tuberculosis is efficient because infected people cough up enormous numbers of mycobacteria, projecting them into the environment, where their outer coat allows them to withstand drying and thus survive for long periods of time in air and house dust.

Pathogenesis

- The pathogenesis of the disease depends on the **history of previous exposure to the organism.**
- **In primary infection**, i.e. infection in individuals `seeing' *M. tuberculosis* for the first time, the ***organisms are engulfed by the alveolar macrophages*** where they can both survive and multiply. Non-resident macrophages are attracted to the site and these also ingest the mycobacteria and carry them via the lymphatics to the local (hilar) lymph nodes. In the lymph nodes the immune response - predominantly a cell-mediated response - is stimulated.
- The body reacts to contain the organisms within `tubercles', **small granuomas consisting of epithelioid cells and giant cells**. The lung lesion plus the enlarged lymph nodes is often called the Ghon (or primary) complex. After a time the material within the **granuloma becomes necrotic and caseous (cheesy)**. In healthy persons the tubercles may heal spontaneously, **become fibrotic or calcified and persist as such for a lifetime**. They will **show up on a chest x-ray as radio-opaque nodules**.
- In a small percentage of people with primary infection, and particularly in the immunocompromised, the mycobacteria invade the blood-stream and cause disseminated disease (`**miliary' tuberculosis).**

•**Secondary tuberculosis** is due to reactivation of dormant mycobacteria

•usually as a consequence of impaired immune function:

- resulting from some other cause such as malnutrition,
- •infection (e.g. AIDS),
- •chemotherapy for treatment of malignancies
- or corticosteroids for treatment of inflammatory diseases.

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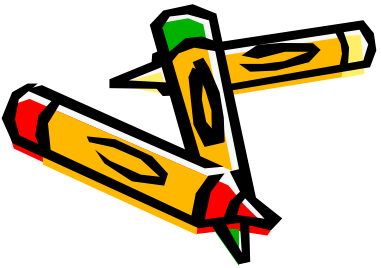
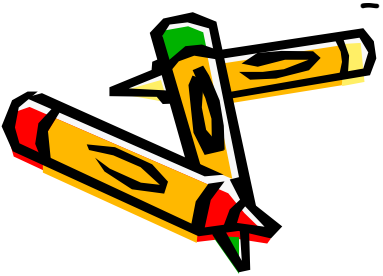


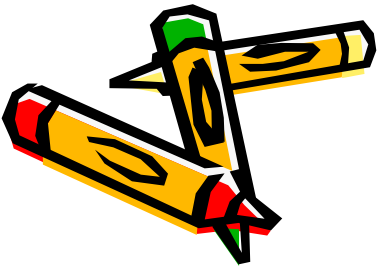
Clinical features

- In contrast to pneumonia, which is usually an acute infection, ***the onset of tuberculosis is insidious***, infection proceeding for some time before the patient becomes sufficiently ill to seek medical attention. **Primary tuberculosis** is usually mild and often asymptomatic, and in 90% of cases does not proceed further. However, in the remaining 10% clinical disease develops.
- **Secondary infection** may occur in almost any organ as the mycobacteria have the ability to colonize almost any site in the body. The clinical manifestations are variable;
  - fatigue,
  - weight loss,
  - weakness
  - and fever are all associated with tuberculosis.
  - a chronic cough productive of sputum, which may be blood-stained as a result of tissue destruction, and necrosis may erode blood vessels which can rupture and causes death through haemorrhage.



Complications

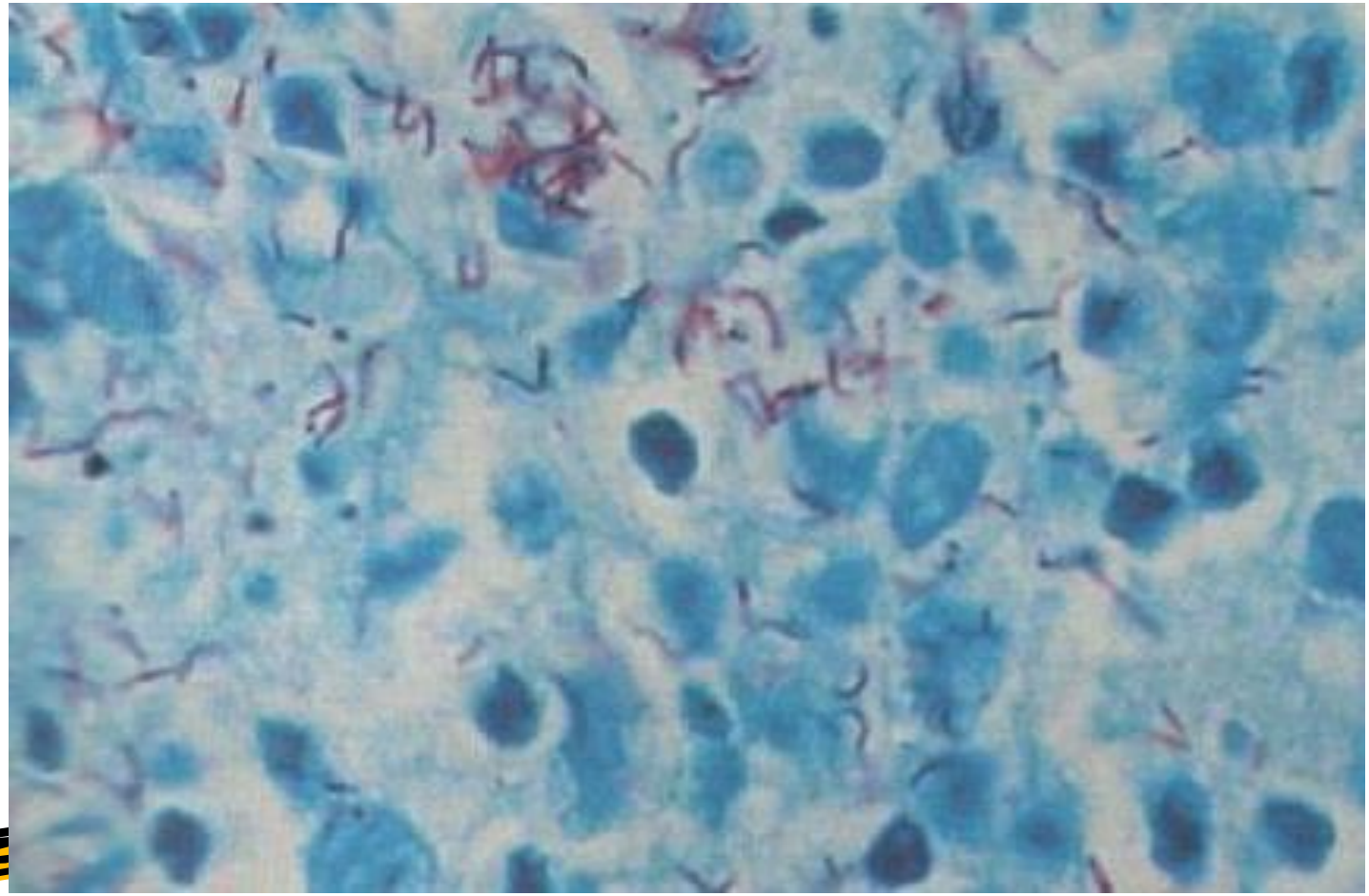
- The complications of *M. tuberculosis* infection of the lungs arise either from **local spread or from dissemination of the organism via the lymphatics and bloodstream to other parts of the body.** This usually occurs at the time of primary infection, and in this way chronic foci are established which may proceed to necrosis and destruction in, for example, the kidney.
- **Alternatively spread may be by extension to a neighbouring part of the lung,** for instance when a tubercle erodes into a bronchus and discharges its contents, or **into the pleural cavity, resulting in a pleural effusion.**



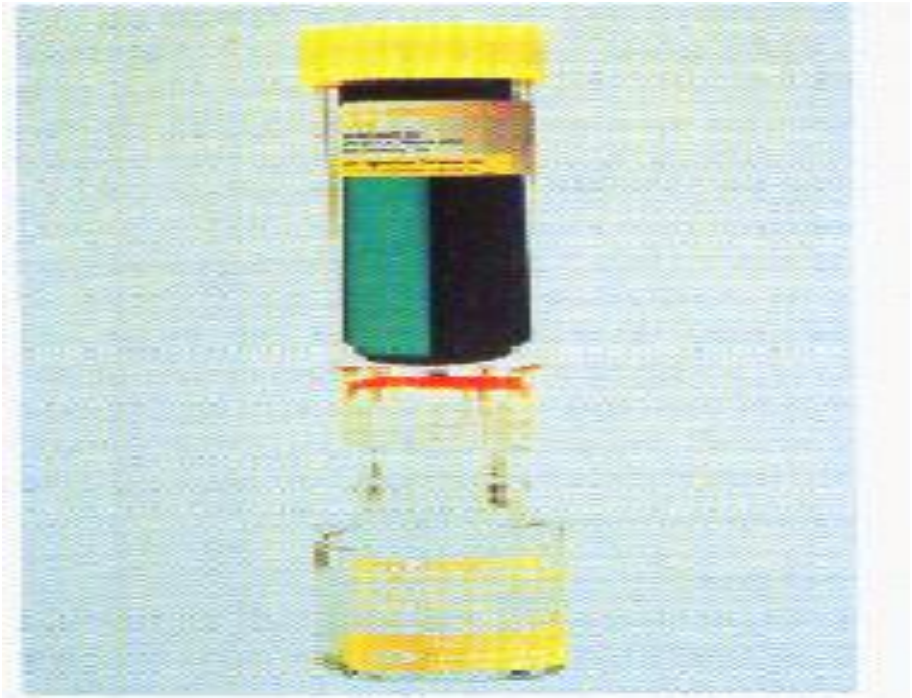
Diagnosis

- The diagnosis of tuberculosis is suggested by the **clinical signs** and symptoms referred to above,
- supported by characteristic **chest x-ray changes**
- and **positive skin test reactivity in the tuberculin (Mantoux) test** .
- These tests are confirmed by **microscopic demonstration of acid-fast rods and culture of *M. tuberculosis***. Microscopic examination of a smear of sputum stained by Ziehl-Neelsen's method or by auramine often reveals masses of acid-fast rods. This result can be obtained within an hour of receipt of the specimen in the laboratory. This is important because *M. tuberculosis* can take up to six weeks to grow in culture (although radiometric methods may reduce the time required for detection) and thus confirmation of the diagnosis is necessarily delayed.
- Further tests are required to identify the species of *Mycobacterium* and to establish susceptibility to antituberculous drugs.

Ziehl Nielsen stain



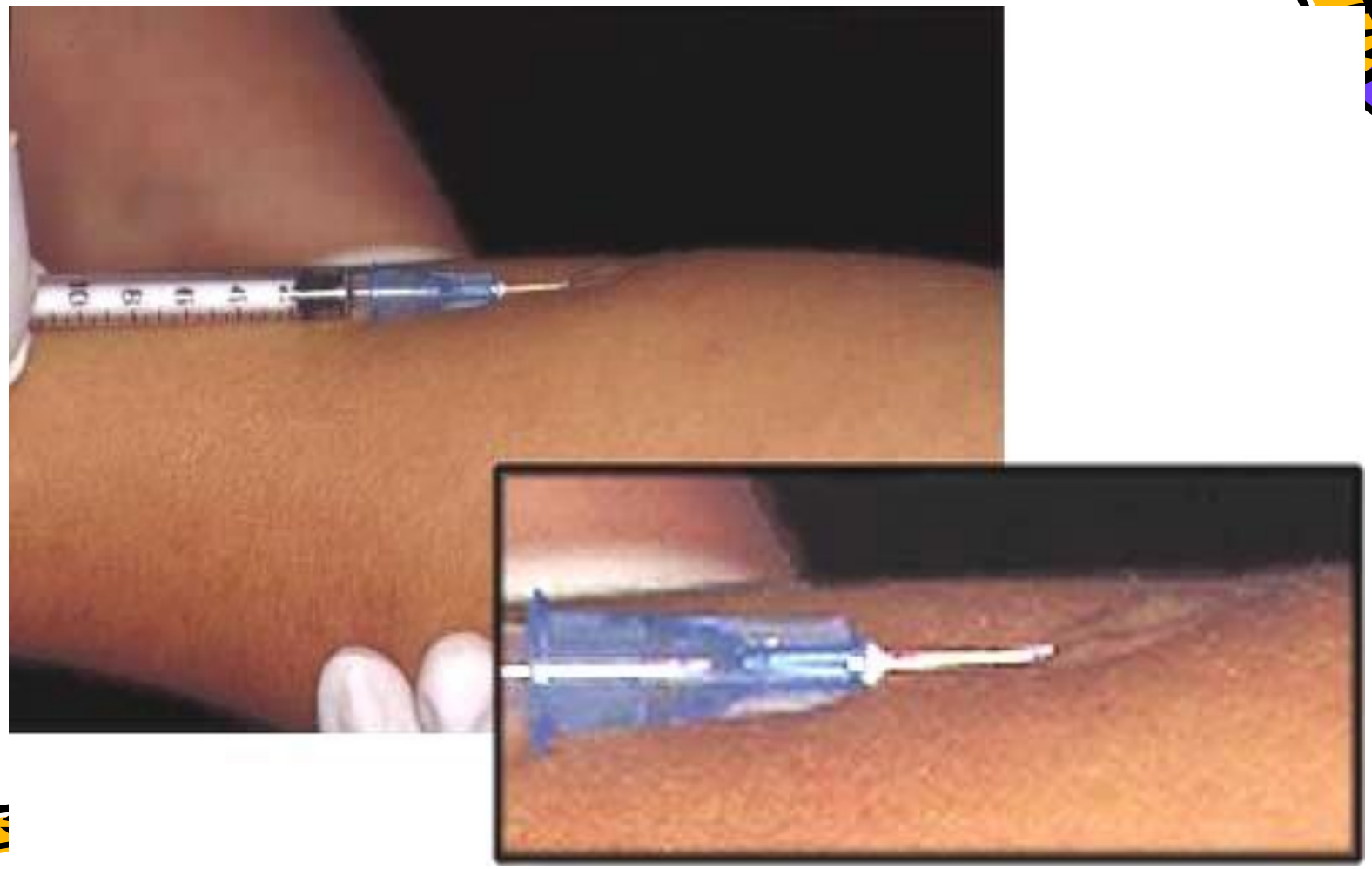
culture

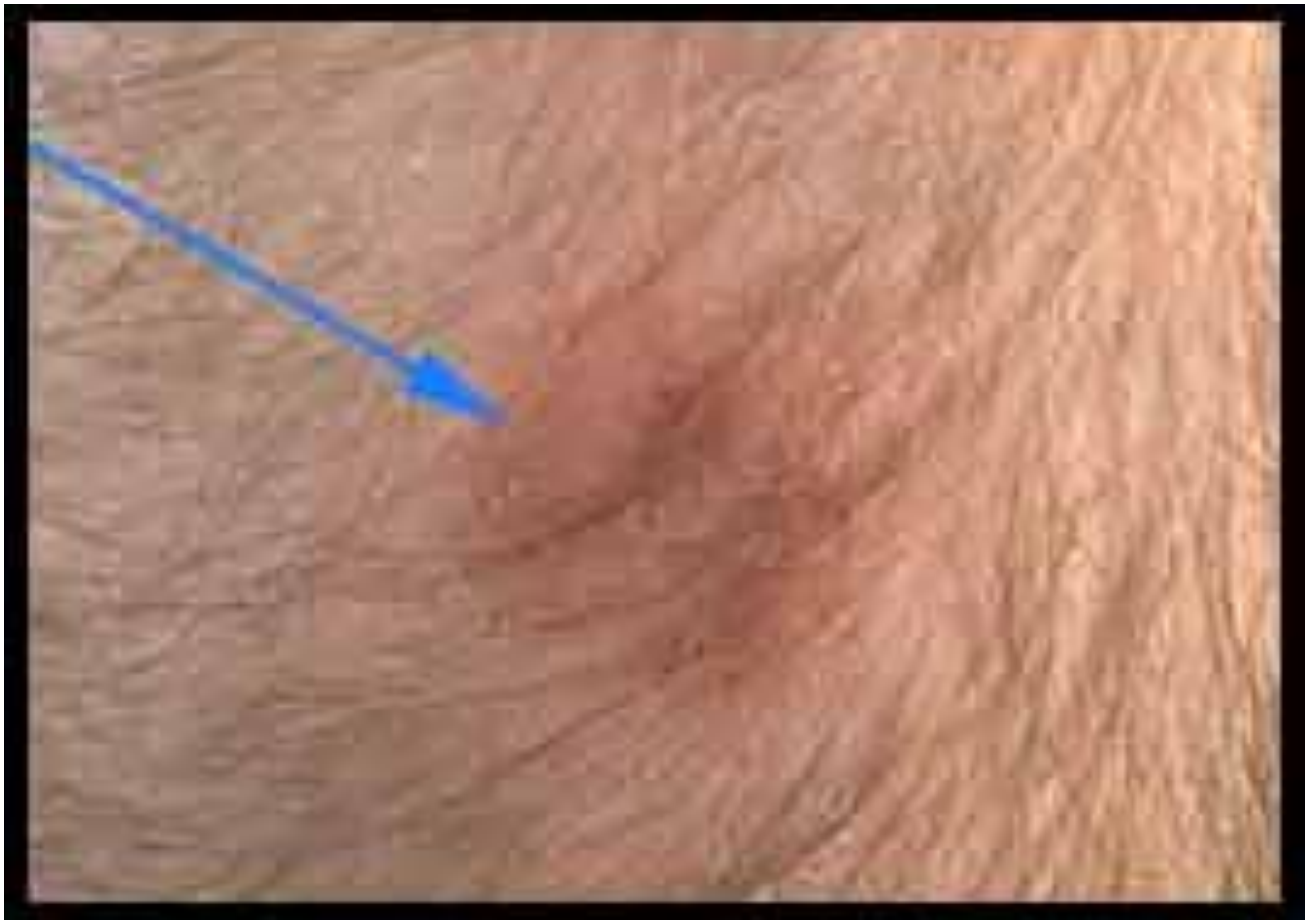


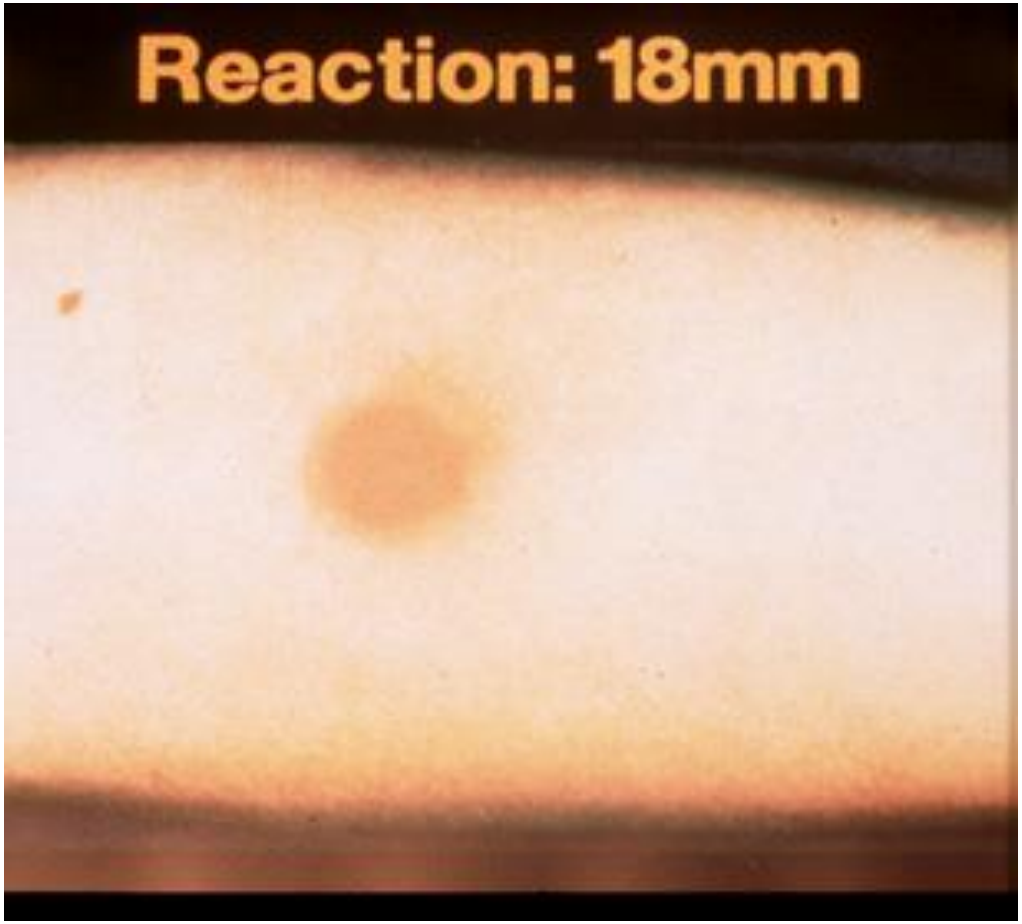
Treatment, Prevention

- Mycobacteria are resistant to most antibacterial agents and specific **antituberculous drugs** have to be used- in ***combination therapy*** (usually three drugs, e.g. isoniazid, rifampin, ethambutol) to prevent emergence of resistance, and ***prolonged therapy*** (minimum 6 months) which is necessary to eradicate these slow-growing intracellular organisms.
- **Immunoprophylaxis.** Immunization with a live attenuatec vaccine, the so-called BCG (bacille Calmette-Guerin) vaccine, has been used effectively in situations where tuberculosis is prevalent. Immunization, which confers positive skin test reactivity, does not prevent infection but it allows the body to react quickly to limit proliferation of the organisms. In areas of low prevalence of disease immunization has largely been replaced by chemoprophylaxis.
- **Chemoprophylaxis-** with isoniazid for one year is recommended for people who have had close contact with a case of tuberculosis. It is also advocated for individuals who show recent conversion to skin test positivity; this is essentially early treatment of subclinical infection rather than prophylaxis.


10 Doses
BCG VACCINE
(FREEZE-DRIED)
Active Immunizing Agent
For Intracutaneous Injection Only.
PASTEUR MÉRIEUX CONNAUGHT



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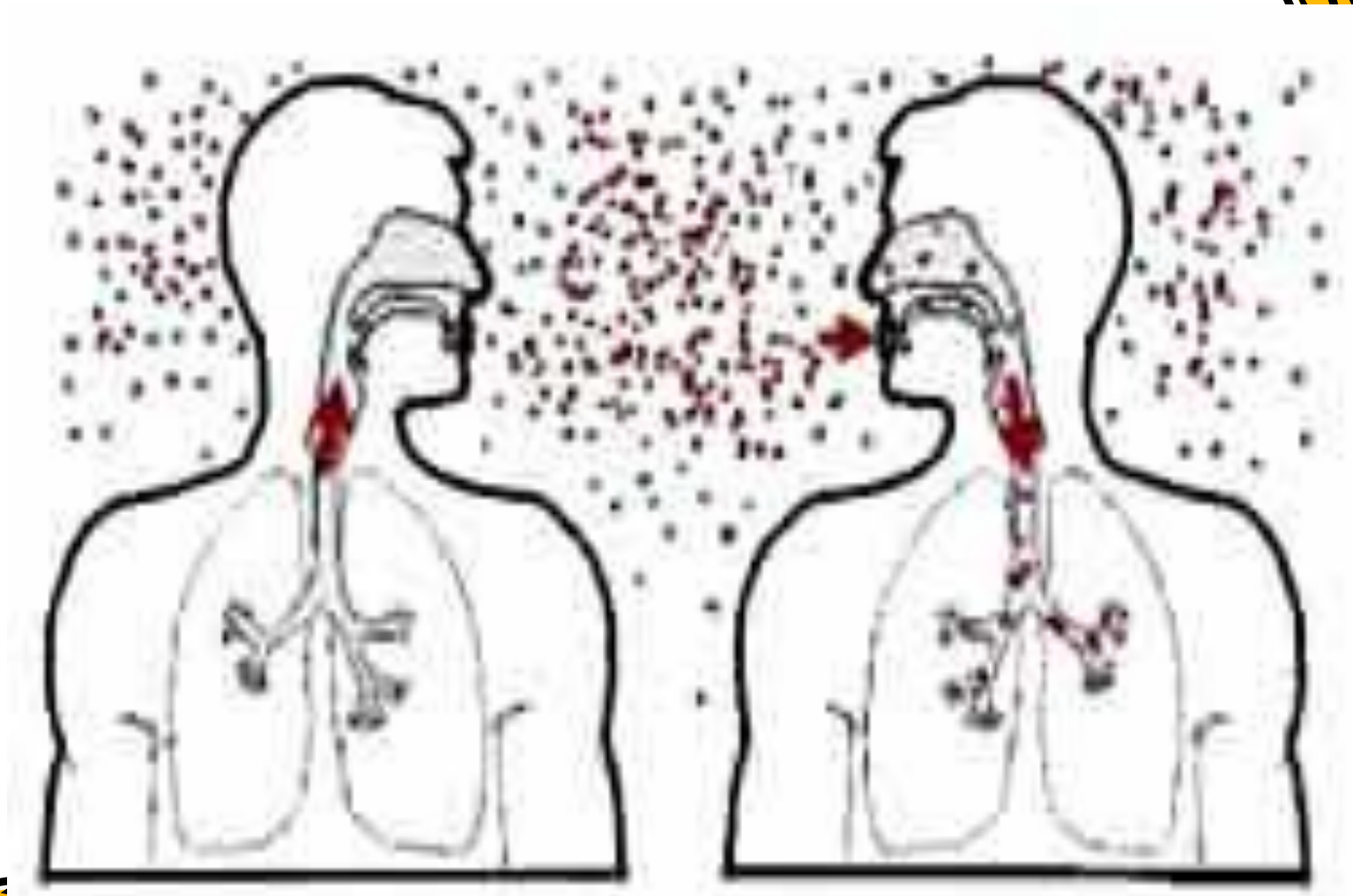


Aspergillosis

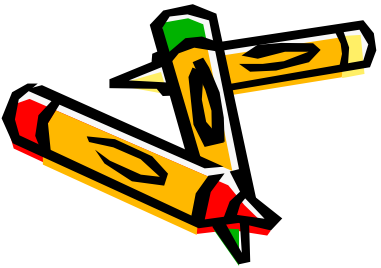
- The genus *Aspergillus* contains many species of fungi which are ubiquitous in the environment.
- They do not form part of the normal flora of man but some species, notably *Aspergillus fumigatus*, are able to cause a range of conditions. These include:
  - **allergic bronchopulmonary aspergillosis** which is, as its name suggests, an allergic response to the presence of aspergillus antigen in the lungs and occurs in patients with asthma.
  - In other patients with preexisting lung cavities or chronic pulmonary disorders, *Aspergillus* may colonize a cavity and grow to produce a fungal ball, a mass of entangled hyphae, called an `**aspergilloma**'. The fungi do not invade the lung tissue but the presence of a large aspergilloma can cause respiratory problems.
  - In the immunosuppressed patient the fungus may invade from the lungs to produce **disseminated disease**.

Cystic fibrosis

- Cystic fibrosis (CF) is **the most common lethal inherited disorder among Caucasians**, with an incidence of approximately 1 in 2500 live births.
- The disease is characterized **by pancreatic insufficiency, abnormal sweat electrolyte concentrations and production of bronchial secretions, with stasis in the lungs and this predisposes to infection.**
- The first invader is ***Staph. aureus*** which causes respiratory distress and lung damage. This can be well controlled by specific anti-staphylococcal chemotherapy. ***Pseudomonas aeruginosa*** *is* the pathogen of paramount importance, often encouraged by its intrinsic resistance to antistaphylococcal agents.
- Most of the lung damage is due to immunological responses to the organisms and to the alginate which forms the mucoid material.

•The third pathogen characteristically associated with cystic fibrosis is **H. *influenzae*,** typically non-encapsulated strains. These organisms may be found in **association with *Staph. aureus* and P. *aeruginosa*;** their pathogenic significance is unclear but they appear to contribute to the respiratory exacerbations experienced by CF patients.

•Although specific antibacterial chemotherapy can reduce the symptoms of infection and improve the quality of life, infections, particularly with P. *aeruginosa*, are impossible to eradicate and are frequently the cause of death in these patients.



Lung abscess

- This is a suppurative infection of the lung, sometimes referred to as `**necrotizing pneumonia**'.
- The most common predisposing cause is **aspiration of respiratory or gastric secretions** as a result of altered consciousness. Thus **the infection is endogenous** in origin and cultures often reveal a mixture of bacteria, with anaerobes such as ***Bacteroides* and *Fusobacterium***.
- Patients with lung abscesses **may have been ill for at least two weeks prior to presentation**.
- They usually produce large amounts of **sputum which if foul-smelling**
- Most **diagnoses** are made from **chest x-rays and the cause confirmed by microbiological investigation**.
- A suitable anti-anaerobic agent such as **metronidazole** should be part of the treatment regimen and treatment may need to be continued for 2-4 months to prevent relapse.

Parasitic infections of the lower respiratory tract

- A number of parasitic infections may localize to the lung, or involve the lung at some stage in their development. Nematodes such as ***Ascaris, Echinococcus granulosus Entamoeba histolytica*** **and the hookworms migrate through the lungs as they move to the small intestine, breaking out of the capillaries around the alveoli to enter the bronchioles**.
- The damage caused by this process, and the development of inflammatory responses can lead to a **transient pneumonitis**. Mild respiratory symptoms may also accompany the migration of schistosome larvae through the lungs.