Respiratory infections

Pavel Drevinek

Layout

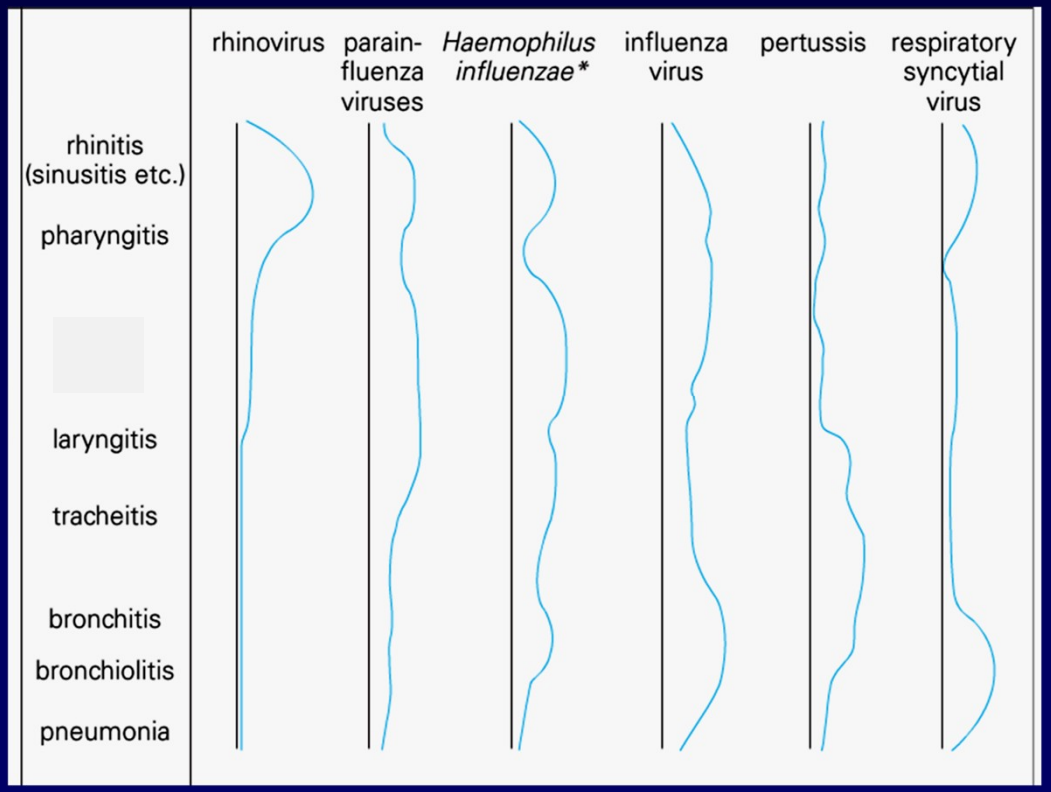
- Introduction
- Material for investigation, examination methods
- Major pathogens
- Upper airway infections incl. tonsillitis and epiglotitis
- Lower airway infections incl. pertussis and diphteria
    - community acquired pneumonia
        - typical agents
        - atypical agents (bacterial, viral)
    - hospital acquired pneumonia

Other: chronic infections, immunocompromised

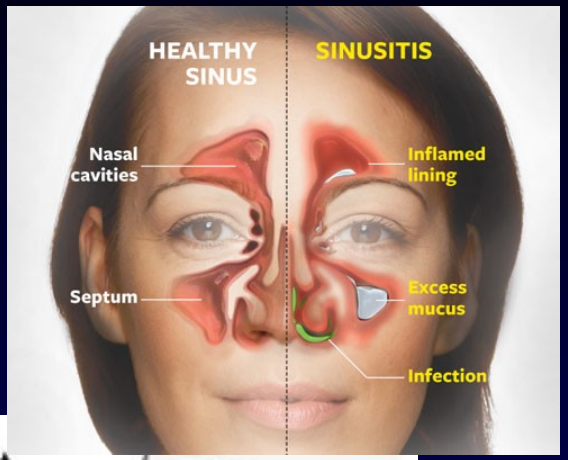
- most common infections worldwide
- often epidemic outbreaks: droplet transmission; direct contact
  seasonal pattern

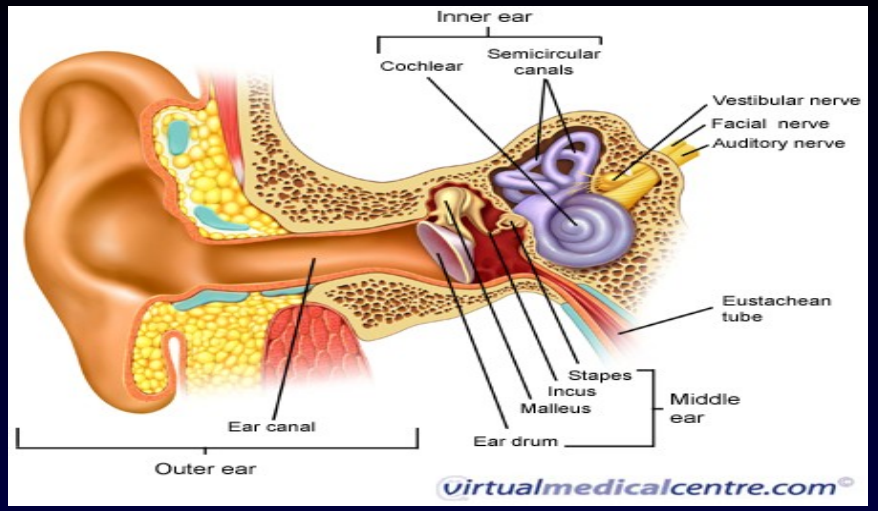
- acute, chronic
- community acquired, nosocomial

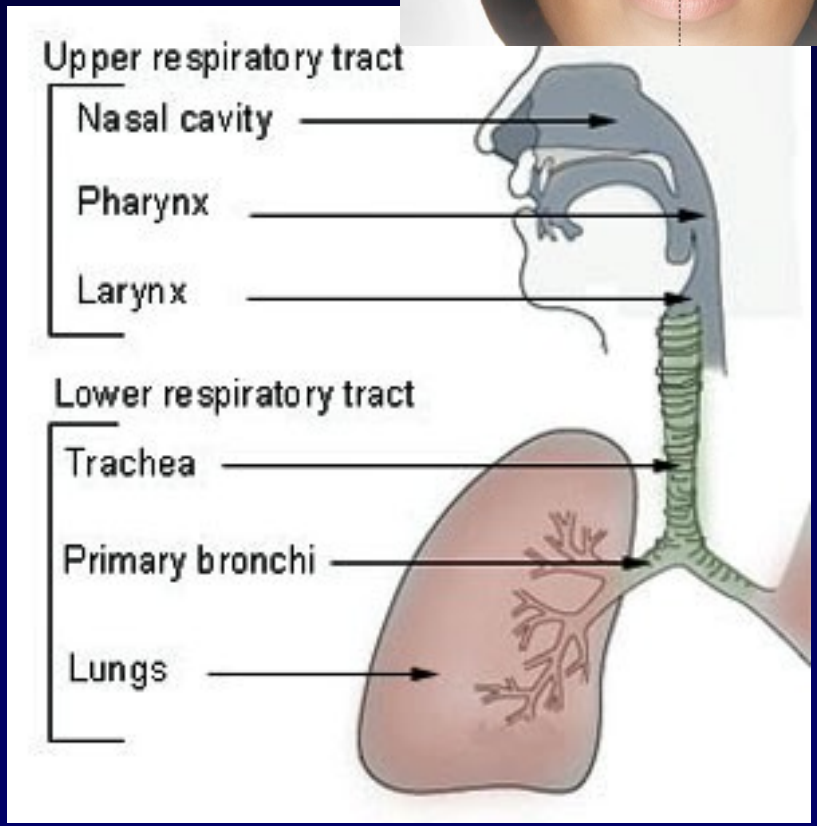
- bacterial, viral (with the risk of bacterial superinfection)
  - the same microorganism can cause various diseases
  - from mild to life threatening

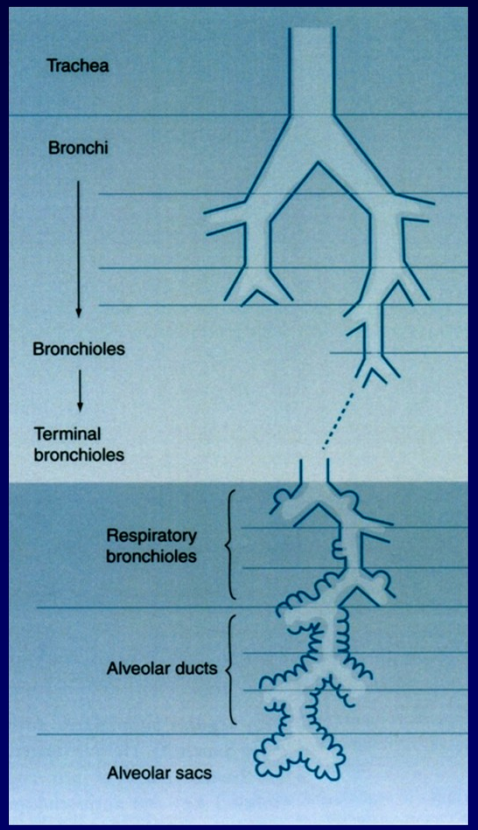


Respiratory tract: anatomy







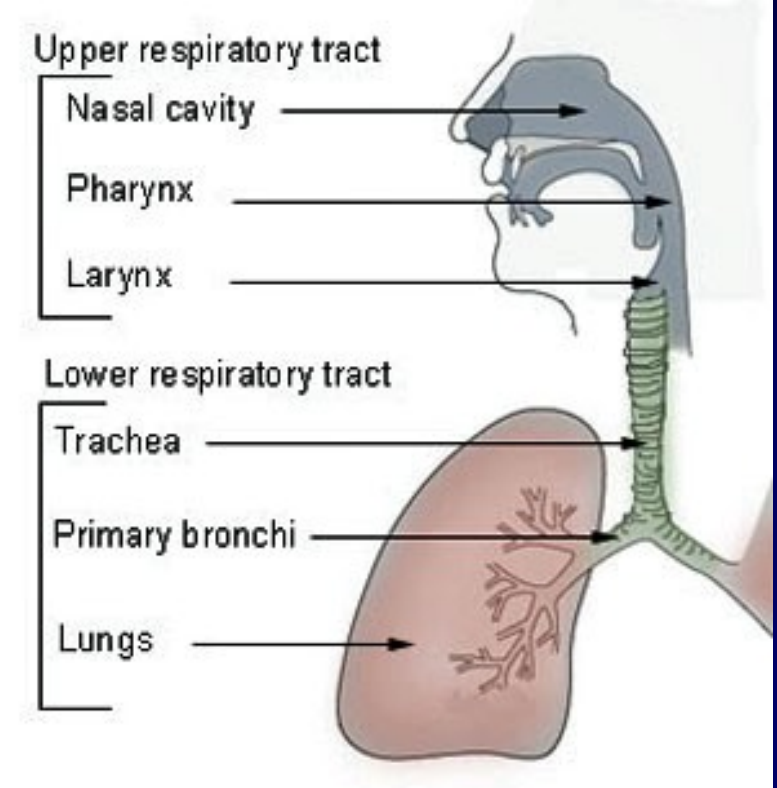


Respiratory tract: one of important ports of entry

- some infections remain there
- some spread further
    - per continuitatem (pneumococcus)
    - via blood (pneumococcus, tuberculosis, measles)
    - systemic effect of toxin (scarlet fever, diptheria, pertussis)

Respiratory tract: naturally colonized

- not every bug means infection (microbiota)



- staphylococci, diphteroids, *S. aureus*
- *H. influenzae*, *S. pneumoniae,*
  viridans streptococci, neisseria, meningococci,
  enterobacteria, candida

- Lung microbiome: streptococci,
haemophilus, anaerobes, pseudomonads
…..

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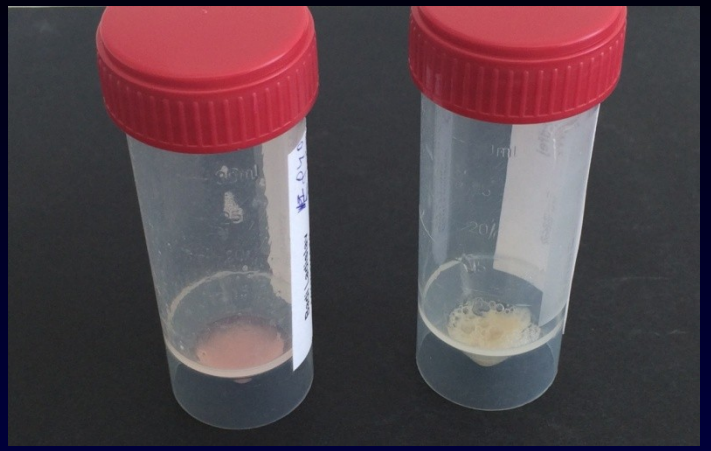
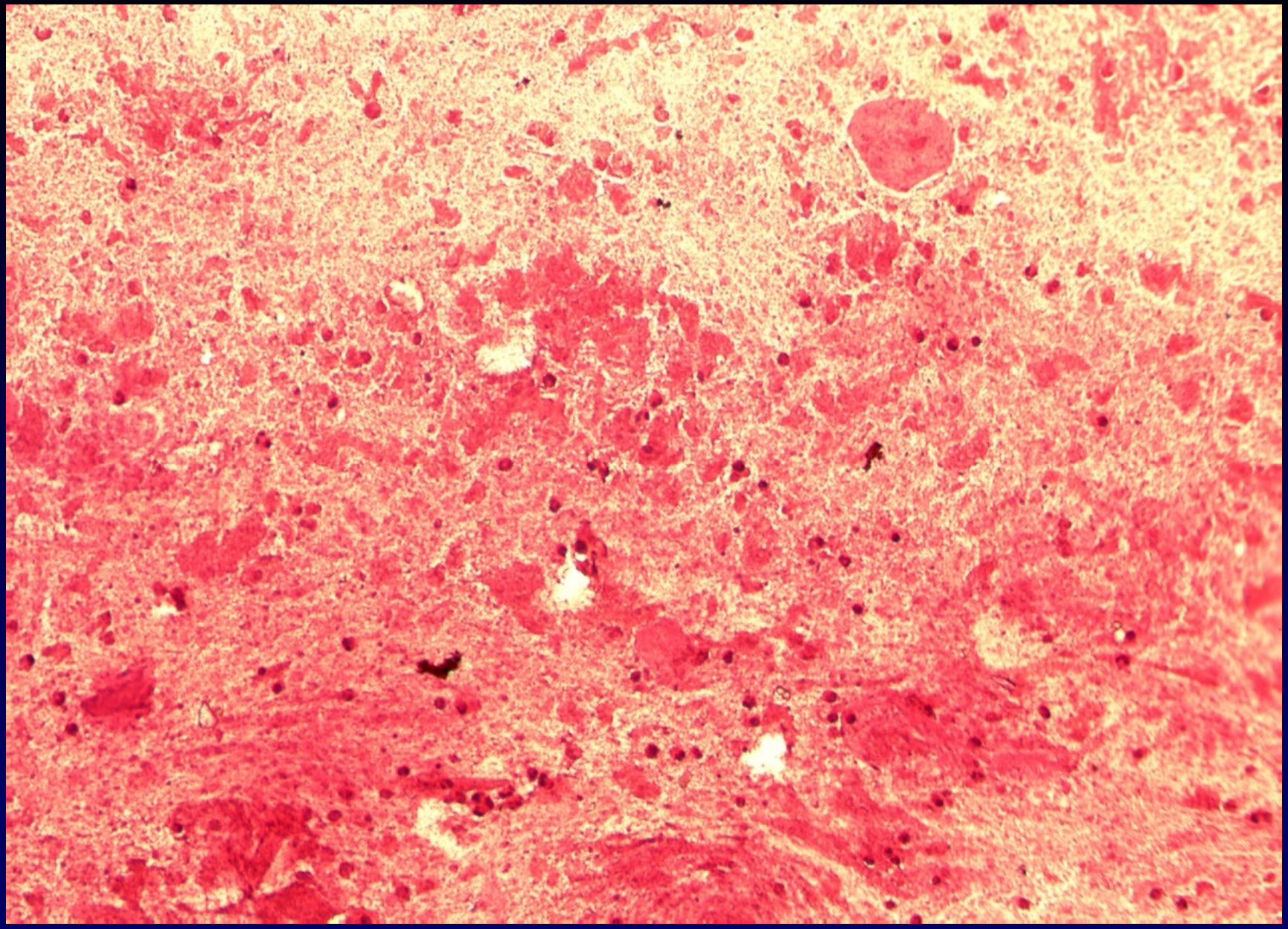
Suitable material for investigation



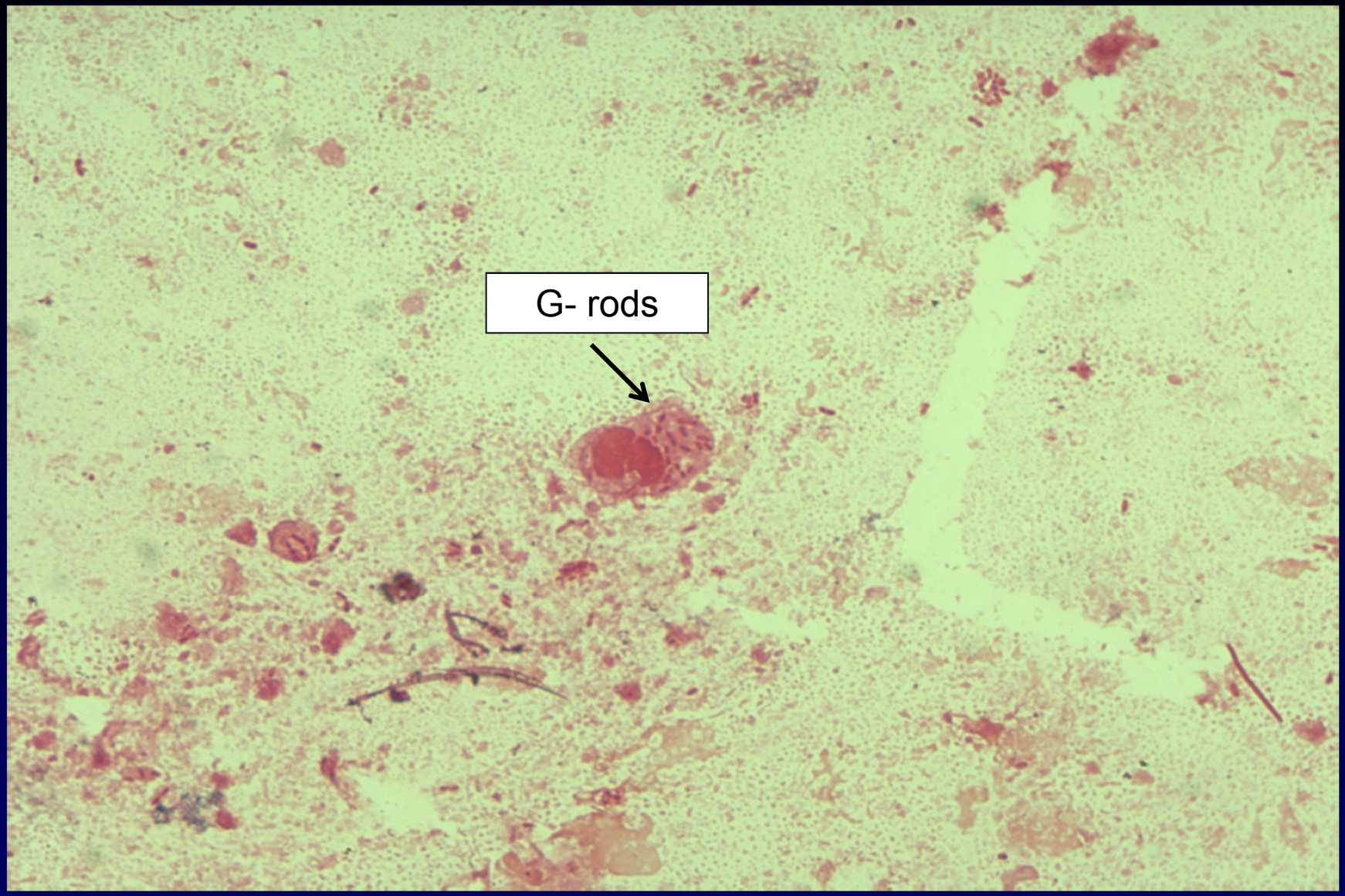
- SPUTUM

  - microscopy (to validate sputum)
  - culture (incl. quantification)
  - molecular genetics in certain cases

- Induced sputum



zoom 10x10

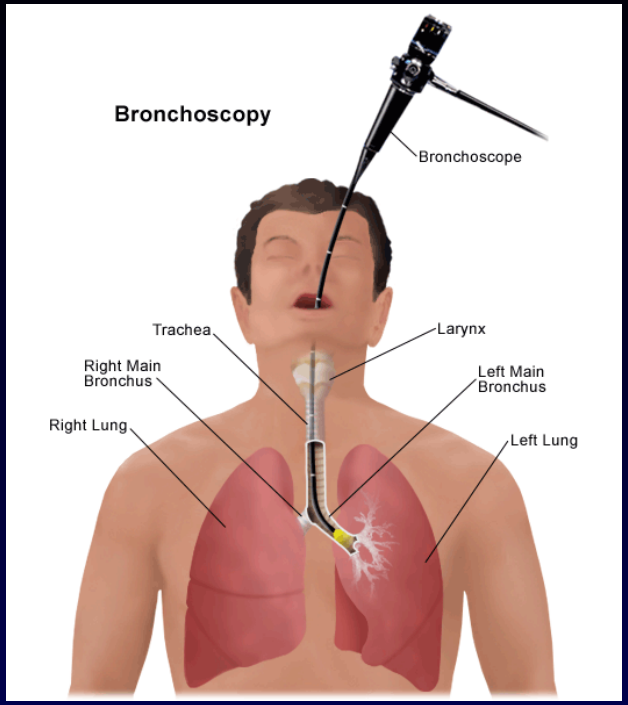


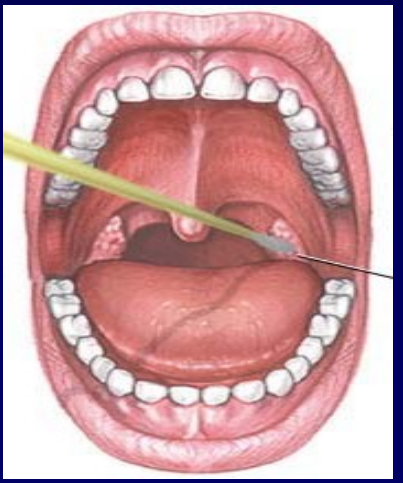
zoom 10x100

- bronchoalveolar lavage (BAL)
  - microscopy, culture, PCR
  - Ag of molds

- throat/cough swab
  - culture
  - Ag (Strep test)

- nasopharyngeal swab
  - viral dg. (PCR)
  - pertussis





- urine
  - pneumococcal Ag (in children low PPV)
  - legionella Ag

- serum
  - mold Ag (glucan; galactomannan ~ aspergillus)
  - antibodies (chlamydia, mycoplasma, pertussis, flu, herpesviruses)

- blood cultures

- pleural fluid

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Key players

Viruses, called respiratory viruses:

orthomyxoviruses: influenza A, B
paramyxoviruses: parainfluenza PIV 1-4, RSV,
metapneumovirus hMPV, measles
picornaviruses: rhinovirus HRV; coxsackie and echovirus (= enteroviruses!)
adenoviruses
coronaviruses HCoV

Bacteria:

S. pneumoniae
H. influenzae
C. pneumoniae
M. pneumoniae
S. aureus
L. pneumophila
M. tuberculosis, NTM

B. pertussis, B. parapertussis
C. diphteriae

Nosocomial infections:
P. aeruginosa
other G- non-fermenters
enterobacteria

Fungi: *Aspergillus* spp., *Pneumocystis jiroveci*

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Rhinitis

• rhinoviruses (also others – e.g. coronaviruses)
mucoid secretion is not a sign of bacterial infection

Sinusitis, otitis media

• viruses
• *S. pneumoniae*, *H. influenzae*, *M. pneumoniae*, *M. catarrhalis*, anaerobes

otitis in young children
complications - mastoiditis, risk of meningitis

Th: amoxicillin

Tonsillopharyngitis

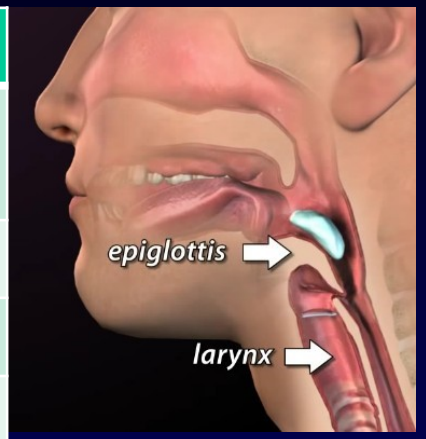
- adenoviruses, EBV
- *S. pyogenes*
- streptococci groups C, G
- *Arcanobacterium heamolyticum*
- *N. gonorrhoeae*

in GAS scarlet fever (when exotoxin is produced)
rheumatic fever (alteration of mitral valve, arthritis, chorea minor, erythema)
glomerulonephritis
peritonsillar abscessus

Th: PNC V for 10 days

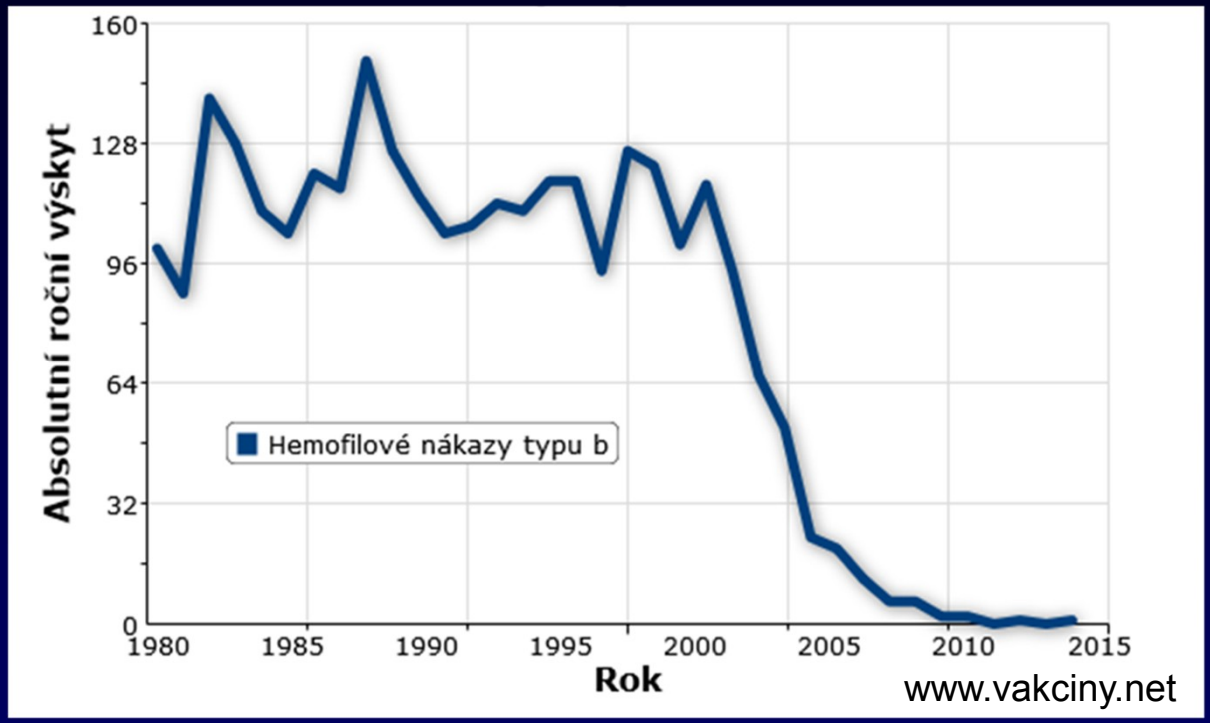
epiglottitis versus laryngitis (subglotic laryngitis, laryngotracheitis)

Epiglottitis	Croup, pseudocroup
H. influenzae type b	viruses (parainfluenza)
rapid onset	upper airway infection
no cough, stridor	barking cough, stridor
fever above 38 deg.	temp below 38 deg.
no swallowing, anxiety	
blood cultures	
swab from epiglottis questionnable	
ATB th! aminoPNC, cephalosporins II., III. gen.	



Invasive *H. influenzae* type b in CR

1999: 54x meningitis, 36x epiglottitis, 6x sepsis, 5x pneumonia



BUT: other groups of *H. influenzae* still out there

H. influenzae non-typeable, types e, f

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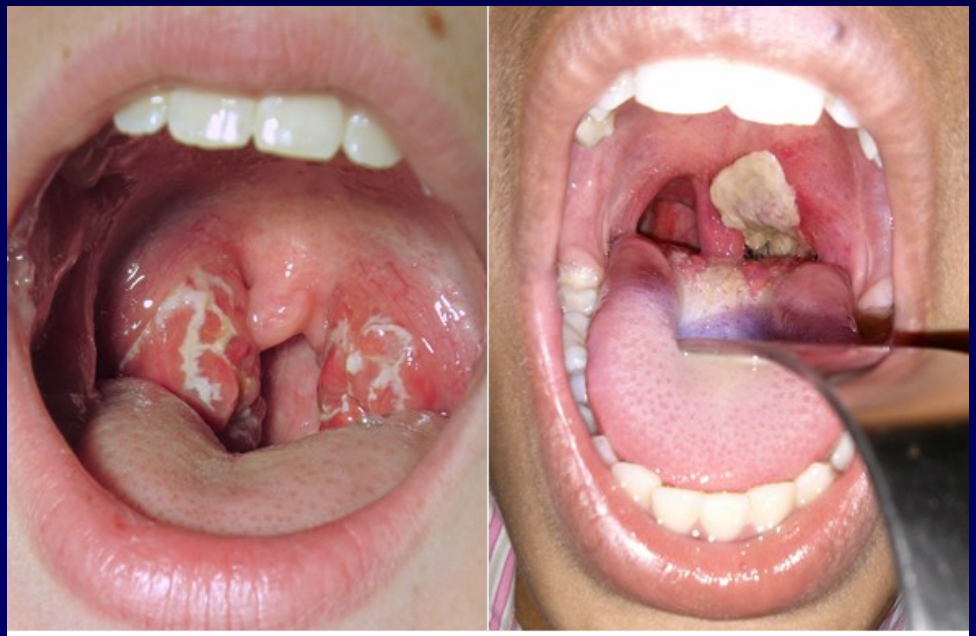
Diphteria

Corynebacterium diphteriae (and other corynebacteria) with production of the toxin (the evidence by PCR)

- tonsillitis, pharyngitis
- laryngitis (true croup) with production of pseudomembranes

- myocard alteration
- neurological problems



Tonsillitis Diphtheria

Pertussis

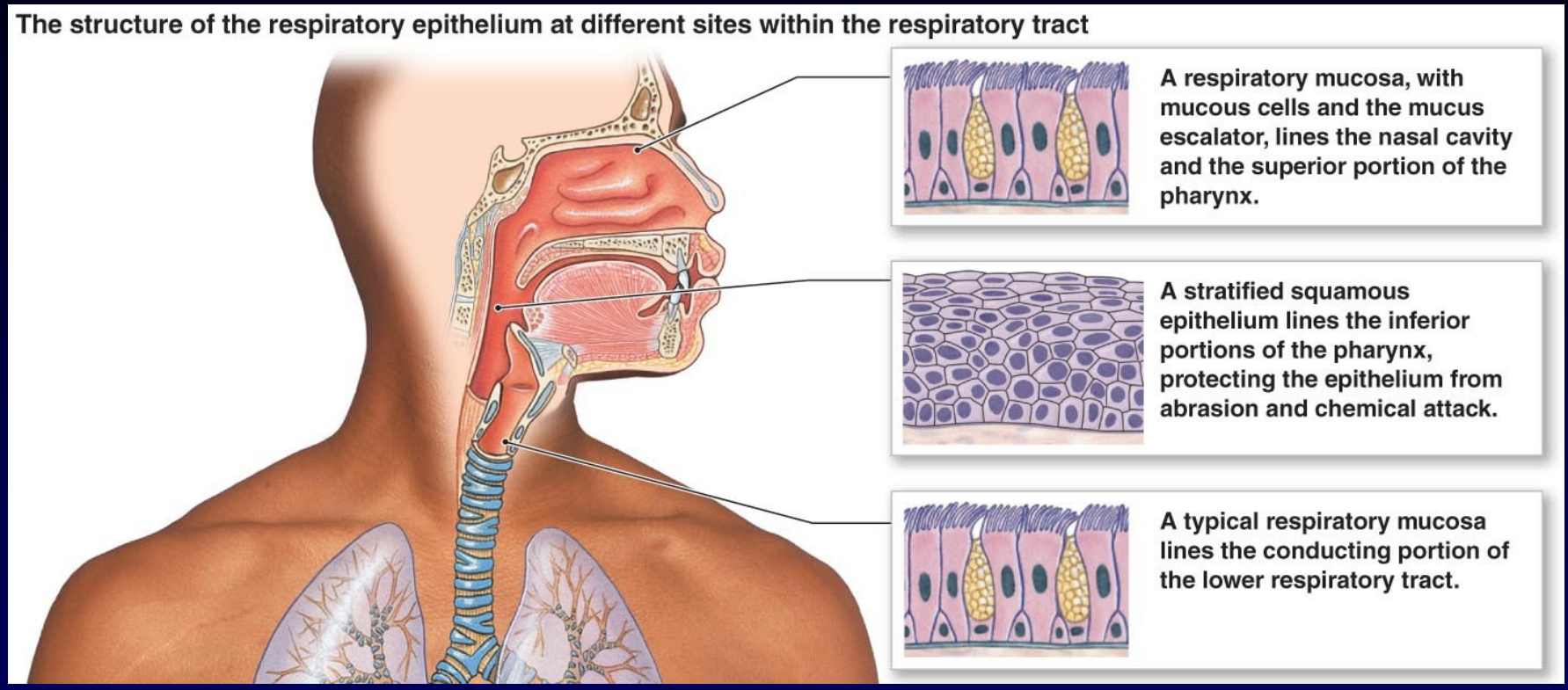
Bordetella pertussis, B. parapertussis

Disease stages:

- catarrhal (common cold)
- paroxysmal (paroxysmal cough, dyspnoe, vomiting)
- convalescent (risk of secondary infections, encephalopathy)

- today more likely atypical course (persistent cough in adults)
- in infants (non-vaccinated) a risk of malignant pertussis:
  - respiratory failure
  - leukocytosis and right-sided heart failure
  - encephalopathy

Dg: culture, PCR, serology



non-invasive disease affecting ciliated epithelium

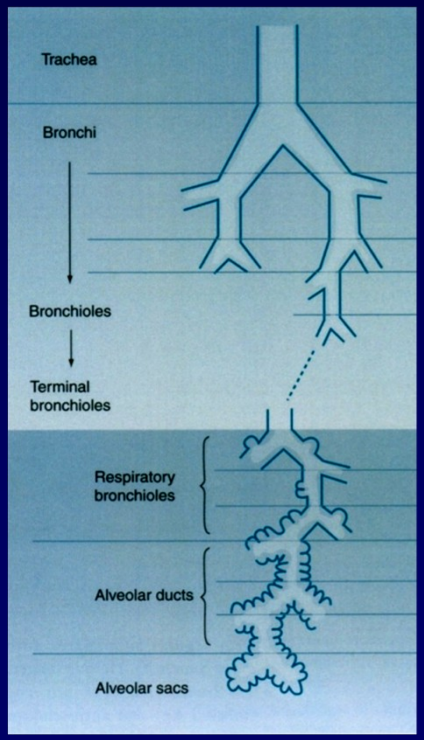
→ nasopharyngeal swab, aspirate

Bronchiolitis (obliterans)

respiratory syncytial virus RSV-A, RSV-B

- in children below 6 months of age, preterm babies
- serious condition

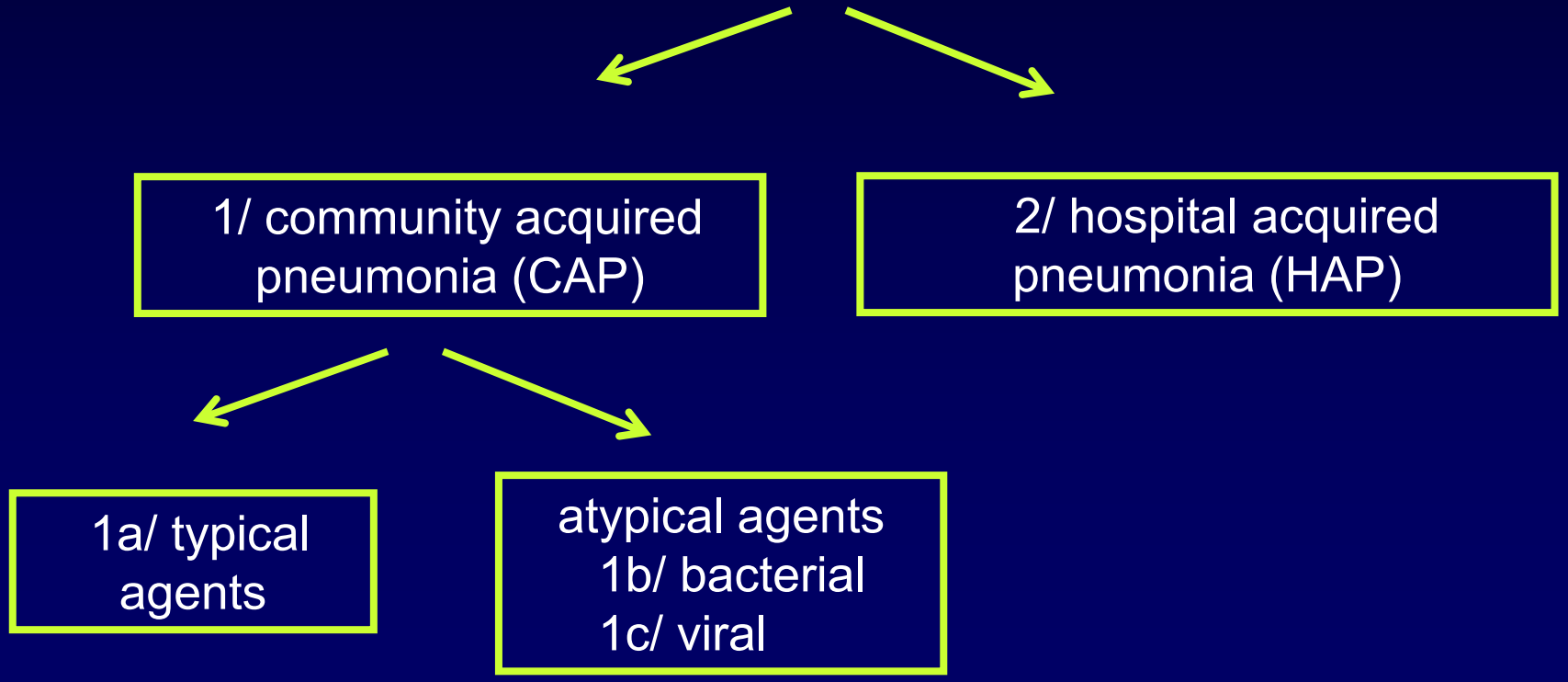
Th: ribavirin + passive immunization (Ab against F protein)



Pneumonia

• infectious condition with corresponding respiratory symptomatology (cough, tachypnoe, dyspnoe, …) and the fresh radiological finding on lungs

• inflammation affecting alveoli, respiratory bronchioli (bronchopneumonia), or also interstitium



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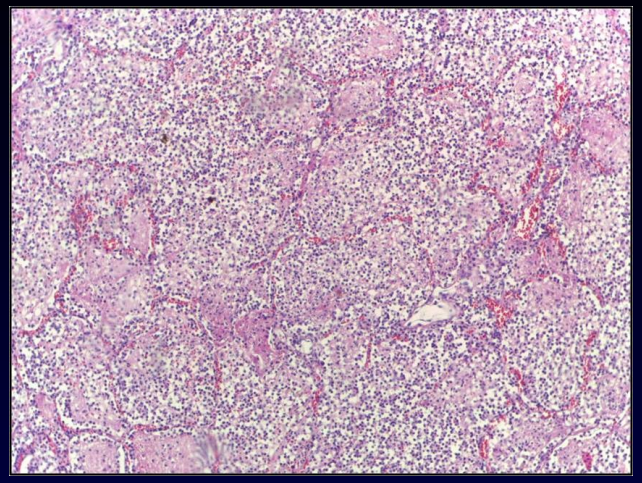
1a/ CAP with typical pathogens



- *S. pneumoniae* (most common)
- *H. influenzae*
- *Moraxella catarrhalis*
- *S. aureus* (secondary pneumonia; production of PVL)
- *K. pneumoniae, E.coli*

Diagnostics: direct methods

- sputum
  - microscopy, culture
  - PCR occasionally
- detection of pneumococcal antigen in urine
- blood cultures

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1b/ CAP with atypical pathogens

sometimes termed atypical pneumonia, walking pneumonia,
several weeks cough

- *Mycoplasma pneumoniae*: former primary atypical pneumonia
- *Chlamydophila pneumoniae*
- *Chlamydophila psittaci*: psittacosis
- *Coxiella burnetii*: Q fever

Diagnostics: indirect methods
- serology; careful interpretation (up to 80% prevalence in healthy)

direct method - PCR

- *Legionella pneumophila*
  - pontiac fever (mild infection, not pneumonia)
  - Legionnaire's disease

Legionella pneumophila

Diagnostics:
- detection of legionella antigen in urine
- culture
- PCR

- serology

24 year old lady
5 days fever 40 ^{o}C, vomiting
3 days cough, with sputum, dyspnoea

CRP 153 mg/l
WBC 8.2x10^{9} /l
x ray: small infiltrates on the bottom right

Microbiology:
urine: antigen S. pneumoniae neg.
antigen L. pneumophila neg.

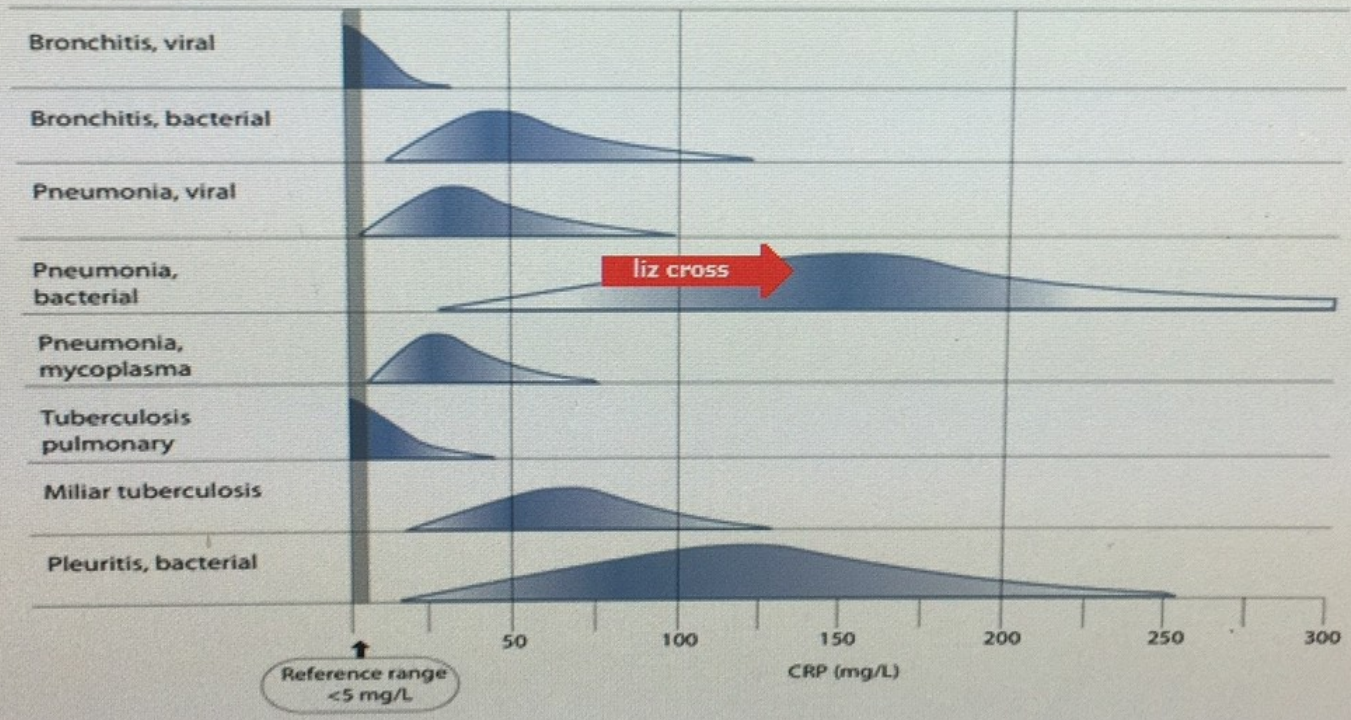
nasopharyngeal swab:

M. pneumoniae	****
C. pneumoniae	neg
C. psittaci	neg
L. pneumophila	neg
P. jiroveci	neg

7 days since the start of therapy with fluorochinolons:
mild cough, no temperature
CRP 12.3 mg/l
x ray: substantial regression of the infiltrates

CRP LEVELS IN LOWER RESPIRATORY TRACT INFECTION

Typically higher values in bacterial infections than in viral infections



ATB therapy of CAP

Pneumococcal pneumonia:

- non complicated - amoxicillin (not hospitalized)
- hospitalization - PNC G or cephalosp. III. gen.

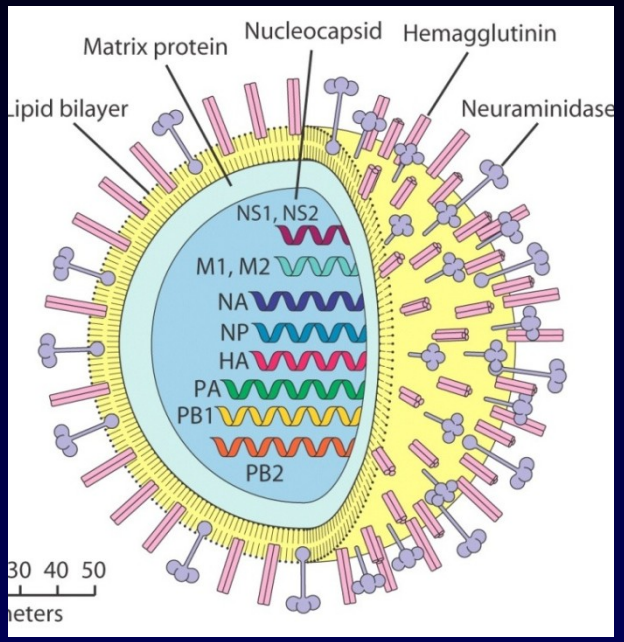
Atypical agents:

- macrolides
- tetracyclines
- respiratory fluoroquinolons (moxifloxacin)

1c/ CAP with atypical pathogen - virus

Influenzavirus type A, B, C

subtypes HxNx (H1N1, H3N2)



Spanish flu 1918 - 1919

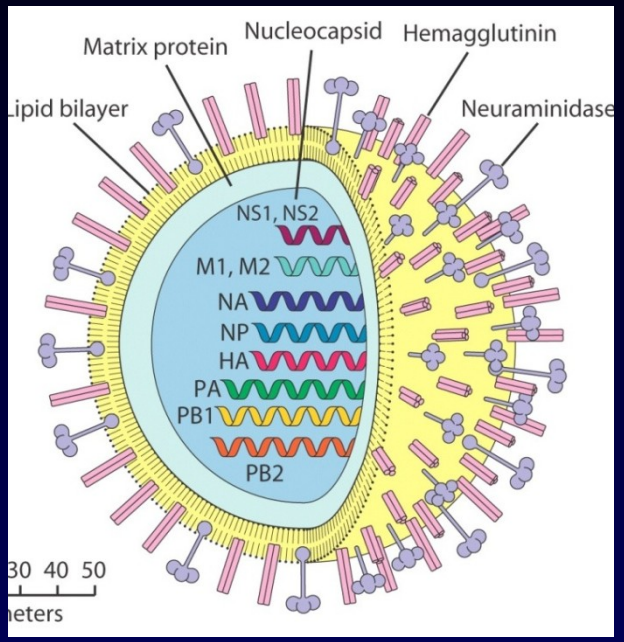
20 - 50 mil. deaths

The Family, 1918 Egon Schiele

1c/ CAP with atypical pathogen - virus

Influenzavirus type A, B, C

subtypes HxNx (H1N1, H3N2)



- tracheobronchitis
- pneumonia
  - primary viral
  - secondary bacterial

Diagnostics:

- antigen detection (low sensitivity)
- PCR

- serology

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2/ HAP

develops min. 48 hours post admission and in association with hospitalization

typically of bacterial origin

Ventilator associated pneumonia (VAP)

secondary colonization of lower airways

- from upper airways and the gut
- from the outside (via personnel)

Early onset (by day 5)

- *S. aureus*
- *S. pneumoniae*
- *H. influenzae*
- *K. pneumoniae, E. coli*

Late onset

- *K. pneumoniae, E. coli …*
- *P. aeruginosa*
- MRSA
- *A. baumannii*

Diagnostics: endotracheal aspirate

(careful interpretation – colonization vs. infection)

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Newborn pneumonia

- *S. agalactiae*
- *Chlamydia trachomatis*

- *K. pneumoniae, E. coli*

Chronic respiratory diseases and chronic infections

- chronic obstructive pulmonary disease (COPN)
- chronic bronchiectasis
- cystic fibrosis (mucoviscidosis)

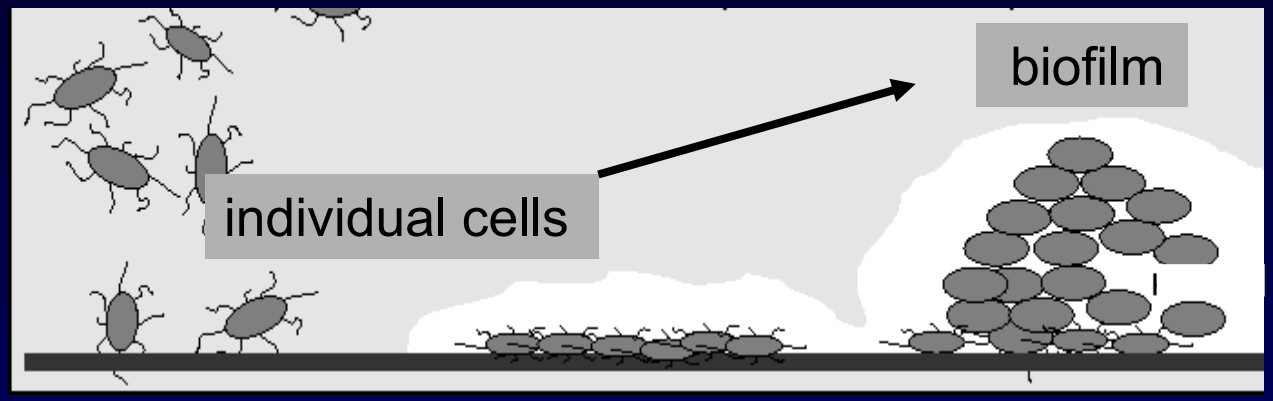
Exacerbations

= worsening of the condition that requires the change of therapy (ATB)

- usual pathogens (respiratory viruses)
- opportunistic pathogens with resistant phenotype, chronic infections

    - *S. aureus*
    - enterobacteria (*K. pneumoniae*)
    - G- nonfermenters
        - *P. aeruginosa*
        - complex *B. cepacia*
        - *Stenotrophomonas maltophilia*
        - *Achromobacter xylosoxidans*

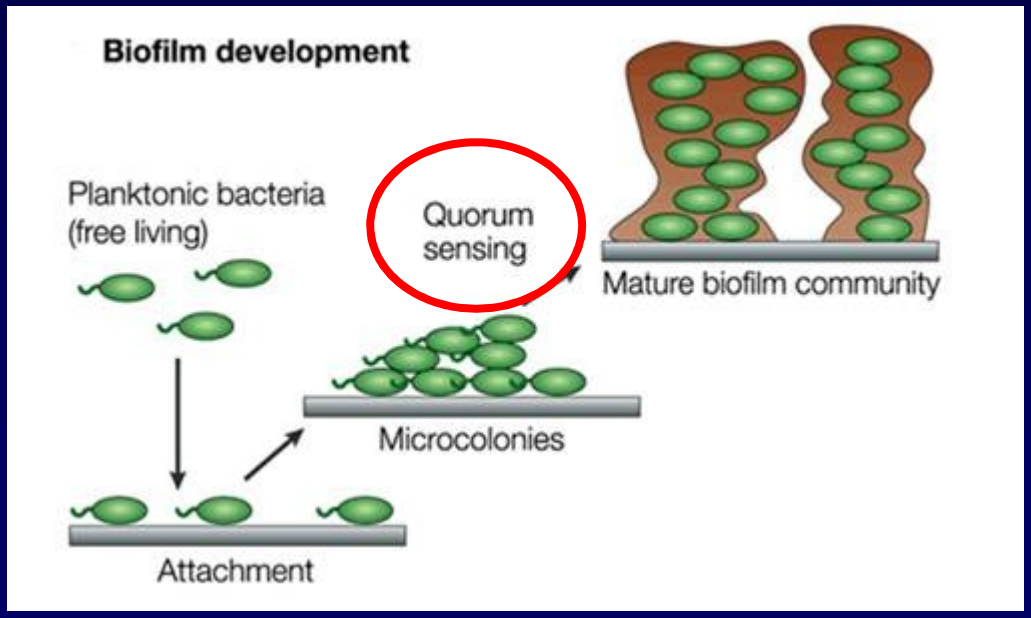
Infection course

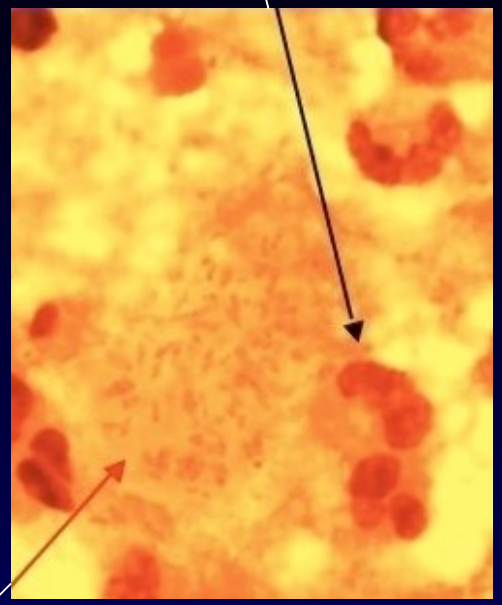


Biofilm

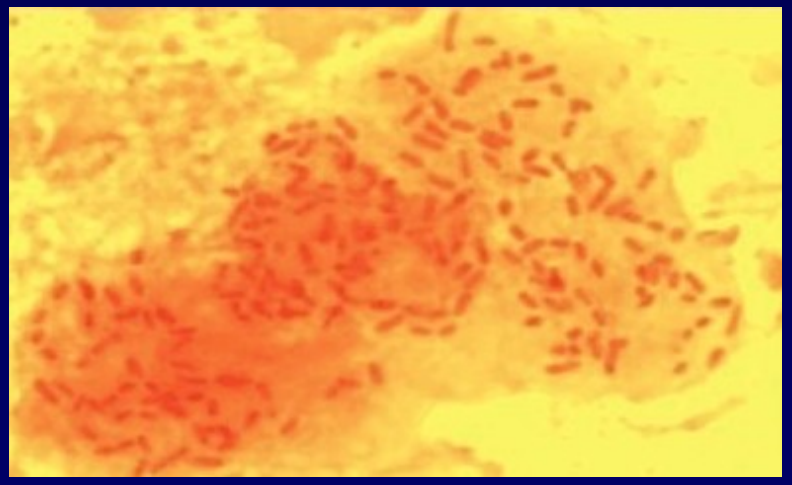
- Aggregate of bacteria embedded in matrix which they produce themeselves (polysaccharides, proteins, DNA)

- Protection against phagocytosis, ATB





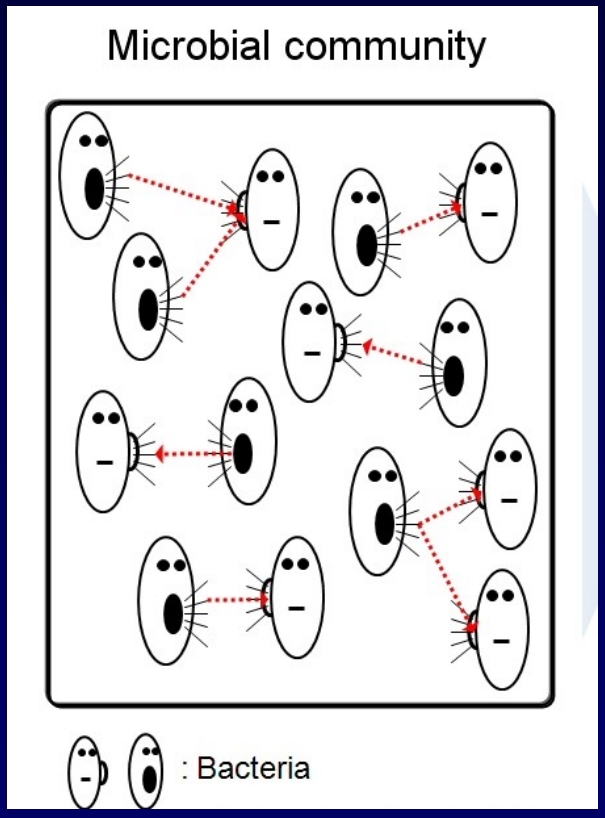
P. aeruginosa biofilm

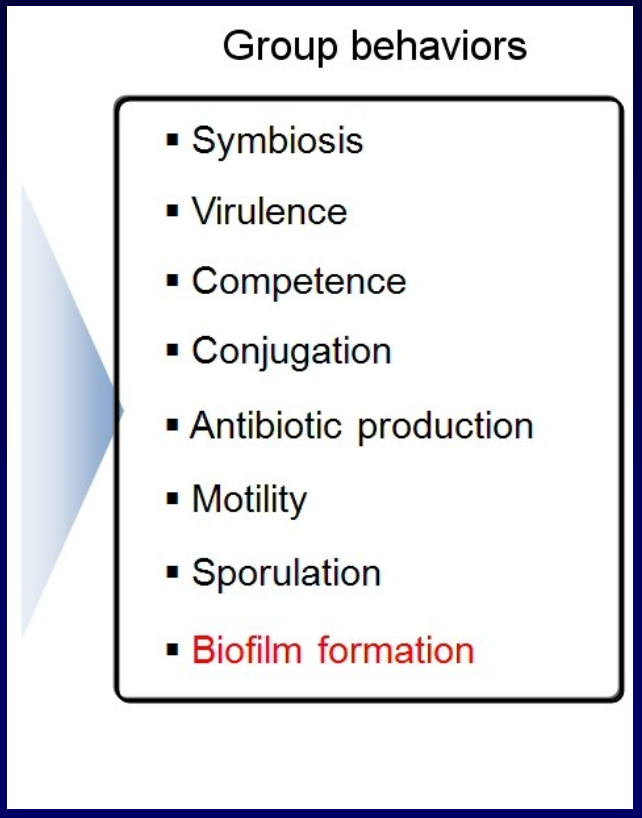


Courtesy: Prof. N. Hoiby, Copenhagen

Quorum sensing

- Cell to cell communication
- Perception of their density, mass
- Synchonizing their behaviour





Immunocompromised and respiratory infections

- haematological malignancies
- AIDS
- after solid or bone marrow transplantation

Oportunistic pathogens of both endogenous and exogenous origin

- CMV
- TB, NTM
- *Pneumocystis jiroveci* (also preterm babies); microscopy, PCR
- fungi

2-month old girl

10 days cough, increased mucus, temperature max. 37.5 ^{o}C
x ray: difuse gentle infiltrates

Microbiology:
culture apirate from upper airways: S. aureus; K. oxytoca

PCR nasopharyngeal swab:
respiratory viruses all neg.

M. pneumoniae	neg
C. pneumoniae	neg
L. pneumophila	neg
P. jiroveci	**

BAL:

M. pneumoniae	neg
C. pneumoniae	neg
L. pneumophila	neg
P. jiroveci	****

Therapy:
Ampicillin/sulbactam --> cotrimoxazol