Respiratory infections

Pavel Drevinek
Department of Medical Microbiology

2nd Faculty of Medicine, Charles University
Motol University Hospital

Layout

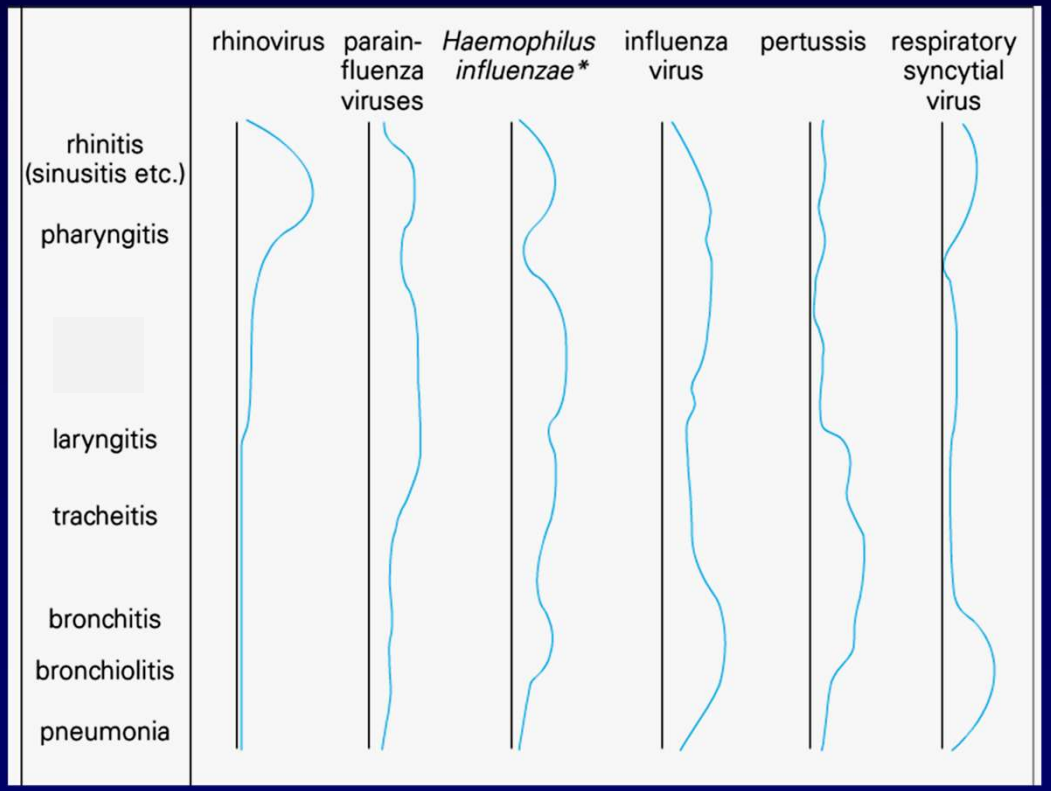
- Introduction
- Material for investigation, examination methods
- Major pathogens
- Upper airway infections
- Lower airway infections
    - community acquired pneumonia
        - typical agents
        - atypical agents (bacterial, viral)
    - hospital acquired pneumonia

Other: chronic infections, immunocompromised

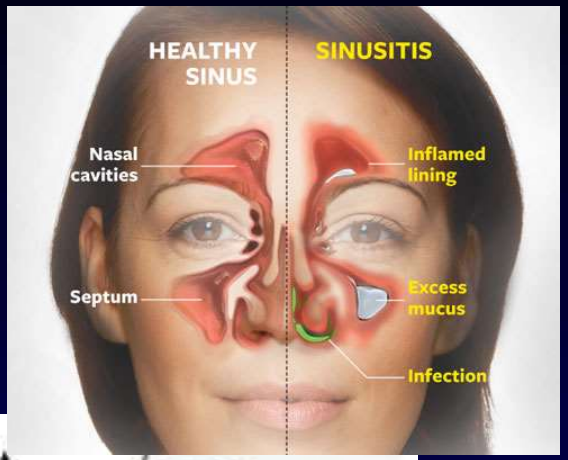
- most common infections worldwide
- often epidemic outbreaks: droplet transmission; direct contact
  seasonal pattern

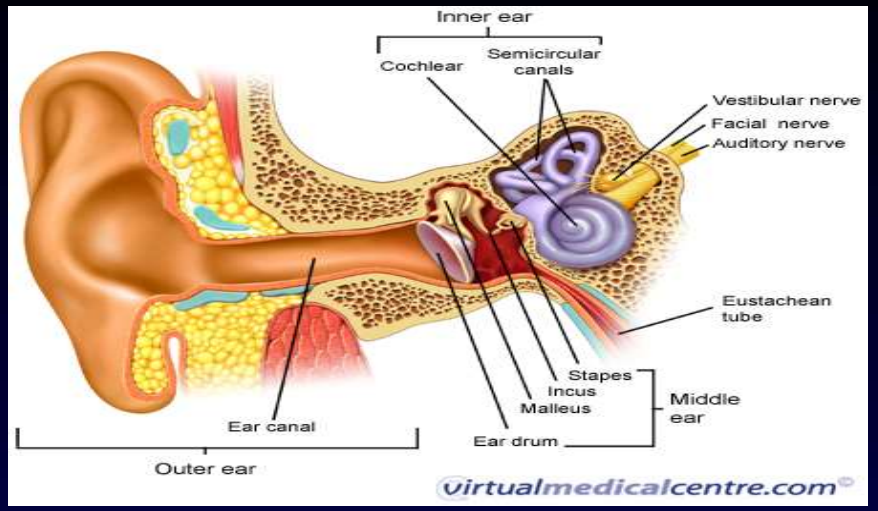
- acute or chronic
- community acquired or nosocomial

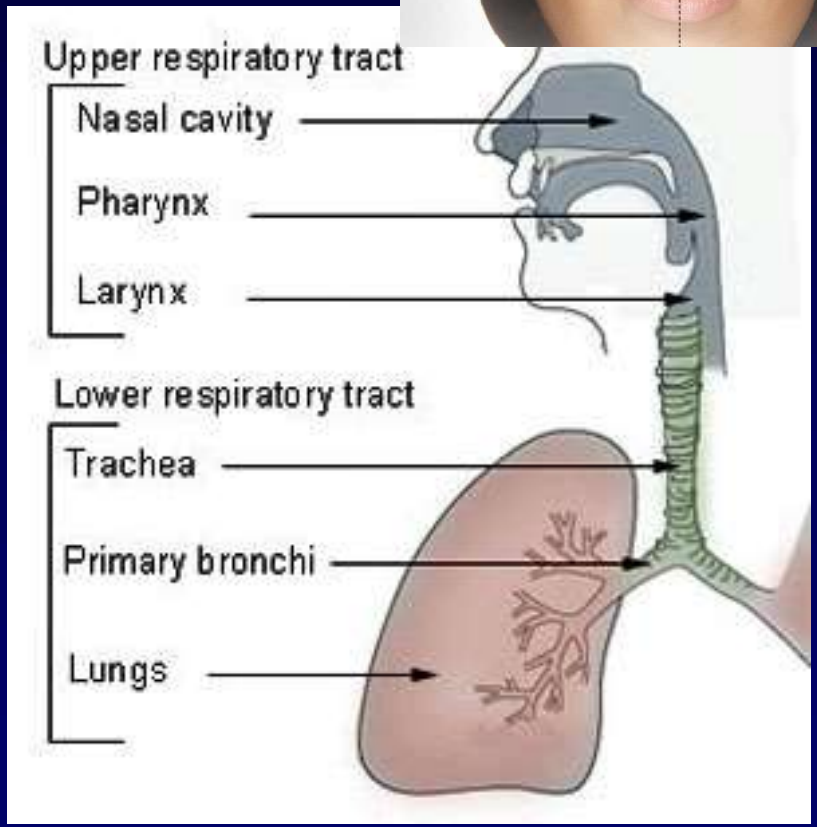
- bacterial or viral (with the risk of bacterial superinfection) ... or fungal
  - the same microorganism can cause different diseases
  - from mild to life threatening



Respiratory tract: anatomy







Conductive zone:

Cilia, mucus (submucosal glands)

Anaerobic growth conditions
- inside sputum

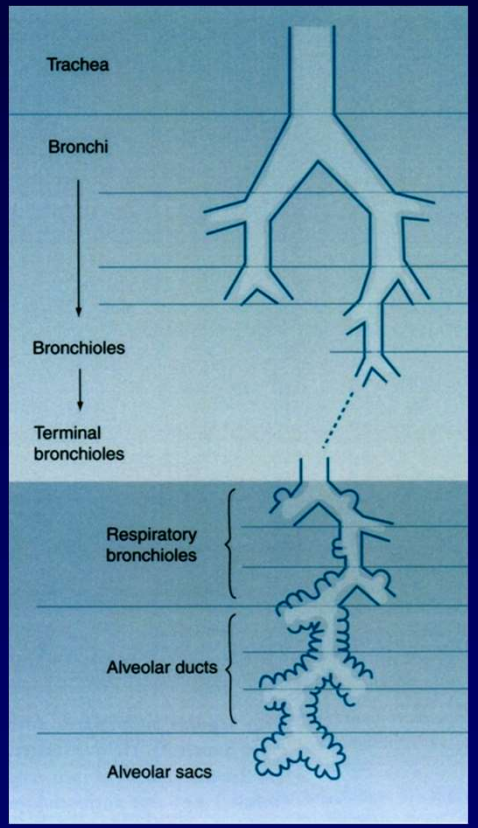
Targeted with inhaled antibiotics

Respiratory zone:

No cilia, no mucus

Mostly aerobic growth conditions

Targeted with systemic antibiotics

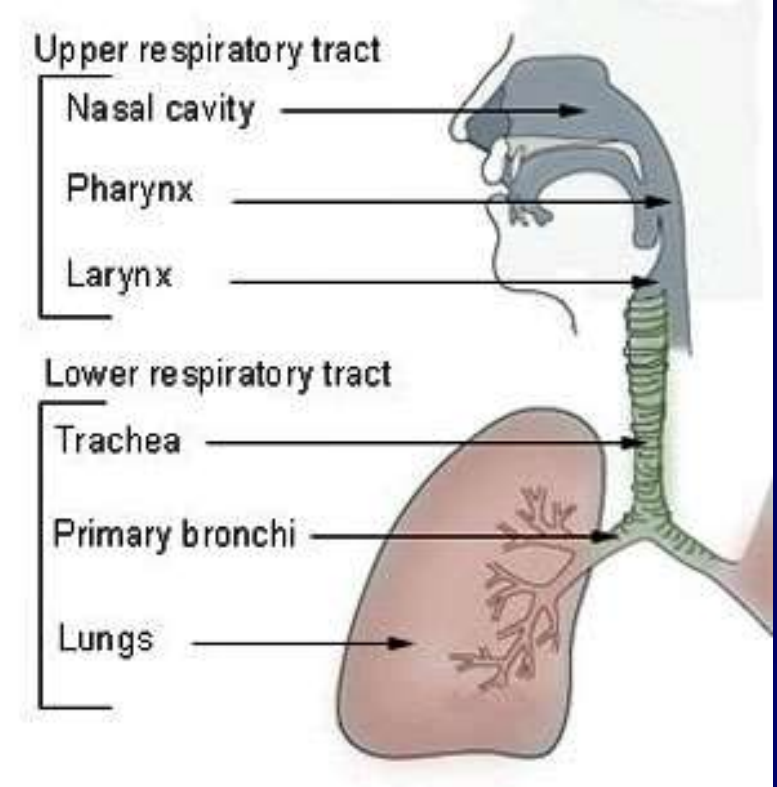


Respiratory tract: one of important ports of entry

- some infections remain there
- some spread further
    - per continuitatem (*S. pneumoniae*)
    - via blood (*S. pneumoniae*, TB, 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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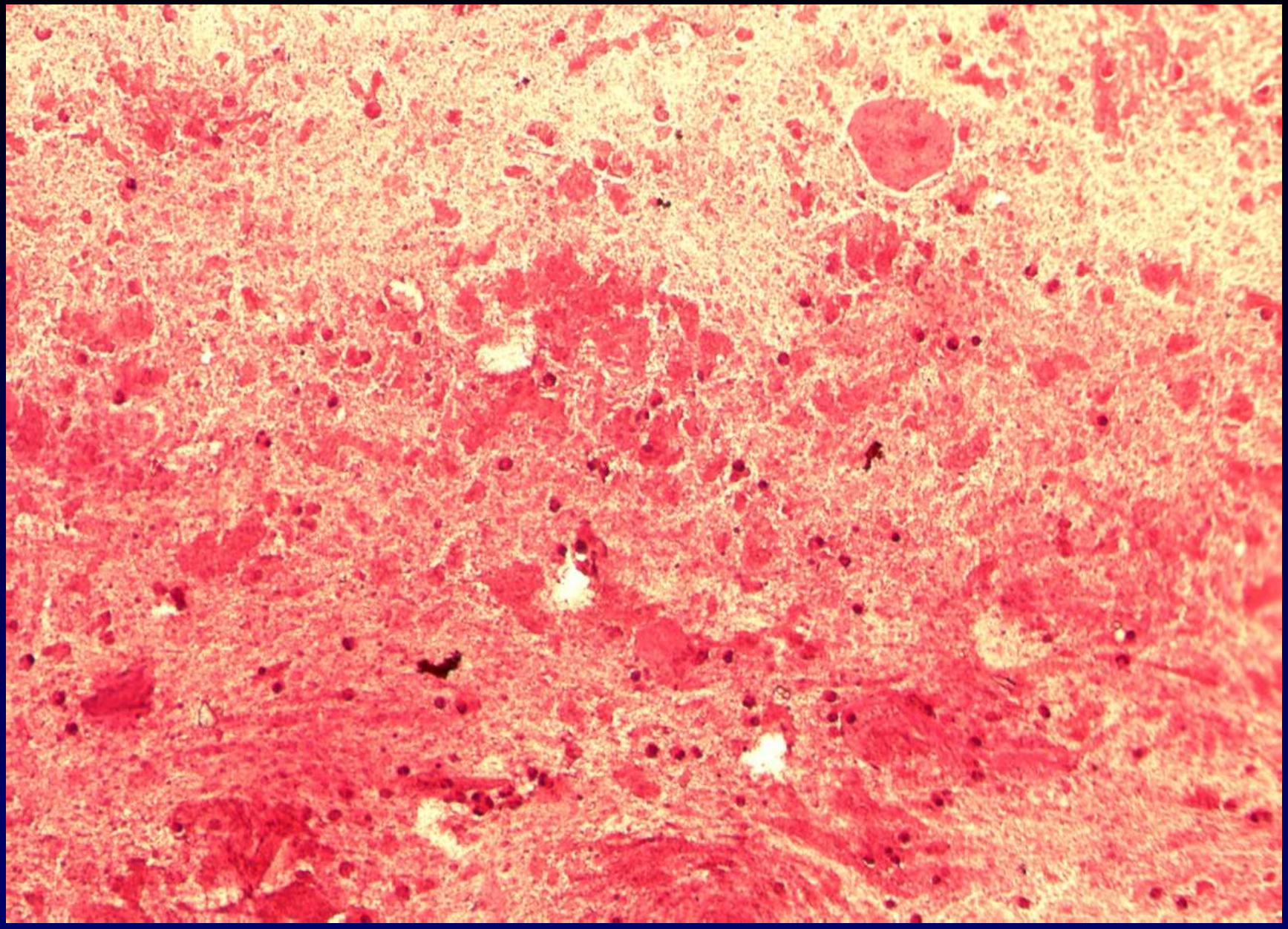
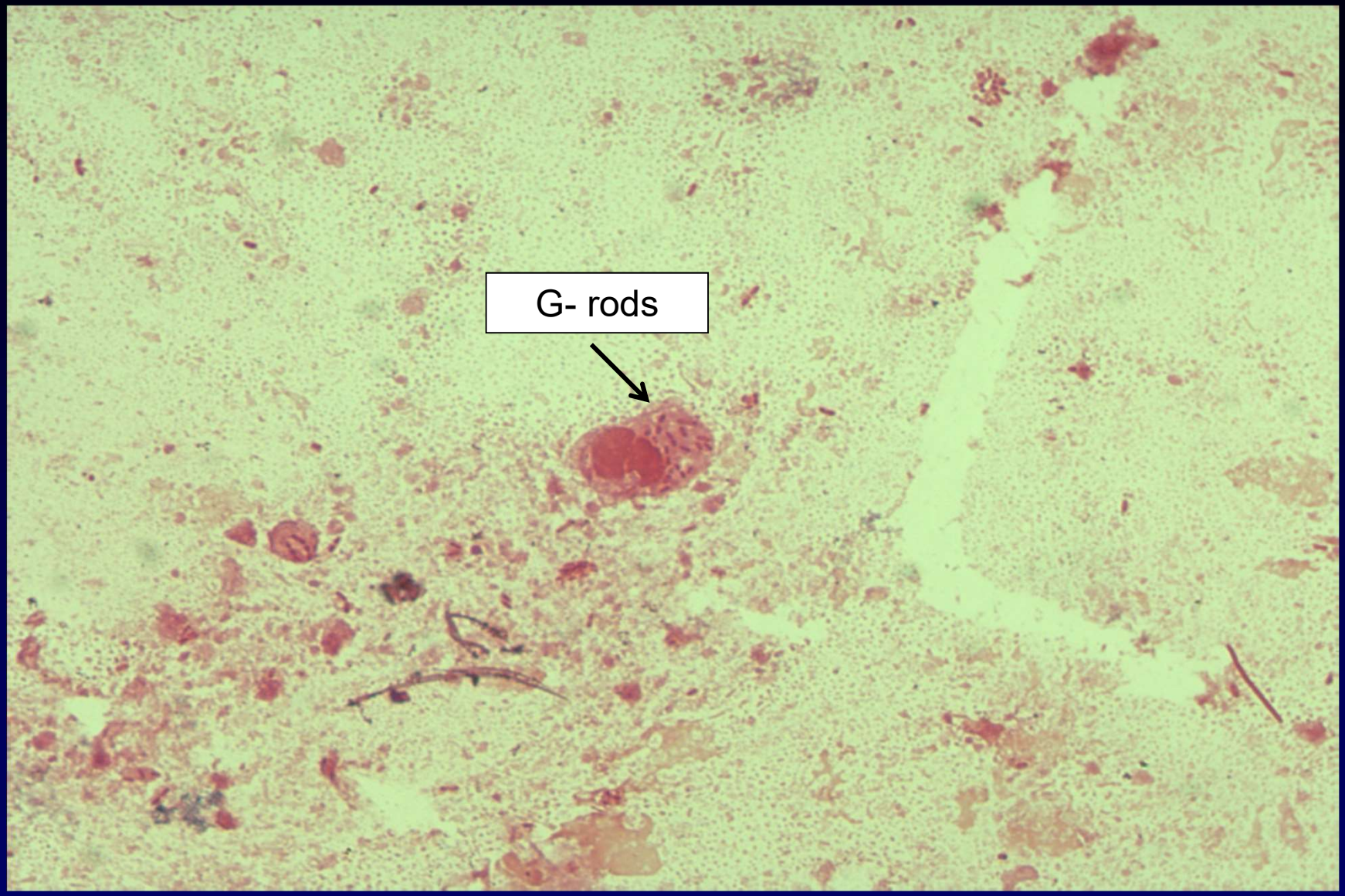
Suitable material for investigation

- SPUTUM

 - microscopy (to validate sputum)



zoom 10x10



zoom 10x100

Suitable material for investigation

- SPUTUM

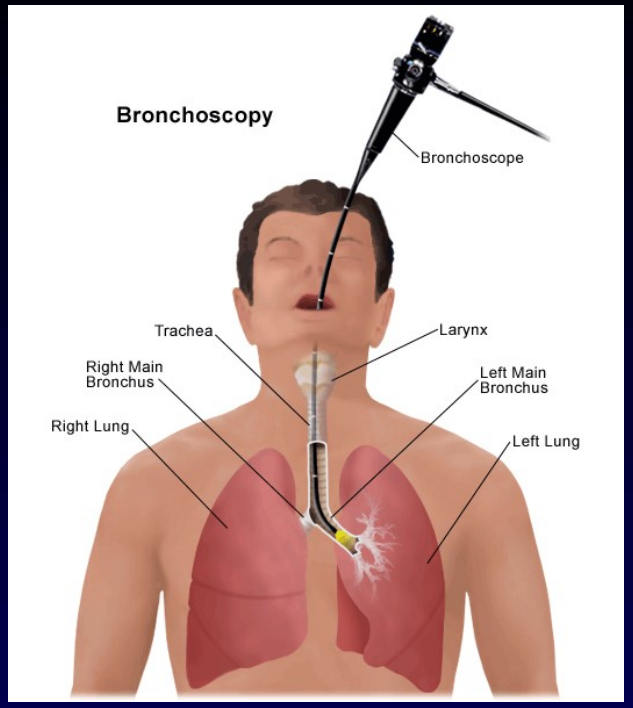
  - microscopy (to validate sputum)
  - culture (incl. quantification)
  - molecular genetics

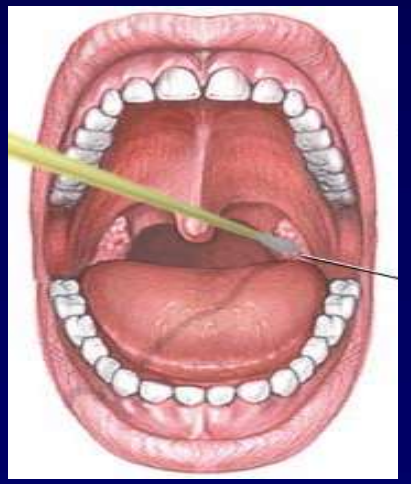
- Induced sputum

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

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

- nasopharyngeal swab
  - viral dg. (PCR, Ag)
  - pertussis, atypical pathogens





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

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

- blood cultures

- pleural fluid

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Key players

Viruses, called respiratory viruses:

orthomyxoviruses: influenza A, B

paramyxoviruses: parainfluenza PIV 1 to 4, RSV,
metapneumovirus hMPV, measles

picornaviruses: rhinovirus HRV; coxsackie and echovirus (= enteroviruses!)

adenoviruses

coronaviruses HCoV

Key players

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

What do the different snot colors mean?

	clear	white	green or yellow	red or pink	brown or orange	black
"normal" or healthy	✓					
allergic sinusitis	✓					
common cold		✓	✓			
fungal infection						✓
injury or irritation				✓	✓	
nonallergic or pregnancy rhinitis	✓			✓		
sinusitis		✓				
smoking/drug use						✓

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 (sore throat)

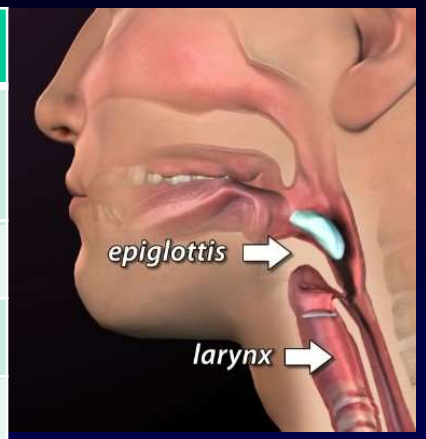
- adenoviruses (often accompanied with conjuctivitis)
- EBV (part of inf mononucleosis)
- *S. pyogenes* (5-15 yrs of age)
- streptococci groups C, G
- *Arcanobacterium heamolyticum*
- *N. gonorrhoeae*

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

Th: GAS: PNC V for 10 days
Arcanobacterium: macrolides

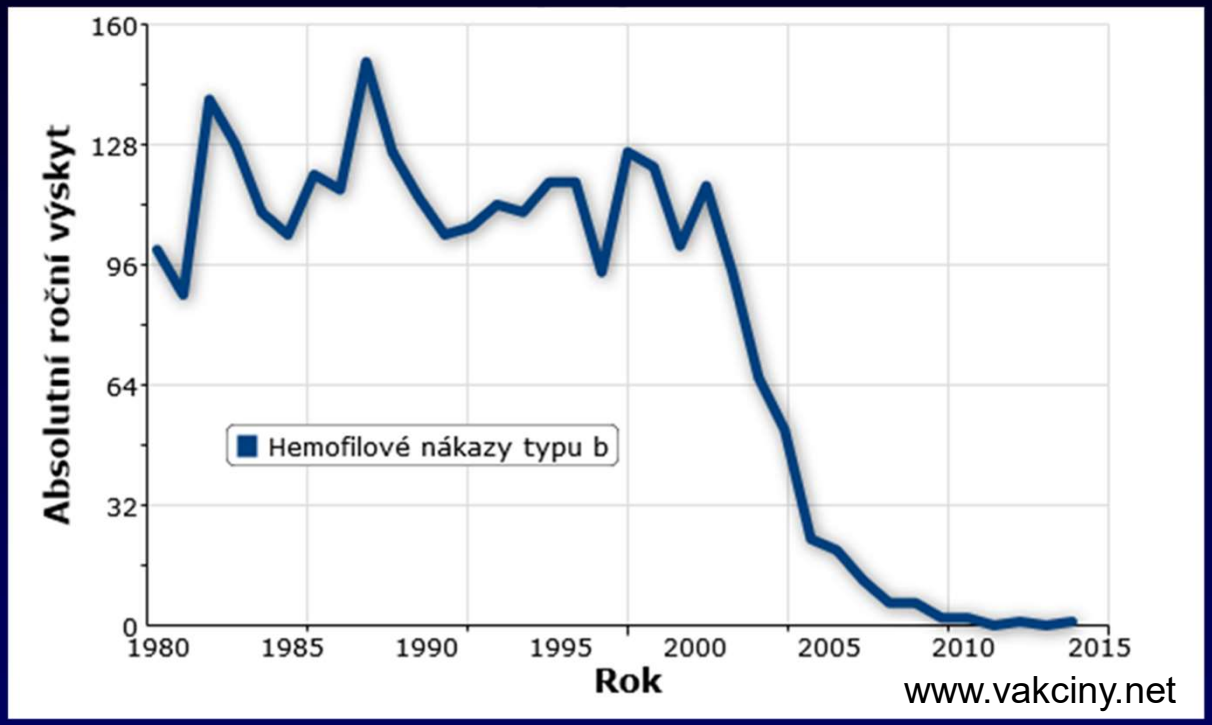
epiglottitis versus laryngitis (subglotic laryngitis, laryngotracheitis)

Epiglottitis	Croup, pseudocroup
H. influenzae type b	viruses (parainfluenza)
rapid onset	upper airway infection
no cough	barking cough
fever above 38 deg. C	temp below 38 deg. C
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 serotypes of *H. influenzae* still out there

H. influenzae non-typeable, types e, f

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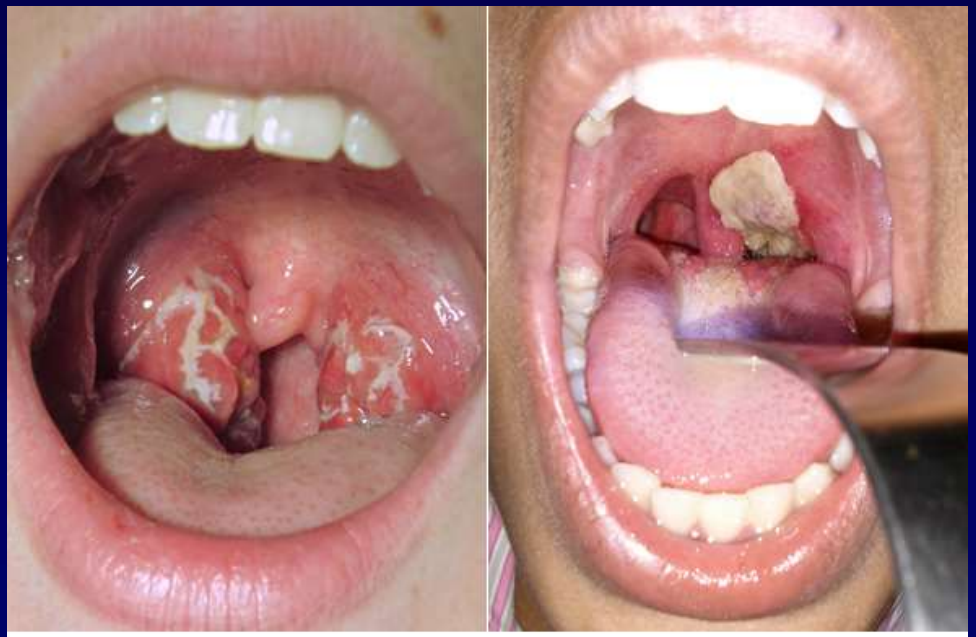
Diphteria

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

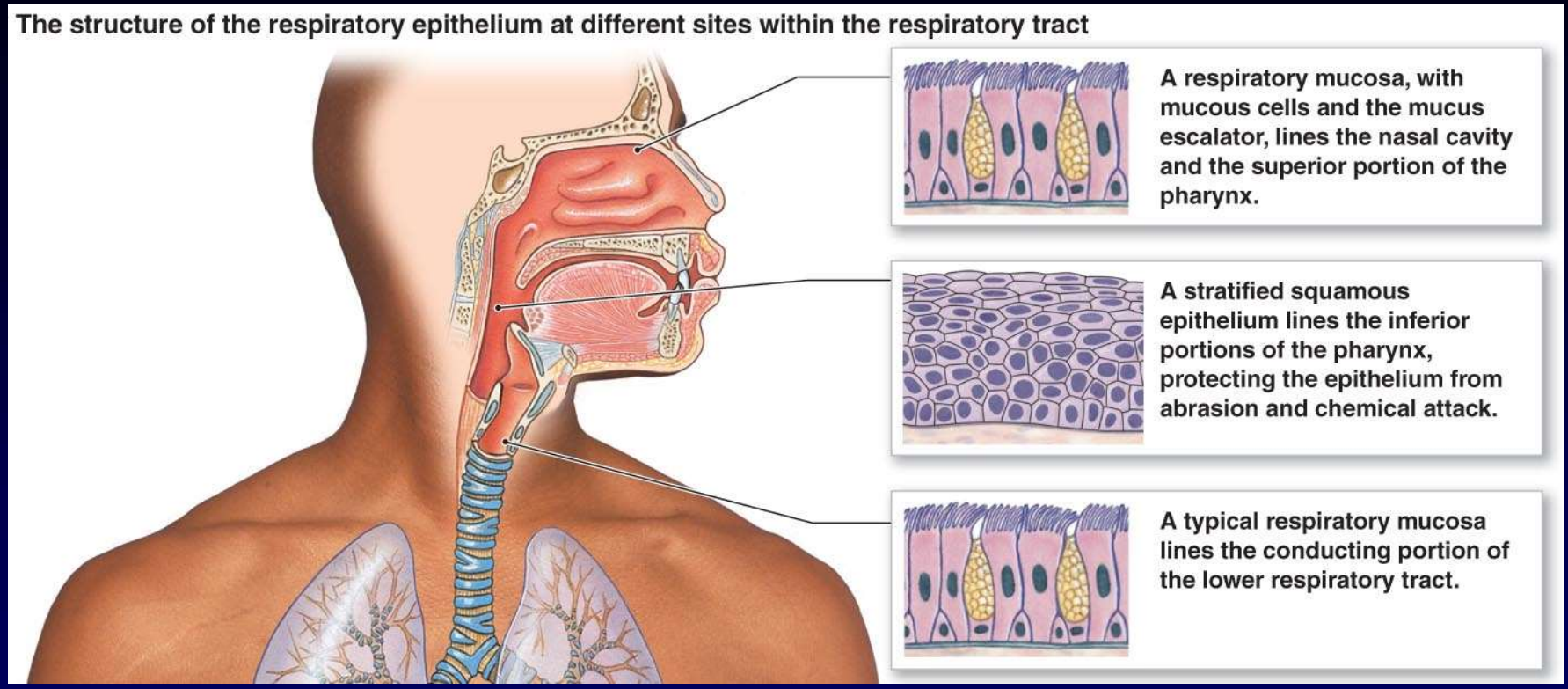
Bordetella pertussis, B. parapertussis

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

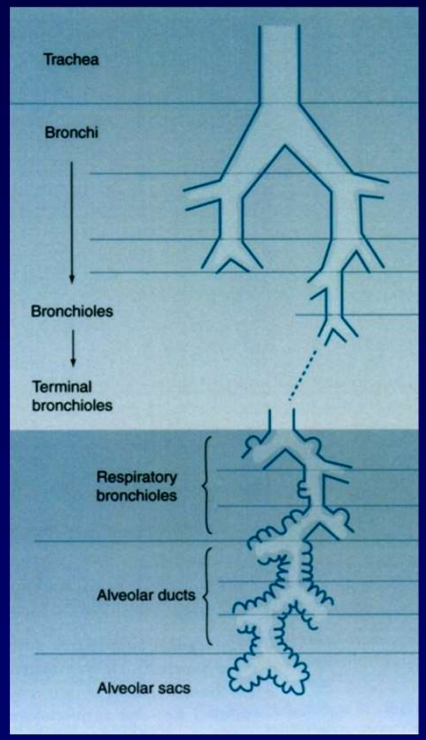
Bronchiolitis (obliterans)

respiratory syncytial virus RSV-A, RSV-B

- in children below 2 years of age (high risk in preterm babies by 6 mo of age)
- serious condition

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

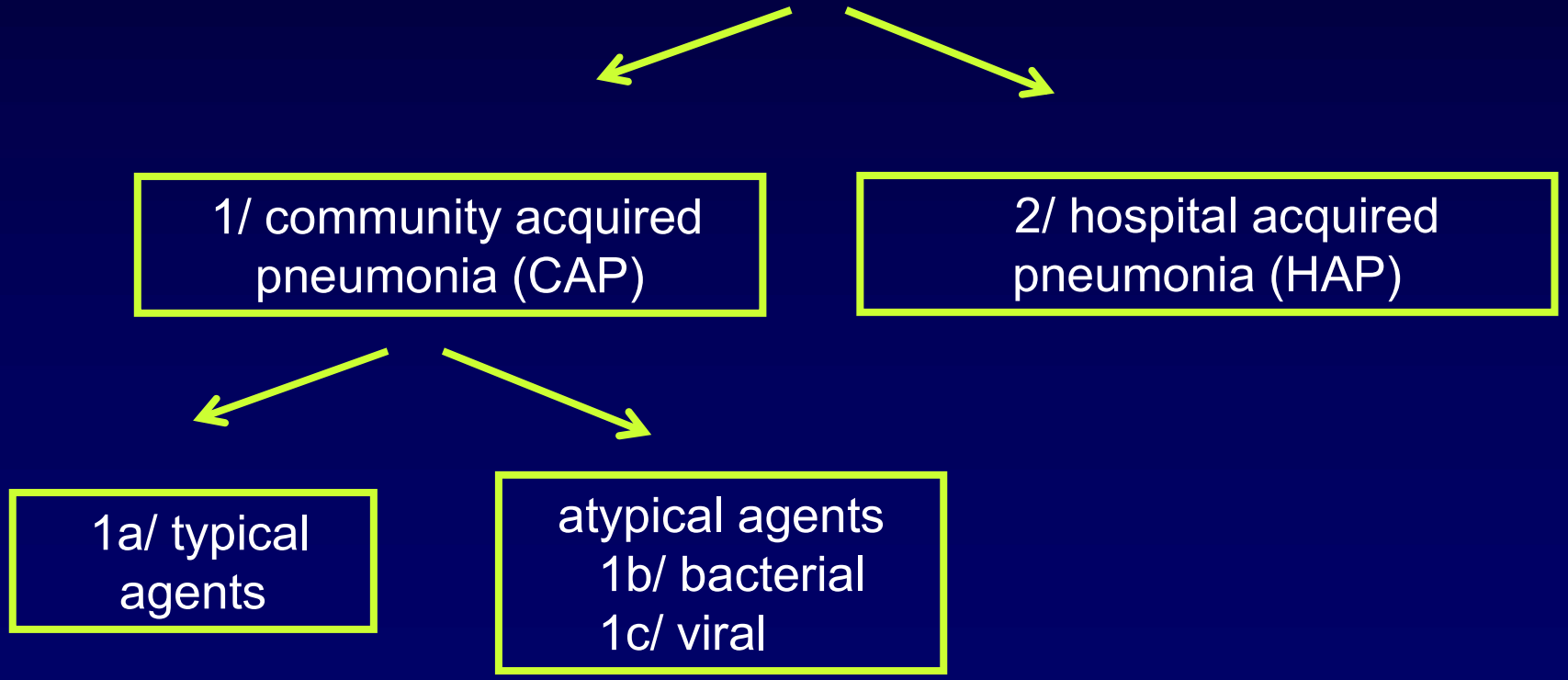
= also as prevention
for infants at risk in winter months



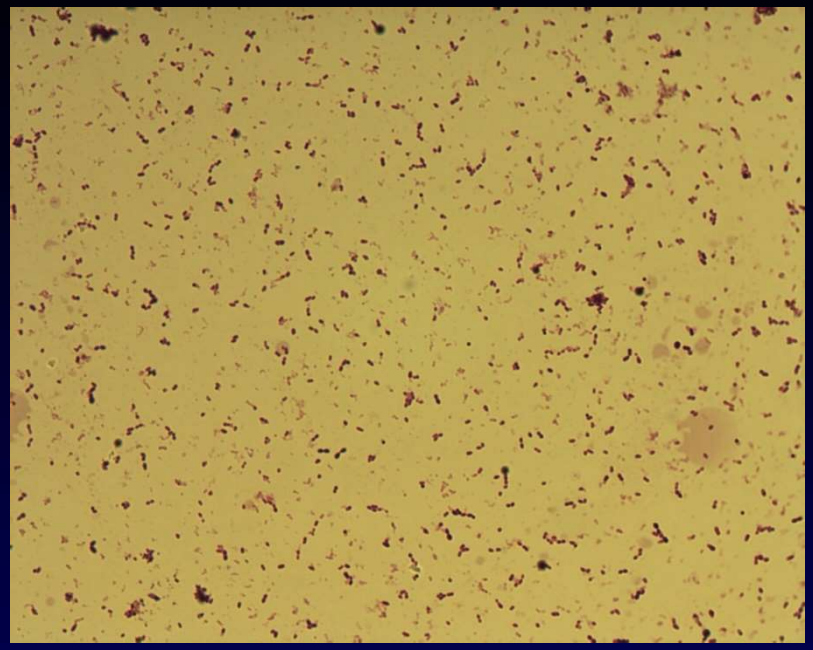
Pneumonia

• 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



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

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

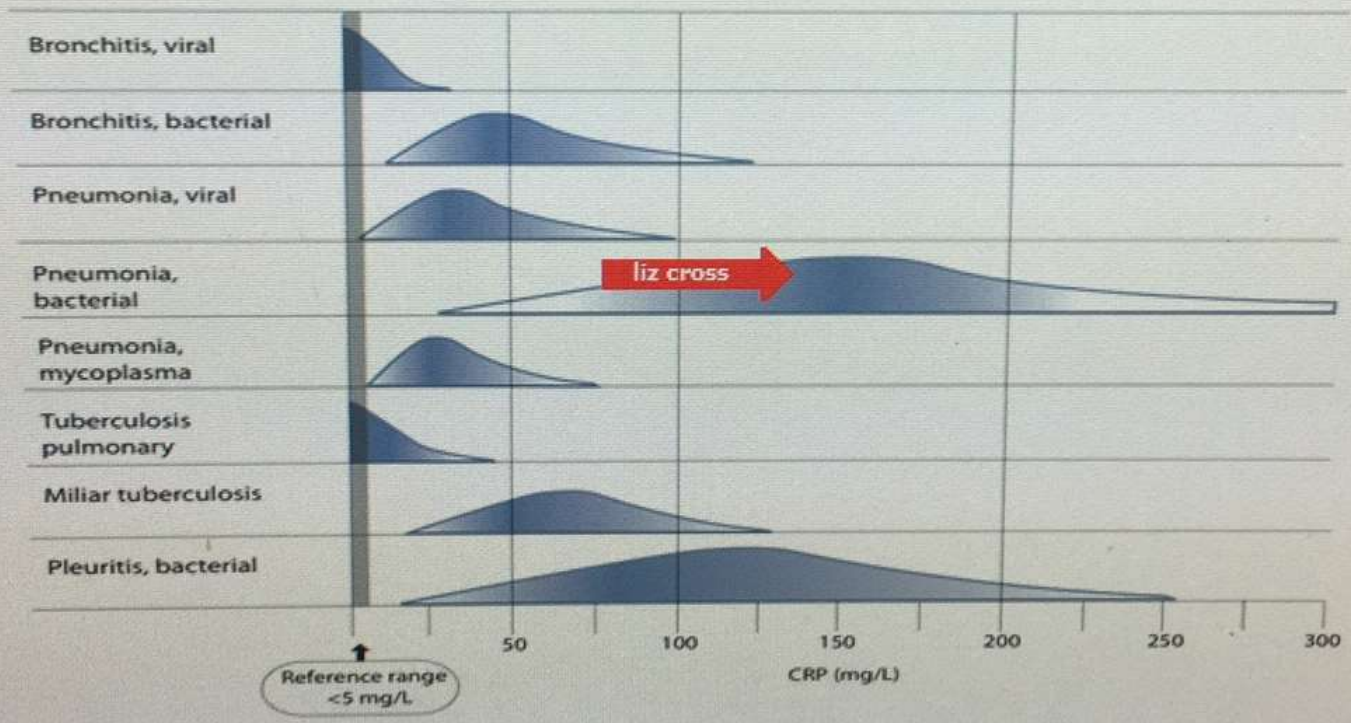
24-year-old lady

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

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

CRP LEVELS IN LOWER RESPIRATORY TRACT INFECTION

Typically higher values in bacterial infections than in viral infections



24-year-old lady

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

1b/ CAP with atypical pathogens

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

Legionella pneumophila

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

- serology

ATB therapy of CAP

Pneumococcal pneumonia:

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

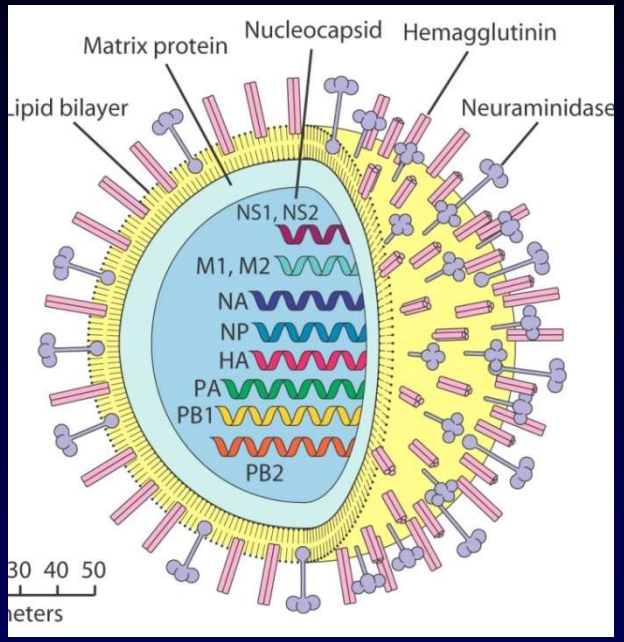
Atypical agents:

macrolides
tetracyclines
respiratory fluoroquinolons (moxifloxacin)

1c/ CAP with atypical pathogen - virus

Influenzavirus type A, B, C

subtypes HxNx (H1N1, H3N2)



Spanish flu 1918 - 1919

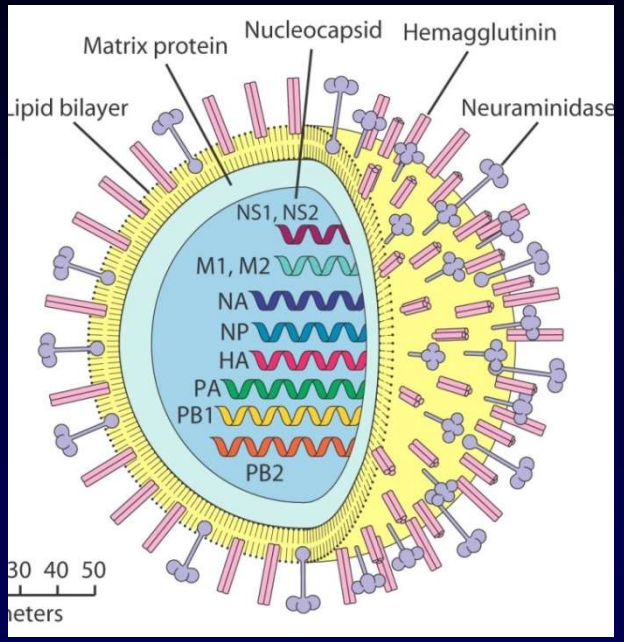
20 - 50 mil. deaths

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:

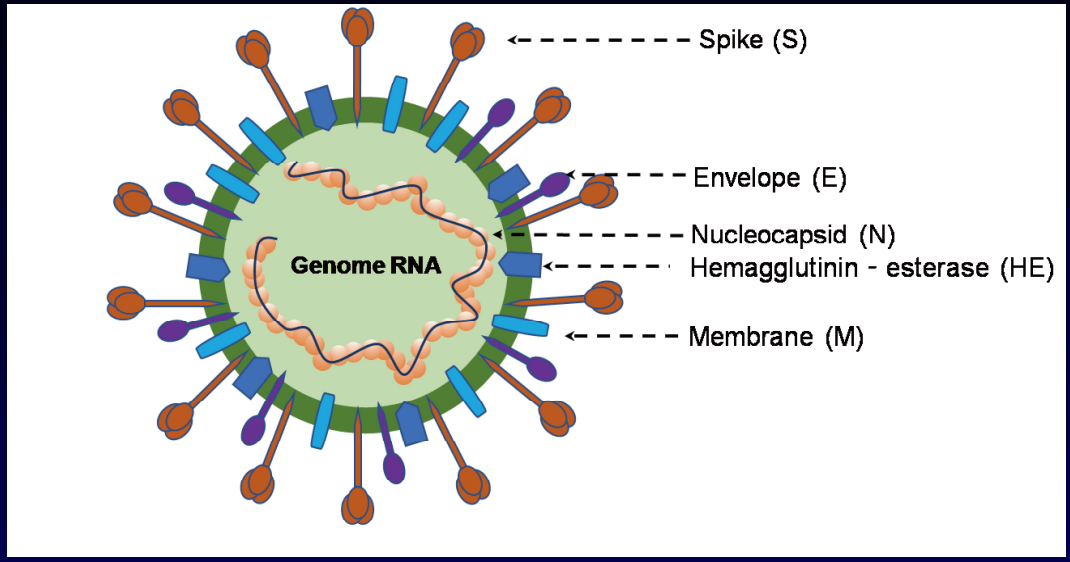
- antigen detection (low sensitivity)
- PCR

- serology

1c/ CAP with atypical pathogen - virus

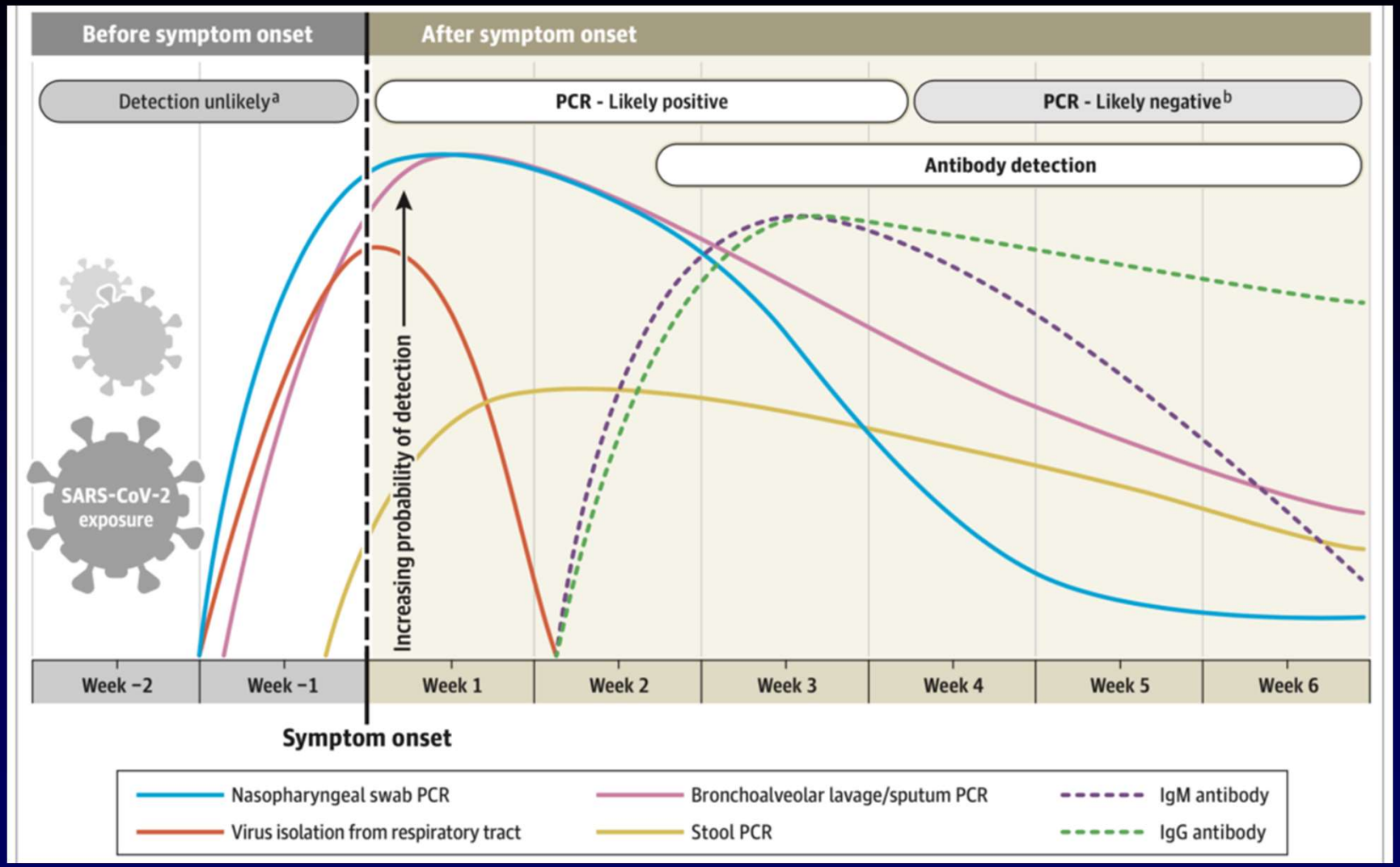
SARS-CoV-2

- asymptomatic course
- pneumonia
  - primary viral (interstitial)
  - secondary bacterial



- Direct detection
  microscopy (EM)
  culture
  antigen detection
  RNA detection

- Indirect detection
  IgM, IgA, IgG



Sethuraman et al. JAMA. 2020.

PCR of SARS-CoV-2

Sample

Extraction of viral RNA

1 hr

RT-PCR

1.5 hr

POCT

60 min

2/ HAP; hospital acquired pneumonia

develops min. 48 hours post admission and in association with hospitalization
typically of bacterial origin

Ventilator associated pneumonia (VAP)

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

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Newborn pneumonia

- *S. agalactiae* GBS
- *Chlamydia trachomatis*

- *K. pneumoniae, E. coli*

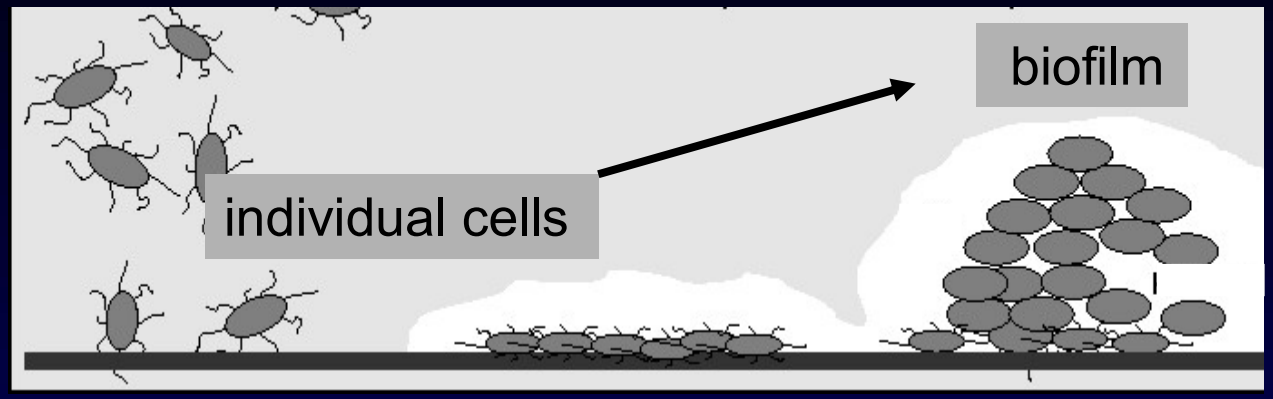
Chronic respiratory diseases and chronic infections

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

- *S. aureus*
- enterobacteria (*K. pneumoniae*)

- G- nonfermenters
  - *P. aeruginosa*
  - complex *Burkholderia cepacia*
  - *Stenotrophomonas maltophilia*
  - *Achromobacter xylosoxidans*

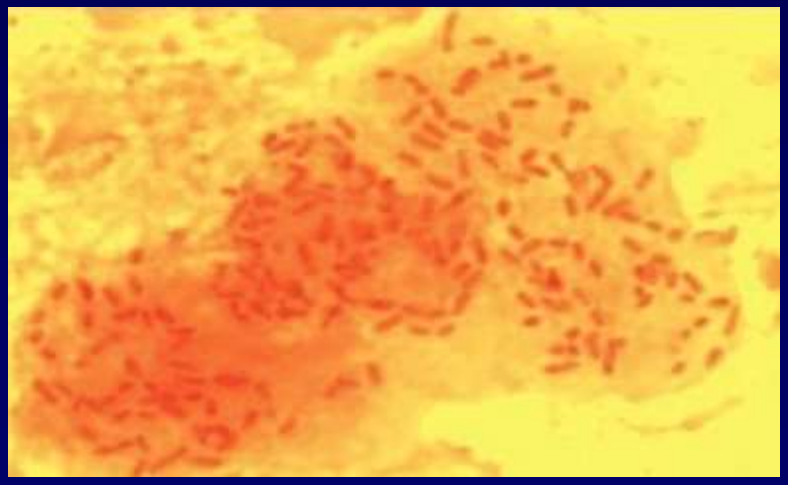
Infection course



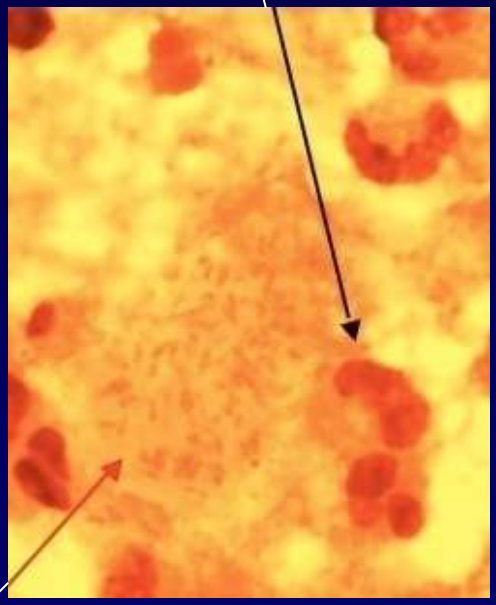
Biofilm

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

- Protection against phagocytosis, ATB



Courtesy: Prof. N. Hoiby, Copenhagen



P. aeruginosa biofilm

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*; microscopy, PCR
- fungi

2-month old girl

10 days cough, increased mucus, temperature max. 37.5 °C
x ray: difuse gentle infiltrates

Microbiology:
culture aspirate 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