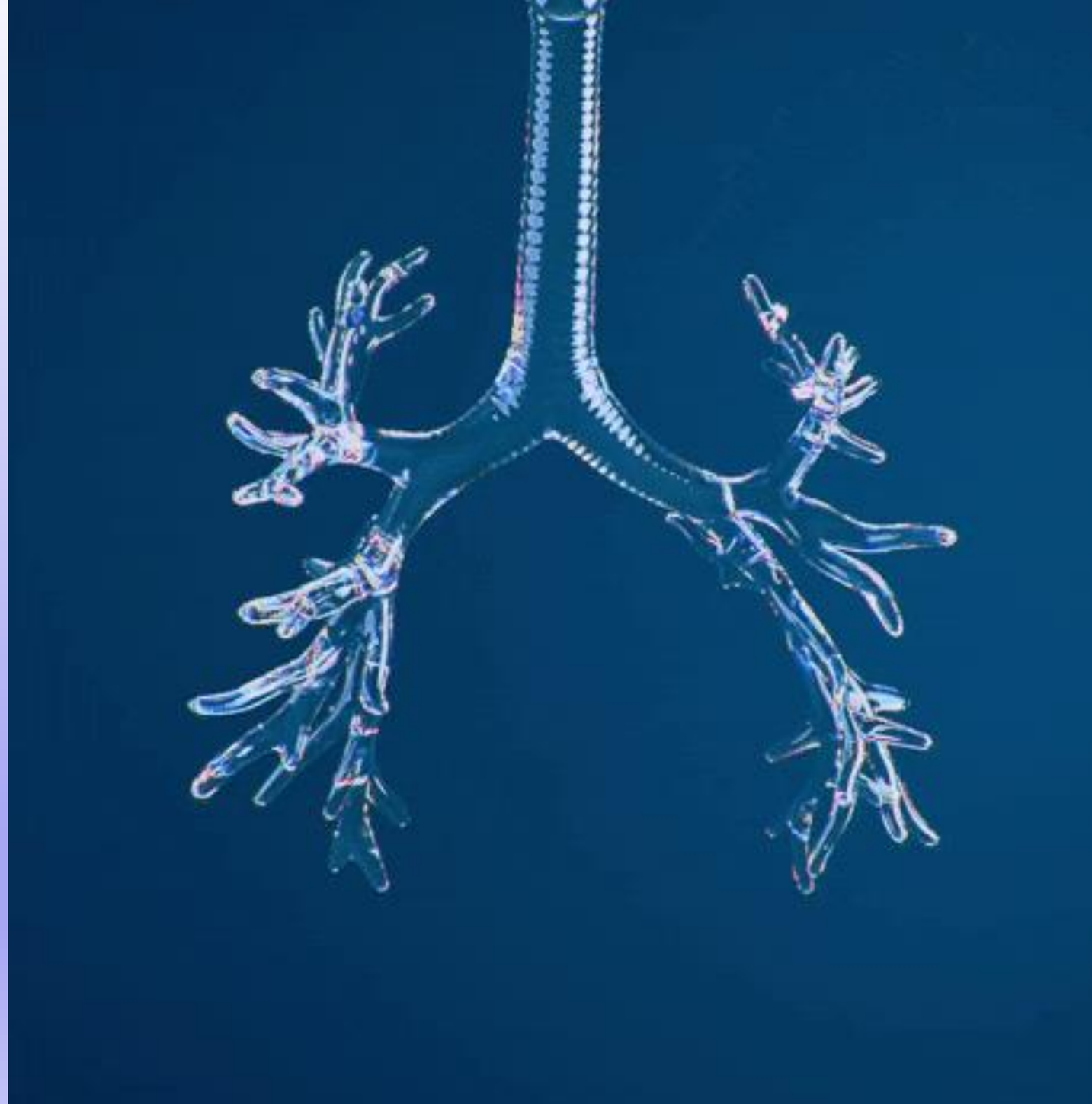
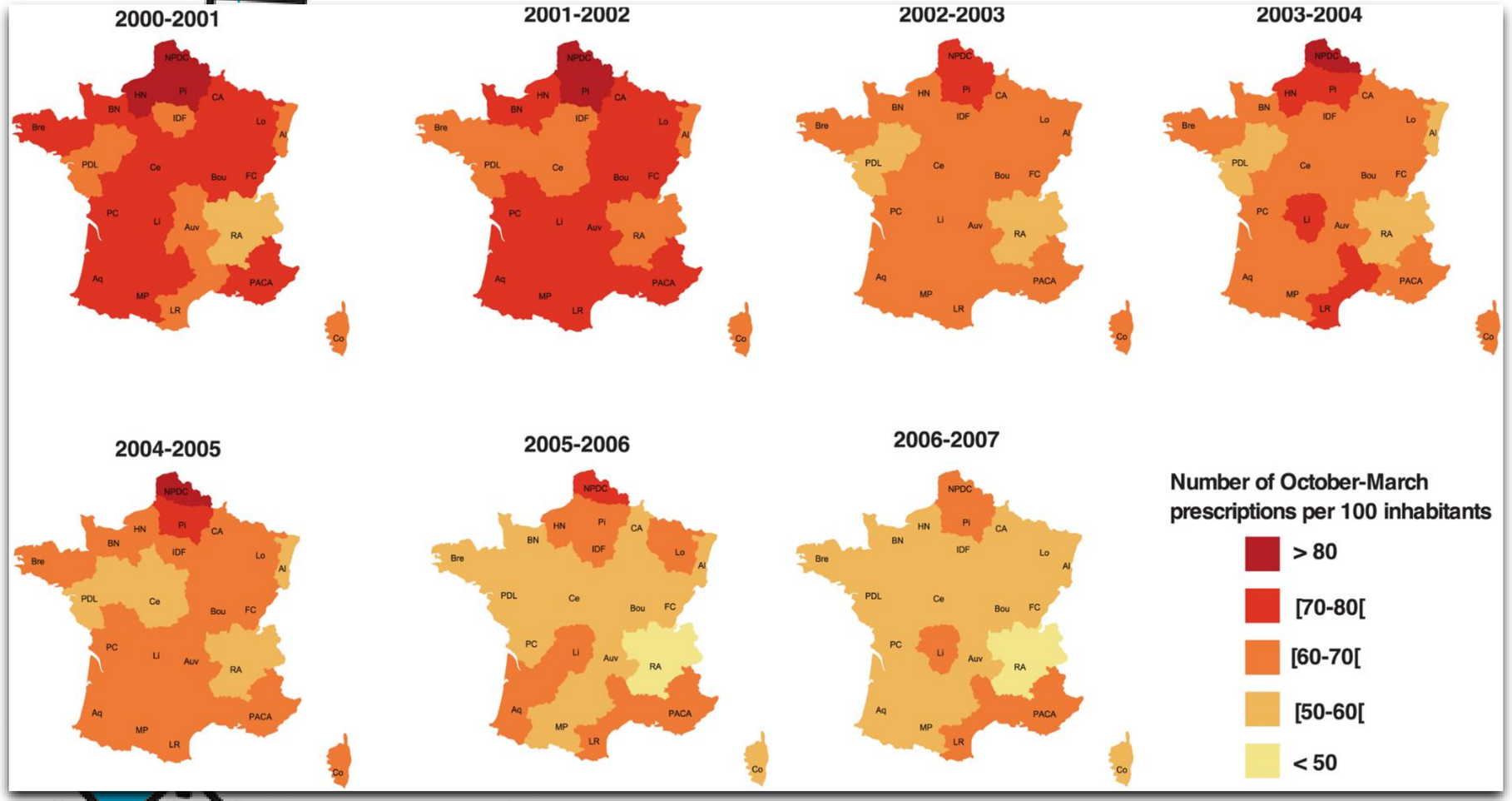
Respiratory tract infections

Martin Slížek



The most common indication for ATB therapy



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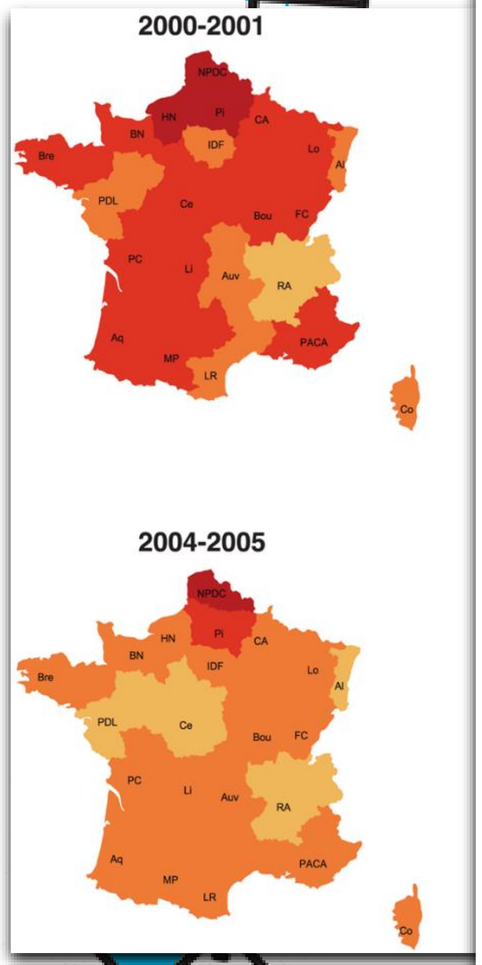
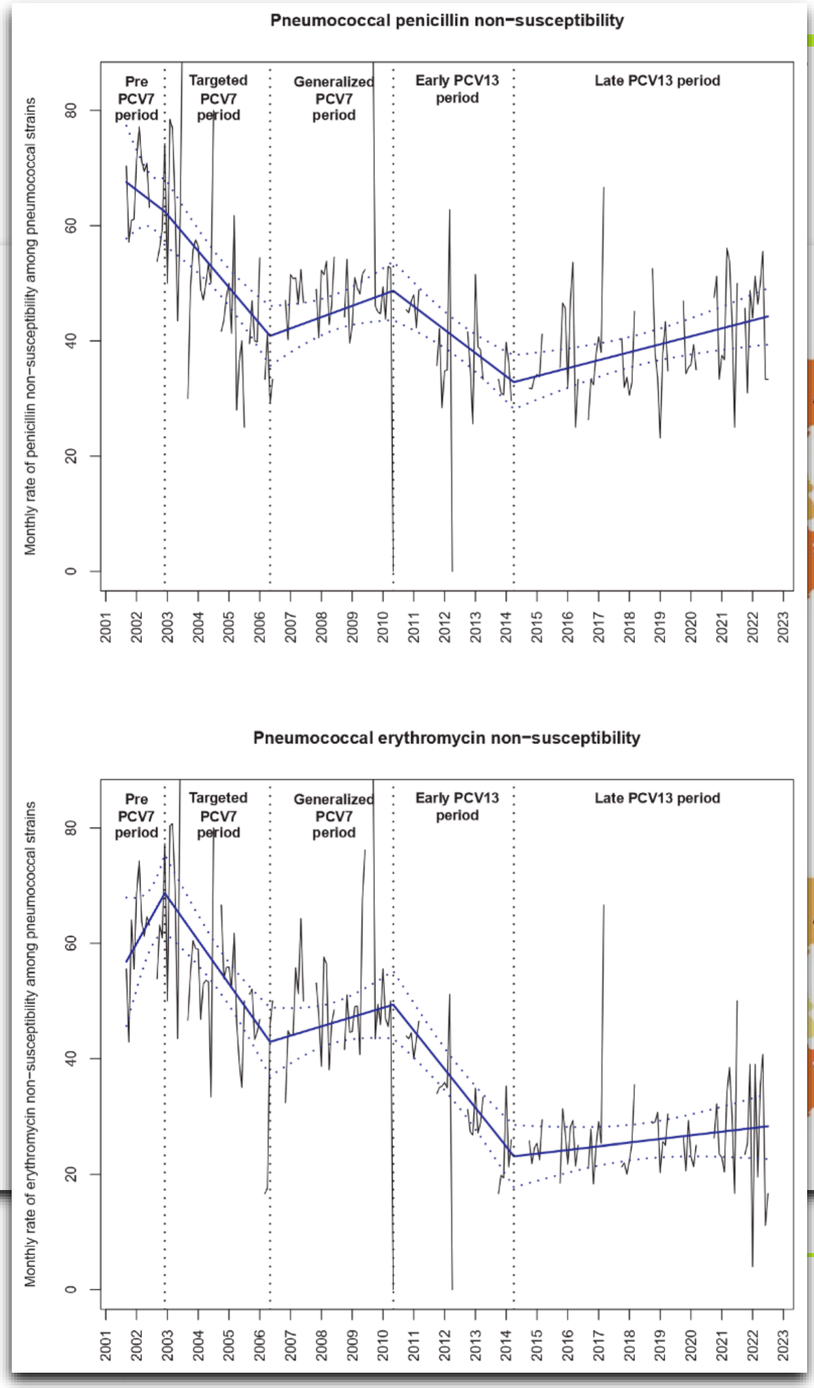
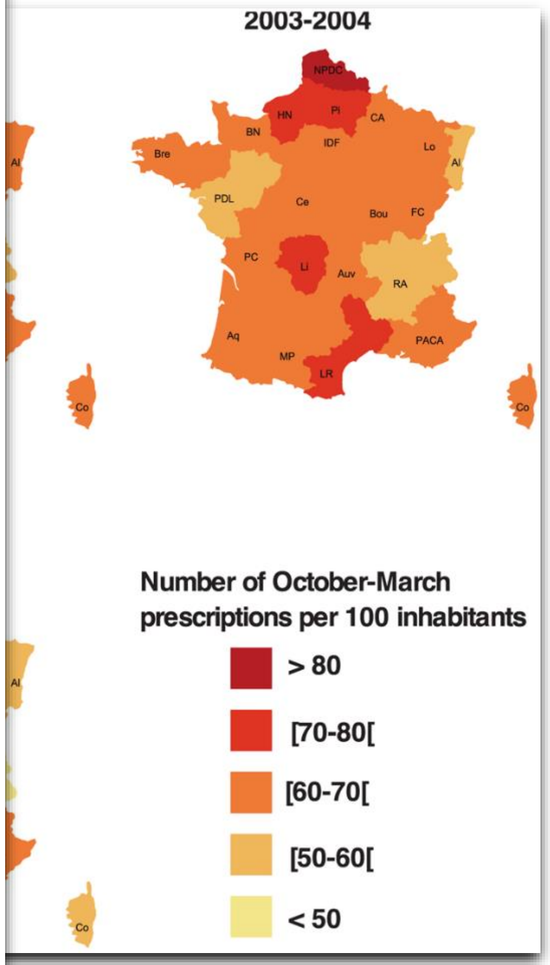






Upper respiratory tract

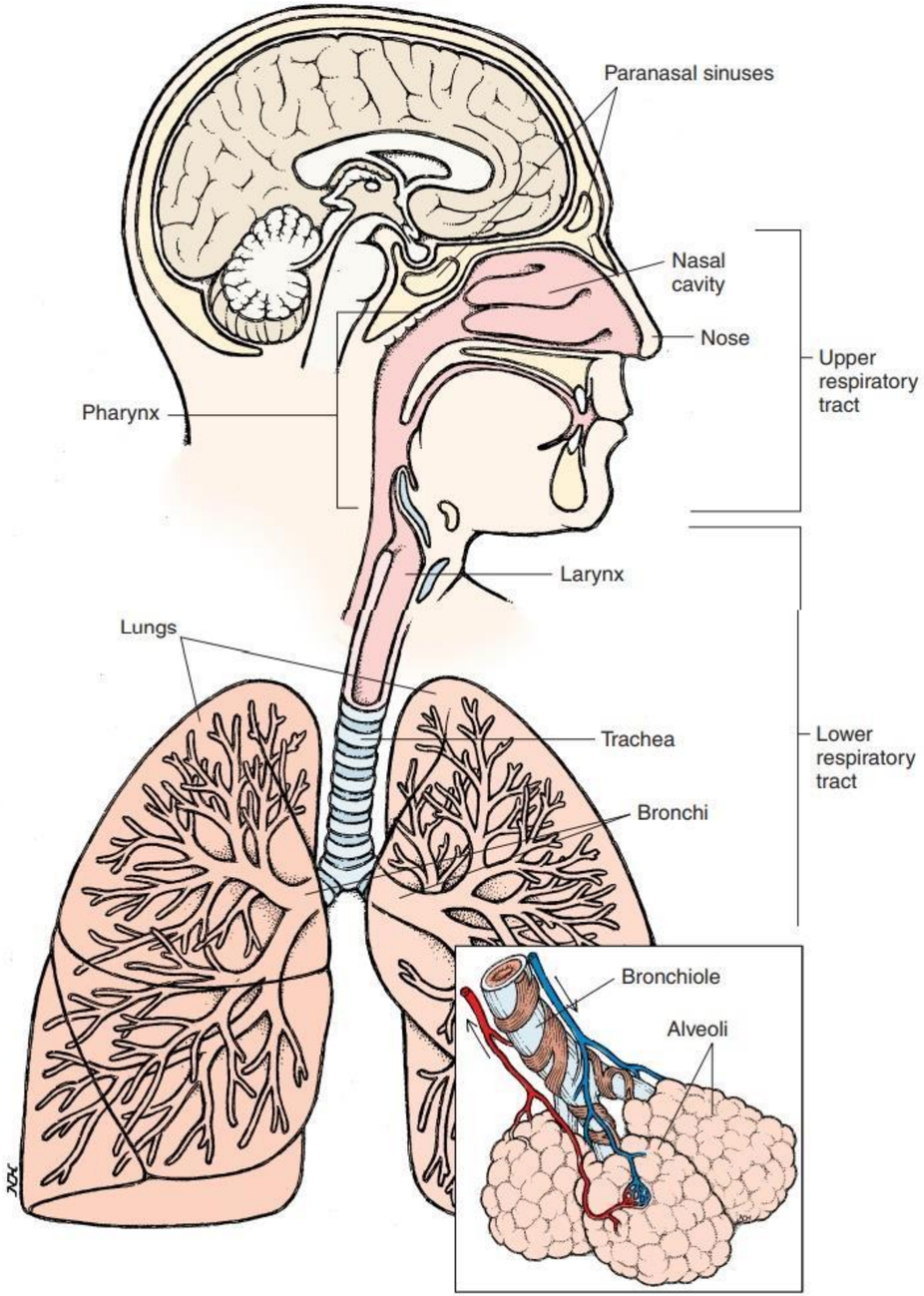


FIGURE The Structures of the Respiratory System (Anterior View)

- proportion of viral infections around 80% (adenoviruses, coronaviruses, rhinoviruses, enteroviruses, influenza, parainfluenza)
- naturally not sterile

Upper respiratory tract

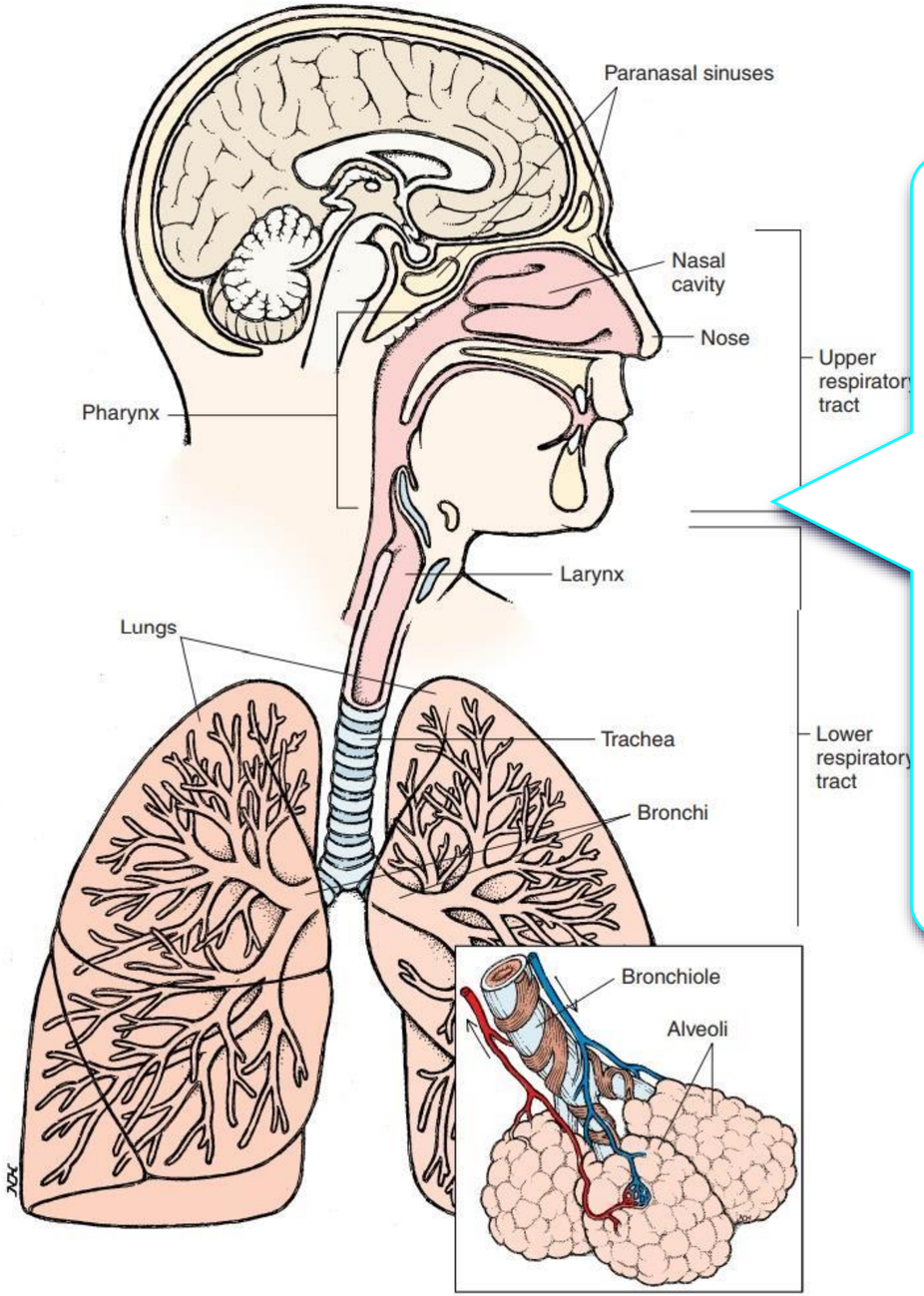
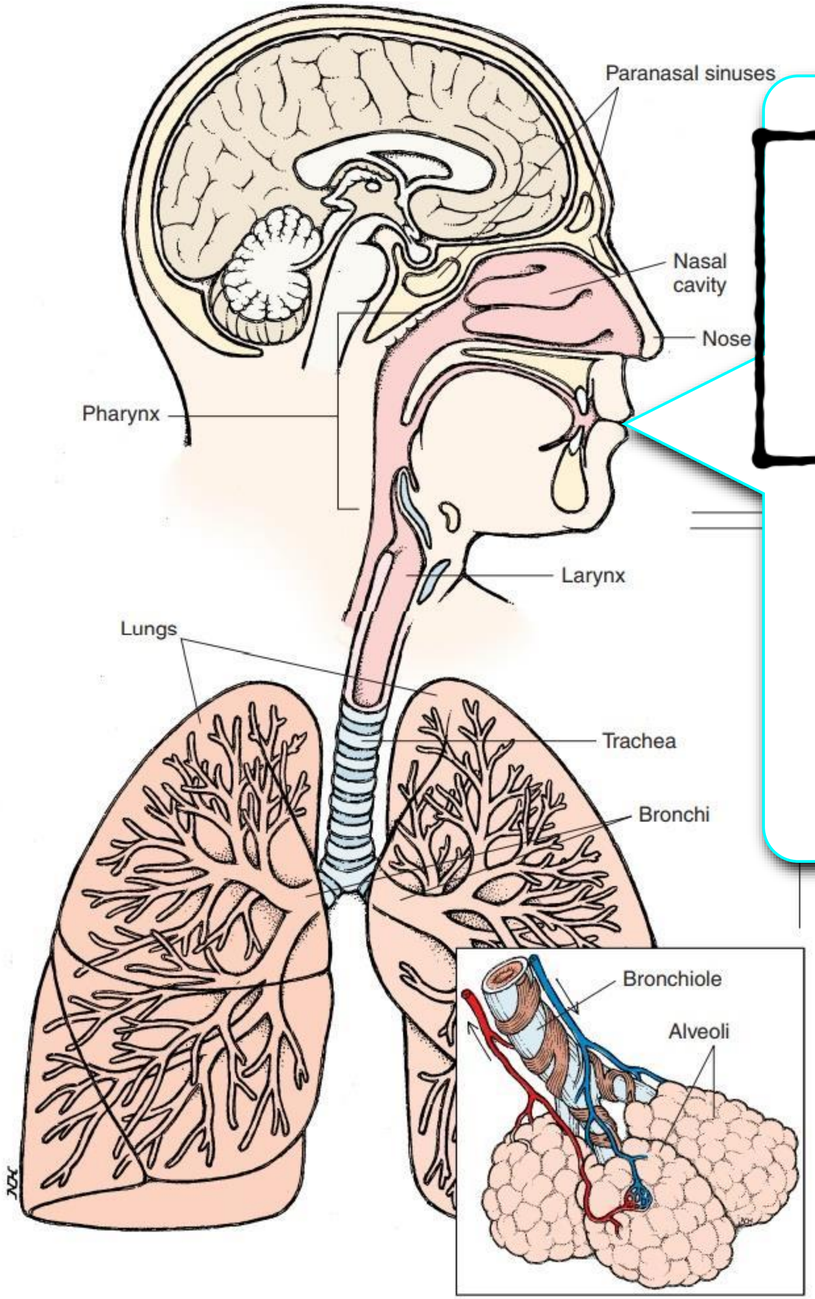


FIGURE The Structures of the Respiratory System (Anterior View)

- Streptococcus pneumoniae 0-50%
- Streptococcus pyogenes 0-9%
- Haemophillus influenzae 5-30%
- Staphylococcus aureus 35-40%
- Neisseria meningitidis 0-15%
- Moraxella catarrhalis 0-15%
- G- bacteria and anaerobes 3%

Upper respiratory tract



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Lower respiratory tract

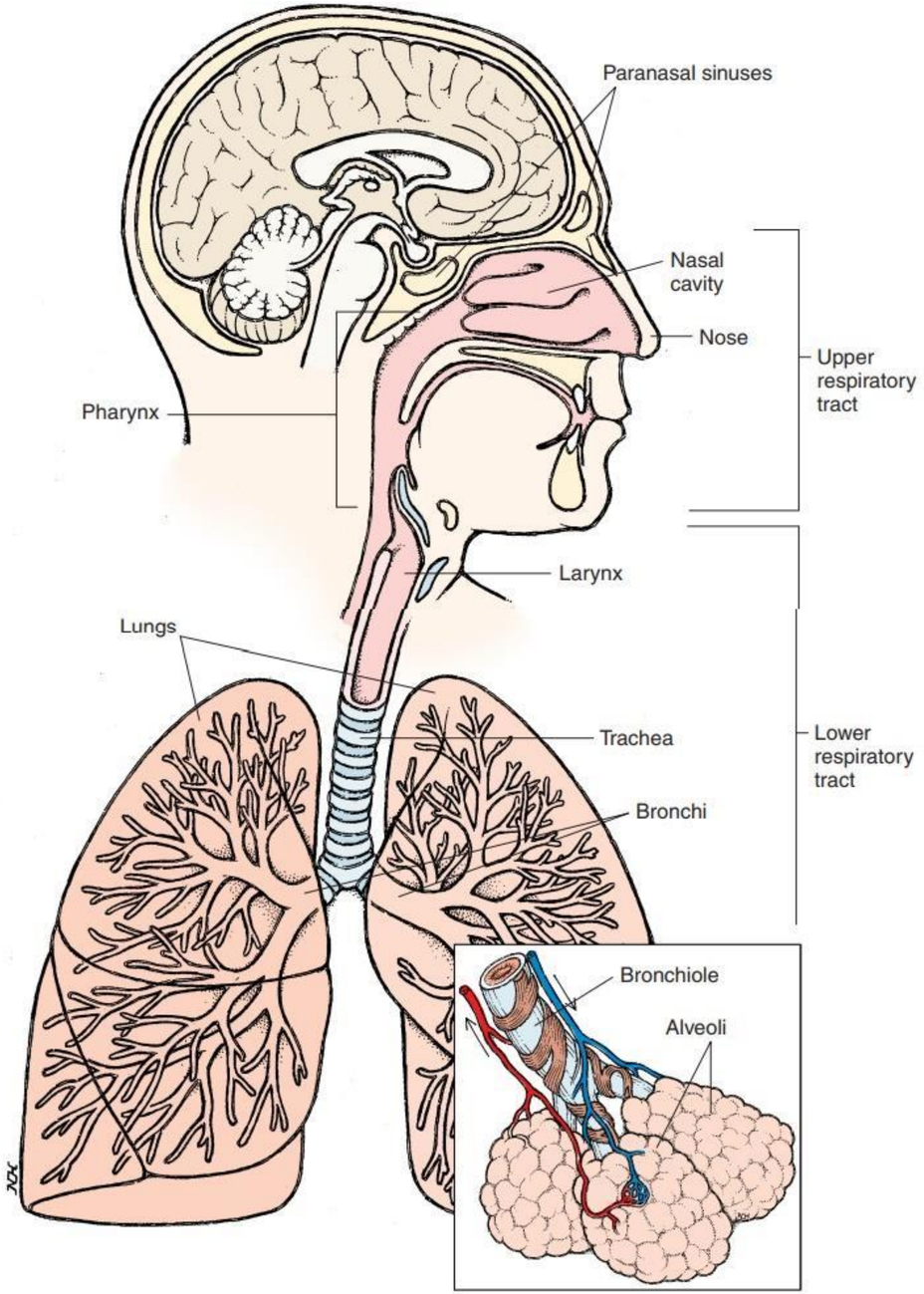

FIGURE The Structures of the Respiratory System (Anterior View)

- primarily sterile
- emphasis on correct material collection is essential (contamination with HCD flora)

Lower respiratory tract

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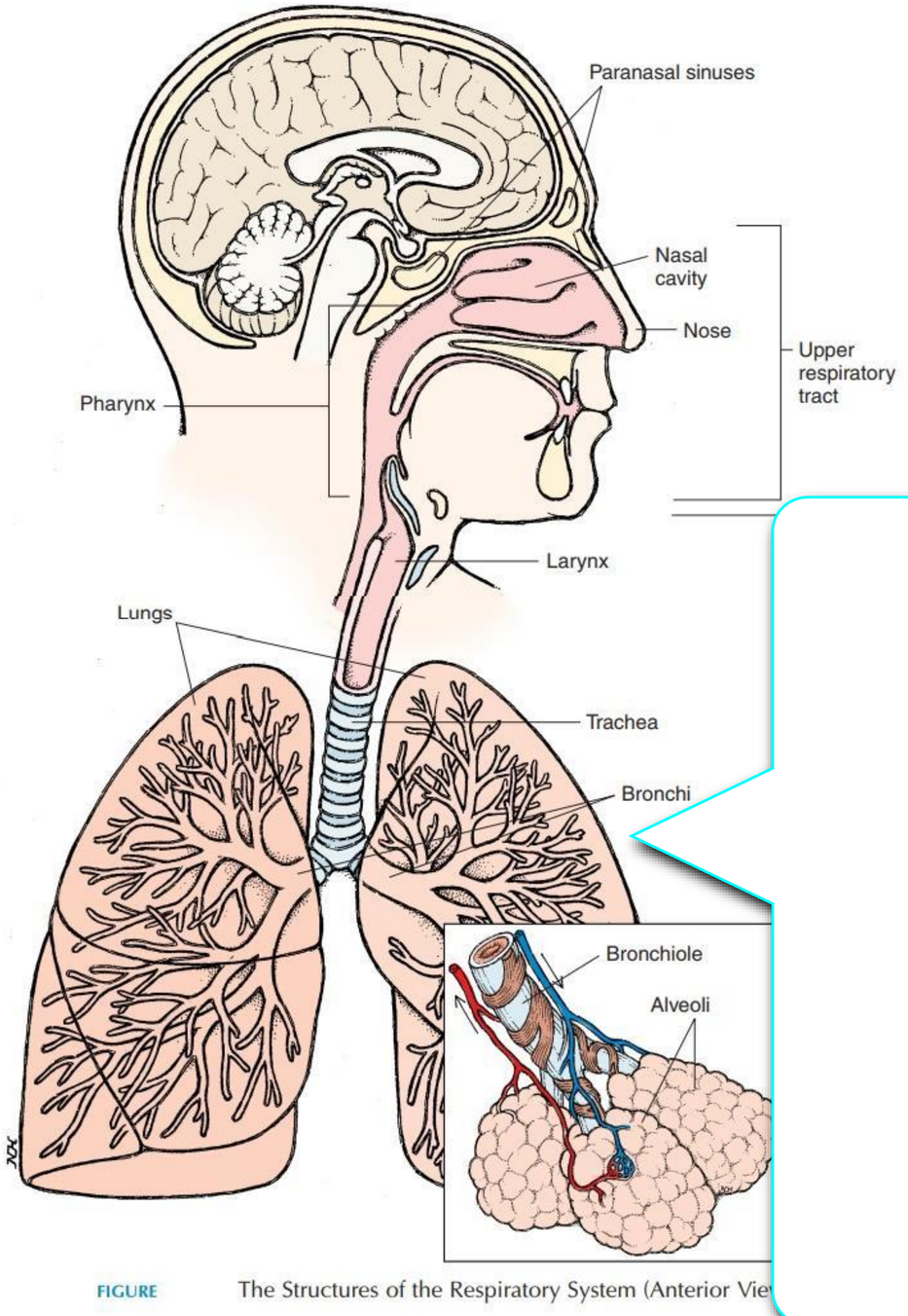


FIGURE The Structures of the Respiratory System (Anterior Vie

THE USUAL SUSPECTS

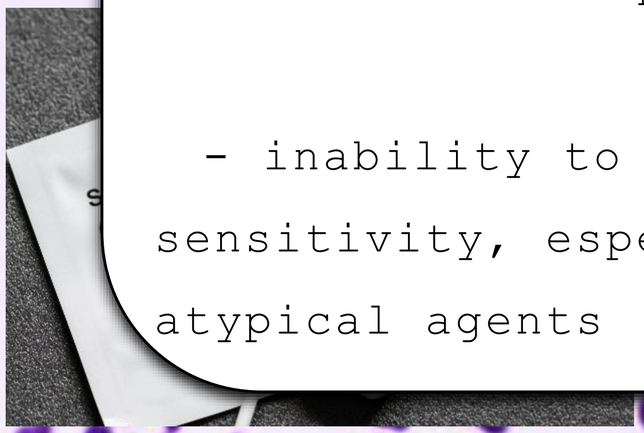
- Streptococcus pneumoniae
- Streptococcus pyogenes
- Haemophillus influenzae
- Staphylococcus **aureus**
- Moraxella catarrhalis
- Mycoplasma pneumoniae
- **Chlamydophila pneumoniae**
- Bordetella pertussis/parapertussis

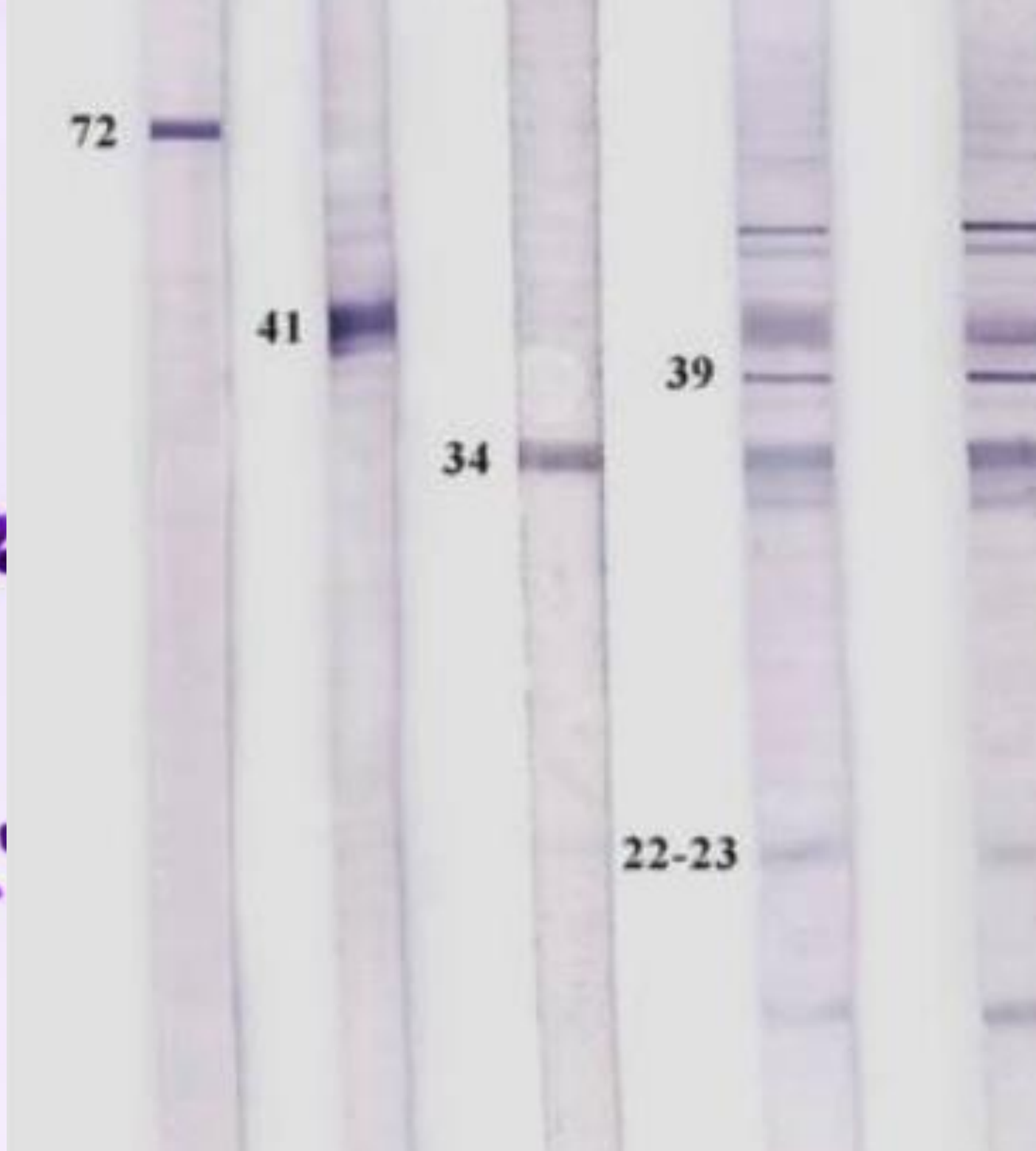
DIRECT METHODS

- usually preferred in the diagnosis of respiratory infections
- high specificity
- early detection of the causative agent

BUT

- inability to perform or low sensitivity, especially for some atypical agents





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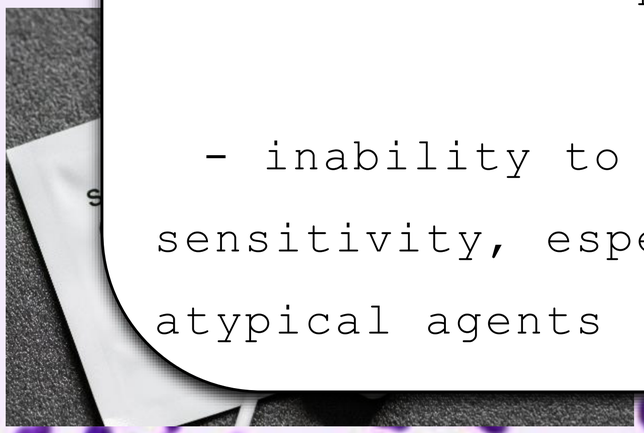

DIRECT METHODS

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BUT

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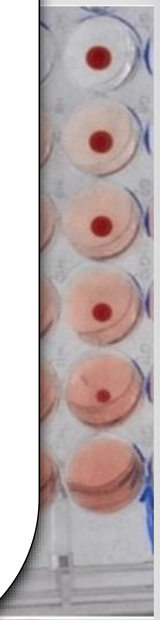
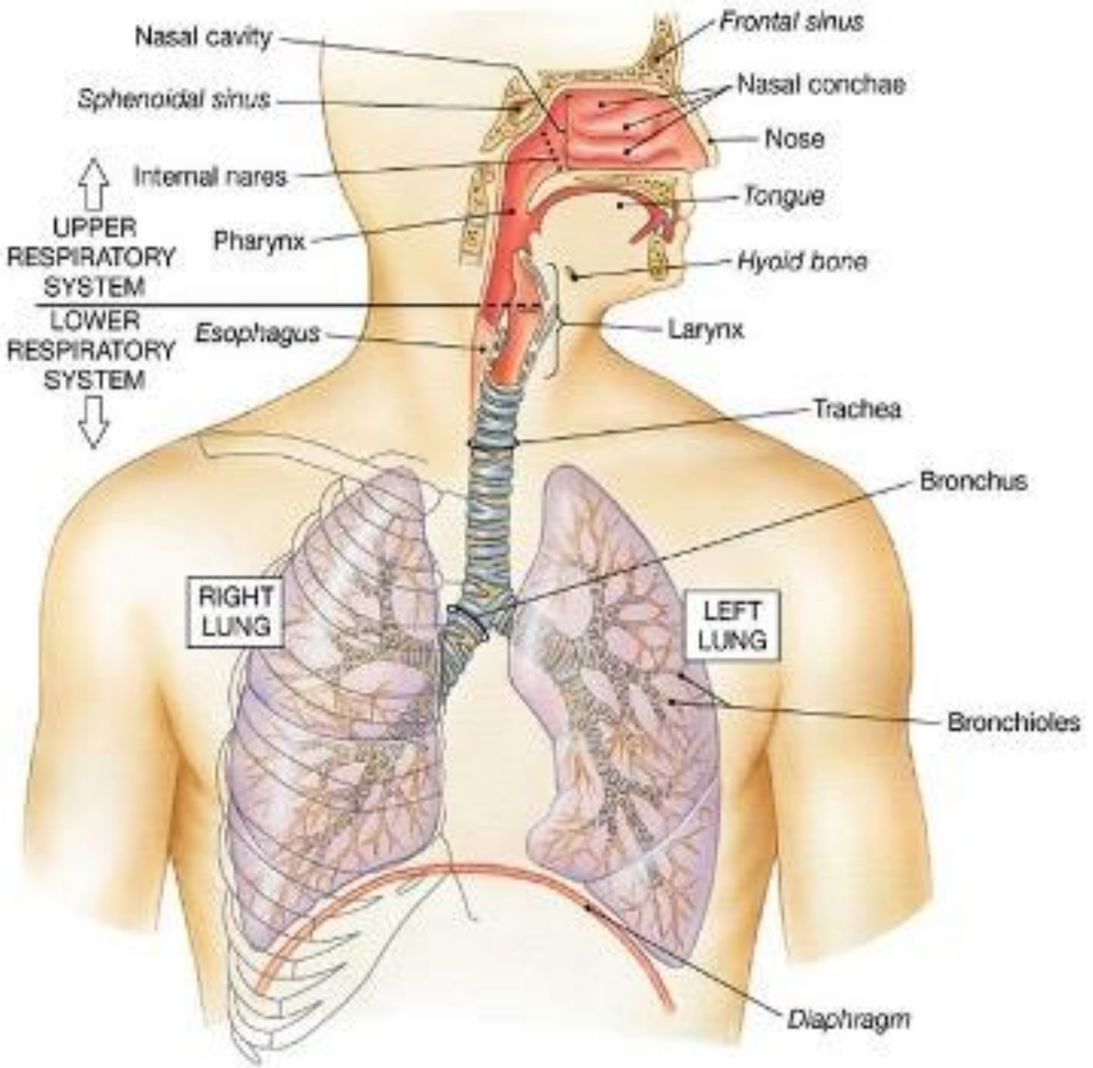
NON-DIRECT METHODS

- generally difficult to interpret results
- often non-specific positivity
- late onset of antibody production
- higher reliability when taking paired serum at a minimum of 10 days apart
- mainly to diagnose atypical agents, sometimes influenza, herpes viruses in immunocompromised



URT infections



Tonsillopharyngitis

- Typical for streptococcal etiology:
  - age 5-15 years
  - winter season (or November-May)
  - fever
  - cervical lymphadenopathy
  - pharyngitis - redness of tonsils, soft palate and uvula, petechiae on palate
  - Absence of other symptoms (rhinitis, cough, conjunctivitis)
  - epidemiological context
  - sudden onset,
  - Significant pain in the throat,
  - scarlatiniform exanthem
  - headaches,
  - vomiting and abdominal pain,
  - excoriations on the nose

- Viral tonsillopharyngitis - conjunctivitis, rhinitis, cough, hoarseness, stomatitis, small ulcerations in the oral cavity, diarrhea

Tonsillopharyngitis

- For streptococc
  - age 5-15 years,
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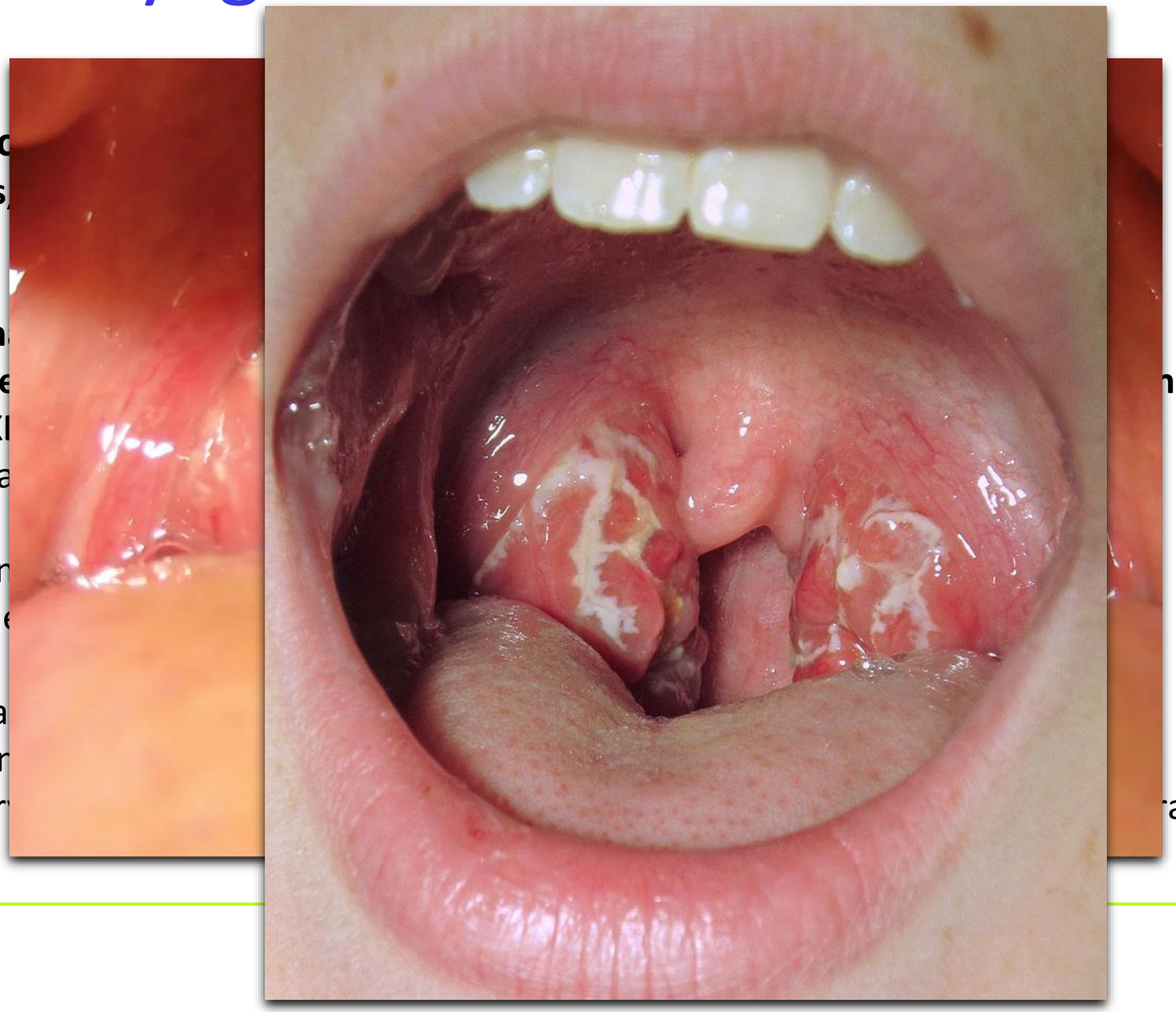

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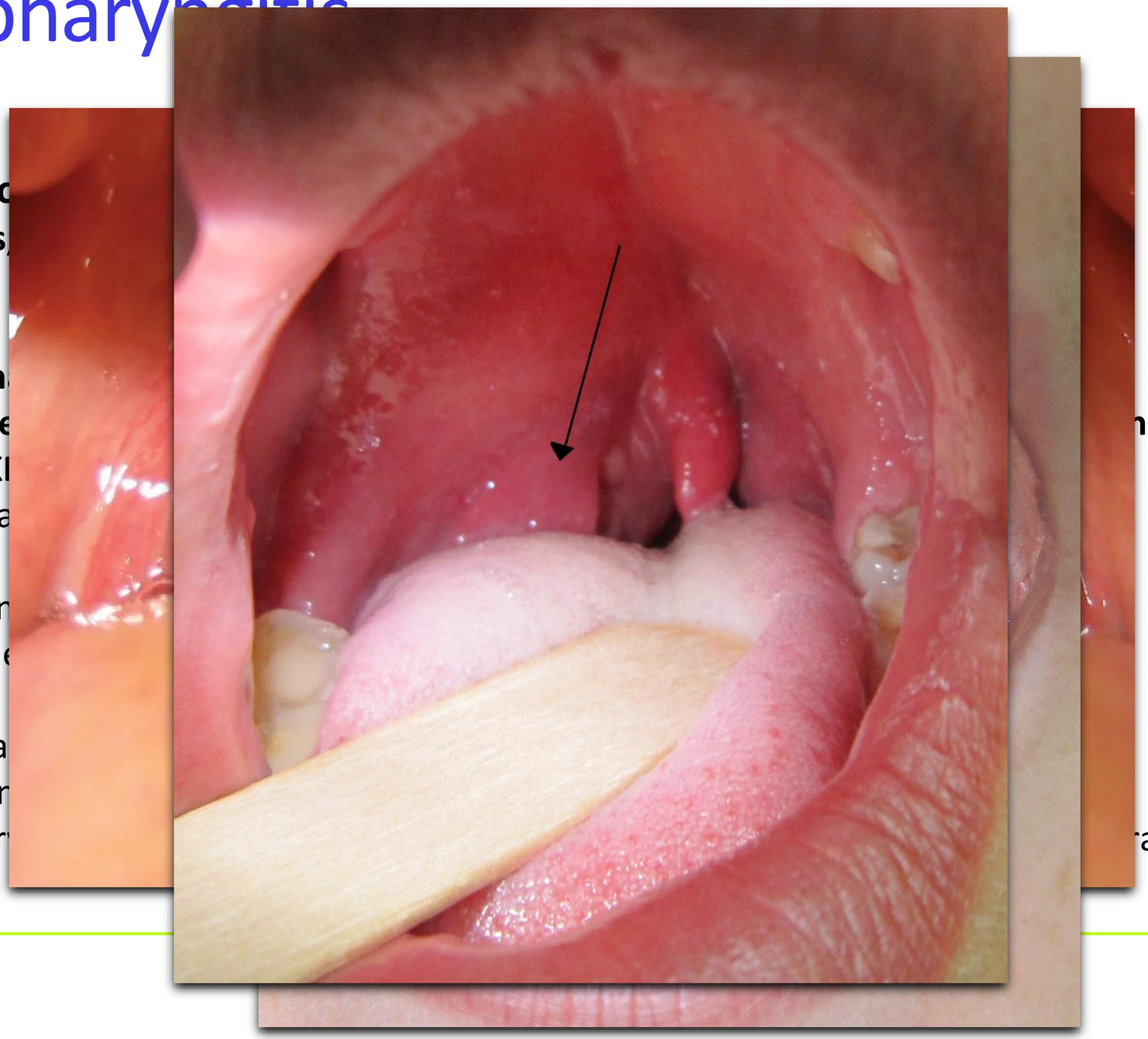

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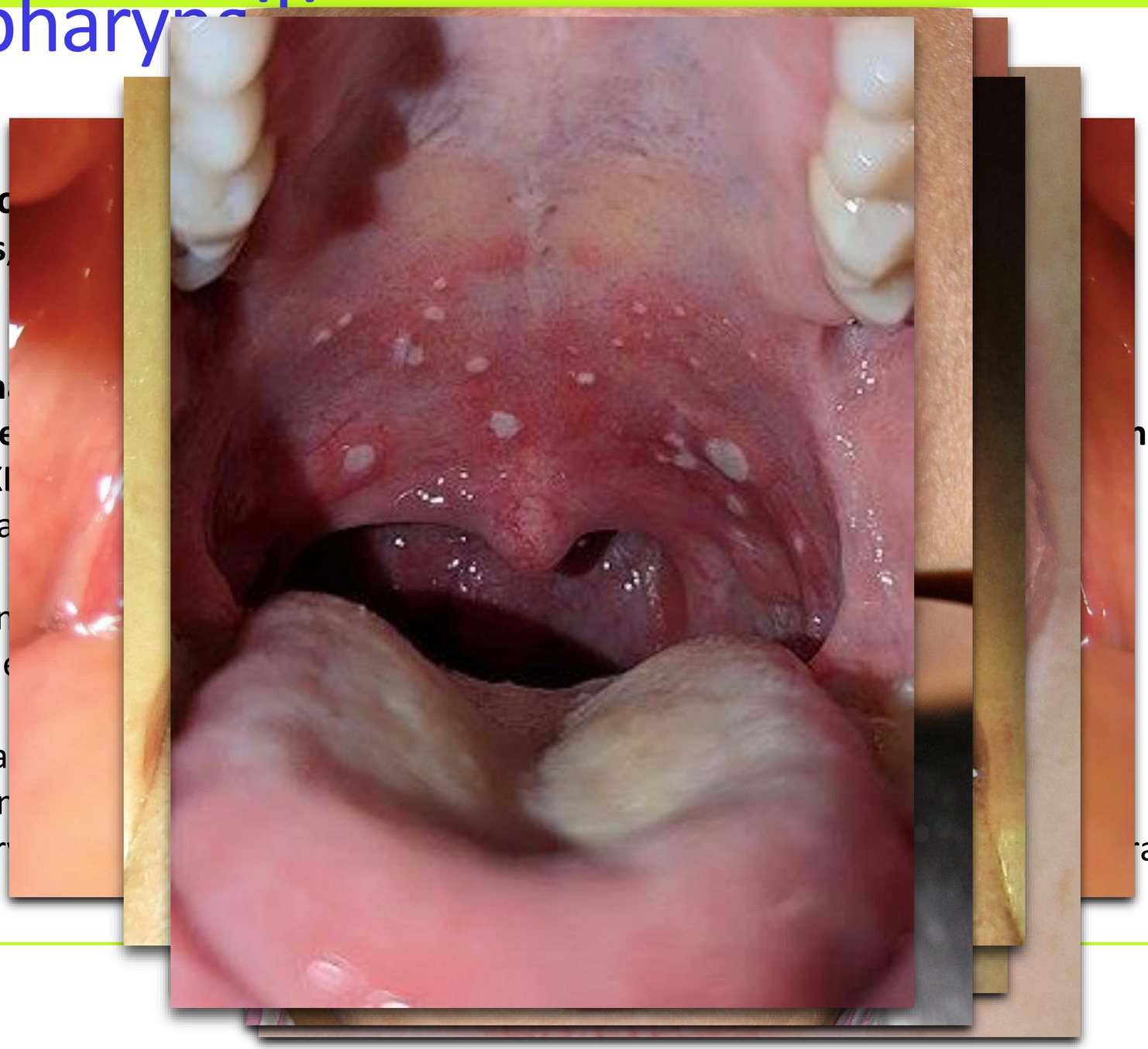

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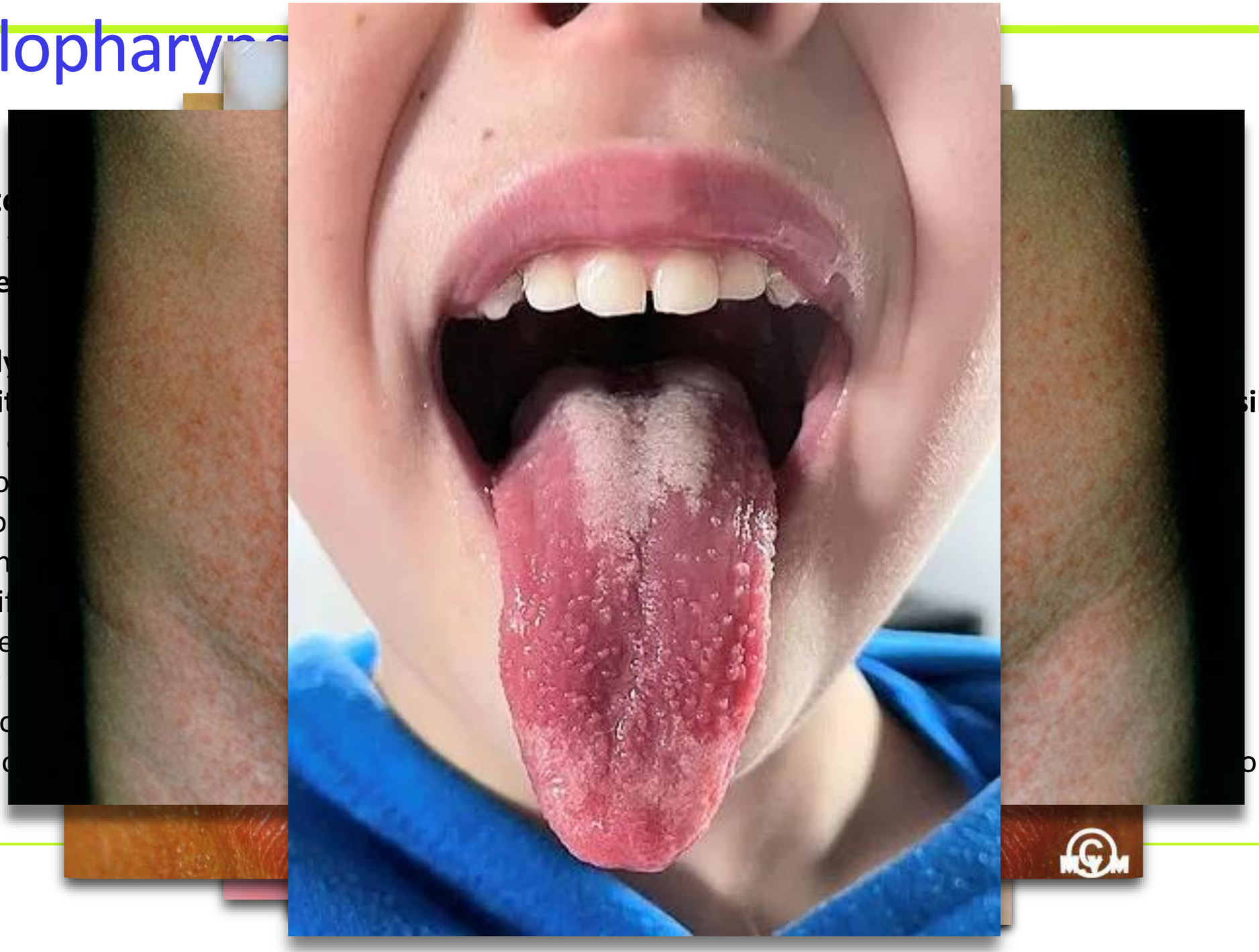
Tonsillopharyn



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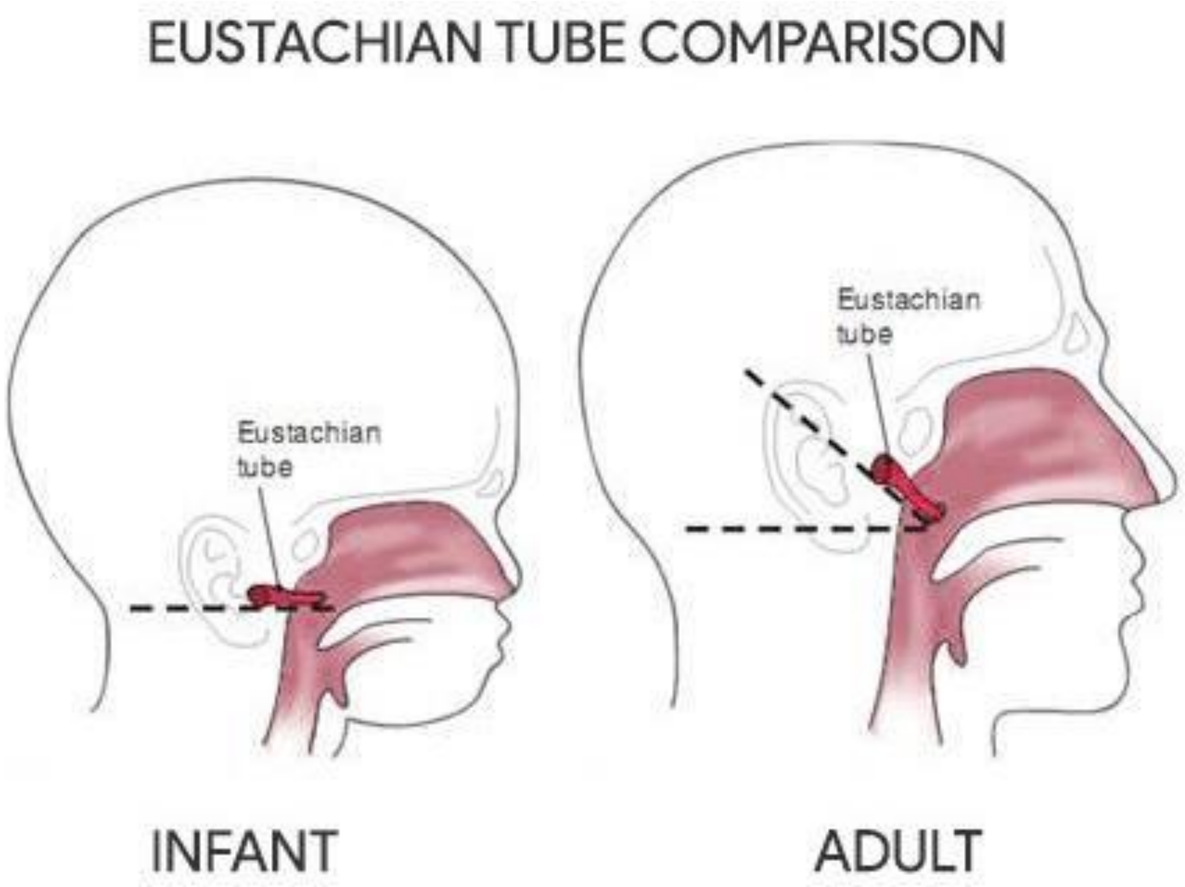
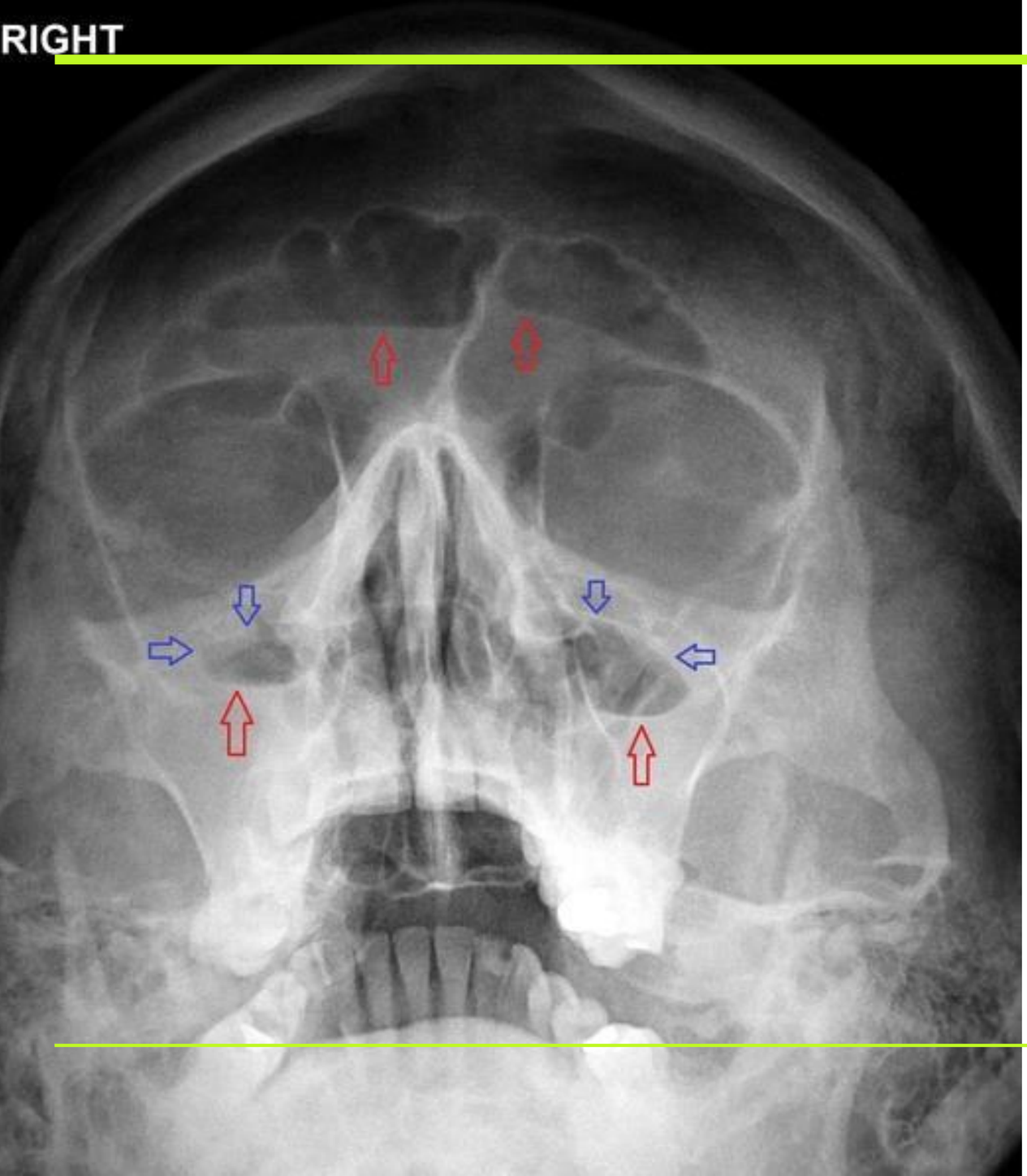
Otitis media acuta



- usually as a complication of other respiratory infections
- bacterial vs. viral 50/50, about 20% dual infection
- Bacterial
  - 80-90% *S.pneumoniae* and *H.influenzae*
  - Th.: amoxicillin, but 80% cure spontaneously even if untreated



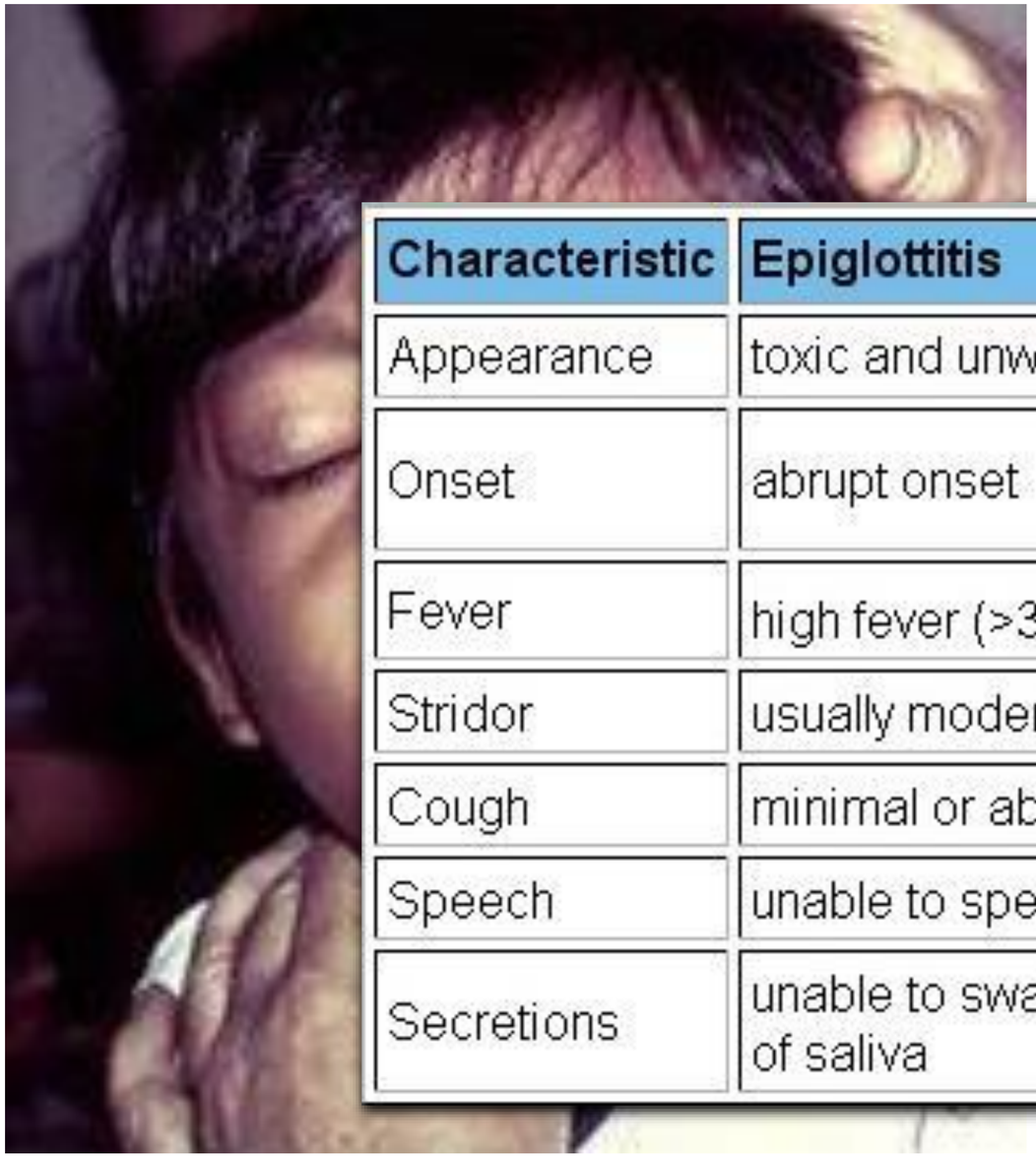
Sinusitis acuta

- initially almost always viral, with time the likelihood of bacterial superinfection increases
- the change in the nature of the secretion may not indicate bacterial inflammation (desquamation of the epithelium and PMN)
- feared complications - purulent meningitis, orbitocellulitis

Acute subglottic laryngitis and epiglottitis

- Epiglottitis
  - since the introduction of universal vaccination against *H.influenzae*
  - Th.: ATB, intensive care
- Laryngitis
  - Viral
  - Th.: oxygen, nebulization of adrenaline, corticosteroids

Acute subglottic laryngitis and epiglottitis



Characteristic	Epiglottitis	Croup
Appearance	toxic and unwell	well looking
Onset	abrupt onset	viral prodrome, slower onset
Fever	high fever (>38.5^{0}C)	moderate fever
Stridor	usually moderate-severe	usually mild-moderate
Cough	minimal or absent	barking, seal-like quality
Speech	unable to speak	hoarse voice
Secretions	unable to swallow, drooling of saliva	able to swallow

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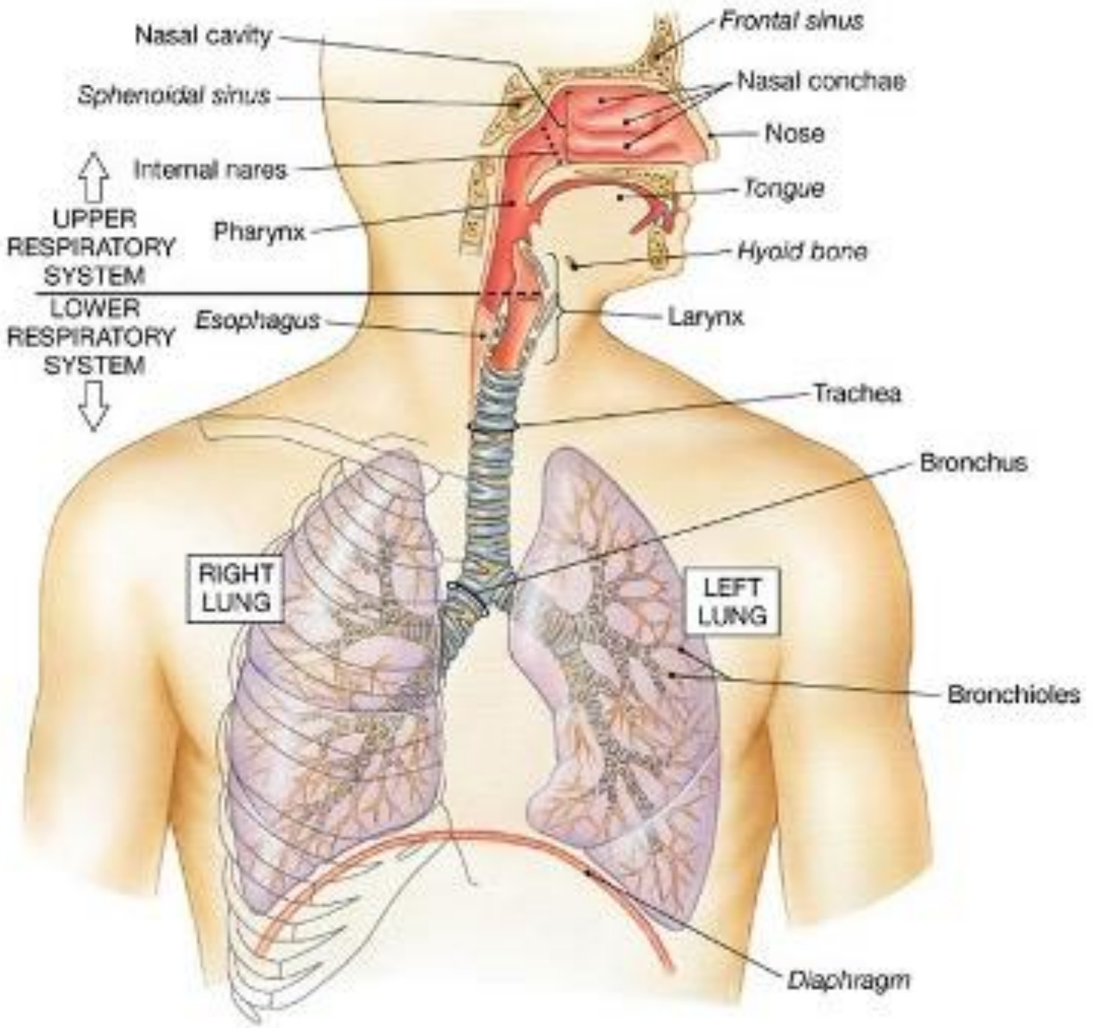
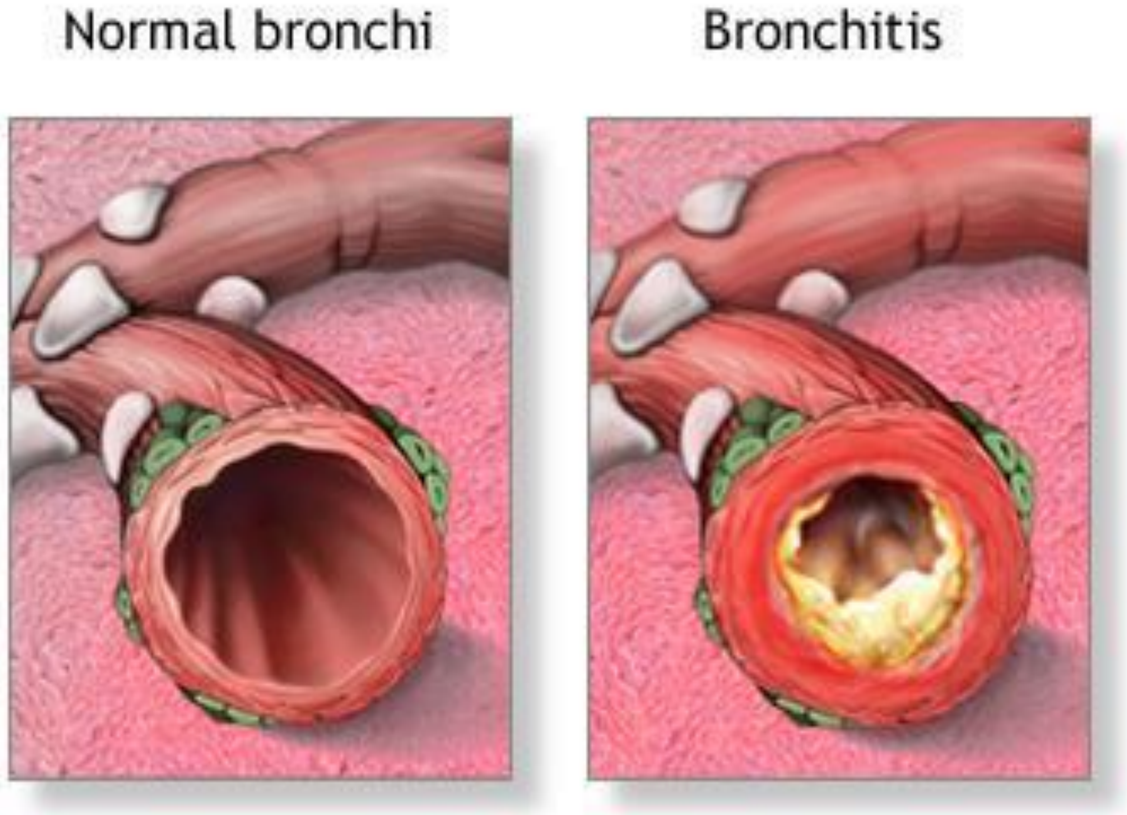
LRT infections

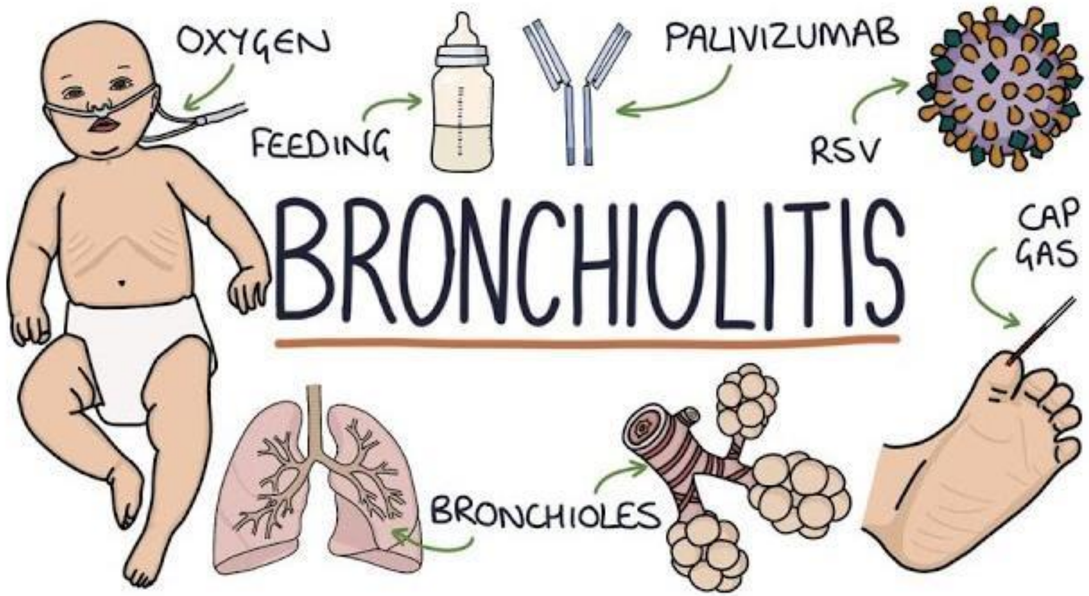


Acute bronchitis

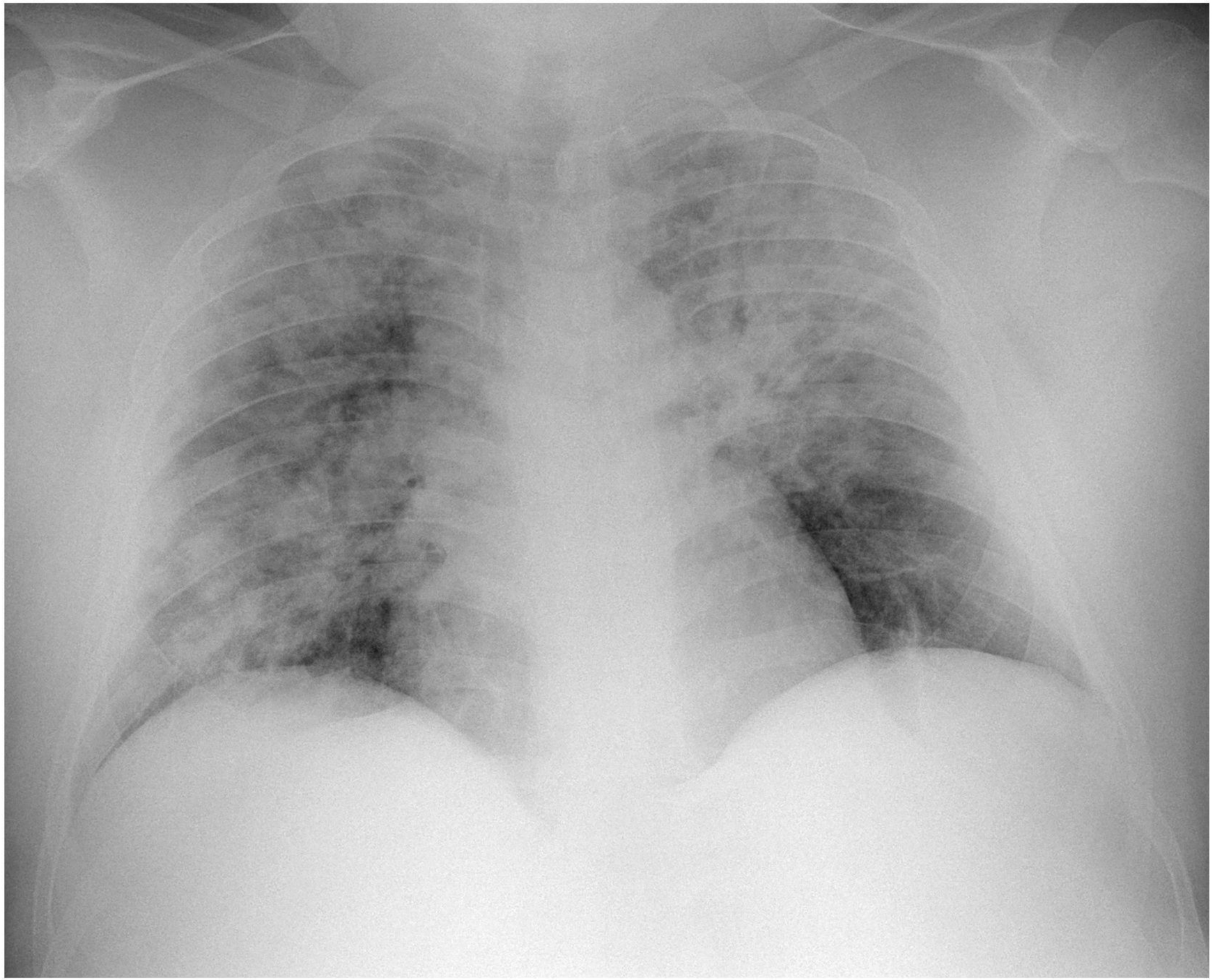


- 50-80% viral aetiology
- Bacterial
  - chlamydia, mycoplasmata, bordetella, haemophilus
  - mixed infections with pneumococci
- Th..:
  - corticosteroids, beta-mimetics, anticholinergics
  - ATB - aminoPNC (with beta-lactamase inhibitors in COPD patients), macrolides or combinations

Acute bronchiolitis



- primarily viral - 70-90% RSV
- Therapy
  - oxygen or ventilation, correction of the internal environment
  - KS and beta-mimetics usually without effect
  - ATB only for known superinfection



Diagnosing pneumonia

- Clinical
  - fever, cough, expectoration, auscultation findings - only in max. 2/3 of patients
- laboratory and imaging
- Microbiology
  - ideally direct methods - sputum, BAL, aspirate, haemoculture, urine antigens
  - Serology
  - even with the use of multiple methods, the aetiology is only clarified in a maximum of 50% of cases

Review > Lancet. 2011 Apr 9;377(9773):1264-75. doi: 10.1016/S0140-6736(10)61459-6. Epub 2011 Mar 22.

Viral pneumonia

Olli Ruuskanen [1], Elina Lahti, Lance C Jennings, David R Murdoch

Affiliations + expand

PMID: 21435708 PMCID: PMC7138033 DOI: 10.1016/S0140-6736(10)61459-6

Free PMC article

Abstract

About 200 million cases of viral community-acquired pneumonia occur every year-100 million in children and 100 million in adults. Molecular diagnostic tests have greatly increased our understanding of the role of viruses in pneumonia, and findings indicate that the incidence of viral pneumonia has been underestimated. In children, respiratory syncytial virus, rhinovirus, human metapneumovirus, human bocavirus, and parainfluenza viruses are the agents identified most frequently in both developed and developing countries. Dual viral infections are common, and a third of children have evidence of viral-bacterial co-infection. In adults, viruses are the putative causative agents in a third of cases of community-acquired pneumonia, in particular influenza viruses, rhinoviruses, and coronaviruses. Bacteria continue to have a predominant role in adults with pneumonia. Presence of viral epidemics in the community, patient's age, speed of onset of illness, symptoms, biomarkers, radiographic changes, and response to treatment can help

Review > Lancet. 20

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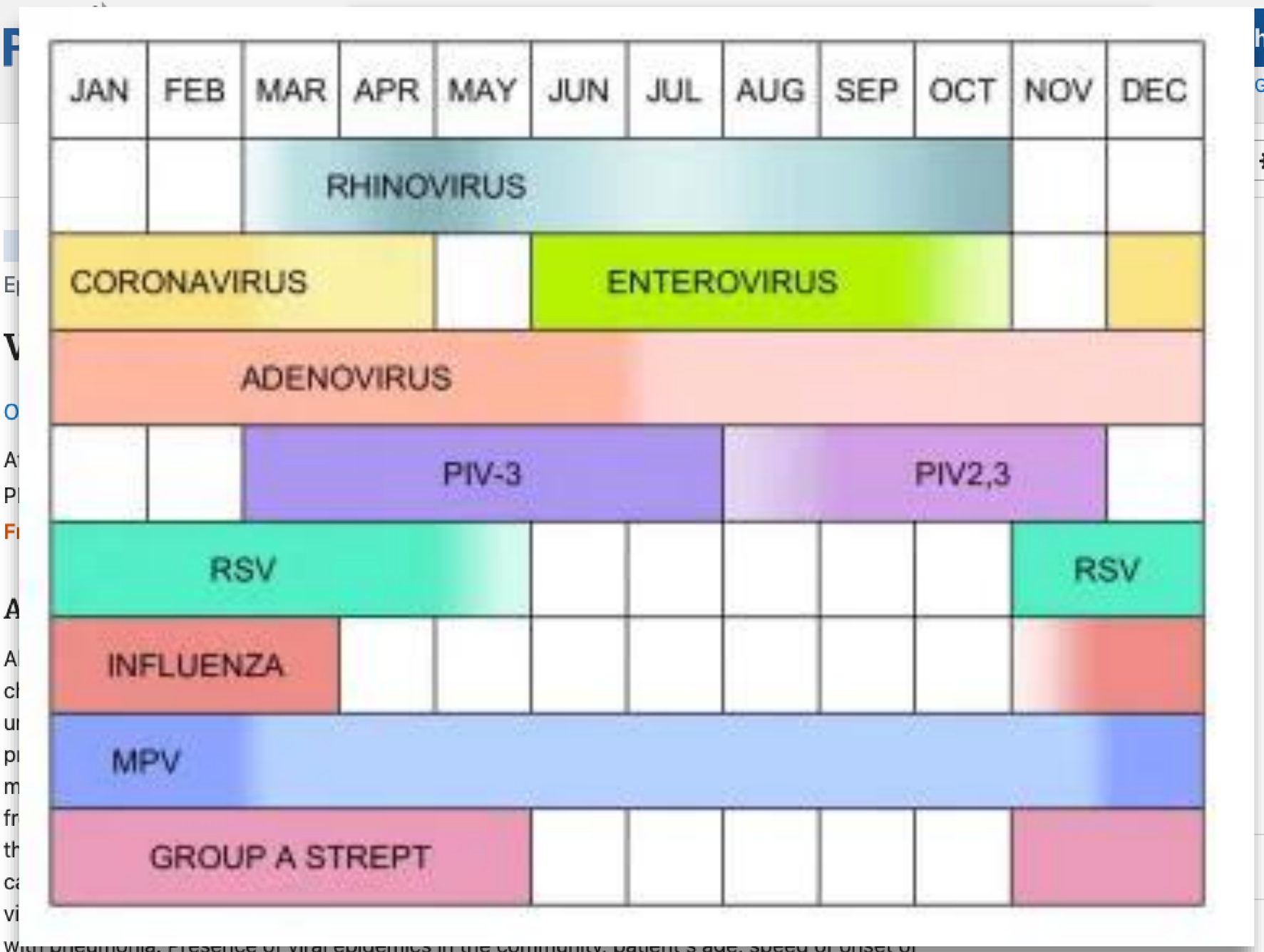
In 2011

- RS viruses most common agents - severe course, 50% immature infants
- Rhinoviruses - implicated in 11-53% of pneumonias
- Influenza, parainfluenza - 5-24% bacterial coinfection
- Adenoviruses - only 2-12%, but severe course, necrotizing pneumonia
- Human metapneumovirus - similar characteristics to RSV



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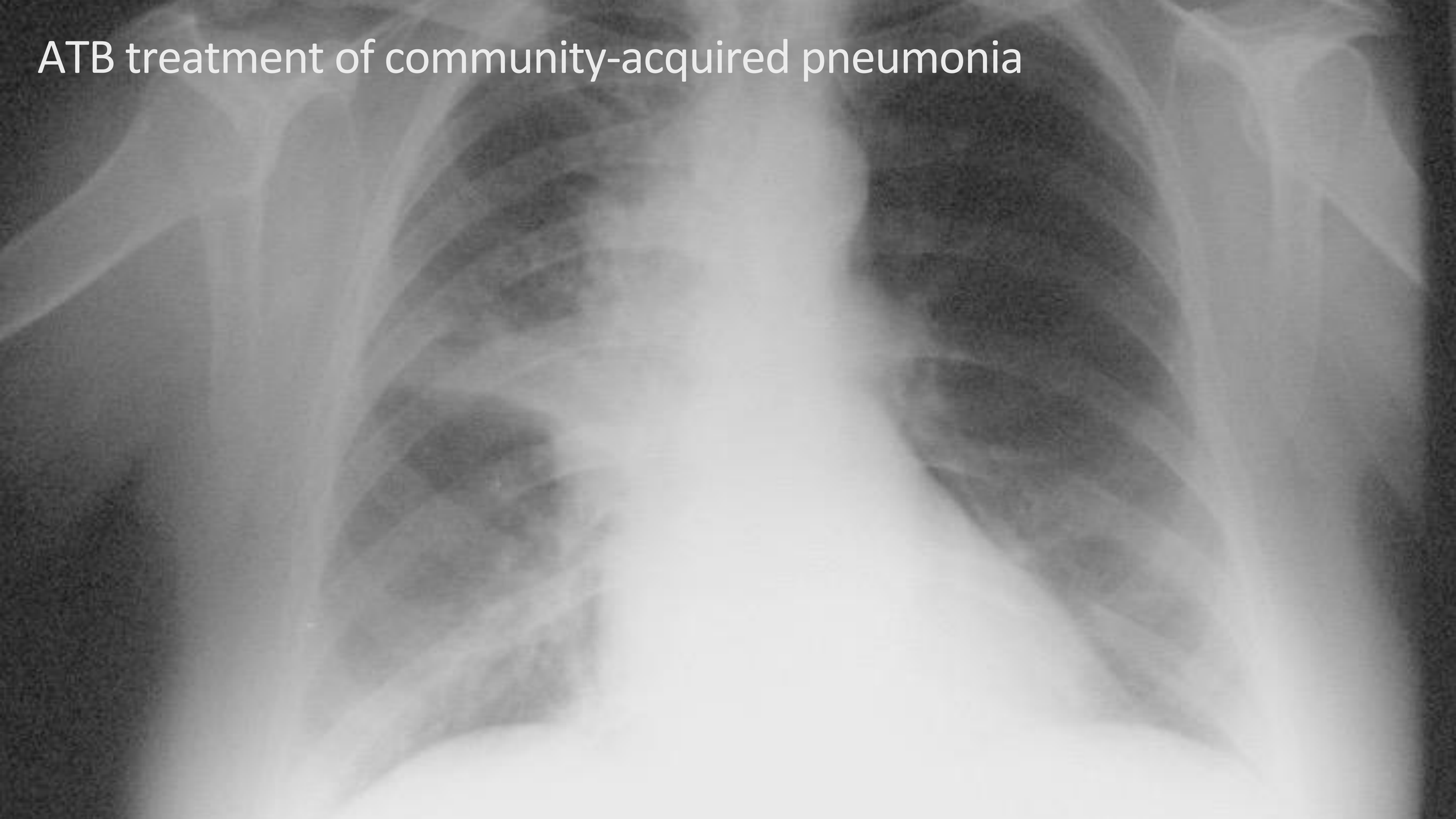
Figures

ATB treatment of community-acquired pneumonia



ATB treatment of community-acquired pneumonia

BETA-LACTAMS

- PENICILLINS
  - AMOXICLAV+AMPICILLIN COMBINATION
  - INH. BETA-LACTAMASE IN PATIENTS AT RISK (COPD)
  - PNC-G IN PROVEN PNEUMOCOCCAL ETIO.
- CEPHALOSPORINS
  - MAINLY 2ND AND 3RD GEN.
  - RELATIVELY LOW RISK OF PNC ALLERGY

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MACROLIDES

- TO COVER ATYPICAL AGENTS (MYCOPLASMA, CHLAMYDIA, LEGIONELLA)
- IN HIGH-RISK PATIENTS, COMBINATION WITH BETA-LACTAM
- HIGHER RISK OF RESISTANCE IN MONOTHERAPY (PNEUMOCOCCI, HAEMOPHILUS)
- CAVE: DRUG INTERACTIONS (LOWER RISK WITH AZITHROMYCIN)

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FLUOROQUINOLONES

- RESPIRATORY - MOXIFLOXACIN
- GOOD TISSUE PENETRATION, COVERAGE OF TYPICAL AND ATYPICAL AGENTS
- RISK OF FMD AND SELECTION OF RESISTANT STRAINS, NOT AS FIRST CHOICE

ATB treatment of community-acquired pneumonias

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  - PNC-G IN PROVEN PNEUMOCOCCAL ETIO.
- CEPHALOSPORINS
  - MAINLY 2ND AND 3RD GEN.
  - RELATIVELY LOW RISK OF PNC ALLERGY

MACROLIDES

- TO COVER ATYPICAL AGENTS (MYCOPLASMA, CHLAMYDIA, LEGIONELLA)
- IN HIGH-RISK PATIENTS, COMBINATION WITH BETA-LACTAM
- HIGHER RISK OF RESISTANCE IN MONOTHERAPY (PNEUMOCOCCI, HAEMOPHILUS)
- CAVE: DRUG INTERACTIONS (LOWER RISK WITH AZITHROMYCIN)

FLUOROQUINOLONES

- RESPIRATORY - MOXIFLOXACIN
- GOOD TISSUE PENETRATION, COVERAGE OF TYPICAL AND ATYPICAL AGENTS
- RISK OF FMD AND SELECTION OF RESISTANT STRAINS, NOT AS FIRST CHOICE

TETRACYCLINES

- BROAD SPECTRUM
- BACTERIOSTATIC
- RISK OF ADVERSE EFFECTS

When to hospitalize?

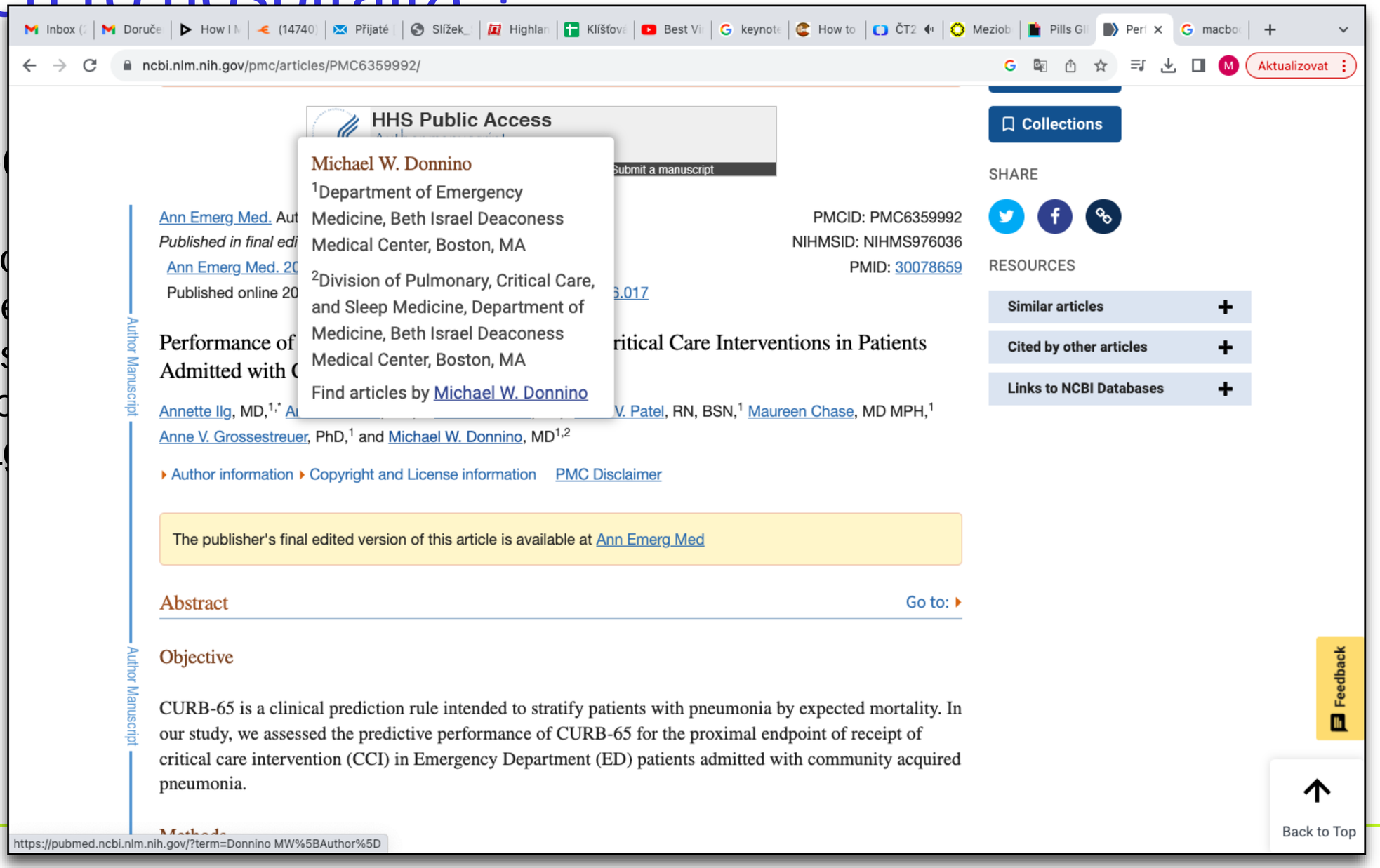
CURB-65

- C - confusion
- U - urea (above 7mmol/l)
- R - respiration (tachypnea above 30/min.)
- B - blood pressure (BP below 90/DBP below 60)
- 65 - age over 65

When to hospitalize?

CURB-

- C - c
- U - ur
- R - re
- B - bl
- 65 - a



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Michael W. Donnino

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Performance of ritical Care Interventions in Patients Admitted with

Annette Ilg, MD,[1,*] A V. Patel, RN, BSN,[1] Maureen Chase, MD MPH,[1] Anne V. Grossestreuer, PhD,[1] and Michael W. Donnino, MD[1,2]

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Abstract

Go to:

Objective

CURB-65 is a clinical prediction rule intended to stratify patients with pneumonia by expected mortality. In our study, we assessed the predictive performance of CURB-65 for the proximal endpoint of receipt of critical care intervention (CCI) in Emergency Department (ED) patients admitted with community acquired pneumonia.

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Predisposing factors in relation to the aetiology of CAP

- alcoholism - S. pneumoniae, anaerobes, G- bacilli

- COPD - S. pneumoniae, H. influenzae, M. catarrhalis, Legionella

- Senior centres and homes - S. pneumoniae, G- bacilli, H. influenzae, S. aureus, anaerobes, Chl. pneumoniae

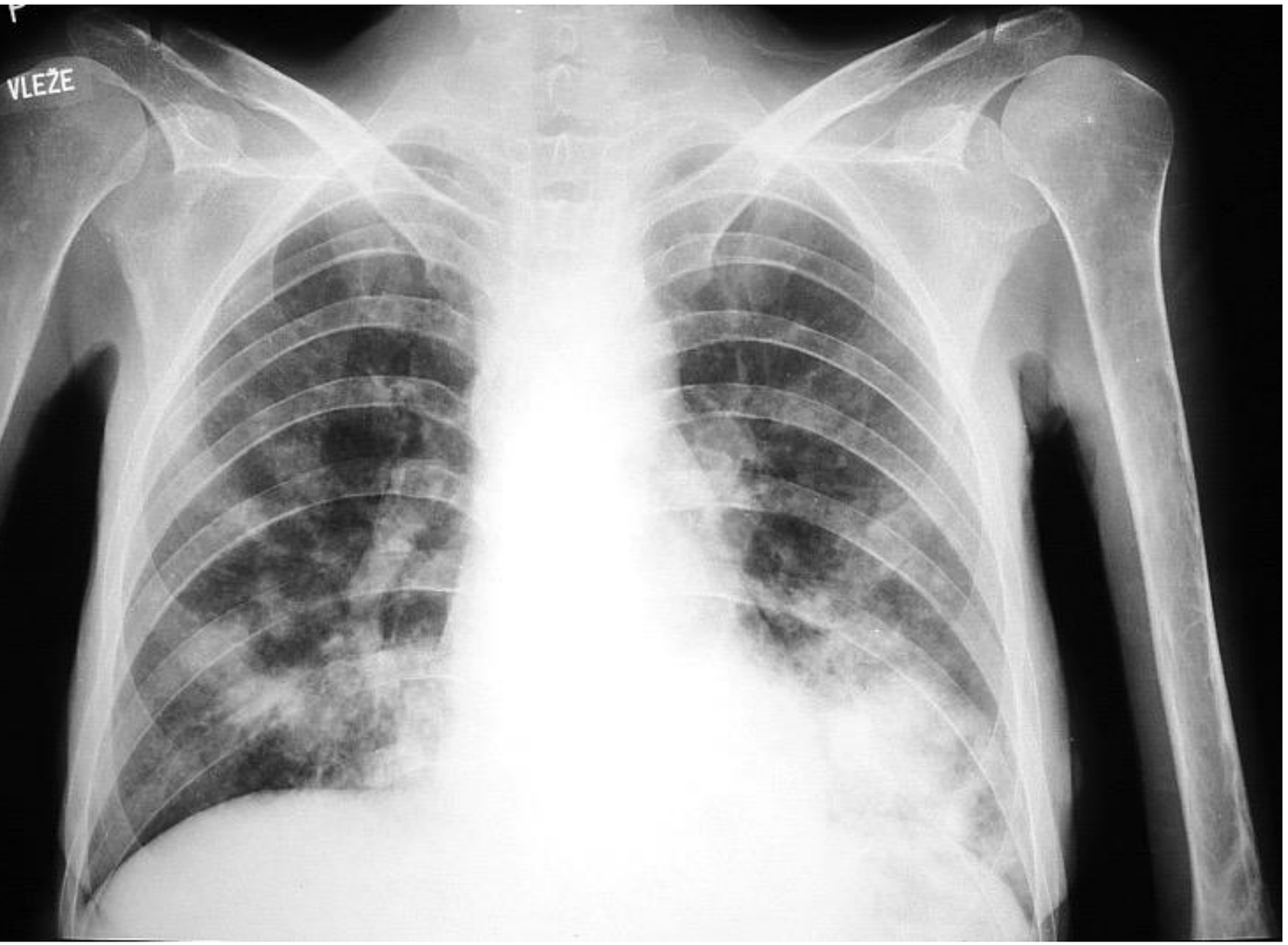
- poor dental hygiene - anaerobes

- epidemic occurrence - Legionella

- influenza epidemics - influenzae virus, S. pneumoniae, S. aureus, S. pyogenes, H. influenzae

- aspiration - anaerobes

- bronchiectasis - S. aureus, P. aeruginosa



Predisposing factors in relation to the etiology of CAP

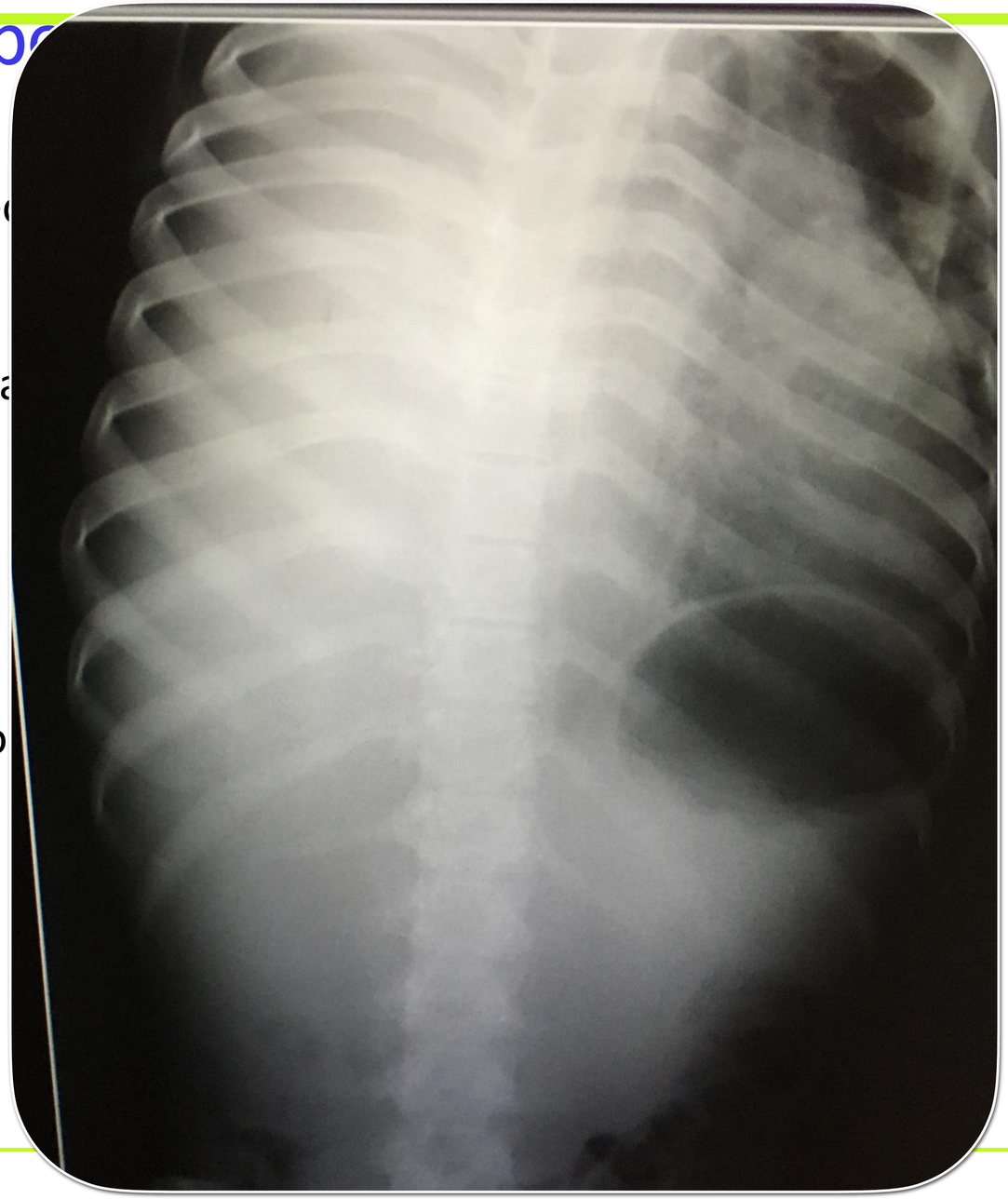
- CF - S. aureus, P. aeruginosa, B. cepacia
- i.v. drug addicts - S. aureus, anaerobes, TB
- airway obstruction - anaerobes
- contact with animals
    - *Chl. psittaci*
    - *F. tularensis*
    - *C. burnetti*
    - Histoplasmosis
- endemic area - coccidiomycosis

Pneumonia unresponsive to treatment

- resistant pathogen (or unrecognised pathogen or polymicrobial flora)
- inadequate ATB treatment
- complications of pneumonia
- misdiagnosis
  - pulmonary embolism
  - cardiac failure
  - non-infectious pneumonia
  - vasculitis
  - malignancy
  - aspirations

Pneumonia unrespo

- resistant pathogen (or unre
- inadequate ATB treatment
- complications of pneumonia
- misdiagnosis
  - pulmonary embolism
  - cardiac failure
  - non-infectious pneumo
  - Vasculitis
  - Malignancy
  - Aspirations



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  - cardiac failure
  - non-infectious pneumo
  - Vasculitis
  - Malignancy
  - Aspirations

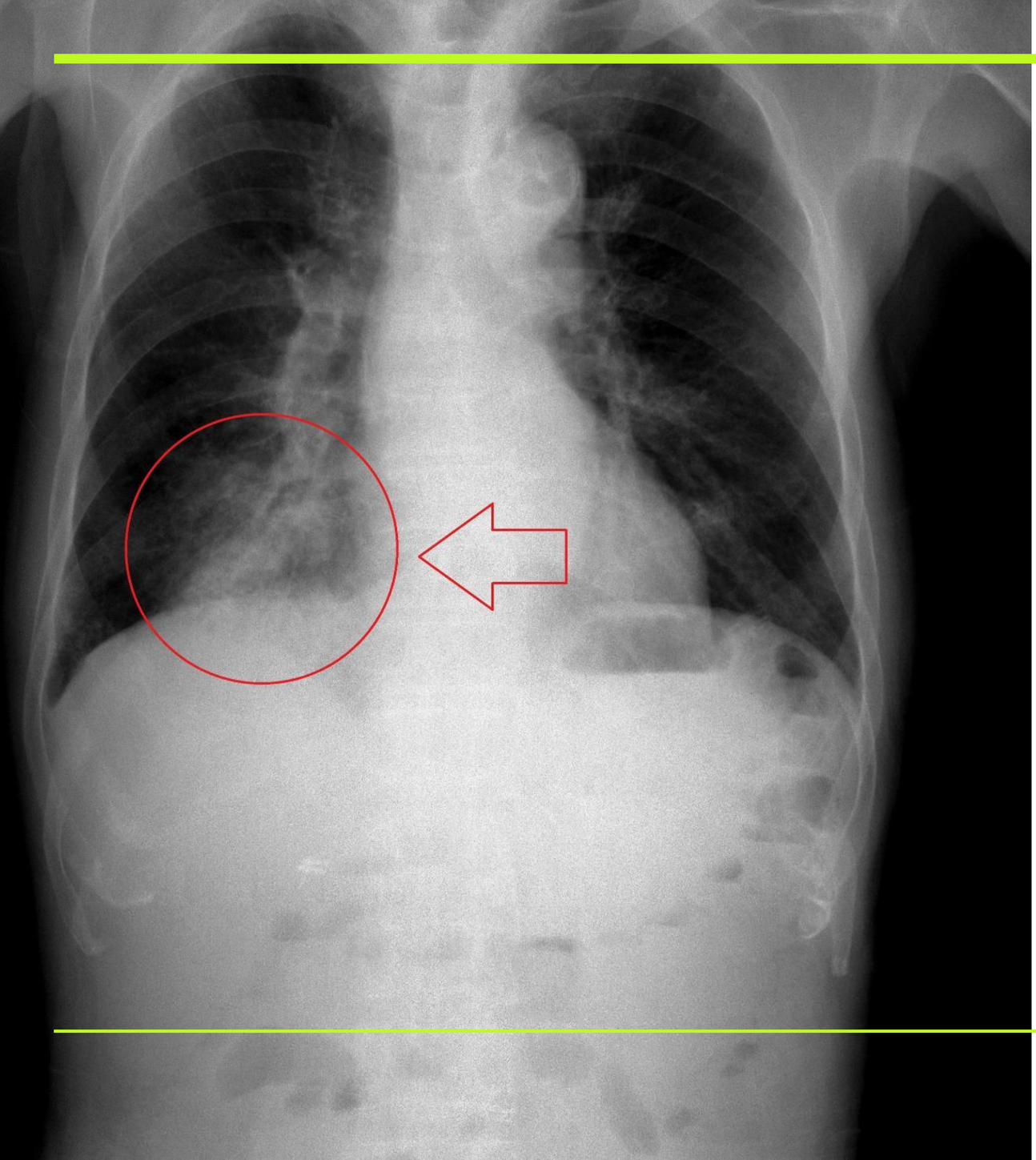
Nosocomial pneumonia

EARLY

- BY THE 4TH DAY AFTER ADMISSION
- USUALLY RATHER ENDOGENOUS FLORA OF THE PATIENT
  - S.AUREUS
  - STR.PNEUMONIAE
  - H.INFLUENZAE
  - M.CATARRHALIS
- ATB USED TO TREAT COMMUNITY-ACQUIRED PNEUMONIA ARE USUALLY SUFFICIENT

LATE

- FROM THE 5TH DAY AFTER ADMISSION
- ESPECIALLY IN VENTILATED PATIENTS
- HIGH RISK OF INFECTION WITH RESISTANT HOSPITAL STRAINS
  - PS.AERUGINOSA
  - KL.PNEUMONIAE
  - PROTEUS, SERRATIA, ACINETOBACTER
  - ST.AUREUS
  - ENTEROBACTERIACEAE
  - ANAEROBES, FUNGI, VIRUSES
- USE OF BROAD-SPECTRUM ATBS OFTEN NECESSARY
  - PIPERACILLIN/TAZOBACTAM
  - CARBAPENEMS
  - CEFTAZIDIME
  - LINEZOLID
  - COLISTIN



Aspiration pneumonia

- risk groups
  - alcoholics, i.v. addicts
  - Seniors
  - Children
  - Patient with swallowing disorders
- often creeping onset, cough with purulent expectoration, weight loss
- X-ray: infiltration in the lower lobes, in S2 and S6
- etio.: flora of the oral cavity, anaerobes, G-bacteria, St.aureus, H.influenzae

Pneumonia in children

Pneumonia in children

BACTERIAL

- CLINICAL FINDINGS
  - EXPECTORATION
  - THE ABSENCE OF OBSTRUCTIVE PHENOTYPES.
  - HIGH FEVERS, RAPID ONSET OF SYMPTOMS
- ELEVATION OF INFLAMMATORY PARAMETERS
  - NEUTROPHILIA ABOVE 9000/UL, MORE THAN 5% OF RODS
  - CRP ABOVE 80MG/L, PCT ABOVE 1UL/L
- RTG
  - ROUND, LOBULAR OR SEGMENTAL INFILTRATE
  - CAVITATION, FLUIDOTHORAX
- ATB
  - USUALLY AMINOPENICILLINS OR MACROLIDES
  - IN NEWBORNS AMPI+GEN OR CEF. 3RD GENE
  - TETRACYCLINES OVER 8 YEARS, QUINOLONES IN CHILDREN NO

Pneumonia in children

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VIRAL

- OFTEN OBSTRUCTIVE PHENOMENA
  - WHISTLING, RETRACTING, PROLONGATION OF EXSPIRATION
  - RATHER SUBFEBRILE
  - SLOWER PROGRESSION
- RTG
  - INDISTINCTLY DEMARCATED INFILTRATES
  - INTERSTITIAL OR PERIBRONCHIAL INFILTRATES, SUBSEPTAL ATELECTASIS
  - BILAT. FINDING
- LOWER INFLAMMATORY PARAMETERS

Pneumonia

BACTE

- CLINICAL FINDINGS
  - EXPECTORATION
  - THE ABSENCE OF OB
    PHENOTYPES.
  - HIGH FEVERS, RAPID
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  - IN NEWBORNS AMPI
    GENE
  - TETRACYCLINES OVER 8 YEARS,
    QUINOLONES IN CHILDREN NO

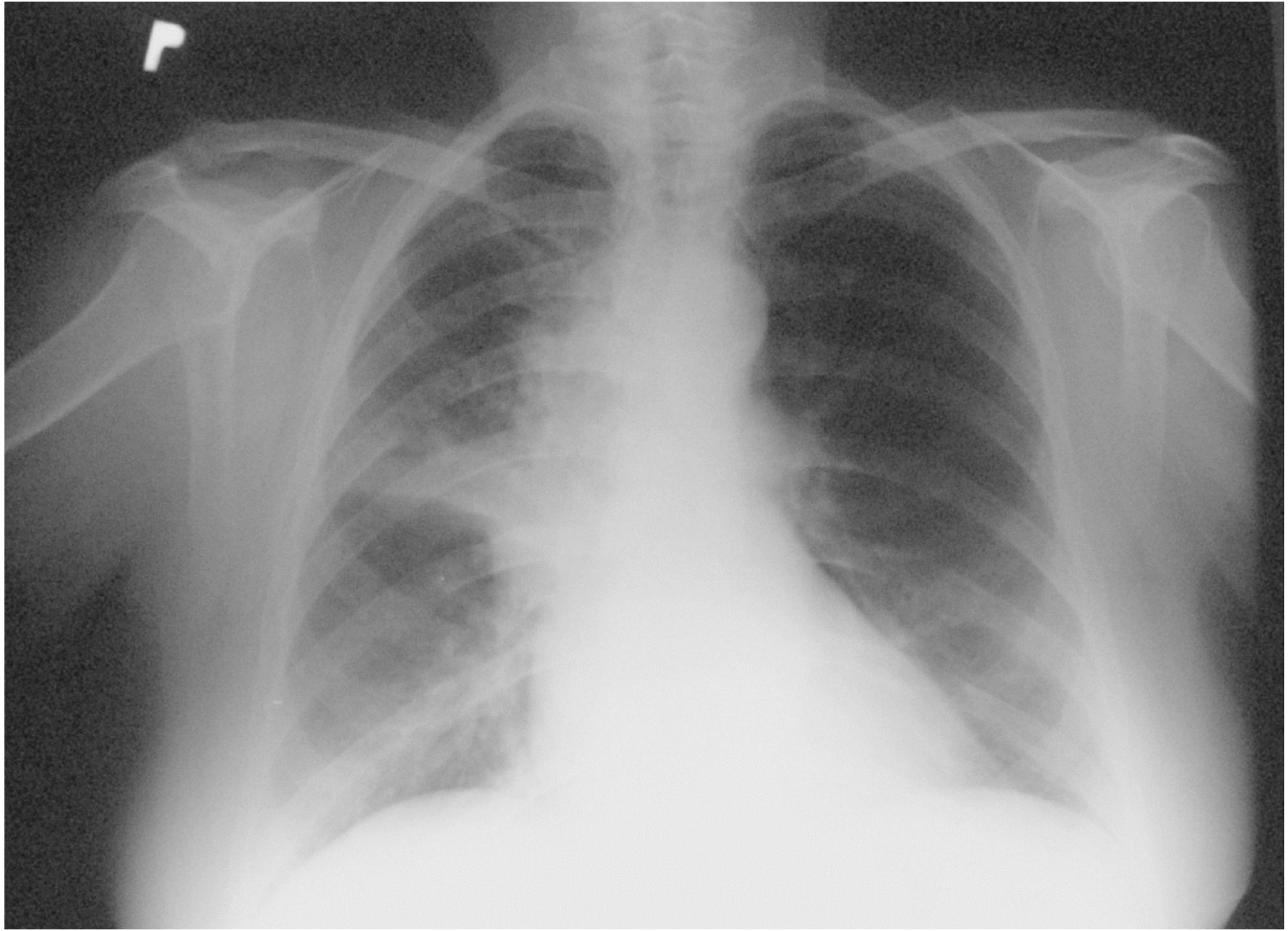
WHEN TO DEFINITELY HOSPITALIZE

- AGE UNDER 2 MONTHS
- DISORDER OF CONSCIOUSNESS
- RESTING STRIDOR, GRUNTING,
  SIGNIFICANT RETRACTION
- CYANOSIS, SATURATION BELOW 92%
- SEVERE MALNUTRITION, EATING DISORDER
- NON-COMPLIANCE FAMILIES
- FAILURE OF OUTPATIENT TREATMENT

VIRAL

CTIVE PHENOMENA
ETRACTING,
N OF EXSPIRATION
EBRILE
RESSION

DEMARCATED INFILTRATES
OR PERIBRONCHIAL
SUBSEPTAL ATELECTASIS
G
MATORY PARAMETERS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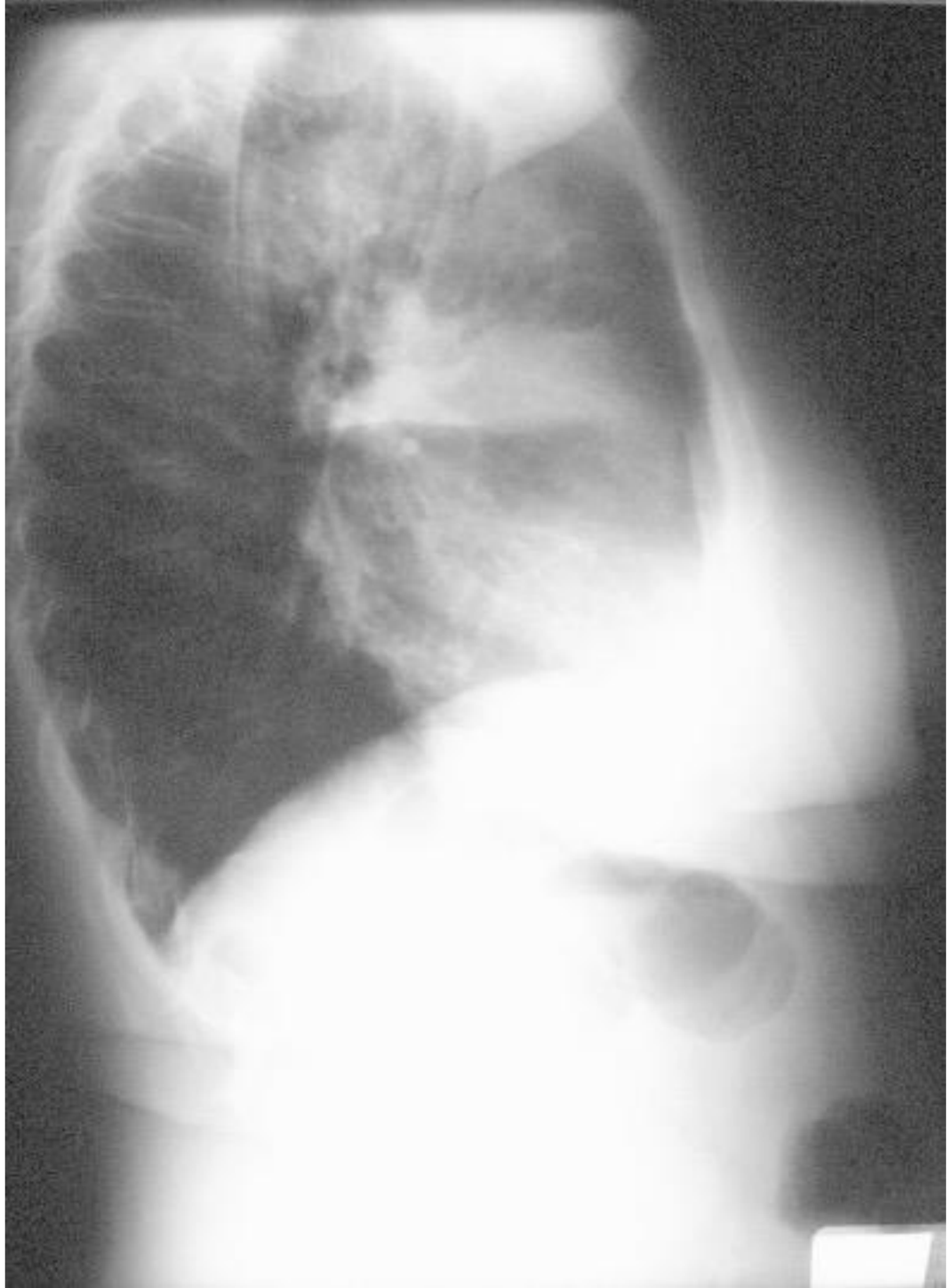
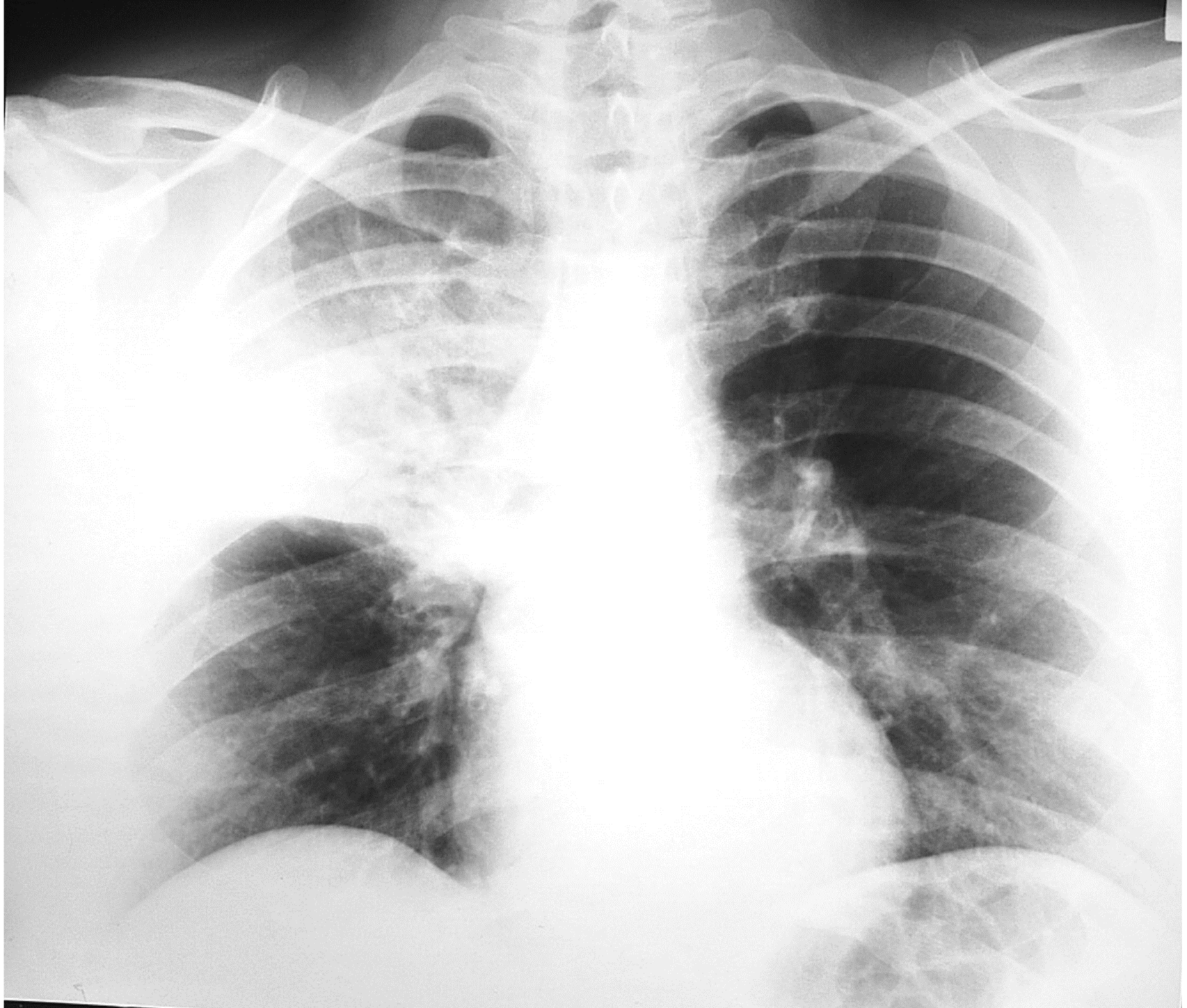
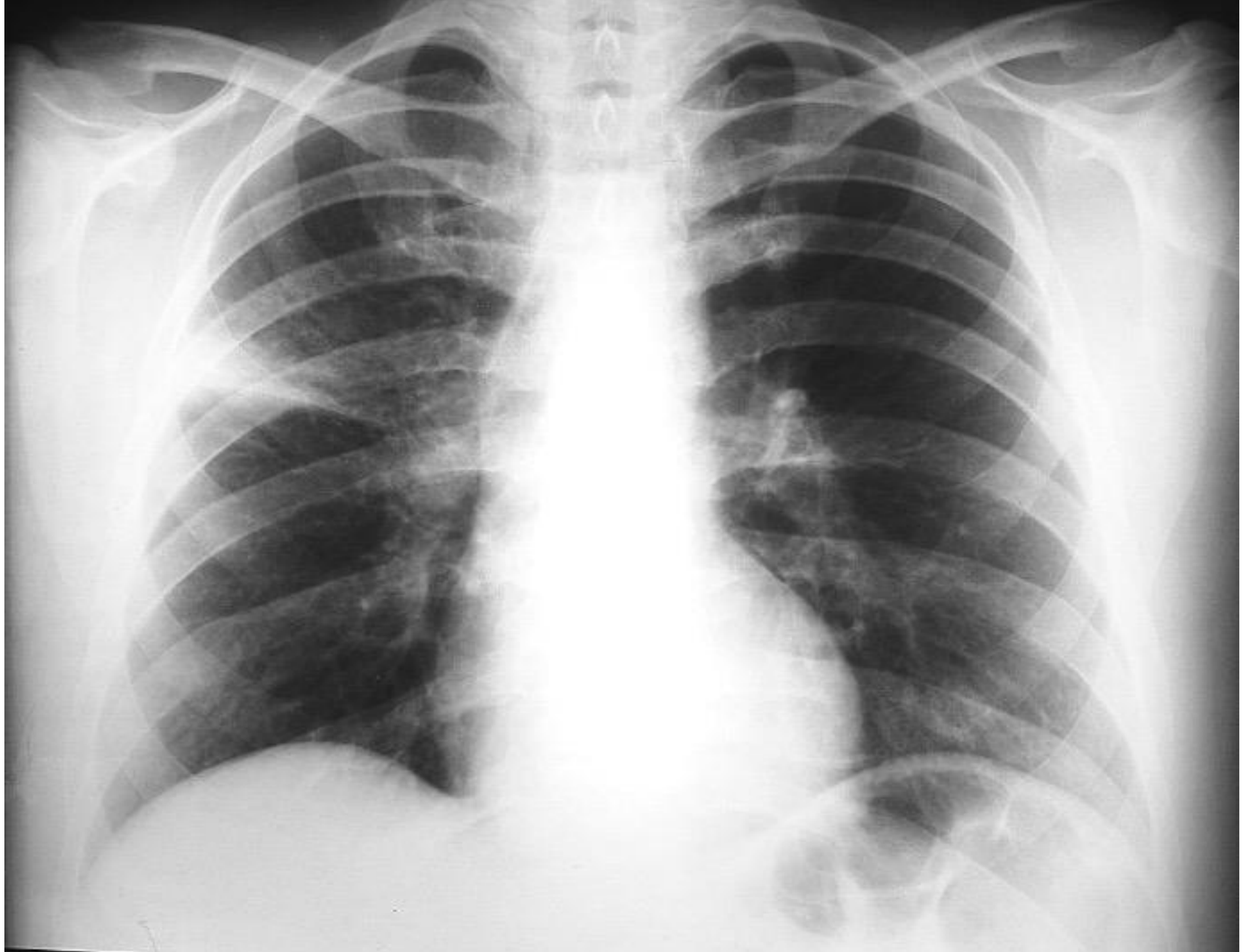






Whooping cough

- *Bordetella pertussis and parapertussis*
  - aerobic G- coccobacillus
  - growth on enriched medium
  - affinity for airway epithelium
  - virulence factors
    - adhesins
    - toxins (pertussis toxin, tracheal cytotoxin)

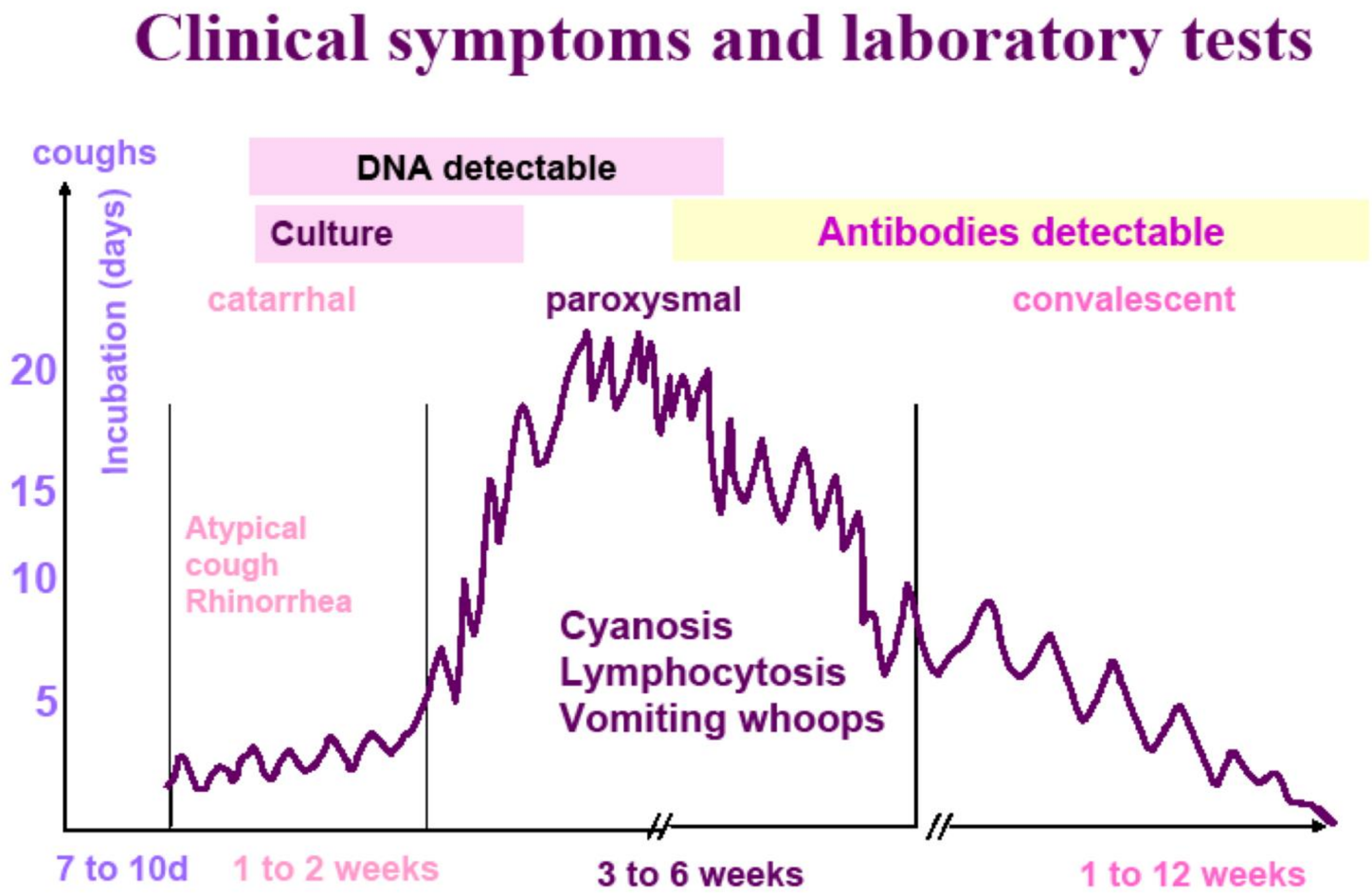
Whooping cough

- droplet infection
- used tol be a common infection - epidemics in 2-5 year cycles
- decrease in incidence after vaccination, now increasing again (shift to higher age category)

Whooping cough

- definition - cough for at least 2 weeks + 1 of the following symptoms (whooping cough, coughing fits, apnoic pauses in infants, gagging after a coughing fit)
- catarrhal, paroxysmal and convalescent stages
- complications - asphyxia, encephalopathy, CNS haemorrhage, pneumothorax, secondary infection
- Therapy: clarithromycin for 7 days od Azithromycin for 5 days

Diagnosis of pertussis



HELIOS Kliniken

Institut Pasteur

Antivirals to treat influenza

M2 protein inhibitors (influenza A only)

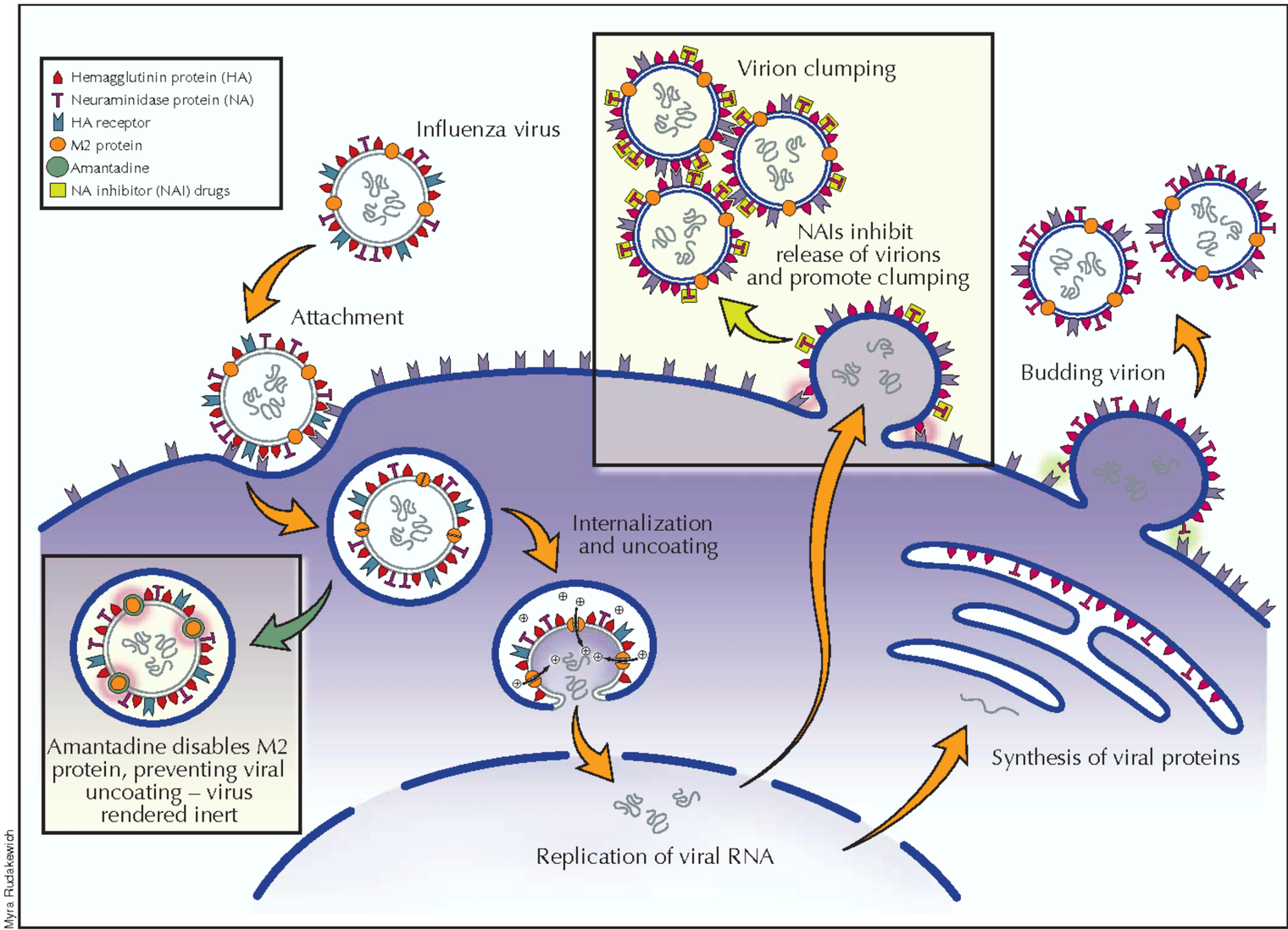
- amantadine (Viregyt K - tbl.)
- rimantadine

Neuraminidase inhibitors

- **oseltamivir (Tamiflu - tbl.)**
- zanamivir (Relenza - inh.)

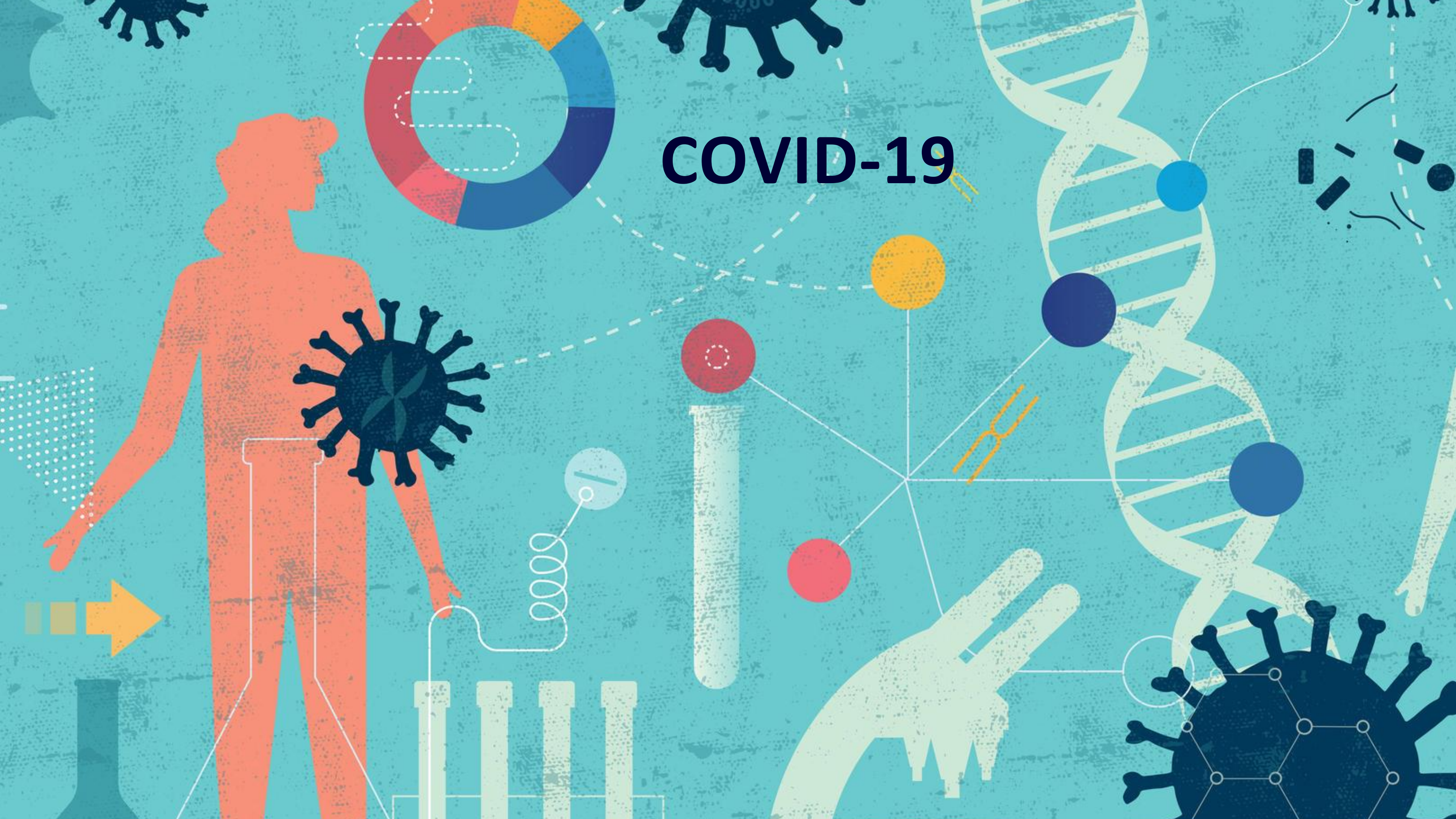
Available at

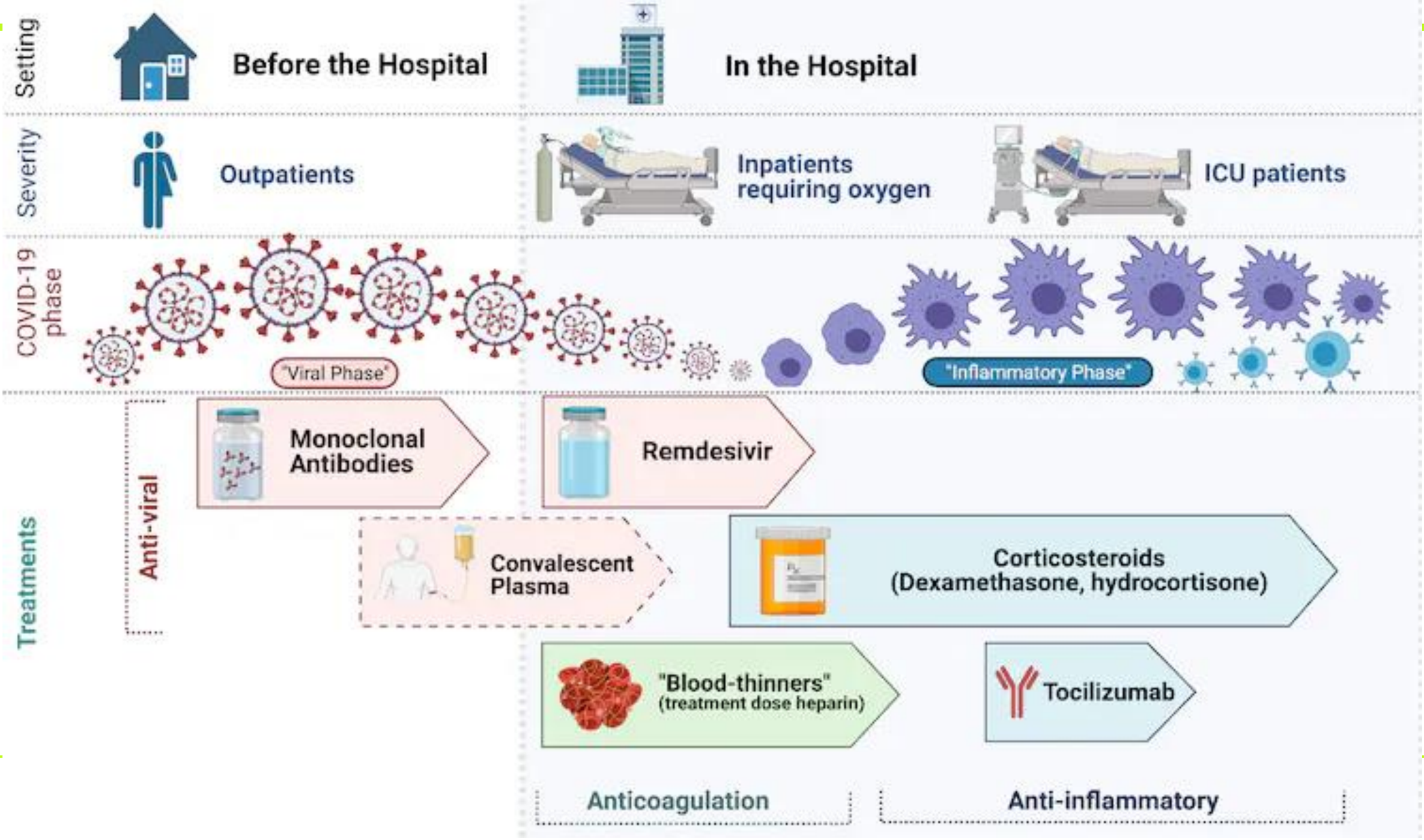
Unavailable

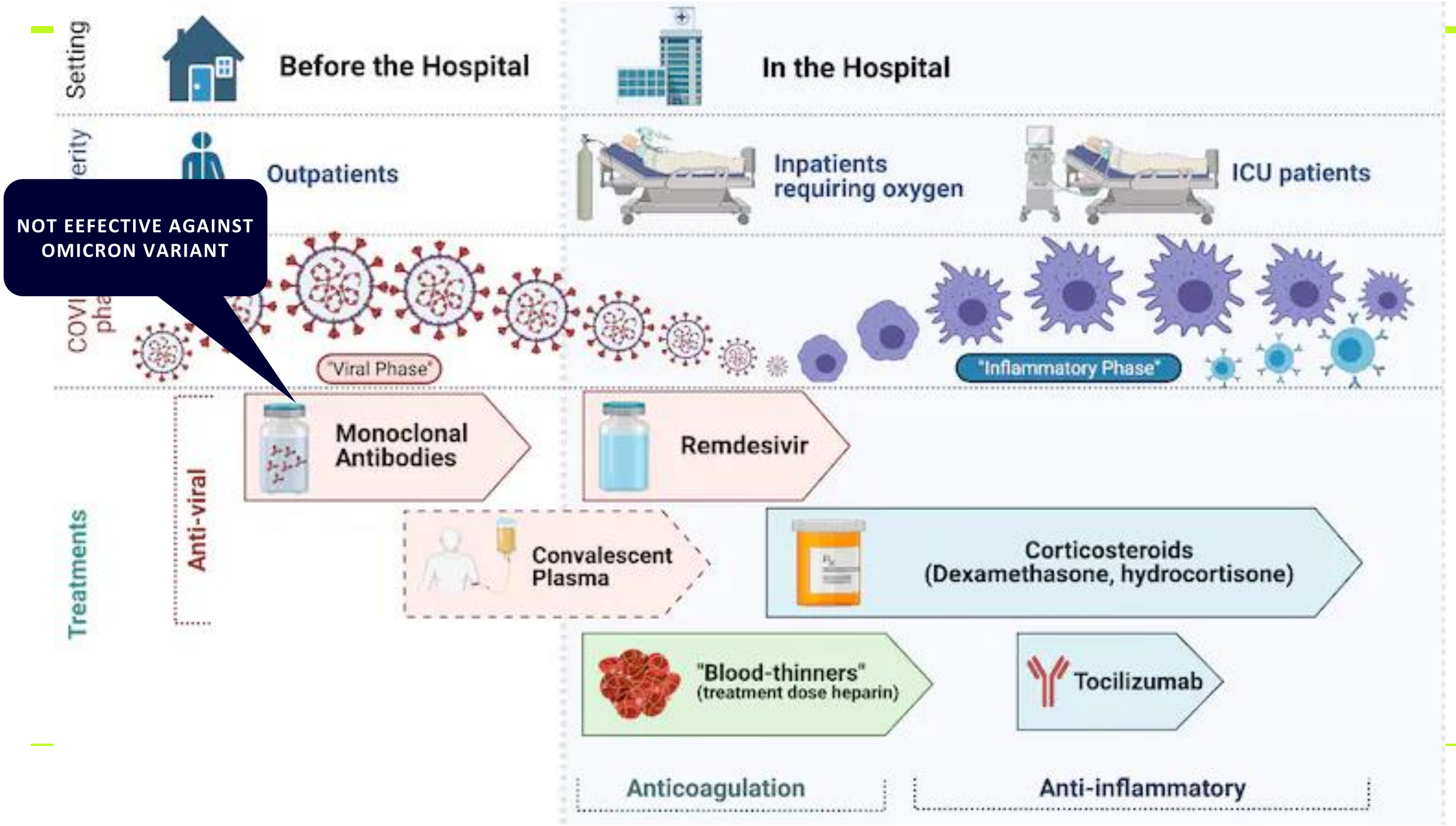


WHO TO TREAT?

- OTHERS WITHIN 48 HOURS OF ARRIVAL AT OWN EXPENSE
- OVER 65 YEARS OF AGE
- CHRON. CV, RESPIRATORY DISEASE, DM, ETC.
- UNDER 2 YEARS OF AGE
- PREGNANT AND UP TO 2 WEEKS POSTPARTUM
- HOSPITALIZED FOR INFLUENZA, REGARDLESS OF THE DURATION OF SYMPTOMS
- SEVERE OR PROGRESSIVE COURSE


COVID-19


Setting
Before the Hospital
In the Hospital
Severity
Outpatients
Inpatients requiring oxygen
ICU patients
COVID-19 phase
"Viral Phase"
"Inflammatory Phase"
Treatments
Anti-viral
Monoclonal Antibodies
Remdesivir
Convalescent Plasma
Corticosteroids (Dexamethasone, hydrocortisone)
"Blood-thinners" (treatment dose heparin)
Tocilizumab
Anticoagulation
Anti-inflammatory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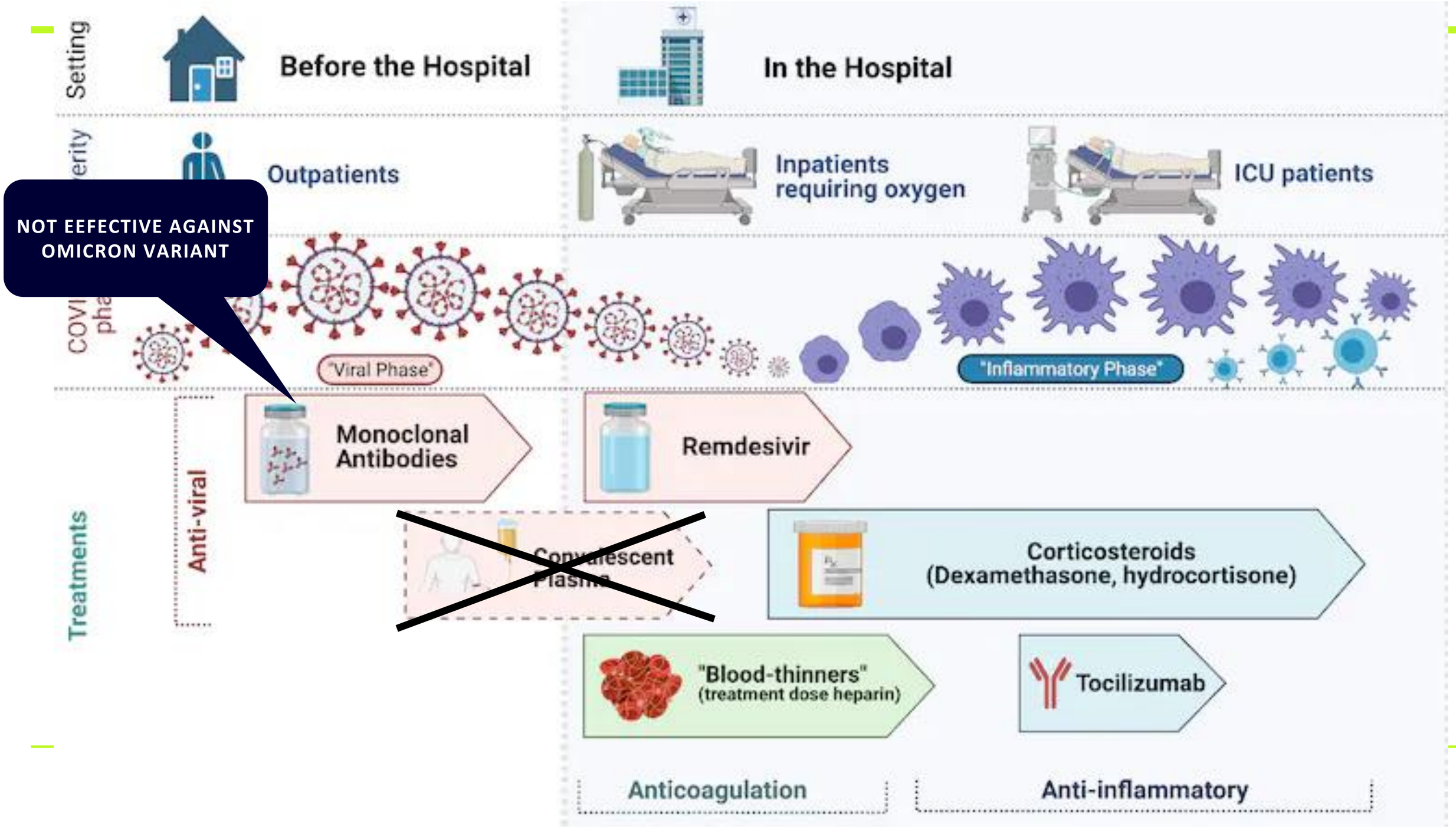
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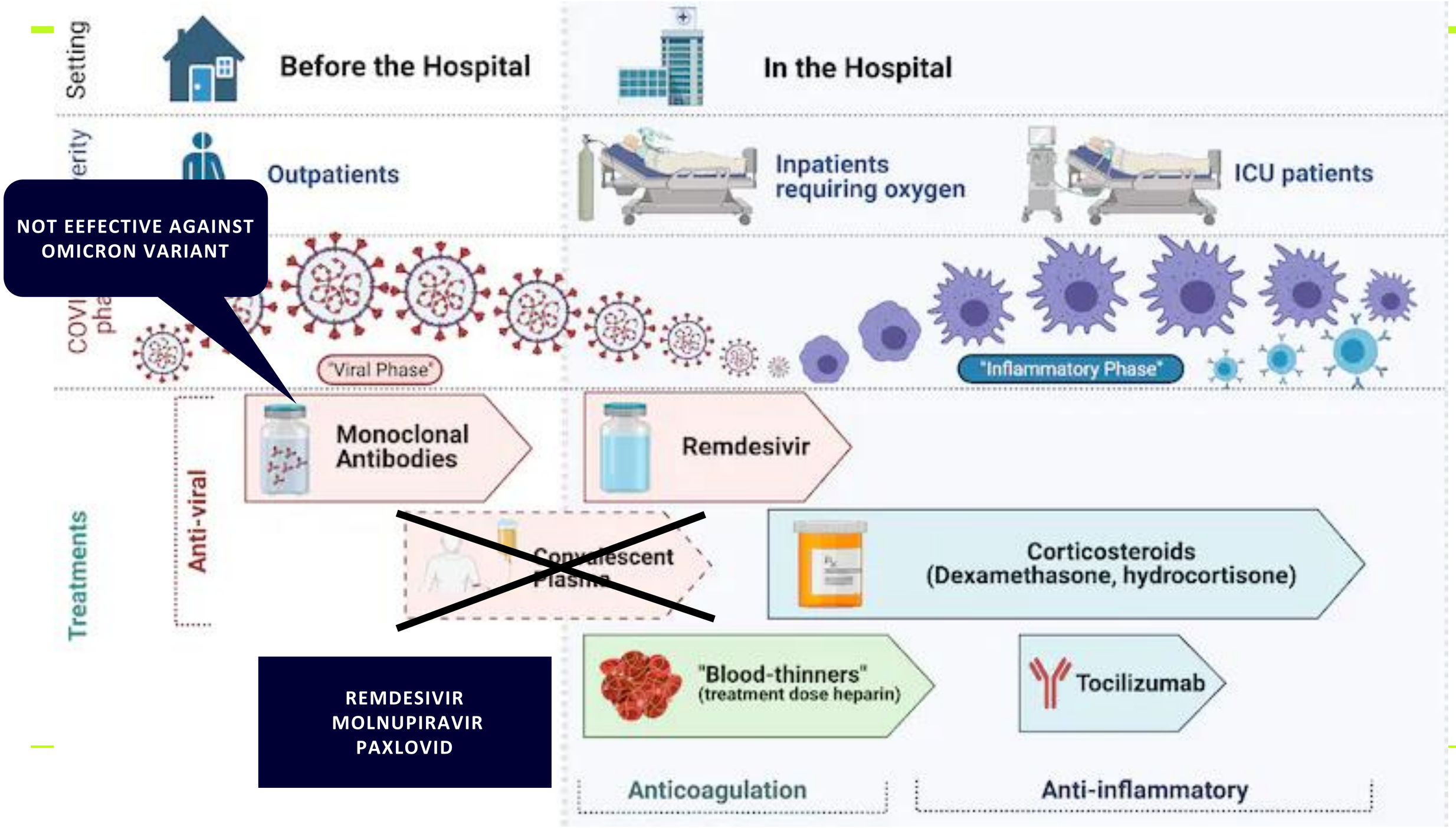
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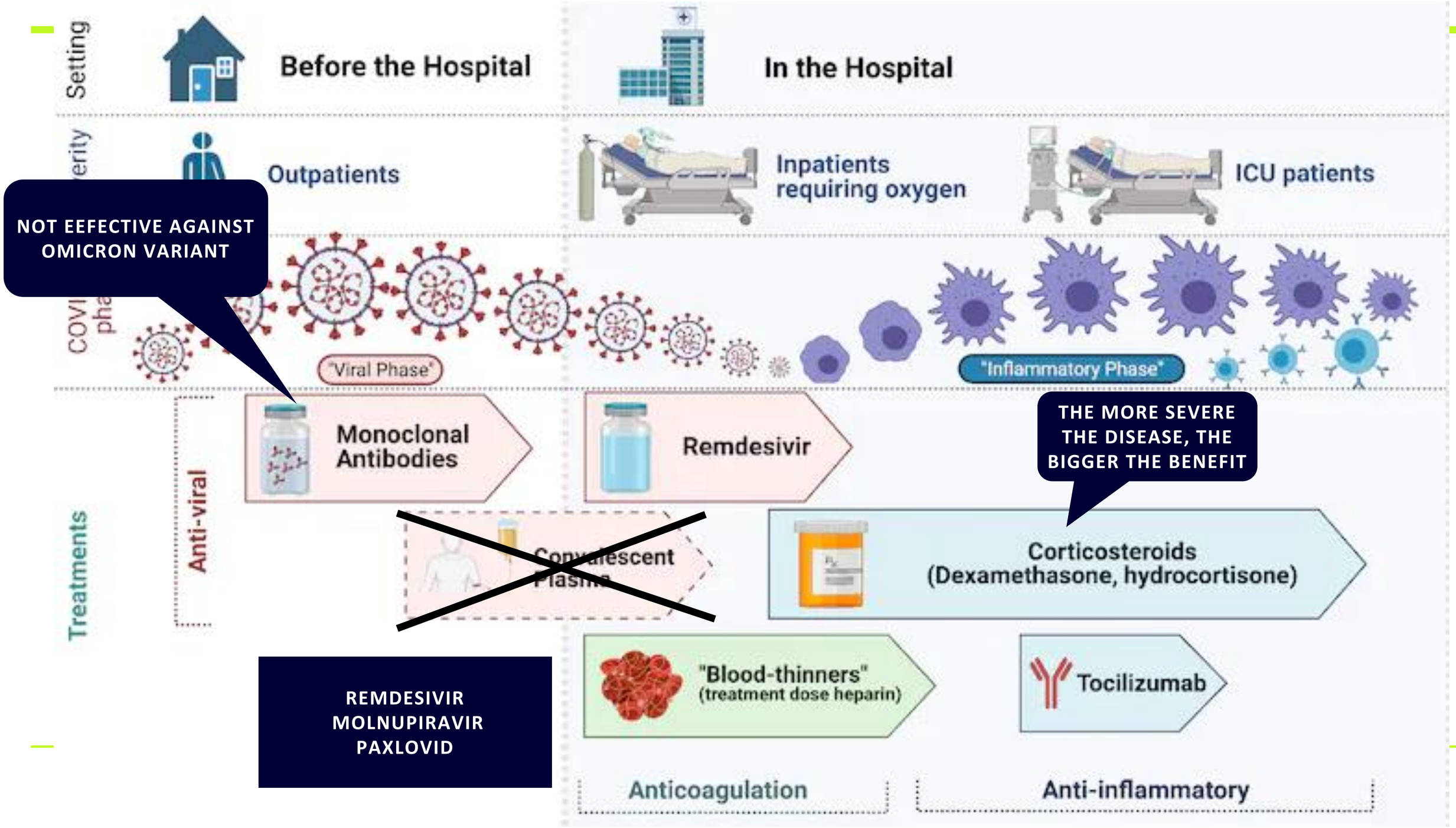
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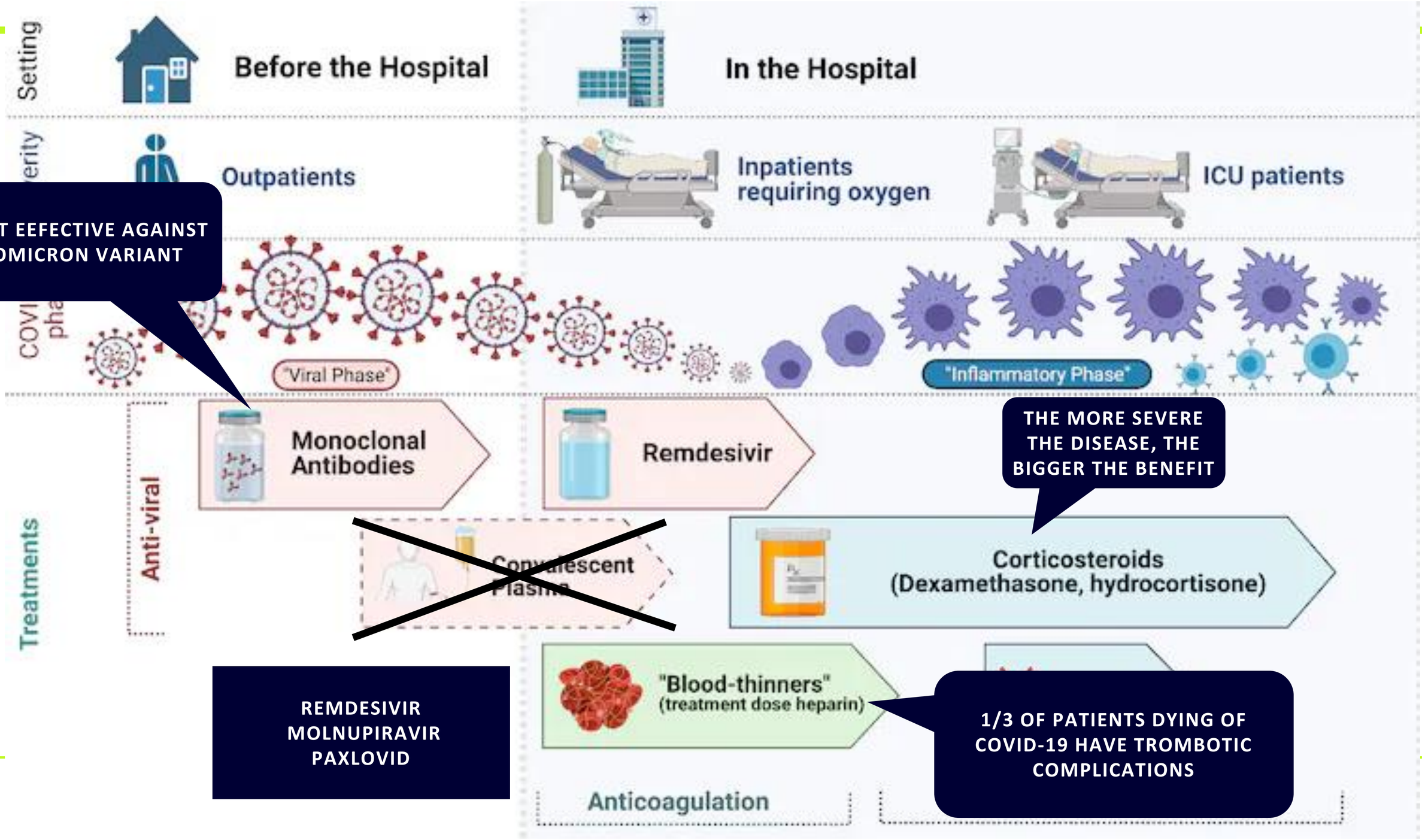
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"Blood-thinners" (treatment dose heparin)
1/3 OF PATIENTS DYING OF COVID-19 HAVE TROMBOTIC COMPLICATIONS
Anticoagulation

Treatments for COVID-19

Drugs/biologics recommended
(monoclonal antibodies, remdesivir, molnupinavir *, paxlovid, systemic corticosteroids, interleukin-6 receptor blockers, Janus Kinase inhibitors, anticoagulants)

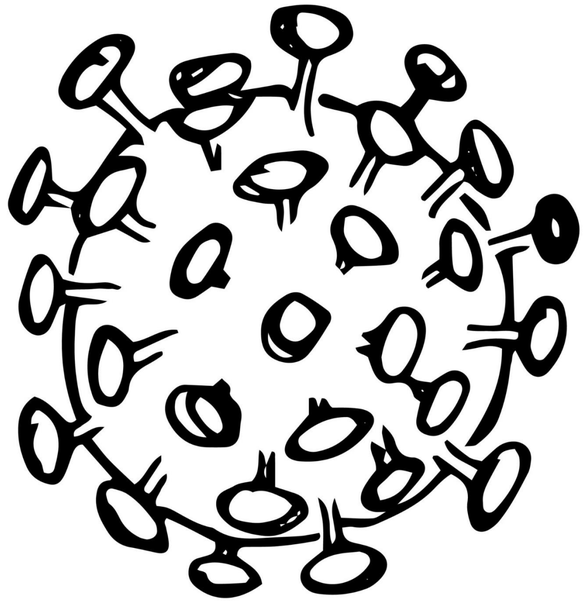
Drugs not recommended
(hydroxychloroquine, chloroquine, ivermectin, fluvoxamine, metformin, colchicine, lopinavir/ritonavir, interferons, convalescent plasma)

Drugs/biologics/cells still under investigation
(complement inhibitors, anti-interleukin-6 antibodies, cell-based therapies)

COVID-19

Drugs with insufficient evidence to recommend for or against
(nitazoxanide, granulocyte-macrophage colony-stimulating factor inhibitors, anakinra, vitamins C, D, and zinc)

Treatment of children with Multisystem Inflammatory Syndrome
(immunomodulatory drugs, antithrombotic agents)



*In some countries health authorities advise against the use of molnupinavir during pregnancy; other countries have chosen not to authorize it at all.

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PMID: 32860962 PMCID: PMC7449662 DOI: 10.1016/j.cmi.2020.08.022

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Abstract

Background: Hydroxychloroquine or chloroquine with or without azithromycin have been widely promoted to treat coronavirus disease 2019 (COVID-19) following early in vitro antiviral effects against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Objective: The aim of this systematic review and meta-analysis was to assess whether chloroquine or hydroxychloroquine with or without azithromycin decreased COVID-19 mortality compared with the standard of care.

Data sources: PubMed, Web of Science, Embase, Cochrane Library, Google Scholar and MedRxiv

Hydroxychlorochin

v.s.

Evidence Based Medicine

- one of the first drugs widely used against COVID-19
- Approved for use all around the world under pressure of public, but with very week evidence regarding efficacy and safety
- Very often used together with azithromycin (including Czechia)

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- Approved for use all around the world under pressure of public, but with very week evidence regarding efficacy and safety
- Very often used together with azithromycin (including Czechia)
- Hydroxychloroquine alone does not reduce mortality in COVID-19 patients
- **Combination of hydroxychoroquine with azithromycine increases mortality in hospitalized patients by up to 27%!!!**