Pathology of the lungs 1

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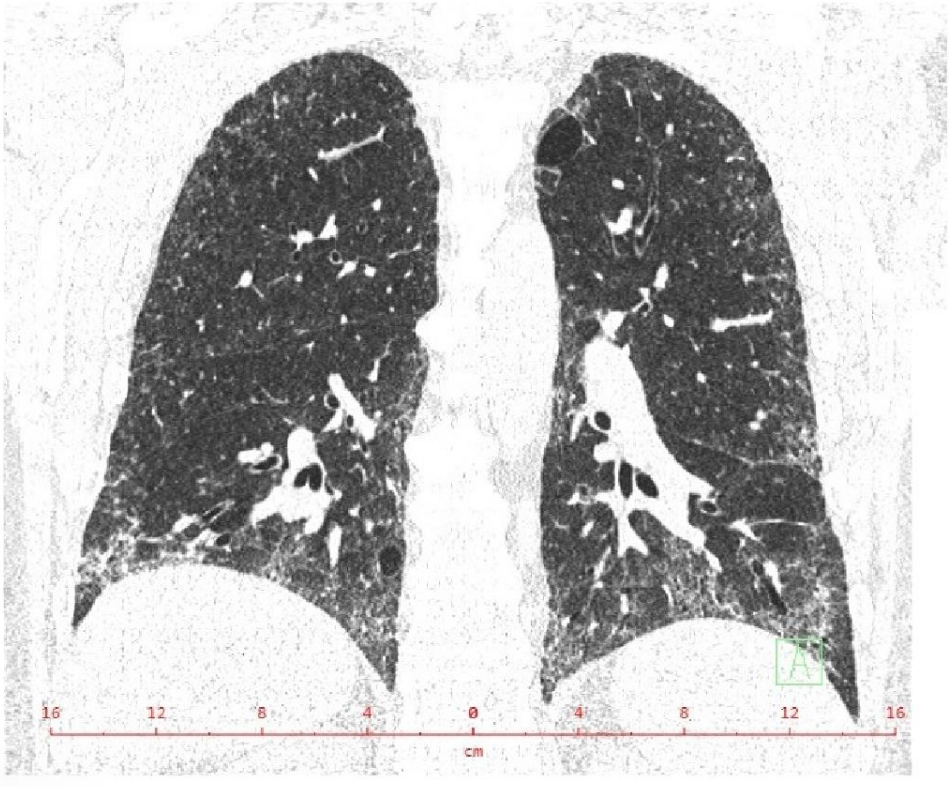

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Diseases of the lungs

1) maformations

2) inflammations

3) tumours

4) obstructive lung diseases

5) restrictive lung diseases

6) vascular lung diseases

Obstructive lung diseases

Obstructive lung diseases

- a group of diseases characterised by **airflow obstruction**

"Acute"

bronchial asthma

Chronic

chronic bronchitis
lung emphysema
bronchiectasis
cystic fibrosis

COPD

Bronchial asthma

Definition

- *asthma bronchiale**
- **chronic** obstructive lung disease with **acute** manifestations
  - long-term disease with recurring acute **asthmatic episodes** of symptoms

- common disease
  - cca 5 % of population, mainly **children** (increasing prevalence)
  - may be associated with COPD

- can be lethal (rarely)
  - severe / long-standing asthmatic episodes

* *asthma cardiale* (pulmonary edema)

Bronchial asthma

Causes (etiology)

- **allergy** triggered hyperreactivity of bronchi
  - associated with other examples of **hypersensitivity** (pollinosis, atopic eczema, eosinophilia, conjunctivitis...)

- **multifactorial** genesis (genetic + environmental factors)
  - **extrinsic** (precipitated by allergens, e.g. plant pollens, mites, fungi, drugs)
  - **intrinsic** (inner idiosyncratic response, e.g. stress, cold, infection)

Bronchial asthma

Developement (pathogenesis)

- developement of **type I hypersensitivity**
  - Ags cross link the **IgE** on **eosinophils** and **mast cells** = fast release of mediators
  - these biomolecules cause **airway obstruction** (bronchospasm, edema) and airway **mucus hypersecretion**

- gradual **remodeling** of bronchial wall
  - acute asthmatic episodes tend to be healed *ad integrum* **except** from frequent / long standing / secondary ones (irreversible damage developes)

Bronchial asthma

Morphology

- **macroscopically** typical mucus filling bronchiolar lumen + hyperinflated lung parenchyma
  - **mucus** is thick and viscous with glassy appearance
  - **hyperinflation** makes the lungs look larger-than-normal as a result of trapped air; diaphragm is in inspiratory position
  - **complications** include acute cor pulmonale and bronchial erosions

Bronchial asthma

Morphology

- **microscopically** changes in brochial mucosa
  - **lumen** shows obturation with mucus plugs (Charcot–Leyden crystals / Curschmann's spirals as a result of degranulation of eosinophils)
  - **epithelium** shows hyperplasia of goblet cells or squamous metaplasia, thick BM
  - **stroma** is edematous and chronically inflamed with eosinophils
  - **mucous glands** are hyperplastic
  - **smooth muscle** is hyperplastic + hypertrophic

Bronchial asthma

Clinical manifestations

- **children** and also adults
  - with allergies (younger age compared to the COPD patients)

- intermittent recurring **asthmatic attacks / episodes**
  - acute exacerbation of breathlessness (**dyspnoea)** of various severity (tachypnoea with long exspirium, anxiety, accessory respiratory muscle contraction, shortness of breath, chest tightness)
  - auscultatory phenomena (stridor, wheezing) / productive cough
  - asymptomatic intervals (except remodeling)

- **complications** can be rarely fatal
  - **status asthmaticus** (long-standing severe / repetitive attack)

COPD

Definition

- chronic obstructive pulmonary / lung / airway disease (COAD)

- **common clinical term** comprising 2 distinct lung diseases
  - **chronic bronchitis** + **lung emphysema** (co-existing in 70 % of cases)

- the **most frequent** disease of lower respiratory system
  - 95 % of patients are smokers

- long-term progress with fatal course
  - the 2nd most common cause of death in the Czech republic (LTx indication)

Chronic bronchitis

Definition

- *bronchitis chronica*

- productive **cough** present for at least 3 months each year for at least 2 years in a roll
  - an exception in the definition of chr. inflammation (along with chr. hepatitis)

- common disease
  - 15 % of population

Chronic bronchitis

Causes (etiology)

- cigarette **smoke-induced** irritation of the brochial mucosa
  - 95 % of patients are smokers (primary / secondary)

- in addition, **inhalation** of air pollution, irritating fumes or dust
  - hazardous exposures (ibdustrial / occupational = coal mining) / repeated acute brochial infections (childhood)
  - remaining 5 % of non-smokers

- **multifactorial** genesis (genetic + environmental factors)
  - affects 50 % of smokers (predisposition is mandatory)

Chronic bronchitis

Developement (pathogenesis)

- **abnormal chronic inflammatory response** to the inhaled smoke particles
  - develops only among the prone smokers

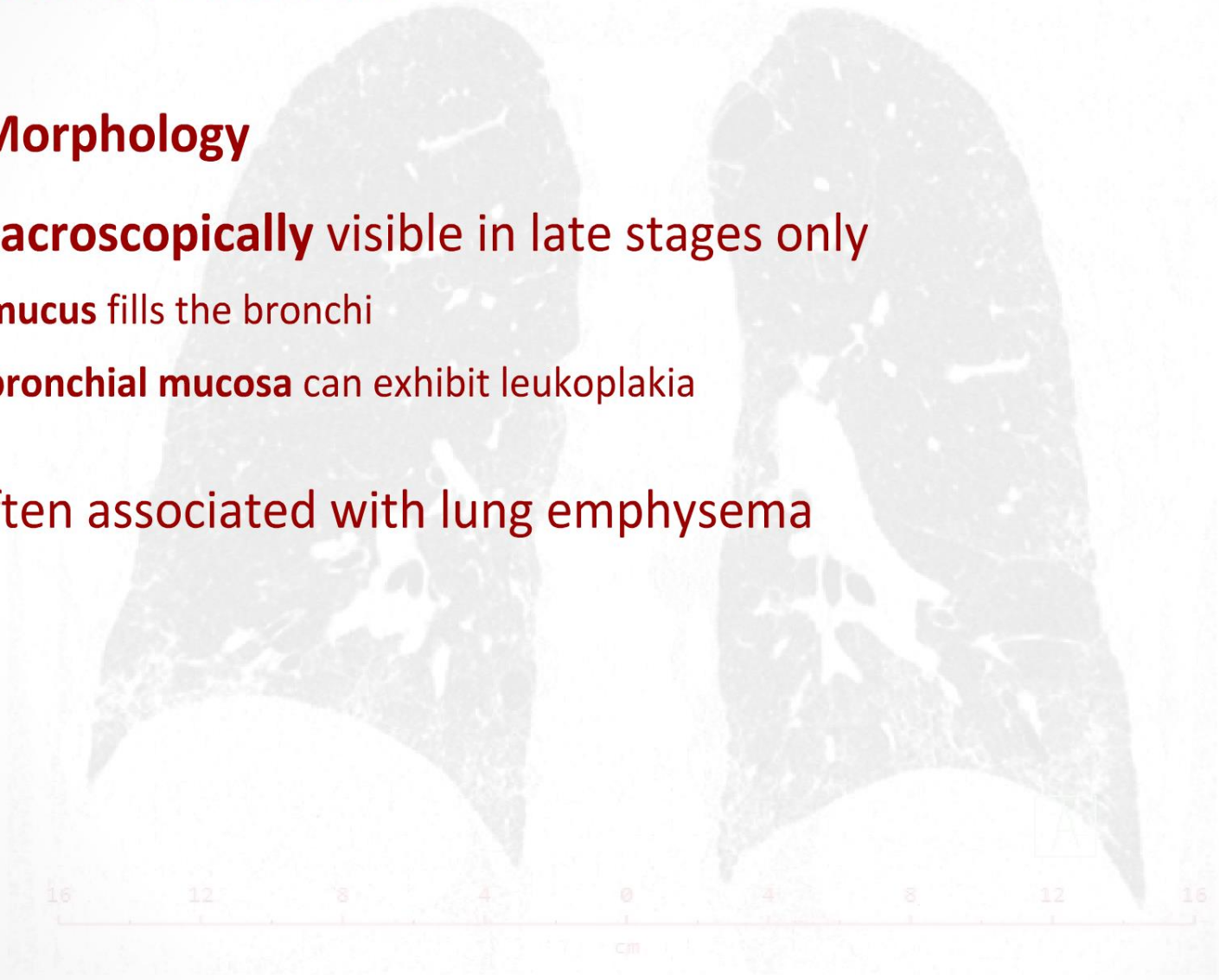
- later on, obstructive **remodeling** of bronchial wall occures
  - compared to bronchial asthma, the COPD is **steady ireversible chronic inflammation** with slow progression and **neutrophilic** participation

Chronic bronchitis

Morphology

- **macroscopically** visible in late stages only
  - **mucus** fills the bronchi
  - **bronchial mucosa** can exhibit leukoplakia

- often associated with lung emphysema



Chronic bronchitis

Morphology

- **microscopically** changes of brochial mucosa:
  - **lumen** obturated with mucus plugs
  - **epithelium** shows hyperplasia of goblet cells or even squamous metaplasia, BM is thicker
  - **stroma** is fibrotic (loss of elasticity) and chronically inflamed with neutrophils (spasm also causes frilling of the mucosa)
  - **mucous glands** are hyperplastic
  - **smooth muscle** is hyperplastic + hypertrophic

- **Reid index** as a marker of glandular hyperplasia
  - ratio between the thickness of the glands : whole lamina propria mucosae
  - the number **above 0,5** confirms hyperplasia (normal index is 0,4 and less)

Chronic bronchitis

Clinical manifestations

- **adults**
  - usually **smokers** (older compared to asthma patients, poorer economic status, prolonged course without exacerbation except from winter)

- phenotype = typically called **"blue bloaters"**
  - combination of **productive cough** (present for years, even bronchorrhoea) + **peripheral cyanosis** (dyspnoea develops into hypoxia)
  - mainly obese smokers with wide chest (usually around 40 years old)

- **complications** can be fatal
  - *cor pulmonale chronicum*, secondary lung infections

Lung emphysema

Definition

- *emphysema pulmonum*,* (pulmonary) emphysema, pneumatosis of the lungs

- abnormal persistent **dilatation of alveolar tree**
  - **distally** from respiratory bronchioli (including)
  - **irreversible** anatomical alteration (destruction of interalveolar septa)

- common disease
  - can be part of COPD / other forms

* there are also subcutaneous and mediastinal emphysema

Lung emphysema

Causes (etiology)

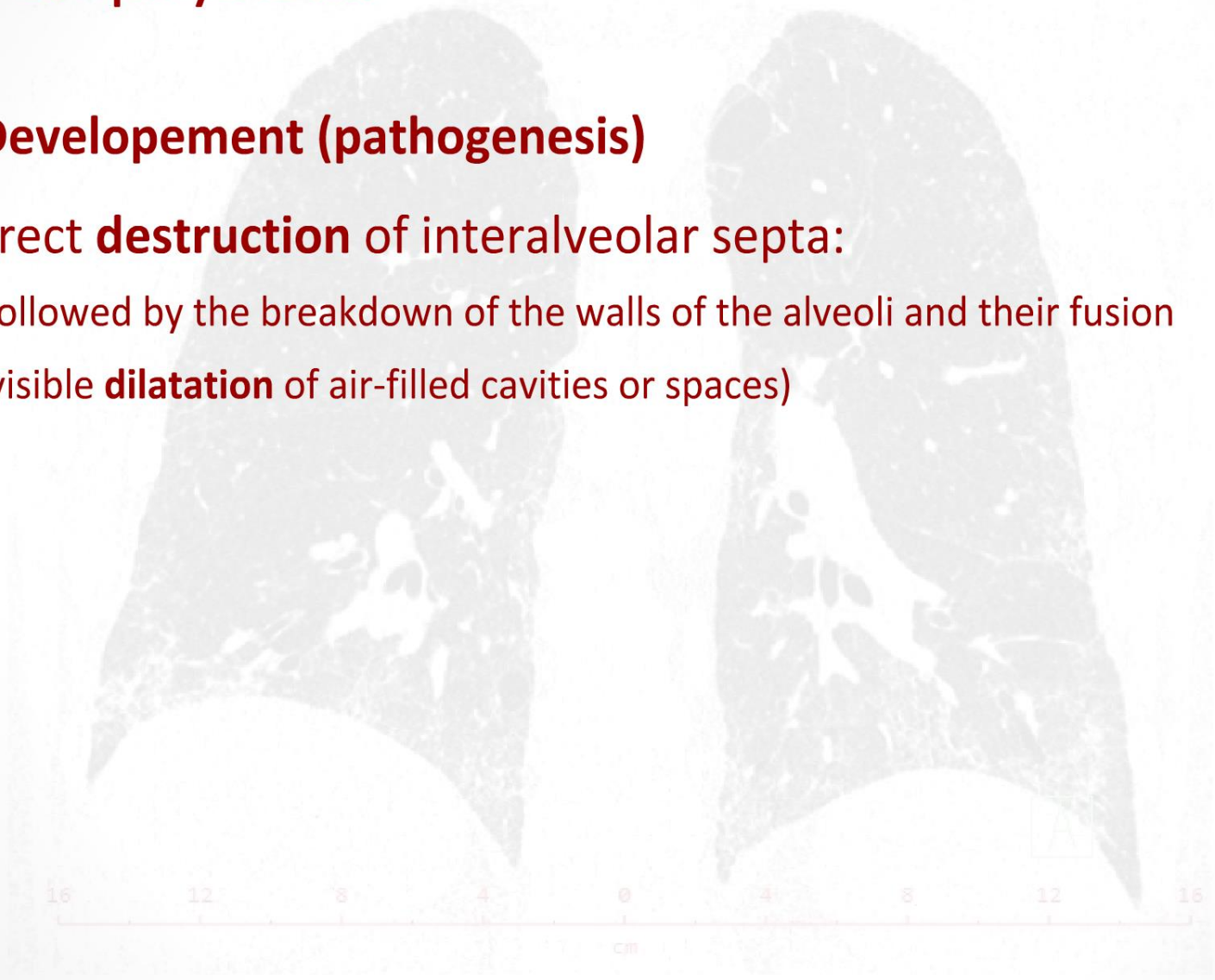
- depends on the **type of emphysema** (2 basic mechanisms)
  - **direct destruction of interalveolar septa** (mainly due to the smoking)
  - **hyperinflation** (pathologically increased lung V at the end of expiration)

- **multifactorial** genesis (genetic + environmental factors)
  - develops in 50 % of smokers (only the prone ones)
  - purely inherited panacinar emphysema represents an exception

Lung emphysema

Developement (pathogenesis)

- direct **destruction** of interalveolar septa:
  - followed by the breakdown of the walls of the alveoli and their fusion (visible **dilatation** of air-filled cavities or spaces)



Lung emphysema

Developement (pathogenesis)

1) centriacinar (centrilobular) emphysema

- the most common one
- destruction of respiratory bronchioles via **smoking**
  - **respiratory b.** represents the most proximal (**central**) airway of alveolar tree (brings air to the group of alveoli called **lung acinus**; several acini = lobulus)

Lung emphysema

Developement (pathogenesis)

2) panacinar (panlobular) emphysema

- genetic disorder called **α-1-antitrypsin deficiency** causes destruction of the whole lung acinus / lobulus
  - **α-1-antitrypsin** normally blocks neutrophil elastase (it is anti-elastase)
  - destruction and dilatation of both **proximal + distal** part of alveolar tree

Lung emphysema

Developement (pathogenesis)

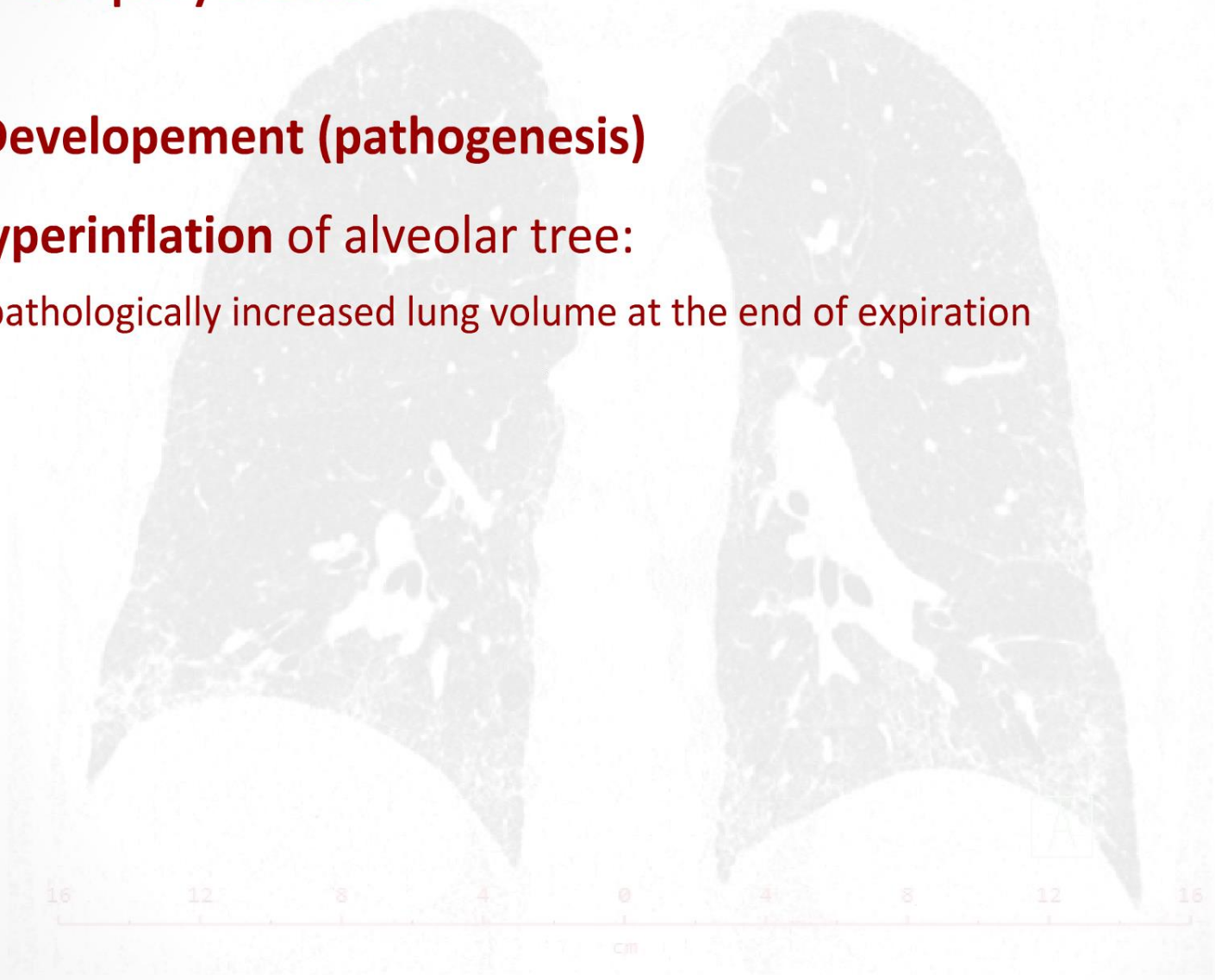
3) distal acinar (paraseptal) emphysema

- **idiopathic** destruction of alveolar wall along acinar septa
  - **alveoli** represent the most distal (**peripheral**) airway of alveolar tree (destruction is be visible mainly in subpleural and paraseptal areas)
  - may be in combination with centriacinar emphysema

Lung emphysema

Developement (pathogenesis)

- **hyperinflation** of alveolar tree:
  - pathologically increased lung volume at the end of expiration



Lung emphysema

Developement (pathogenesis)

1) irregular (localized / focal) emphysema

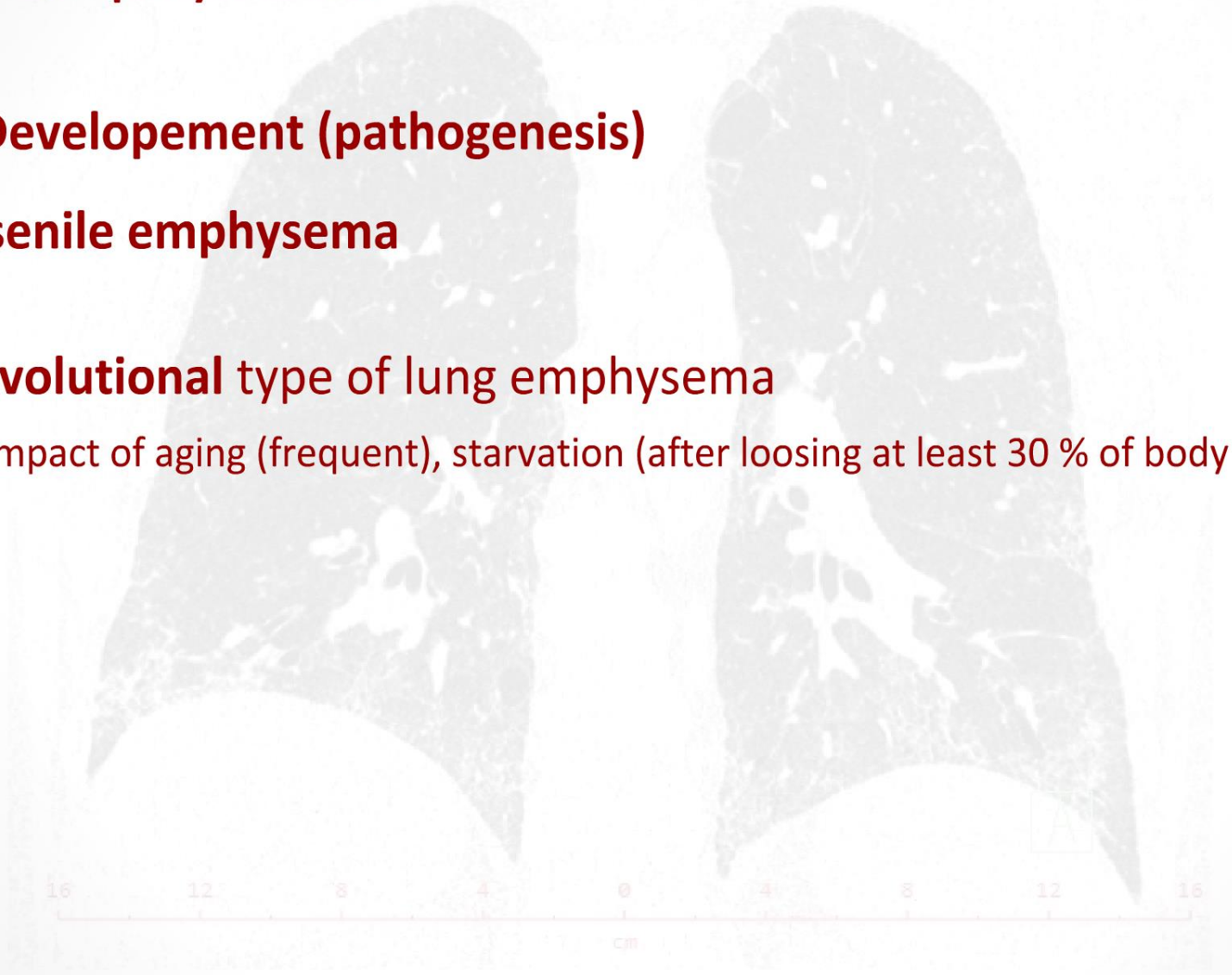
- **para- / paracicatricial** emphysema adjacent to fibrosis
  - dilatation of alveoli adjacent to areas of **scarring** (*cicatrix*)
  - caused by silicosis, granulomatous infection, pneumonia, pulmonary infarction or an operation
- **hereditary** emphysema caused by developmental defect
  - Down syndrome, congenital airway malformations

Lung emphysema

Developement (pathogenesis)

2) senile emphysema

- **involutional** type of lung emphysema
  - impact of aging (frequent), starvation (after loosing at least 30 % of body weight)



Lung emphysema

Developement (pathogenesis)

3) compensatory emphysema

- dilatation of **residual** lung parenchyma
  - portion of the lung increases in size, if another portion is destroyed or temporarily useless
  - after surgical resection (of lobe = lobectomy / whole lung = pulmectomy)

Lung emphysema

Morphology

- **macroscopically** lung parenchyma gets hyperinflated
  - **hyperinflation** makes the lungs look larger-than-normal as a result of trapped air; diaphragm is in inspiratory position
  - barrel-shaped **chest** with horizontal ribs
  - air-filled cystic spaces known as **blebs or bullae** beneath visceral pleura
  - **complications** include chronic cor pulmonale

Lung emphysema

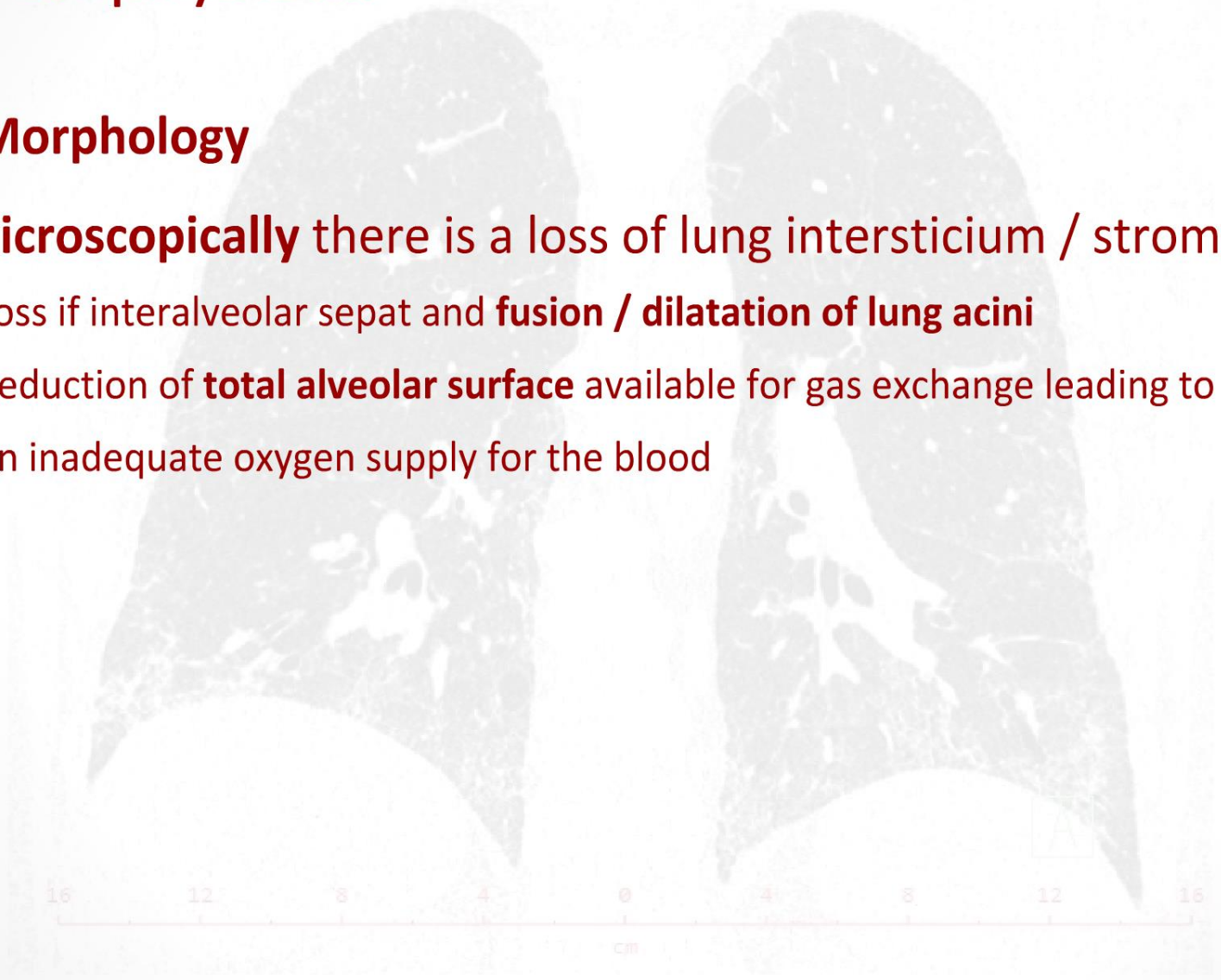
Morphology

- distribution can reveal the specific type of emphysema:
  - **centriacinar** affects mainly central areas of superior lobes (lung apices)
  - **panacinar** is diffuse with predisposition to lower lobes
  - **distal acinar** affects mainly peripheral areas of superior lobes (lung apices)

Lung emphysema

Morphology

- **microscopically** there is a loss of lung intersticium / stroma
  - loss if interalveolar sepat and **fusion / dilatation of lung acini**
  - reduction of **total alveolar surface** available for gas exchange leading to an inadequate oxygen supply for the blood



Lung emphysema

Clinical manifestations

- **adults**
  - **centriacinar** is the most common one, mainly old smokers
  - **panacinar** affects young non-smokers (accompanied by liver cirrhosis)
  - **distal acinar** young tall and skinny individuals (spontaneous PNO)

- phenotype = typically smokers called **"pink puffers"**
  - **pink** (no cyanosis) and **puffy** (out of breath); rarely cough (non-productive)
  - usually skinny smokers with barrel-shaped chest (age around 60 years)

- **complications** can be fatal
  - *cor pulmonale chronicum*, secondary lung infections, PNO

Bronchiectasis

Definition

- *bronchiectasis*

- abnormal persistent **dilatation of bronchial tree**
  - **proximally** from terminal bronchioli (including)
  - **ireversible** anatomical alteration (destruction of bronchi(ol)ar wall)

- relatively rare nowadays

Bronchiectasis

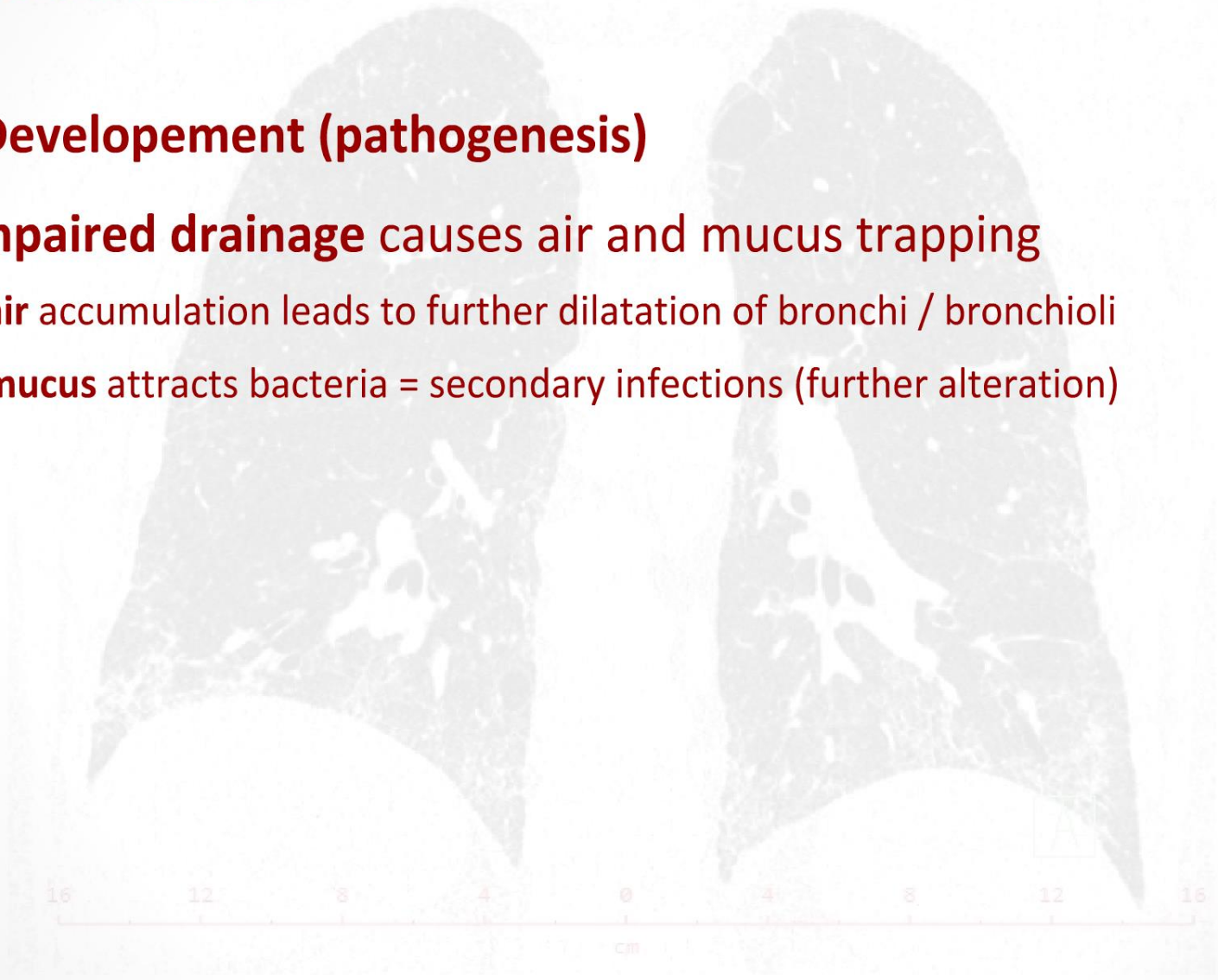
Causes (etiology)

- dilatation occures due to the **destruction** of bronchial wall
  - **focall** distally after obstruction (tumour, foreign body, mucus plug)
  - **diffuse** following severe inflammation (adenoviruses, measles, pertussis, TBC), in terrain of defect in host defense (immunodeficiency, CF, aspiration, neuromuscular disorders, Kartagener syndrome...)
  - majority of causes stays unrevealed (50-80 %)

Bronchiectasis

Developement (pathogenesis)

- **impaired drainage** causes air and mucus trapping
  - **air** accumulation leads to further dilatation of bronchi / bronchioli
  - **mucus** attracts bacteria = secondary infections (further alteration)



Bronchiectasis

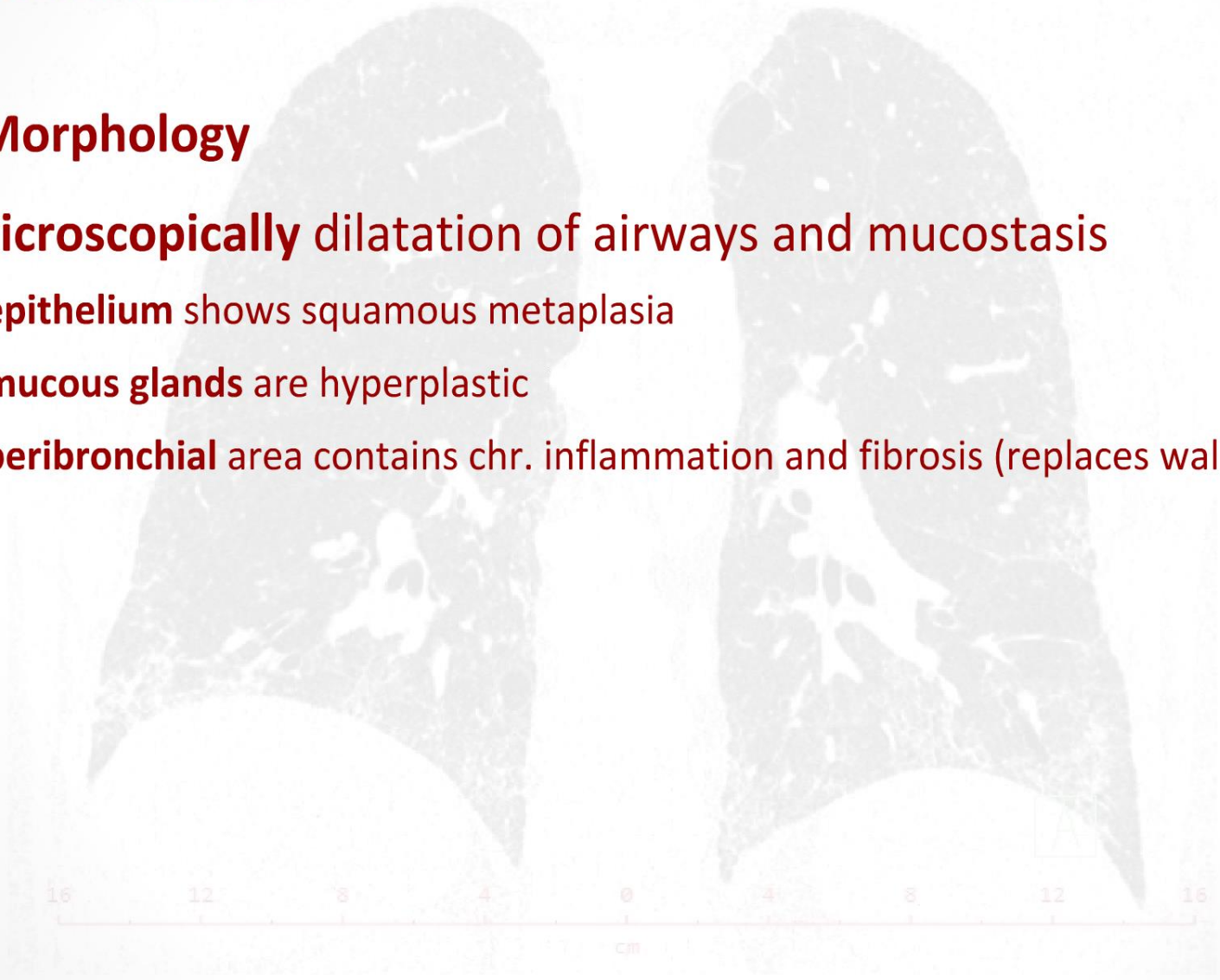
Morphology

- **macroscopically** visible dilatation of bronchial tree
  - **cylindrical** (the most common one, tubular uniform enlargement of bronchi)
  - **saccular** (focal outpouching of bronchial wall)
  - **varicose** (tortuosity caused by alternation of intermittent narrowed and dilated segments in long axis)

Bronchiectasis

Morphology

- **microscopically** dilatation of airways and mucostasis
  - **epithelium** shows squamous metaplasia
  - **mucous glands** are hyperplastic
  - **peribronchial** area contains chr. inflammation and fibrosis (replaces wall)



Bronchiectasis

Clinical manifestation

- **children** as well as **adults**
  - diffuse form is more typical in childhood

- productive cough resulting in dyspnoea

- **complicatons** can be rarely fatal
  - *cor pulmonale chronicum*
  - secondary lung infections (abscess pneumonia)
  - aspergilloma (pseudotumorous clump of mold in saccular bronchiectasis)
  - AA amyloidosis
  - dysplasia or SCC

Restrictive lung diseases

Restrictive lung diseases

- a group of lung diseases with **interstitial** fibrosis / inflammation

Acute

ARDS / IRDS

Chronic

Interstitial lung disease (ILD) / diffuse parenchymal lung disease (DPLD)

secondary:
- EAA
- smoking associated ILD
  - drug induced ILD
  - autoimmune induced ILD
  - pneumoconiosis

idiopathic:
- IPF (UIP)
- NSIP
- COP
- LIP
  - eosinophilic pneumonia
  - pleuropulmonal fibroelastosis
  - alveolar proteinosis

pulmonary granulomatosis

- sarcoidosis
- immune (vasculitis, RA)
- infectious

ARDS

Definition

- **A**cute / **A**dult **R**espiratory **D**istress **S**yndrome
  - **clinical** term
  - premature newbors = **IRDS** (**I**nfant **R**espiratory **D**istress **S**yndrome)

- **acute** restrictive lung disease
  - **trias** = rapid onset + severe hypoxemia + widespread inflammation (RTG)
  - part of **acute lung injury (ALI)** next to the DAH

- relatively common disease with fatal outcome
  - the most common cause of RI

ARDS

Causes (etiology)

- provoked by **diffuse acute injury** to lung interstitium

- **endogenous** causes
  - usually **shock**, rarely vasculitis, systemic autoimmune diseases...

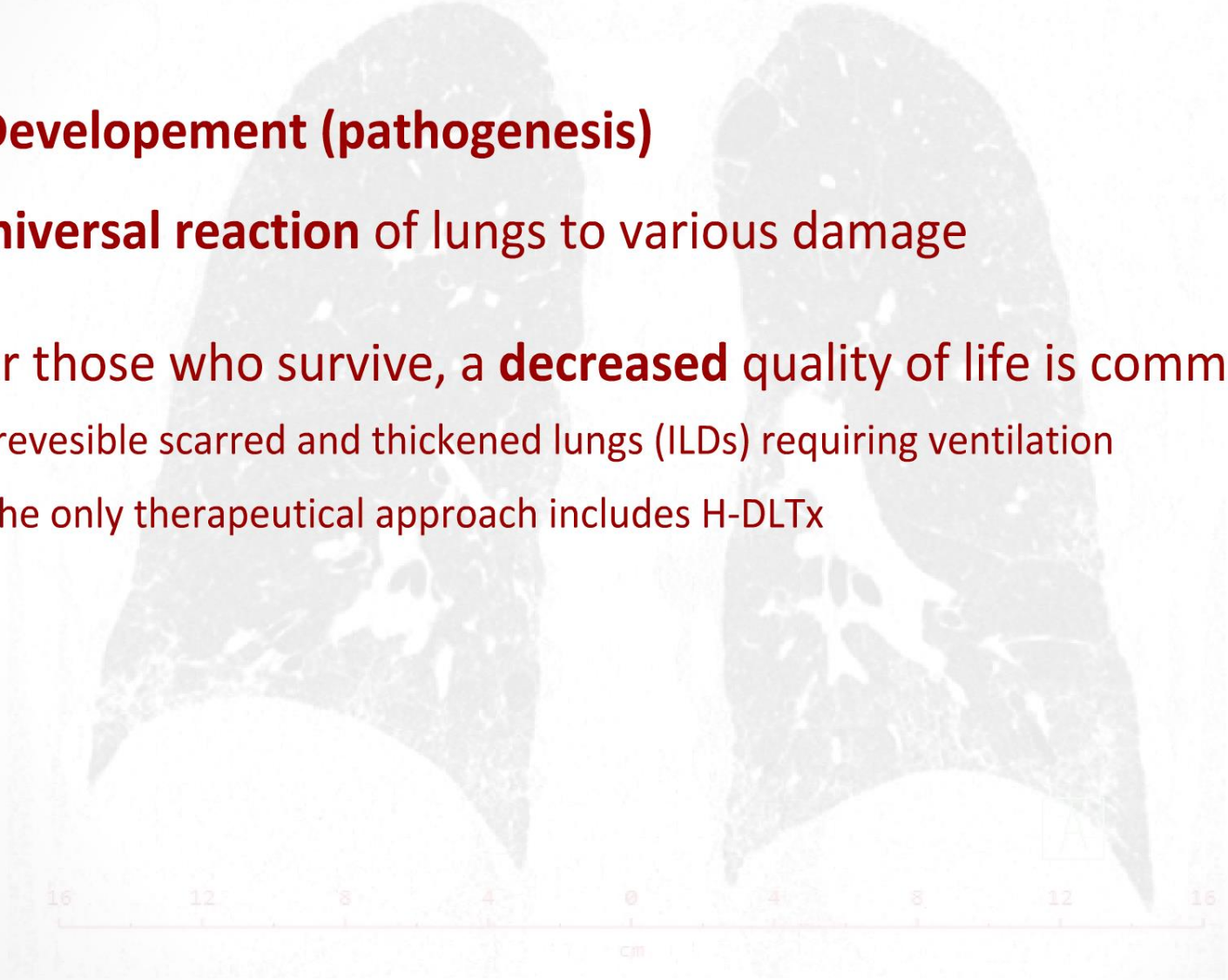
- **exogenous** causes
  - **inhalation** (toxins, corrosives, SAVO), **aspiration** (drowning, gastric juice), **sepsis**, **lung trauma** (pulmonary contusion, burns), acute pancreatitis, DIC, **tumours** (leukaemia, lymphomas), **iatrogenic** (radiation, drugs)...

ARDS

Developement (pathogenesis)

- **universal reaction** of lungs to various damage

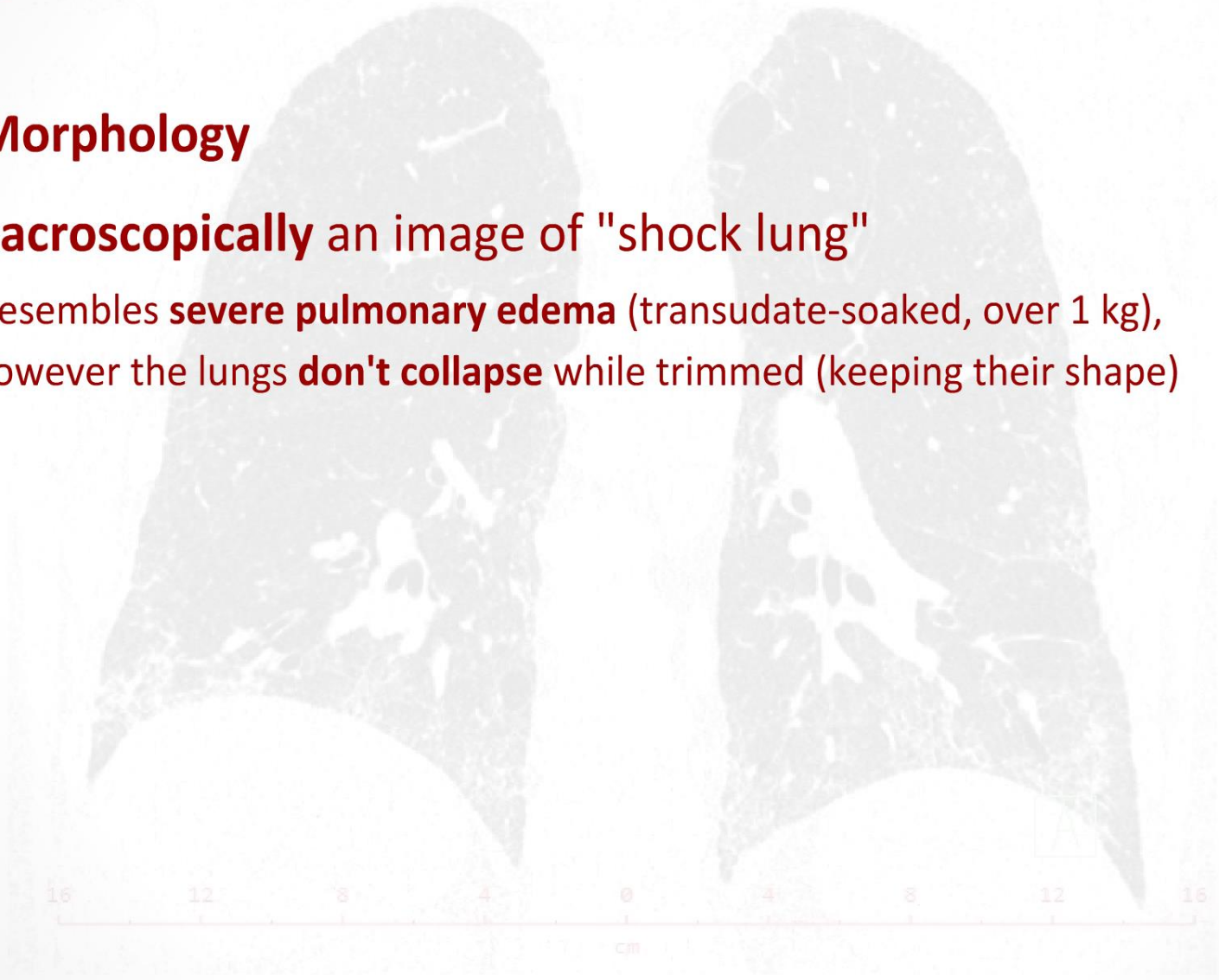
- for those who survive, a **decreased** quality of life is common
  - irevesible scarred and thickened lungs (ILDs) requiring ventilation
  - the only therapeutical approach includes H-DLTx



ARDS

Morphology

- **macroscopically** an image of "shock lung"
  - resembles **severe pulmonary edema** (transudate-soaked, over 1 kg), however the lungs **don't collapse** while trimmed (keeping their shape)



ARDS

Morphology

- **microscopically** called **DAD** (**D**iffuse **A**lveolar **D**amage)
  - **pathologic** term
  - **exsudative phase** (destruction of interstitial capillaries and flooding of lungs' aveoli with fibrin deposits = "hyaline membrane disease")
  - **proliferative phase** (interstitial fibrosis, hyperplasia of class II pneumocytes, carnifications (OP), bronchiolization of the alveoli from terminal bronchioli)

ARDS

Clinical manifestation

- **children** as well as **adults**
  - ARDS / IRDS

- destruction of parenchyma results in **severe RI** and pulmonary hypertension with ***cor pulmonale chronicum***
  - good prognosis cannot be expected even after survival of the acute phase
  - prone to the secondary infections

ILDs

Definition

- interstitial lung diseases (ILDs) / diffuse parenchymal lung diseases (DPLDs)

- a group of **chronic** restrictive lung diseases
  - characterised by **interstitial fibrosis** followed by decrease of lung volume (mutual patogenesis, clinical manifestation and imaging)
  - individual diagnoses based on **histopathological** image
  - sometimes **lymphangioleiomyomatosis** is included (but it's PEComa)

- relatively rare diseases with fatal outcome
  - irreversible damage resulting in RI

ILDs

Causes (etiology)

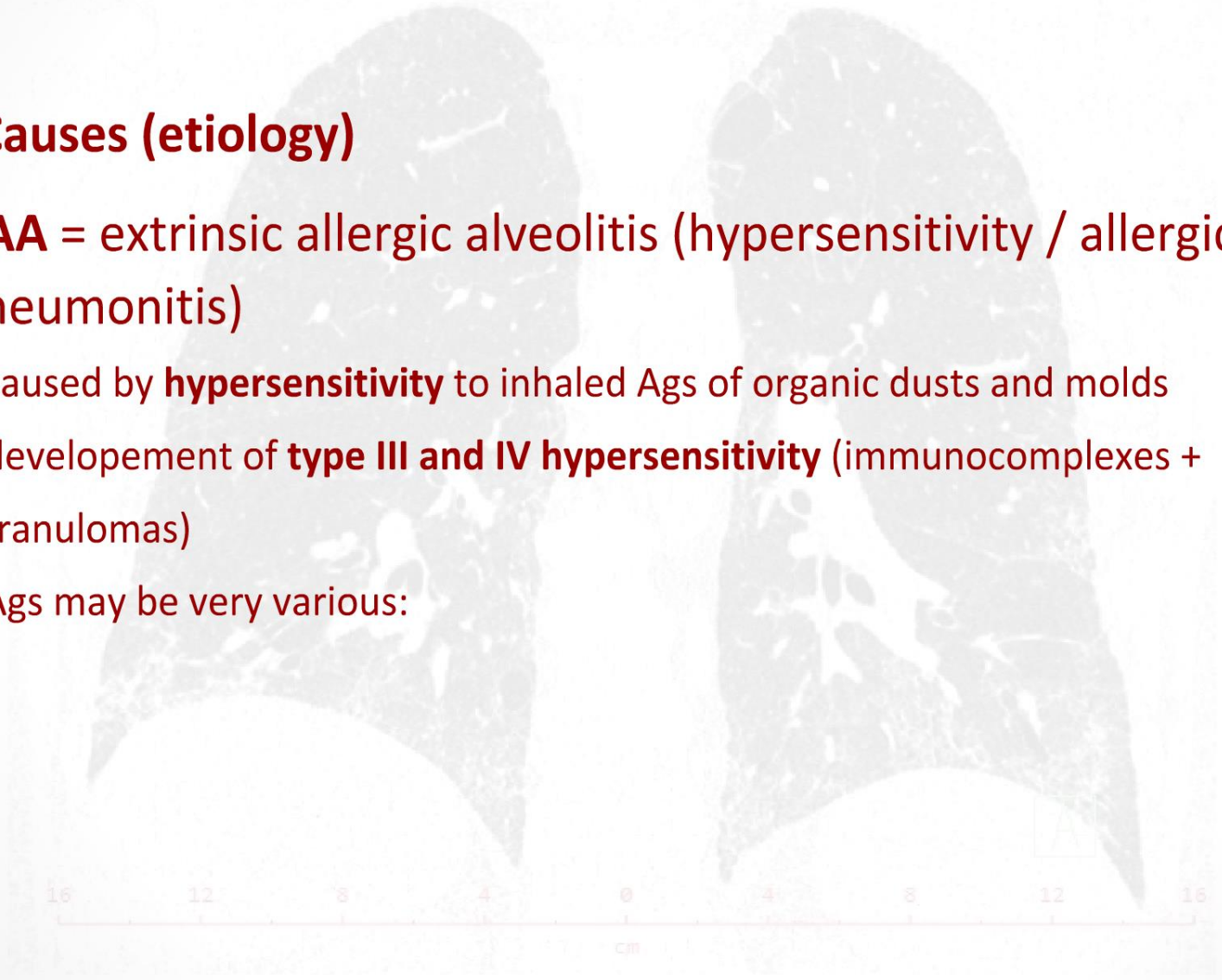
- **known** causes
  - EAA, smoking associated ILDs, drug induced ILDs, autoimmune induced ILDS and pneumoconiosis

- **idopathic** (cryptogenic) causes
  - IPF (UIP), NSIP, COP, LIP, eosinophilic pneumonia, pleuropulmonal fibroelastosis, alveolar proteinosis

ILDs

Causes (etiology)

- **EAA** = extrinsic allergic alveolitis (hypersensitivity / allergic pneumonitis)
  - caused by **hypersensitivity** to inhaled Ags of organic dusts and molds
  - developement of **type III and IV hypersensitivity** (immunocomplexes + granulomas)
  - Ags may be very various:



ILDs

Causes (etiology)

- **EAA** = extrinsic allergic alveolitis (hypersensitivity / allergic pneumonitis)
  - bird droppings (bird fancier's lung)
  - moldy hay (farmer's lung)
  - cocaine (crack lung)
  - moldy bagasse (bagassosis)
  - moldy barley (malt worker's lung)
  - moldy maple bark (maple bark disease)
  - dust-contaminated grain (miller's lung)
  - mushroom compost (mushroom worker's l.)
  - compost (compost lung)
  - peat moss (peat moss worker's lung)
  - moldy cork dust (suberosis)
  - wood (japanese summer house HP)
  - cheese casings (cheese-washer's lung)
  - mist m. (metalworking fluids HP)
  - mist from hot tubs ("hot tub lung")
  - mollusc shell dust (mollusc shell HP)
  - paints, resins (isocyanate HP)
  - plastics (trimellitic anhydride HP)
  - Be (beryliosis)
  - moldy grapes (wine-grower's lung)

ILDs

Causes (etiology)

- **smoking related ILDs** = a group of restrictive lung diseases
  - chronic irritation of lung interstitium via nicotinism
  - **DIP** (desquamative interstitial pneumonia)
  - **RB** (respiratory bronchiolitis-interstitial lung disease)
  - **pulmonary Langerhans cell histiocytosis**
  - **SRIF** (smoking-related intersticial fibrosis)
  - **CPFE** (combined pulmonary fibrosis and emphysema)

ILDs

Causes (etiology)

- **drug induces ILDs** = over 200 drugs + radiation
  - cytostatic drugs, immunosupression, heroine, hydralazine, amiodaron...

- **autoimmune induced ILDs** = autoimmune pneumonitis
  - **collagenosis** (SLE, Sjörgen's syndrome, sclerodermia, dermatomyositis / polymyositis)

- **pneumoconioses** = inhalation of anorganic dusts
  - **silicosis** (see General pathology)
  - **asbestosis** (see General pathology)
  - **beryliosis** (see General pathology)
  - **coal workers pneumoconiosis** (see General pathology)

ILDs

Causes (etiology)

- **IPF** = idiopathic pulmonary fibrosis (clinical term)
  - **histopathology** term is **UIP** (**U**sual **I**nterstitial **P**neumonia)
  - **idiopathic** primarily **proliferative** (fibrosing) interstitial lung inflammation (multifactorial developement = genetic factors, cytokines, PMN, smoking)
  - the most common and dangerous ILDs (frequent cause of RI among elders)

ILDs

Causes (etiology)

- **NSIP** = non-specific interstitial pneumonia
  - **idiopathic** primarily **proliferative** (fibrosing) interstitial lung inflammation, histopathology different from UIP (more favorable than IPF)

- **COP** = cryptogenic organizing pneumonia
  - uniform non-pecific **pathological healing** of lung **without** known cause
  - same process reacts to known causes (infection, toxic substaces, drugs, tumours...)

- **LIP** = lymphoid interstitial pneumonia
  - **idiopathic chronic inflammatory** (lymphocytic) interstitial lung infiltration
  - associated with HIV, autoimmune diseases (+ risk of MALT lymphoma)

ILDs

Developement (pathogenesis)

- there are **2 ways of ILD manifestation** possible:

- **primary chronic** pneumonitis
  - chronic **(fibro)productive interstitial** pneumonia from the very start
  - usually **irevesible**
  - IPF, NSIP, smoking related ILDs

- **secondary chronic** pneumonitis
  - **acute** pneumonitis anticipates (repeated episodes leading to chronicity)
  - acute phase is **reversible** (chronic phase of reparation is ireversible)
  - EAA, LIP, COP

ILDs

Developement (pathogenesis)

- one way or the other, the ILDs lead to **restrictive disorder and RI** with pulmonary hypertension
  - developement of **cor pulmonale chronicum** follows as a result

ILDs

Morphology

- **macroscopically** interstitial fibrosis (stiff thickened lung)
  - **irregular** = patchy fibrosis in predilective areas of the lung (EAA, smoking related ILDs, IPF, COP)
  - **regular** = diffuse fibrosis of the whole interstitium (NSIP, LIP, late ARDS)

- fibrosis results in **"honeycomb lung"**
  - variably sized blebs in a background of densely scarred lung tissue
  - **terminal fibrotic change** + compensatory emphysema + bronchiectasis

- diagnosis often requires biopsy (even HR-CT is not enough)

ILDs

Morphology

- **microscopically** it's possible to distinguish every single IDL
  - **biopsy** provides particular ILD diagnosis

ILDs

Morphology

- **EAA** finding depends on the stage of the disease
  - **acute** = florid inflammation in the peribronchiolar area (neutro-, eosinophils)
  - **chronic** = lymphocytic inflammation within interstitium, granulomas, fibrosis

ILDs

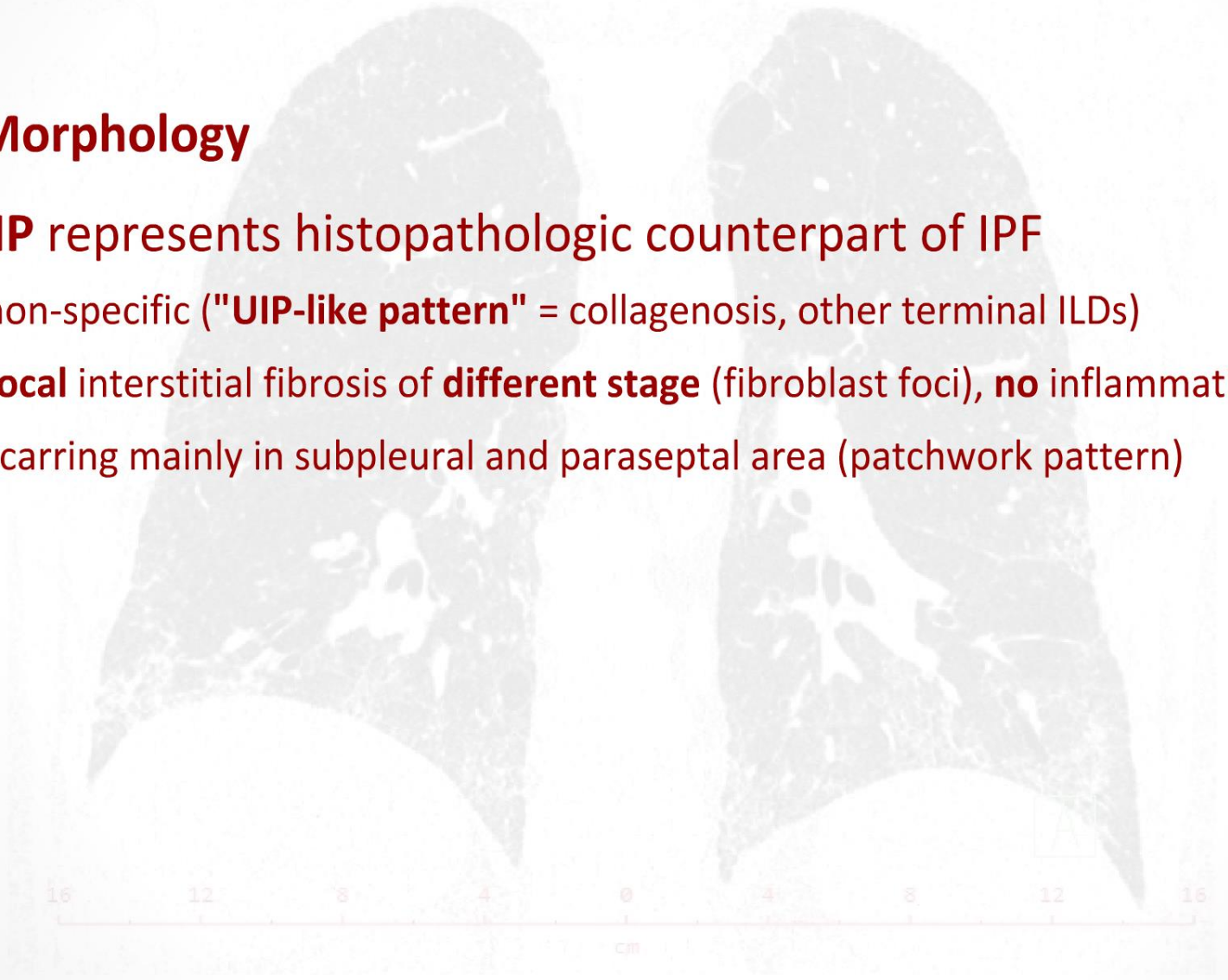
Morphology

- **smoking related ILDs** = a group of restrictive lung diseases
  - **DIP** = alveoli contain smokers macrophages ("desquamation"), mild fibrosis
  - **RB** = smokers macrophages, respiratory bronchial wall thickening
  - **pulmonary Langerhans cell histiocytosis** = non-tumorous accumulation of Langerhans cells, macrophages and eosinophils in the peribronchiolar and subpleural area followed with fibrosis
  - **SRIF** = asymptomatic hyalinization of interalveolar septa (disease?)
  - **CPFE** = combination of UIP + COPD

ILDs

Morphology

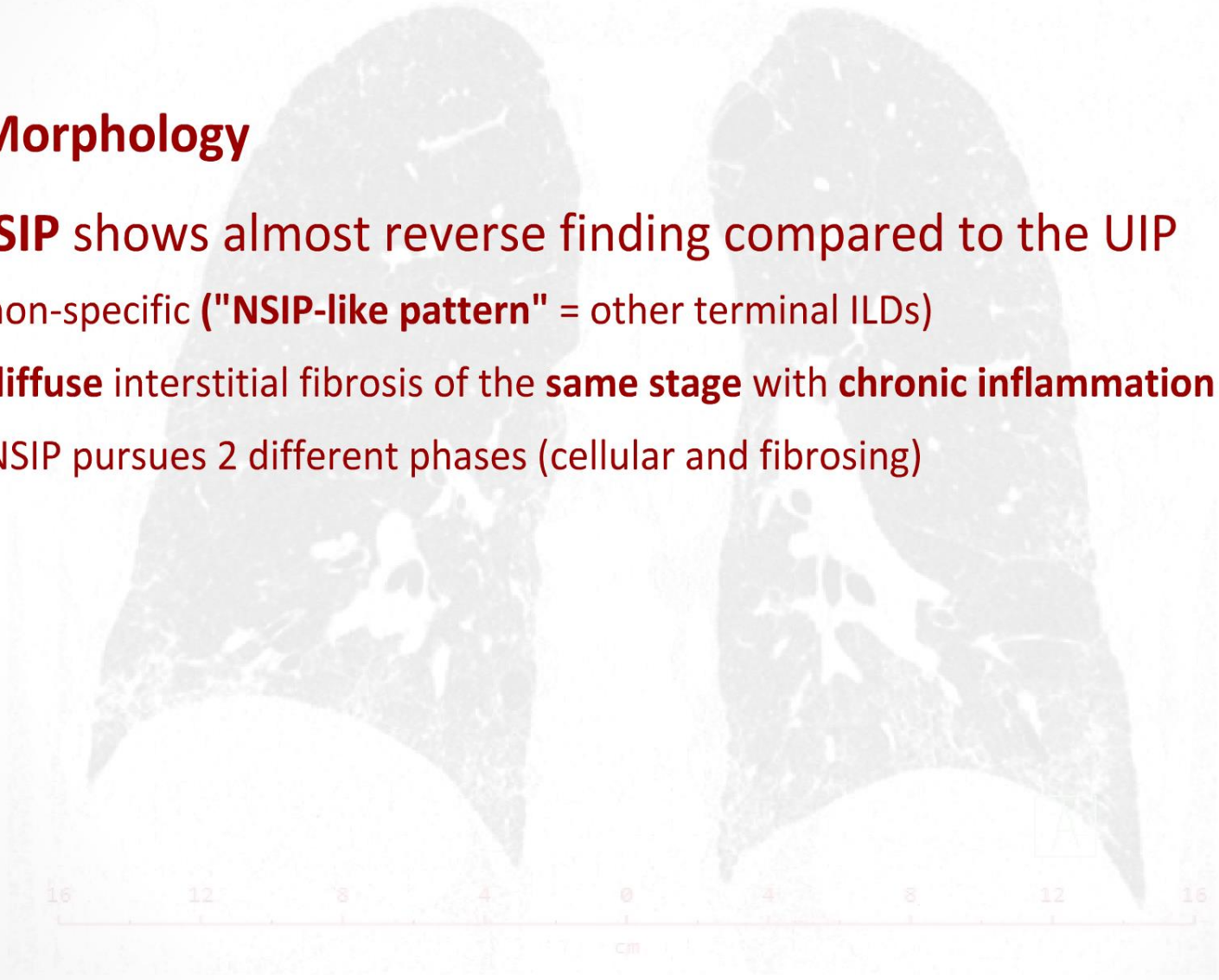
- **UIP** represents histopathologic counterpart of IPF
  - non-specific (**"UIP-like pattern"** = collagenosis, other terminal ILDs)
  - **focal** interstitial fibrosis of **different stage** (fibroblast foci), **no** inflammation
  - scarring mainly in subpleural and paraseptal area (patchwork pattern)



ILDs

Morphology

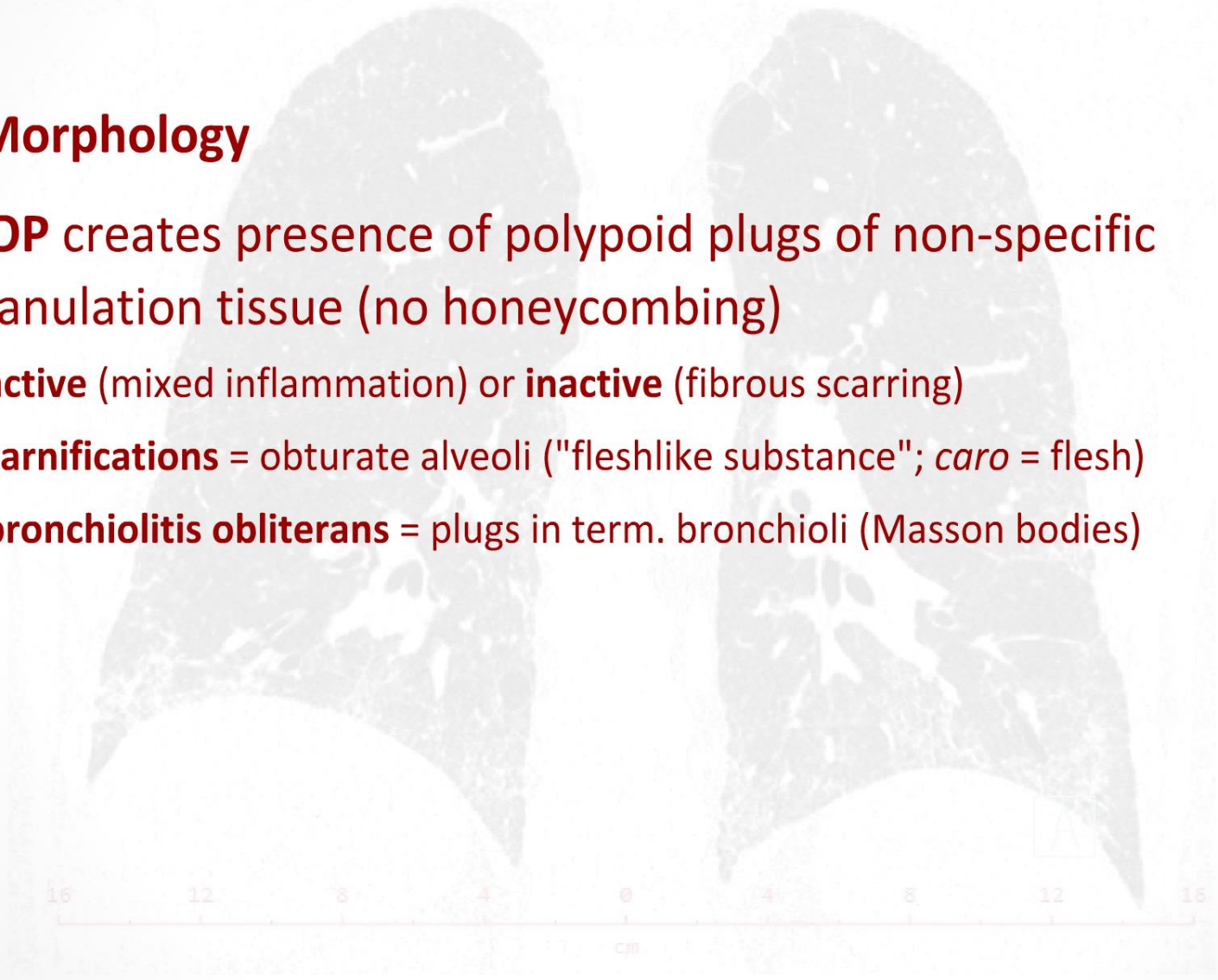
- **NSIP** shows almost reverse finding compared to the UIP
  - non-specific **("NSIP-like pattern"** = other terminal ILDs)
  - **diffuse** interstitial fibrosis of the **same stage** with **chronic inflammation**
  - NSIP pursues 2 different phases (cellular and fibrosing)



ILDs

Morphology

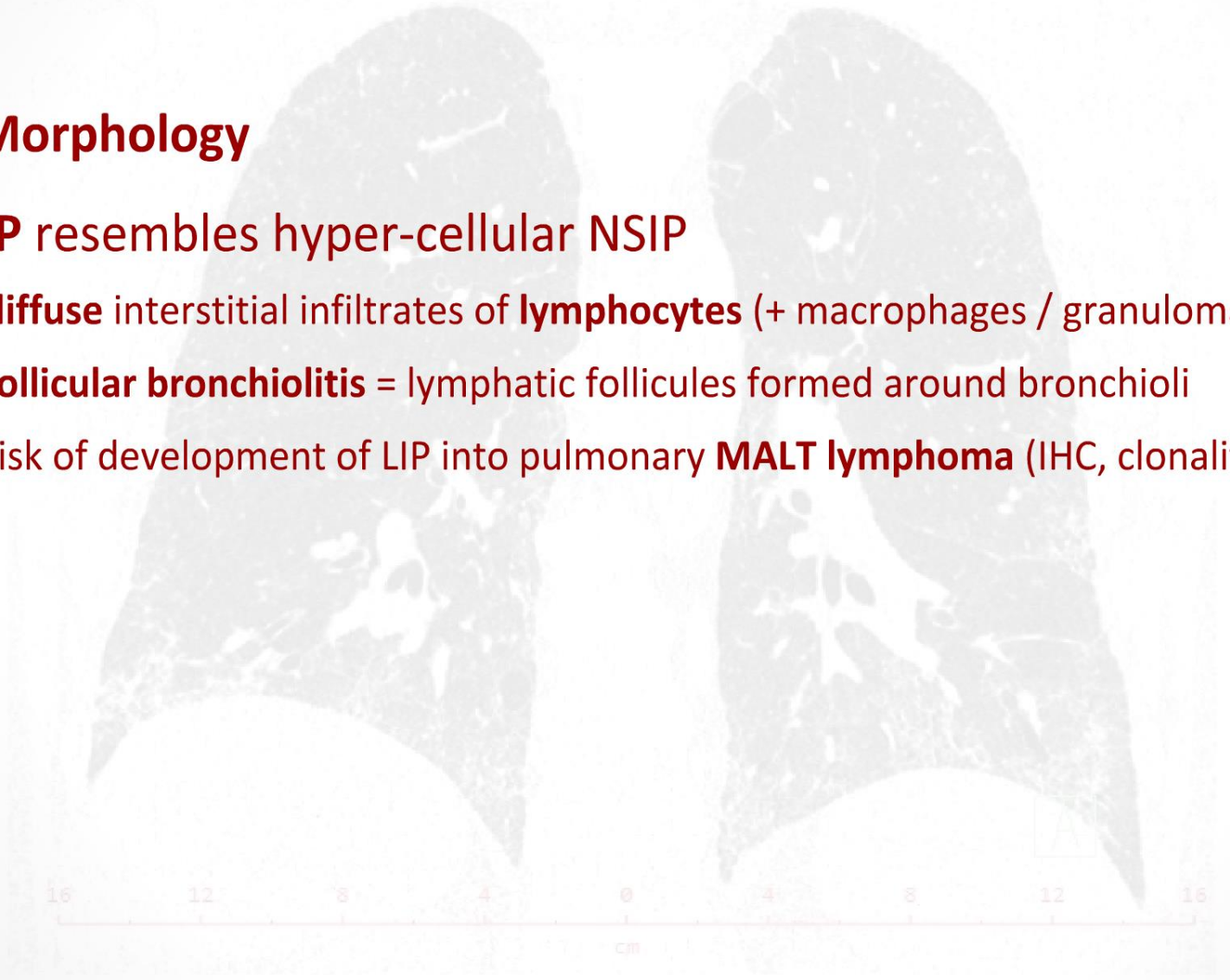
- **COP** creates presence of polypoid plugs of non-specific granulation tissue (no honeycombing)
  - **active** (mixed inflammation) or **inactive** (fibrous scarring)
  - **carnifications** = obturate alveoli ("fleshlike substance"; *caro* = flesh)
  - **bronchiolitis obliterans** = plugs in term. bronchioli (Masson bodies)



ILDs

Morphology

- **LIP** resembles hyper-cellular NSIP
  - **diffuse** interstitial infiltrates of **lymphocytes** (+ macrophages / granulomas)
  - **follicular bronchiolitis** = lymphatic follicules formed around bronchioli
  - risk of development of LIP into pulmonary **MALT lymphoma** (IHC, clonality)



ILDs

Clinical manifestation

- **adults**
  - smokers as well as non-smokers (depends on ILD type)

- lung fibrosis leads to the **severe RI** with pulmonary hypertension and **cor pulmonale chronicum**
  - progressive **dyspnoea** with dry cough (survival approximately 4 years)
  - auscultatory phenomena (wheezing)
  - **acute** forms (EAA) can be manifested with fever

- accompanying symptoms of **hypoxia**
  - **digital clubbing** of fingers and nails (*digiti Hippocratici*)

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