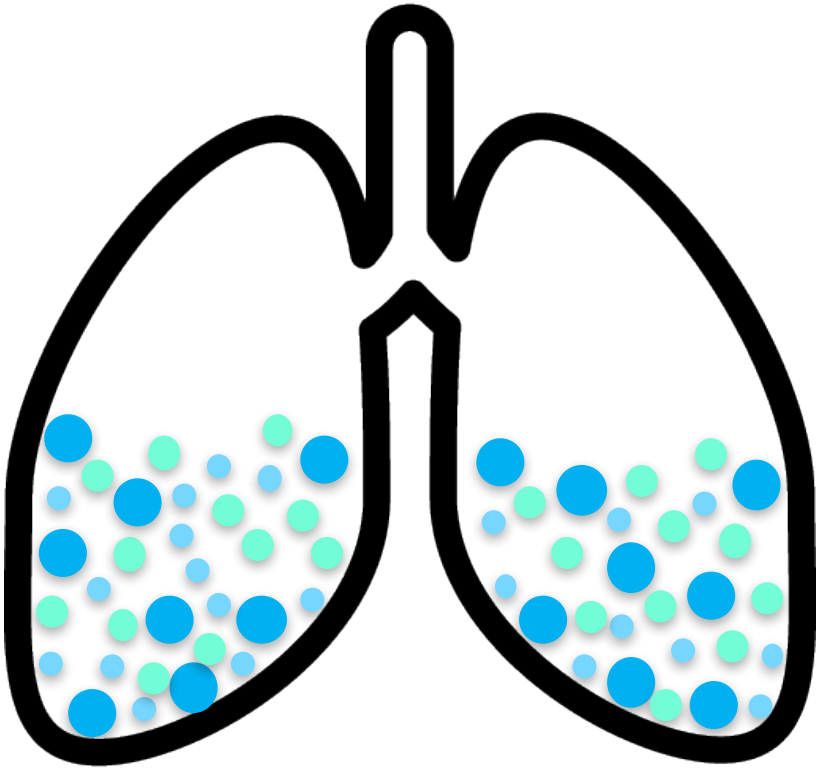
Doenças Pulmonares Difusas



heldernovaisbastos.pt
pneumologia

Doenças Pulmonares

Ácino e interstício

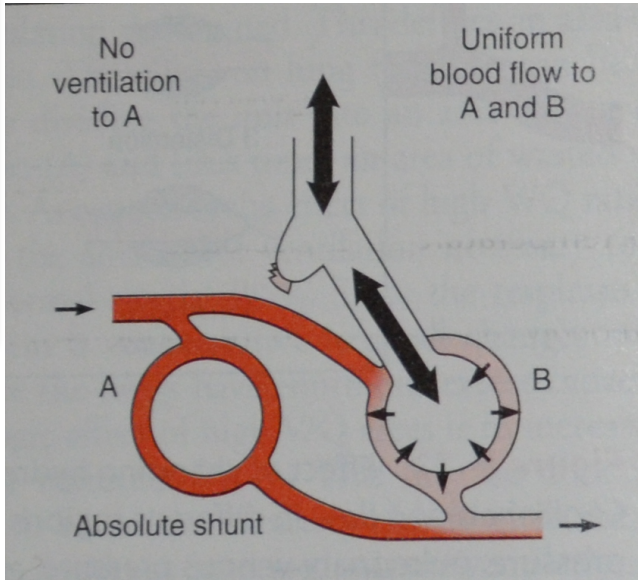
- Edema pulmonar
- Pneumonia
- Hemorragia
- Lesão Alveolar Difusa
- Dças do interstício ou Dças Pulmonares Difusas

Vias aéreas

- DPOC
- Bronquiectasias
- Asma

Vasculatura pulm.

- Hipertensão pulmonar
- TEP



McPhee's Pathophysiology of Disease, 4th ed

Definição de DPD

Grupo heterogéneo de doenças

I. Algumas de etiologia conhecida, outras idiopáticas

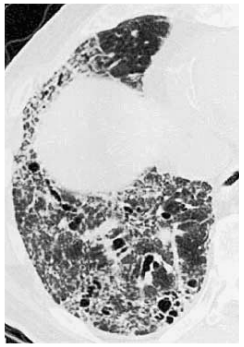
II. Podem envolver o interstício, alvéolos, vias aéreas periféricas ou vasos

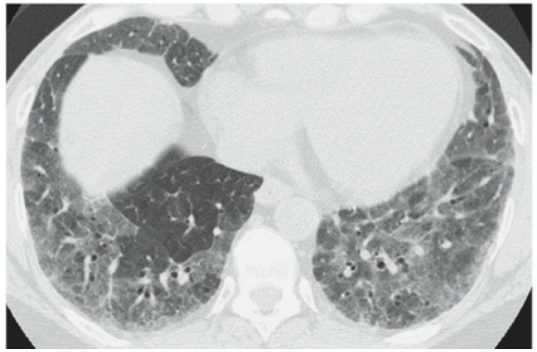
III. Acumulação variável de células efectoras inflamatórias e de matriz extracelular

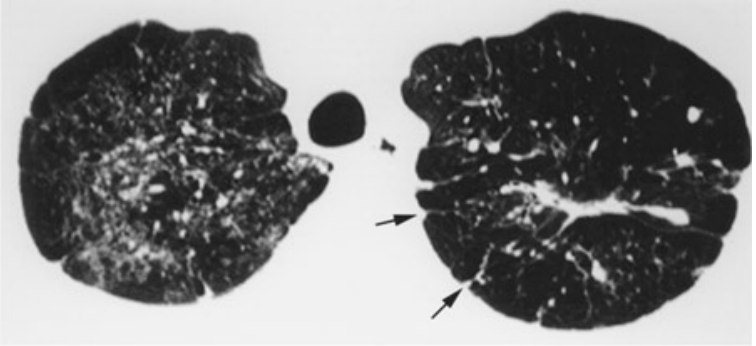
IV. Causam alterações da fisiologia pulmonar (geralmente restritivo) e nas trocas gasosas

V. Apresentação clínica aguda ou crónica (mais comum)

VI. Doença definida por critérios clínicos, radiológicos e patológicos







I. Etiologia conhecida *versus* idopáticas

DPD de etiologia conhecida (~35%)

1. Exposição inorgânica

Pneumoconioses (asbestos, silica, carvão, metais pesados)

2. Exposição orgânica

Pneumonite de hipersensibilidade (pássaros, feno, bolores, micobatérias)

TABLE 54-2 Occupational Interstitial Lung Disease

Occupation	Type of ILD	Exposure
Electrician Plumber Pipe fitter Construction worker Ship builder Insulation installer	Asbestosis	Asbestos
Stone cutter Miner Sand blaster	Silicosis	Crystalline silica dust
Metal grinder	Giant cell interstitial pneumonia Hard metal lung disease	Hard metals Cobalt Tungsten carbide
Metal worker Factory workers Nuclear weapons Aircrafts Electronics Ceramics Golf clubs Bicycle frames	Berylliosis	Beryllium
Coal worker	Coal worker's pneumoconiosis	Coal dust
Paint sprayer Plastic worker	Chemical worker's lung	Isocyanates
Bird breeder	Bird breeder's lung	Bird droppings Bird feathers
Farm worker Haying Mushroom compost	Farmer's lung Mushroom worker's lung	Thermophilic bacteria
Office worker	Humidifier lung Ventilation pneumonitis	Fungi/Molds
Lifeguard	"Hot tub" hypersensitivity pneumonitis	*Mycobacteria*

Fishman's Pulmonary Diseases and Disorders

I. Etiologia conhecida *versus* idopáticas

DPD de etiologia conhecida (~35%)

3. Iatrogénica

- Induzida por fármacos (amiodarona, metotrexato, quimioterapia)
- Induzida por radiação

(http://www.pneumotox.com)

4. Pós-infecciosa

5. Relacionadas com o tabagismo

- DIP (Pneumonia Intersticial Descamativa)
- RBILD (Bronquiolite Respiratória)
- LCH (Histiocitose de células de Langerhans)

6. Associadas com conectivites

- Artrite Reumatóide
- Esclerodermia / Esclerose sistémica
- Polimiosite/dermatomiosite
- LES
- S.Sjogren

TABLE 54-3 Drugs Implicated in Interstitial Lung Disease

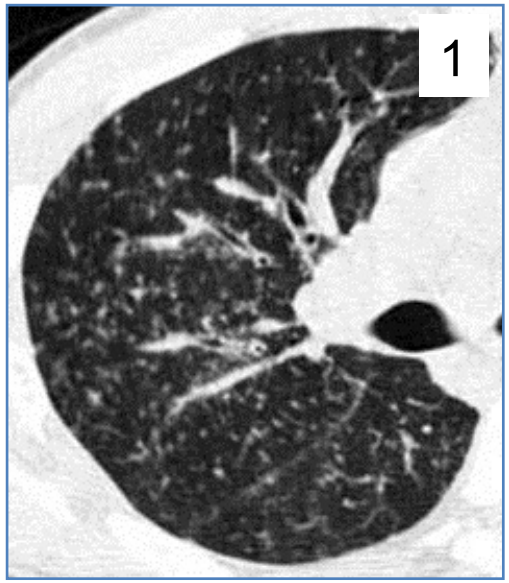
Antibiotics	**Chemotherapeutic**
Nitrofurantoin	All-trans retinoic acid (ATRA)
Minocycline	Alpha-interferon
Cephalosporins	Antithymocyte globulin
Antiarrhythmic	Bleomycin
Amiodarone	Busulfan
Tocainide	Carmustine (BCNU)
Anti-inflammatory	Chlorambucil
Azathioprine	Colony-stimulating factors (GM-CSF)
Etanercept	Cyclophosphamide
Gold salts	Cytosine arabinoside
Infliximab	Docetaxel
Methotrexate	Geftinib
NSAIDs	Gemcitabine
Penicillamine	Interleukin-2
Sulfasalazine	Irinotecan
Neurologic/Psychiatric	Melphalan
Carbamazepine	Mitomycin C
Phenytoin	Paclitaxel
Drugs of Abuse	Procarbazine
Cocaine	Vinorelbine
Heroin	**Other**
Talc	Bacille Calmette-Guérin (BCG)
	Mineral oil
	Radiation

Source: Data from Camus. Drug-induced and iatrogenic infiltrative lung disease. Clinics in Chest Med. 2004;25:479–519.

Fishman's Pulmonary Diseases and Disorders

I. Etiologia conhecida *versus* idopáticas

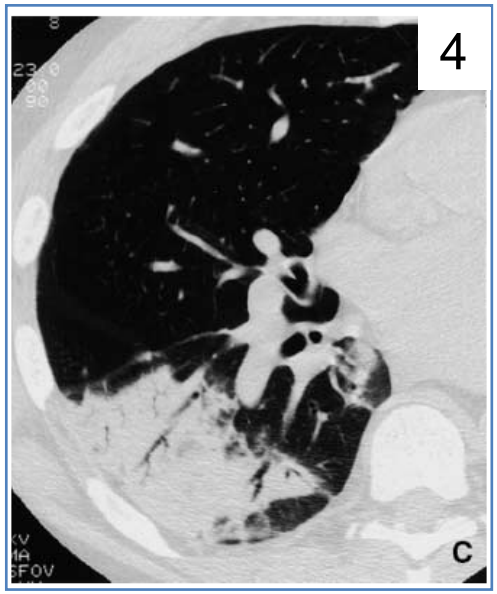
DPD de etiologia desconhecida (~65%)

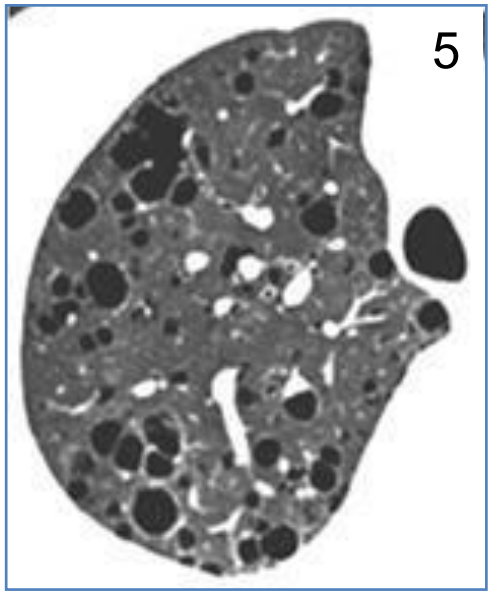


DPD de etiologia desconhecida (~65%)

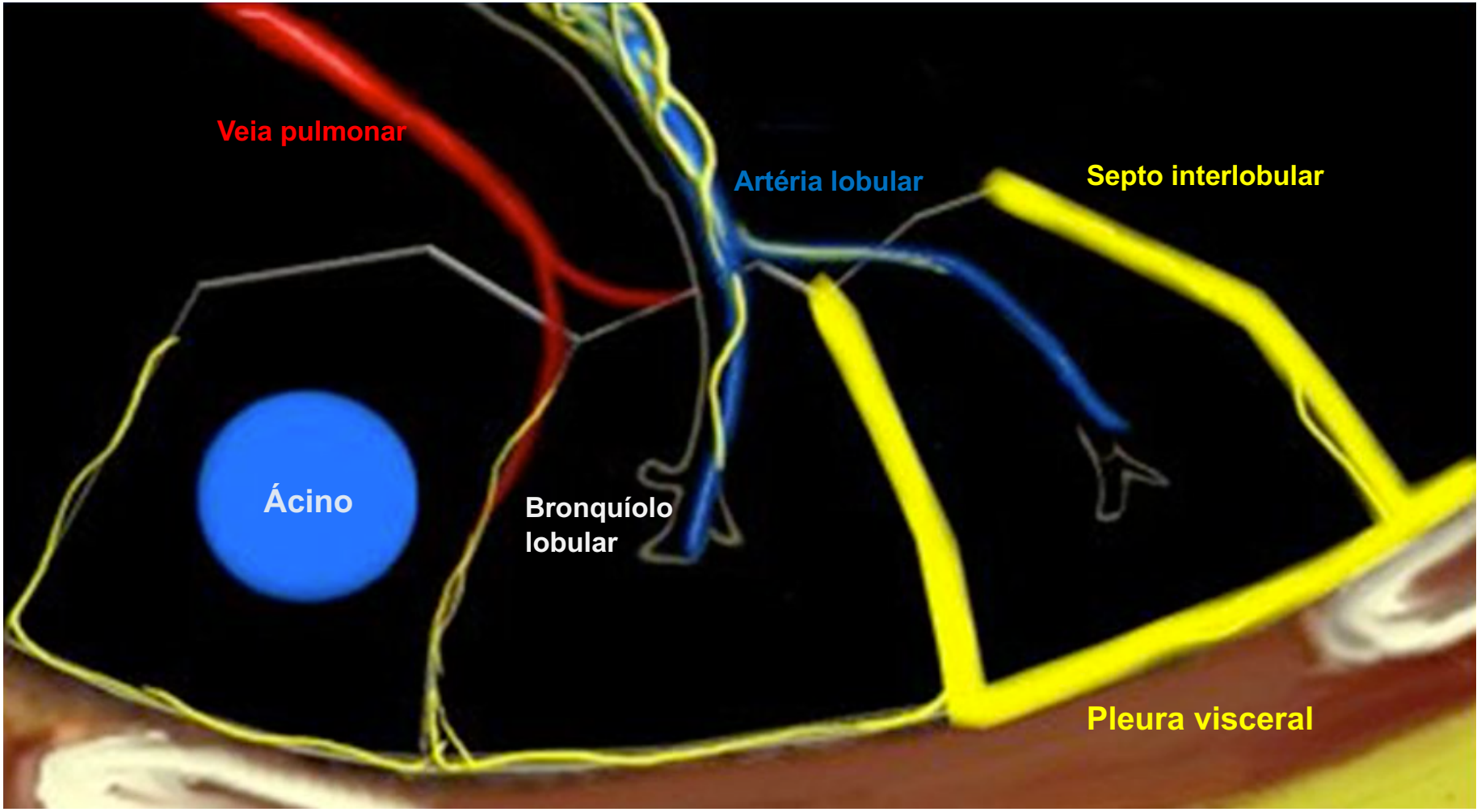
1. Sarcoidose
2. UIP/IPF (>50%)
3. NSIP (~1/3)
4. COP (raro)
5. LIP (muito raro)
6. AIP (muito raro)

Pneumonias intersticiais idiopáticas



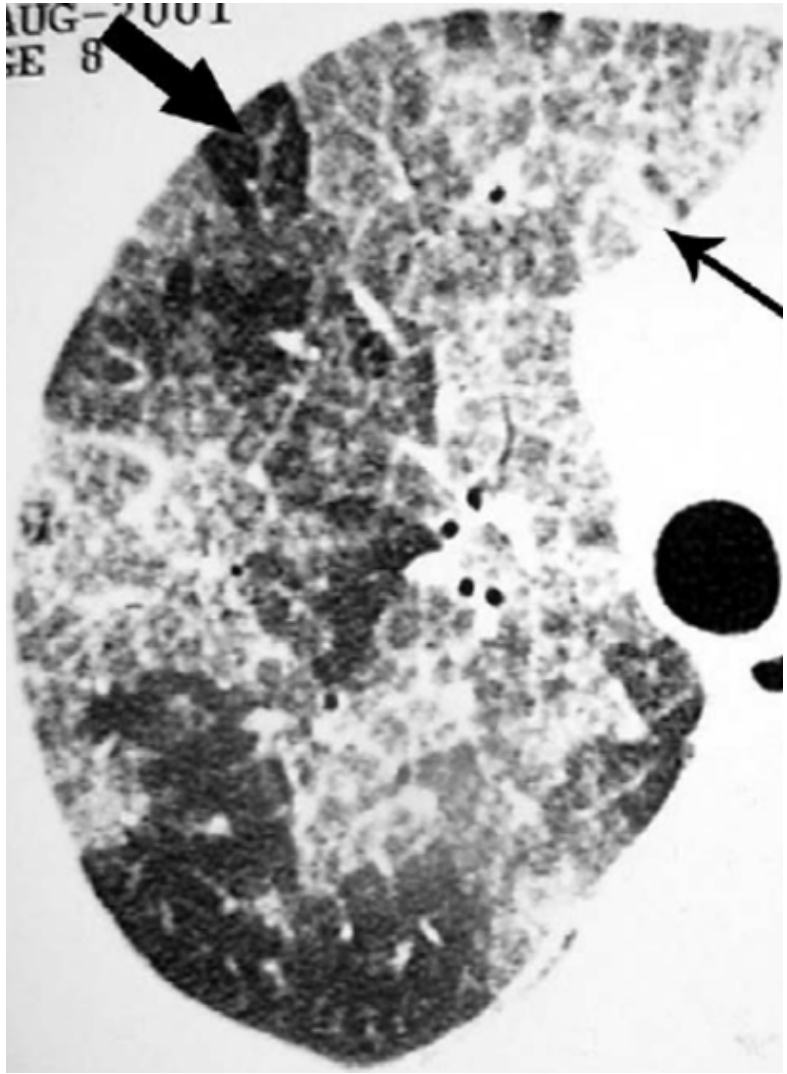


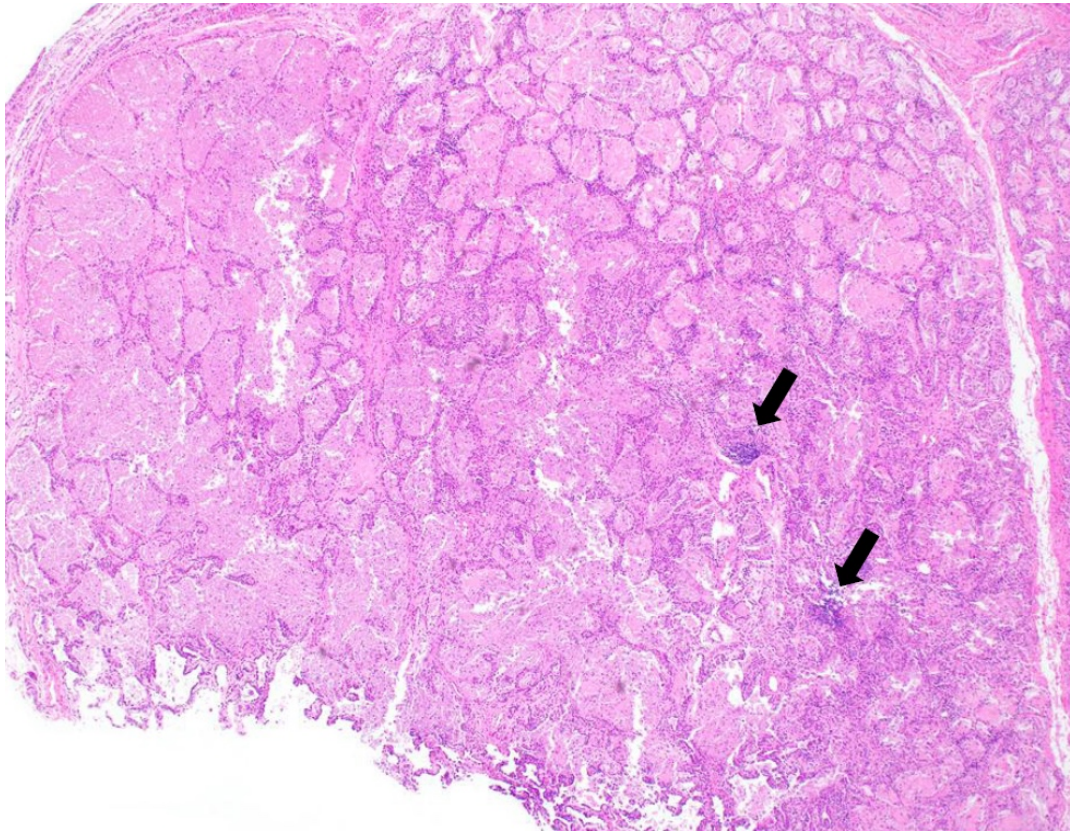
II. Envolvem o interstício, alvéolos, vias aéreas periféricas ou vasos



Ácino – Unidade estrutural e funcional

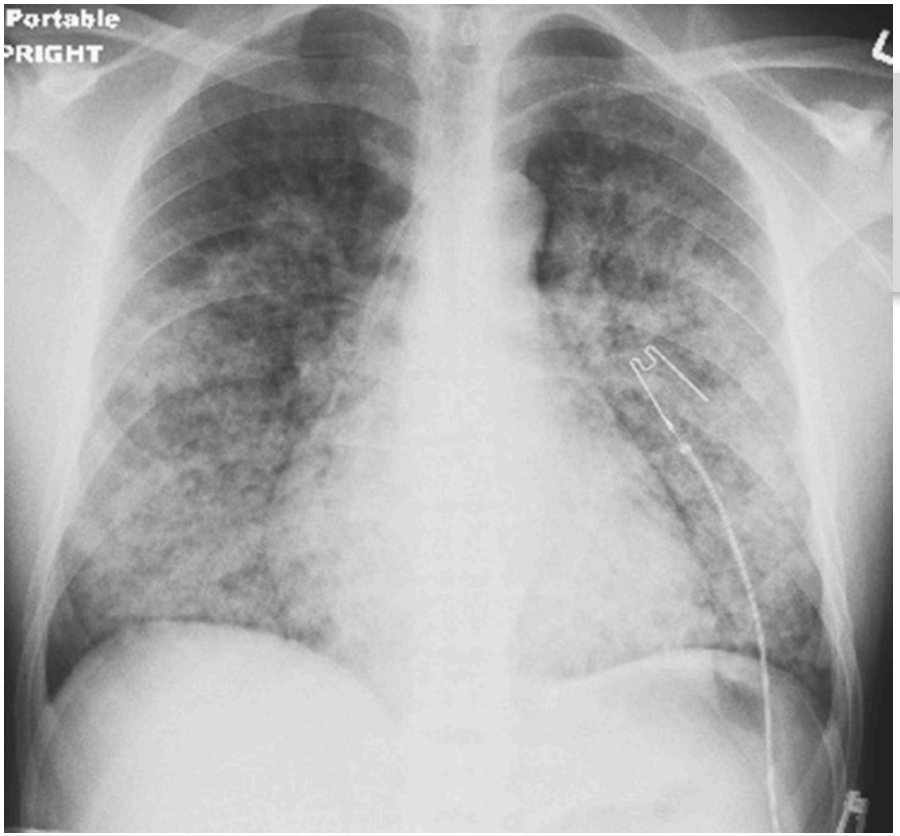
Proteinose alveolar

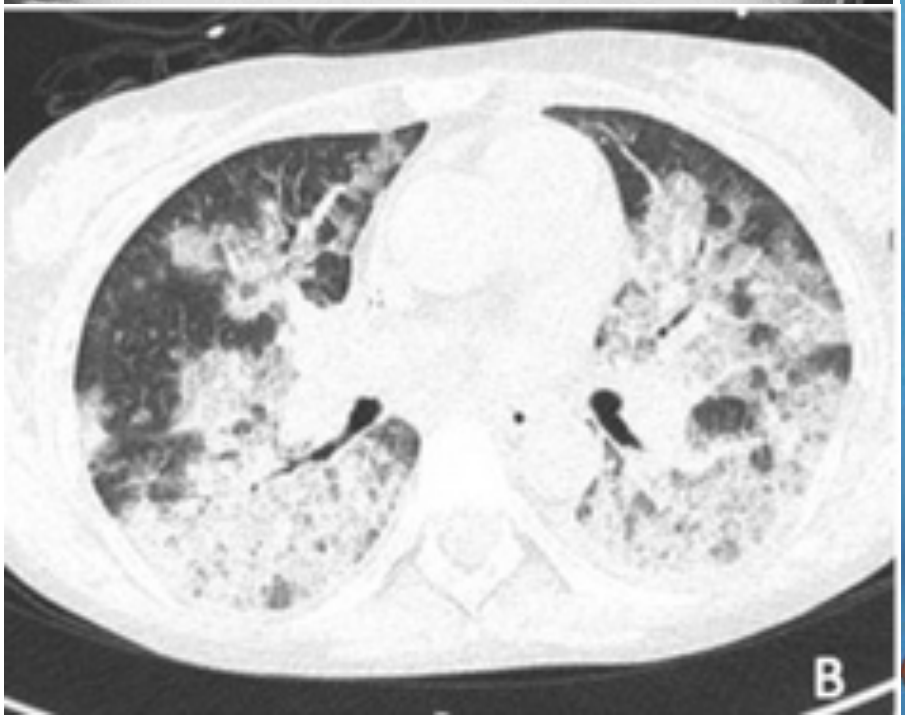




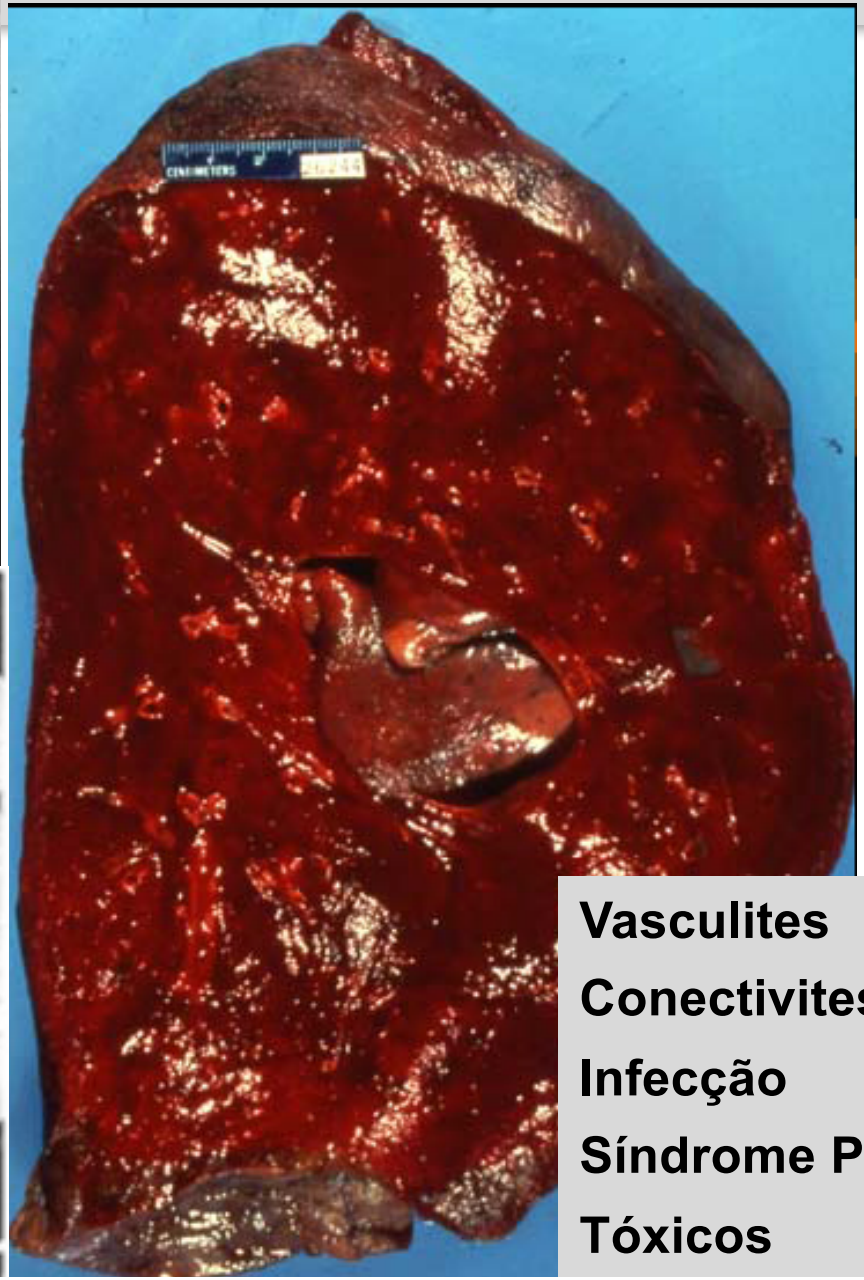
Envolvimento difuso dos espaços intra-alveolares por material amorfo,granular e eosinofílicos; o interstício está expandido por células inflamatórias crónicas que formam agregados densos

Espessamento dos septos interlobulares e opacidades em “vidro-despoldo”





Hemorragia Alveolar



Vasculites

Conectivites

Infecção

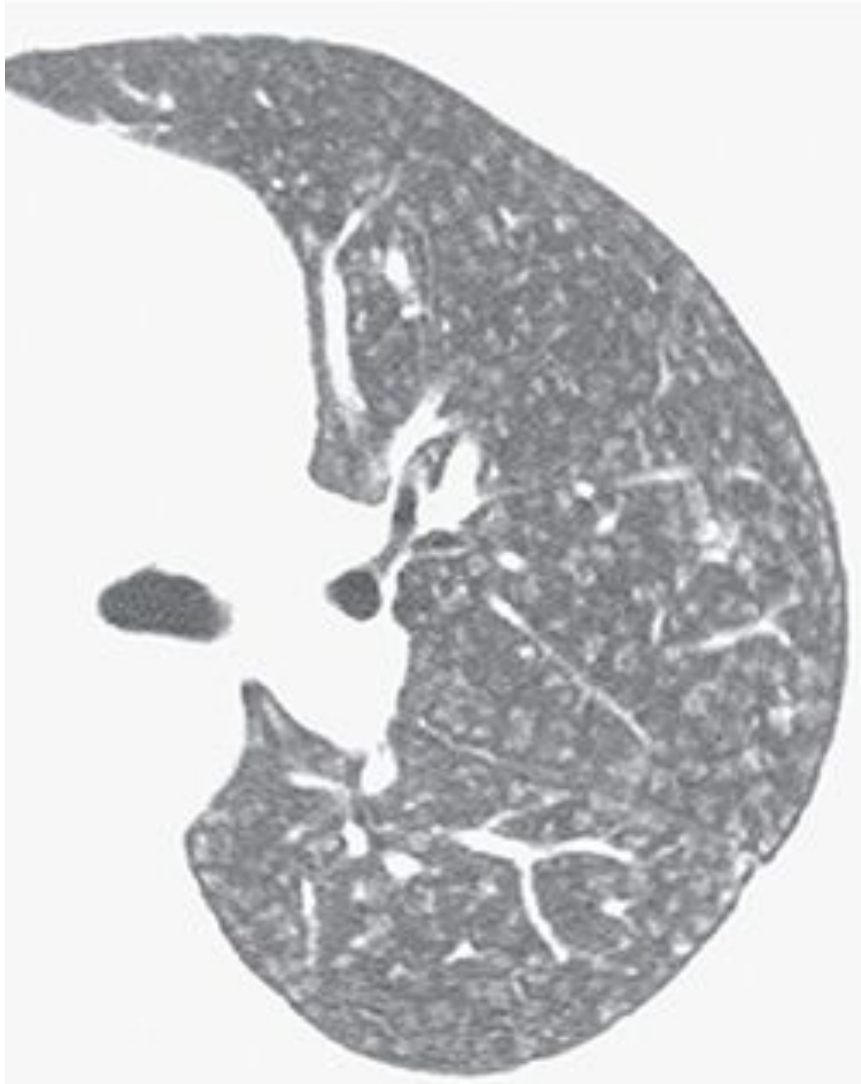
Síndrome Pulmão-Rim

Tóxicos

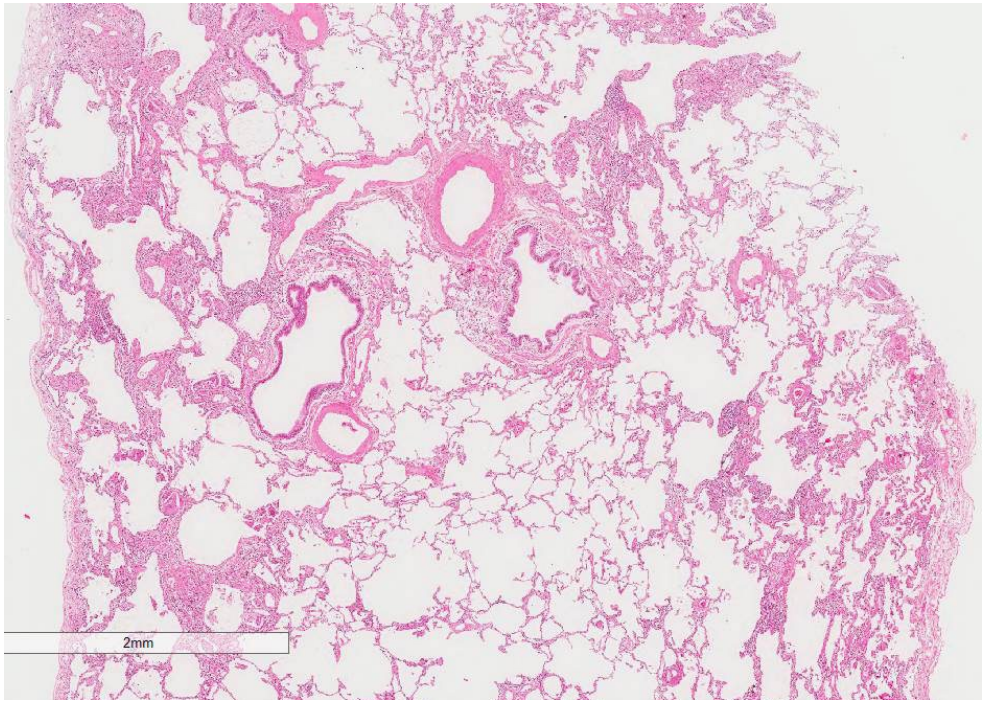
Causas de Hemorragia Alveolar Difusa

Vasculites	Granulomatose de Wegener, Poliangite microscópica, S. Churg-Strauss, etc
Conectivites	Lupus Eritematoso Sistémico, Artrite Reumatóide, Esclerose sistémica, etc
Outras causas imunes	Síndromes Pulmão-Rim (S. Goodpasture, GN pauci-imune, GN com depósito de imunocomplexos circulantes), S. Hemolítico Urémico, etc
Infecções	Leptospirose, Aspergilose invasiva, etc
Fármacos e tóxicos	Propiltiouracilo, imunossupressores, quimioterápicos, anti-coagulantes, antiagregantes plaquetários, cocaína, cannabis, etc
Outros	Transplante (medula óssea e órgão sólido), Barotrauma,

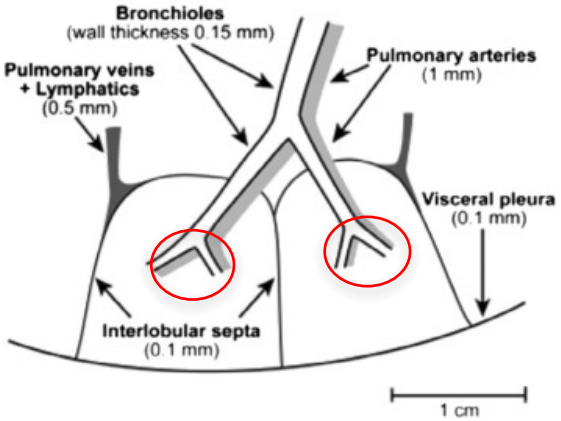
Pneumonite de hipersensibilidade



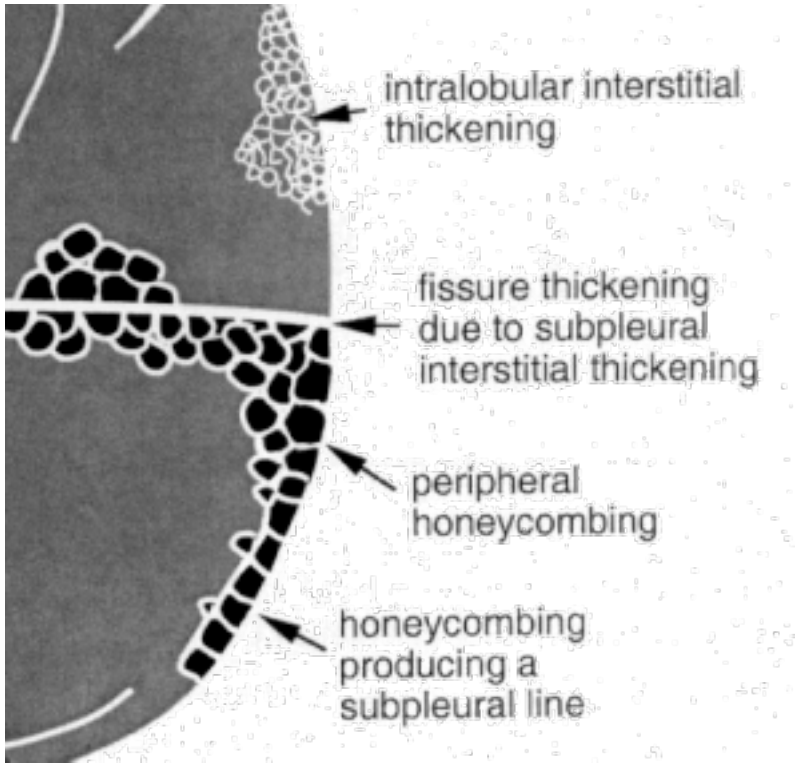
Micronódulos em “vidro-despolido” centrilobulares

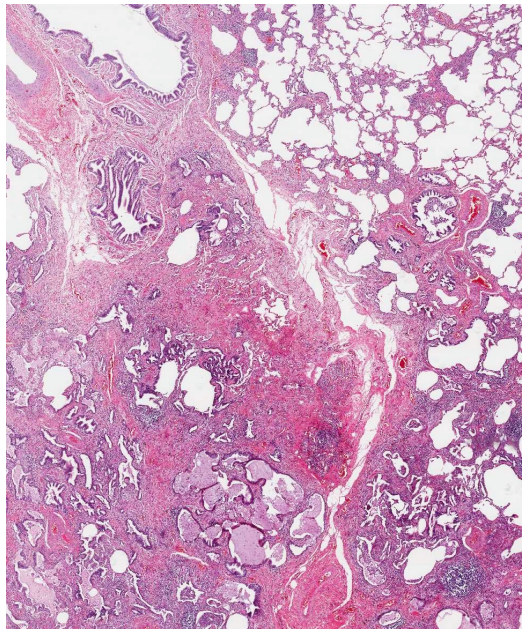


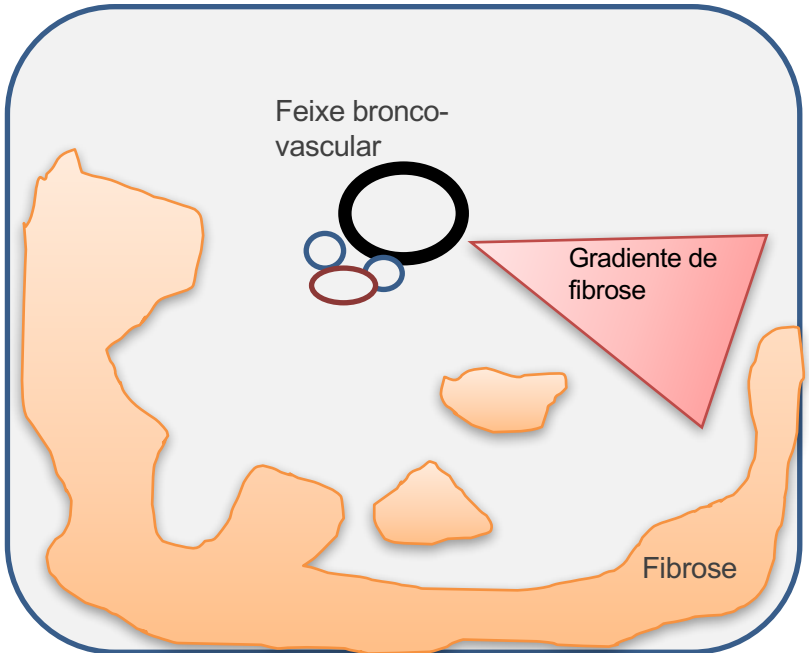
Infiltrado linfocítico bronquiolocêntrico com células gigantes



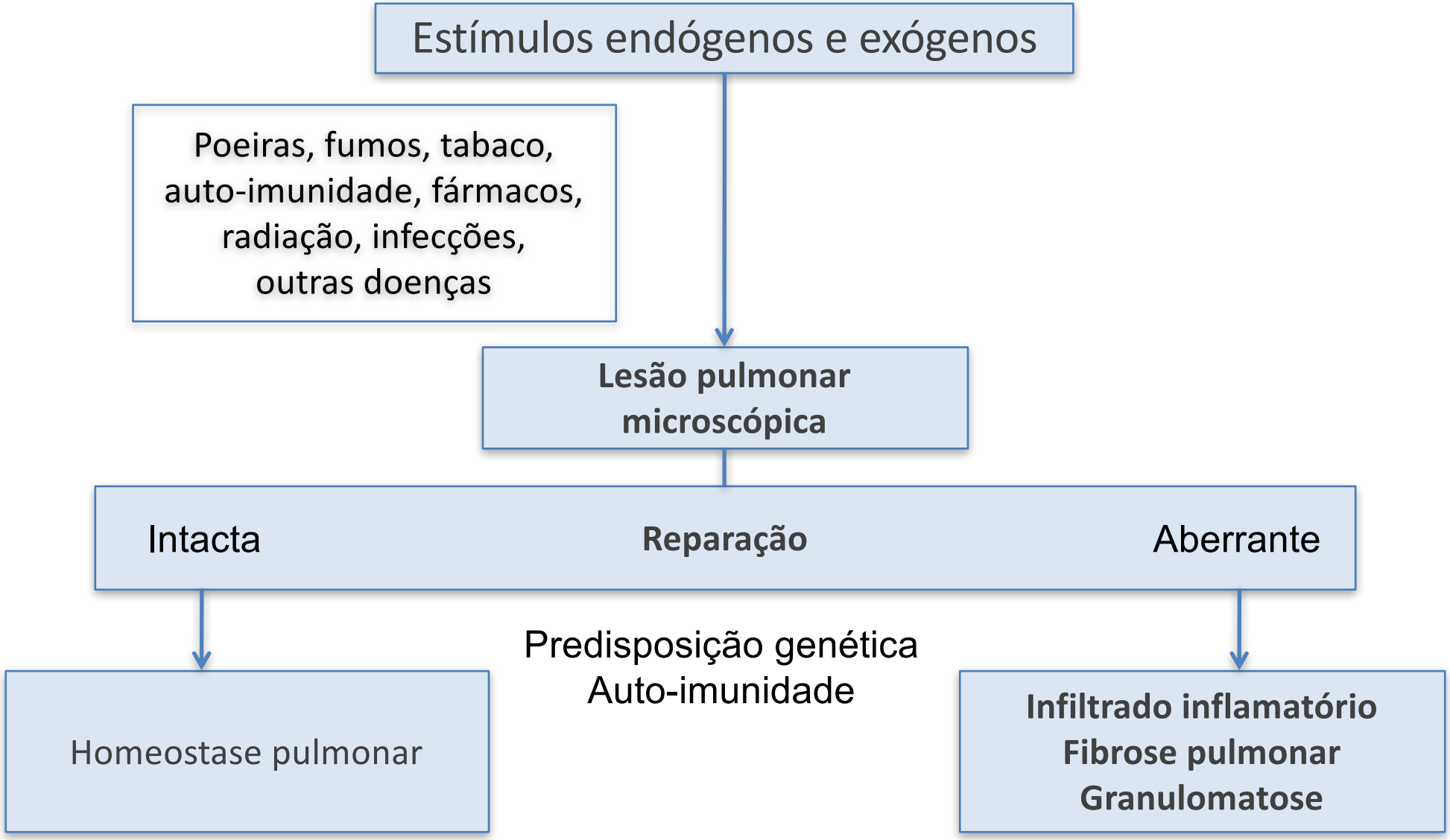
Padrão UIP (Pneumonia Intersticial Usual)



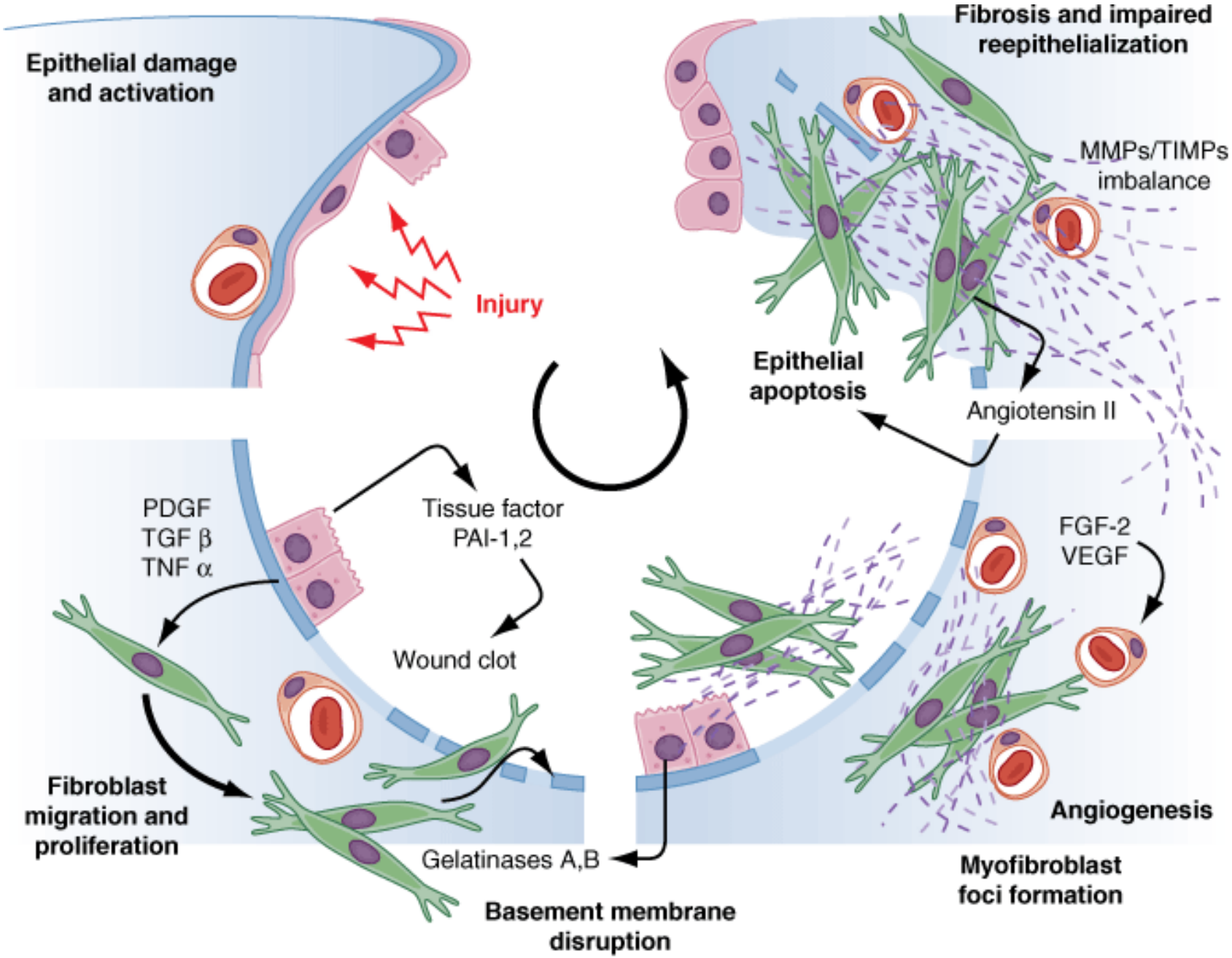




III. Acumulação de células efectoras inflamatórias e de matriz extracelular



Baseado em Harrison's Principles of Internal Medicine



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

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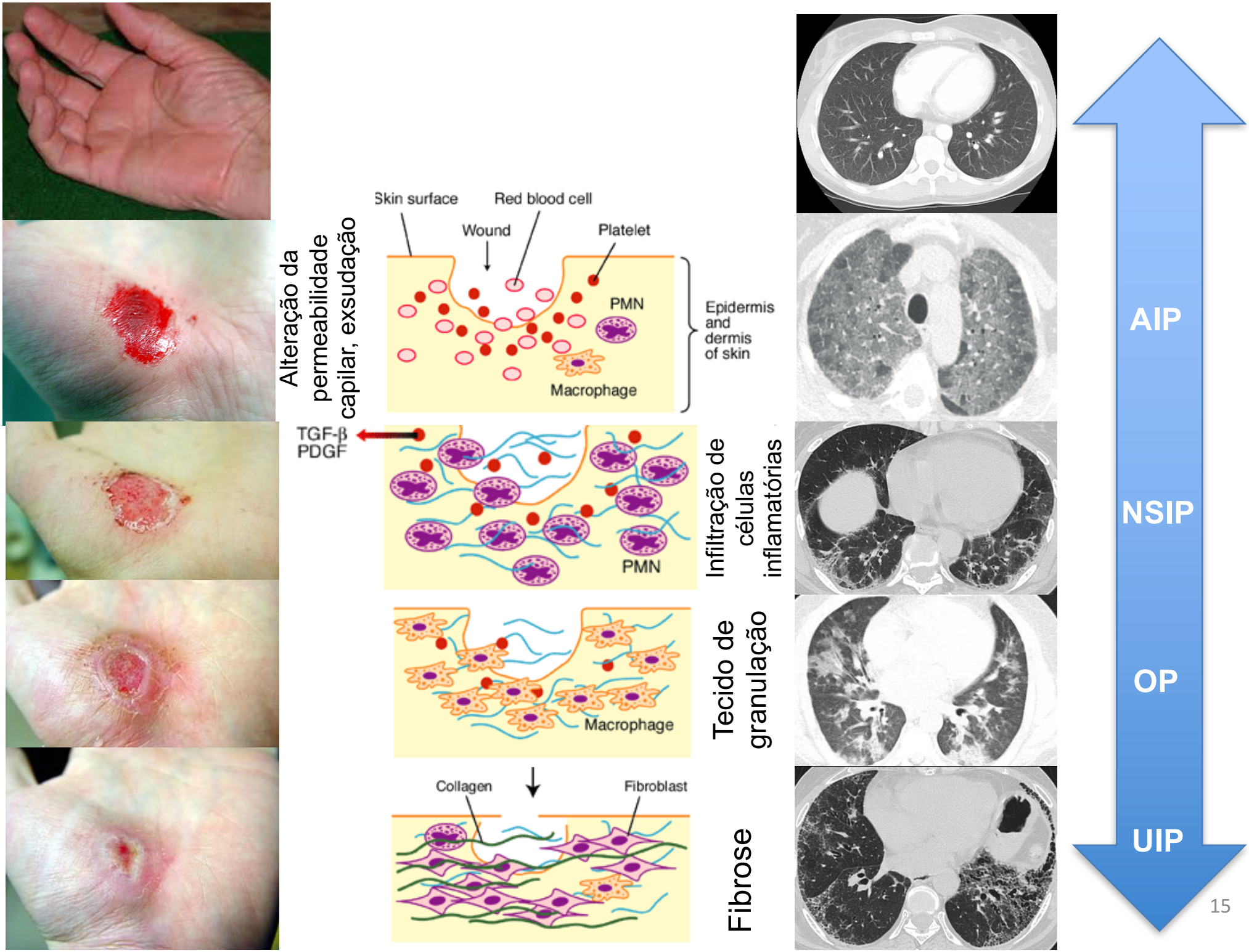
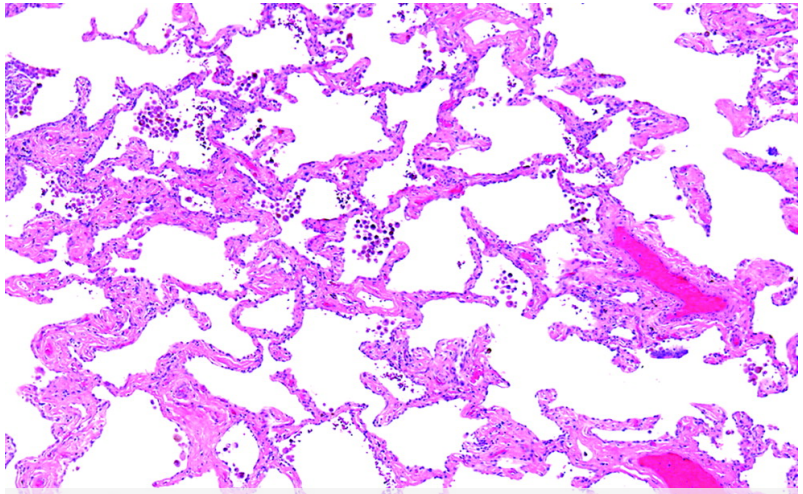
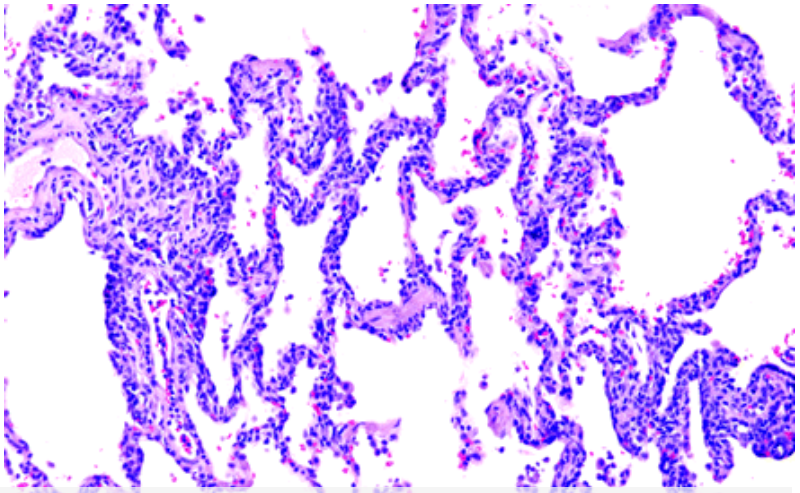

Alteração da permeabilidade capilar, exsudação
Skin surface
Red blood cell
Wound
Platelet
PMN
Macrophage
Epidermis and dermis of skin
TGF-β
PDGF
PMN
Infiltração de células inflamatórias
Macrophage
Tecido de granulação
Collagen
Fibroblast
Fibrose
AIP
NSIP
OP
UIP

Alveolite, infiltrado inflamatório intersticial, fibrose

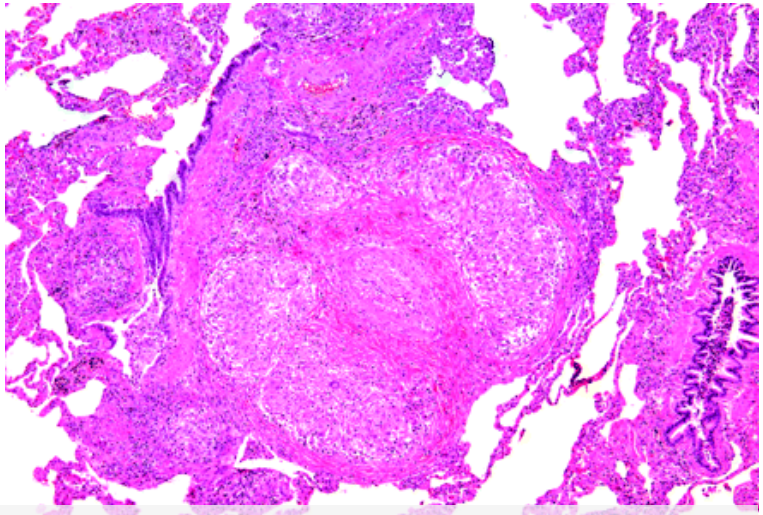


Fibrose intersticial e discreto infiltrado inflamatório (NSIP, HP)

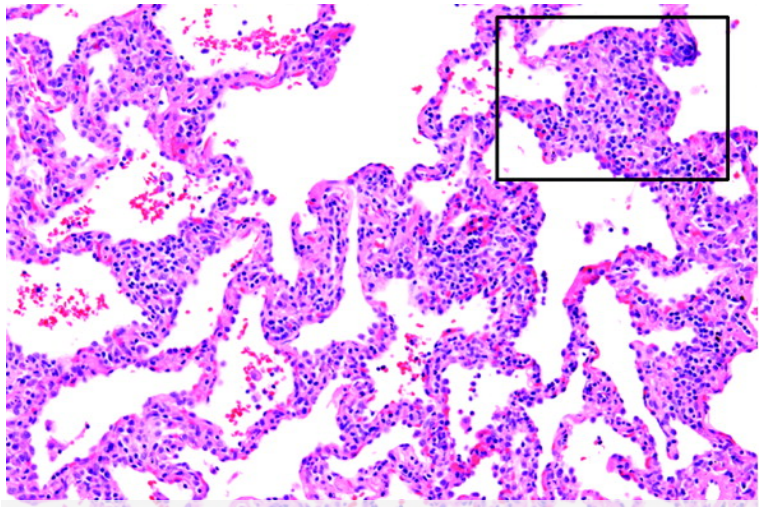


Infiltrado inflamatório marcado, com LBA revelando alveolite linfocítica (NSIP, HP)

Granuloma

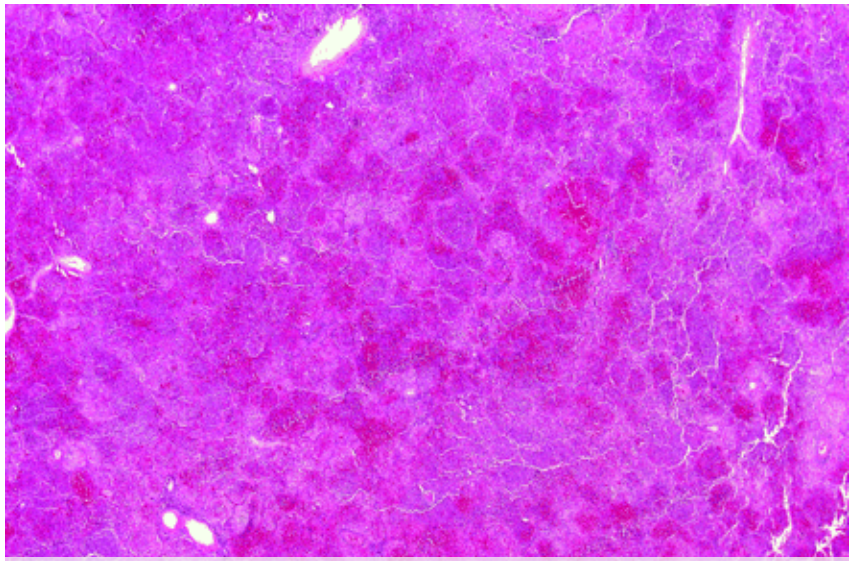


Granuloma sarcóide (sarcoidose)

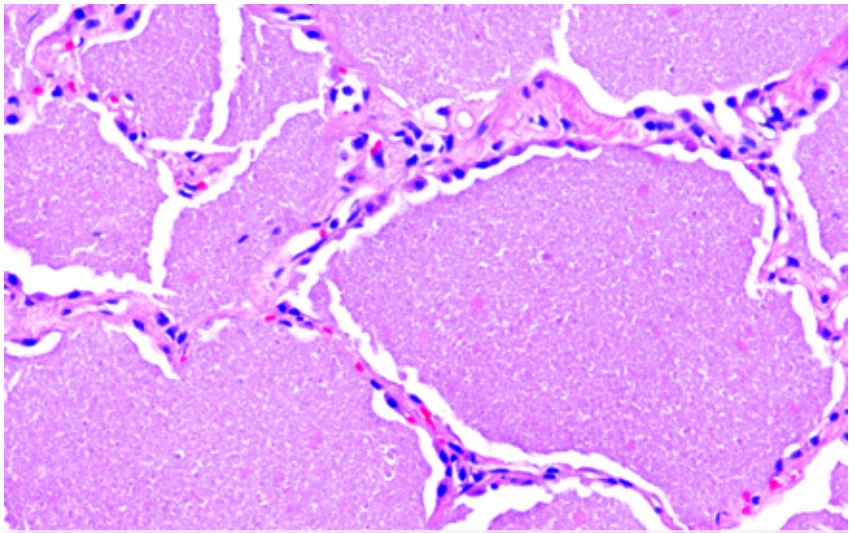


Infiltrado plasmocitário, granuloma laxo (HP)

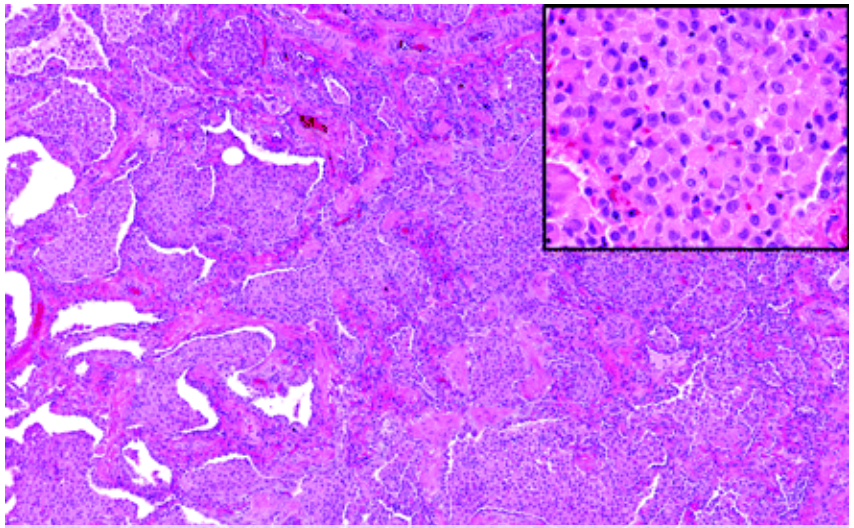
Preenchimento alveolar



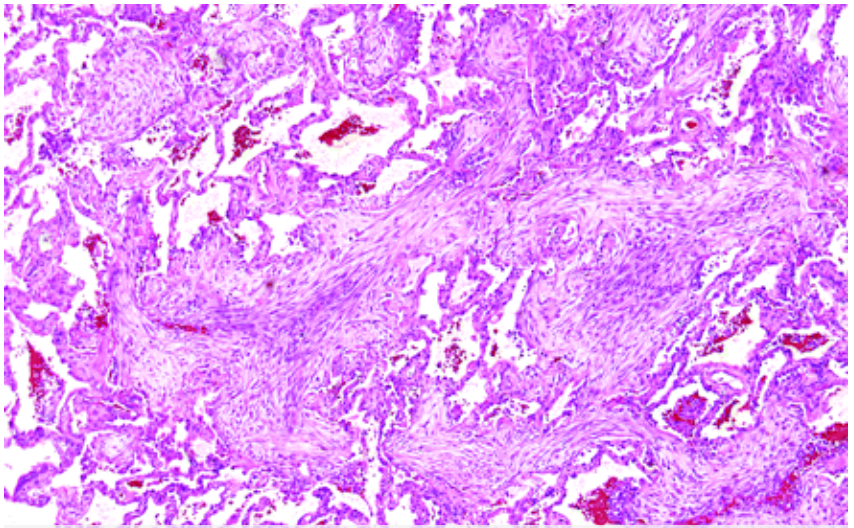
Hemorragia alveolar difusa



Preenchimento alveolar por material eosinofílico amorfo (proteinose alveolar)

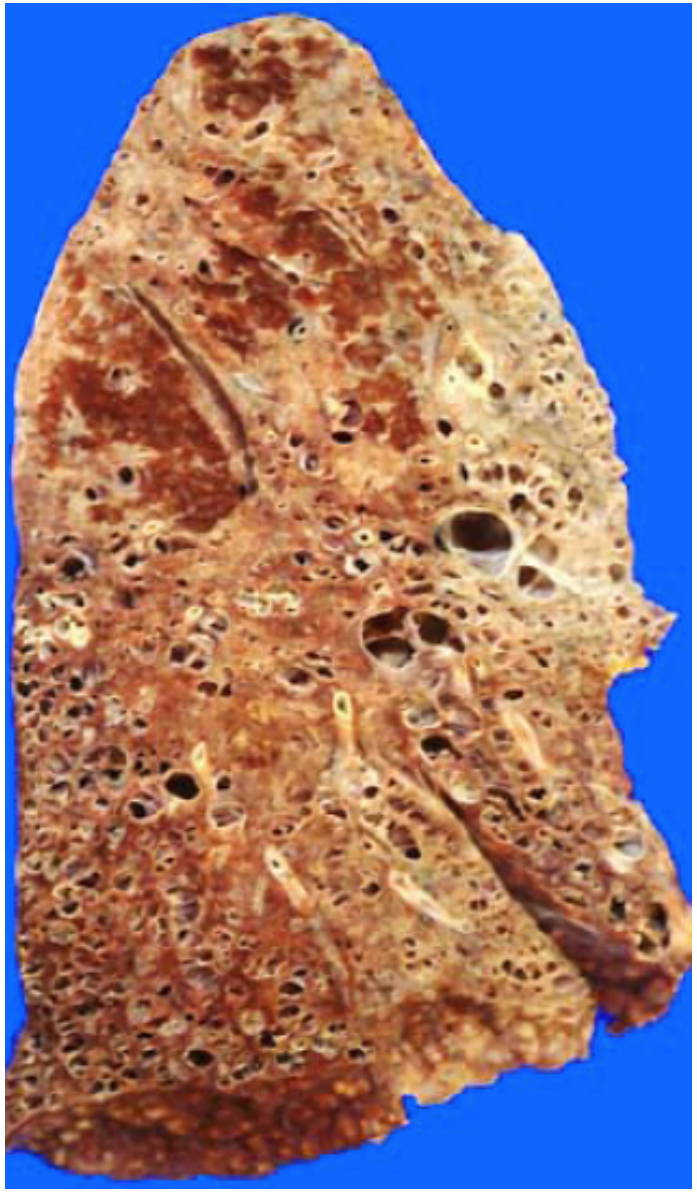


Preenchimento alveolar por ”toalhas” de macrófagos (DIP)



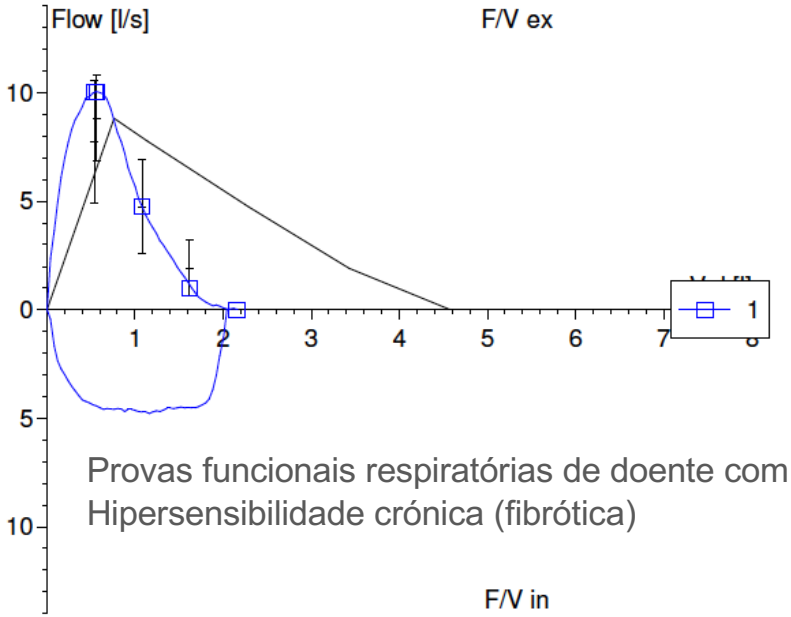
Preenchimento alveolar por “tufos” de fibroblastos imaturos (COP)

IV. Alterações da fisiologia pulmonar



Consequências funcionais:

- Aumento de retracção elástica pulmonar
- Diminuição da *compliance* pulmonar (doenças restritivas)
- Discordância V/Q e *shunt*
- Aumento da espessura da membrana alvéolo capilar (déf. difusão)

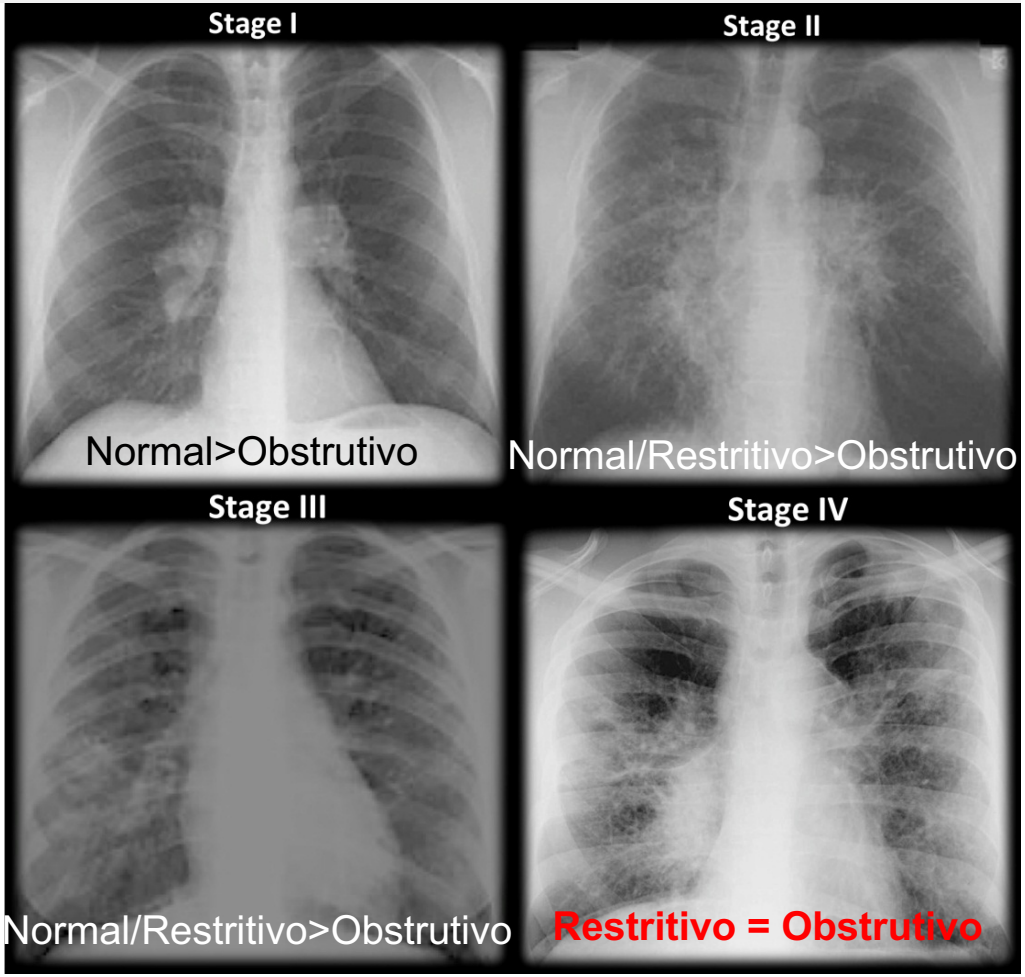


FVC	47%
FEV1	52%
IT	88%
TLC	45%
DLCO	41%

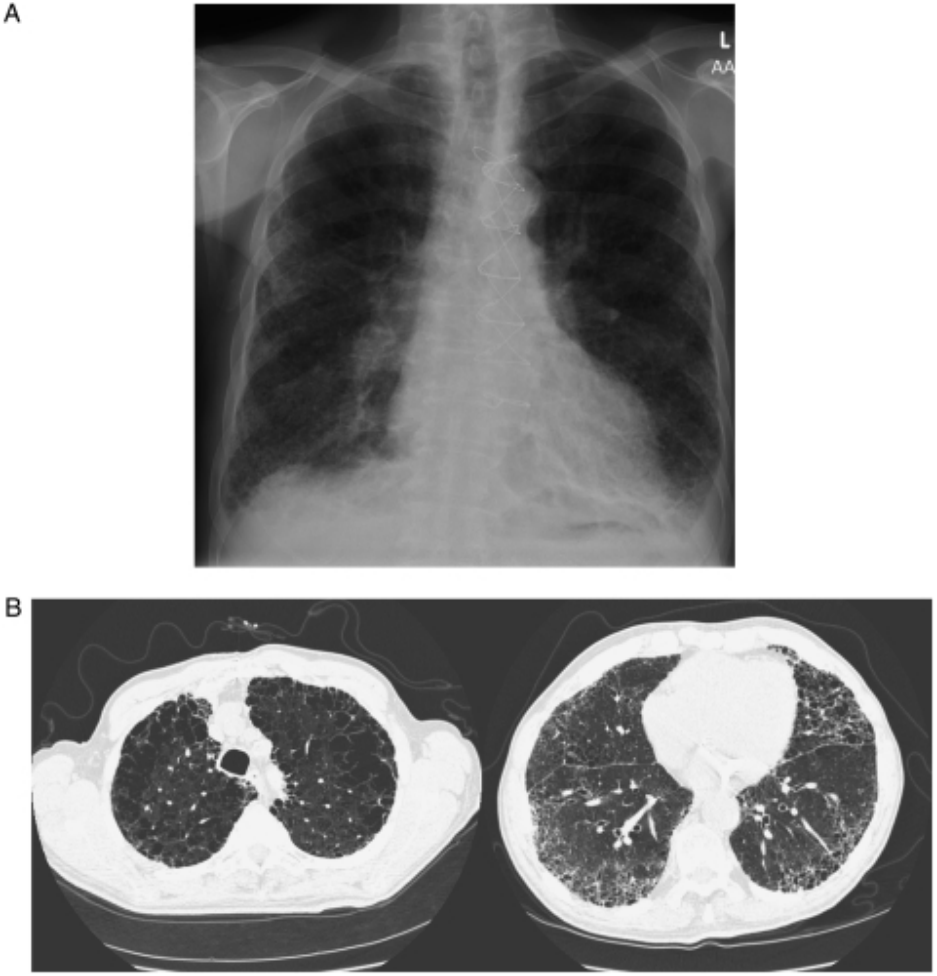
Provas funcionais respiratórias de doente com Pneumonite de Hipersensibilidade crónica (fibrótica)

Doenças Pulmonares Difusas também podem causar alterações ventilatórias obstrutivas

Sarcoidose

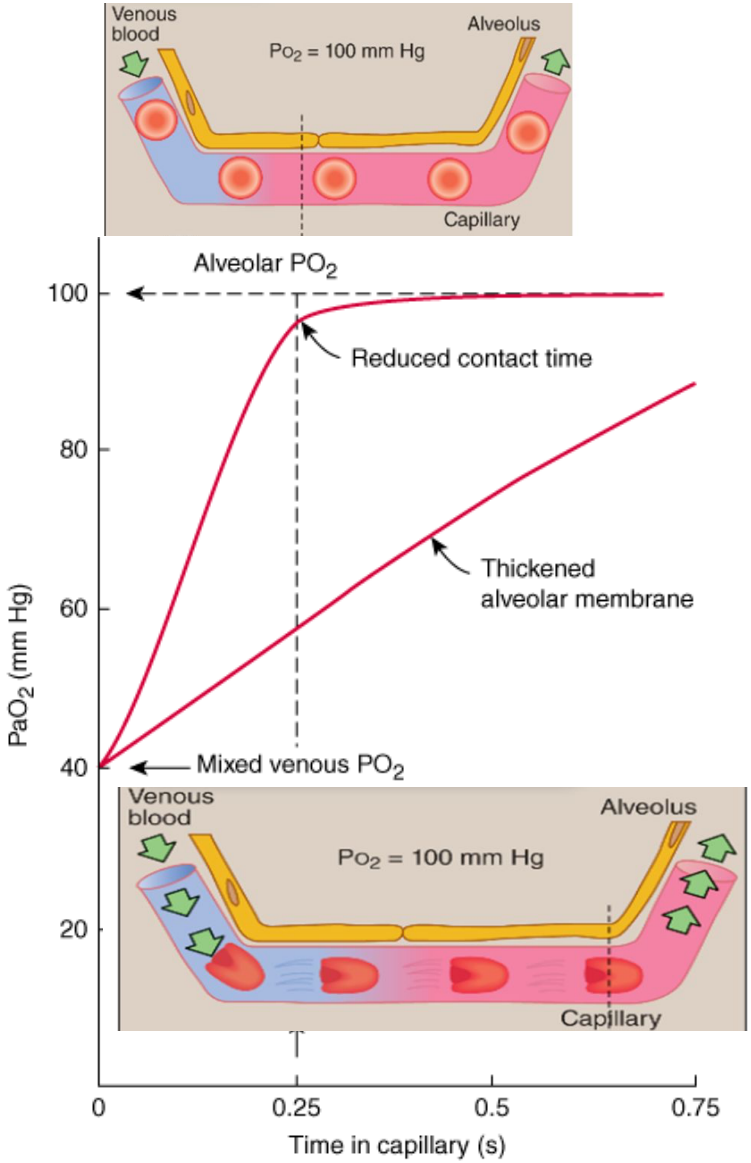


Combinação fibrose pulmonar e enfisema



Chest. 2012 Jan; 141(1): 222–231

Outras: HP, LCH, LAM, Silicose crónica



Source: McPhee SJ, Hammer GD: *Pathophysiology of Disease: An Introduction to Clinical Medicine, 6th Edition*: http://www.accessmedicine.com

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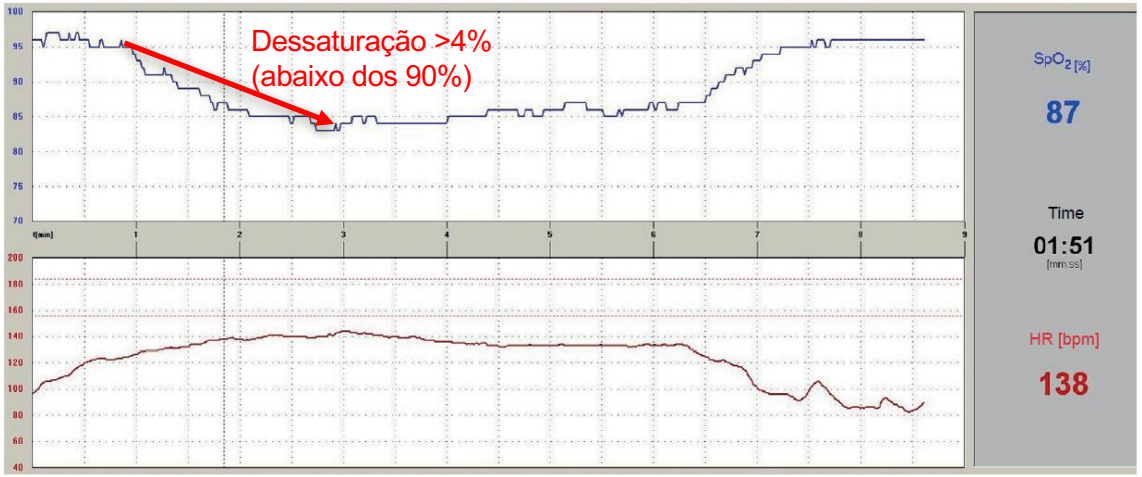
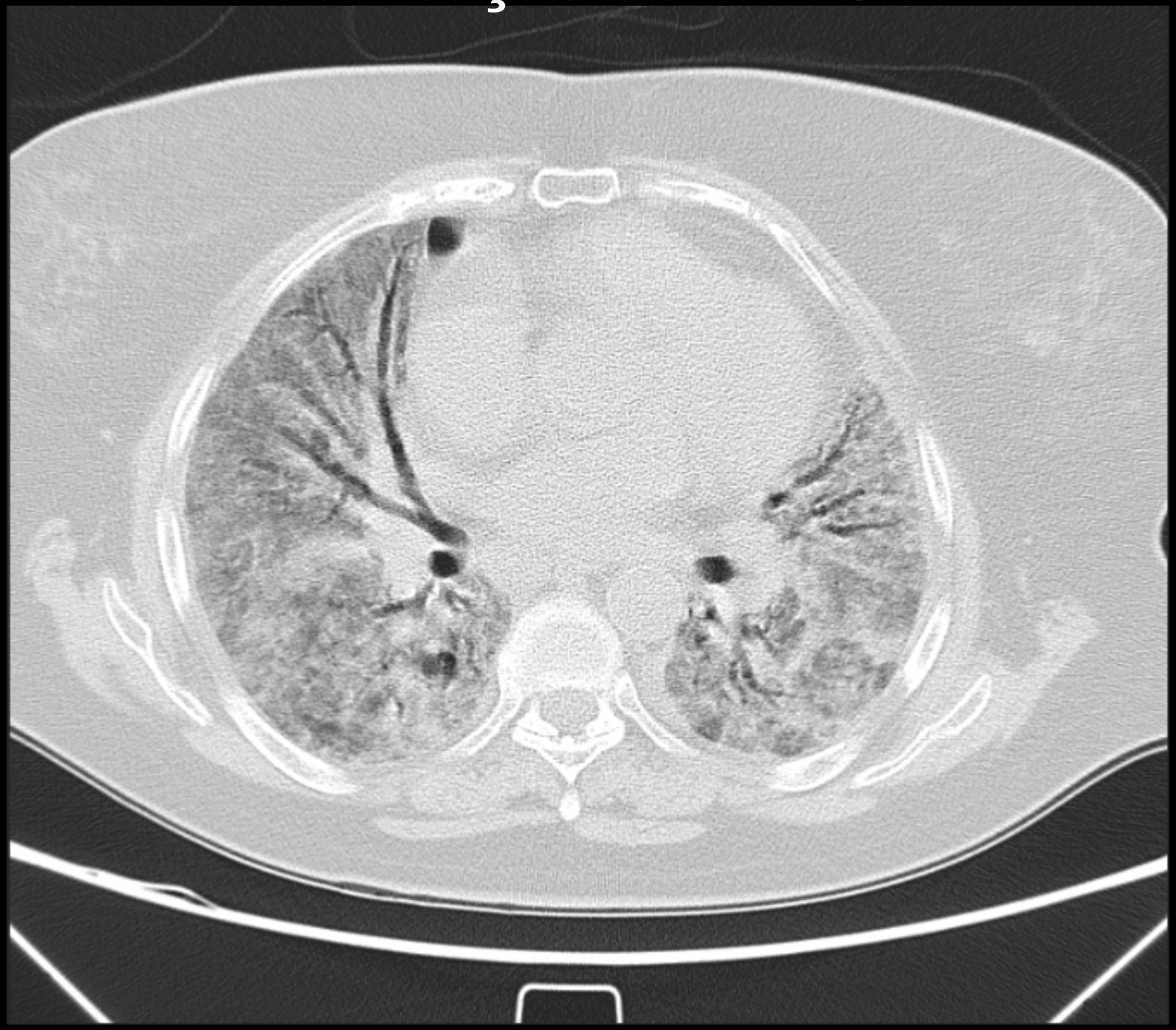
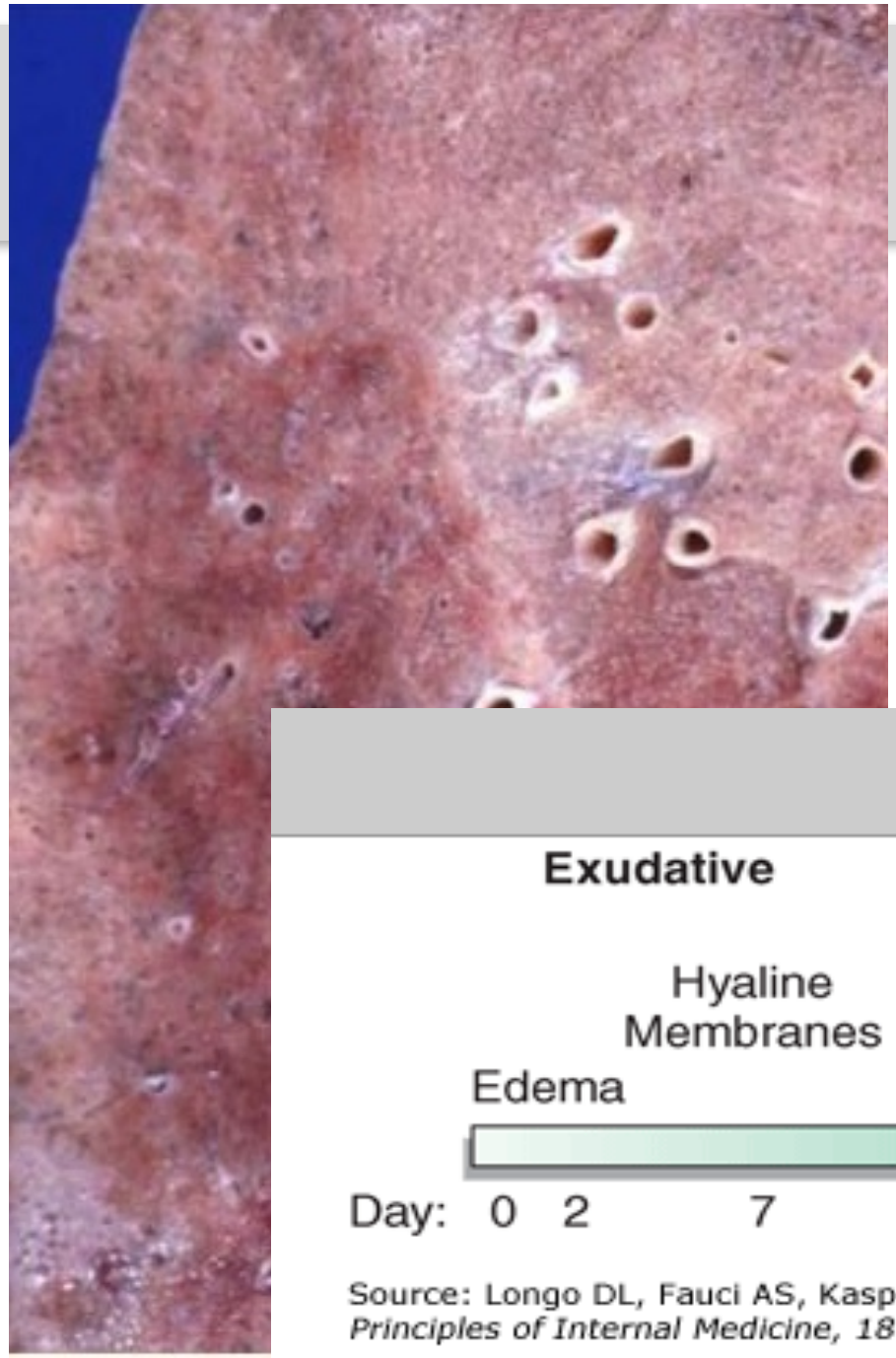
Prova de marcha de 6 minutos

- Avaliação do estado funcional (basal e monitorização) e indicador de prognóstico
- Afectada primariamente pela alteração da membrana alvéolo-capilar



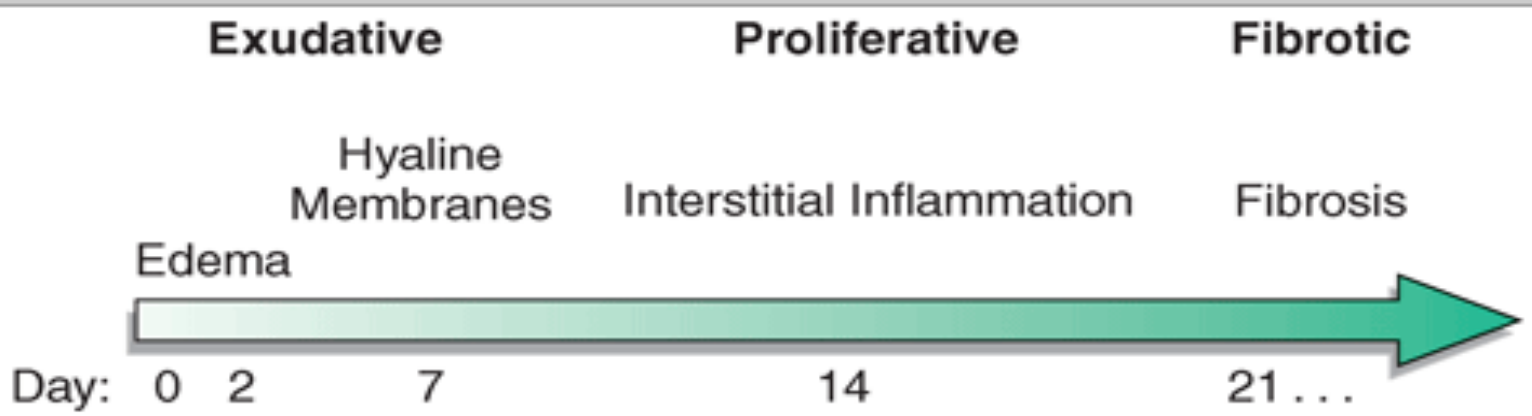
Exacerbação de DPD / AIP





Dano Alveolar Difuso .

Padrão histo-patológico caracterizado por membranas hialinas revestindo os alvéolos em estádios iniciais, posteriormente com proliferação dos pneumócitos tipo II e em estádios finais com inflamação e fibrose.



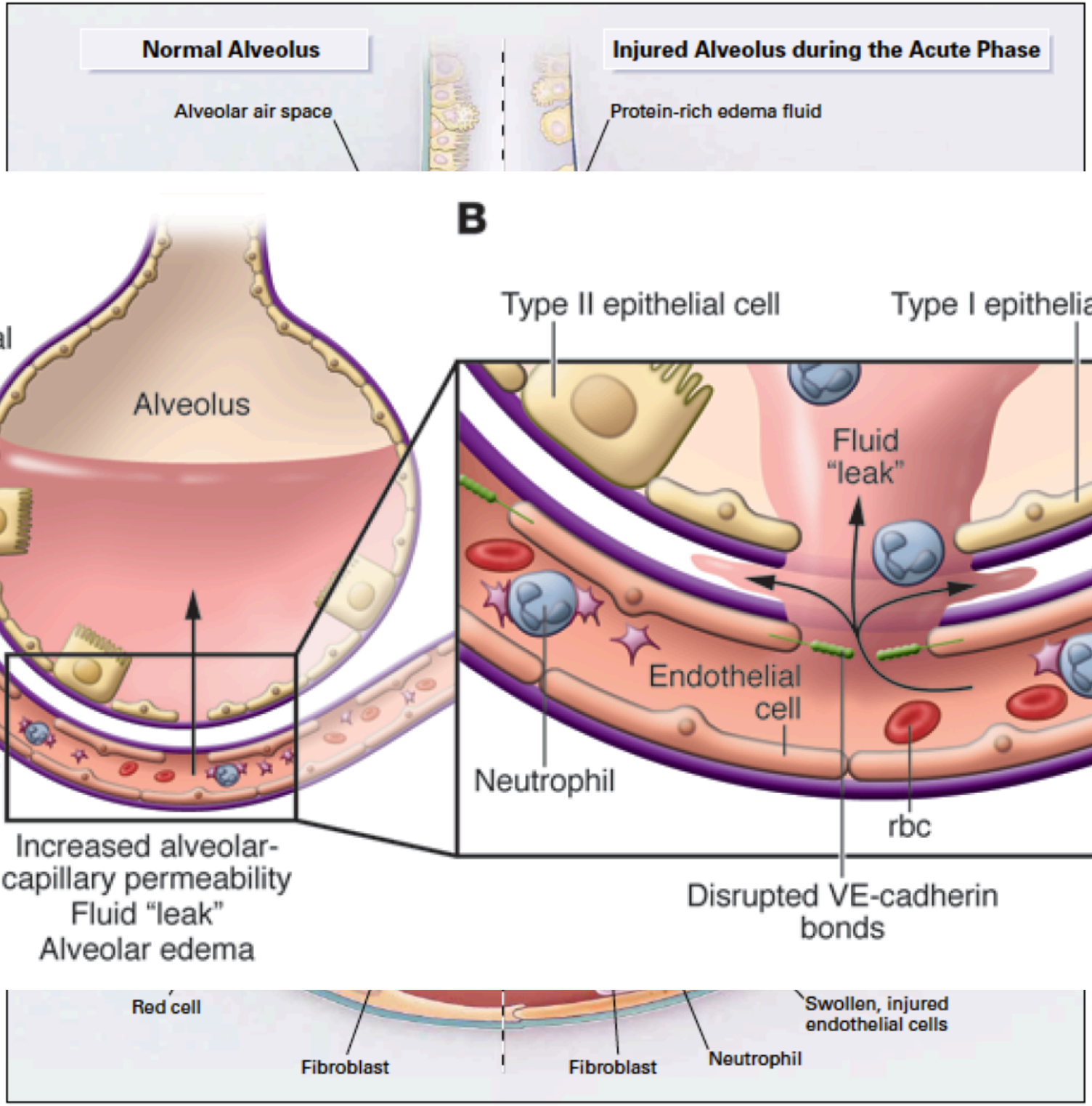
Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

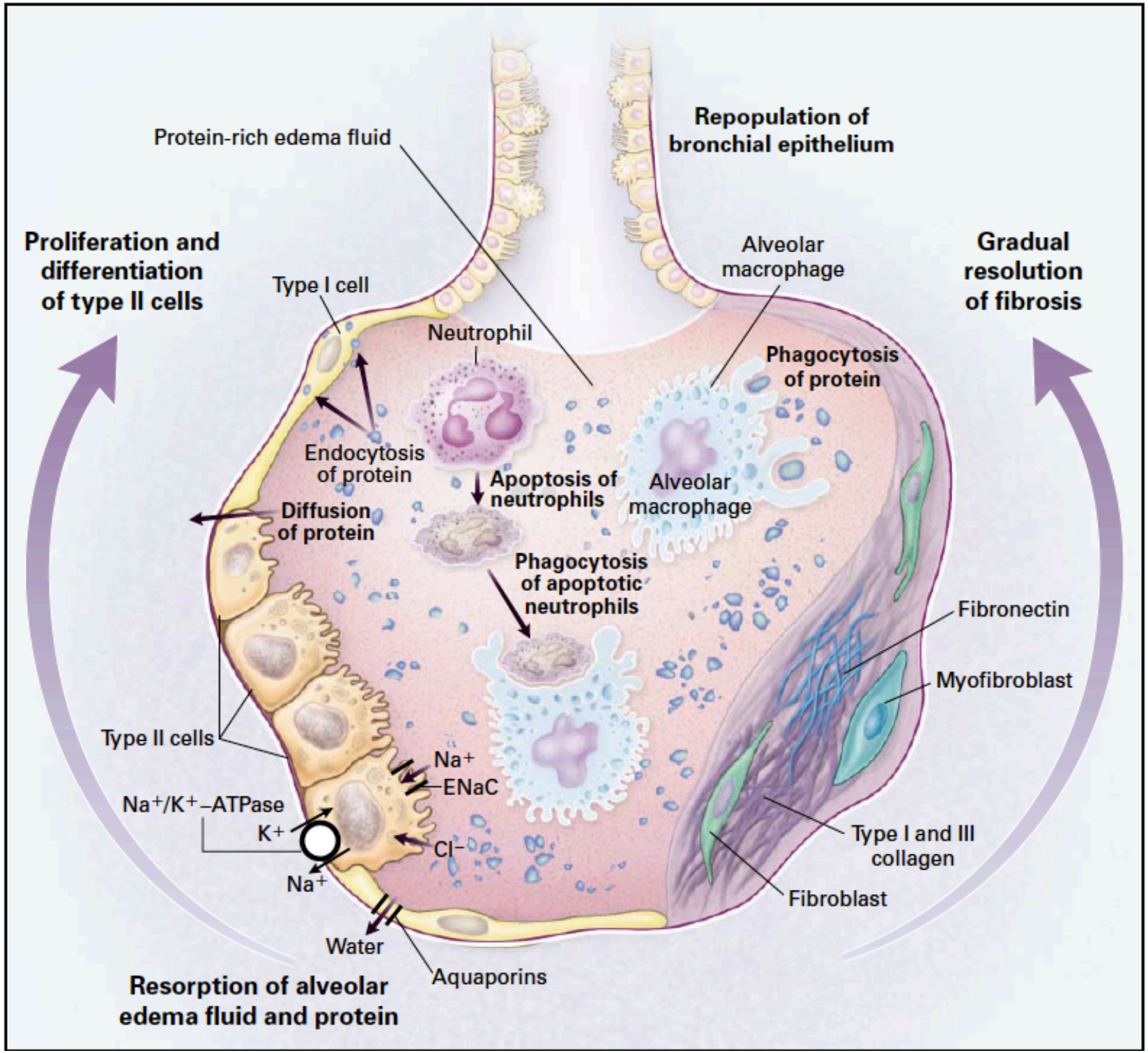
ARDS – *Acute Respiratory Distress Syndrome*

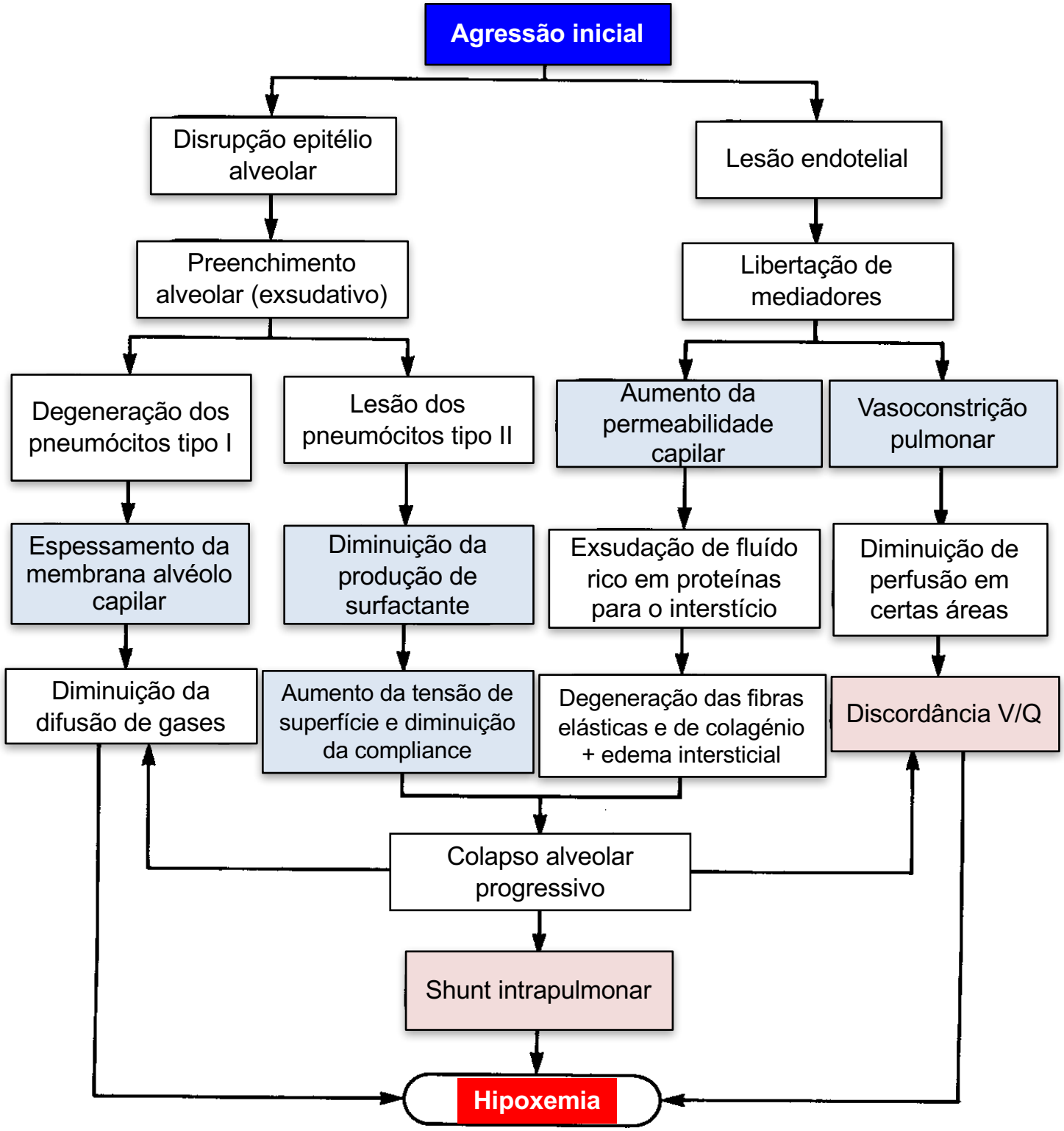
TABLE 2. CLINICAL DISORDERS ASSOCIATED WITH THE DEVELOPMENT OF THE ACUTE RESPIRATORY DISTRESS SYNDROME.

DIRECT LUNG INJURY	INDIRECT LUNG INJURY
Common causes	**Common causes**
Pneumonia	Sepsis
Aspiration of gastric contents	Severe trauma with shock and multiple transfusions
Less common causes	**Less common causes**
Pulmonary contusion	Cardiopulmonary bypass
Fat emboli	Drug overdose
Near-drowning	Acute pancreatitis
Inhalational injury	Transfusions of blood products
Reperfusion pulmonary edema after lung transplantation or pulmonary embolectomy	

N Eng J Med 2000;342(18):1334-1349


Normal Alveolus
Injured Alveolus during the Acute Phase
Alveolar air space
Protein-rich edema fluid
A
B
Interstitial space
Alveolus
Capillary
Increased alveolar-capillary permeability
Fluid "leak"
Alveolar edema
Type II epithelial cell
Type I epithelial cell
Fluid "leak"
Endothelial cell
Neutrophil
Platelet
rbc
Disrupted VE-cadherin bonds
Red cell
Fibroblast
Fibroblast
Neutrophil
Swollen, injured endothelial cells


Protein-rich edema fluid
Repopulation of bronchial epithelium
Proliferation and differentiation of type II cells
Gradual resolution of fibrosis
Type I cell
Alveolar macrophage
Neutrophil
Phagocytosis of protein
Endocytosis of protein
Apoptosis of neutrophils
Alveolar macrophage
Diffusion of protein
Phagocytosis of apoptotic neutrophils
Fibronectin
Myofibroblast
Type II cells
Na+
ENaC
Na+/K+–ATPase
K+
Cl−
Na+
Type I and III collagen
Fibroblast
Water
Aquaporins
Resorption of alveolar edema fluid and protein


Agressão inicial
Disrupção epitélio alveolar
Lesão endotelial
Preenchimento alveolar (exsudativo)
Libertação de mediadores
Degeneração dos pneumócitos tipo I
Lesão dos pneumócitos tipo II
Aumento da permeabilidade capilar
Vasoconstrição pulmonar
Espessamento da membrana alvéolo capilar
Diminuição da produção de surfactante
Exsudação de fluído rico em proteínas para o interstício
Diminuição de perfusão em certas áreas
Diminuição da difusão de gases
Aumento da tensão de superfície e diminuição da compliance
Degeneração das fibras elásticas e de colagénio + edema intersticial
Discordância V/Q
Colapso alveolar progressivo
Shunt intrapulmonar
Hipoxemia

Consequências

Perturbação das trocas gasosas

•Hipoxemia

– Discordância V/Q

– Shunt

• Aumento de CO2

– Hipoventilação

Diminuição da distensibilidade (*compliance*)

– Pulmões pequenos e rígidos – pressões elevadas

Hipertensão pulmonar

– Multifactorial (vasoconstrição hipóxica, compressão vascular pelo aumento da pressão nas VA, acidose, colapso das VA)

V. Apresentação clínica aguda ou crónica

TABLE 54-1 Time Course of Disease Onset

Acute
Cryptogenic organizing pneumonia
Acute eosinophilic pneumonia
Acute hypersensitivity pneumonitis
Diffuse alveolar hemorrhage
Acute interstitial pneumonia
Acute exacerbation of idiopathic pulmonary fibrosis or other ILDs
Subacute to Chronic
Connective tissue disease–associated ILD
Idiopathic pulmonary fibrosis
Sarcoidosis
Chronic hypersensitivity pneumonitis
Occupational lung disease
Nonspecific interstitial pneumonia
Desquamative interstitial pneumonitis
Respiratory bronchiolitis interstitial lung disease
Lymphocytic interstitial pneumonia
Chronic eosinophilic pneumonia

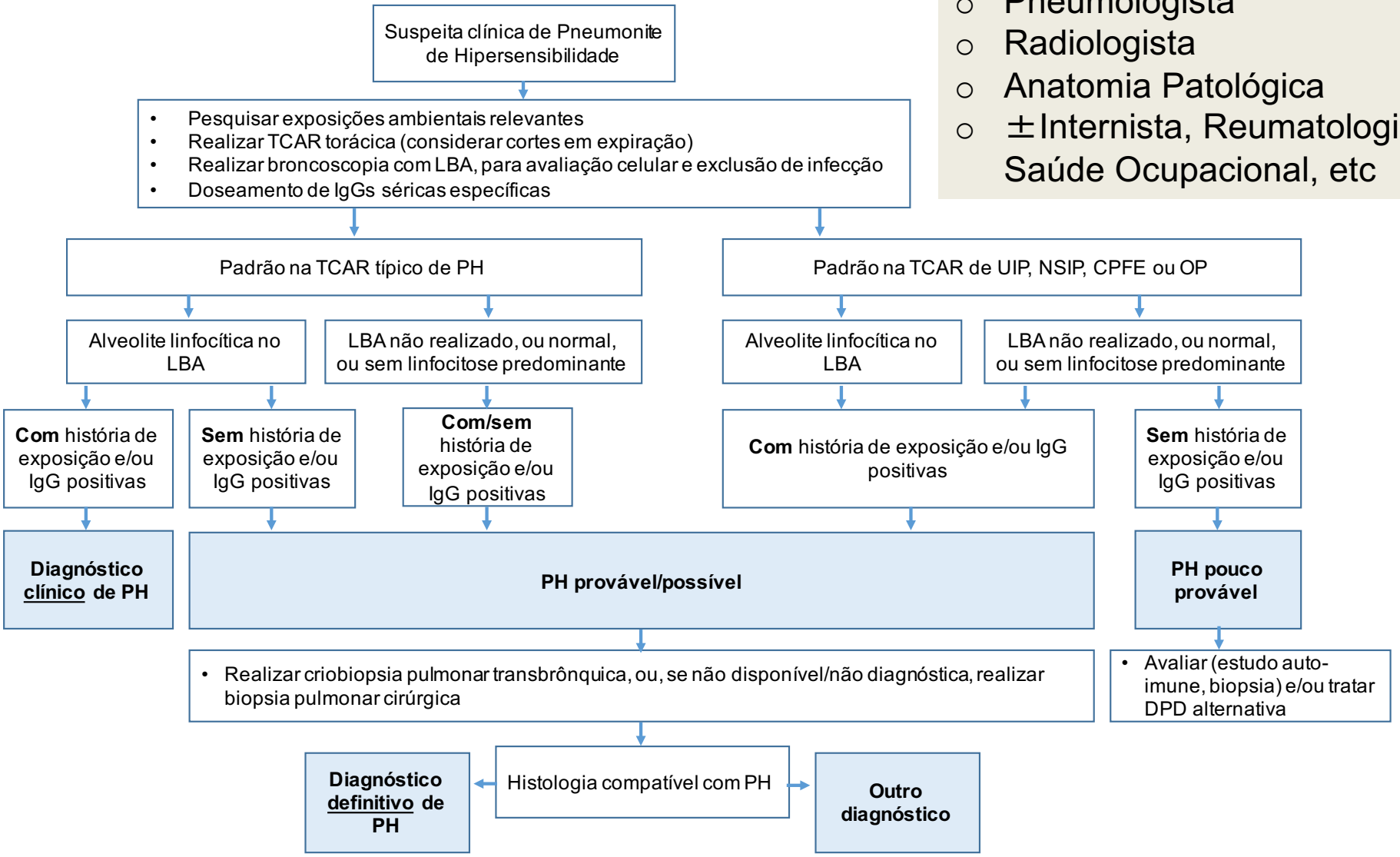
Fishman's Pulmonary Diseases and Disorders

VI. Avaliação multidisciplinar

O exemplo da Pneumonite de Hipersensibilidade

In Cap. "Pneumonite de Hipersensibilidade" (Mota PC, Bastos HN, Guimarães S, Cunha R)

- Pneumologista
- Radiologista
- Anatomia Patológica
- ±Internista, Reumatologista, Saúde Ocupacional, etc



Doenças Pulmonares Difusas

Causa conhecida
- Conectivites
- Toxicidade farmacológica
- Ocupacional (pneumoconioses)
- Induzida por radiação
- ...

Pneumonias intersticiais idiopáticas

Fibrosante
- Fibrose Pulmonar Idiopática (FPI)
- Pneumonia Intersticial Não Específica (NSIP)

Relacionada com o tabaco
- Bronquiolite respiratória (RB-ILD)
- Pneumonia Intersticial Descamativa (DIP)

Aguda/subaguda
- Pneumonia Intersticial Aguda (AIP)
- Pneumonia Organizativa Criptogénica (COP)

Raras
- Pneumonia Intersticial Linfocítica (LIP)
- Fibroelastose pleuro-parenquimatosa (PPFE)

Inclassificável

Granulomatosas
- Sarcoidose
- Pneumonite de hipersensibilidade
- Beriliose
- Vasculites (Wegener, Churg-Strauss)

Outras
- Proteinose alveolar pulmonar
- Pneumonia eosinofílica
- LAM
- Histiocitose pulmonar de células de Langerhans
- ...

ERS/ATS, Am J Respir Crit Care Med Vol 188, Iss. 6, pp 733–748, Sep 15, 2013; King et al. *Am J Respir Crit Care Med.* 2000;161:646; 2. Travis et al. *Am J Respir Crit Care Med.* 2002;165:277. 3. ATS/ERS Guideline. IPF: Diagnosis and Treatment. 2000; 4. ATS/ERS Guideline. Classification of the Idiopathic Interstitial Pneumonias. 2002; 5. Harrison's Principles of Internal Medicine 17th ed.