Poumon auto-immun

Jacques Cadranel

Service de Pneumologie - Centre de Compétences

Maladies rares pulmonaires

Principales maladies auto-immunes

- Non spécifiques d'organe
  - Polyarthrite rhumatoïde (PR)
  - Maladie de Gougerot-Sjögren (GS)
  - Lupus érythémateux disséminé (LED)
    - Syndrome des anti-phospholipides (SAPL)
  - Sclérodermie systémique (SS)
    - Connectivite mixte (CM)
  - Poly- (PM), dermato-myosites (DPM)
  - Polychondrite atrophiante (PC)
  - Spondylarthrite ankylosante (SPA)
  - **Vascularites**

Goldblatt F, Lancet 2013, 382:797

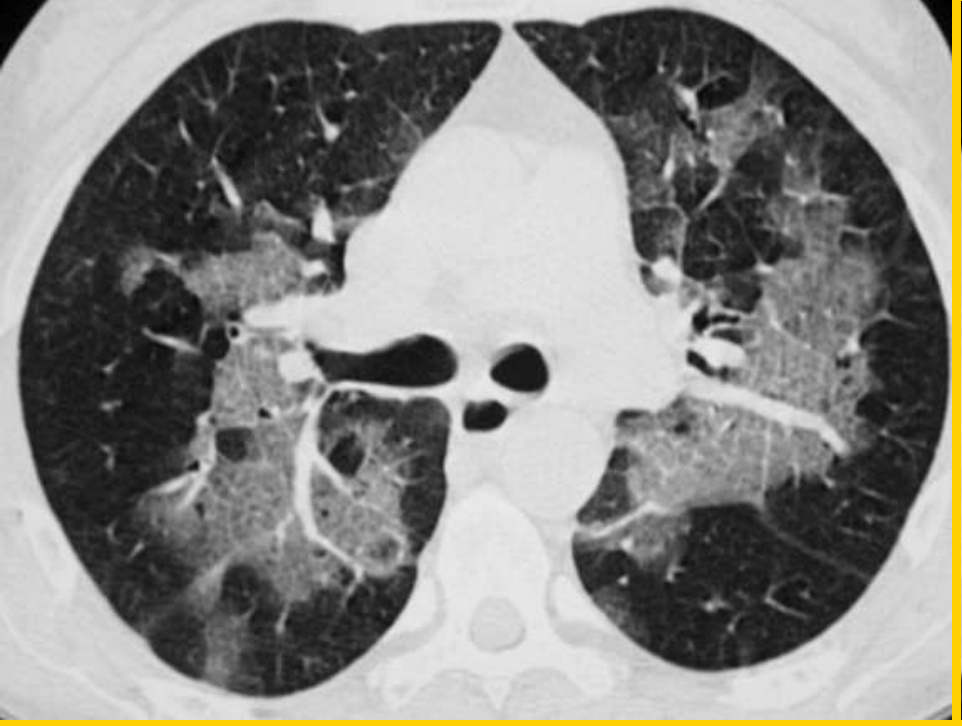
Principales maladies auto-immunes

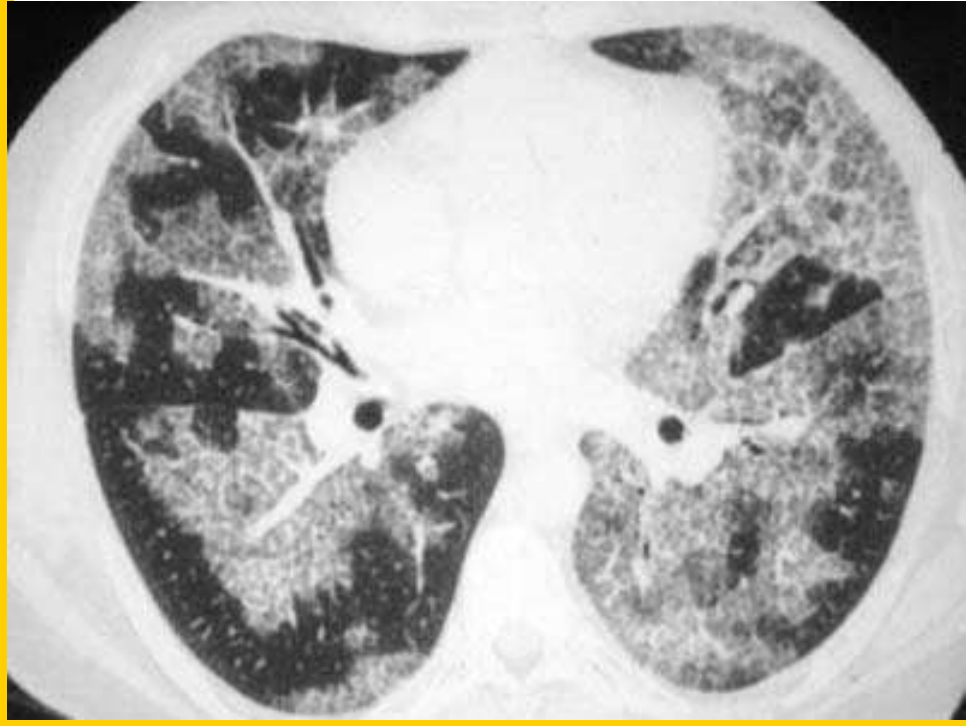
- Connectivites spécifiques d'organe
  - Glandes endocrines
    - Thyroïdite, maladie d'Addison, diabète ID, polyendocrinopathies
  - Tube digestif
    - Maladie de Biermer, maladie coeliaque

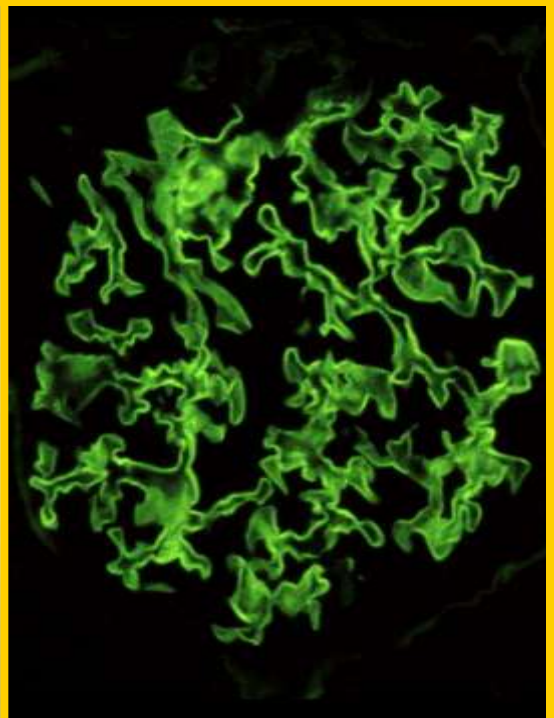
Poumon ?

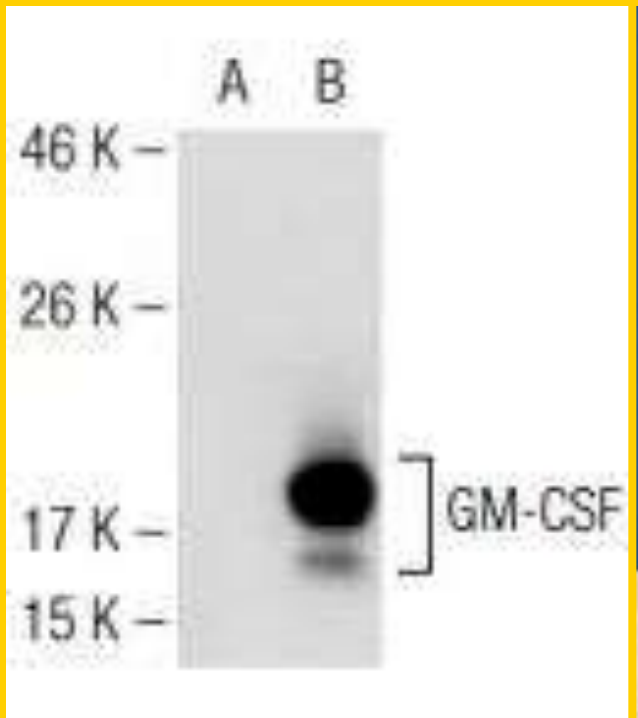
  - Peau
    - Pemphigus, pemphigoïde bulleuse, vitiligo
  - Foie
    - Hépatites auto-immunes, cirrhose biliaire primitive

Goldblatt F, Lancet 2013, 382:797








A
B
46 K –
26 K –
17 K –
15 K –
GM-CSF

Pneumopathies auto-immunes

- *"Interstitial Pneumonia with Auto-immune Feature" ERS Task-Force*

PID +

Symptom/Sign	Serologic Test
Weight loss	Antinuclear antibody titer ≥ 1:160
Dry eyes/dry mouth	Antidouble-stranded DNA
Oral ulcers	Anti-ribonucleoprotein antibody
Dysphagia	Anti-Smith antibody
Gastroesophageal reflux	Anti-Scl-70
Hand ulcers	Anti-Ro antibody (anti-SSA)
Raynaud phenomenon	Anti-La antibody (anti-SSB)
Leg/foot swelling	Rheumatoid factor
Joint pain/swelling	Anticyclic citrullinated peptide antibody (aCCP)
Morning stiffness	Anti-Jo-1 antibody
Rash	Antineutrophil cytoplasmic antibody
Proximal muscle weakness	CK
Photosensitivity	Aldolase

Fischer A, Chest 2010, 138:251

Diagnostic des connectivites

Polyarthrite rhumatoïde (6/10pts)

A. Atteinte articulaire (0 à 5)
B. Sérologie, FR ou anti-CCP (0 à 3)
C. Synd. inflammatoire, CRP ou VS (0 à 1)
D. Durée des symptômes, ≥ 6 sem. (0 à 1)

Sclérodermie systémique

1. Acrosclérose/sclérose diffuse (1)
2. Ulcération digitale ou sclérodactylie ou **fibrose pulmonaire** (2/3)

Gougerot Sjögren

1. Syndrome sec buccal
2. Syndrome sec occulaire
3. Biopsie des glandes salivaires (score de Chilsom ≥ 3)
4. Atteinte objective des glandes salivaires (flux salivaire, sialographie, scintigraphie)
5. Ac anti-SSA et/ou SSB

Défini = 4/5 dont BGSA ou Auto-AC; 3 des critères objectifs

Po

1.
2.
3.
4.

Déf

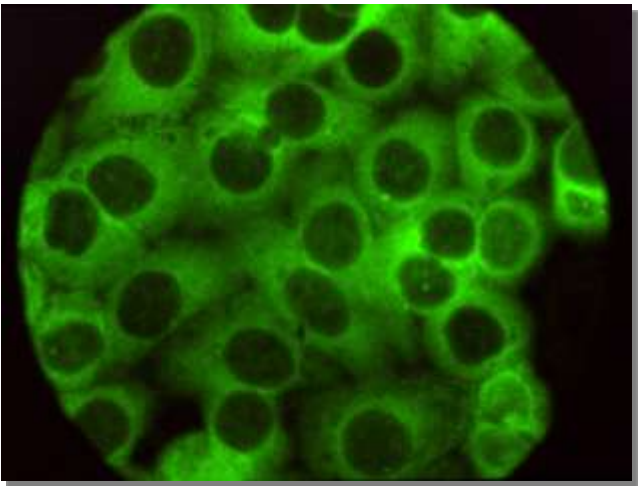
Lupus érythémateux disséminé (4/11)

1. Eruption malaire en “loup“
2. Lupus discoïde
3. Photosensibilité
4. Ulcération orale ou nasopharyngée
5. Polyarthrite non érosive
6. **Pleurésie ou péricardite**
7. Protéinurie ou hématurie
8. Convulsions ou psychose
9. Anémie hémolytique, leucopénie thrombopénie, lymphopénie
10. Anti-DNA natif, anti-SM, anti-phospholipide
11. FAN > 1/320

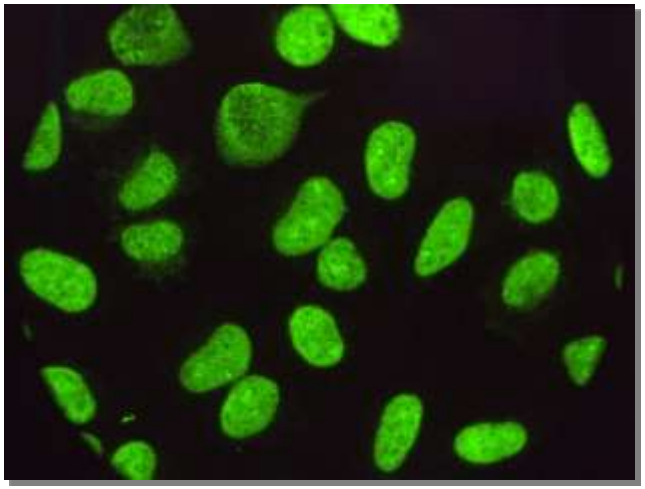
Kristin B, Clin Chest Medidine 2010, 31; Vij R, Chest 2013, 14

Diagnostic des connectivites

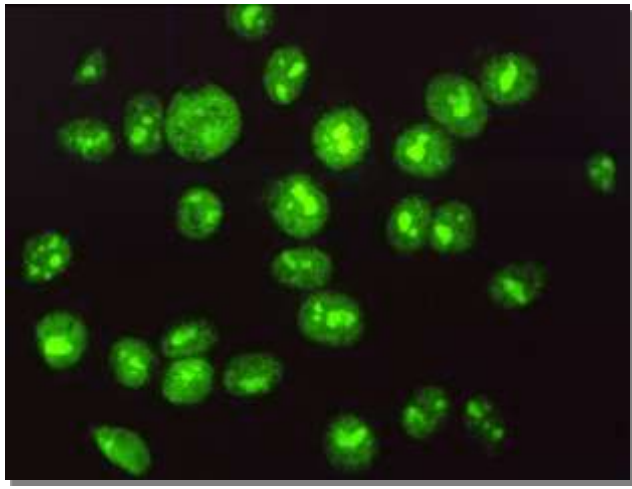
- Intérêt des anticorps anti-nucléaires sériques



“cytoplasmique“



“nucléaire“
homogène/moucheté



“nucléolaire“

Recherche d’une spécificité : immunodiffusion, ELISA, Dot-Blot

Sally E, Clin Chest Medicine 2010, 31:416; Goldblatt F, Lancet 2013, 382:797

Diagnostic des connectivites

- Intérêt des anticorps anti-nucléaires sériques

Auto-Ac	PR	GS	LED	SS	PM/DPM
AAN	40%*	70-95%	90-98%	70-90%	40-50%
FR	66-85%	30-70%*	15-25%*	10-50%*	10-40%*
Anti-CCP	56-74%				
Anti-SSA/SSB		60-80%/50%	30-50%/10-15%		
Anti-DNA			40-60%		
Anti-Sm			20-30%		
Anti-Scl70				30-35%/70% PID*	
Anti-PM-Scl				25%	8%
Anti-centromère				8%/40-80% CREST*	
Anti-t-RNA synth.					25%/50 PID*

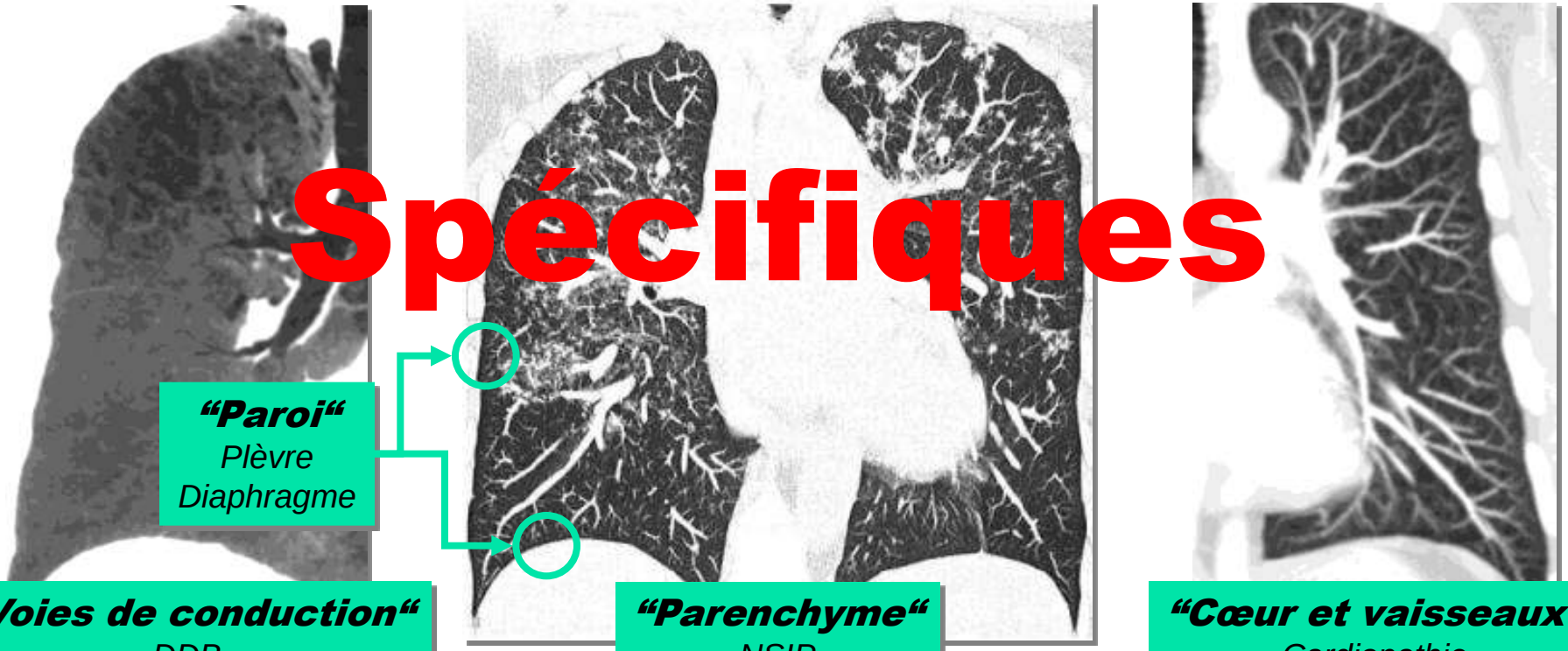
*Tzelepis GE, Eur Respir J 2008, 31:11; Goldblatt F, Lancet 2013, 382:797

Epidémiologie des connectivites

Connectivite	Age	F:M ratio	Incidence	Commentaires
PR	40-60	7,5-9	20-30/10^5	Rôle du tabac
GS	40-50	9	10-50/10^5	
LED	15-40	6-10	1-10/10^5	Risque familial, > afro-américains
SS	30-50	5-14	0,6-19/10^5	Risque familial, facteur environnemental, PID chez caucasiens
PM-DPM	10-15/ 45-60	2,5	0,2-1/10^5	Risque de cancer associé

Goldblatt F, Lancet 2013, 382:797

Connectivites et atteintes respiratoires



Spécifiques

"Paroi"
Plèvre
Diaphragme

"Voies de conduction"
DDB
Bronchiolite/BF
Emphysème
Kystes

"Parenchyme"
NSIP
UIP
LIP/MALT
DAD
DIP

"Cœur et vaisseaux"
Cardiopathie
Péricardite
HTAP/HTP
HIA

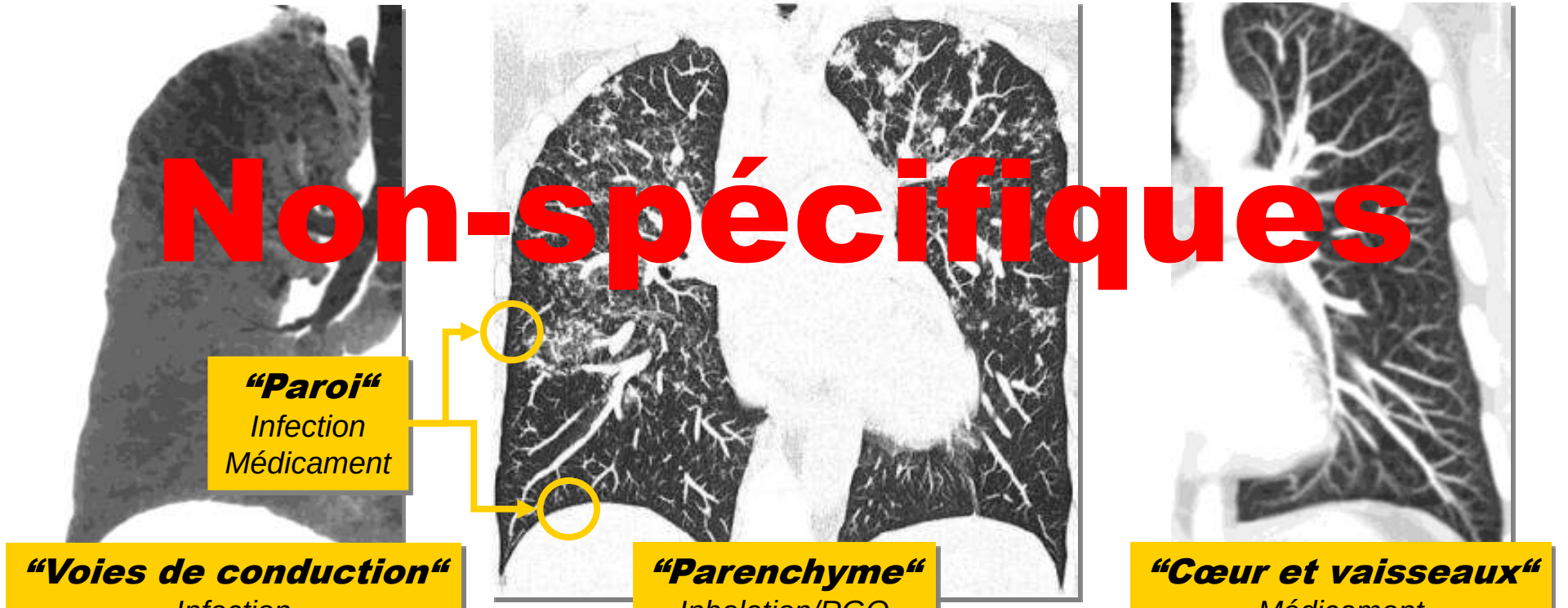
Raghu G, Clin Chest Med 2004, 25:409

Connectivites et atteintes respiratoires

- Maladies cardio-vasculaires
  - Maladies auto-immunes
    - Risque augmenté de maladie cardio-vasculaire au cours des maladies auto-immunes, RR=2,9 à 1 an (LEAD, PM/DPM, PAN)
  - LEAD
    - Risque augmenté d'IDM chez femmes (35-45 ans), RR=52
    - Péricardites et valvulopathies
    - Insuffisance cardiaque droite diastolique
  - SS
    - Athérosclérose accélérée
    - Insuffisance cardiaque droite diastolique, HTAP, (HTP)
  - PM/DPM
    - Péricardites et valvulopathies
    - Insuffisance cardiaque droite diastolique

Goldblatt F, Lancet 2013, 382:797

Connectivites et atteintes respiratoires



Non-spécifiques

"Paroi"
Infection
Médicament

"Voies de conduction"
Infection
Médicament

"Parenchyme"
Inhalation/RGO
Infection
Tumeur
Médicament

"Cœur et vaisseaux"
Médicament

Raghu G, Clin Chest Med 2004, 25:409

Atteintes multi-compartiments

	ILD	Airways	Pleural	Vascular	DAH
Systemic sclerosis	+++	–	–	+++	–
Rheumatoid arthritis	++	++	++	+	–
Primary Sjögren's syndrome	++	++	+	+	–
Mixed CTD	++	+	+	++	–
Polymyositis/ dermatomyositis	+++	–	–	+	–
Systemic lupus erythematosus	+	+	+++	+	++

Table 1: **CTDs and common pulmonary manifestations**

Fischer A, Lancet 2012, 380:689

Atteintes multi-compartiments

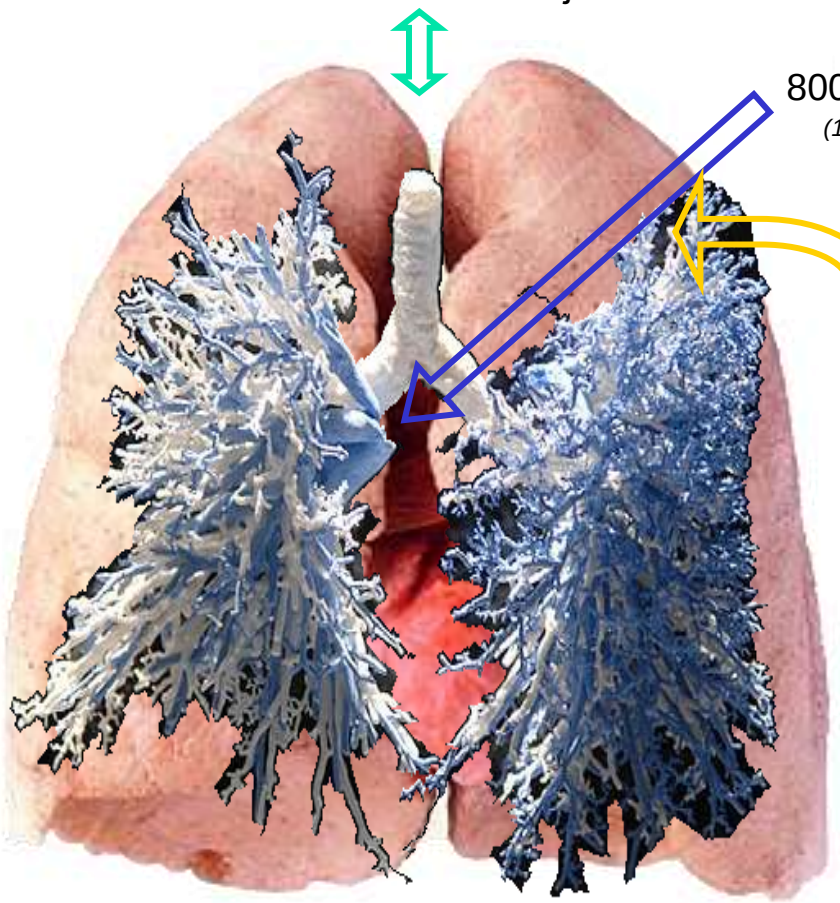
Lung Manifestations of the Rheumatic Diseases[a]

	RA	SLE	PSS	DM/PM	MCTD	Sjögren Syndrome
Pleural inflammation, fibrosis, effusions	X	X	X	X	X	X
Airway disease						
Inflammation (bronchiolitis)	X	X		X	X	X
Constrictive bronchiolitis	X				X	
Bronchiectasis	X				X	
Follicular bronchiolitis	X	X			X	X
Interstitial disease	X	X	X	X	X	X
Acute (DAD), with or without hemorrhage	X	X	X	X	X	
Subacute/organizing (OP pattern)	X	X	X	X	X	X
Subacute cellular	X	X	X	X	X	X
Chronic cellular and fibrotic	X	X	X	X	X	X
Eosinophilic infiltrates	X				X	
Granulomatous interstitial pneumonia	X	X			X	
Vascular diseases; hypertension/vasculitis	X	X	X	X	X	X
Parenchymal nodules	X					
Apical fibrobullous disease	X		X		X	
Lymphoid proliferation (reactive, neoplastic)	X		X		X	

Schneider F, Arch Path Lab Med 2012, 136:1242

Physiopathologie ?

12 000 litres d'air/j



8000 litres de sang/j

(100% du Q cardiaque,

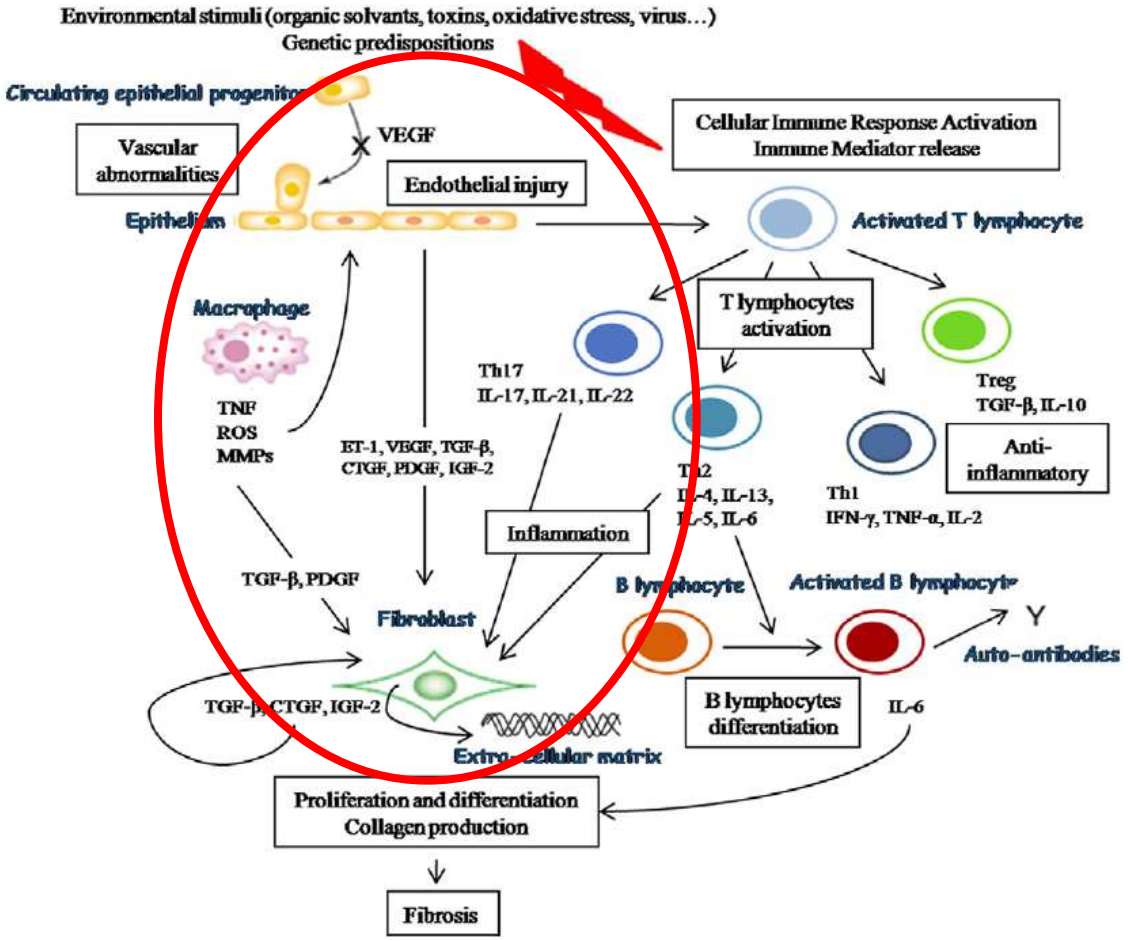
¢ du sang, auto-ac)

Canal thoracique

(100% des Ly et DC efférents)

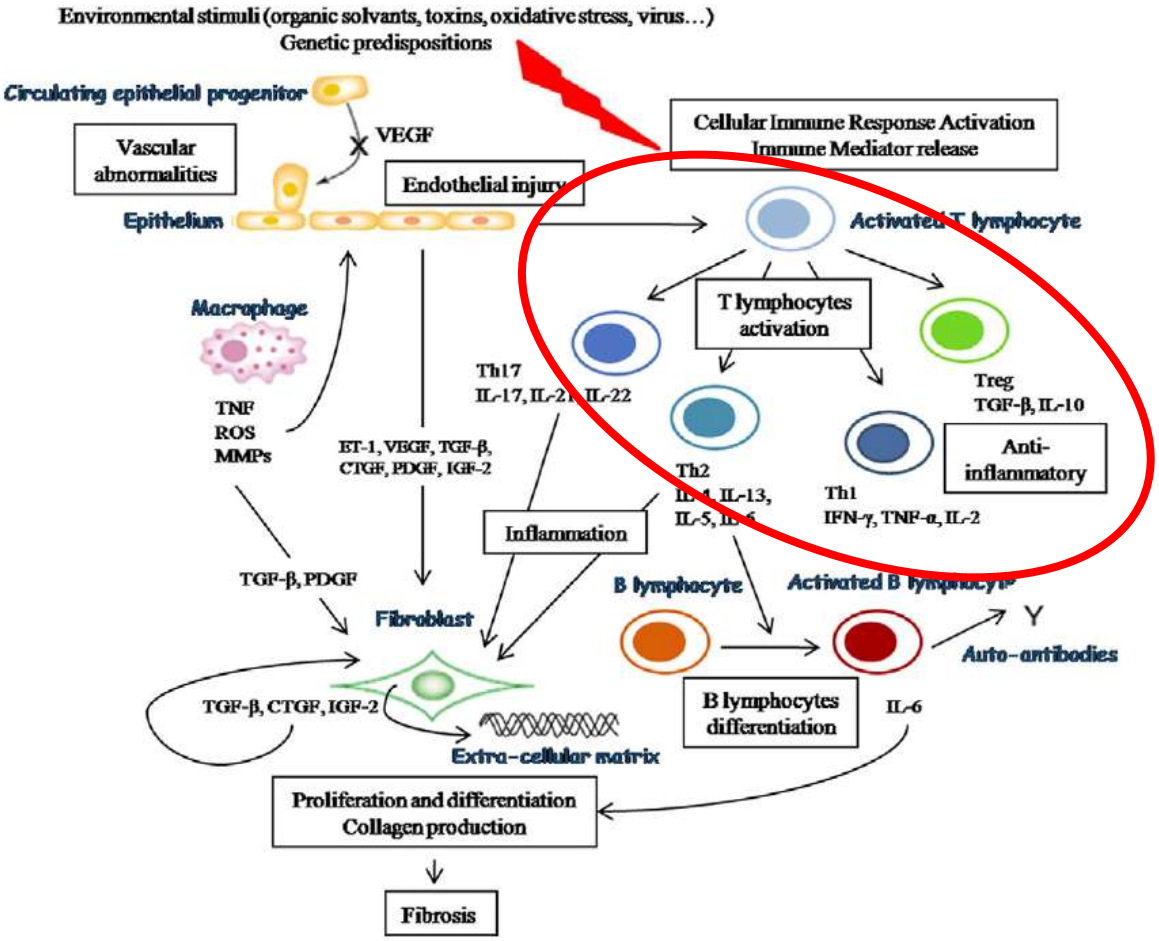
≈ 210 m^2 de surface d'échange

Physiopathologie ?



Baraut J, Autoimmunity Reviews 2010, 10:65

Physiopathologie ?



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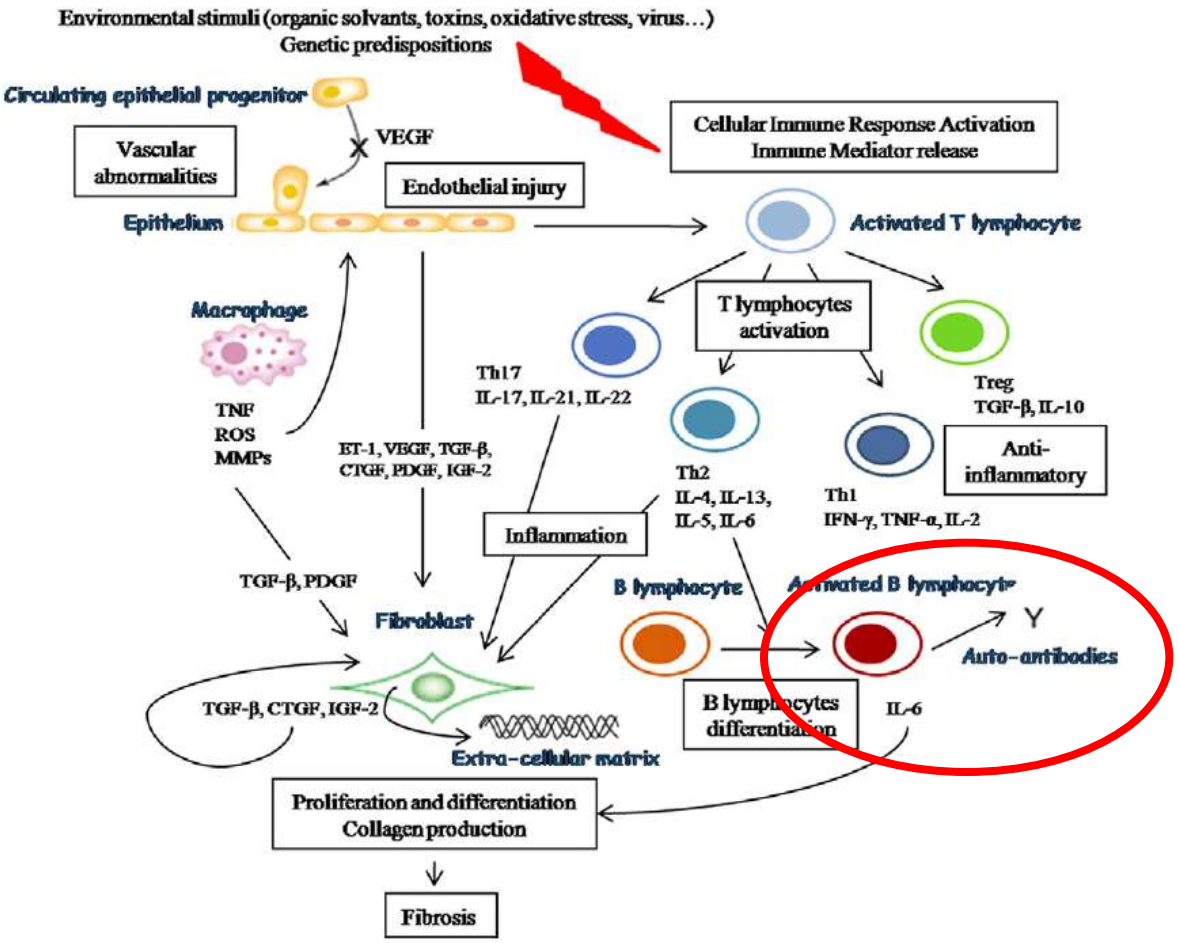
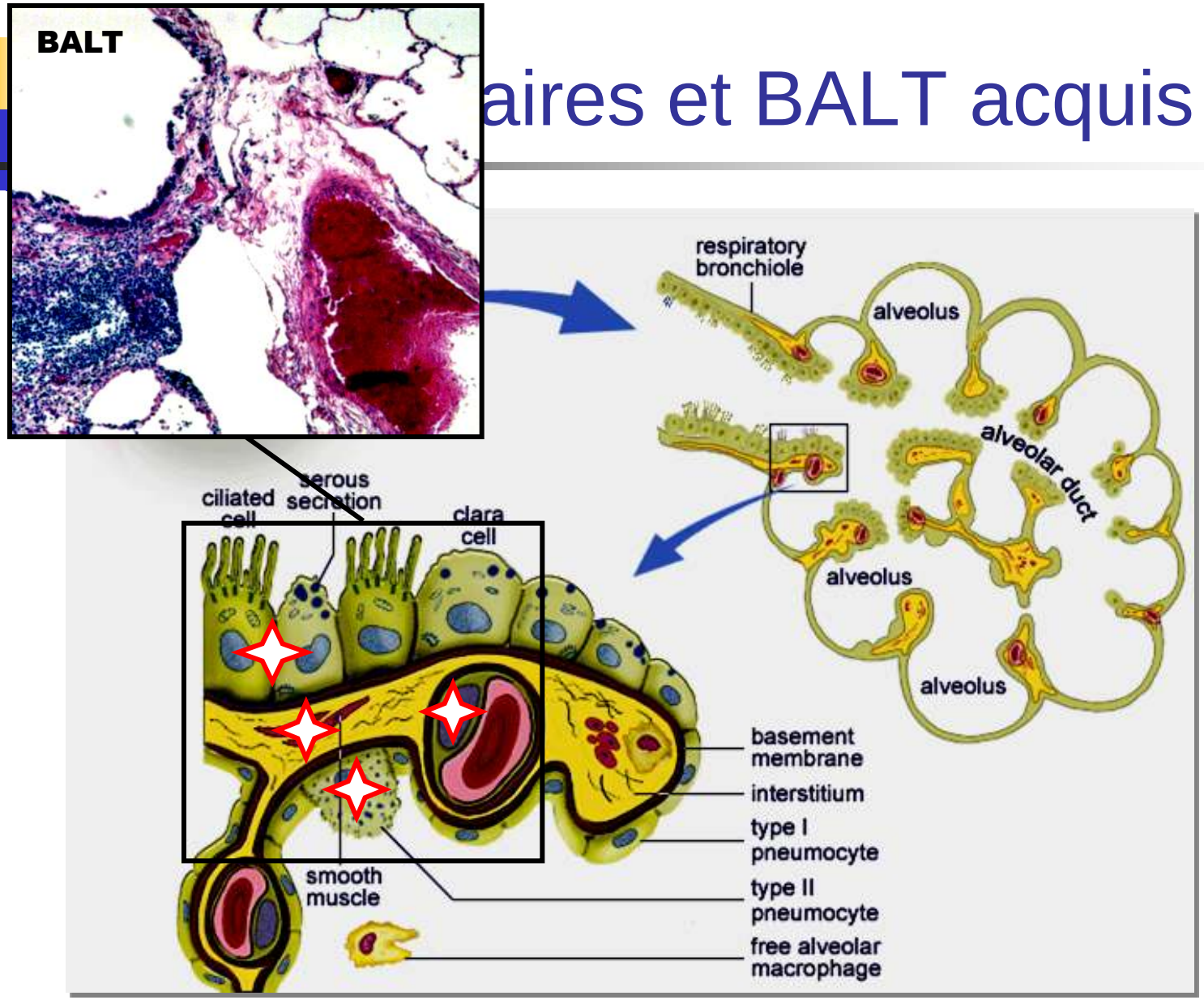
Physiopathologie ?

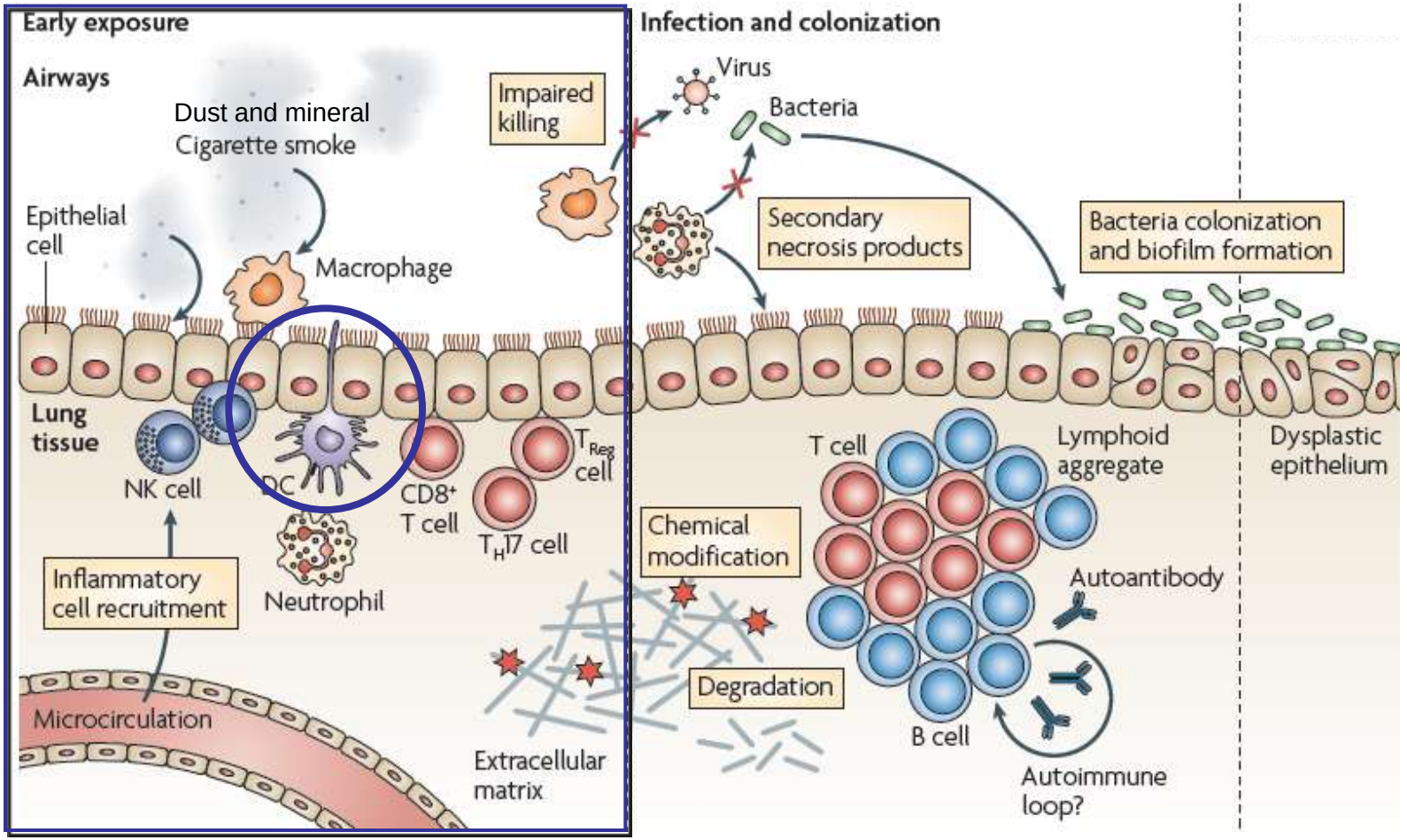


Baraut J, Autoimmunity Reviews 2010, 10:65

aires et BALT acquis



Rôle de l'environnement ?



Stämpfli MR, Nature Rev Immuno 2009, 9:377

Rôle du tabac ?

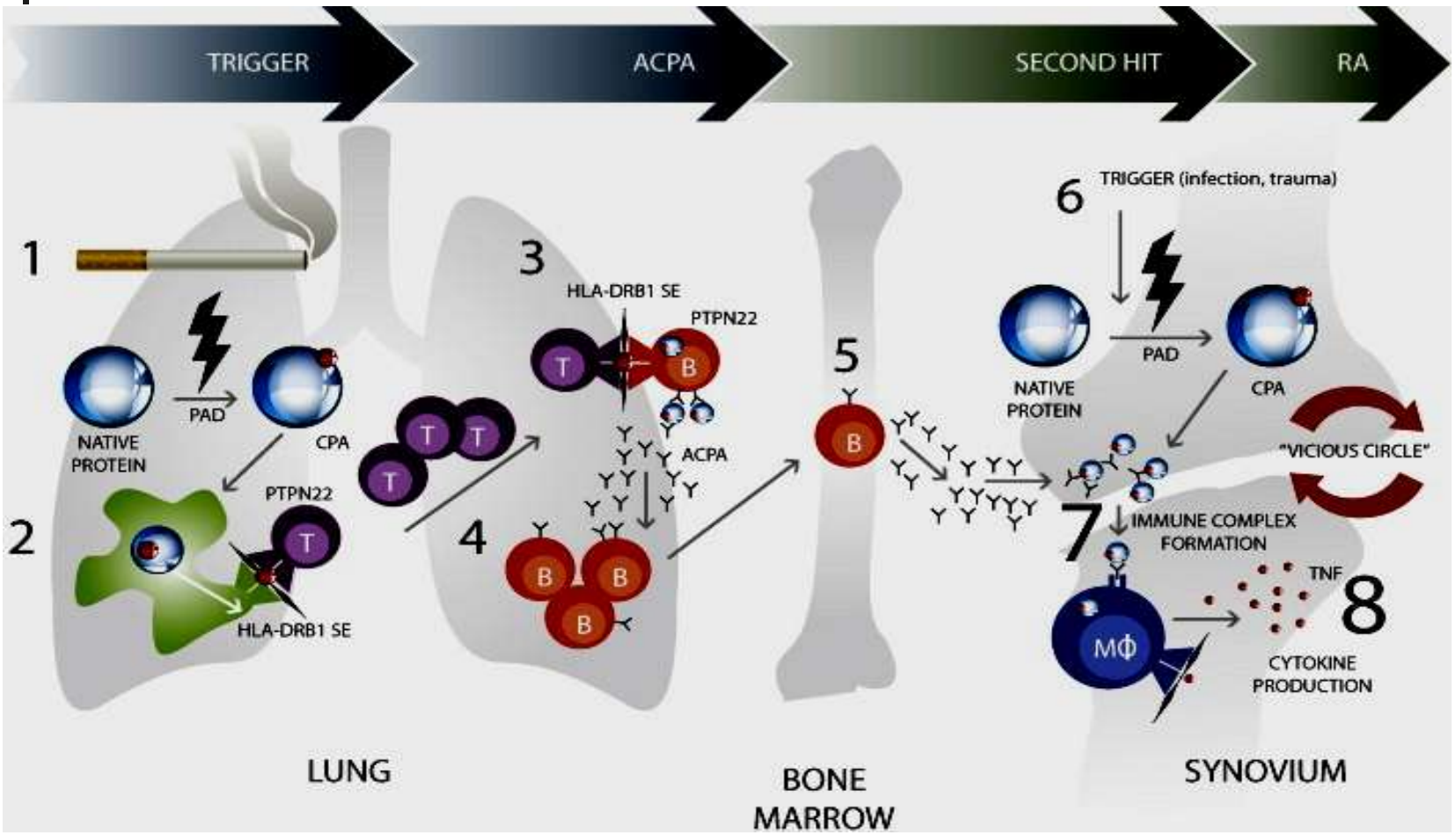
Table 1. Clinical features of smoking-related interstitial lung diseases (ILDs)

	HX	RBILD	AcuteEP	DIP	FibroEmph	IPF	RA-ILD
Smoking %	>90	100		90	100	41–83	
Age	3rd and 4th decades	3rd–5th decades	2nd and 4th decades	3rd–5th decades	Middle aged and older	Middle aged and older	5th-6th decades
Male:female ratio	1:1	Slight male dominance	2:1	Nearly 2:1		1:1 to 1:2	
Occurrence in children	Rare	No	Yes	Rare	No	Rare	No
Onset	Insidious	Insidious	Acute	Insidious	Insidious	Insidious	Insidious
Presenting symptoms	Dyspnoea and cough	Dyspnoea and cough	Dyspnoea and cough	Dyspnoea and cough	Dyspnoea and cough	Dyspnoea and cough	Dyspnoea and cough
Crackles	Usually absent	50%	?	60%	Nearly all	Nearly all	Great majority
Clubbing	Rare	Rare	Rare	Nearly 50%	50–70%	50–70%	
Chest radiograph	Interstitial/cystic nodular with basilar sparing	Interstitial or normal	Patchy opacities	Interstitial, patchy ground glass	Upper lobe emphysema associated with lower lobe fibrosis	Interstitial, honeycombing with basilar predominance	Lower lobe interstitial lung disease
HRCT	Nodules and cysts; basilar sparing	Patchy ground glass	Patchy opacities /ground glass	Ground glass with lower lung predominance	Upper lobe emphysema associated with interstitial, honeycombing	Subpleural honeycombing, basilar predominance	Lower lobe interstitial infiltrates or honeycombing
Pulmonary function	Obstructive or restrictive	Mixed defect or normal	Restrictive	Restrictive	Mixed defect or normal	Restrictive	Restrictive
Treatment	Smoking cessation, steroids?	Smoking cessation, steroids	Steroids	Smoking cessation, steroids	Bronchodilators and inhaled steroids	Pirfenidone?	Steroids and immunosuppressive treatment
Response to steroids	Fair	Good	Good	Good	Poor	Poor	Variable
Prognosis	Good	Good	Variable	Good	Poor	Poor	Variable
Complete recovery possible	Yes	Yes	Yes	Yes	No	No	No

PLCH: pulmonary Langerhans' cell histiocytosis; RB: respiratory bronchiolitis; AEP: acute eosinophilic pneumonia; DIP: desquamative interstitial pneumonia; CPFE: combined pulmonary fibrosis and emphysema; IPF: idiopathic pulmonary fibrosis; RA: rheumatoid arthritis; HRCT: high-resolution computed tomography. Modified from [26].

Cerri S, Eur Respir Mon 2011

Rôle du tabac dans la PR ?



Klaserskog, Seminars in Immunology 2011, 23:92

Poussières et minéraux ?

Table 3 Multivariate analysis of certain specified occupational exposures among men with adjustment for age and smoking; analysis of: 74 incident cases and 382 referents; and 176 cases and 630 referents in the pooled material

	Incident cases			Pooled material		
Exposure	No. of exposed (cases/referents)	LOR	95% CI	No. of exposed (cases/referents)	LOR	95% CI
Asphalt	2/3	6.4	0.4 to 109.2	9/4	4.0	0.5 to 31.2
Asbestos	12/19	2.5	1.0 to 6.8	24/33	1.6	0.8 to 3.3
Organic dust	31/80	2.1	0.9 to 4.9	63/140	1.4	0.8 to 2.5
Vibrations	27/47	2.0	0.9 to 4.4	59/98	2.2	1.3 to 3.8
Mineral dust*	11/20	1.8	0.6 to 5.5	25/41	1.9	0.8 to 4.2
Crops and/or forage	22/60	1.6	0.2 to 10.7	65/122	3.2	0.9 to 11.8
Mineral oils	26/52	1.6	0.7 to 3.4	44/87	1.2	0.7 to 2.1
MMMF	9/20	1.5	0.4 to 4.9	13/37	0.7	0.3 to 1.9
Fertilisers	17/40	1.4	0.3 to 7.4	47/79	1.7	0.6 to 4.8

Table 4 Multivariate analysis of occupational categories among women with adjustment for age and smoking; analysis of: 160 incident cases and 368 referents; and 339 cases and 627 referents in the pooled material

	Incident cases			Pooled material		
Occupation (NYK codes)	No. of exposed (cases/referents)	LOR	95% CI	No. of exposed (cases/referents)	LOR	95% CI
Printmakers, process engravers, etc (801–809)	4/2	5.5	0.9 to 32.6	8/4	3.0	0.9 to 10.3
ADP workers (251–259)	4/4	3.0	0.7 to 12.5	5/5	2.1	0.6 to 7.3
Post and telegraph personnel (671–689)	11/11	2.0	0.8 to 4.9	23/21	1.7	0.9 to 3.3
Millers and bakers (821–822)	3/3	1.5	0.3 to 7.9	6/6	1.5	0.5 to 4.8
Packers and warehouse workers (881–889)	4/4	1.5	0.3 to 6.1	9/10	1.2	0.5 to 3.1
Hairdressers and beauticians (941–949)	4/5	1.4	0.4 to 5.6	11/10	1.8	0.7 to 4.3
Engineers and technicians (001–009)	2/4	1.2	0.2 to 6.7	2/8	0.4	0.1 to 2.1

Klaserskog, Seminars in Immunology 2011, 23:92

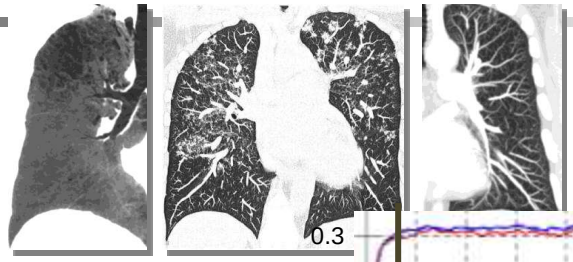
Connectivites et atteintes respiratoires

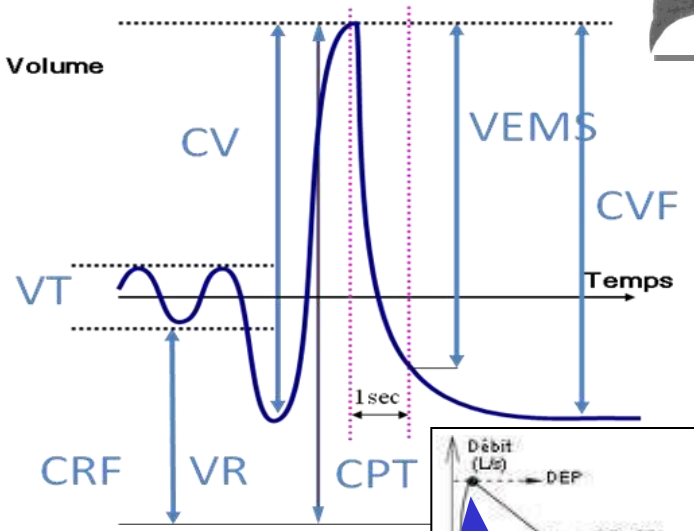
	ILD	Airways	Pleural	Vascular	DAH
Systemic sclerosis	+++	–	–	+++	–
Rheumatoid arthritis	++	++	++	+	–
Primary Sjögren's syndrome	++	++	+	+	–
Mixed CTD	++	+	+	++	–
Polymyositis/ dermatomyositis	+++	–	–	+	–
Systemic lupus erythematosus	+	+	+++	+	++

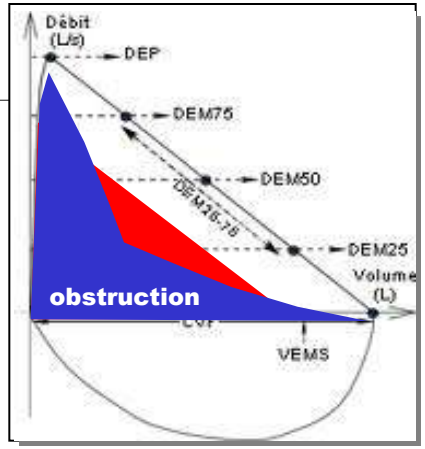
Table 1: **CTDs and common pulmonary manifestations**

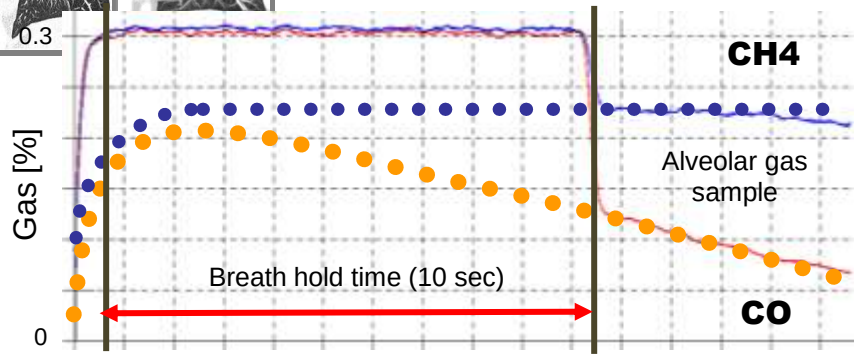
Fischer A, Lancet 2012, 380:689

Connectivites et atteintes respiratoires

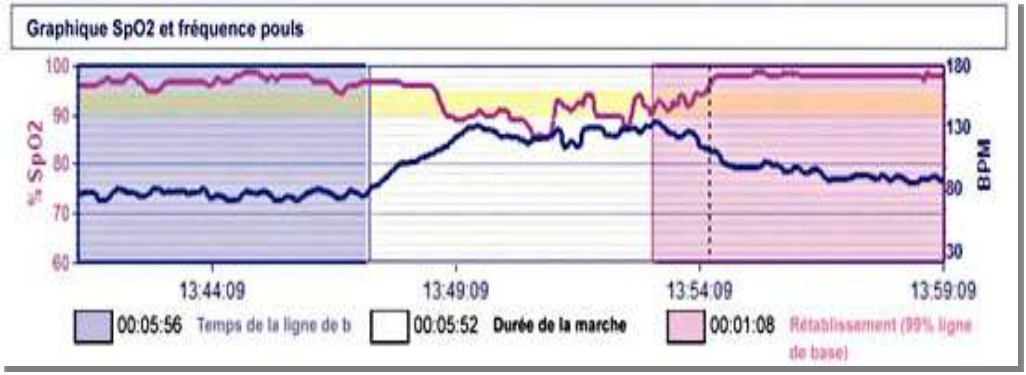






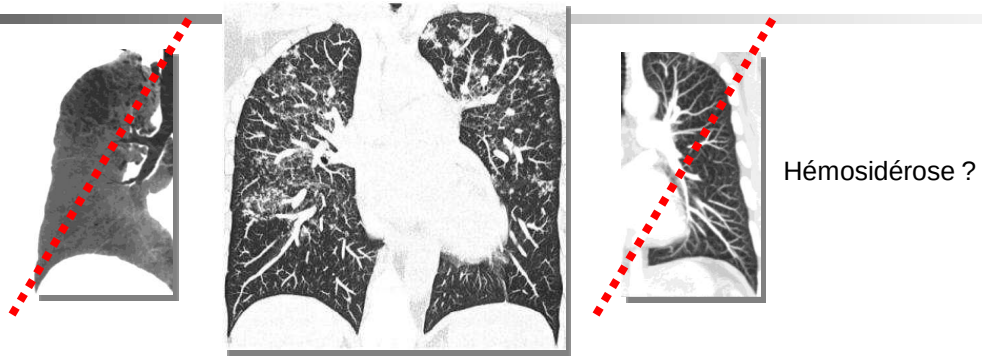


Mesure de la DLCO et DLCO/VA



Test de marche, distance, nadir SaO2

Connectivites et atteintes respiratoires

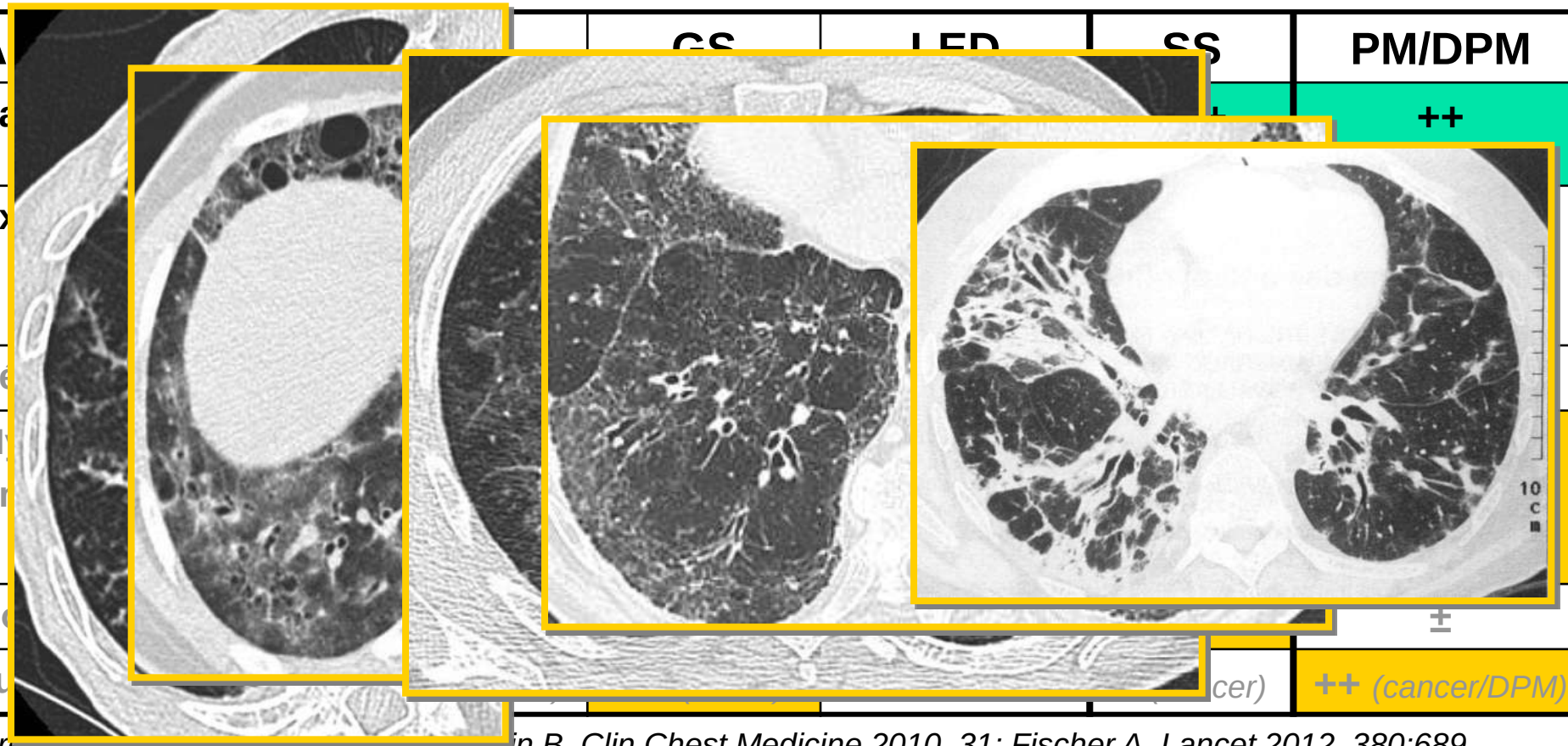


Hémosidérose ?

- Aspect macroscopique le plus souvent normal
- Biopsies bronchiques peu contributives
  - sauf si anomalies endobronchiques
  - systématiques en cas de distribution lymphatique
  - aspiration bronchique pour analyse bactériologique
- Lavage bronchoalvéolaire
  - ≈ 150 à 300 ml sérum; récupération ≥ 50%
  - numération formule + microbiologie
  - techniques complémentaires, fonction des hypothèses : phénotypage B et T, K/L, réarrangement des Ig, PAS, Perls
- Biopsies pulmonaires par voie endoscopique
  - opacités alvéolaires +++
  - OP, NSIP/OP, MALT, granulomatose…

Caractéristique	Normal	Fumeur
N cellules (ml)	100-200	400-800
% macrophages	>90%	>95%
% lymphocytes	<15%	<5%
% neutrophiles	≤3%	≤3%
% éosinophiles		
% mastocytes		
% Ly CD3	>90%	>90%
% Ly CD4	60%	40%
% Ly CD8	40%	60%
CD4:CD8	2-3	0,5-1,5
% Ly B	<3%	<3%

Connectivites et atteintes respiratoires



A	GS	LED	SS	PM/DPM
Pa				++
Vx				
Sé				
My Pr				
Ca				±
Tu			cer)	++ (cancer/DPM)

Crestani B, Allergy 2005; 60:713; Khalil N, Clin Chest Medicine 2010, 31; Fischer A, Lancet 2012, 380:689

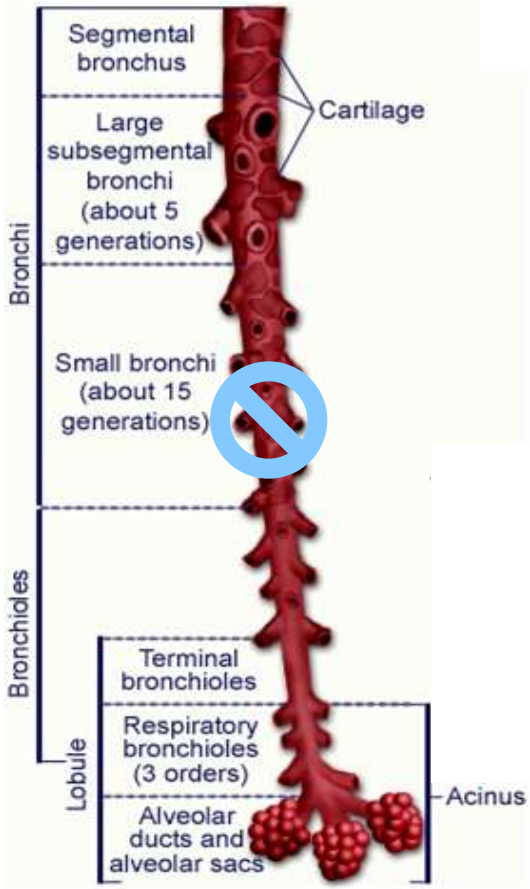
Connectivites et atteintes respiratoires

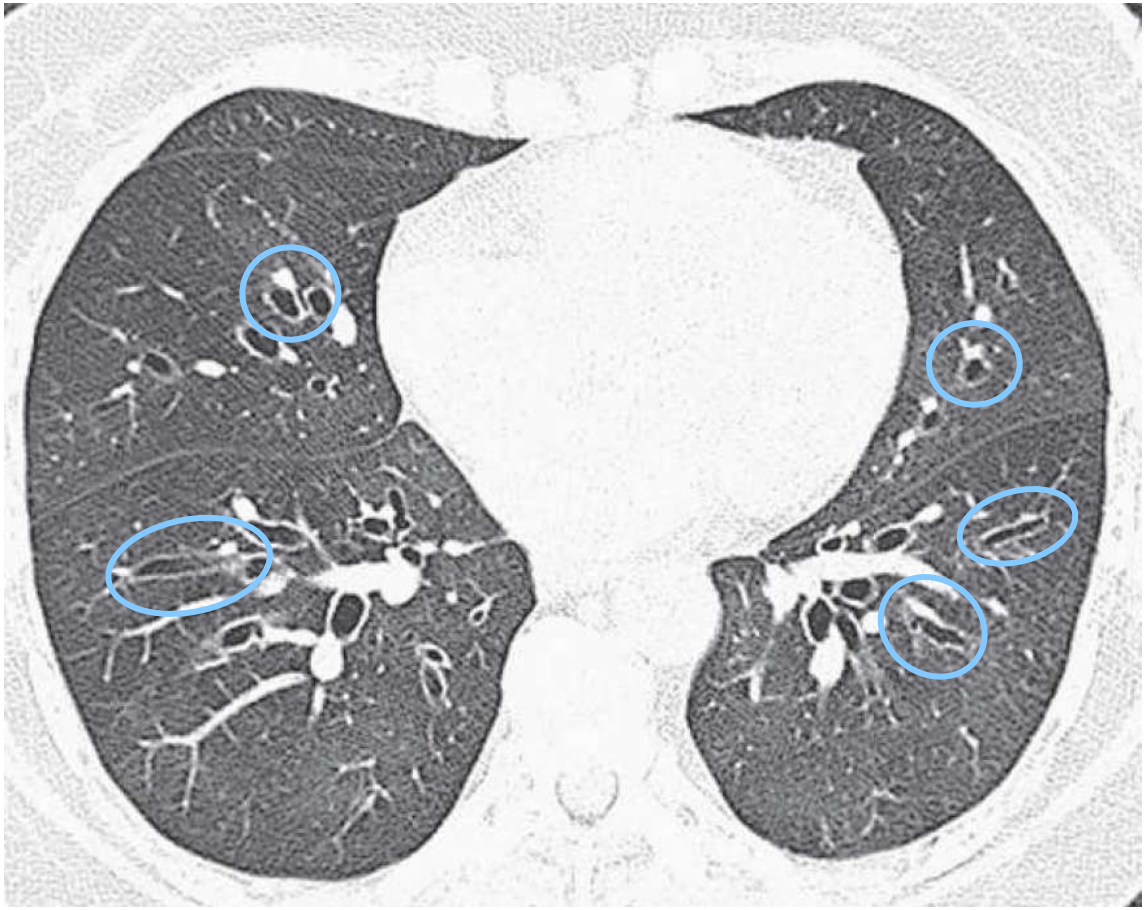
Table 3—*Clinical Pearls for CTD-ILD*

CTD	Diagnosis	Management
Systemic sclerosis	Esophageal dilation on HRCT scan increases clinical suspicion.	Esophageal dysfunction and gastroesophageal reflux are common. Annual screening for pulmonary hypertension is recommended by the WHO.
Rheumatoid arthritis	Consider drug-induced pneumonitis for new or worsening ILD.	Radiographic and histopathologic findings of UIP portend a worse prognosis. Tobacco cessation is strongly recommended.
Dermatomyositis and polymyositis	Myositis may be subtle and present after ILD. Myositis-associated and -specific antibodies aid in diagnosis.	Early treatment with prednisone and additional immunosuppressive agents may improve outcomes.
Sjögren syndrome	Cysts on HRCT scan increase clinical suspicion.	Severe ILD, with UIP on HRCT scan and pathology, has been reported. LIP may be less common than other histopathologic patterns.

Vij R, Chest 2012, 143:814

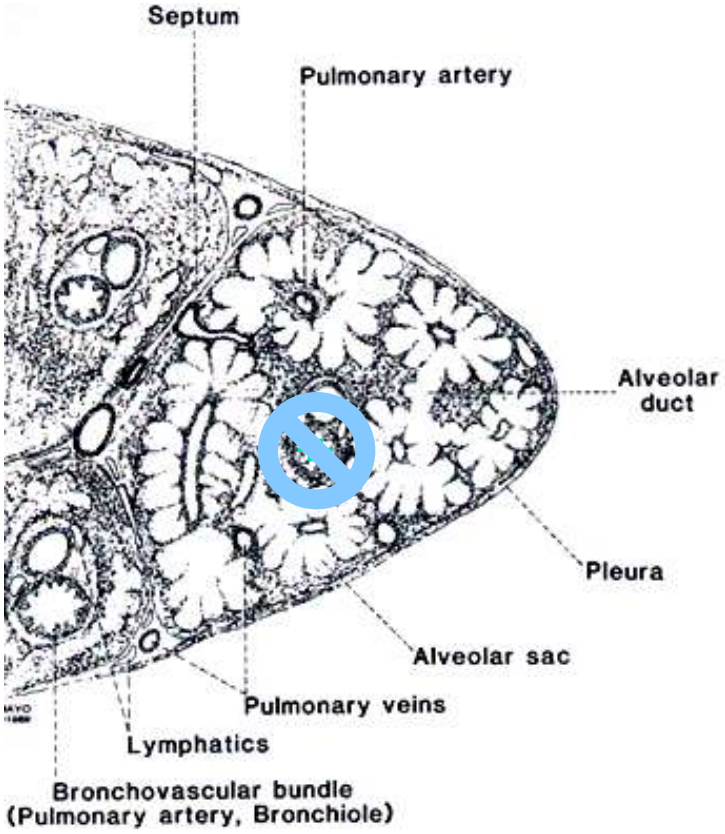
Atteinte des voies aériennes

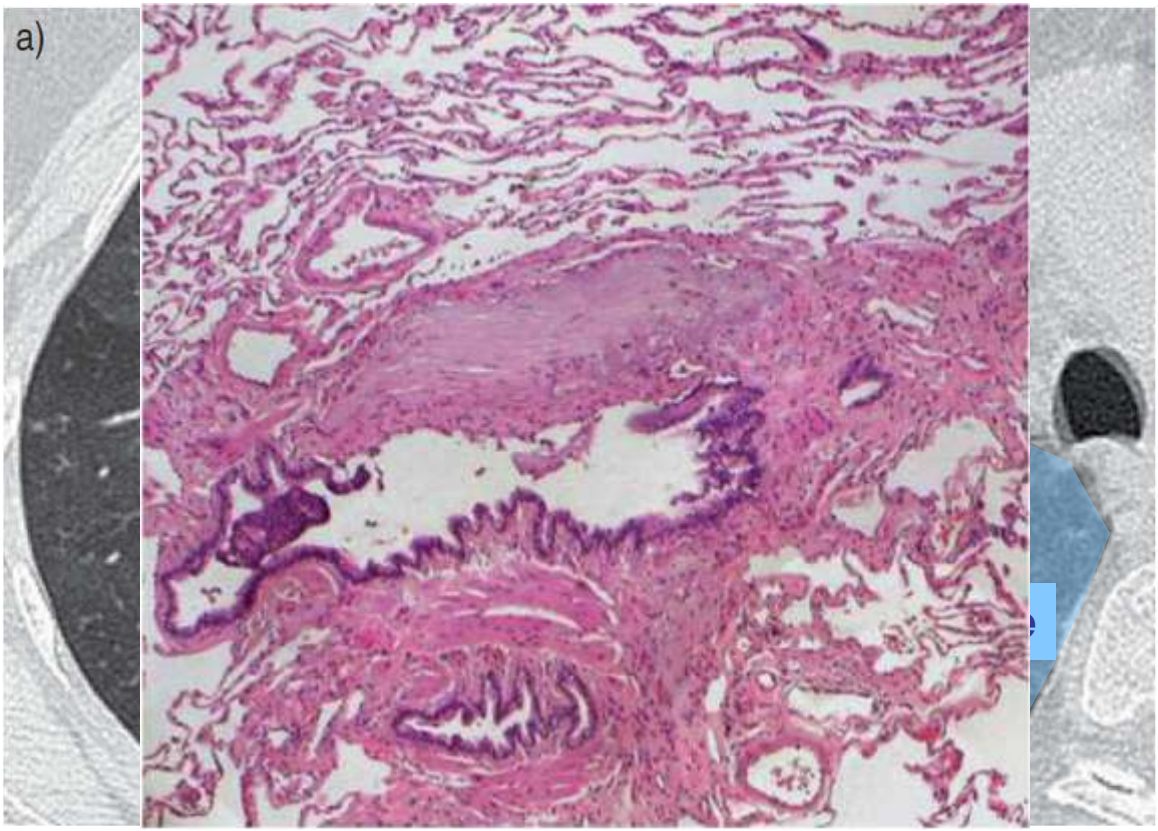




Webb WR, Radiology 2006, 239:322; Hansell DM, Radiology 2008, 246:69; Schneider F, Arch Path Lab Med 2012, 136:1242; Capobianco J, RadioGraphics 2012, 32:33

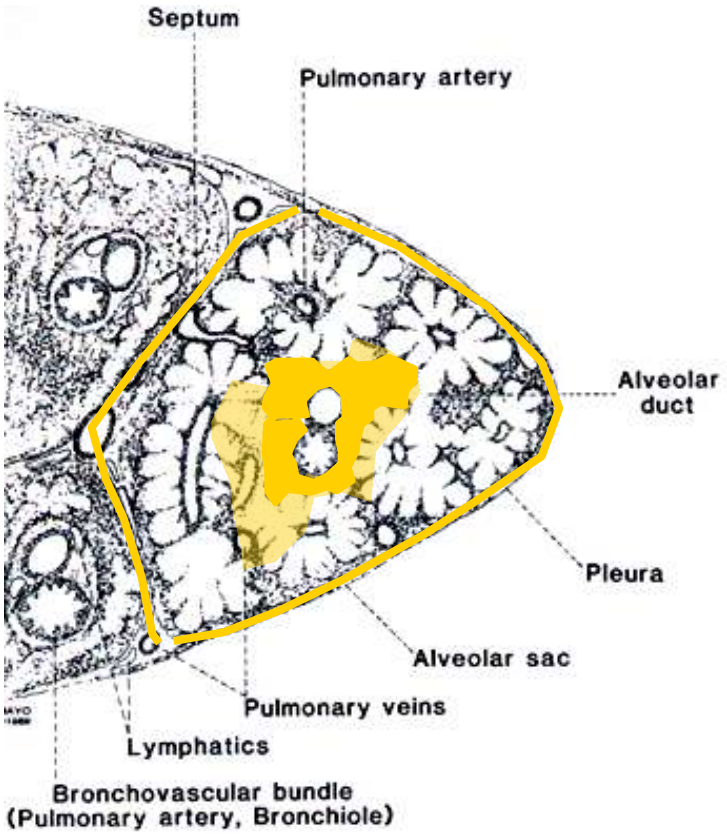
Atteinte des voies aériennes

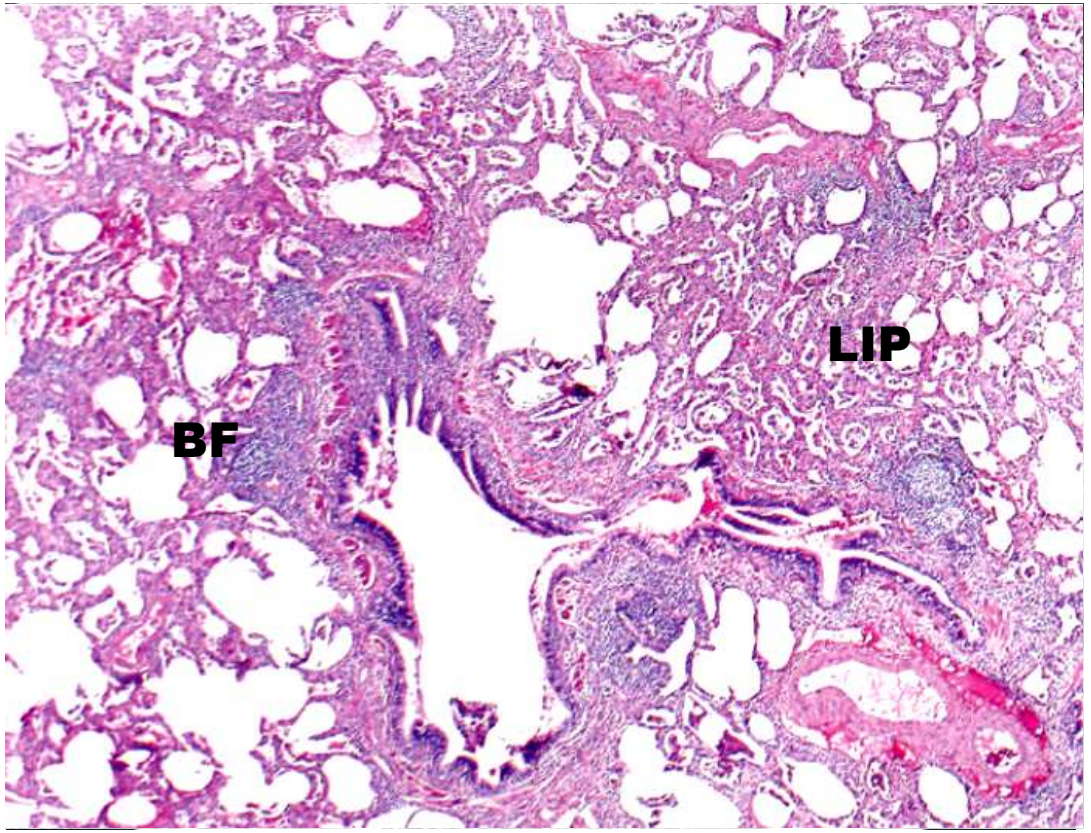




Webb WR, Radiology 2006, 239:322; Hansell DM, Radiology 2008, 246:69; Schneider F, Arch Path Lab Med 2012, 136:1242; Capobianco J, RadioGraphics 2012, 32:33; Poletti V, Eur Respir Mon 2011

Hyperplasie lymphoïde/BALT…





Webb WR, Radiology 2006, 239:322; Hansell DM, Radiology 2008, 246:69; Schneider F, Arch Path Lab Med 2012, 136:1242; Capobianco J, RadioGraphics 2012, 32:33

Hyperplasie lymphoïde/BALT…

Table 2

Characteristics of iBALT in patients with interstitial lung disease

No.	Patient	Diagnosis	FDCs[A]	B cells	T cells	No. follicles	No. GCs[B]
RA							
RA1	191-88	NSIP pattern and FB	+	+	+	15 (small)	NF
RA2	150-00	NSIP pattern with UIP-like lesions and FB	++	++	+	40 (medium)	6
RA3	192-04	UIP pattern	NF	++	+	57 (small)	20
RA4	314-01	UIP pattern and FB	++	+++	++	58 (medium)	18
RA5	208-00	NSIP pattern and FB	++	+++	++	50 (medium)	20
RA6	179-01	NSIP pattern with UIP-like lesions	++	++	++	80 (medium)	28
RA7	181-03	NSIP pattern with UIP-like lesions and FB	+++	+++	+++	96 (large)	80
RA8	547-99	NSIP, UIP lesions, and FB	+	+	+	14 (medium)	2
RA9	72-00	NSIP and FB	+	+	+	17 (medium)	2
SS							
SS1	147-05	Primary SS, NSIP pattern, FB, RA	++	++	+	40 (medium)	10
SS2	731-02	RA, secondary SS, NSIP,	+	+	+	20 (medium)	2
SS3	296-05	Primary SS, RA, NSIP, UIP	+	+	+	32 (medium)	5

Rangel-Moreno J, J Clin Invest 2006,116:3183

Connectivites et lymphome

Table 2 | Associations between ARD and increased risks of NHL and BCNHL subtypes

SLE	RA	SS	Study
Overall increased risk of NHL			
4.6 (1.0–2.2)*	1.5 (1.1–1.9)*	6.1 (1.4–27)*	Smedby *et al.* (2006)[11]
2.69 (1.68–4.30)	1.06 (0.87–1.29)*	Overall: 6.56 (3.10–13.9); primary: 4.75 (1.79–12.6); secondary: 9.57 (2.90–31.6)	Smedby *et al.* (2008)[12]
3.3 (2.1–5.3)	1.6 (1.4–1.9)	Overall: 11.7 (5.7–24); primary: 17.7 (6.3–50); secondary: 7.7 (2.3–25)	Mellemkjaer *et al.* (2008)[13]
1.5 (1.2–1.9)	1.2 (1.1–1.3)	1.9 (1.5–2.3)	Anderson *et al.* (2009)[14]
No difference	1.6 (0.7–3.7)	∞ (1.4–∞)	Ansell *et al.* (2010)[15]
Overall increased risk of BCNHL			
2.44 (1.49–3.99)	No difference	Overall: 6.52 (3.061–3.93); primary: 4.97 (1.86–3.29); secondary: 9.11 (2.72–30.46)	Smedby *et al.* (2008)[12]
Increased risk of MZL			
ND	1.4 (0.5–3.5)	28 (4.4–176)*	Smedby *et al.* (2006)[11]
7.52 (3.39–16.7)	No difference	Overall: 30.6 (12.3–76.1); primary: 23.1 (7.16–74.6); secondary: 44.6 (10.6–187)	Smedby *et al.* (2008)[12]
2.8 (1.7–4.7)‡	1.2 (1.0–1.6)	Overall: 6.6 (4.6–9.5)*; primary: 7.1 (4.4–12); secondary: 5.9 (3.5–10)	Anderson *et al.* (2009)[14]
ND	0.5 (0.1–4.3)	∞ (7.3–∞)	Ansell *et al.* (2010)[15]

Dias C, Nature Reviews. Rheumatology 2011

Lymphome du BALT et connectivites

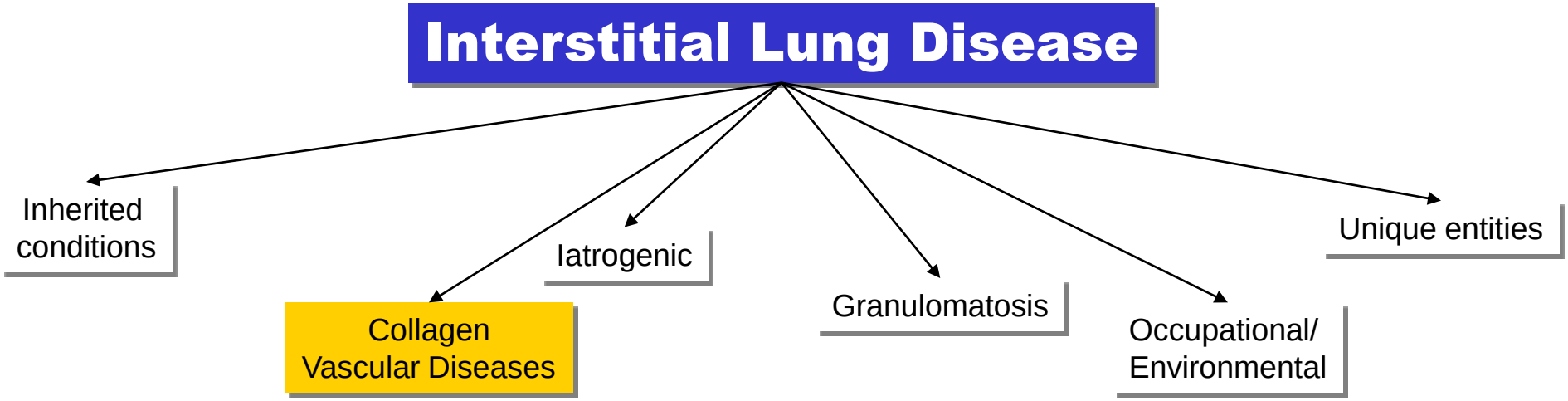
TABLE 1 Main clinical and biological characteristics of the

10 patients had autoimmune disease at diagnosis, including systemic lupus erythematosus (n=2), rheumatoid arthritis (n=1) and Sjogren's syndrome (n=5), and four more patients had undifferentiated connective tissue disease similar to Sjogren's syndrome [16].

Active or former tobacco use	24 (37)
Respiratory tract infection	6 (9)
Including tuberculosis	4 (6)
Autoimmune background	10 (16)
Respiratory symptoms	37 (58)
B symptoms	14 (22)
Cytopenia	12 (19)
LDH level more than twice the upper limit	2 (3)

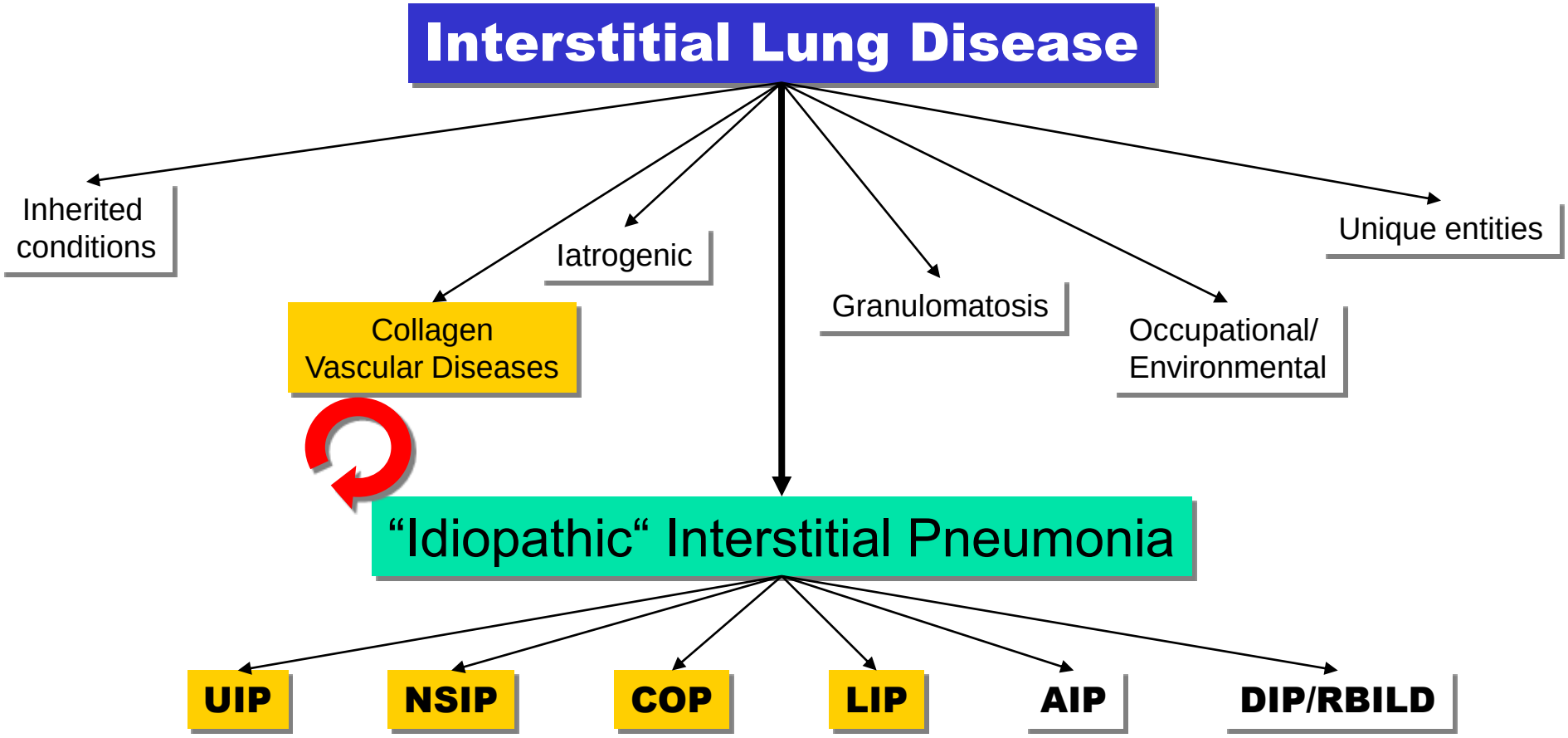
Rangel-Moreno J, J Clin Invest 2006,116:3183; Borie R, Eur Respir J 2010, 34:1

PID et connectivites



Raghu G, Clin Chest Med 2004, 25:409

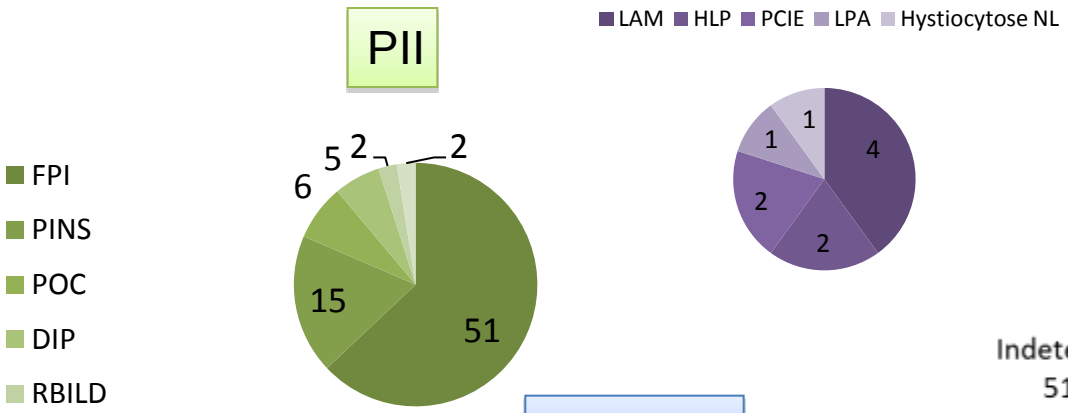
PID et connectivites

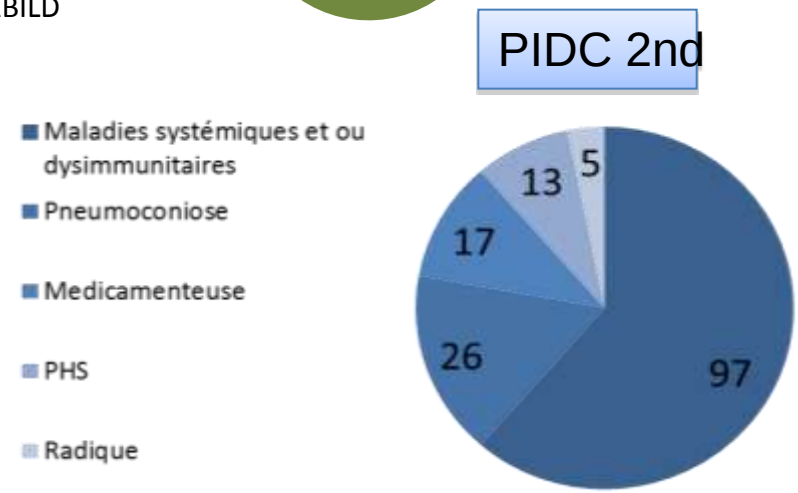


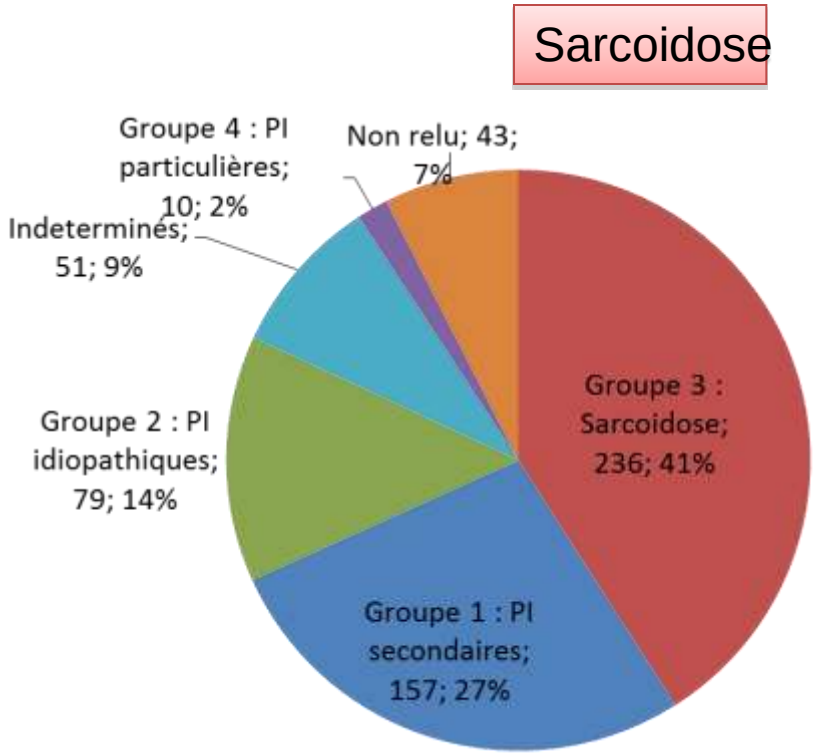
Raghu G, Clin Chest Med 2004, 25:409

PID et connectivites

PID 93, n=576







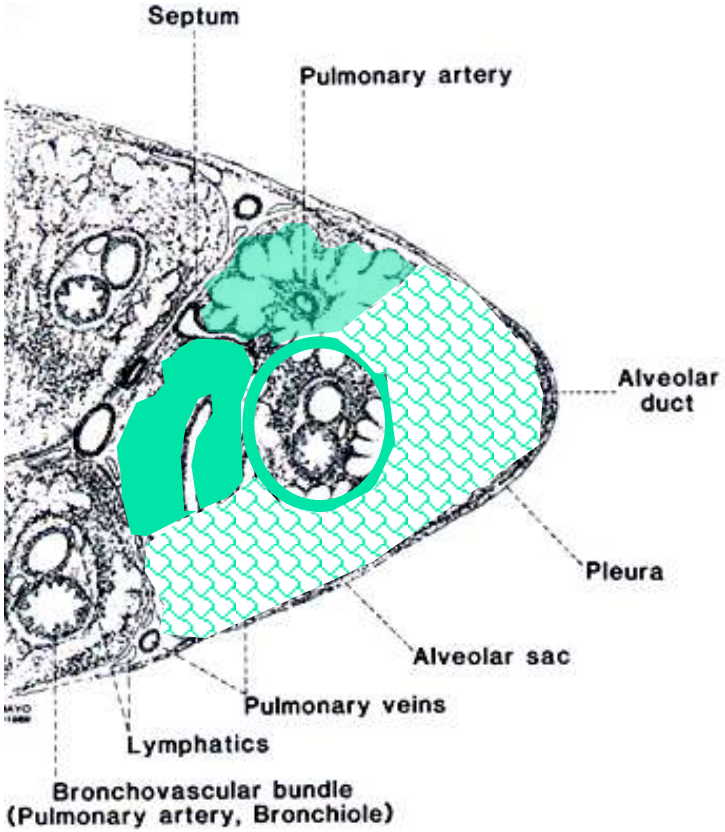
Connectivites et PID

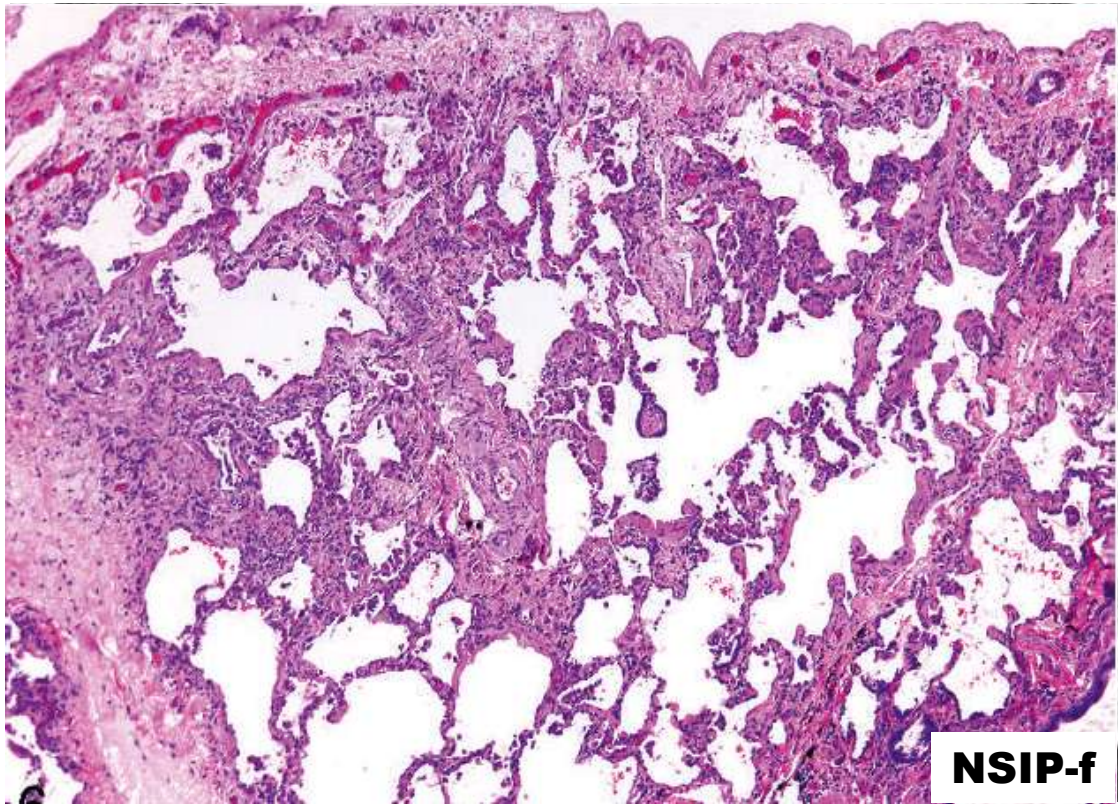
TABLE 1 Types of interstitial lung disease encountered in connective tissue diseases

	SSc	PM/DM	PSS	RA	SLE	MCTD
Usual interstitial pneumonia	++	++	+	++	+	+
Nonspecific interstitial pneumonia	++++	++++	+	+	++	++
Cryptogenic organising pneumonia	+	++	+	+	+	-
Diffuse alveolar damage	+	++	+	+	++	-
Lymphocytic interstitial pneumonia	-	-	+++	-	-	-

Tzelepis GE, Eur Respir J 2008, 31:11

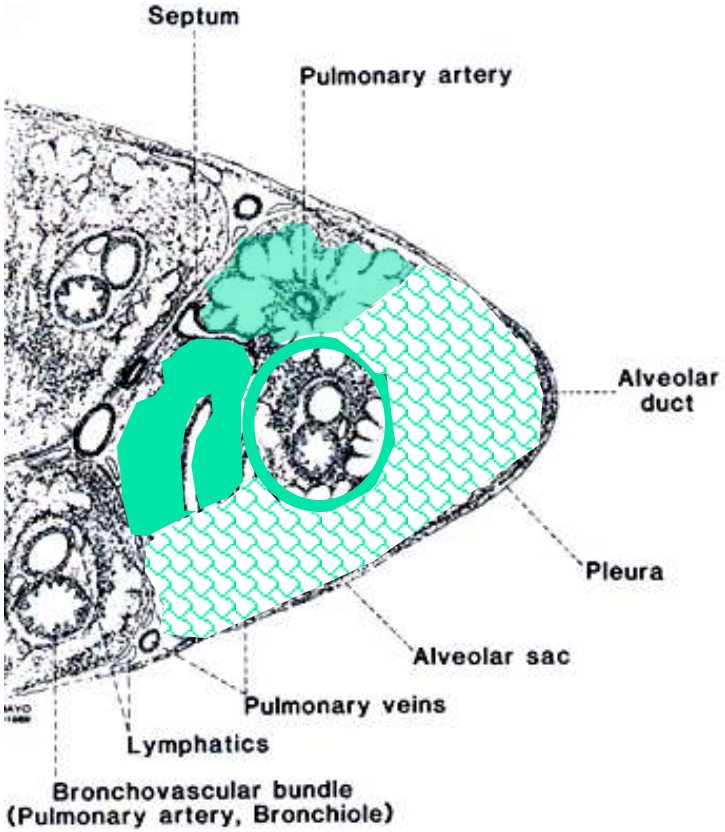
Atteinte parenchymateuse/NSIP

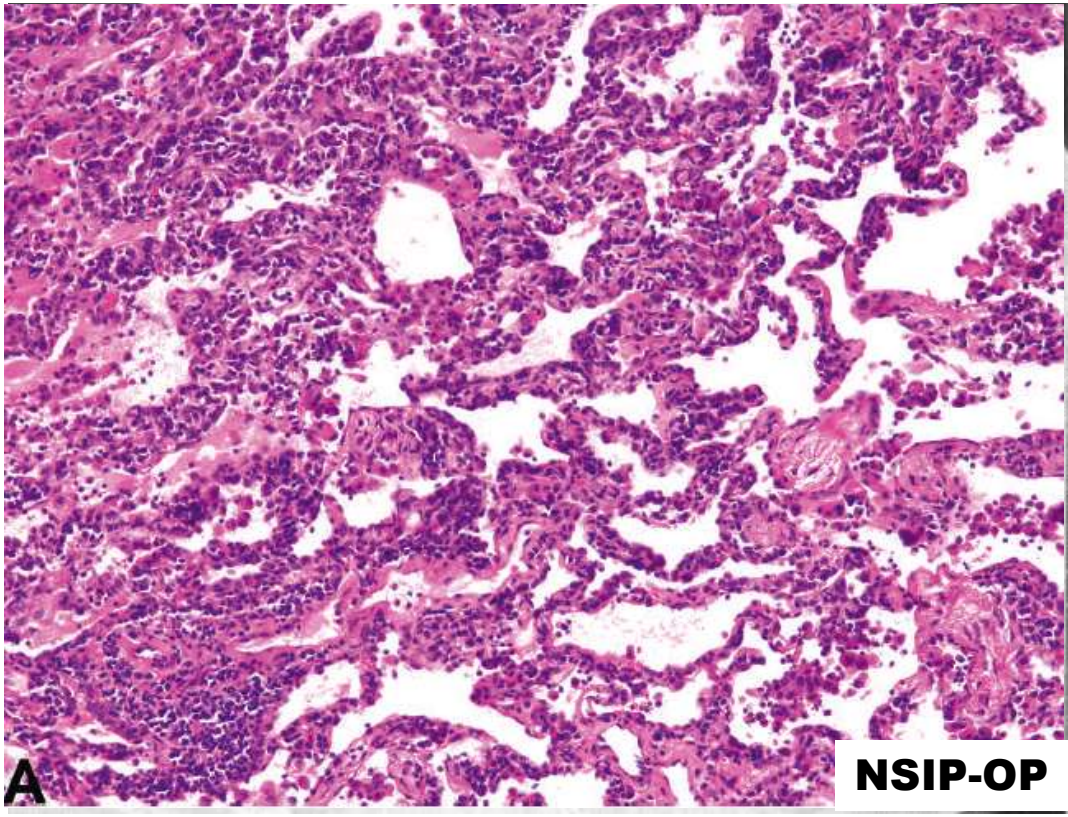




Webb WR, Radiology 2006, 239:322; Hansell DM, Radiology 2008, 246:69; Schneider F, Arch Path Lab Med 2012, 136:1242; Capobianco J, RadioGraphics 2012, 32:33

Atteinte parenchymateuse/OP





Webb WR, Radiology 2006, 239:322; Hansell DM, Radiology 2008, 246:69; Schneider F, Arch Path Lab Med 2012, 136:1242; Capobianco J, RadioGraphics 2012, 32:33

Connectivites et PID

TABLE 1. PATHOLOGIC PATTERNS OF LUNG FIBROSIS IN THE CLINICAL SETTINGS OF IDIOPATHIC AND COLLAGEN VASCULAR DISEASES: RELATIVE FREQUENCY OF FIBROTIC NONSPECIFIC INTERSTITIAL PNEUMONIA

	Number of Subjects	NSIP, n (%)
Idiopathic	269	66 (24.5)
Rheumatoid arthritis	28	10 (35.7)
Scleroderma	35	23 (65.7)
Dermatomyositis–polymyositis	8	7 (87.5)
Sjögren syndrome	11	7 (63.6)
Systemic lupus erythematosus	1	1 (100)
Mixed connective tissue disease	5	5 (100)
Polymyalgia rheumatica	2	2 (100)
CREST syndrome	2	2 (100)
Undifferentiated	1	0

Park JH, Am J Resp Crit Care 2007:175, 705

PID et connectivites, pronostic

269 IIP vs. 93 CVD-IP

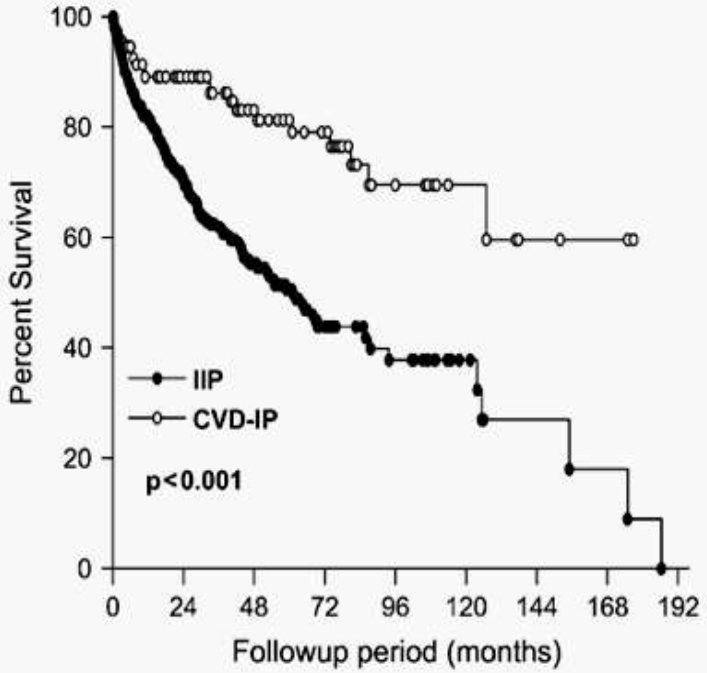


Figure 1. Survival of total subjects with idiopathic interstitial pneumonia (IIP) and interstitial pneumonia associated with collagen vascular disease (CVD-IP).

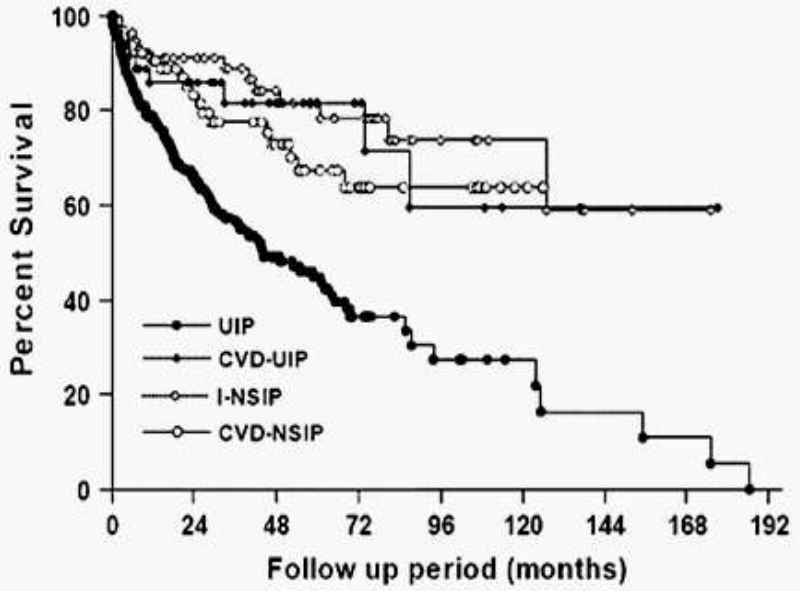
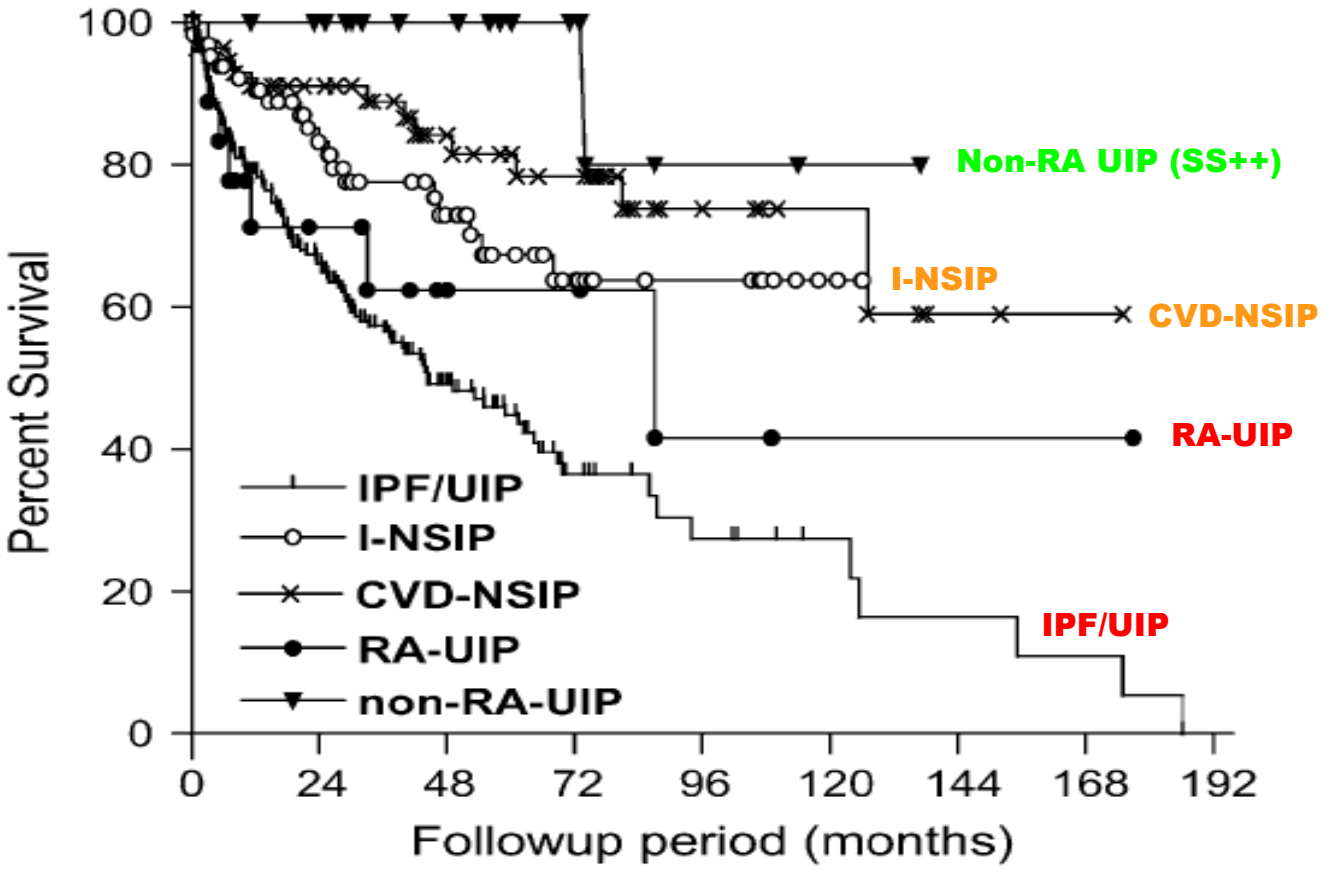


Figure 2. Comparison of the survival curves of all subject groups. CVD-UIP = usual interstitial pneumonia associated with collagen vascular disease; CVD-NSIP = nonspecific interstitial pneumonia associated with collagen vascular disease; I-NSIP = idiopathic nonspecific interstitial pneumonia; UIP = usual interstitial pneumonia.

Park JH, Am J Resp Crit Care 2007:175, 705

Atteinte parenchymateuse/UIP/NSIP/OP



Park JH, Am J Resp Crit Care 2007:175, 705

Atteinte parenchymateuse/UIP/NSIP/OP

Table 2—*Proposed Therapies for CTD-ILD*[a]

Medication	Dose[b]	Disease
Prednisone	0.5-1 mg/kg/d up to 60 mg/d	SSc, RA, DM, PM, SS
Methylprednisolone	1 g/d IV for 3 d	Acute worsening CTD-ILD
Azathioprine	1-2 mg/kg/d	SSc, RA, DM, PM, SS
Cyclophosphamide	1-2 mg/kg/d po or 500-1,000 mg IV pulse every 4 wk	SSc, RA
Mycophenolate mofetil	1.0-1.5 g bid	SSc, RA, DM, PM
Tacrolimus	1 mg bid	DM, PM
Rituximab	375 mg/wk, 4 wks or 1 g at d1 and d15	SSc, RA, DM, PM, SS

Vij R, Chest 2012, 143:814

Connectivites indifférenciées

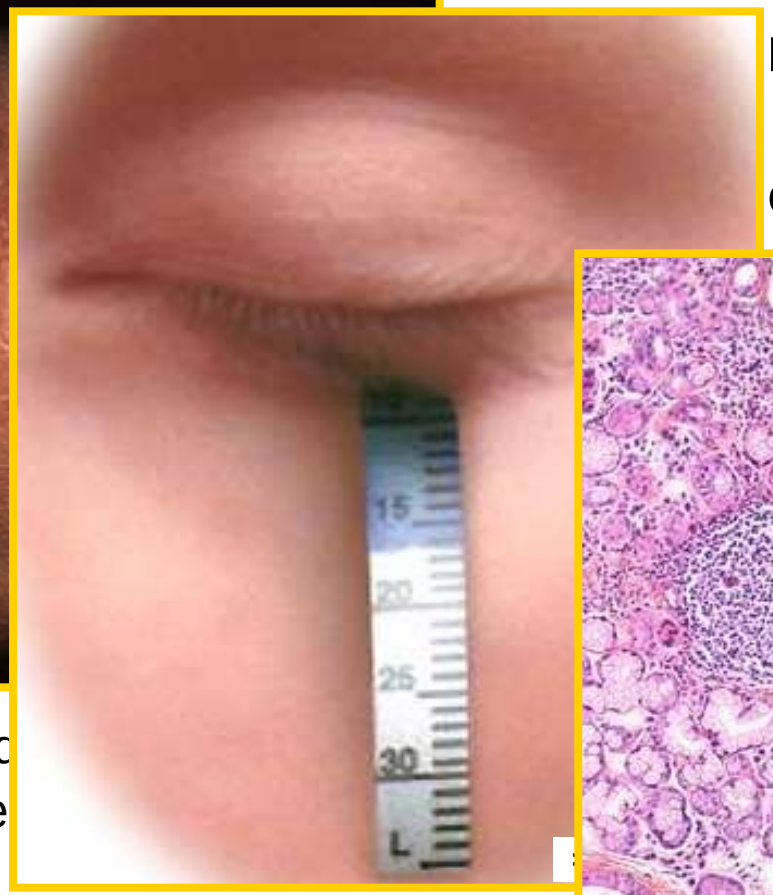
- Situation clinique fréquente
- Eviter une BPTO futile
- Prédire l'atteinte d'autres organes
- Apporter des éléments pronostiques sur l'atteinte respiratoire
- Permettre d'adapter le traitement
- Mieux comprendre la physiopathologie de ces maladies

Connectivites indifférenciées

- ≈ 25% des malades avec caractéristiques de maladies auto-immunes restent “non classés“
- 65-94% de ces malades ne développent pas dans le temps de connectivites déterminées (PR, SS, LED, GS, PM/DPM, CM…)
- Concept de, *“undifferentiated connective tissue disorder“…*

Mosca M, Nature Clin Pract - Rheumatology 2008, 4:328; Fischer A, Chest 2010, 138:251

PR et GS indifférenciées/frustes



nte pulmonaire

caractéristique

- difficulté d
- Valeur de

Tzelepis GE, ERJ 2008, 31:11; Lee HK, Chest 2005, 127:2019; Param *J Respir Crit Care 2005, 171: 632; Vij R, Chest 2012, 143:814*

PM/DPM indifférenciées/frustes

- 5 à 64% des PM/DPM développent une PID; 1/3 inaugurales
- PM/DPM avec PID prédominante
  - 20 à 30% dans les séries de *Douglas et al* et *Marie et al*
- PID et DPM amyopathic
  - 10 à 20% des DM n'ont pas d'atteinte myopathique
  - 13% présentent une PID
  - chronique vs aigüe/subaigüe avec mortalité importante

Tzelepis GE, ERJ 2008, 31:11; Douglas WW, AJRCCM 2001, 164:1182; Marie I, Arthritis and Rheum 2002, 74:614; Gerami P, J Am Acad Dermatol 2006,54:597; Vij R, Chest 2012, 143:814

PM/DPM indifférenciées/frustes

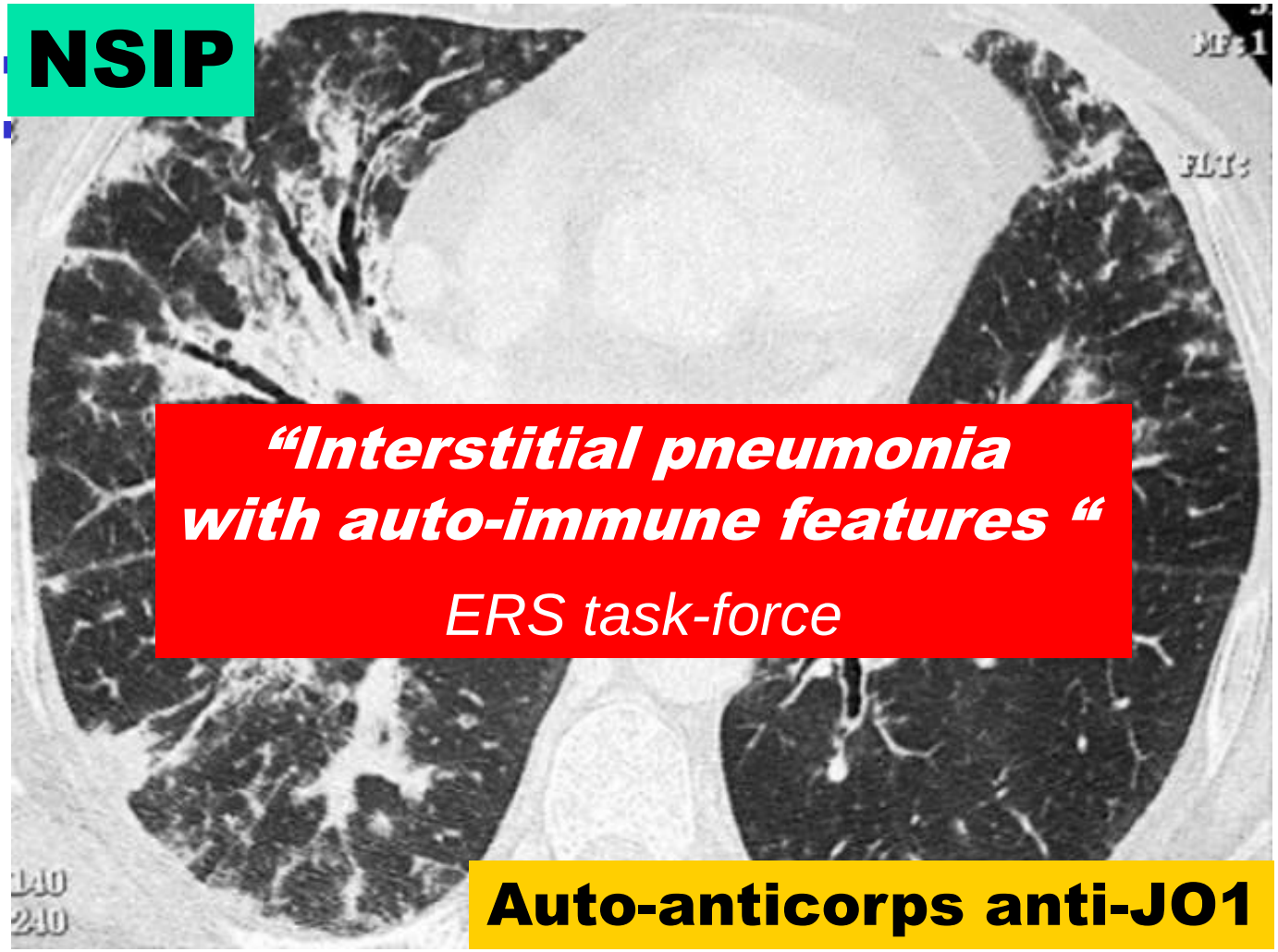
t-RNA synthetase

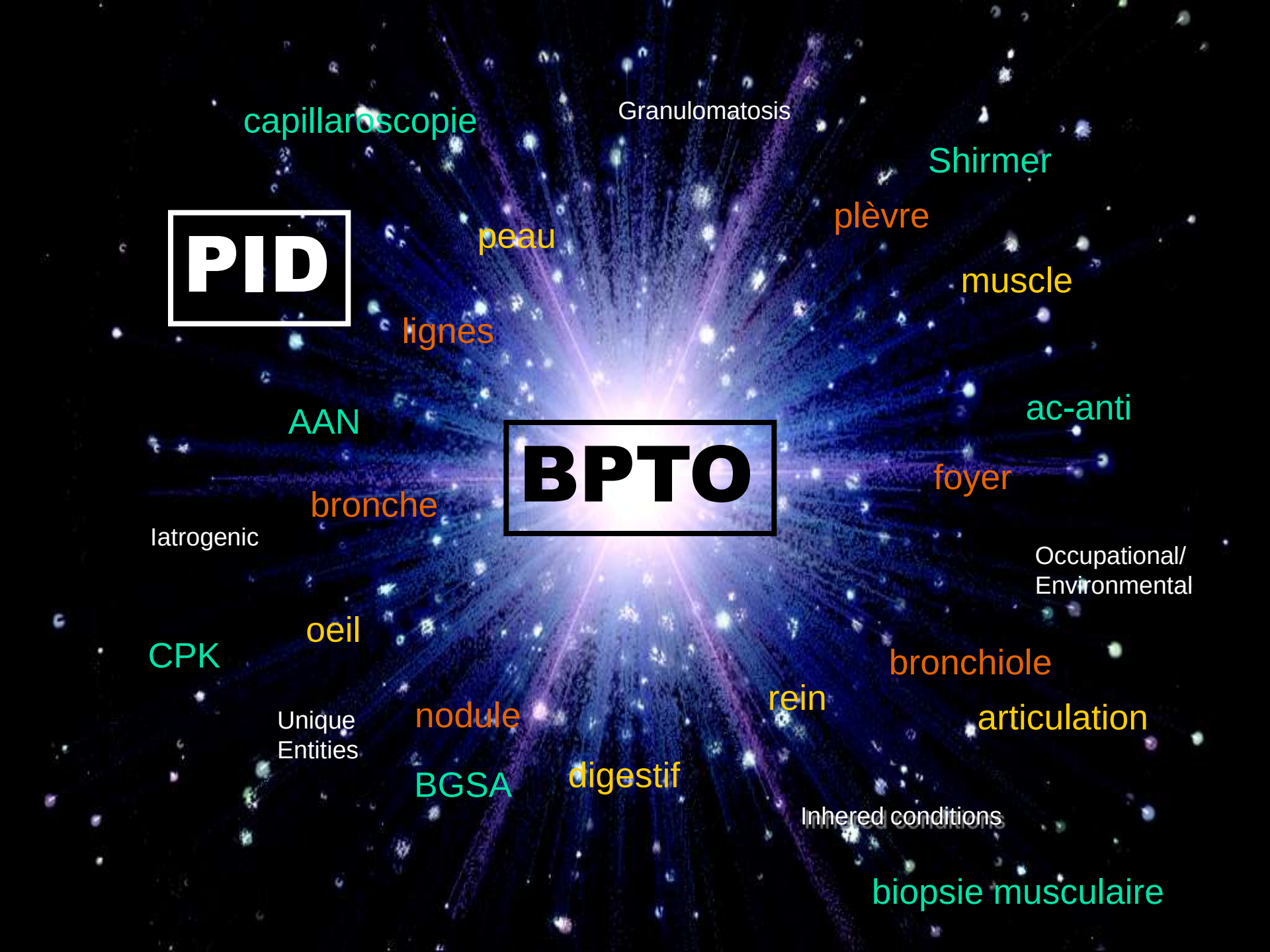
nti-synthétases; >90% sont

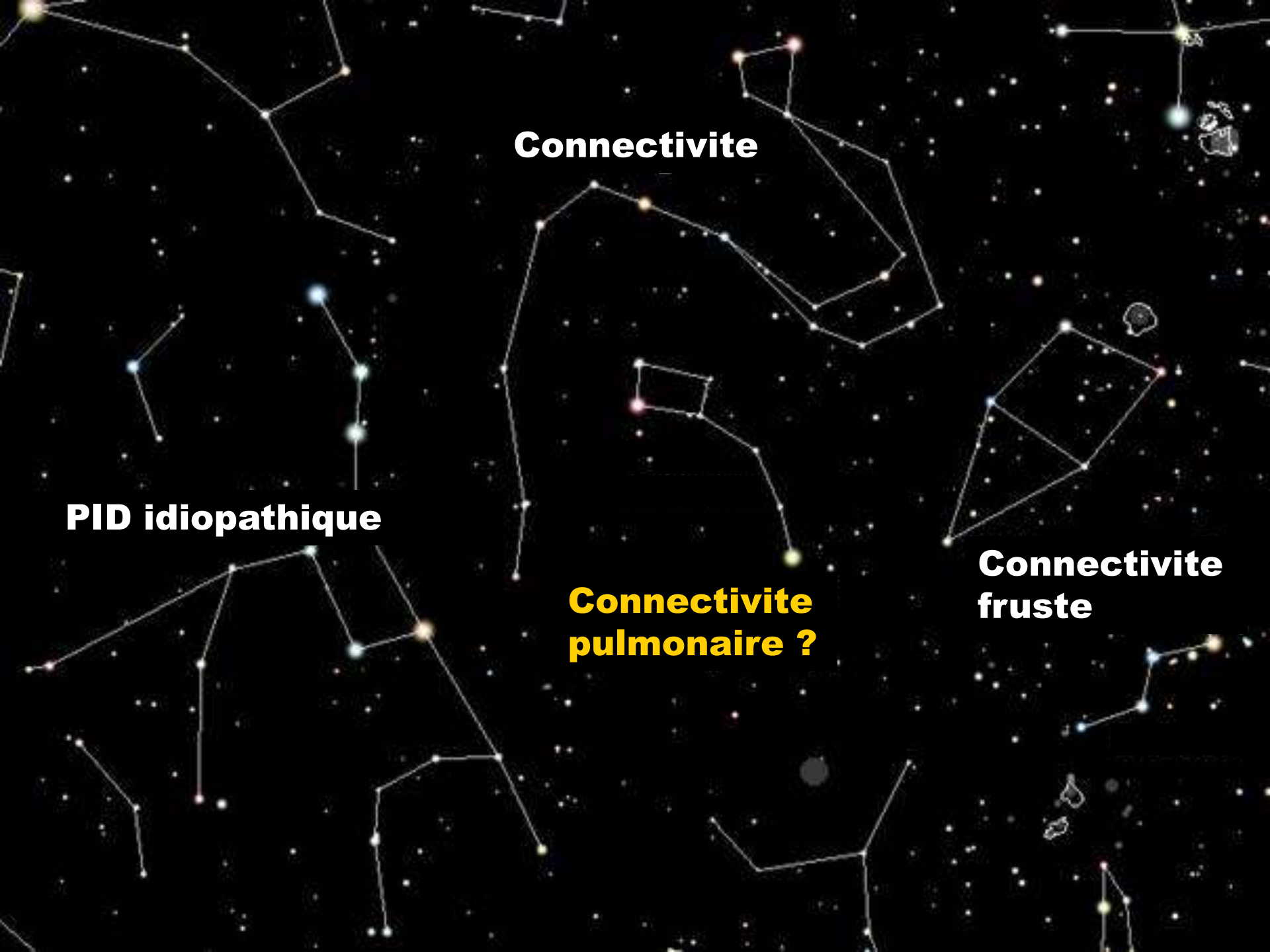
tent des anti-synthétases:

Tzelepis GE, ERJ 2008, 31:11; Mar
Chmiel JF, J Rheumatol 1995, 22:762; Vij R, C

Pneumonie interstitielle auto-immune




capillaroscopie
Granulomatosis
Shirmer
plèvre
PID
peau
muscle
lignes
ac-anti
AAN
BPTO
foyer
bronche
Iatrogenic
Occupational/
Environmental
oeil
CPK
bronchiole
rein
articulation
Unique
Entities
nodule
BGSA
digestif
Inhered conditions
biopsie musculaire


Connectivite
PID idiopathique
Connectivite pulmonaire ?
Connectivite fruste