Explorations Fonctionnelles Respiratoires

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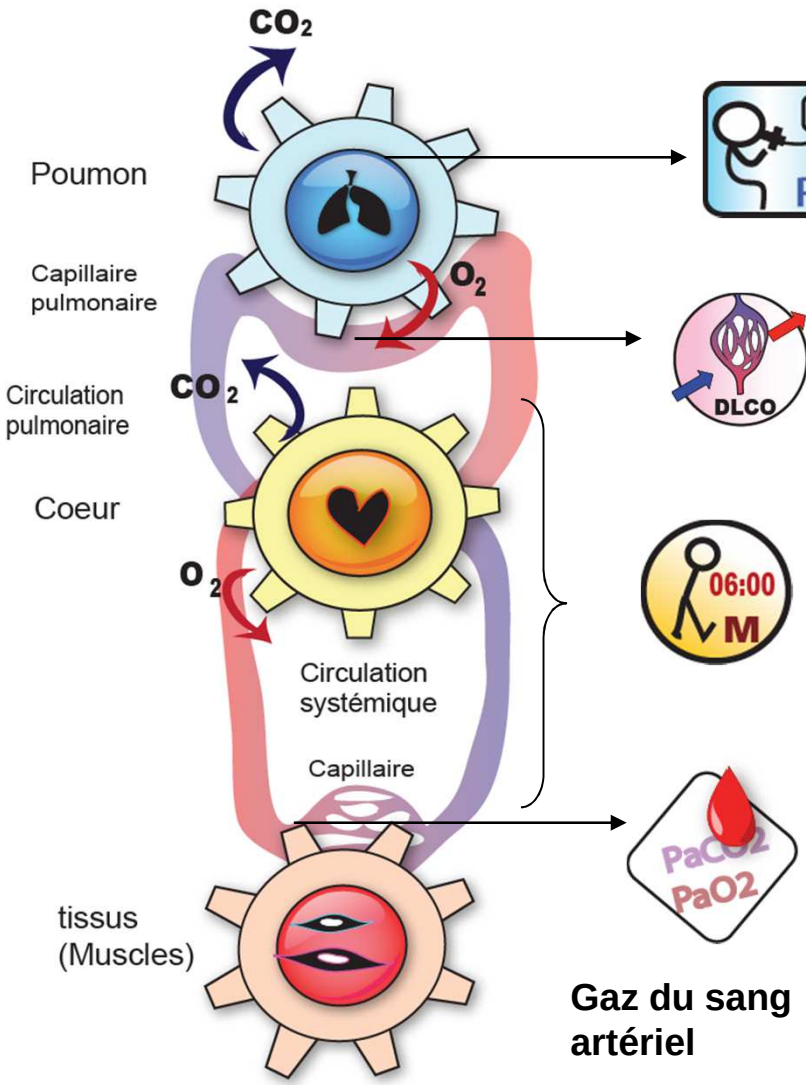
Pourquoi explorer ?



Spirométrie - Pléthysmographie (CVF, CPT…)

Capacité de diffusion DLCO, Dm et Vc

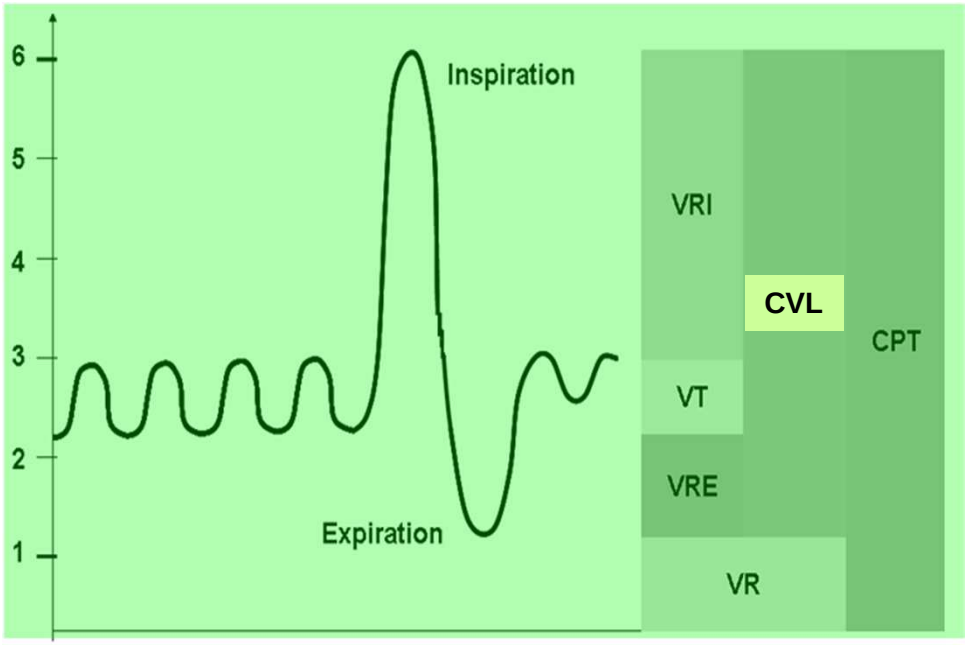
Test de marche de 6 minutes

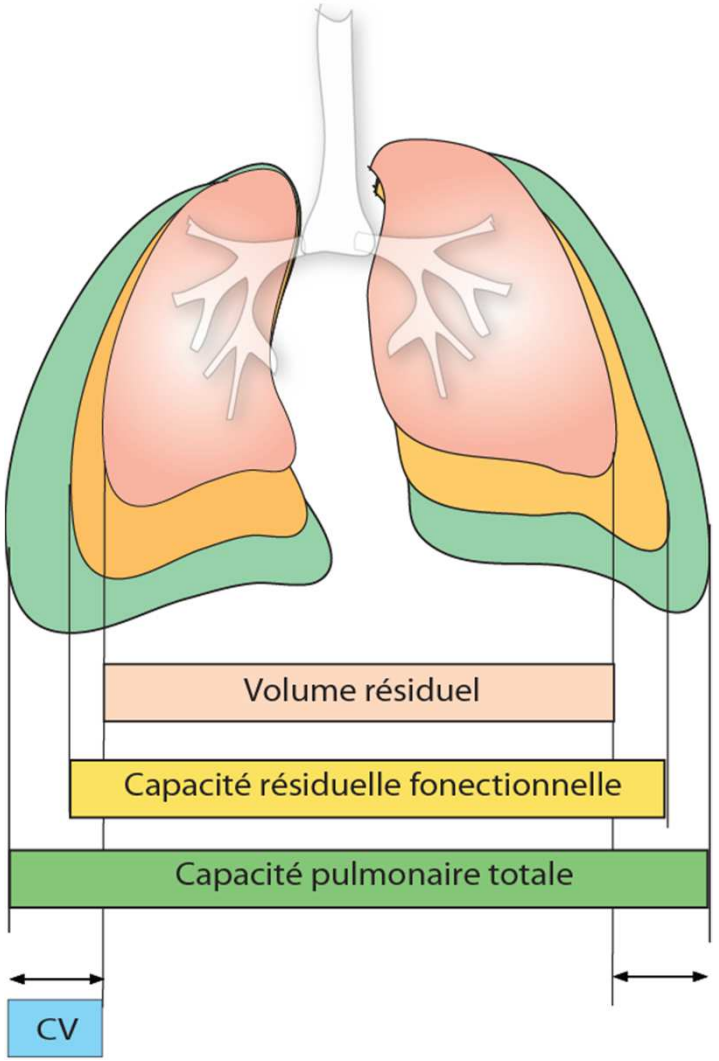
Gaz du sang artériel

Buts

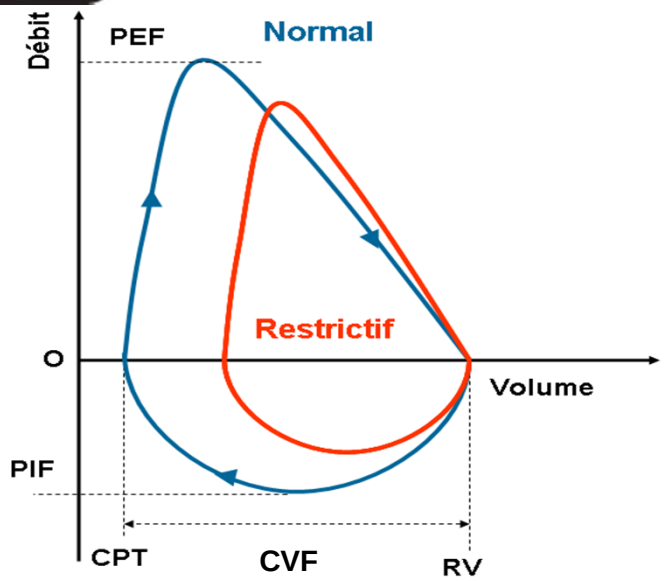
- **Valeur diagnostique (dépister les atteintes pulmonaires)**
- **Valeur pronostique (évaluer le retentissement clinique et/ou la réponse aux traitements)**

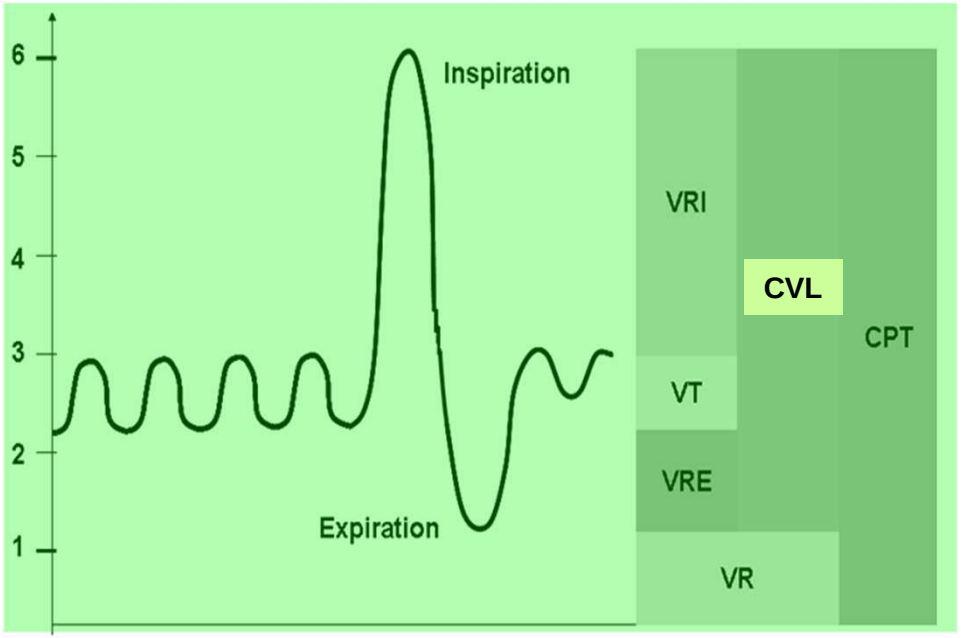
Ventilation pulmonaire : Mesure des volumes





Ventilation : Mesure des volumes pulmonaires et des débits respiratoires





Capacité vitale: tous les volumes mobilisables

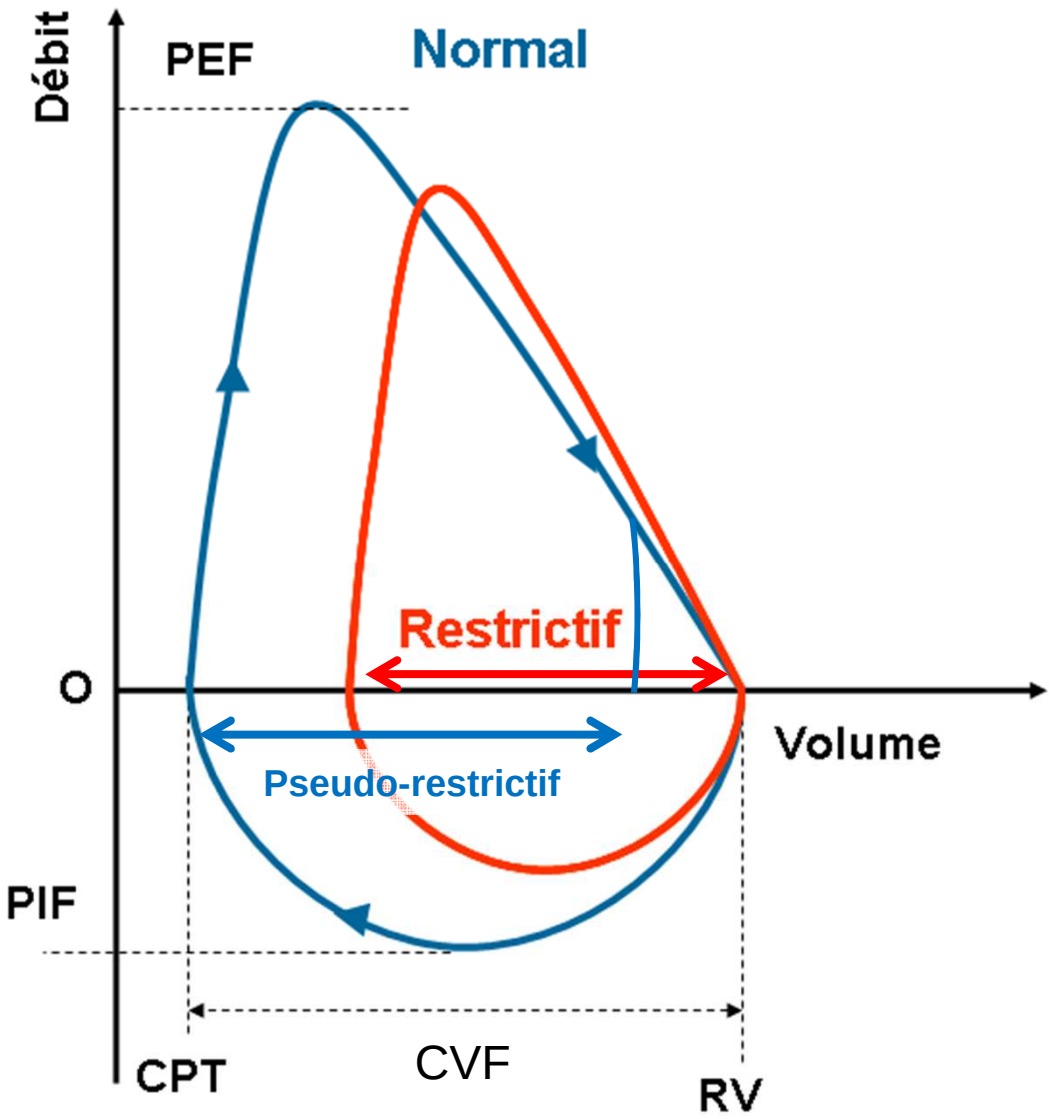
CV = VT+VRE+VRI

CVF est mesurée lors d'un expiration forcée (Courbe de débit-volume)

Capacité pulmonaire totale

CPT = CV+ VR

L'atteinte pulmonaire dans la SSC est définie par un trouble ventilatoire **restrictif**
CPT < 80% des valeurs théoriques (et/ou CVF < 80%)

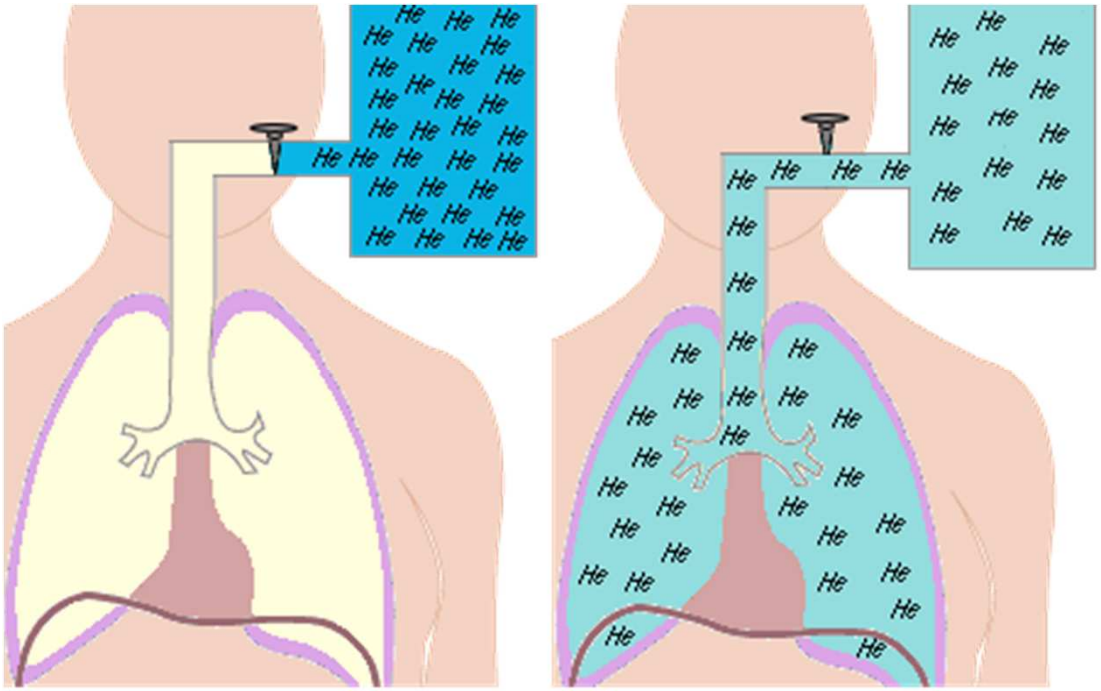

Débit
PEF
Normal
Restrictif
O
Volume
Pseudo-restrictif
PIF
CPT
CVF
RV

Dilution à l'Hélium

Capacité résiduelle fonctionnelle :
volume d'air restant dans les poumons à la fin d'une expiration normale.

CRF=VRE+VR

Pléthysmographie ou Dilution à l'Hélium

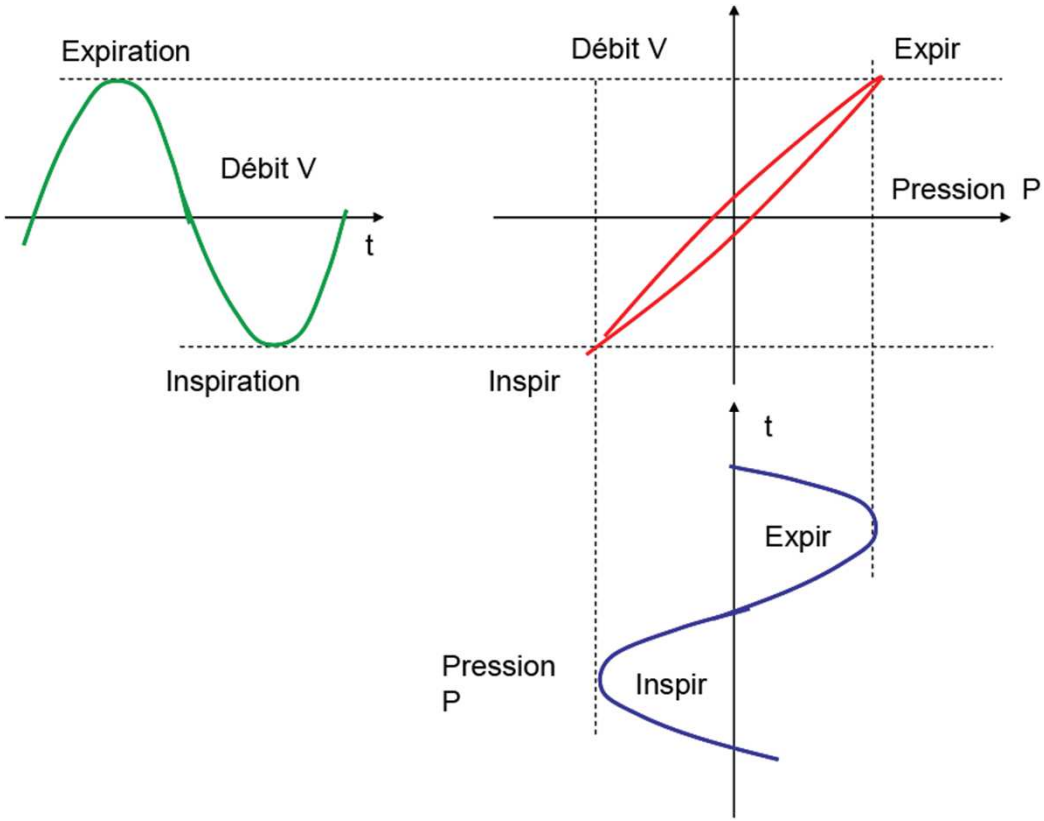


$$V_{SPIR} \cdot C_1 = V_x \cdot C_2 \qquad V_x = VR + VRE$$

$$VR = \frac{V_{SPIR} \cdot C_1}{C_2} - VRE - V_{SPIR}$$

Méthode de dilution à l'hélium (gaz inerte)

Pléthysmographie corporelle totale



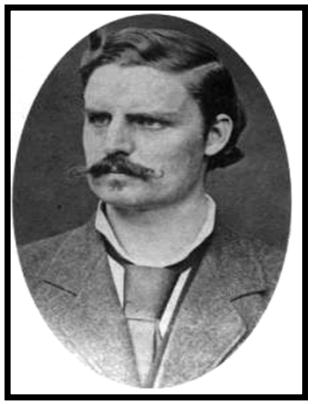
Pléthysmographie

PV = Constant (Boyle)
→$P_1V_1 = P_2V_2$

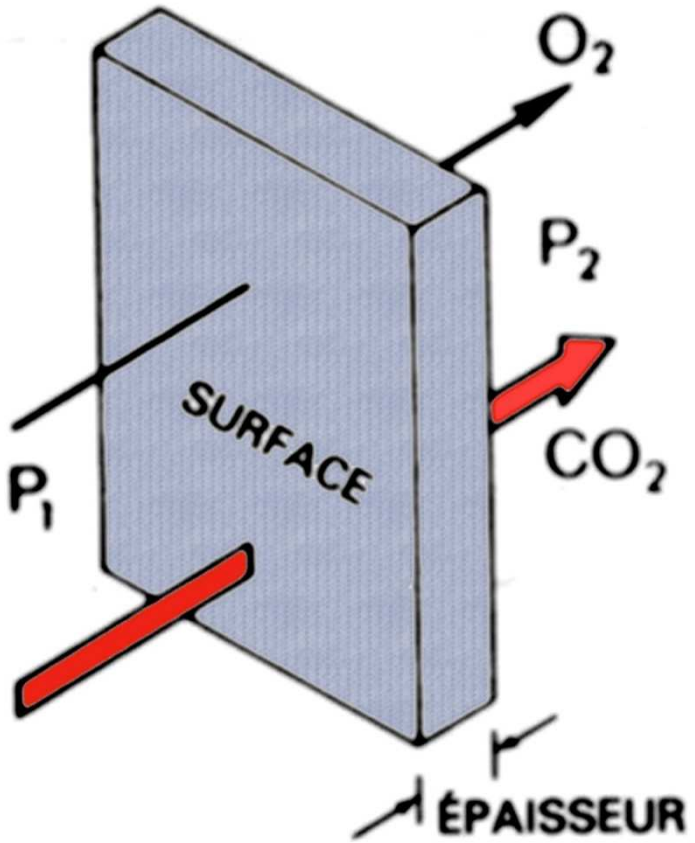
→CRF. PB = (CRF + ΔV) x (PB + ΔP)

Simplifié : CRF = - (ΔV/ ΔP) x (PB + ΔP)

ΔV/ ΔP : pente de la courbe Pression/Volume = Compliance pulmonaire



Adolf Eugene FICK
(1829 -1901)

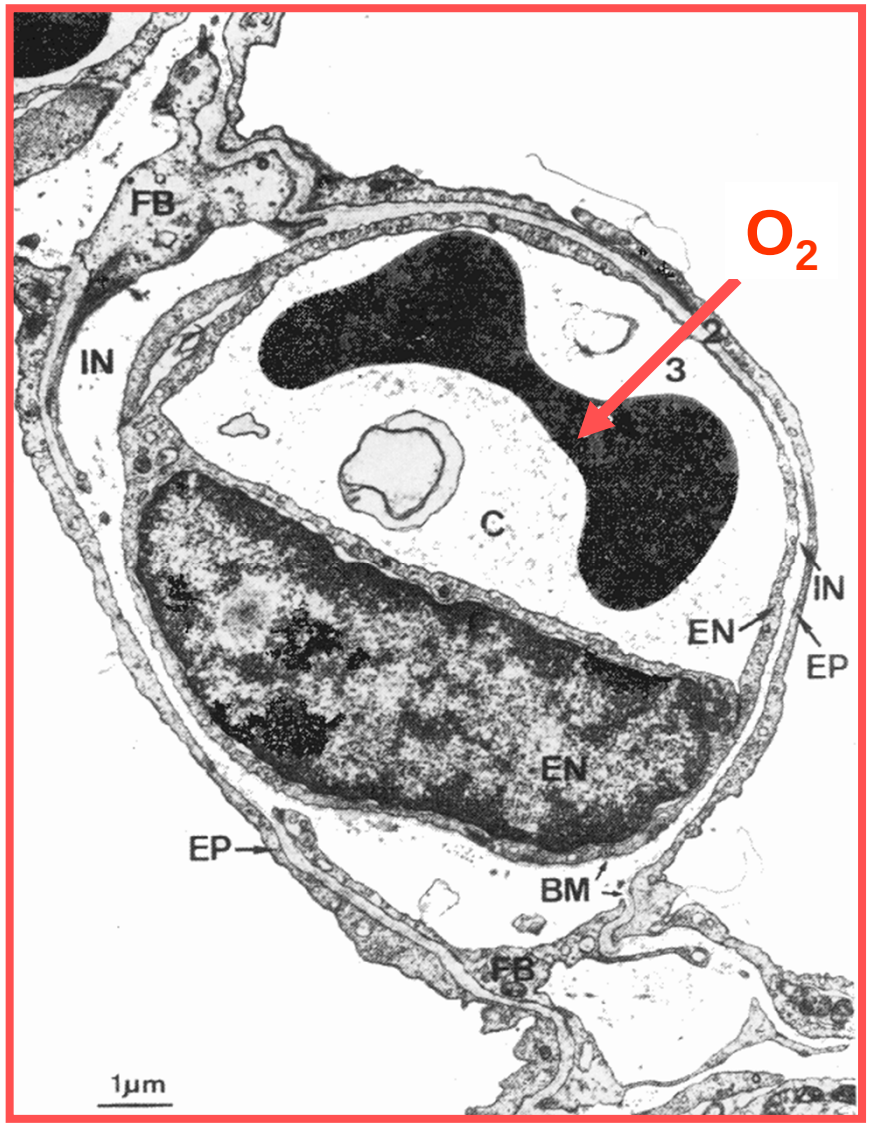


Tous les gaz passent à travers la paroi alvéolaire par **diffusion passive**.

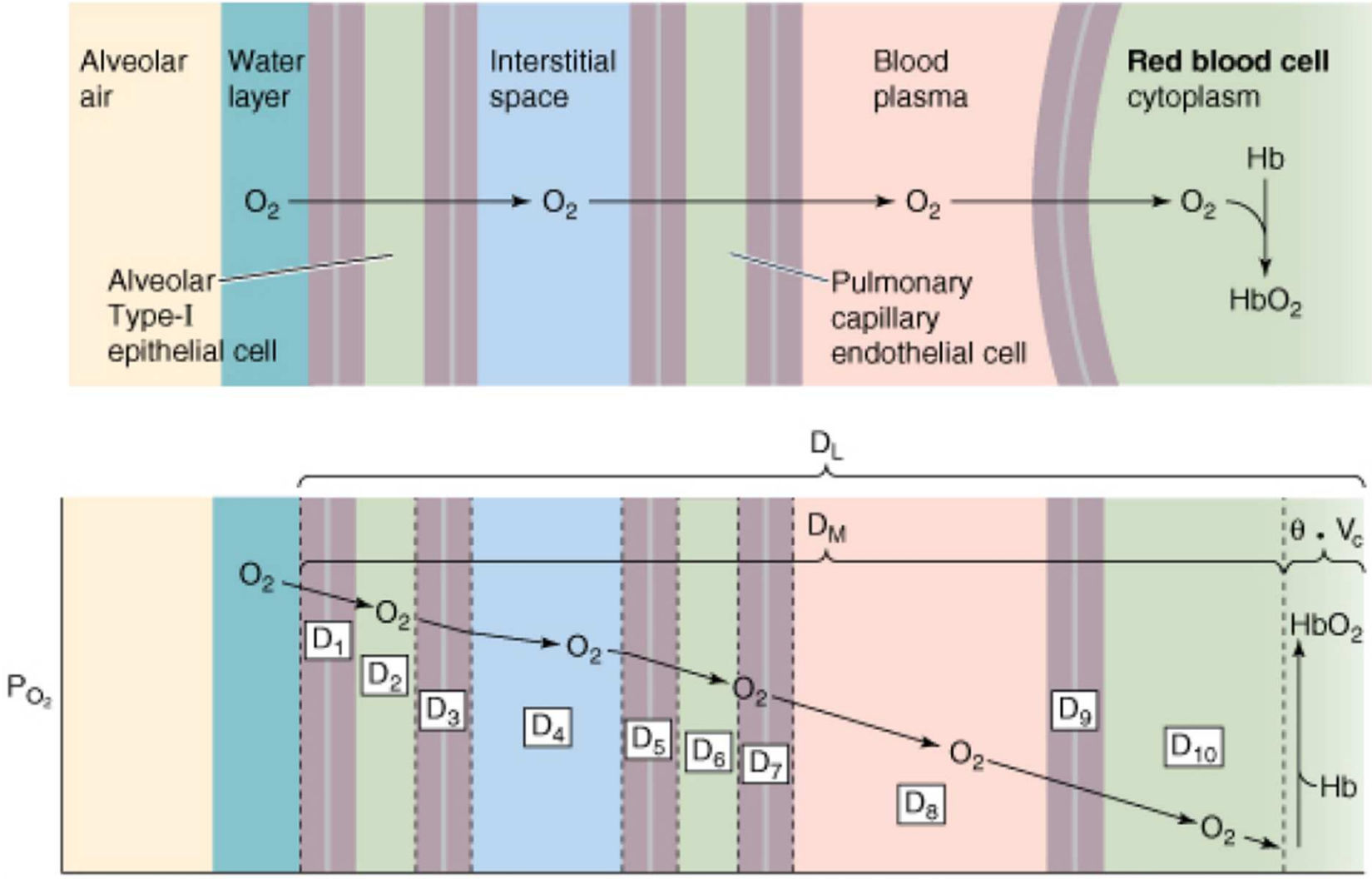
Le débit de transfert d'un gaz à travers une couche de tissu (Loi de Fick) est :

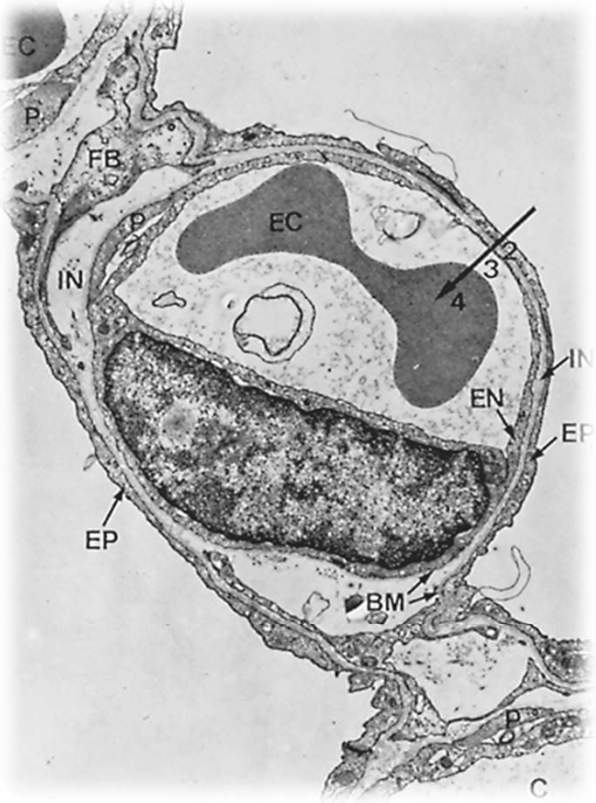
1. proportionnel à la **surface** du tissu
2. proportionnel à la **différence de pression** partielle du gaz de part et d'autre de la barrière alvéolo-capillaire
3. proportionnel à la **solubilité** du gaz
4. inversement proportionnel à l'**épaisseur** du tissu
5. inversement proportionnel à son **poids moléculaire**

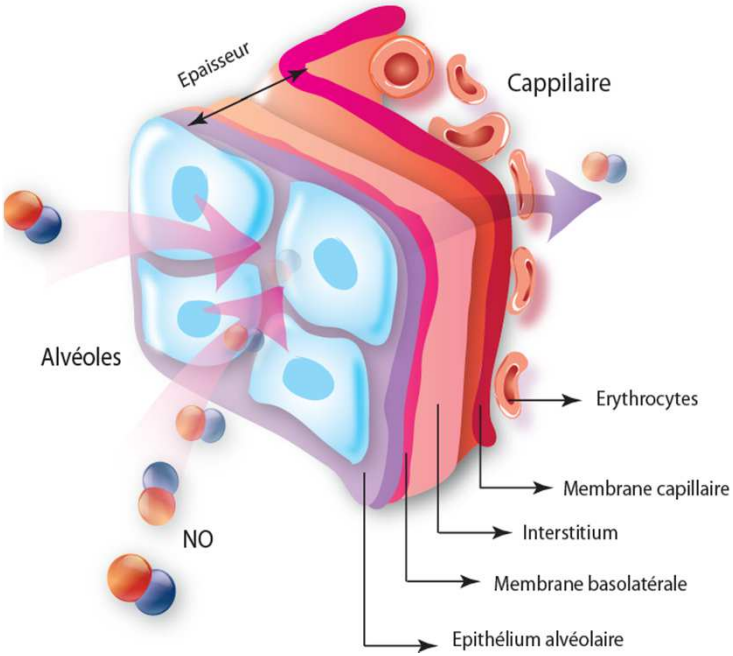
La barrière alvéolo-capillaire



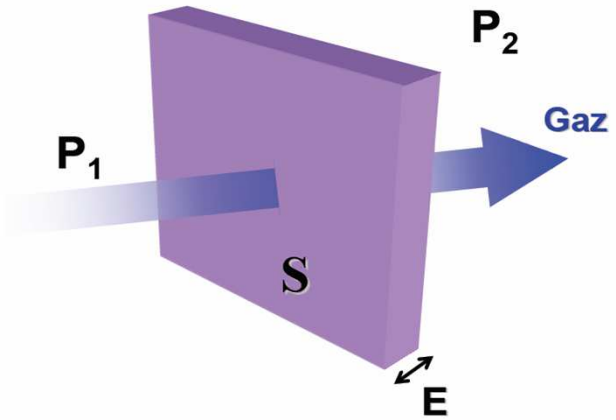
1. Surfactant
2. Épithélium alvéolaire
3. Espace interstitiel
4. Endothélium capillaire
5. Plasma (du capillaire pulmonaire)
6. Milieu intérieur du globule rouge
7. Hémoglobine







La loi de Fick



$$\dot{V}gaz \propto \frac{S}{E} \cdot D \cdot \Delta P \qquad D \propto \frac{Sol}{\sqrt{PM}}$$

Diffusion

$$\dot{V}_{gaz} = \frac{S}{E} \times \Delta P \times D$$

$$D \approx \frac{Sol}{\sqrt{PM}}$$

$$\dot{V}_{gaz} = D_{L,gaz} \times \Delta P$$

$$D_{L,gaz} = \frac{S}{E} \times D$$

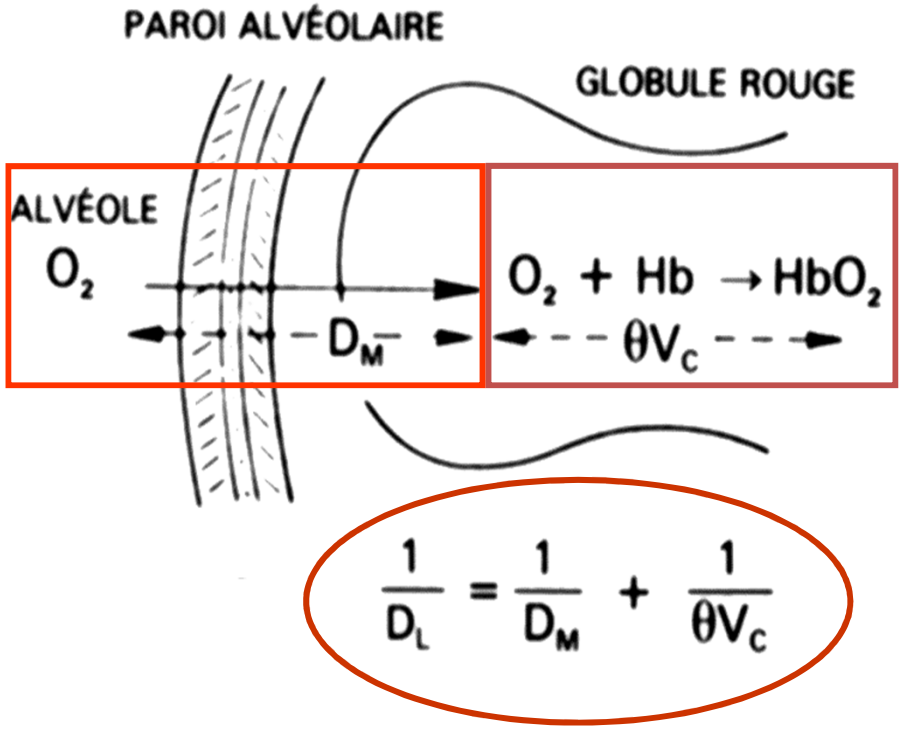
$$D_{L,gaz} = \frac{\dot{V}_{gaz}}{\Delta P}$$

$$R = \frac{\Delta P}{\dot{V}_{gaz}}$$

$D_{L,gaz}$ est l'expression de l'inverse d'une résistance

Résistance globale à la diffusion

La diffusion de l'O_2 de l'alvéole à l'hémoglobine peut être considéré en 2 étapes :

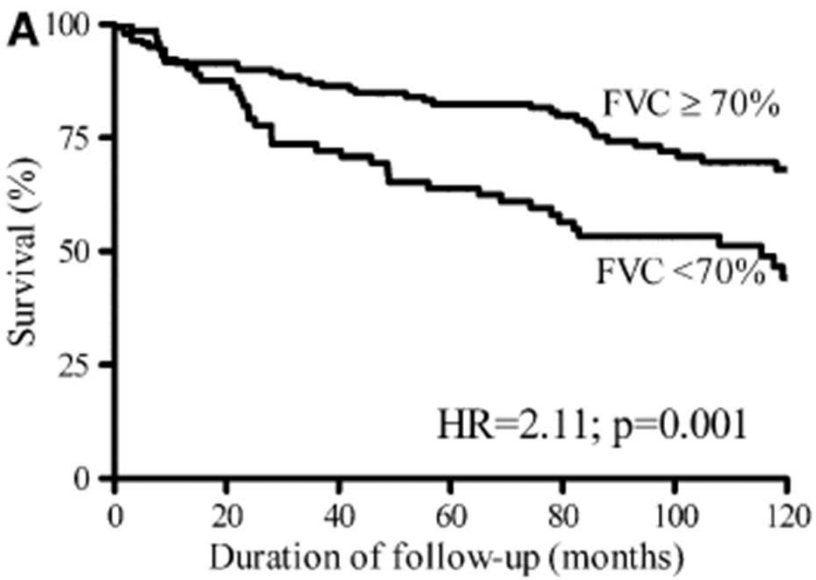


1. Diffusion de l'O_2 à travers la barrière alvéolo-capillaire caractérisée par le facteur membranaire (D_M)

2. Combinaison de l'O_2 avec l'Hb, caractérisée par la vitesse de liaison de l'O_2 à l'Hb (θ) multiplié par le volume capillaire pulmonaire (Vc)

La résistance globale à la diffusion est égale à la somme des deux résistances correspondantes.

Trouble restrictif et CVF



Goh NS, Desai SR et col.

Am J Respir Crit Care Med. 2008 Jun 1;177(11):1248-54

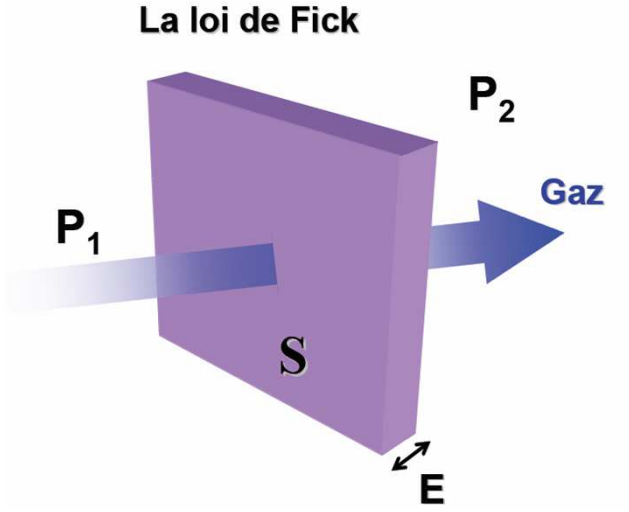
Patterns of pulmonary function in smoking and nonsmoking patients with progressive systemic sclerosis

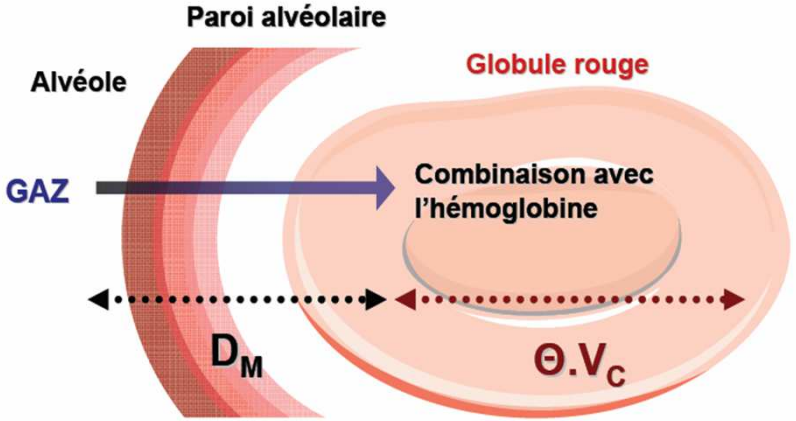
Silvia A. Quadrelli · Luciana Molinari · Lorena M. Ciallella · Martin Bosio · Alejandro Salvado

Item	Smokers (n = 12)	Nonsmokers (n = 34)	P
Age	53.92 ± 13.7	50.24 ± 12	0.383
FVC (% predicted)	78.26 ± 18.2	83.83 ± 15.3	0.350
FEV1 (% predicted)	83.91 ± 21.4	84.33 ± 14.4	0.950
FEV1/FVC (% predicted)	82.10 ± 6.8	78.83 ± 16.9	0.373
TLC (% predicted)	84.12 ± 21.3	97.18 ± 15.2	0.036
RV/TLC (% predicted)	37.44 ± 8.4	48.18 ± 16.3	0.011
DLCO (% predicted)	73.67 ± 21.3	79.92 ± 19.2	0.268

Rheumatol Int. 2009 (E-pub)

Diffusion alvéolo-capillaire
DLCO et ses composantes





$$\frac{1}{D_L} = \frac{1}{D_M} + \frac{1}{\theta . V_C}$$

$$Débit\ de\ gaz\ diffusé\ \dot{V} = DL \times \Delta P$$

$$Où\ DL \propto \frac{S}{E} \times \frac{Sol}{\sqrt{Pm}}$$

$$Capacité\ de\ diffusion\ DL = \frac{\dot{V}}{\Delta P}$$

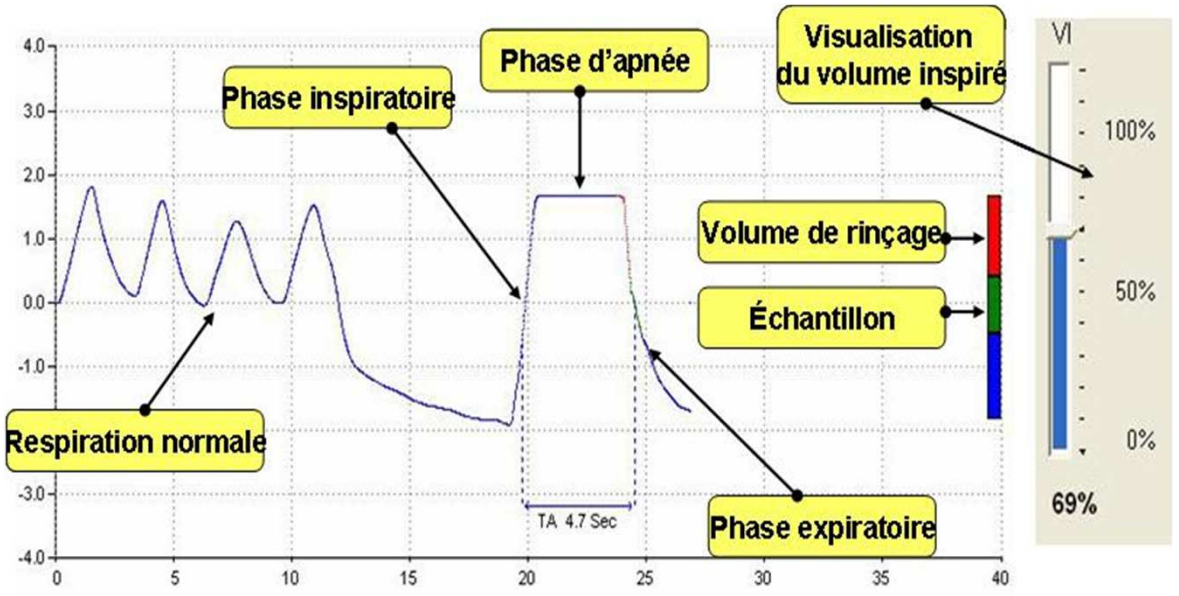
DL - Capacité de diffusion pour un gaz

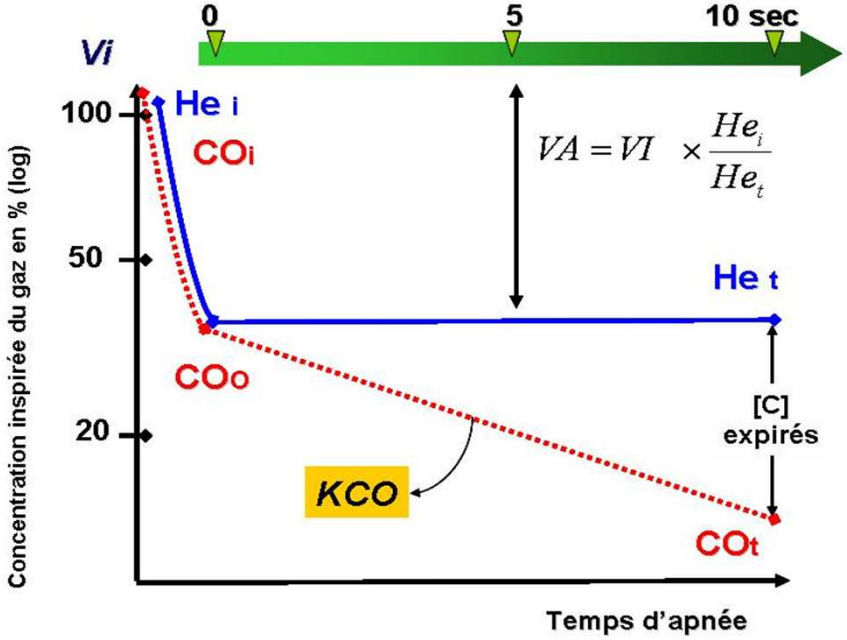
Dm - Conductance membranaire

Théta - Vitesse de capture spécifique par l'hémoglobine

Vc - Volume capillaire


DLCO


Phase inspiratoire
Phase d'apnée
Visualisation du volume inspiré
Volume de rinçage
Échantillon
Respiration normale
Phase expiratoire
TA 4.7 Sec
VI
100%
50%
0%
69%


Vi
0
5
10 sec
He i
COi
VA = VI × He_i / He_t
He t
COo
[C] expirés
KCO
COt
100
50
20
Concentration inspirée du gaz en % (log)
Temps d'apnée

DLCO = KCO x VA

Dm et Vc

CO $$\frac{1}{DLCO} = \frac{1}{DmCO} + \frac{1}{\theta_{CO} \times Vc}$$

NO $$\frac{1}{DLNO} = \frac{1}{DmNO} + \frac{1}{\theta_{NO} \times Vc}$$

$$\Rightarrow DLNO = DmNO$$

Affinité et vitesse de réaction

$$NO - Hb >> CO - Hb$$

$$\Rightarrow \frac{1}{\theta NO} >> \frac{1}{\theta CO}$$

CO $$DmCO = \frac{S}{E} \times \frac{\alpha CO}{\sqrt{PmCO}}$$

NO $$DmNO = \frac{S}{E} \times \frac{\alpha NO}{\sqrt{PmNO}}$$

$$\rightarrow \frac{DmNO}{DmCO} = \sqrt{\frac{PmCO}{PmNO}} \times \frac{\alpha NO}{\alpha CO}$$

coefficient $a \approx 1{,}97$

$$DLNO = DmNO = DmCO \times a$$

Dm

$$DLNO = DmCO \times a$$

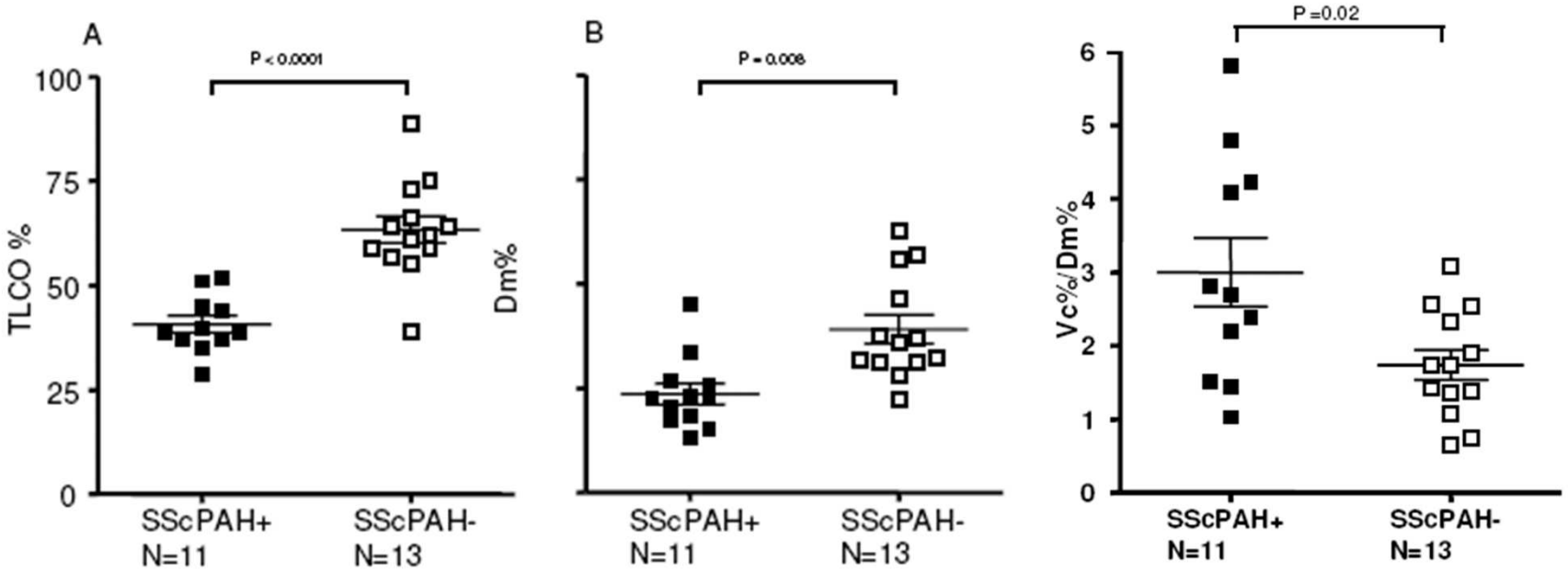
$$\Rightarrow DmCO = \frac{DLNO}{a}$$

Vc

$$\frac{1}{DLCO} = \frac{1}{DmCO} + \frac{1}{\theta_{co} \times Vc}$$

$$\Rightarrow Vc = \frac{1}{\left[\frac{\theta_{CO}}{DLCO} - \frac{\theta_{CO}}{DmCO}\right]}$$

Dm et Vc



Overbeek MJ et col.

Respir Res. 2008 Oct 1;9:68

Test de marche de 6 minutes

Paramètres

Distance parcourue en 6 minutes

Saturation en O_2
(capteur frontal / Syndrome de Raynaud)

Niveau de dyspnée: Indice de Borg

± gaz du sang : PaO_2, lactate,…

Variables	Résultats
Distance parcourue (Médian) m	450 (150–660)
Patients dont la Distance < 400 m, No.(%)	31 (28%)
Patients avec une désaturation ≥ 4%, No. (%)	31 (28)
% de désaturation moyenne chez les patients avec ΔSat ≥ 4%	6,87 %
% de désaturation moyenne chez les patients avec ΔSat ≥ 4%	0,57 %

Villalba et al. Chest 2007; 131: 217-22.

3. EXERCISE VARIABLES AND THEIR REPRODUCIBILITY IN PATIENTS WITH CT FEATURES TYPICAL OF IPF

	Exercise Indices Given as Mean (SD) Values	SD_{diff}	SD_{diff}/Mean Value (%)
6-Minute walk (n = 17)			
Resting Borg dyspnea score*	0 (0–3.5)	Kw = 0.73†	NA
Post-Borg dyspnea score*	3.2 (1.7)	Kw = 0.82†	NA
Distance, m	398.9 (136.5)	16.5	4.1
O_2 desaturation	10.4 (5.2)	2.6	25.0
Desaturation to 88% or lower	NA	K = 1.00*	NA
Maximal exercise testing (n = 13)			
Vo_2max, % pred	59.5 (21.1)	7.2	12.1
Post-Borg dyspnea score*	3.6 (2.5)	Kw = 0.81†	NA
O_2 desaturation	9.3 (4.6)	2.8	30.1
O_2 desaturation, adjusted for Vo_2max	17.1 (10.3)	6.9	40.4

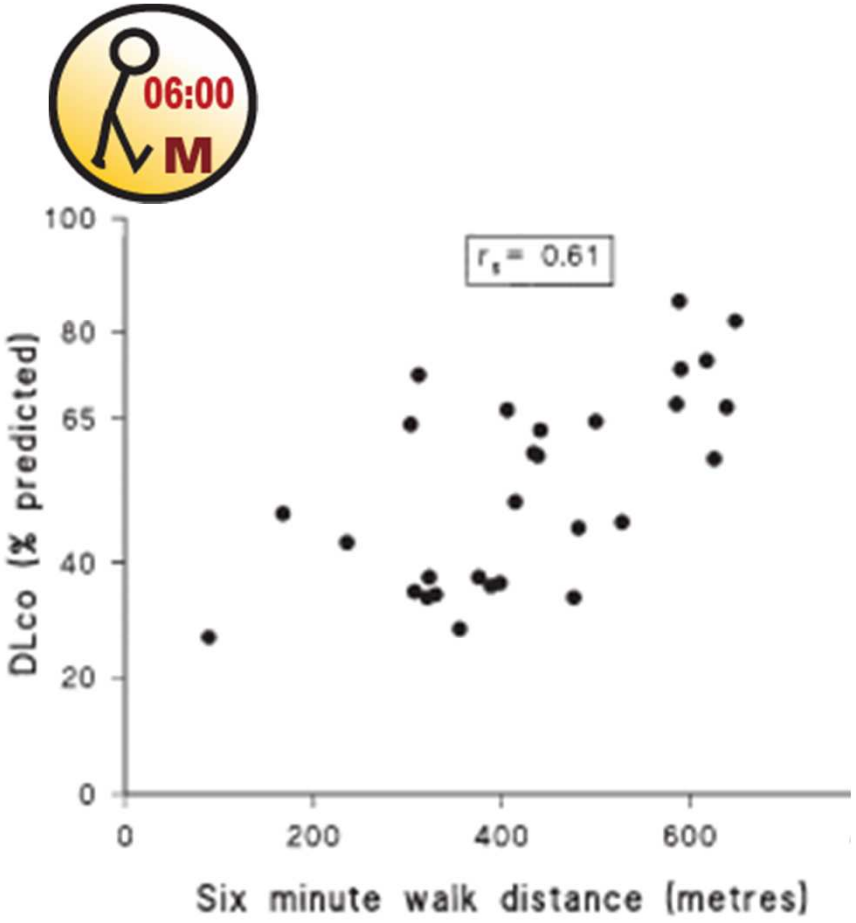
Definition of abbreviations: CT = computed tomography; IPF = idiopathic pulmonary fibrosis; K = nonweighted κ coefficient of agreement; Kw = weighted κ coefficient of agreement; NA = not applicable; SD_{diff} = SD of differences between measurements.

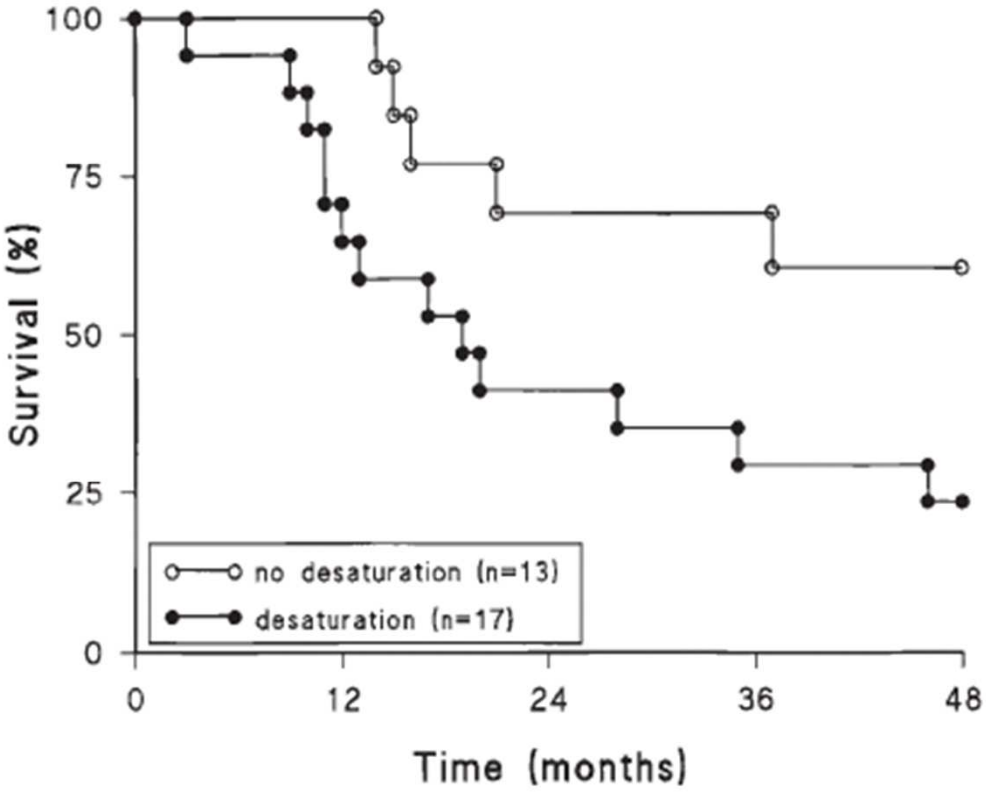
Variables are expressed as the mean of two measurements, the SD_{diff} between the two measurements, given as absolute values and as percentages of the mean of the two measurements in 17 patients with high-resolution computed tomography appearances typical of idiopathic pulmonary fibrosis.

* The reproducibility of desaturation to 88% or lower during the 6-minute walk is stated as the (nonweighted) κ coefficient of agreement (K).

† The reproducibility of Borg dyspnea scores is stated as the weighted κ coefficient of agreement (Kw).

Eaton et al. Am J Respir Crit Care Med 2005; 171: 1150-7.





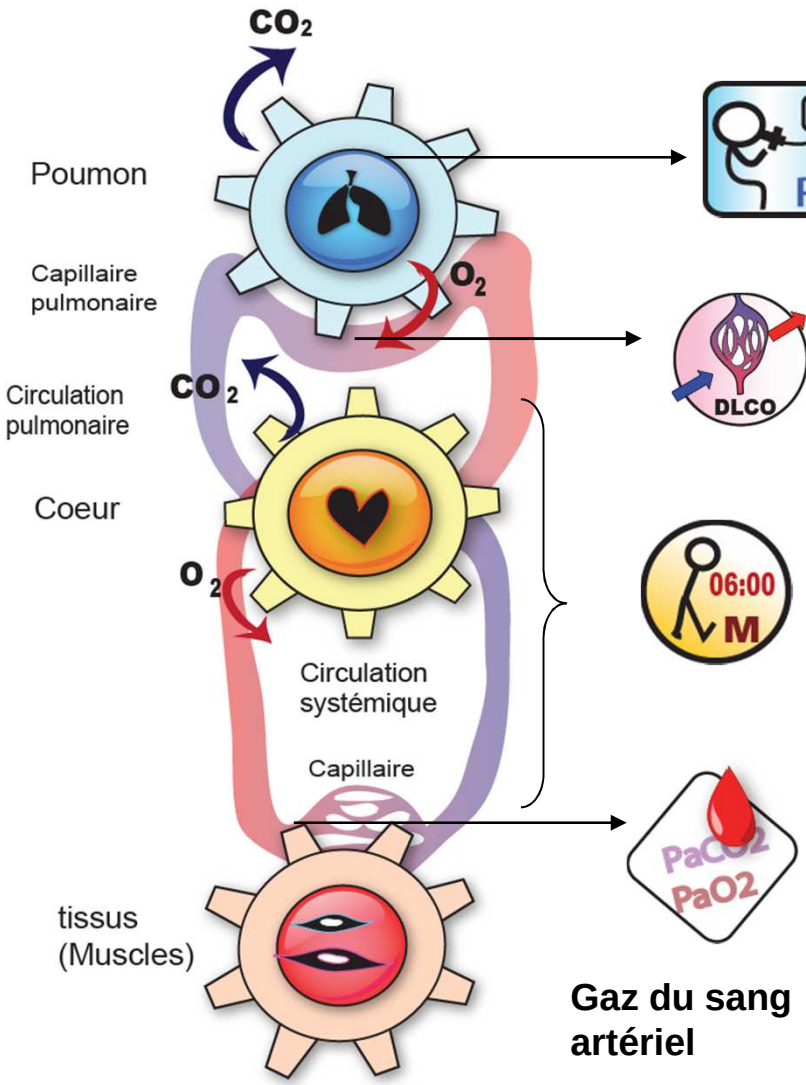
Eaton et al. Am J Respir Crit Care Med 2005; 171: 1150-7.

Variables	Walk Distance p Value	ΔSat p Value
Sexe	0.34	1.00
Race	0.72	0.34
Age	**0.008***	**0.02***
Durée de la maladie	0.84	0.95
Anticorps Antinucléaires	0.11	0.21
Anti-Scl-70	0.20	**< 0.001***
Dyspnée	**0.003***	**< 0.001***
Radio thoracique (fibrose)	**0.05***	**< 0.001***
CVF < 80%	0.15	**< 0.001***
CT ground-glass opacity	0.88	0.02*
PASP	**0.036***	0.01*
Désaturation	**< 0.001***	-
Distance	-	**< 0.001***

Six-minute walk test for the evaluation of pulmonary disease severity in scleroderma patients.

Villalba et al. Chest 2007; 131: 217-22.

Pourquoi explorer ?



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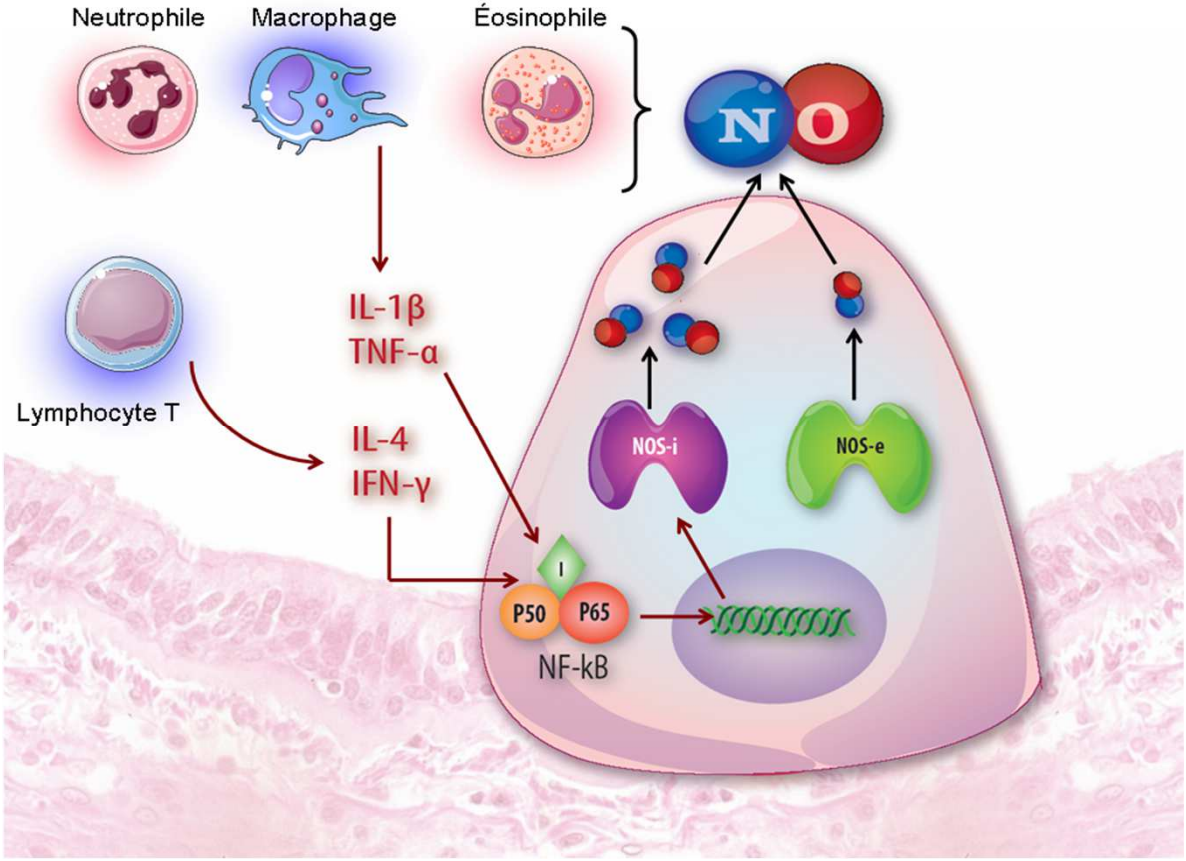
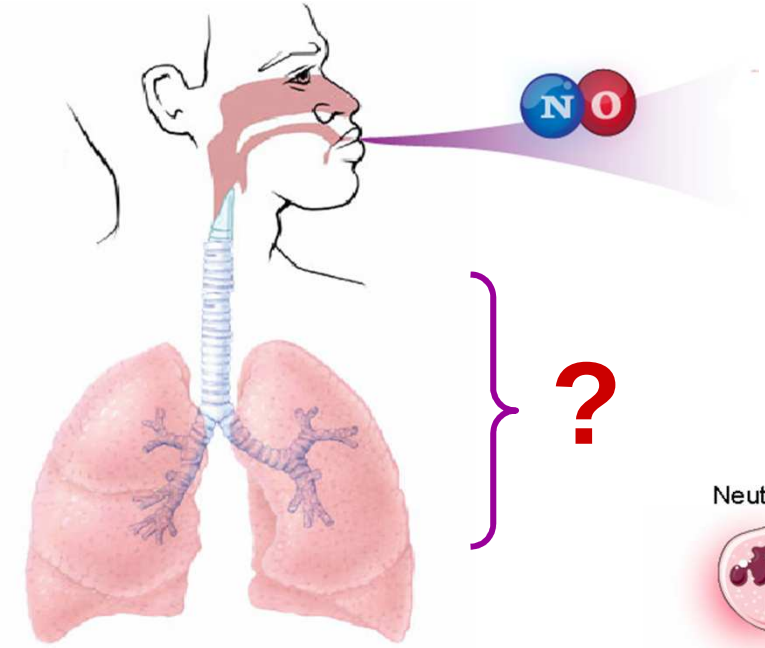
Evaluation de l'état inflammatoire : par la mesure du NO exhalé





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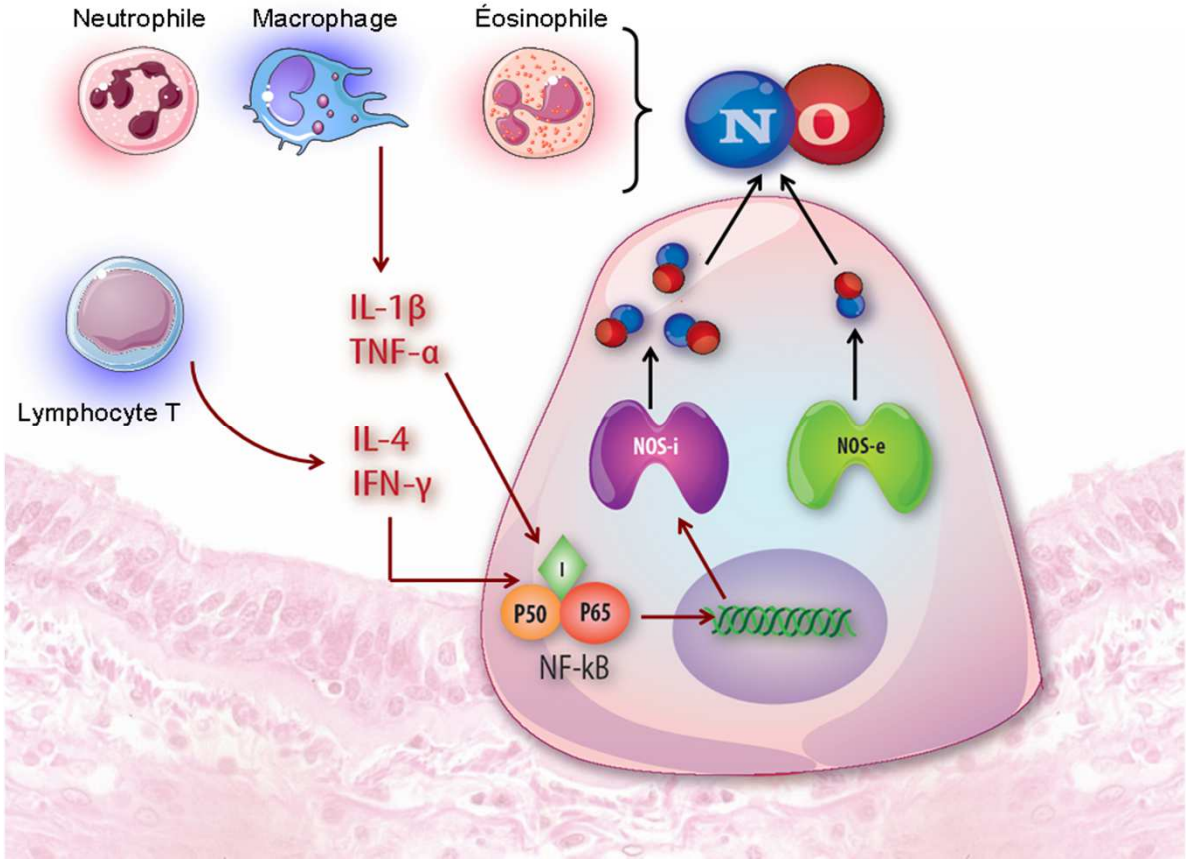
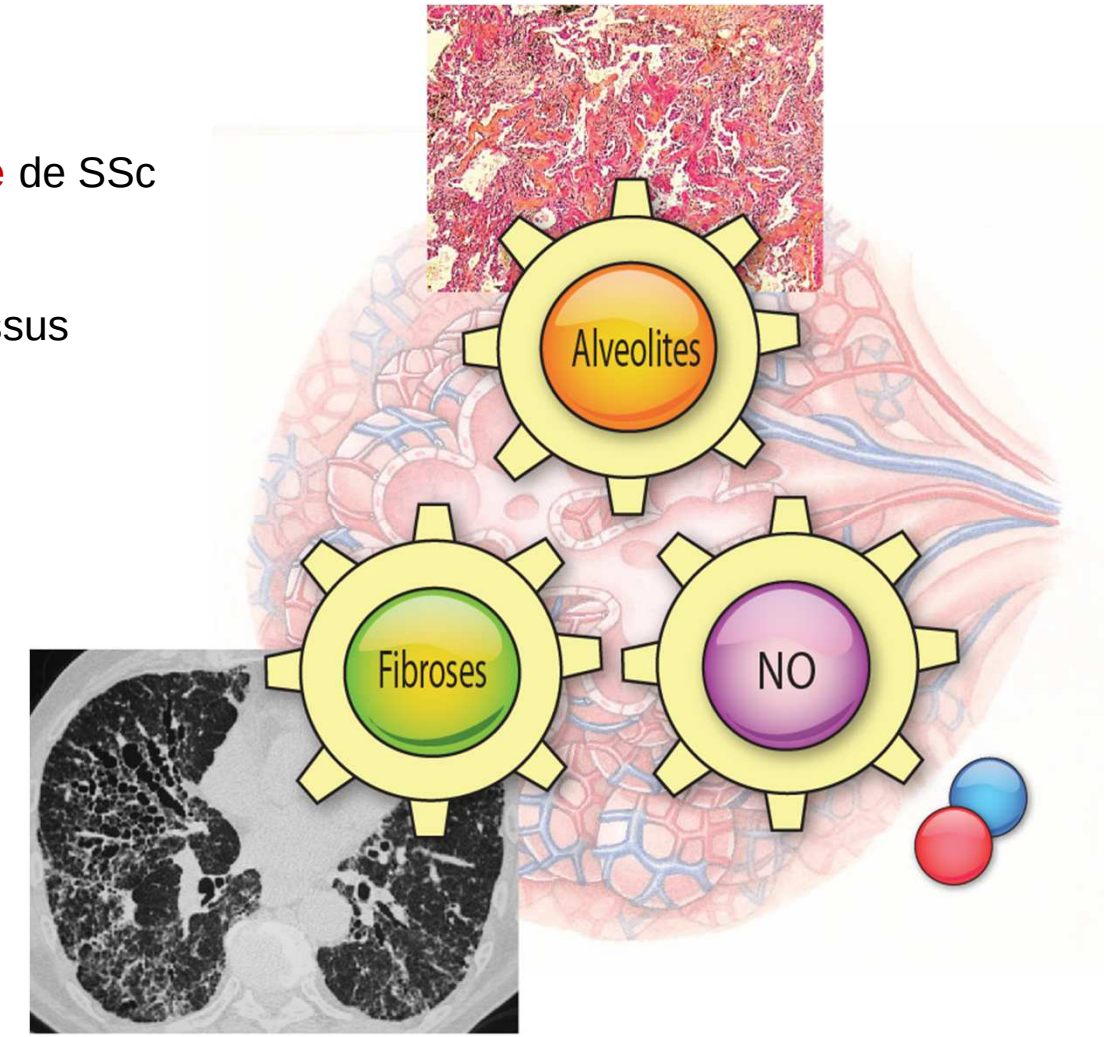
Evaluation de l'état inflammatoire : Par NO exhalé



Evaluation de l'état inflammatoire : par la mesure du NO exhalé

Physiopathologie de SSc

Inflammation
Destruction des tissus
Fibroses



Evaluation de l'état inflammatoire par la mesure du NO exhalé

Physiopathologie de SSc

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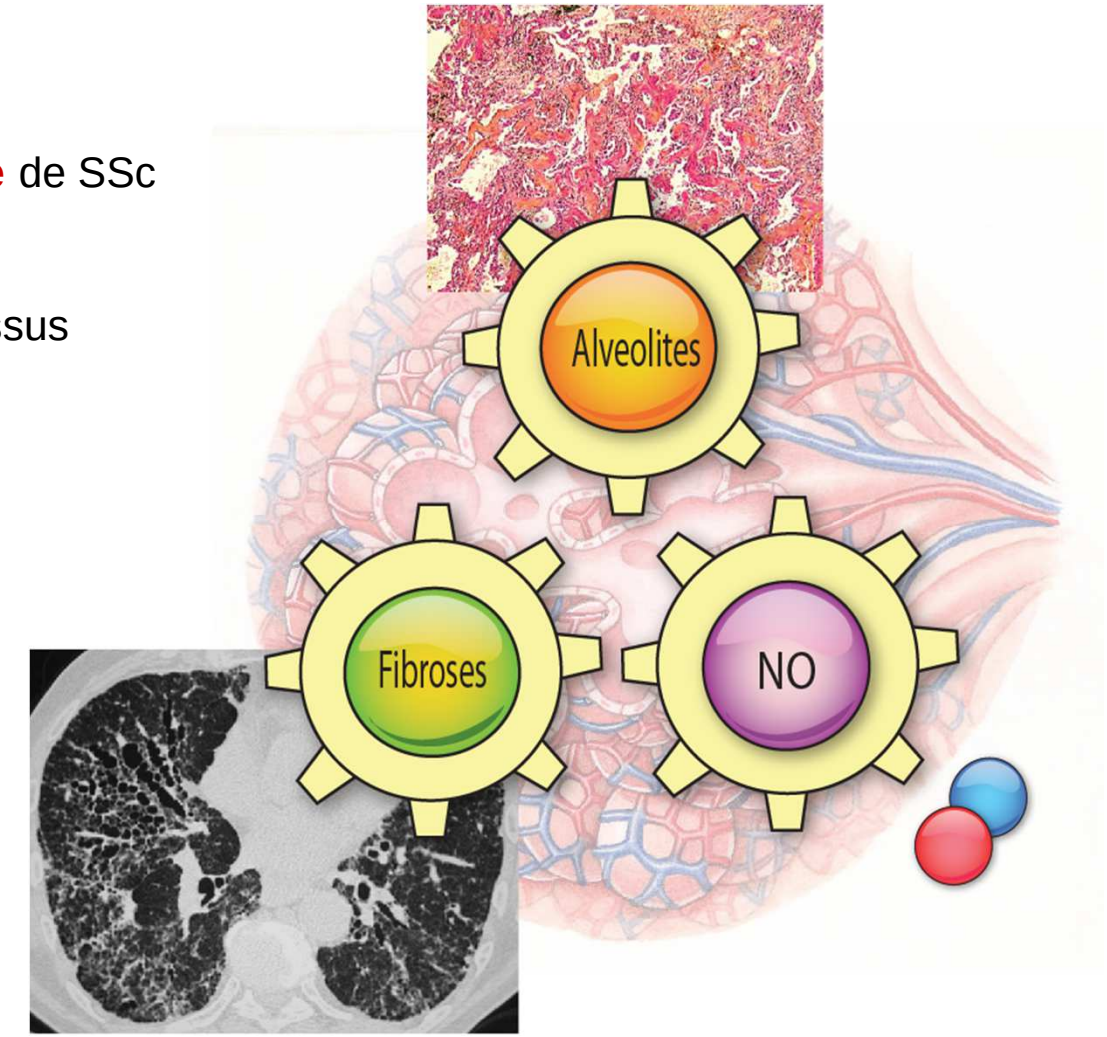
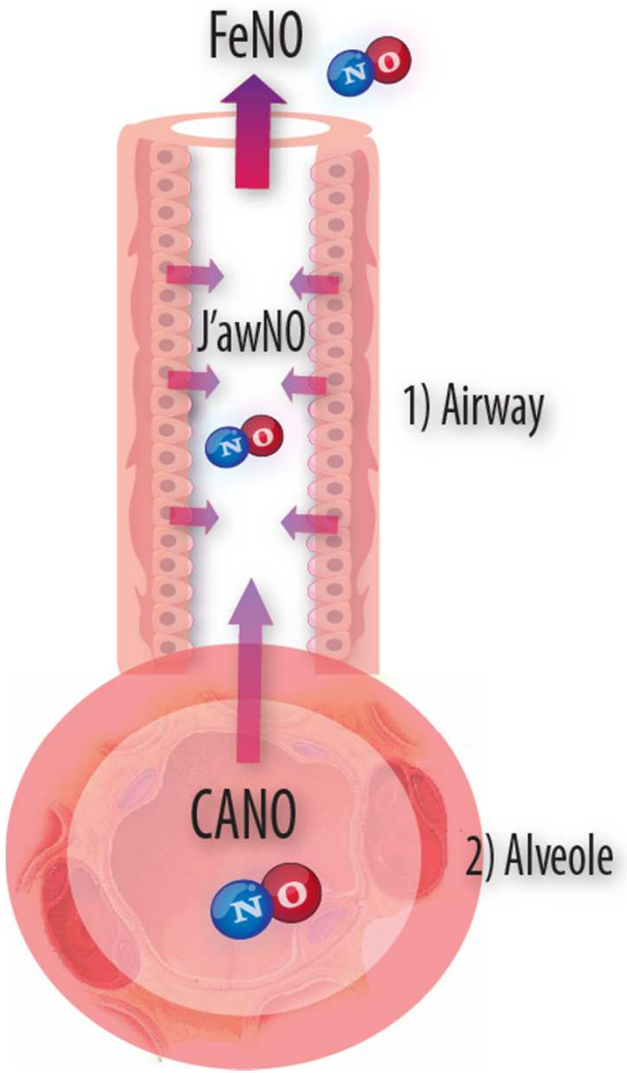
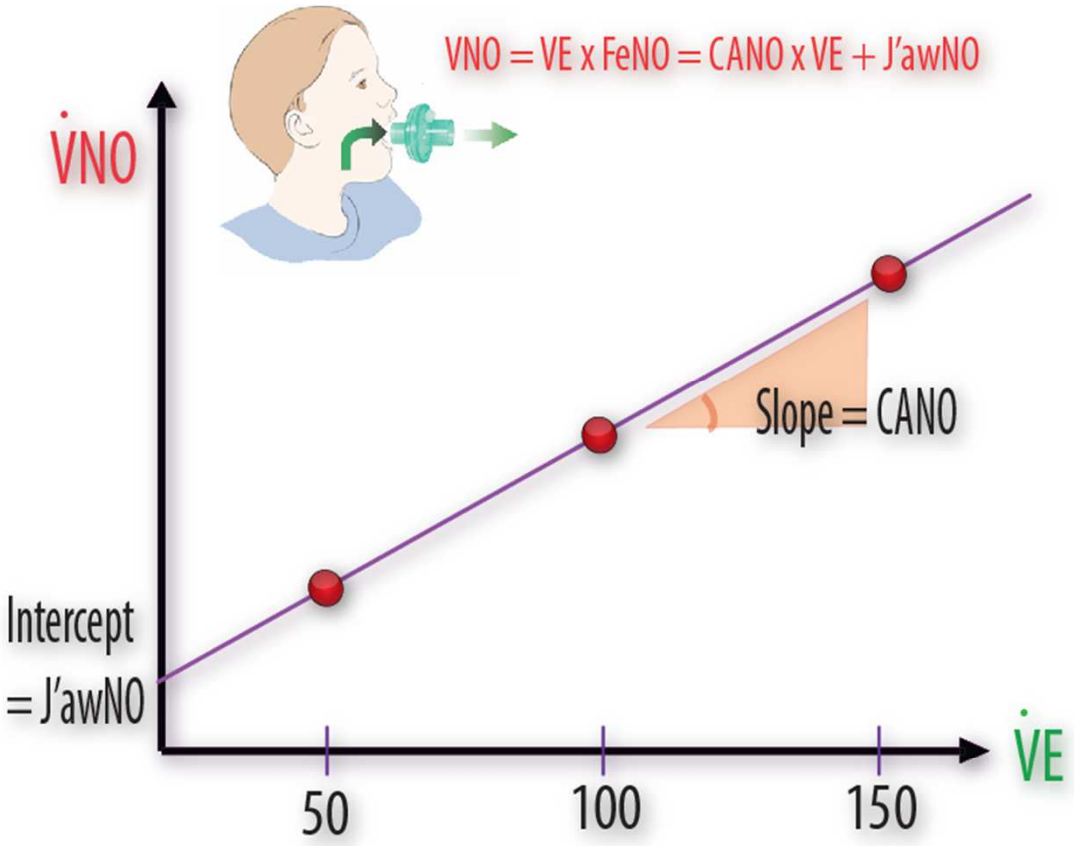
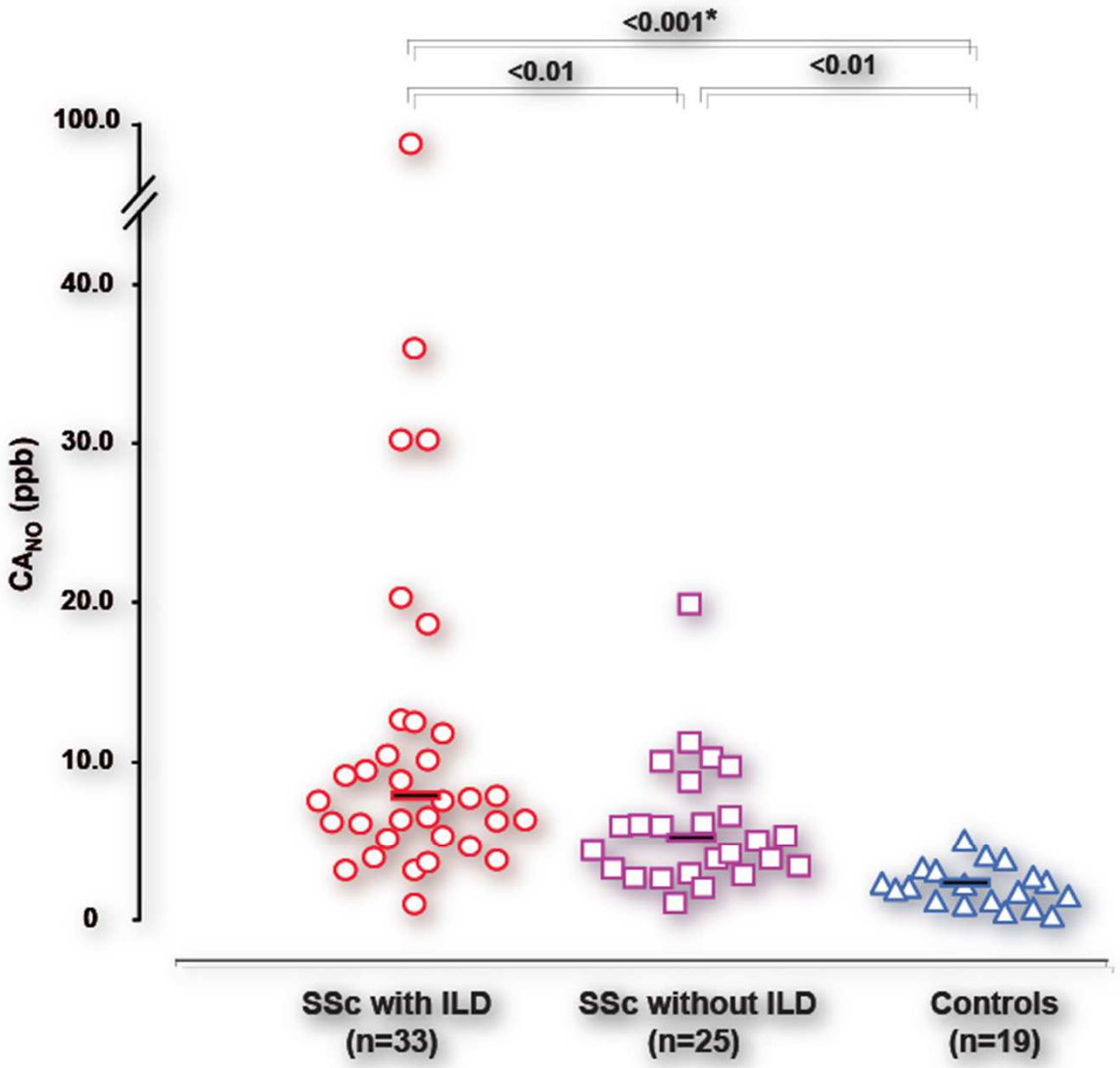


Modèle de 2 compartiments

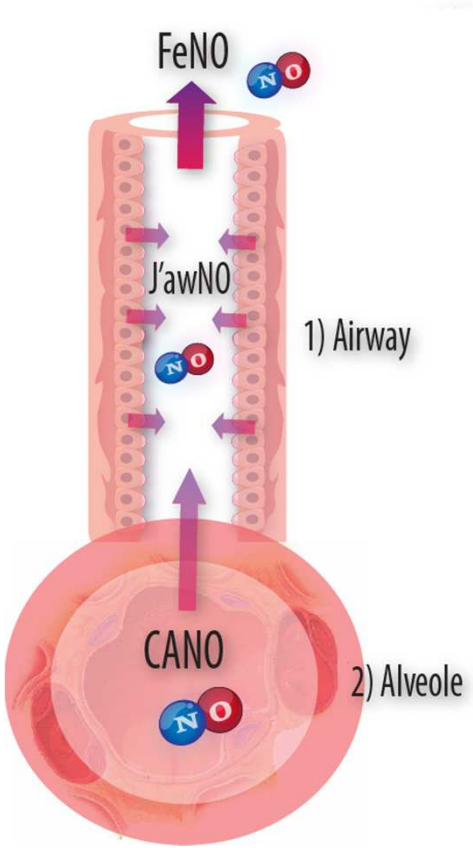


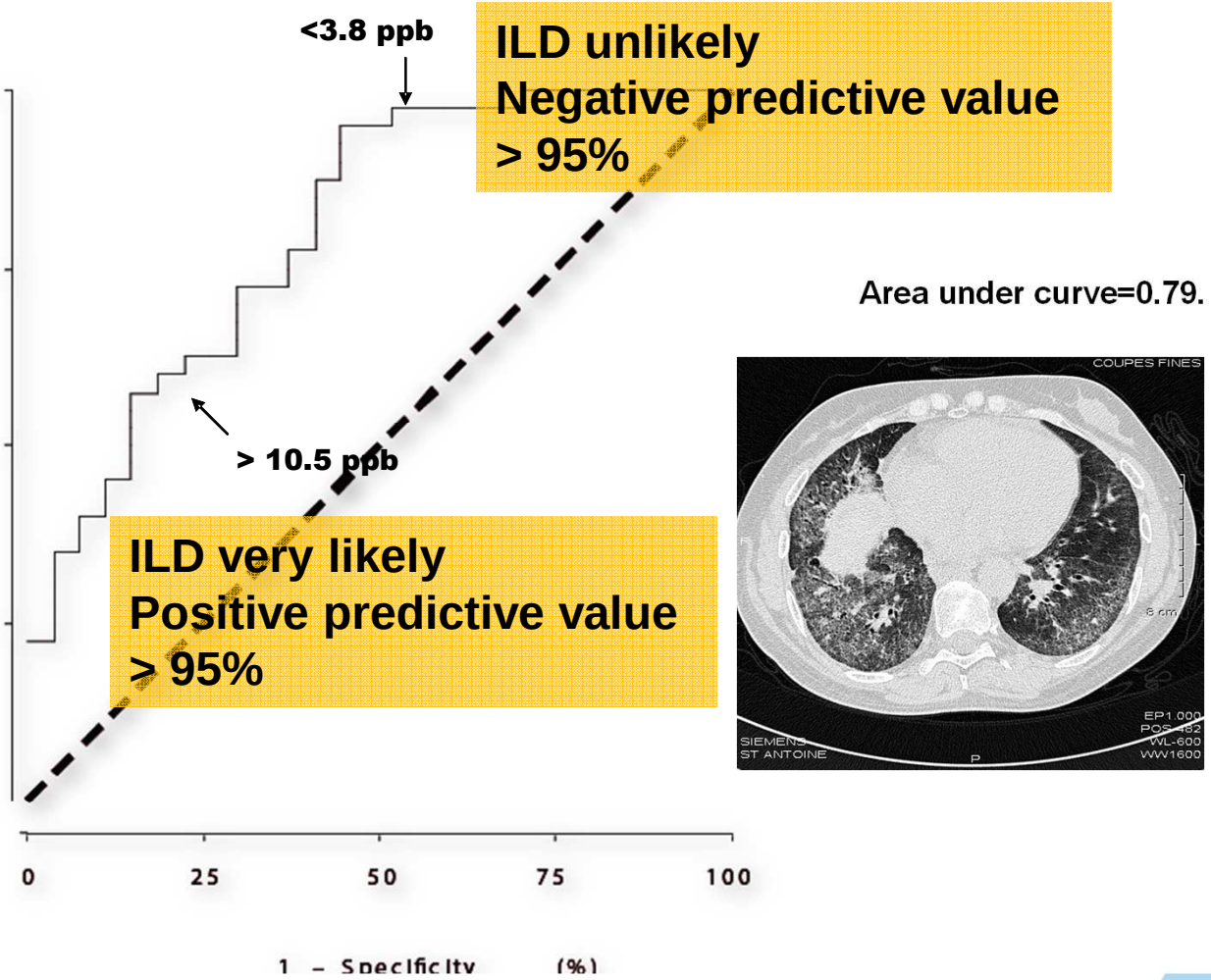


Tsoukias & George. JAP 1998; 85: 653-66.



Tiev et al. Eur Respir J 2007; 30: 26-30

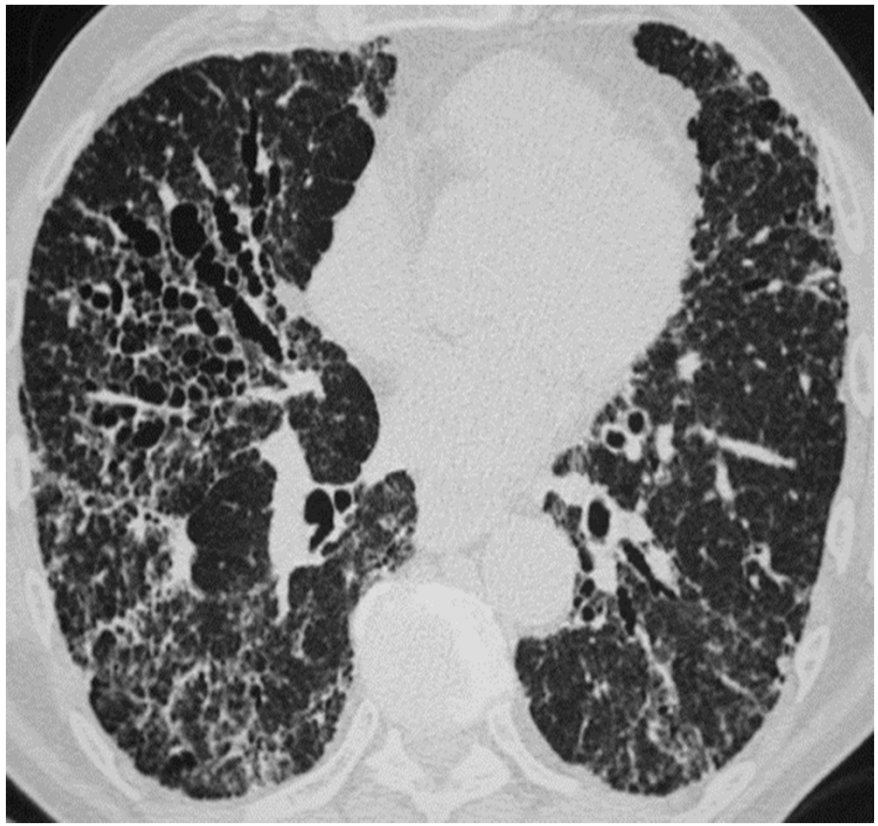




Tiev et al. Sarcoidosis Vasc Diffuse Lung Dis 2009; 26: 32-8**.**

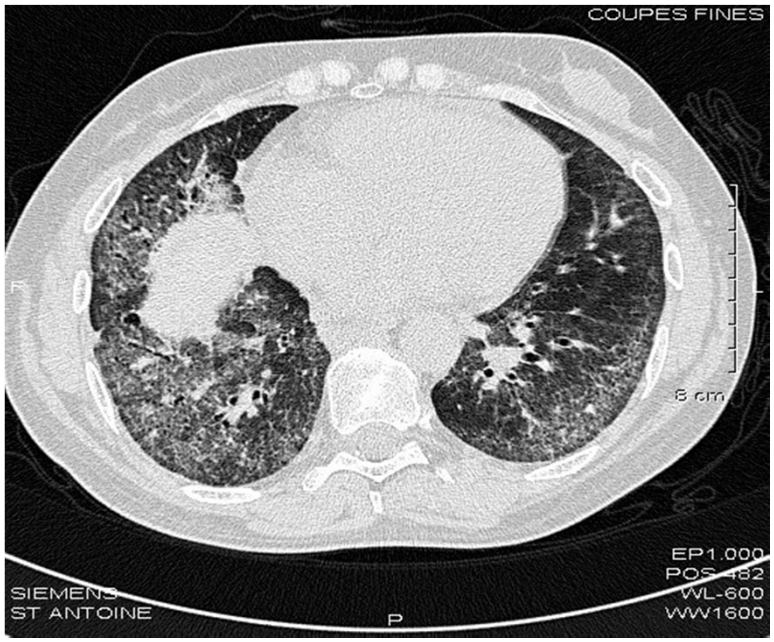
Cytokines involved in scleroderma ILD

Lymphocyte	**IL-2**
	IL-4
	IL-5
	INF–γ
Macrophage	**IL-8**
	TNF-α
	Fibronectine
	PDGF, IGF-1
	TGF-β



Results

C_ANO and TLC	- 0.37	p<0.01
C_A NO and DLCO	- 0.34	p<0.01
C_A NO and lung fibrosis Score	0.39	p<0.01



Tiev et al. Eur Respir J 2007; 30: 26-30.

Interim conclusion

- Increased alveolar concentration of nitric oxide (C_{ANO}) is related to the severity of interstitial lung disease (ILD) in systemic sclerosis (SSc).

- However, cutoff levels of C_{ANO} to rule in, or to rule out, the presence of ILD in individual patients are unknown.

Tiev et al. Am J Respir Crit Care Med 2008; 177: A45.

Subjets & Methods

- **Sera** from 40 SSc patients and 10 healthy controls.
- **Pulmonary fibroblast proliferation** was assessed by BrdU labeling index at 72h of culture.
- **Myofibroblast conversion** was detected by α-smooth muscle actin expression.

Hua-Huy et al. Am J Respir Crit Care Med 2008; 177: A45.

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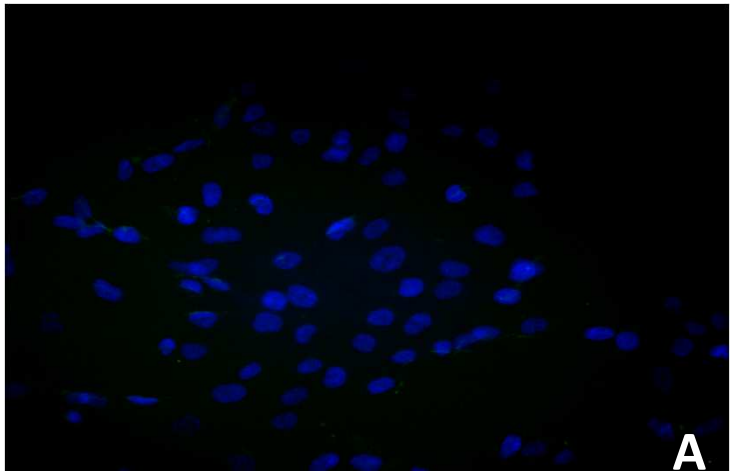
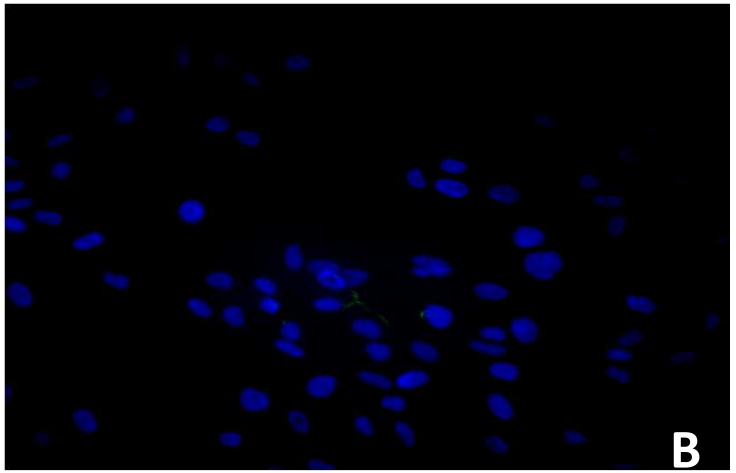
Immunofluorescence staining of α-smooth muscle actin

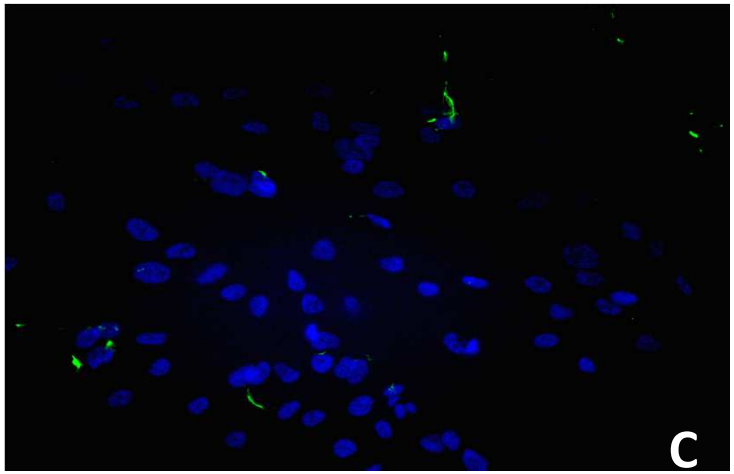
Negative control (FBS)



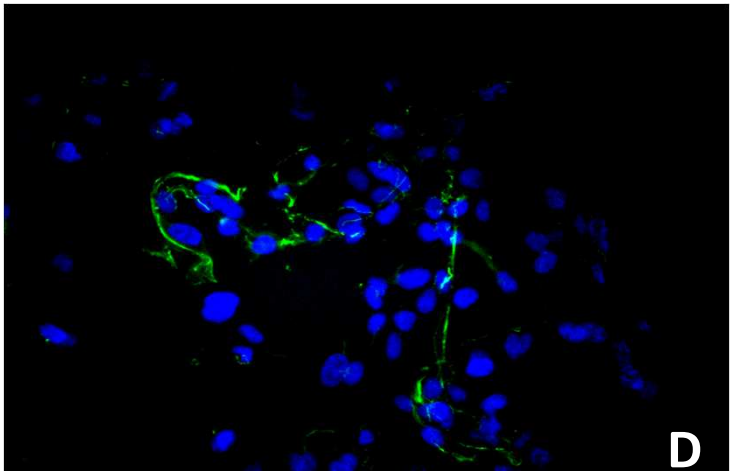
Healthy subjects



Patients with $C_ANO \leq 5ppm$

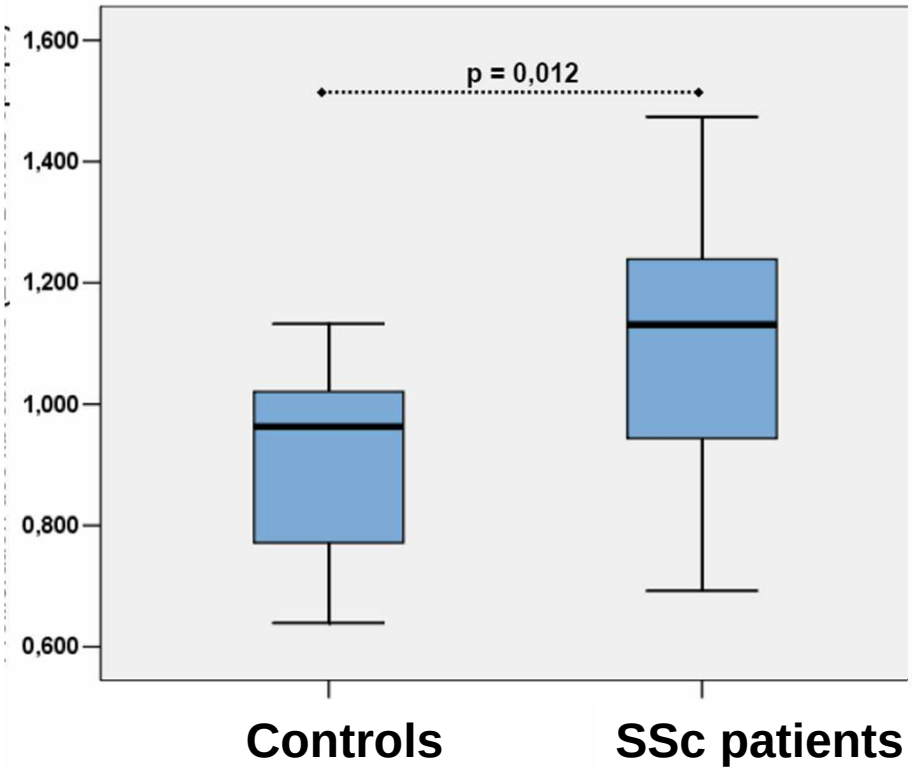


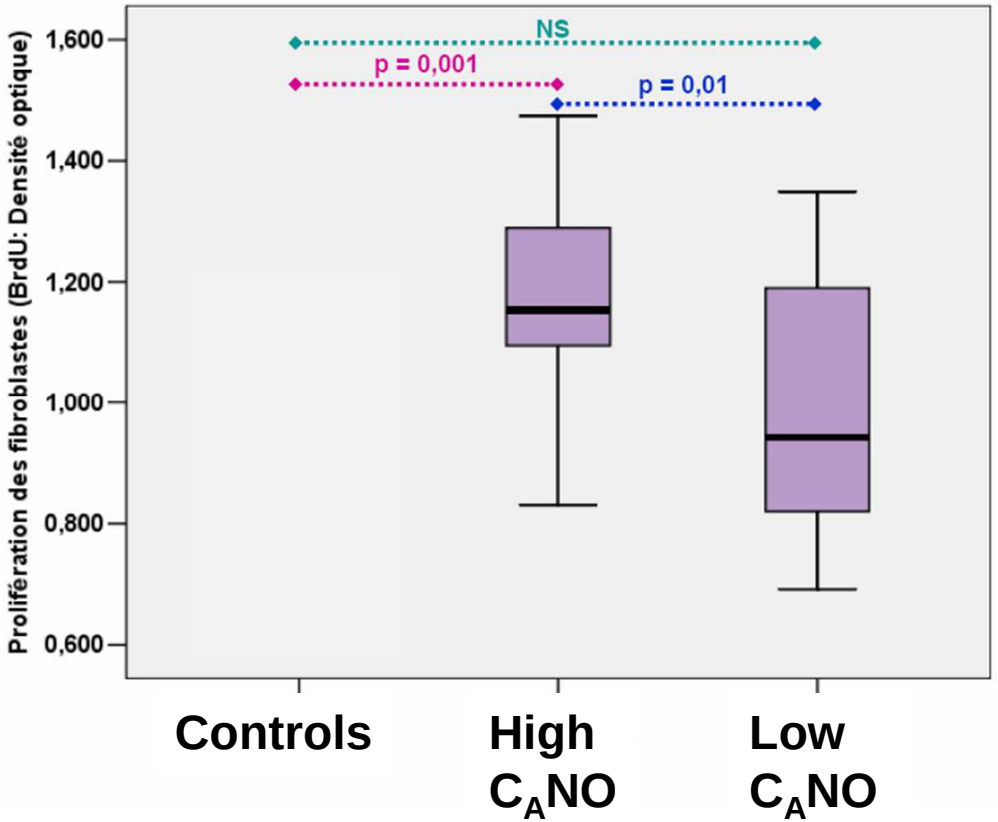
Patients with $C_ANO > 5ppm$



Hua-Huy et al. J Rheumatol 2010; 37: 1680-7.

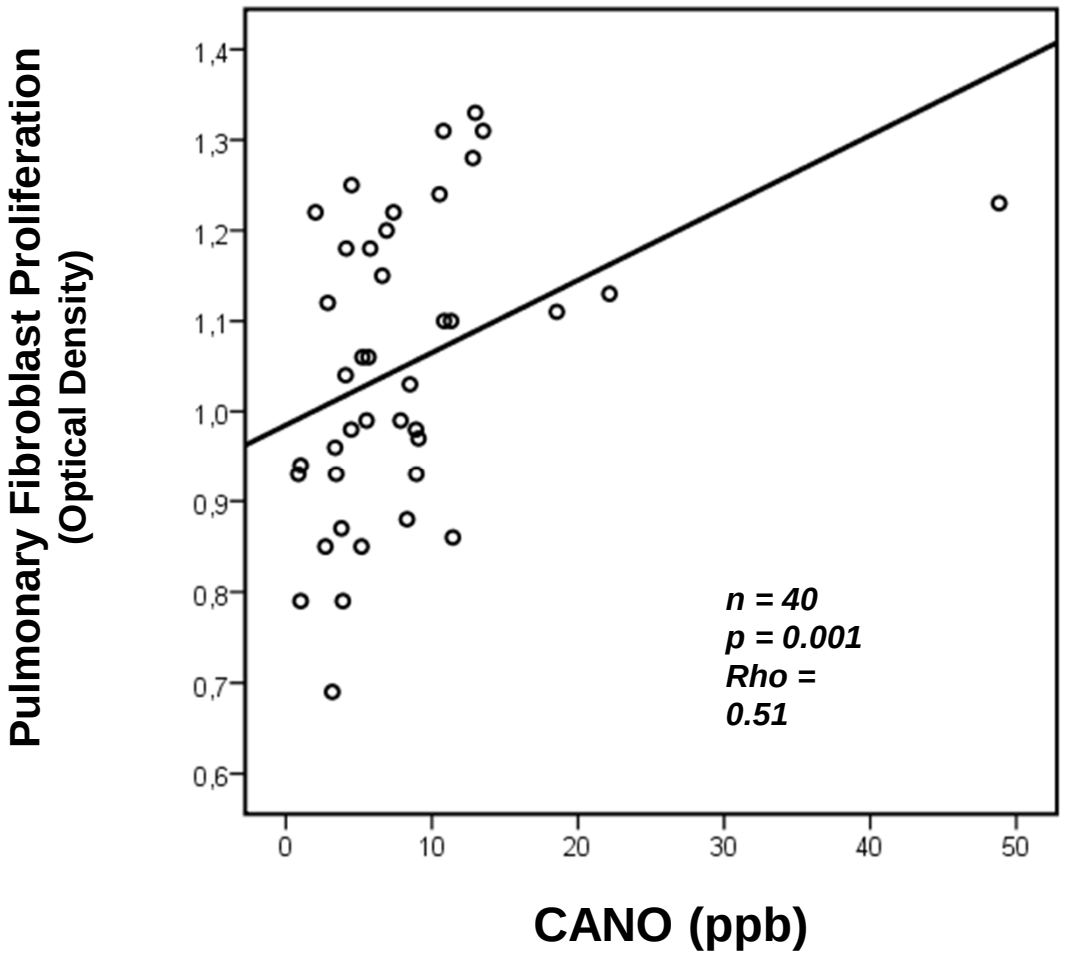
Results



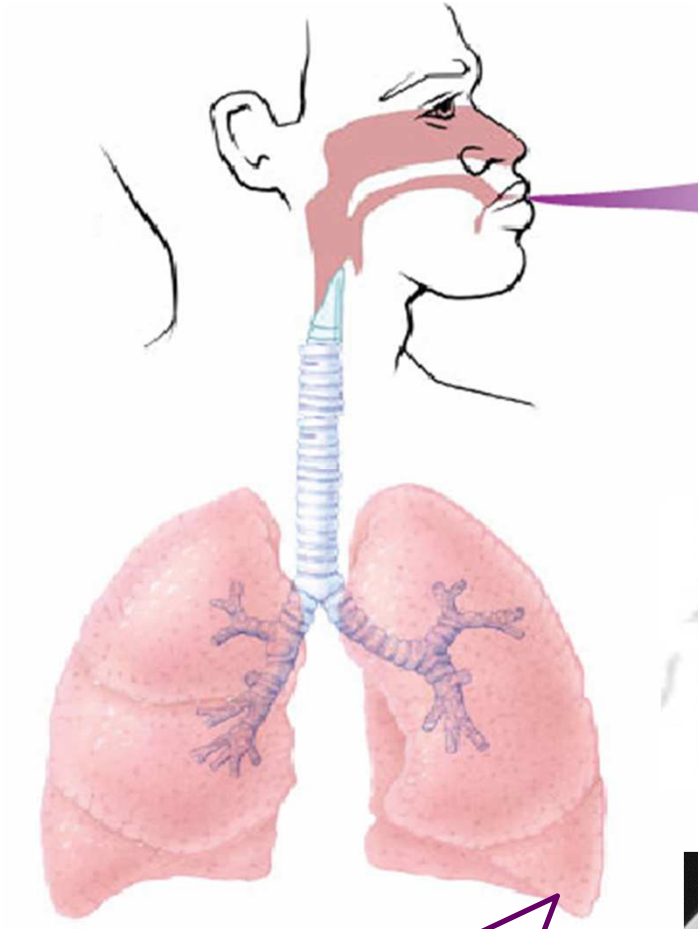


Hua-Huy et al. J Rheumatol 2010; 37: 1680-7.

Correlation between C_ANO and pulmonary fibroblast proliferation

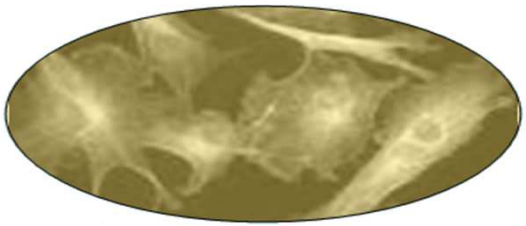


Hua-Huy et al. Am J Respir Crit Care Med 2008; 177: A45.



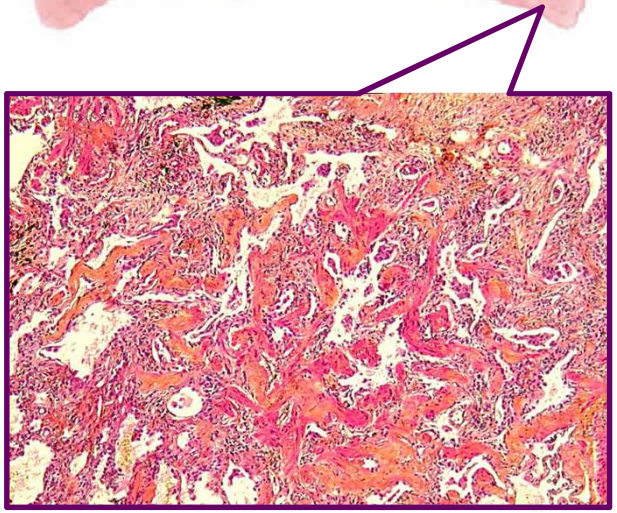
NO

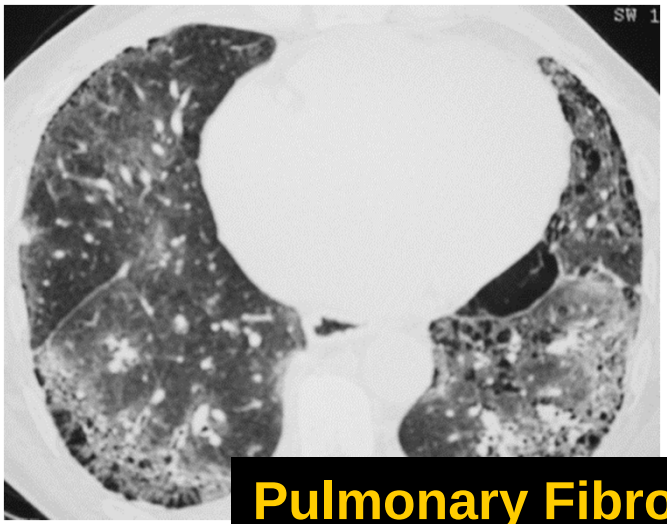
?



Lung Fibroblasts Proliferation

Impaired Lung function





Pulmonary Fibrosis