

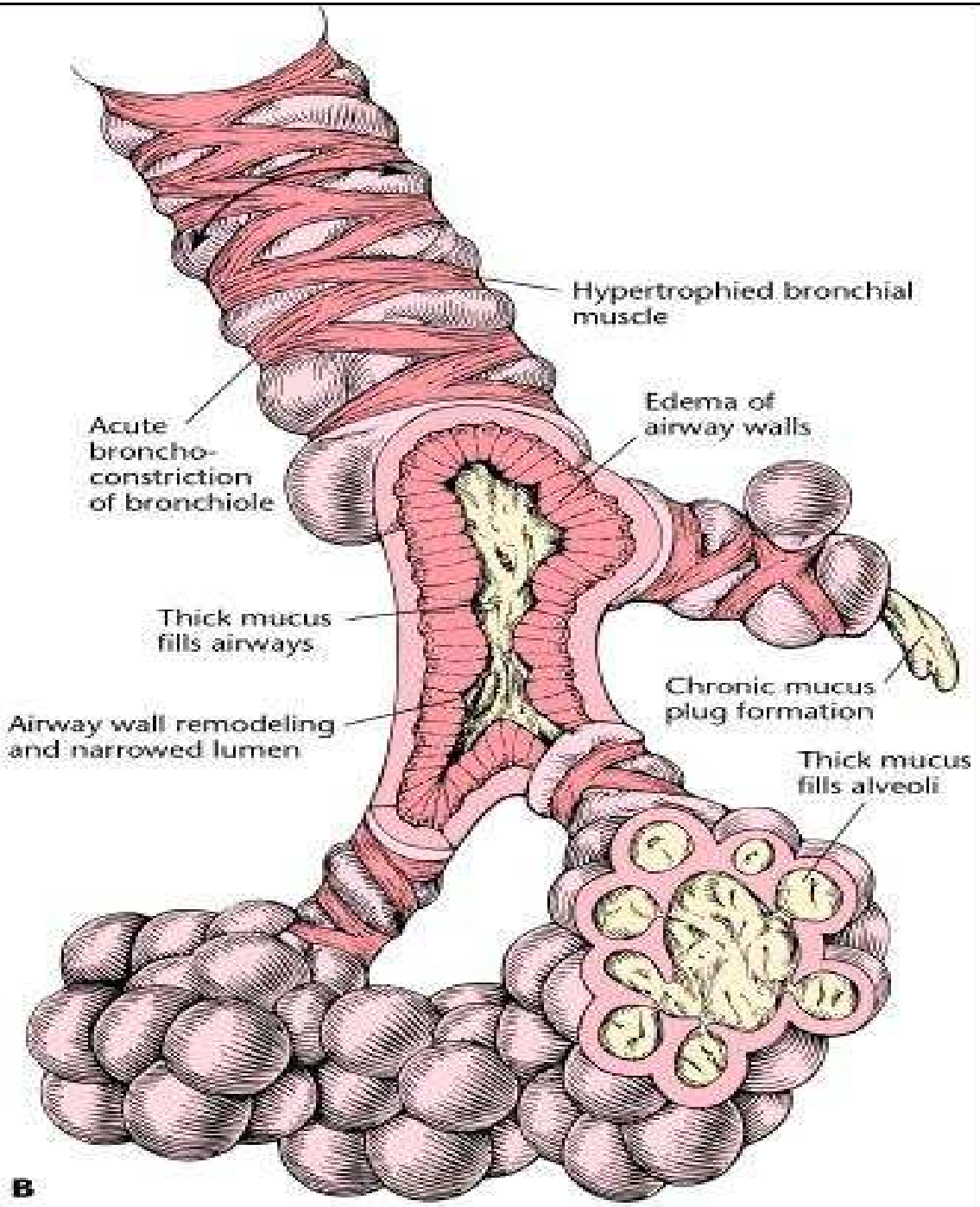
L'articolo dell'anno sulla patologia respiratoria

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Small Airway Disease in Asthma and COPD

Clinical Implications

Maarten van den Berge et al.

Department of Pulmonology, University

Medical Center Groningen, University of Groningen,
Groningen, The Netherlands .

CHEST 2011; 139(2): 412 - 423

Nonostante l'importanza delle piccole vie aeree nell'asma, il numero di studi riguardante la loro patologia è sorprendentemente scarso, ciò è dovuto con molta probabilità alla inaccessibilità di tale sito anatomico.

CHEST 2011; 139(2): 412 - 423

Table 1—Overview of Lung Function Tests for SA Obstruction

Lung Function Test	Able to Detect SA Abnormality	Reproducibility	Burden on Patients
Δ FVC at PC ₂₀	Closely related to: -disease severity ^{8,16} -MCh-induced air trapping (CT scan) -maximal airway response (gas trapping) ⁹	Reproducibility comparable to PC ₂₀ ⁸ 1-wk reproducibility good	Bronchial challenge test Performing complete FVC maneuver twice at each dose is strenuous Relatively time-consuming (20-60 min)
FVC/SVC	Detects and monitors SA disease in BOS after lung transplantation ¹²	Poor 1-wk reproducibility	Noninvasive Low cost, not time-consuming (5 min)
<u>FEF_{25%-75%}</u>	Closely related to: -Air trapping (CT scan) ^{17,18} -FEF _{25%-75%} is often normal when FEV ₁ /FVC \geq 75% ¹⁹	Within-subjects variance 5% in healthy subjects (vs 3% for FEV ₁) ²⁰	Noninvasive Low cost Not time-consuming (5 min)
<u>Impulse oscillometry</u>	Closely related to: -FEF _{25%-75%} ²¹ -MCh-induced changes in ventilation heterogeneity ²²	Fair reproducibility (< 95% CI for natural variability) ²³	Noninvasive Relatively low cost Relatively time-consuming (30 min)
SBNW test: closing volume	Closely related to: -Alveolar NO in severe asthma ²⁴ Closing volume is increased in patients with recurrent exacerbations ²⁵	Poor 1-wk reproducibility Small interobserver variability	Noninvasive Relatively low cost Difficult measurement to perform without flow restrictor

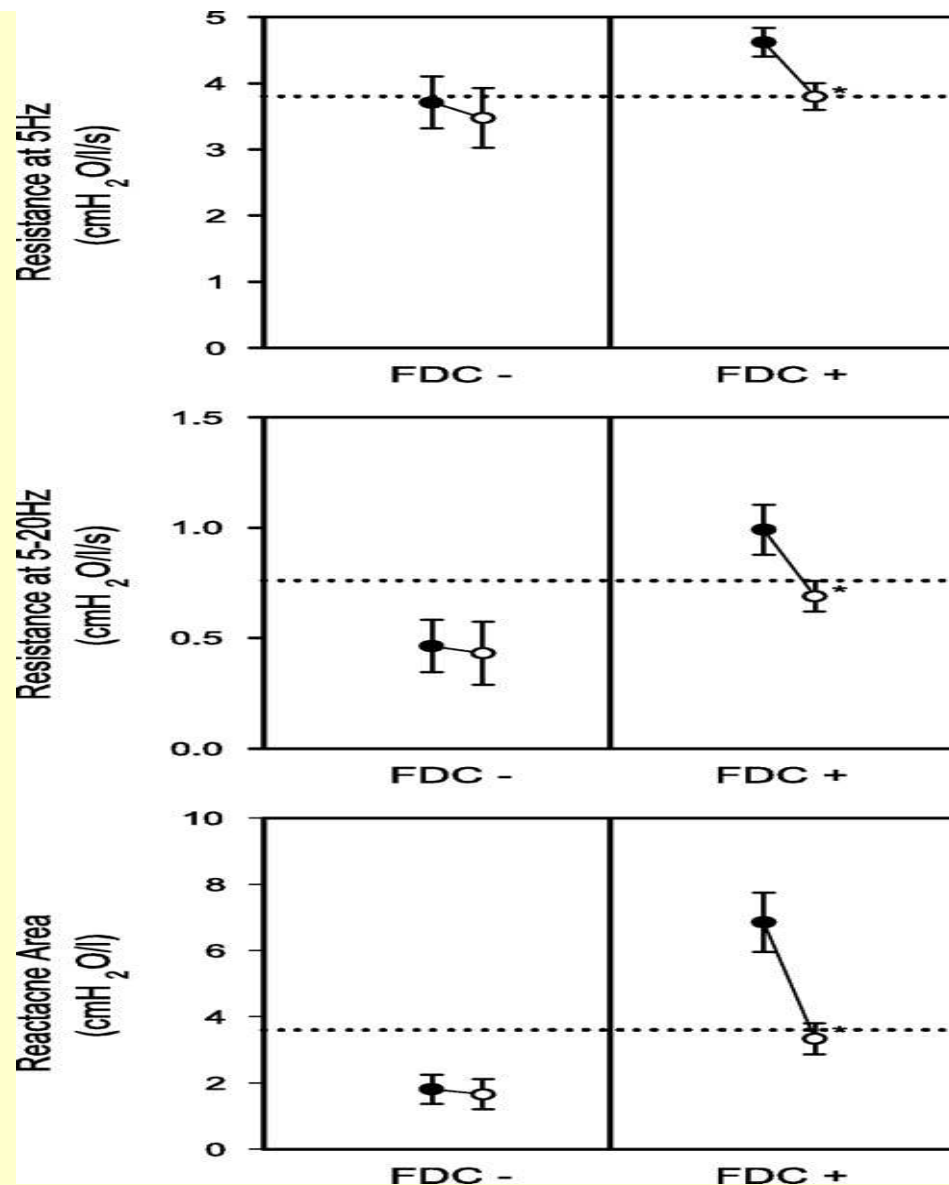
Impulse oscillometry versus
Assessment of respiratory
mechanics over time with
oscillometry might offer
additional insights into the
response of asthmatic patients
to therapy

Distal Airway Function in Symptomatic Subjects With Normal Spirometry Following World Trade Center Dust

Exposure *Beno W. Oppenheimer, et al. CHEST 2007; 132:1275-1282)*

One hundred seventy-four subjects with normal spirometry results were included. Six exposure scenarios were defined:

1. initial dust cloud
2. dust cleanup
3. involvement in rescue /recovery
4. residence near the WTC site
5. employment near the WTC site
6. a group with unspecified exposure.



Resistance at 5 Hz (top), resistance at 5 to 20 Hz (center), and reactance area (bottom) and their response to bronchodilator (• = before bronchodilator; ○ = after bronchodilator) are shown for subjects without FDC (n = 6) or with FDC (n = 37).

Oppenheimer B W et al. Chest
2007;132:1275-1282

MCh-induced air trapping with CT scan

Closely related to:
- Δ FVC at PC₂₀
-FEF_{25%-75%} and FEF_{50%}^{17,18}
-Bronchial NO
-RV/TLC^{16,26,27}

Good 6-wk reproducibility

Time-consuming (~70 min)
Radiation load is unfavorable
Relatively high cost
Time-consuming (~70 min including MCh challenge)

RV/TLC

Closely related to:
-Alveolar NO in severe asthma²⁴
-Air trapping (CT scan)^{17,18,26}

Fair reproducibility²⁶

Noninvasive
Relatively time-consuming (30 min)

Alveolar and bronchial NO

Alveolar NO related to:
-RV/TLC and closing volume in severe asthma²⁴
-Ventilation heterogeneity in stable asthma²⁰
Bronchial NO related to air trapping (CT scan)

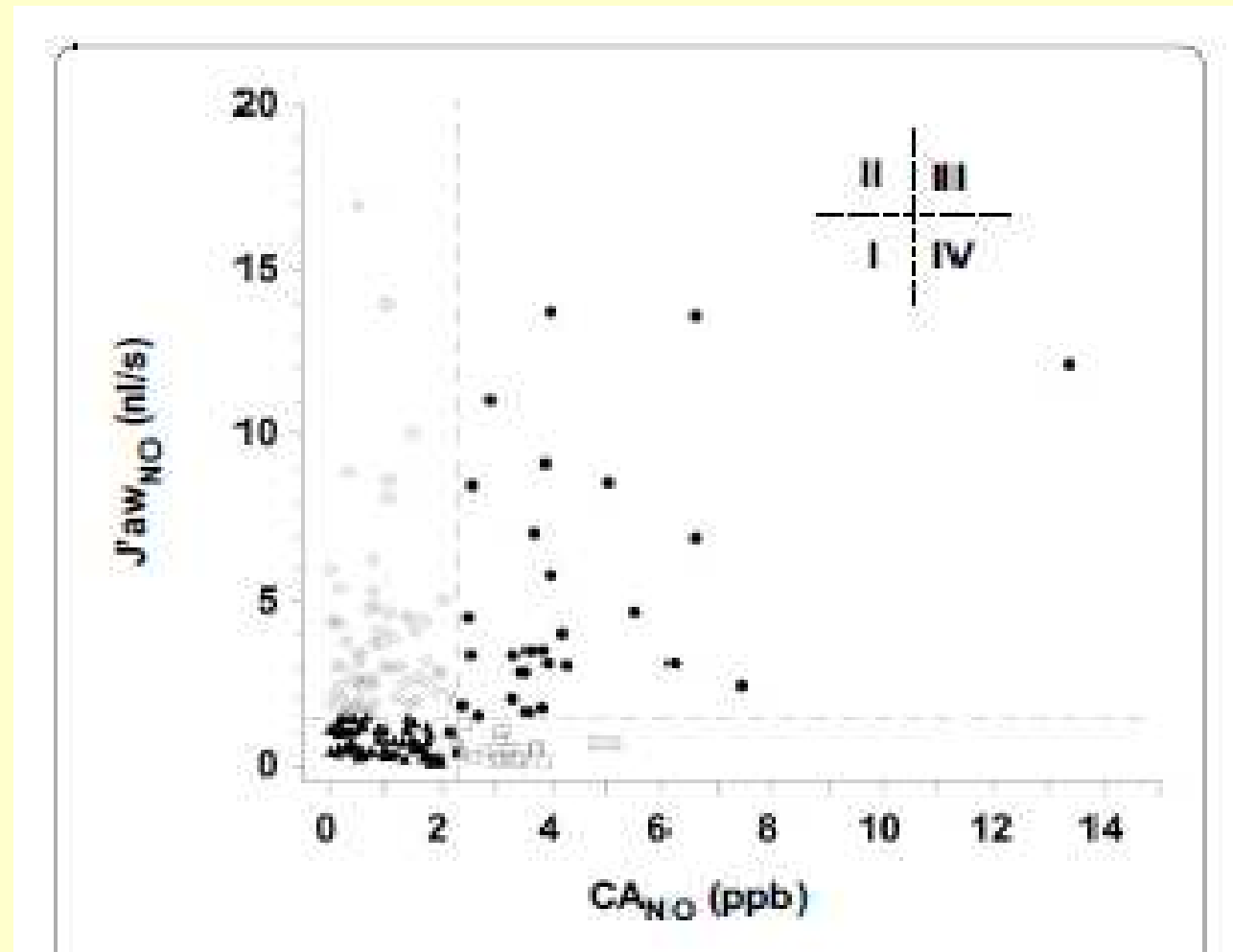
High intraclass coefficient (95%-99%)³⁰
Day-to-day and within-hours reproducibility good³⁰

Noninvasive
Relatively time-consuming (20 min)

Clinical patterns in asthma based on proximal and distal airway nitric oxide categories

Puckett *et al. Respiratory Research* 2010, **11**:47

200 children with asthma
and 21 non-asthmatic



DIFFERISCONO LE PICCOLE
VIE AEREE NEI PAZIENTI
CON ASMA DA QUELLE DEI
CONTROLLI SANI?

- VI E' UN MAGGIORE SPESSORE
DELLE PARETI BRONCHIALI, SIA
INTERNE CHE ESTERNE, CAUSATO
DALL'INFIAMMAZIONE CRONICA

Differiscono le piccole vie aeree nelle sottopopolazioni di asmatici?

- Maggiore ispessimento delle pareti in: Asma fatale
- Maggiore presenza di cellule infiammatorie in: Asma fatale, Asma severo ed Asma notturno
- Air trapping più significativo, visualizzato con CT scanning quantitativo, nell'asma fatale

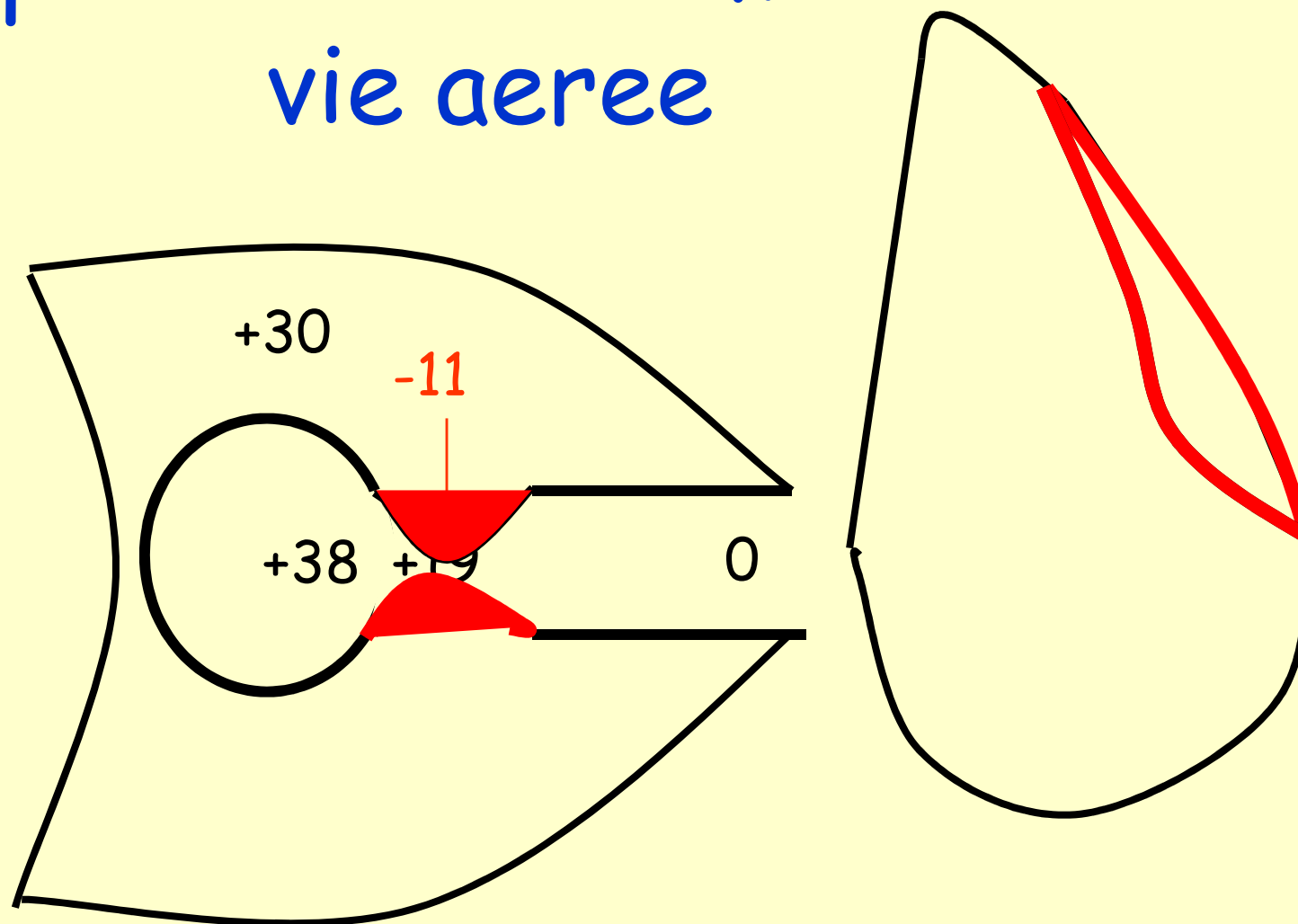
C'è differenza tra
l'infiammazione nelle vie aeree
prossimali ed in quelle distali

- L'eterogeneità riscontrata in numerosi studi e la differenza strutturale esistente tra alte e basse vie aeree, non consentono di trarre conclusioni definitive

C'è differenza tra pareti interne ed esterne delle piccole vie aeree?

- Ci sono indicazioni sulla maggiore infiammazione della parete esterna, con una compartecipazione della regione peribronchiolare. (maggiore collassabilità delle piccole vie aeree)

Compressione dinamica delle vie aeree



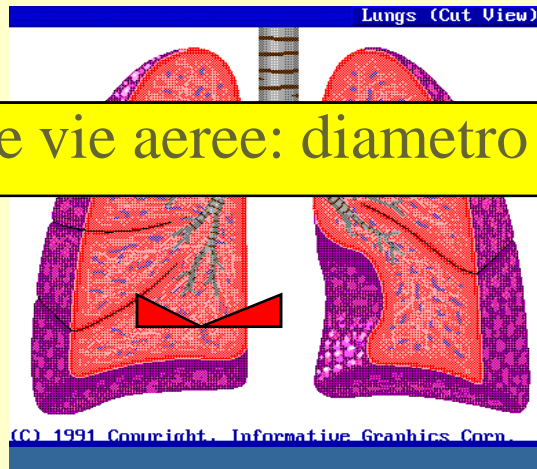
Fine-Espirazione

Distal Lung

La zona silente

Mead J et al. – J Appl Physiol 1970 ; 28: 596

Piccole vie aeree: diametro < 2 mm



Studi fisiopatologici evidenziano che l'unità "Distal Lung", che include le piccole vie aeree (< 2 mm) ed il parenchima polmonare, partecipa alla patogenesi dell'Asma.

M. Kraft Eur Respir J 1999; 14: 1403-1417

The importance and features of the distal airways in children and adults

J Allergy Clin Immunol 2009;124:S84-7. EW. Gelfand, and M Kraft

L'aumento delle resistenze delle vie aeree periferiche prima o in assenza di un coinvolgimento delle vie aeree prossimali, spiega i valori normali del FEV1 in molti bambini con asma.

Diversi studi hanno dimostrato l'anormalità dei flussi parziali (FEF 25% - 75%) in bambini asmatici con valori del FEV1 normali.

Location

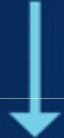
Generation ▼

Trachea

Bronchi



Bronchioles

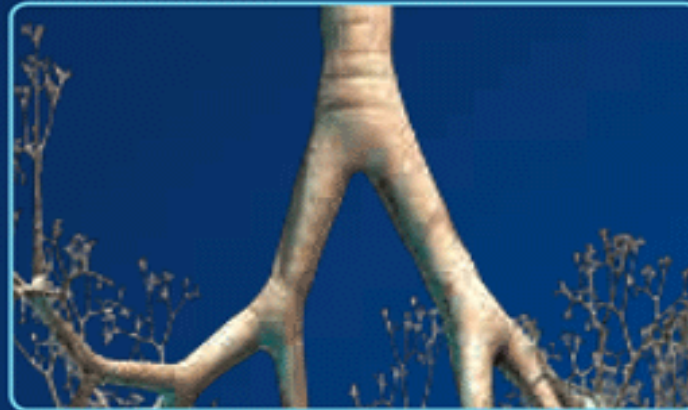


Terminal bronchioles

Respiratory bronchioles

Alveolar ducts

Alveolar sacs



0

1

2

3

4

5



16

17

18

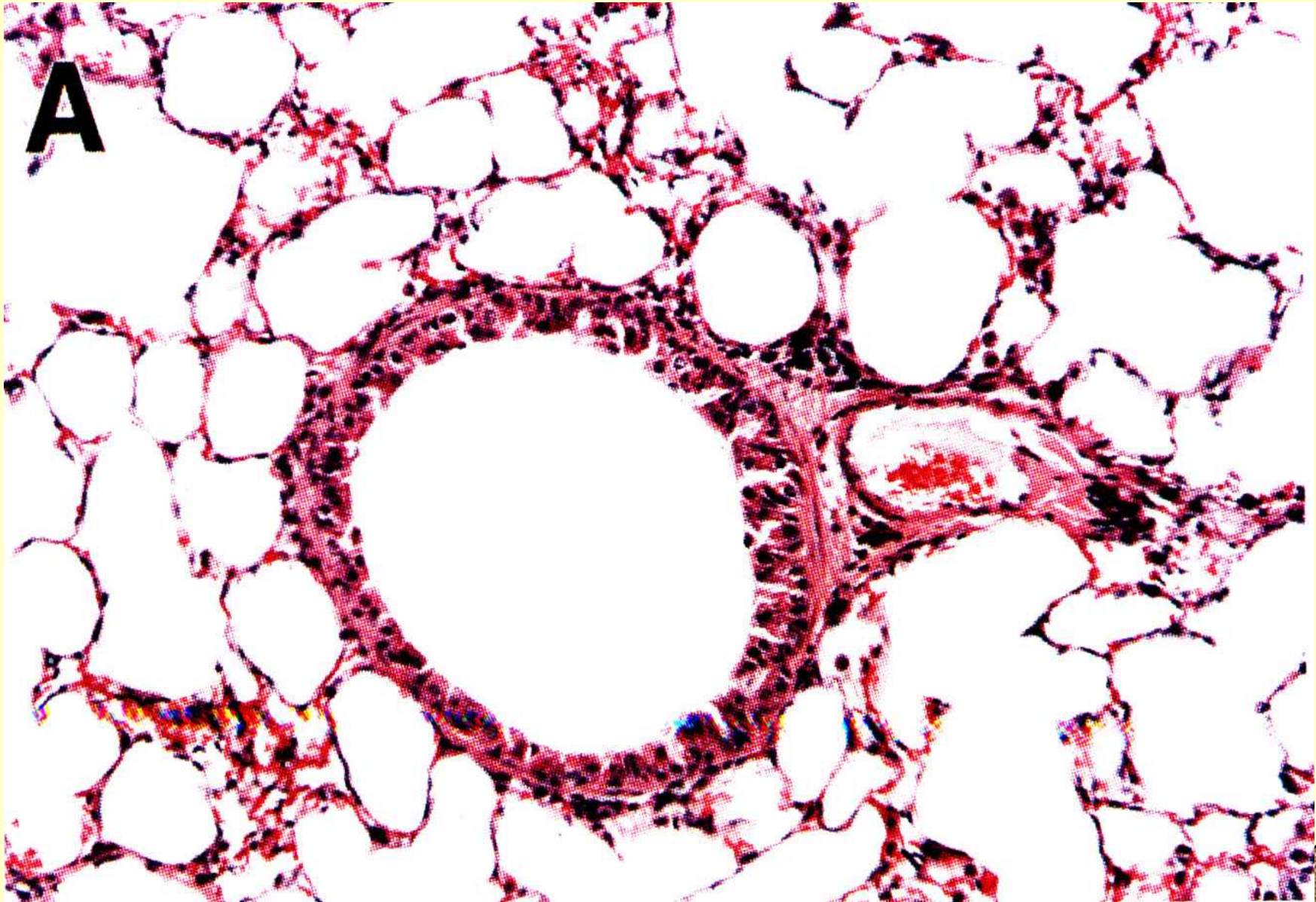
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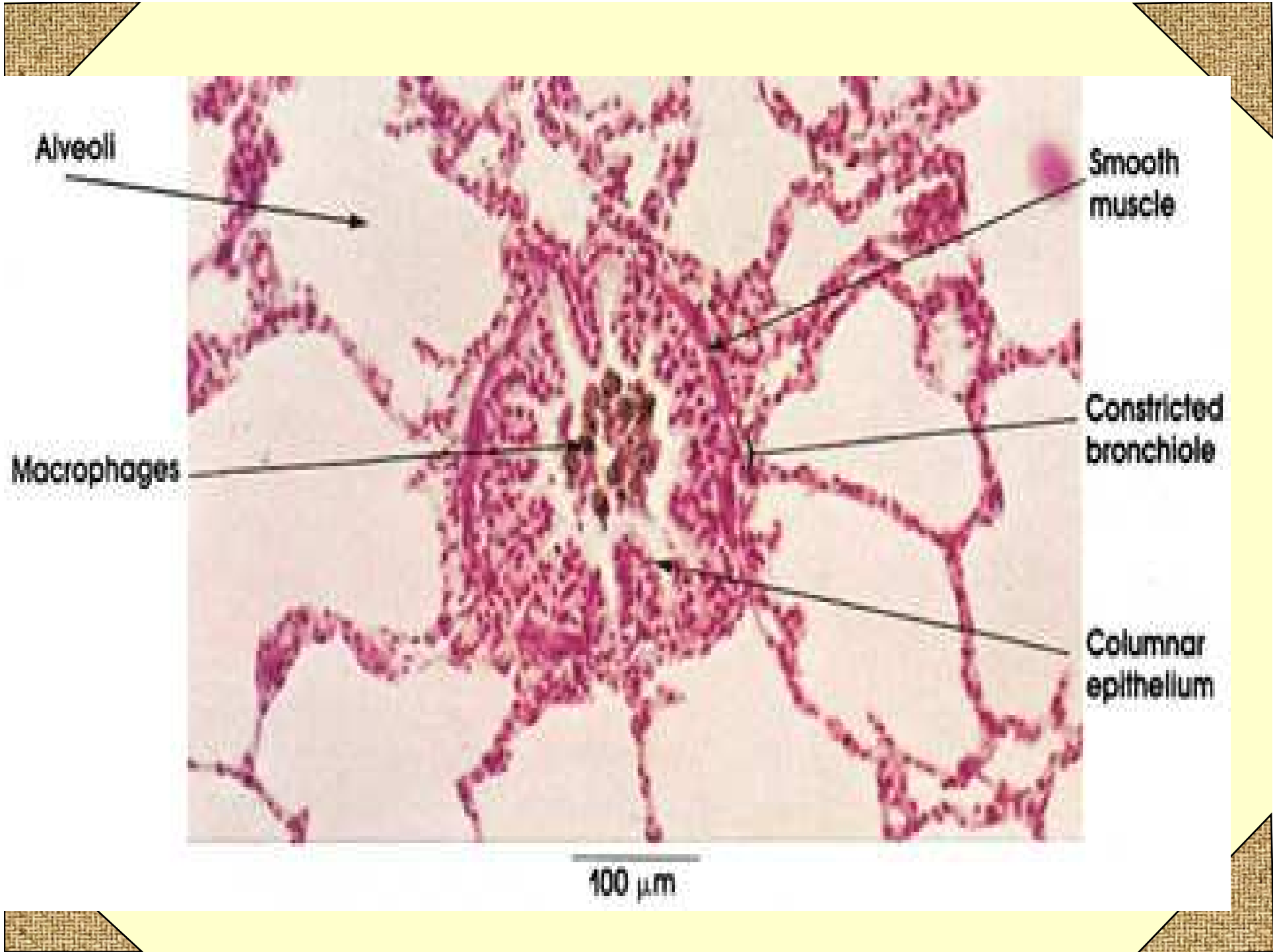
T₃ 20

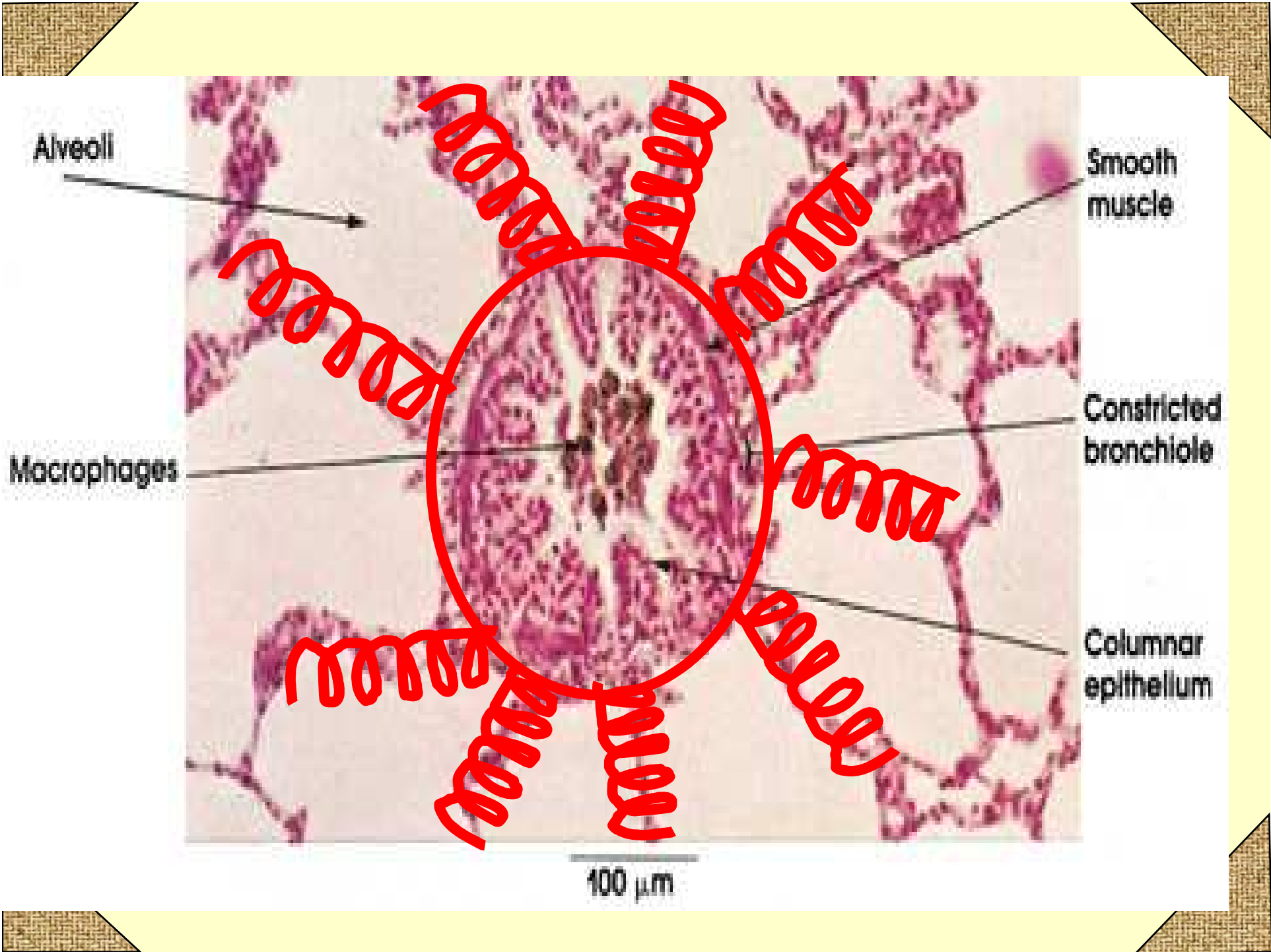
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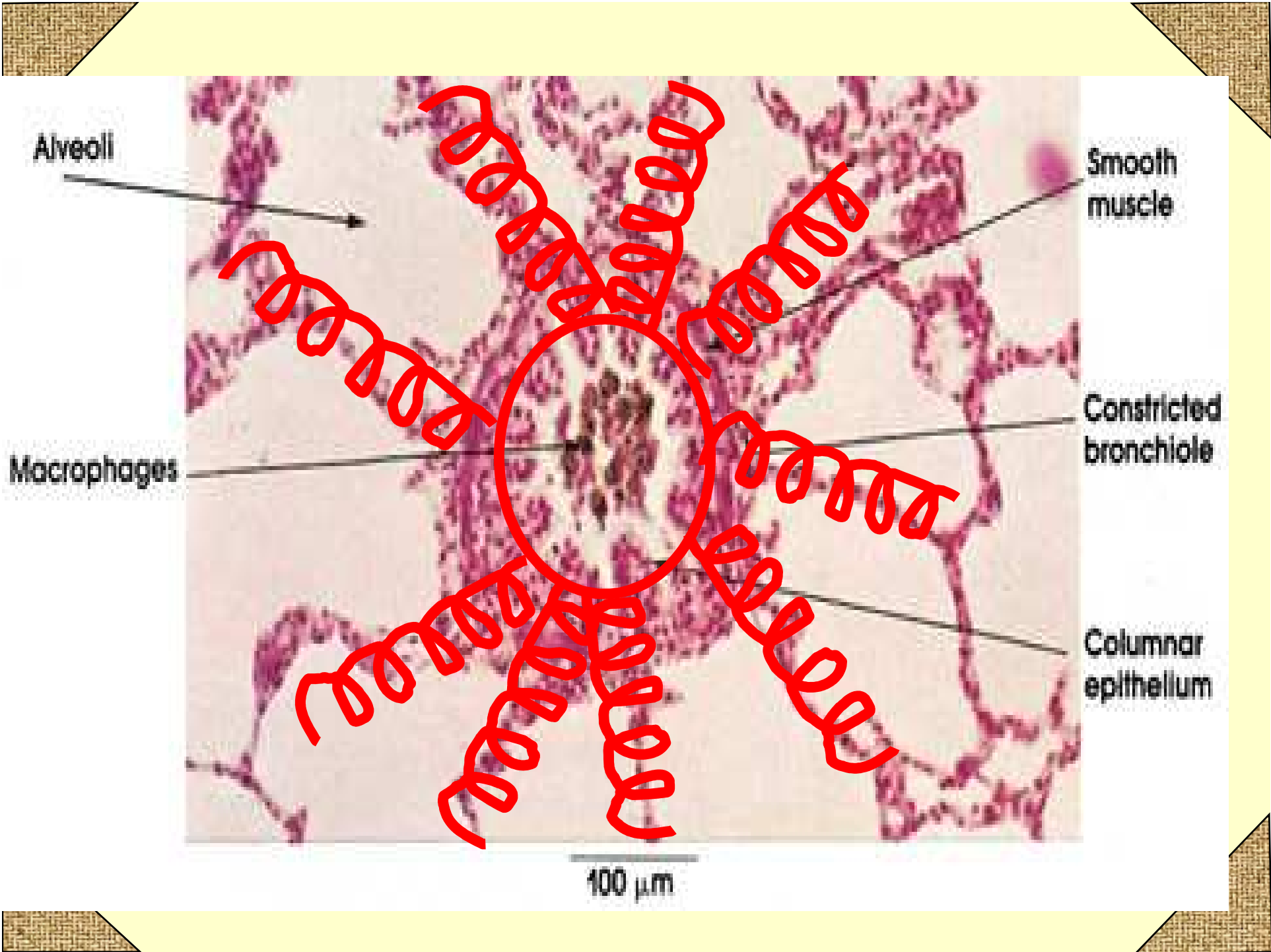
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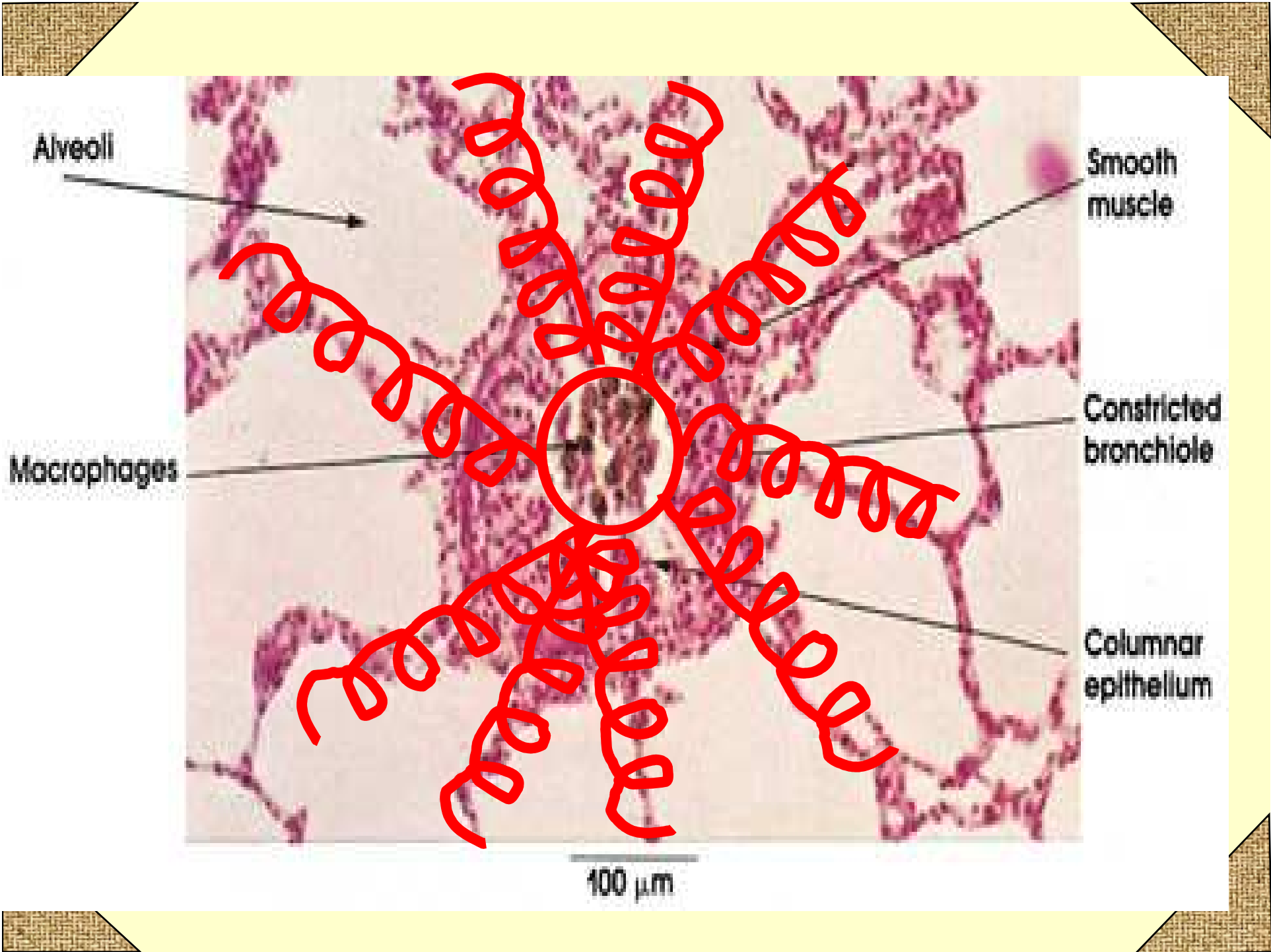
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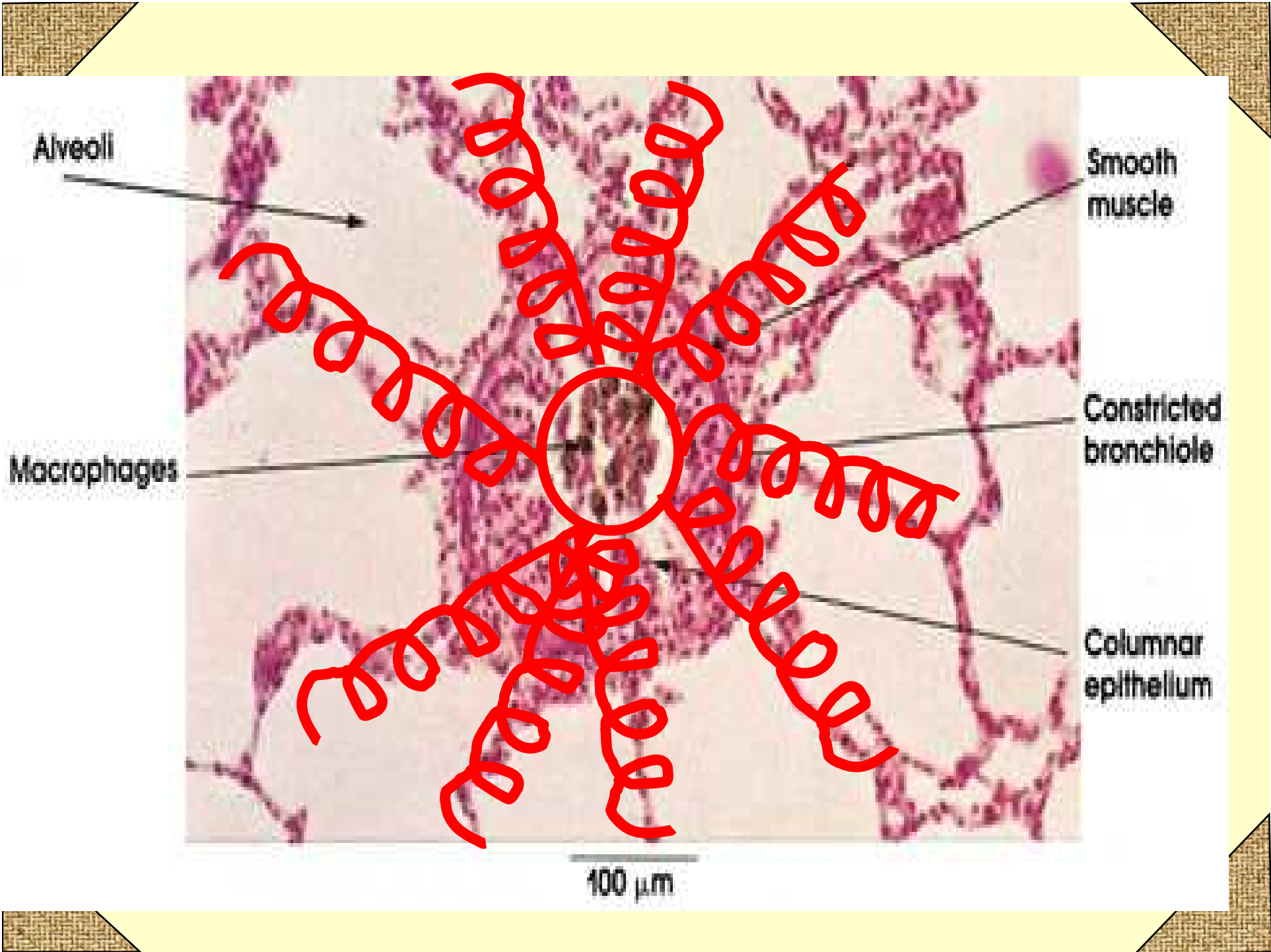


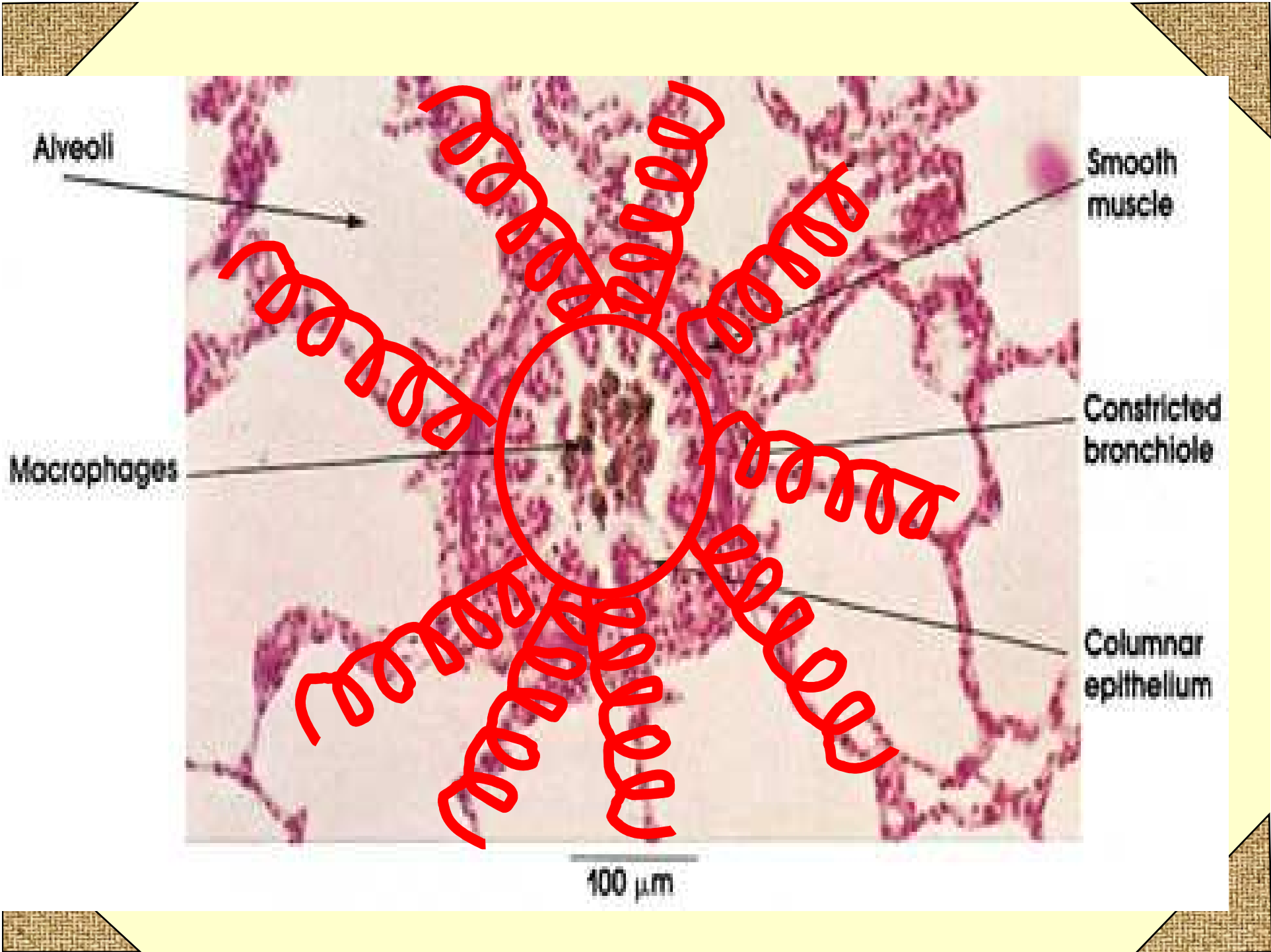


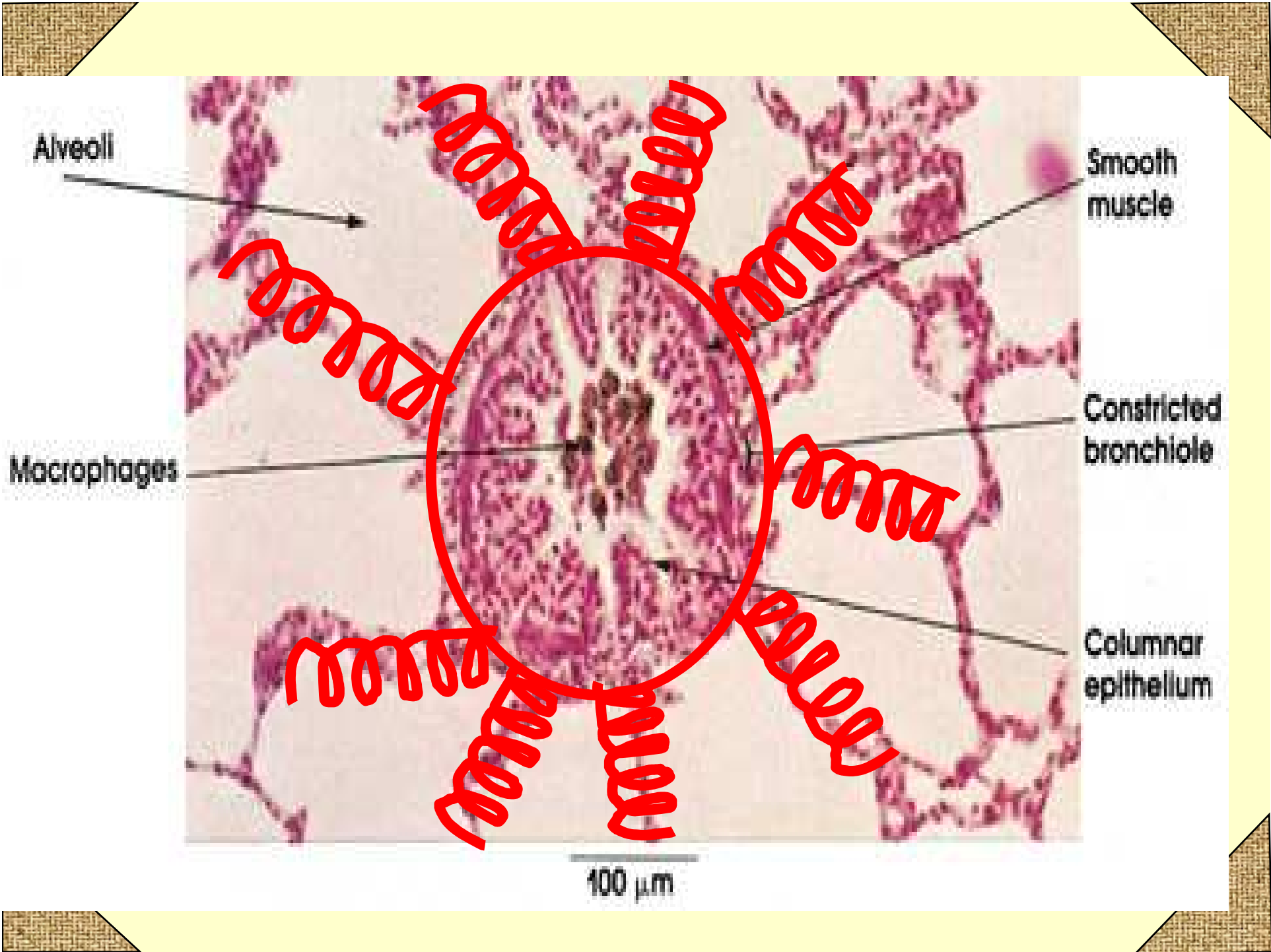


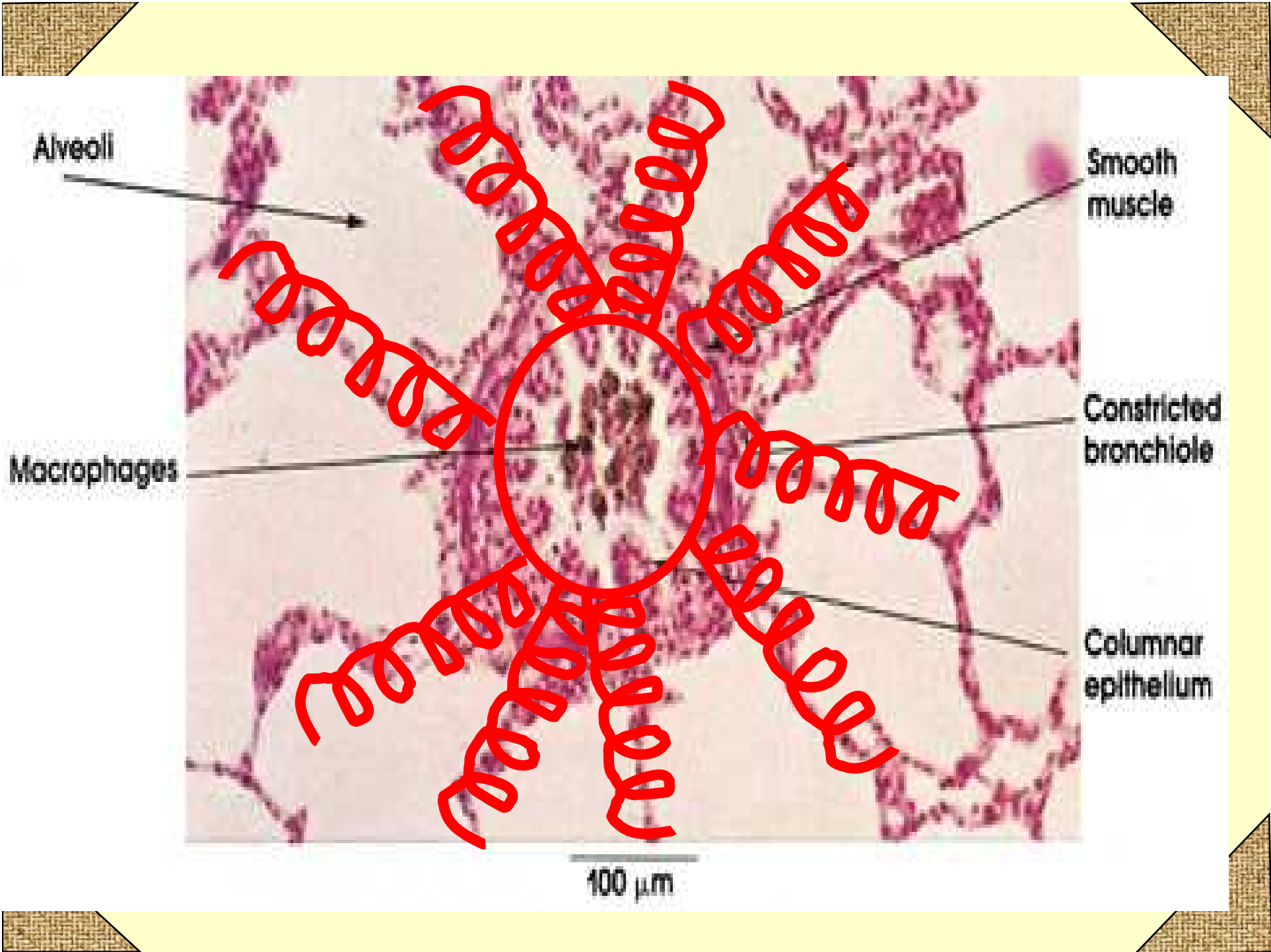


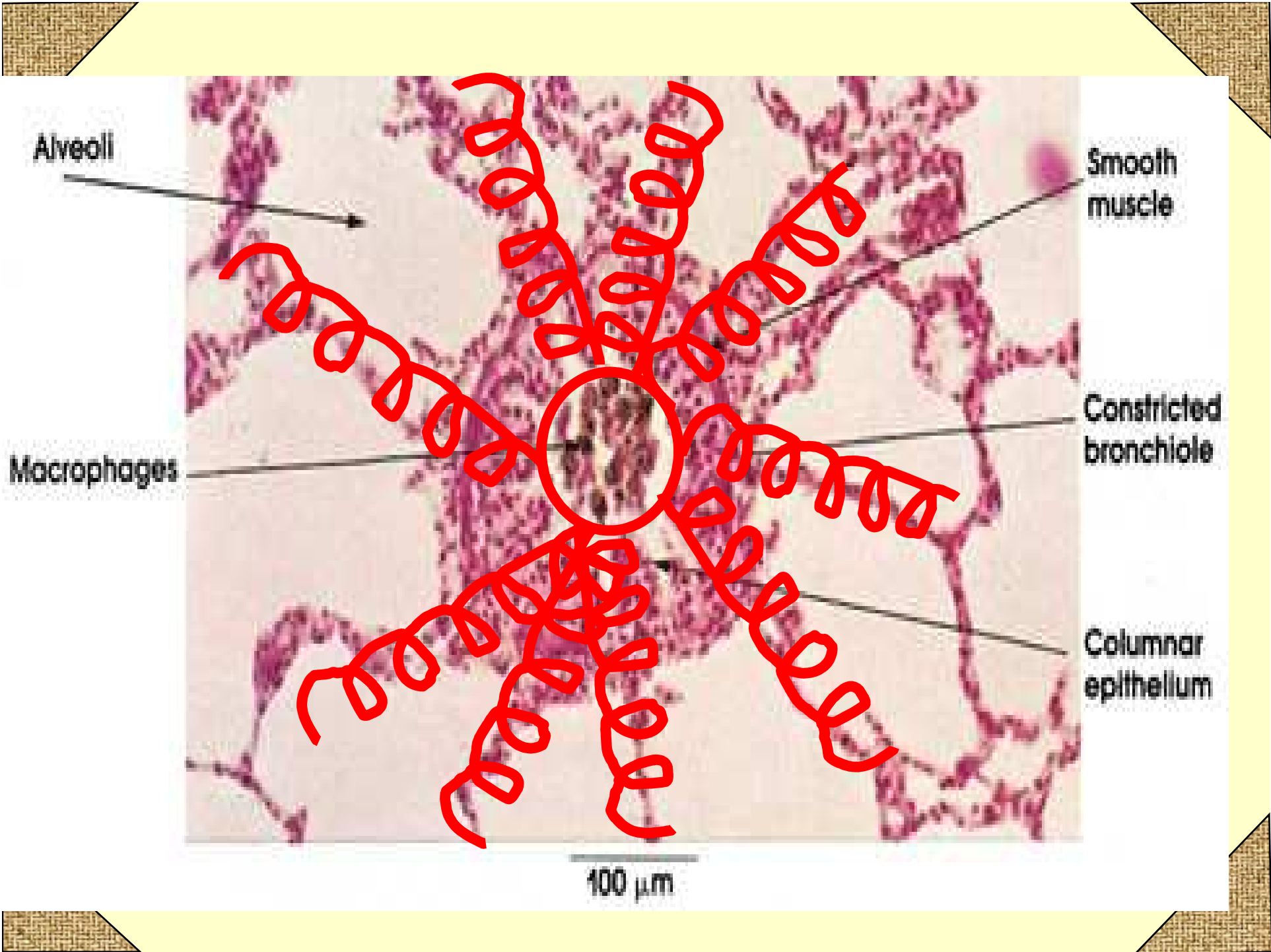


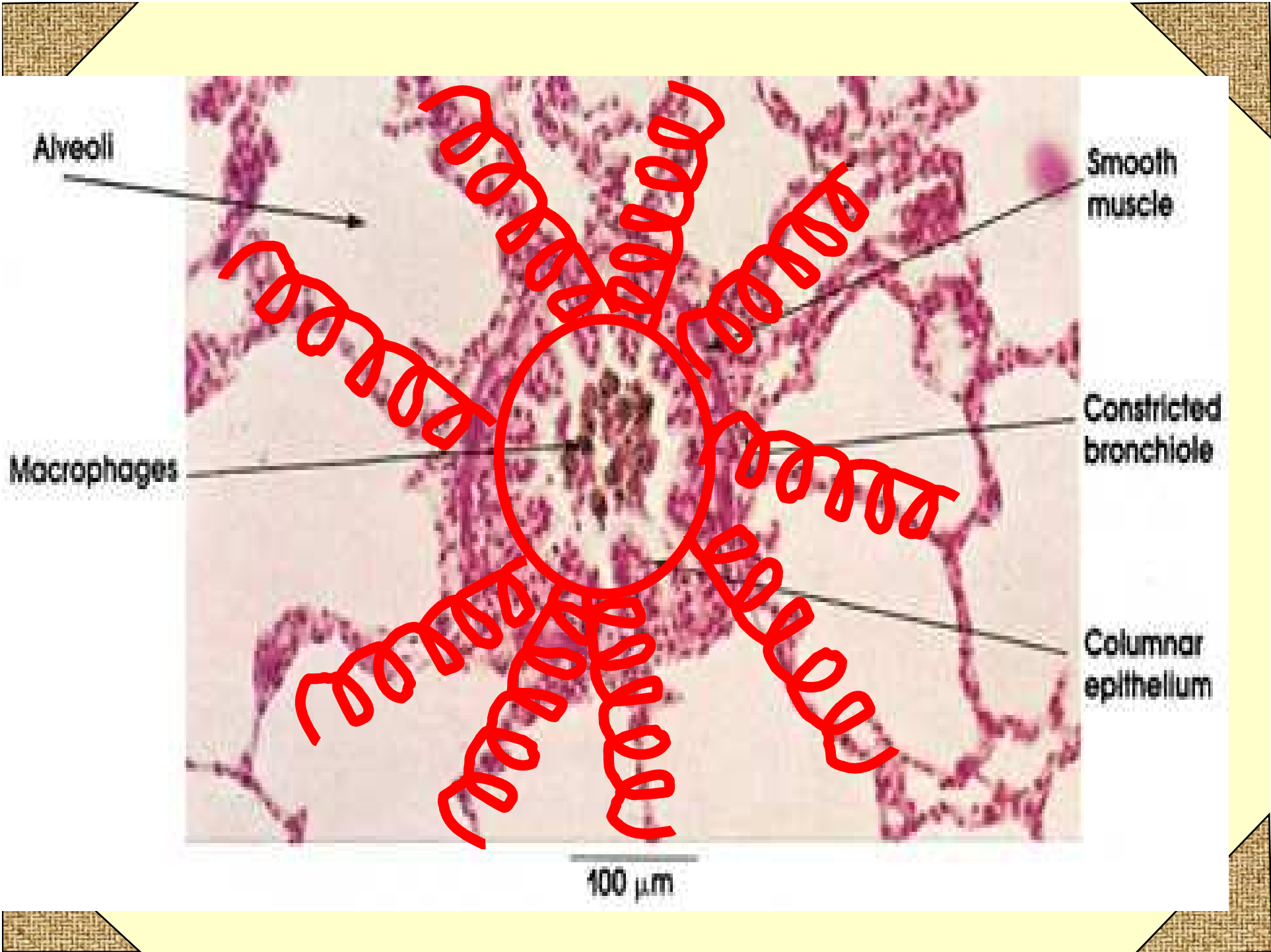


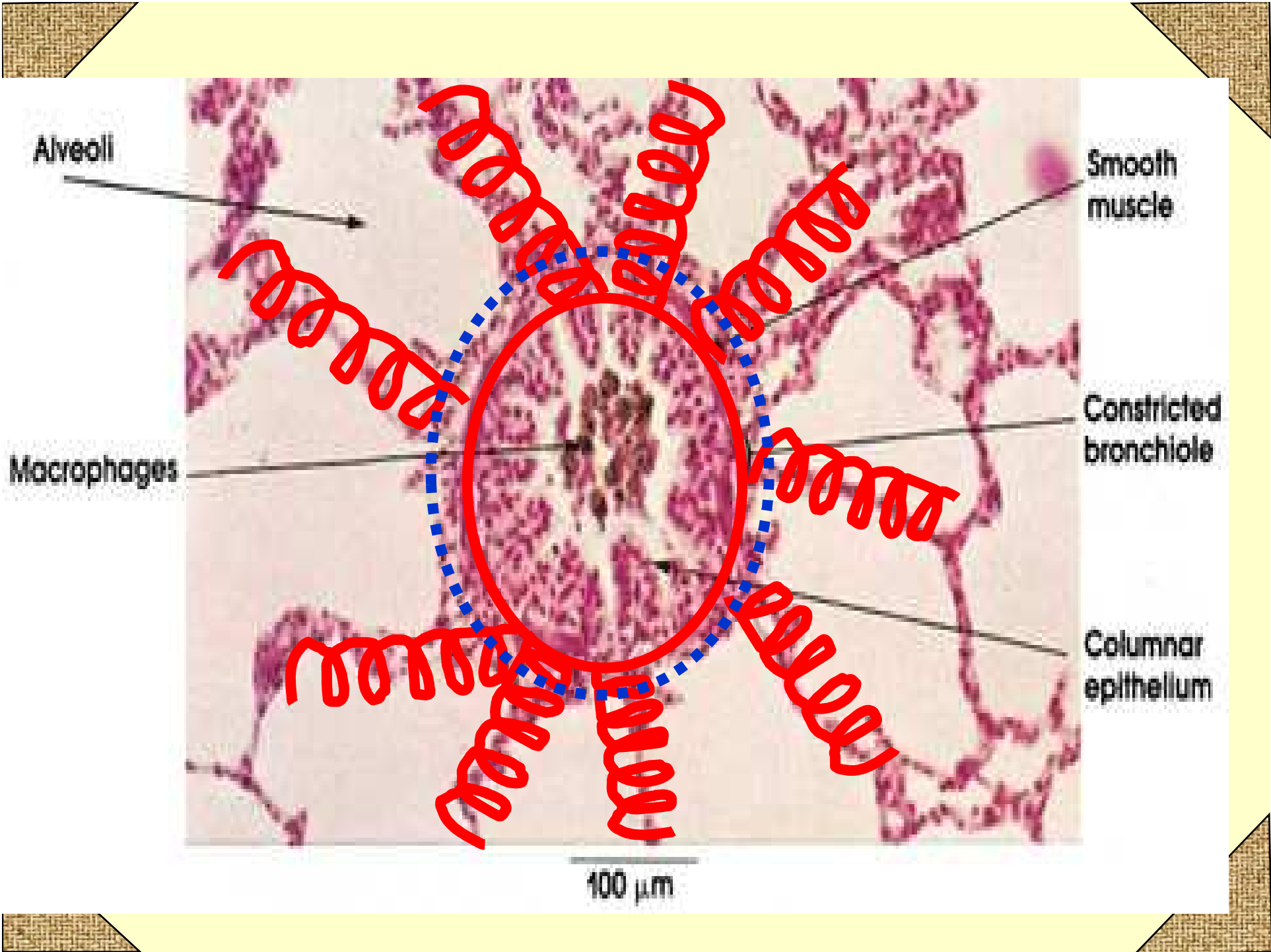


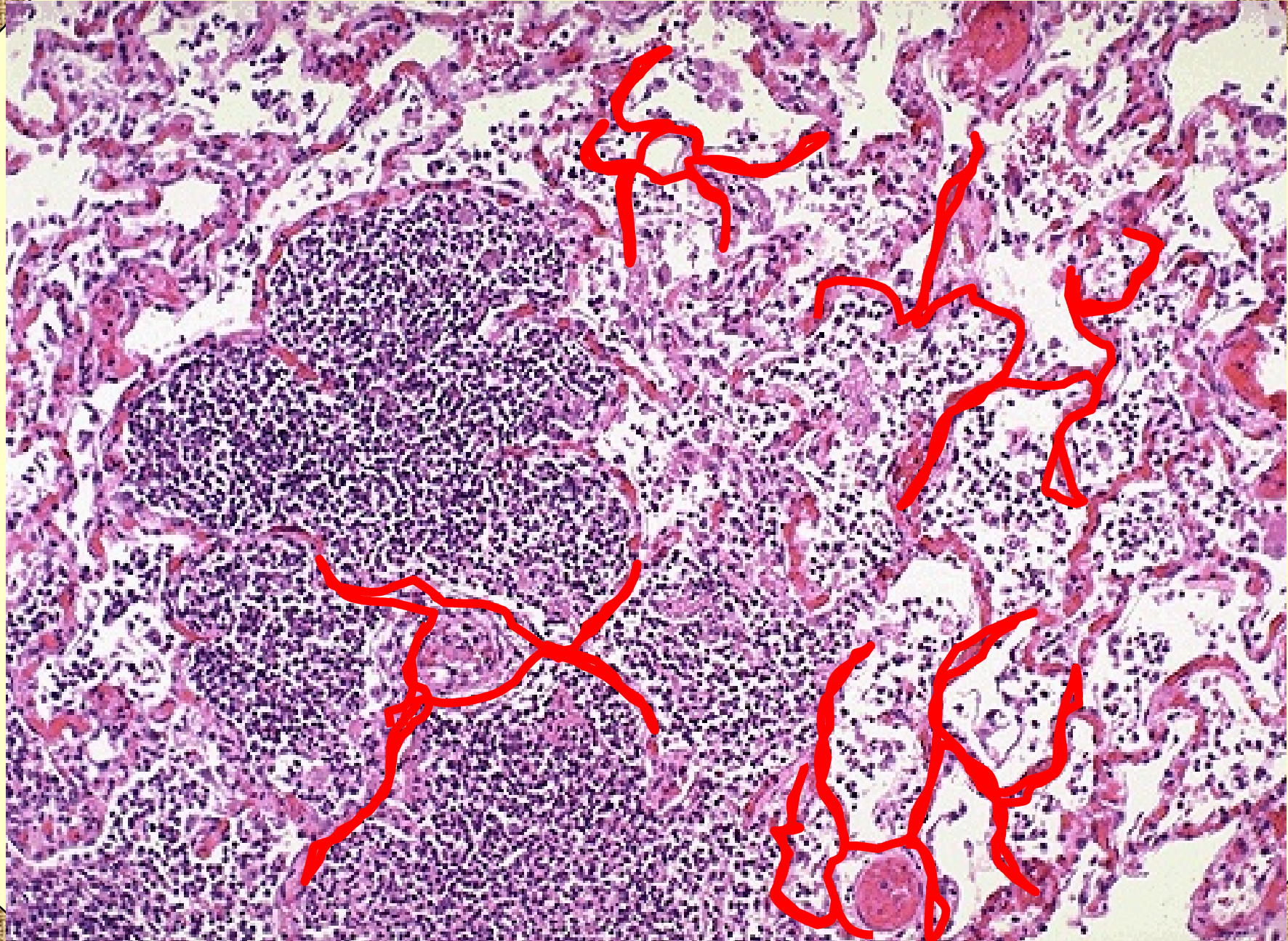












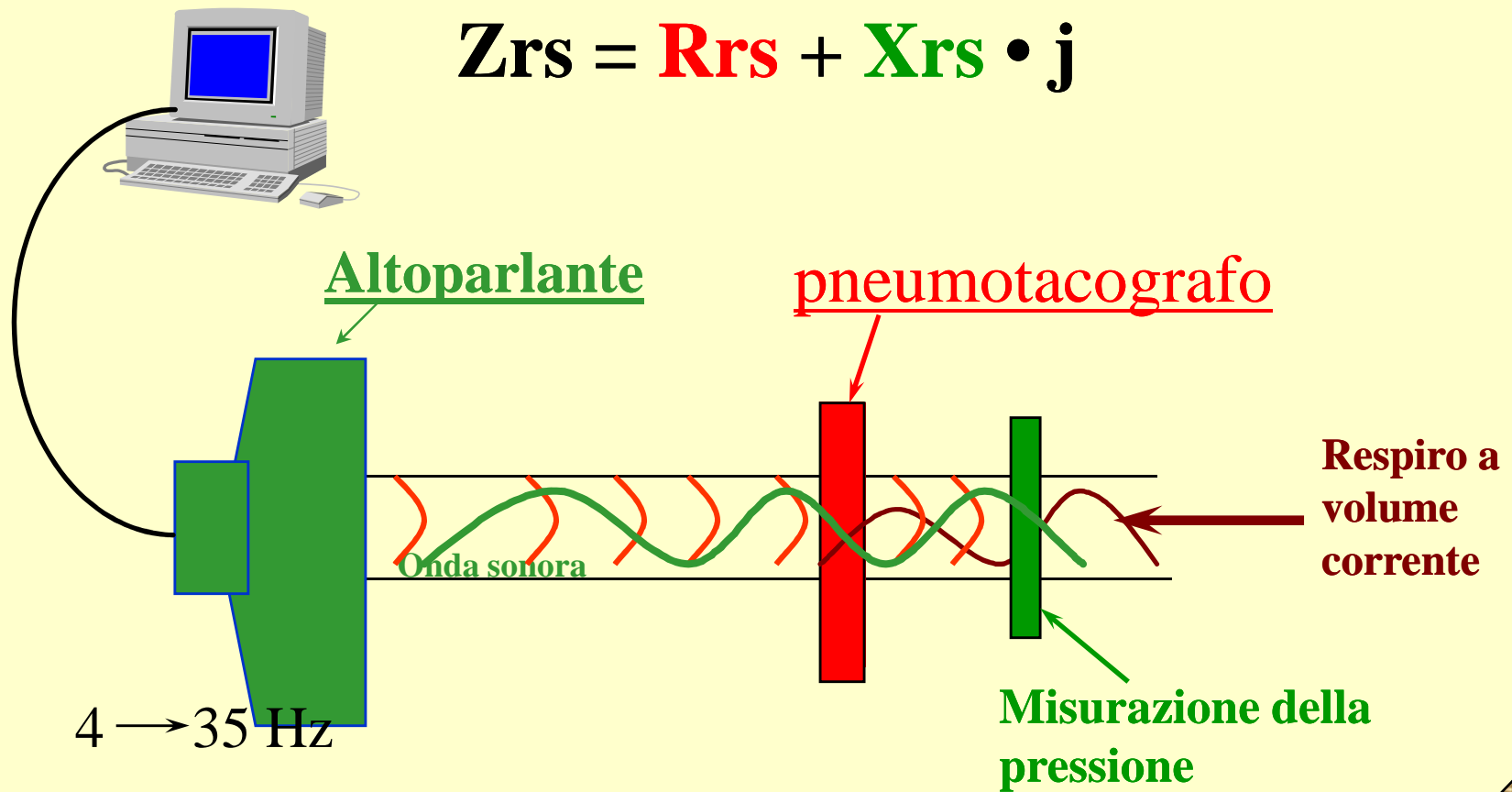
Variazioni nelle piccole vie aeree correlano con la funzione polmonare?

- Gli studi sono pochi e su piccola popolazione.
- E' stata vista comunque correlazione sia nell'asma notturno che nell'asma lieve.

La Diagnosi

Principio dell'Oscillometria Forzata

$$Z_{rs} = R_{rs} + X_{rs} \cdot j$$





La Terapia

CFC

A



HFA

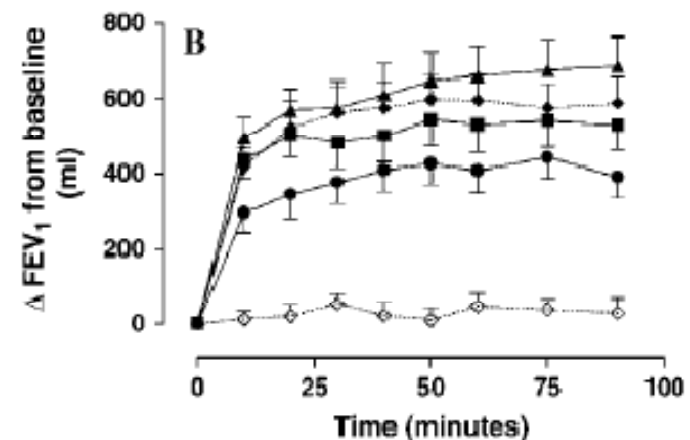
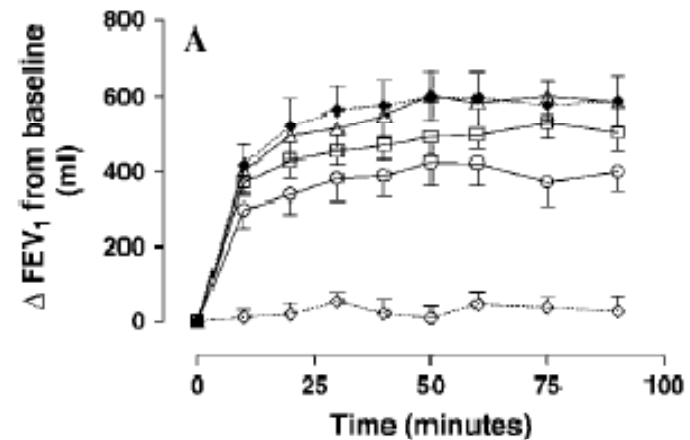
B



Regional Lung Deposition and Bronchodilator Response as a Function of Beta 2-Agonist Particle Size.

Am J Respir Crit Care Med Vol 172. pp 1497–1504, 2005 Omar S. Usmani, Martyn F. Biddiscombe, and Peter J. Barnes

FEV₁ time-response profile curves. Placebo (dashed line, open diamonds) and albuterol metered-dose inhaler 200 mcg (dotted line, closed diamonds) are shown on both graphs. Monodisperse albuterol aerosols are shown as follows: 1.5 μm (circles), 3 μm (squares), and 6 μm (triangles) at (A) 15-mcg (open symbols) and (B) 30-mcg (closed symbols) doses. Data are presented as means (of 12 patients) of the maximal change in each patient's individual FEV₁ response (from baseline value) at each time point SEM.



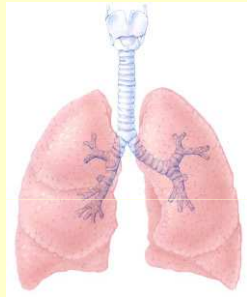
Fenotipi

- **Vie aeree prossimali** (fino alla 16° generazione)
- **Vie aeree distali** (dalla 16° generazione)
- **Vie aeree distali + prossimali**

Il periodo postnatale

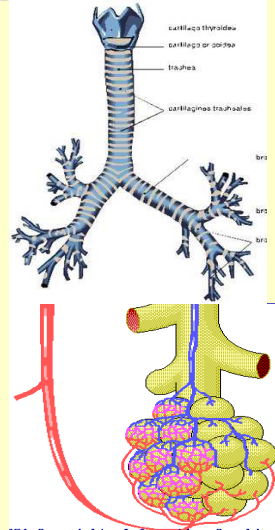
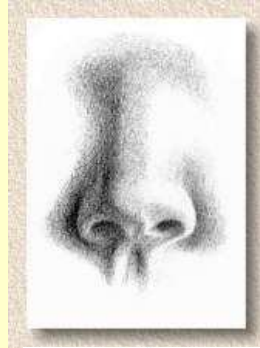
- Al momento della nascita sono riconoscibili circa 25-50 milioni di **strutture simil-alveolari** che assumeranno l'aspetto di alveoli maturi soltanto dopo circa due mesi di vita, per effetto dell'adattamento alla respirazione.
- Il loro numero aumenta sino ai primi 2-8 anni di vita, quando raggiungere i 300 milioni circa.
- L'aumento del numero degli alveoli si realizza con modalità simili a quelle della vita intrauterina, cioè per l'ulteriore segmentazione delle strutture alveolari già esistenti e per l'**alveolarizzazione dei bronchioli**.
- Successivamente l'accrescimento dei polmoni continua sino alla età adulta, realizzandosi però soltanto nel senso di un incremento di volume, proporzionale all'aumento delle dimensioni corporee.

0-3 anni



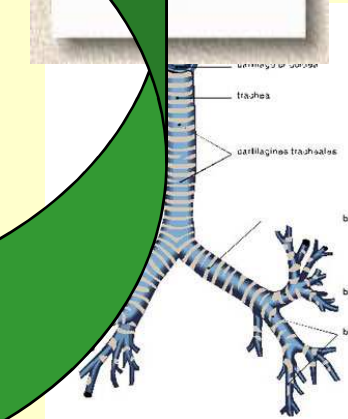
50 mln alveoli

3-8 anni

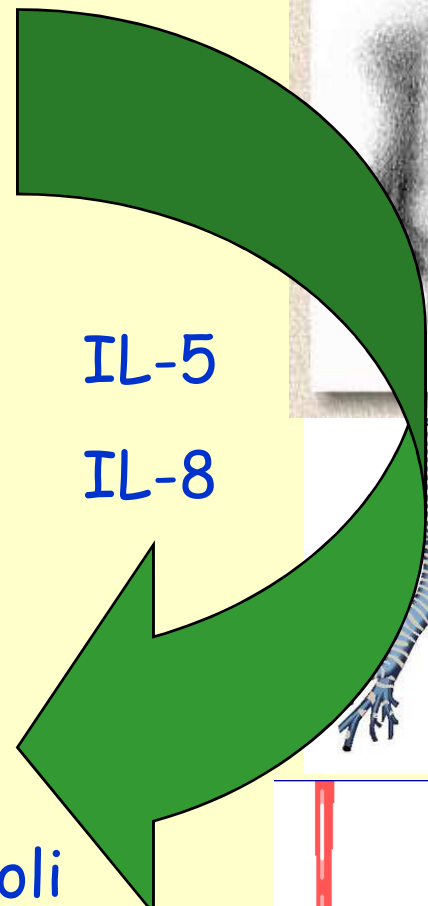


300 mln alveoli

adulto



300 mln alveoli



IL-5

IL-8