

BI 121 Lecture 13

I. Announcements Optional notebook check today. Discussion-Review followed by final exam tomorrow. Q?

II. Introduction to PFT Lab 6 Pulmonary Function Testing

III. Respiratory System LS ch 12, DC Module 7, SI Fox +...

A. Steps of respiration? External vs. cellular/internal?

LS fig 12-1 pp 345-7

B. Respiratory system anatomy LS fig 12-2 p347, DC, SI Fox +...

C. Histology LS fig 12-4 pp 347-9, DC

D. How do we breathe? LS fig12-12, fig12-25 pp 349-56, 373-8

E. Gas exchange LS fig 12-19 pp 362-5

F. Gas transport LS tab 12-3 pp 365-70

IV. Physiology of Cigarette Smoking

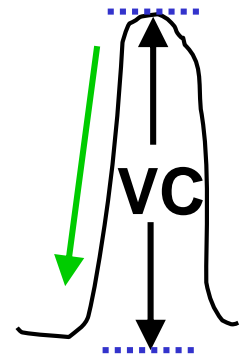
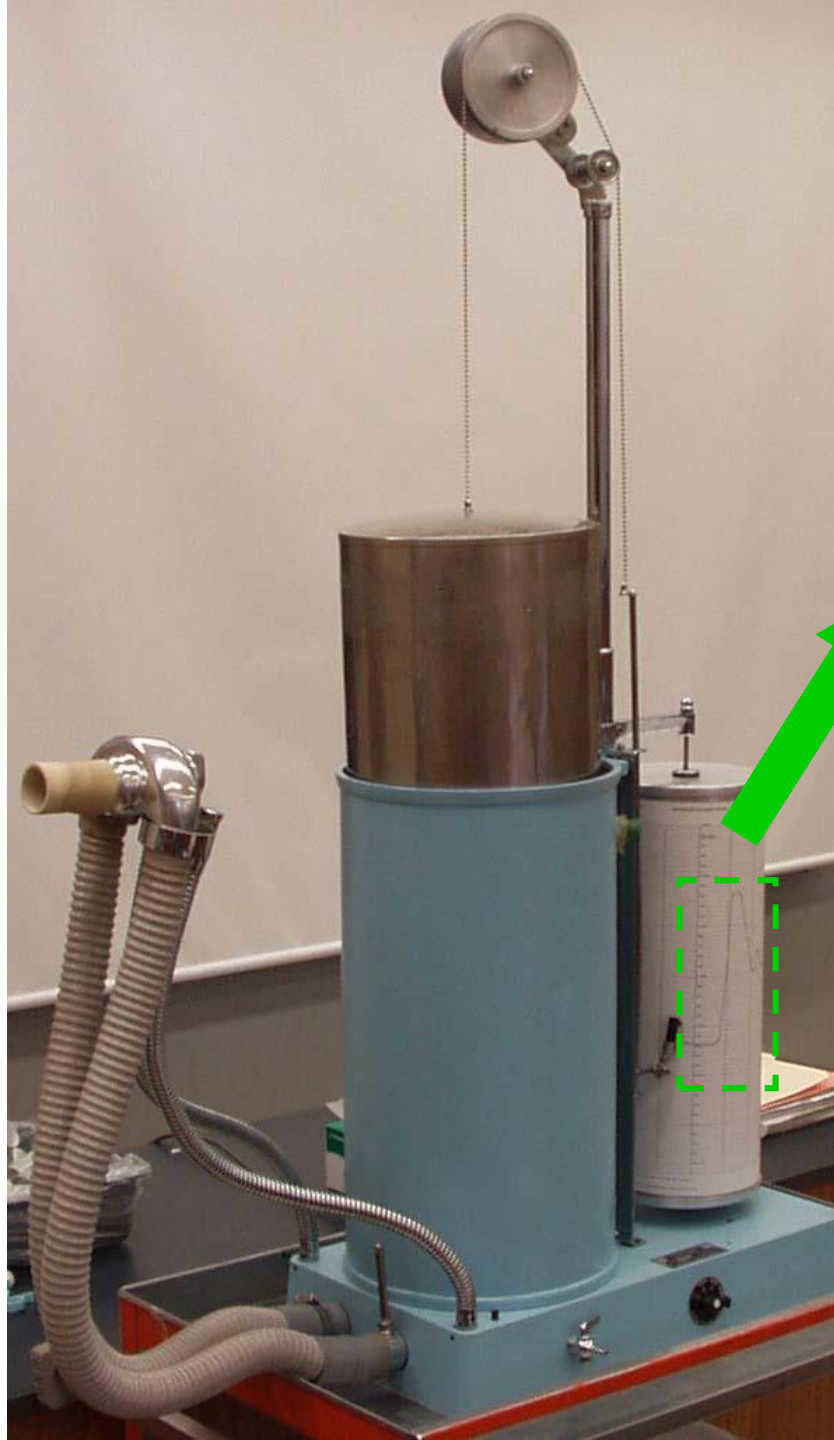
A. ANS, autonomic nerves & nicotine? Route of chemicals,...

B. Emphysema? 2nd-hand smoke?... p 356, 365

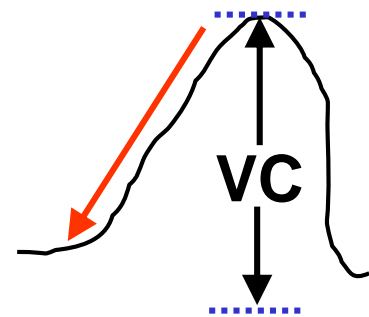
C. UO Smoke-Free since Fall 2012! Help is available!

Respirometer →
measures **complete
Pulmonary Function
Test or PFT!**

NB: Should be able to
blow out $\geq 75 - 85\%$ of
VC/FVC in 1 second!
That's $FEV_{1.0}/FVC \geq$
 $0.75 - 0.85$. If less,
may indicate asthma
or other lung disease.

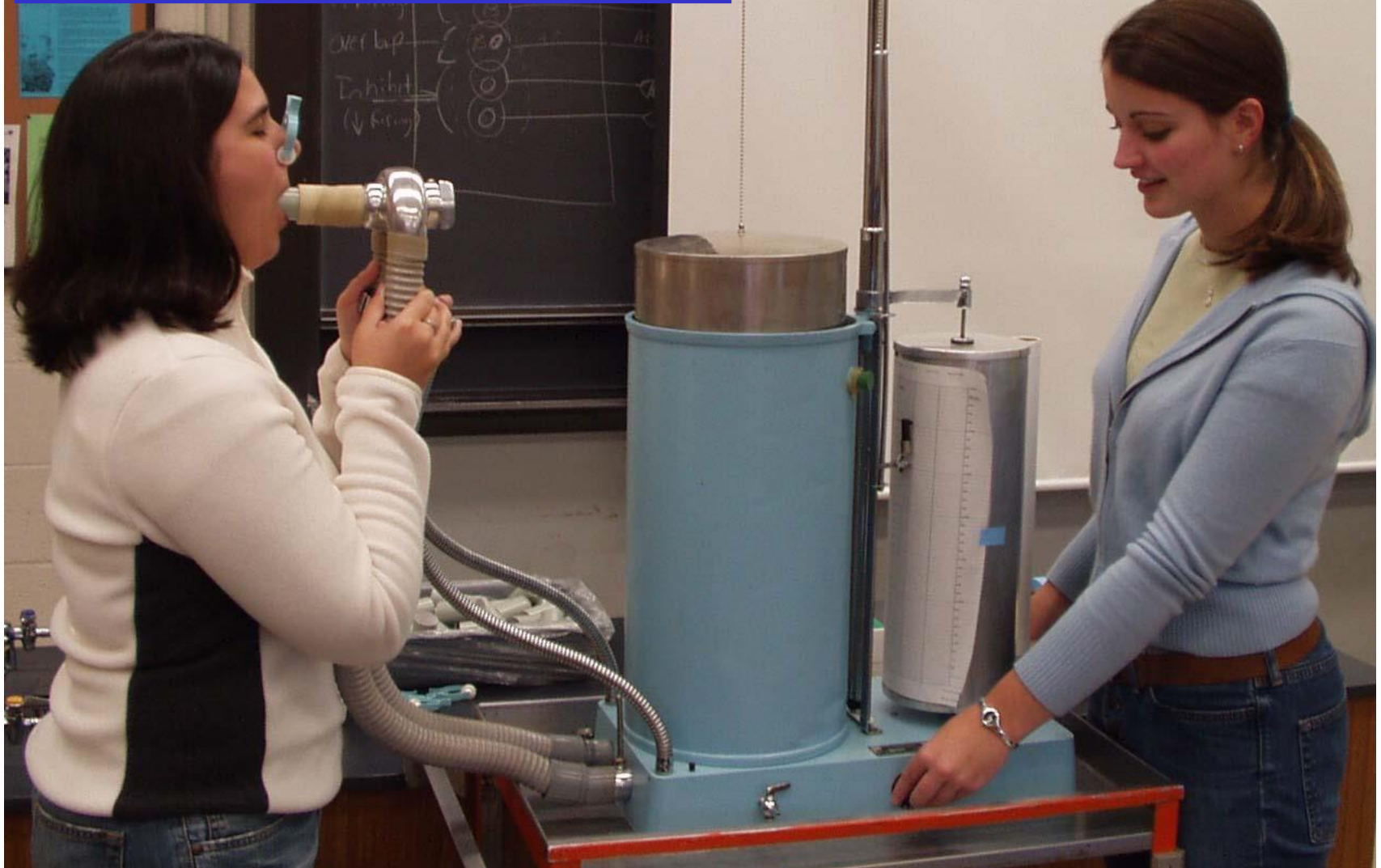


**Normal =
Steep**

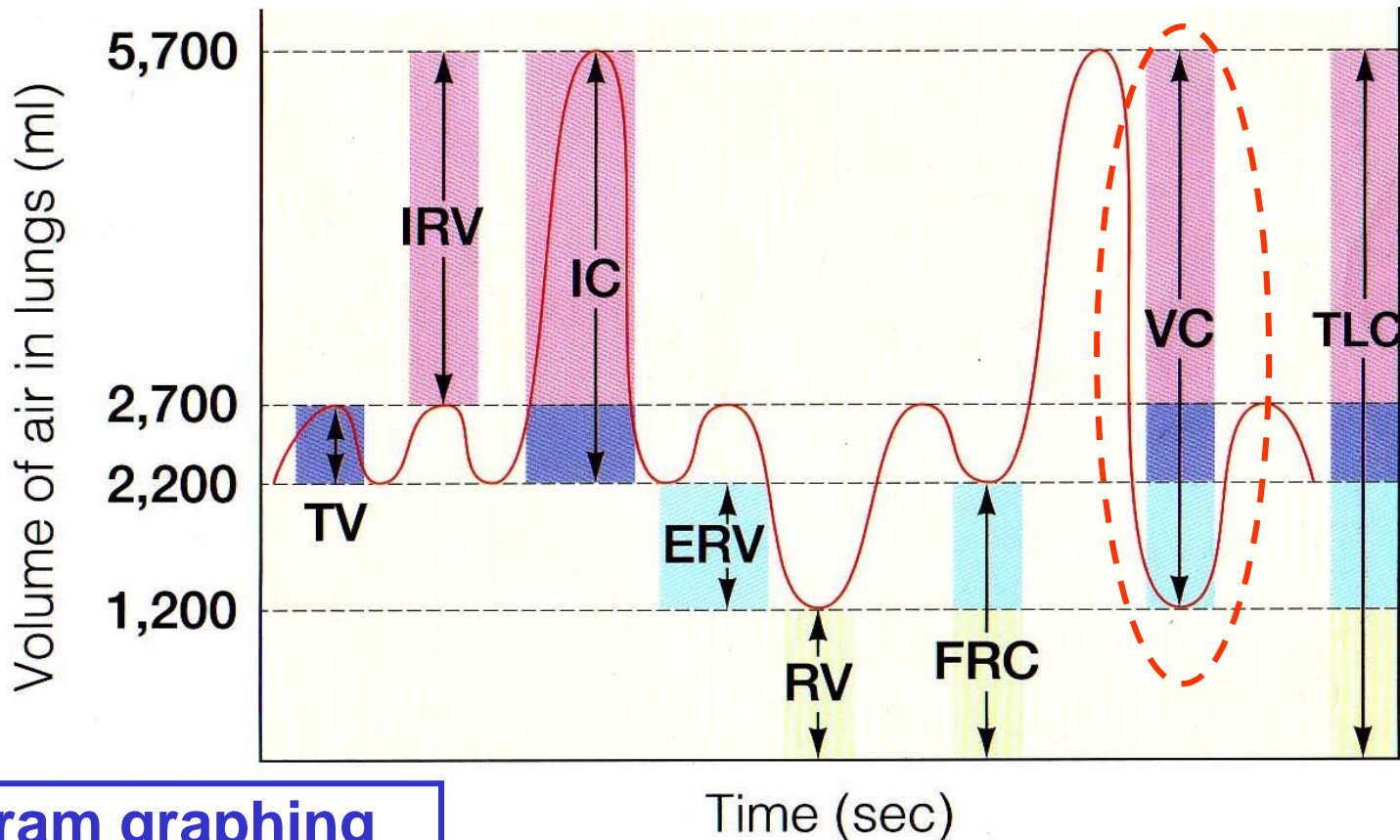


**Abnormal =
Flatter
Downslope
(eg, Asthma)**

PFT → measures all lung volumes & capacities (sum of ≥ 2 volumes). Subject relaxes & breathes normally into and out of tank.



Normal Spirogram of Healthy Young Adult Male



**Spirogram graphing
complete *PFT* from
computer simulation.**

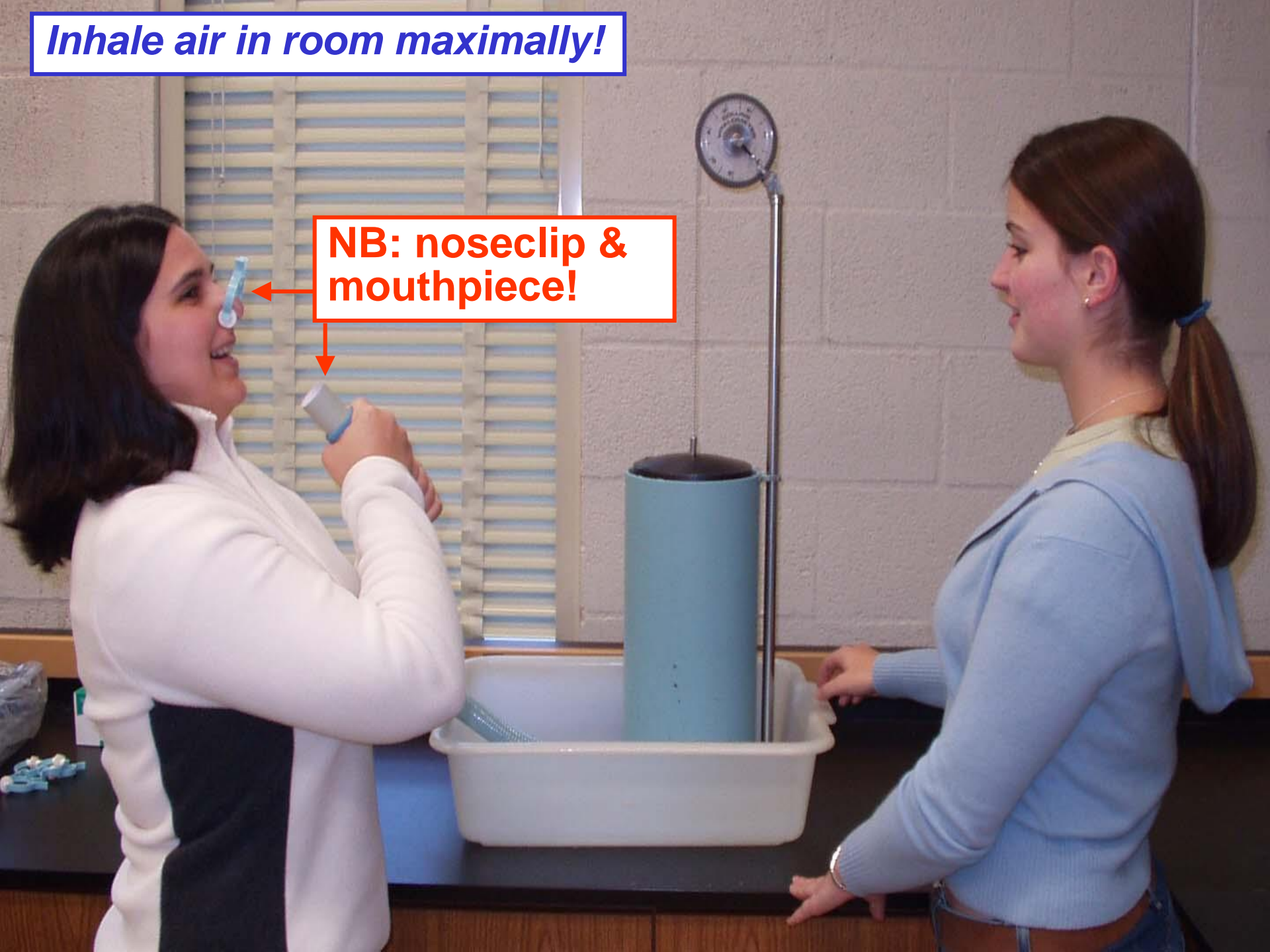
- TV = Tidal volume (500 ml)
- IRV = Inspiratory reserve volume (3,000 ml)
- IC = Inspiratory capacity (3,500 ml)
- ERV = Expiratory reserve volume (1,000 ml)
- RV = Residual volume (1,200 ml)
- FRC = Functional residual capacity (2,200 ml)
- VC = Vital capacity (4,500 ml)
- TLC = Total lung capacity (5,700 ml)

***Vitalometer* → Can only measure Vital Capacity (VC). No graph paper, so no time component.**



Inhale air in room maximally!

NB: noseclip & mouthpiece!



Exhale into tube maximally!



More modern-day computerized Pulmonary Function Testing



*Complete with HH!
Happy Helpers!*

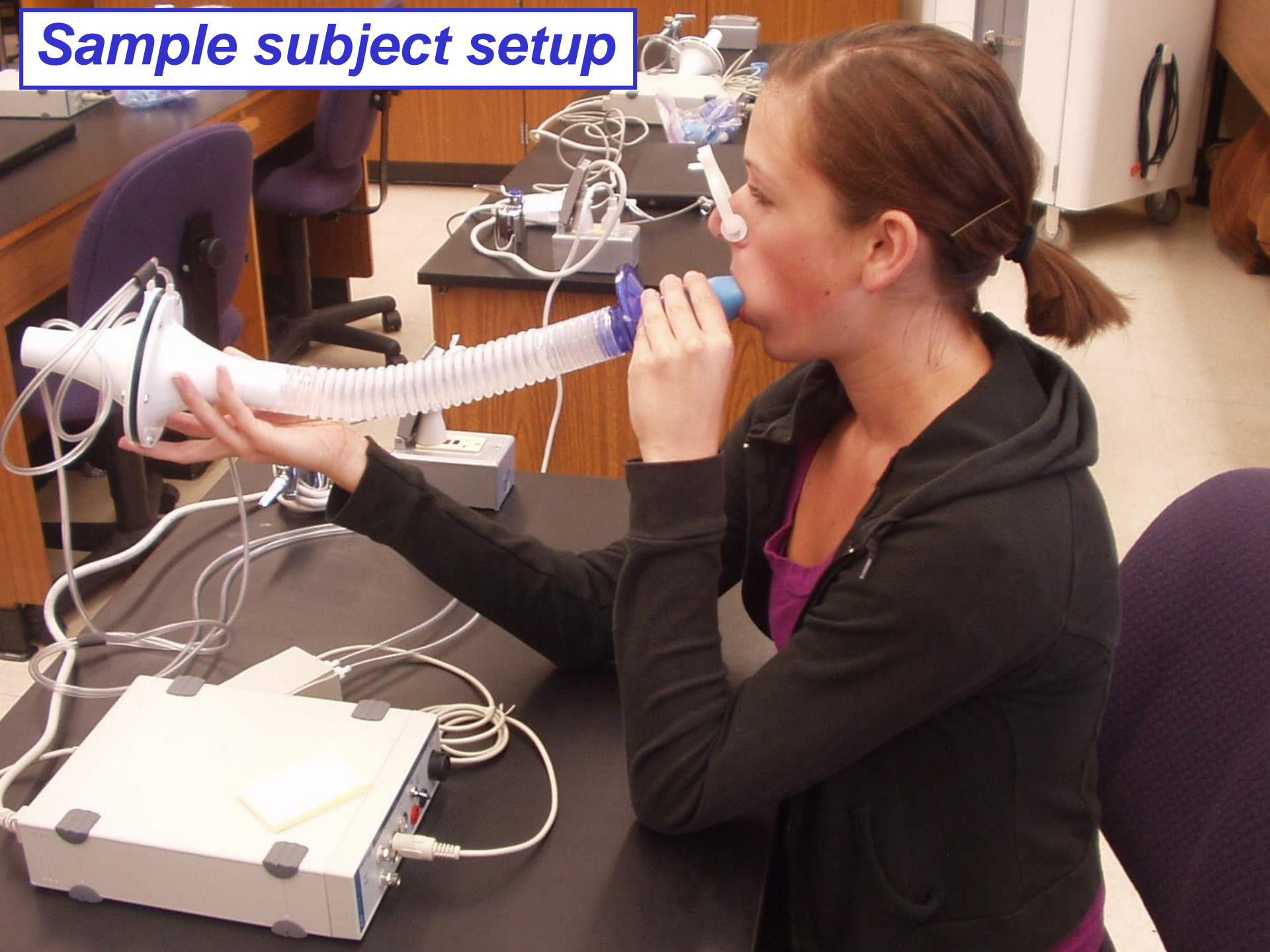


**How to put
together?**

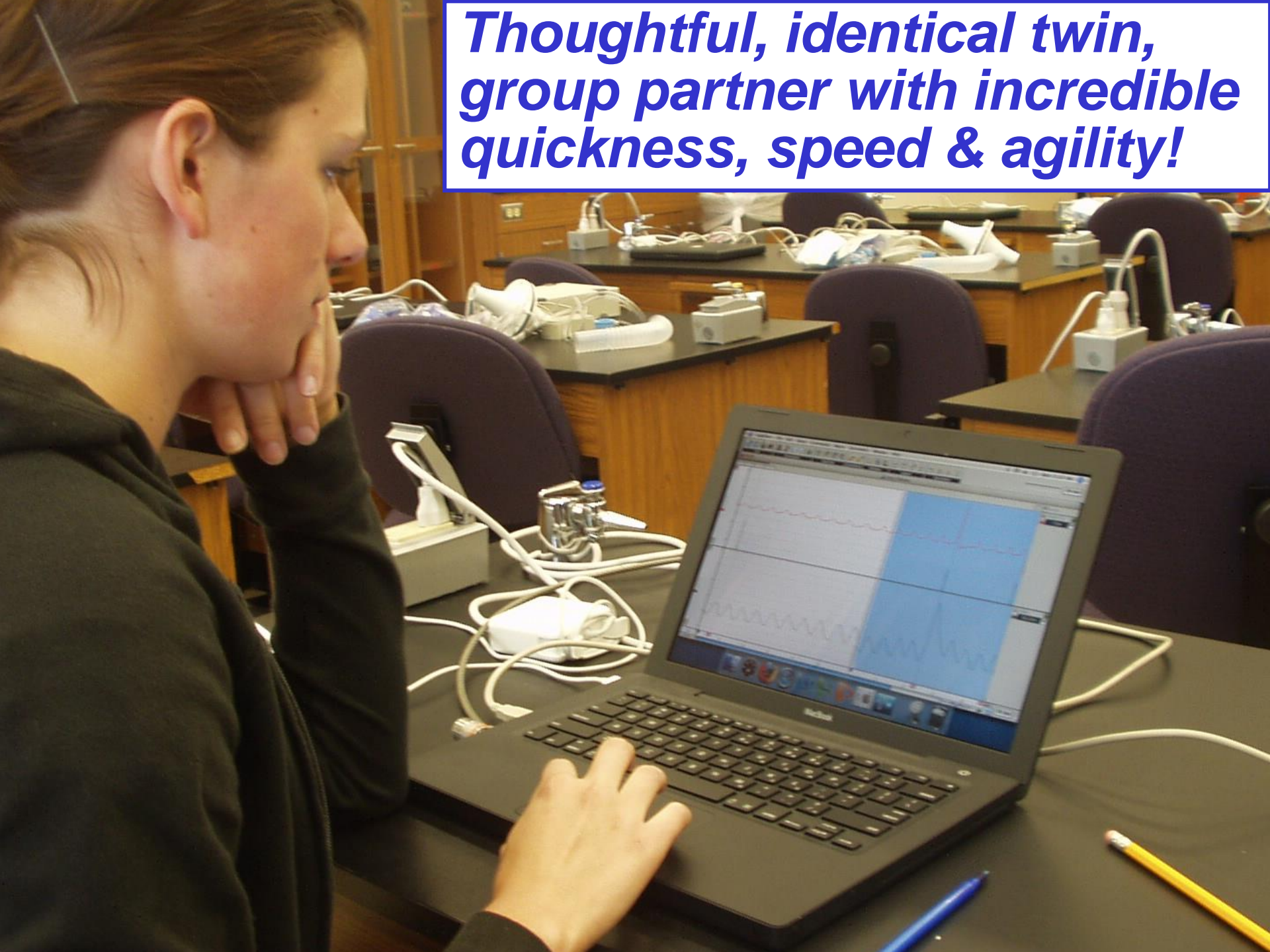
Viola!!



Sample subject setup

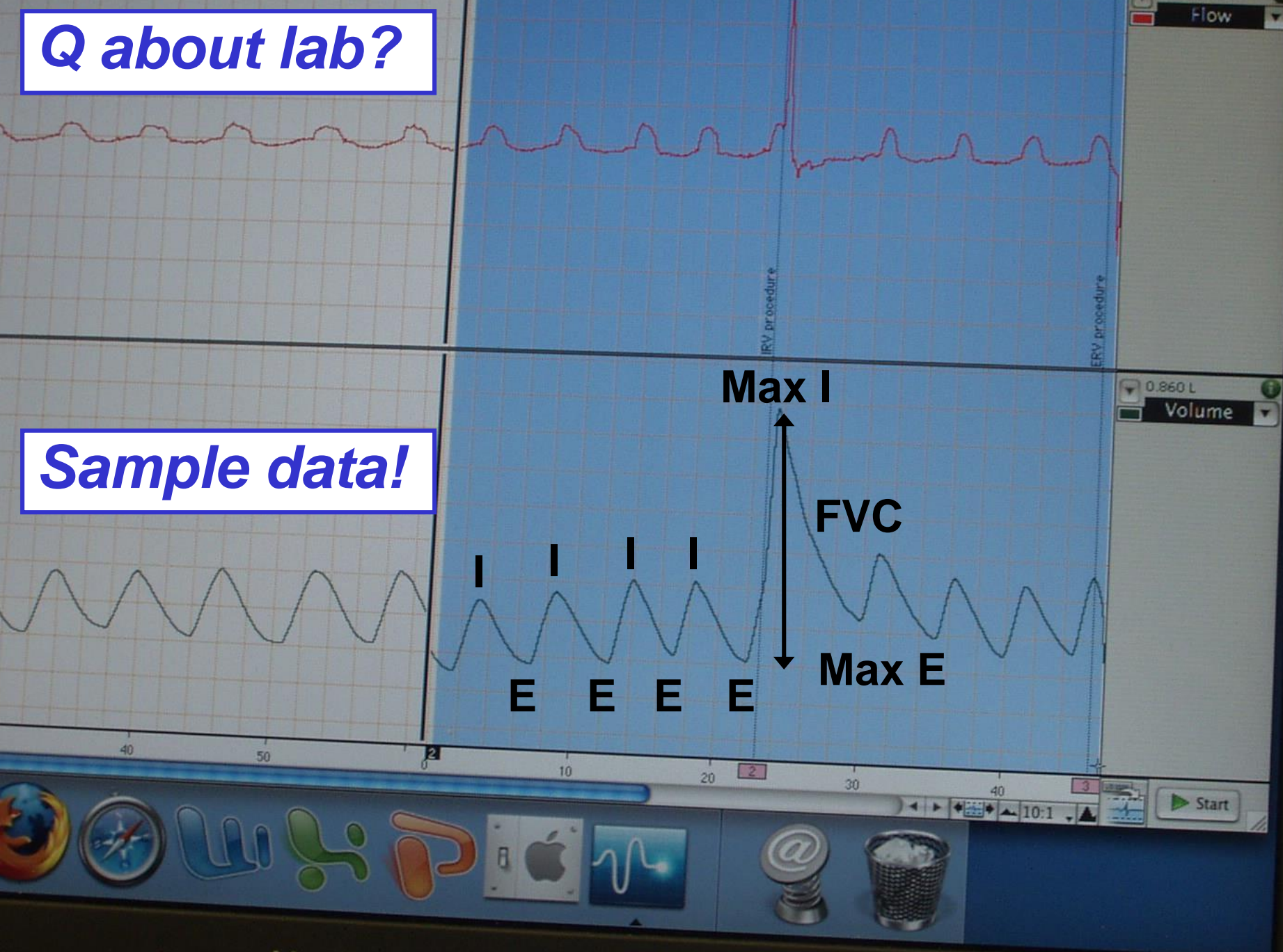


***Thoughtful, identical twin,
group partner with incredible
quickness, speed & agility!***



Q about lab?

Sample data!



MacBook

Lombo's simplified steps!

1 Breathe in & out!



2 Cross membranes!



3 Move with blood!

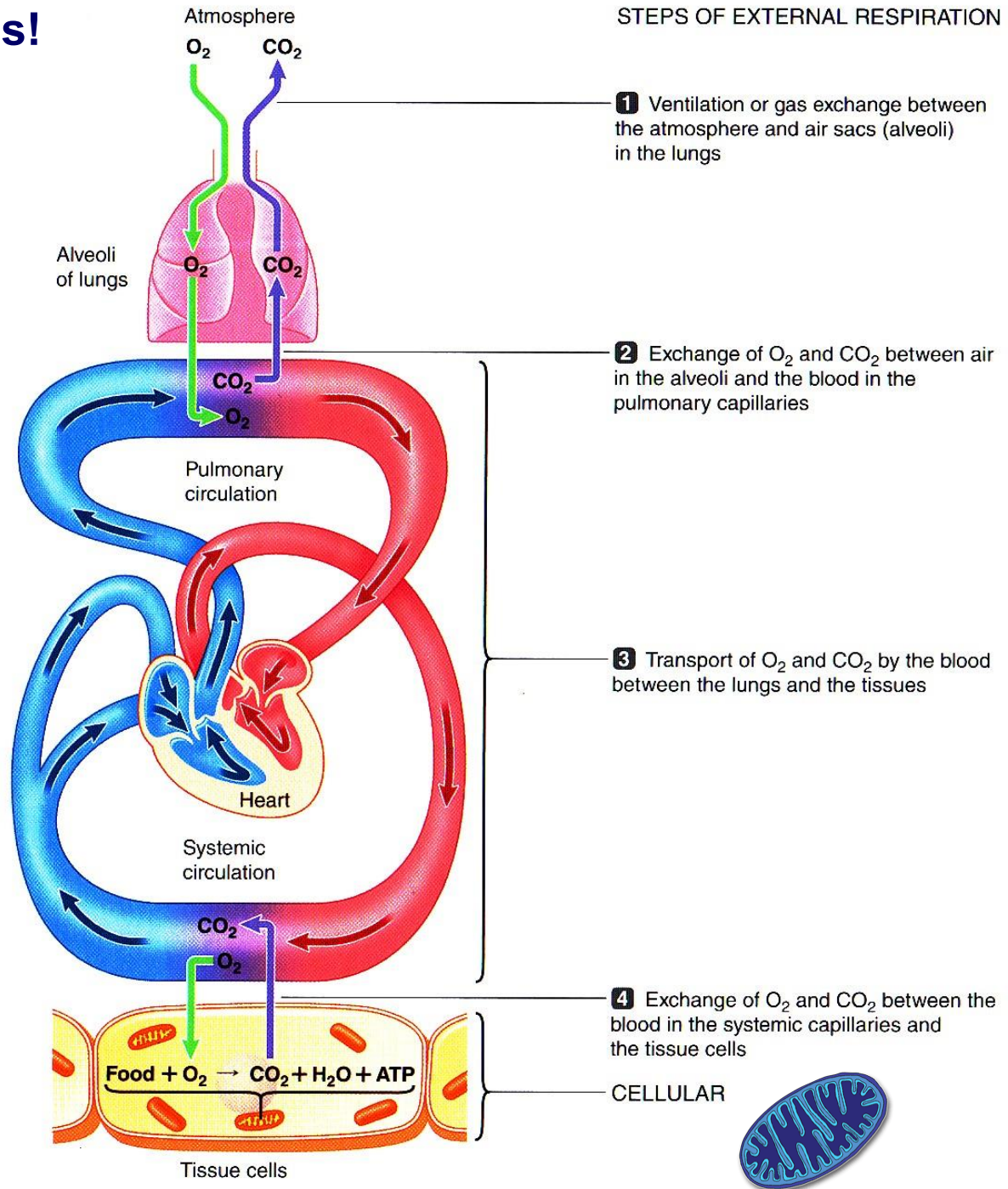
Go with the flow!



4 Cross membranes!

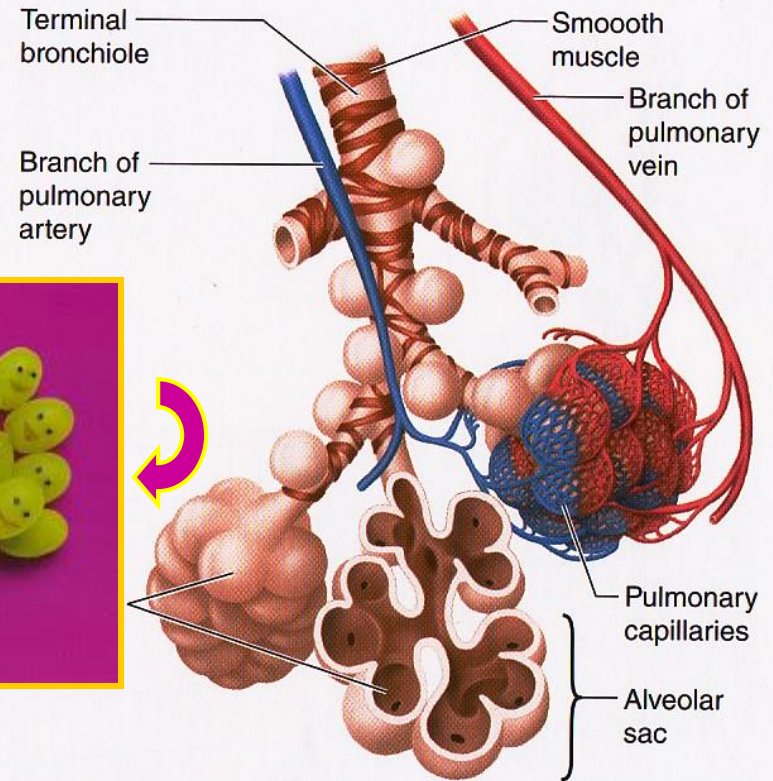
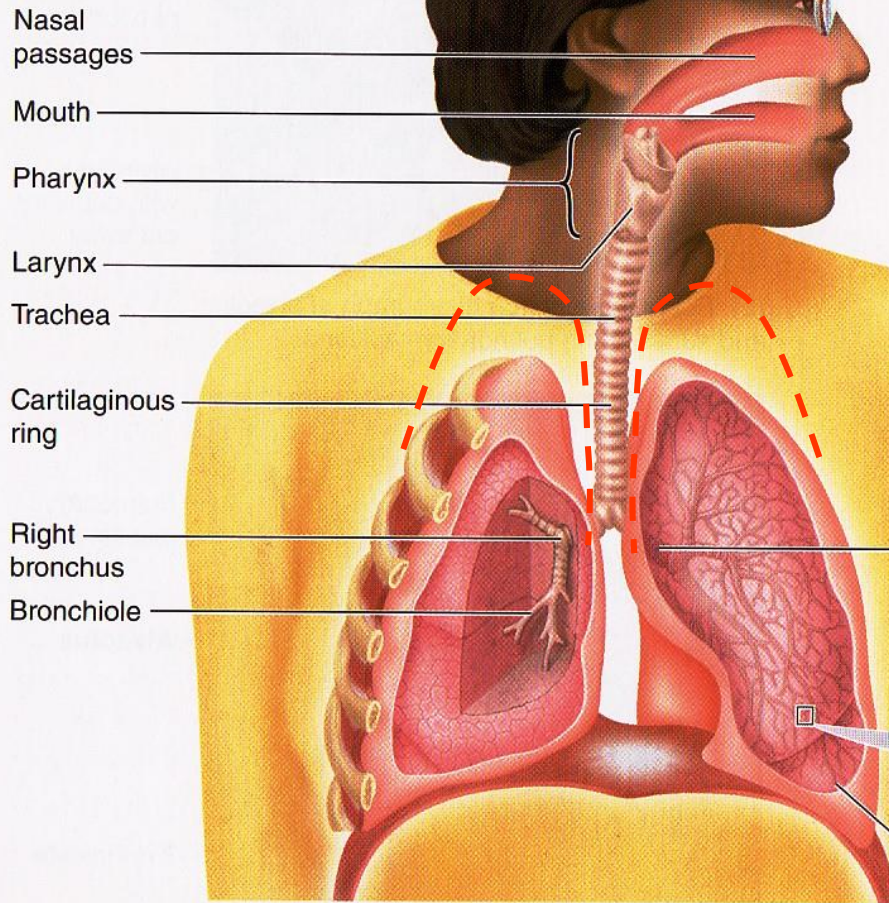


STEPS OF EXTERNAL RESPIRATION

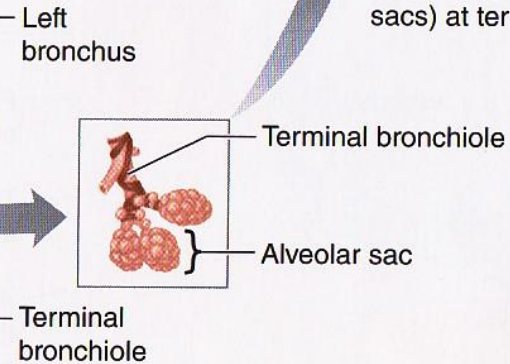


Respiratory System Anatomy

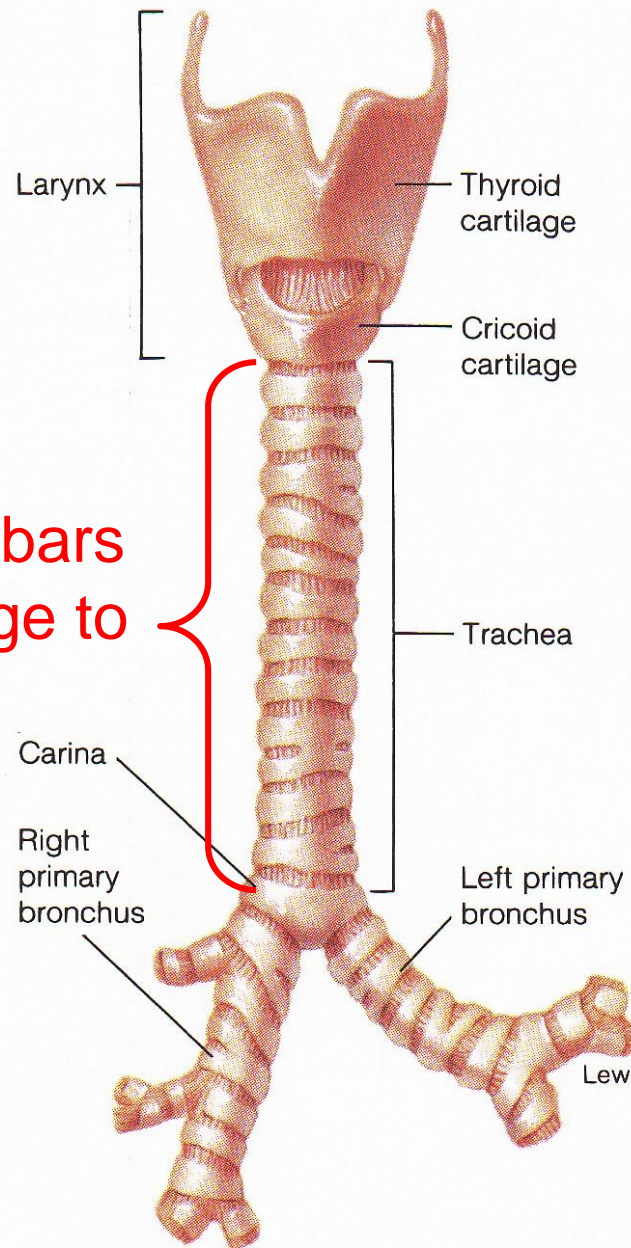
NB: In vivo,
Cupola or peak
of each lung
goes into neck
> clavicle line!

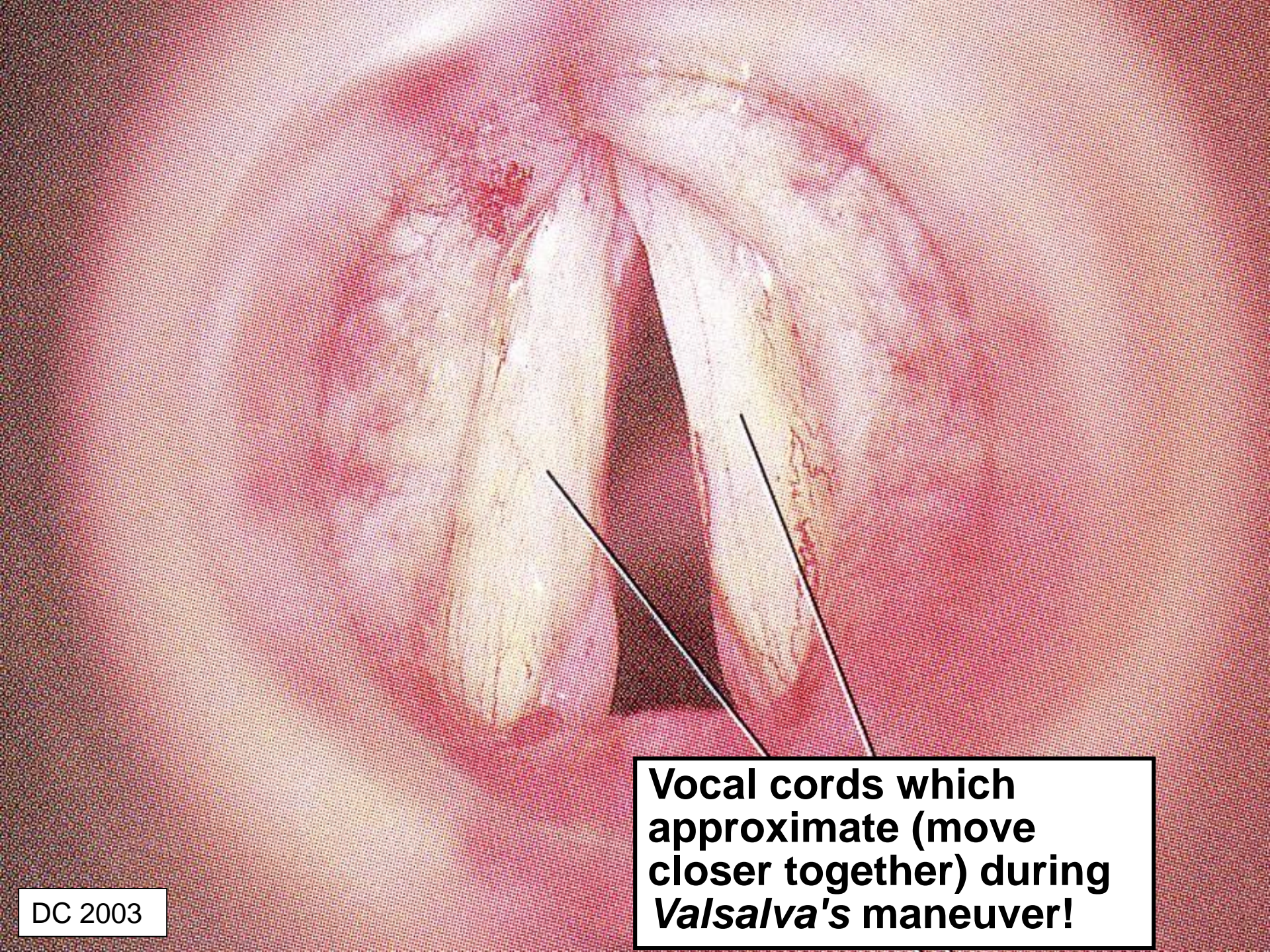


(b) Enlargement of alveoli (air sacs) at terminal ends of airways



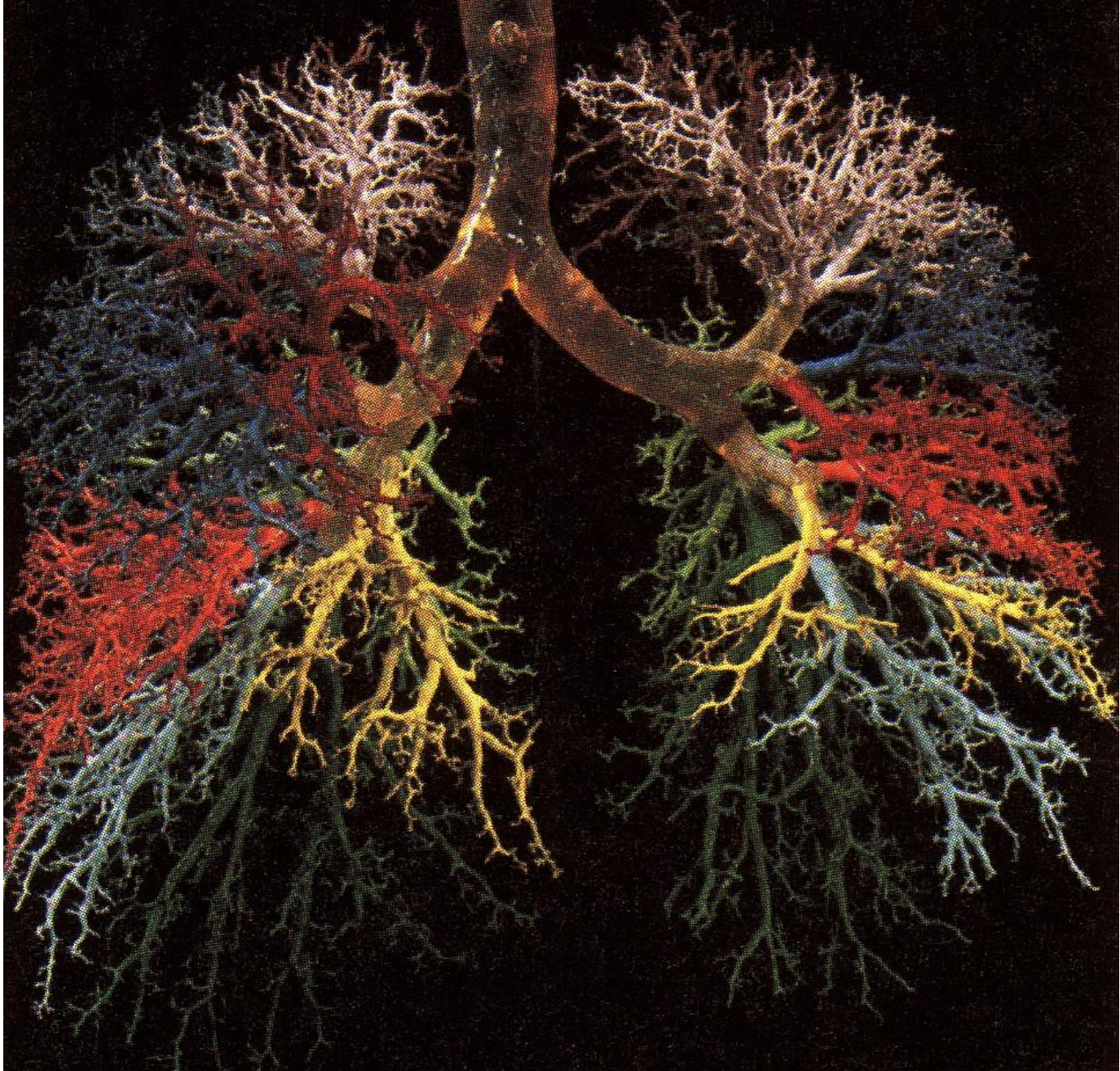
16-20 C-shaped bars
of hyaline cartilage to
prevent collapse



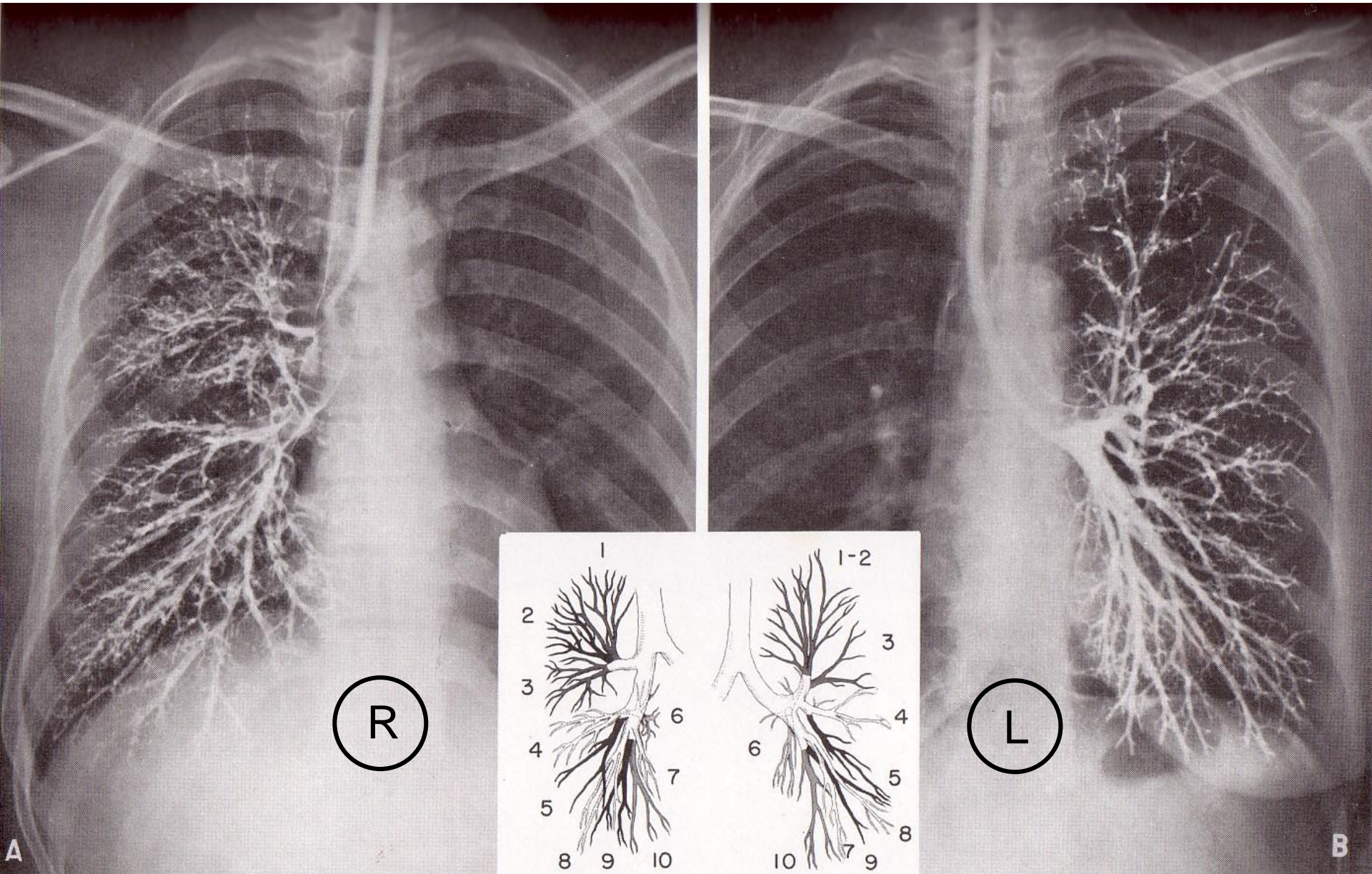


Vocal cords which approximate (move closer together) during *Valsalva's* maneuver!

Pulmonary Latex Cast with Colored Segmentation

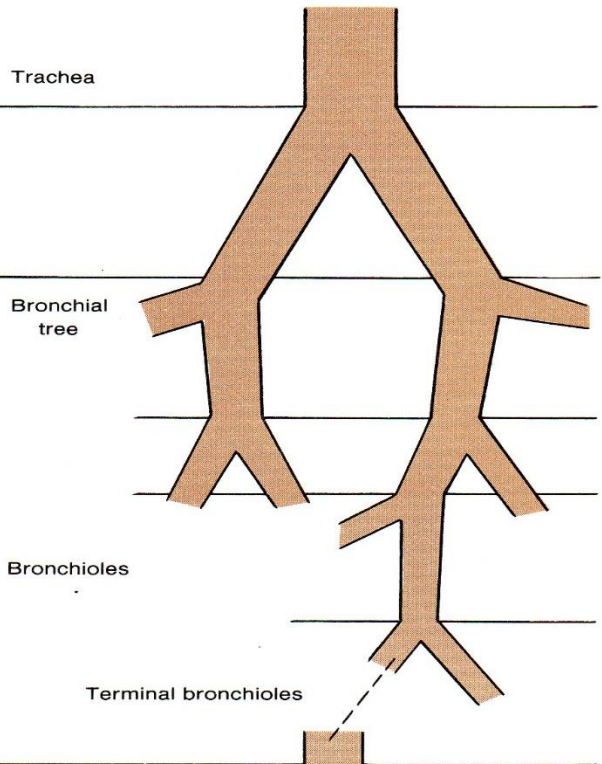


Bronchograms (posteroanterior)



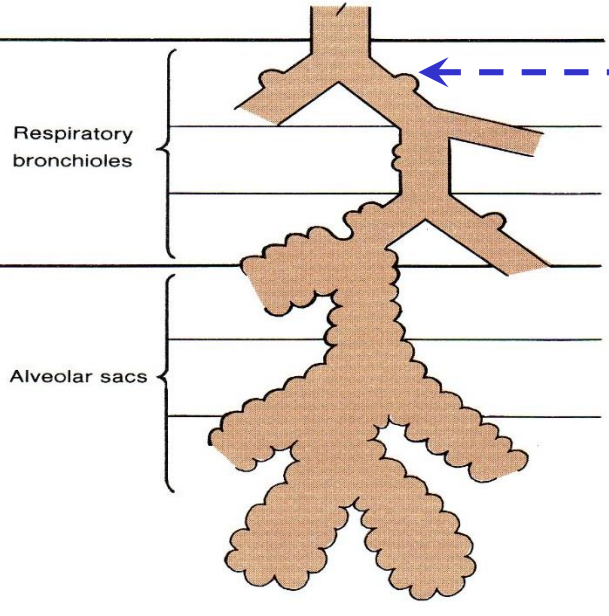
Source: Gardner, Gray, O'Rahilly, *Anatomy*, fig 29-11, p 295.

Conductive Zone



No Gas Exchange

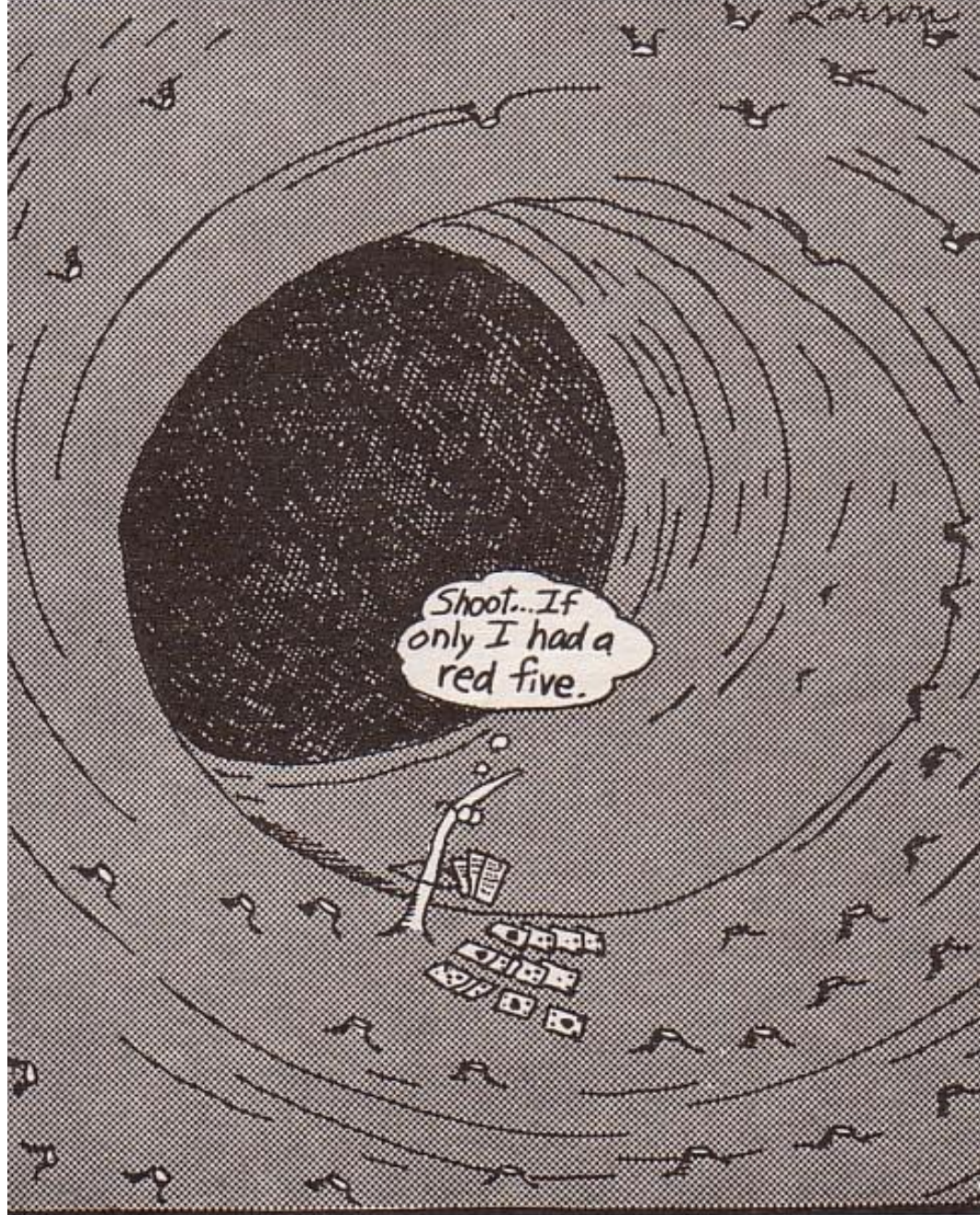
Respiratory Zone



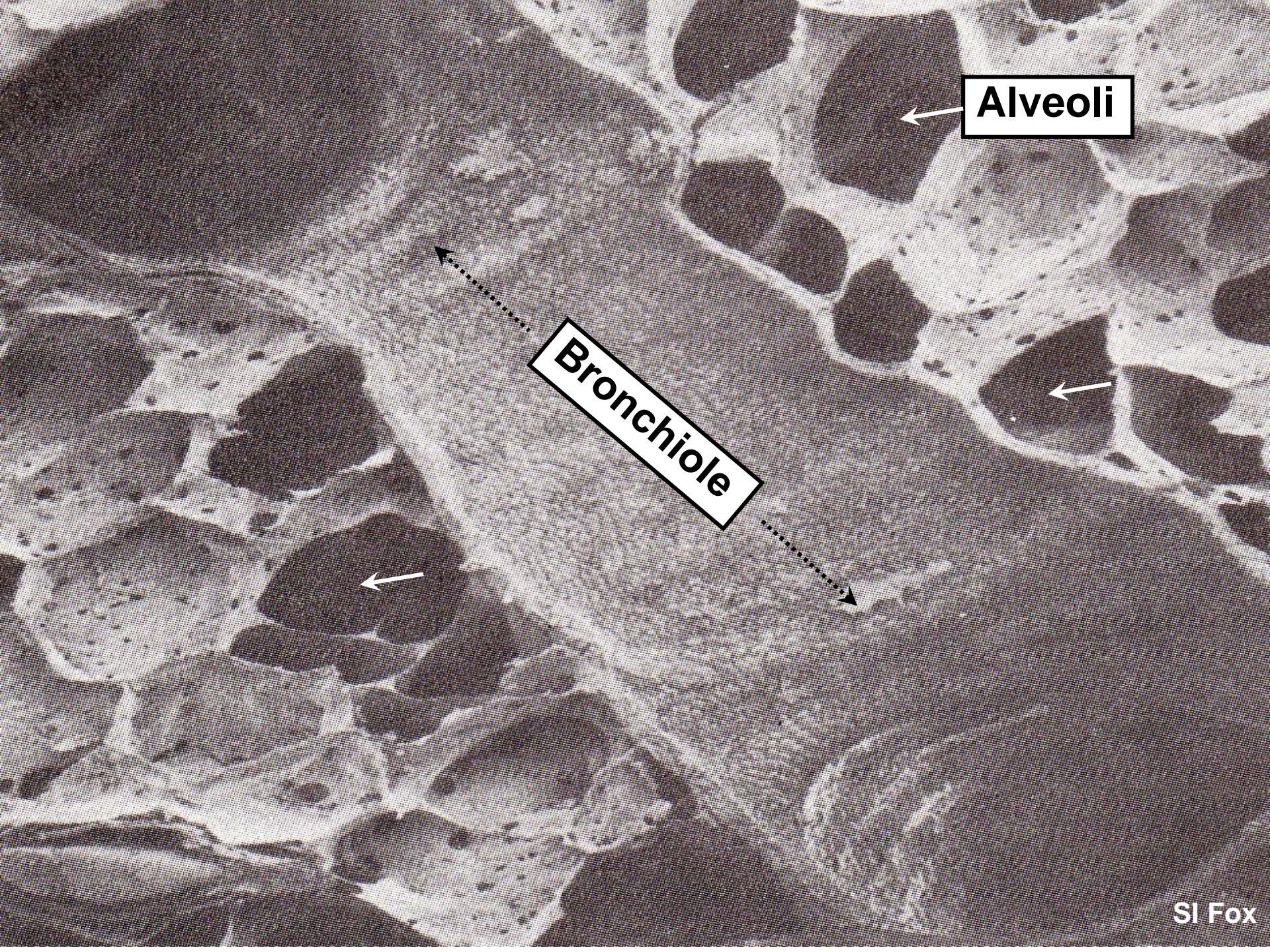
-1st alveolar outpouching!

Gas Exchange





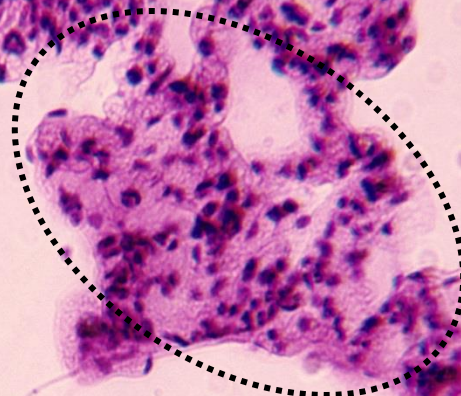
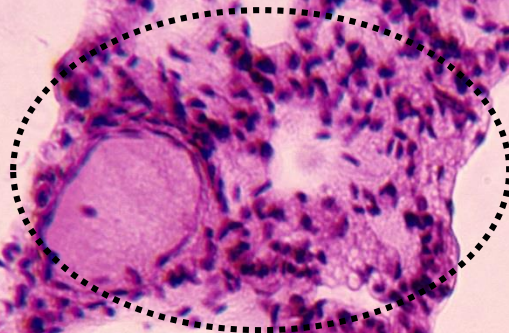
The last cilium on a smoker's lung



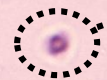
Alveoli

Bronchiole

Capillaries with rbcs!



← Alveoli →



White Blood Cell

Muscles of Ventilation

Accessory muscles of inspiration
(contract only during forceful inspiration)

Sternocleidomastoid

Scalenus

Internal intercostal muscles

Sternum

Ribs

External intercostal muscles

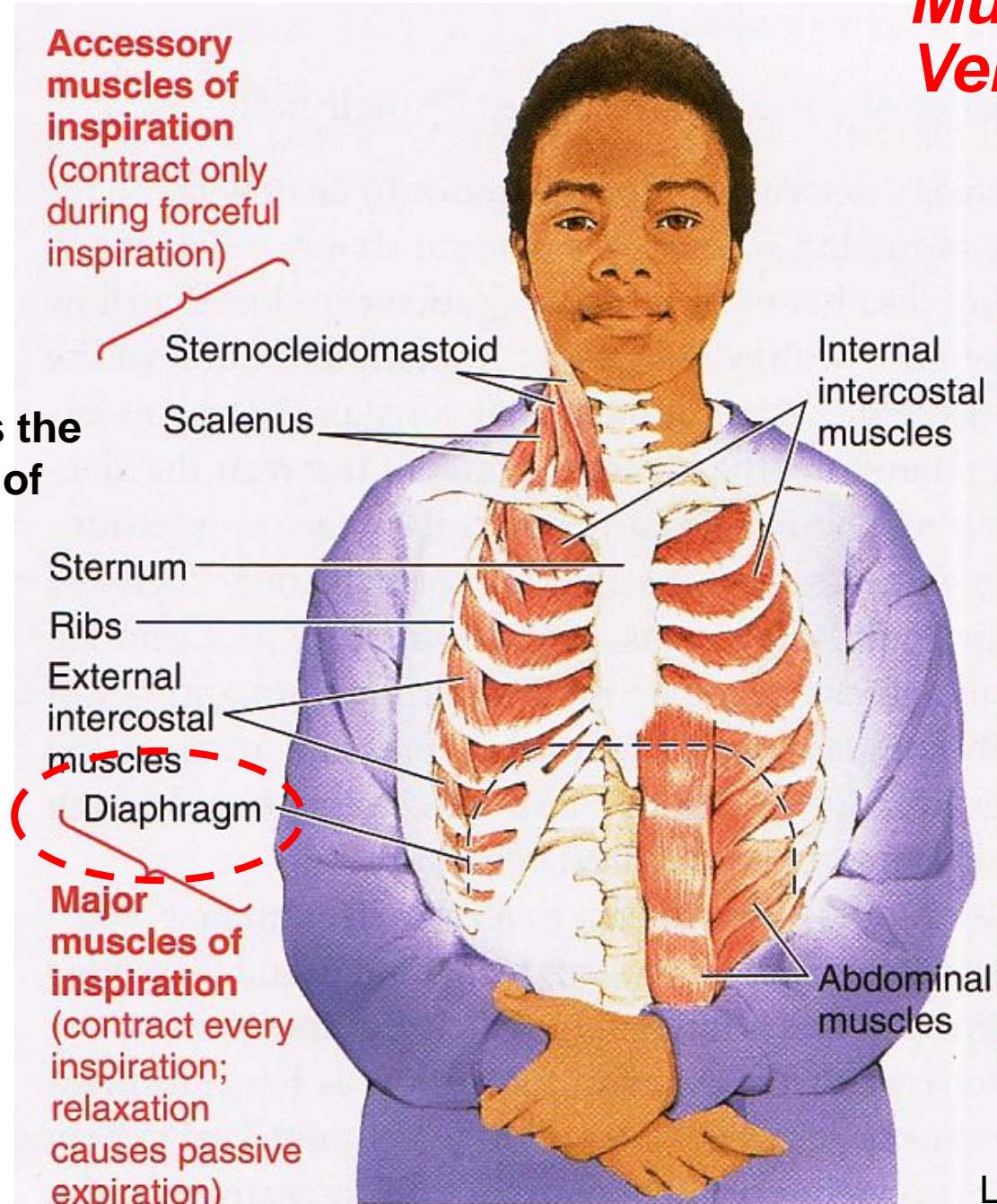
Diaphragm

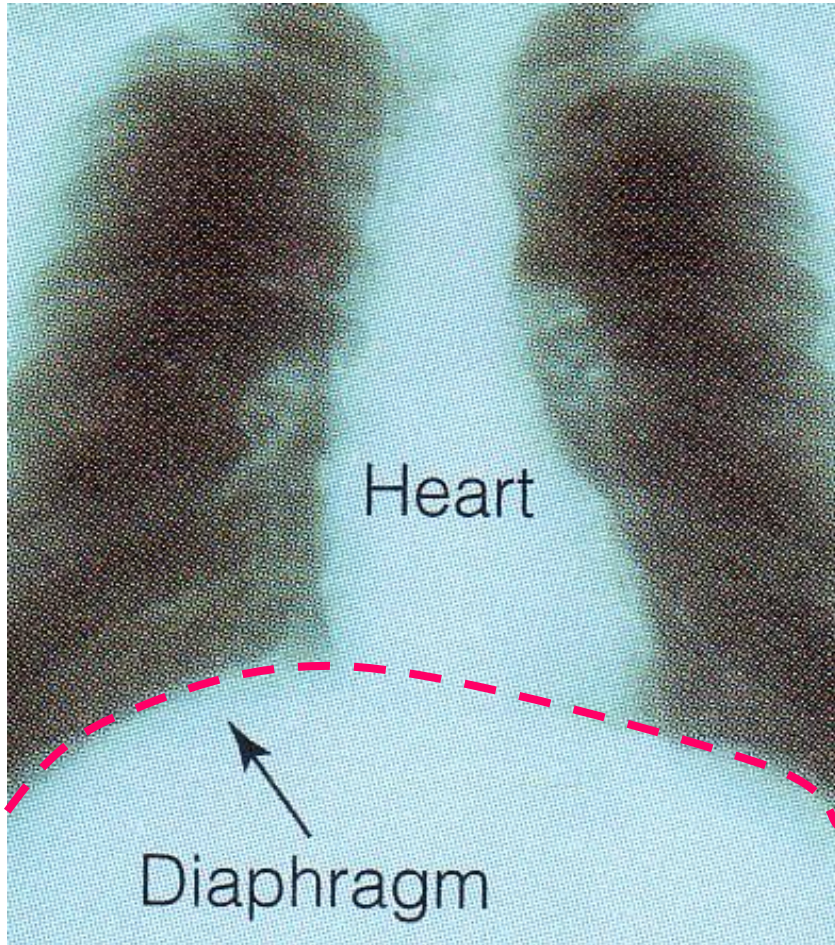
Major muscles of inspiration
(contract every inspiration; relaxation causes passive expiration)

Abdominal muscles

Muscles of active expiration
(contract only during active expiration)

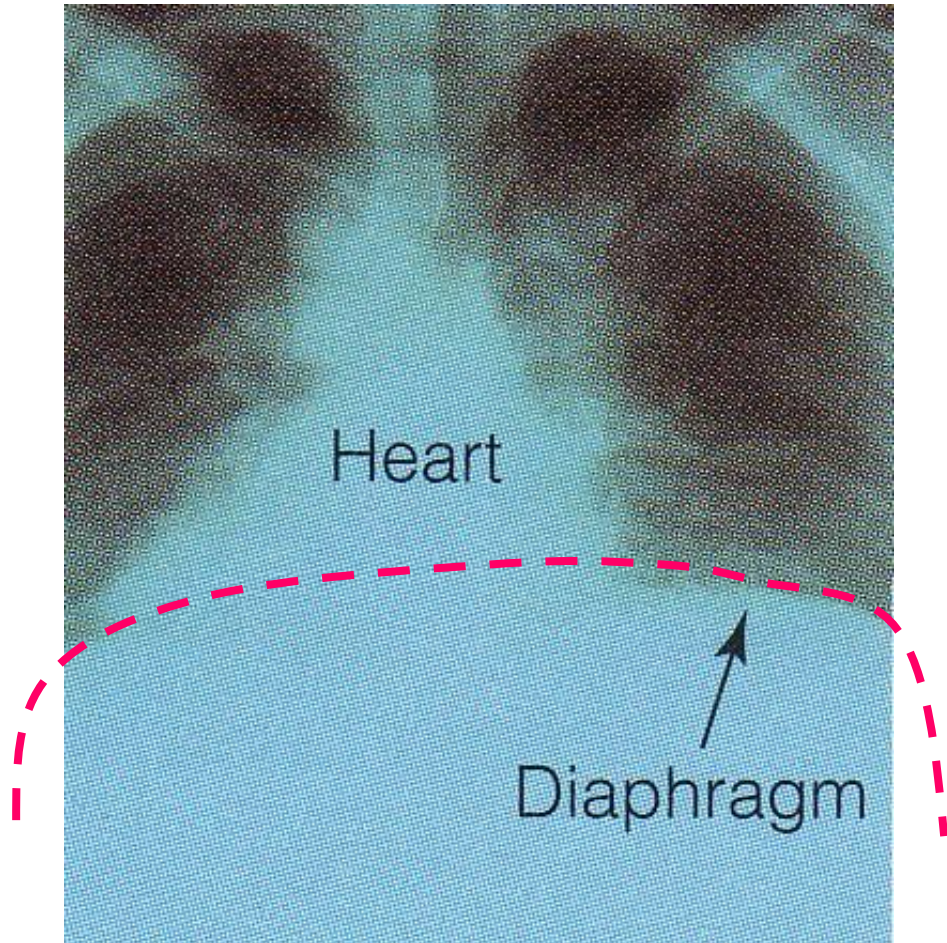
NB: Diaphragm is the chief muscle of ventilation!





Inhale (active)

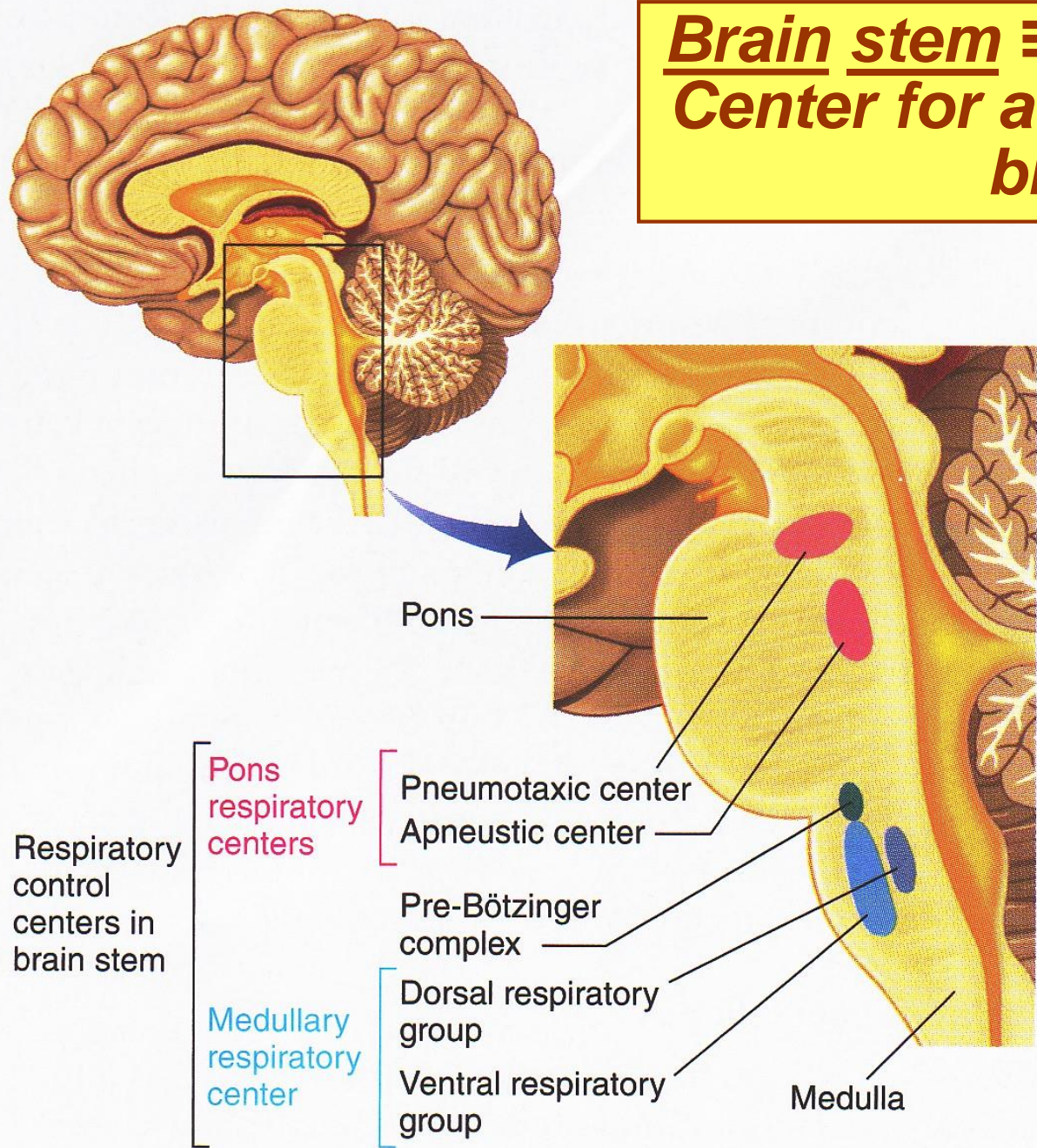
Contract & flatten diaphragm



Exhale (passive @ rest)

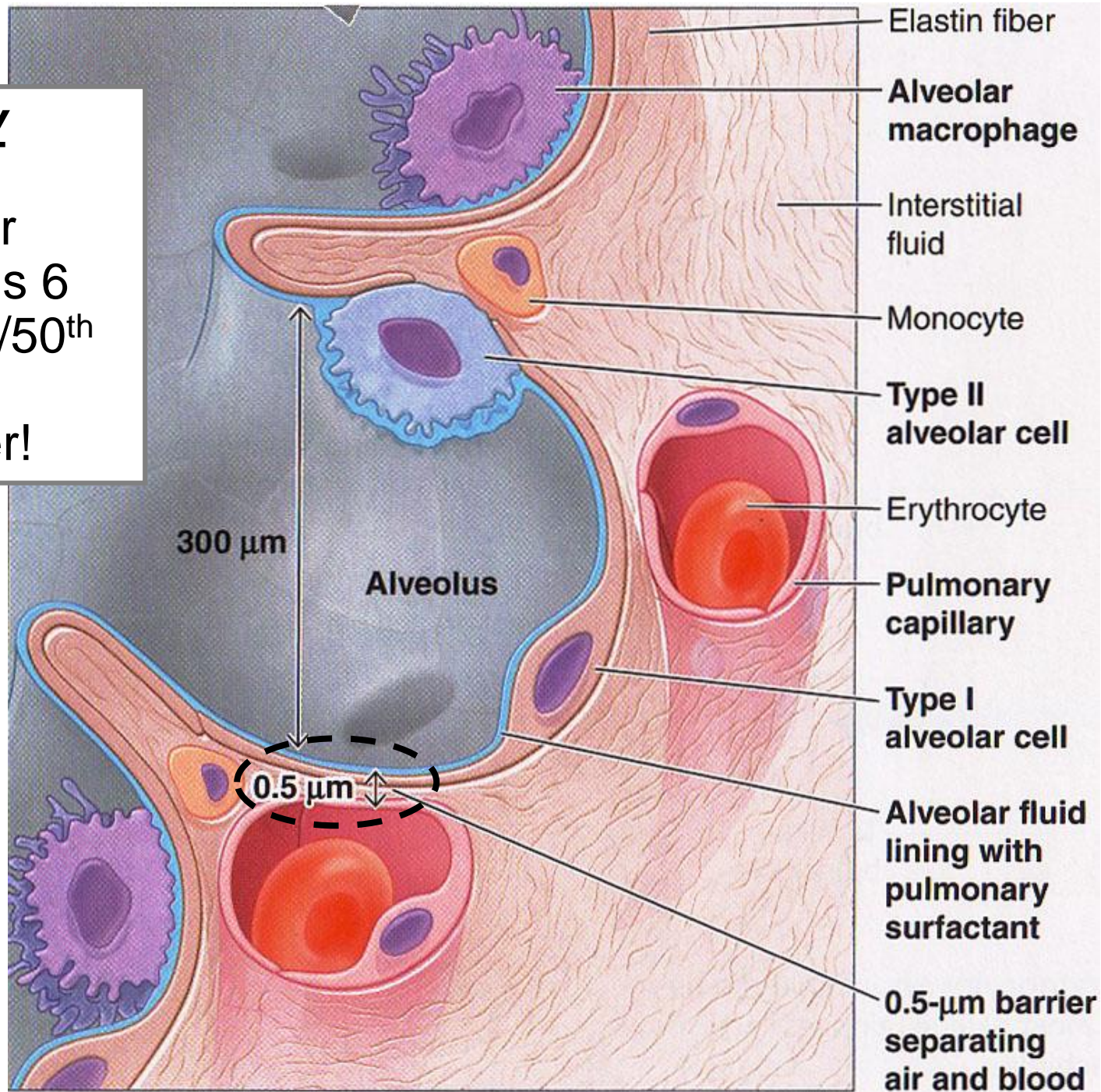
Relax & pouch up diaphragm!

Brain stem ≡ Control Center for automatic breathing!

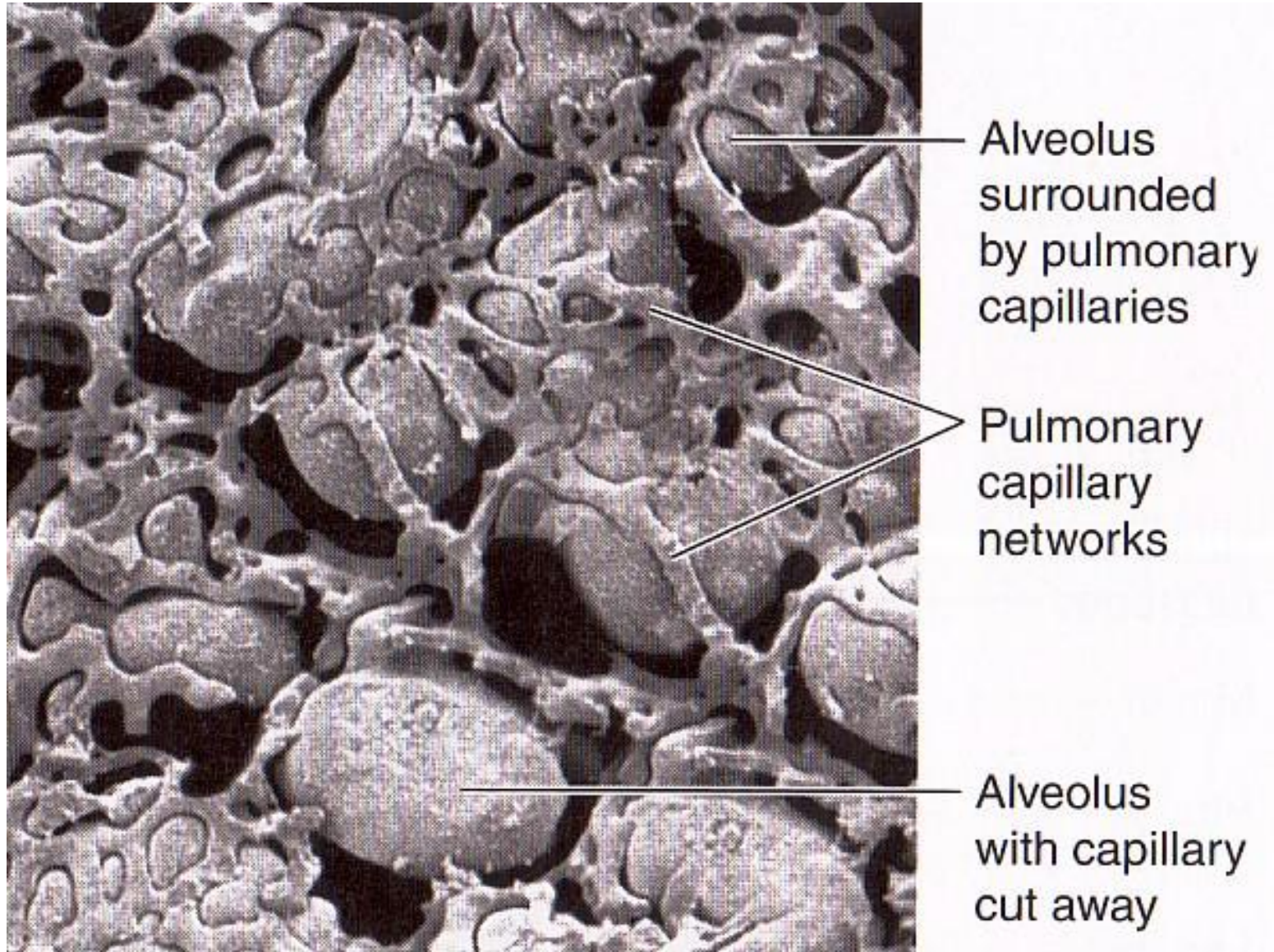


Respiratory membrane

separates air from blood, is 6 layers, yet 1/50th thickness of tracing paper!



Alveoli are surrounded by jackets of capillaries!



Gas Exchange

CO₂ LOW

O₂ HIGH

Across pulmonary capillaries:

O₂ partial pressure gradient from alveoli to blood = 60 mm Hg (100 → 40)

CO₂ partial pressure gradient from blood to alveoli = 6 mm Hg (46 → 40)

Across systemic capillaries:

O₂ partial pressure gradient from blood to tissue cell = 60 mm Hg (100 → 40)

CO₂ partial pressure gradient from tissue cell to blood = 6 mm Hg (46 → 40)

Numbers are mm Hg pressure.

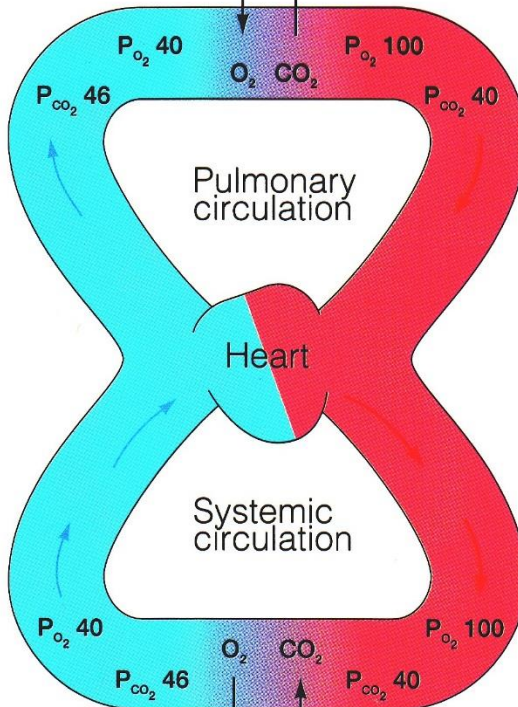
Inspired air

P_{O₂} 160

P_{CO₂} 0.3

P_{O₂} 100 P_{CO₂} 40

Alveolus



P_{O₂} < 40

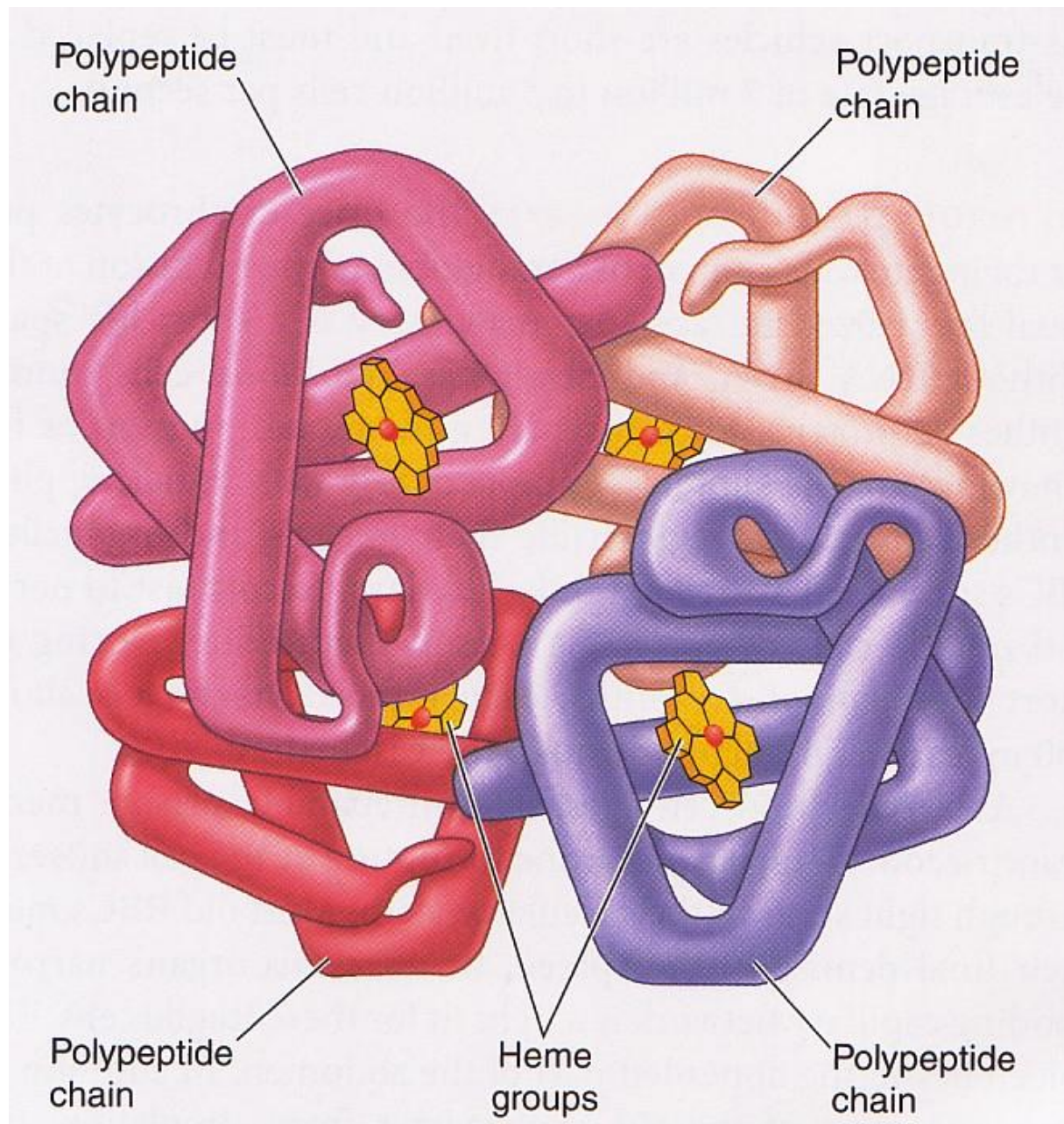
P_{CO₂} > 46

Tissue cell

CO₂ HIGH

O₂ LOW

O₂ is carried mainly by red blood cell hemoglobin!



▲ TABLE 12-3

Methods of Gas Transport in the Blood

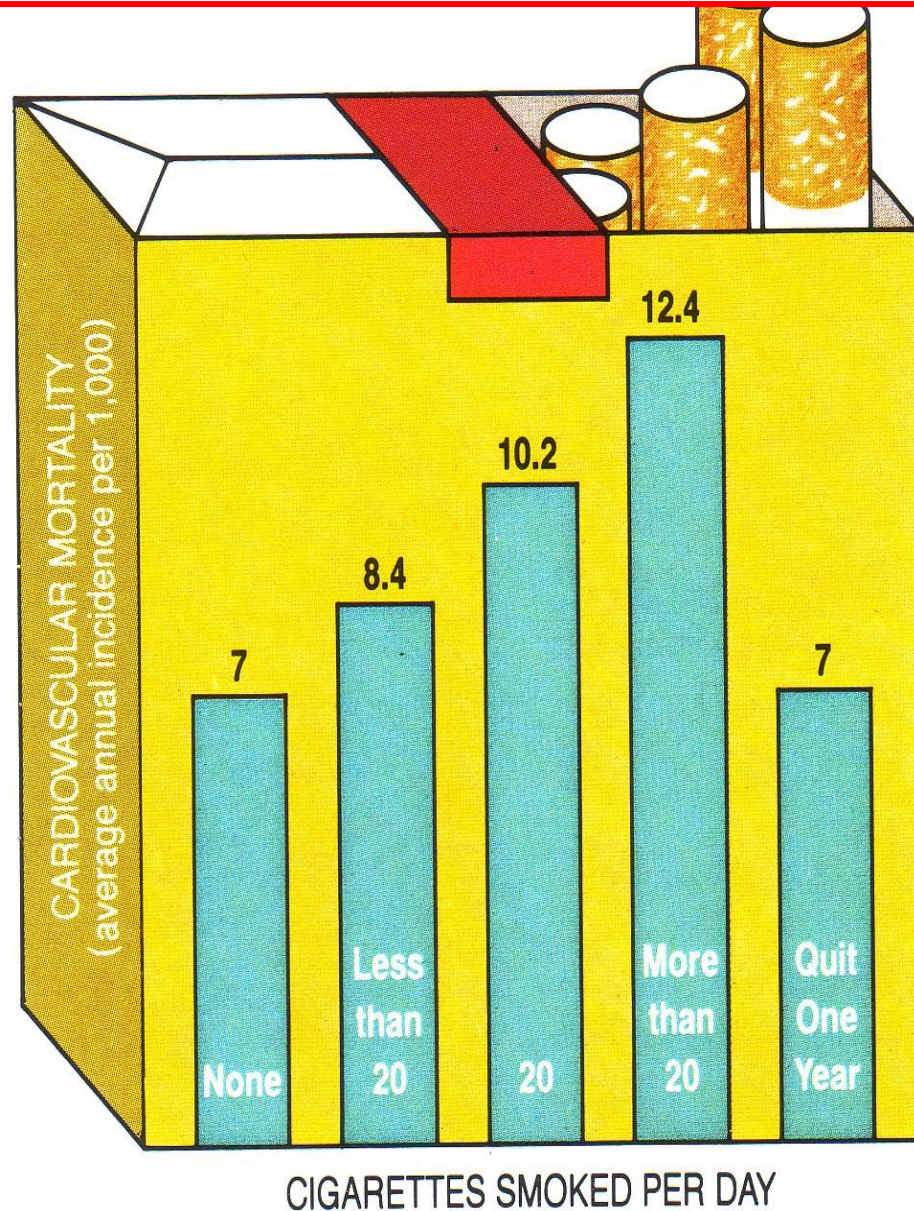
GAS	METHOD OF TRANSPORT IN BLOOD	PERCENTAGE CARRIED IN THIS FORM
O_2	Physically dissolved	1.5
	Bound to hemoglobin	98.5
CO_2	Physically dissolved	10
	Bound to hemoglobin	30
	As bicarbonate (HCO_3^-)	60

American Cancer Society Great American Smoke Out!

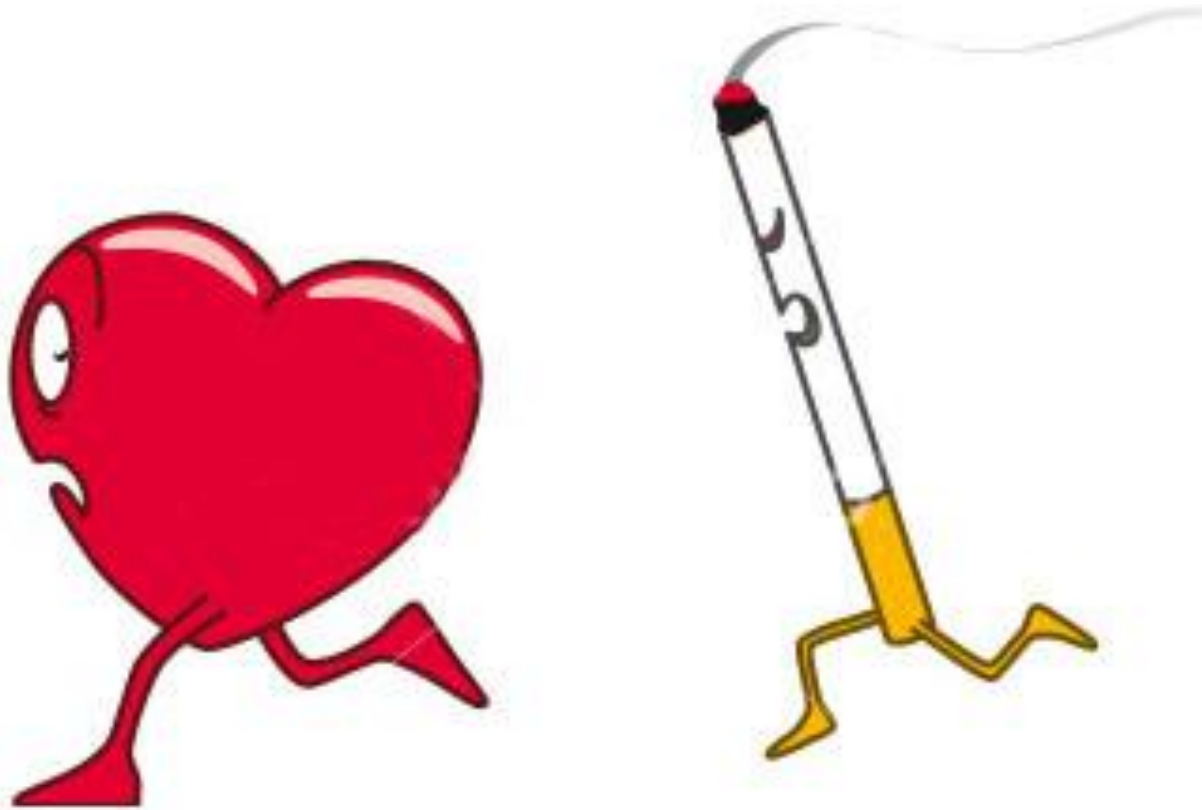


**[http://www.cancer.org/healthy/stayawayfromtobacco/
greatamericansmokeout/](http://www.cancer.org/healthy/stayawayfromtobacco/greatamericansmokeout/)**

Cigarette Smoking: #1 Preventable Cause of Premature Death in the US



***Not only the Lungs, but the Heart, Brain & 100s
of Other Tissues & Organs Adversely Affected!***



Tobacco smoke = Deadly mix of > 7000 chemicals!

[http://www.cdc.gov/tobacco/data_statistics/sgr/
50th-anniversary/index.htm#fact-sheets](http://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/index.htm#fact-sheets)

[http://www.cdc.gov/tobacco/data_statistics/sgr/
2010/consumer_booklet/chemicals_smoke/](http://www.cdc.gov/tobacco/data_statistics/sgr/2010/consumer_booklet/chemicals_smoke/)

Cancer-causing Chemicals



Formaldehyde
Used to embalm dead bodies



Benzene
Found in gasoline



Polonium 210
Radioactive and very toxic



Vinyl chloride
Used to make pipes

Toxic Metals



Chromium
Used to make steel



Arsenic
Used in pesticides



Lead
Once used in paint



Cadmium
Used in making batteries

Poison Gases



Carbon monoxide
Found in car exhaust



Hydrogen cyanide
Used in chemical weapons



Ammonia
Used in household cleaners



Butane
Used in lighter fluid



Toluene
Found in paint thinners

Tobacco smoke contains a deadly mix of **more than 7,000 chemicals**. Hundreds are toxic. About 70 can cause cancer. Here are some of the chemicals.

Tobacco-free Campus

For better health,
smoking and use of
tobacco products are
prohibited everywhere
on our property.



UO's Josh Buehler

U.S. Surgeon General
Regina Benjamin

SMOKE AND TOBACCO-FREE UNIVERSITY



September 1, 2012

For a healthier community and cleaner
environment, the University of Oregon
will be smoke and tobacco free



Ready to Quit Tobacco?

Visit tobaccofree.uoregon.edu for free and low cost resources



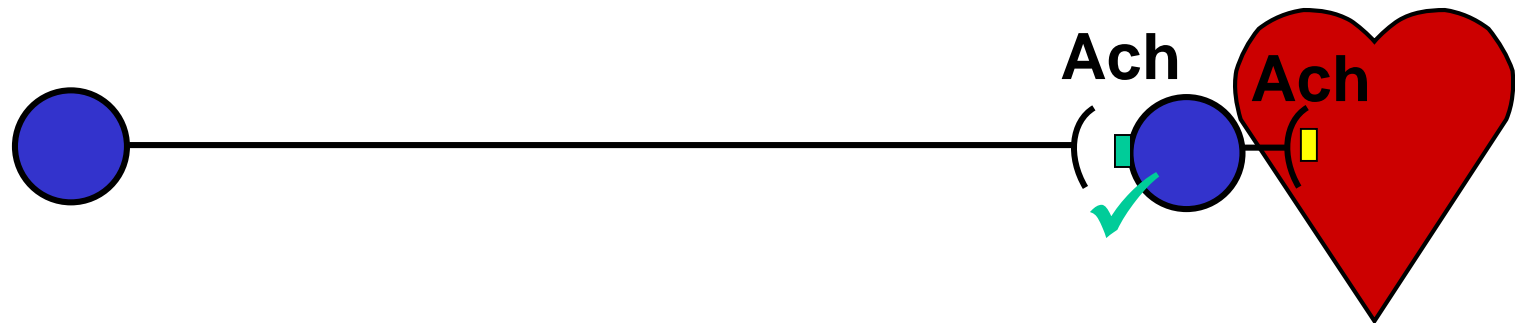
UNIVERSITY OF OREGON

tobaccofree.uoregon.edu



For a healthier community and cleaner
environment, the University of Oregon
is smoke and tobacco-free.

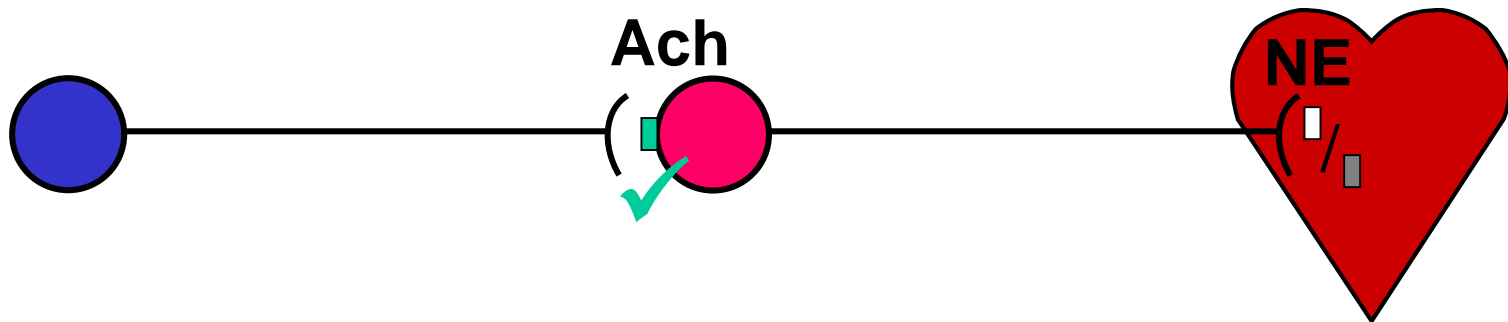
Parasympathetic



Ach = Acetylcholine

- = Nicotinic Receptor
- = Muscarinic Receptor

Sympathetic



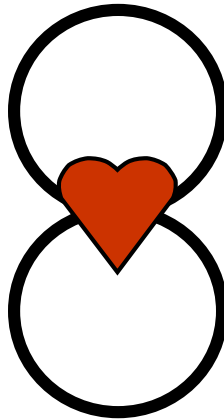
NE = Norepinephrine

- = α Receptor (α_1 , α_2)
- = β Receptor (β_1 , β_2)

Cigarettes ≡ Patient-Assisted Drug-Delivery System Inhaling Bypasses the Systemic Circulation & Is Powerfully Reinforcinging!



Pulmonary

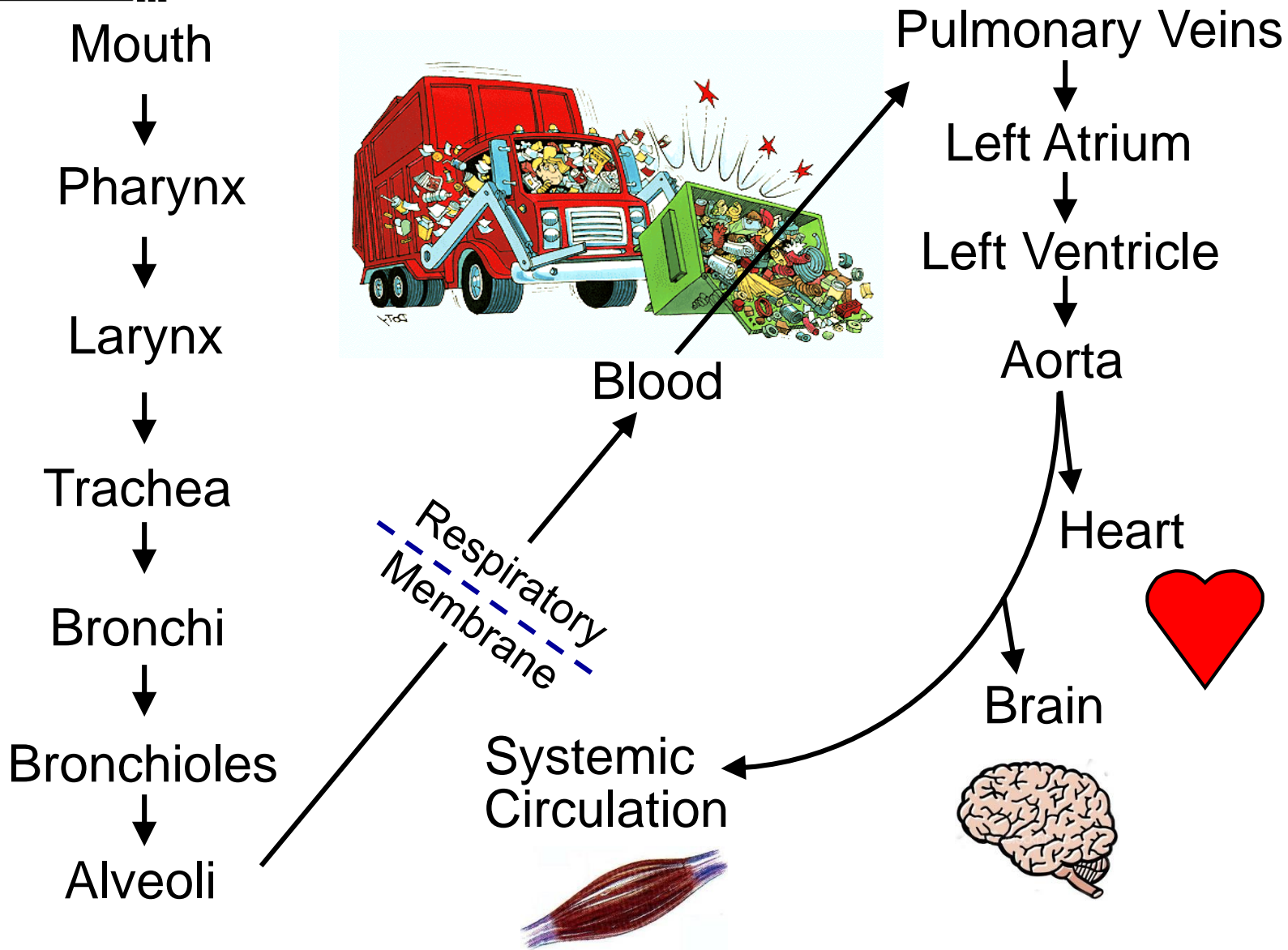


Systemic



Tracing the Route of Cigarette Smoke

Puff to Brain Time 5 to 8 seconds!!



OUTDOOR SYSTEMS

Recreation? Relaxation?

Keep it Basic



ACROSS

- 1. Celebrity
- 5. Nickname
- 8. Deep voice
- 12. Press clothes
- 13. Male name
- 14. Lotion

17. Used to

18. Agr

19. A

21. _____ of the Month

24. Corral

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
		A	M	E																									
		T	R	O	N																								
		L	E	N																									
		M	A																										

15. B A S I S

16. E L I

17. A L O E

18. L U R E

19. R I M

20. A I M E D

21. F L A V O R

22. A R M

15 mg "tar," 1.0 mg nicotine av. per cigarette by FTC method.

SURGEON GENERAL'S WARNING: CIGARETTE SMOKE CONTAINS CARBON MONOXIDE.

Keep it Basic?

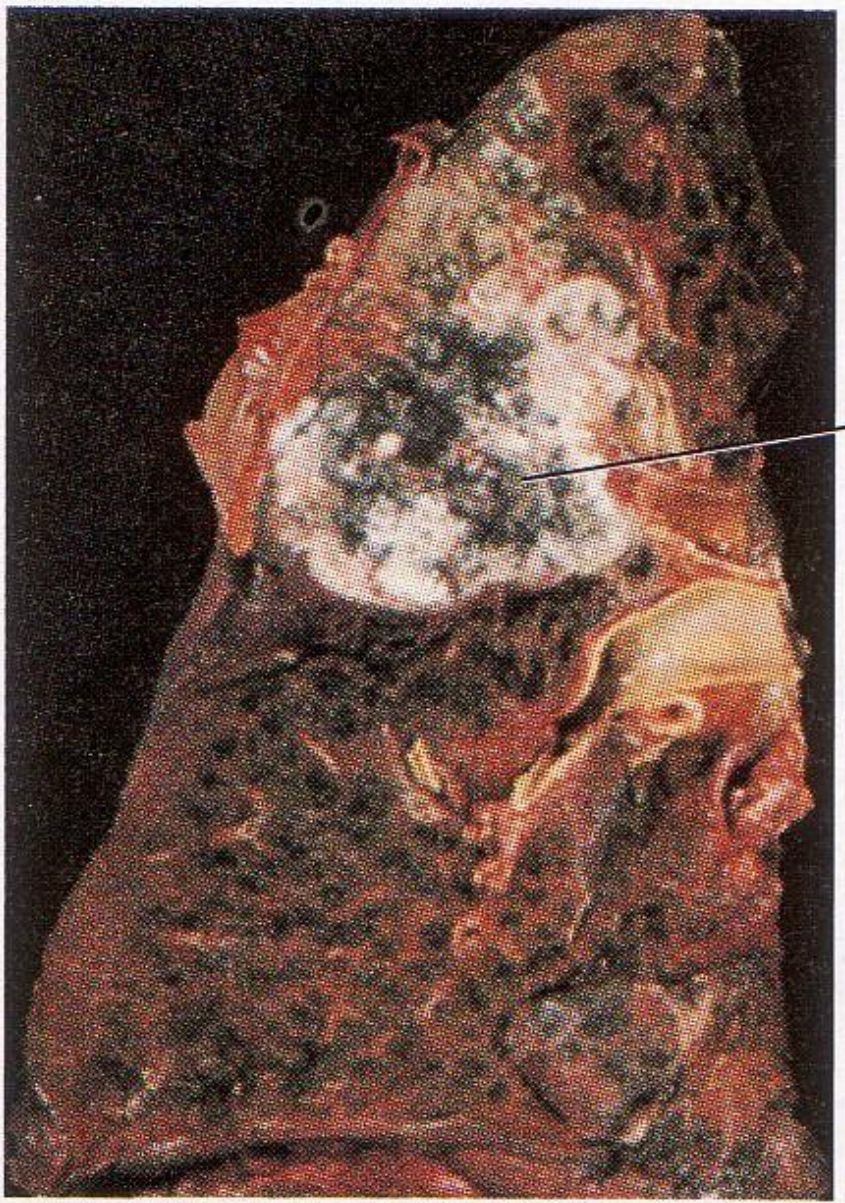
**Cigarette smoking is the
most important
preventable cause of
premature death in the
U.S. accounting for
443,000 annual deaths.**

[http://www.cdc.gov/tobacco/data_statistics/fact_sheets/
health_effects/tobacco_related_mortality/#cigs](http://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/tobacco_related_mortality/#cigs)

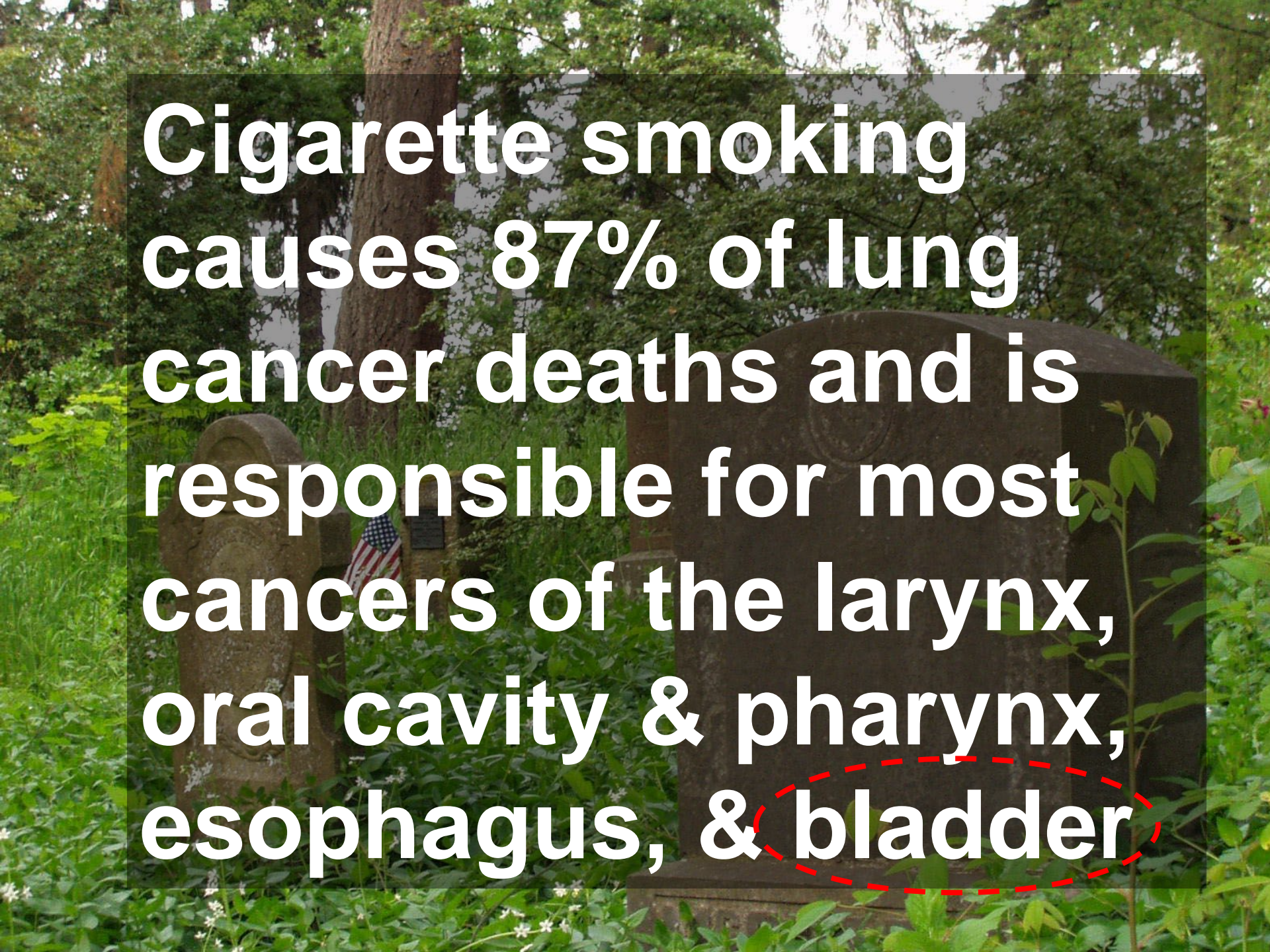
We know about lung cancer, but what about...?



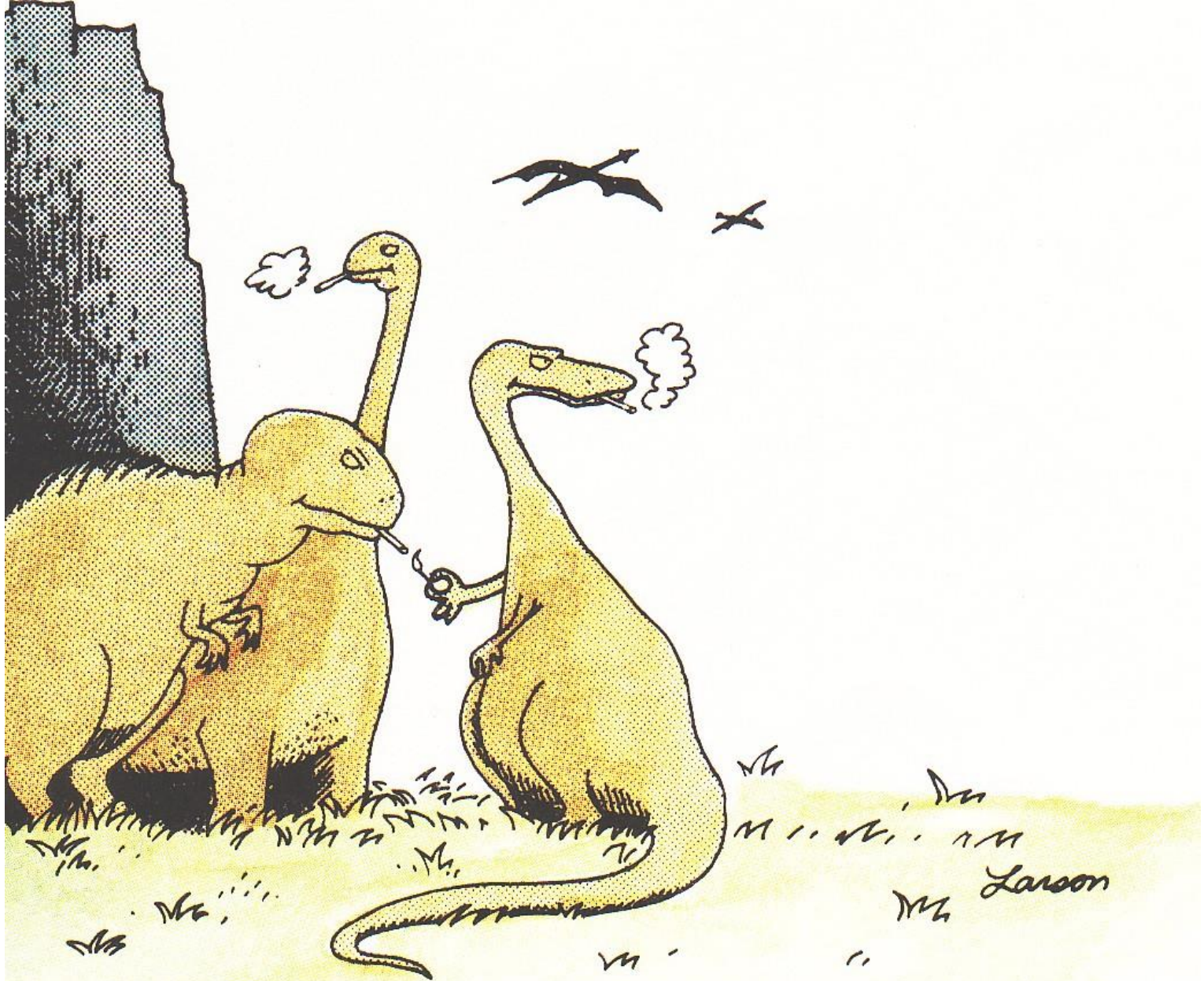
(a)



(b)

A photograph of a cemetery with several tombstones and lush green trees in the background. A semi-transparent grey text box is overlaid on the image, containing white text. The word 'bladder' in the text is circled with a red dashed line.

Cigarette smoking causes 87% of lung cancer deaths and is responsible for most cancers of the larynx, oral cavity & pharynx, esophagus, & bladder



The real reason dinosaurs became extinct

Macho Man?

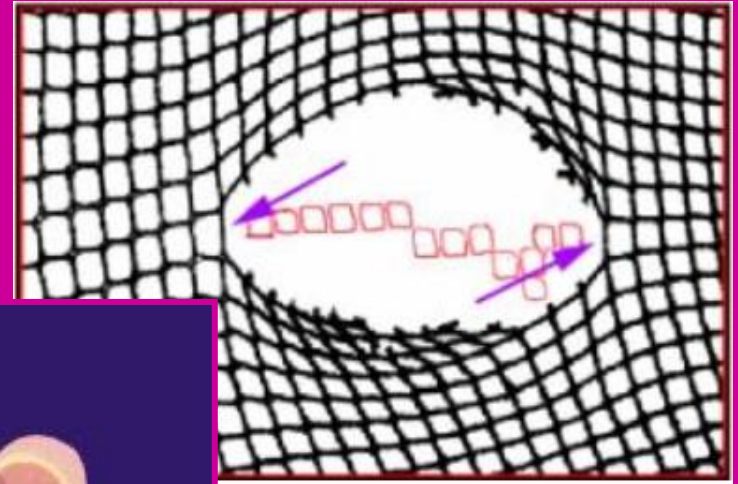
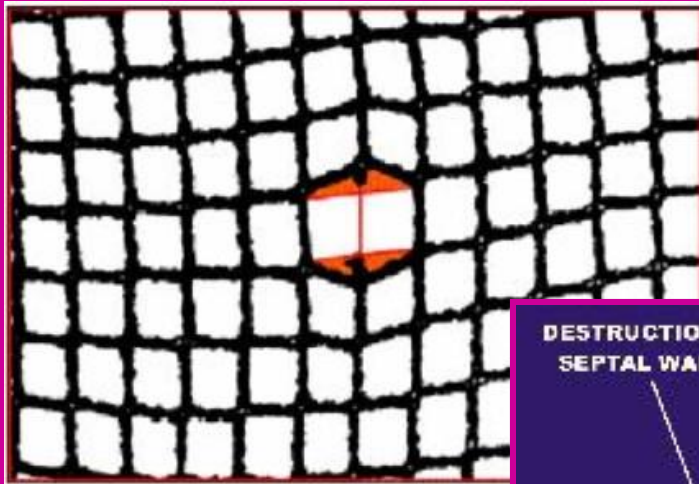


Bob, I've got Emphysema.

WARNING: Cigarette Advertising Makes
Smoking Look Cool And Cowboys Look Stupid.

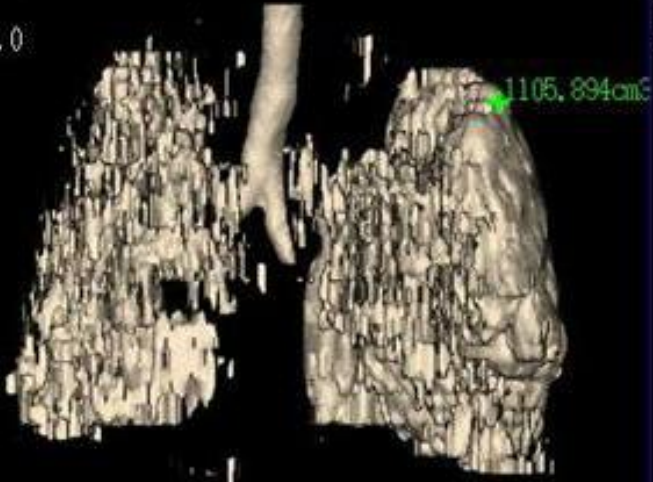
0A1405

Emphysema ≡ Corrosion of Alveolar Walls with ↓ SA & Labored Breathing

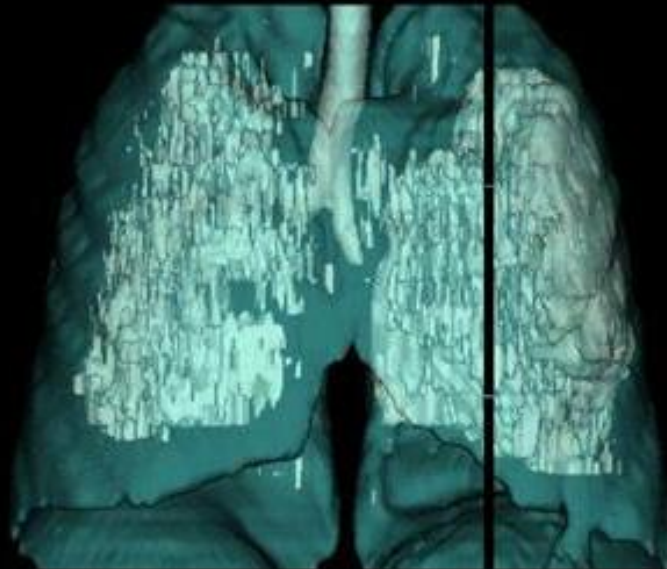
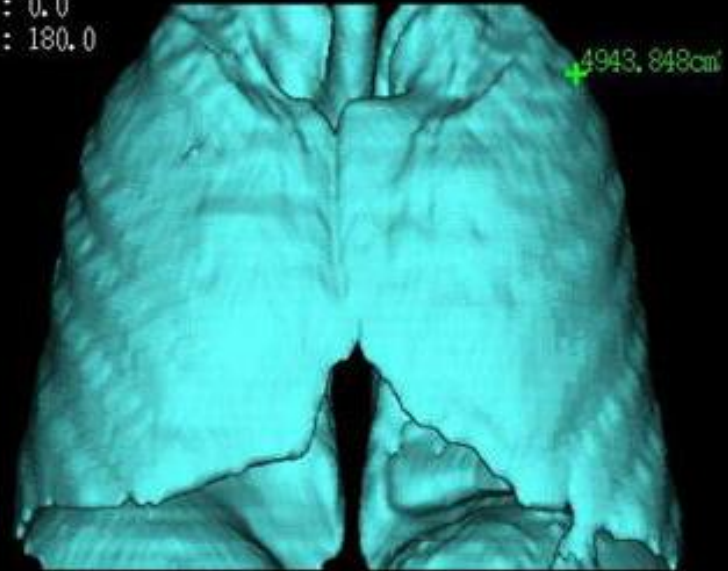


CT Densitovolumetry in Heavy Smoker with Emphysema Indicating ~ 22% Compromise of Lung Parenchyma

Y : 0.0
Z : 180.0



Y : 0.0
Z : 180.0



SOURCE: Corrêa da Silva, 2001, from *Emphysema Imaging* Ali Nawaz Khan

<http://www.realityunfiltered.com/>



Terrie Hall, who has appeared in television commercials for Tobacco.Reality.Unfiltered., started smoking when she was 18. She smoked two packs a day for twenty-two years before she was diagnosed with throat cancer. She had a permanent tracheotomy and has fought cancer seven times. The photo to the right is of Terrie as a teenager. Photos: Tobacco.Reality.Unfiltered.



Why you have to tell your gynecologist you smoke. Even if it's only at parties.

©AMP 2008 03/11/08

You figure an occasional cigarette can't hurt, and you really don't want to listen to the "stop smoking" lecture from your doctor. But if you want any type of hormonal birth control, smoking is a vitally important issue.

Hormonal birth control is a prescription drug, and while the risks are rare, they can be serious, and smoking, even a little, increases the risks, especially if you're over 35.

Risks include blood clots, stroke, and heart attack. If you have a history of these conditions or certain cancers, you shouldn't use hormonal birth control.

Of course, you should tell your healthcare professional if you could be pregnant, and because hormonal birth control doesn't protect against HIV or sexually transmitted diseases, learn how to stay safe and healthy.

Hormonal birth control has been used safely by millions of women for 45 years, and is 99% effective when used correctly.

It could be a good choice for you. To find out, talk to your healthcare professional. And to help you get started, there's a list of questions to ask at: www.orthowomenshealth.com



Be smart about your body.
Be smart about your birth control.

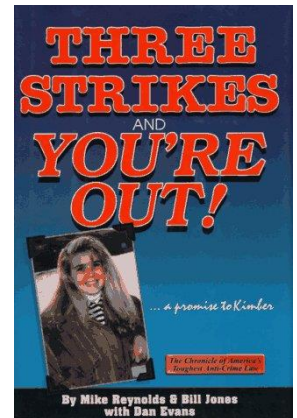
On the Pill & Smoke?

Increased Risk of:

1. Blood Clots

2. Heart Attack

3. Strokes!



**Breathing 2nd-hand
smoke for as little as
1/2 hr activates
platelets almost as
much as if you were a
pack-a-day smoker**

2nd-hand smoke is the 3rd leading preventable cause of death in the US!

A photograph of a man in a tuxedo with a cigarette in his mouth, looking at a woman. The text "Mind if I smoke?" is overlaid on the image.

"Mind if I smoke?"

"Care if I die?"

Each year ~45,000 Americans die due to 2nd-hand smoke exposure!

News: Health, Toxicology, Pollution

Health risks of e-cigarettes emerge

Vaping pollutes lungs with toxic chemicals and may even make antibiotic-resistant bacteria harder to kill

By JANET RALOFF 4:31PM, JUNE 3, 2014



<https://www.sciencenews.org/article/health-risks-e-cigarettes-emerge>

DEEP BREATH Half of the pollutant vapors inhaled by an e-cigarette user may make it into the lungs, a new study finds.

Magazine issue: Vol. 185 No. 13, June 28, 2014

Electronic cigarettes, marketed as safer than regular cigarettes, deliver a cocktail of toxic chemicals including carcinogens into the lungs, new studies show. Using e-cigarettes may even make bacterial infections resistant to antibiotics, according to one study.

Engineers developed e-cigarettes several years ago to provide tobacco users a smoke-free source of nicotine. The devices heat up a liquid that a user inhales, or “vapes.” Because e-cigarettes burn nothing, they release no smoke.

“There’s no question that a puff on an e-cigarette is less toxic than a puff on a regular cigarette,” says Stanton Glantz, director of the Center for Tobacco Control Research and Education at the University of California, San Francisco. But few studies have looked at the toxicity of their vapors. As a result, scientists have been circumspect about describing e-cigarettes as safe.

For a May 13 review in *Circulation*, Glantz and his team pored over emerging data on what vapers are inhaling and found, he says, greater risk than scientists had thought. E-cigarettes deliver high levels of nanoparticles, the researchers found, which can trigger inflammation and have been linked to asthma, stroke, heart disease, and diabetes (*SN: 7/18/09, p. 26*). The levels “really raise concerns about heart disease and other chronic conditions where inflammation is involved,” he says.

E-cigarettes are no longer niche products, he and others note. Vaping product sales last year were projected to hit an estimated \$1.7 billion, report Li-Lun Chen and Corinne Husten of the Food and Drug Administration’s Center for Tobacco Products in Rockville, Md., in a special May issue of *Tobacco Control* on e-cigarettes. E-cigarette sales may exceed those of traditional cigarettes within 10 years, the pair reports. At least 1 in 5 smokers has tried e-cigarettes, as have 10 percent of U.S. high school students, according to the U.S. Centers for Disease Control and Prevention.

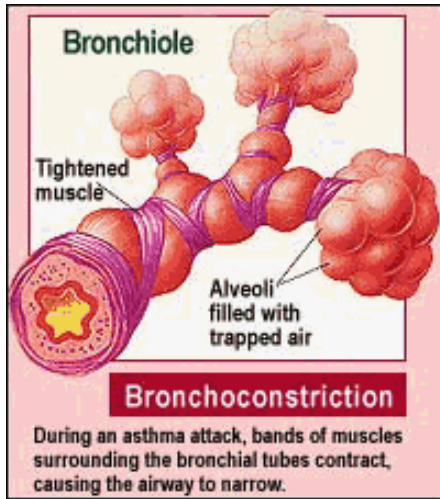
Those people may think vaping is safe, but FDA has seen no data establishing anything like that, writes the agency’s Priscilla Callahan-Lyon in the same journal. She reviewed data from 18 studies on e-cigarettes’ vapors and found that most contain at least traces of the solvents in which nicotine and flavorings had been dissolved. Those solvents, she reports, are known as lung irritants.

And the solvents can transform into something even more worrisome: carbonyls. This group includes known cancer-causing chemicals, such as formaldehyde, and suspected carcinogens, such as acetaldehyde. Because early e-cigarettes didn’t deliver the same powerful hit of nicotine that burning tobacco does, engineers developed second-generation technology that allows users to increase an e-cigarette’s voltage, and thus temperature, to atomize more nicotine per puff.

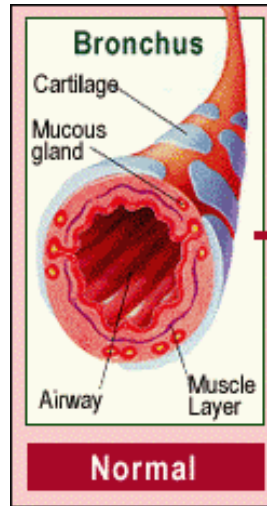


More than 250 different brands of electronic cigarettes are available on the market (a few examples shown), and many dozens of solutions are used to generate the devices’ vapors.

SMOKING ≡ ASTHMA?



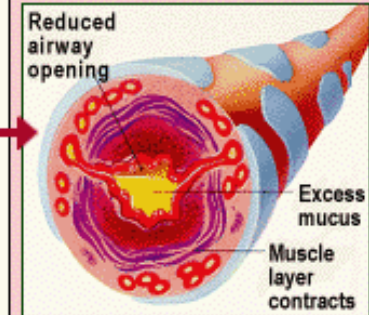
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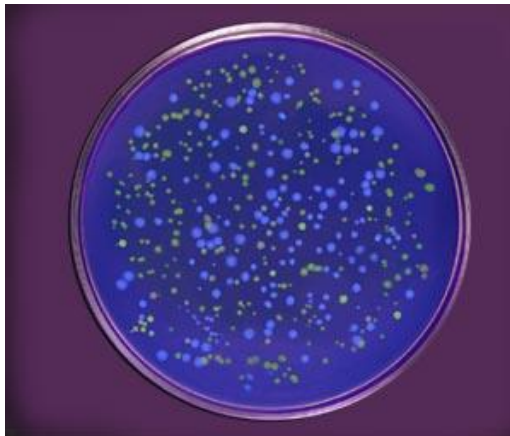
Asthma Triggers

- Allergens
- Drugs
- Exercise
- Occupational stimuli
- Infections
- Environmental changes
- Air pollutants
- Chemical irritants
- Emotions
- Weather/Temp.
- Food additives

Inflammation

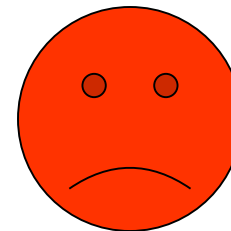


=



Petri-dish Effect

Ugh!!
Cough!
Cough!!



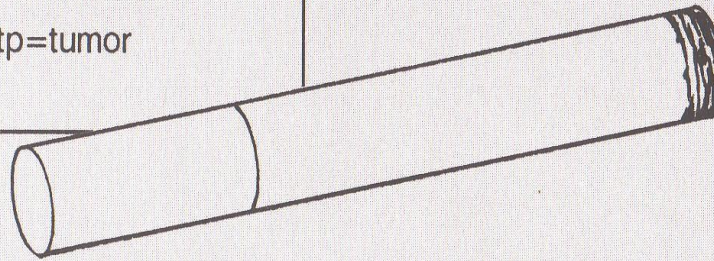
Source: *Reducing the Health Consequences of Smoking: 25 Years of Progress. A Report of the Surgeon General, 1989*

(per cigarette)

4-aminobiphenyl	c	140 ng
benz(a)anthracene	c	40-200 ng
benzene	c	400 μ g
benz(o)pyrene	c	40-70 ng
carbon monoxide	t	26.8-61 mg
formaldehyde	c	1,500 μ g
hydrazine	c	90 ng
hydrogen cyanide	t	14-110 μ g
2-naphthylamine	c	70 ng
nitrogen oxides	t	500-2,000 μ g
N-nitrosodimethylamine	c	200-1,040 ng
N-nitrosodiethanolamine	c	43 ng
N-nitrosopyrrolidine	c	30-390 ng
phenol	tp	70-250 μ g
polonium 210	c	.5 - 1.6 pCi
quinoline	c	15-20 μ g
o-toluidine	c	3 μ g

Note: c=carcinogenic; t=toxic; tp=tumor promoter

TOLOUIDINE
AMINOBIIPHENYL
BENZENE
BENZ(A)ANTHRACENE
NITROSODIMETHYLAMINE
QUINOLINE
HYDRAZINE
PHENOL
CARBON MONOXIDE



**Some Toxic and Cancer-Causing Agents
You Breathe When You Are Exposed To Other People's Tobacco Smoke**

phoric Acid, Pimenta Leaf Oil, Pine Needle Oil, Pine Oil, Scotch, Pineapple
ntrate, alpha-Pinene, beta-Pinene, D-Piperitone, Piperonal, Pipsissewa L
Potassium Sorbate, 1-Proline, Propenylguaethol, Propionic Acid, Propyl
Hydroxybenzoate, Propylene Glycol, 3-Propylideneephthalide, Prune Juice
ne, Pyroligneous Acid And Extract, Pyrrole, Pyruvic Acid, Raisin Juice Co
mol, Rose Absolute and Oil, Rosemary Oil, Rum, Rum Ether, Rye Extract,
age Oleoresin, Salicylaldehyde, Sandalwood Oil, Yellow, Sclareolide, Ska
; Snakeroot Oil, Sodium Acetate, Sodium Benzoate, Sodium Bicarbonate
nate, Sodium Chloride, Sodium Citrate, Sodium Hydroxide, Solanone, Spe
ct, Gum and Oil, Sucrose Octaacetate, Sugar Alcohols, Sugars, Tagetes
ic Acid, Tea Leaf and Absolute, alpha-Terpineol, Terpinolene, Terpinyl Ac
3-Tetrahydroquinoxaline, 1,5,5,9-Tetramethyl-13-Oxatricyclo(8.3.0.0(4,9))
5, and 3,4,5,6-Tetramethylethyl-Cyclohexanone, 2,3,5,6-Tetramethylpyraz
chloride, Thiazole, 1-Threonine, Thyme Oil, White and Red, Thymol, Tobac
pherols (mixed). Tolu Balsam Gum and Extract Tolu aldehydes para-Tol

TOBACCO ADDITIVES

The tobacco industry has acknowledged that nearly 600 chemicals are added to cigarettes. It is not clear, however, how much of the various additives are used or which combinations appear together. Some of the chemicals among cigarette additives most questioned by tobacco opponents include:

■ **Megastigmatrienone:** A flavoring that tobacco companies contend is found naturally in grapefruit juice.

■ **Dehydromenthofuro lactone:** A flavoring that tobacco companies say is found in peppermint.

■ **Ethyl furoate:** Found naturally in coffee, kiwi and peanuts.

■ **Maltitol:** A sweetener used in chewing gum and diabetic candy.

■ **Sclareolide:** A synthetic form of a naturally occurring tobacco element.

■ **Ammonia:** A processing aid.

■ **Methoprene:** An insecticide that toxicologists say is biodegradable.

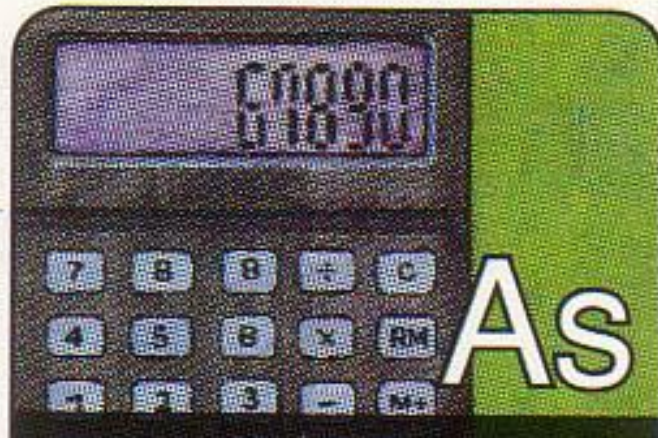
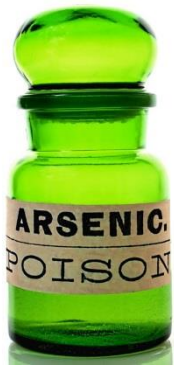
■ **Other additives:** Yeast, wine, caffeine, beeswax, beta carotene, chocolate, coconut oil.



freebase nicotine!!

Ammonia converts nicotine, the addictive agent in tobacco, into a more volatile form, Pan-kow said. "Ammonia is the thing that helps tobacco companies hook the smoker by providing a means of delivering the nicotine."


Last October a former tobacco industry employee revealed that secret industry documents indicated that ammonia was added to tobacco to double the impact of nicotine. The Oregon Graduate Institute study confirms the contention that



As

Arsenic 33

- o Shotgun pellets
- + Metal for mirrors
- v Glass, lasers
- v **Light emitting diodes=LED**
- x 74.9216



Po

Polonium 84

- o **Nuclear batteries**
- o Neutron source
- o Antistatic agents
- o Film cleaner
- x (209)



Sunflowers are planted along with our organic tobacco to attract beneficial insects to protect our organic crops...



To be buried with sunflowers?
Compost?

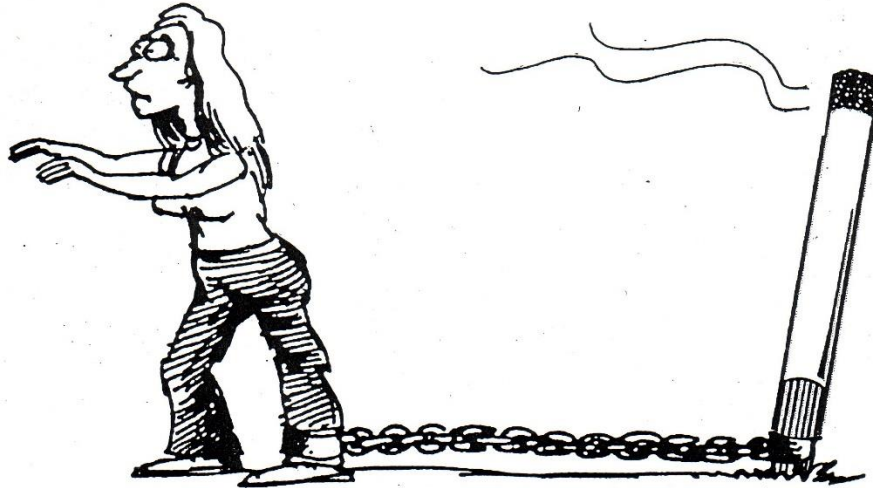


Cigarettes & 2nd-hand smoke!!

...and to **avoid** the use of chemical pesticides.



Cigarettes got you on a tight leash?



Free Yourself

Smoking Cessation

Workshop

Wednesdays, 3:30-4:30 p.m.
January 22 to March 5, 1997

Student Health Center, Medical Library
Free to UO students

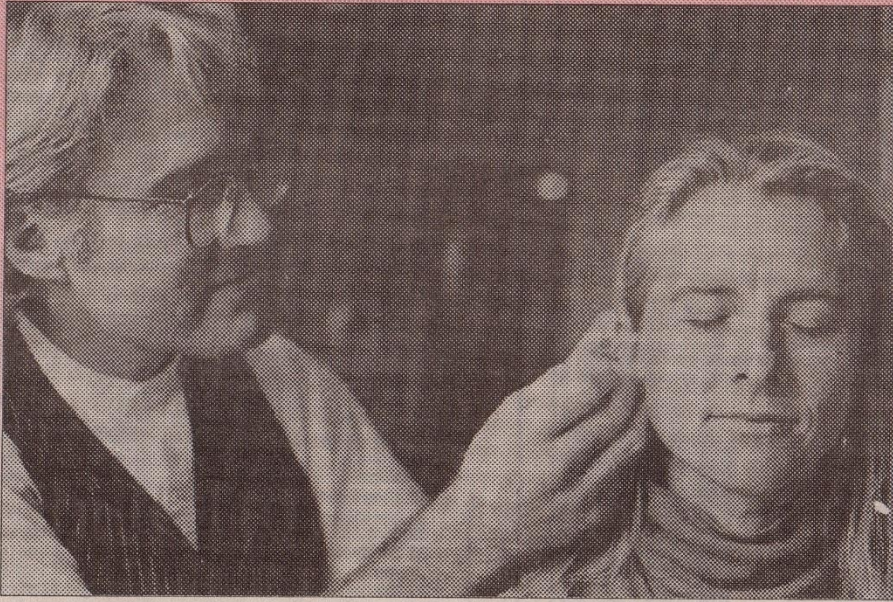
Call 346-4456 to register



***...Thanks for helping us
for almost 20 yr!!***

Stop Smoking Through Acupuncture

If you're serious about quitting the smoking habit, now's your chance.
In honor of the great American Smoke Out



Tom Williams, a licensed acupuncturist in Eugene, provides stop-smoking treatments to relieve cravings and irritability at the four-session stop smoking workshop that begins at the Health Center November 18th in conjunction with the Great American Smokeout on November 19th. Call 346-4456 to sign up.

Educational Session*

Wednesday, November 18, 4-5 pm

*You must attend this session in order to receive acupuncture treatment.

Acupuncture Sessions

Thursday, November 19, 4-6 pm

Friday, November 20, 4:30-6 pm

Monday, November 23, from 4:30-6 pm

All sessions meet in the medical library in the basement of the University Health Center.

**Space is limited, so sign up now
by calling the Health Education
office at 346-4456.**

\$30 fee that will be donated to the American Lung Association is requested.

UNIVERSITY

HEALTH CENTER

We're a matter of degrees ◆

Open daily 8 a.m. to 6 p.m., except Tuesdays (9 a.m.) and Sundays (10 a.m.).
Appointments and after hours: 346-2770 • Web: darkwing.uoregon.edu/~uoshc

Nicotine Addiction & Help Quitting Smoking

[http://www.cancer.org/healthy/stayawayfromtobacco/guide
toquittingsmoking/guide-to- quitting-smoking-help-phys-nrt](http://www.cancer.org/healthy/stayawayfromtobacco/guide-toquittingsmoking/guide-to- quitting-smoking-help-phys-nrt)

2nd-Hand Smoke or ETS & 3rd-Hand Smoke?

[http://www.cancer.org/cancer/cancercauses/tobaccocancer/
secondhand-smoke](http://www.cancer.org/cancer/cancercauses/tobaccocancer/secondhand-smoke)

2nd-Hand Smoke Addictive?

[http://www.ncbi.nlm.nih.gov/pubmed?term=2nd%20hand
%20smoke%20addictive](http://www.ncbi.nlm.nih.gov/pubmed?term=2nd%20hand
%20smoke%20addictive)

<http://www.ncbi.nlm.nih.gov/pubmed/20211642>

<http://www.ncbi.nlm.nih.gov/pubmed/19936715>

<http://www.ncbi.nlm.nih.gov/pubmed/21840504>

