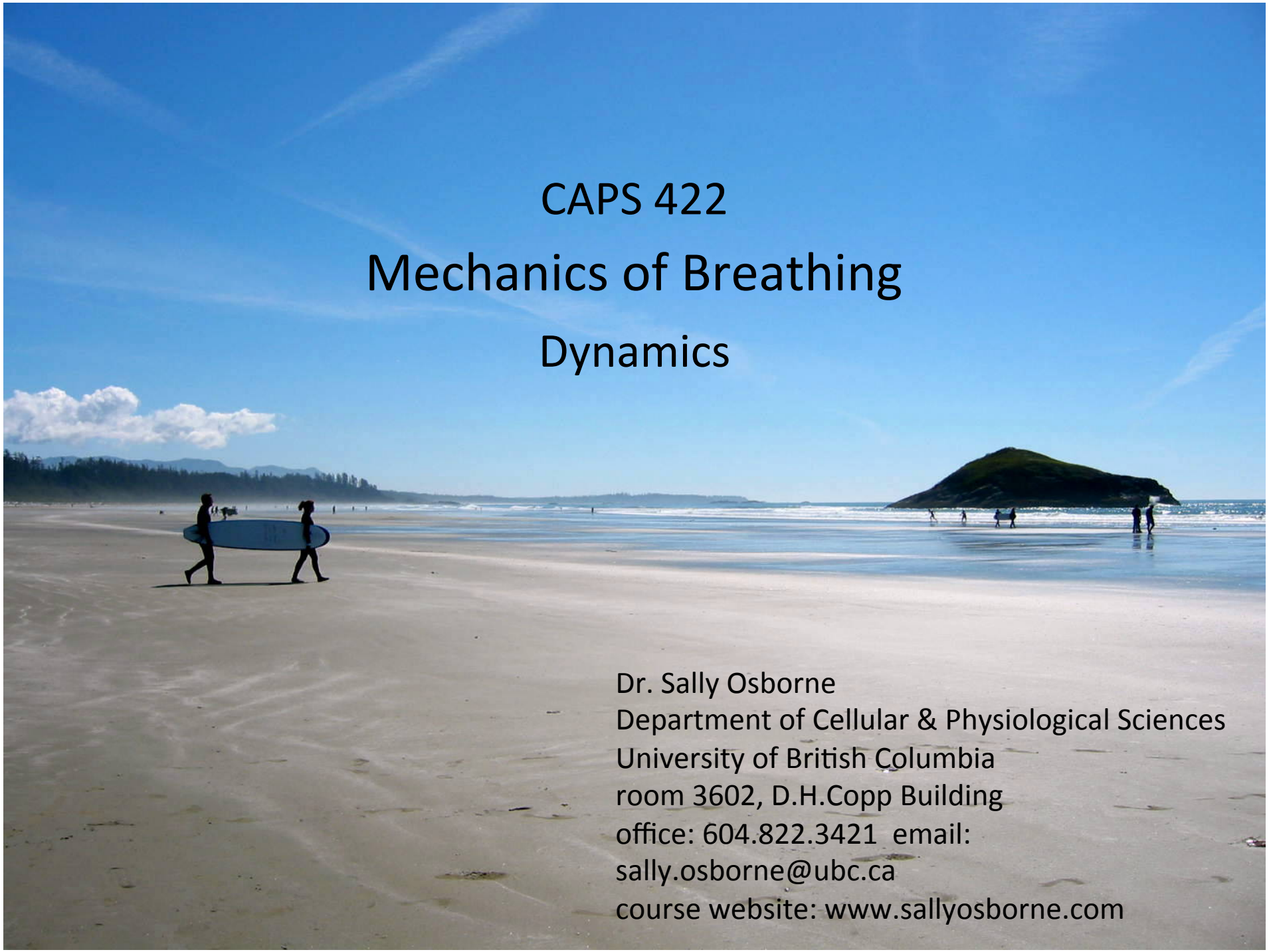

CAPS 422

Mechanics of Breathing

Dynamics

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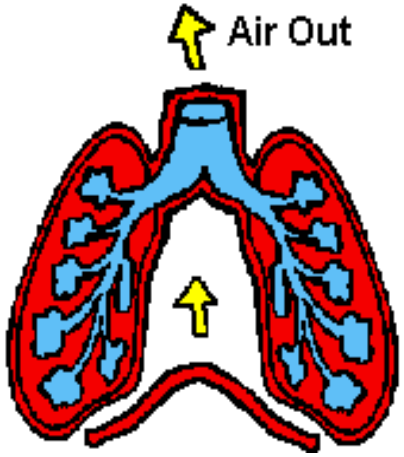
Airway Resistance

A Key Factor in Movement of Air In & Out of the Lungs

The total resistance to flow of air in the airways (R_{aw}) is very little about 250 fold less than that encountered generating the same airflow through a smokers pipe.



2 **cm H_2O/L/sec**

500 **cm H_2O/L/sec**

!

Airway Resistance

A Key Factor in Movement of Air In & Out of the Lungs

Resistive Forces

1. **Inertia** of the respiratory system (negligible)
2. **Friction**

   I) lung & chest wall tissue surfaces gliding past each other

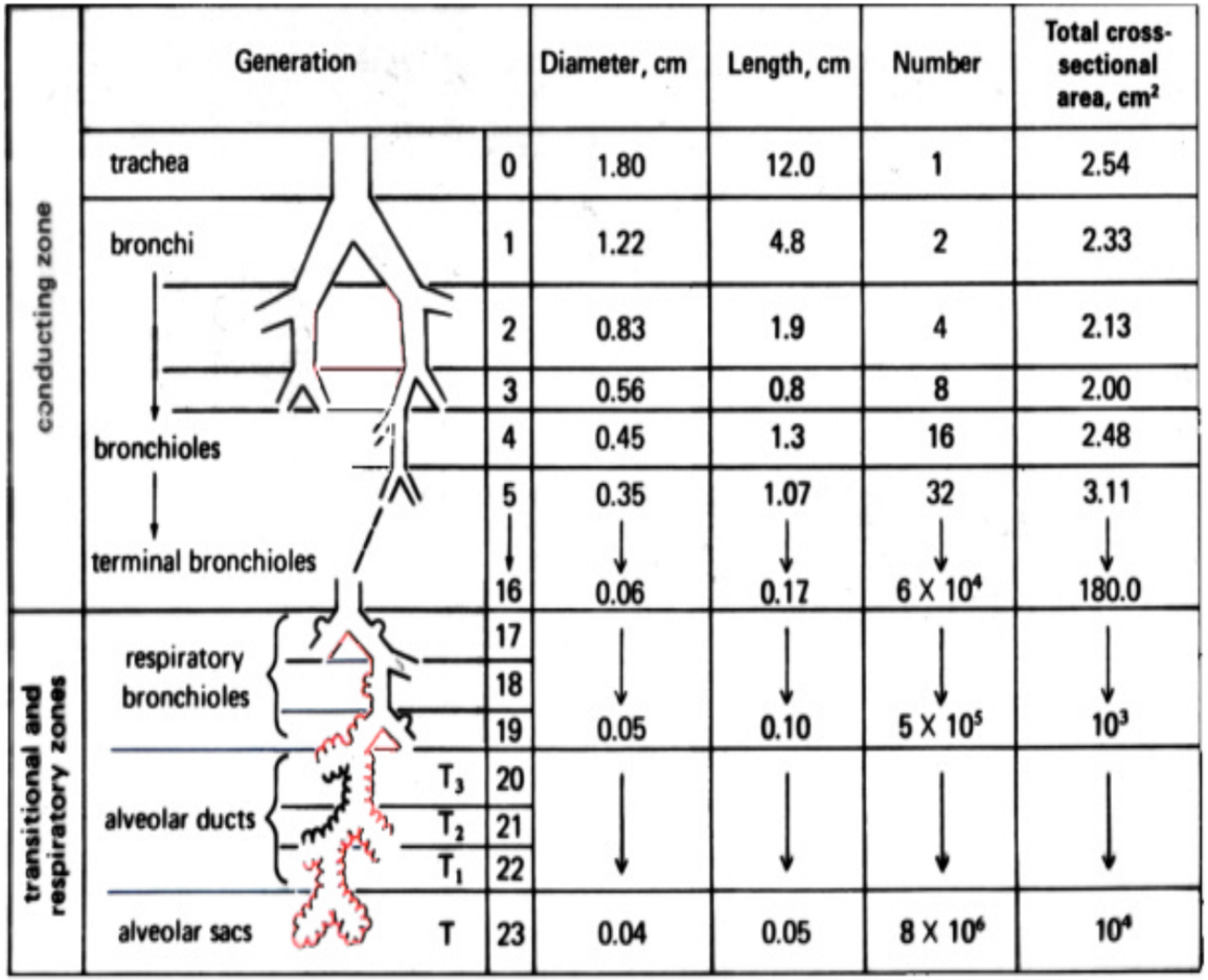
   II) lung tissue past itself during expansion

   III) frictional resistance to flow of air through the airways (80%)

Flow In Airways Of Different Size

Arranged In Parallel

Distinguish between individual airway size indicated by radius/cross sectional area & generation airways size indicated by the sum of radii in parallel or the total cross sectional of a given generation



	Generation		Diameter, cm	Length, cm	Number	Total cross-sectional area, cm^2
conducting zone	trachea	0	1.80	12.0	1	2.54
	bronchi	1	1.22	4.8	2	2.33
		2	0.83	1.9	4	2.13
		3	0.56	0.8	8	2.00
	bronchioles	4	0.45	1.3	16	2.48
	terminal bronchioles	5 ↓ 16	0.35 ↓ 0.06	1.07 ↓ 0.17	32 ↓ 6×10^4	3.11 ↓ 180.0
transitional and respiratory zones	respiratory bronchioles	17	↓	↓	↓	↓
		18				
		19	0.05	0.10	5×10^5	10^3
	alveolar ducts	T_3 20	↓	↓	↓	↓
		T_2 21				
		T_1 22				
	alveolar sacs	T 23	0.04	0.05	8×10^6	10^4

Airflow in the Lungs 3 Patterns/Regimes

1. Laminar
2. Turbulent
3. Transitional [distributed laminar]

The General Relationship Between

Pressure, Flow & Resistance

$$\Delta P \propto \dot{V} \times R$$

$$R \propto \Delta P / \dot{V}$$

units of resistance = cm H_2O/L/sec

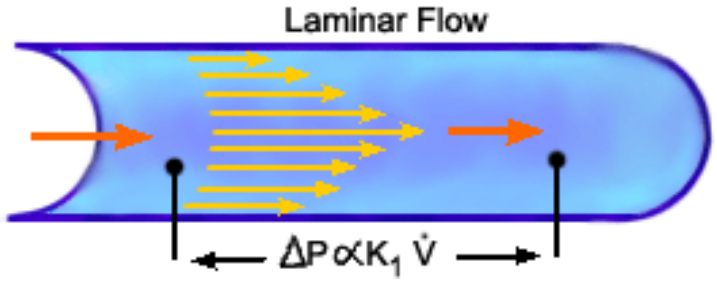
At peak flow during quiet inspiration:

$$R_{aw} = P_A - P_B / \dot{V} = -1.0 \text{ cm } H_2O / -0.5 \text{ L/sec} = 2 \text{ cm } H_2O/L/sec$$

-ve flow indicates flow into the lungs in contrast to +ve flow air exiting the lungs

This General Relationship Applies

When Flow is Laminar governed by Poiseuille's Law



Features of laminar flow

- silent, slow
- streamline, parabolic flow profile
- Poiseuille flow: proportional to driving pressure
- in smaller airways (< 2 mm diameter)

$\Delta P \propto \dot{V} \times R$

$R \propto \Delta P / \dot{V}$

$R = 8 \eta L / \pi r^4$ where η=viscosity L= length r = radius

$R \propto 1 / r^4$

Jean Louis Marie Poiseuille (1797-1869)

French Physician & Physiologist

- studied @École Polytechnique (Paris)
- trained in physics & mathematics
- interested in flow of blood in rigid narrow tubes
- formulated the mathematical expression relating pressure, flow and resistance
- first to have used the mercury manometer to measure blood pressure in dogs to quantify oscillations in blood pressure with respiratory phase and changes with aging
- the unit of viscosity "poise" is in his honor

Flow Changes from Laminar to Turbulent

when Reynolds Number exceeds 2000

$$\text{Reynolds number} = \frac{\rho \times Ve \times D}{\eta}$$

ρ= density of fluid
Ve= linear velocity of fluid
D = diameter of tube
η = viscosity of fluid

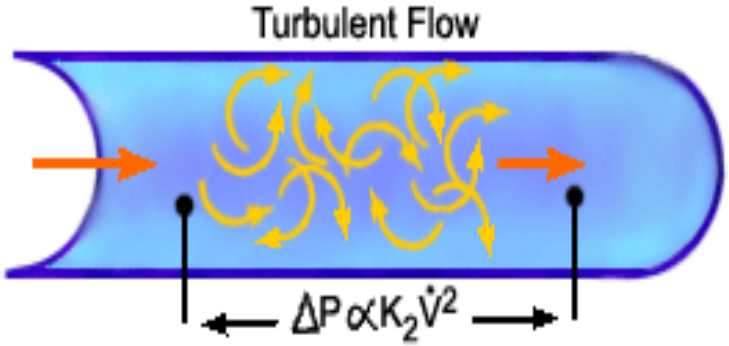
Turbulent flow tends to take place when gas density, linear velocity & tube radius are large.

The linear velocity (cm/sec) of gas in a tube is calculated by dividing the flow rate (L/sec) by tube area (cm^2). Once again, tube area refers to total cross sectional area of the airways of a given generation.

Where is the linear velocity of gas greatest in the lungs?

Pressure, Flow & Resistance Relationship

When Flow is Turbulent

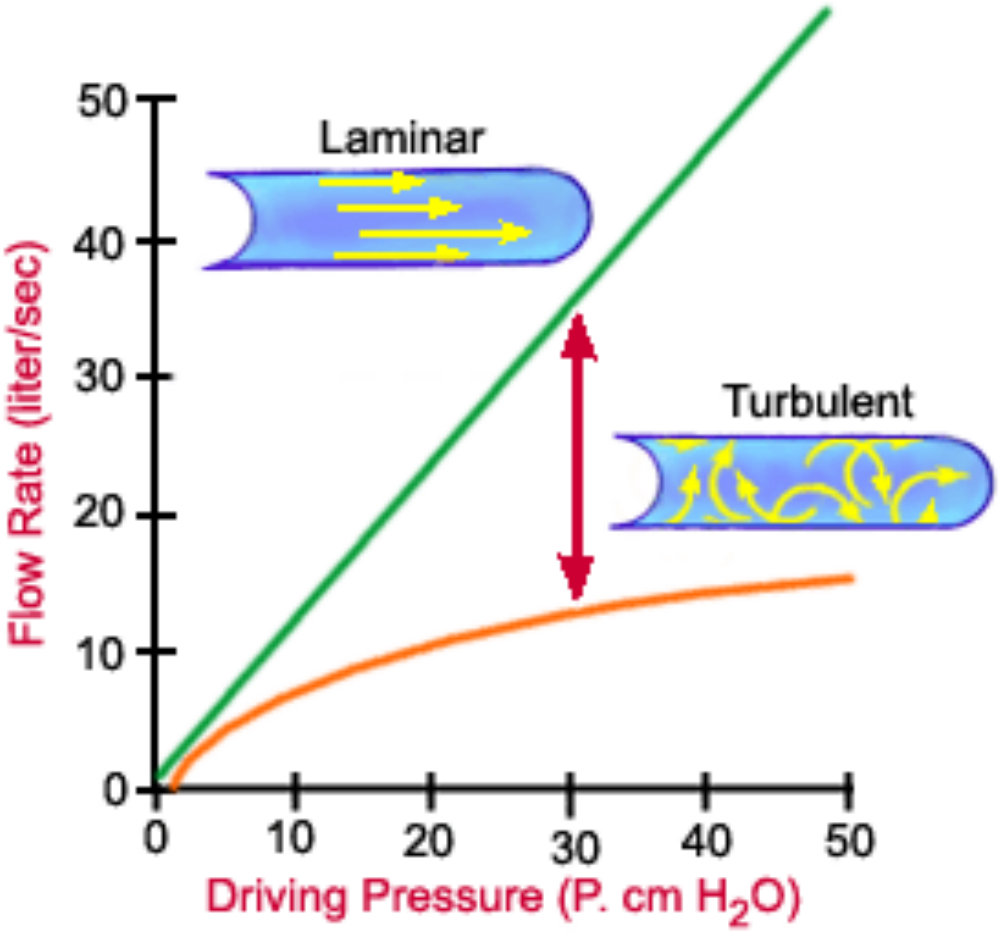


Features of Turbulent Flow

- axial & radial with blunt flow profile
- noisy & rapid
- resistance depends more on density than viscosity [nb. use of Heliox instead of air in patients with airway obstruction]
- in larger airways

Pressure, Flow & Resistance Relationship

Comparing Laminar & Turbulent Flow



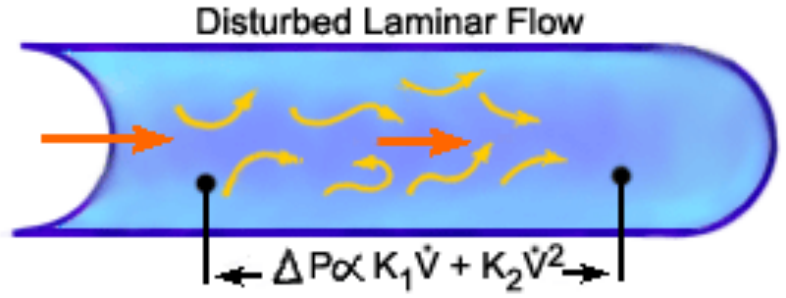
Increasing driving pressure results in greater laminar flow compared to turbulent flow.

This because with turbulent flow regime some of the driving pressure is expended in generating radial flow.

Pressure, Flow & Resistance Relationship

When Flow is Transitional (Distributed Laminar)

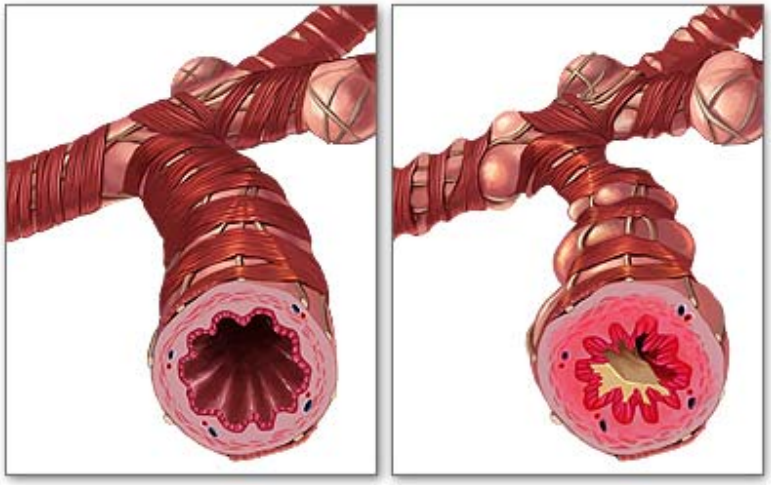
- Airflow is transitional throughout most of tracheobronchial tree. The energy required to produce this flow is intermediate between laminar & turbulent flow.



- Due to the many bifurcations of the tracheobronchial tree, flow becomes laminar at very low Reynolds number (<1 compared to <2000 in simple tubes). In the lungs laminar flow occurs in small airways distal to the terminal bronchioles.

- In the trachea where the radius is large linear velocities reach high values [during exercise, during a cough] flow is turbulent.

Regulation of Airway Resistance & Control of Airway Smooth Muscle



Bronchoconstriction

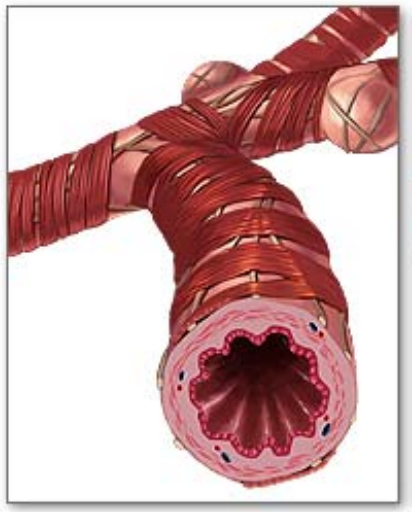
Physiologic control factors

- parasympathetic stimulation, Ach via M_3 receptors (*predominant autonomic control)*
- decreased Pco_2 in airways

Pathologic control factors *released by cells located in the airway wall: epithelial cells, inflammatory cells & myocytes themselves)*

- Inflammatory: Histamine, Tryptase, Prostanoids (PGF α , PGD2,TXA2, Cysteinyl leukotrienes, Endothelin (see also SRS-A, slow reacting substance of anaphylaxis)
- Neurotransmitter: Acethylcoline, Neurokinine A, Substance P, Calcitonin Gene Related Peptide
- α adrenergic agonists

Regulation of Airway Resistance & Control of Airway Smooth Muscle



Bronchodilation

Physiologic control factors

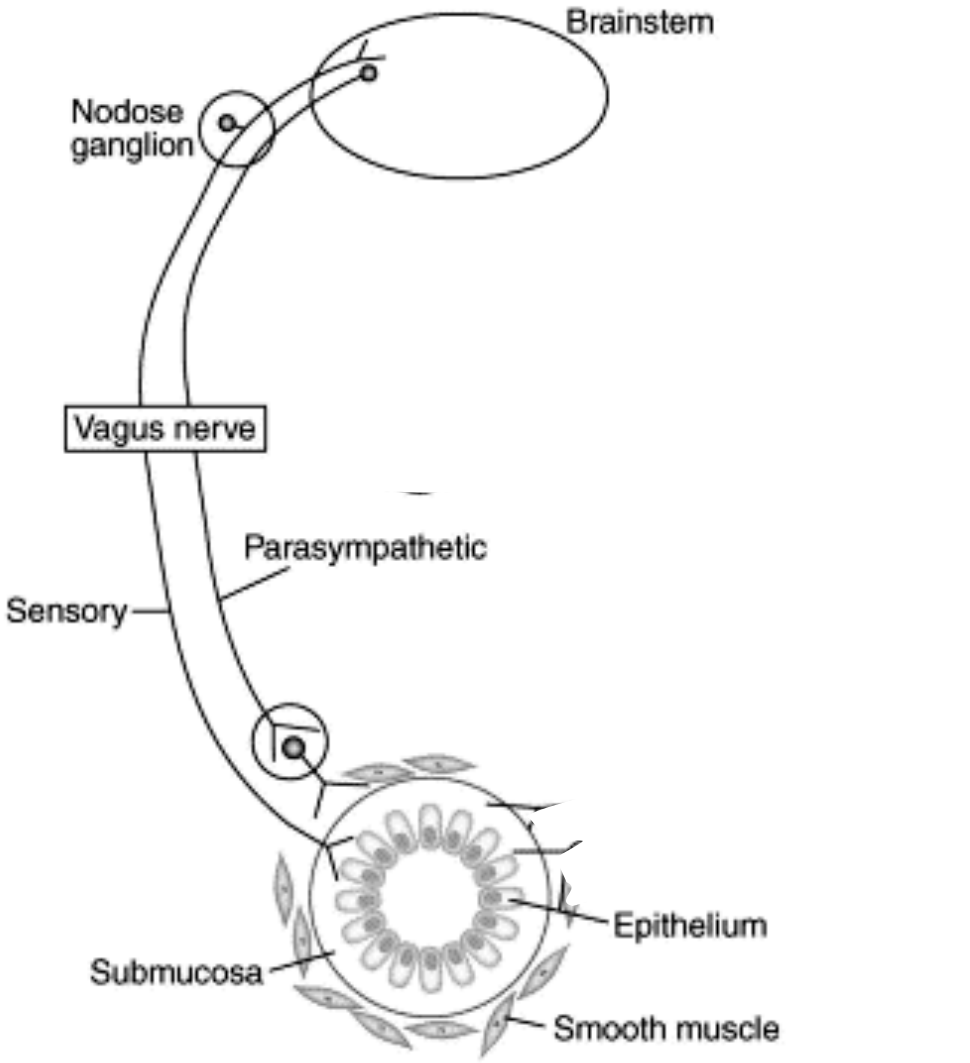
- sympathetic stimulation β_2 receptors *(little adrenergic innervation & minimal effect)*
- circulating adrenergic agonists (adrenaline/epinephrine; note key use of β_2 adrenergic agonists in asthma therapy]
- Nitric oxide (NO), Vasoactive Intestinal Peptide (VIP)
- increased Pco_2 in airways
- decreased Po_2 in airways

Pathologic control factors

- Prostanoids (PGE2,PG12)

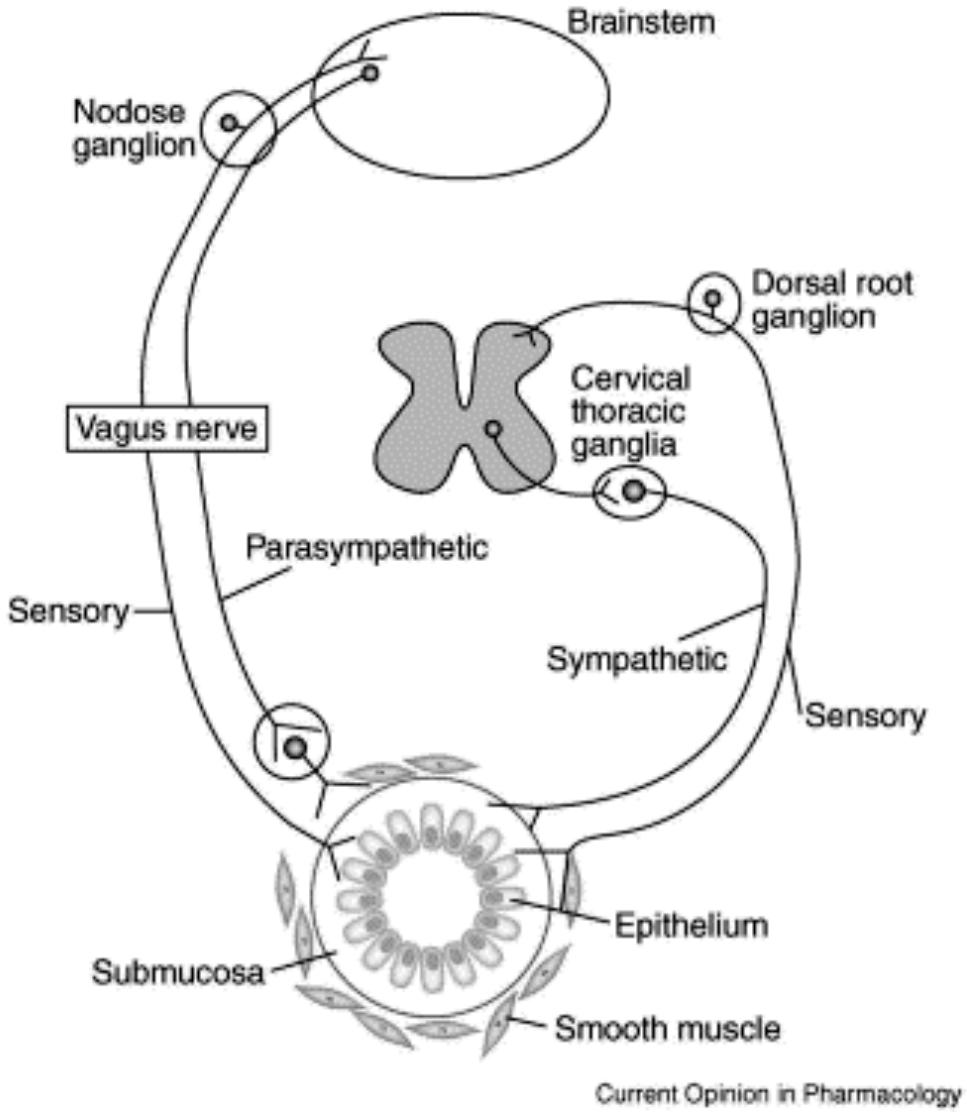
Innervations of airway smooth muscle in man is predominantly parasympathetic ...

In humans, the vagus nerves provide the parasympathetic innervations to the bronchial smooth muscle. The trachea is innervated by the superior & recurrent laryngeal nerves, branches of the vagus nerve.



Innervations of airway smooth muscle in man is predominantly parasympathetic ...

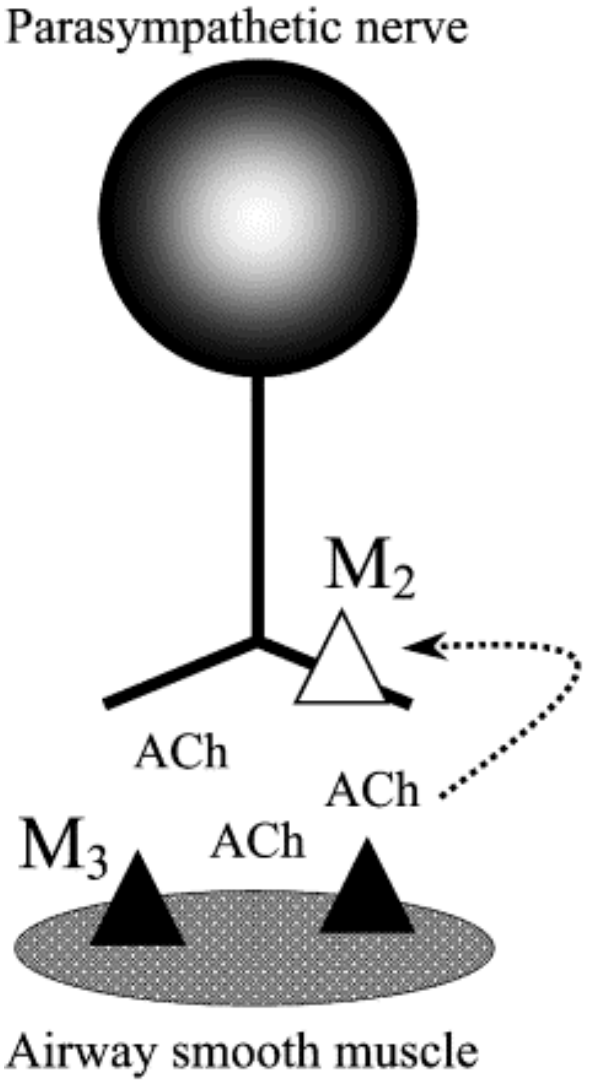
In other mammalian species, there is greater sympathetic innervations of the airway smooth muscle



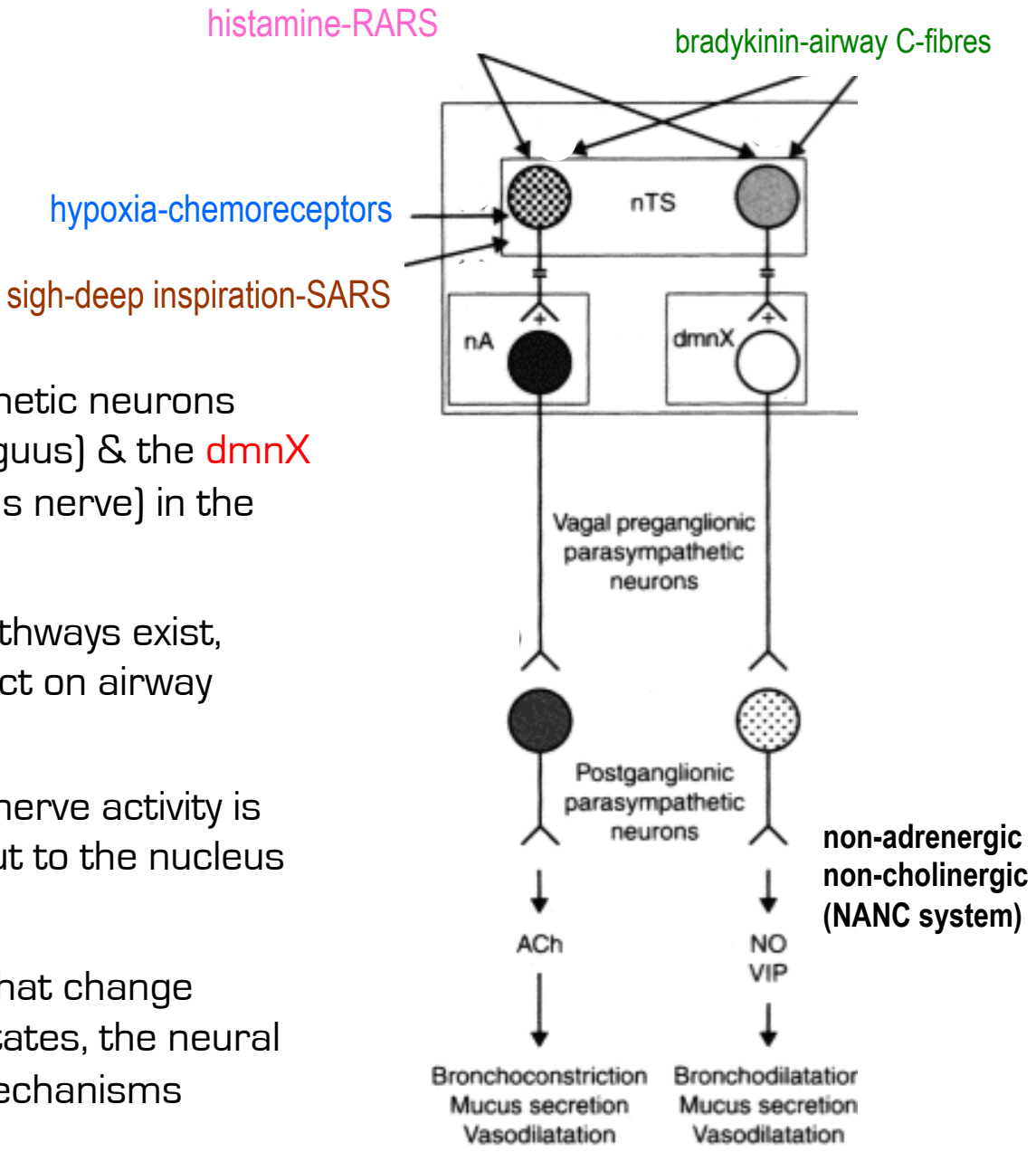
Muscarinic Receptors on Airway Smooth Muscle & Nerves

- Postganglionic, parasympathetic nerves innervate the airway smooth muscle where they release acetylcholine (ACh).
- ACh stimulates M_3 muscarinic receptors on the smooth muscle to cause contraction.
- At the same time, ACh stimulates M_2 muscarinic receptors located on the postganglionic nerves.

  Stimulation of M_2 autoreceptors:
  1) limits further acetylcholine release
  2) inhibits β adrenoceptor-induced bronchodilation by preventing activation of adenylate cyclase and Ca^{2+}-dependent K^+ channels.



Neural Pathways Controlling Airway Function



- vagal preganglionic parasympathetic neurons originate in the nA (nucleus ambiguus) & the dmnX (dorsal motor nucleus of the vagus nerve) in the medulla

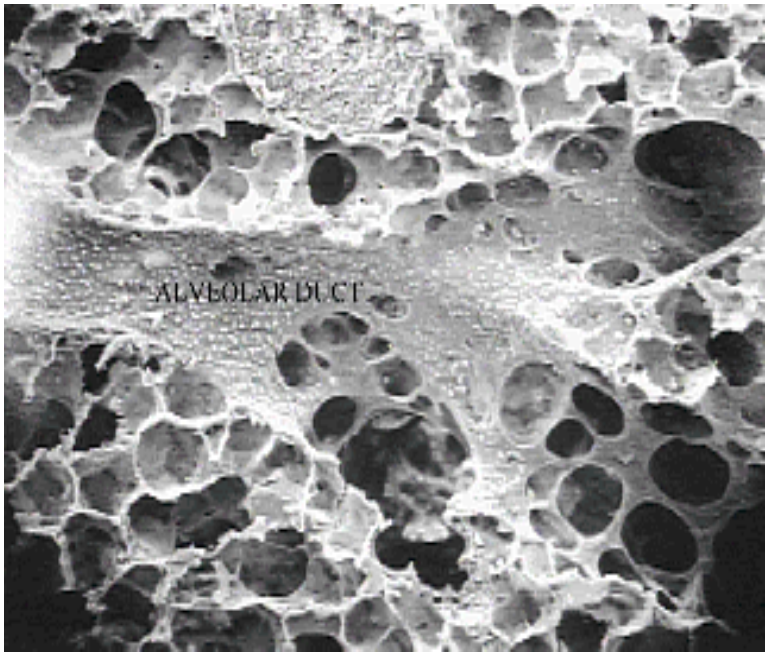
- two distinct parasympathetic pathways exist, differing with respect to their effect on airway smooth muscle tone.

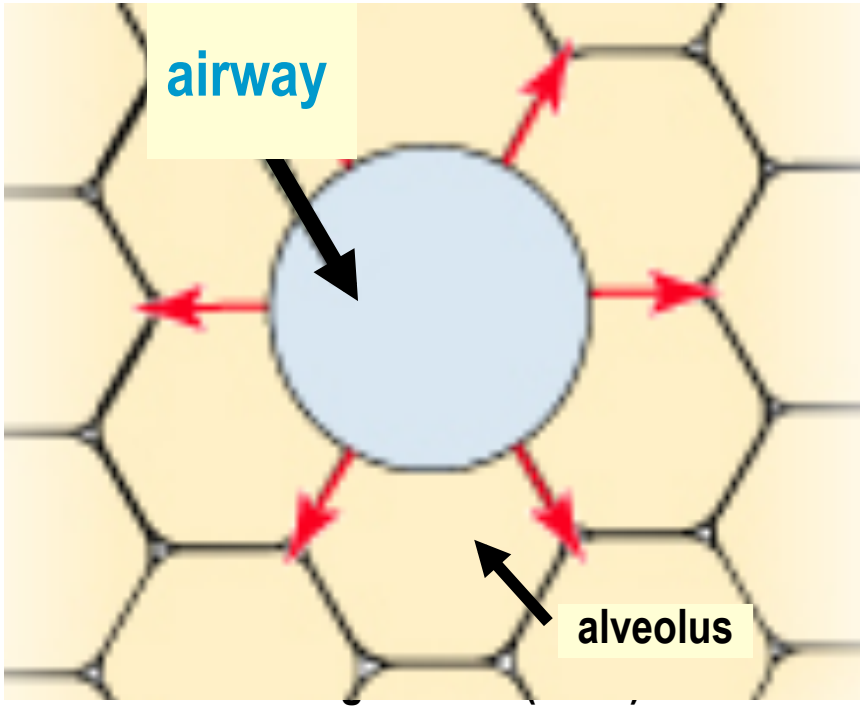
- parasympathetic preganglionic nerve activity is reflexly regulated by afferent input to the nucleus tractus solitarius (nTS)

- current emphasis: substances that change smooth muscle tone in disease states, the neural pathway & signal transduction mechanisms involved

Regulation Of Airway Resistance Through Passive Mechanisms Controlling Airway Caliber

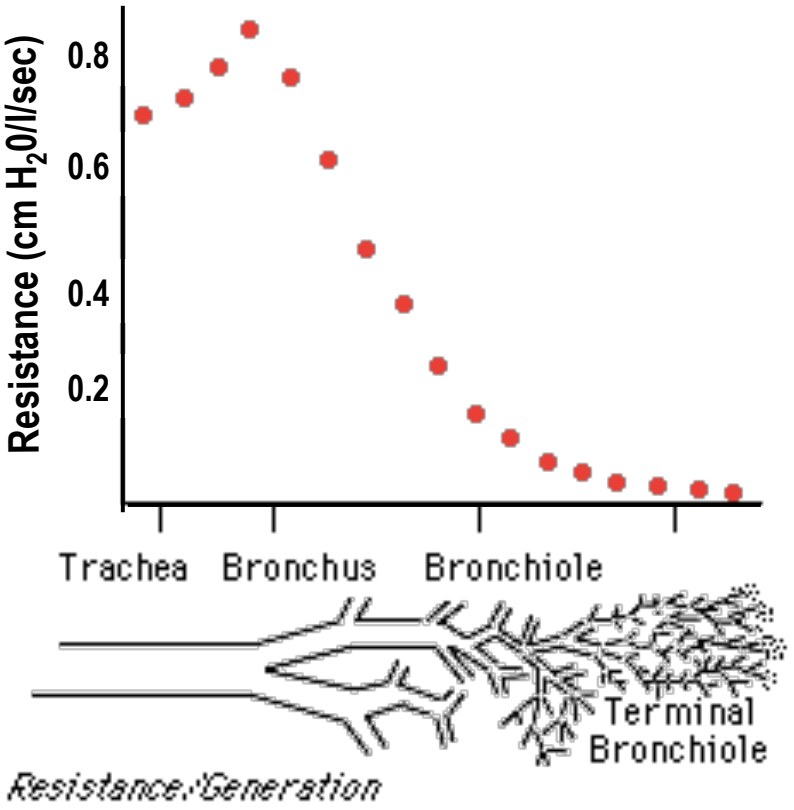
- airway radius
- alveolar tethering [increased radial traction on neighboring airways with lung inflation]





Airways Resistance [R_{aw}]

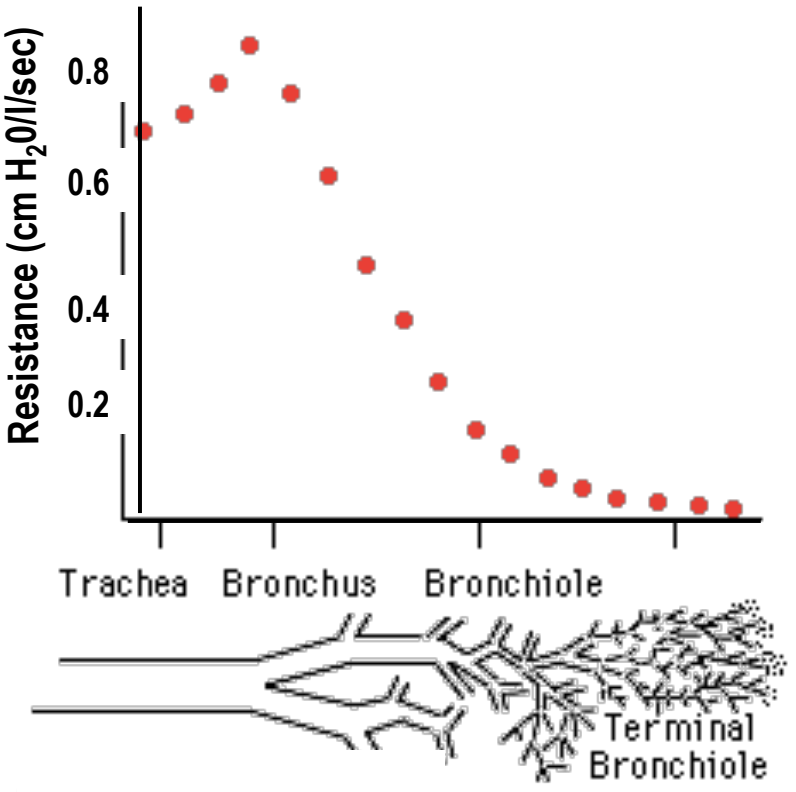
- due to its smaller radius, a single small airway provides more resistance than a single large airway.
- however, in the lungs, resistance to air flow at a given generation, depends on the number of parallel pathways present & the total cross sectional area (sum of all the radii).



Airways Resistance (R_{aw})

In health, the larger and mid size airways are the major site of resistance to flow of air owing to their small relative cross sectional area.

In most common disease states, the smaller airways are the major site of resistance to flow of air because of a reduction in their luminal size.



The contribution of smaller airways to total resistance is little due to their numerous parallel branching resulting in a large overall cross sectional area.

Clinical/Indirect Approach To Airway Resistance

Measuring Maximal Airflow

Knowledge of Raw important for diagnosis and treatment of patients with "obstructive" lung disease with increased airflow limitation.

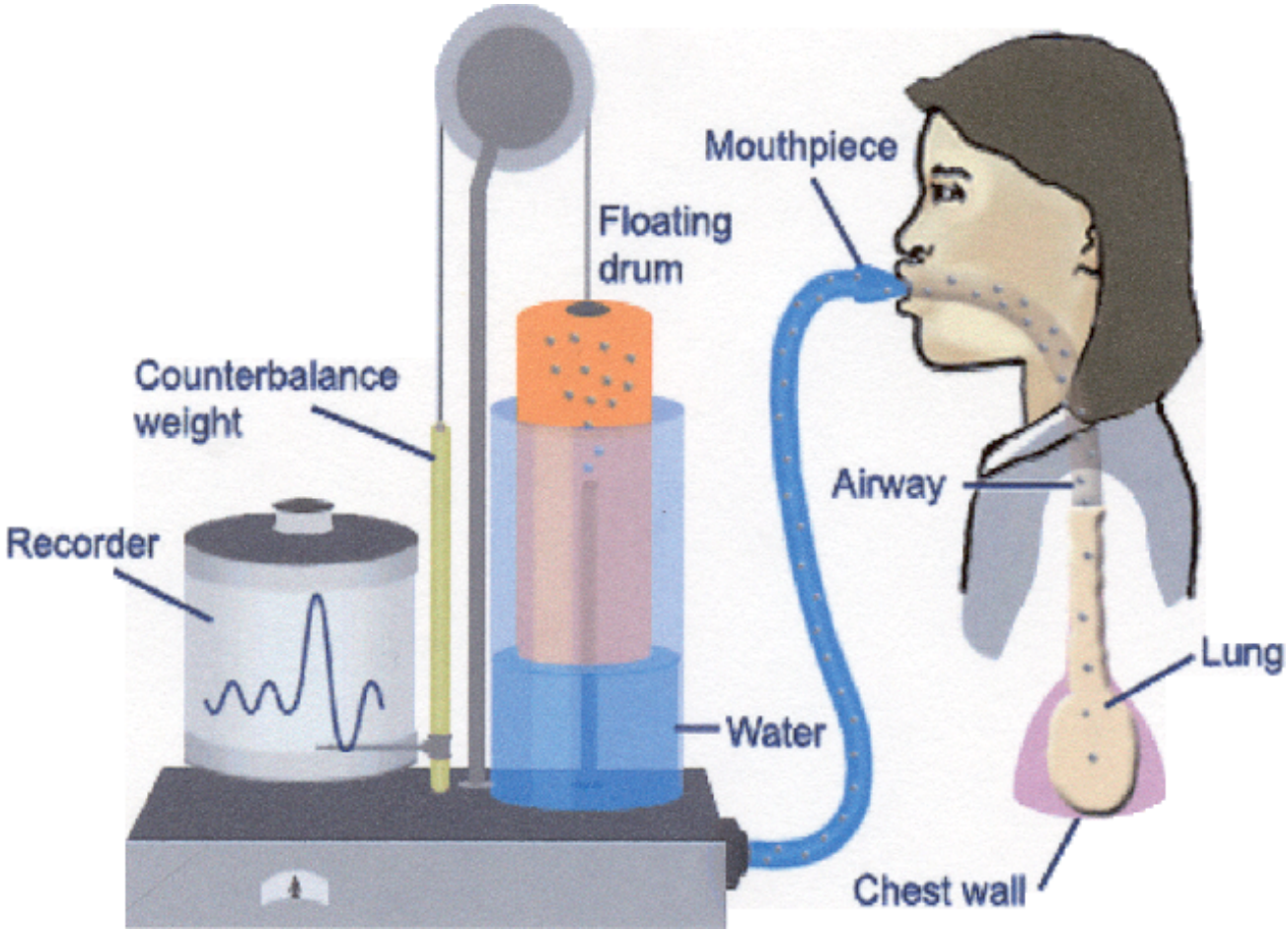
- asthma: airway inflammation & hyperresponsiveness (bronchoconstriction)
- chronic bronchitis: chronic mucus production with cough for 3 months in 2 consecutive years emphysema: permanent enlargement of alveoli & destruction of alveolar walls

What do you think happens to airflow, the harder a person forces air out of their lungs? The harder the person forces air out, the greater the airflow. Surprisingly, only true at low flows.

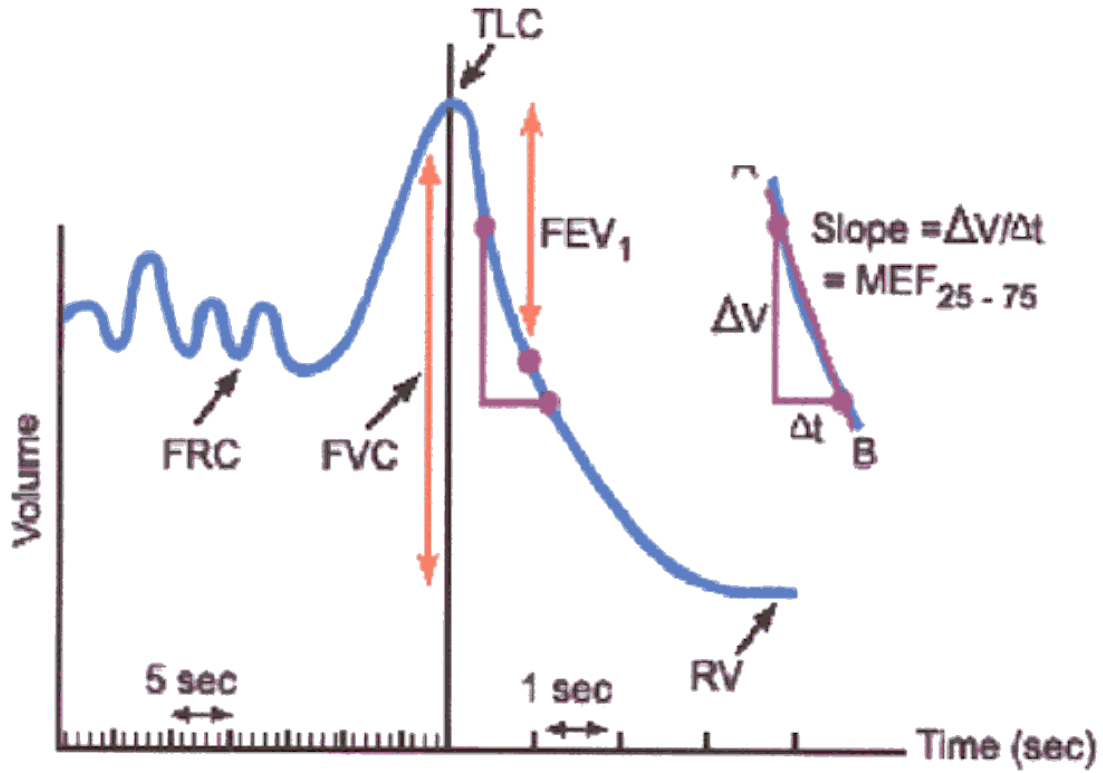
ONCE FLOW REACHES A CERTAIN MAXIMUM, NO MATTER HOW HARD THE EXPIRATORY MUSCLES PUSH, FLOW WILL NOT INCREASE. THIS PHENOMENON IS CALLED AIRFLOW LIMITATION.

Key pulmonary function tests are based on measurement of flow during a maximal voluntary expiration [**FVC: Forced Vital Capacity**]

Spirometer


Mouthpiece
Floating drum
Counterbalance weight
Recorder
Airway
Lung
Water
Chest wall

Expiratory Forced Vital Capacity Maneuver

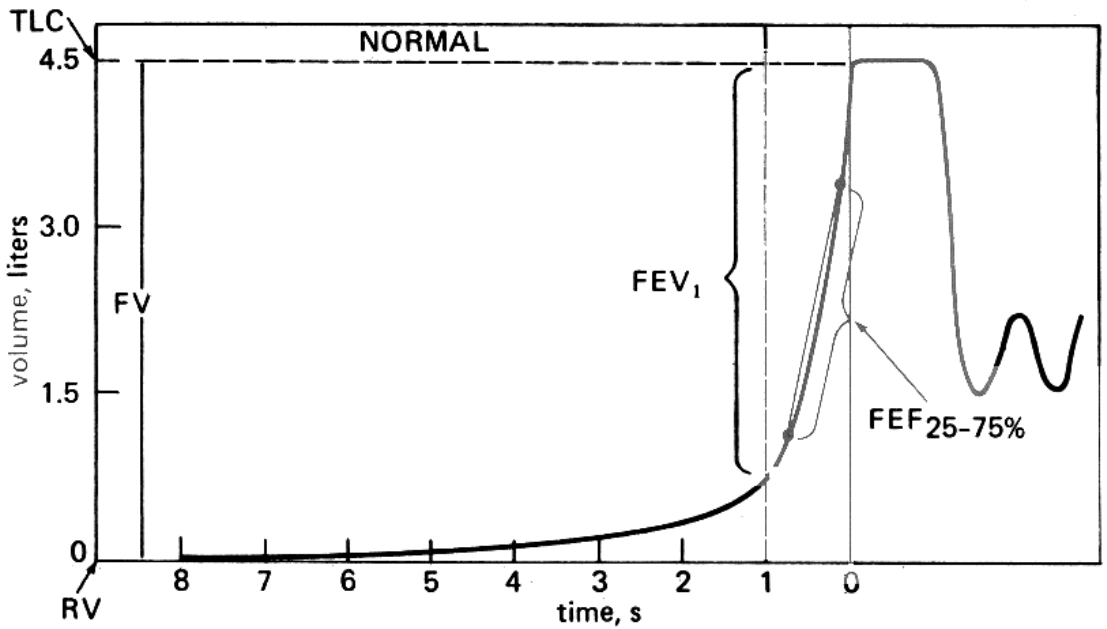


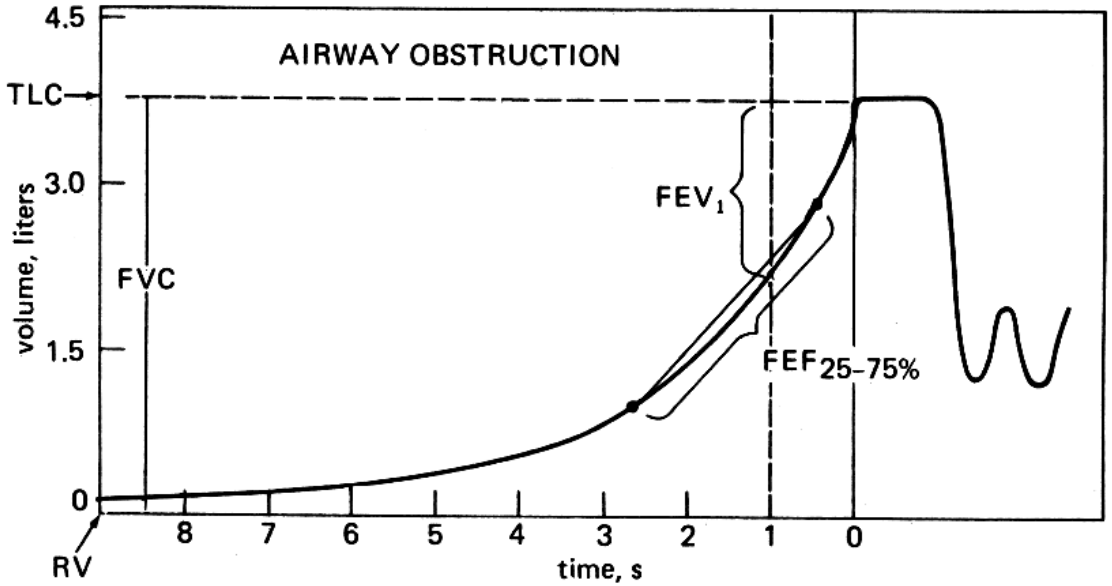
- FEV1/FVC= 80%
- FEF 25-75

  a.k.a.

  MEF25-75

  MMEFR

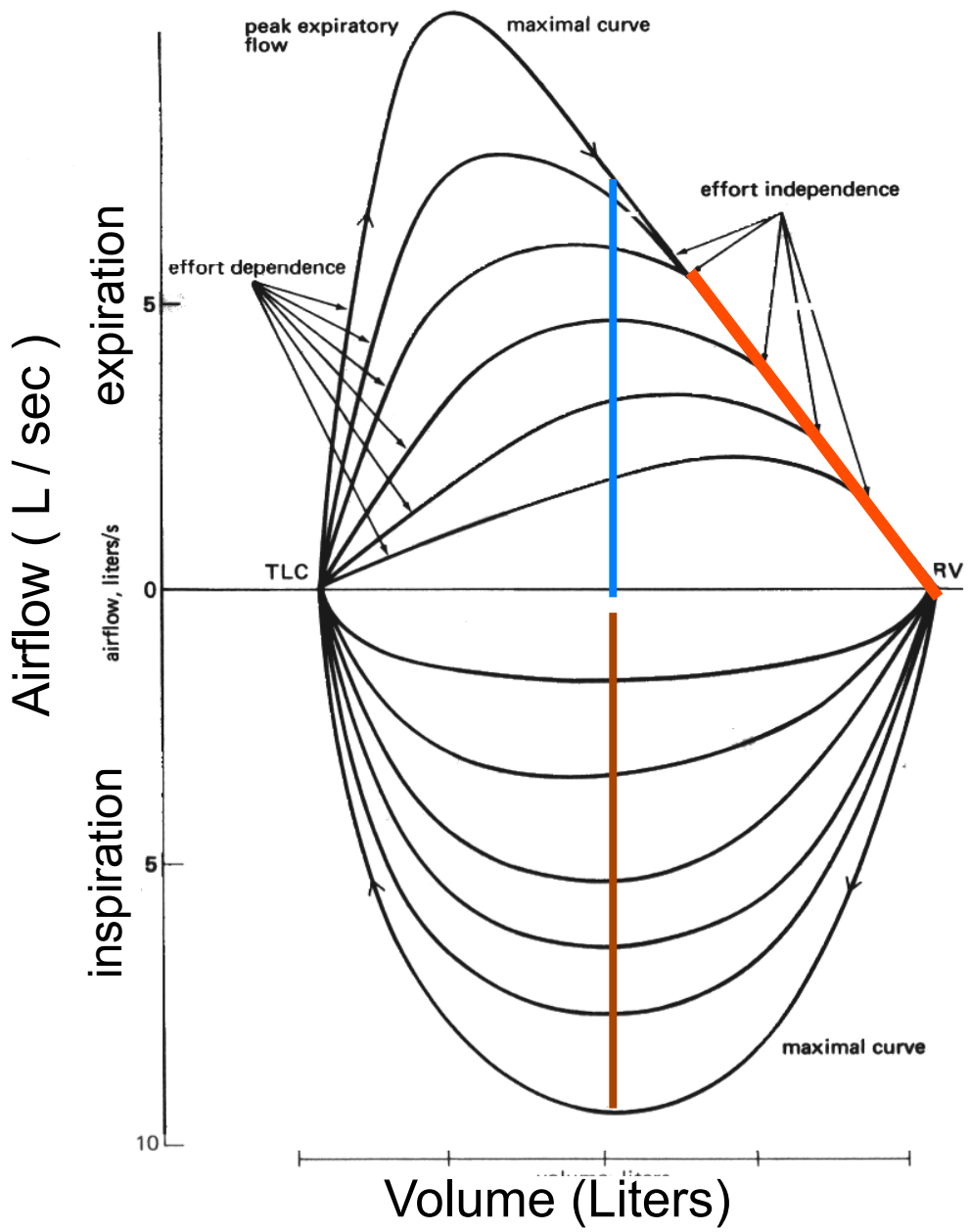

NORMAL
TLC
4.5
3.0
1.5
0
volume, liters
FV
FEV1
FEF25–75%
RV
8
7
6
5
4
3
2
1
0
time, s


AIRWAY OBSTRUCTION
4.5
TLC
3.0
1.5
0
volume, liters
FVC
FEV1
FEF25–75%
RV
8
7
6
5
4
3
2
1
0
time, s

The Flow-Volume Loop

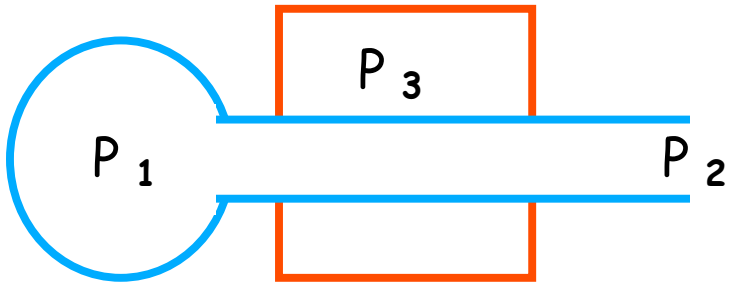
$\dot{V}E_{50} / \dot{V}I_{50} = 0.9$

How come this ratio is not one?



The Starling Resistor

A simple model of maximal expiratory flow limitation



P_1 = pressure in the alveolus
P_2 = pressure a the airway opening
P_3 = intrapleural pressure

If $P_2 > P_3$ driving pressure = $P_1 - P_2$
If $P_3 > P_2$ driving pressure = $P_1 - P_3$

Passive Quiet Expiration
from 0.5 L above FRC

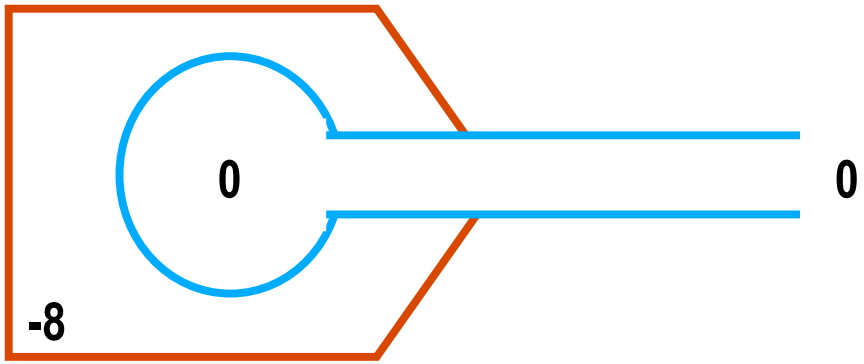
END OF INSPIRATION

at about 0.5L above FRC

P_{TP}= 0-(-8)=8 cm H_2O distending pressure = elastic recoil of the lungs

$P_A = P_{el} + P_{pl}$

flow=0



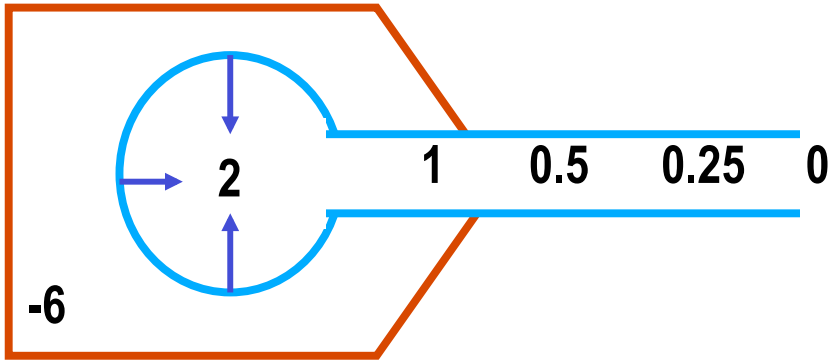
BEGIN QUIET EXPIRATION

at about 0.5L above FRC

inward recoil of the lungs sets a driving pressure= 2 cm H_2O

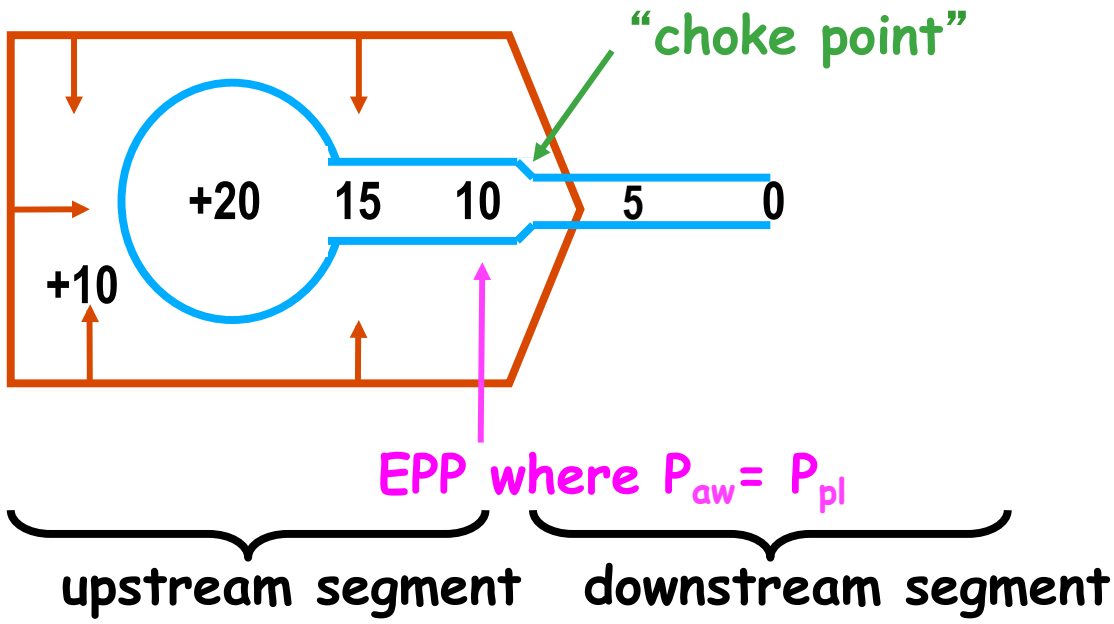
P_{TP}= 2-(-6)= 8 cm H_2O

flow=0



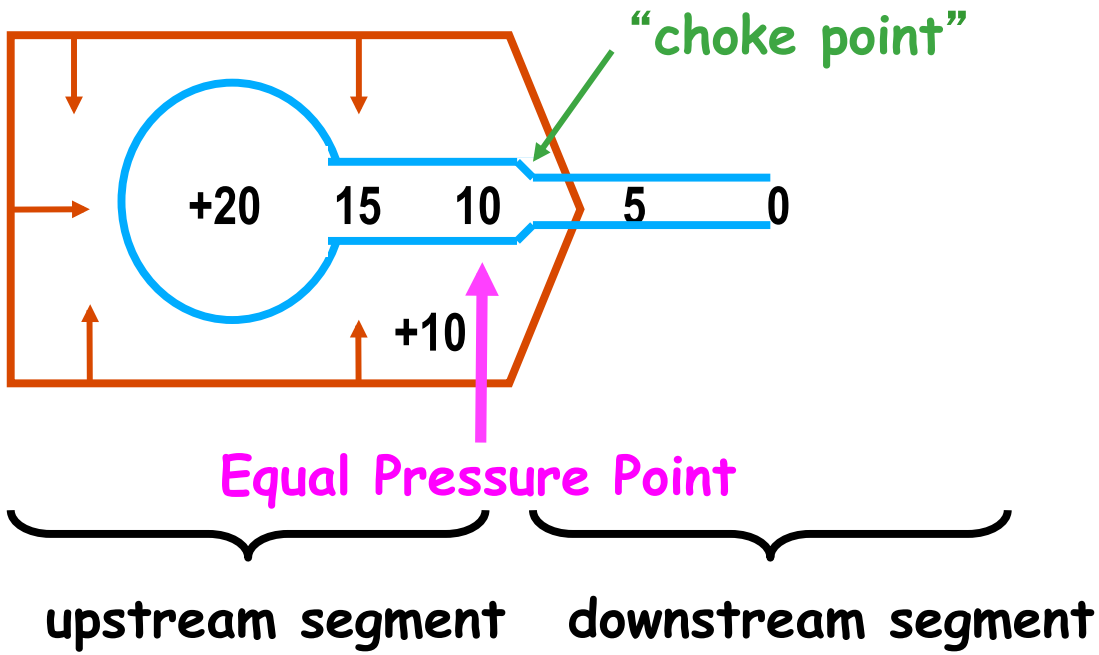
In both cases, lung volume & transpulmonary pressure are equal. Expiratory flow requires establishing a driving force set by the passive recoil of the lungs.

Forced Expiration At The Same Lung Volume



At any given lung volume, expiratory flow increases with increasing effort (+ve Ppl) until a give Ppl beyond which increasing Ppl does not increase expiratory flow. Flow becomes limited when a choke point and a flow limiting segment develops downstream an Equal Pressure Point where the transmural pressure across the airway is zero.

Forced Expiration At The Same Lung Volume



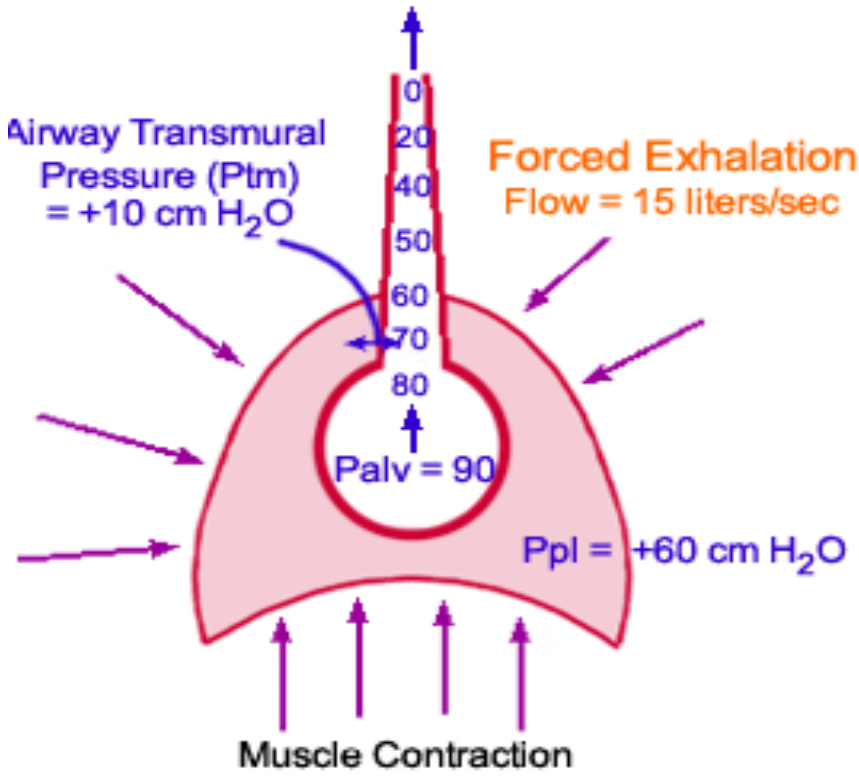
Driving pressure

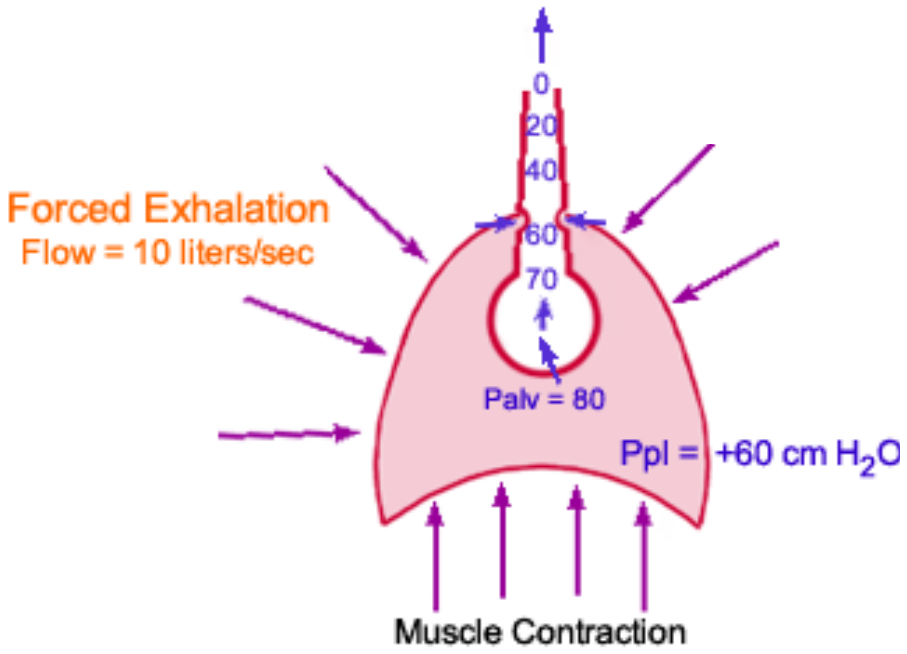
- upstream segment [Paw >Ppl]: driving pressure= Paw_1-Paw_2= 20-10=10 cm H20
- downstream segment [Ppl>Paw] driving pressure=Paw-Ppl =P_{TP} - ve =potential compression if there is no cartilagenous support or alveolar tethering.

Mechanism of Airflow Obstruction

Forced Expiration from TLC to RV (FVC maneuver)

Dynamic Compression Hypothesis





As expiration continue, there is less driving pressure, volume decreases, inward recoil diminishes, pressure dissipates in the airways as it overcomes frictional airways resistance, and EPP moves upstream towards the alveolus.

Determinants of Maximal Expiratory Flow

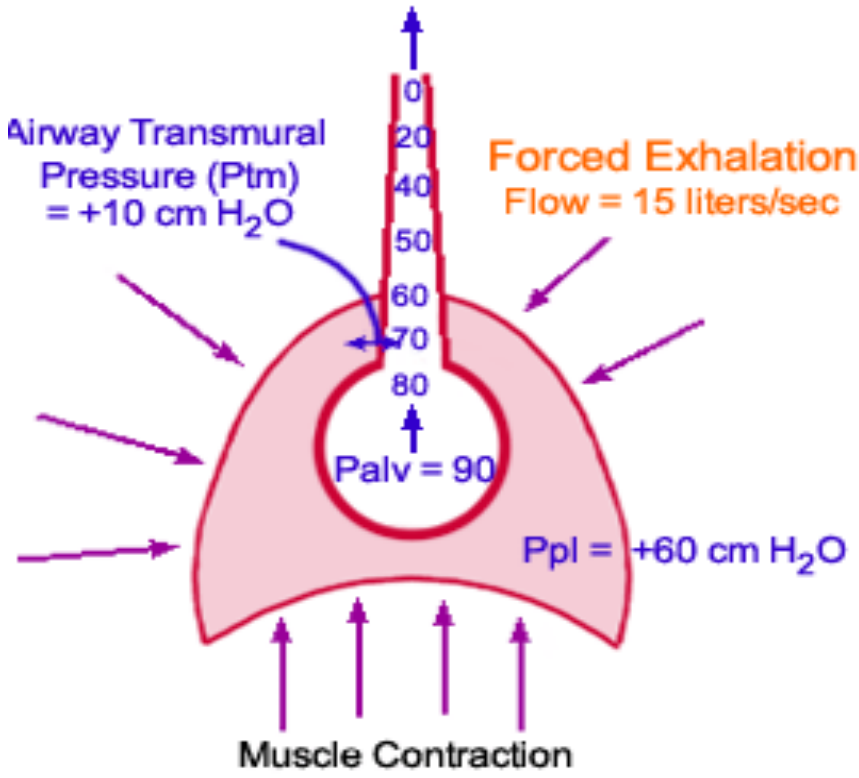
1. expiratory muscle strength prior to development of EPP (early in expiration-reflected in Peak Expiratory Flow, PEF)
2. airway resistance of the upstream segment
3. lung compliance/elastic recoil of the airways of the downstream segment

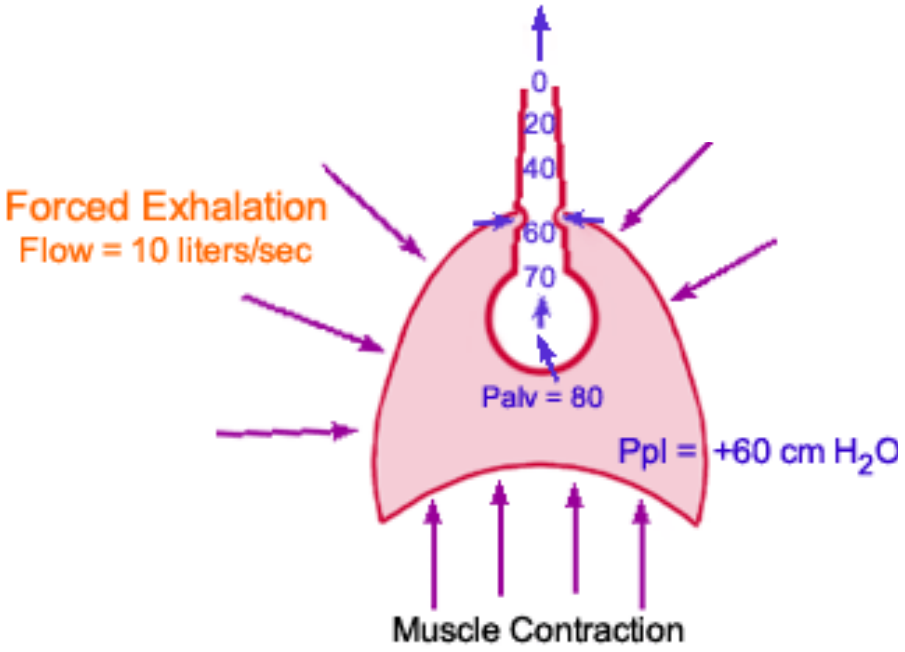
Team work: As these 3 characteristics change with disease abnormalities develop in maximal flow. Provide examples.

Mechanism of Airflow Obstruction

Forced Expiration from TLC to RV (FVC maneuver)

Dynamic Compression Hypothesis





As expiration continue, there is less driving pressure, volume decreases & inward recoil diminishes; pressure dissipates in the airways as it overcomes frictional airways resistance; and the EPP moves upstream towards the alveolus.

The Flow Volume Loop & Airway Obstruction

Fixed Obstruction

- foreign bodies / tumors
- scarring/stiffening of upper airways

Variable Extrathoracic Obstruction

- tumors
- fat deposits
- weakened pharyngeal muscles [obstructive sleep apnea]
- tracheomalacia/chondromalacia
- paralyzed vocal chords
- enlarged lymph nodes
- inflammation

Variable Intrathoracic Obstruction

- tumors