Airway Physiology
Essentials for Intensivists

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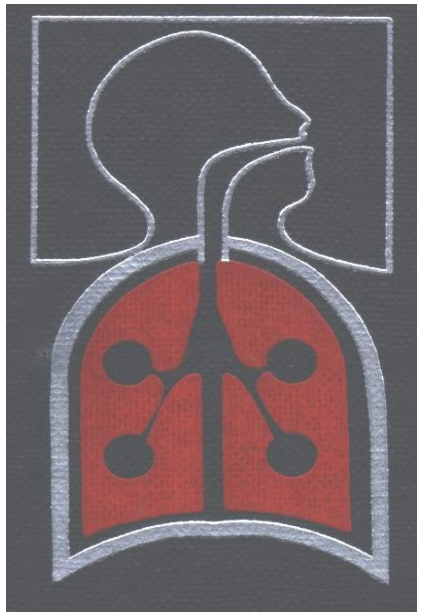


Airway and Physiology

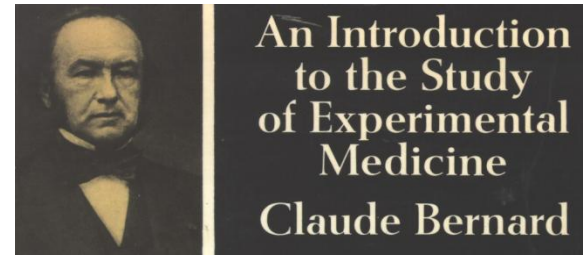
生理学

- Airway
  - Conduit – environment
  - Nose to Air Sacs

- Physiology: the Logic of Life
  - Stimulus – Response; Mechanisms of function
  - Framework: Understanding and Direction
  - Constancy of internal environment: norms and limits
  - Adaptations to maintain homeostasis
  - Survival (cell / organism) in a changing environment

Captions: The Normal Lung by John F Murray; The Logic of Life Edited by CAR Boyd & D Noble

Airway Physiology



- General: Integrity of Structure for Survival
  - Protection –can override other functions
  - Growth / Maintenance / Structural Adaptations
  - Defense against Invasion from inside or outside
- Specific Function in Breathing: Stable Conduit for Transport of Vital Material for Gas Exchange
  - Interaction with environment
  - Links with pulmonary and systemic circulations
  - Clinical Relevance
- Each of functions must support the other

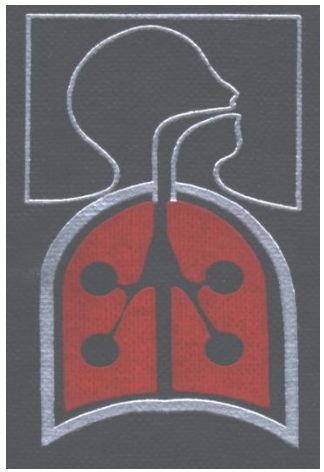
Breathing

- Dictionary: air inhaled and exhaled
- Physiologist: motor act for gas exchange

- Breathing is a coordinated motor act by which tightly controlled muscular activities ensure the airway is protected and has optimal supra- and sub-glottic volumes to provide a stable platform for ventilation with an ensuing efficiency of gas exchange and transport.

Caption: Cover of Breathing by Arend Bouhuys, Grune and Stratton 1974

Respiration in Changing Environments
Airway and Breathing ... and Circulation



Stimuli

Precedence Routing
Limit Recognition

Major Response

Normal or No Response

Airway Effectiveness: a stable patency

Constancy of optimal upper and lower airway volumes

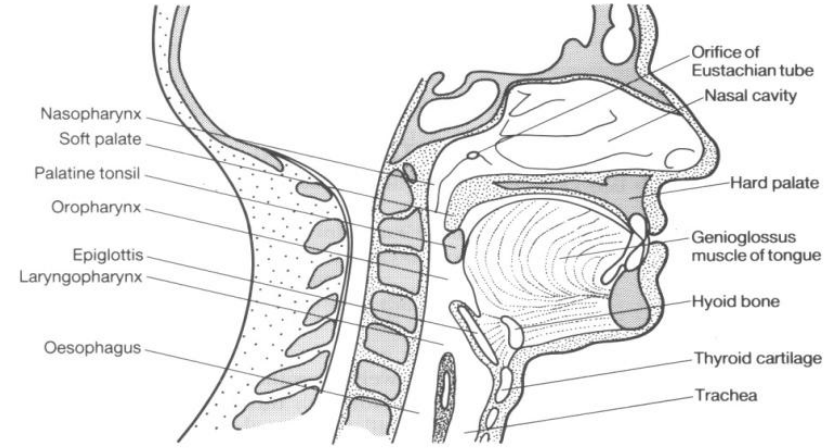
Control Focus: physicochemical (structural) and active neural mechanisms for control of airway volume(s)

Captions: Covers The Normal Lung by John F Murray 1986 & Breathing by Arend Bouhuys 1974

Aims

- Review Airway Structure and Function
- Importance of Airway Volume

Nose



Reflexes: Irritation
Dive Reflex
Sneezing and Sniffing
Negative pressure: open pharynx & larynx

Motor
Nasal Cycle: resistances of two sides
alters every 2-4 hours – 80% humans

Crutch reflex: Axilliary stimulation –
ipsilateral increase in resistance

Nasal “valves”: alae nasae muscles
patency of narrowest region of the nose

Air-conditioning → protects lower airway mucosa
Inspiration: warm → humidity;
Expiration: colder → heat & water recovery

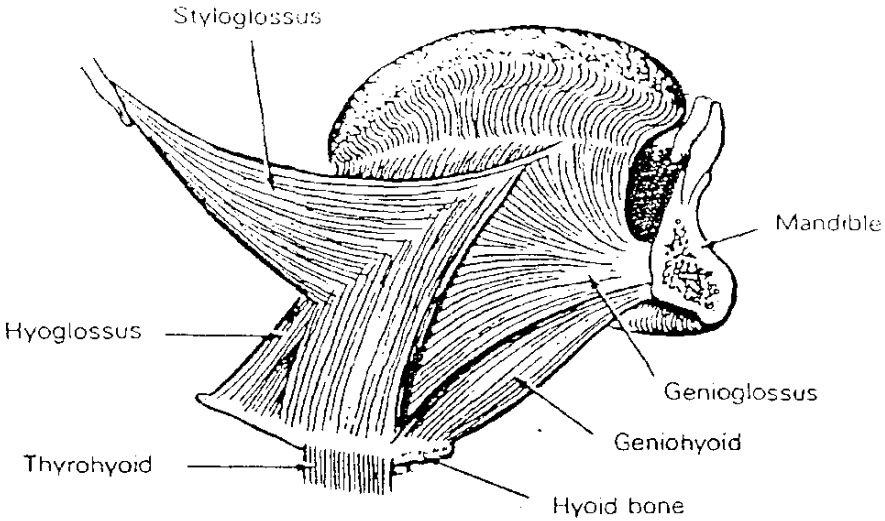
Dogs: inspired air -40 to +40^{o}C → fully saturated with water vapor (BTPS) just below larynx

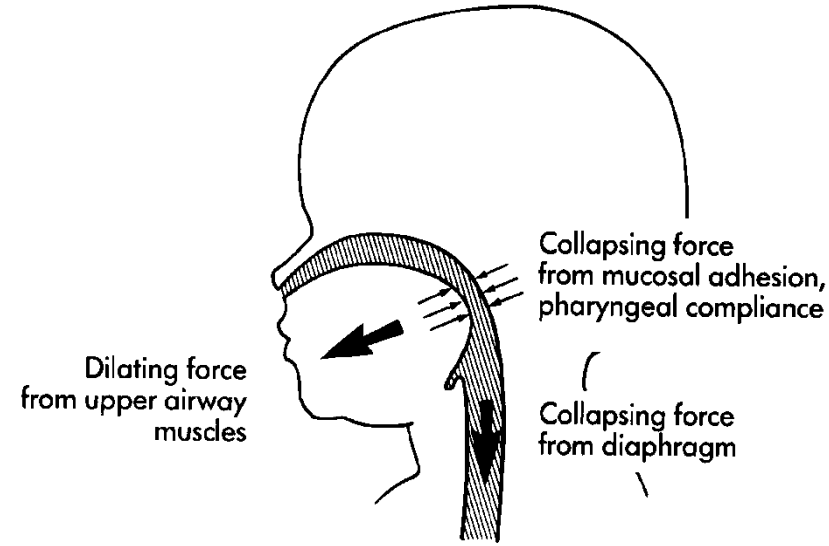
Resistance: adult x 2 mouth: exercise & sighing

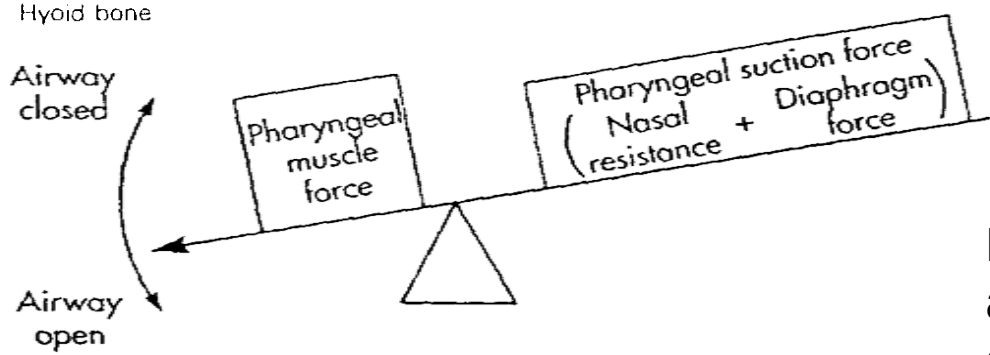
Newborn: lower nasal than mouth resistance
Obligate nose breather: Flow directed to larynx

Widdicombe JG Clin Chest Med 1986; 7:159-170
Nunn, JF In Applied Respiratory Physiology 4th Edition Butterworth Heinemann 1993

Pharyngeal Patency





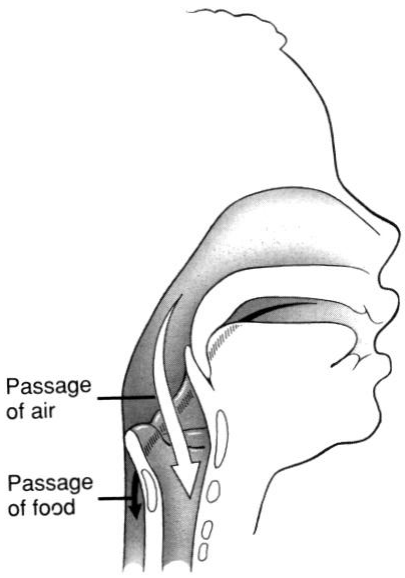


Pharyngeal Patency
Muscle Function
Sleep & ↓ Tone
Obesity

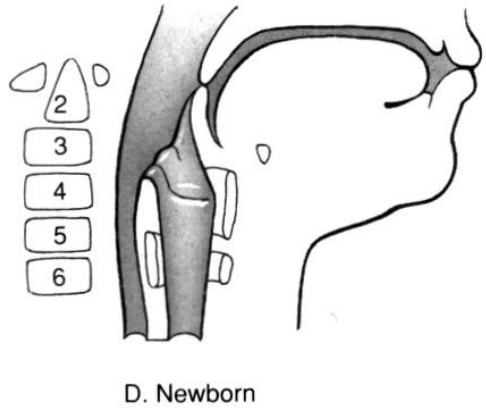
Does not explain mixed apnea as apnea with airway closure precedes diaphragmatic effort

Thach BT 1983. In SIDS, Academic Press;
Motoyama EK In Basic Principles in Pediatric Anesthesia Chap 2
Idiong N et al. J Pediatr 1998; 134:796-798

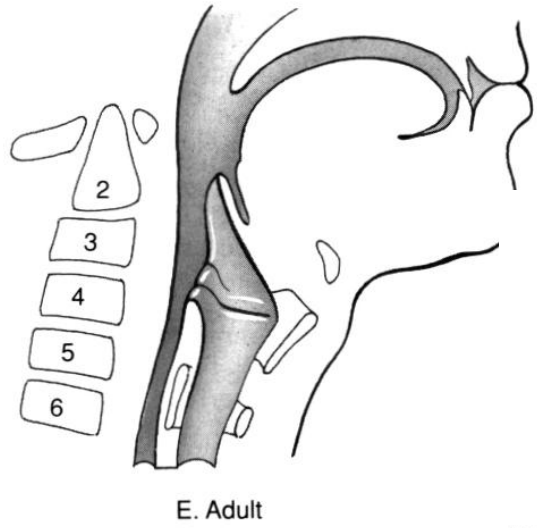
Naso- and Oropharynx



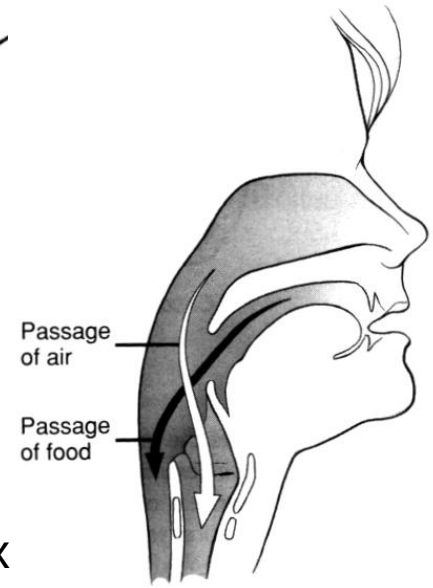
High Larynx
Breathe & Feed
Baby “Talk”



D. Newborn



E. Adult

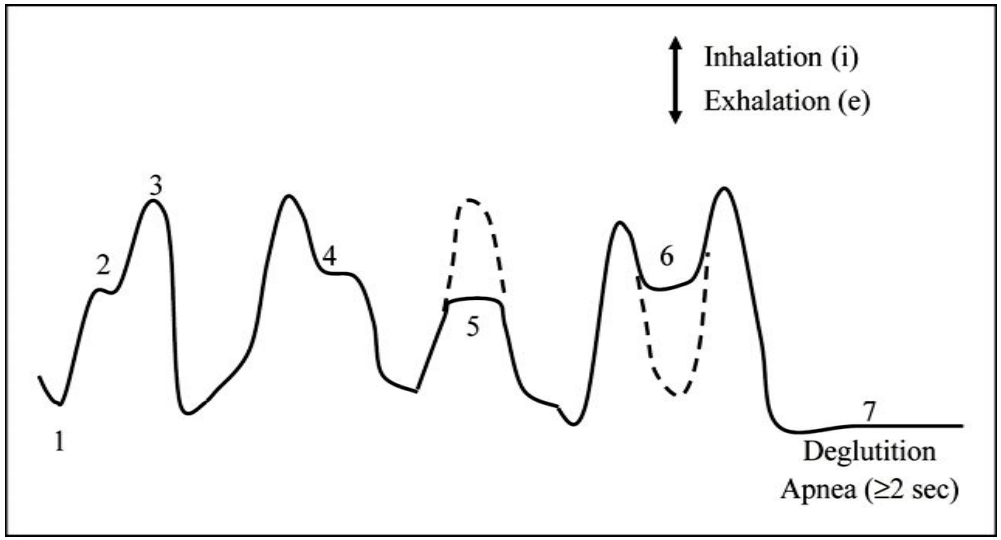


Lower Larynx
Cross Road
Speech

O’Connor DM. In: The Pediatric Airway Myer III CM, Cotton RT, Shott SR. JP Lippincott Co. 1995

Suck – Swallow – Breathe

[waiting for the “light bulb” to go on]



Swallowing: Glottis closes

Preterm Infants & Swallowing

1. at Start of Inspiration / End Expiration
2. during Inhalation
3. at End-Inspiration / Start Expiration
4. during Exhalation
5. interrupting Inspiration
6. interrupting Exhalation
7. with no respiration occurring

Normal Coordination: S - S – B = 1:1:1 or 2:2:1
& no apnea / bradycardia / desaturations / aspiration

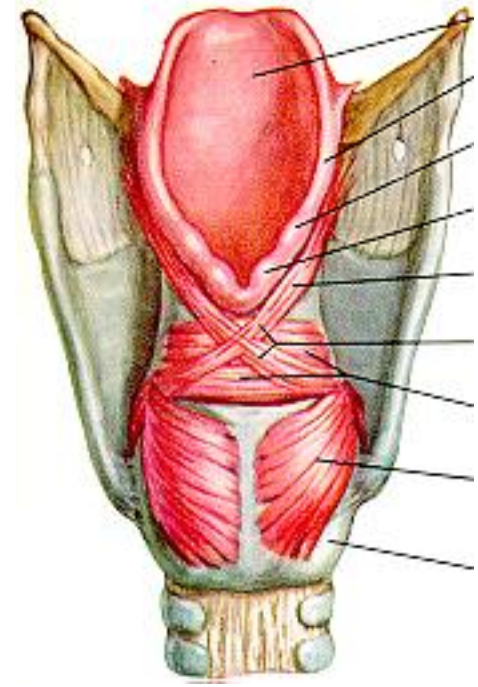
Term at > 2 weeks ~55% swallows start inspiration (1) and end-inspiration (3)
Preterm ~ 55% swallows in apnea (7)

“Safe” swallowing: at start inspiration / during apnea

Lau, C. NeoReviews 2006; 7:e19-27

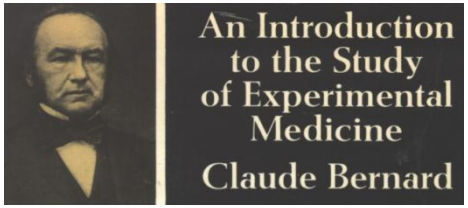
Laryngeal Functions

- Valve : Motor Control of Flow in Breathing
- Sensory: pressure; flow; temperature
- Chemoreflex: Protection
- Airway Closure
- Dive Reflex
- Speech and …Song!

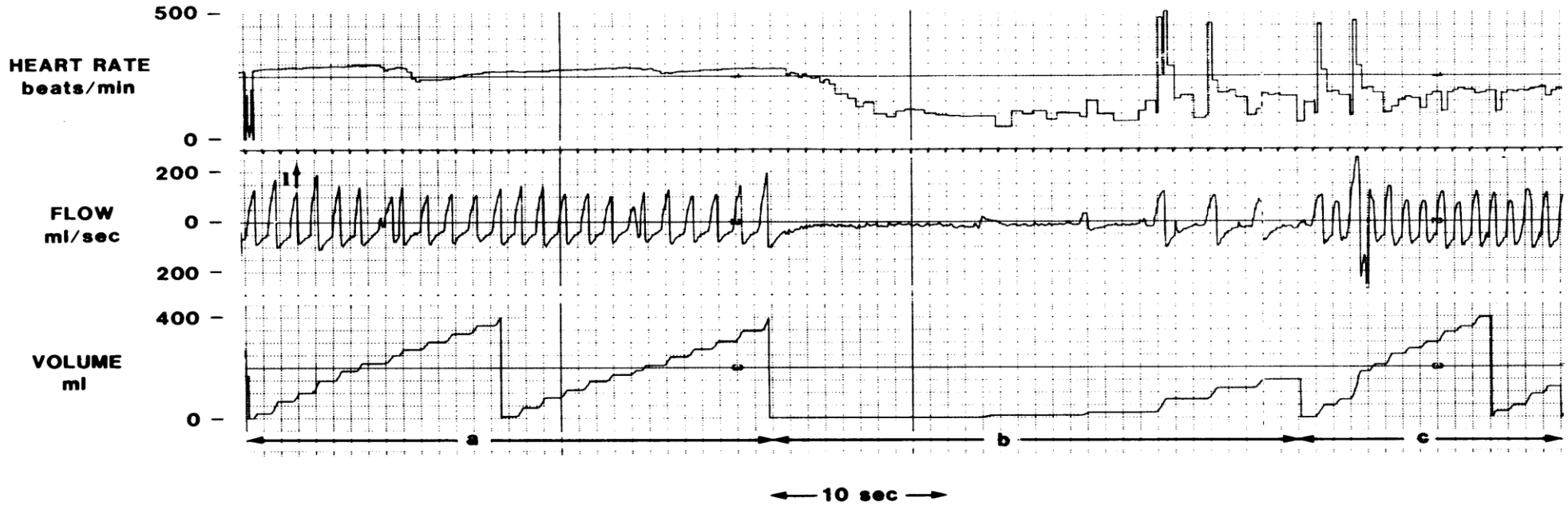


Bartlett D Jr. Physiol Rev 1989; 69:33-57; (Respiratory Functions) Sant'Ambrogio G, Tsubone H, Sant'Ambrogio F Respir Physiol 1995; 102:1-16 (Sensory Information)

Apnea – SLN – Dive Reflex



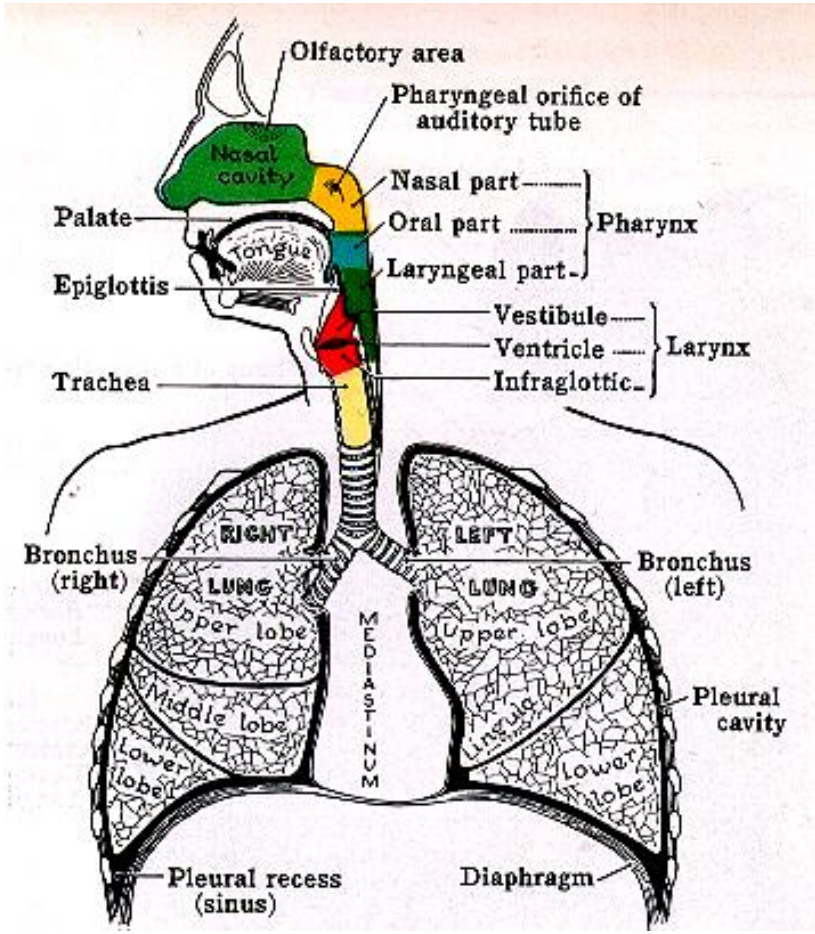
Environmental Challenge: Airway Protection is Paramount & linked to Circulatory Protection

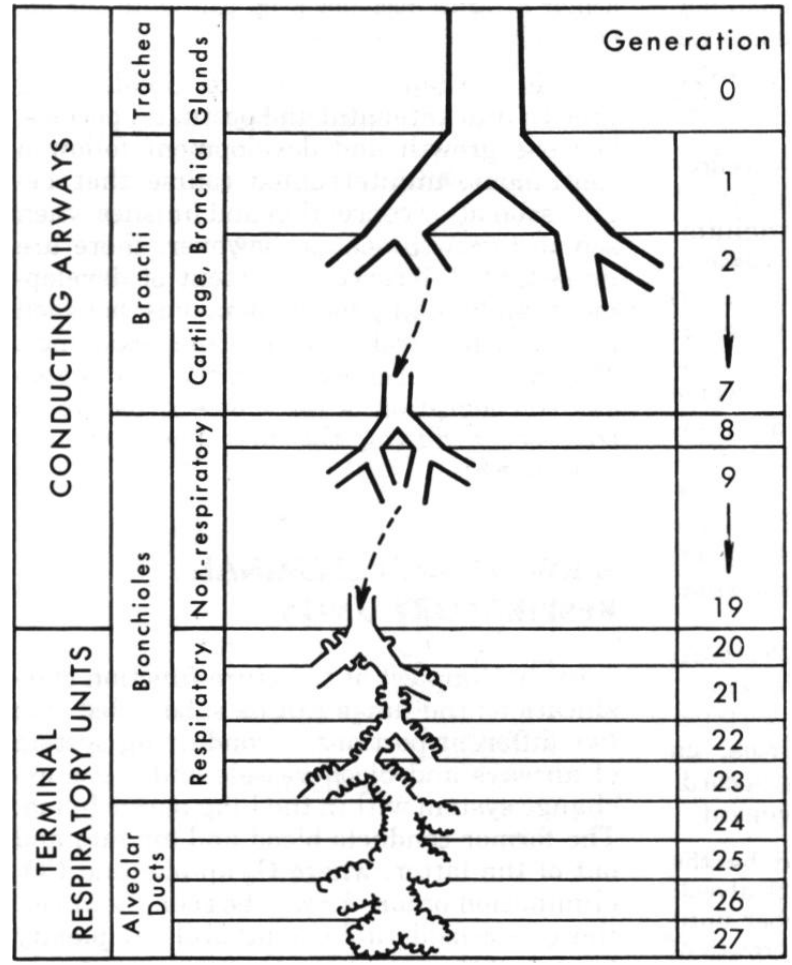


Dive reflex is present in the fetus

Hutchison AA. Pediatric Pulmonology 1987; 3:317 - 323.
Perkett EA, Vaughn RL. Acta Paediatr Scand 1982; 71:969 - 972

Lower Airway: Structure





Upper Airway
Lower Airway

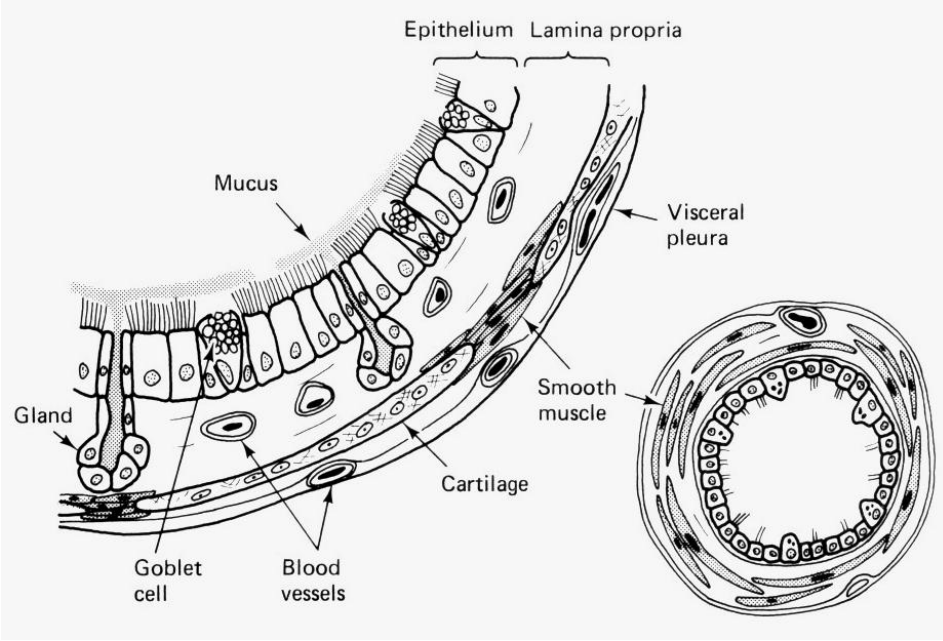
Irregular Dichotomous branching → even gas distribution

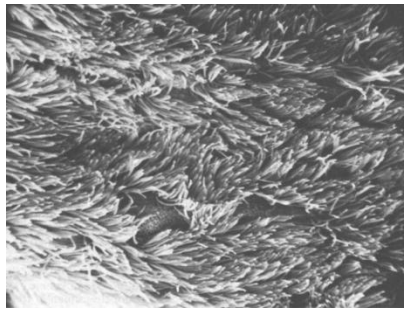
Huge increase in surface area in terminal respiratory units compared to more proximal conducting airways

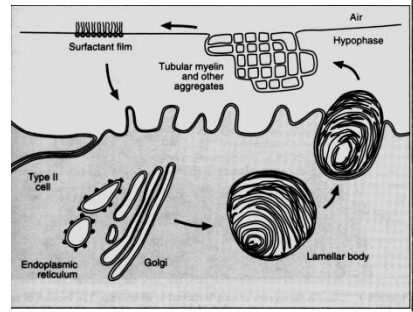
Lower Airway Volume : Sub-Glottic Volume / “Lung” Volume; Relative: Tidal Volume

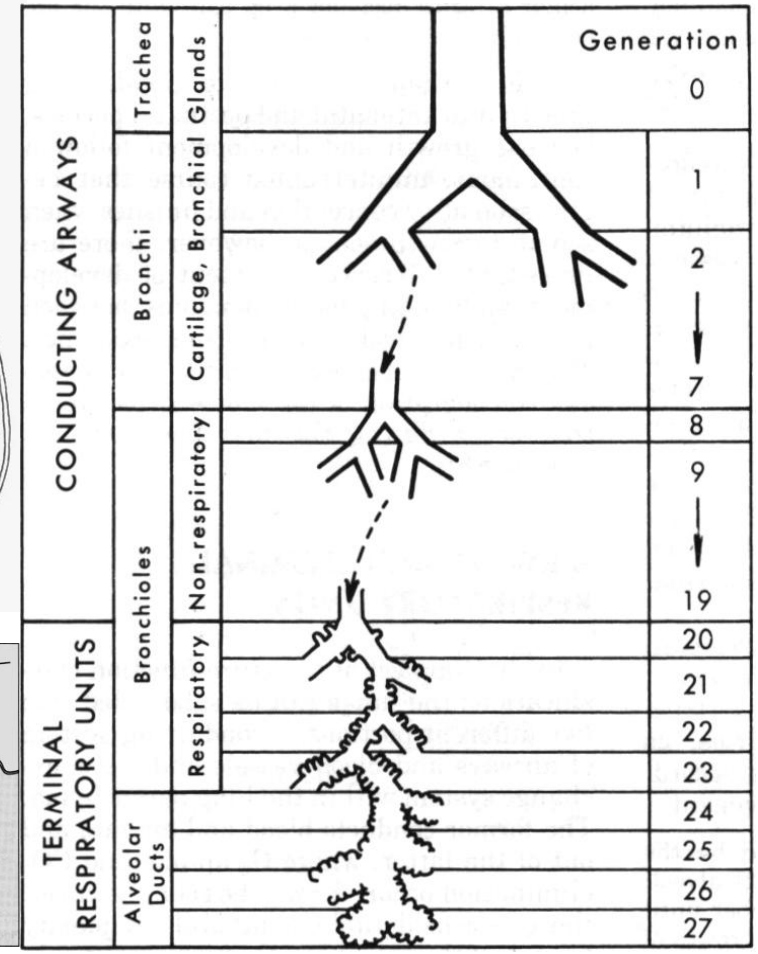
In Grant JCB An Atlas of Anatomy Livingstone 1962.
In: Murray JF The Normal Lung 2nd Edition WB Saunders 1986.

Lower Airway Optimal Volume









Cricoid Tethering

Wall: Cartilage

Mucus Clearance

Wall: Smooth Muscle Tone

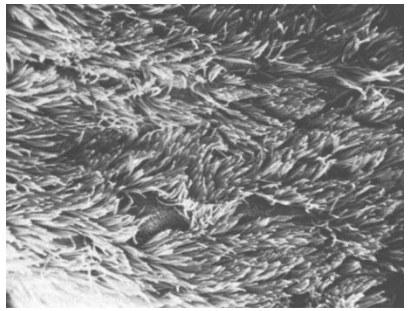
Transpulmonary Pressure

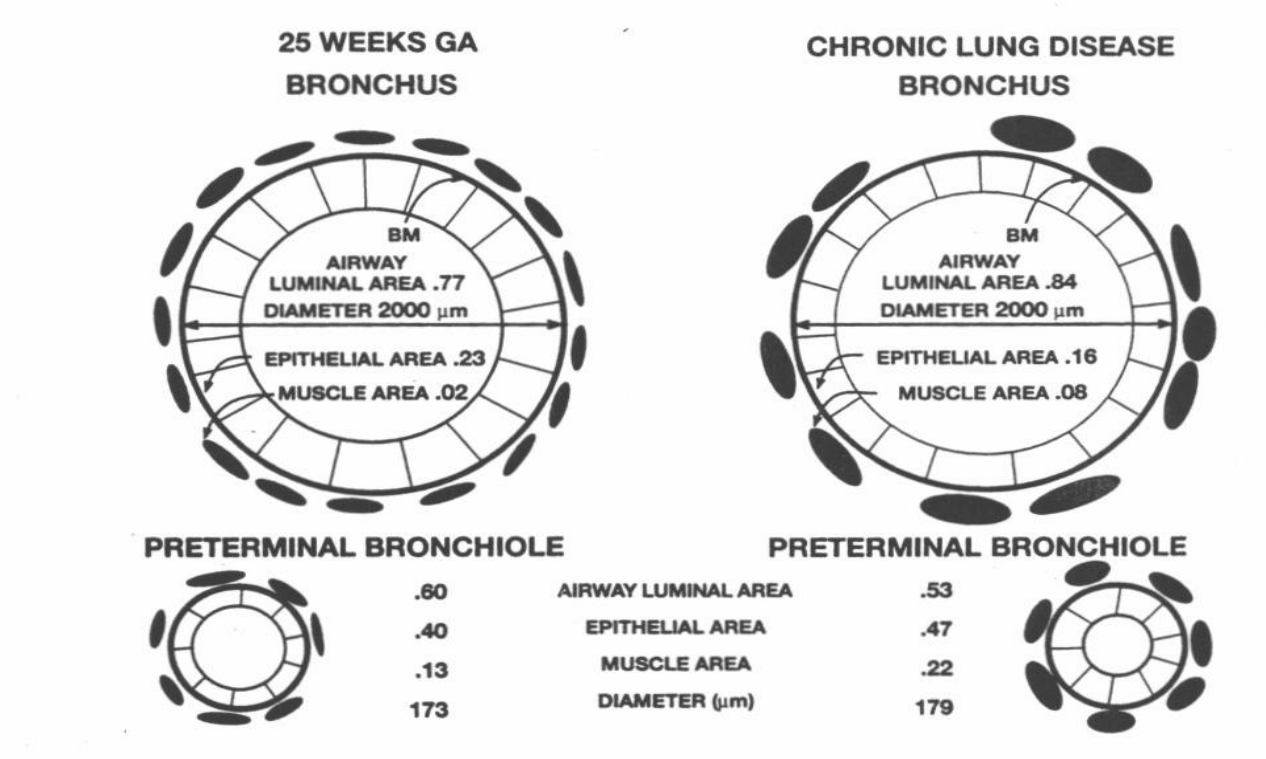
Radial Traction of Tissue Forces

Surfactant Interdependence of Air Sacs

In: Respiratory Physiology 2nd Ed. J Widdicombe & A Davies Edward Arnold 1991 p 45.
In: The Normal Lung 2nd Edition Murray JF WB Saunders 1986

Preterm Airway Smooth Muscle

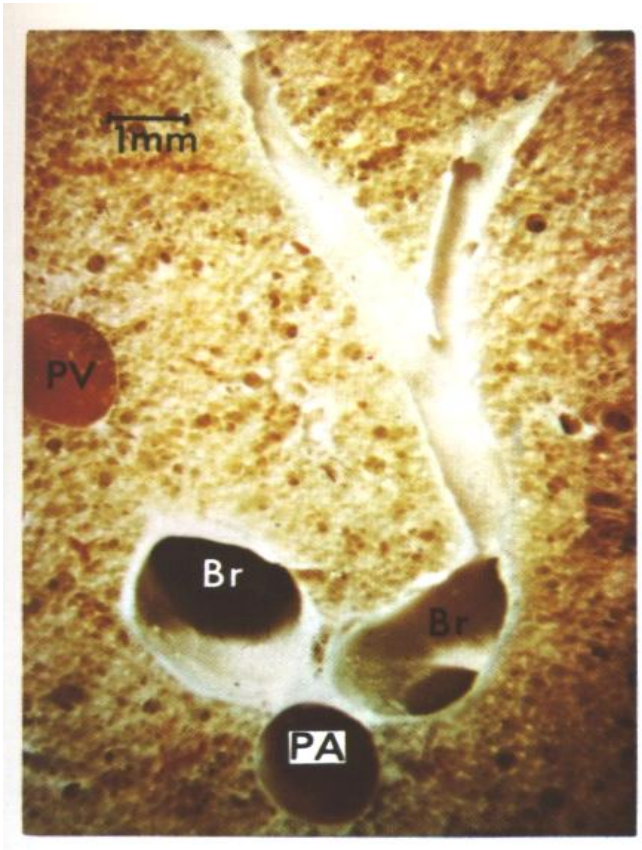


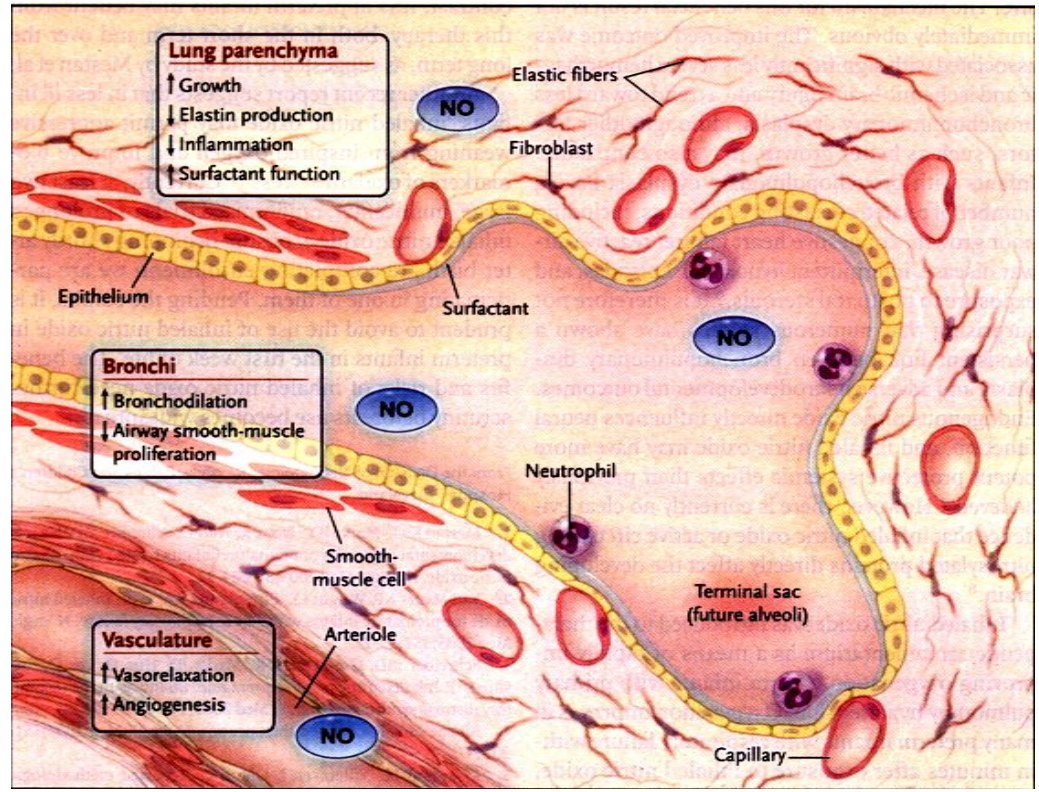


From 23 weeks to term airway muscle in smallest preterminal bronchiole to bronchi. Fetal smooth muscle has phasic activity. Fluid movement is proximal to distal. No S/M in animal model → lung hypoplasia

Sward-Comunelli S et al. J Pediatr 1997; 130:570-576
In: Murray JF The Normal Lung 2nd Edition WB Saunders 1986.

Interaction with Circulations





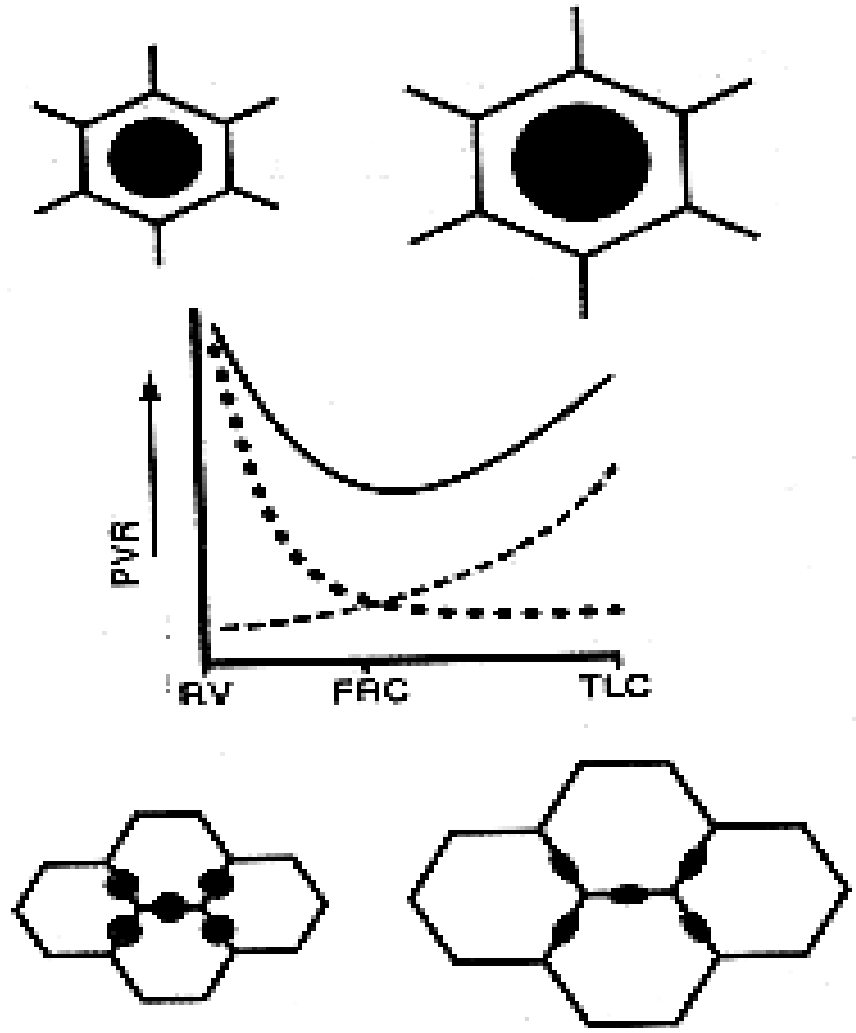
Pre-acinar arteries and veins follow the development of the conducting airways
Intra-acinar vessels follow the development of the gas exchange airways
Nitric Oxide & Bronchial Derived Relaxing Factor; Vagal afferents & efferents: Sinus Arrhythmia

In Nunn, JF In Applied Respiratory Physiology 4th Edition Butterworth Heinemann 1993
Martin RJ NEJM

Airway Volume and Pulmonary Circulation

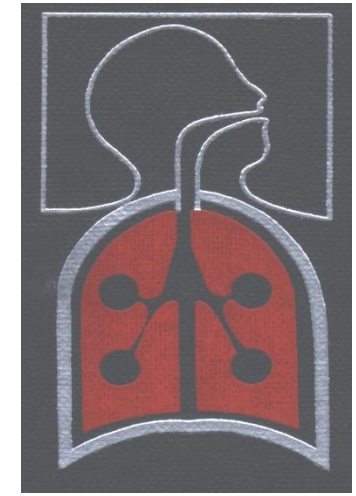
Under-inflation: pulmonary resistance increased

Over-inflation: pulmonary resistance increased
lung tissue injury & capillary stress injury



In: Neonatal Respiratory Diseases T Hansen, TR Copper, LE Weisman 1998; Handbooks in Health Care

Importance of Sub-Glottic Airway Volume

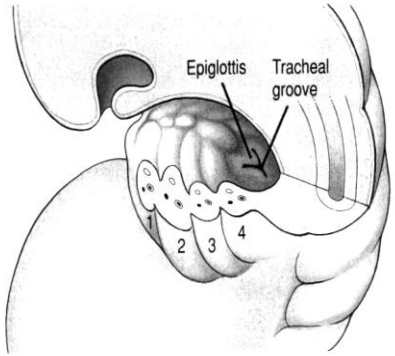


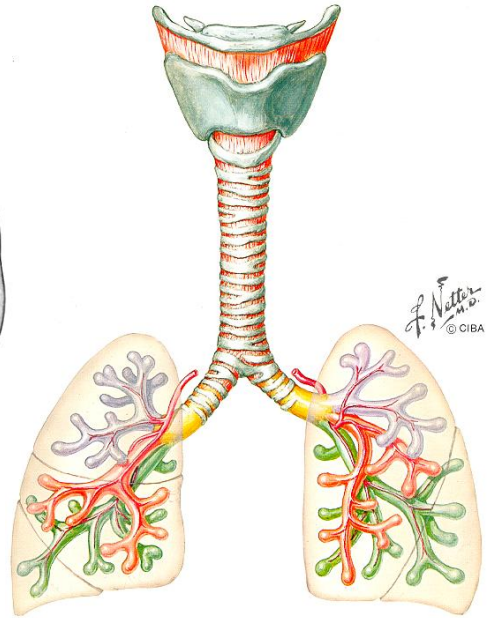
- Respiratory distress warning signs that draw a crowd:
  suboptimal sub-glottic airway volume

- Main Focus:
  - How does the fetus control airway volume?
  - What are the determinants and limits for airway volume?
  - How do structural / physicochemical properties of the respiratory system impact on sub-glottic volume?
  - How do active, neuromechanical adjustments in breathing pattern optimize sub-glottic volume?
  - How does therapy affect homeostasis?

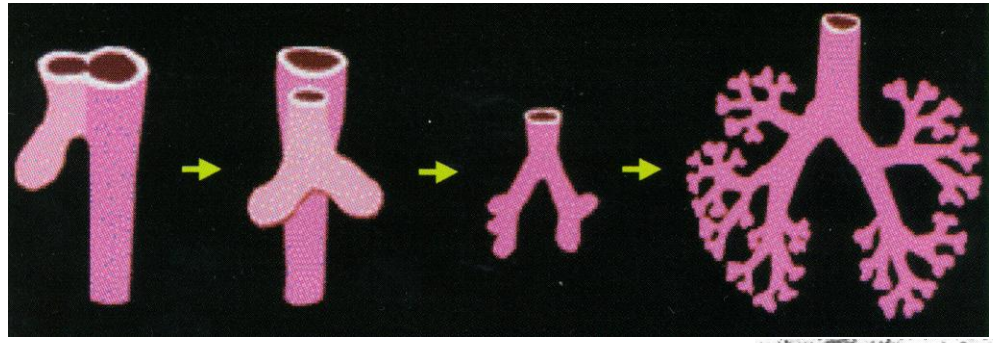
Human Airway Development

Pharynx Larynx
Embryogenesis
4-7 wks ……7-8 weeks

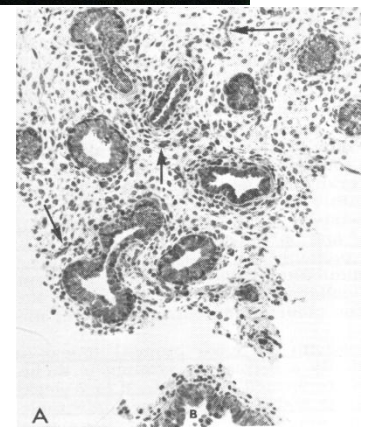




Branching Morphogenesis
4-7 wks … Pseudoglandular 8-16 wks
Foregut Endoderm & Thoracic Mesoderm



Thoracic Mesenchyme: CT, Airway Muscle & Vasculature



Conducting airways formed by 16th week

FGF-7,10, ptc, Gli & Hox genes, Shh, TTF-1,
FGFR-2, HNF-3β, RA & RAR; TGF- β, EGF, EGF-R

O'Connor DM. In: The Pediatric Airway Myer III CM, Cotton RT, Shott SR.
JP Lippincott Co. 1995; Crelin ES Clin Symposia 1975; 27:1-28; Volpe, MV Neo Resp Dis 1999; 9:1-11.

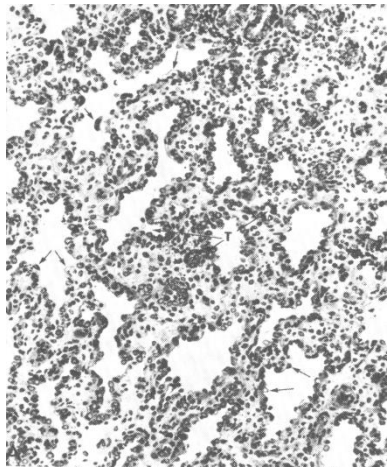
Terminal Airway Development:
Canalicular & Terminal Sac / Alveolar

Canalicular
(17-26 wks)

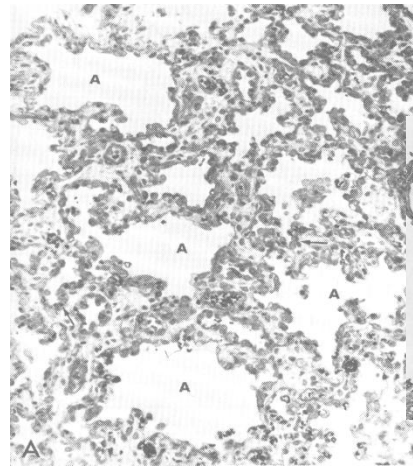
Terminal Sac
(27-32/36 wks)

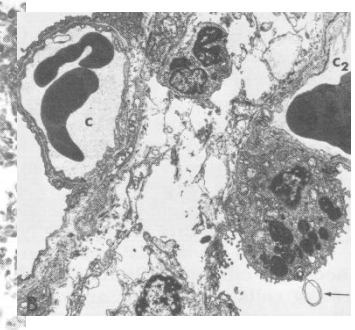
Alveolar
(>36 wks)

22 wks 500g

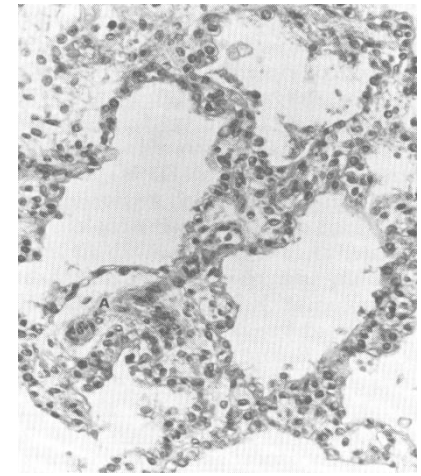


27 wks 1000g

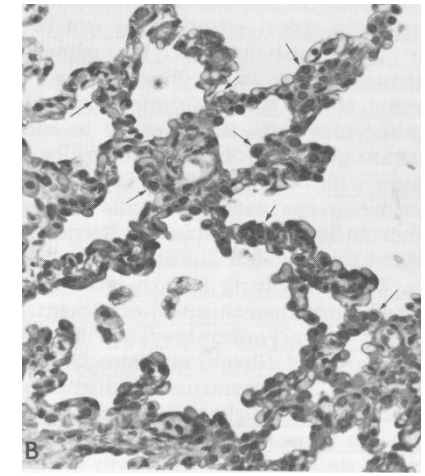




32wks 1700g



40wks 3500g

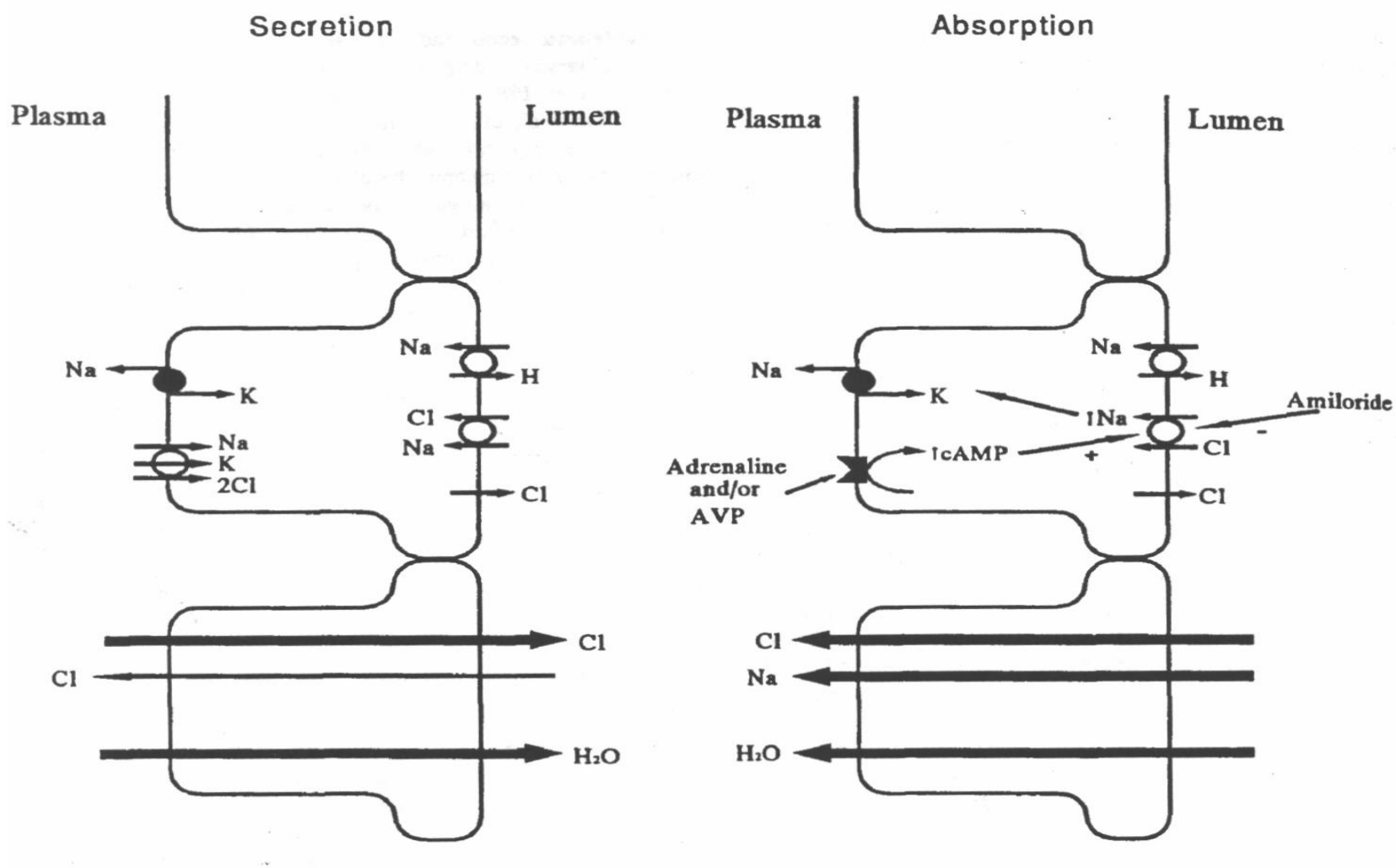


Hox genes, TTF-1, HNF-3β, PDGF-A & B; EGFR, RA & RAR; TGF-β & TGF-β R

Glucocorticoids, DHT, TTF-1, HNF-3β, EGF, EGF-R, RA, RAR,Thyroid hormone

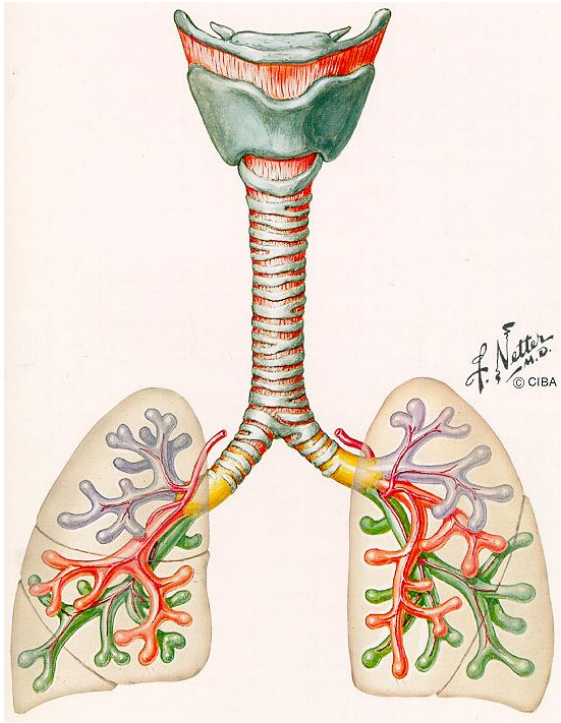
Stahlman MT, Gray ME Clin Perinatol 1978; 5:181-196.
Volpe, MV Neo Resp Dis 1999; 9:1-11.

Fetal Airway: Liquid Secretion & Absorption



Harding R, Hopper SB J Appl Physiol 1996; 81:209-224

Fetal Lung Volume, Fetal Breathing: Growth

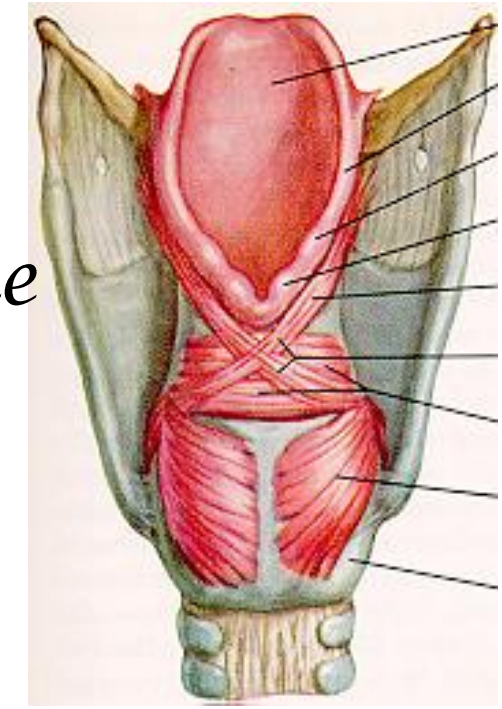


Larynx 7-8 weeks

Lung Liquid / Volume

Fetal Breathing

Airway Growth

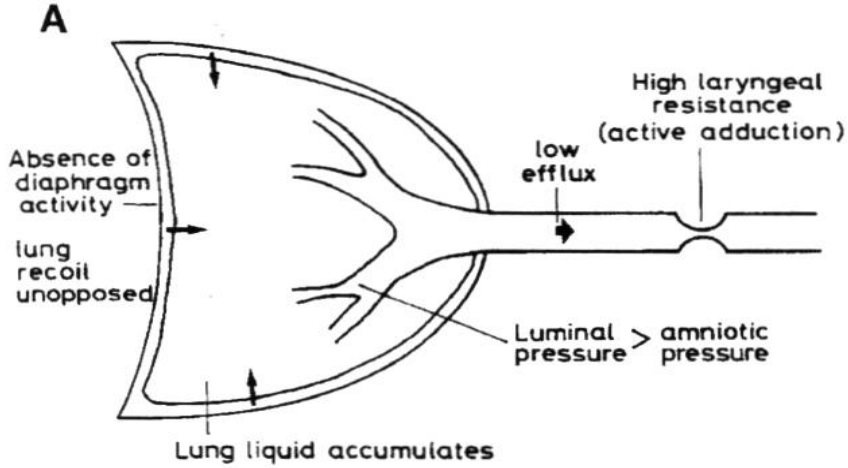


Fetal Breathing: "…thoracic gymnastics in preparation for the great extrauterine function of atmospheric respiration."
Ballantyne JW. Manual of Antenatal Pathology and Hygiene 1902: p.144

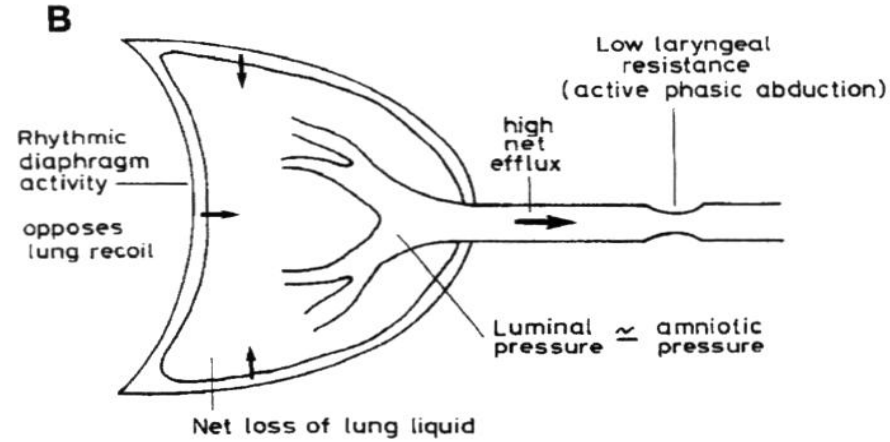
Crelin ES Clin Symposia 1975; 27:1-28; Saunders, WH Clin Symposia 1964; 67-99

Upper Airway Control of Airway Liquid Volume

High – Voltage State (NREM)



Low Voltage State (REM)

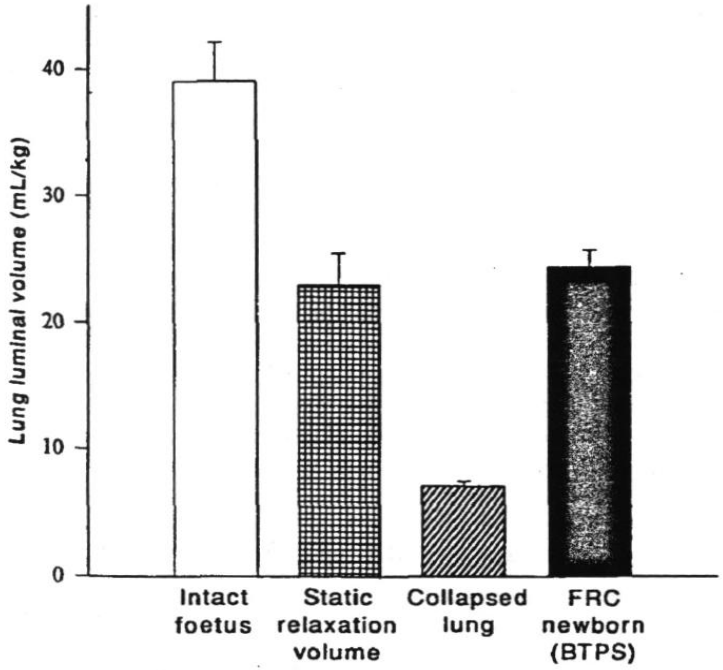


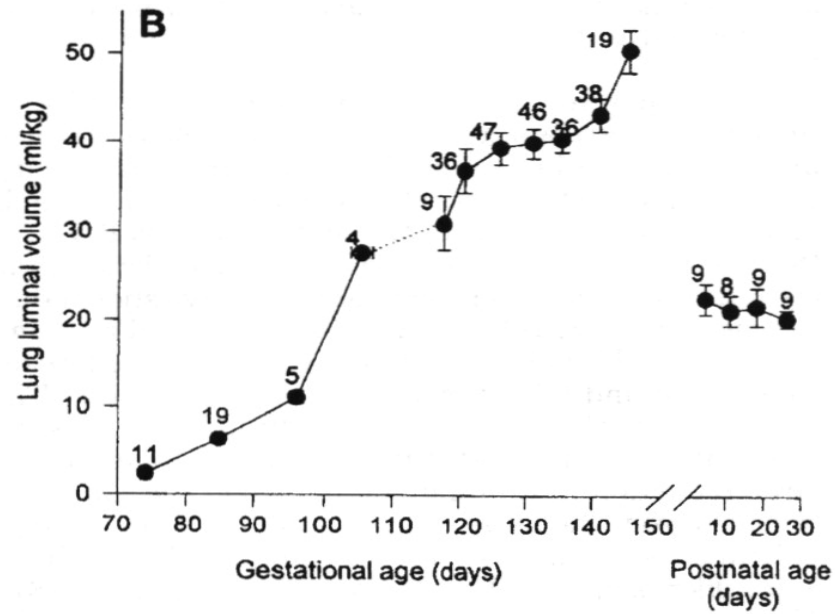
In utero there is no surface tension. The chest wall is compliant.

In NREM maximum lung expansion with apnea occurs.
REM chest wall tone is lacking: maybe mimics minimal lung volume.
Could REM and NREM sleep be times when we test our limits / alter growth patterns to fit changing functional needs?

Harding R, Hopper SB J Appl Physiol 1996; 81:209-224

Fetal Lung Volume is High





Motor mechanisms (laryngeal NREM and diaphragmatic REM) are set in place that maintain fluid volume .
Airway volume of the fetus is high compared to the newborn.
Fetal breathing is focused on the control of lung volume.
Airway volume control is a major challenge at birth.

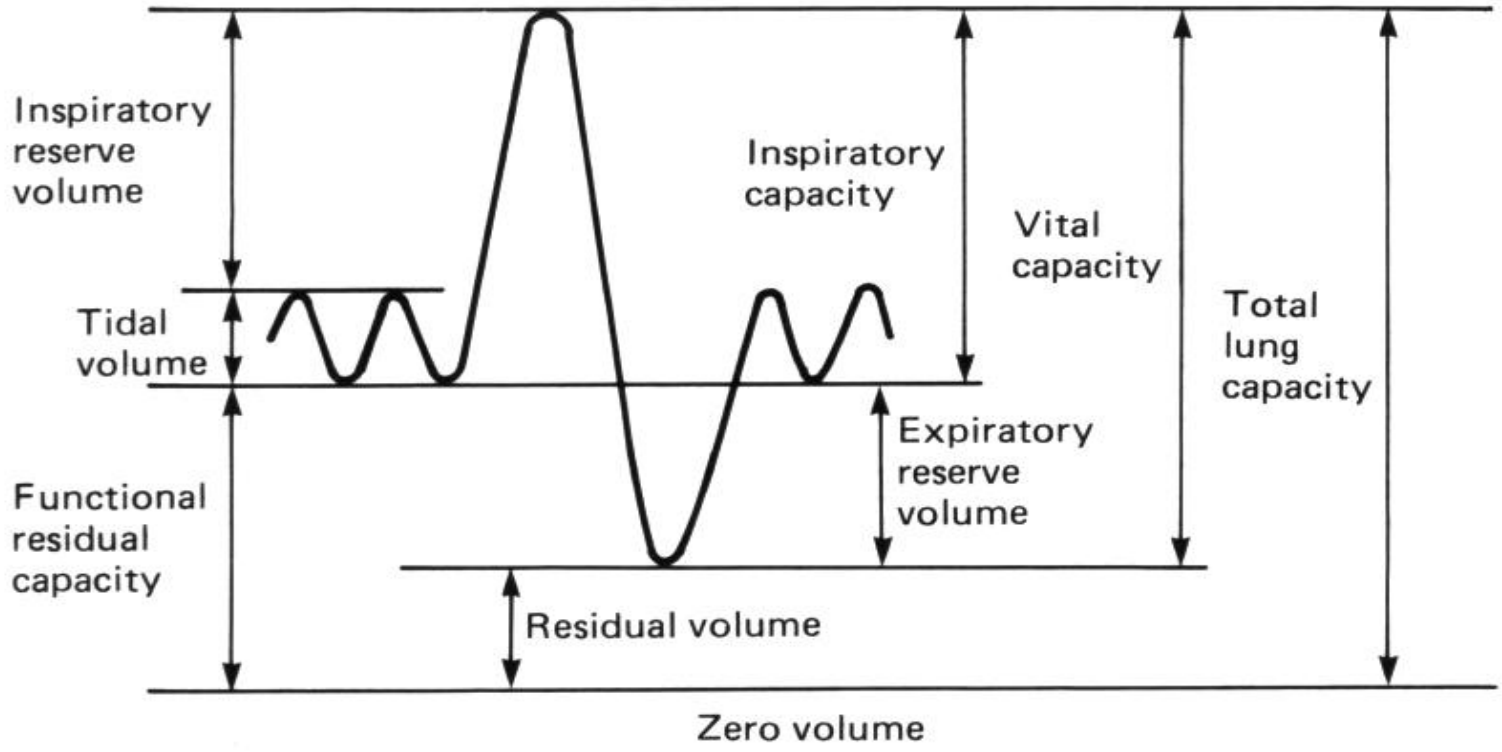
Hopper SB, Harding R Clin Exp Pharmacol Physiol 1995; 22:235-247

What are Normal Airway Volumes?

Upper Limit

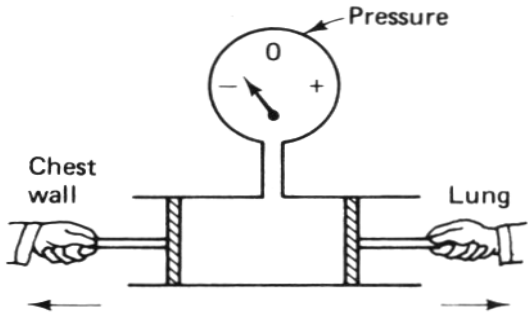
Normal

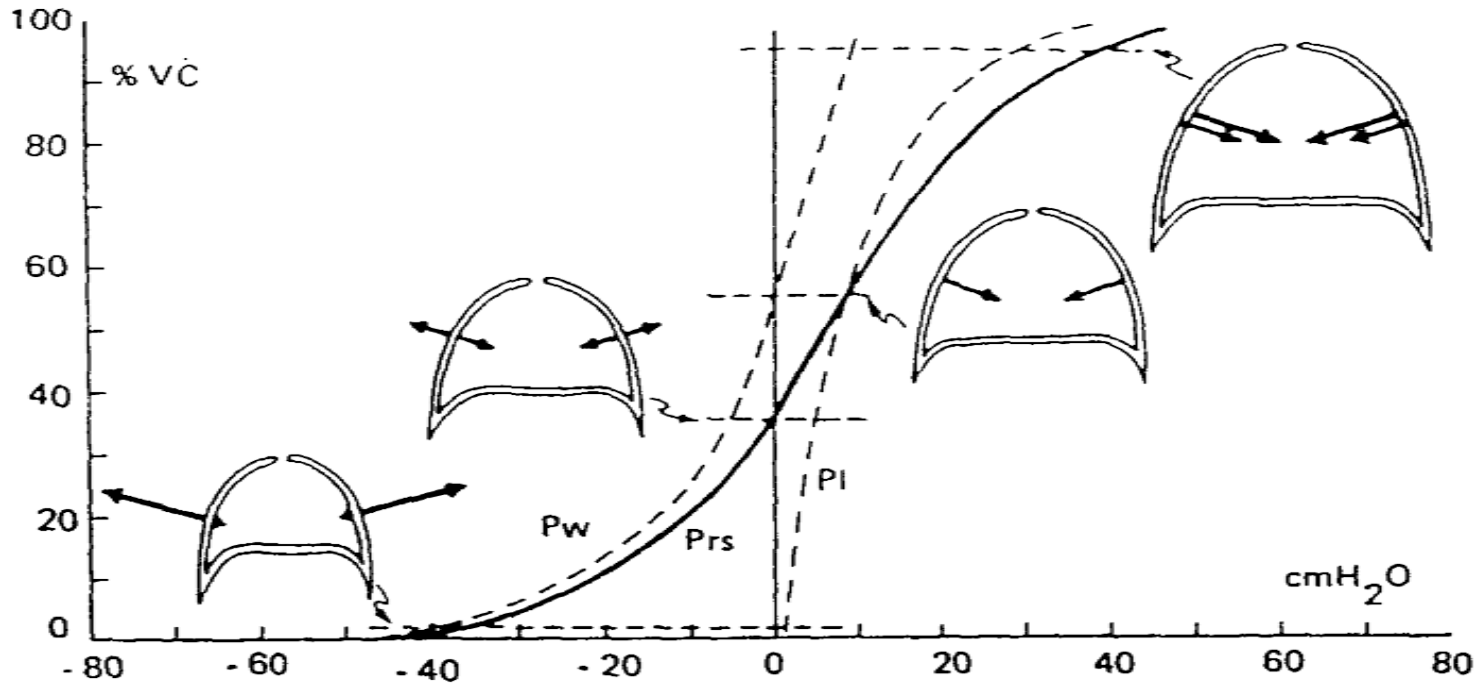
Lower Limit



Nunn, JF In Applied Respiratory Physiology 4th Edition Butterworth Heinemann 1993

Where do we “want’ to breathe?
Limits of collapse and stretching

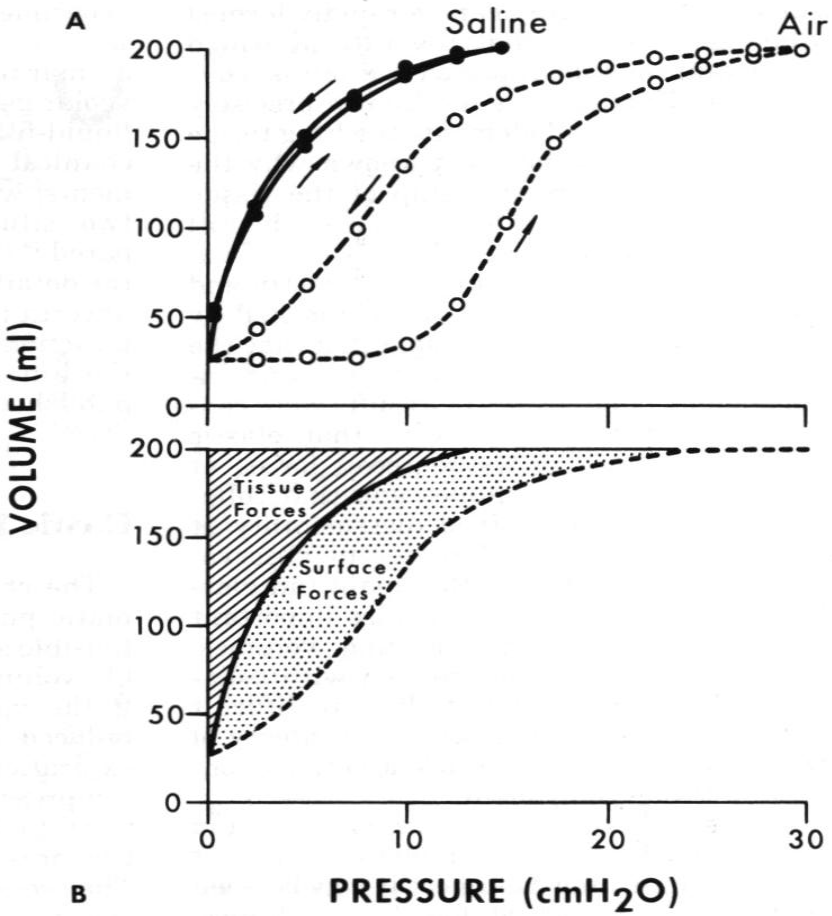




We want to breathe at a point where the sub-glottic volume is set passively.

In: Respiratory Physiology 2nd Ed. J Widdicombe & A Davies Edward Arnold 1991
Agostini E, Mead J. In Fenn WO, Rahn H Handbook of Physiology 1986.

Why is our elasticity “imperfect”?



Opening from RV to TLC: Sigmoid Curve
Slow start to inspiration and expiration

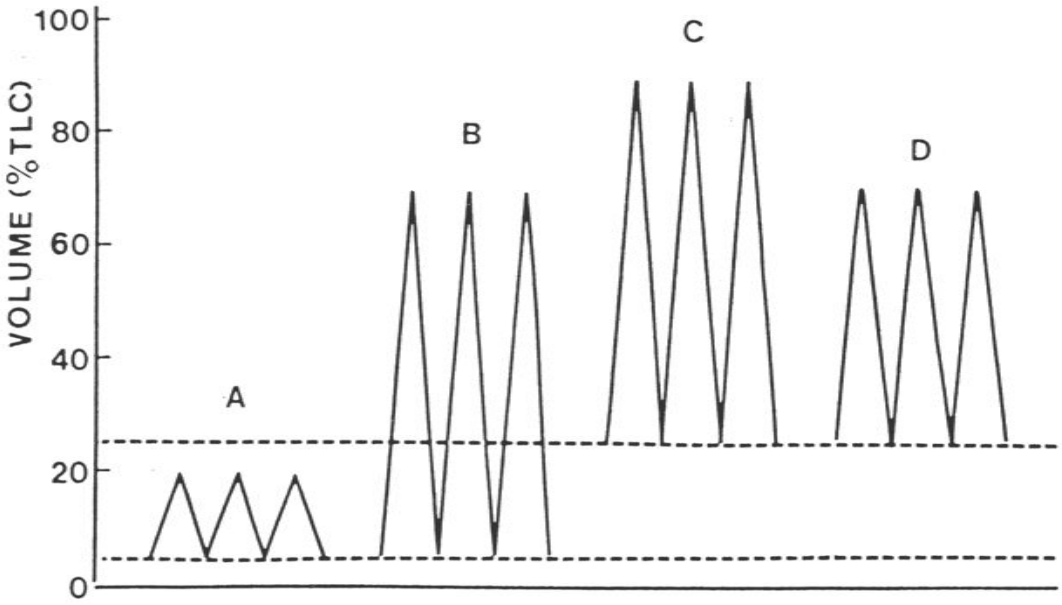
Recruit in inspiration; Resist overexpansion
Delay decay on expiration

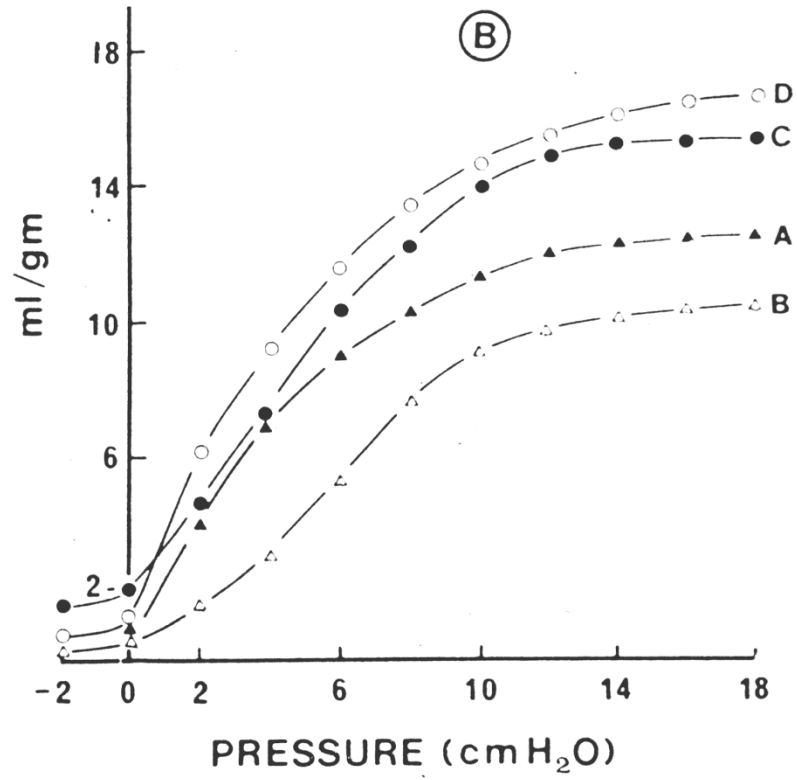
Hysteresis: “The failure of a property that has been changed by an external agent to return to its original value when the cause of the change is removed.” Gk husterein: to be behind, come later

The imperfect curve allows expiration to occur effectively although the flow is barely a “breeze”.

Murray JF In The Normal Lung 2nd Edition WB Saunders 1986

Expansion from Low Volume

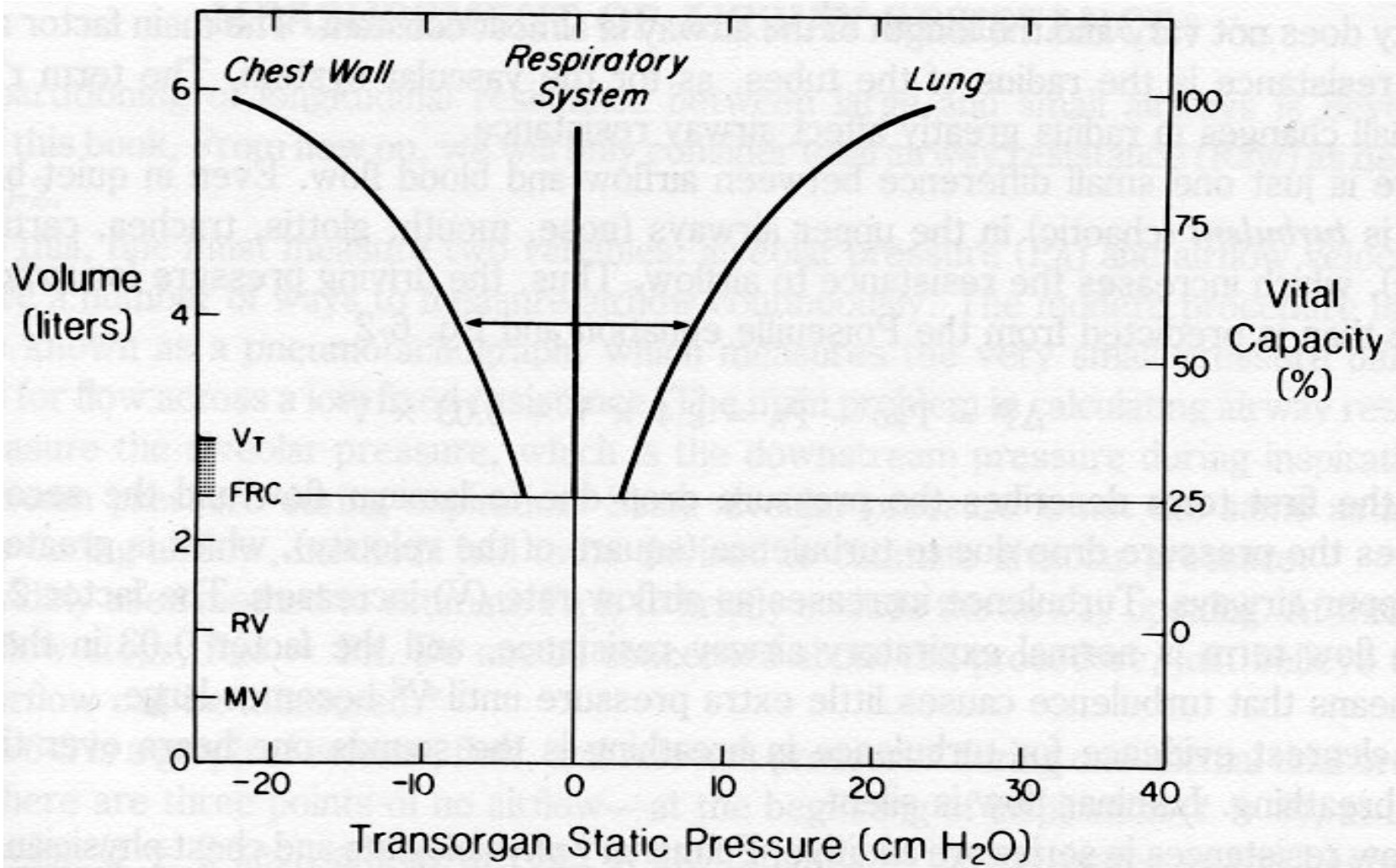




Where we start to breathe from and the relative change (strain =ΔV/V) is important

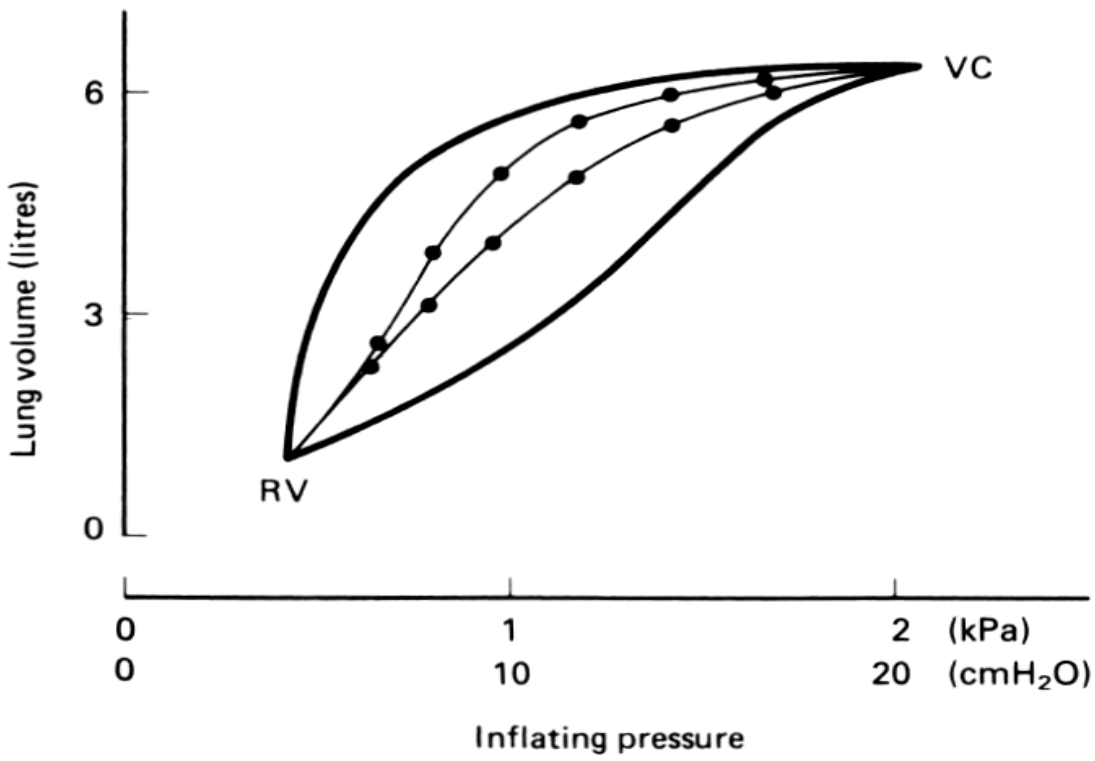
Wyszogordski, I et al. J Appl Physiol 1975; 38:461-466.

Mechanics - Dynamic



Staub, NC. In: Basic Respiratory Physiology Churchill Livingstone, 1991

Hysteresis due of Airway Resistance

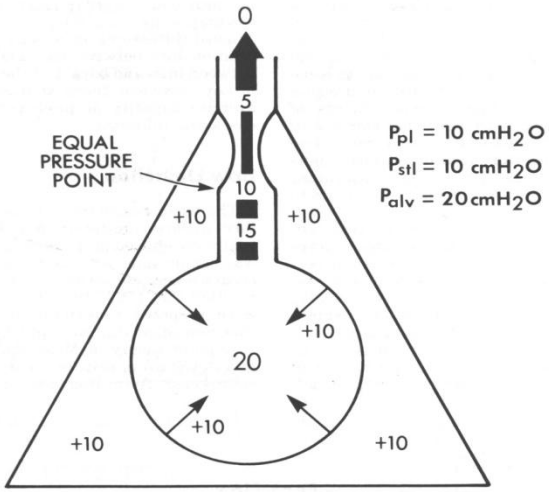


With open air sacs the hysteresis due to surface forces is small.

The higher the resistance of the conducting airways results in “ballooning” of the loops that also show hysteresis – a characteristic of bronchoconstriction.

In: Respiratory Physiology 2nd Ed. J Widdicombe & A Davies Edward Arnold 1991

Resistance & Airway Collapse: Flow-Related & Volume-Related

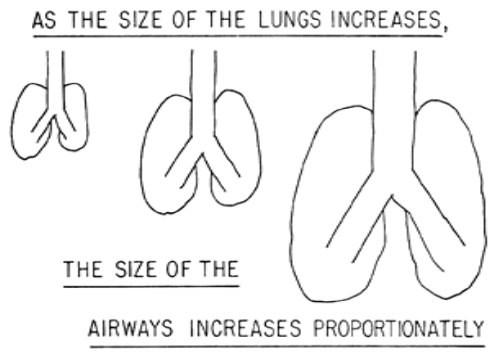


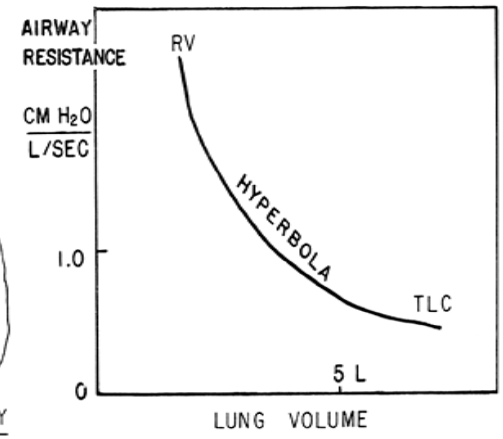
<u>Flow-Related</u> Airway Collapse

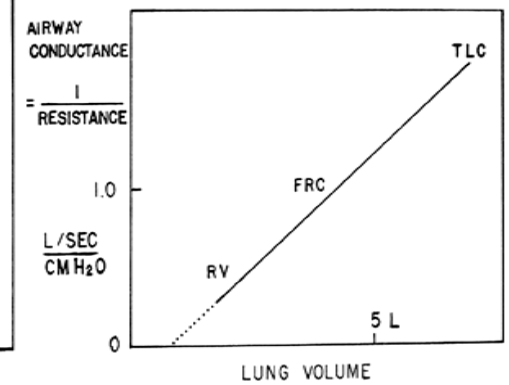
During a forced expiration when intra & extraluminal pressures are equal a decrease in tube size limits expiratory flow.

<u>Volume-Related</u> Airway Collapse

Parenchymatous air sacs and airways are attached. Air sac volume has a large impact on airway conducting airway volume. Resistance increases at low volume.

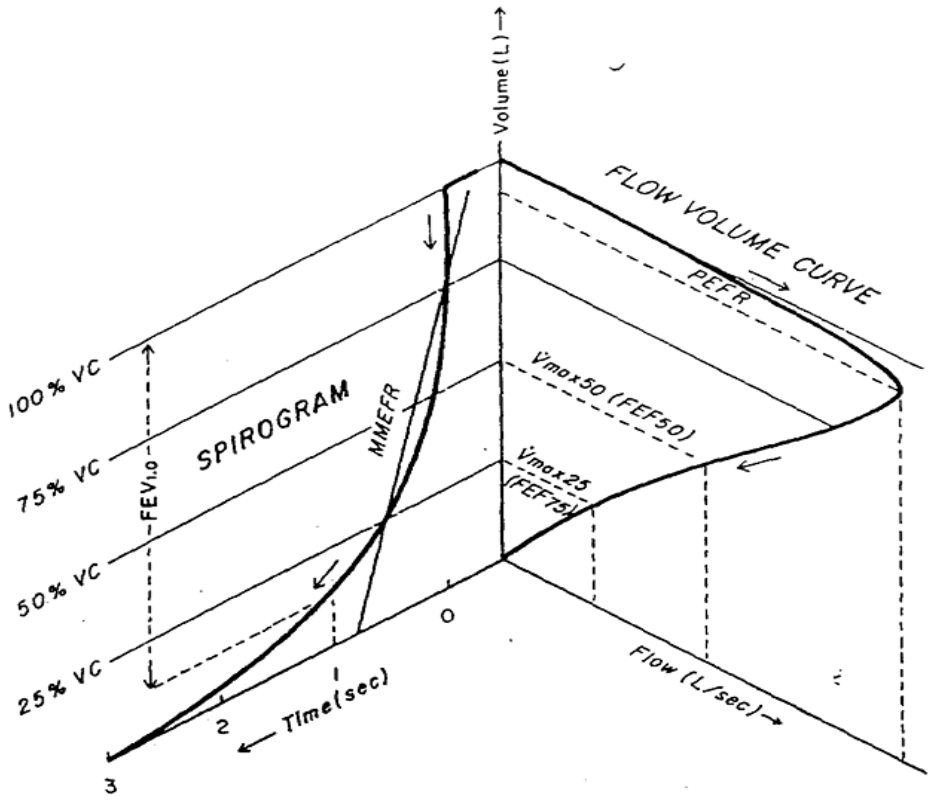


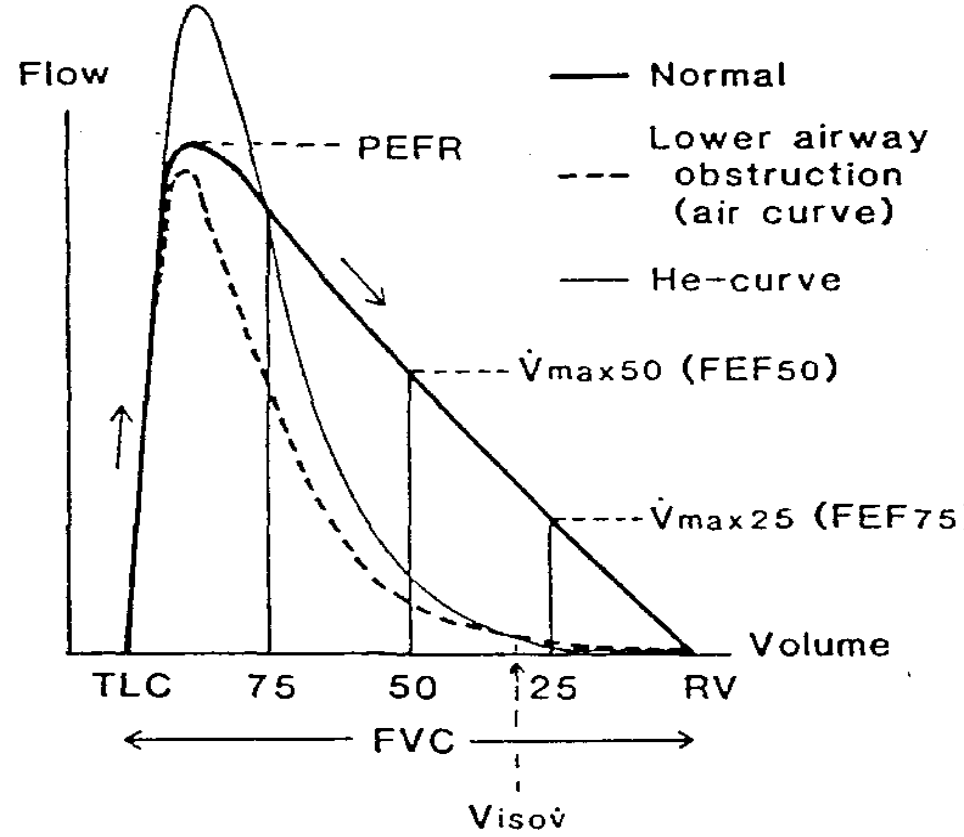




Murray JF In The Normal Lung 2nd Edition WB Saunders 1986;
DuBois AB In Fenn WO, Rahn H eds. Handbook of Physiology, 1984

Flow at given Airway Volume / Size



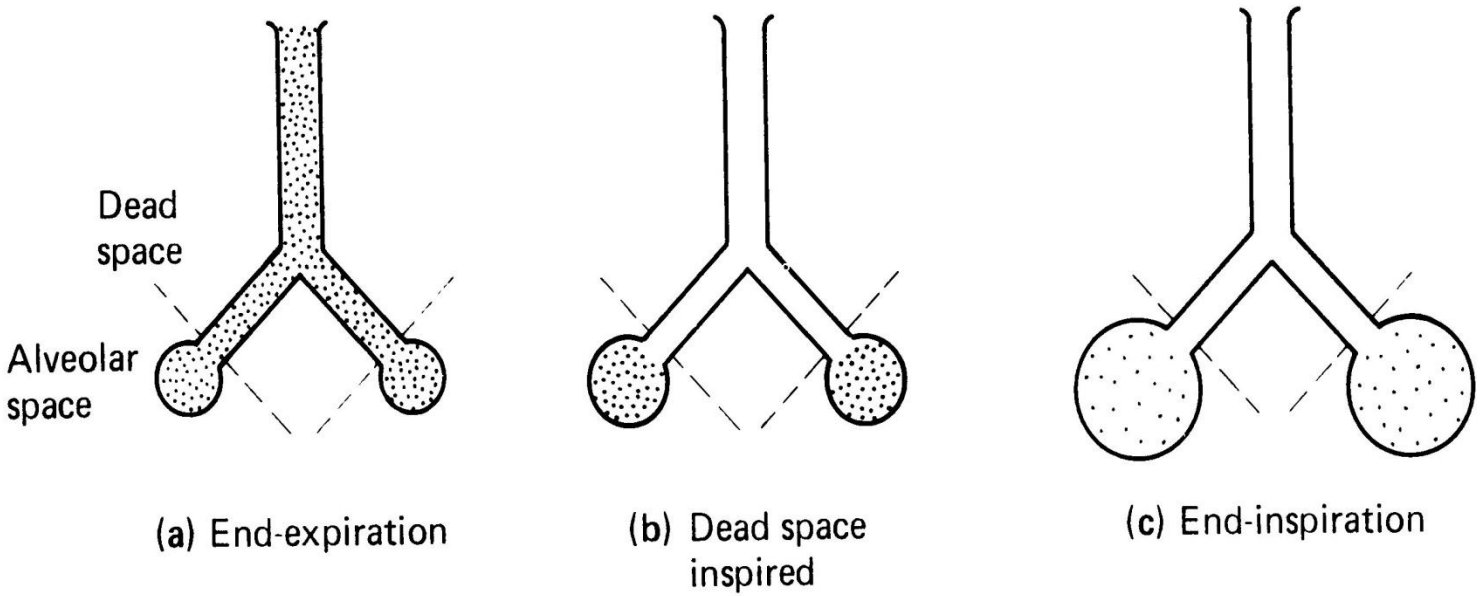


Dynamic Mechanics: Resistance: Bronchomotor Tone ; Secretions; Transairway wall tension

Unit of Flow-Volume = time

Motoyama EK In Basic Principles in Pediatric Anesthesia Chap 2

Relative Hysteresis



Conducting Airway (CA) Dead Space

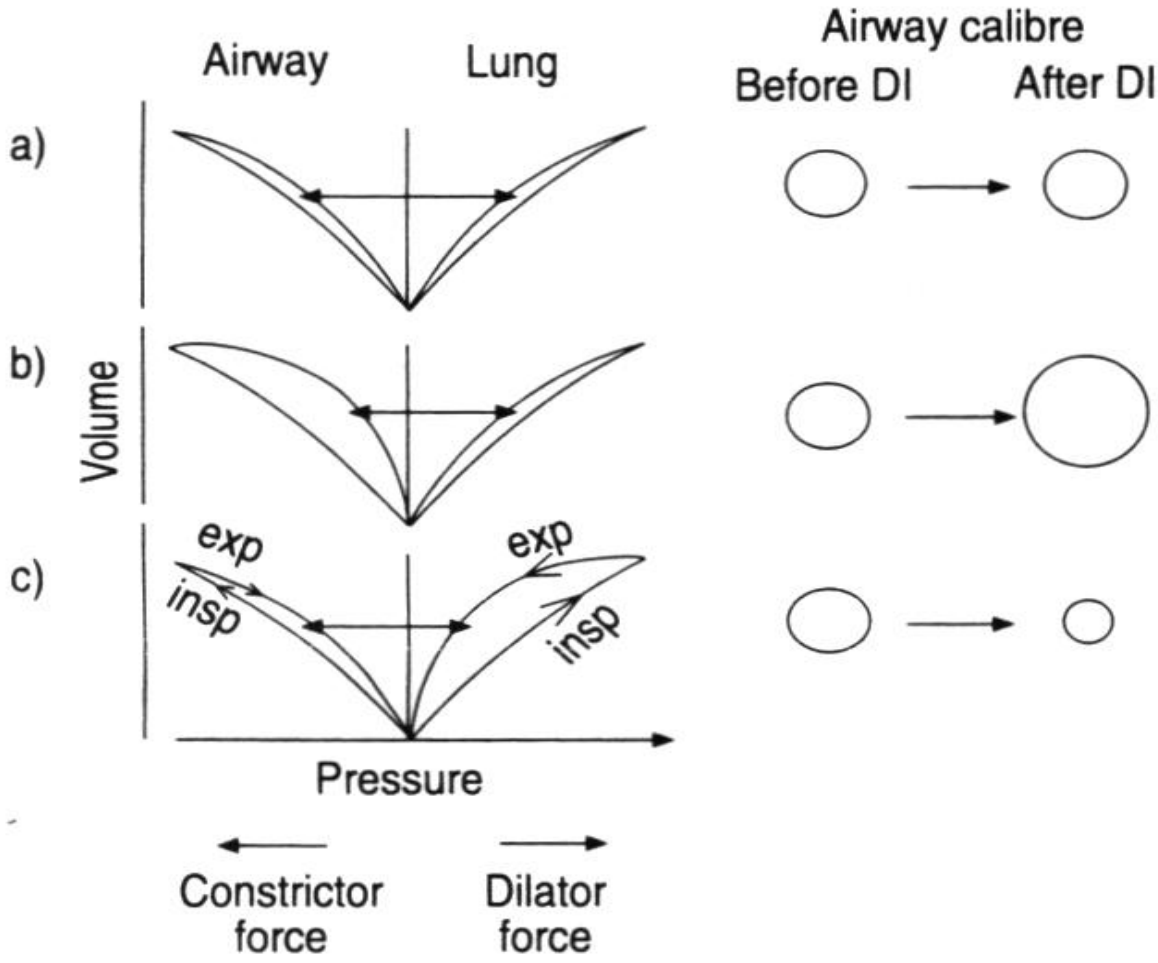
Parenchymal Air Sacs (PA) Majority of FRC

Expiratory Flow = Driving Pressure (Pst_L) / Resistance

At a set point in expiration if CA is relatively more open (↑DS) than the PA ("FRC") then expiratory flow improves.
A deep inspiration in some asthmatics results in this.

In: Respiratory Physiology 2nd Ed. J Widdicombe & A Davies Edward Arnold 1991.

Relative Hysteresis: Bronchomotor Tone and Parenchymal Surface Tension



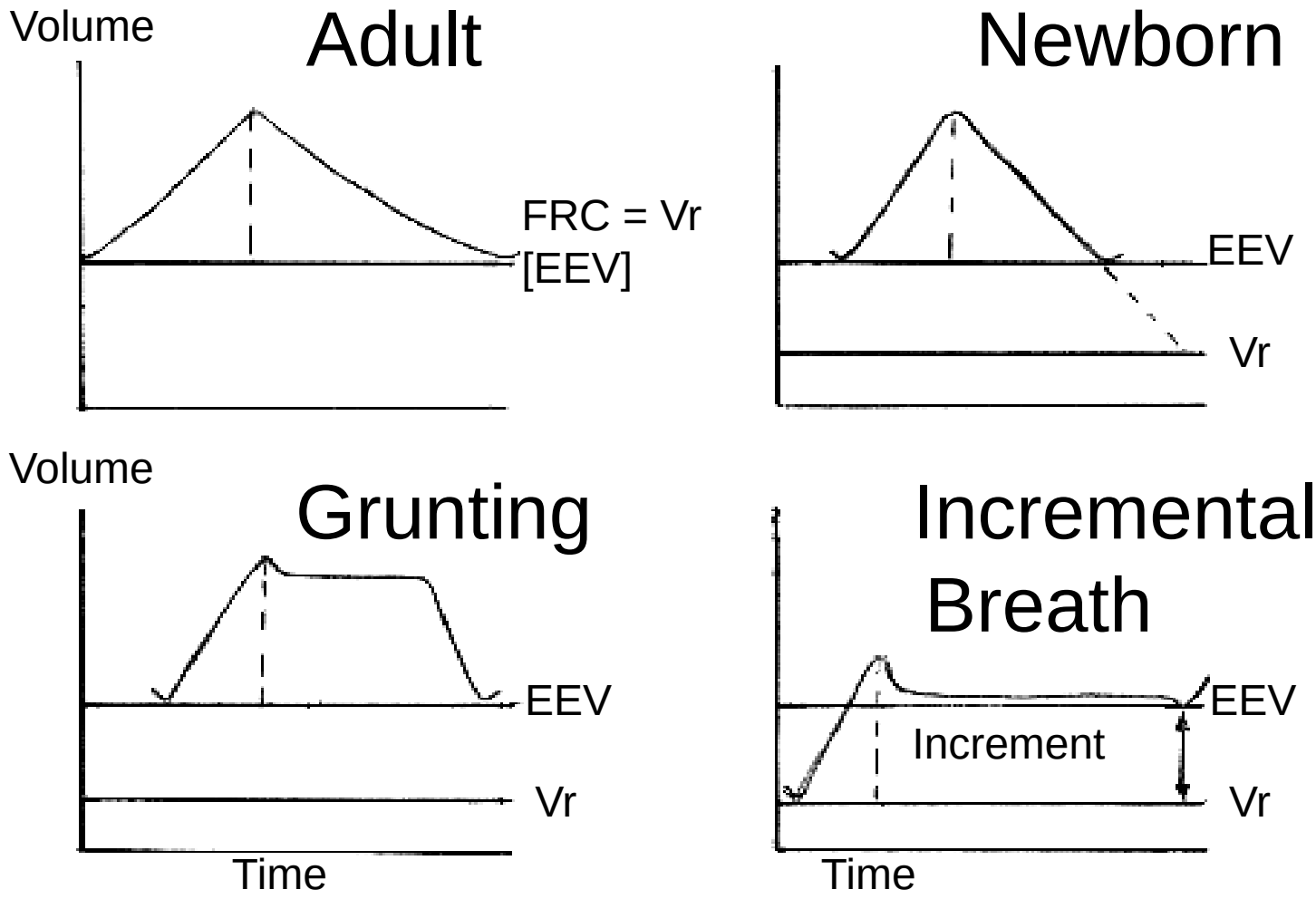
Equal Hysteresis
Equal Recoils
No Change in Vmax

CA > PA Hysteresis
PA > CA Recoil
Vmax improves
Milder Asthma

CA < PA hysteresis
PA < CA Recoil
Vmax decreases
“Inflammatory” Asthma

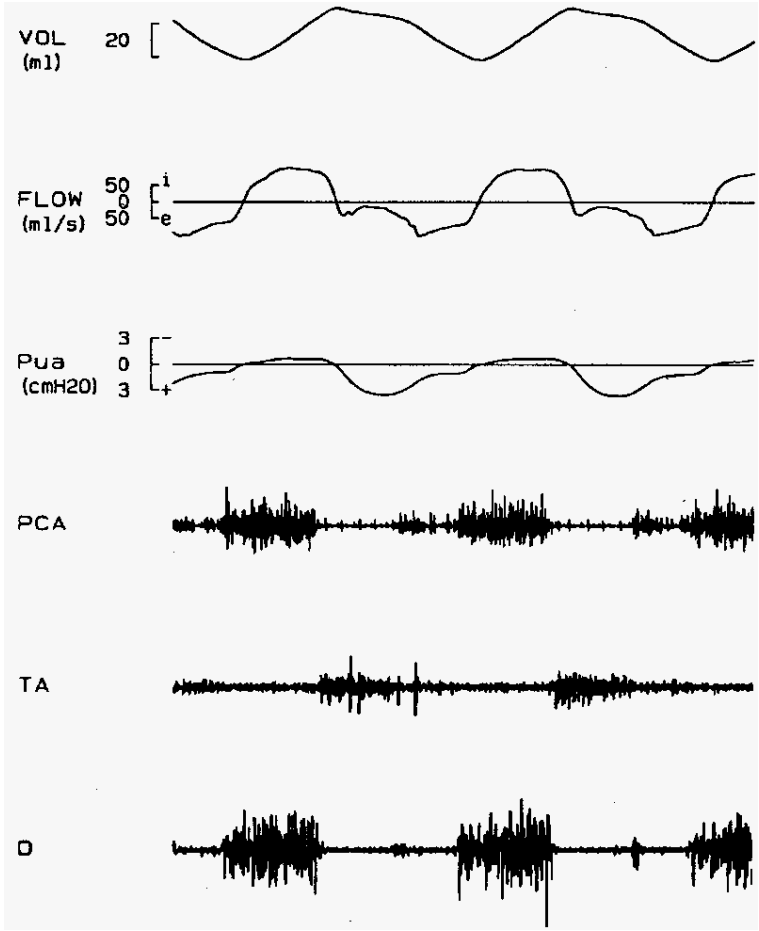
Pellegrino R et Al. Eur Respir J 1998; 12:1219-1227

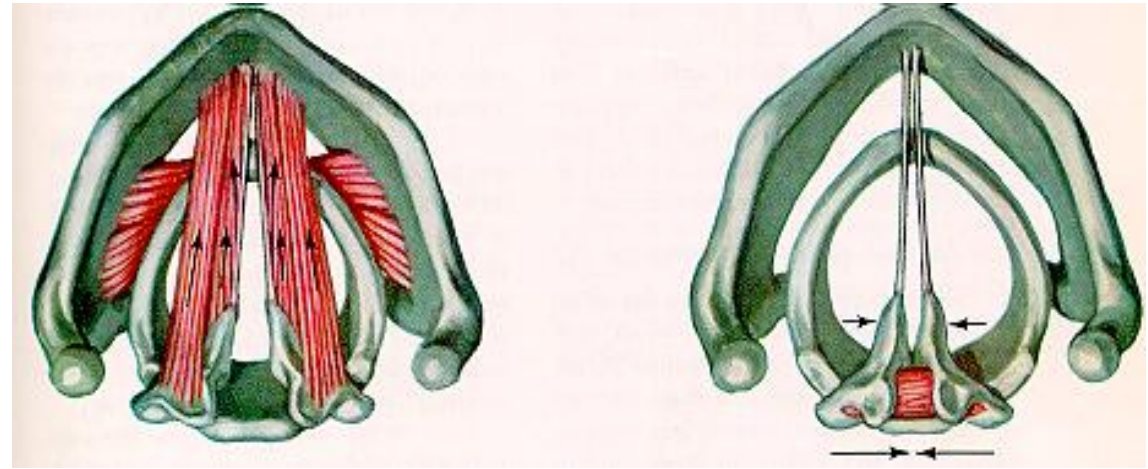
How is airway volume actively maintained?



Hutchison AA, Bignall S Arch Dis Child (in press)

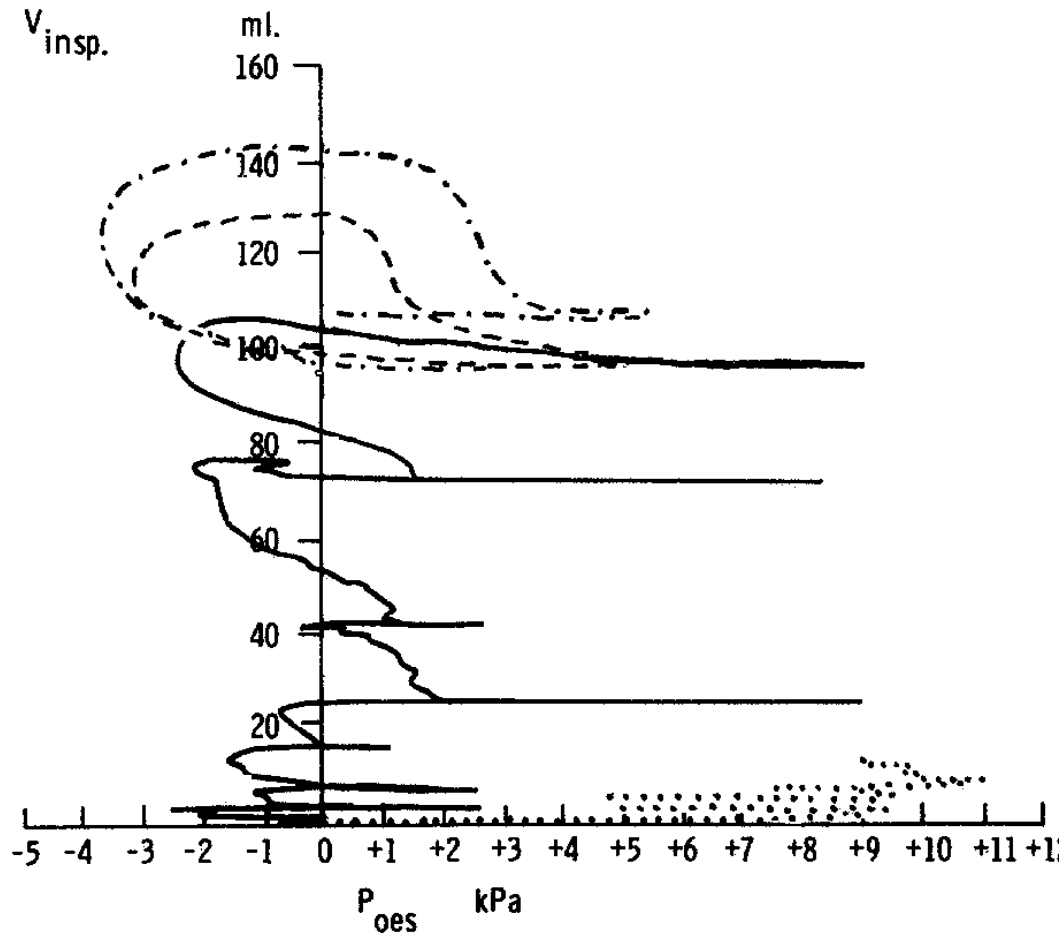
Laryngeal Closure: Thyroarytenoid





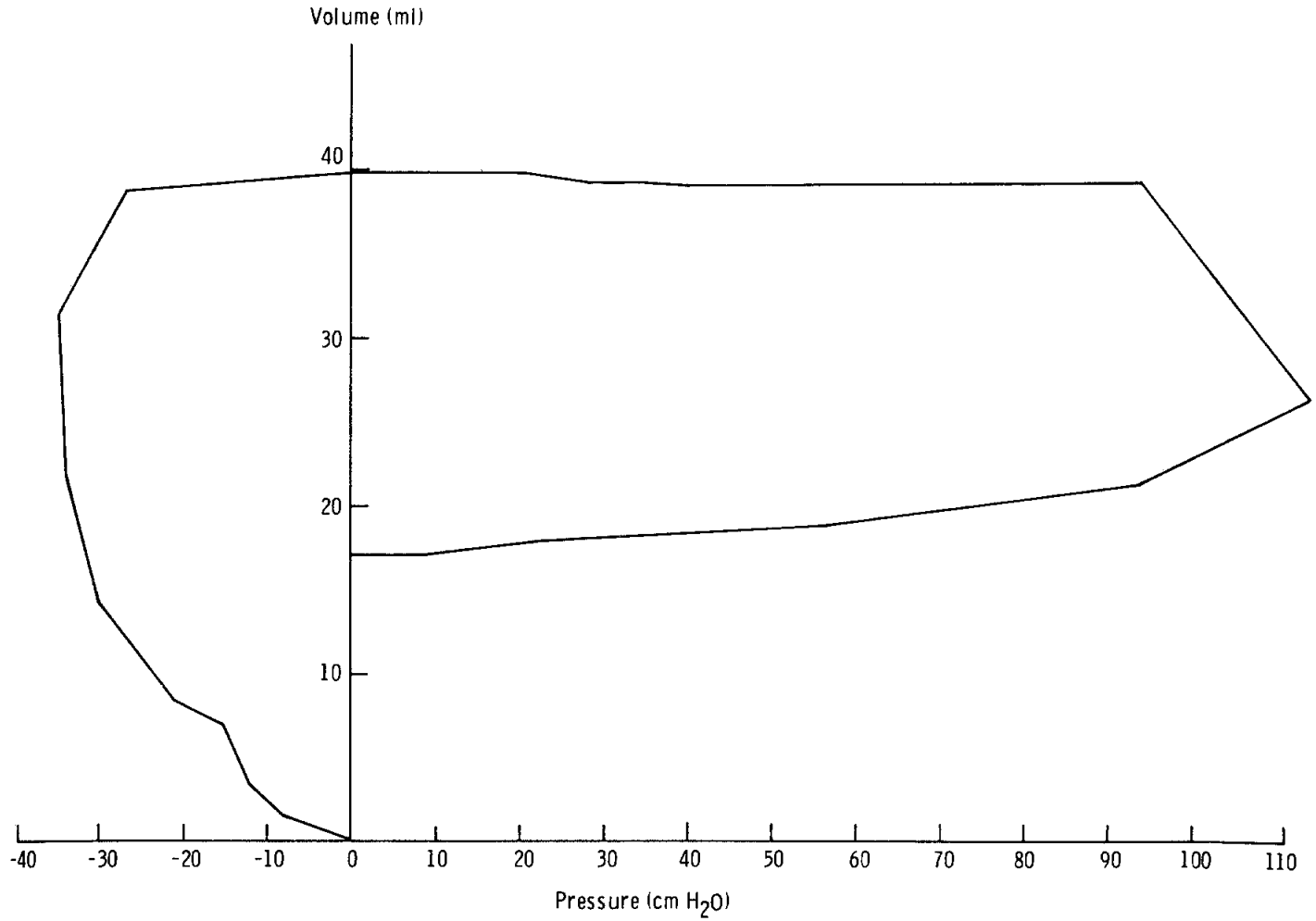
Hutchison AA et al. J Appl Physiol 1993; 75:121-131.
Saunders, WH Clin Symp 1964; 67-99

Birth - EEV Increment



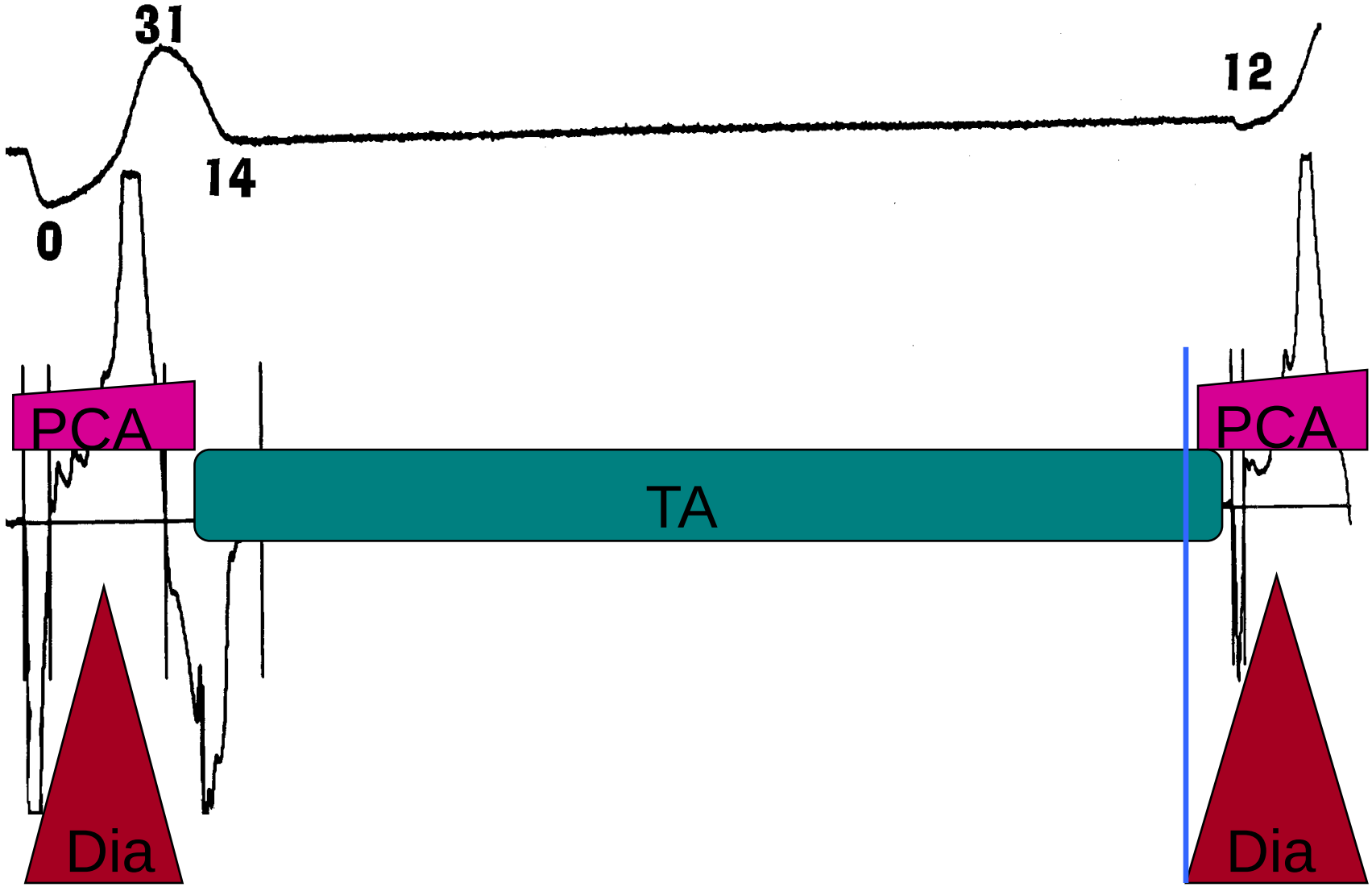
Saunders RA, Milner AD J Pediatr 1978; 93:667-673.

Birth - First Breath



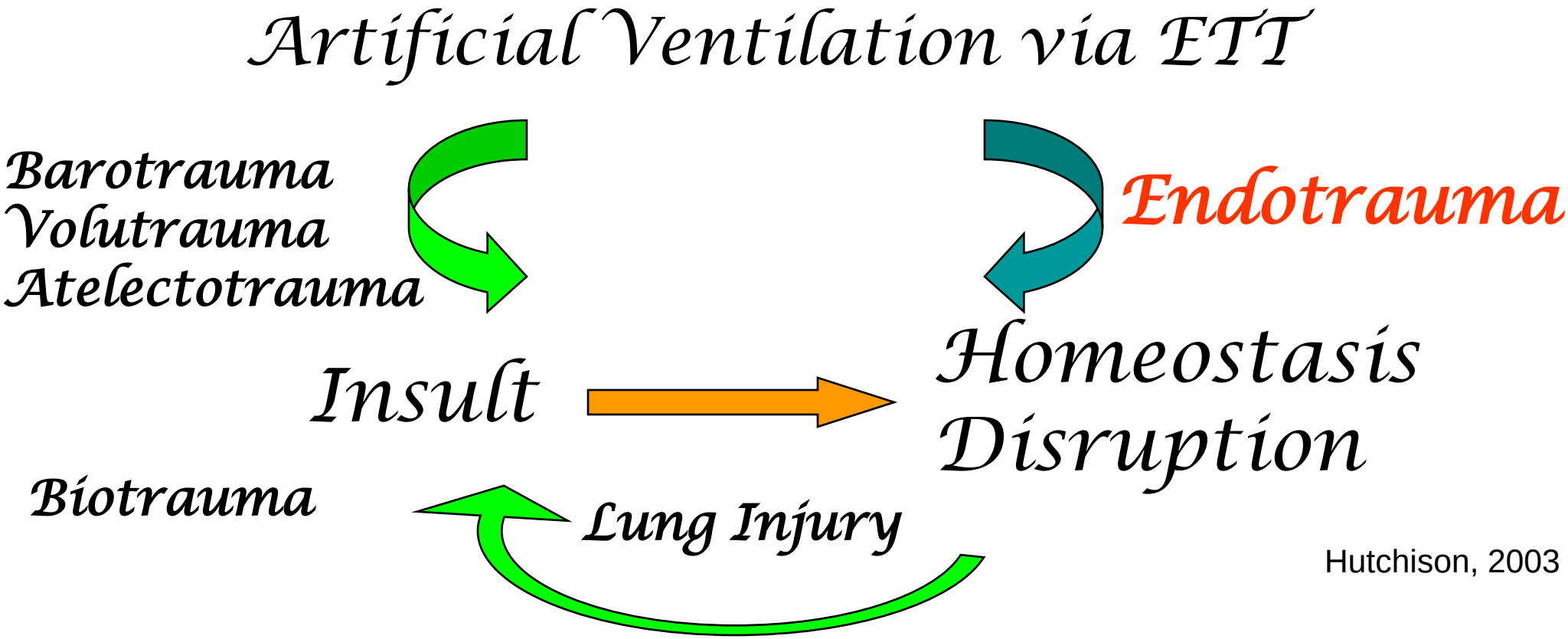
Milner AD, Yvas H J Pediatr 1982; 101:879-886.

Incremental Breath



Modified from Hutchison AA Acta Pediatr Scand 1994; 83:241-248

Ventilator-Induced Lung Disease



Endotrauma: injury resulting from the disruption of homeostasis that occurs during and sometimes after artificial ventilation through an endotracheal tube.

Hutchison AA, Bignall S Arch Dis Child (in press)

Airway Physiology Essentials

Critical Importance of Control of Sub-Glottic Volume

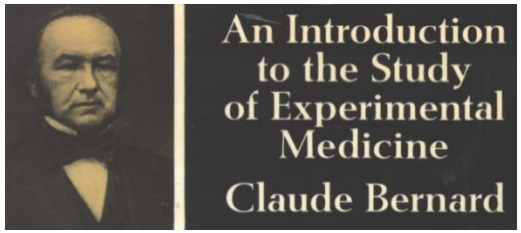
Protection and Maintenance: Humidity / Airway Closure

Preparation of Fetal Life: Lung and Vascular Bed Growth

Airway Volumes: Mechanisms of Norms and Limits

Breathing patterns aim to maintain an optimal sub-glottic volume

Therapy may disrupt airway volume homeostatic mechanisms



Environment – Norms & Limits - Constancy