Airway Physiology
Essentials for Intensivists

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Airway and Physiology

• 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

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: Axilliiary 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 +40ºC → 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
Pharyngeal Patency

Muscle Function
Sleep & ↓ Tone
Obesity

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

Motoyama EK In Basic Principles in Pediatric Anesthesia Chap 2
Naso- and Oropharynx

High Larynx
Breathe & Feed
Baby “Talk”

Lower Larynx
Cross Road
Speech

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!

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

Dive reflex is present in the fetus

Lower Airway: Structure


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

Upper Airway

Irregular
Dichotomous branching
→ even gas distribution

Huge increase in surface area in terminal respiratory units compared to more proximal conducting airways
Lower Airway Optimal Volume

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
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

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.
# Terminal Airway Development: Canalicular & Terminal Sac / Alveolar

<table>
<thead>
<tr>
<th>Stage</th>
<th>Remarks</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar (&gt;36 wks)</td>
<td>32wks 1700g 40wks 3500g</td>
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</tbody>
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- 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
Fetal Airway: Liquid Secretion & Absorption

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

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?

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.

What are Normal Airway Volumes?

Upper Limit

Normal

Lower Limit

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.

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

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.

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

Flow-Related Airway Collapse

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

Volume-Related 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.

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

Expiratory Flow = Driving Pressure ($P_{st_L}$) / 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.

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

How is airway volume actively maintained?

Hutchison AA, Bignall S Arch Dis Child (in press)
Laryngeal Closure: Thyroarytenoid

Saunders, WH Clin Symp 1964; 67-99
Birth - EEV Increment

Birth - First Breath

Incremental Breath

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)
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