Objective Assessment of Lung Disease

Pharmacotherapy II, January 2020

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Objectives

- **Understand the physiology of abnormal ventilation and gas exchange**
- **Be able to recognize abnormalities in ventilation, oxygenation, and acid-base balance from the Arterial Blood Gases report**
- **Be able to utilize the results of the following Pulmonary Function Tests for assessing and monitoring patients with asthma, COPD, or pulmonary fibrosis: lung volumes, FEV_1, FVC, FEV_1/FVC, PEF, DL_{CO}, bronchodilator reversibility, bronchoprovocation, 6-min walk**

Clinical Uses of Blood Gases

- Most Common:
  - Ventilation and gas exchange
  - Acid-base status

- Less Common:
  - Superior vena caval O_2 saturation
  - Oxygen delivery
  - Oxygen consumption/metabolic rate

Abbreviations

P = partial pressure of gas

C = concentration or content

S = HGB %saturation

a = arterial

A = alveolar

I = inspired air

v = venous

c = capillary

$\bar{v}$ = mixed venous

$\mathring{V}$ = flow or ventilation rate

$\mathring{V}/Q$ = ventilation/perfusion

Normal Arterial Blood Values

- ***Measured***

  pH 7.36-7.44

  PaO_2 >80 mmHg

  $PaCO_2$ 34-46 mmHg

- ***Computed***

  HCO_3 22-26 mmol/L (or mEq/L)

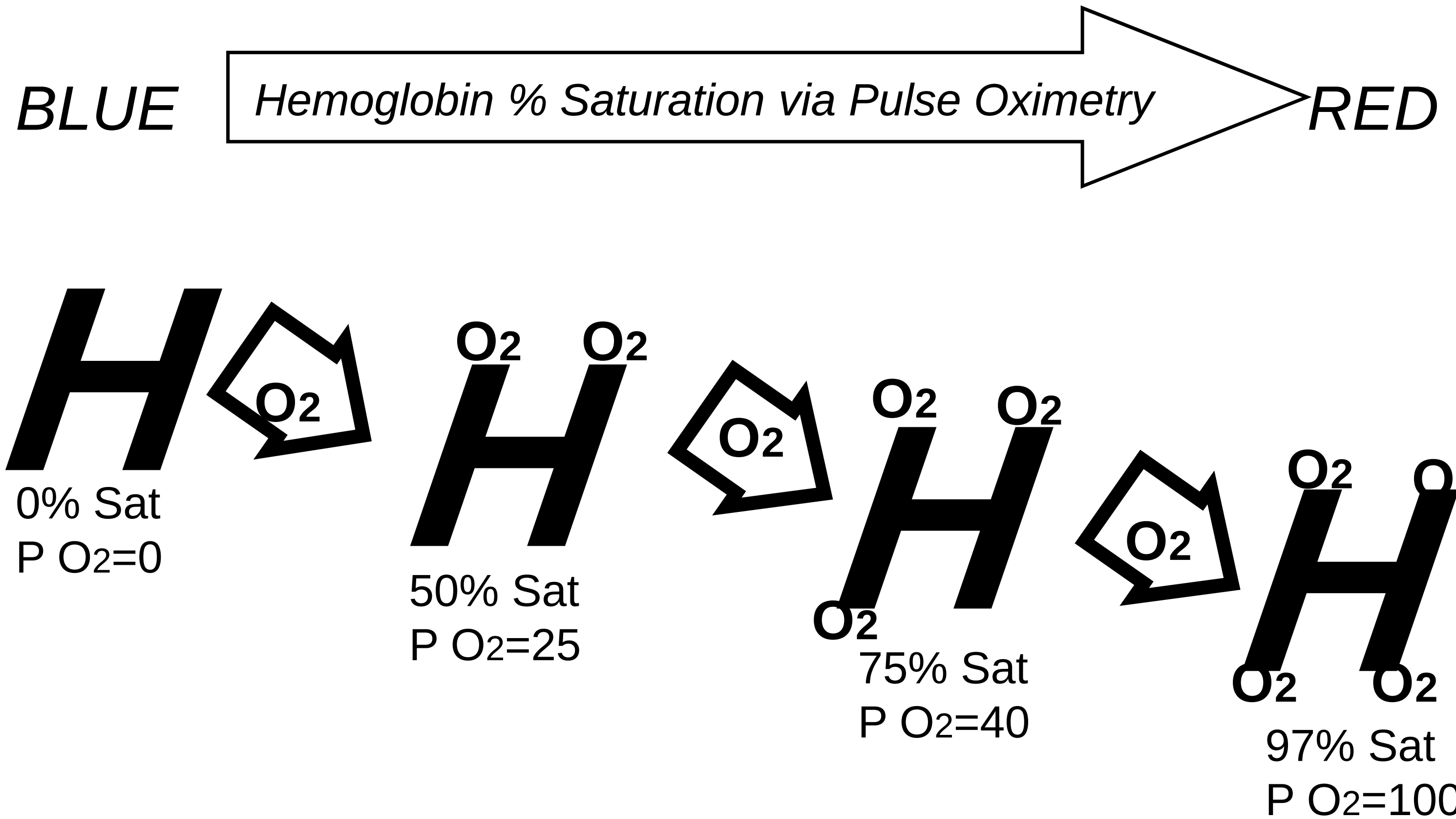
  Base Excess -2.5 to +2.5 mmol/L (or mEq/L)

  SaO_2 >94% (may also be measured directly)

Noninvasive Alternatives

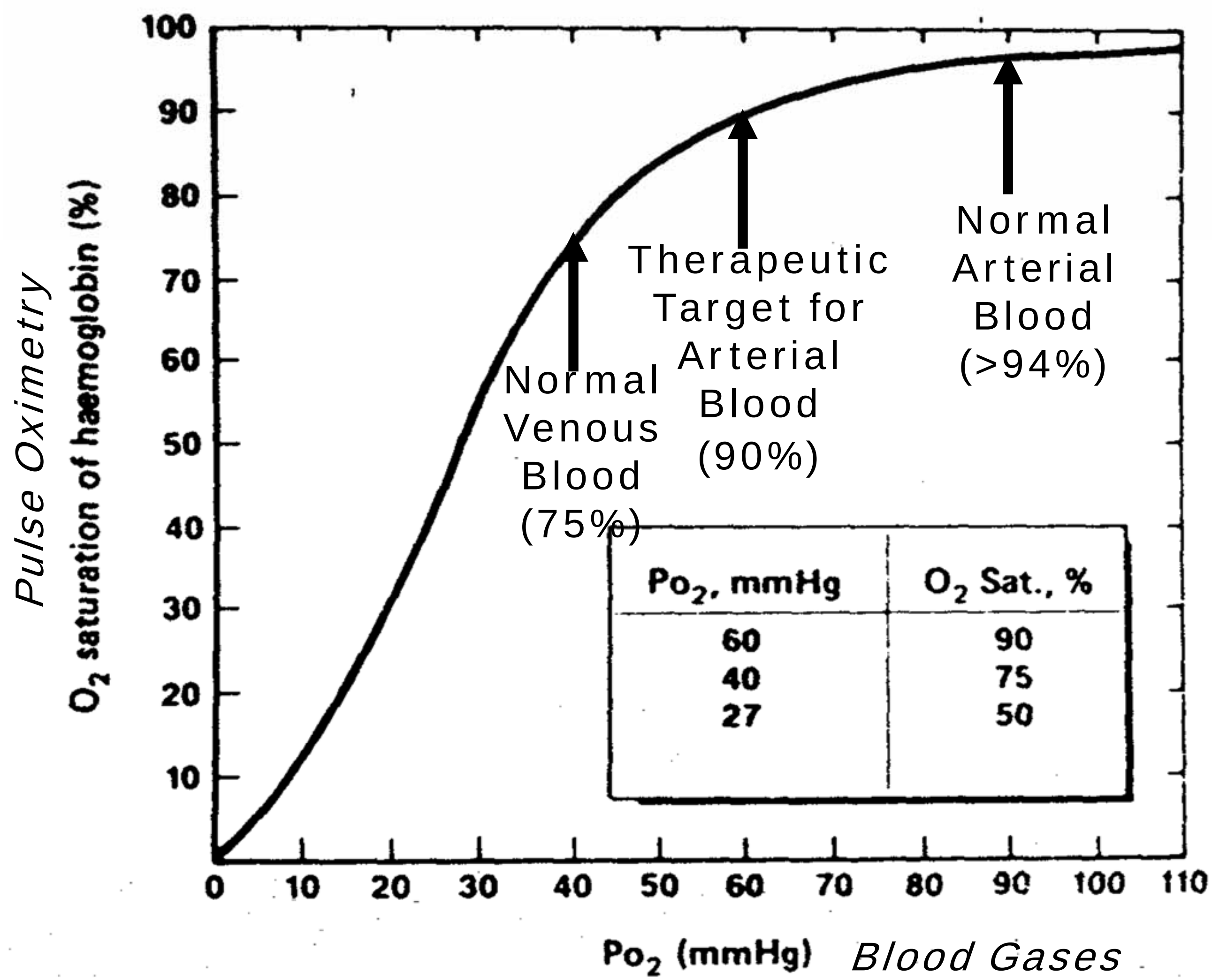
- ***Pulse Oximetry (SpO_2)***- estimate of SaO_2 using spectrophotometric measure at nail bed

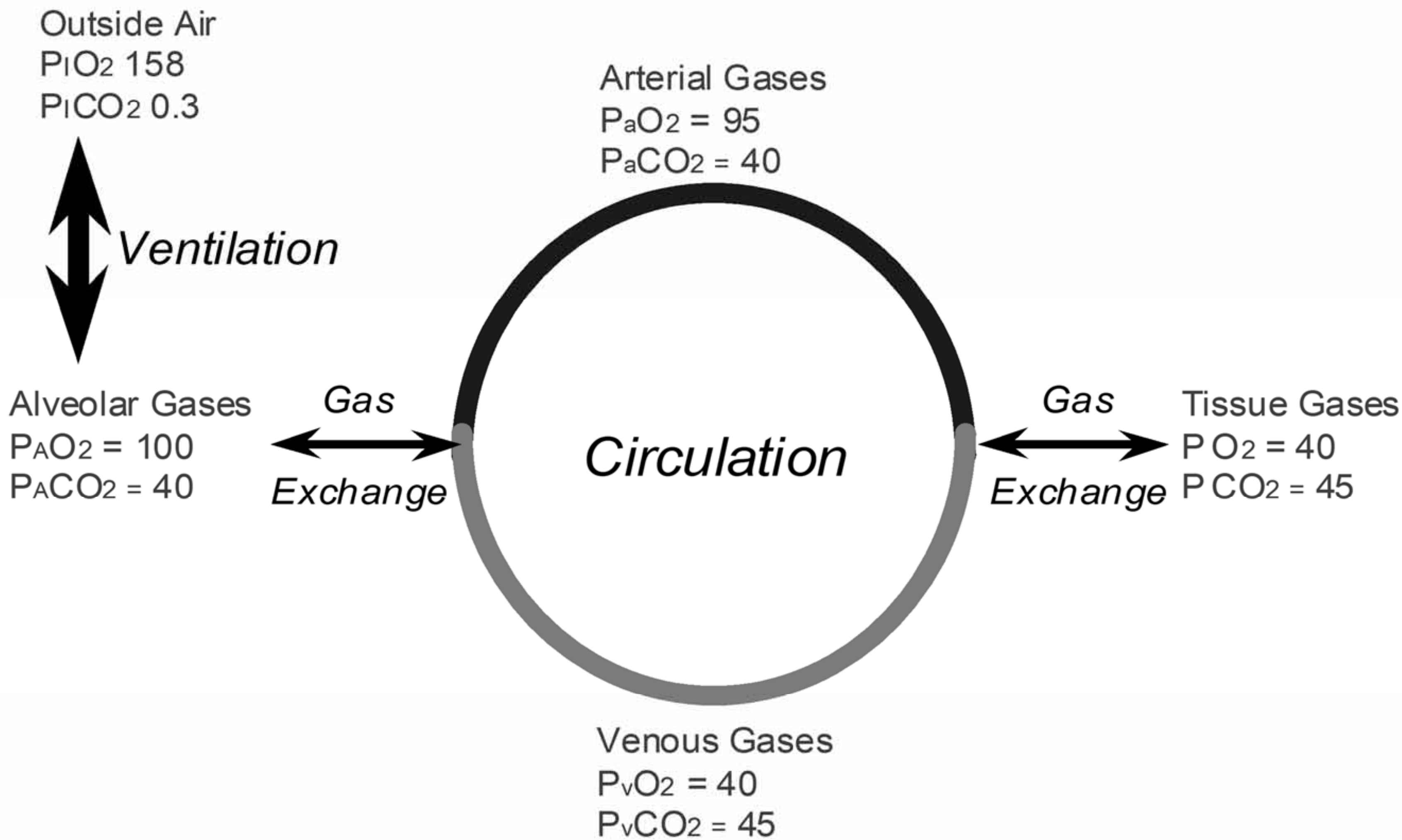
- **Others not used commonly:**
  - ***Transcutaneous electrodes***- most useful in thin-skinned neonates
  - ***Expired gases***- end-tidal gas concentrations reflect alveolar gases



BLUE
Hemoglobin % Saturation via Pulse Oximetry
RED
H
O2
0% Sat
P O2=0
O2 O2
H
O2
50% Sat
P O2=25
O2 O2
H
O2
O2
75% Sat
P O2=40
O2 O2
H
O2 O2
97% Sat
P O2=100

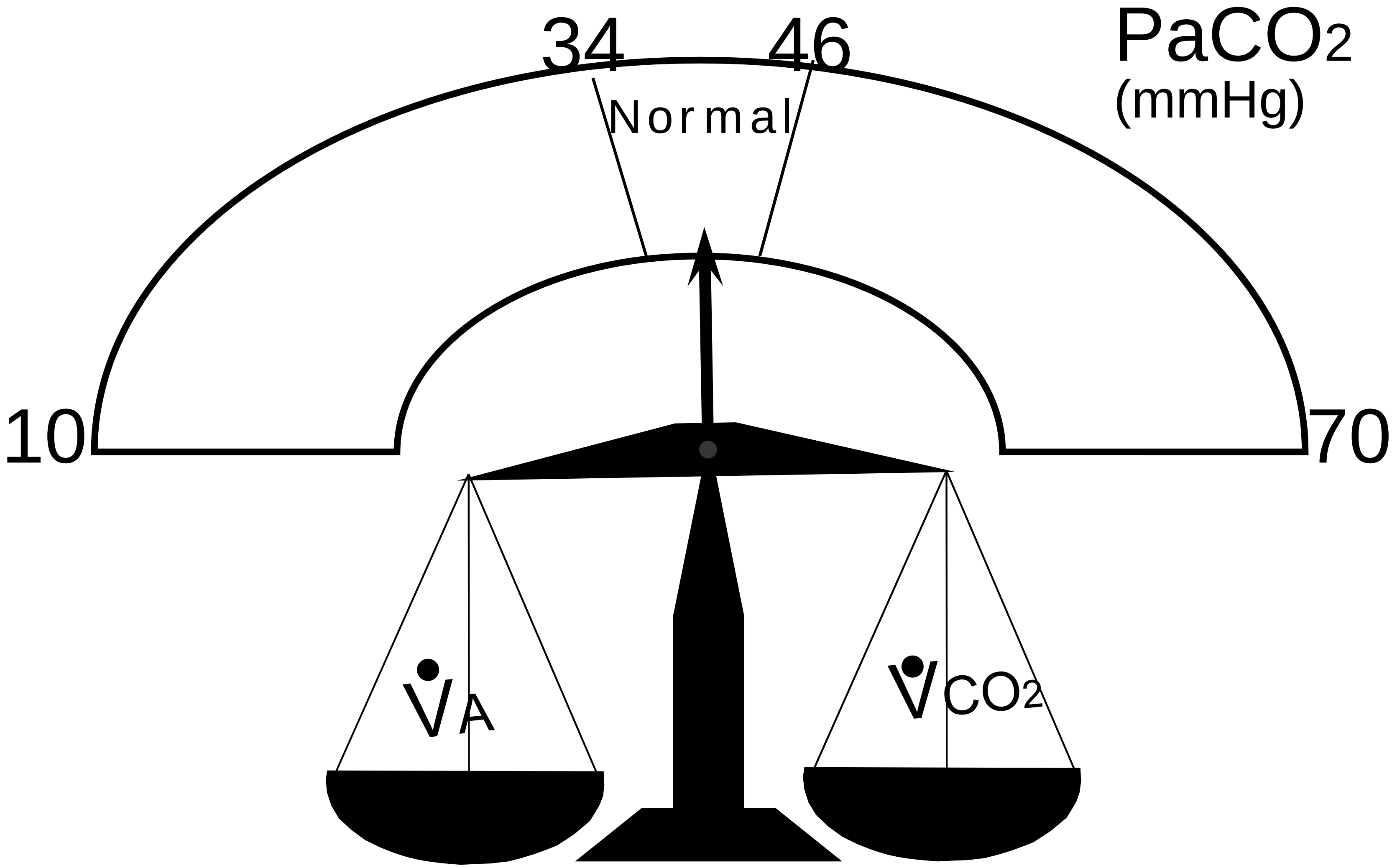
HGB Saturation vs PaO_2

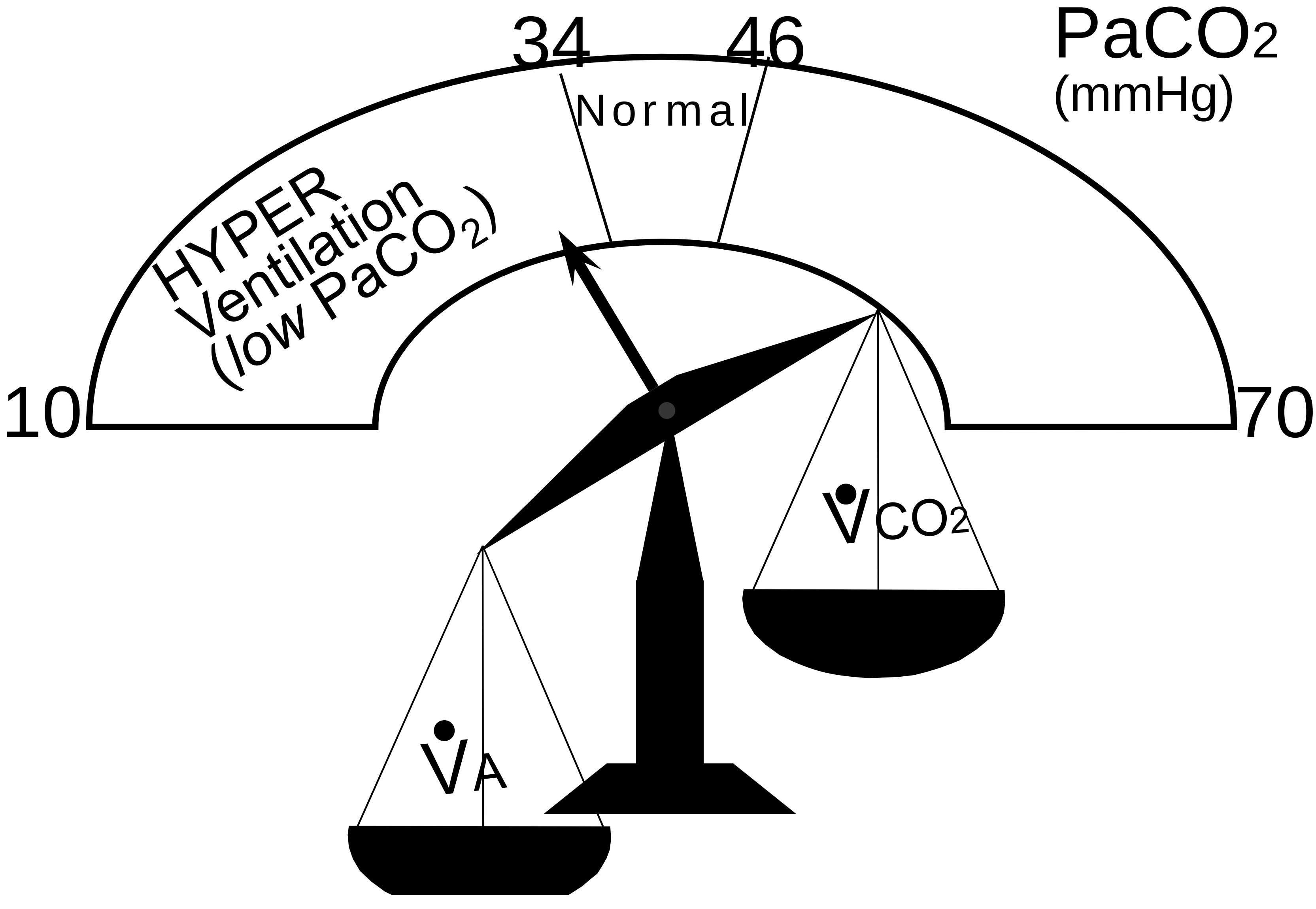


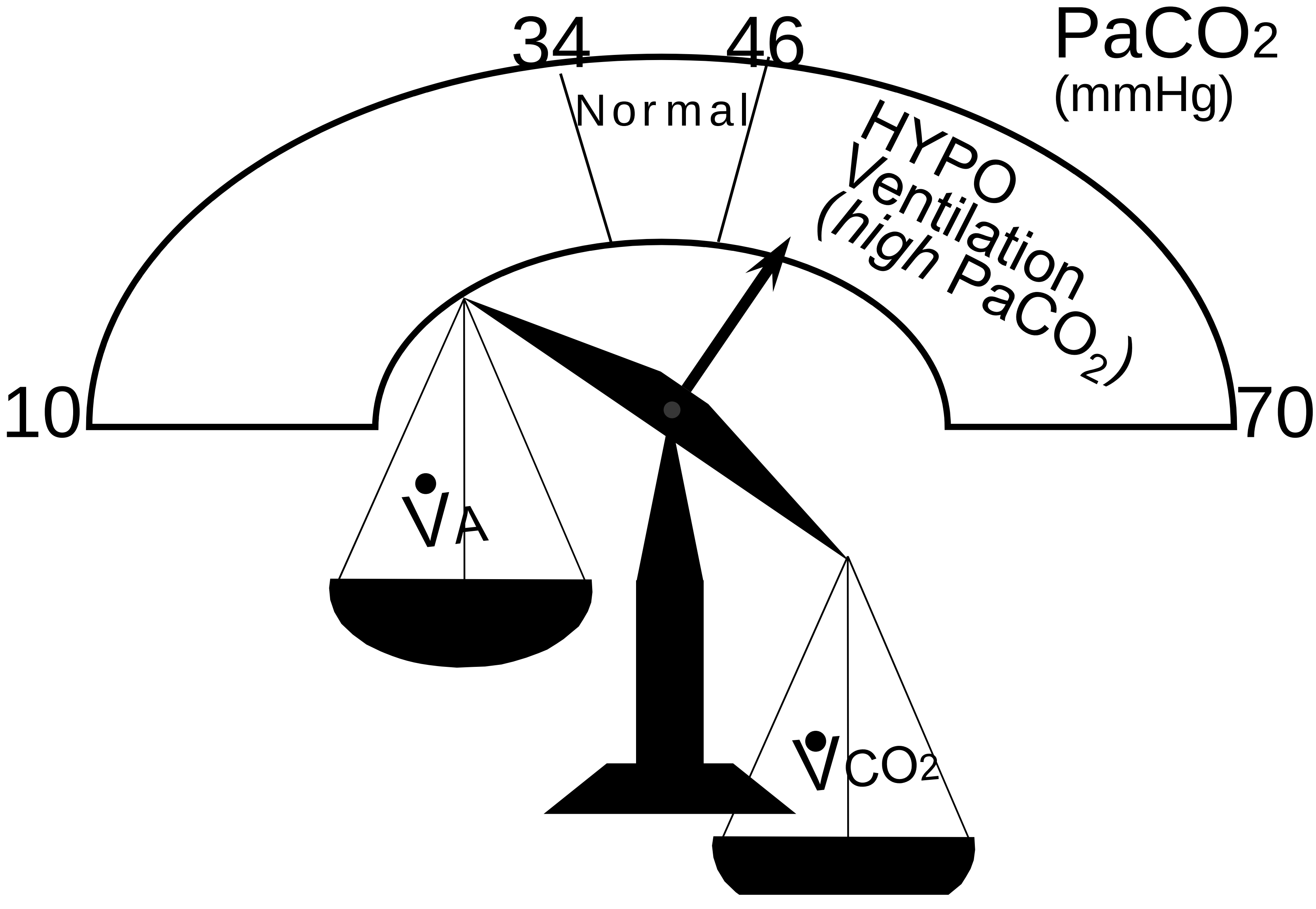

Outside Air
P_IO_2 158
P_ICO_2 0.3
Ventilation
Arterial Gases
$P_aO_2 = 95$
$P_aCO_2 = 40$
Alveolar Gases
$P_AO_2 = 100$
$P_ACO_2 = 40$
Gas
Exchange
Circulation
Gas
Exchange
Tissue Gases
$PO_2 = 40$
$PCO_2 = 45$
Venous Gases
$P_vO_2 = 40$
$P_vCO_2 = 45$

Ventilation

$PaCO_2$ on the Arterial Blood Gases report is an indicator of *Hyper*ventilation or *Hypo*ventilation


34
46
PaCO2
(mmHg)
Normal
10
70
V̇A
V̇CO2


34
46
PaCO2
(mmHg)
Normal
HYPER
Ventilation
(low PaCO2)
10
70
V̇CO2
V̇A

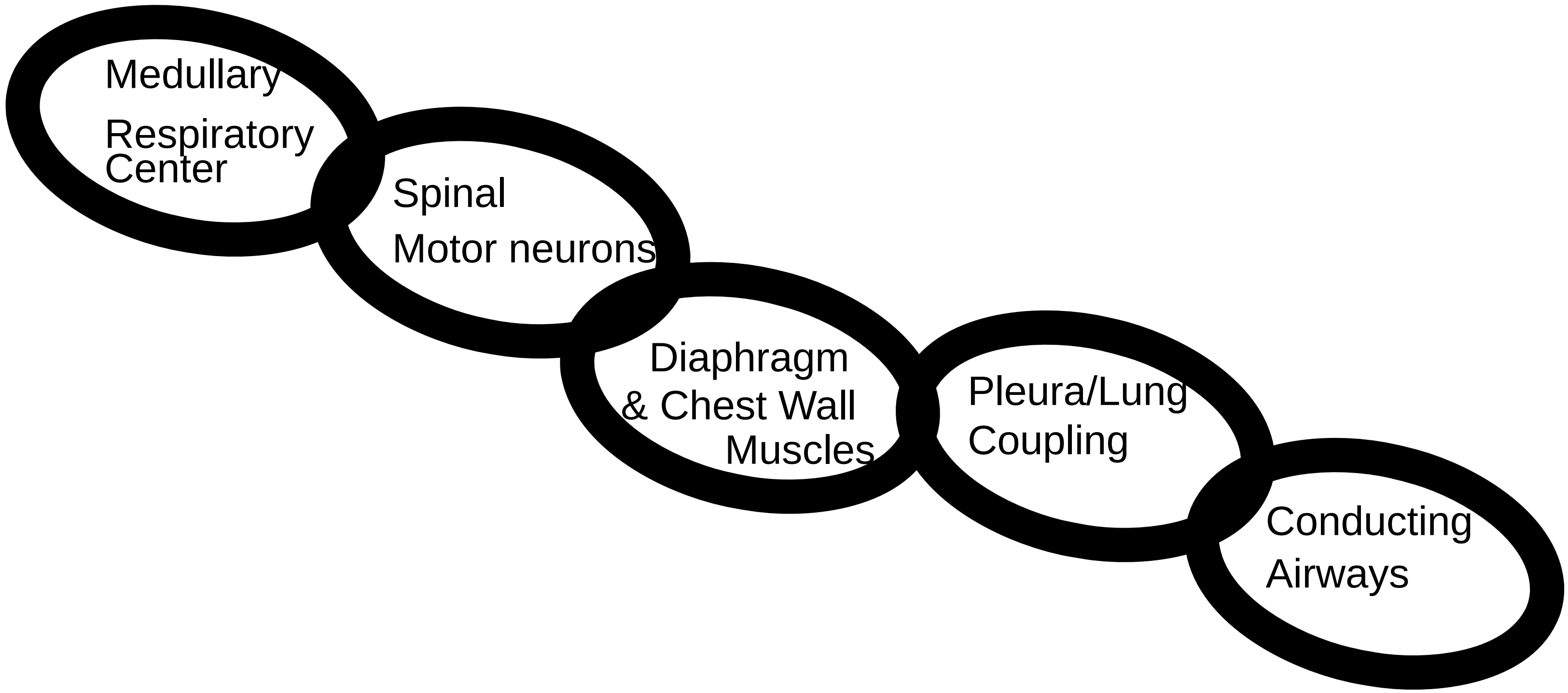


34
46
PaCO2
(mmHg)
Normal
HYPO
Ventilation
(high $PaCO_2$)
10
70
$\dot{V}_A$
$\dot{V}CO_2$

Ventilation

- Normally matched with CO_2 production
- *Mismatch* of ventilation and CO_2 production results in hyperventilation or hypoventilation
- $PaCO_2$ changes *quickly* during mismatch
- *Hyper*ventilation results when there is an abnormal stimulus to breathe, e.g. acidemia, hypoxia, salicylate toxicity, head injury, panic attack, pregnancy
- *Hypo*ventilation results when the patient cannot ventilate sufficiently to keep up with CO_2 production - when severe this becomes *Ventilatory Failure*

Ventilation Chain



Ventilatory Failure

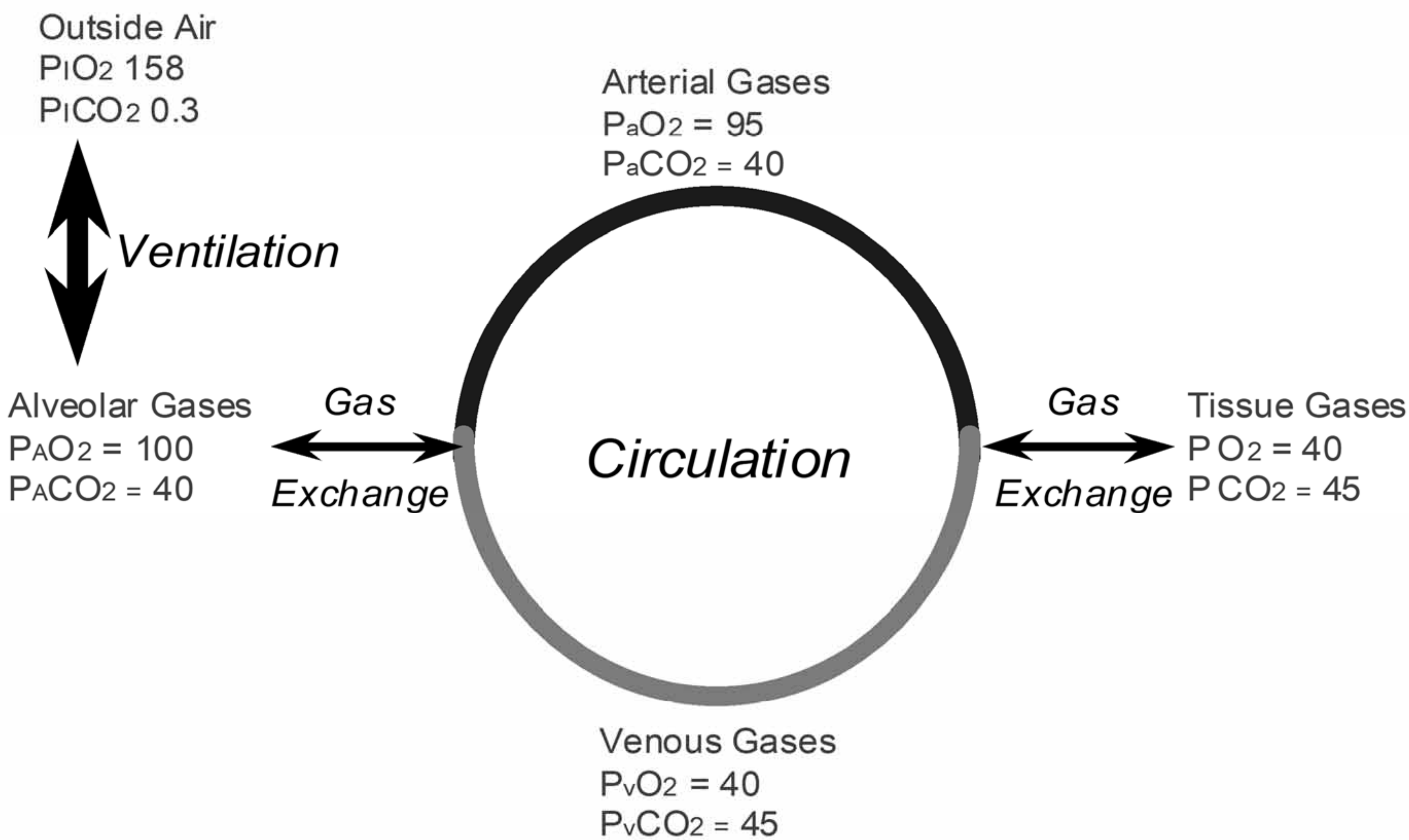
Medullary Respiratory Center
- Head injury
- Drug O.D.

Spinal Motor neurons
- Spinal injury
- Degenerative nerve disease

Diaphragm & Chest Wall Muscles
- Paralyzing drugs
- Muscle fatigue/weakness
- Muscular dystrophy

Pleura/Lung Coupling
- Pneumothorax
- Pleural effusion
- Bronchopleural fistula

Conducting Airways
- Severe airway obstruction
- Foreign object
- Tracheal stenosis


Outside Air
PIO2 158
PICO2 0.3
Ventilation
Arterial Gases
PaO2 = 95
PaCO2 = 40
Alveolar Gases
PAO2 = 100
PACO2 = 40
Gas
Exchange
Circulation
Gas
Exchange
Tissue Gases
P O2 = 40
P CO2 = 45
Venous Gases
PvO2 = 40
PvCO2 = 45

Causes of Hypoxia (low PaO_2)

Low alveolar P_AO_2

- **Hypoventilation (↓ in PaO_2 ≈ ↑ in $PaCO_2$)**
- **Low inspired air P_IO_2 (high altitude; poor air supply)**
- **Responds well to oxygen Rx**

Ventilation/Perfusion mismatch

- **most common cause of hypoxia in lung diseases**
- **Responds well to oxygen Rx**

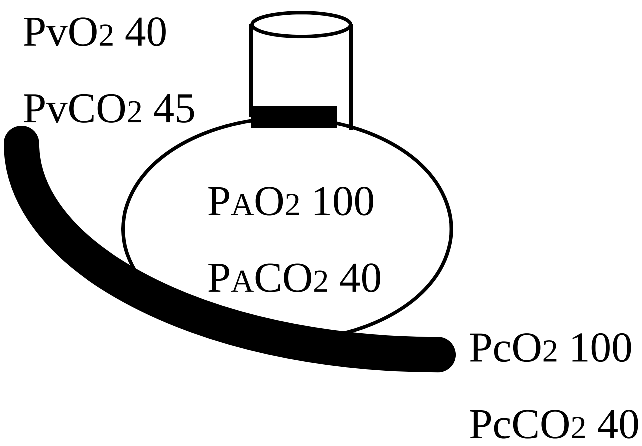
Decreased rate of gas diffusion

- **hypoxia worse during exertion than at rest**
- **Responds to oxygen Rx**

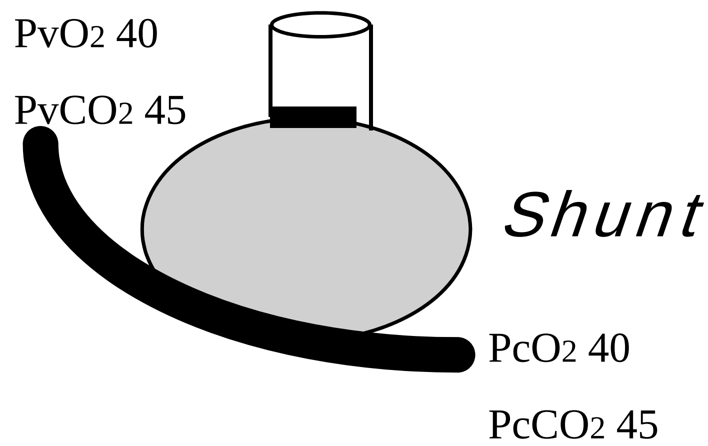
Venous- Arterial shunt

- **Anatomic (septal defect; patent ductus arteriosus; patent foramen ovale- PFO)**
- **Physiologic (collapsed or fluid-filled alveoli)**
- **Does *not* respond to oxygen Rx**

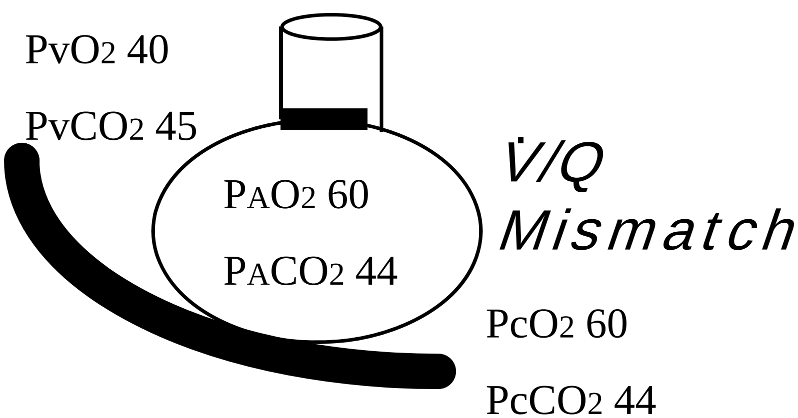
Normal



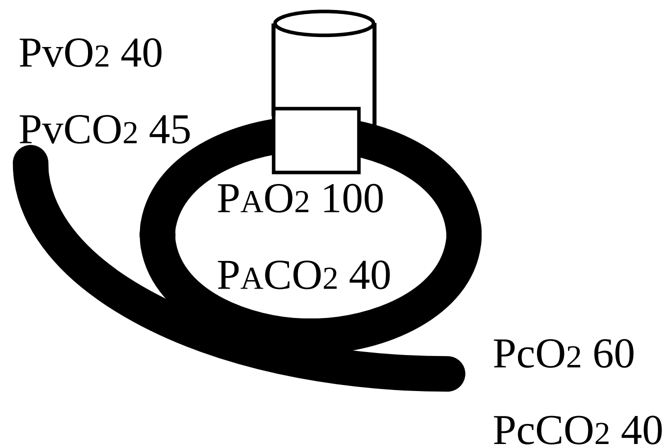
No Ventilation



Poor Ventilation



Slow Diffusion



Oxygen Supplement

Nasal Cannula

Mask

BMJ 1998;317:798

Acid-Base Assessment using the CO_2/HCO_3^- Buffer System

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

$$pH = 6.1 + \log \left([HCO_3^-] / [CO_2 + H_2CO_3] \right)$$

- **CO_2 : the conjugate *acid*; regulated by ventilation; called the "respiratory component"**
- **HCO_3^- : the conjugate *base*; regulated by kidneys; called the "metabolic component"**
- **Base Excess: mEq/L titration of blood with acid (+) or base (-) to pH 7.40 ; a more precise & quantitative measure of the *metabolic* component**

Acid-Base Imbalance

Metabolic Acidosis

- **BE and HCO_3^- less than normal**

Metabolic Alkalosis

- **BE and HCO_3^- above normal**

Respiratory Acidosis

- **$PaCO_2$ above normal (hypoventilation)**

Respiratory Alkalosis

- **$PaCO_2$ less than normal (hyperventilation)**

Clinical Assessment of Arterial Blood Gases

Step 1: evaluate ***Ventilation (also the Respiratory Component of acid-base status)***, using $PaCO_2$

Step 2: evaluate ***Oxygenation***, using PaO_2
(note if oxygen supplement is being used)

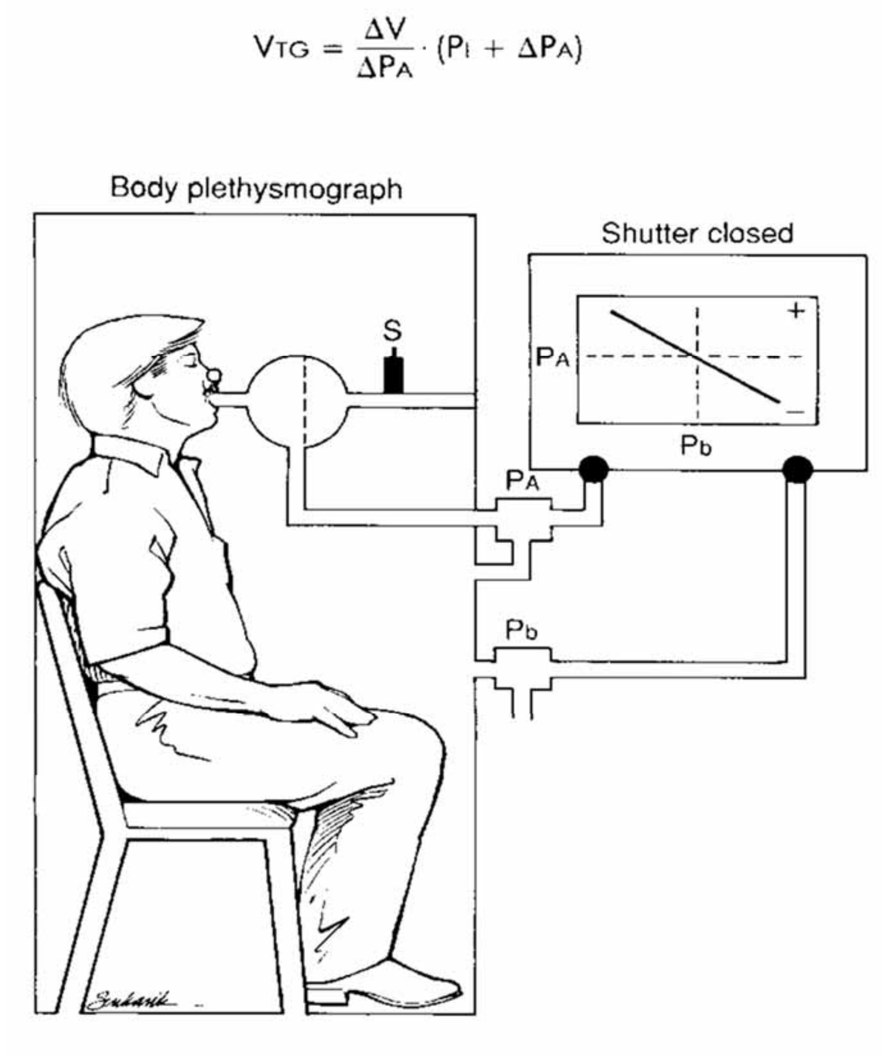
Step 3: evaluate ***pH***

Step 4: evaluate the ***Metabolic Component*** of acid-base status (BE, HCO_3)

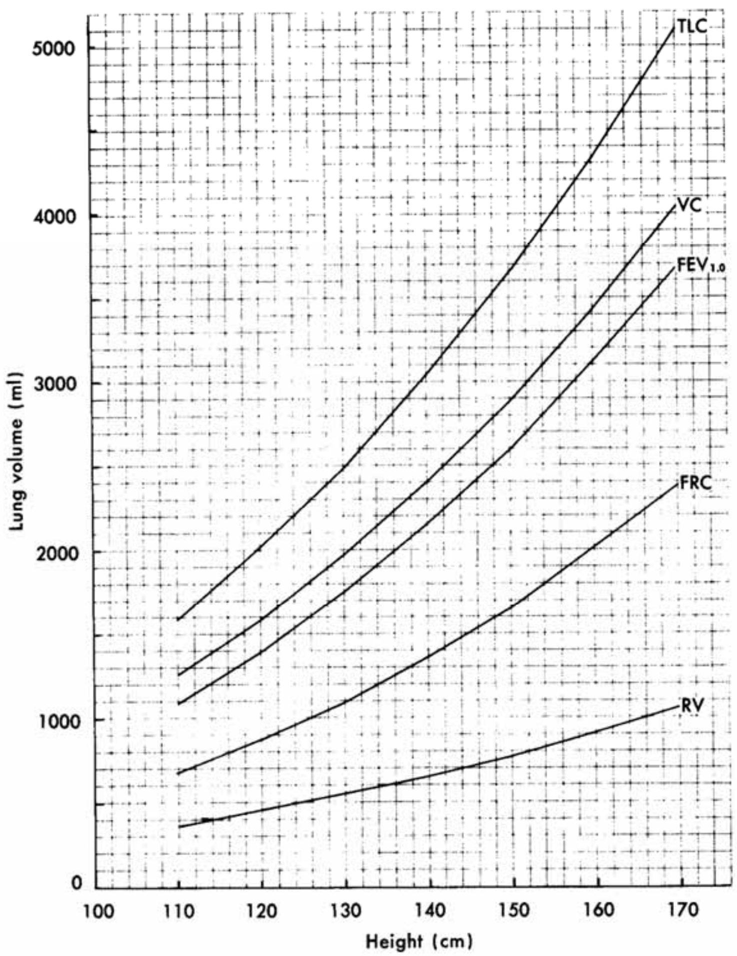
Basic Pulmonary Function Tests

- **Measurements of lung and expired air volumes, airflow rates, and alveolar gas diffusion**
- **Range of technology: simple (peak flow, spirometry) to advanced (TLC, D_{LCO})**
- **Results reported both as measured values and as % predicted for the person's age, size, sex and race**

Boyle's Law Method for Lung Volume Measurements



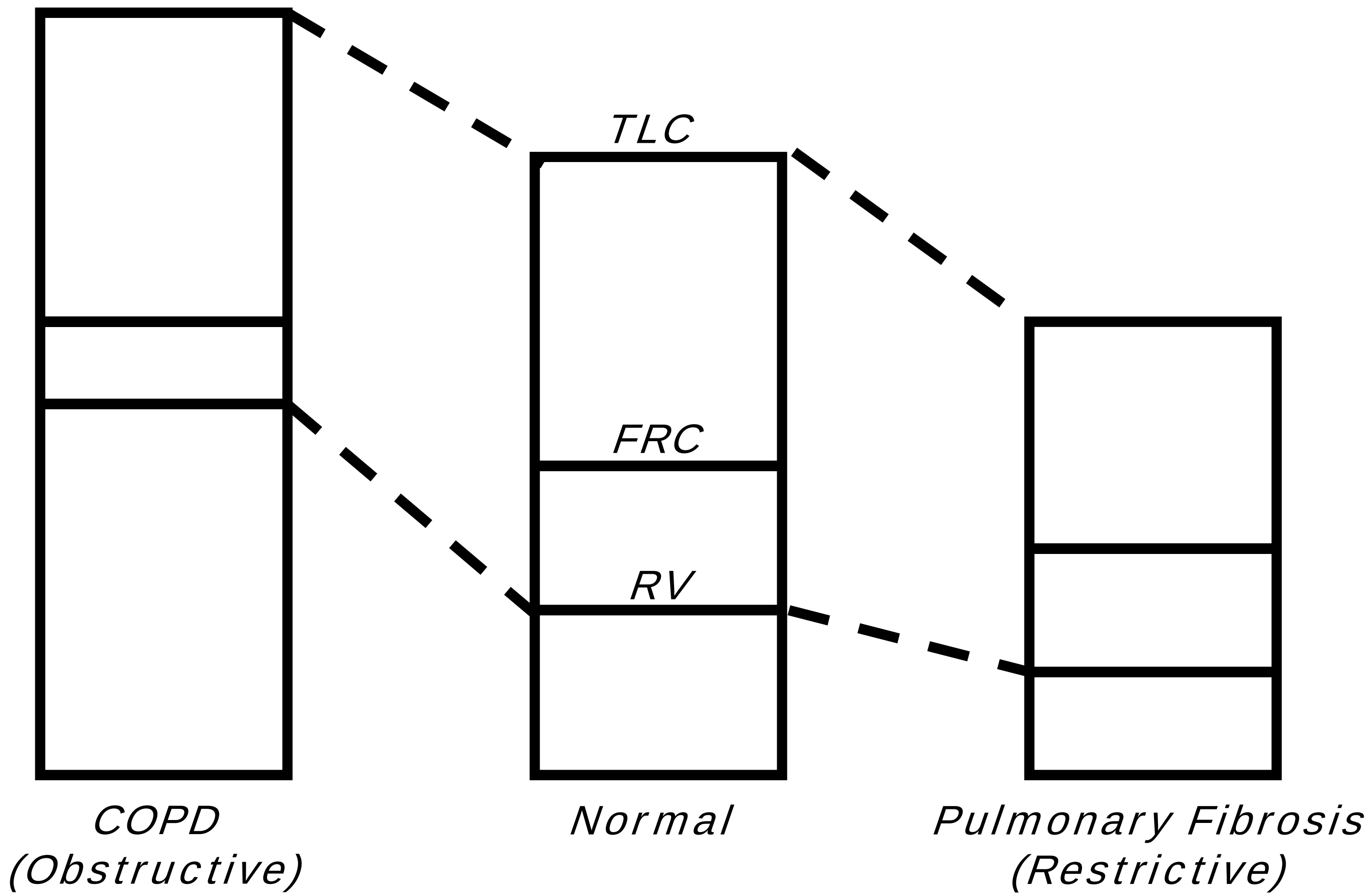
SUMMARY CURVES FOR PREDICTING
NORMAL VALUES IN CHILDREN



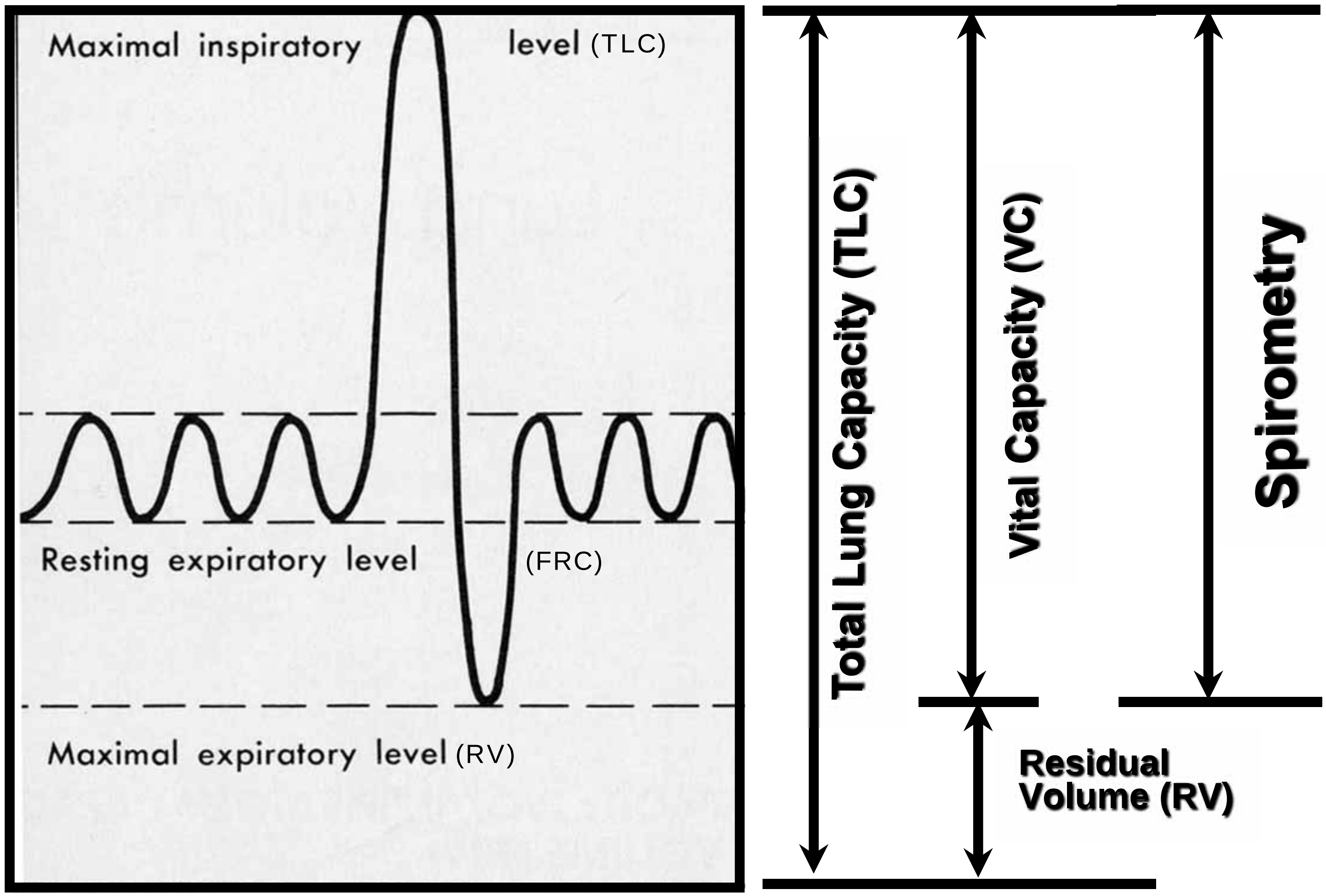
"Predicted" values for pulmonary function tests are the expected average values for individuals with normal lungs, adjusted for body size, sex, age and race

In addition, values for the upper or lower limits of normal may be reported along with the predicted values

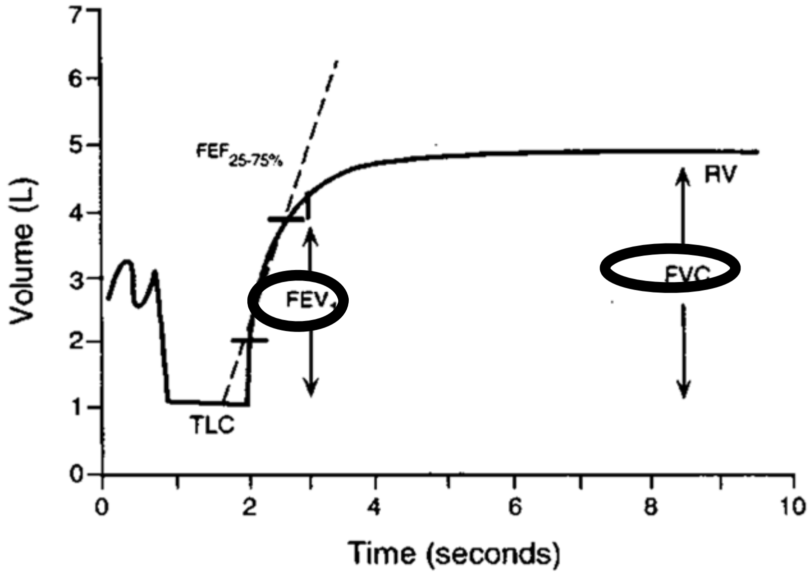
Lung Volumes in Lung Disease

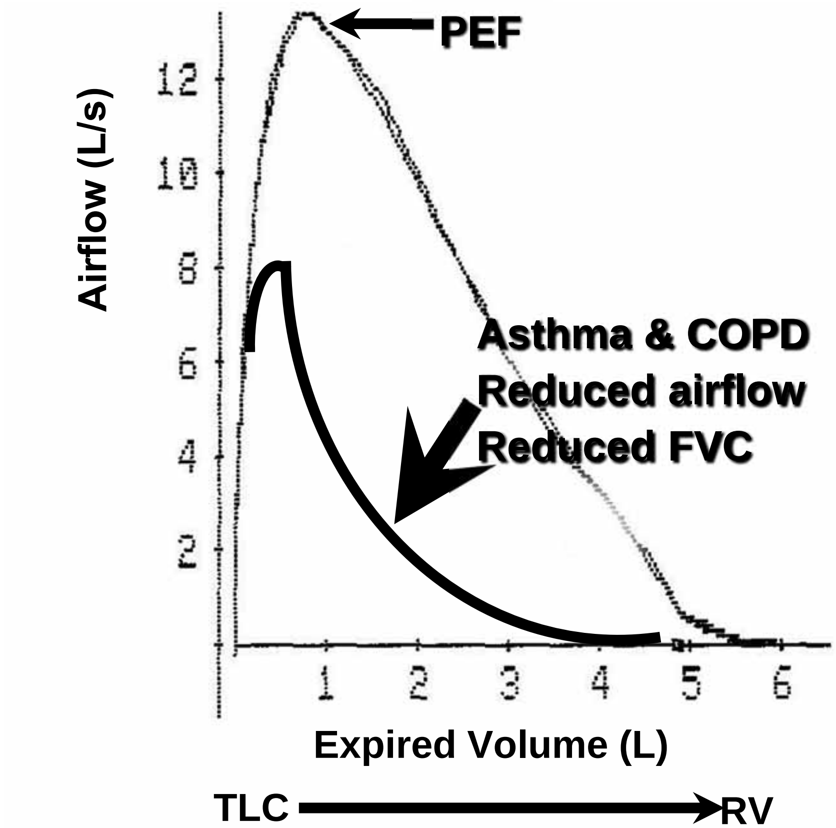


Lung Volumes

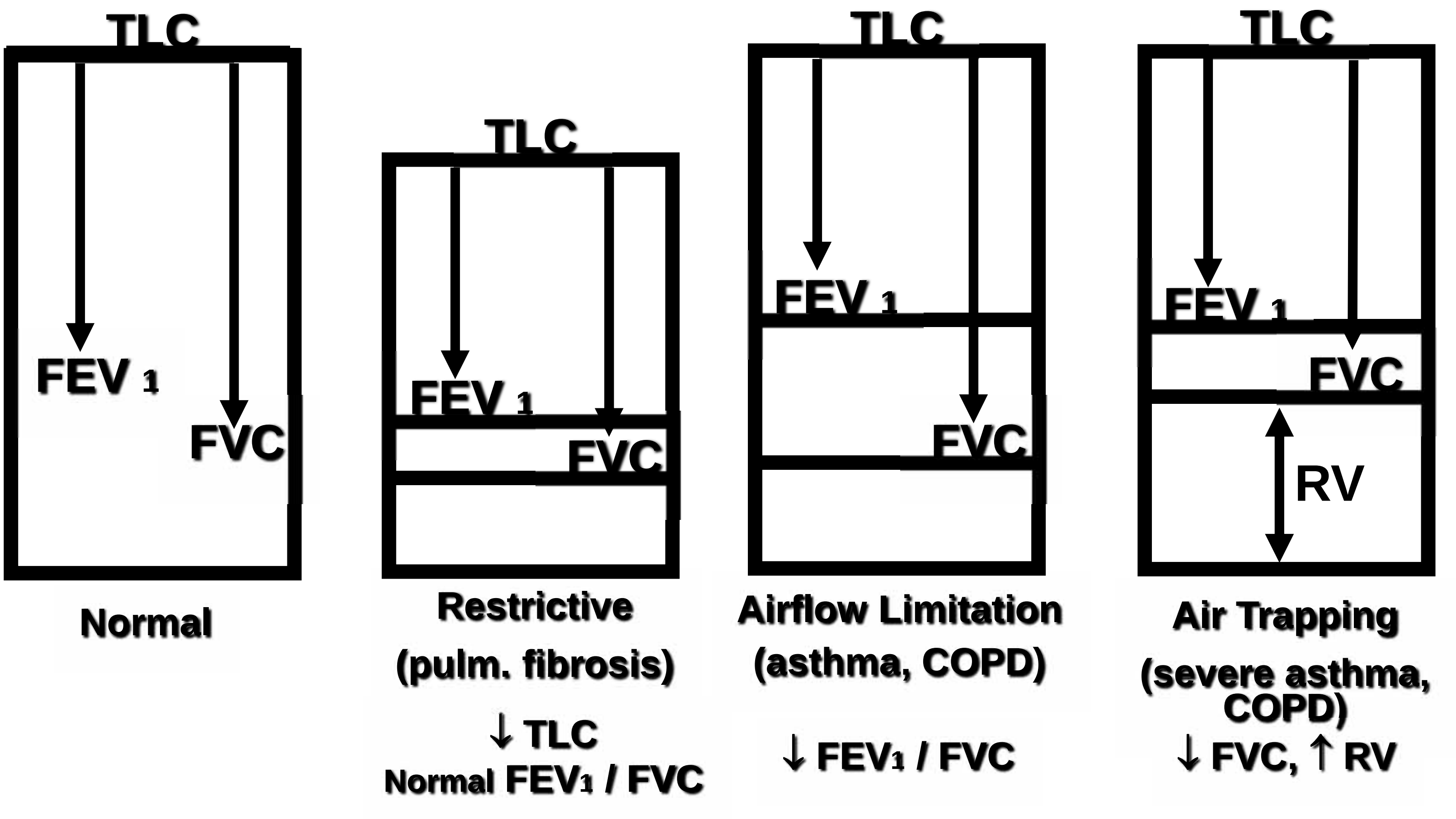


Spirometry: Detection of Airway Obstruction





Causes of Changes in FEV_1



Example: a healthy 22 year old male

Lung Volumes

- TLC 6.0 L
- VC 4.8 L
- RV 1.2 L (20% of TLC)

Spirometry

- FVC 4.8 L
- FEV_1 4.0 L
- FEV_1/FVC 0.83
- PEF 10.0 L/s (600 L/min)

Diffusing Capacity (DLco)

- Measurement of diffusion rate of carbon monoxide across the alveolar-capillary membranes
- DLco is reduced in pulmonary fibrosis (reduced rate of gas diffusion), emphysema (reduced alveolar surface area), and any other disease that results in loss of alveolar numbers or function (pulmonary edema, pneumonia, surgical removal, etc.)
- DLco is useful for monitoring patients that are taking drugs with potential pulmonary toxicity, to detect early changes that may still be reversible

Patterns of PFT Abnormalities

Test	Restrictive Disease *(e.g. Pulm. Fibrosis)*	Obstructive Disease *Asthma*	*COPD*
TLC	Decreased	Normal to Increased	Increased
RV	Decreased (%TLC normal)	Normal to Increased	Increased
FVC	Decreased	Normal to Decreased	Decreased
FEV_1	Decreased	Decreased	Decreased
FEV_1/FVC	Normal	Decreased	Decreased
PEF	Decreased	Decreased	Decreased
DLco	Decreased (fibrosis)	Normal	Decreased

Exhaled Nitric Oxide (eNO)

- NO a relatively stable free radical gas
  - Generated from arginine by NO synthases (NOS)
  - Numerous physiological functions
  - Most airway cells (resident and inflammatory) can express NOS, and NOS may be induced in epithelial cells during inflammation
- Some of the NO generated by airway cells is carried in exhaled air, and elevated eNO may be an indicator of inflammation in the airways

How Can We Use eNO?

- **Asthmatics with ↑eNO may be more likely to improve with antiinflammative Rx**
  - **possible use to guide choice of controller Rx**
- **eNO usually decreases with inhaled steroid Rx**
  - **Indicator that pt is using the Rx**
  - **Guide for tapering steroid to lowest effective dose**
- **Caveats- eNO also is *reduced* by some inflammatory processes that increase conversion of NO to nonvolatile stable nitrates, by ↓ airway pH, & by exposure to tobacco smoke**
- **eNO has been approved by FDA for assessing asthma, but has not yet found a clear role in asthma diagnosis & treatment**

2011 Practice Guidelines for eNO Use in Asthma

TABLE 5. GENERAL OUTLINE FOR $F_{E_{NO}}$ INTERPRETATION: SYMPTOMS REFER TO COUGH AND/OR WHEEZE AND/OR SHORTNESS OF BREATH*

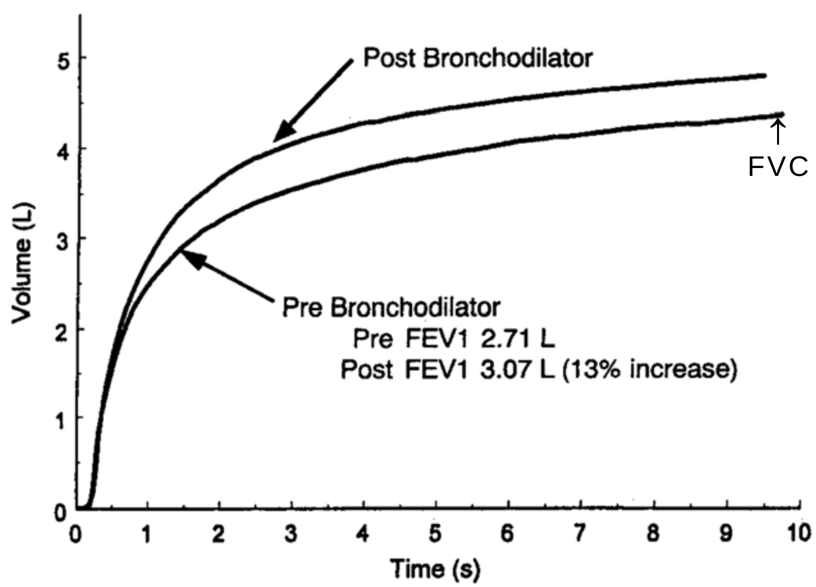
	$F_{E_{NO}}$ < 25ppb (<20 ppb in children)	$F_{E_{NO}}$ 25–50 ppb (20–35 ppb in children)	$F_{E_{NO}}$ > 50 ppb (>35 ppb in children)
		Diagnosis	
Symptoms present during past 6+ wk	Eosinophilic airway inflammation unlikely Alternative diagnoses Unlikely to benefit from ICS	Be cautious Evaluate clinical context Monitor change in $F_{E_{NO}}$ over time	Eosinophilic airway inflammation present Likely to benefit from ICS
		Monitoring (in Patients with Diagnosed Asthma)	
Symptoms present	Possible alternative diagnoses Unlikely to benefit from increase in ICS	Persistent allergen exposure Inadequate ICS dose Poor adherence Steroid resistance	Persistent allergen exposure Poor adherence or inhaler technique Inadequate ICS dose Risk for exacerbation Steroid resistance
Symptoms absent	Adequate ICS dose Good adherence ICS taper	Adequate ICS dosing Good adherence Monitor change in $F_{E_{NO}}$	ICS withdrawal or dose reduction may result in relapse Poor adherence or inhaler technique

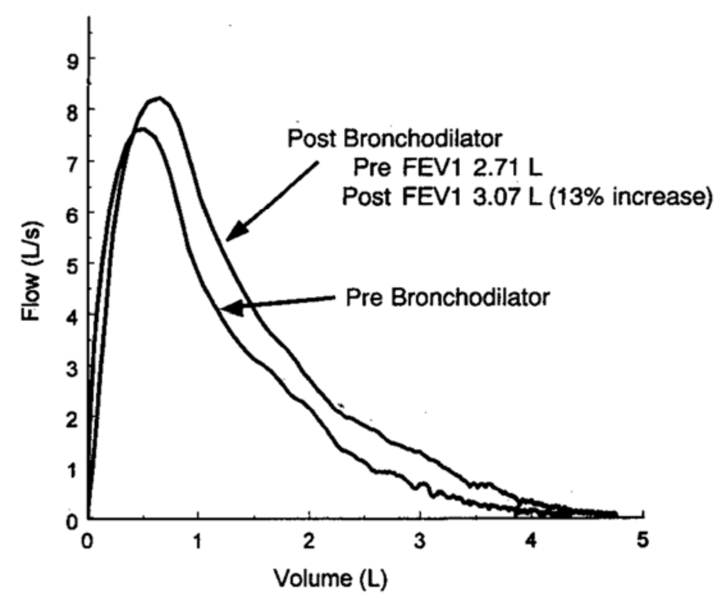
Definition of abbreviations: $F_{E_{NO}}$ = fraction of exhaled nitric oxide; ICS = inhaled corticosteroid.

*The interpretation of $F_{E_{NO}}$ is an adjunct measure to history, physical exam, and lung function assessment. *See* text and Tables 3 and 4 for other details.

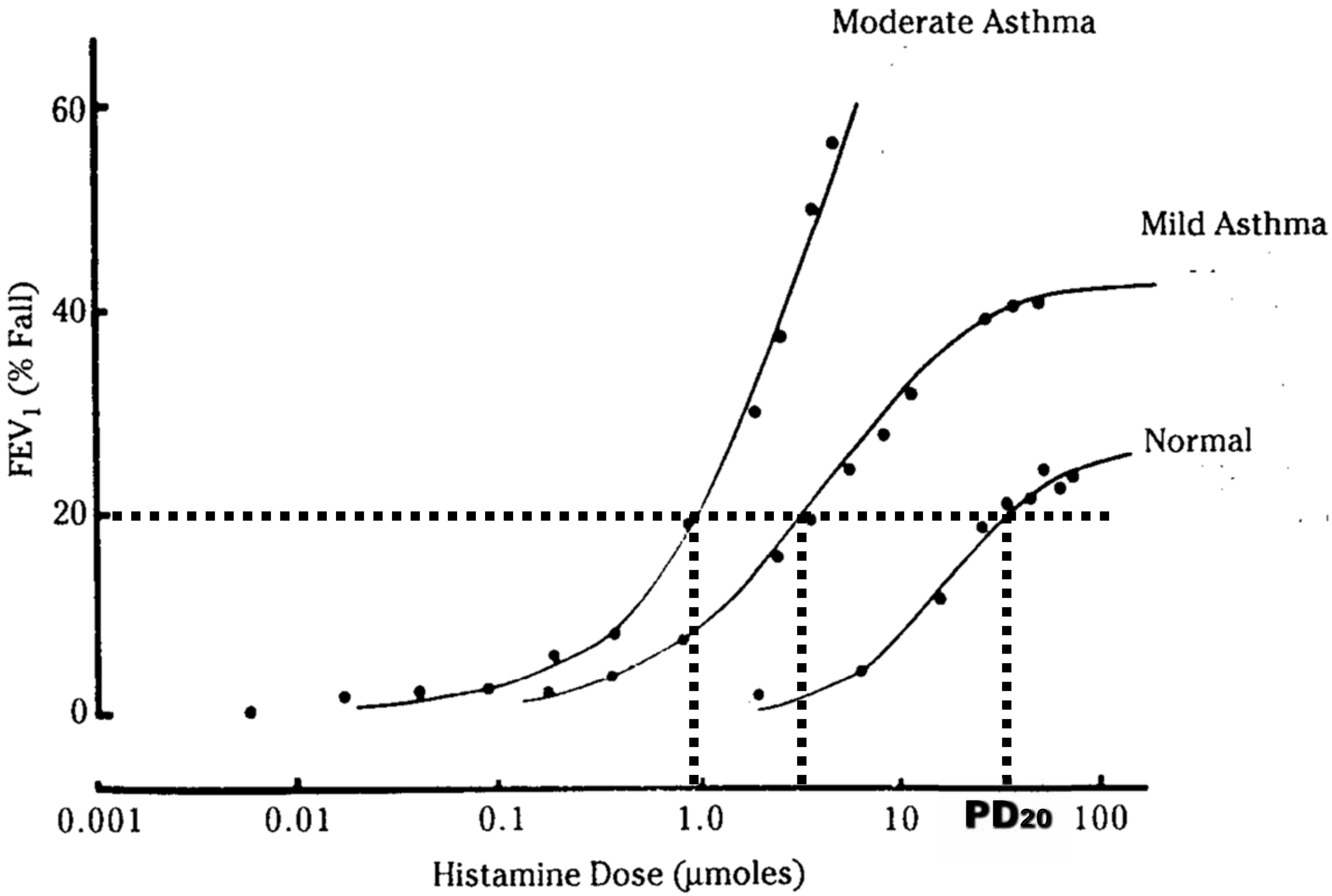
Am J Respir Crit Care Med 2011; 184:602.

Reversibility with Bronchodilation in Asthma





Airway Hyperresponsiveness



Woolcock, Am Rev Respir Dis 1984; 130:71

Assessing Exercise Tolerance

- ***COPD or Pulmonary Fibrosis***- ability to perform physical activities
  - 6 minute walk
    - Record total distance covered in 6 minutes
    - Monitor SpO_2 for desaturation during exercise
    - Symptom scale for dyspnea & leg fatigue
- ***Asthma***- airway obstruction associated with exercise
  - Document changes in PEF or FEV_1 with exercise
  - Standardized test using treadmill and dry air

Blood Gas Study Problem #1

pH 7.39, $PaCO_2$ 53, PaO_2 55, HCO_3 31, BE +5.0

Ventilation	*Hypoventilation*
Oxygenation	*Decreased*
pH	*Normal range*
Metabolic Component	*Increased*
Acid-Base Status	*Resp. acidosis + met. alkalosis*
Clinical problem	*Chronic bronchitis and emphysema*

Blood Gas Study Problem #2

pH 7.49, $PaCO_2$ 30, PaO_2 100, HCO_3 23, BE 1.2

Ventilation	*Hyperventilation*
Oxygenation	*Normal to increased*
pH	*Alkalemia*
Metabolic Component	*Normal*
Acid-Base Status	*Respiratory alkalosis*
Clinical problem	*Acute psychogenic hyperventilation*

Blood Gas Study Problem #3

pH 7.45, $PaCO_2$ 33, PaO_2 64, HCO_3 24, BE 1.1

Ventilation	*Hyperventilation*
Oxygenation	*Decreased*
pH	*Alkalemia*
Metabolic Component	*Normal*
Acid-Base Status	*Respiratory alkalosis*
Clinical problem	*Acute asthma exacerbation*

Blood Gas Study Problem #4

pH 7.32, $PaCO_2$ 51, PaO_2 59, HCO_3 27, BE 0.5

Ventilation	*Hypoventilation*
Oxygenation	*Decreased*
pH	*Acidemia*
Metabolic Component	*Normal*
Acid-Base Status	*Respiratory acidosis*
Clinical problem	*Acute pulmonary failure (ARDS)*

Blood Gas Study Problem #5

pH 7.25, $PaCO_2$ 53, PaO_2 80, HCO_3 27, BE 0.5

Ventilation	*Hypoventilation*
Oxygenation	*Low end of normal range*
pH	*Acidemia*
Metabolic Component	*Normal*
Acid-Base Status	*Respiratory acidosis*
Clinical problem	*Drug overdose-induced coma*

Blood Gas Study Problem #6

pH 7.39, $PaCO_2$ 40, PaO_2 187, HCO_3 25, BE 0.9

Ventilation	*Normal*
Oxygenation	*Increased*
pH	*Normal*
Metabolic Component	*Normal*
Acid-Base Status	*Normal*
Clinical problem	*Uncomplicated postop on oxygen supplement*

Blood Gas Study Problem #7

pH 7.58, $PaCO_2$ 36, PaO_2 108, HCO_3 33, BE 11

Ventilation	*Normal*
Oxygenation	*Increased*
pH	*Alkalemia*
Metabolic Component	*Increased*
Acid-Base Status	*Metabolic alkalosis*
Clinical problem	*Post-bicarbonate Rx; on oxygen supplement*

Blood Gas Study Problem #8

pH 7.00, $PaCO_2$ 13, PaO_2 131, HCO_3 2, BE -29

Ventilation	*Hyperventilation*
Oxygenation	*Increased*
pH	*Acidemia*
Metabolic Component	*Decreased*
Acid-Base Status	*Metabolic acidosis + resp. alkalosis*
Clinical problem	*Diabetic ketoacidosis; on oxygen supplement*

Blood Gas Study Problem #9

pH 7.15, $PaCO_2$ 49, PaO_2 53, HCO_3 17, BE -12

Ventilation	*Hypoventilation*
Oxygenation	*Decreased*
pH	*Acidemia*
Metabolic Component	*Decreased*
Acid-Base Status	*Combined resp. & met. acidosis*
Clinical problem	*Severe pneumonia and septic shock with lactic acidosis*

Blood Gas Study Problem #10

pH 7.52, $PaCO_2$ 45, PaO_2 83, HCO_3 39, BE +15

Ventilation	*Normal range (almost hypo-)*
Oxygenation	*Normal range (low end)*
pH	*Alkalemia*
Metabolic Component	*Increased*
Acid-Base Status	*Metabolic alkalosis*
Clinical problem	*Vomiting repeatedly for several days*

Blood Gas Study Problem #11

pH 7.55, $PaCO_2$ 12, PaO_2 30, HCO_3 11, BE -6

Ventilation	*Hyperventilation*
Oxygenation	*Hypoxia*
pH	*Alkalemia*
Metabolic Component	*Decreased*
Acid-Base Status	***Metabolic acidosis + respiratory alkalosis***
Clinical problem	*Healthy climber on Mt. Everest*