A Potpourri of Blood Gas Info That You Probably Don’t Know

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Objectives for Session

- Review basic interpretation of blood gas results.
- Discuss issues in temperature-correction of blood gas results.
- Calculate Pulmonary Shunt fraction.
- Describe how pleural fluid pH (and other) tests can be used to evaluate pleural diseases:
  - Transudates vs Exudates.
  - Reference or interpretive intervals
- Discuss the effects of sulfhemoglobin on cooximetry results.
- Discuss the stability of blood gas samples and why so much disagreement.
- Describe how to minimize effects of pneumatic transport on pO_2 results.

Arterial Blood Gas Report

			Reference Range
PATIENT TEMP, ARTERIAL	37.0		
FIO2, ARTERIAL	21	%	
pH, BLOOD ARTERIAL	7.40		[7.35-7.45]
pCO2, ARTERIAL	40	mmHg	[35-45]
pO2, ARTERIAL	96	mmHg	[75-100]
P/F Ratio	457		[>400]
BASE EXCESS,ARTERIAL	0	mmol/L	[-3-3]
BICARBONATE, ARTERIAL	25	mmol/L	[20-28]
CO2 TOTAL, ARTERIAL	26	mmol/L	[21-30]
HEMOGLOBIN, ARTERIAL	*8.3	g/dL	[13.7-17.3]
%O2 HEMOGLOBIN, ARTERIAL	95.8	%	[94.0-99.0]
%CO HEMOGLOBIN, ARTERIAL	1.8	%	[0.0-2.0]

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Interpretive Data (%)

Non-Smokers: 0-2.0

Smokers: 1-2 packs/day: 0-5.0

Smokers: 3-4 packs/day: 0-9.0

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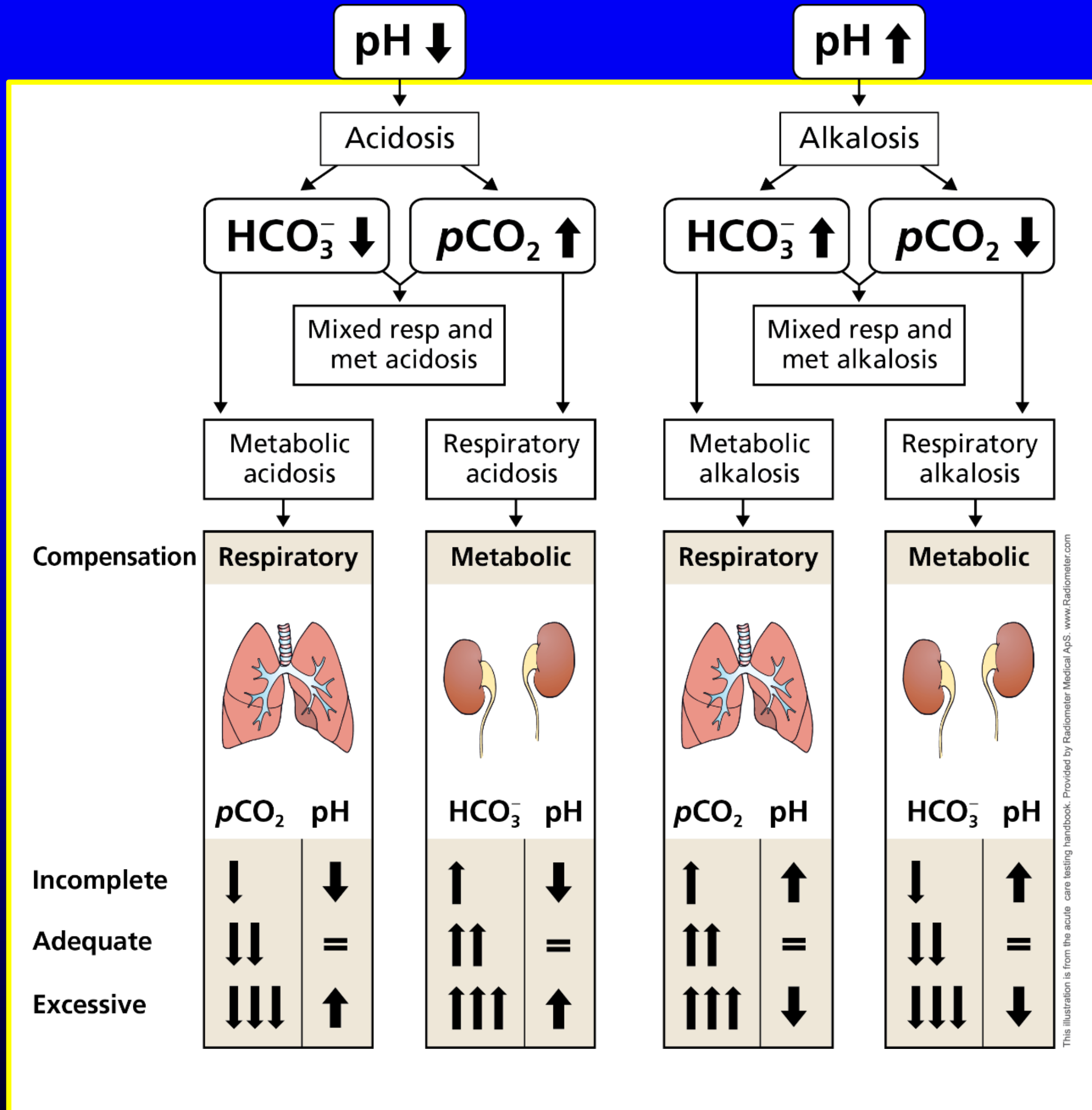
%METHEMOGLOBIN, ARTERIAL	*1.7	%	[0.4-1.5]
VOLUME % O2, ARTERIAL	*11.4	mL/dL	[15.0-24.0]

Interpreting Lab Results in Acid-Base Disorders and Appropriate Compensation



Causes of Metabolic Acidosis

- ***Lab diagnosis:*** **A decreased pH and HCO_3.**
  - **Hypoxemic / Ischemic**
    - **Related to pulmonary, cardiac, and/or metabolic function, decreased blood flow, mitochondria dysfunction, etc**
    - **Blood lactate often a marker**
  - **High Anion Gap acidosis:**
    - **Related to increased anion generation: lactate, ketoacids, ethanol, methanol, Tylenol, ethylene glycol, etc**
  - **Normal Anion Gap acidosis**
    - **GI loss of bicarbonate (gain of Cl^-): diarrhea**
    - **Kidney: RTA: Increased loss of HCO_3 or increased retention of H^+**
    - **Decreased aldosterone: promotes loss of Na^+ / gain of K^+ and H^+**

Disorder	Decreased	Increased/Gained
Diarrhea	HCO_3^-	Cl^-
Renal tubular acidosis	HCO_3^-	Cl^-
Lactate acidosis	HCO_3^-	Lactate
Ketoacidosis	HCO_3^-	Ketoacids

Causes of Respiratory Acidosis

- ***Lab diagnosis:*** **A decreased pH and increased pCO_2.**
  - **Hypoventilation**
    - **May be from trauma, drugs, airway obstruction, etc**
    - **Depressed ventilation = Increased pCO_2**
  - **Impaired pulmonary gas exchange**

Source	Disorder	Lab Results Increased	Lab Results Decreased
Central Nervous System	Ventilation failure: brain injury, drugs (opioids), respiratory muscle failure	pCO_2	pH, pO_2
Pulmonary	Impaired pulmonary gas exchange: shunts, dead space, damaged alveoli. COPD, ARDS	pCO_2	pH, pO_2
Other	Insufficient mechanical ventilation	pCO_2	pH, pO_2

Causes of Metabolic Alkalosis

Lab diagnosis: An increased pH and HCO_3.

- Kidney: Gain of bicarbonate often related to Na^+ / K^+ / Cl^- movements:
  - » Urinary loss of Cl^- can lead to increased retention of HCO_3
  - » Increased aldosterone: Gain of Na^+ = loss of K^+ / H^+ and gain of HCO_3
- GI absorption of HCO_3
  - » Excess HCO_3 administration
- Loss of acidic upper GI fluids: vomiting

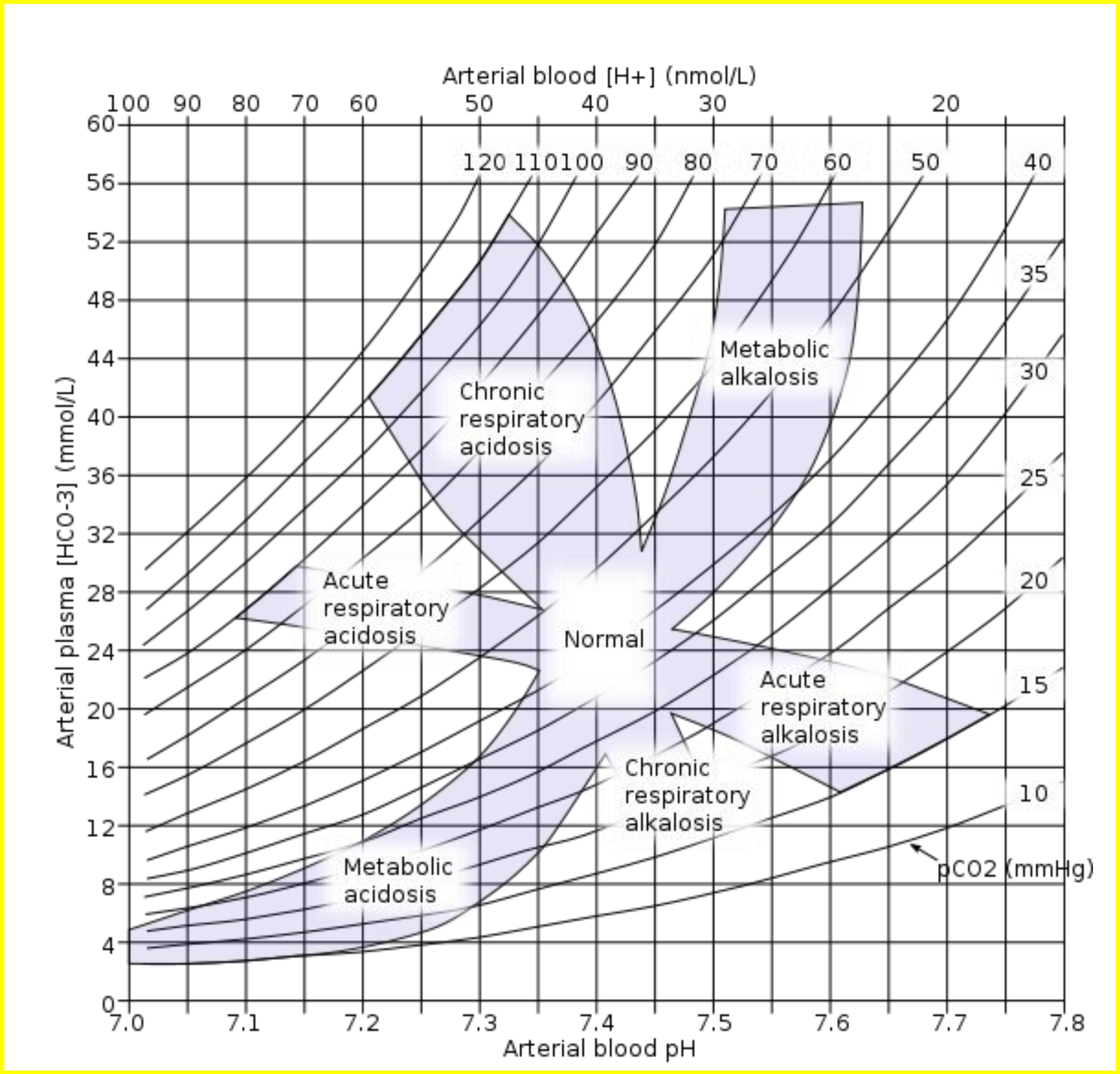
Note: Very little HCO_3 or other alkaline substances are produced by metabolism: Ammonia is produced, but it is 98% NH_4^+ and 2% NH_3.

Causes of Respiratory Alkalosis

- ***Lab diagnosis:*** **An increased pH and decreased pCO_2.**
  - **Hyperventilation:**

Source	Cause
Central Nervous System	Hyperventilation: Panic/Anxiety disorders
	Stroke, brain trauma, encephalitis, tumors
Drugs and Toxins	Overdoses of salicylate, catecholamines, nicotine, others
	Progesterone stimulates respiratory center (pregnancy)
Pulmonary conditions	Hypoxemia leading to hyperventilation: Pneumonia, pulmonary edema or embolism, pulmonary shunting
Miscellaneous	Pregnancy (progesterone)
	Severe anemia
	Excessive mechanical ventilation

Nomogram for Interpreting Acid-Base Status



- Left Y-axis is plasma HCO_3 in mmol/L.
- Curved lines represent constant pCO_2 values in mmHg.
- Upper X-axis is H^+ concentration in nmol/L.

NOTE: These relationships may not hold in complex acid-base disorders.

From Huckfinne, Wikimedia Commons; Public domain

Case Example #1 Acid-Base Disturbance

65y F with neuromuscular weakness and infection. Difficulty breathing, on 50% oxygen.

pH 7.07	*(7.35-7.45)*
p_aCO_2 **85** *mmHg*	*(35 - 45 mmHg)*
p_aO_2 **143** *mmHg*	*(80 - 108 mmHg)*
HCO_3 **25** *mmol/L*	*(21-28 mmol/L)*

Acute respiratory acidosis (on supplemental oxygen)

Evaluating Blood Oxygenation

Some Blood Oxygenation Terminology

- pO_2: The partial pressure of O_2 gas in arterial (p_aO_2) or venous (p_vO_2) blood.
- p_AO_2 or A: The pO_2 of alveolar air.
- $FI\ O_2$: The % of oxygen contained in the air that a person is breathing ("*fraction* of *inspired oxygen*").
- Alveolar – arterial pO_2 difference (A – a)
- pO_2 : FIO_2 Ratio (P/F Ratio)
- Pulmonary Dead Space
- Pulmonary Shunt

Processes for Getting Oxygen from the Atmosphere to Cells and Mitochondria

- Air intake by breathing or ventilation
- Air enters alveoli
- Pulmonary gas exchange:
  - Functional alveoli: healthy membranes and good blood flow to alveoli [A-a, dead space, shunt]
- Oxygenation of blood and Hb
- Oxygen transport to tissues and cells:
  - Adequate Hb and good systemic blood flow
- Oxygen release and diffusion into cells
- Oxygen utilization by mitochondria

Reference Intervals for Blood Gases

Test	Age Range	Reference Interval	
		Venous	**Arterial**
pH	18 – 76 y	7.32 – 7.42	7.35 – 7.45
pCO_2 (mmHg)	18 – 70 y	38 – 51	32 – 45
pO_2 (mmHg)	20 – 39 y	-	83 – 108
	40 – 76 y	-	70 – 100
sO_2 (%)		-	>95
Base Excess	18 – 70 y	-1.9 to +4.5	-3.0 to +2.8
HCO_3^- mmol/L	18 – 70 y	22 – 30	21– 29
% Oxyhemoglobin, FO_2Hb	All	-	>94%
CO-Hb	Adult	Non-smoker: < 2% Smoker: 5 – 10%	
Met-Hb	Adult	$\leq$ 1%	

Klaestrup E, et al. Reference intervals and age and gender dependency for arterial blood gases and electrolytes in adults. Clin Lab Med 2011; 49: 1495-1500.

Temperature Correction of Blood Gas Results

- Blood gas measurements are performed at 37 °C.
- The decision to correct the blood gas test results to the body temperature is a never-ending debate and depends on the regional practice and the clinical situation.
- Since the solubilities of oxygen and carbon dioxide vary with the patient's core body temperature, equations to correct the pH, pCO_2, and pO_2 for the patient's core body temperature have been derived.

Temperature Correction of pO_2

The temperature correction of pO_2 is complicated because:

- the solubility coefficient of oxygen varies with temperature, and…
- the hemoglobin affinity also varies with temperature.

An equation that directly calculates the pO_2 (in mmHg) at a desired temperature (T in ^{o}C) is from Ashwood, et al 1983 , who modified the Severinghaus 1979 equation from natural log to decimal log (base 10):

$$pO_2(T) = pO_2(37\ ^\circ C) \times 10^{\left(\frac{5.49\times10^{-11}\times pO_2^{3.88}+0.071}{9.72\times10^{-9}\times pO_2^{3.88}+2.30}\right)\times\left(T-37\ ^\circ C\right)}$$

Ashwood ER, Kost G, Kenny M. Temperature correction of blood gas and pH measurements. Clin Chem 1983; 29(11): 1877-1885.

Severinghaus, J.W. (1979) Simple, Accurate Equations for Human Blood O2 Dissociation Computations. Journal of Applied Physiology, 46, 599-602.

Temperature Correction of pH

- **Severinghaus published an equation for correcting pH to the patient's temperature for pH ranging from 6.65 to 7.80:**

$$pH(T) = pH\ (37°C) – [0.0146 + 0.0065 \times (pH\ (37°C) – 7.40) \times (T – 37°C)]$$

Reference:

Severinghaus JW. Blood gas calculator. J Appl Physiol 1966; 21(3): 1108-1116. Doi: 10.1152/jappl.1966.21.3.1108

Optimal Management of pH During Hypothermic Cardiopulmonary Bypass is a Continuing Debate

The two main strategies:

- **To "correct" pH to the patient's body temperature (pH-stat) or interpret the results as reported by the blood gas analyzer at 37 °C (α-stat).**

Published reports conclude that:

- **Results not corrected for body temperature (α-stat) led to better neurological outcomes in adults who underwent cardiopulmonary bypass.**
- **3 of 4 studies on pediatric cardiopulmonary bypass patients concluded that test results corrected for body temperature (pH-stat) led to better outcomes.**

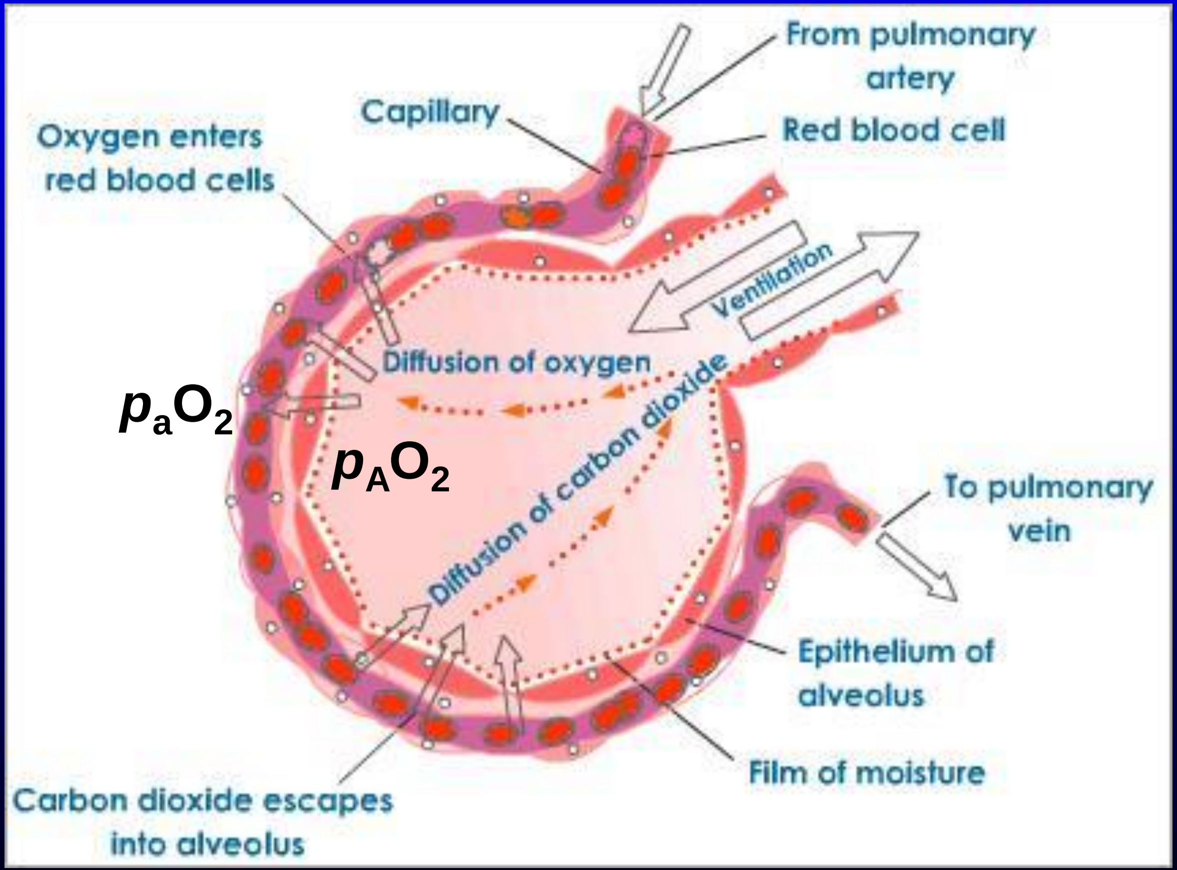
Conclusions Regarding Management of pH During Hypothermic Cardiopulmonary Bypass

- Overall Conclusions:
- At temperatures above 32 °C, there is little clinical or physiological significance, and below 25 °C, the difference is profound.
- Although the two strategies are frequently debated, the difference is of little actual relevance in most adult cardiac surgery because most cases are performed either for a short duration or at mild hypothermia when there is little clinical or physiological significance .

The A-a Difference or Gradient

Definition of A-a difference

- Difference between alveolar oxygen (p_AO_2) and arterial oxygen (p_aO_2) = A-a.
- Normal A-a difference: 5-15 mmHg ages up to 50 y



Calculating the Alveolar pO_2 (p_AO_2)

Alveolar p_AO_2 = (*Atm pressure* – pH_2O_{alv}) x FI-O_2 – ($pCO_{2\,art}$ / R)

R = 0.8 = Respiratory quotient; related to CO_2 production

Alveolar p_AO_2 = [*Atm pressure* – pH_2O_{alv}] x 0.21 – pCO_2/0.8

p_AO_2 = [*760 – 47*] x 0.21 – 1.25 x pCO_2

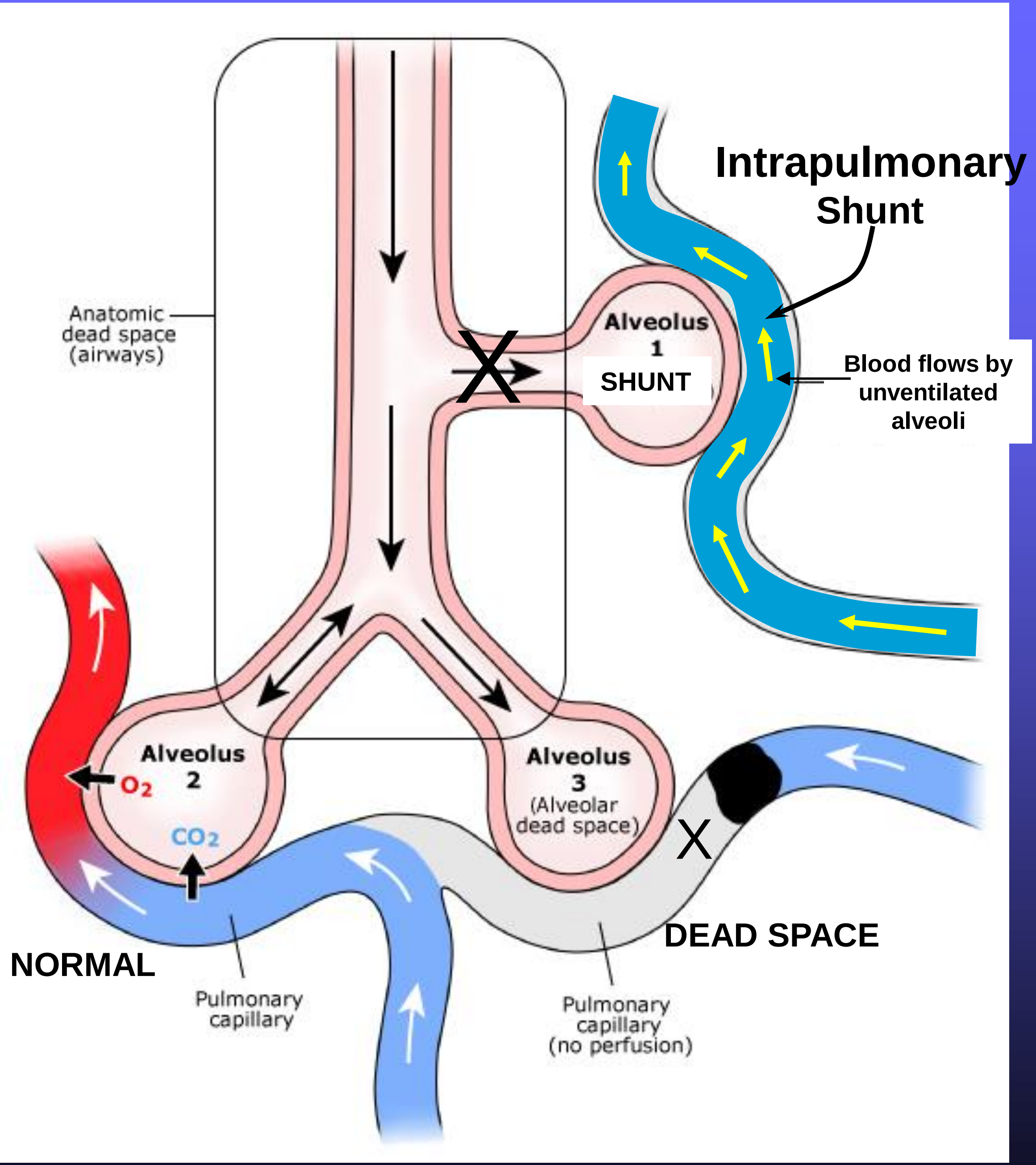
***Example*: Person breathing 100% oxygen and pCO_2 = 40 mmHg**

p_AO_2 = 713 mmHg x 1.00 – 1.25 x 40

p_AO_2 = 663 mmHg

Pulmonary Dead Space and Shunt

Examples of Normal Alveoli and Those with Dead Space and Shunt



Pulmonary Shunt

Poor alveolar ventilation with good blood flow

- **Shunt: Alveolar blood passes by unventilated alveoli, with no gas exchange.**
- **Excess Pulmonary Shunt may be caused by:**
  - **Pneumonia, pulmonary edema, ARDS, collapsed alveoli (atelectasis), and any arteriovenous passages.**
- **Characteristics:**
  - **A poor response to O_2 therapy** *(alveoli less efficient in oxgenation)*
  - **A calculated shunt of >8%.**

(Sarkar M, et al. Mechanisms of hypoxemia. Lung India 2017; 34: 47-60)

Evaluation of Pulmonary Shunt

All calculations of Shunt Fraction are approximations

- First, have patient breath 100% oxygen for 20 minutes.
- To calculate shunt fraction, collect arterial and venous blood.
- Measure blood gases and cooximetry on both.
- Use lots of equations to calculate the shunt fraction:
- O_2 content = sO_2 x 1.34 x [Hb] + 0.003 pO_2
- Alveolar pO_2 (p_AO_2) = (760 – 47 mmHg) x $FI\text{-}O_2$ - $p_aCO_2/0.8$
- Shunt fraction = $(c_{pc}O_2 – c_{art}O_2) / (c_{pc}O_2 – c_{ven}O_2)$

*	*Cane RD, et al. Unreliability of oxygen tension-based indices in reflecting intrapulmonary shunting in critically ill patients. Crit Care Med 1988; 16: 1243-5.*

Calculating Physiologic Shunt from Actual Data on a Healthy Person Breathing 100% O_2 for 20 minutes

Measured Parameters	
$FI\text{-}O_2$	**1.00**
Barometric pressure (*p*B)	**760 mmHg**
Respiratory Quotient (R)	**0.8**
Hb	**15.2 g/dL**
saO_2 and $spcO_2$	**0.993**
paO_2	**587 mmHg**
$paCO_2$	**38 mmHg**
pvO_2	**40 mmHg**
svO_2	**0.781**

Calculated Parameters	
Alveolar p_AO_2	**665 mmHg**
Arterial O_2 dissolved in plasma (paO_2 x 0.003 mL/dL / mmHg)	**1.76 mL/dL**
Venous O_2 dissolved in plasma (pvO_2 x 0.003)	**0.12 mL/dL**
Arterial O_2 content	**22 mL/dL**
Venous O_2 content	**16 mL/dL**
Art – Ven O_2 content difference	**6.0 mL/dL**
Pulmonary capillary O_2 content	**22.2 mL/dL**
Shunted blood (Qs) =	**0.20**
Total blood flow (Qt) =	**6.22**
Qs / Qt = shunted fraction = 22.2 – 22 / 22.2 - 16	**0.032 = 3.2%**

Data from Gerald Zavorsky; UC Davis Resp Therapist and member of CLSI C46 3rd Edition Committee

Much Easier Evaluation of Pulmonary Shunt

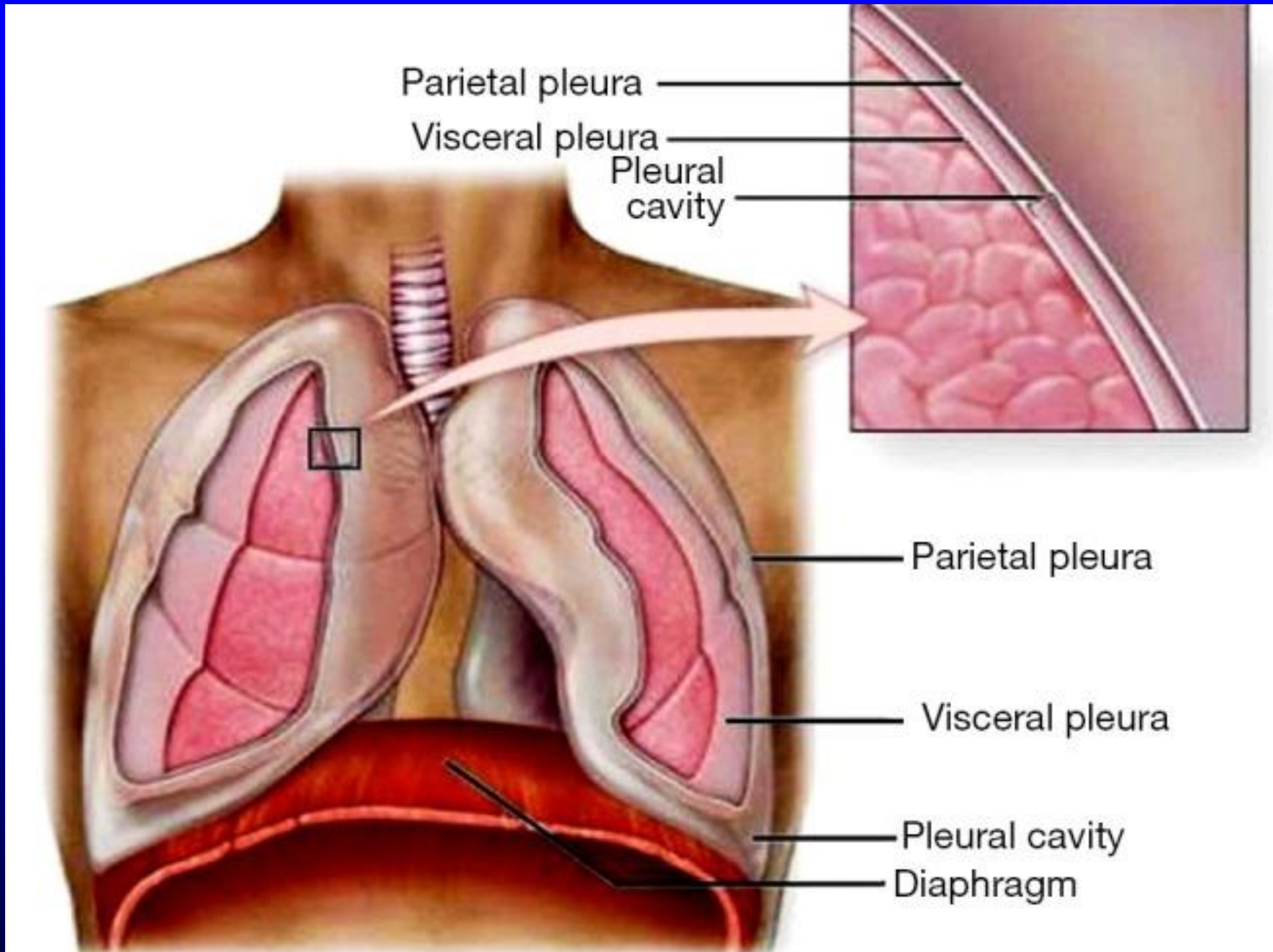
- OR…You can estimate the shunt fraction from sO_2 measured by pulse oximetry or blood gas analyzer:
- The patient breaths 100% oxygen for 20 minutes:
  - If sO_2 remains below 95%, a shunt is likely
  - If sO_2 increases to 98% or above, a shunt is unlikely **

*** Craig Rackley, MD; Duke critical care pulmonologist*

Evaluating Test Results in Pleural Fluid

- Pleural fluid pH and other tests can be used to evaluate pleural diseases:
  - Transudates vs Exudates.
  - Reference or interpretive intervals

Gross Anatomy of the Pleural Cavity



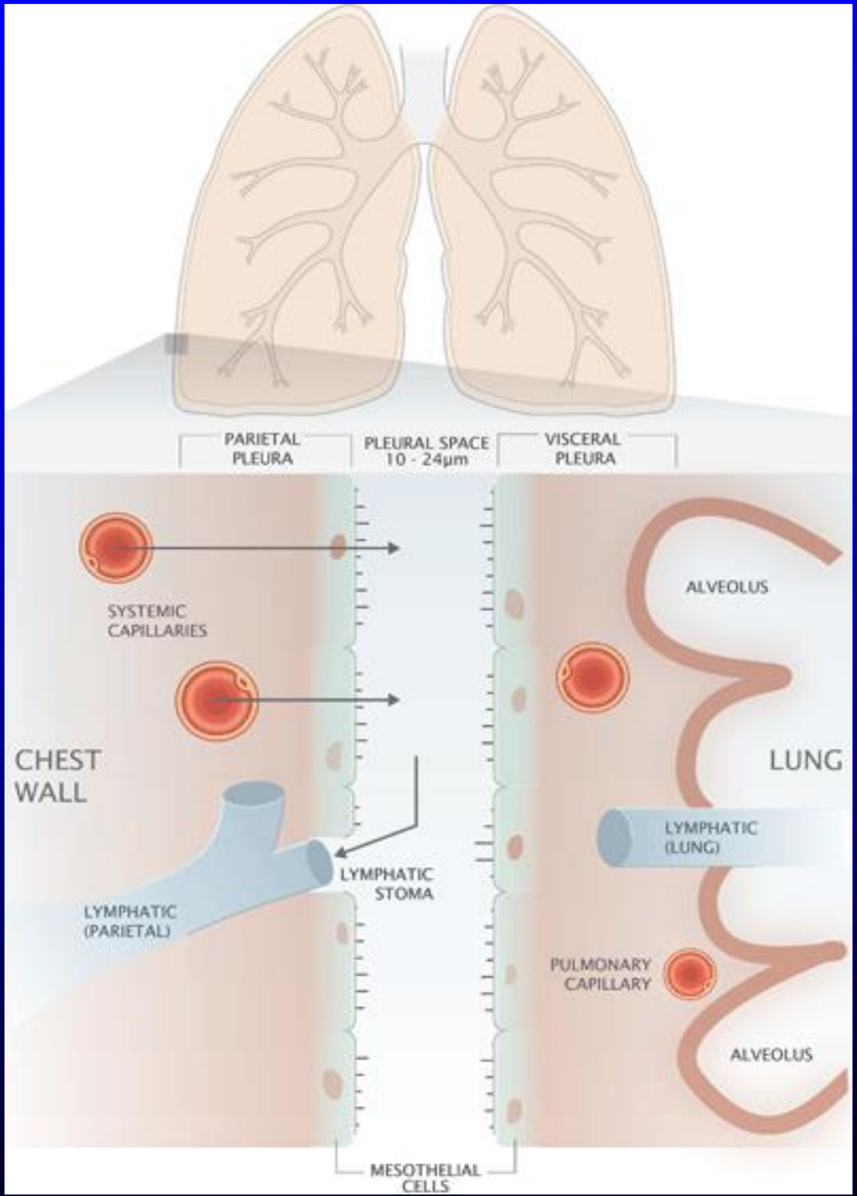
The plural cavity or space is a very thin layer: ~0.02 mm.

Healthy lungs contain only a few mL of pleural fluid.

PF acts as a lubricant to allow the layers to slide during breathing.

from: Charalampidis C, et al. Pleura space anatomy. J Thorac Dis 2015; 7(S1): S27-S32.

Diagram of the Pleural Space



From: Higgins C. Clinical aspects of pleural fluid pH. Acutecaretesting.org Oct 2009

Causes of Transudates vs Exudates

Transudates:
- Heart failure*
- Cirrhosis
- Nephrotic syndrome
- Hypoalbuminemia
- Hypothyroidism

Exudates:
- Pneumonia*
- Malignancy*
- Tuberculosis
- Pulmonary embolism*
- Esophageal rupture
- SLE
- Pancreatitis
- Post coronary bypass surgery
- Drug induced.

Transudates **are caused by pressure imbalances that lead to fluid accumulation in pleural space.**

Exudative processes **are more serious, with loss of pleural integrity.**

Criteria for Pleural Fluid (PF) Exudate

- Measure:
  - Serum total protein (g/L) and LDH (U/L)
  - Pleural fluid total protein and LDH (U/L)
  - Pleural fluid pH
- Calculate:
  - Total Protein PF:Serum ratio
  - LDH PF:Serum ratio
- Criteria for Exudate:
  - PF:Serum TP ratio > 0.5, or
  - PF:Serum LDH ratio > 0.6, or
  - PF LDH > 200 U/L
  - PF pH < 7.45
    - » **Normal pleural fluid pH ~7.60 – 7.68**
    - » Estimate from very old study on humans; Consistent with animal studies; PF has high HCO_3^-

Pleural Fluid pH Associated with Various Pulmonary Diseases

pH

<6.5	<7.30	7.30	7.40	7.45	7.55	7.60

Esophageal Rupture

Typically has the lowest PF pH.

A pH <6.0 is virtually diagnostic of esophageal rupture

pH 6.29 – 7.28 Pneumonia:
Empyema stage, with;
Pus,
Growth of fibrous layer

pH < 7.30
Malignancy;
Rheumatic Disease

pH 6.70 – 7.21 Pneumonia:
Fibinopurulent stage, with:
Bacteria,
Neutrophils,
Fibrin forms in pleura

pH 7.33 – 7.47 Early Pneumonia:

Exudative Stage; usually no complications

CHF:
pH >7.40;
Usually within 0.04 pH of arterial pH

Normal pH of Pleural Fluid:
7.60-7.68

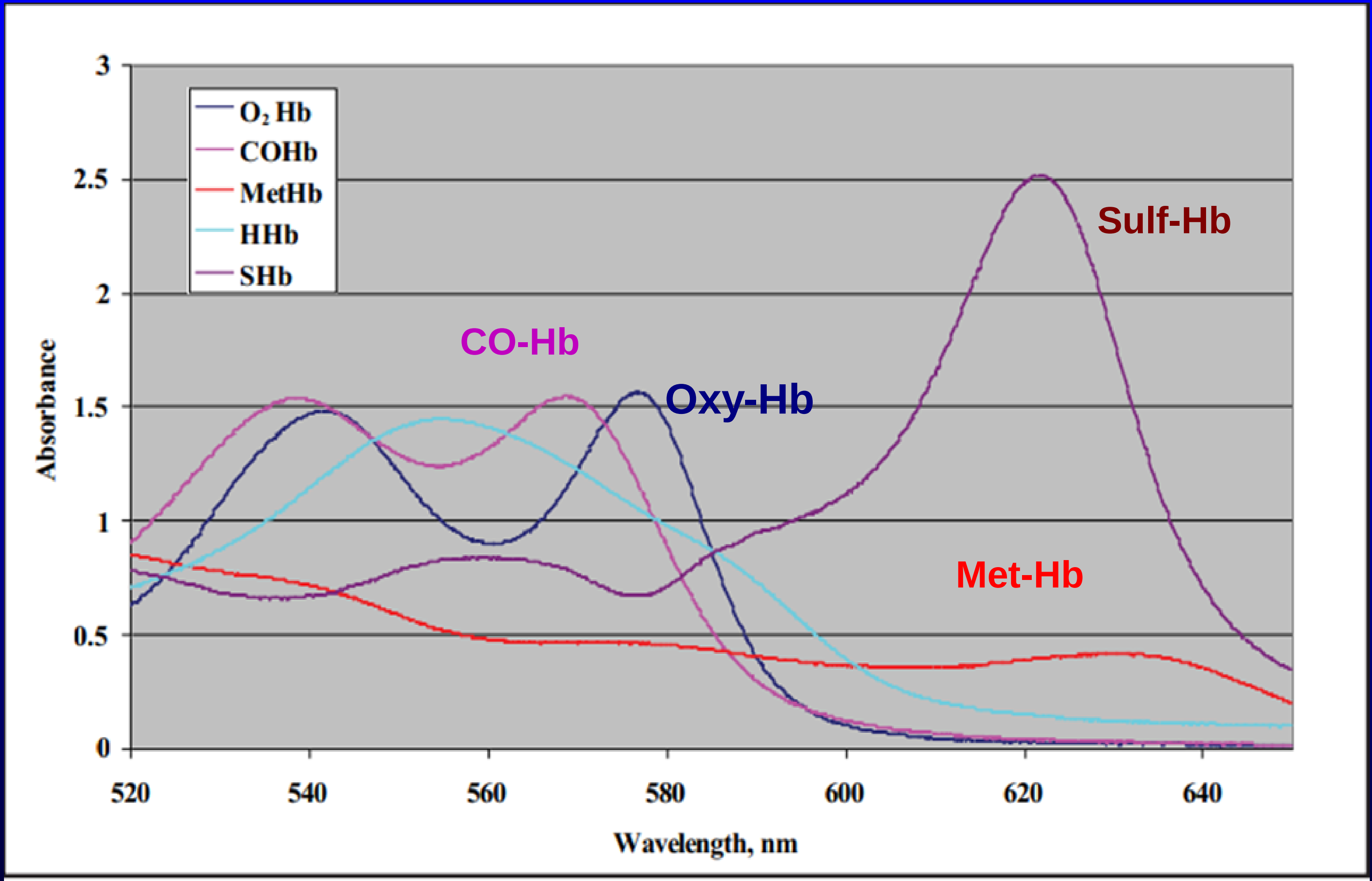
Duke BG Lab does about 1000 body fluid pH's / year.

Sulfhemoglobin (S-Hb): The 3rd and Forgotten Dyshemoglobin

- S-Hb is a rare hemoglobinopathy
  - Results from Sulfur binding irreversibly to Hb = non-functional Hb.
  - Caused by several medications: dapsone, sulfamexazole, sumatriptan, phenacetin, et al.
- Sulfhemoglobinopathy typically presents as cyanosis that is not improved by oxygen supplementation.
  - Symptoms can start to appear at [S-Hb] >5%

Absorption Spectra of Hb Derivatives

Sulf-Hb absorbs strongly over the wavelength ranges in cooximetry causing interference if not corrected



From: Pamidi P, Mansouri S, DeAbreau M, Kim D. Sulf-Hb detection and correction to cooximetry measurements on the GEM Premier 4000 critical care analyzer. Poster presented at AACC Annual Meeting July 2007; San Diego CA.

Sulf-Hb Detection and Correction

- S-Hb absorbs strongly over the wavelength ranges in cooximetry causing interference if not corrected:
  - Most modern blood gas/coox instruments detect S-Hb and attempt to correct other Hb results
  - S-Hb measured in “background” and not usually reported if less than 3% of total Hb.
  - From 3-10%, S-Hb is detected and reported and used to correct other Hb results.
    - Flags as “Corrected for Sulf-Hb”
  - Above 10%, S-Hb interference it too great
    - Flags as “Sulf-Hb interference detected”

Proper Collection of Blood Gas Specimens

- **Essentials:**
  - **Eliminate exposure to atmosphere or air bubbles.**
  - **Minimize cell metabolism**
  - **Analyze ASAP!**
- **Plastic syringes are permeable to oxygen.**
  - Markedly at cold temps: 0-4ºC
  - Slightly at cooler room temps: 20-24ºC
- **Cells metabolize O_2 and produce CO_2**
  - Faster at warmer temps
  - Longer handling time = more metabolism = greater changes

Stability of Blood Gases (mostly pO_2)

Handling of Blood Gas Specimens:

How long is too long?

- ***p*O_2 is the main concern**
  - Studies claim anywhere from immediate (10-15 min) to 40 min or longer:
- **Pneumatic tube transport can affect *p*O_2**
  - With agitation, even small air bubbles will affect ***p*O_2**
  - Cushioning of syringes in tube carrier will help
  - Magnitude of change depends on several factors
- **Cannot use vacutainers for blood gas specimens!!**
  - Plastic tubes produce CO from irradiation during manufacturing process.

Representative Changes in pO_2 for Various Leukocyte and Platelet Counts

WBC Count x 10^9/L	Original *p*O2 (mmHg)	Decrease in pO_2 (mmHg)	Time (min) at RT	Reference
55	130	-40	~30	Fox [4]
99	"	-62	~30	"
276	"	-95	30	"
490	"	-100	30	"
Normal range <11	88	-9	10	Chillar [6]

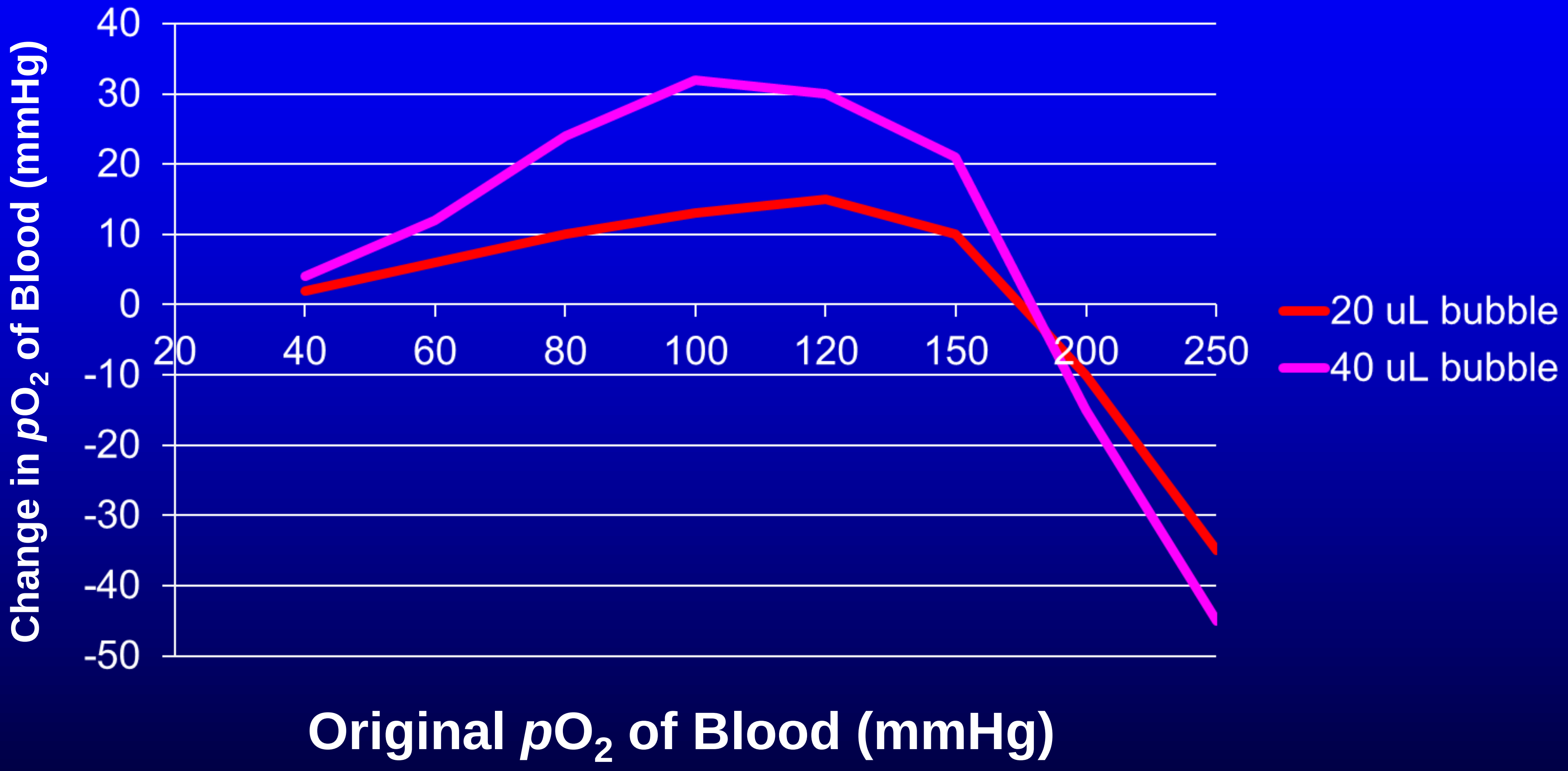
The frequency of elevated WBC counts above 50 x 10^9/L or platelet counts above 500 x 10^9/L was noted to be about 1% of patients at two major hospitals [7]. At another major medical center, for all samples with complete blood counts, 4.2% had WBC counts over 100 x 10^9 cells/L, and only about 0.2 % of samples had WBC counts between 50 and 100 x 10^9/L [8[JTP1]].

Pre-analytic Error: Trapped Air

- **Trapped air can significantly lower or raise pO_2 of blood sample** ($\%O_2$Hb and O_2 Content also affected).
- **Variables:**
  - **Volume of trapped air in syringe.**
  - **Agitation of syringe (pneumatic tube transport)**
  - **Number and size of air bubbles**
  - **Original pO_2 of sample**
  - **Original [Hb] and $\%O_2$Hb levels:**
    - **Oxygen buffering by Hb = less effect at low $\%O_2$Hb levels**
    - **Greater effect at lower Hb levels**

Pneumatic Tube Transport:

Changes in Blood pO_2 with 20 uL and 40 uL Air Bubbles Added to 1 mL Blood



Toffaletti JG, McDonnell EH. Effect of small air bubbles on changes in blood pO_2 and blood gas parameters: calculated vs measured effects. Website: http://acutecaretesting.org; July 2012.

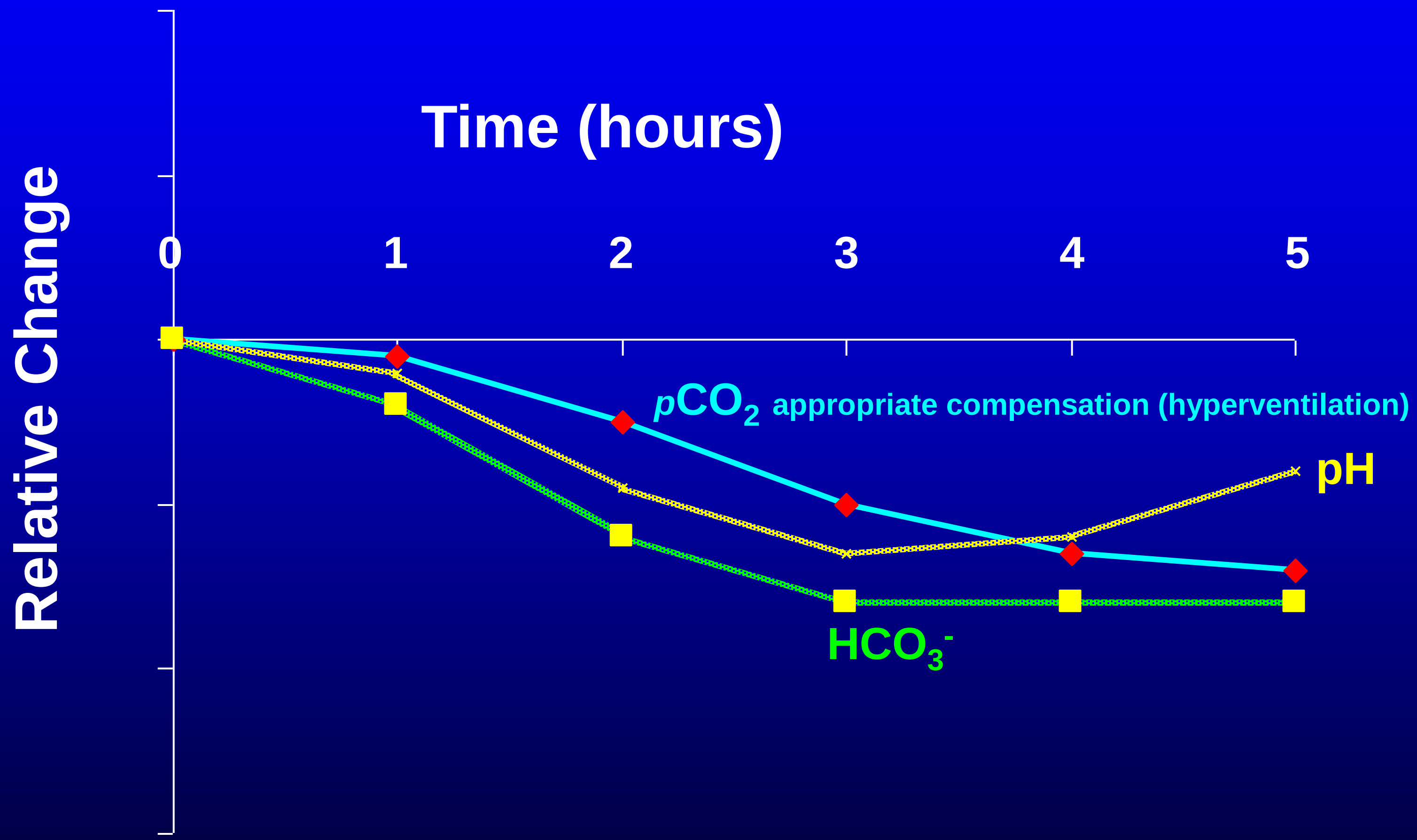
Minimizing Agitation of Blood in Syringes during Pneumatic Transport

That’s All Folks!

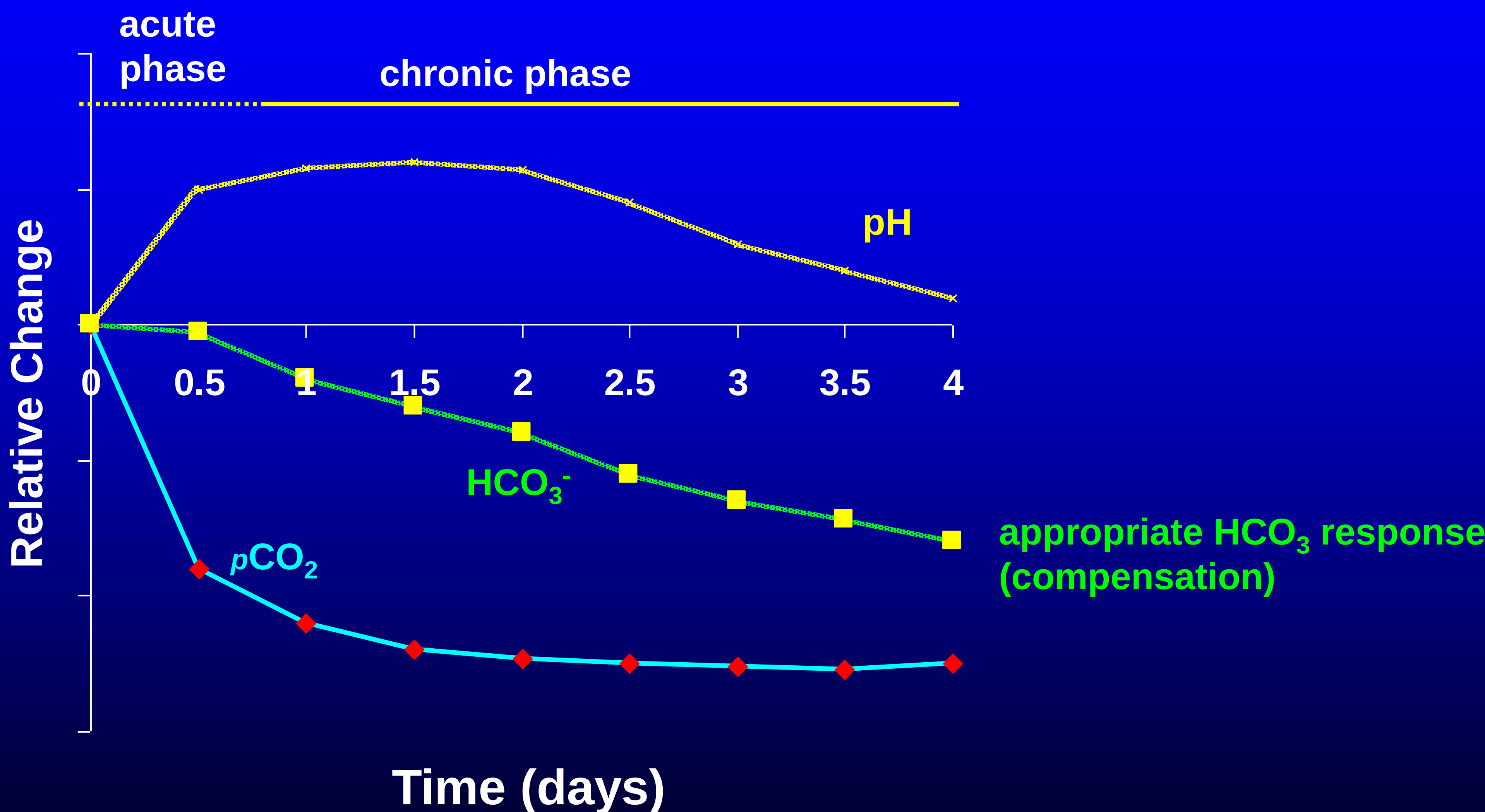
Compensation in Acid-Base Disorders

- The compensation response attempts to restore the ratio of HCO_3^- / pCO_2 to normal (~0.60).
- Appropriate compensation is time-dependent:
  - a metabolic pH disorder activates a fast respiratory response (pCO_2) or
  - a respiratory pH disorder activates a slow metabolic (renal) response (HCO_3^-).
- Compensation ceases as pH is restored (or close) to normal.

Appropriate pCO_2 and pH Responses in Metabolic Acidosis (decreased HCO_3)



Appropriate HCO_3 and pH Responses in Respiratory Alkalosis (decreased pCO_2)



Factors that Affect Changes in pO_2 in blood after collection:

- • The initial pO_2 of the blood (section 2.3.4)
- • The Hb concentration and O2 saturation, as related to the oxygen buffering capacity of Hb (section 1.3.1.9).
- • Exposure of blood to air (section 2.3.4)
- • Agitation of the specimen, as with pneumatic tube transport (Section 2.3.4)
- • The temperature of blood in storage
- • The time delay from collection to analysis (section 2.5.4)
- • Concentrations of leukocytes and platelets, and the types of leukocytes (section 2.3.6)
- • Collection container:
- Plastic syringe; glass syringe; evacuated tube
- The permeability of syringes to oxygen (section 2.5.1): type of plastic, wall thickness, and syringe geometry that affect permeability to oxygen: surface area of syringe to volume of blood in syringe. {148} {151} {152} {153} (As noted, glass syringes are impermeable to gases).