Evolution of Blood Gas Analysis - Focusing on the Source of Impaired O_2 Supply to the Tissue

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Agenda

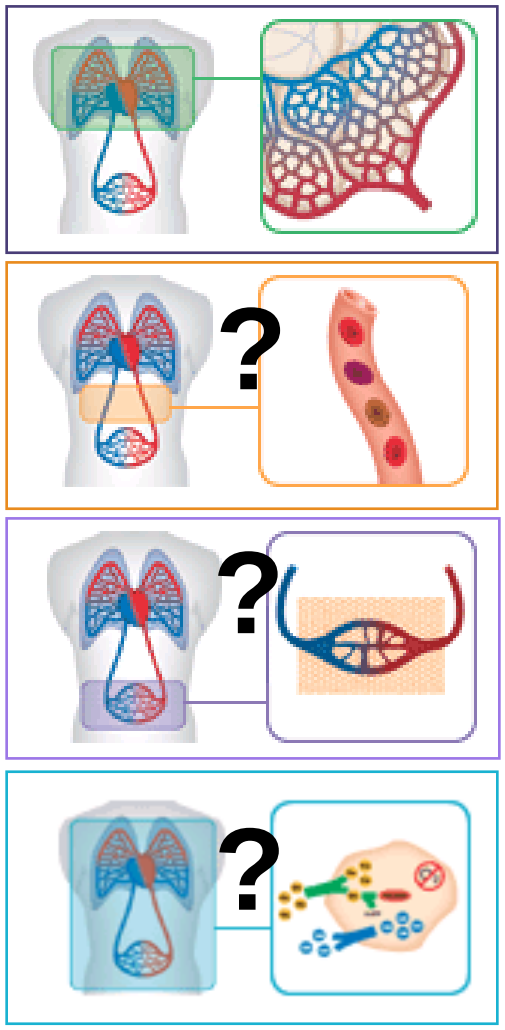
Part 1

- Why measure blood gases
- Overview of acid-base disturbances
- Use of the Acid- Base Chart

Part 2 (Today)

- Full value of the pO_2 assessment via
  - Oxygen uptake, Oxygen transport, Oxygen release
- Why a measured saturation is the best
- Assessment of tissue perfusion - Lactate

The traditional picture



Oxygen uptake

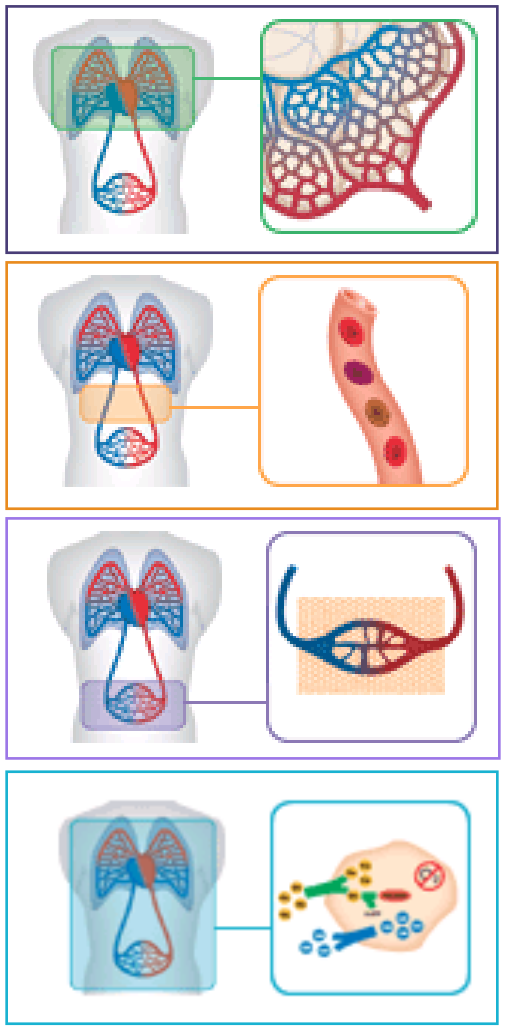
Oxygen transport

Oxygen release

Tissue oxygenation

- Traditionally, $pO_2(a)$ has been the sole parameter used for evaluation of patient oxygen status

The traditional picture



Oxygen uptake

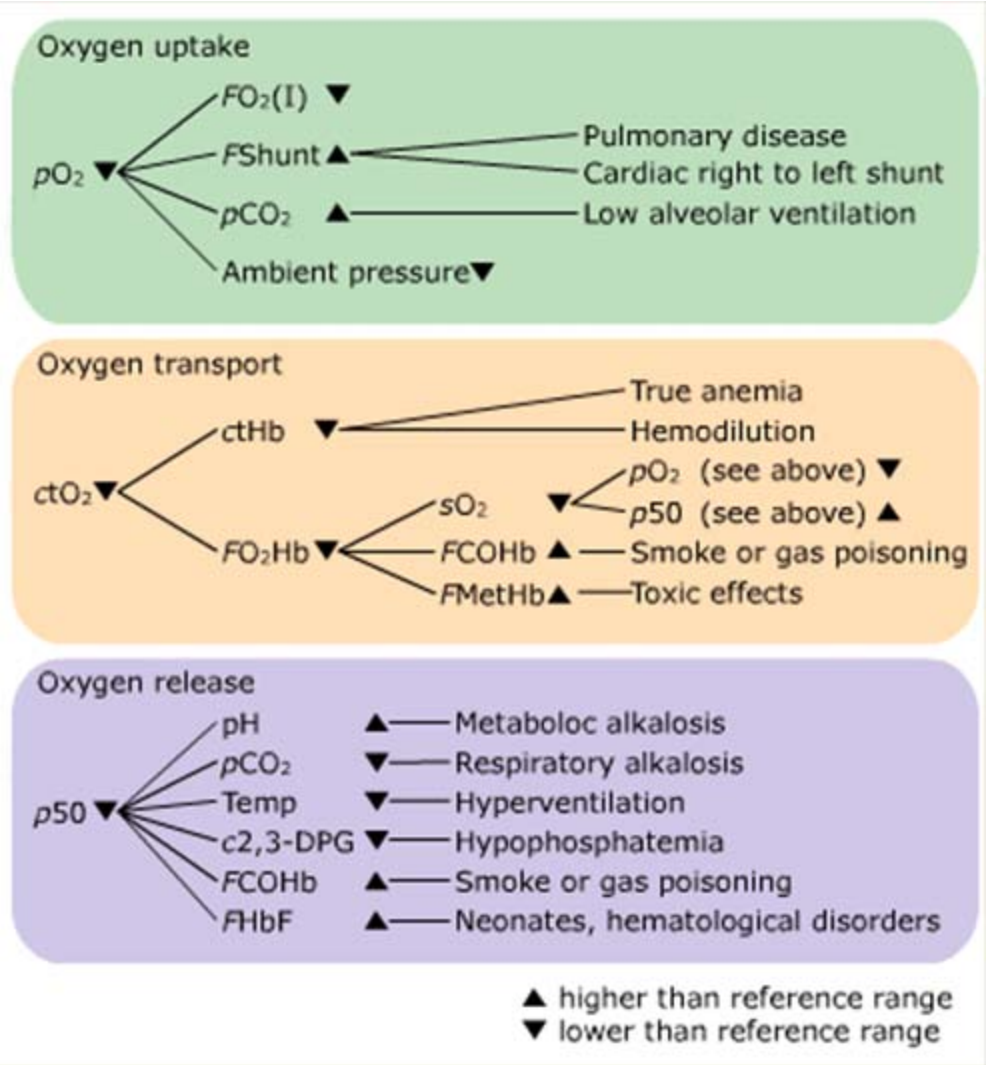
Oxygen transport

Oxygen release

Tissue oxygenation

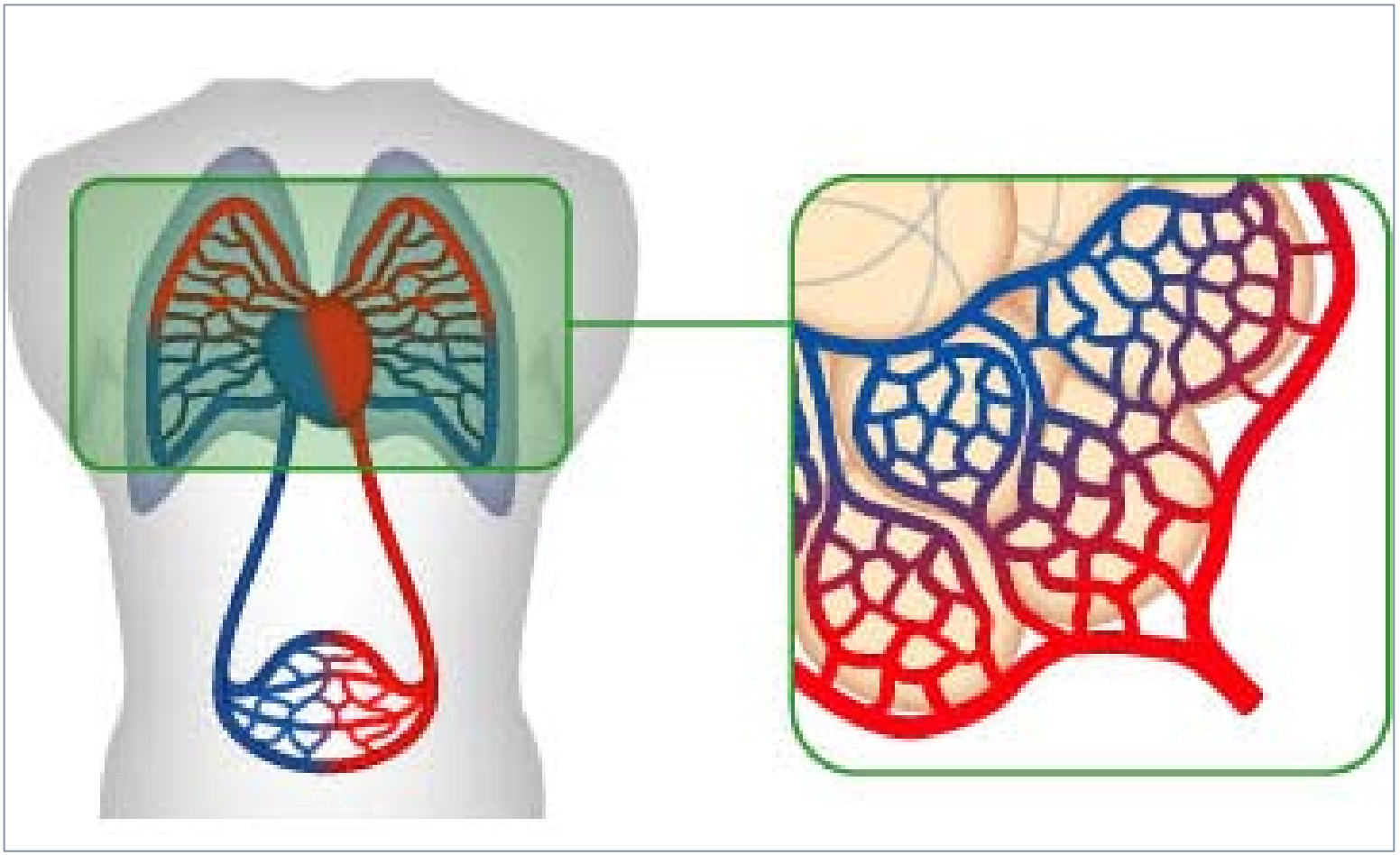
- Traditionally, $pO_2(a)$ has been the sole parameter used for evaluation of patient oxygen status
- For a complete evaluation of the oxygen status, it is necessary to consider lactate and all parameters involved in oxygen uptake, transport, and release

Example of a flowchart

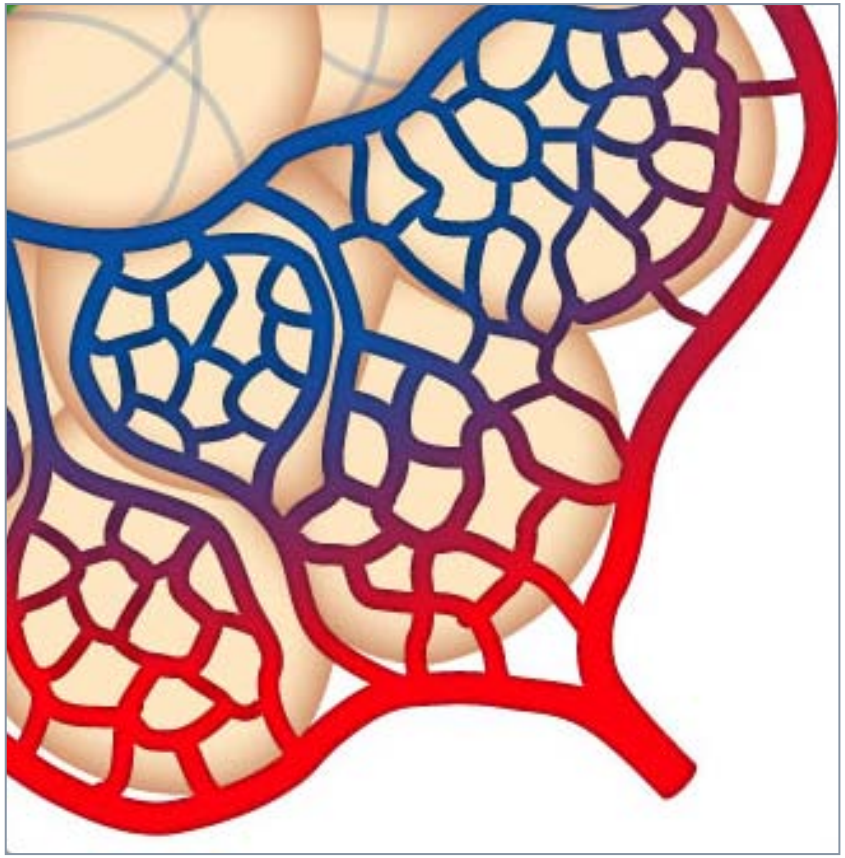


[Adapted from different textbooks and Siggaard-Andersen, O et al. Oxygen status of arterial and mixed venous blood. Crit Care Med. 1995 Jul;23(7):1284-93.

Phase one: Oxygen uptake

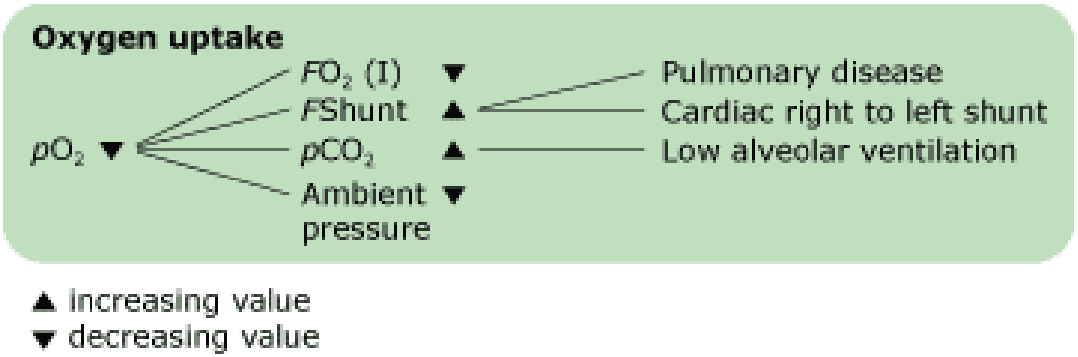


pO_2(a) – the key parameter



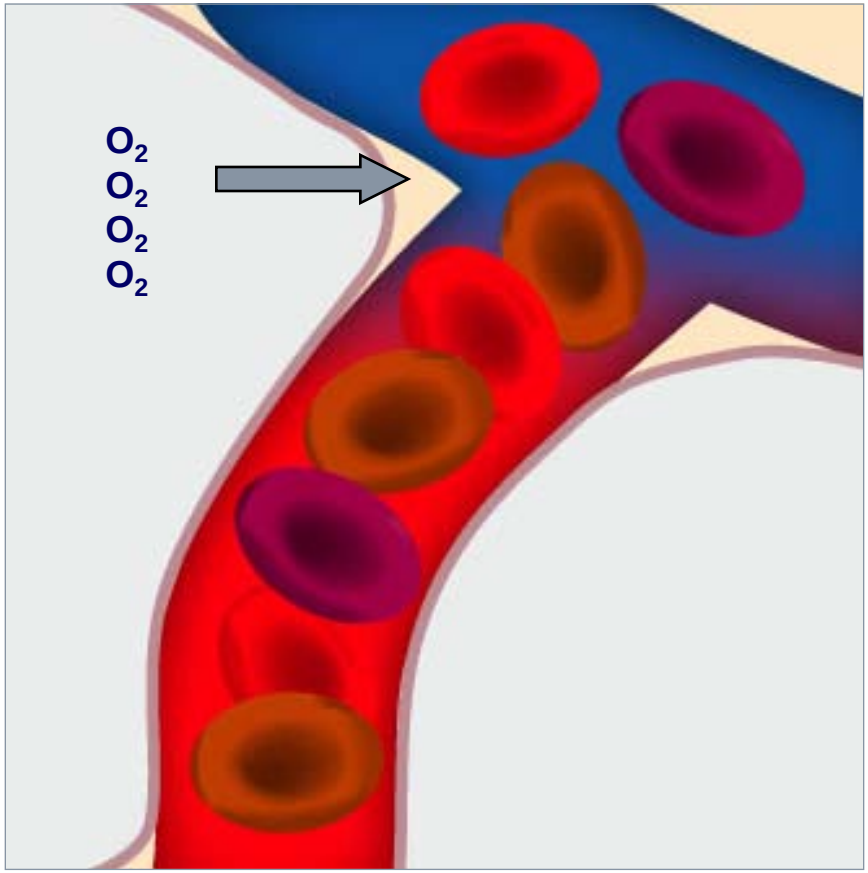
- pO_2(a) is the key parameter for evaluation of oxygen uptake in the lung
- When the pO_2(a) is low, the supply of oxygen to cells might be compromised

Conditions affecting pO_2(a)



- The amount of oxygen ***FO*$_2$(I)** available
- The degree of intra- and extrapulmonary shunting ***F*Shunt**
- Hypercapnia, high blood ***p*CO$_2$**
- The ambient pressure ***p*(amp)**

FO_2(I) – fraction of inspired oxygen



- Oxygen diffuses from the alveoli into the blood
- The higher the oxygen content of the air, the higher pO_2(a)
- Breathing room air equals an FO_2(I) of 21 %
- A patient breathing supplemental oxygen may have a pO2(a) as high as 400 mmHg (and the oxygen saturation is normal)

Evaluation of PO_2 in Adult, Neonatal, and Geriatric Patients Breathing Room Air

Arterial PO_2 (mmHg)	Condition
above 80	Normal for adult ($\leq$ 60 y)
above 70	*Adequate for age $\geq$ 70 y*
above 60	*Adequate for age $\geq$ 80 y*
50 to 75	Normal neonatal at 5 min
60 to 90	Normal neonatal at 1-5 days
40 to 60/70/80	*Moderate to mild hypoxemia*
below 40	Severe hypoxemia

Evaluating Arterial Oxygenation in Patients Breathing O_2-Enriched Air

$FI\text{-}O_2$ (%)	Lowest Acceptable PO_2 (mmHg)
30	150
40	200
50	250
80	400
100	500

Patients with a lower PO_2 may be assumed to be hypoxic on room air.

Estimated FI-O_2 of Air When Breathing 100% Oxygen from Nasal Cannula

Rough estimate:

For each L/min of oxygen flow, add 4% to the estimated FI-O_2 of air in the room, usually 21%.

Example: What is the estimated FIO_2 of the air being inhaled by a person receiving 2 L/min oxygen from a nasal cannula?

Goals of Oxygen Therapy

- Treat hypoxemia
- Decrease work of breathing
  - Hyperventilation typical response to hypoxemia.
- Decrease myocardial work
  - Increased cardiac output is a mechanism to compensate for hypoxemia.

*F*Shunt

FShunt is the fraction of venous blood not oxygenated when passing the pulmonary capillaries

Examples of different types of shunt

Intrapulmonary respiratory shunt:

- Also called ventilation-perfusion disturbance
- Incomplete oxygenation in lung
- Lung diseases with inflammation or edema that causes the membranes to thicken

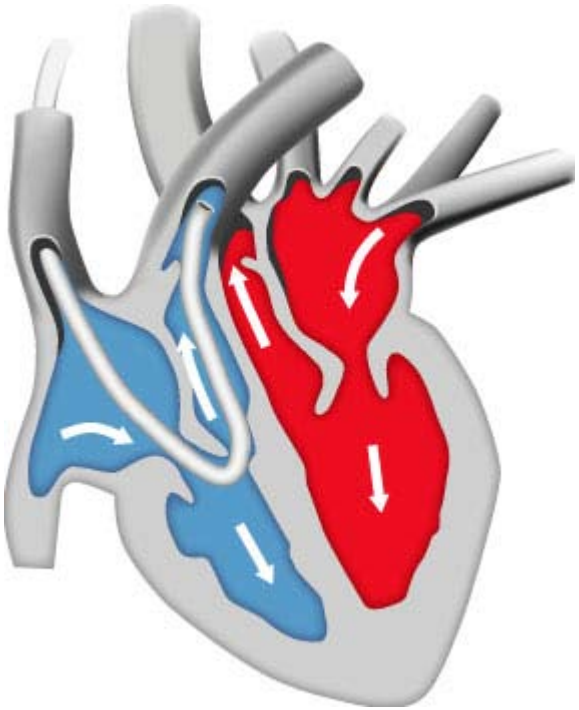
Intrapulmonary circulatory shunt:

- Incomplete oxygenation in lung
- Insufficient blood perfusion of the lungs

Cardiac shunt:

- By some called true shunt
- Heart defects allowing venous blood from left chamber of heart to enter right chamber

*F*Shunt – measured vs calculated



- Shunt is calculated with values from simultaneously drawn arterial and mixed venous samples
  - The mixed venous sample must be drawn from the pulmonary artery, as indicated in the illustration
- A simpler and faster way to estimate *F*Shunt is from a single arterial sample
  - Assuming that the arterio-venous difference is normal, i.e. extraction of 5.1 mL O_2 per dL blood

Hypercapnia, high pCO_2

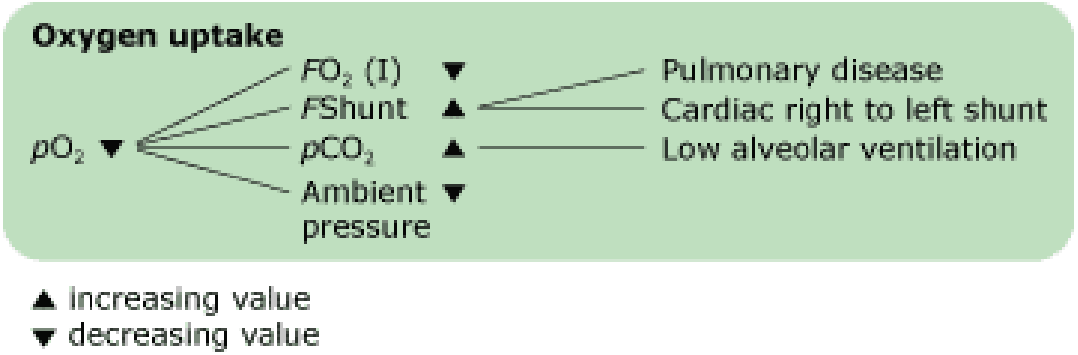
- Strong hypercapnia significantly decreases alveolar pO_2, a condition known as hypoventilatory hypoxemia

- The hypoxemia develops because the alveolar gas equation dictates a fall in pO_2(a);

$$pO_2(A) = pO_2(air) - pCO_2(A)/RQ$$

- At any given barometric pressure, any increase in alveolar pCO_2 (caused by hypoventilation) leads to a fall in alveolar pO_2 and therefore also in arterial pO_2

Oxygen uptake – a recap



- The amount of oxygen ***FO*$_2$(I)** available
- The degree of intra- and extrapulmonary shunting ***F*Shunt**
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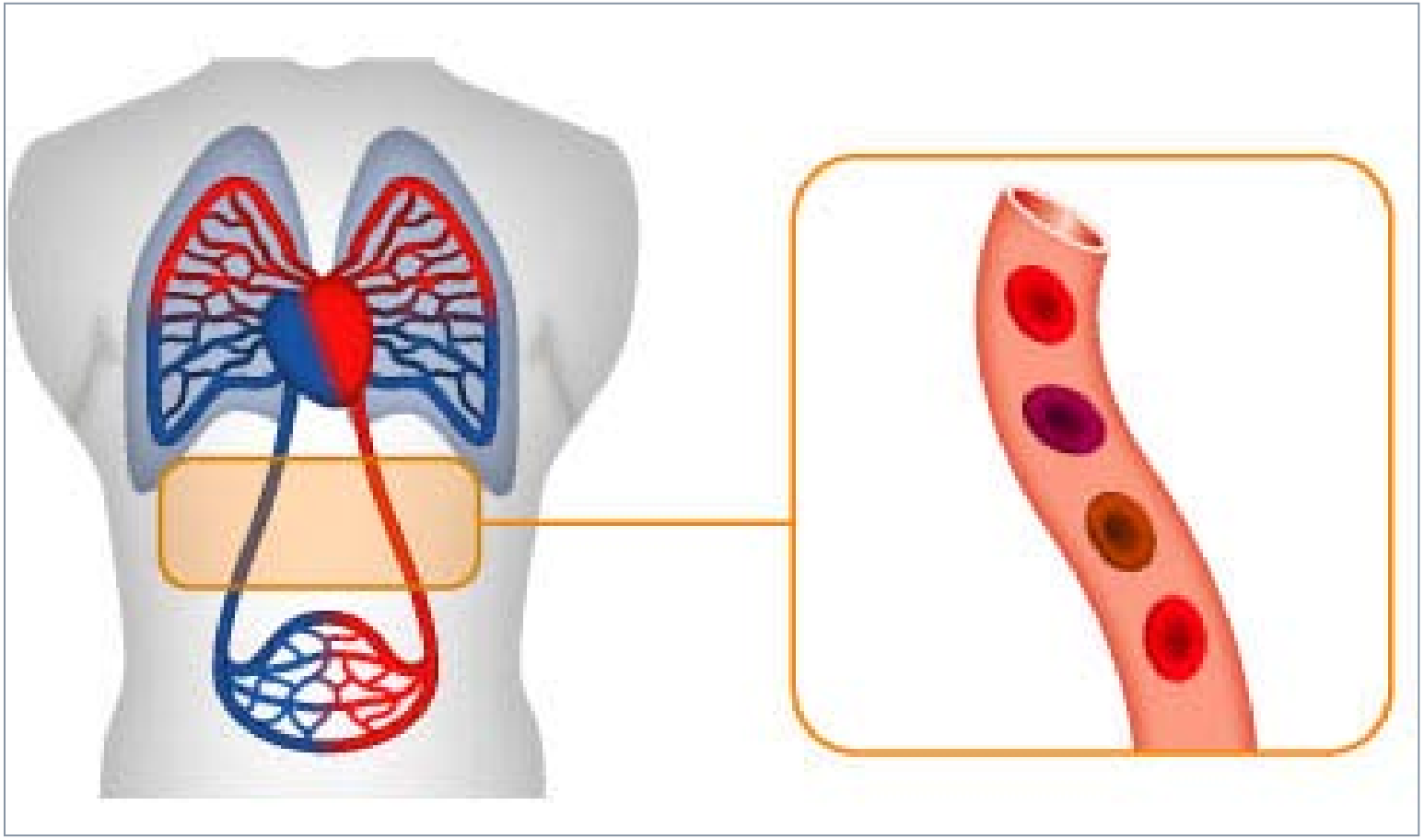
- The ambient pressure ***p*(amp)**

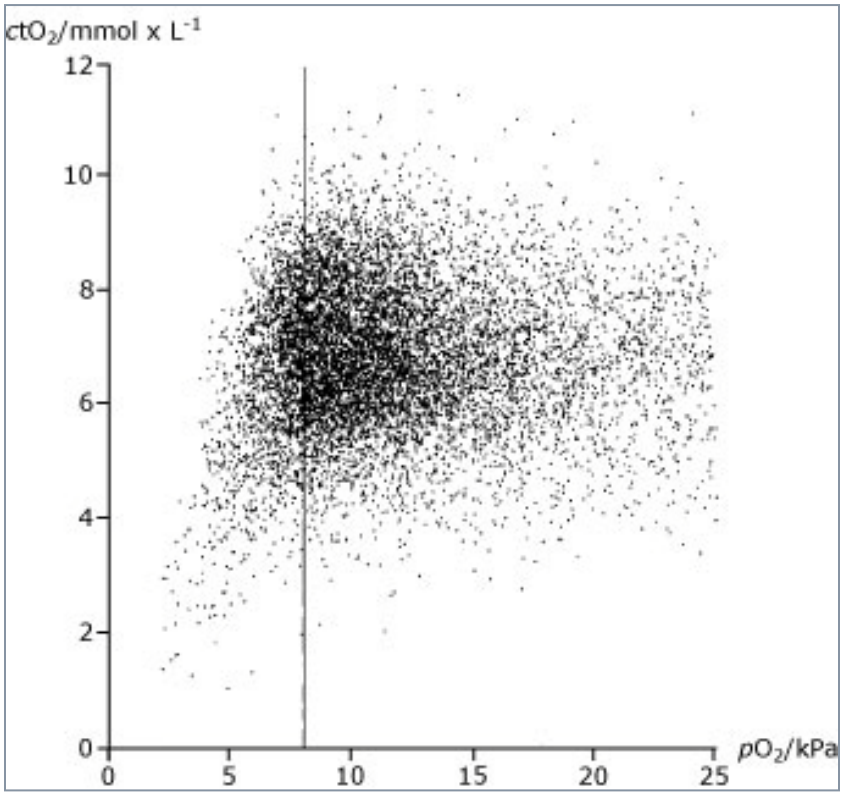
Phase two: Oxygen transport



ctO_2 – the key parameter

- Oxygen content, ctO_2 is the key parameter for evaluating the capacity for oxygen transport
- When ctO_2 is low, the oxygen delivery to the tissue cells may be compromised

Does ctO_2/pO_2 correlate?



- A multicenter study on 10079 blood samples [1]
- ctO_2/pO_2 correlation unpredictable
- ctO_2 is almost independent of pO_2, so full information is needed
- E.g. pO_2 of 60 mmHg (8 kPa) corresponds to a ctO_2 of 4.8 – 24.2 mL/dL

[1] Gøthgen IH et al. Variations in the hemoglobin-oxygen dissociation curve in 10079 arterial blood samples. Scand J Clin Lab Invest 1990; 50, Suppl. 203:87-90

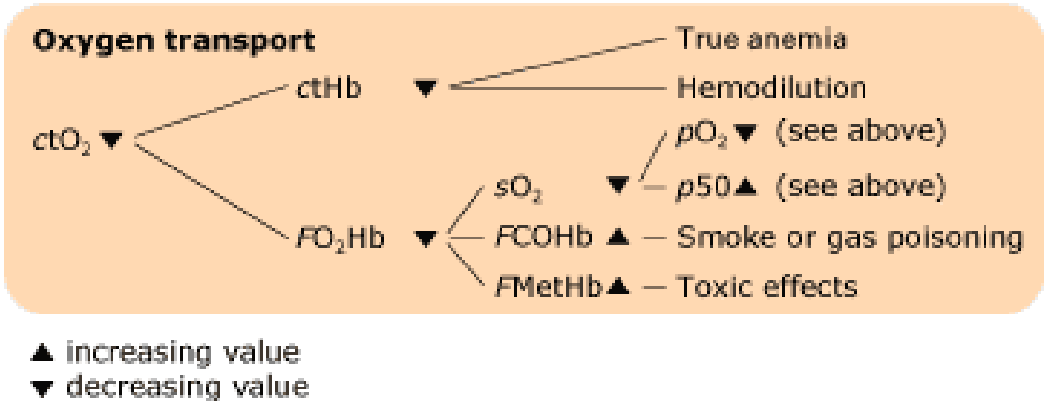
Oxygen content

- The blood's oxygen content, ctO_2, is the sum of
  - Oxygen bound to hemoglobin and
  - Physically dissolved oxygen
- 98% of oxygen is carried by hemoglobin
- The remaining 2% is dissolved in a gas form
- ctO_2 normal range 18.8-22.3 mL/dL

$$ctO_2 = sO_2 \times ctHb \times (1 - FCOHb - FMetHb) + \alpha O_2 \times pO_2$$

α is the solubility coefficient of oxygen in blood

Conditions affecting ctO_2

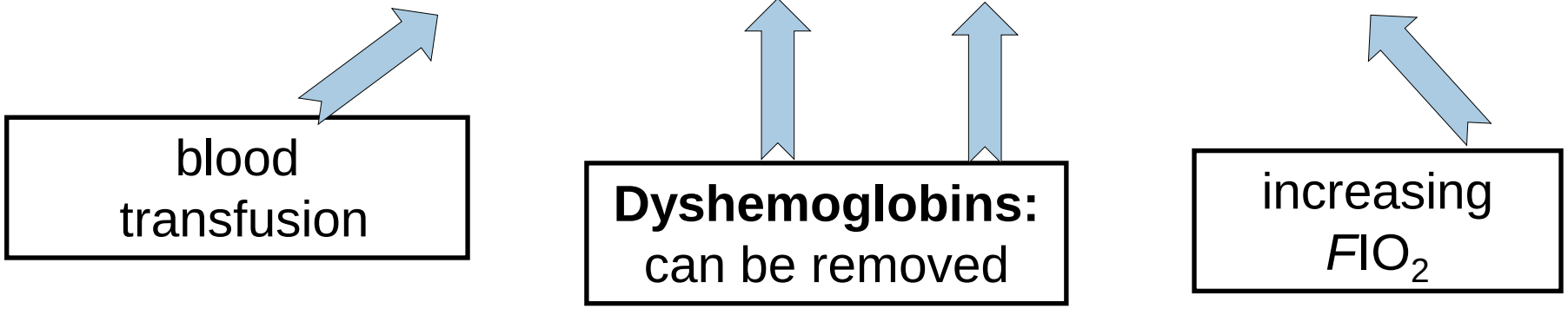


- The concentration of hemoglobin ***ctHb***
- The fraction of oxygenated hemoglobin ***F*O_2Hb**
- The arterial oxygen saturation **sO_2**
- The presence of dyshemoglobins ***F*COHb** and ***F*MetHb**

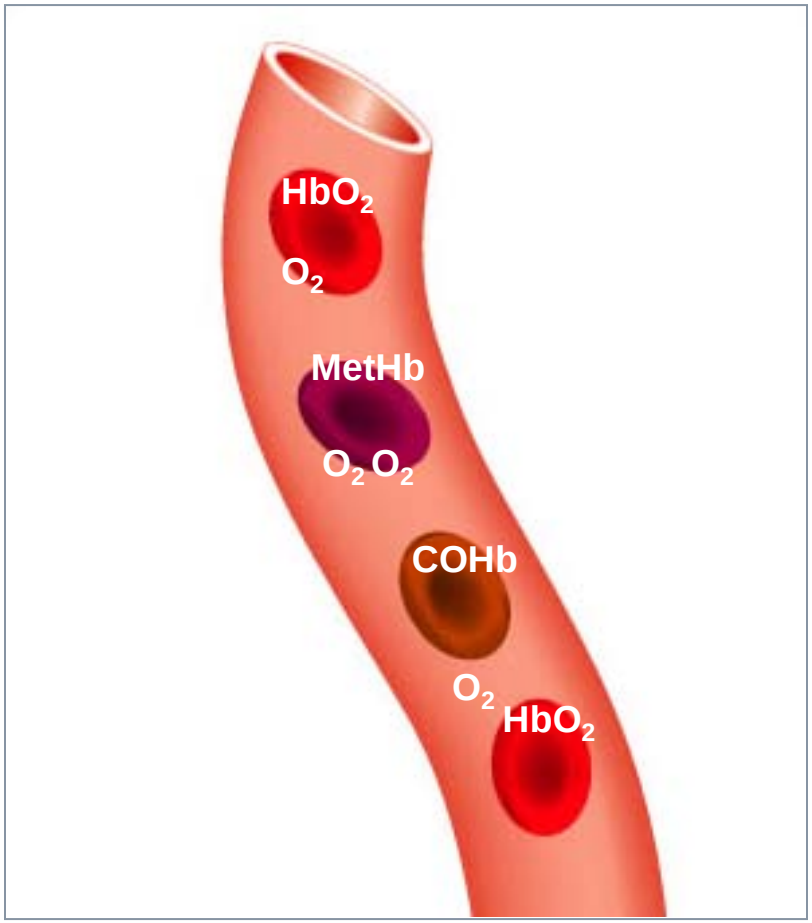
Improving ctO_2

- The oxygen content can be improved by the variable factors in the equation

$$ctO_2 = sO_2 \times ctHb \times (1 - FCOHb - FMetHb) + \alpha O_2 \times pO_2$$



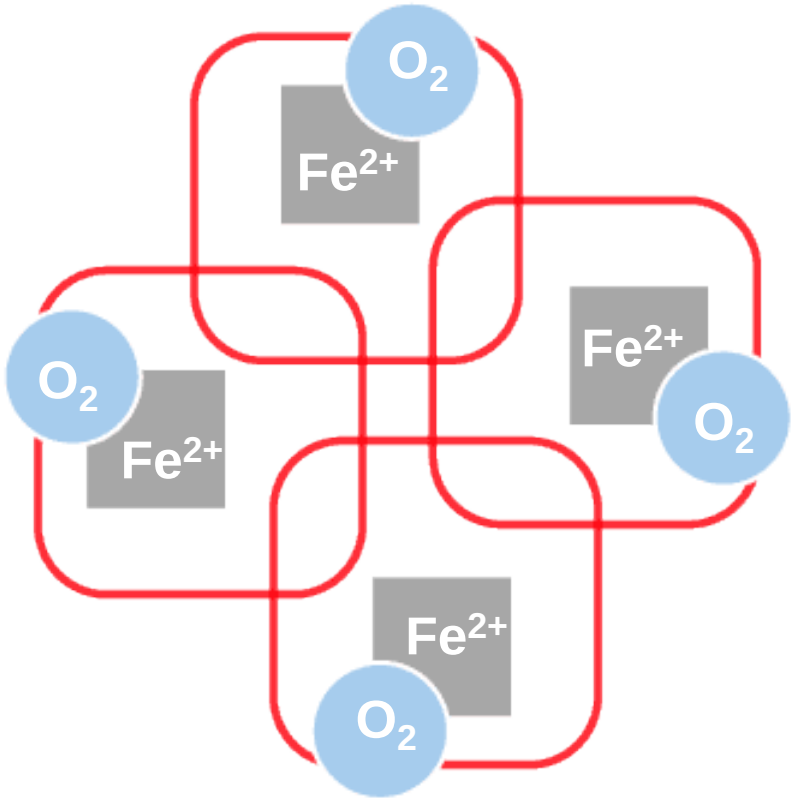
Types of hemoglobin



tHb	Total hemoglobin
HHb	Reduced hemoglobin
O_2Hb	Oxyhemoglobin
COHb	Carboxyhemoglobin
MetHb	Methemoglobin

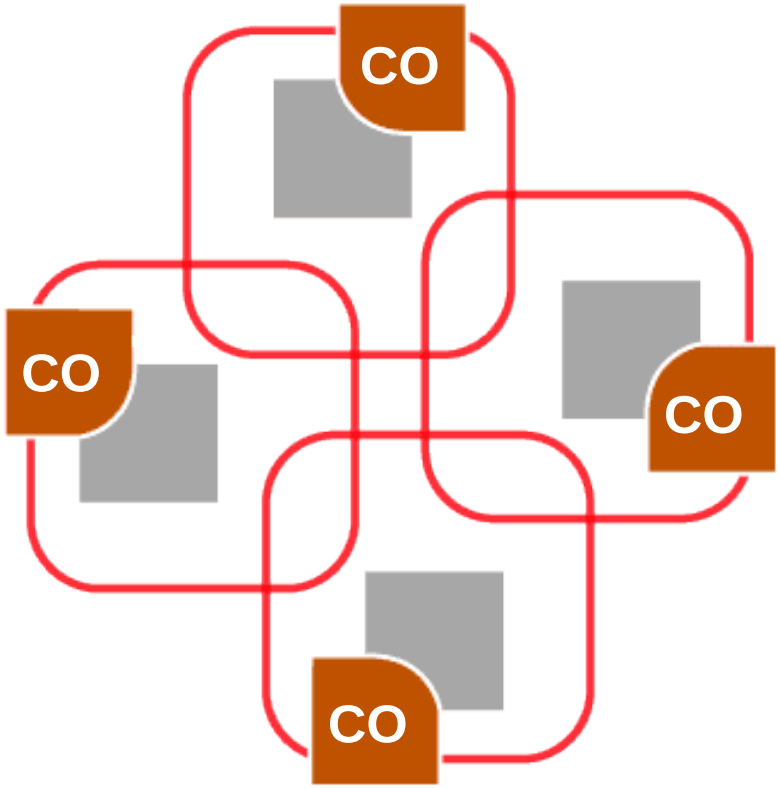
- tHb is defined as the sum of $HHb + O_2Hb + COHb + MetHb$
- COHb and MetHb are called dyshemoglobins because they are incapable of oxygen transport

Hemoglobin



- Hemoglobin consists of 4 identical subunits
- Each subunit contains an iron atom, Fe^{2+}
- Each iron can bind to one oxygen molecule, O_2
- Oxygen binding is cooperative
- Typical reference range is 12-17 g/dL

Carboxyhemoglobin



- Causes of raised COHb:
  - Increased endogeneous production of CO
  - Breathing air polluted with CO (carbon-monooixde poisoining)
- CO's affinity to Hb is 210 times higher than that of O_2
- The blood turns cherry-red, but is not always evident
- COHb is normally less than 1-2 % but in heavy smokers up to 10 %

Endogeneous increase in COHb

- Hemolytic condition leads to heme catabolism and thus increased production of CO [1]
- Hemolysis induced increase in COHb can be up to 4 % but 8.3 % is also reported [2]
- Slight increase in COHb is also a feature of a inflammatory disease, and is thus also seen in critically ill patients [3]

[1] Higgins C. Causes and clinical significance of increased carboxyheomoglobin. www.acutecaretesting.org . Oct 2005.
[2] Necheles T, Rai U, Valaes T. The role of hemolysis in neonatal hyperbilirubinemia as reflected in carboxyhemoglobin values. Acta Paediatr Scand. 1976; 65: 361-67
[3] Morimatsu H, Takahashi T, Maeshima K et al. Increased heme catabolism in critically ill patients: Correlation among exhaled carbon monoxide, arterial carboxyhemoglobin and serum bilirubin IX {alpha} concentrations. Am J Physiol Lung Cell Mol Physiol. (EPub) 2005 Aug 12th doi:/0.1152/ajplung.00031.2005

COHb intoxication

- COHb intoxication may be deliberate or accidential
- In the US is accounts for 40,000 ED visits and between 5 and 6,000 death a year (2004) [1]
- Sources of CO – common [2]
  - Fire, motor-vehicle exhaust and faulty domestic heating systems
  - Less commonly, gas ovens, paraffin (kerosene) heaters and even charcoal briquettes

[1] Kao L. Nanagas K. Carbon monoxide poisoning. Emerg Clin N Amer 2004; 22: 985-1018
[2] Higgins C. Causes and clinical significance of increased carboxyheomoglobin. www.acutecaretesting.org . Oct 2005.

Relationship COHb

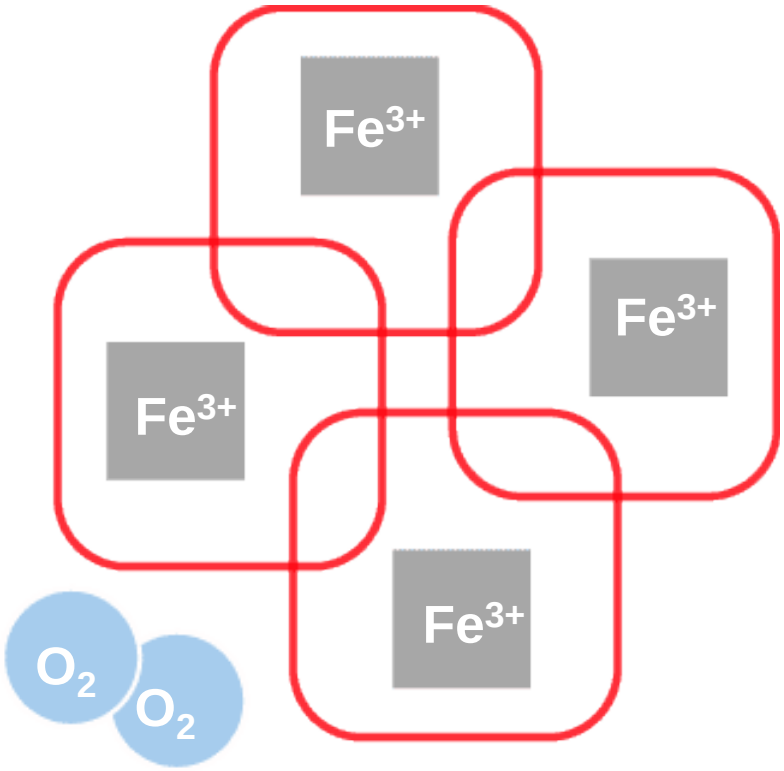
CO conc. in inspired air (ppm)	COHb in blood %	Examples of typical symptoms
70	10	No appreciable effect except shortness of breath on vigorous exertion, possible tightness across forehead
120	20	Shortness of breath on moderate exertion, occasional headache
220	30	Headache, easily fatigued, judgement disturbed, dizziness, dimness of vision
350-520	40-50	Headache, confusion, fainting, collapse
800-1200	60-70	Unconsciousness, convulsions, respiratory failure, death if exposure continues
1950	80	Immediately fatal

[1] Higgins C. Causes and clinical significance of increased carboxyheomoglobin. www.acutecaretesting.org . Oct 2005.

Clinical cases - Carboxyhemoglobin

Read three interesting case stories in ”Causes and clinical significance of increased carboxyheomoglobin” by Chris Higgins on www.acutecaretesting.org

Methemoglobin



- Methemoglobin is formed when blood is exposed to oxidizing agents, oxidizing the iron atom: $Fe^{2+} \Rightarrow Fe^{3+}$
- MetHb has a very low affinity to O_2
- The blood typically turns dark brown

Causes for increased methemoglobin

- Inherited – very seldom
- Acquired – more frequent
- Acquired methemoglobinemia occurs when hemoglobin is oxidized in a rate faster by which methemopglobin is reduced
- Drugs or toxins that may cause methemoglobinemia
  - Acetanilide, p-aminosalicylic acid, amyl nitrate, aniline, benzocaine, cetacaine, chloroquinone, clorfazimine, dapsone, hydroxylamine, isobutyl nitrite, lidocaine, mafenide acetate, menadione, metoclopramide, naphthoquinone, nitric oxide, nitrobezene, nitroethane, nitrofurane, nitroglycerin, nitroprusside, paraquat, phenacitin, phenazopyridine, prilocaine, primaquine, resorcinol, silver nitrate, sodium nitrate, sodium nitrite, sodium valproate, sulphonamide anitibiotics, trinitrotoluene

[1] Higgins C. Methemoglobin. www.acutecaretesting.org . Oct 2006.

Effect of MetHb

MetHb in blood %	Examples of typical symptoms
2-10	Is typically well tolerated and, in an otherwise healthy individual, is asymptomatic
10-15	Typically first sign of tissue hypoxia is cyanosis with skin taking on a classically blue/slate gray appearance. Symptoms: more profound hypoxia, including increased heart rate, headache, dizziness and anxiety, accompany deepening cyanosis as methemoglobin rises above 20 %.
>50	May be associated with increasing breathlessness and fatigue. Confusion, drowsiness and coma Methemoglobin
>70	May be fatal

Symptoms of methemoglobinemia are generally more severe in a patient who has some pre-existing condition (e.g. anemia, respiratory or cardiovascular disease) that compromises oxygenation of tissues.

[1] Higgins C. Methemoglobin. www.acutecaretesting.org . Oct 2006.

Clinical cases - Methemoglobin

Read three interesting case stories in ”Methemoglobin” by Chris Higgins on www.acutecaretesting.org

Case

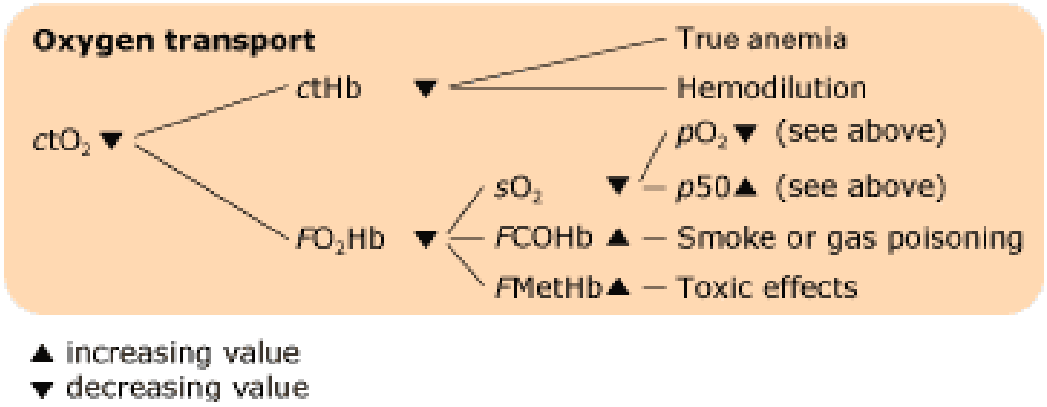
- A 84-year-old man had undergone a left hemicolectomy for bowel torsion. After 10 days he became hypotensive, tachypneic, oliguric, progressively acidotic, and anemic. Also, the patient had passed bloody stools
- *c*tO_2 normal range: 18.8-22.3 mL/dL

1) With a *F*O_2(I) of 0.6 a blood sample showed
   - pH = 7.25
   - *p*CO_2 = 29 mmHg
   - *p*O_2 = 169 mmHg
   - **ctHb = 4.2 g/dL**
   - *s*O_2 = 98 %
   - **ctO$_2$ = 6.08 mL/dL**

2) After bicarbonate and blood had been administered i.v.
   - pH = 7.35
   - *p*CO2 = 24 mmHg
   - *p*O2 = 169 mmHg
   - **ctHb = 7.8 g/dL**
   - *s*O2 = 98 %
   - **ctO2 = 10.8 mL/dL**

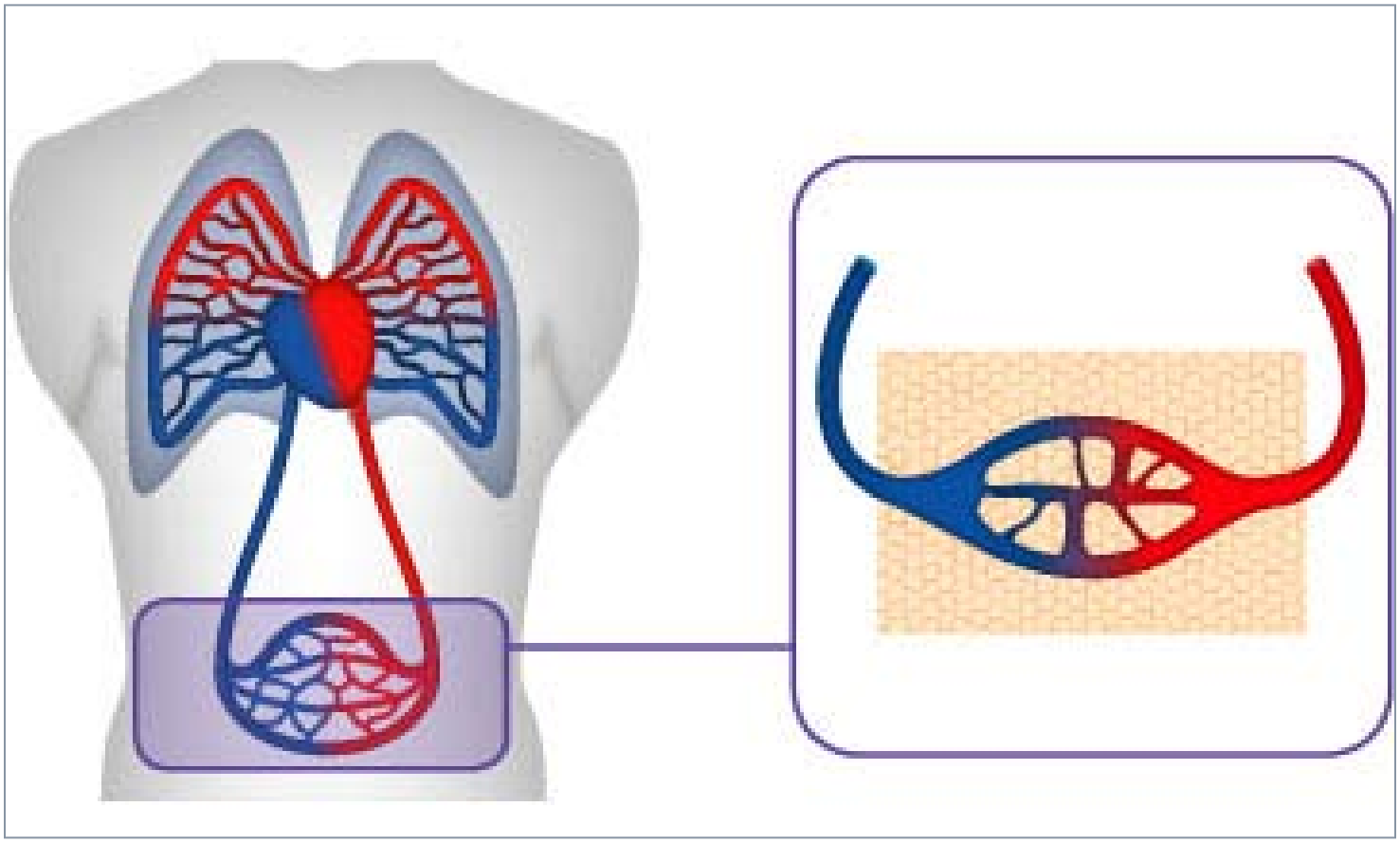
This case is not a real life case – it is made for illustration purposes only

Oxygen transport – a recap

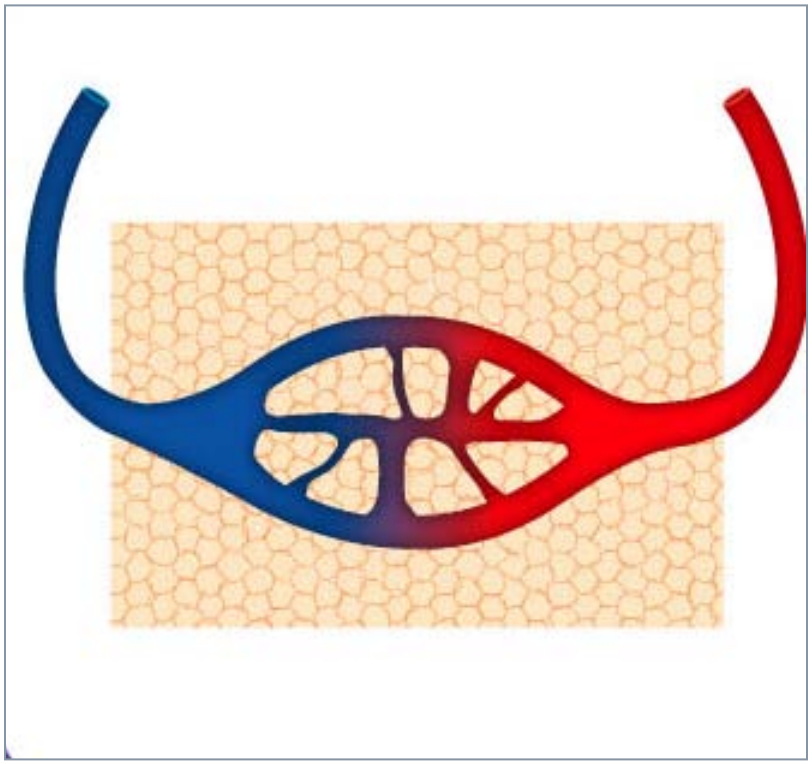


- The concentration of hemoglobin ***ctHb***
- The fraction of oxygenated hemoglobin ***F*O$_2$Hb**
- The arterial oxygen saturation **sO$_2$**
- The presence of dyshemoglobins ***F*COHb** and ***F*MetHb**

Phase three: Oxygen release

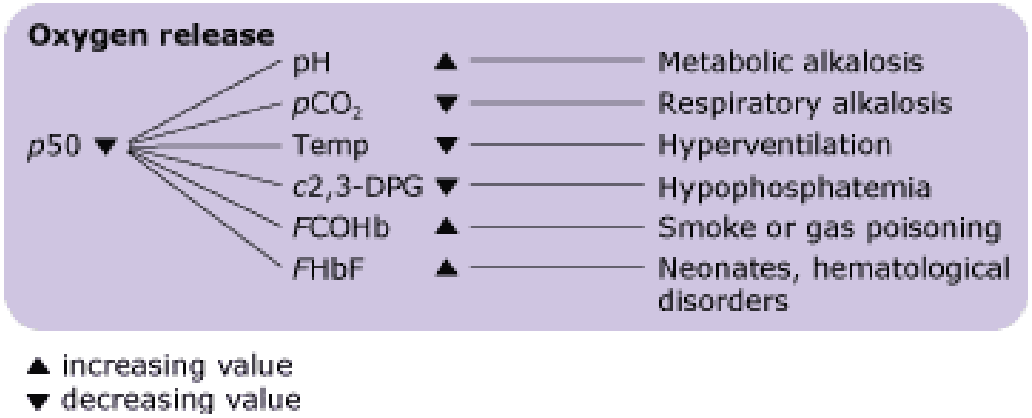


Conditions affecting release



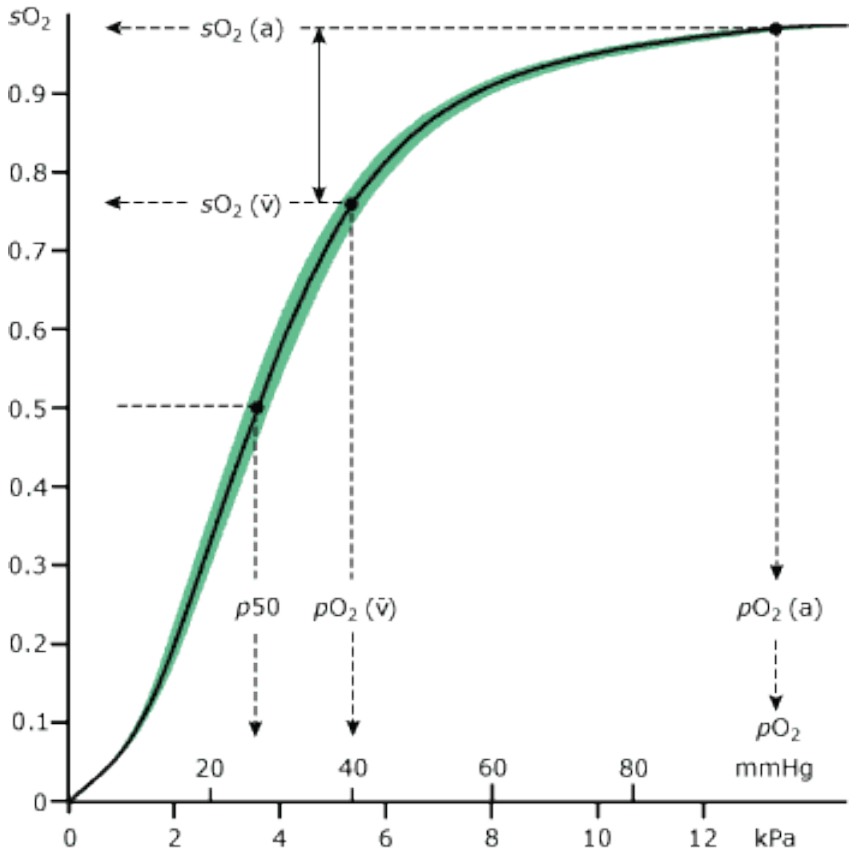
- Oxygen release depends primarily on:
- The arterial and end-capillary oxygen tensions and ctO_2
- The hemoglobin-oxygen affinity expressed by the *p*50 value
- *p*50 is the key parameter for evaluation of oxygen release from hemoglobin

Conditions affecting *p*50



- The hemoglobin-oxygen affinity is expressed by the oxygen dissociation curve (ODC), the position of which is expressed by the ***p*50** value
- As illustrated in the flowchart, several conditions can affect the *p*50 value

*p*50 and the ODC curve

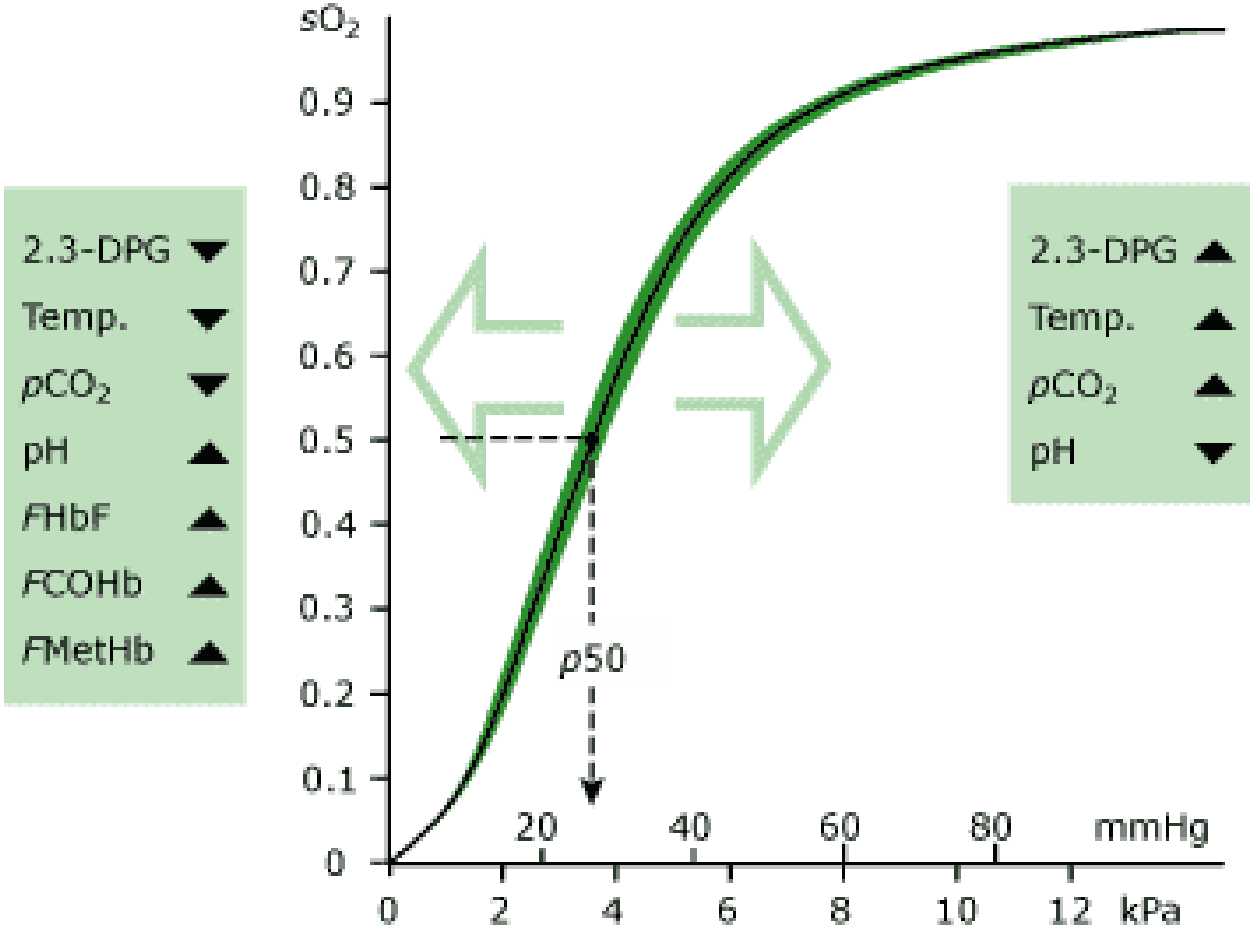


The *p*50 is the oxygen tension at half saturation (sO_2 = 50 %) and reflects the affinity of hemoglobin for oxygen

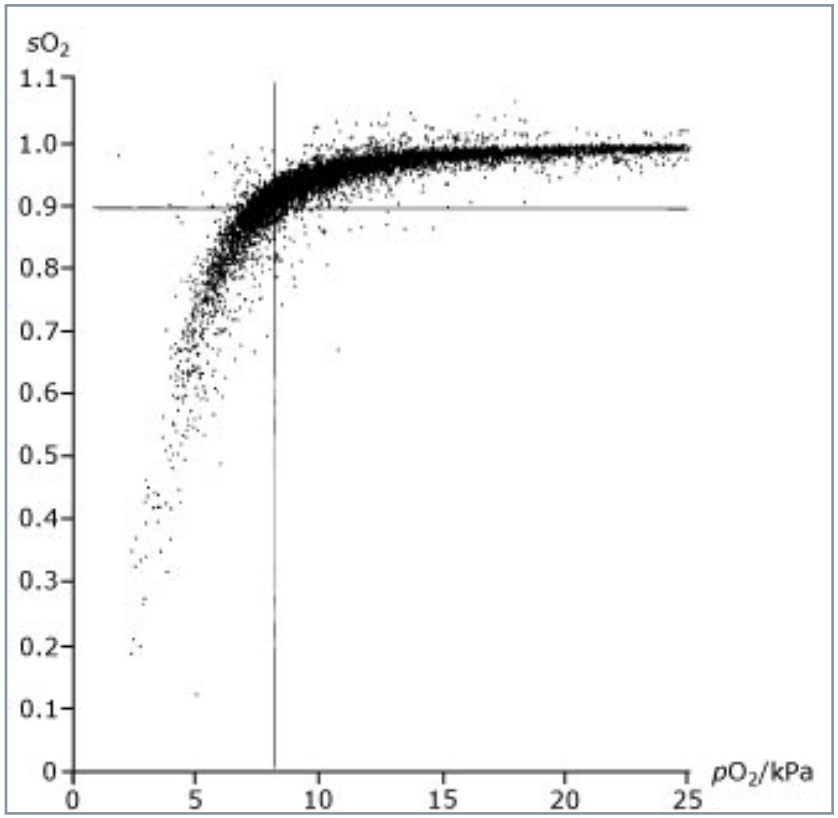
Different factors affect the position of the ODC, and *p*50 express the position of the curve

Typical reference range: 25-29 mmHg

Conditions affecting position of ODC



Can *p*50 be read from the ODC curve? [1]



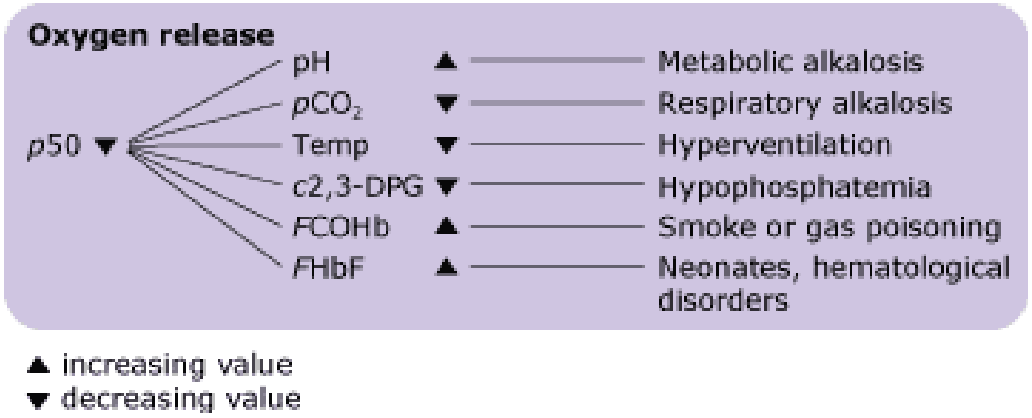
If sO_2 = 90 % then pO_2 = 29-137 mmHg (4–18 kPa)

If pO_2 = 60 mmHg (8 kPa) then sO_2 = 70-99%

Conclusion: Need information about *p*50 via measurement of the factors affecting ODC (MetHb, COHb etc)

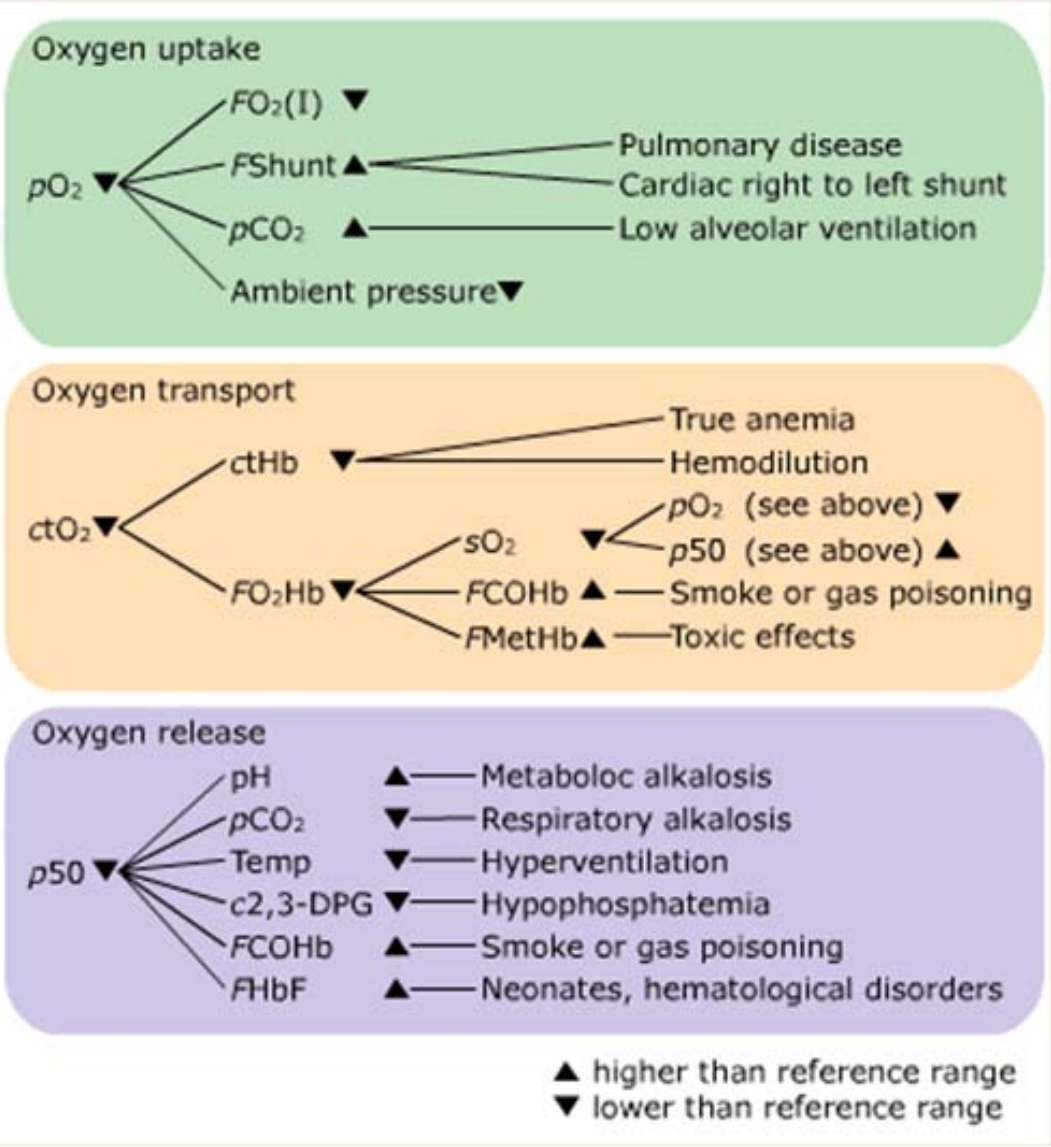
[1] Gøthgen IH et al. Variations in the hemoglobin-oxygen dissociation curve in 10079 arterial blood samples. Scand J Clin Lab Invest 1990; 50, Suppl. 203:87-90

Oxygen release – a recap



- The hemoglobin-oxygen affinity is expressed by the oxygen dissociation curve (ODC), the position of which is expressed by the ***p*50** value
- As illustrated in the flowchart, several conditions can affect the *p*50 value

Some cases using the Flowchart



Case

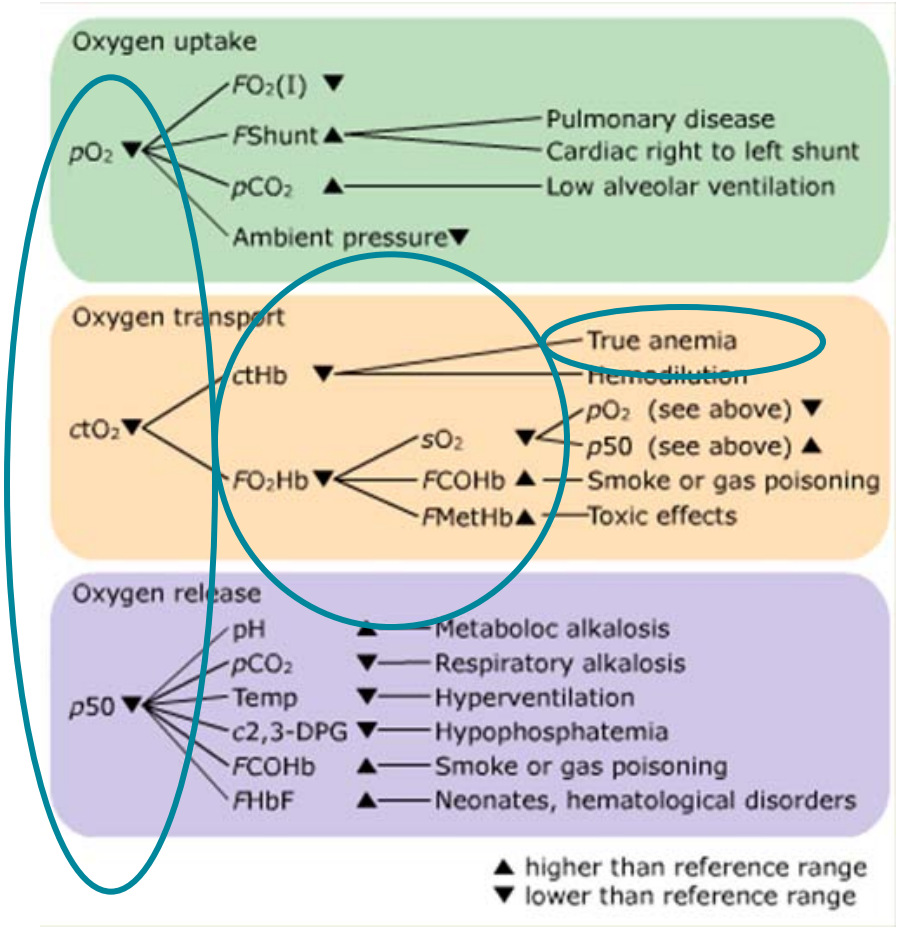
- 75-year-old woman
- Suffering from anemia, probably due to an ulcer
- What to do?
- Some of the results from the lab showed

pH = 7.40 (7.35-7.45)
pCO$_2$ = 40 mmHg (35-48)
pO$_2$ = 98 mmHg (83-108)
FO$_2$(I) = 0.21
ctHb = 9.0 g/dL (12.0-17.5)
ctO$_2$ = 8.8 mg/dL (18.8-22.3)

sO$_2$ = 97 % (95-99)
FMetHb =0.005 (.002-.008)
FCOHb =0.005 (0.0 – 0.008)
Temp = 37 °C
p50 = 25.5 mmHg (24-28)

This case is not a real life case – it is made for illustration purposes only

Case



pO_2 98 mmHg
ctO_2 8.8 mg/dL
p50 25.5 mmHg

ctHb 9.0 g/dL
No DysHb

True anemia

This case is not a real life case – it is made for illustration purposes only

Case

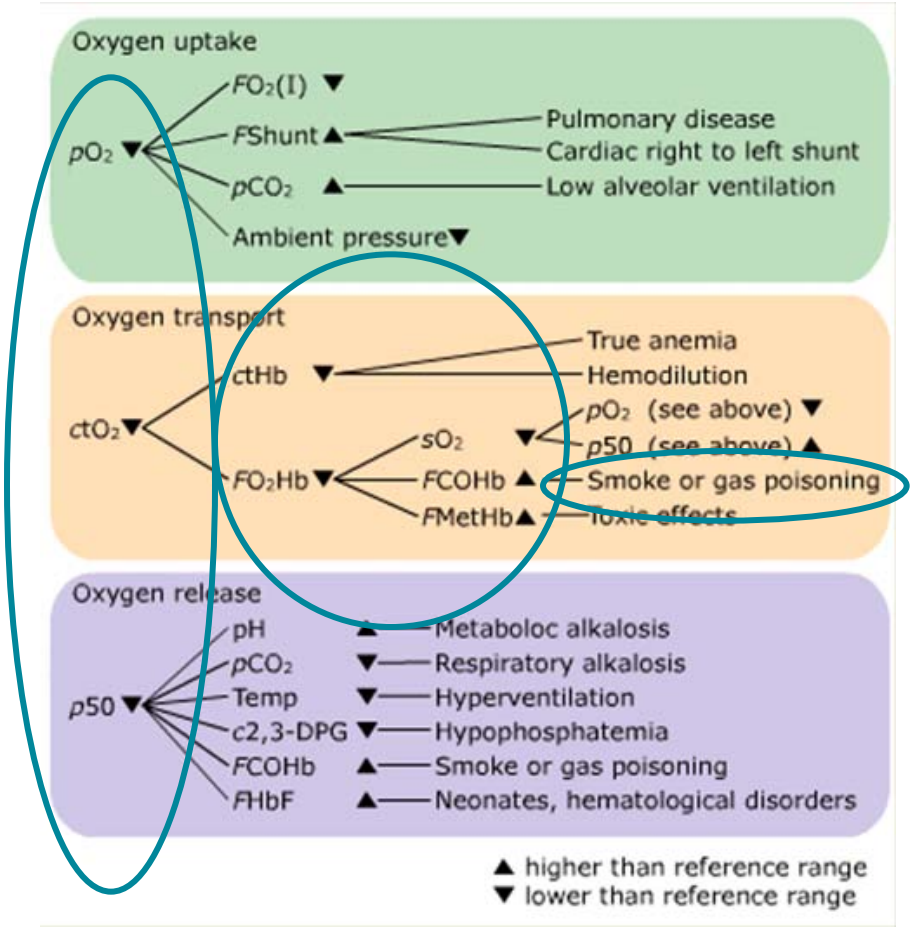
- 40-year-old man
- Exposed to smoke from a fire
- Some of the test results showed

pH = 7.400 (7.35-7.45)
pCO_2 = 40 mmHg (35-48)
pO_2 = 98 mmHg (83-108)
$FO_2(I)$ = 0.21
*c*tHb = 14.5 g/dL (12.0-17.5)
ctO_2 = 16.6 mL/dL (18.8-22.2)

sO_2 = 97 % (95-99)
*F*MetHb =0.005 (0.002-0.008)
*F*COHb =0.300 (0.0-0.008)
Temp = 37 °C
*p*50 = 26.3 mmHg (24-28)

This case is not a real life case – it is made for illustration purposes only

Case



pO_2 98 mmHg
ctO_2 16.6 mg/dL
p50 26.3 mmHg

ctHb 14.5 g/dL
COHb 30%

CO poisoning

This case is not a real life case – it is made for illustration purposes only

Case

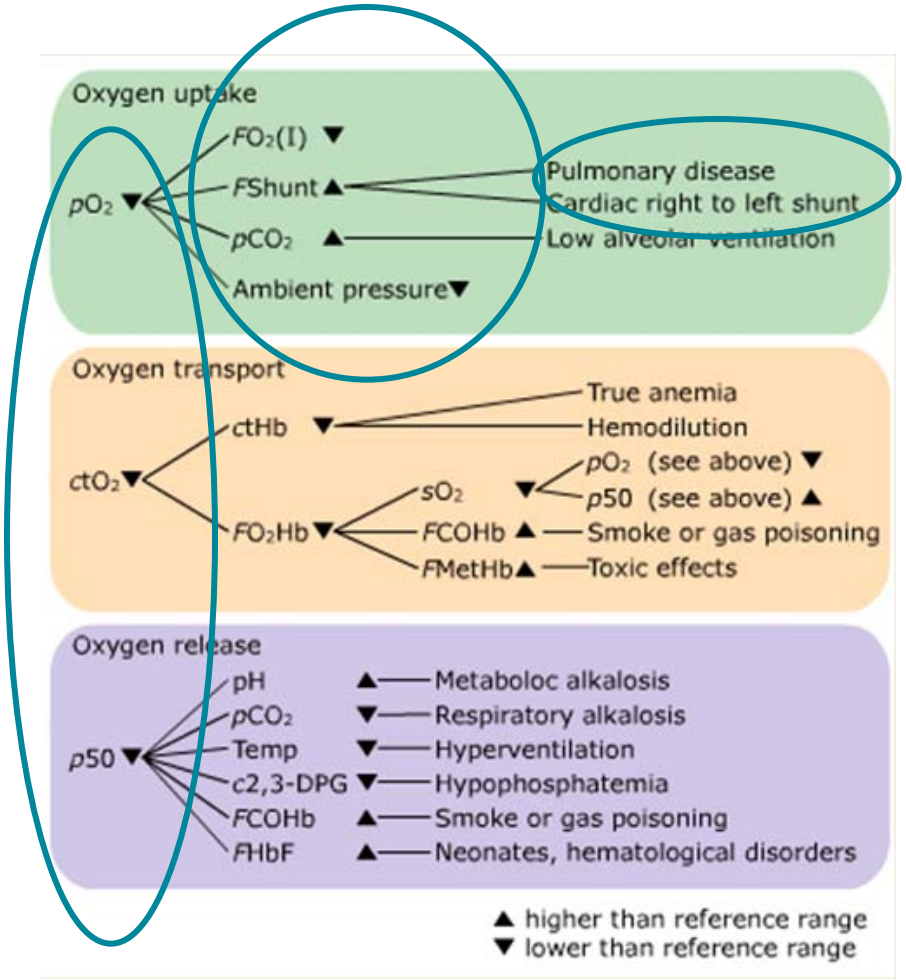
- 15-year-old boy
- Severe asthmatic attack
- Some of the test results showed

pH = 7.350 (7.35-7.45)
pCO_2 = 35 mmHg (35-48)
pO_2 = 60 mmHg (83-108)
$FO_2(I)$ = 0.21
$ctHb$ = 14.5 g/dL (12.0-17.5)
ctO_2 = 15.8 mL/dL (18.8-22.3)

sO_2 = 80 % (95-99)
FMetHb =0.005 (0.002-0.008)
FCOHb =0.005 (0.0-0.008)
Temp = 37 °C
$p50$ = 37 mmHg (24-28)

This case is not a real life case – it is made for illustration purposes only

Case



pO_2 60 mmHg
ctO_2 15.8 mg/dL
p50 37 mmHg

pCO_2 35 mmHg

Asthma

This case is not a real life case – it is made for illustration purposes only

Oxygen saturation, sO_2

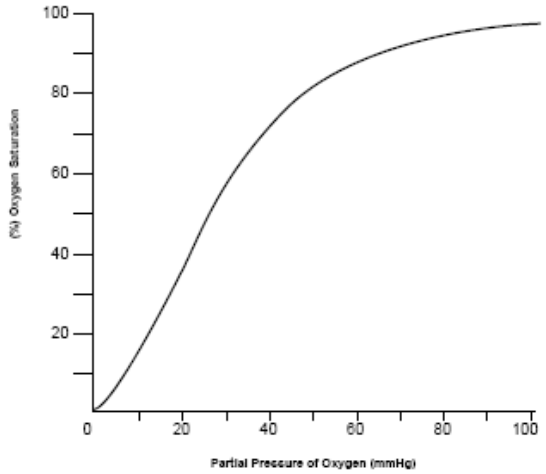
$$sO_2 = \frac{cO_2Hb}{cO_2Hb + cHHb} \times 100\ \%$$

- sO_2 is defined as
  - The percentage of oxygenated hemoglobin in relation to the amount of hemoglobin capable of carrying oxygen
- Typical reference interval 95-99 %
  - High sO_2:
    - Indicates that there is sufficient utilization of actual oxygen transport capacity
  - Low sO_2:
    - Indicates that the patient can likely benefit from supplemental oxygen
- No information about tHb, COHb, MetHb, ventilation or O_2-release to tissue

3 different ways to get sO_2

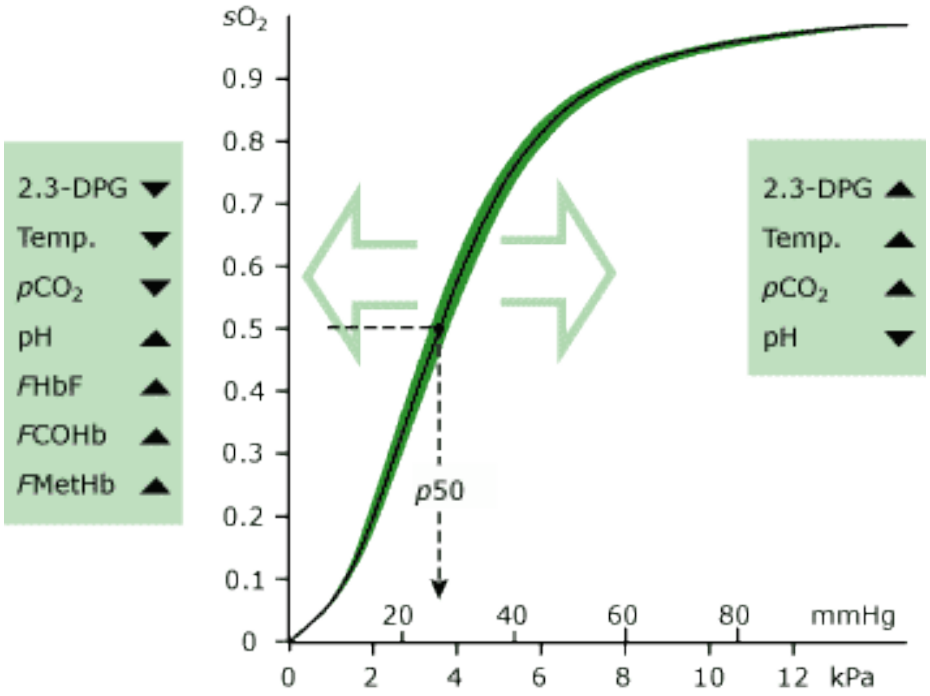
1. BG analyzer **with** CO-OX:
   - Measured by the CO-oximeter
   - Golden standard
2. BG analyzer **without** CO-OX:
   - Calculated from a pO2(a) via the ODC curve
3. Pulse oximeters

$$sO_2 = \frac{cO_2Hb}{cO_2Hb + cHHb} \times 100\ \%$$

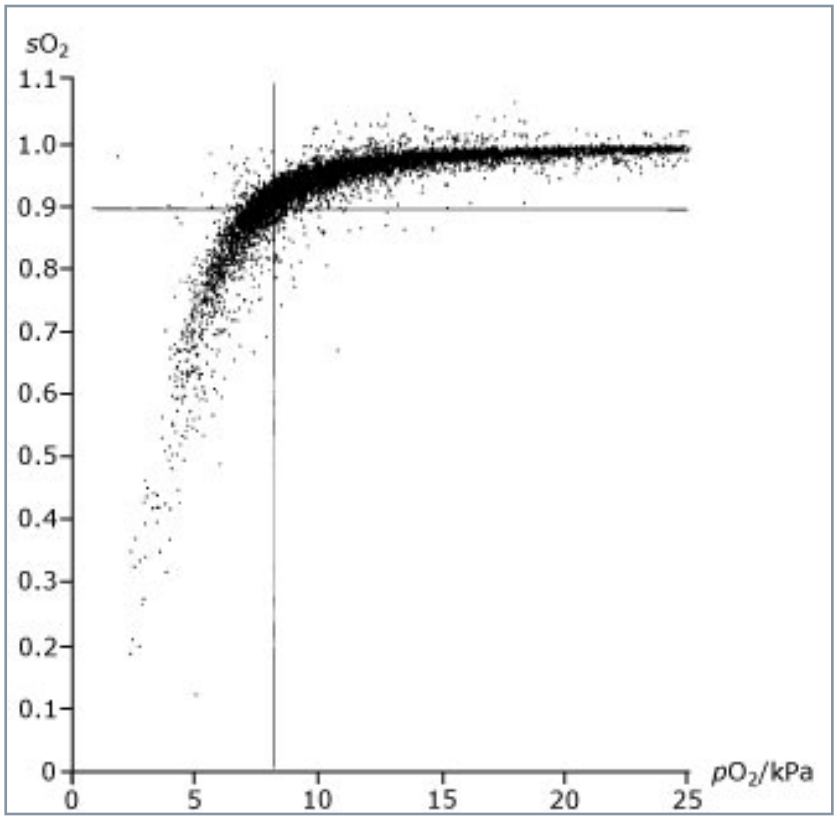


BGA without CO-OX

- CALCULATED sO_2 dependents on
  - Available information (parameters)
  - Algorithm applied by manufacturer



Correlation of pO_2 and sO_2 in real life [1]



- If sO_2 = 90% then
  pO_2 = 29-137 mmHg (4 – 18 kPa)
- If pO_2 = 60 mmHg (8 kPa) then
  sO_2 = 70-99%
- At pO_2 = 45 mmHg (6 kPa) and
  - pH = 7.25, then sO_2 = 80 %
  - pH = 7.40, then sO_2 = 88 %

[1] Gøthgen IH, Siggaard-Andersen O, Kokholm G. "Variations in the hemoglobin-oxygen dissociation curve in 10079 arterial blood samples“ By. Scand J Clin Lab Invest 1990; 50, Suppl. 203:87-90

Why measured over calculated sO_2

- Several studies are supporting the importance of using a measured sO_2 and not calculated
  - CLSI [1]*: "Clinically significant errors can result from incorporation of such an estimated value for sO_2 in further calculations such as shunt fraction"*
  - Breuer [2]: *"No calculation mode can be performed with constant accuracy and reliability when covering a wide range of acid-base values. If sO_2 values are used for further calculations, e.g. for determination of cardiac output, measured values are preferred"*

[1] Blood gas and pH analysis and related measurements: Approved Guidelines, National Committee for Clinical Laboratory Standards C46-A2, 29; 2009
[2] Breuer HWM et al. Oxygen saturation calculation procedures: a critical analysis os six equations or the determination of oxygen saturation. Intensive Care Med 1989; 15: 385-89

A reliable sO_2 (and pO_2) matters

	pO_2(a)	sO_2(a)
Hypoxemia - severe	6.0 kPa/45 mmHg	~80 %
Hypoxemia –moderate	8.0 kPa/60 mmHg	~91 %
Hypoxemia - mild	9.3 kPa/70 mmHg	~94 %
Normoxemia	10.6 kPa/80 mmHg	~96 %
Normoxemia	13.3 kPa/100 mmHg	~98 %
Hyperoxemia	16.0 kPa/120 mmHg	~98 %
Hyperoxemia - marked	20.0kPa/150 mmHg	~99-100 %

Pulse oximetry

- SpO_2
- Reflects the utilization of the current oxygen transport capacity
- Continuous monitoring
- Noninvasive method
- Easy and convenient
- 37 out of 42 pulse oximeters companies reported best analytical performance as 1SD of +/- 2 % [1, 2]

[1] From www.fda.gov as accessed September 2010,
[2] www.reillycomm.com as accessed in 2007

Pulse oximeters in the ICU

- Reputation: 90'ies studies conclude like these:
  - *"We conclude that the accuracy of the tested nine pulse oximeters does not enable precise absolute measurements, specially at lower oxygen saturation ranges" [1]*
  - *"Infants with acute cardiorespiratory problems, pulse oximetry unreliably reflects $pO_2(a)$, but may be useful in detecting clinical deterioration [2]*
- A 2010 publication [3]
  - *"The accuracy of pulse oximetry to estimate arterial oxygen saturation in critically ill patients has yielded mixed results. Both the degree of inaccuracy, or bias, and its direction has been inconsistent"…"analysis demonstrated that hypoxemia (sO2(a) < 90) significantly affected pulse oximeter accuracy. The mean difference was 4.9 % in hypoxemic patients and 1.89 % in non-hypoxemic patients (p < 0.004). In 50 % (11/22) of cases in which SpO2 was in the 90-93 % range the sO2(a) was <90 % ".*
- A 2012 publication [4]
  - *"Despite its accepted utility, it is not a substitute for arterial blood gas monitoring as it provides no information about the ventilatory status and has several other limitations".*

[1] Würtemberger G. Accuracy of nine commercially available pulse oximeters in monitoring patients with chronic respiratory insifficiency. Monaldi Arch Chest Dis 1994; 49: 348-353
[2] Walsh, M. Relationship of pulse oximetry to arterial oxygen tension in infants. Crit Care Med 15; 12: 1102-05.
[3] Wilson et al. The accuracy of pulse oximetry in emergency department patients with severe sepsis and septic shock: a retrospective cohort study. BMC Emergency Medicine 2010; 10:9
[4] Kipnis, E et al. Monitoring in the Intensive Care . Critical Care Research and Practice, Volume 2012, Article ID 473507, doi:10.1155/2012/473507

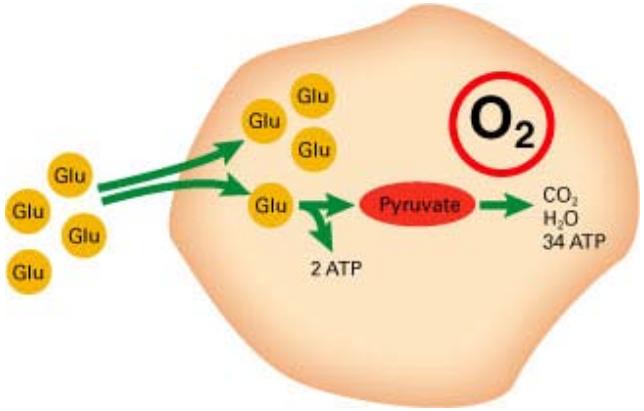
Oxygen saturation - Summary

- GOLDEN STANDARD is the oxygen saturation measured by the CO-oximeter analysis
- Other oxygen saturation methods have various limitations
- Oxygen saturation does not give information on oxygen delivery, ventilation, etc.

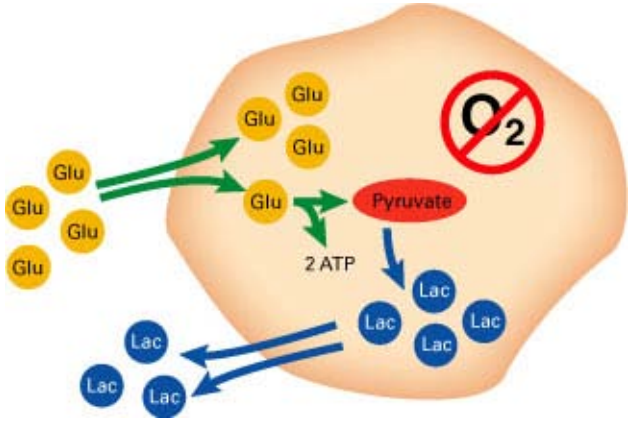
Does the oxygen get to the tissue?

- Lactate is a waste product from anaerobic metabolism
  - Takes place when there is insufficient oxygen delivery to tissue cells
  - Thus lactate is an early sensitive indicator imbalance between tissue oxygen demand and oxygen supply

Aerobic metabolism

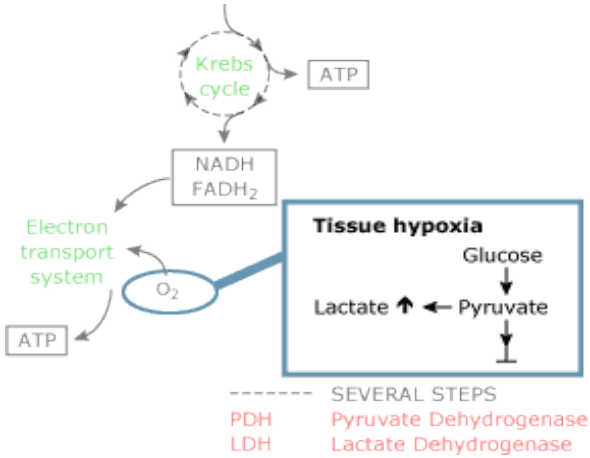


Anaerobic metabolism



Lactate is used….

- ……as a tool for
  - Diagnostically, admitting and triaging patients
  - As a marker of tissue hypoperfusion in patients with circulatory shock
  - As an index of adequacy of resuscitation after shock
  - As a marker for monitoring resuscitation therapies
  - Prognostically, as a prognostic indicator for patient outcome.



From: Bakker J. Increased blood lactate levels: a marker of…? www.acutecaretesting.org Jun 2003

When to measure lactate?

- When there are signs and symptoms such as
  - Rapid breathing, nausea, hypotension, hypovolemia and sweating that suggest the possibility of reduced tissue oxygenation or an acid/base imbalance
  - Suspicion of inherited metabolic or mitochondrial disorder.

Data shows that…..

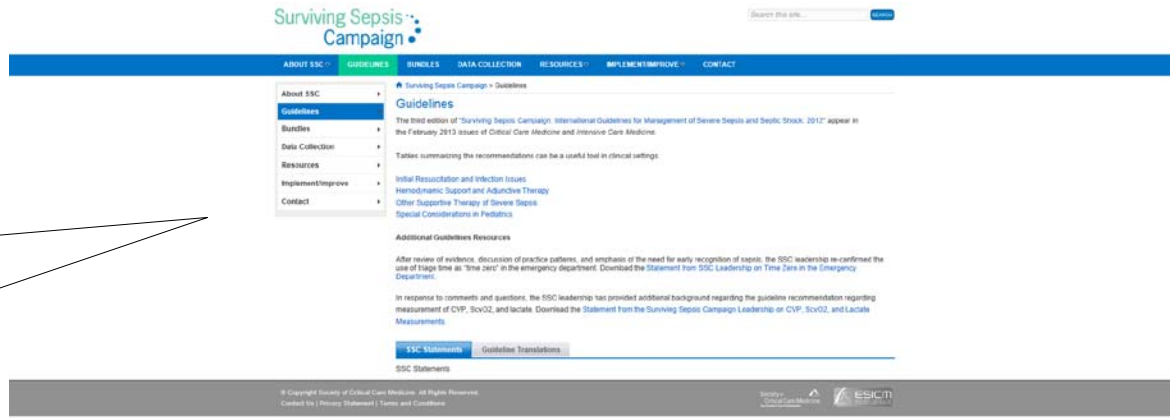
- Lactic acidosis
  - Occurs in approximately 1% of hospital admissions[1].
  - Has a mortality rate greater than 60% and approaches 100% if hypotension also is present [1].
- Elevated lactate
  - Have been demonstrated to be associated with mortality in both emergency departments and hospitalized patients [2, 3, 4, 5].

[1] Burtis CA, Ashwood ER, Bruns DE. In: Tietz textbook of Clinical Chemistry and molecular diagnostics, 5th edition. St. Louis: Saunders Elsevier, 2012.
[2] Dellinger RP, Levy MM, Rhodes A et al. Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012. Crit Care Med, 2012; 41: 580-637
[3] Shapiro NI, Howell MD, Talmor D et al. Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med, 2005; 45; 524-528.
[4] Trzeciak S, Dellinger RP, Chansky ME et al. Serum lactate as a predictor of mortality in patients with infection. Intensive Care Med, 2007; 33; 970-977.
[5] Mikkelsen ME, Miltiades AN, Gaieski DF et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and stock. Crit Care Med. 2009; 37; 1670-1677

Surviving sepsis

- The surviving sepsis campaign care bundle recommends, among others, to measure lactate within 3 hours of admission.
- If lactate is elevated a second lactate measure could be completed within 6 hours [1].

Read more at
www.survivingsepsis.org



[1] Dellinger RP, Levy MM, Rhodes A *et al*. Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012. Crit Care Med, 2012; 41: 580-637

Hyperlactatemia and lactic acidosis

- Hyperlactatemia:
  - Is typically defined as a lactate >2.0 mmol/L
  - Occurs when the rate of lactate release from peripheral tissue exceeds the rate of lactate removal by liver and kidneys
- Lactic acidosis
  - If lactate is > 3-4mmol/L there is increasing risk of associated acidosis
  - The combination of hyperlactatemia and acidosis is called lactic acidosis, which is a disruption of acid/base balance.

Lactic acidosis A and B

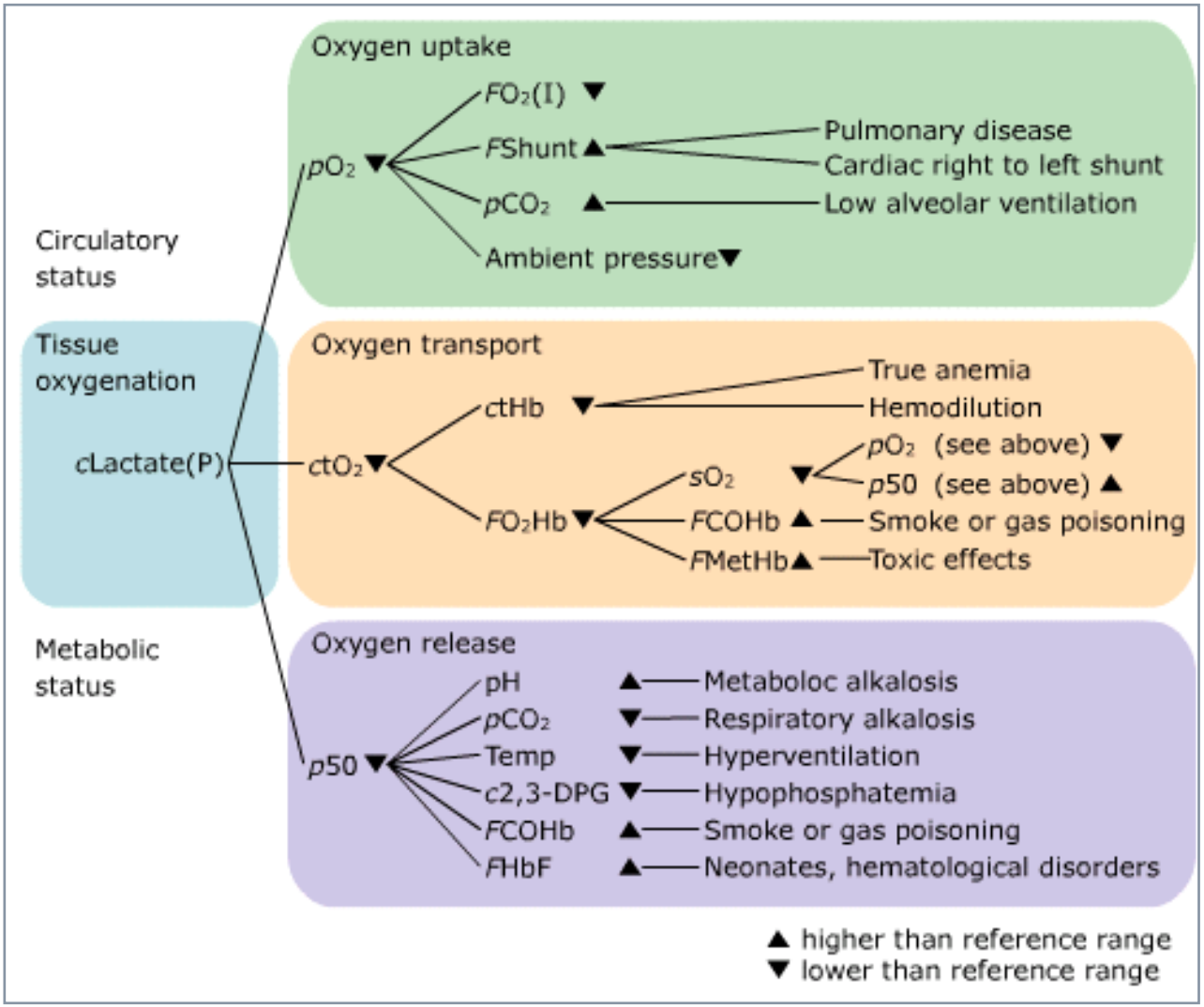
- Type A (hypoxic)
  - Inadequate oxygen uptake in the lungs and/or to reduced blood flow resulting in decreased transport of oxygen
  - E.g.: Shock from blood loss/sepsis, myocardial, infarction/cardiac arrest, congestive heart failure, pulmonary edema, severe anemia, severe hypoxemia , carbon monoxide poisoning
- Type B (metabolic)
  - Conditions that increase the amount of lactate in the blood but are not related to a decreased availability of oxygen
  - E.g.: Liver disease, Kidney disease, Diabetic ketoacidosis (DKA), Leukemia, HIV, glycogen storage diseases (like glucose-6-phosphatase deficiency), server infections – both systemic sepsis and meningitis, strenuous exercise
  - Drugs and toxins typically represent the most common cause of type B lactic acidosis

Lactic acidosis and pH

- No universal agreement for definition of lactic acidosis [1]
- Lactic acidosis is the most common cause of metabolic acidosis [2].
- Lactic acidosis may not necessarily produce acidemia in a patient as it depends on [1]
  - Magnitude of hyperlactatemia
  - Buffering capacity of the body
  - Coexistence of other conditions that produce tachypnea and alkalosis (eg, liver disease, sepsis).
- Thus, hyperlactatemia or lactic acidosis may be associated with acidemia, a normal pH, or alkalemia [1]

[1] Acutecaretesting Handbook 2013 – Radiometer Medical - in press
[2] Cassaletto J. Differential diagnosis of metabolic acidosis. Emerg Med Clin N Amer, 2005; 23: 771-87.

Lactate and oxygen uptake, transport and release [1]



[1] Adapted from different textbooks and Siggaard-Andersen, O et al. Oxygen status of arterial and mixed venous blood. Crit Care Med. 1995 Jul;23(7):1284-93.

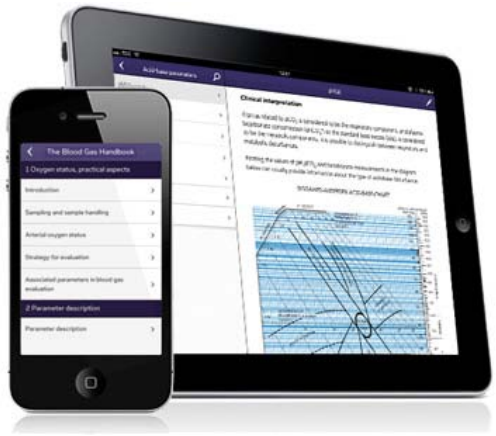
Summary

ABG test	Units	Examples of reference interval	Short summary
pH	pH	7.35–7.45	Indicates the acidity or alkalinity of blood. pH is the indispensable measure of acidemia or alkalemia.
pCO_2(a)	mmHg (kPa)	M 35–48 (4.7-6.4) F 32–45 (4.3–6.0)	pCO_2 is the carbon dioxide partial pressure in blood. pCO_2(a) is a reflection of the adequacy of alveolar ventilation in relation to the metabolic state.
Bicarbonate (HCO_3^-)	mmol/L	M 22.2-28.3 F 21.2-28.3	Standard HCO_3^- is standardized with the aim to eliminate effects of the respiratory component on the HCO_3^-. HCO_3^- is classified as the metabolic component of acid-base balance.
Base excess (BE)	mmol/L	M -3.2-1.8 F -2.3-2.7	BE predicts the quantity of acid or alkali to return the plasma in vivo to a normal pH under standard conditions. BE may help determine whether an acid/base disturbance is a respiratory, metabolic for mixed metabolic/respiratory problem Base(Ecf) is independent from changes on pCO_2 and is also called ”in-vivo base excess” or ”standard base excess” (SBE).
pO_2(a)	mmHg (kPa)	83-108 (11.1-14.4)	pO_2 is the oxygen partial pressure in blood. The pO_2(a) is an indicator of the oxygen uptake in the lungs.
sO_2(a)	%	95-99	sO_2(a) is the percentage of oxygenated hemoglobin in relation to the amount of hemoglobin capable of carrying oxygen and indicates if there is sufficient utilization of actual oxygen transport capacity.
Hemoglobin (Hb)	g/dL (mmol/L)	M 13.5-17.5 (8.4–10.9) F 12.0-16.0 (7.4–9.9)	tHb is defined as the sum of HHb+O_2Hb+COHb+MetHb. tHb is a measure of the potential oxygen-carrying capacity.
ctO_2	mmol/L	M 23.3-29.7 F 22.3-28.4	ctO_2 is the blood’s oxygen content and is the sum of oxygen bound to hemoglobin and physically dissolved oxygen. ctO_2 reflects the integrated effects of changes in the arterial pO_2, the effective hemoglobin concentration and the hemoglobin affinity.
$p50$	mmHg (kPa)	24–29 (3.2-3.9)	$p50$ is the oxygen tension at half saturation and reflects the affinity of hemoglobin for oxygen.
MetHb	%	0–1.5	MetHb is formed when blood is exposed to certain oxidizing agents. MetHb has a very low affinity to O_2 resulting in decreased oxygen-carrying capacity.
COHb	%	0.5-1.5	COHb is primarily formed when breathing air polluted with CO. COHb is not capable of transporting oxygen.
Lactate	mg/dl (mmol/L)	4.5–14.4 (0.5-1.6)	Lactate is a waste product from anaerobic metabolism. Lactate is an early sensitive indicator imbalance between tissue oxygen demand and oxygen supply.

Read more

- Sources for Scientific knowledge about acute care testing

acutecaretesting.org
Your knowledge site



Blood gas app
- for smartphones and tablets

Avoid preanalytical errors app
- for smartphones