1. Oxygen transport & delivery.
2. Regulation of blood pressure and volume

Dr. Rubina Aman
MICU PIMS
MCCM Module 2
20/10/09
“The First Concern”

“the first concern in any life-threatening illness
is to maintain
an adequate supply of oxygen
to sustain oxidative metabolism”

[Marino 2nd ed.]
The transport system for oxygen is separated into 4 components:

taken together, these form the “oxygen transport variables”
The Oxygen Transport Variables

- Oxygen Content \([\text{CaO}_2]\)
- Oxygen Delivery \([\text{DO}_2]\)
- Oxygen Uptake \([\text{VO}_2]\)
- Extraction Ratio \([\text{ER}]\)
Oxygen Content (1)

The oxygen in the blood is either bound to hemoglobin or dissolved in plasma. The sum of these two fractions is called the Oxygen Content.

\[ CaO_2: \text{the Content of Oxygen in Arterial Blood} \]

\[ \text{Hb} = \text{Hemoglobin (14 g/dl)} \]
\[ \text{SaO}_2 = \text{Arterial Saturation (98 %)} \]
\[ \text{PaO}_2 = \text{Arterial PO2 (100 mmHg)} \]
Oxygen Content (2)

\[ \text{CaO}_2 = (1.34 \times \text{Hb} \times \text{SaO}_2) + (0.003 \times \text{PaO}_2) \]

(amount carried by Hb) + (amount dissolved in plasma)

\[ \text{CaO}_2 = (1.34 \times 14 \times 0.98) + (0.003 \times 100) \]

\[ \text{CaO}_2 = 18.6 \text{ ml/dl} \quad (\text{ml/dl} = \text{vol} \% ; 18.6 \text{ vol} \%) \]

* at 100 % Saturation, 1 g of Hb binds 1.34 ml of Oxygen!
Oxygen Content (3)

- $\text{PaO}_2$ contributes *little* to the Oxygen Content!
- $\text{PaO}_2$ is **NOT** an important measure of arterial oxygenation!
- $\text{SaO}_2$ is more important variable for assessing the oxygenation of arterial blood!

*the PaO$_2$ should be reserved for evaluating the efficiency of pulmonary gas exchange*
Hemoglobin vs. PaO₂: CaO₂

- Arterial oxygenation is based on 3 factors:
  - Hb
  - SaO₂
  - PaO₂

- A 50% reduction in Hb leads to a direct 50% reduction in CaO₂
- A 50% reduction in PaO₂ leads to a 20% reduction in CaO₂
The Oxygen Dissociation curve
**CaO\textsubscript{2}:**

PaO\textsubscript{2} influences oxygen content only to the extent that it influences the saturation of hemoglobin.

Hypoxemia (*i.e. a decrease in PaO\textsubscript{2}* ) has a relatively SMALL impact on arterial oxygenation if the accompanying change in SaO\textsubscript{2} is small!
**Oxygen Delivery** (1)

**DO₂**: the Rate of Oxygen Transport in the Arterial Blood

* it is the product of Cardiac Output & Arterial Oxygen Content

\[ \text{DO}_2 = Q \times \text{CaO}_2 \]

Cardiac Output, Q, can be “indexed” to body surface area

Normal C.I. : 2.5 - 3.5 L/min-m²

By using a factor of 10, we can convert vol % to ml/min
Oxygen Delivery \(^{(2)}\)

\[
\text{DO}_2 = Q \times \text{CaO}_2
\]

\[
\text{DO}_2 = 3 \times (1.34 \times \text{Hb} \times \text{SaO}_2) \times 10
\]

\[
\text{DO}_2 = 3 \times (1.34 \times 14 \times .98) \times 10
\]

\[
\text{DO}_2 = 551 \text{ ml/min}
\]

Normal Range (CO): 800 – 1000 ml/min

Normal Range (CI): 520 - 720 ml/min/m\(^2\)
Oxygen Uptake  \textit{oxygen supply} for tissue metabolism \textsuperscript{(1)}

The Fick Equation:

Oxygen Uptake is the Product of Cardiac Output and the Arteriovenous Difference in Oxygen Content

\[ \text{VO}_2 = Q \times [(\text{CaO}_2 - \text{CvO}_2)] \]

Oxygen Delivery:

\[ \text{DO}_2 = Q \times \text{CaO}_2 \times 10 \]
Oxygen Uptake

\[ \text{VO}_2 = Q \times \text{Hb} \times 13.4 \times (\text{SaO}_2 - \text{SvO}_2) \]
Oxygen Uptake \(^{(3)}\)

The Fick Equation:

\[ \text{VO}_2 = Q \times (\text{CaO}_2 - \text{CvO}_2) \]
\[ \text{VO}_2 = Q \times [(1.34 \times \text{Hb}) \times (\text{SaO}_2 - \text{SvO}_2) \times 10] \]
\[ \text{VO}_2 = 3 \times [(1.34 \times 14) \times (.98 - .73) \times 10] \]
\[ \text{VO}_2 = 3 \times [46] \]
\[ \text{VO}_2 = 140 \text{ ml/min/m}^2 \]

Normal \(\text{VO}_2\): 110 - 160 ml/min/m\(^2\)
Extraction Ratio (1)

The fractional uptake of oxygen from the capillary bed

$O_2ER$: derived as the Ratio of Oxygen Uptake to Oxygen Delivery

$$O_2ER = \frac{VO_2}{DO_2} \times 100$$

$O_2ER = \frac{130}{540} \times 100$  
Normal Extraction  
$O_2ER = 24\%$  
$32\%$
Control of Oxygen Uptake

the uptake of oxygen from the microcirculation is a set point that is maintained by adjusting the Extraction Ratio to match changes in oxygen delivery.

the ability to adjust $O_2$ Extraction can be impaired in serious illness.
The Normal Response: O\textsubscript{2}ER \hspace{1cm} (1)

The Normal Response to a Decrease in Blood Flow is an Increase in O\textsubscript{2} Extraction sufficient enough to keep VO\textsubscript{2} in the normal range

\[ VO_2 = Q \times Hb \times 13.4 \times (SaO_2 - SvO_2) \]

- \( Q = 3; \) \( VO_2 = 3 \times 14 \times 13.4 \times (.97 - .73) = 110 \text{ ml/min} \)

- \( Q = 1; \) \( VO_2 = 1 \times 14 \times 13.4 \times (.97 - .37) = 109 \text{ ml/min} \)
The Normal Response: $O_2ER$ (2)

- The Drop in Cardiac Index is BALANCED by an Increased $(SaO_2 - SvO_2)$ Difference…and $VO_2$ remains Unchanged

- Note the drop in $SvO_2$ from 97 % to 37 % !!

- This association between $SvO_2$ & $O_2ER$ is the Basis for $SvO_2$ Monitoring

*The Ability to Adjust Extraction is a feature of all vascular beds except the Coronary Circulation & the Diaphragm!*
The $\text{DO}_2 - \text{VO}_2$ Curve (1)

$\text{VO}_2 = \text{DO}_2 \times \text{O}_2\text{ER}$

- Maximum $\text{O}_2\text{ER}$
- Normal
- $\text{VO}_2$ becomes supply-dependent
- Critical $\text{DO}_2$

Diagram shows the relationship between $\text{DO}_2$ and $\text{VO}_2$, with critical and normal points indicated.
The $\text{DO}_2 - \text{VO}_2$ Curve (2)

- As $\text{O}_2$ delivery decreases below normal, the ER increases proportionally to keep $\text{VO}_2$ constant.

- When ER reaches its maximum level (50 – 60%), further decreases in $\text{DO}_2$ are accompanied by proportional decreases in $\text{VO}_2$.

- Critical $\text{DO}_2$
  - The $\text{DO}_2$ at which consumption becomes supply-dependent.
  - The point at which energy production within the cell becomes oxygen-limited.
The $\text{DO}_2 - \text{VO}_2$ Curve \(^{(3)}\)

- **Flat Portion of the Curve**
  - $\text{VO}_2$ Flow - Independent
  - $\text{O}_2$ Extraction varies in response to Blood Flow ($\text{VO}_2$ Constant)

- **Linear Portion of the Curve**
  - $\text{VO}_2$ Flow - Dependent
  - Indicates a defect in oxygen extraction from the microcirculation
  - Extraction is fixed and $\text{VO}_2$ becomes directly dependent on Delivery

- **Critical Level of Oxygen Delivery**
  - The Threshold $\text{DO}_2$ needed for Adequate Tissue Oxygenation
  - If $\text{DO}_2$ falls below this level, oxygen supply will be sub-normal
The critical $\text{DO}_2$ in anesthetized patients is around 300 ml/min.

However, in critically-ill patients, the Critical $\text{DO}_2$ varies widely from 150 – 1000 ml/min…

[Leach et al. Dis Mon. 1994;30:301-368]
Mixed Venous Oxygen

By rearranging the Fick Equation, the determinants of Venous Oxygen are:

\[ \text{VO}_{2} = \text{Q} \times \text{Hb} \times 13 \times (\text{SaO}_{2} - \text{SvO}_{2}) \]

\[ \text{SvO}_{2} = \text{SaO}_{2} - (\text{VO}_{2}/\text{Q} \times \text{Hb} \times 13) \]

* the most prominent factor in determining \( \text{SvO}_{2} \) is \( \text{VO}_{2}/\text{Q} \)

Causes of a Low \( \text{SvO}_{2} \):

- Hypoxemia
- Increased Metabolic Rate
- Low Cardiac Output
- Anemia
Remember: Mixed Venous

In Critically-Ill Patients, augmenting the extraction ratio
(in response to a change in oxygen delivery)
may not be possible!

In these patients, the Venous Oxygen Levels may change
little in response to changes in Cardiac Output!

thus, the Relationship
between CO (Q) and Mixed Venous Oxygen must be
determined before using SvO$_2$ or PvO$_2$ to monitor
changes in DO$_2$ or VO$_2$
Oximetry

Arterial Oxygen Saturation can be estimated but Venous Oxygen Saturation MUST be Measured!

- *Due to the shape of the Oxyhemoglobin Curve*
- *The arterial Sat falls on the flat portion & can be safely estimated*
- *The venous Sat (68 - 77%) falls on the Steep Portion and can vary significantly even with small errors in estimation!*
• 50 % Sat...PO$_2$ 25

• Mixed Ven. Sat 75...PO$_2$ 40
"Right-shift: off-loading"

- Acidosis
- Elevated temperature
- Elevated CO₂
- Increased 2,3-DPG
Tissue \( \text{O}_2 \)-Balance

- Oxygen supply to the tissues is the rate of \( \text{O}_2 \) uptake from the microcirculation
  - \( \text{VO}_2 \) & ER

- The metabolic requirement for oxygen is the rate at which oxygen is metabolized to water within the mitochondria
  - \( \text{MRO}_2 \)

- Because oxygen is NOT stored in the tissues, \( \text{VO}_2 \) must match \( \text{MRO}_2 \) if aerobic metabolism is to continue

  \textit{when matching occurs, glucose is completely oxidized to yield 36 moles of ATP}
Oxygen Balance

when matching occurs, glucose is completely oxidized to yield 36 moles of ATP

- When matching is not equal (\( VO_2 \) is less than \( MRO_2 \)), a portion of the glucose is diverted to the production of lactate in an attempt to salvage energy

- Per mole of glucose converted through anaerobic metabolism, 2 moles of ATP are gained (47 kcal)
Dysoxia

the condition in which the production of ATP is limited by the supply of oxygen

when cell dysoxia leads to a measurable change in organ function….SHOCK
**VO₂ Deficit**

- In ICU patients, a VO₂ that falls below the normal range (*i.e.* below 100 ml/min), can be used as evidence of impaired tissue oxygenation.

- Studies have shown a direct relationship between the magnitude of the VO₂ deficit and the risk of multiorgan failure.

  [Dunham et al. CCM 1991;19:231-243]
Oxygen Debt

The cumulative VO$_2$ deficit is referred to as the “oxygen debt”.

In ICU patients, there may be a progressive and linear relationship between VO$_2$ & DO$_2$. 
Monitoring of $\text{O}_2$ Transport

The transport variables provide no information about the ADEQUACY of tissue (cellular) oxygenation… because that requires a measurement of metabolic rate.
Interpreting the Transport Variables

- **Low VO$_2$:**
  - Indicates a tissue oxygen deficit
  - “Oxygen Debt”
    - The total VO$_2$ deficit over time
    - Remember the direct relationship exists between magnitude of the oxygen debt and subsequent risk of multiorgan failure

- **Normal VO$_2$:**
  - Requires a blood lactate level to determine the adequacy of global tissue oxygenation
Correcting a VO₂ Deficit (1)

- **Step 1: CVP or PWP**
  - If low, infuse volume to normalize filling pressure
  - If normal or high, go to step 2

- **Step 2: CO**
  - If low & filling pressures not optimal…infuse volume
  - If low & filling pressures high, start DOBUTAMINE & titrate keep CI > 3 L/min/m² *(some believe 5)*
     - If blood pressure is also low, start DOPAMINE or LEVOPHED
  - If CI > 3, proceed to Step 3.
Correcting a VO₂ Deficit

Step 3: VO₂ (Oxygen Uptake)
- If VO₂ is less than 100 ml/min/m², use VOLUME
  - to goal of CVP 8 – 12; PWP 18 – 20
  - inotropic therapy to achieve a CI > 4.5 L/min/m²
- Correct Hb if less than 8 g/dl (some say 10 g/dl)
- If VO₂ is greater than 100 ml/min/m², proceed to Step 4.

Step 4: Blood Lactate
- Lactate > 4 with other signs of shock (i.e. organ failure, low BP), decrease METABOLIC RATE – via sedation or paralysis (? Pentobarbital coma)
- Lactate 2 – 4...controversial!
- Lactate < 2...observe
Role of Serum Lactate (1)

• An elevated lactate indicates that VO$_2$ is less than the metabolic rate

• The approach must then be to either decrease the metabolic rate or increase the VO$_2$

*achieving a supranormal level of VO$_2$ may be difficult*

*and carries risks*
## Serum Lactate (2)

<table>
<thead>
<tr>
<th>Ability to Identify a Fatal Outcome</th>
<th>Whole Blood or Plasma Lactate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt; 2 mmol/L</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>89%</td>
</tr>
<tr>
<td>Specificity</td>
<td>42</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>58</td>
</tr>
</tbody>
</table>

Optimizing Oxygen Transport: The Steps

Filling Pressures

Cardiac Output

$VO_2$

Serum Lactate
# Oxygen Transport Variables

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery ( (DO_2) )</td>
<td>500 - 800 ml/min</td>
</tr>
<tr>
<td>Uptake ( (VO_2) )</td>
<td>110 - 160 ml/min</td>
</tr>
<tr>
<td>Extraction Ratio (ER)</td>
<td>22 - 32 %</td>
</tr>
<tr>
<td>Mixed Venous ( \text{PO}_2 )</td>
<td>33 - 53 mmHg</td>
</tr>
<tr>
<td>Mixed Venous ( \text{SO}_2 )</td>
<td>68 - 77 %</td>
</tr>
</tbody>
</table>

**\( DO_2 \) & \( VO_2 \) can be indexed to body surface area**
Regulation of Blood Pressure and blood volume
Arterial Blood Pressure (BP)

The lateral pressure generated by the pumping action of the heart on the wall of arteries per unit area.

OR

Pressure inside big arteries (aorta & big vessels).

- Measured in (mmHg), & sometimes in (cmH$_2$O),
  
  $1 \text{ mmHg} = 1.36 \text{ cmH}_2\text{O}.$

- Of 2 components:
  - systolic ... (= max press reached) = 110-130 mmHg.
  - diastolic ... (= min press reached) = 70-90 mmHg.

In normal adult $\approx 120/80 \text{ mmHg}.$
Arterial Blood Pressure (continued)

- **Pulse pressure** = Systolic BP – Diastolic BP.
- **Mean arterial pressure** = Diastolic BP + 1/3 Pulse press.
Factors determining ABP:

Blood Pressure = Cardiac Output $\times$ Peripheral Resistance

- **BP depends on:**
  1. Cardiac output $\Rightarrow$ CO = SV $\times$ HR.
  2. Peripheral resistance.
Regulation of ABP:

- Maintaining B.P. is important to ensure a steady blood flow (perfusion) to tissues.

- B.P. **regulated neurally** through centers in medulla oblongata:
  1. Vasomotor Center (V.M.C.), or (pressor area):
     - \(\Rightarrow\) Sympathetic fibers.
  2. Cardiac Inhibitory Center (C.I.C.), or (depressor area):
     - \(\Rightarrow\) Parasympathetic fibers (vagus).
Regulation of ABP (continued)

Cardiac control centers in medulla oblongata

1. Cardiac accelerator center (V.M.C)
   - Sympathetic n. fibers
2. Cardiac inhibitory center (C.I.C)
   - Parasympathetic n. fibers
Regulatory mechanisms depend on:

- **a. Fast acting reflexes:**
  Concerned by controlling CO (SV, HR), & PR.

- **b. Long-term** Concerned mainly by regulating the blood volume.
Regulation of CO:

- A fast acting mechanism.
- CO regulation depends on the regulation of:
  - a. Stroke volume, &
  - b. Heart rate
Regulation of the CO:

Cardiac output = Stroke volume \times Heart rate

- Mean arterial pressure
- End diastolic volume (EDV)
- Contraction strength
- Sympathetic neuron
- Parasympathetic neuron
- Frank-Starling relationship
Regulation of Peripheral Resistance (PR):

A fast acting mechanism controlled through several reflex mechanisms:

- Baro receptors reflex.
- Chemo receptors reflex.
- Vasomotor reflexes.
- Hormonal
1. Baroreceptors reflex:

- Baroreceptors are receptors found in carotid sinus & aortic arch.
- Are stimulated by changes in BP.

\[ \uparrow \text{BP} \rightarrow \] Baroreceptors

\[ \downarrow \text{V.M.C} \rightarrow \text{Sympathetic} \rightarrow \text{Vasodilatation} \& \downarrow \text{TPR} \]

\[ \uparrow \text{C.I.C} \rightarrow \text{Parasympathetic} \rightarrow \text{Slowing of SA node} \downarrow \text{HR} \& \downarrow \text{CO} \]
2. Chemoreceptors reflex:

- Chemoreceptor in carotid & aortic bodies.
- Stimulated by hypoxia ($\downarrow O_2$), hypercapnia ($\uparrow CO_2$), & pH

![Diagram showing the chemoreceptors reflex mechanism:]

- Haemorrhage $\rightarrow \downarrow BP$
- Hypoxia
- $\rightarrow$ Chemoreceptors
- $\rightarrow$ C.I.C
- $\rightarrow$ Parasympathetic
- $\rightarrow$ Adrenal medulla
- $\rightarrow$ Sympathetic
- $\rightarrow$ Vasoconstriction & $\uparrow TPR$
- $\rightarrow$ HR
3. Other Vasomotor Reflexes:

1. **Atrial stretch receptor reflex:**
   \[ \uparrow \text{Venous Return} \Rightarrow ++ \text{atrial stretch receptors} \Rightarrow \text{reflex vasodilatation \& } \downarrow \text{BP.} \]

2. **Thermoreceptors:** (in skin/or hypothalamus)
   - Exposure to heat \(\Rightarrow\) vasodilatation.
   - Exposure to cold \(\Rightarrow\) vasoconstriction.

3. **Pulmonary receptors:**
   Lung inflation \(\Rightarrow\) vasoconstriction.
4. Hormonal Agents:

- Nor Adrenalin $\Rightarrow$ vasoconstriction.
- Adrenalin $\Rightarrow$ vasoconstriction (except in sk. ms.).
- Angiotensin II $\Rightarrow$ vasoconstriction.
- Vasopressin $\Rightarrow$ vasoconstriction.
Regulation of Blood Volume:

- A long-term regulatory mechanism.
- Mainly renal:
  1. Renin-Angiotensin System.
  2. Anti-diuretic hormone (ADH), or vasopressin.
  3. Low-pressure volume receptors.
1. Renin-Angiotensin System:

- Most important mechanism for Na⁺ retention in order to maintain the blood volume.
- A drop of renal blood flow & or ↓ Na⁺, stimulates volume receptors in juxtaglomerular apparatus to secrete:

Renin ► Angiotensin System ► aldosterone.
Renin-Angiotensin System:

↓ renal blood flow &/or ↓ Na⁺

++ Juxtaglomerular apparatus of kidneys
(considered volume receptors)

Renin

Angiotensinogen → Angiotensin I

(Lungs) Converting enzymes

Angiotensin III
(powerful vasoconstrictor)

Angiotensin II
(powerful vasoconstrictor)

Aldosterone

N.B. Aldosterone is the main regulator of Na⁺ retention.
2. Anti-diuretic hormone (ADH), or vasopressin:

- Hypovolemia & dehydration stimulate the osmo receptors in the hypothalamus,
- Release of ADH from posterior pituitary gland.
- ADH causes water re absorption at kidney tubules.
3. Low-pressure volume receptors:

Atrial natriuritic peptide (ANP) hormone, is secreted from the wall of right atrium to regulate Na$^+$ excretion in order to maintain blood volume.
Clinical application: Shock

- Stage I: reversible, compensated shock
  - Body reacts to maintain BP → $\uparrow$HR, vasoconstriction. BP remains within normal range

- Stage II: reversible, noncompensated shock
  - Body reacts to maintain BP → $\uparrow$HR, vasoconstriction. BP drops below adequate range (SBP 70). Can be reversed by medical treatment

- Stage III: irreversible shock
  - Body is fighting to maintain adequate BP without success → HR is very high → not enough O2 for cardiac, brain cells to survive → damages. Cannot be reversed by medical treatment

- Death
summary

- $\text{PaO}_2$----efficacy of gas exchange, determines the $\text{Sao}_2$.
- $\text{Sao}_2$----arterial oxygenation and Hb saturation
- Hb ----Oxygen Content
- CO ----Oxygen delivery
- Oxygen uptake--Arteriovenous Difference in Oxygen Content
- Cellular metabolism ----Oxygen extraction
- Blood pressure----Blood flow to tissues