**Factors Affecting Gas Exchange at the Lung**

**The PAO2 defines the upper limit to PaO2**

Factors that affect the “A-a” difference:

1. **Shunt**
   - in newborns, patent ductus arteriosus or foramen ovale
   - in adults, pathology
2. **Diffusion Limitation**
   - particularly during exercise in horses, but also in some people
3. **V-Q inequality – mismatch of perfusion and ventilation**
   - can be caused by disease
   - worsens during intense exercise even in healthy people

**Right to Left Shunt**

- Deoxygenated blood “leaks” through the shunt from the right side to the left (systemic) side.
- Normal: bronchial supply for larger airways, can account for up to 4 mmHg reduction in PaO2.
- Abnormal: Can occur through a patent ductus arteriosus or septal defect (for examples)
- Rare in adults
- Causes dilution of oxygenated blood, lowers PaO2
- Clinically diagnosed by 100% O2 breathing
Diffusion Limitation

- Equilibrium between PAO2 and PaO2 is not reached
- DOES NOT AFFECT PaCO2 (Why?)
- Can be caused by any factor that affects diffusion
  - BGB area or thickness (loss of lung due to surgery, etc.)
  - Pressure gradient (altitude)
- Can occur during exercise due to reduced time for diffusion
  - Capillary transit time may decrease from ~0.75 sec to only 0.25 sec
  - Extreme case in race horses – PaO2 drops to 50’s or 60’s, A-a difference is 40-50 mmHg!
  - Can occur in humans, particularly in elite athletes with very high cardiac output

Ventilation/Perfusion Matching

- Review: Pulmonary circuit
  - Same rate of flow (L/min) as systemic circuit
    - Cardiac output systemic = Cardiac output pulmonary
  - Minute ventilation, also measured in L/min
- When standing, most of the blood flow is to the base of the lung
  - Due to gravitational force

Ventilation-Perfusion Relationships

- Ventilation/perfusion ratio
  - Indicates matching of blood flow to ventilation
    - Ideal: ~1.0
- Base
  - Overperfused (ratio <1.0)
  - Extreme case – ratio near 0 - perfusion with no ventilation
    - physiological shunt, as with collapsed alveoli or severe pulmonary edema
- Apex
  - Underperfused (ratio >1.0)
  - Extreme case – ratio near infinity – ventilation with no perfusion, as with blocked or collapsed blood vessel
EXERCISE: Rest-to-Work Transitions

- Initially, ventilation increases rapidly
  - Then, a slower rise toward steady-state
- Both tidal volume and respiratory rate increase
  - At low intensities tidal volume changes more
- PO₂ and PCO₂ are maintained (homeostatically regulated parameters)
Ventilation during Exercise:
Intensity Effects

- Linear increase in ventilation with intensity up to ~55-75% of VO₂max
  - VE and VO₂ are matched – rise in parallel
- Ventilation increases exponentially beyond this point
  - VE and VO₂ become unmatched – VE increases faster than VO₂
- Ventilatory threshold (Tvent) or breakpoint
  - Inflection point where V̇E parts with VO₂ and begins to increase exponentially

VO₂ and VE versus Intensity

![Graph showing VO₂ and VE versus Intensity](image)

Data Based on Hopkins et al. 1998

Respiration During Exercise in a Hot Environment

During prolonged submaximal exercise:

- Ventilation tends to drift upward
- In panting animals, VE increases rapidly to increase respiratory evaporative heat loss
- PaCO₂ tends to fall, slightly in humans, more rapidly and more extremely in panting animals
- Higher ventilation in heat is strongly related to thermoregulation in panting animals, is probably also related in humans
PaCO₂ during 30 min at ~50% VO₂max in sheep

Body Temperature and PaCO₂ During Exercise

<table>
<thead>
<tr>
<th>Body Temp (°C)</th>
<th>PaCO₂ (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>30</td>
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<td>30</td>
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<td>25</td>
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<tr>
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</table>

Minutes of Exercise

Changes in $V_E$ and PaCO₂ During Exercise in a Hot/Humid Environment

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>$V_E$ (L/min)</th>
<th>PaCO₂ (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>40</td>
<td>41</td>
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<tr>
<td>10</td>
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<tr>
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<td>21</td>
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<tr>
<td>30</td>
<td>10</td>
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</tbody>
</table>

Exercise time (min)

Ventilatory Response to Exercise: Trained vs. Untrained

- VE is lower at any given intensity below the ventilatory threshold
  - Mechanism not known, but parallels lower VO₂ at any given submaximal intensity
- Ventilatory threshold occurs at a higher work rate
- pH maintained at a higher work rate, i.e., higher lactate threshold, better buffering (tighter homeostasis)
- In elite athletes, particularly women, there may be a drop in PaO₂ with high intensity exercise
  - Due mainly to V/Q inequality, diffusion limitation, relative hypoventilation (especially in older people, women)
More extreme
Than usual
(horse like)

Effects of Endurance Training on Ventilation During Exercise

Respiration during Exercise:
Locomotor-Respiratory Coupling

- Coupling is characterized by an integer ratio between respiratory rate and step rate, e.g. 1:1 or 2:1 (breathes:strides)
- Coupling is characterized by “phase lock” – inspiration occurs during specific part of the stride
- 1:1 coupling is the rule in galloping dogs, horses, etc.
- Coupling is found during running and flight in birds
- Coupling of 1:1, 2:1 and other ratios is found in humans on bikes, running, and of course swimming
- Coupling is more common in trained than untrained humans
Control of Ventilation

- Respiratory control center
  - Located in the medulla (part of brainstem)
  - Inspiratory and expiratory neurons
- Receives neural and humoral input
  - Neural input from motor cortex, other “higher” centers
  - Neural input from respiratory neurons in pons
  - Neural (GTO, spindles) and humoral feedback from muscles
  - Humoral feedback from central and peripheral chemoreceptors

Location of the Brain Stem
Respiratory Control Centers

Chemoreceptors

- Peripheral chemoreceptors
  - Aortic arch chemoreceptor
  - Carotid bodies
    - Carotid sinus nerve carries messages
    - Detect PaO₂, PaCO₂, H⁺, and K⁺ in arterial blood
- Central chemoreceptors
  - Located in the medulla
  - PCO₂ and H⁺ concentration in cerebrospinal fluid
Effect of Increasing $\text{PaCO}_2$ on Minute Ventilation

Effect of Decreasing $\text{PaO}_2$ on Minute Ventilation

Ventilatory Control During Exercise

- At exercise onset, $\text{VE}$ increases immediately
  - Due to feedforward control?
  - Neural feedback from muscles
  - After a few seconds, humoral feedback

- Incremental submaximal exercise
  - Linear increase in ventilation with intensity due to:
    - Central command (motor cortex, "higher" centers)
    - Humoral feedback from chemoreceptors
    - Neural feedback

- Heavy exercise
  - Exponential rise above ventilatory breakpoint
  - Increasing blood $\text{H}^+$
  - Increasing body temperature
Ventilatory Control During Submaximal Exercise

Do the Lungs Limit Exercise Performance?

- Submaximal exercise
  - Pulmonary system not seen as a limitation

- Maximal exercise
  - Not thought to be a limitation in healthy individuals at sea level
  - May be limiting in elite endurance athletes
    - Flow limitations in older people due to increased lung compliance
    - Flow and diffusion limitations in women due to smaller lungs than men of same body size