Exercise Physiology

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Outline

• Basics of Exercise Physiology
  – Cellular respiration
  – Oxygen utilization \((QO_2)\)
  – Oxygen consumption \((VO_2)\)
  – Cardiovascular responses
  – Ventilatory responses

• Exercise Limitations
  – In normal healthy individuals

• Cardiopulmonary Exercise Testing
Gas Transport Mechanisms: coupling of cellular (internal) respiration to pulmonary (external) respiration

- The major function of the cardiovascular as well as the ventilatory system is to support cellular respiration.
- Exercise requires the coordinated function of the heart, the lungs, and the peripheral and pulmonary circulations to match the increased cellular respiration.

- Wasserman K: *Circulation* 1988;78:1060
Exercise and Cellular Respiration

Exercise requires the release of energy from the terminal phosphate bond of adenosine triphosphate (ATP) for the muscles to contract.
Cellular Respiration
Cellular Respiration:
Mechanisms Utilized by Muscle to Generate ATP

Mechanisms for ATP generation in the muscle

1. Aerobic oxidation of substrates (carbohydrates and fatty acids)
2. The anaerobic hydrolysis of phosphocreatine (PCr)
3. Anaerobic glycolysis produces lactic acid

Each is critically important for normal exercise response and each has a different role
Major Metabolic Pathways During Exercise
Aerobic Oxidation of CHO and FA to Generate ATP

• The major source of ATP production
• Only source of ATP during sustained exercise of moderate intensity
Aerobic Oxidation of CHO and FA to Generate 36 ATP

Glycogen → NADH + H+ → Lactate → 3 ATP → 6 H2O + 6 CO2

Pyruvate → acetyl-CoA → Krebs cycle → NADH + H+ → Electron transport chain → 36 ATP

Mitochondria
Anaerobic Hydrolysis of Phosphocreatine (PCr) to Generate ATP

- Provides most of the high energy phosphate needed in the early phase of exercise
- This is used to regenerate ATP at the myofibril during early exercise
- PCr is an immediate source of ATP regeneration
The Glycolytic Pathway: Uses Glycogen to Generate ATP

• Produces ATP from glycogen without the need for \( O_2 \) \( \rightarrow \) results in production of lactic acid

• The energy produced by anaerobic glycolysis is relatively small for the amount of glycogen consumed

• The consequence is lactate accumulation
Anaerobic Glycolysis: Uses Glycogen to Generate 3 ATP

Glycogen → Pyruvate → Lactate

- 3 ATP
- NADH + H+

Pyruvate → acetyl-CoA → Krebs cycle

- NADH + H+
- Electron transport chain
- 36 ATP

Mitochondria

6 H₂O + 6 CO₂ → 6 O₂
During exercise, when does anaerobic glycolysis occur?

- Exercising muscle energy needs cannot be met entirely by $O_2$ and PCr-linked ATP generation
- Exercising muscles cells are critically $O_2$-poor
- Exercising muscle fibers have different balances of oxidative versus glycolytic enzymes
  - Low intensity: recruit fibers that are primarily oxidative
  - High intensity: recruit fibers that primarily rely on glycolytic pathway
Oxygen Utilization (QO$_2$)
Exercise results in increased oxygen utilization (QO₂) by muscles

- Increased extraction of O₂ from the blood

During exercise the muscle has
  - Increase in temperature
  - Increase in [H⁺]

Bohr Effect:
  - Right shift on dissociation curve
  - Decrease Hb-O₂ affinity at muscle
  - Augments O₂ diffusion into the exercising muscles

http://www.anaesthesiaw.com/images/ODC_3.jpg
Exercise results in increased oxygen utilization ($QO_2$) by muscles

- Increased extraction of $O_2$ from the blood
- Dilation of peripheral vascular beds
- Increased cardiac output
- Increase in pulmonary blood flow
  - recruitment and vasodilation of pulmonary bed
- Increase in ventilation
In Steady State Conditions

\[ \text{QO}_2 = \text{VO}_2 \]
Coupling of cellular (internal) respiration to pulmonary (external) respiration

At steady-state: oxygen consumption per unit time (VO$_2$) and carbon dioxide output (VCO$_2$) = oxygen utilization (QO$_2$) and carbon dioxide production (QO$_2$). Thus, external respiration measured at the mouth represents internal respiration.

Wasserman K: *Circulation* 1988;78:1060
Oxygen Consumption (VO₂)
Oxygen Consumption ($VO_2$)

- $VO_2$ is the difference between the volume of gas inhaled and the volume of gas exhaled per unit of time

$$VO_2 = [(V_i \times F_{IO_2}) - (V_E \times F_{EO_2})]/t$$

- $V_i$ and $V_E$ = volumes of inhaled and exhaled gas
- $t$ = time period of gas volume measurements
- $F_{IO_2}$ and $F_{EO_2}$ = $O_2$ concentration in the inhaled and mixed gas
Oxygen Consumption (VO$_2$)

**Oxygen Delivery**
- LUNGS
  - ventilation, gas exchange
- HEART
  - CO, SV, HR
- CIRCULATION
  - pulmonary, peripheral, Hgb

**Oxygen Utilization**
- MUSCLES
  - limbs, diaphragm, thoracic
Determinants of VO$_2$

- VO$_2$ is interrelated to blood flow and O$_2$ extraction

- Fick Equation

\[ VO_2 = CO \times (CaO_2 - CvO_2) \]

- VO$_2$ = oxygen consumption
- CO = cardiac output
- CaO$_2$ = arterial oxygen saturation
- CvO$_2$ = venous oxygen saturation
- CaO$_2$ – CvO$_2$ = arteriovenous O$_2$ content difference →
  is related to O$_2$ extraction by tissues

- CaO$_2$ = (1.34 x Hb x SaO$_2$) + (0.003 x PaO$_2$)
- CvO$_2$ = (1.34 x Hb x SvO$_2$) + (0.003 x PvO$_2$)
**VO₂ Max**

Maximum Oxygen Consumption

- VO₂ increases linearly until SV, HR, or tissue extraction approaches its limitations → VO₂ plateaus

- VO₂ max is the point at which there is no further increase in VO₂ despite further increases in workload.
• What is normal?
  > 30 ml/kg/min

• Average individual
  – 30-50 ml/kg/min

• Athletes
  – 60-70 ml/kg/min

- Laughlin, Am J Physiol 1999; 277: S244
Reduced VO$_2$ Max
(less than 30 ml/kg/min)

- Oxygen transport
  - CO, O$_2$-carrying capacity of the blood
- Pulmonary limitations
  - mechanical, gas exchange
- Oxygen extraction at the tissues
  - tissue perfusion, tissue diffusion
- Neuromuscular or musculoskeletal limitations

Decreased Exercise Capacity
Anaerobic Threshold (AT)
Anaerobic Threshold

The VO$_2$ at which anaerobic metabolism contributes significantly towards the production of ATP
Anaerobic Threshold

The VO$_2$ at which anaerobic metabolism contributes significantly towards the production of ATP

- A non-invasive estimate of cardiovascular function
- Normal AT: > 40% of predicted VO$_2$ max
- Average individual AT: 50-60% predicted VO$_2$ max
- Low AT (< 40% predicted max VO$_2$ max)
  - Indicates early hypoxia of exercising muscles
  - Suggests cardiovascular or pulmonary vascular limitation
Anaerobic Threshold

The VO$_2$ at which anaerobic metabolism contributes significantly towards the production of ATP

• AT demarcates the upper limit of a range of exercise intensities that can be accomplished almost entirely aerobically

• Work rates below AT can be sustained indefinitely

• Work rate above AT is associated with progressive decrease in exercise tolerance
VCO₂
Carbon Dioxide Output

- The body uses CO₂ regulation to compensate for acute metabolic acidosis
- CO₂ increases due to bicarbonate buffering of increased lactic acid production seen at high work rates (anaerobic metabolism).
  \[
  H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O
  \]
- As tissue lactate production increases [H⁺], the reaction is driven to the right
Anaerobic Threshold

The VO₂ at which anaerobic metabolism contributes significantly towards the production of ATP

$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$
Cardiovascular Responses to Dynamic Exercise
Cardiovascular Responses to Dynamic Exercise

- Increase in cardiac output (CO = HR x SV)
  - Increase in heart rate (HR)
  - Increase in stroke volume (SV)

- Increase in SBP

- DBP remains stable +/- decreased
Cardiac Output Increases with Dynamic Exercise

• As work intensity rises, the proportion of CO distributed
  – skeletal muscle increases
  – viscera decreases

• Exercise Hyperemia
  – Increased blood flow to cardiac and skeletal muscles during exercise

- Laughlin, Am J Physiol 1999; 277: S244
Predicted Maximum Heart Rate

• Standard equation
  \[ \text{Max HR} = 220 - \text{age} \]

• Alternative equation
  \[ \text{Max HR} = 210 - (\text{age} \times 0.65) \]

• Both have similar values for < 40 years old

• Standard method underestimates peak HR in older people
Oxygen Pulse\((O_2\text{ pulse})\)

- Oxygen pulse = \(VO_2\text{ max}/\text{max HR}\)
- Reflects the amount of oxygen extracted per heart beat
- Estimator of stroke volume (SV)*
  - Modified Fick Equation: \(VO_2/HR = SV \times C(a-v)O_2\)

*Assumption that at max work rate, \(C(a-v)O_2\) is constant, thus change in \(O_2\) pulse represents change in SV
Heart Rate, Stroke Volume and Cardiac Output Increase with Dynamic Exercise

Increase in cardiac output (CO = HR x SV)

Early in exercise:
- Increase in HR and SV

Late in exercise:
- Primarily due to HR
- SV plateaus

- ATS / ACCP Statement of CPET; AJRCCM 2003;167:211-77
Effects of Dynamic Exercise on Blood Pressure

- Marked Rise in SBP
  - Linear increase
  - Nml ≤ 200 mmHg

- Minimal Change in DBP
  - May decrease a little

- Moderate rise in MAP

SBP increase is due to increased cardiac output, NOT increased peripheral resistance

- Laughlin, Am J Physiol 1999; 277: S244
Abnormal Blood Pressure Responses to Dynamic Exercise

• Abnormal patterns of SBP response to exercise
  – Fall, reduced rise, excessive rise
  – Increase to > 200 mmHg

• Most alarming → FALL in SBP
  – Indicates a potential serious cardiac limitation
  – CHF, ischemia, aortic stenosis, central venous obstruction
Respiratory System
Responses to Dynamic Exercise
Pulmonary Responses to Exercise

• Ventilation ($V_E$) increases
  
  $V_E = \text{tidal volume (VT)} \times \text{respiratory rate (RR)}$
  
  – Increase in VT (depth of breath)
  – Increase in RR

• Arterial oxygen pressure ($\text{PaO}_2$)
  – Does not significantly change

• Arterial oxygen saturation ($\text{SaO}_2$)
  – Does not significantly change

• Alveolar-Arterial $\text{O}_2$ Pressure Difference [$P(\text{A-a}) \text{O}_2$]
  – Gradient widens
Ventilation Increases with Dynamic Exercise

\[ \text{VE} = \text{VT} \times \text{RR} \]

- Ventilatory demand is dependent on:
  - Metabolic requirements
  - Degree of lactic acidosis
  - Dead space

- In healthy adults:
  - Peak exercise \( \text{VE} \approx 70\% \) of the Maximum Voluntary Ventilation (MVV)

ATS / ACCP Statement of CPET; AJRCCM 2003;167:211-77
Respiratory Rate, Tidal Volume and Ventilation Increase with Dynamic Exercise

Increase in ventilation ($V_E = V_T \times RR$)

Early in exercise:
- Increase in RR and $V_T$

Late in exercise:
- Primarily due to RR
- $V_T$ plateaus

- ATS / ACCP Statement of CPET; AJRCCM 2003;167:211-77
Respiratory Rate and Tidal Volume Exercise Response in Patient with COPD

- ATS / ACCP Statement of CPET; AJRCCM 2003;167:211-77
Pulmonary Gas Exchange

• Efficient pulmonary gas exchange is critical for a normal exercise response

• Pulmonary gas exchange indices
  – $\text{PaO}_2$
  – $\text{P(A-a)O}_2$ difference
PaO$_2$ and SaO$_2$ Response to Dynamic Exercise

• PaO$_2$ response to exercise
  – Normal Individuals
    • No significant change
  – Endurance-trained athletes
    • Can see significant decrease in PaO$_2$ at maximal exercise

• SaO$_2$ response to exercise
  – Normal individuals
    • No significant change
Alveolar-Arterial $O_2$ Pressure Difference $P(A-a)O_2$

- Difference between alveolar oxygen pressure ($P_{A\text{O}_2}$) and the arterial oxygen pressure ($P_{a\text{O}_2}$)

- “A-a gradient”

- Normal A-a gradient at rest
  - Normal is 4 – 16, usually < 10 mm Hg*
  - Increases with age due to increase in V/Q mismatch
  - Age correction

*This range from ATS CPET guidelines, multiple different normal ranges exist
Defer to ranges provided earlier in course
Response of A-a gradient to Dynamic exercise

• In normal individuals
  – A-a gradient increases with exercise
  – May increase to > 20 mm Hg during exercise

• P(A-a)O₂ increased during exercise due to
  – V/Q mismatching
  – O₂ diffusion limitation
  – Low mixed venous O₂

• Abnormal A-a gradients with exercise
  – Greater than 35 mm Hg indicates pulmonary abnormality
What mechanism limits exercise in healthy individuals?
What mechanism limits exercise in healthy individuals?

- VE is not the limiting factor
  - at maximal exercise there is ample ventilatory reserve

- Pulmonary gas exchange is not the limiting factor
  - At maximal exercise SaO₂ and PaO₂ are near baseline

- Metabolic and contractile properties of the skeletal muscles are not the limiting factors

- Maximal exercise is limited by CARDIAC OUTPUT
Cardiopulmonary Exercise Testing
What is a Cardiopulmonary Exercise Test (CPET)?

Simultaneous study of the cardiovascular and ventilatory systems response to known exercise stress via measurement of gas exchange at the airway.
Cardiopulmonary Exercise Testing
Why do we perform CPETs?

• Distinguish between normal and diseased state

• Determine etiology of exercise intolerance
  – Isolate system(s) responsible for the patient’s symptoms

• Assess severity of disease

• Assess the effect of therapy

• Pre-operative assessment of thoracotomy
What physiologic parameters are obtained during a CPET?

- $\text{VO}_2\text{ max}$ (maximum oxygen consumption)
- Continuous electrocardiogram (ECG), HR
- BP measurements every 1-2 minutes
- Continuous $\text{SaO}_2$ (arterial $\text{O}_2$ saturation)
- Maximum minute ventilation ($\text{VE max}$)
- $\text{O}_2$ pulse (calculated)
Two Key Values Obtained During a CPET

Oxygen Consumption ($VO_2$)

Anaerobic Threshold (AT)
In Conclusion
Exercise Physiology is Complex

Many elements of exercise physiology not discussed: autonomic responses, neurological responses, and sensory aspects of exercise.