Exercise Physiology

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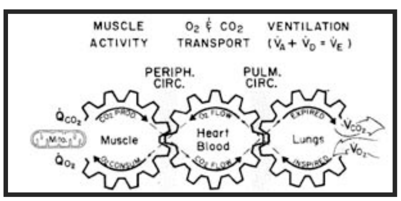
Outline

- 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



- Wasserman K: *Circulation* 1988;78:1060

- 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.

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

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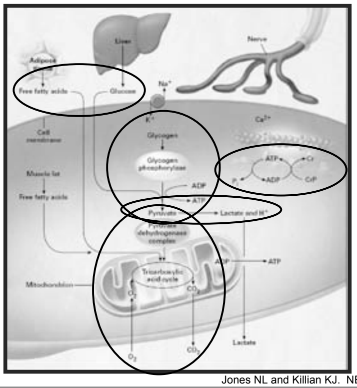
Major Metabolic Pathways During Exercise



Jones NL and Killian KJ. NEJM 2000;343:632

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

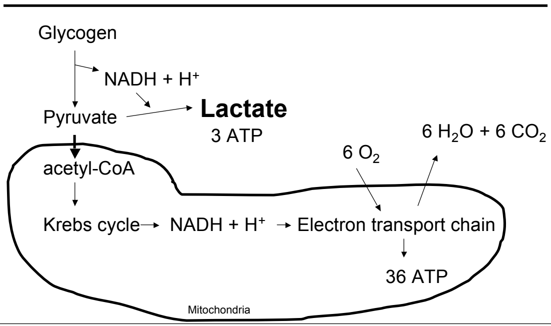
Anaerobic Hydrolysis of Phosphocreatine (PCr) to Generate ATP

- 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 → 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 ATP



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

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Oxygen Utilization (QO_2)

Exercise results in increased oxygen utilization (QO_2) by muscles

- Increased extraction of O_2 from the blood

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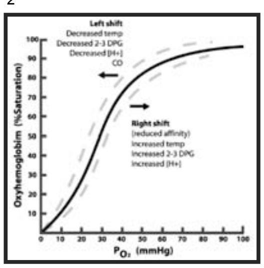
During exercise the muscle has
- Increase in temperature
- Increase in [H^+]

Bohr Effect:
- Right shift on dissociation curve
- Decrease Hb-O_2 affinity at muscle
- Augments O_2 diffusion into the exercising muscles



http://www.anaesthesiauk.com/images/ODC_3.jpg

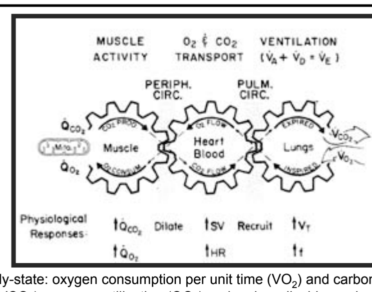
Exercise results in increased oxygen utilization (QO_2) by muscles

- 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

$QO_2 = VO_2$

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.

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Oxygen Consumption (VO_2)

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

$$VO_2 = [(V_I \times F_{I_{O_2}}) - (V_E \times F_{E_{O_2}})]/t$$

- V_I and V_E = volumes of inhaled and exhaled gas
- t = time period of gas volume measurements
- $F_{I_{O_2}}$ and $F_{E_{O_2}}$ = O_2 concentration in the inhaled and mixed gas

VO_2 Max

Maximum Oxygen Consumption

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

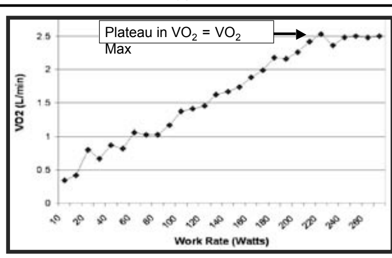
$$VO_2 = CO \times (CaO_2 - CvO_2)$$

- 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

- $CaO_2 = (1.34 \times Hb \times SaO_2) + (0.003 \times PaO_2)$
- $CvO_2 = (1.34 \times Hb \times SvO_2) + (0.003 \times PvO_2)$

VO_2 Max

Maximum Oxygen Consumption

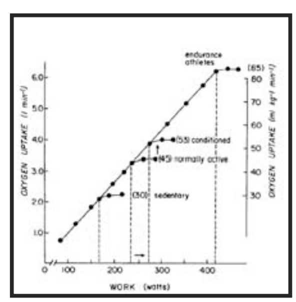


- VO_2 increases linearly until SV, HR, or tissue extraction approaches its limitations → VO_2 plateaus
- VO_2 max is the point at which there is no further increase in VO_2 despite further increases in workload.

VO_2 Max

Maximum Oxygen Consumption

- What is normal?
  > 84% predicted (L/min)
  > 30 ml/kg/min
- Average individual
  - 30-50 ml/kg/min
- Athletes
  - 60-70 ml/kg/min
- Lance Armstrong
  - 85 ml/kg/min



- Laughlin, Am J Physiol 1999; 277: S244

A Reduced VO_2 Max
(less than 84% predicted (L/min) or 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

The VO_2 at which anaerobic metabolism contributes significantly towards the production of ATP

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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 max 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

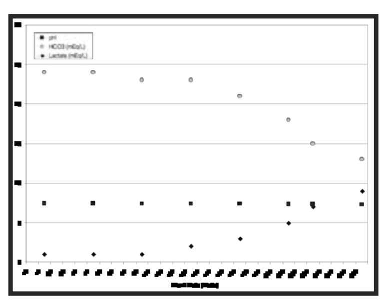
VCO_2
Carbon Dioxide Output

- The body uses CO_2 regulation to compensate for acute metabolic acidosis
- CO_2 increases due to bicarbonate buffering of increased lactic acid production seen at high work rates (anaerobic metabolism).

$$H^+ + HCO3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$$

- As tissue lactate production increases [H^+] the reaction is driven to the right

Anaerobic Threshold
The VO_2 at which anaerobic metabolism contributes significantly towards the production of ATP



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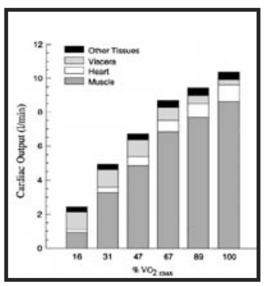
Cardiovascular Responses to Dynamic Exercise

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



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Predicted Maximum Heart Rate

- Standard equation

  Max HR = 220 - age
- Alternative equation

  Max HR = 210 – (age x 0.65)
- Both have similar values for < 40 years old
- Standard method underestimates peak HR in older people

Oxygen Pulse(O_2 pulse)

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

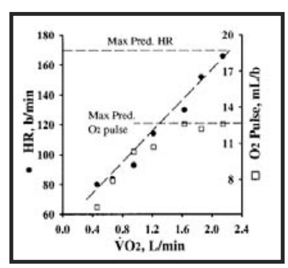
*Assumption that at max work rate, $C(a\text{-}v)O_2$ is constant, thus change in O_2 pulse represents change in SV

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

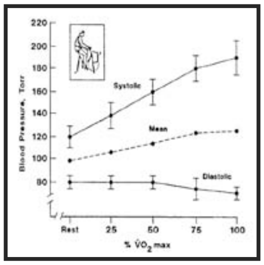
Late in exercise:
- Primarily due to HR
- SV plateaus



- 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



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

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

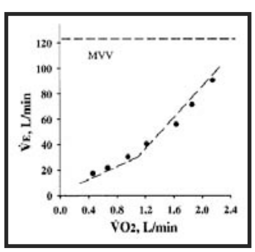
- Ventilation (V_E) increases

  V_E = tidal volume (V_T) + respiratory rate (RR)
  - Increase in V_T (depth of breath)
  - Increase in RR
- Arterial oxygen pressure (PaO_2)
  - Does not significantly change
- Arterial oxygen saturation (SaO_2)
  - Does not significantly change
- Alveolar-Arterial O_2 Pressure Difference [P(A-a) O_2]
  - Gradient widens

Ventilation Increases with Dynamic Exercise

($V_E = V_T + RR$)

- Ventilatory demand is dependent on:
  - Metabolic requirements
  - Degree of lactic acidosis
  - Dead space
- In healthy adults:
  - Peak exercise V_E ≈ 70% of the Maximum Voluntary Ventilation (MVV)



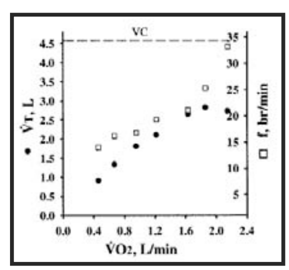
ATS / ACCP Statement of CPET; AJRCCM 2003;167:211-77

Respiratory Rate, Tidal Volume and Ventilation Increase with Dynamic Exercise

Increase in ventilation ($V_E = V_T + RR$)

Early in exercise:
- Increase in RR and V_T

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



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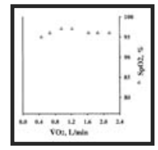
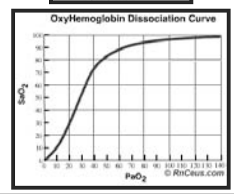
Pulmonary Gas Exchange

- Efficient pulmonary gas exchange is critical for a normal exercise response
- Pulmonary gas exchange indices
  - PaO_2
  - $P(A\text{-}a)O_2$ 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 $P(A\text{-}a)O_2$

- Difference between alveolar oxygen pressure (PAO_2) and the arterial oxygen pressure (PaO_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
- $P(A\text{-}a)O_2$ increased during exercise due to
  - V/Q mismatching
  - O_2 diffusion limitation
  - Low mixed venous O_2
- 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?

- V_E is not the limiting factor
  - at maximal exercise there is ample ventilatory reserve
- Pulmonary gas exchange is not the limiting factor
  - At maximal exercise SaO_2 and PaO_2 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?

- VO_2 max (maximum oxygen consumption)
- Continuous electrocardiogram (ECG), HR
- BP measurements every 1-2 minutes
- Continuous SaO_2 (arterial O_2 saturation)
- Maximum minute ventilation (VE max)
- O_2 pulse (calculated)

Two Key Values Obtained During a CPET

Oxygen Consumption (VO_2)

Anaerobic Threshold (AT)

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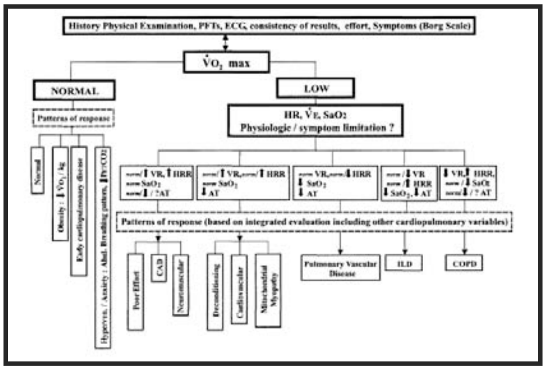
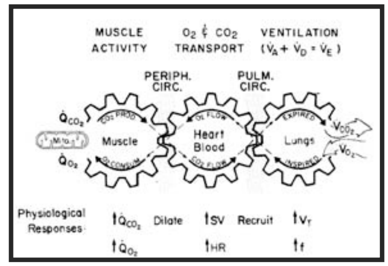


In Conclusion
Exercise Physiology is Complex



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