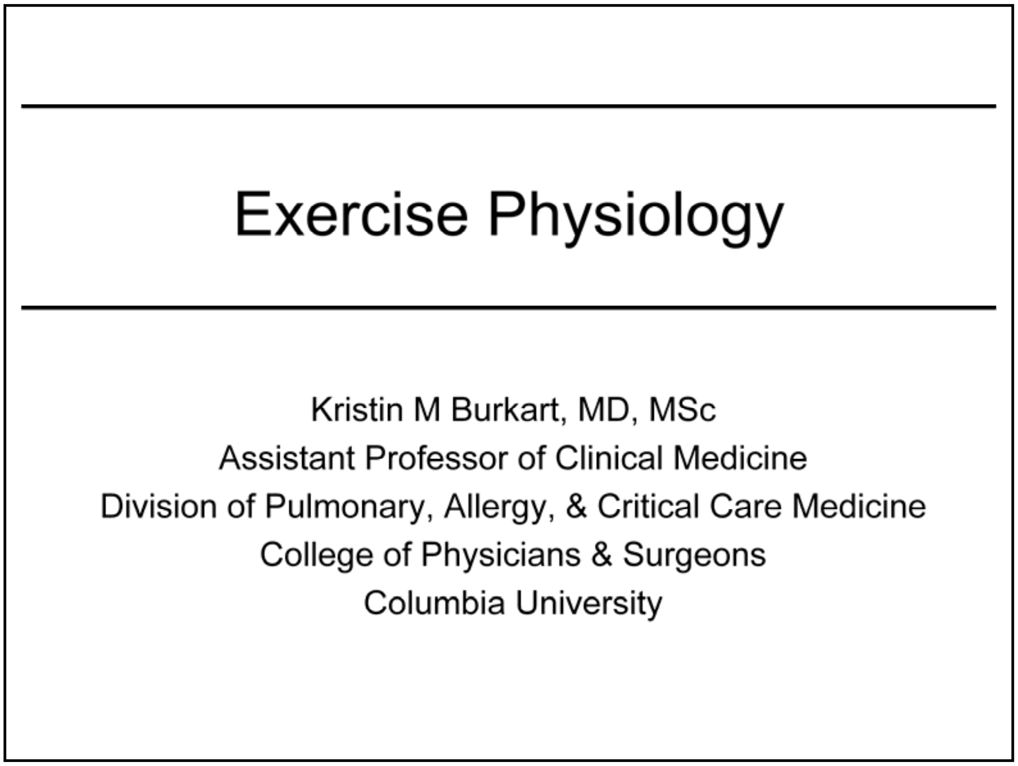
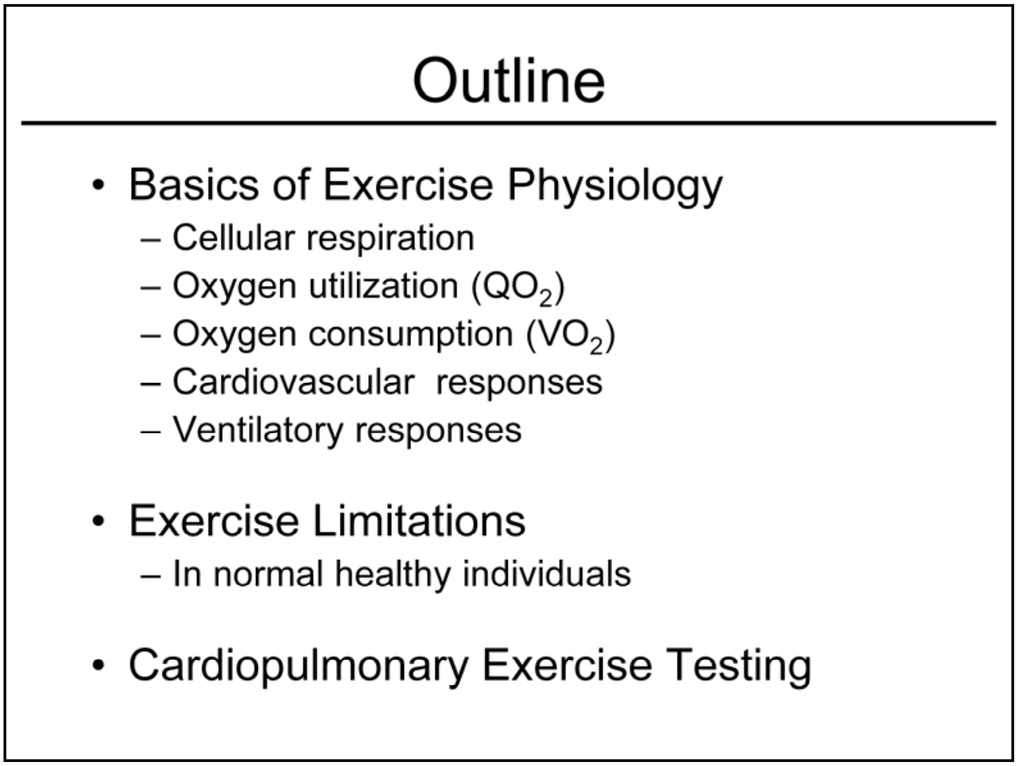


Exercise Physiology

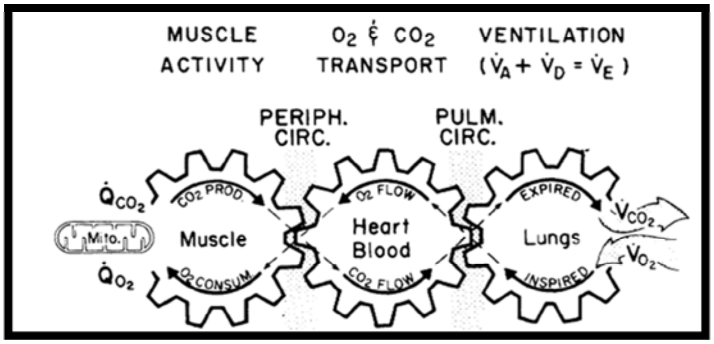
Kristin M Burkart, MD, MSc
Assistant Professor of Clinical Medicine
Division of Pulmonary, Allergy, & Critical Care Medicine
College of Physicians & Surgeons
Columbia University



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



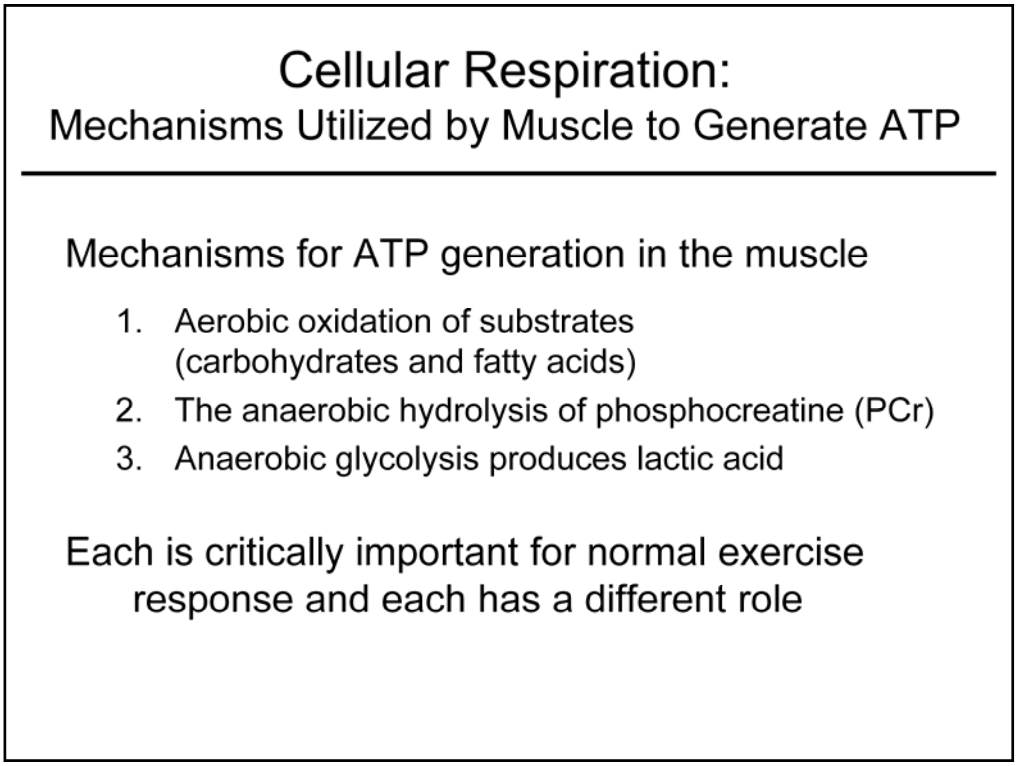
- Wasserman K: *Circulation* 1988;78:1060

- 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

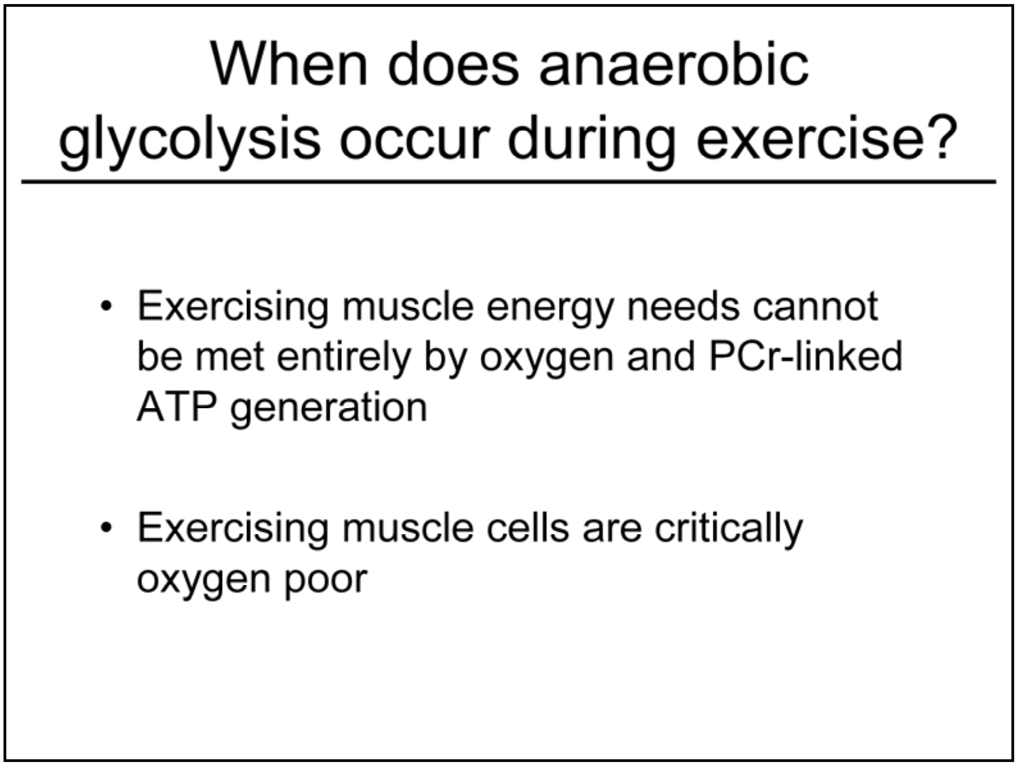


Cellular Respiration:
Mechanisms Utilized by Muscle to Generate ATP

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



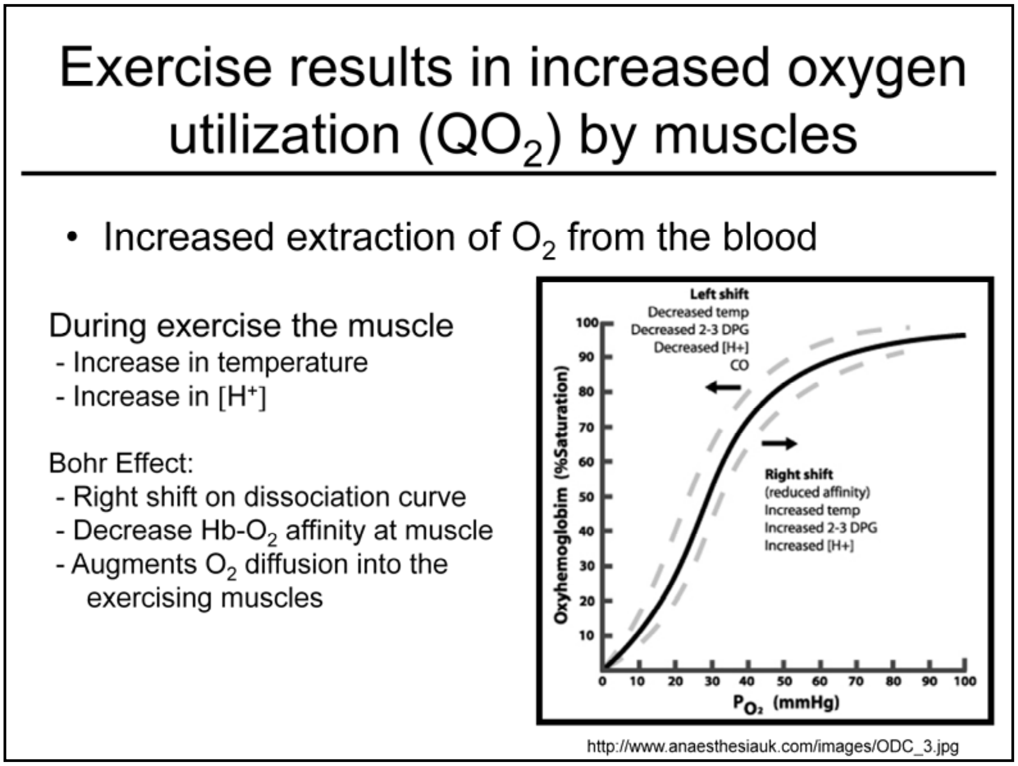
When does anaerobic glycolysis occur during exercise?

- Exercising muscle energy needs cannot be met entirely by oxygen and PCr-linked ATP generation
- Exercising muscle cells are critically oxygen poor

Oxygen Utilization (QO_2)

Exercise results in increased oxygen utilization (QO_2) by muscles

- Increased extraction of O_2 from the blood



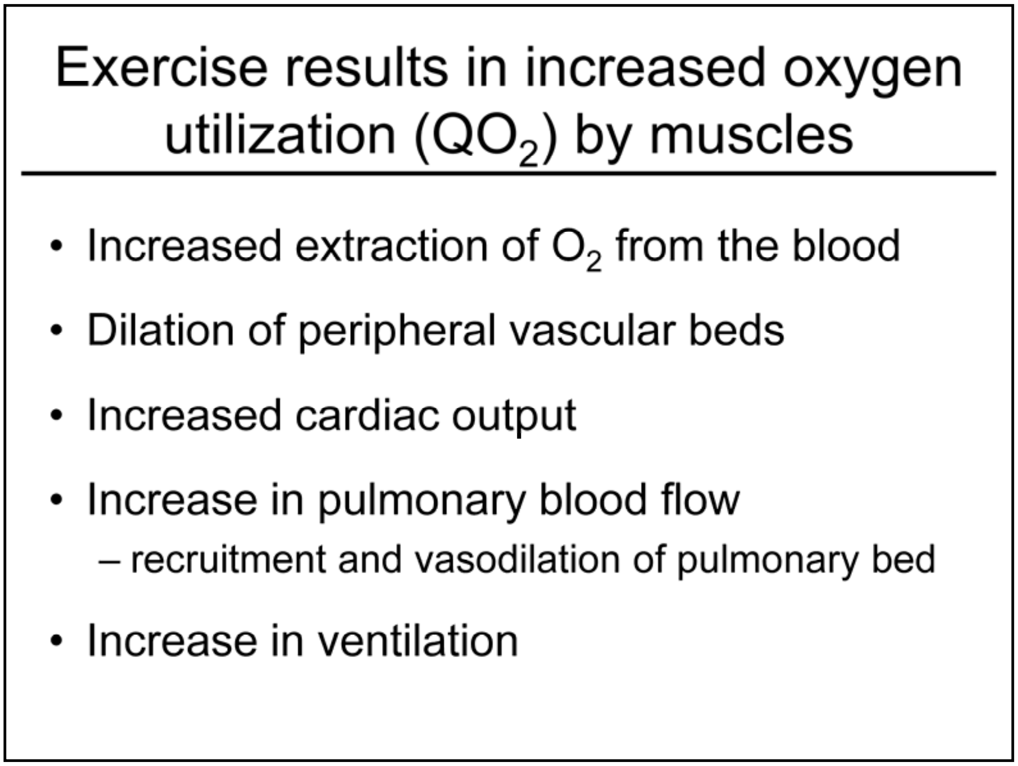
Exercise results in increased oxygen utilization (QO_2) by muscles

- Increased extraction of O_2 from the blood

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

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

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

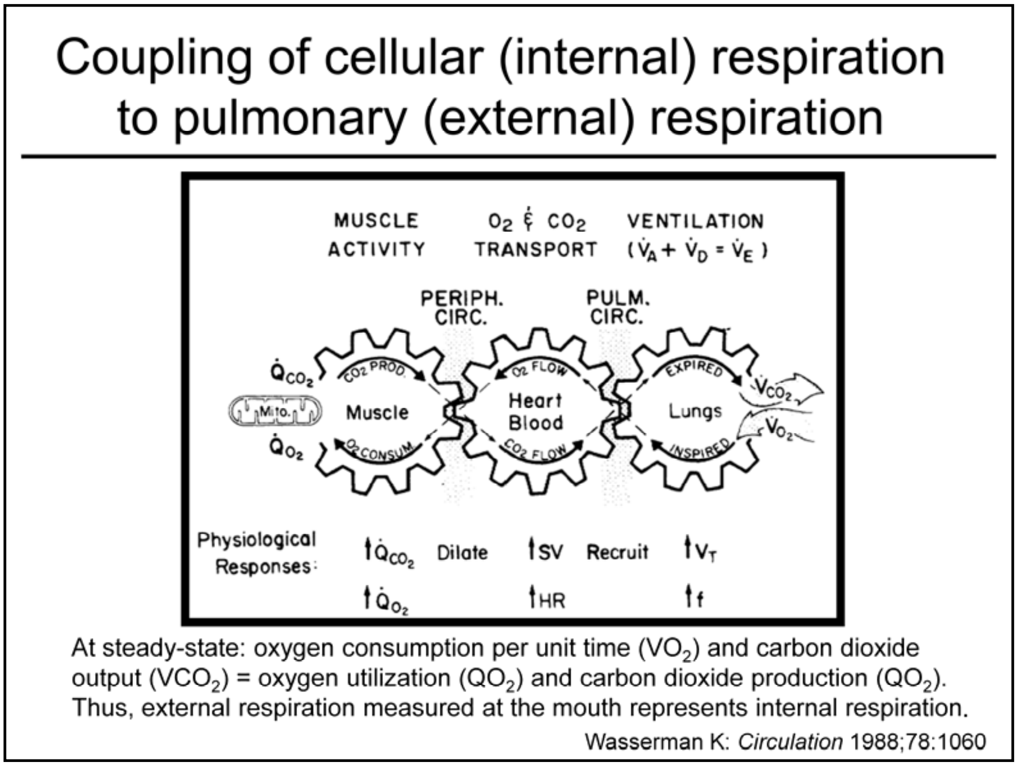


Exercise results in increased oxygen utilization (QO_2) by muscles

- 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

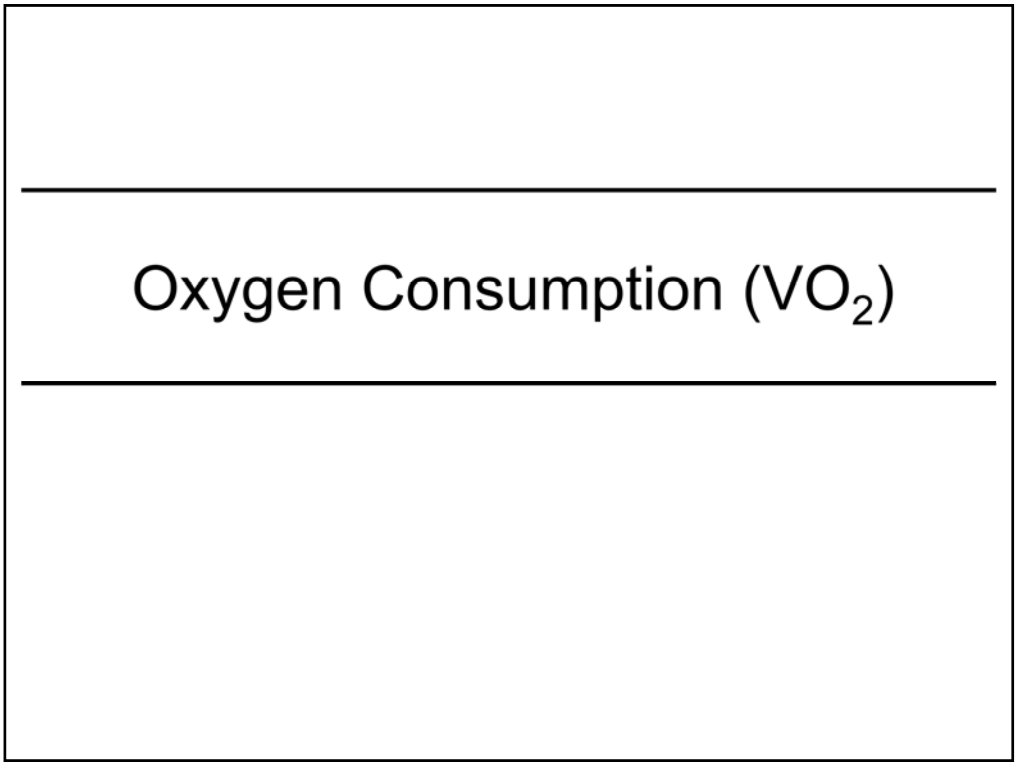
$$QO_2 = VO_2$$



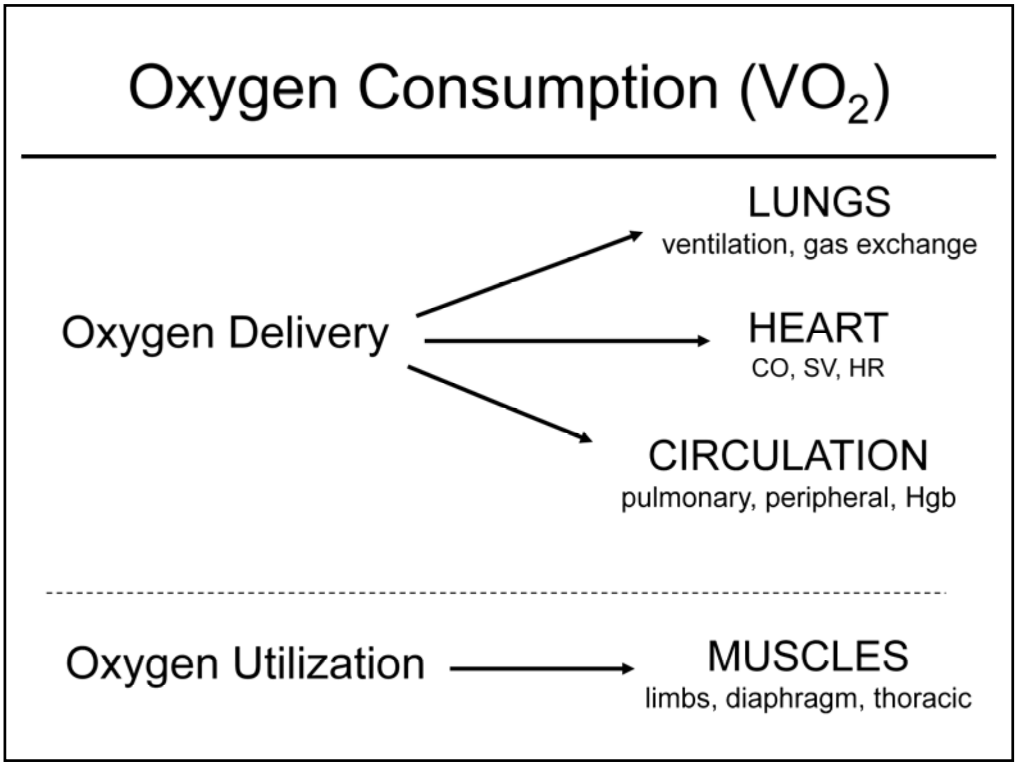
Coupling of cellular (internal) respiration to pulmonary (external) respiration

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.

Wasserman K: *Circulation* 1988;78:1060



Oxygen Consumption (VO_2)



Oxygen Consumption (VO_2)

Oxygen Delivery

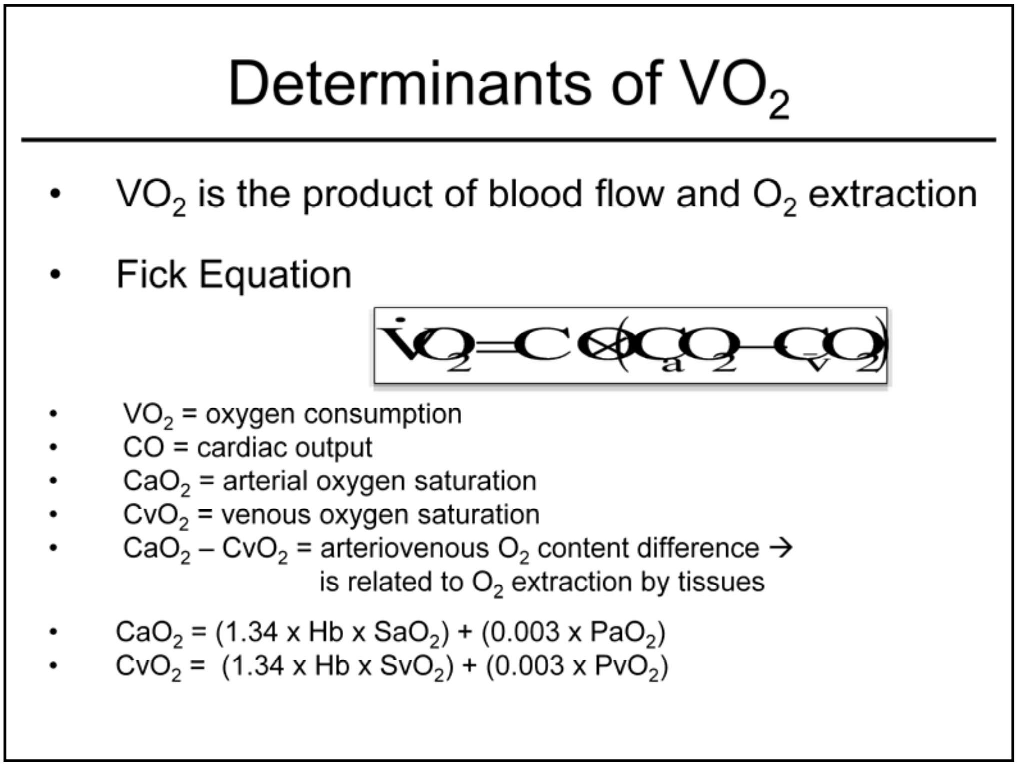
LUNGS
ventilation, gas exchange

HEART
CO, SV, HR

CIRCULATION
pulmonary, peripheral, Hgb

Oxygen Utilization

MUSCLES
limbs, diaphragm, thoracic



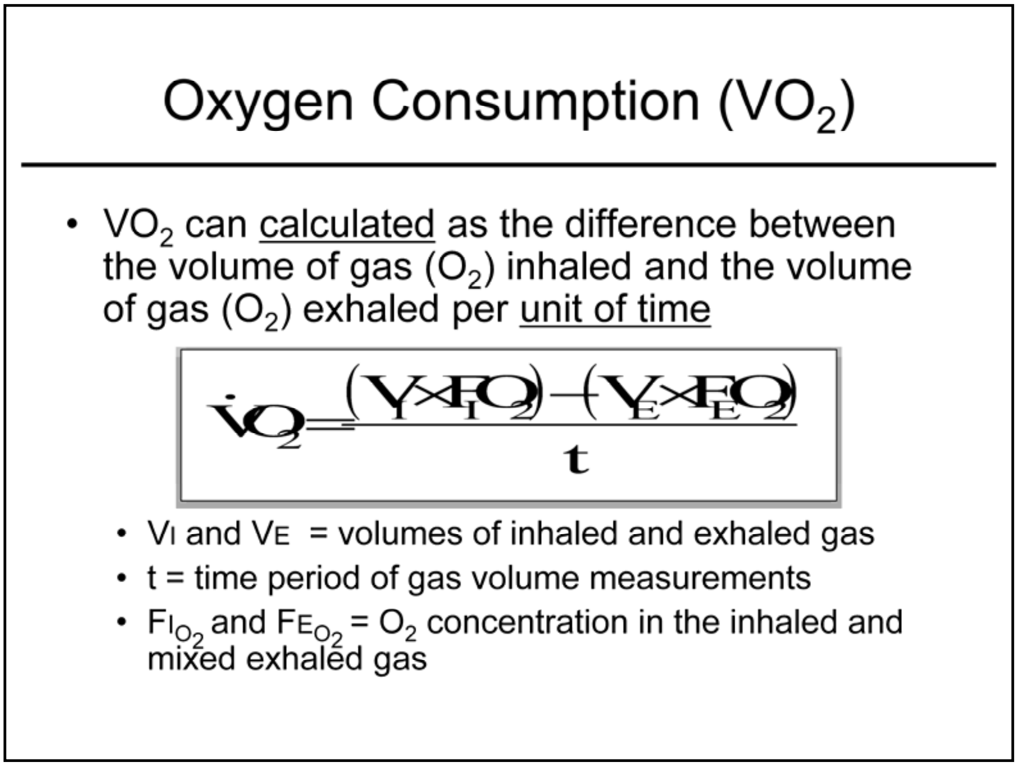
Determinants of VO_2

- VO_2 is the product of blood flow and O_2 extraction
- Fick Equation

$$\dot{V}O_2 = CO \times (C_aO_2 - C_{\bar{v}}O_2)$$

- 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

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

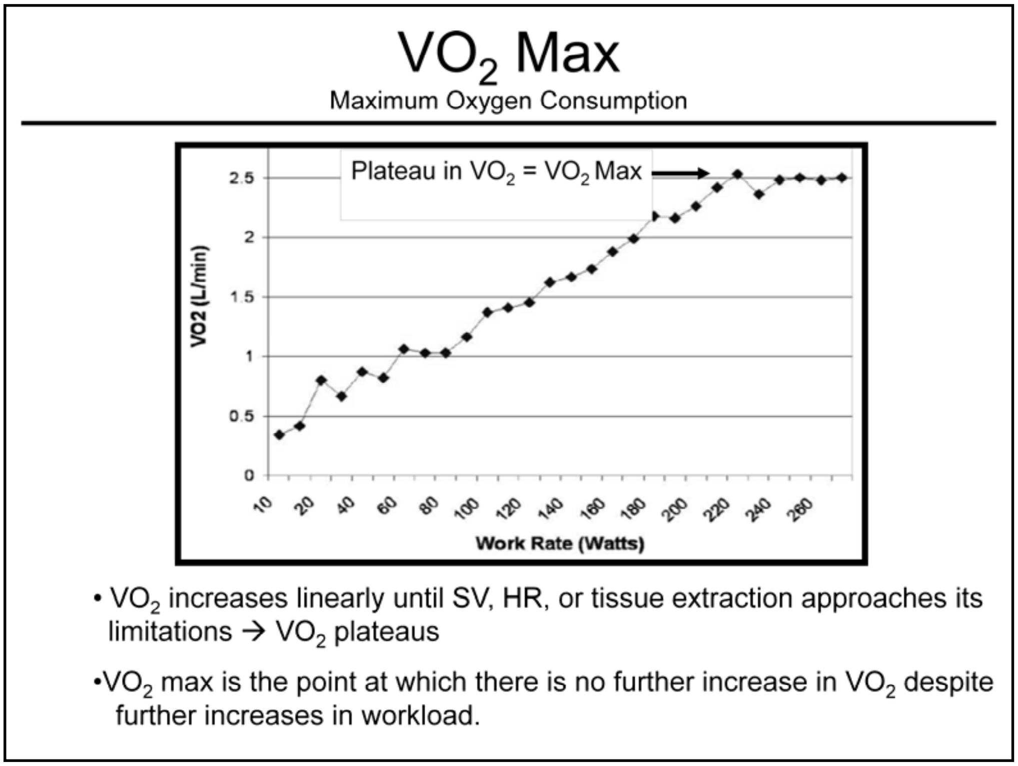


Oxygen Consumption (VO_2)

- VO_2 can calculated as the difference between the volume of gas (O_2) inhaled and the volume of gas (O_2) exhaled per unit of time

$$\dot{V}O_2 = \frac{(V_I \times F_I O_2) - (V_E \times F_E O_2)}{t}$$

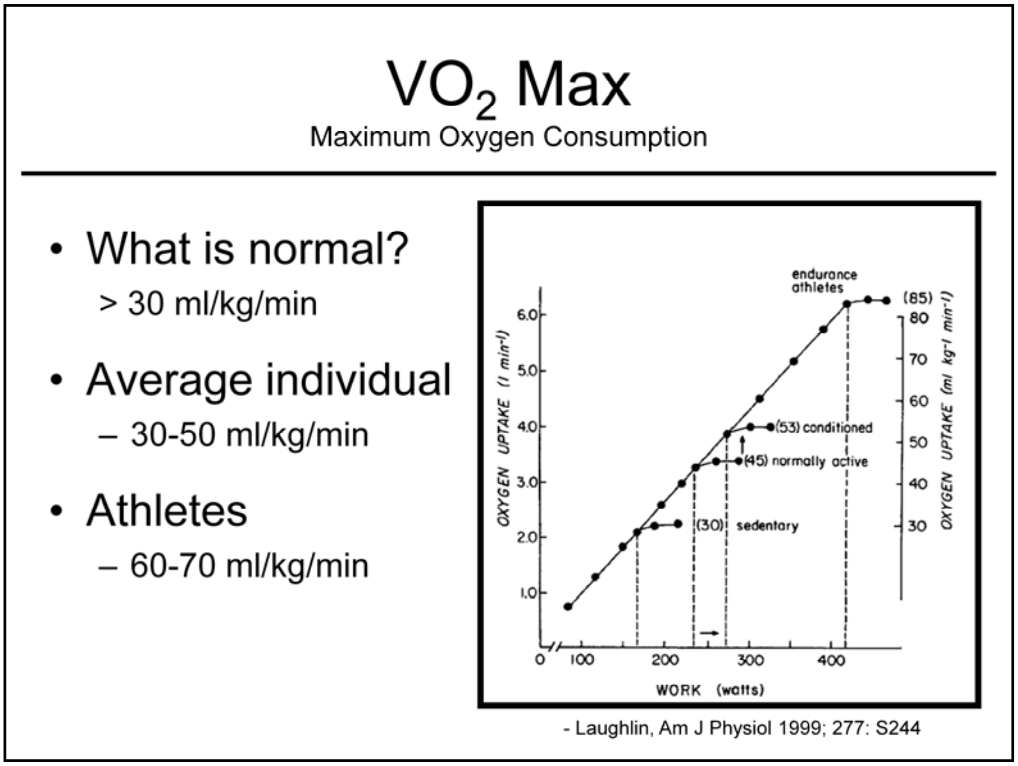
  - V_I and V_E = volumes of inhaled and exhaled gas
  - t = time period of gas volume measurements
  - $F_{I_{O_2}}$ and $F_{E_{O_2}}$ = O_2 concentration in the inhaled and mixed exhaled gas



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.

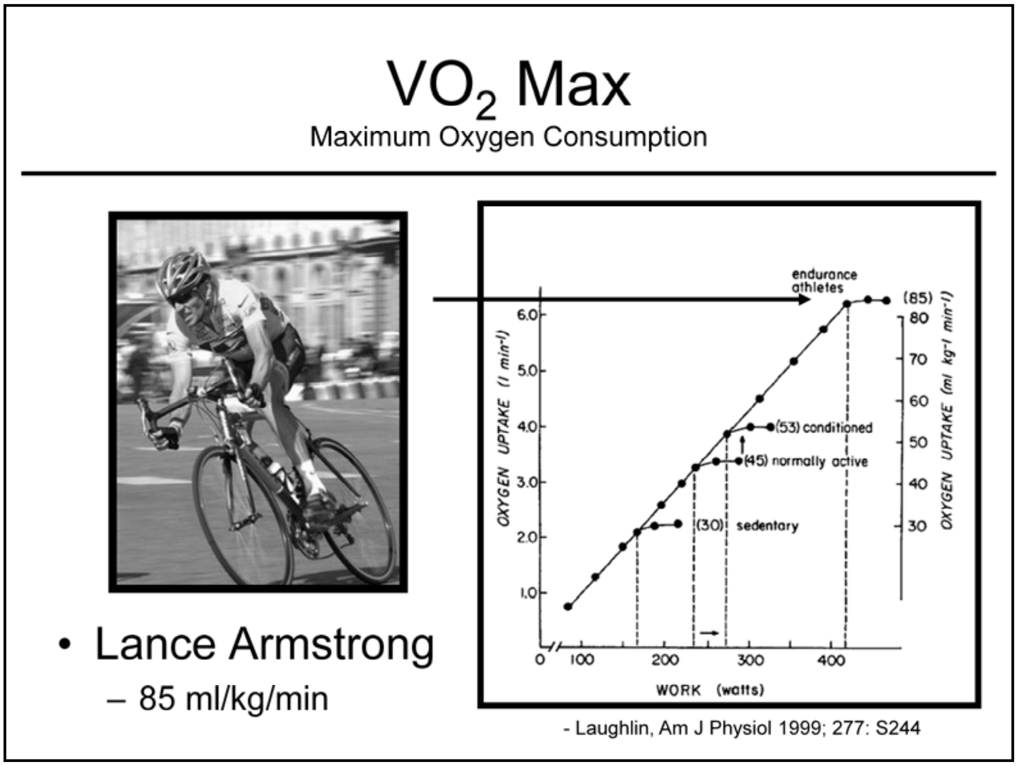


VO$_2$ Max

Maximum Oxygen Consumption

- What is normal?
  > 30 ml/kg/min
- Average individual
  - 30-50 ml/kg/min
- Athletes
  - 60-70 ml/kg/min

- Laughlin, Am J Physiol 1999; 277: S244

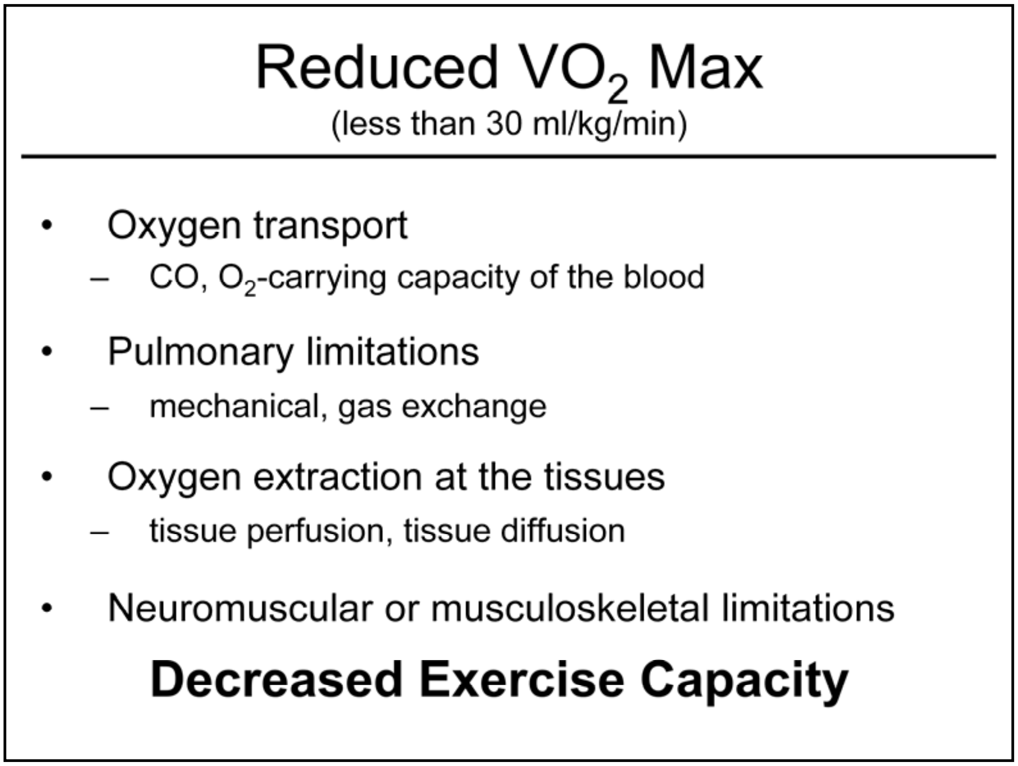


VO_2 Max

Maximum Oxygen Consumption

- Lance Armstrong
  - 85 ml/kg/min

- Laughlin, Am J Physiol 1999; 277: S244

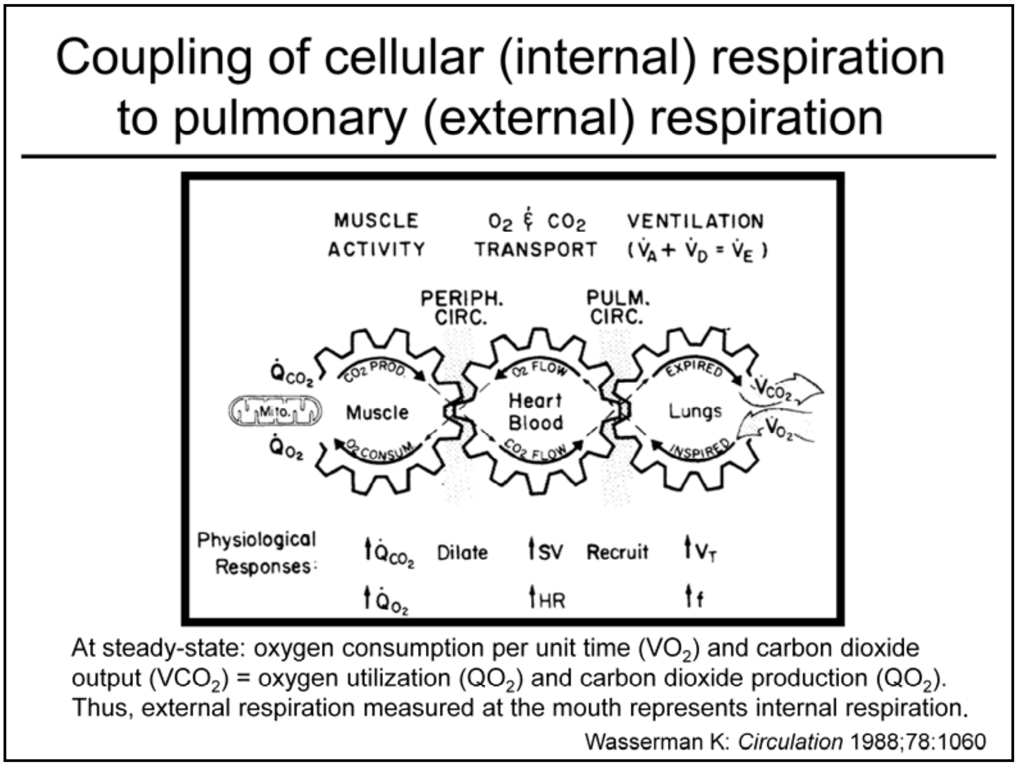


Reduced VO_2 Max

(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

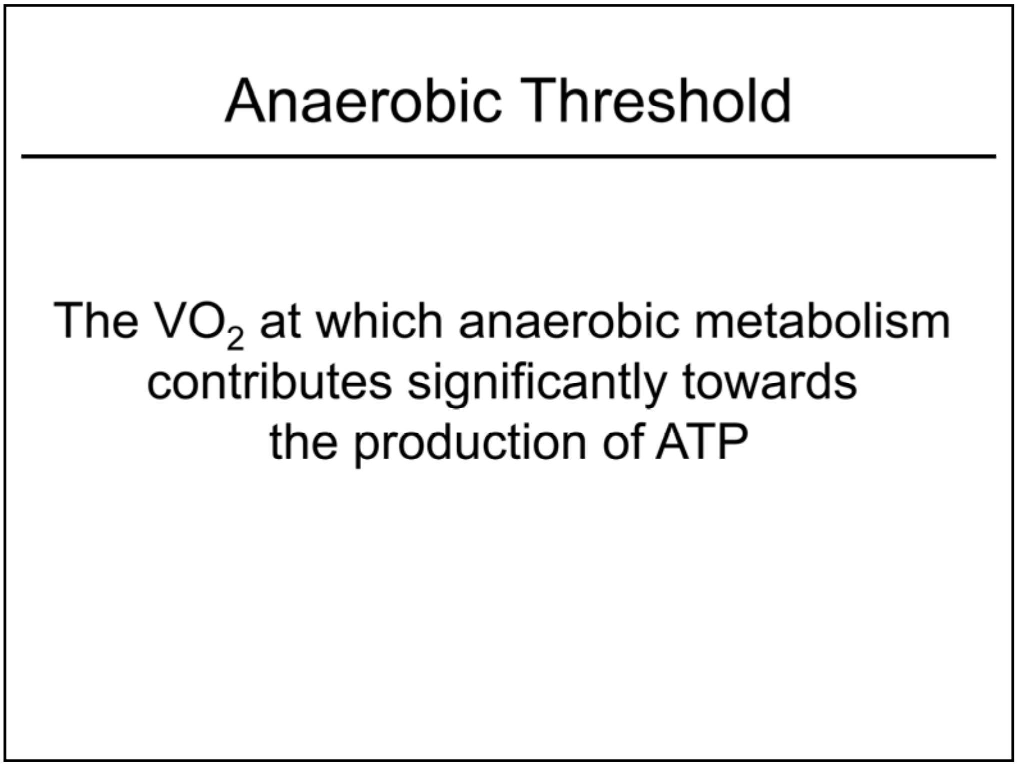


Coupling of cellular (internal) respiration to pulmonary (external) respiration

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

Anaerobic Threshold (AT)



Anaerobic Threshold

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

Anaerobic Threshold

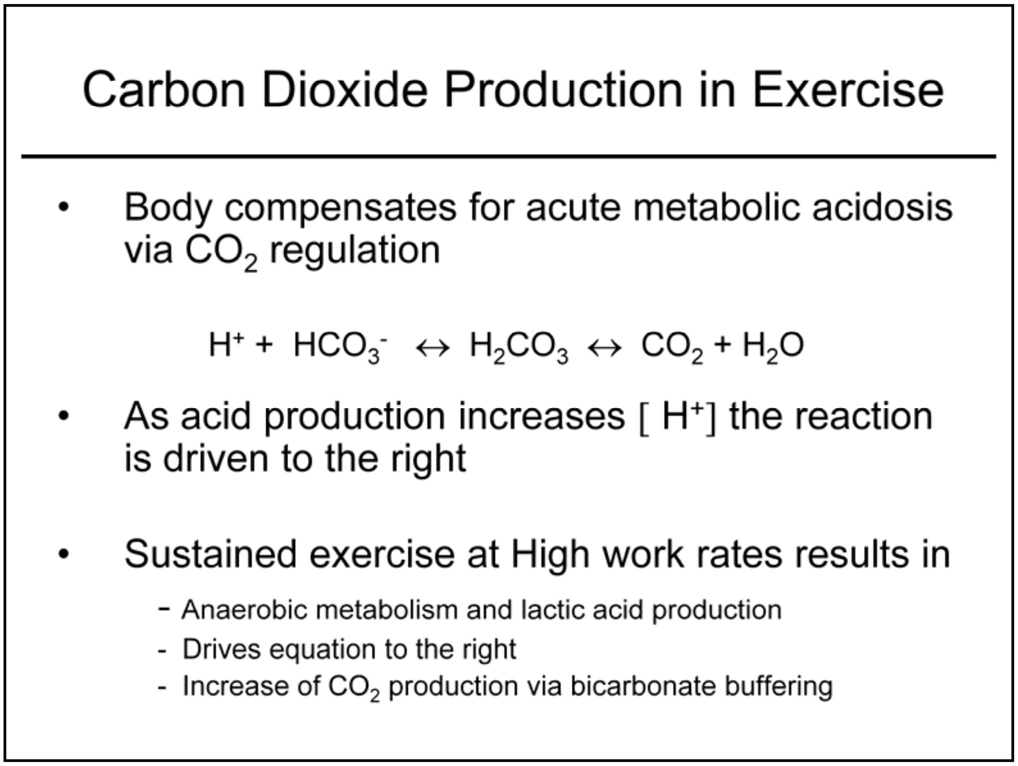
The VO_2 at which anaerobic metabolism
contributes significantly towards the production of ATP

- 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, pulmonary disease causing desaturation, or underlying mitochondrial abnormality

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

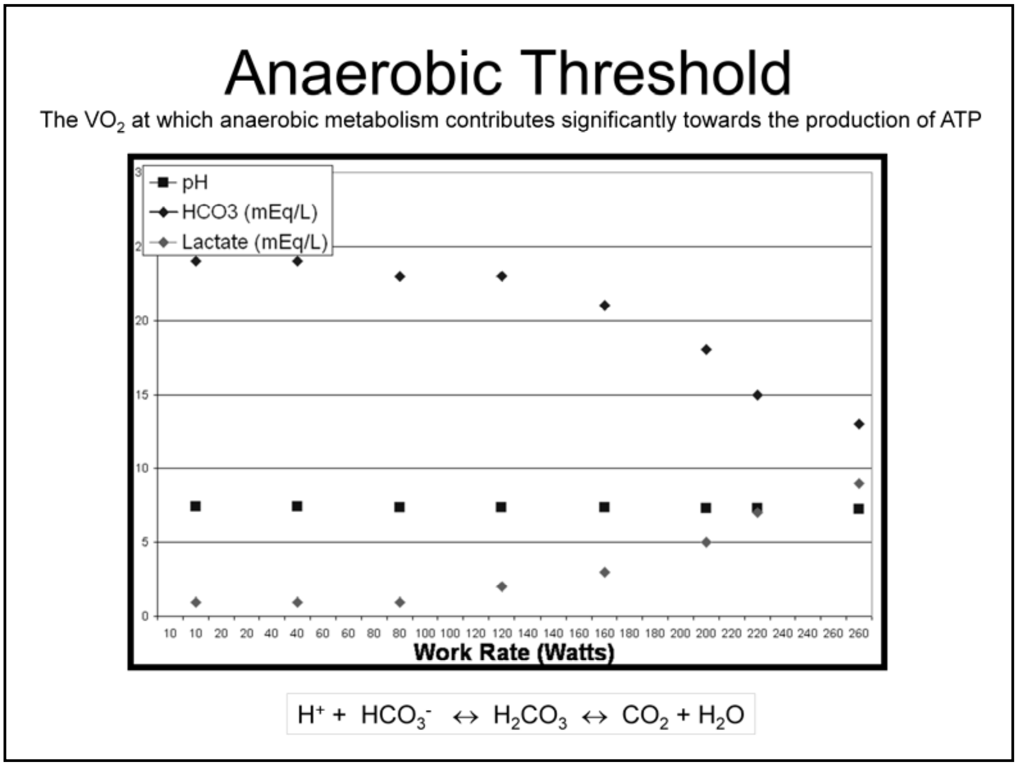


Carbon Dioxide Production in Exercise

- Body compensates for acute metabolic acidosis via CO_2 regulation

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$$

- As acid production increases [H^+] the reaction is driven to the right
- Sustained exercise at High work rates results in
  - Anaerobic metabolism and lactic acid production
  - Drives equation to the right
  - Increase of CO_2 production via bicarbonate buffering

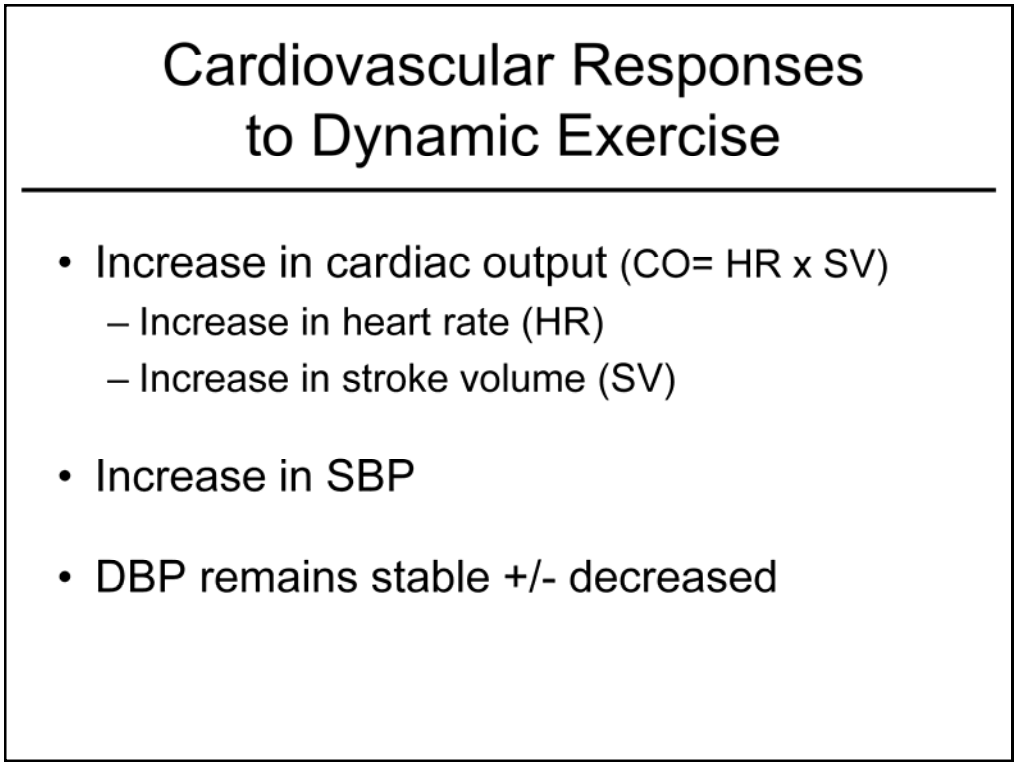


Anaerobic Threshold

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

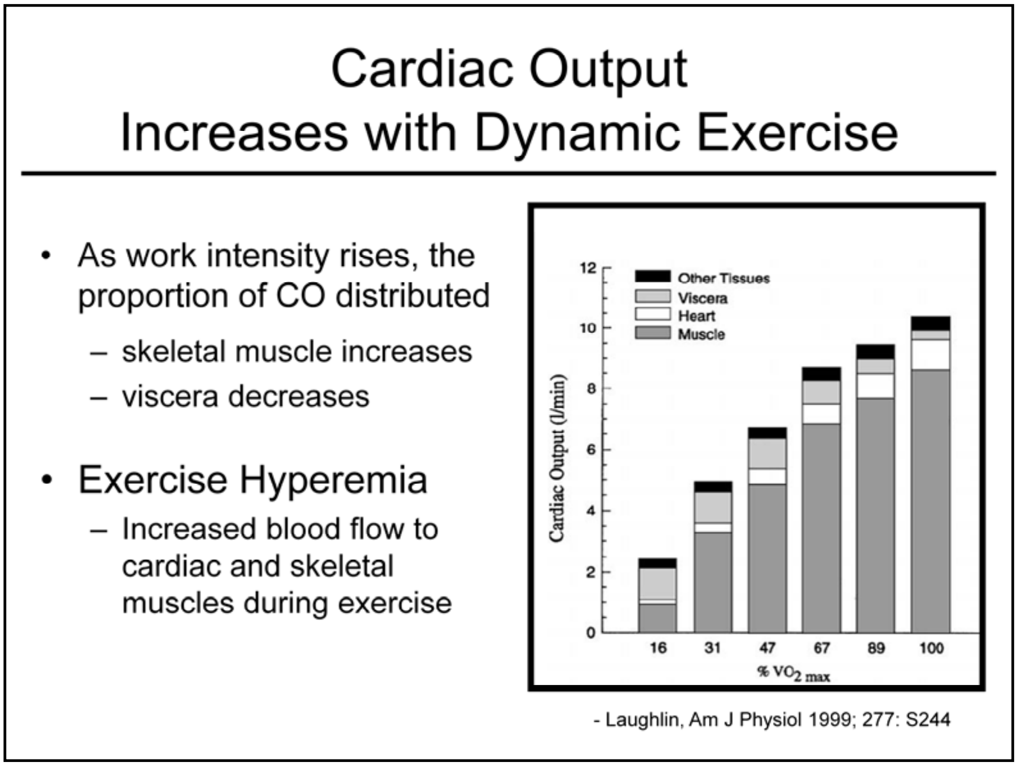
$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$

Cardiovascular Responses to Dynamic Exercise



Cardiovascular Responses to Dynamic Exercise

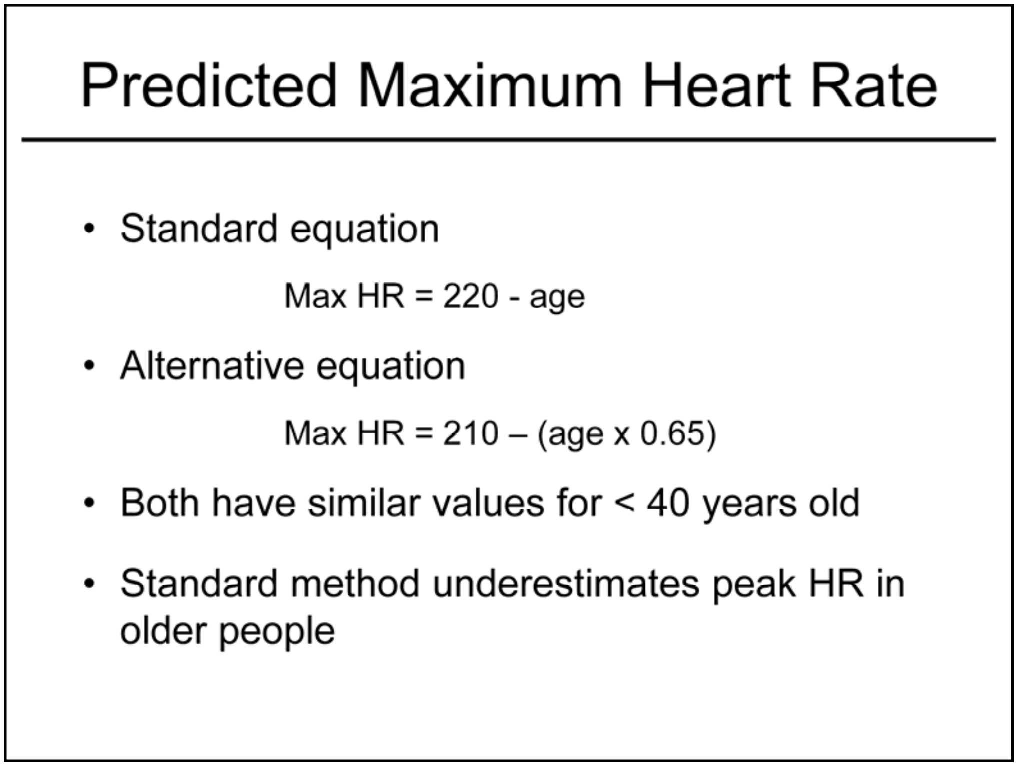
- Increase in cardiac output (CO= HR x SV)
  - Increase in heart rate (HR)
  - Increase in stroke volume (SV)
- Increase in SBP
- DBP remains stable +/- decreased



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

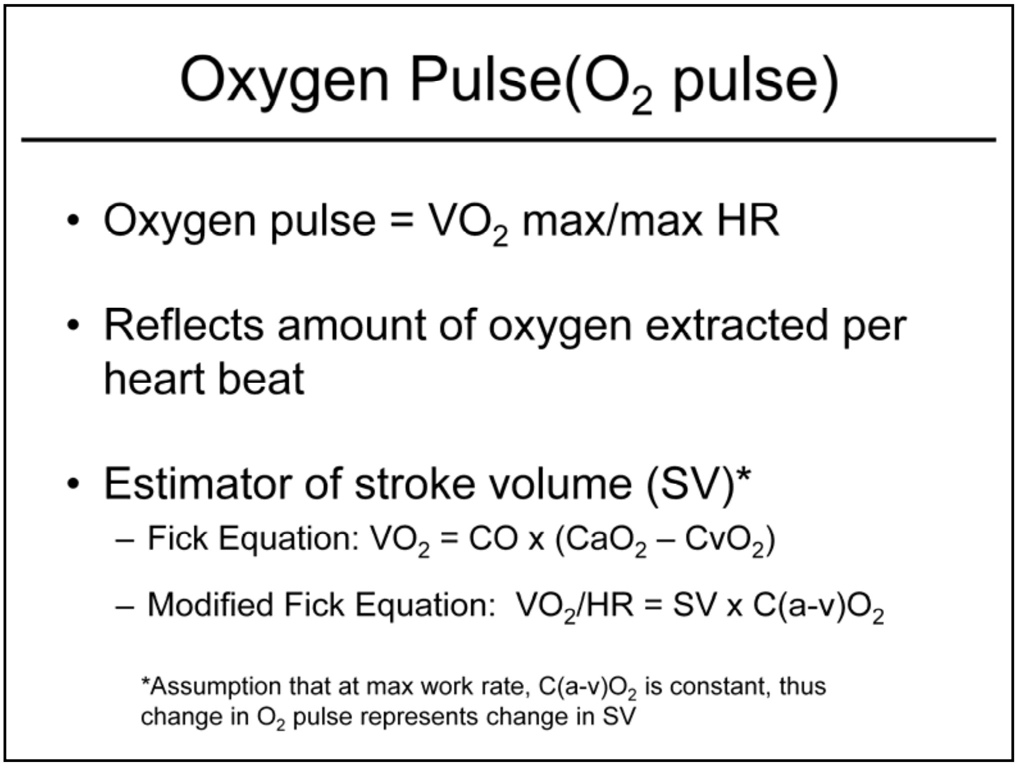
- Standard equation

  Max HR = 220 - age

- Alternative equation

  Max HR = 210 – (age x 0.65)

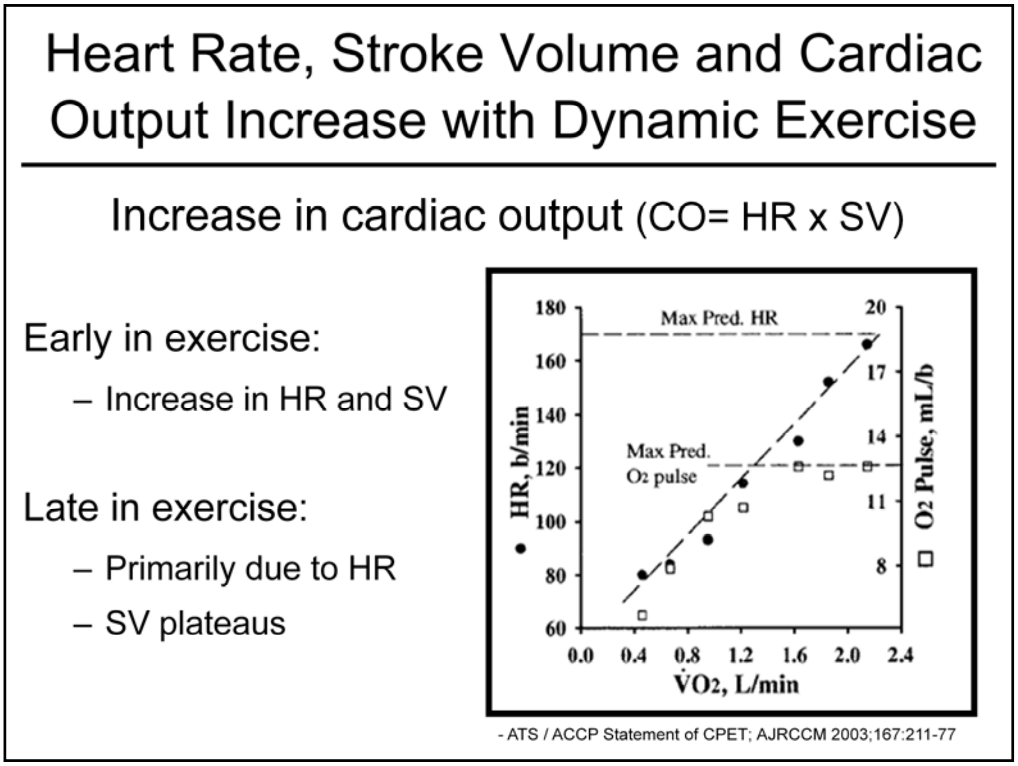
- Both have similar values for < 40 years old
- Standard method underestimates peak HR in older people



Oxygen Pulse(O_2 pulse)

- Oxygen pulse = VO_2 max/max HR
- Reflects amount of oxygen extracted per heart beat
- Estimator of stroke volume (SV)*
  - Fick Equation: $VO_2 = CO \times (CaO_2 - CvO_2)$
  - 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)

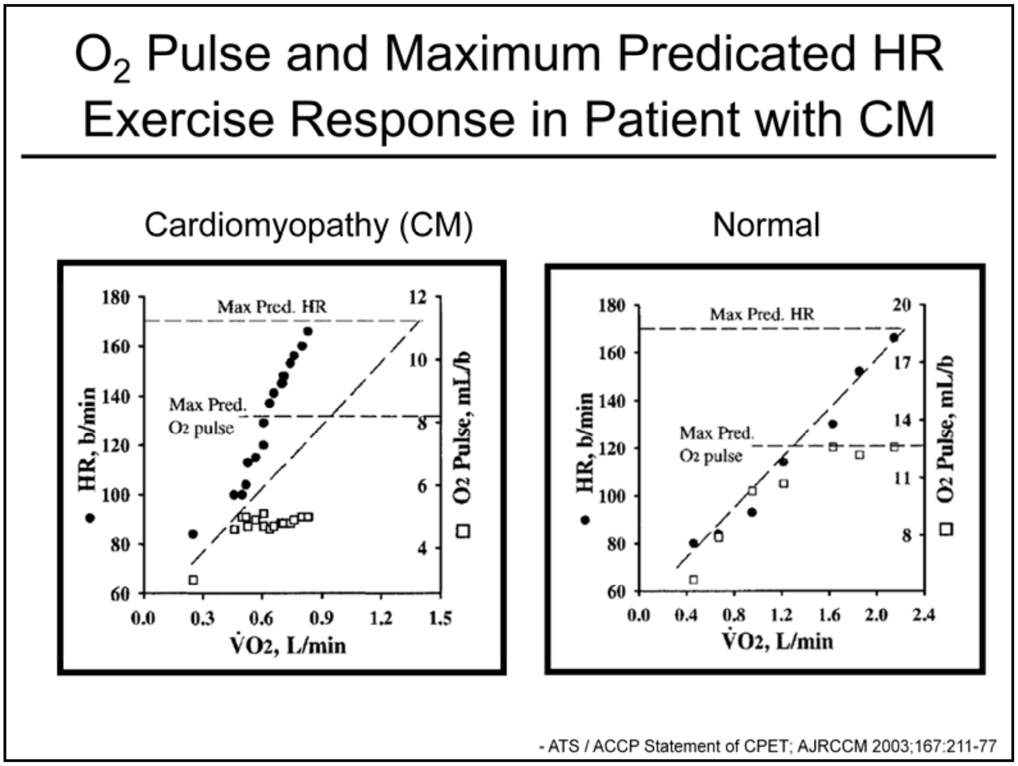
Early in exercise:

- Increase in HR and SV

Late in exercise:

- Primarily due to HR
- SV plateaus

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

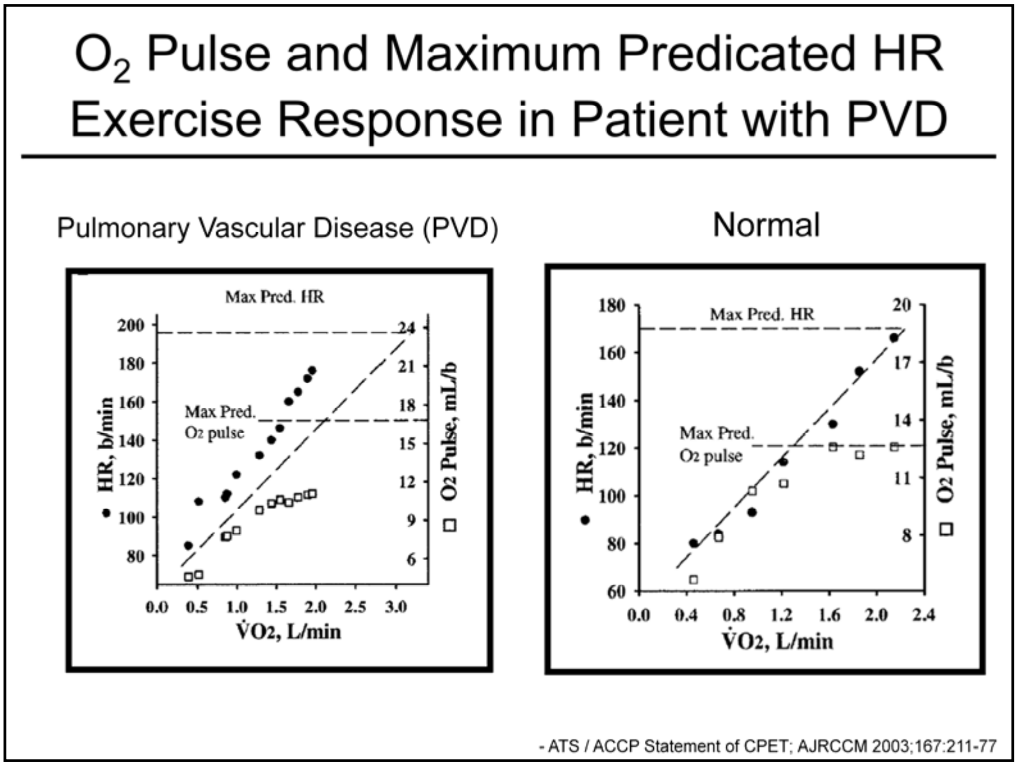


O$_2$ Pulse and Maximum Predicated HR Exercise Response in Patient with CM

Cardiomyopathy (CM)

Normal

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



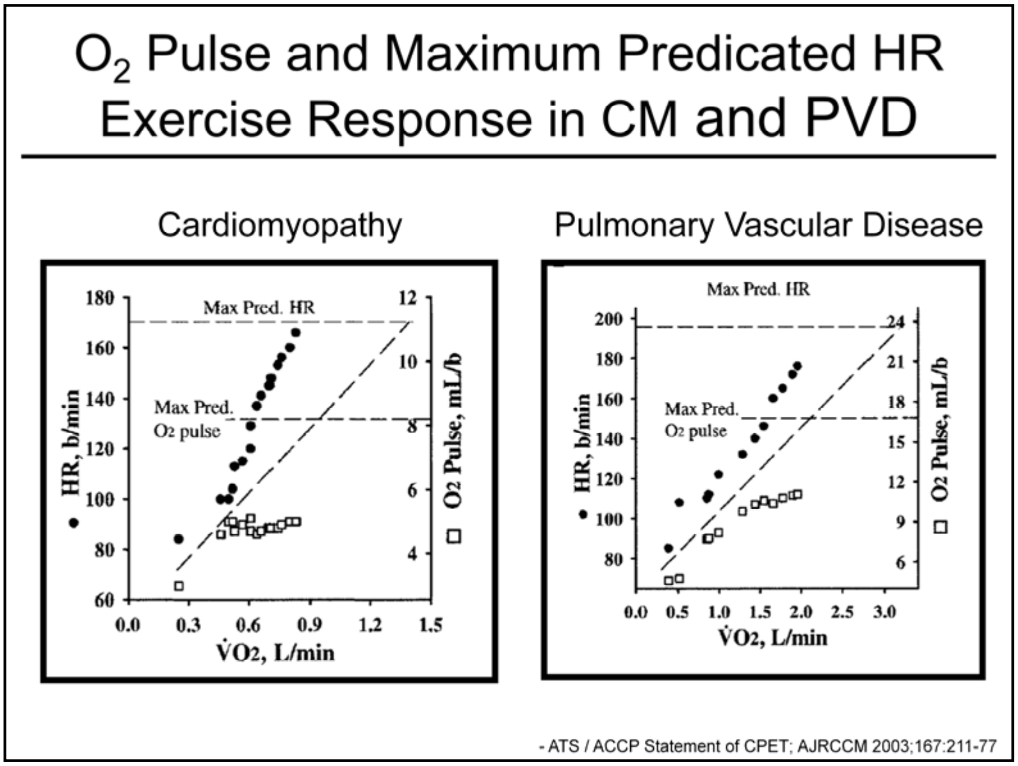
O_2 Pulse and Maximum Predicated HR Exercise Response in Patient with PVD

Pulmonary Vascular Disease (PVD)

Normal

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

.

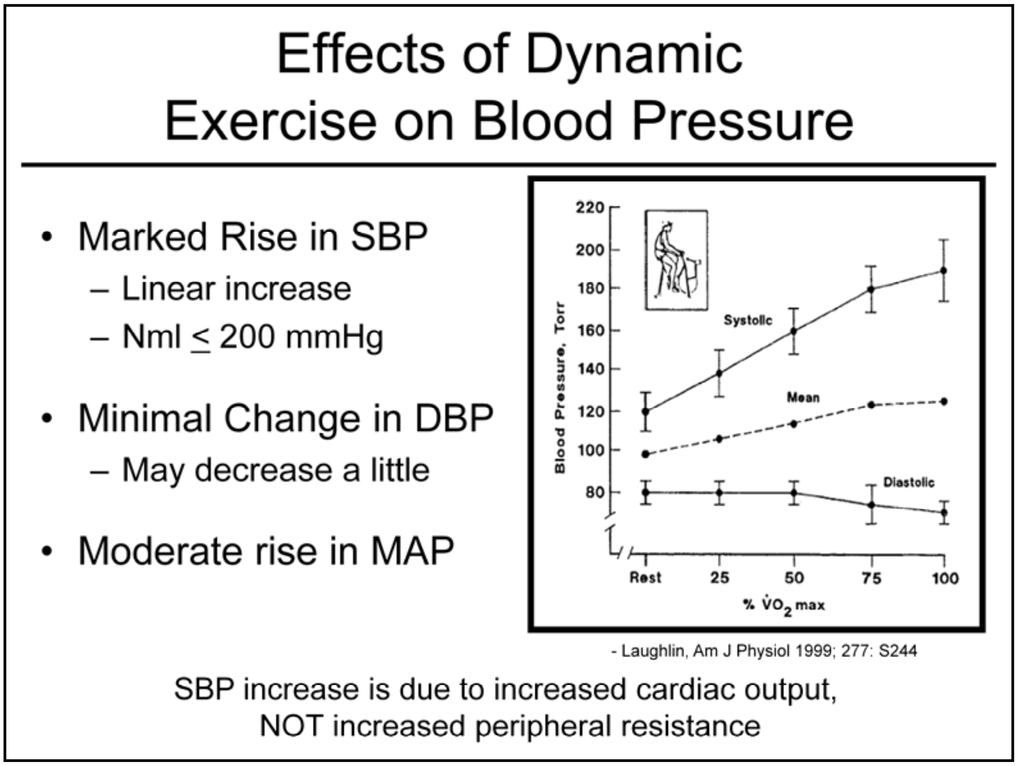


O_2 Pulse and Maximum Predicated HR Exercise Response in CM and PVD

Cardiomyopathy

Pulmonary Vascular Disease

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

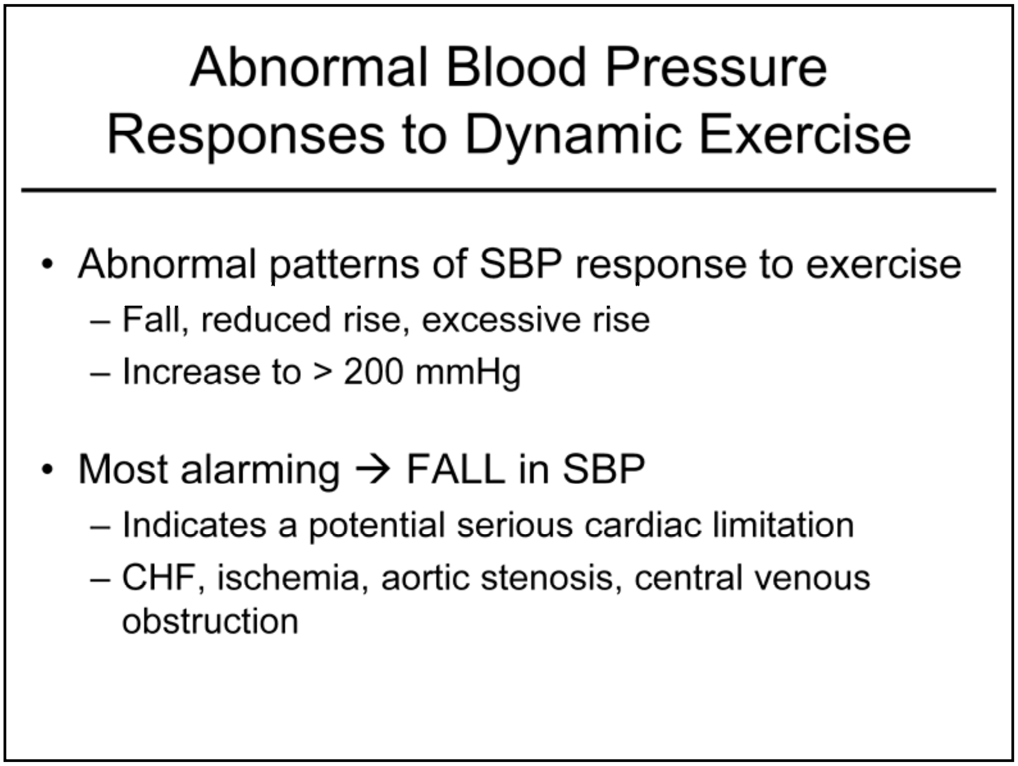


Effects of Dynamic Exercise on Blood Pressure

- Marked Rise in SBP
  - – Linear increase
  - – Nml ≤ 200 mmHg
- Minimal Change in DBP
  - – May decrease a little
- Moderate rise in MAP

- Laughlin, Am J Physiol 1999; 277: S244

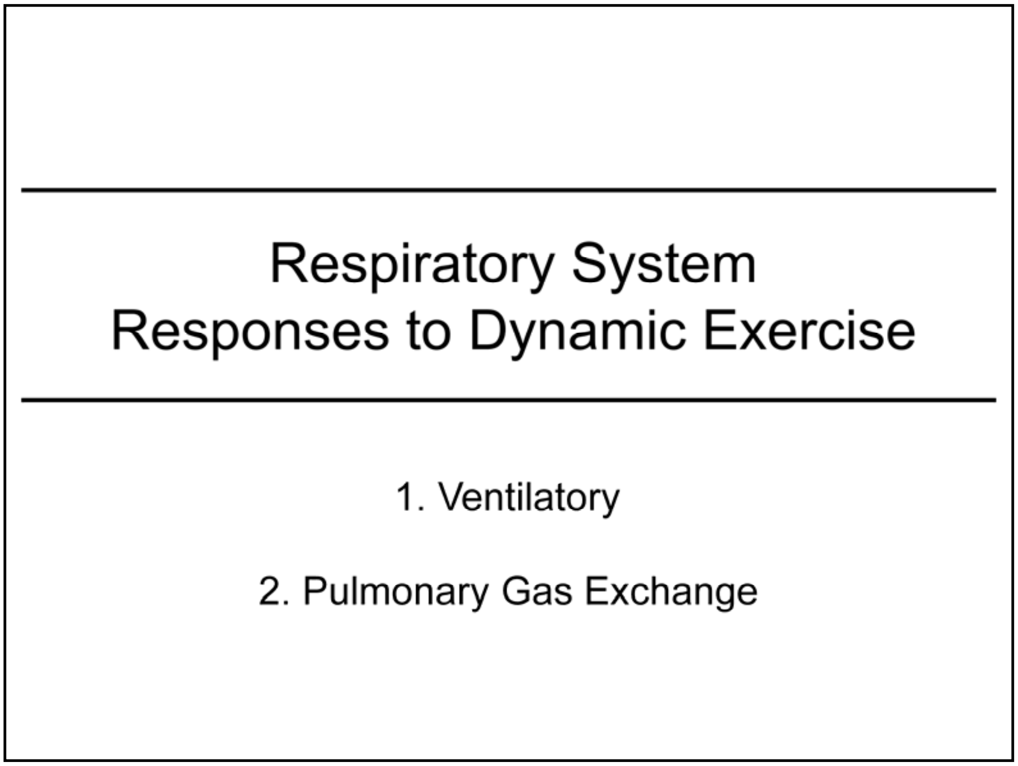
SBP increase is due to increased cardiac output,
NOT increased peripheral resistance



Abnormal Blood Pressure Responses to Dynamic Exercise

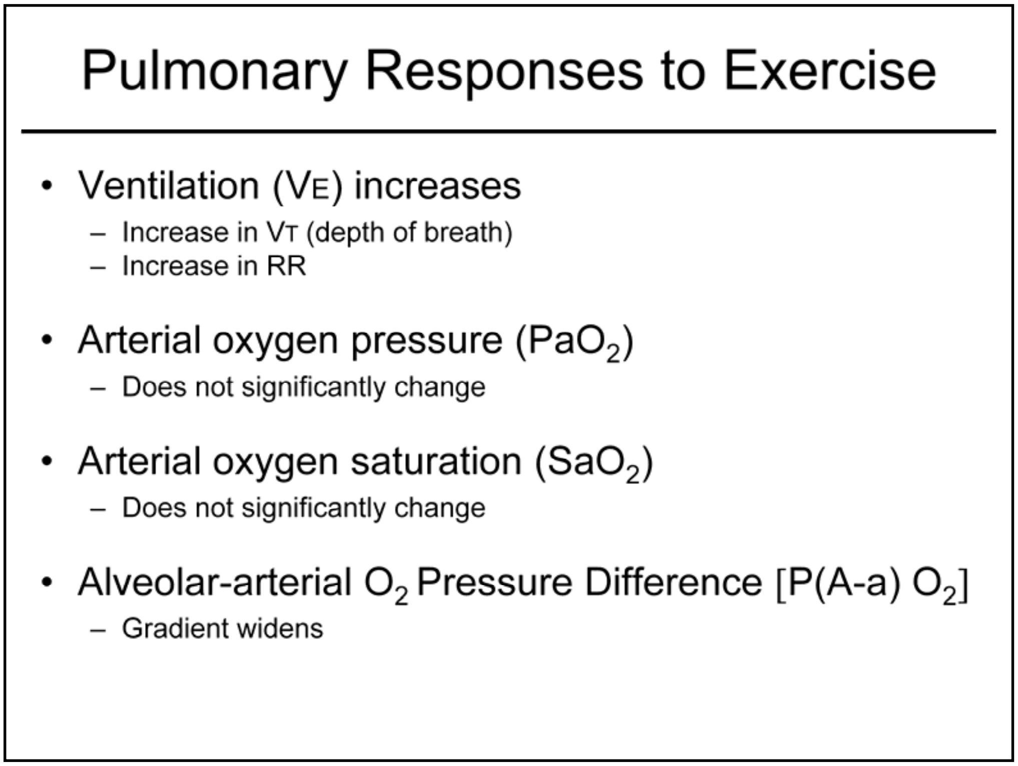
- Abnormal patterns of SBP response to exercise
  - Fall, reduced rise, excessive rise
  - Increase to > 200 mmHg
- Most alarming → FALL in SBP
  - Indicates a potential serious cardiac limitation
  - CHF, ischemia, aortic stenosis, central venous obstruction

Other



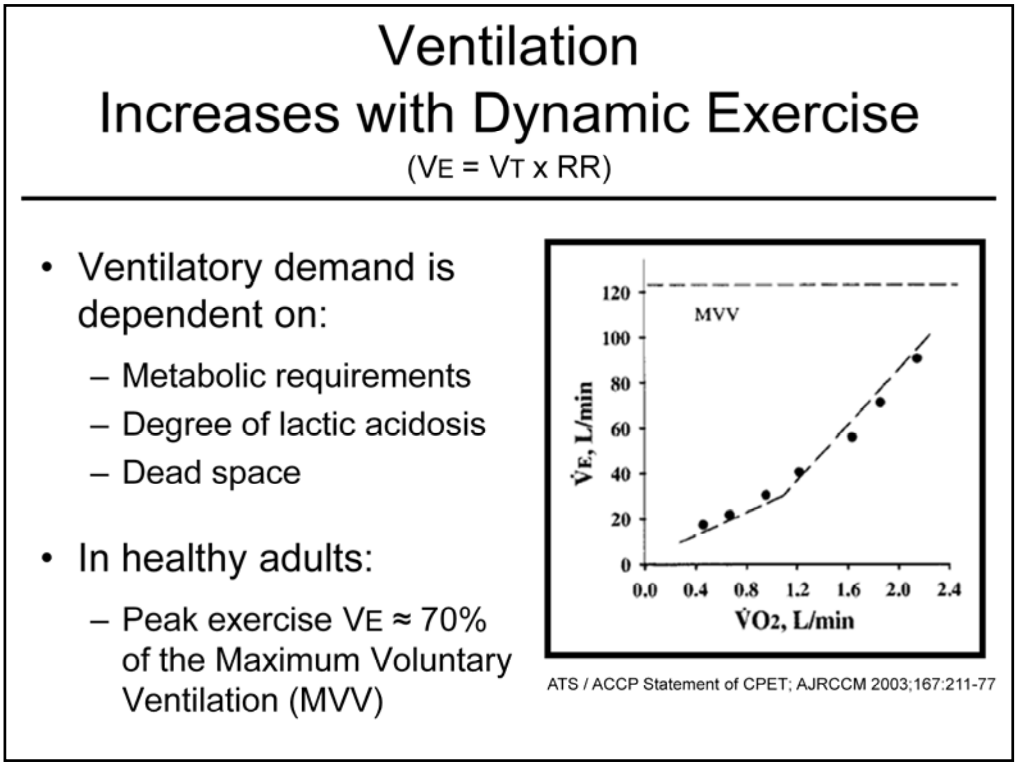
Respiratory System
Responses to Dynamic Exercise

1. Ventilatory
2. Pulmonary Gas Exchange



Pulmonary Responses to Exercise

- Ventilation (V_E) increases
  - 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 [$P(A\text{-}a)\ O_2$]
  - Gradient widens

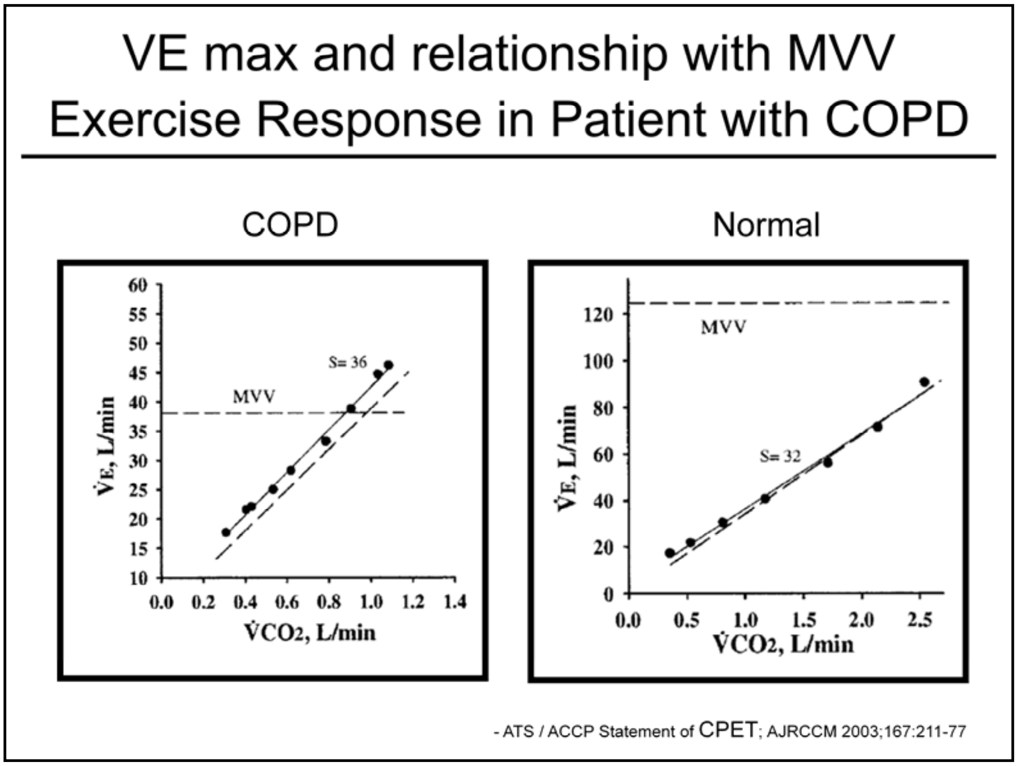


Ventilation Increases with Dynamic Exercise

(VE = VT x RR)

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

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

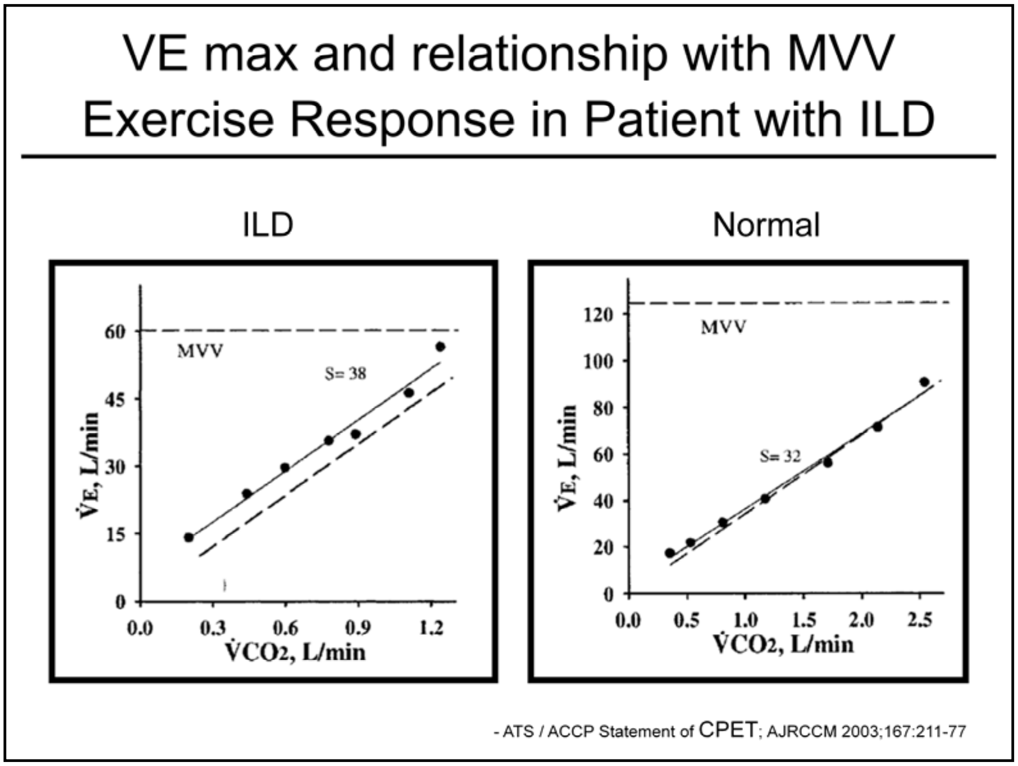


VE max and relationship with MVV Exercise Response in Patient with COPD

COPD

Normal

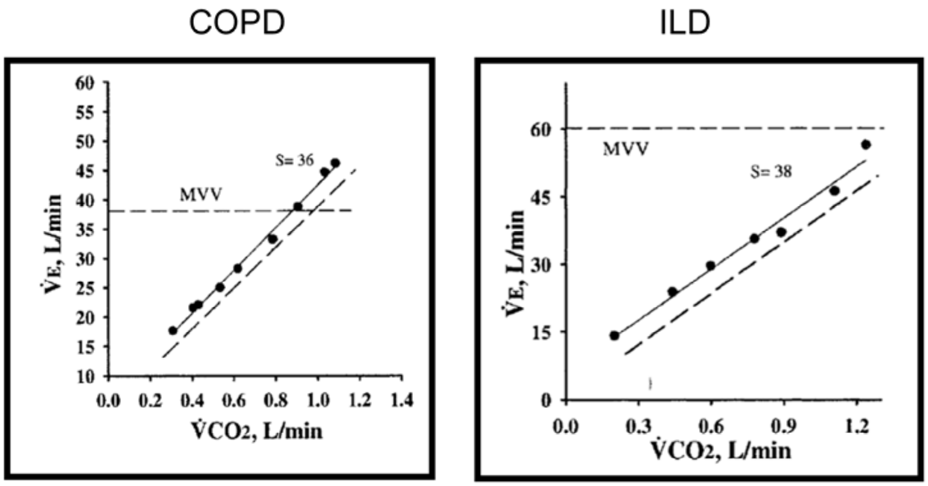
- ATS / ACCP Statement of CPET; AJRCCM 2003;167:211-77



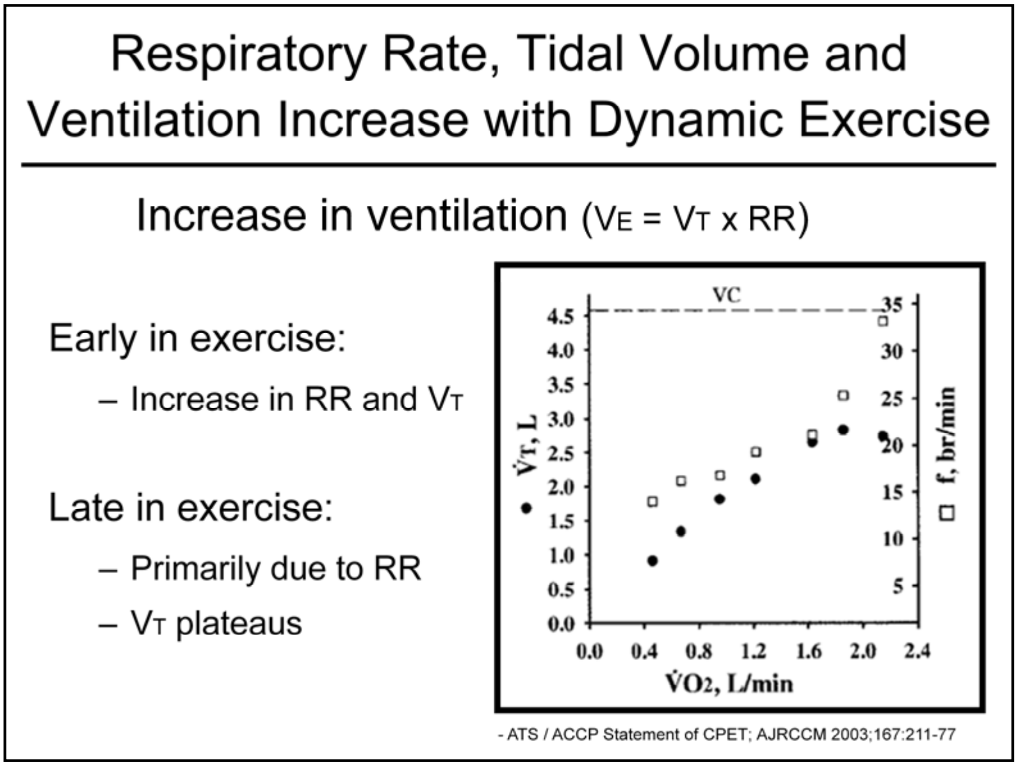
VE max and relationship with MVV Exercise Response in Patient with ILD

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

VE max Relative to MVV in Patients with COPD and ILD During Exercise



- 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:

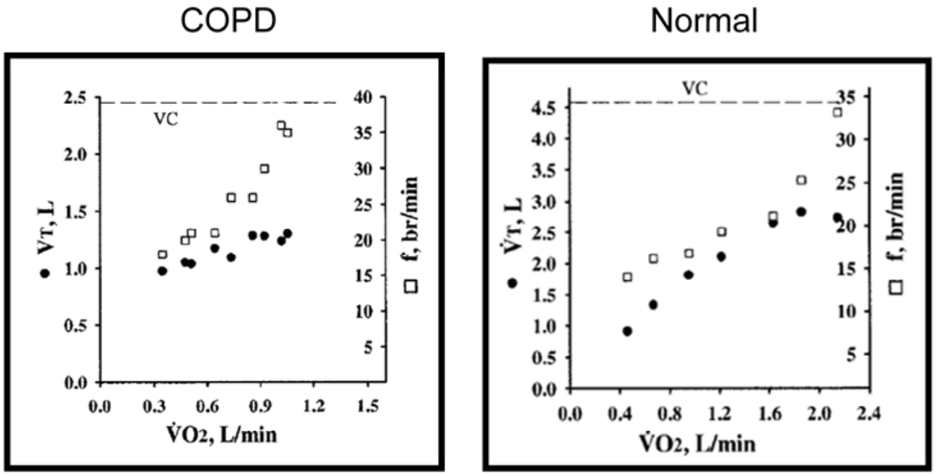
- Increase in RR and V_T

Late in exercise:

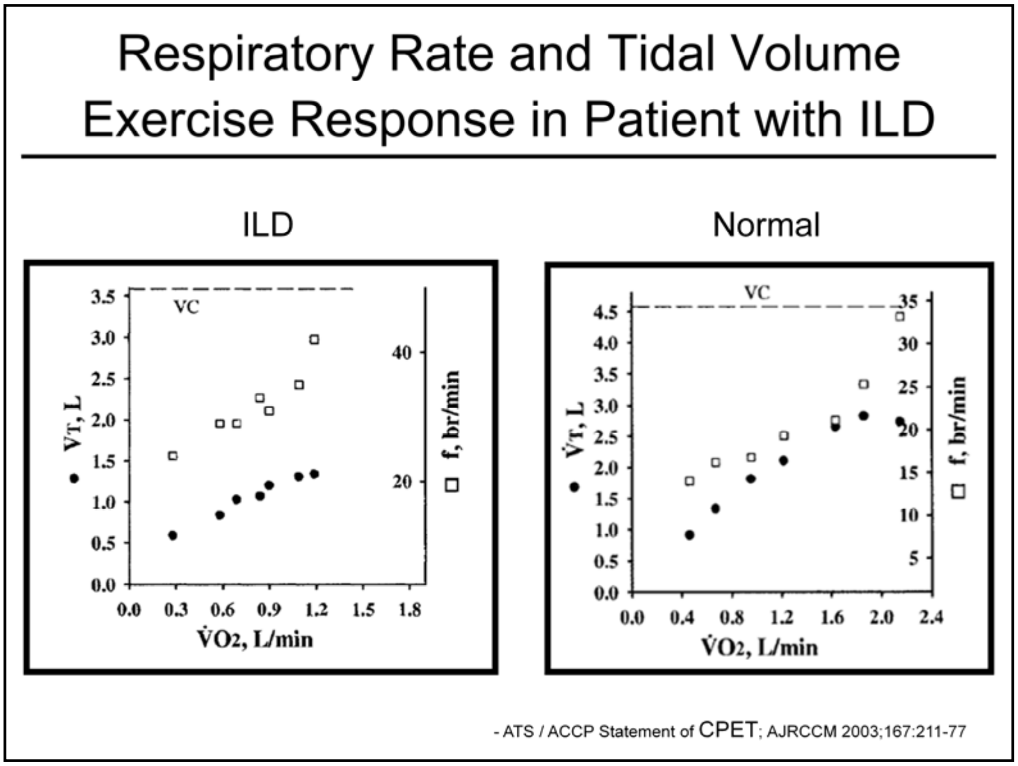
- Primarily due to RR
- V_T plateaus

- 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



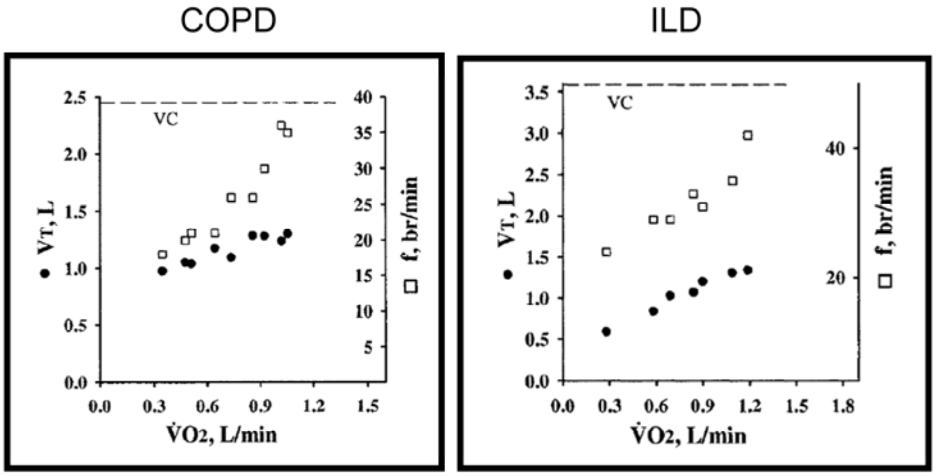
Respiratory Rate and Tidal Volume Exercise Response in Patient with ILD

ILD

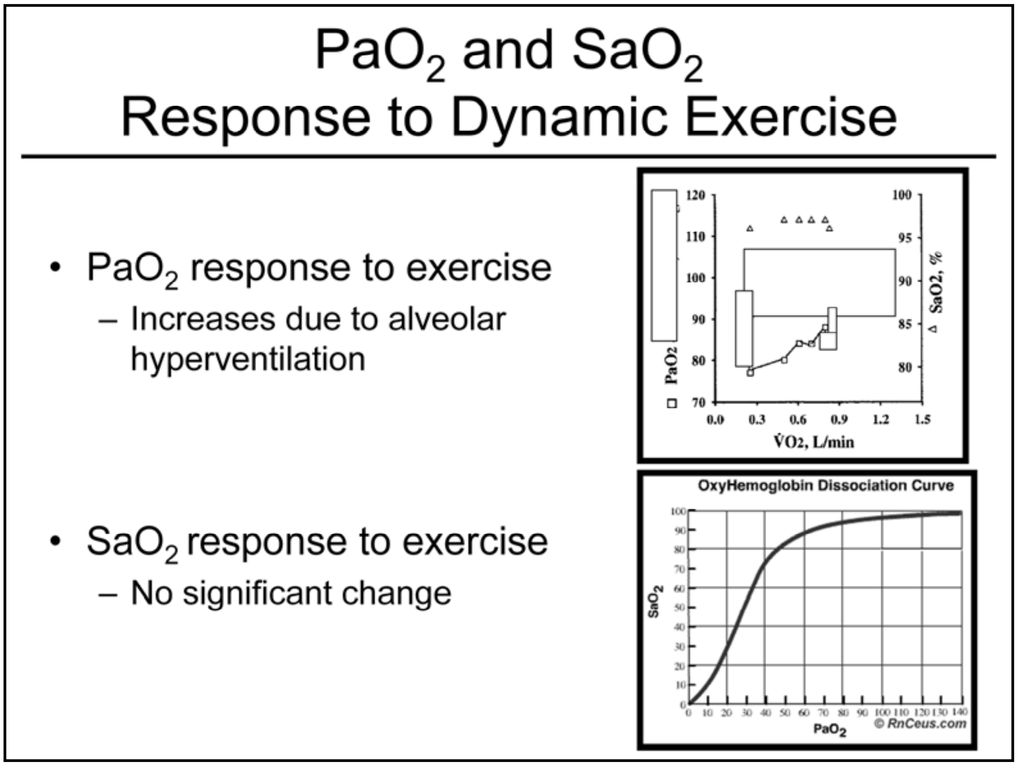
Normal

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

Respiratory Rate and Tidal Volume Exercise Response in COPD and ILD



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

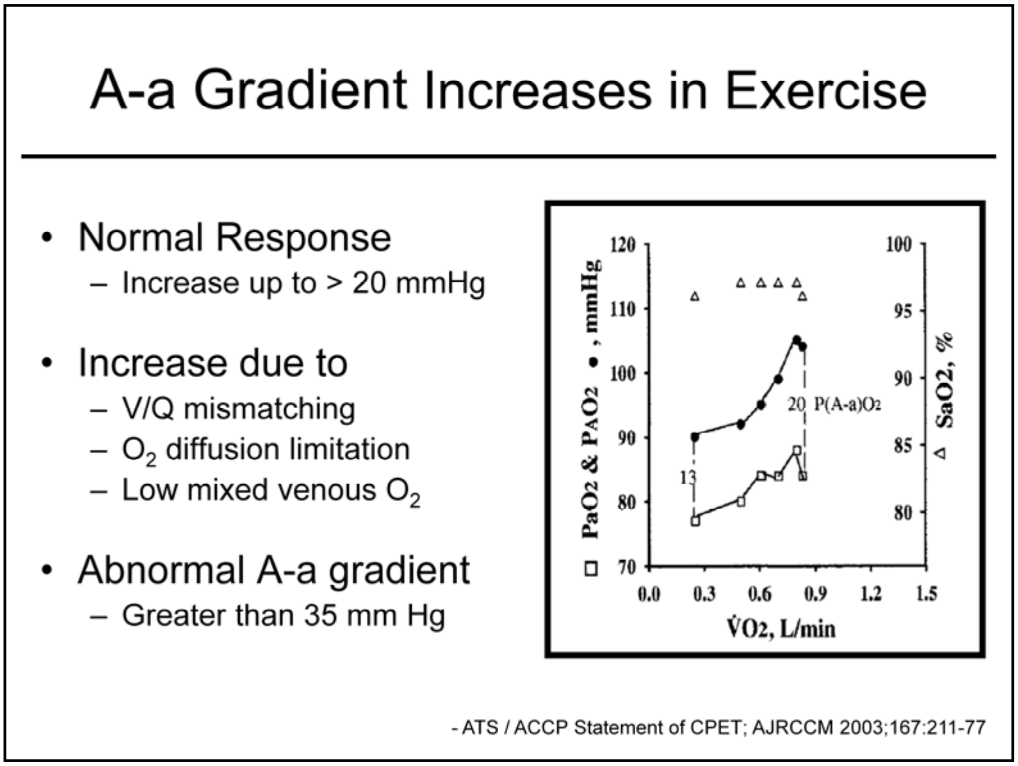


PaO_2 and SaO_2 Response to Dynamic Exercise

- PaO_2 response to exercise
  - Increases due to alveolar hyperventilation
- SaO_2 response to exercise
  - 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”



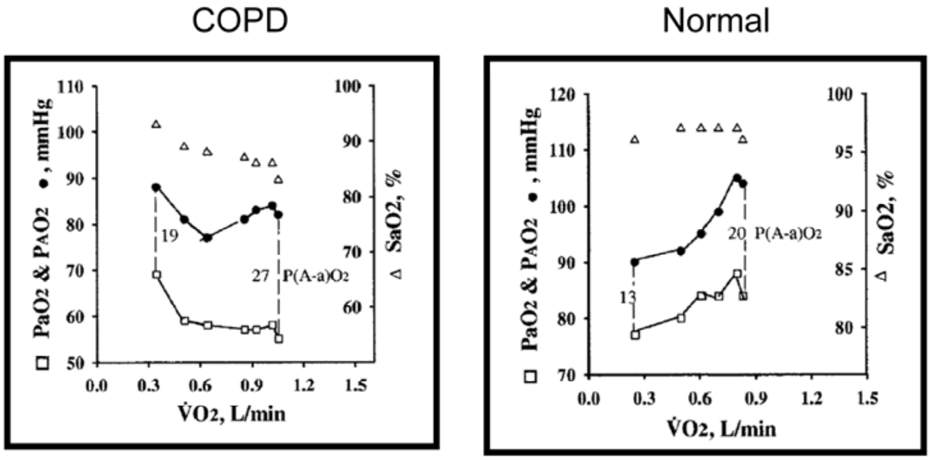
A-a Gradient Increases in Exercise

- Normal Response
  - Increase up to > 20 mmHg
- Increase due to
  - V/Q mismatching
  - O_2 diffusion limitation
  - Low mixed venous O_2
- Abnormal A-a gradient
  - Greater than 35 mm Hg

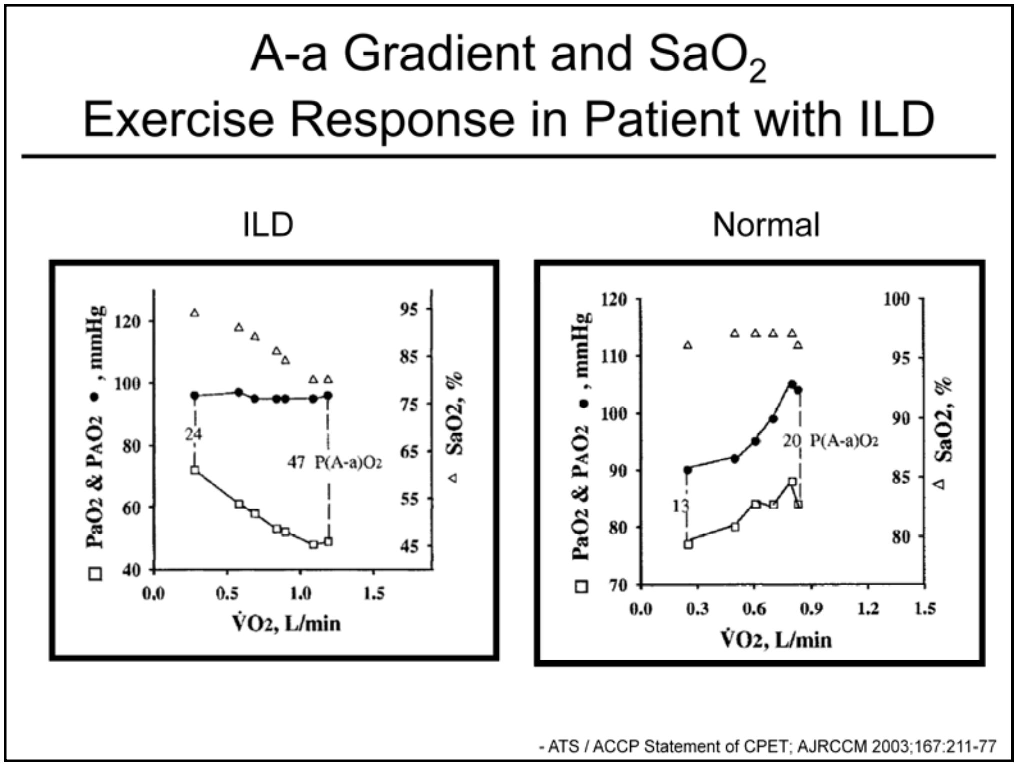
- ATS / ACCP Statement of CPET; AJRCCM 2003;167:211-77

Kristin M Burkart, MD, MSc
Assistant Professor of Clinical Medicine

A-a Gradient and SaO_2
Exercise Response in Patient with COPD



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

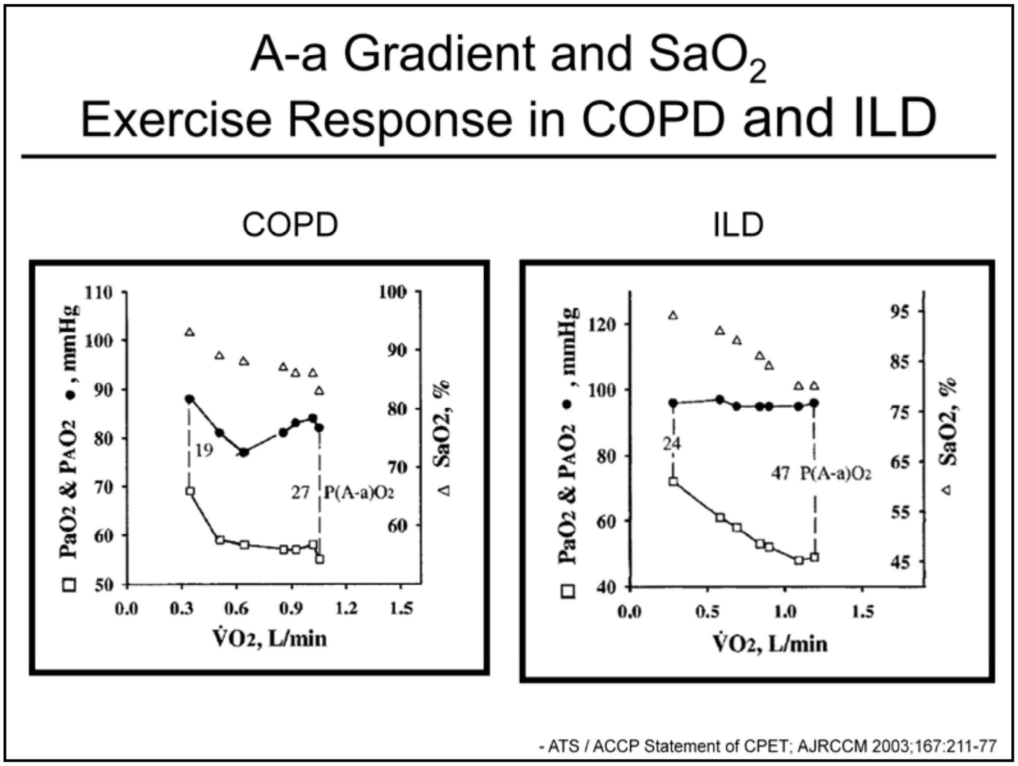


A-a Gradient and SaO_2 Exercise Response in Patient with ILD

ILD

Normal

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

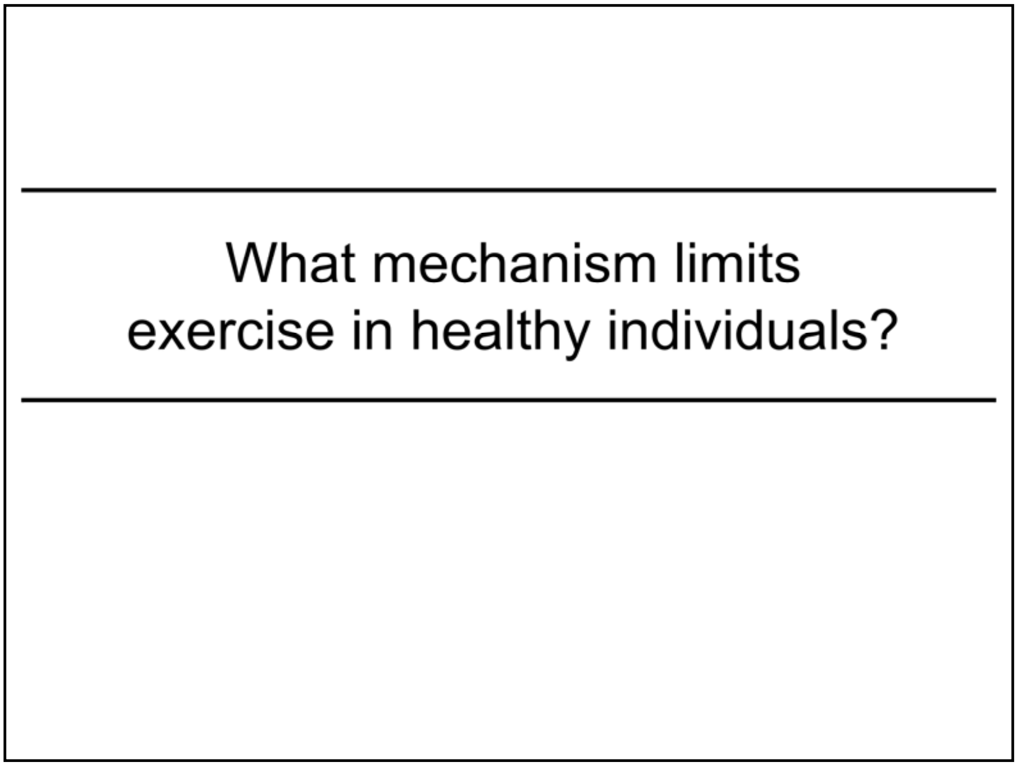


A-a Gradient and SaO_2 Exercise Response in COPD and ILD

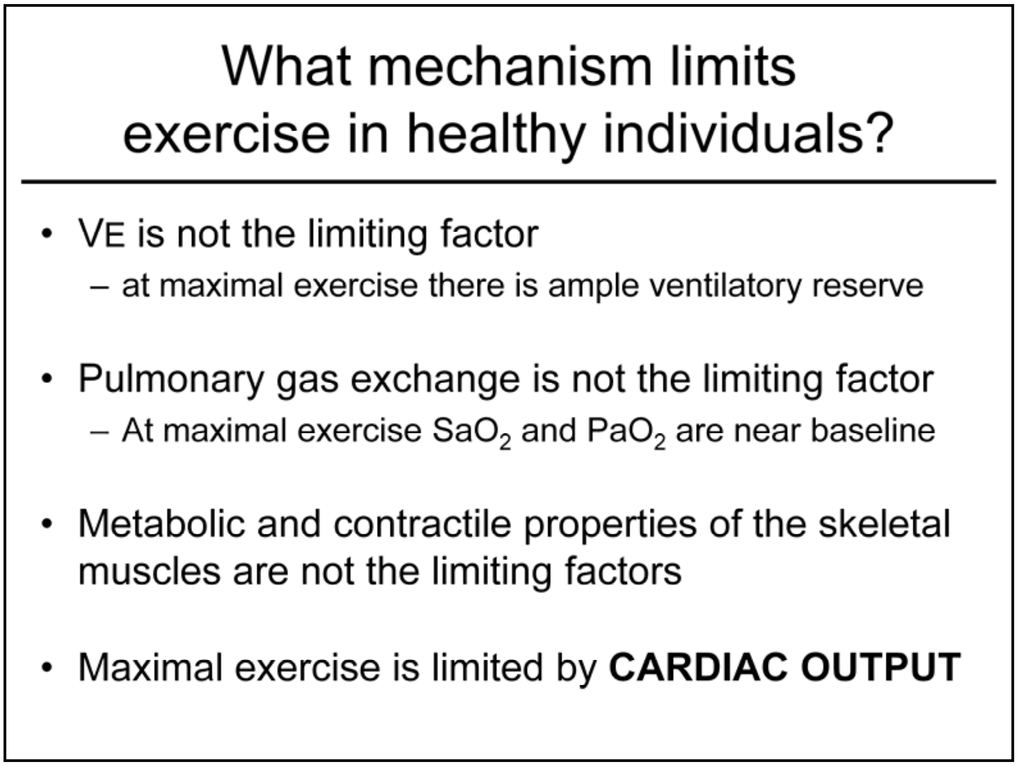
COPD

ILD

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



What mechanism limits exercise in healthy individuals?

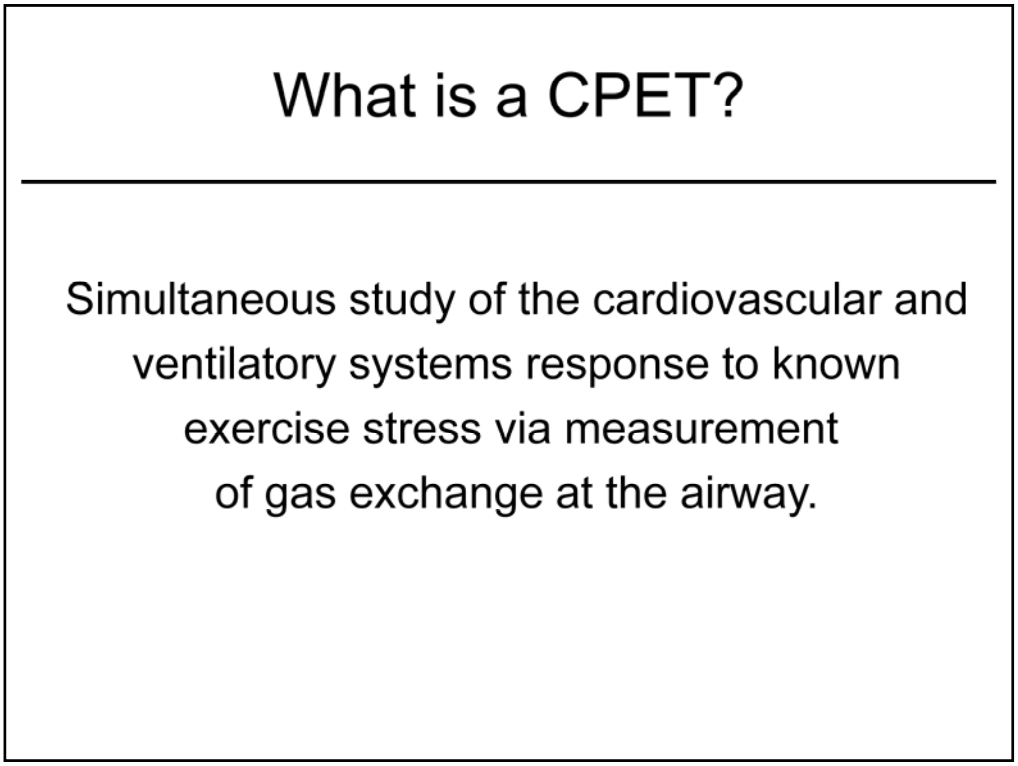


What mechanism limits exercise in healthy individuals?

- 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 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**

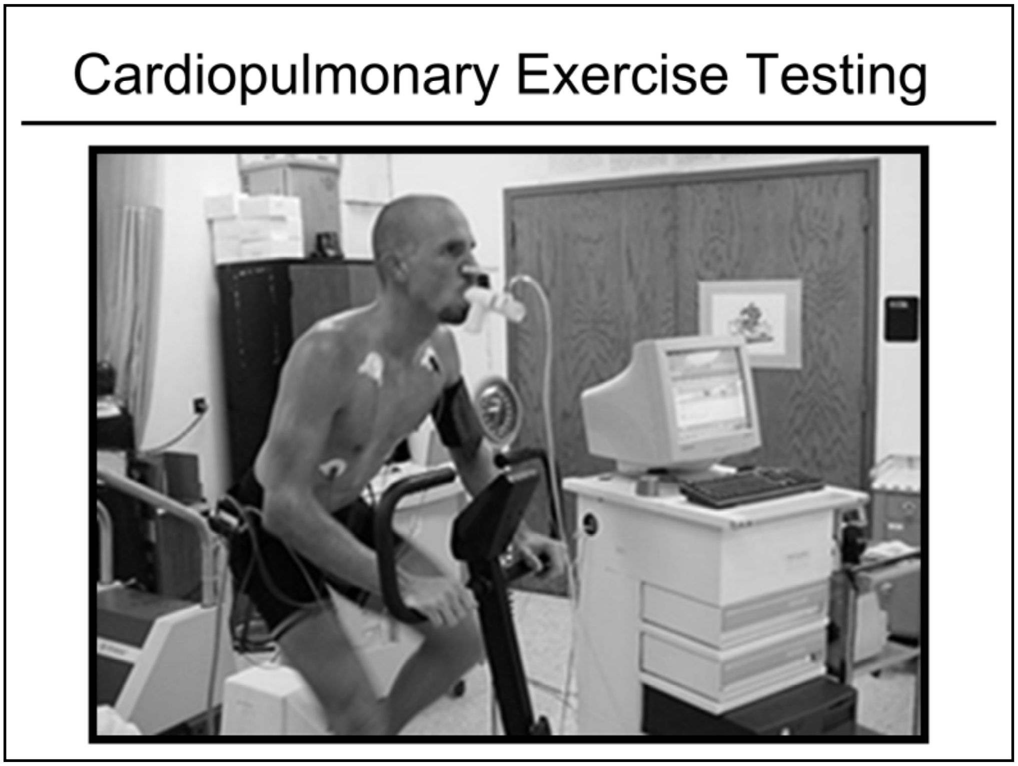
How do we assess cardiopulmonary limitations to exercise?

Cardiopulmonary exercise test (CPET)



What is a CPET?

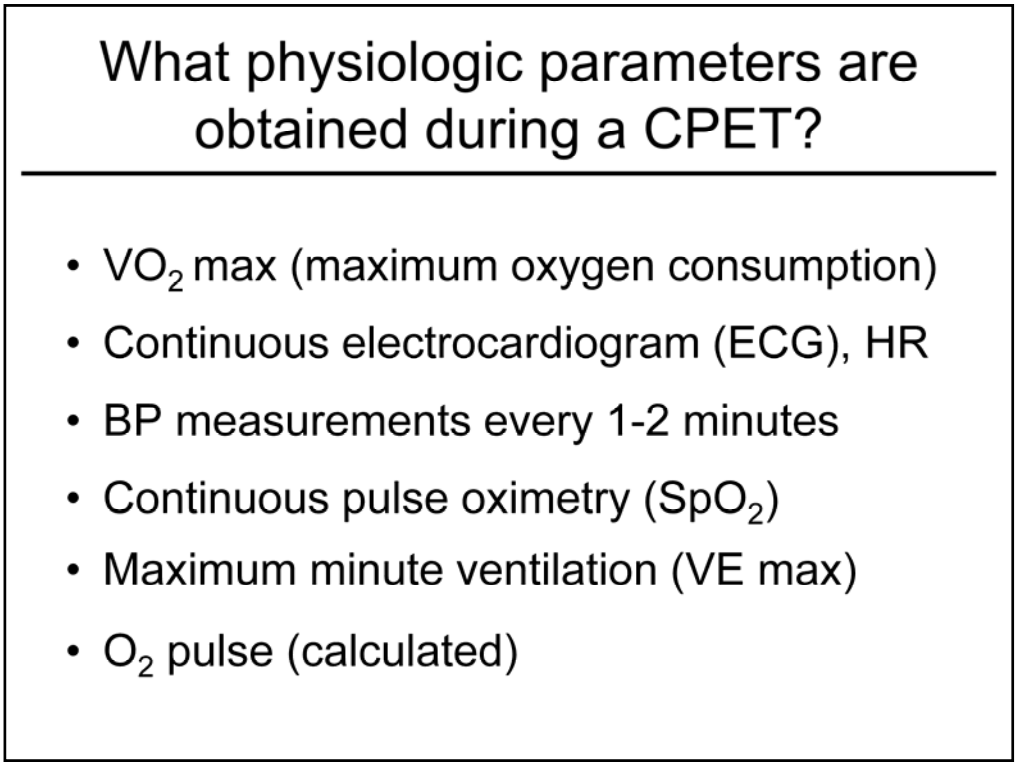
Simultaneous study of the cardiovascular and ventilatory systems response to known exercise stress via measurement of gas exchange at the airway.



Cardiopulmonary Exercise Testing

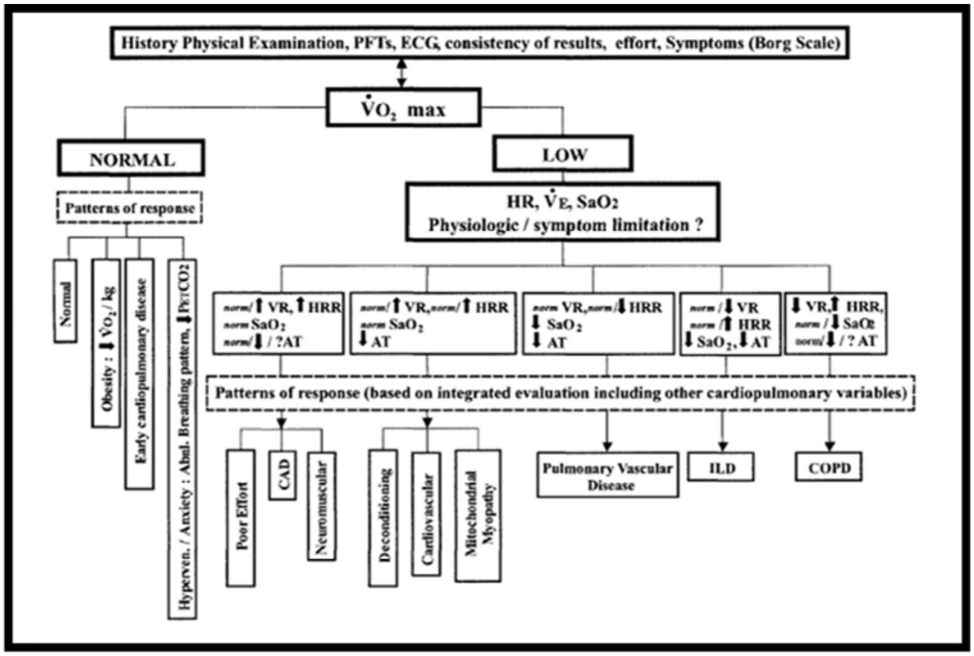
Why do we perform CPETs?

- 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

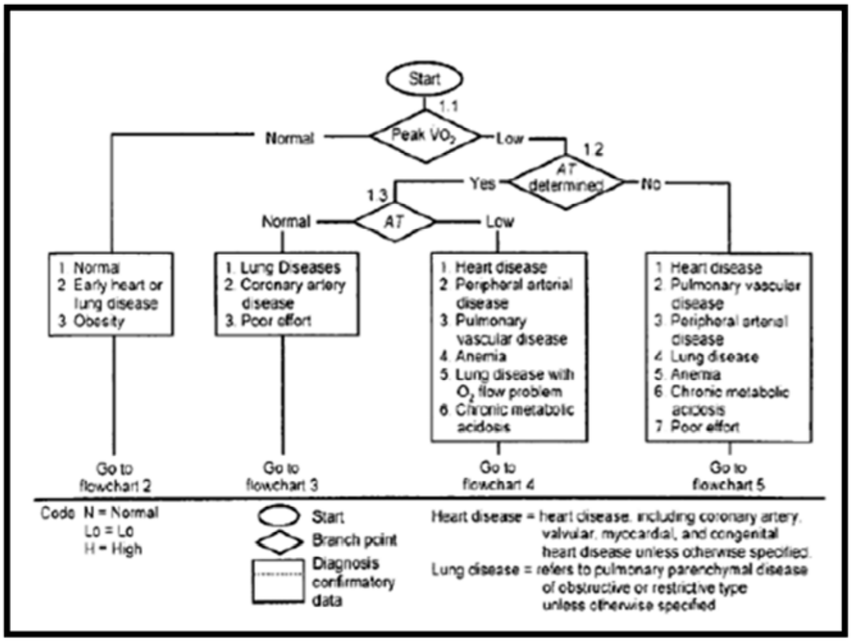


What physiologic parameters are obtained during a CPET?

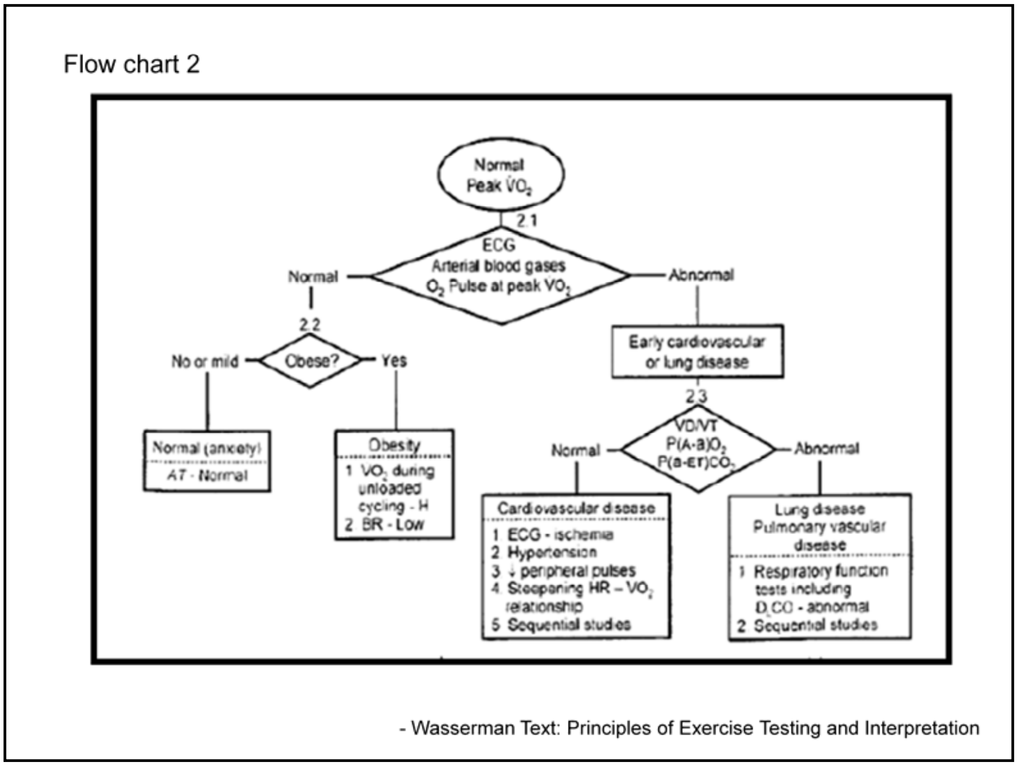
- VO_2 max (maximum oxygen consumption)
- Continuous electrocardiogram (ECG), HR
- BP measurements every 1-2 minutes
- Continuous pulse oximetry (SpO_2)
- Maximum minute ventilation (VE max)
- O_2 pulse (calculated)



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



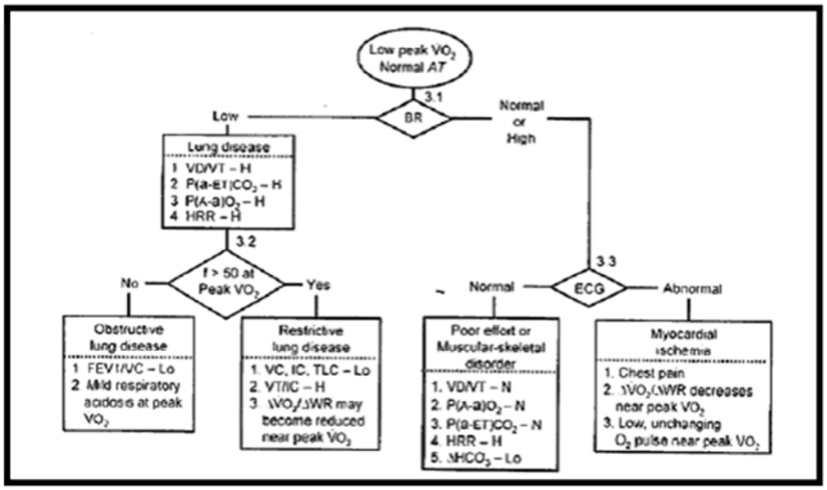
- Wasserman Text: Principles of Exercise Testing and Interpretation



Flow chart 2

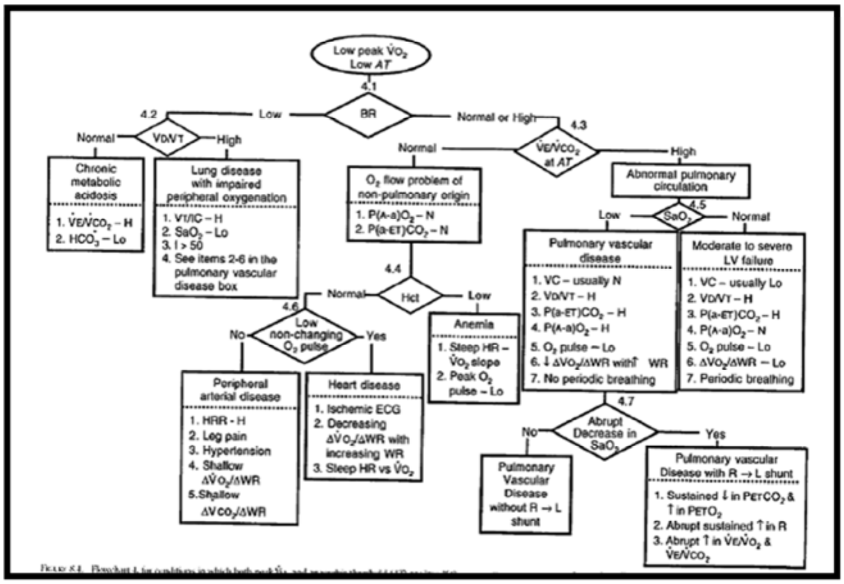
- Wasserman Text: Principles of Exercise Testing and Interpretation

Flow chart 3



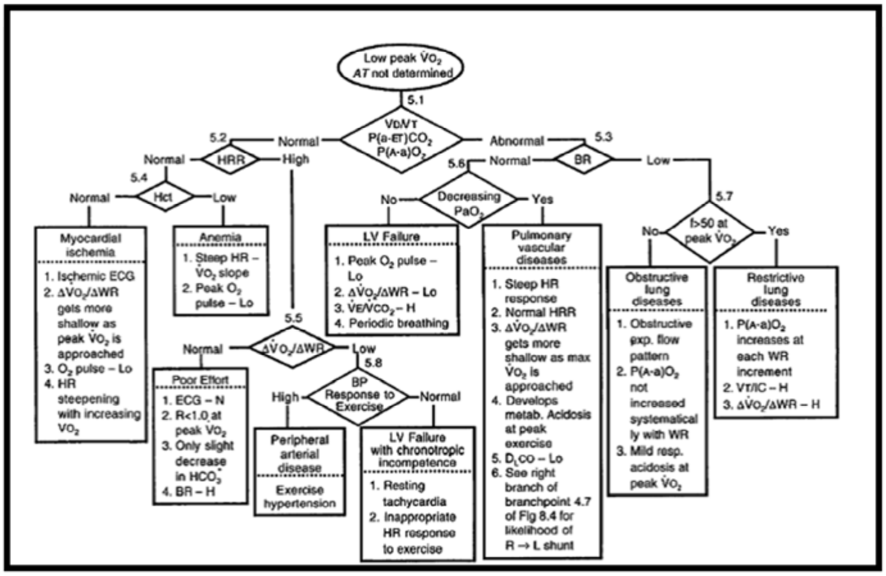
- Wasserman Text: Principles of Exercise Testing and Interpretation

Flow chart 4

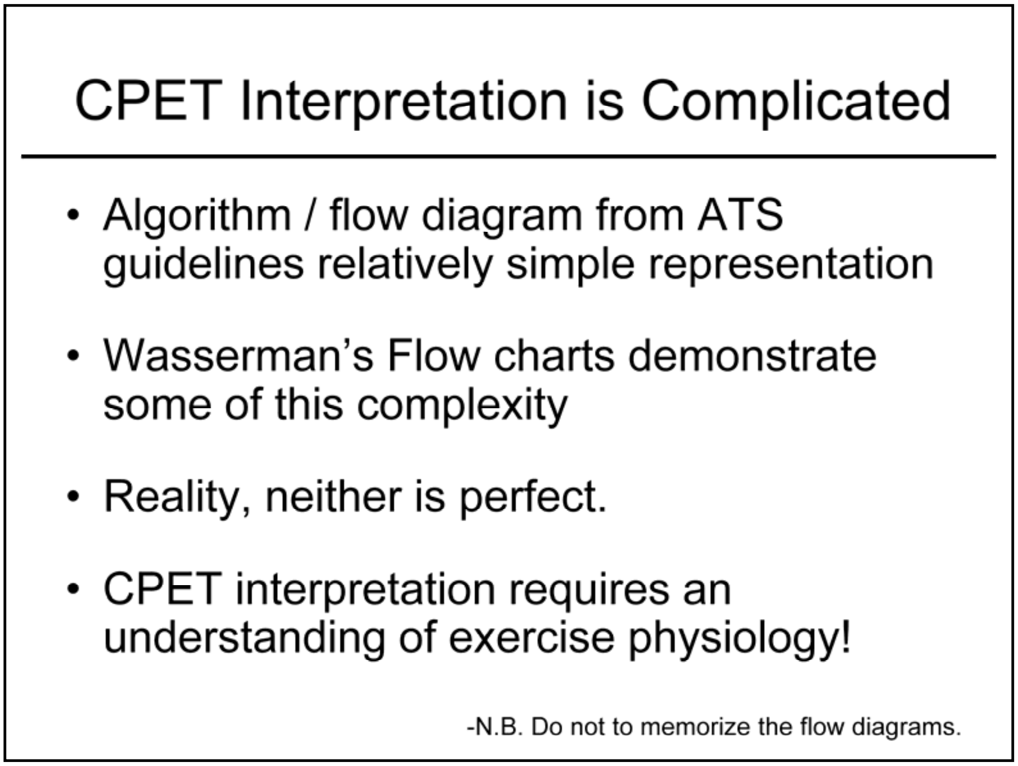


- Wasserman Text: Principles of Exercise Testing and Interpretation

Flow chart 5



- Wasserman Text: Principles of Exercise Testing and Interpretation

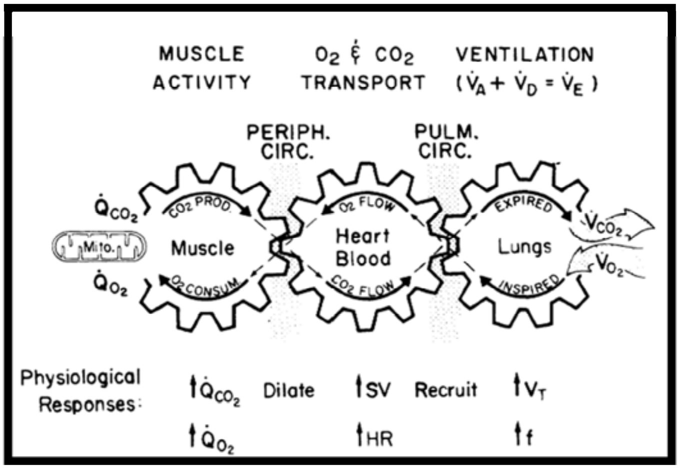


CPET Interpretation is Complicated

- Algorithm / flow diagram from ATS guidelines relatively simple representation
- Wasserman’s Flow charts demonstrate some of this complexity
- Reality, neither is perfect.
- CPET interpretation requires an understanding of exercise physiology!

-N.B. Do not to memorize the flow diagrams.

In Conclusion:
Exercise Physiology is Complex



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