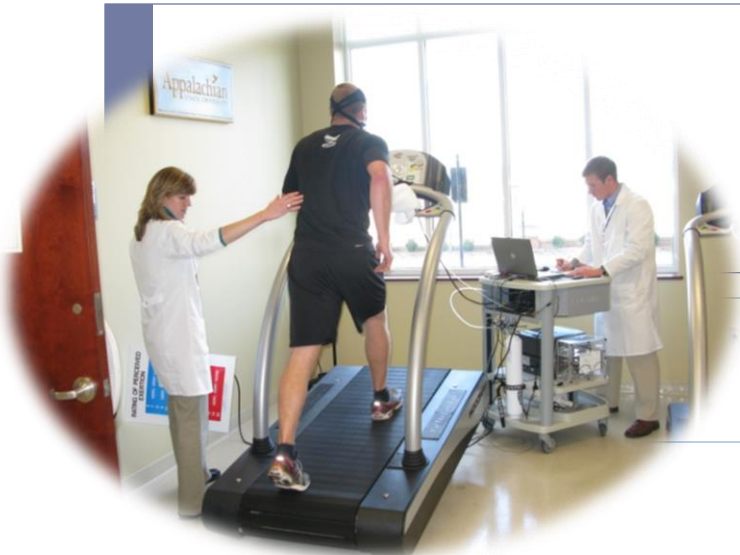




Cardiopulmonary Exercise Testing (CPET)



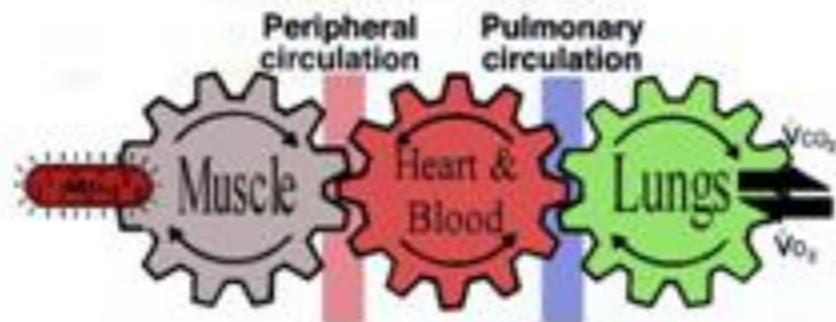
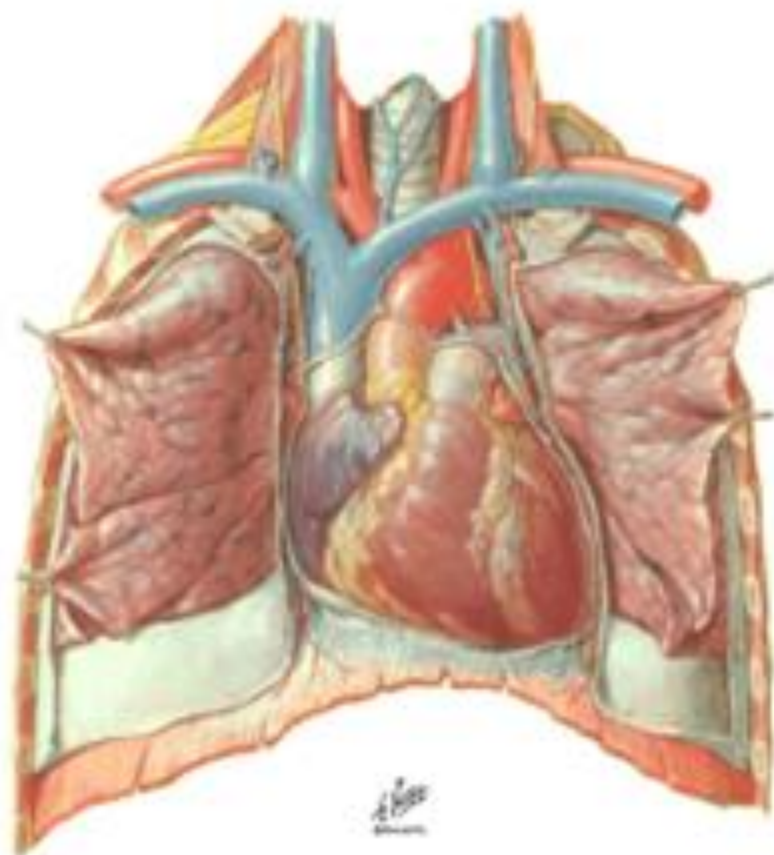
Cardiopulmonary exercise testing (CPET) provides a global assessment of the integrative exercise responses involving the pulmonary, cardiovascular, hematopoietic, neuropsychological, and skeletal muscle system, which are not adequately reflected through the measurement of individual organ system function.



The Cardiopulmonary System

It is not just the heart
or lungs...

Everything works
together



ONE INTEGRATED SYSTEM

The goal of cardiopulmonary exercise testing is to evaluate the organs and systems involved in the exercise response , under conditions of progressively intense physical stress. Exercise testing involves large muscle groups, usually the lower extremity muscles as in running on treadmill or pedaling on cycle ergometer.



Physical exercise requires the interaction of physiological mechanisms that enable the cardiovascular and respiratory systems to support the increased energy demands of contracting muscles.

Patients with chronic heart and/or pulmonary diseases often complain of a progressive reduction in exercise tolerance; in early stages of the diseases, when pulmonary function tests could be normal, clinical manifestations sometimes occur only when the heart, the lungs and the skeletal muscular apparatus are stressed, like during exercise.

Exercise intolerance results when a subject is unable to sustain a required work rate (W_R) sufficiently long for the successful completion of the task and can be clinically expressed by symptoms such as: dyspnea (breathlessness), especially in patients with pulmonary diseases, limb fatigue and weakness, particularly in patients with heart diseases and limb pain or claudication in patients with peripheral vascular occlusive disease



American Thoracic Society/ American College of Chest Physicians

ATS/ACCP Statement on Cardiopulmonary Exercise Testing

THIS JOINT STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS) AND THE AMERICAN COLLEGE OF CHEST PHYSICIANS (ACCP) WAS ADOPTED BY THE ATS BOARD OF DIRECTORS, MARCH 1, 2002 AND BY THE ACCP HEALTH SCIENCE POLICY COMMITTEE, NOVEMBER 1, 2001

TABLE 1. INDICATIONS FOR CARDIOPULMONARY EXERCISE TESTING

In practice, CPET should be considered when specific questions remain unanswered after consideration of basic clinical data including history, physical examination, chest radiographs, resting pulmonary function tests, and resting electrocardiogram (ECG).

- Cystic fibrosis
- Exercise-induced bronchospasm

Specific clinical applications

- Preoperative evaluation
 - Lung resectional surgery
 - Elderly patients undergoing major abdominal surgery
 - Lung volume resectional surgery for emphysema (currently investigational)
- Exercise evaluation and prescription for pulmonary rehabilitation
- Evaluation for impairment–disability
- Evaluation for lung, heart–lung transplantation

Definition of abbreviation: $\dot{V}O_2$ = oxygen consumption.

Adapted by permission from Reference 27.

Exercise Testing Protocols

- 1- Maximal incremental cycle ergometry protocols
- 2- Maximal incremental treadmill protocols.

The work rate can be incremented at regular interval with a combination of speed and grade.

(MET) metabolic equivalent is defined as the equivalent of the resting metabolic oxygen requirement .

One metabolic equivalent equals 3.5ml /kg /minute

Exercise capacity (in METS) is a powerful predictor of mortality among men referred for exercise testing

- 3- constant work rate protocols .This protocol is particularly for monitoring responses to a spectrum of therapeutic interventions including cardiopulmonary rehabilitation, bronchodilators, also useful for the analysis of exercise tidal – volume loops and dynamic hyperinflation,

Gas exchange kinetics, and validation of pulmonary gas exchange during incremental exercise testing.

Important Parameters to Monitor

Parameter	Definition
VO_2	Volume of oxygen consumed per minute.
VCO_2	Volume of carbon dioxide produced per minute.
VO_2/kg	Volume of oxygen consumed per minute normalized for body weight.
METS	VO_2 normalized (1 MET = 3.5 ml $\text{O}_2/\text{kg}/\text{min}$)
R	Respiratory exchange ratio (VCO_2/VO_2). It shows the substrate the person is using for their primary source of fuel.
HR	Heart rate
VE	Minute ventilation, the amount of air a person is moving in and out of their lungs.
BR	Breathing reserve, the percentage of maximal ventilation a person has remaining during exercise.
Rf	Respiratory frequency, the rate of breathing.

INDICATIONS FOR CPET

Evaluation of exercise tolerance

- Determination of functional impairment or capacity (peak $\dot{V} \text{ O}_2$)
- Determination of exercise-limiting factors and pathophysiologic mechanisms

Evaluation of undiagnosed exercise intolerance

- Assessing contribution of cardiac and pulmonary etiology in coexisting disease
- Symptoms disproportionate to resting pulmonary and cardiac tests
- Unexplained dyspnea when initial cardiopulmonary testing is nondiagnostic

Evaluation of patients with cardiovascular disease

- Functional evaluation and prognosis in patients with heart failure
- Selection for cardiac transplantation
- Exercise prescription and monitoring response to exercise training for cardiac rehabilitation

▶ (special circumstances; i.e., pacemakers)

Evaluation of patients with respiratory disease

- Functional impairment assessment
- Chronic obstructive pulmonary disease

Establishing exercise limitation(s) and assessing other potential contributing factors, especially occult heart disease (ischemia)

Determination of magnitude of hypoxemia and for O₂ prescription

When objective determination of therapeutic intervention is necessary and not adequately addressed

by standard pulmonary function testing



- Interstitial lung diseases

Detection of early (occult) gas exchange abnormalities

Overall assessment/monitoring of pulmonary gas exchange

Determination of magnitude of hypoxemia and for O₂ prescription

Determination of potential exercise-limiting factors

Documentation of therapeutic response to potentially toxic therapy

- Pulmonary vascular disease (careful risk–benefit analysis required)
- Cystic fibrosis
- Exercise-induced bronchospasm



Specific clinical applications

- Preoperative evaluation

Lung resectional surgery

Elderly patients undergoing major abdominal surgery

Lung volume resectional surgery for emphysema

(currently investigational)

- Exercise evaluation and prescription for pulmonary rehabilitation
- Evaluation for impairment–disability
- Evaluation for lung, heart–lung transplantation



TABLE 8. ABSOLUTE AND RELATIVE CONTRAINDICATIONS FOR CARDIOPULMONARY EXERCISE TESTING

Absolute	Relative
Acute myocardial infarction (3–5 days)	Left main coronary stenosis or its equivalent
Unstable angina	Moderate stenotic valvular heart disease
Uncontrolled arrhythmias causing symptoms or hemodynamic compromise	Severe untreated arterial hypertension at rest (> 200 mm Hg systolic, > 120 mm Hg diastolic)
Syncope	Tachyarrhythmias or bradyarrhythmias
Active endocarditis	High-degree atrioventricular block
Acute myocarditis or pericarditis	Hypertrophic cardiomyopathy
Symptomatic severe aortic stenosis	Significant pulmonary hypertension
Uncontrolled heart failure	Advanced or complicated pregnancy
Acute pulmonary embolus or pulmonary infarction	Electrolyte abnormalities
Thrombosis of lower extremities	Orthopedic impairment that compromises exercise performance
Suspected dissecting aneurysm	
Uncontrolled asthma	
Pulmonary edema	
Room air desaturation at rest \leq 85%*	
Respiratory failure	
Acute noncardiopulmonary disorder that may affect exercise performance or be aggravated by exercise (i.e. infection, renal failure, thyrotoxicosis)	
Mental impairment leading to inability to cooperate	

The most important parameter monitored during an incremental CPET are:

The oxygen uptake ($\dot{V}'\text{O}_2$ ml or l/min; ml or l/kg/min) and in particular:
 $\dot{V}'\text{O}_2$ max (maximal oxygen uptake) is the highest level of oxygen utilization for the oxidation of energy substrates and is defined as the $\dot{V}'\text{O}_2$ at which performance fails to increase $\dot{V}'\text{O}_2$ by 150 ml/min **despite the increase in work rate**. It is determined by the maximal cardiac output, the arterial O_2 content, the fractional distribution of the cardiac output to the exercising muscle and the ability of the muscle to extract O_2 .

$\dot{V}'\text{O}_2$ peak (or maximum $\dot{V}'\text{O}_2$) is the highest $\dot{V}'\text{O}_2$ attained at maximal effort; sometimes subjects (and all patients with cardiac and/or pulmonary diseases) **can not sustain the work rate to the point of oxygen limitation** ($\dot{V}'\text{O}_2$ max)

It is convenient to express oxygen uptake in multiples of sitting, resting requirements. The metabolic equivalent (MET) is a unit of sitting, resting oxygen uptake (3.5 mL O_2 per kilogram body weight per minute [$\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$])



O₂ Consumption

What are O₂ consumption and CO₂ production?

- 1) Inspired O₂ – Expired O₂ = VO₂ (Oxygen Consumed)
- 2) Expired CO₂ – Inspired CO₂ = VCO₂ (Carbon Dioxide Production)



Aerobic Power ($\dot{V}'O_2$ vs Work Rate ml/watt). This relationship reflects the amount

of O_2 utilized by the exercising subject in relation to the quantity of external work performed; it gives important information concerning the coupling of external work to cellular respiration. During incremental tests, its value increases linearly and the slope ($\Delta\dot{V}'O_2/\Delta\text{Watt}$) of $\approx 10 \pm 1.0$ ml/min/watt is similar in all sedentary subjects; in trained athletes, the steepness of the slope can be greater ($\approx 11 \pm 1.0$), while is lower in patients with inadequate O_2 availability to the exercising muscles muscular impairment (Cardiovascular diseases, Chronic Obstructive Pulmonary Disease, Myopathies, neuromuscular disorders, malnutrition).

This slope is important because it measures the aerobic work efficiency. It is suggested to measure this slope only for the part of the incremental exercise performed below AT (from the end of unloaded exercise up the AT outbreak



Physiological basis of CPET

O₂ uptake determined by cellular O₂ demand up to some level that equates maximal rate of O₂ transport .

VO₂ max or VO₂ peak (plateau)

VO₂ increase linear as external work

The slope of VO₂ versus external work reflects the efficiency of metabolic conversion of chemical potential energy to mechanical work and the mechanical efficiency of the musculoskeletal system. Decrease value of this relationship most often indicates inadequacies of O₂ transport as may occur with disease of the heart , lungs, or circulation .

VO₂ increase with increasing external work approach limit which is the best index of aerobic capacity and gold standard for cardiorespiratory fitness.

VO₂ in average person 3.5ml/min/kg (250ml/min)

VO₂max is equal 15 times the resting value 30- 50 ml/min/kg

Athletes is 20 times 80 ml/min/kg .

$\dot{V}O_2$ peak decrease reflect

1. Problems with O_2 transport , cardiac output , O_2 carrying capacity of blood .
2. Pulmonary limitation (mechanical , control of breathing , gas exchange)
3. O_2 extraction of the tissues (tissue perfusion , tissue diffusion)
4. Neuromuscular in musculoskeletal limitation.

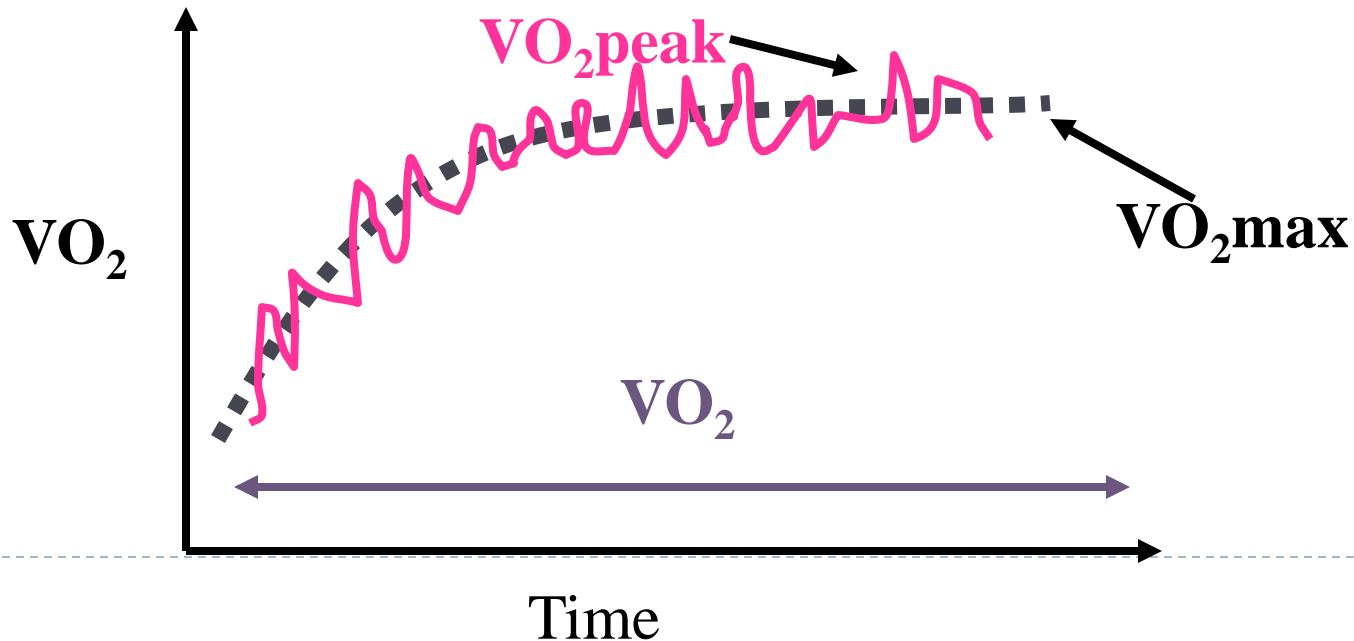


METABOLIC MEASUREMENT

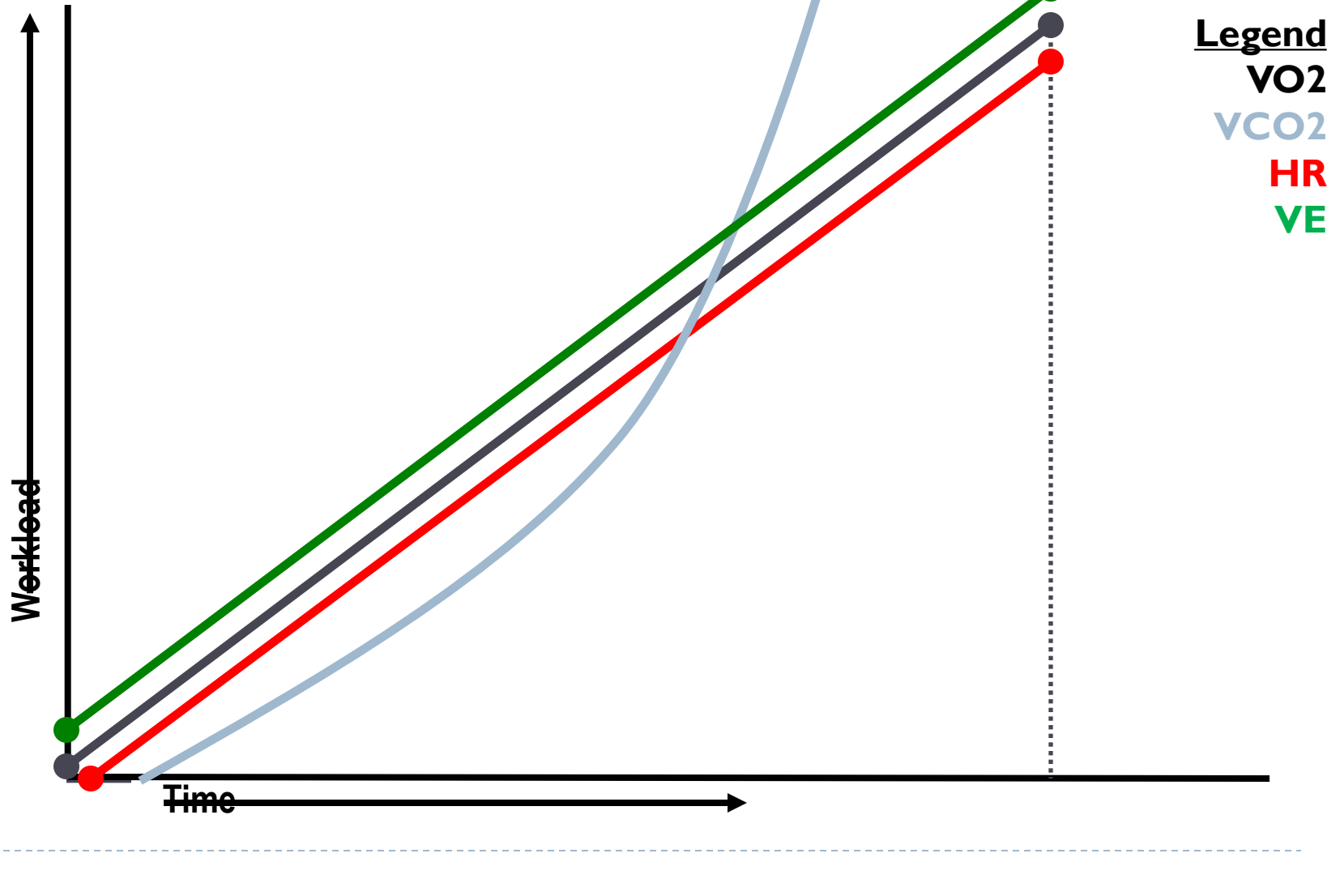
Volume of oxygen consumption $\dot{V}O_2$:

$\dot{V}O_2$ max: Maximum volume of oxygen consumption

$\dot{V}O_2$ peak: Highest volume of oxygen consumption



Normal Physiologic Responses



Vo₂max is the best index of aerobic capacity and the gold standard for cardiorespiratory fitness



(VO₂max) Assessing the test results

Maximal Oxygen Uptake

Normal is $\geq 85\%$ of predicted at maximal exercise

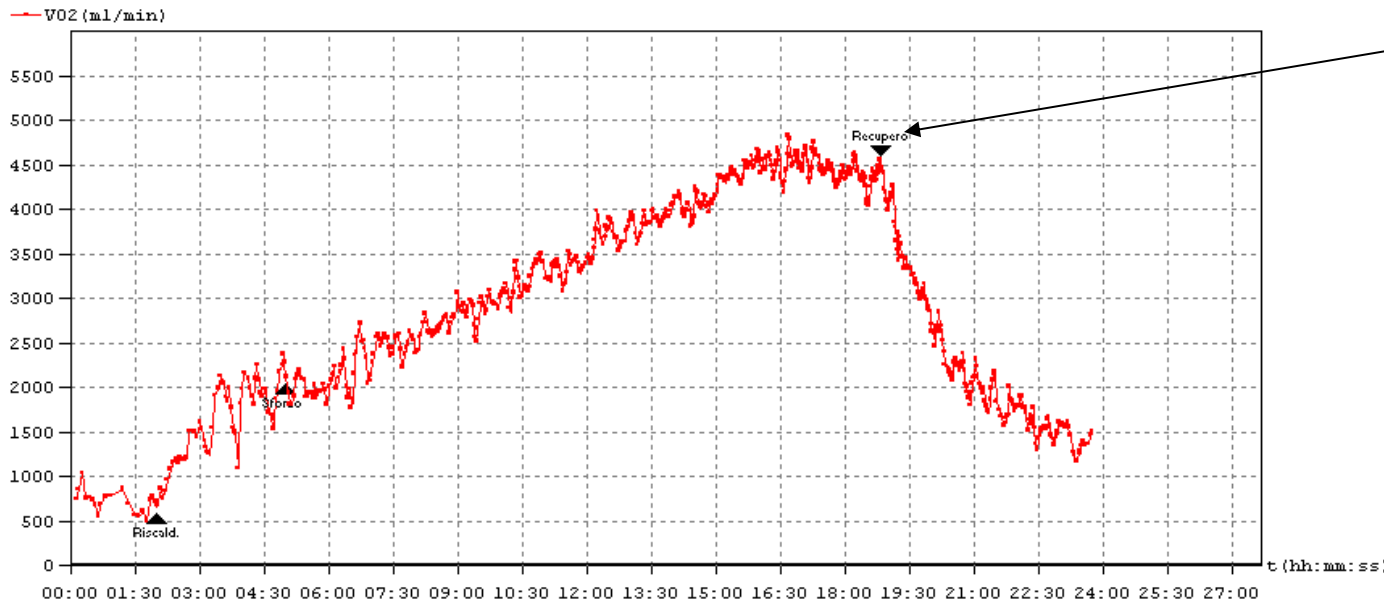
$< 85\%$ is abnormal. Causes include:

Cardiovascular limitation

Respiratory limitation

Deconditioning

Subject “quit” (symptom-limitation or poor effort)



VO₂max!!

The carbon dioxide output ($\dot{V}'\text{CO}_2$ ml or l/min; ml or l/kg/min), is the amount

of CO_2 cleared by the lungs per unit of time. Taken with $\dot{V}'\text{O}_2$ in the steady state condition, $\dot{V}'\text{CO}_2$ provides important information regarding the substrate mixture undergoing catabolism. It is essential for the non-invasive determination of the Anaerobic Threshold.

The $\dot{V}'\text{CO}_2$ response during incremental exercise is linear with respect to work rate; however, at high intensity work rates (above AT) the $\dot{V}'\text{CO}_2$ profile steepens both with respect to work rate and $\dot{V}'\text{O}_2$; this reflects the generation of additional CO_2 from the bicarbonate (HCO_3^-) component of the buffering of lactic acid in muscle and blood. The consequence is that $\dot{V}'\text{CO}_2$ increases faster than $\dot{V}'\text{O}_2$ with increasing work rate.



CO₂ output VCO₂

CO₂ is much more soluble in tissues and blood and weak acid because of solubility its measured at mouth and because of weak acid its used for regulation to compensate for acute metabolic acidosis .

The steeper slope reflects the CO₂ generated in excess of that produced by aerobic metabolism due to bicarbonate buffering of increase lactic acid .

VCO₂ increase in anaerobic metabolism as result of chemical reaction H⁺ from lactate and dissolved CO₂



Increase lactate $\rightarrow H^+ \rightarrow CO_2$

Hyperventilation

\rightarrow wash of CO₂ \rightarrow \downarrow of CO₂ BY BODY STORES GAS EXCHANGE



RER respiratory quotient (RQ) tissue fuel

RQ = 1.0 indicates metabolism of carbohydrates

RQ = 0.7—1.0 indicates mixture of fat and carbohydrates or protein

RER usually measured by gas exchange of mouth

RER is a function of $\dot{V}O_2$ its value obtained from ratio of $\dot{V}CO_2$ and $\dot{V}O_2$.

AT (Anaerobic threshold)

Its expressed as a percentage of the predicted value of $\dot{V}O_2$ max (% $\dot{V}O_2$ max predicted).

Cellular basis

GLYCOGENE \rightarrow *PYROVATE* enter TCA via acetylcOA

And breakdown of fats to produce acetylcOA .

Further processing of acetylcOA in the TCA cycle and electron transport chain produces ATP needed for muscle contraction .

In low exercise muscle fibers that are primarily oxidative are recruited but as intensity increases , fibers that rely primarily on glycolytic pathways are recruited, thus increasing the output of lactic acid.

The extra acid produced causes increase in V_{CO_2} by buffering of CO_2 in blood .

Deconditioning is often associated with chronic illness and should be considered as a contributing factor to exercise tolerance ,reduced VO_2 peak and exercise intolerance in patients with mitochondrial myopathy.



Anaerobic, Lactic and Lactic Acidosis Threshold, (AT, LT and LAT) are different

definition of the level of exercise above which aerobic energy production is supplemented by anaerobic mechanisms and is reflected by an increase in lactate in muscle and arterial blood.

Direct estimation of AT can be done by measuring directly blood lactate or standard bicarbonate; the start, from baseline levels, of blood lactate increase or bicarbonate fall corresponds to the lactic threshold (LT) or lactic acidosis threshold (LAT) respectively.

Indirect or non-invasive estimation of AT be done using different methods.



Respiratory exchange ratio (R or RER).
This is the ratio of $V'CO_2$ to $V'O_2$ and

reflects tissue metabolic activity; during incremental exercises, it rises from values ≈ 0.8 to maximum values ≈ 1.1 (in normal subjects, the highest level of an incremental exercise can be considered maximal only when $R > 1.08$).

R also reflects metabolic substrate utilization, but only when is measured during steady state conditions.



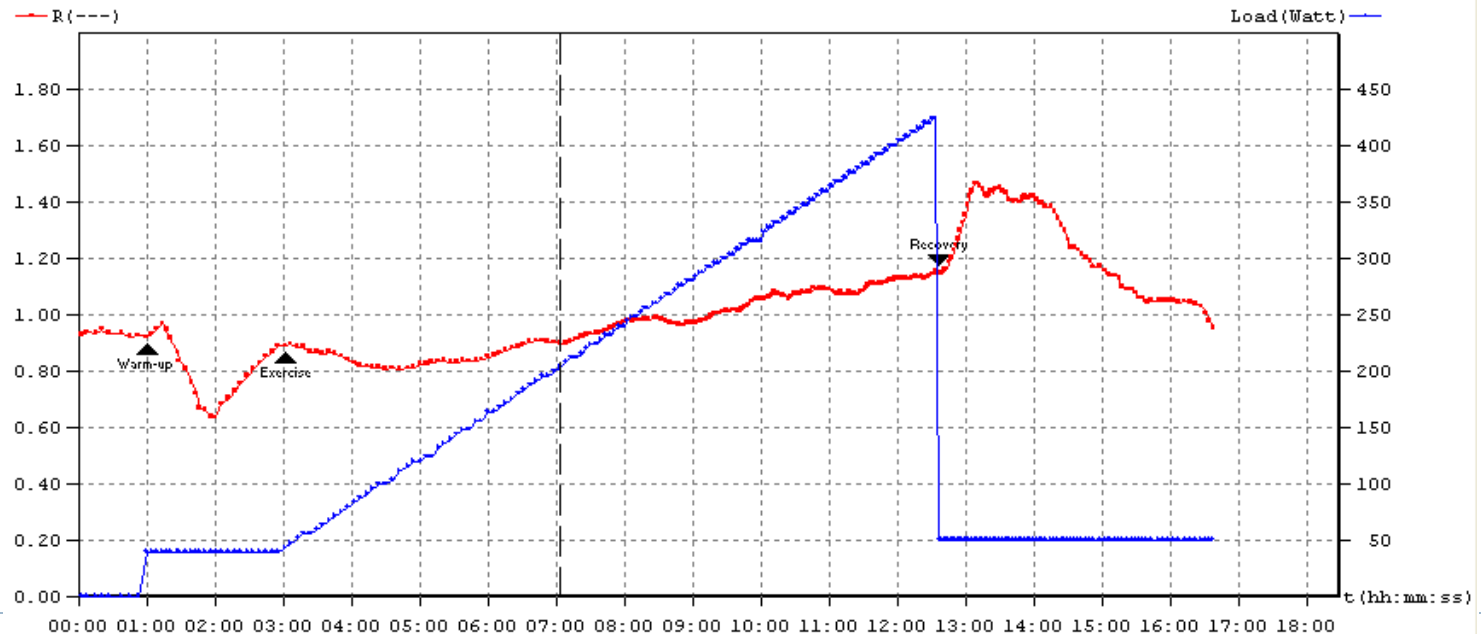
(R) Assessing the test results

R (or RQ or RER)

$R > 1.09$ indicates “maximal
exercising muscle effort” ▶

REST = 0.70 – 0.90 ▶

MAX = 1.10 – 1.30 ▶



Preliminary requirements for exercise testing.

1-spirometry and MVV should be measured ,and lung volumes and DLco can be included if clinically warranted.

2- if hypoxemia is clinically suspected , resting arterial blood gases should be obtained.

3-a recent hemogram and electrolytes should be determined if warranted.

4- patients who smoke should asked to abstain from smoking for at least 8 hours

5-consultation with a cardiologist is recommended, when appropriate ,for patients with a history of coronary artery disease .

6-for functional evaluation and disability , patients should be tested with their optimal medication regimen.

7-the morning of test , patients should not exercise and have a light breakfast no less than 2 hours before the test.

8-patients should come to laboratory in exercise clothing , including tennis shoes.

9- at day of the test ,a consent form must be signed, properly dressed , place the ECG electrodes and indwelling arterial catheter if necessary .A supine resting 12 lead ECG should be obtained and used as the standard ECG tracing for determination of resting abnormalities before exercise testing.



INDICATIONS FOR EXERCISE TERMINATION

Chest pain suggestive of ischemia

Ischemic ECG changes

Complex ectopy

Second or third degree heart block

Fall in systolic pressure 20 mm Hg from the highest value during the test

Hypertension (250 mm Hg systolic; 120 mm Hg diastolic)

Severe desaturation : SpO₂ 80% when accompanied by symptoms and signs of severe hypoxemia

Sudden pallor

Loss of coordination

Mental confusion

Dizziness or faintness

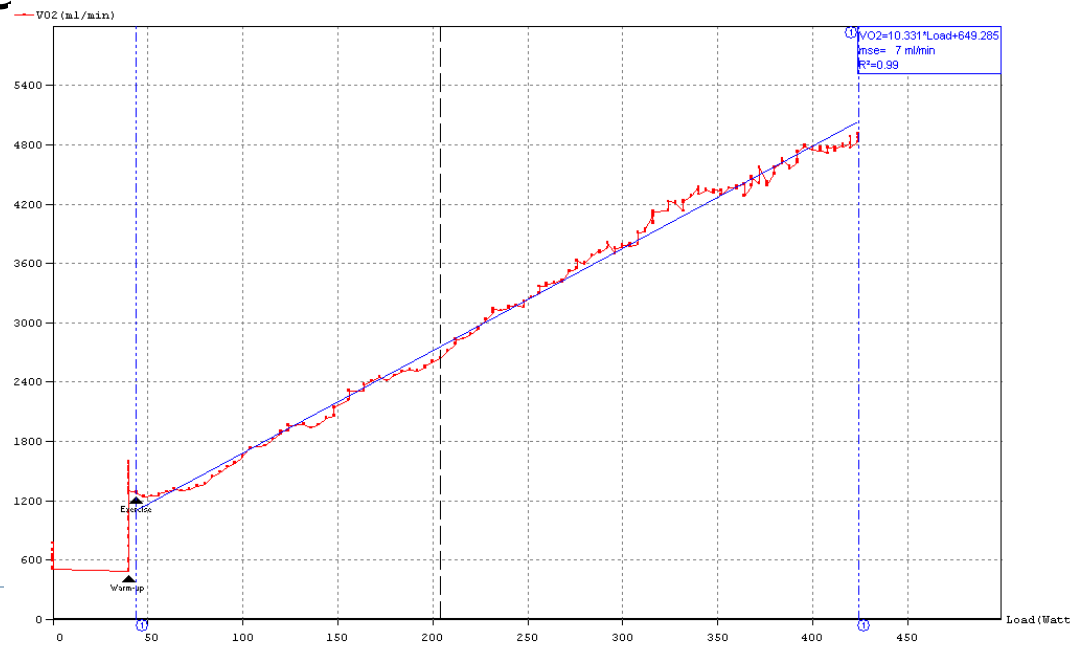
Signs of respiratory failure



Assessing the results (W, VO2, HR)

Workload, HR, VO2 (Ramping protocols)

- ▶ Linear increase in all 3 to > 85% predicted in normal
- ▶ VO2 and/or HR increase at a slower rate relative to work rate in disease



Breathing reserve (BR), also called ventilatory reserve, can be expressed either

as the difference between the Maximum Voluntary Ventilation (MVV) and the maximum exercise ventilation in absolute terms or this difference as a fraction of MVV; at peak exercise, normal subjects have a BR ≥ 11 l/min or 10 to 40% of the MVV.

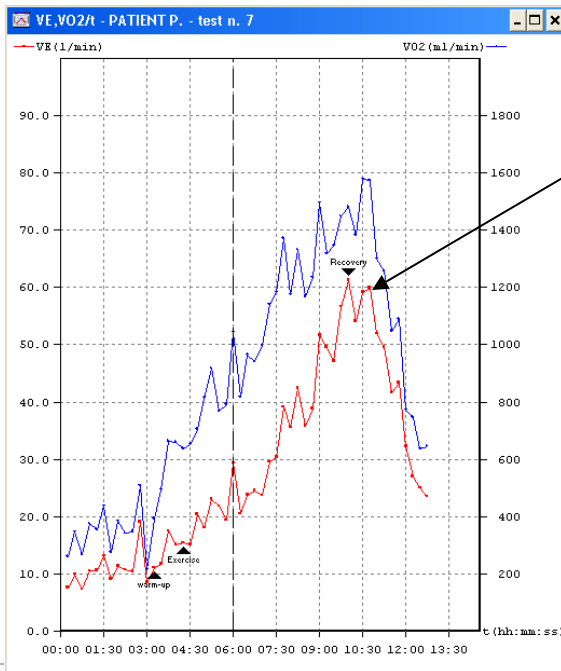
MVV represents the theoretical highest level of ventilation that a subject can achieve and can be directly measured after 1-minute (or after 15 seconds \times 4) maximal ventilatory effort at rest or indirectly by multiplying FEV₁ (forced expiratory volume after 1 second) by 40.



Assessing the test results (BR)

Breathing Reserve (BR%)

- ❖ Normal is at $\geq 30\%$ at maximal exercise
- ❖ Calculated by: $[1 - (V_{Emax}/FEV1 \times 40)] \times 100$ or $[1 - (V_{Emax}/MVV)] \times 100$
- ❖ $< 30\%$ at maximal exercise indicates a respiratory limitation



@VO₂max ~ 1600

V_Emax ~ 60 L/min

FEV₁ = 3.5 L → MVV = 3.5 * 40 = 140 L/min

BR = $(1 - 60/140)\% = 57.1\% > 30\%$

predicted

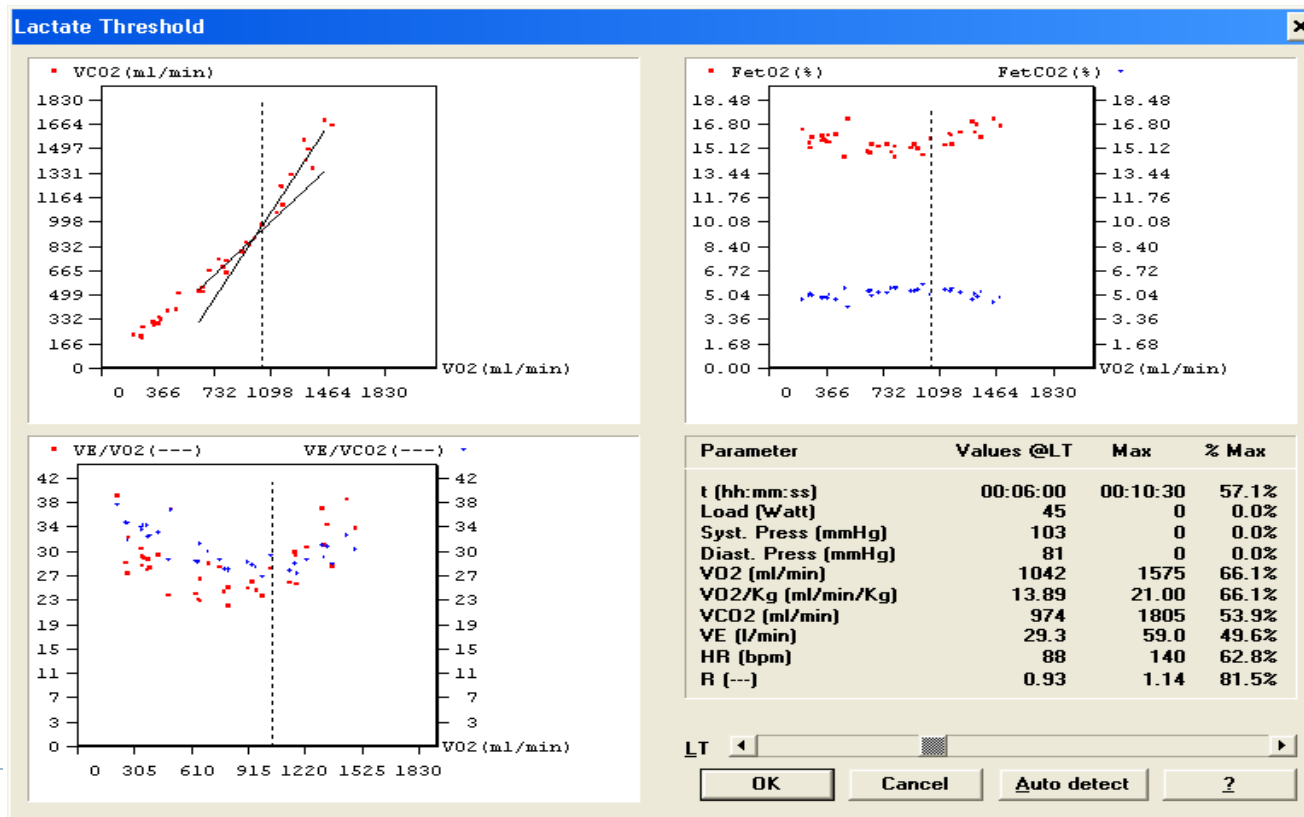
Conclusions:

NO Ventilatory limitation!

(VO₂@LT) Assessing the test results

VO₂ @ LT (Anaerobic or Lactate Threshold)

Normal is $\geq 40\%$ of the predicted VO₂max ▶
< 40% indicates a cardiovascular limitation ▶



How to Measure

Equations

Inspired O₂ content
(20.93% at sea level)

Mixed expired O₂
Content (Measured)

$$VO_2 = (20.93 - F_{eO_2}) \times VE$$

$$VCO_2 = (F_{eCO_2} - 0.03) \times VE$$

Mixed expired CO₂
Content (Measured)

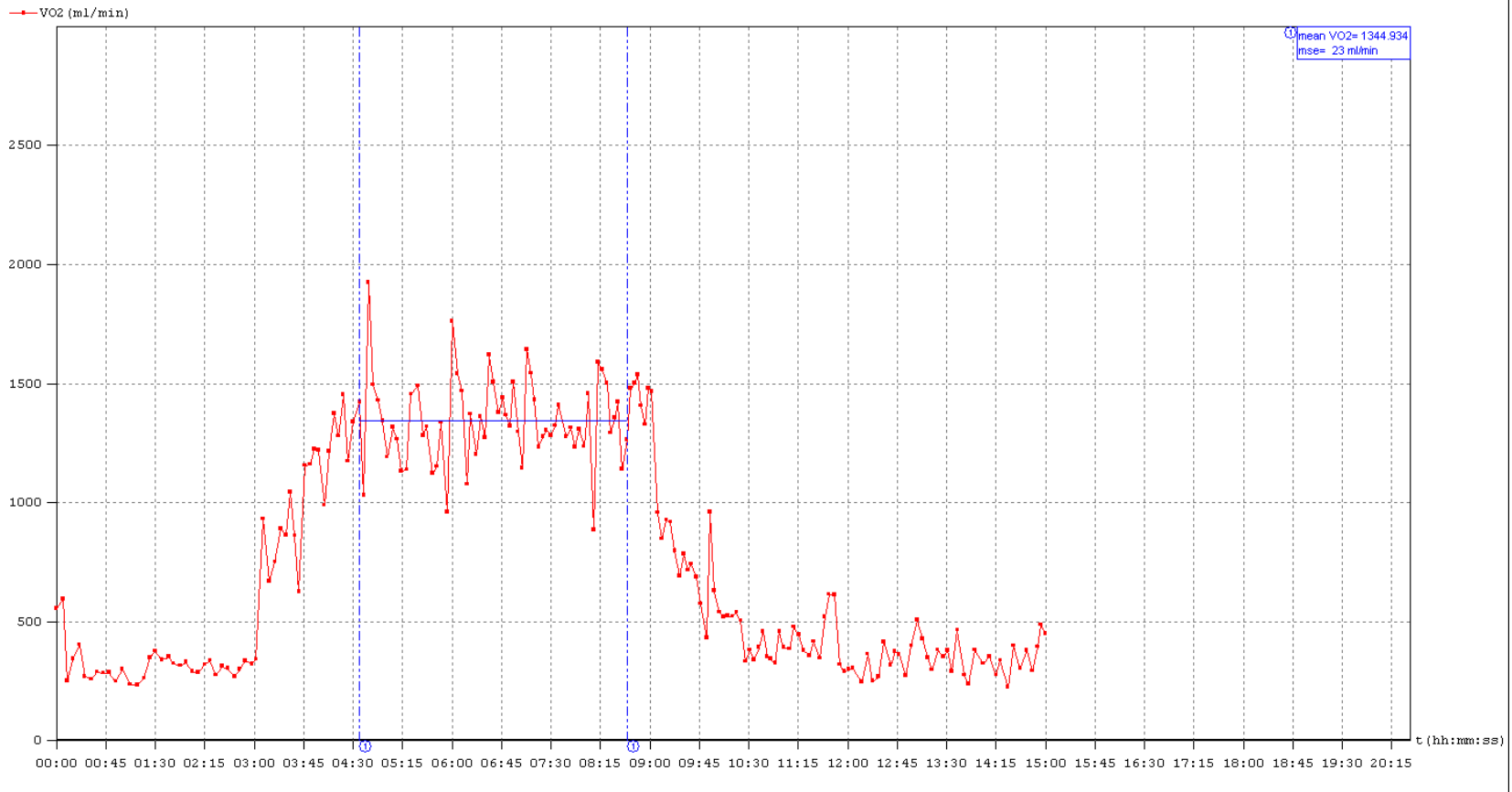
Inspired CO₂ content
(0.03% at sea level)

Expired
Ventilation
(Measured)



Oxygen Demand

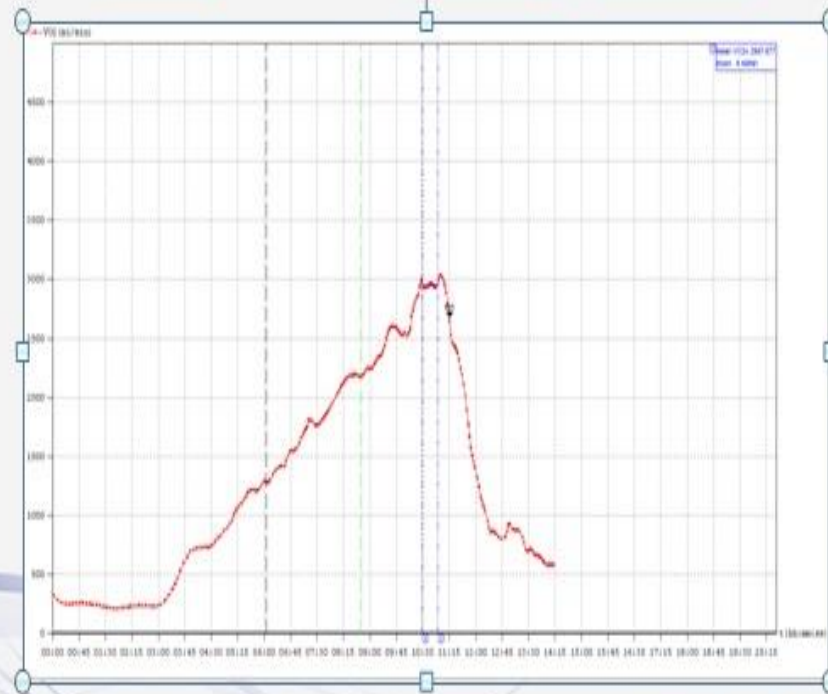
During sub-max Physical Activity



When Physical activity is at sub maximal level all the energy required (except at the beginning of exercise) can be supplied by aerobic metabolism, thus the Oxygen reaches a Plateau after a certain time form the exercise starts. Usefull for the measurement of EE per specific activity. In the picture the VO2 is for an exercise of around 100 Watt

Oxygen Demand

During maximal Intensity Exercise



COSMED
Pulmonary Function Equipment

During an incremental load exercise to maximal exertion, VO_2 increases till a plateau (VO_2 max). Which defines the maximal Aerobic Power in sport medicine (the maximal amount of ATP that can be created with an aerobic metabolism), but also the Cardiorespiratory Fitness in clinical setting, as it define the efficiency of the Cardiopulmonary and vascular functions.

In Diseases subject the value of VO_2 max is inferior that in Healthy subject

Interpretation: Sub-maximal Effort

Criteria

- ❖ **$R < 1.09$**
- ❖ **$VO_{2max} < 85\%$**
- ❖ **$VO_2 @ LT = 40\%$ or not reached**
- ❖ **$HR < 85\%$**
- ❖ **$VO_2/HR < 80\%$**
- ❖ **$BR\% \geq 30\%$**

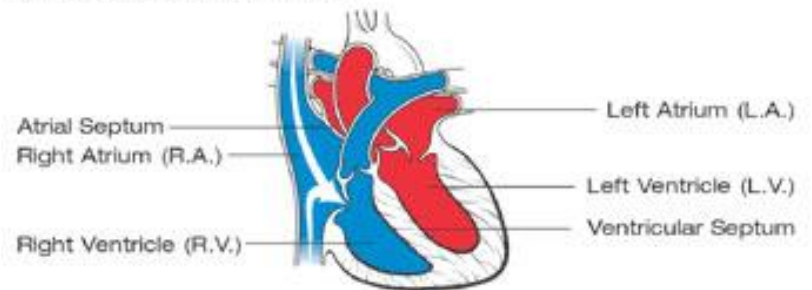


Interpretation: Cardiovascular limitation

Criteria

- ❖ **R usually > 1.09**
- ❖ **VO_{2max} usually $< 85\%$**
- ❖ **$VO_2 @ LT < 40\%$**
- ❖ **HR usually $> 85\%$**
- ❖ **VO_2/HR usually $< 80\%$ and may drop**
- ❖ **$BR\% \geq 30\%$**

A. Chambers of the heart



Interpretation: Respiratory limitation

Criteria

- ❖ **R usually > 1.09**
- ❖ **VO₂max usually $< 85\%$**
- ❖ **VO₂ @ LT $> 40\%$ or not reached**
- ❖ **HR usually $< 85\%$**
- ❖ **VO₂/HR usually $< 80\%$**
- ❖ **BR% $< 30\%$**

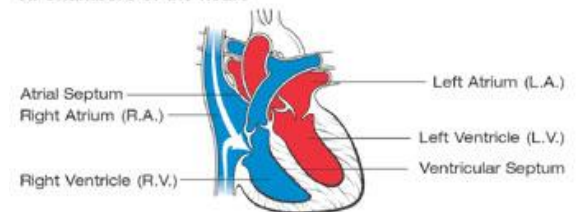


Interpretation: Combined Cardiovascular and Respiratory Limitation

Criteria

- ❖ **R usually > 1.09**
- ❖ **VO_{2max} usually $< 85\%$**
- ❖ **$VO_2 @ LT < 40\%$**
- ❖ **HR usually $< 85\%$**
- ❖ **VO_2/HR usually $< 80\%$ and may**
- ❖ **$BR\% < 30\%$**

A. Chambers of the heart



Interpretation: Deconditioned Subject

Criteria

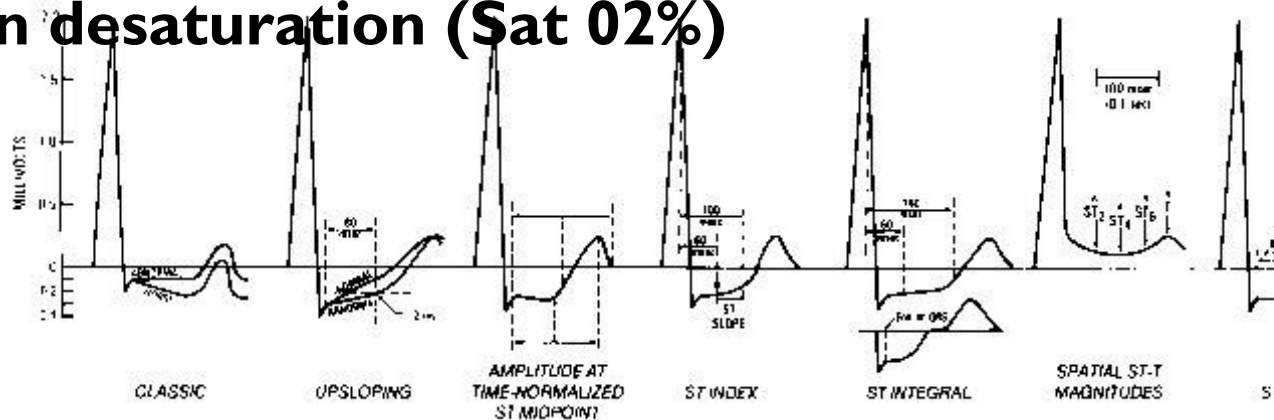
- ❖ **$R > 1.09$**
- ❖ **$VO_{2max} < 85\%$**
- ❖ **$VO_2 @ LT > 40\%$**
- ❖ **$VO_2/HR > 80\%$**
- ❖ **$HR > 85\%$**
- ❖ **$BR\% \geq 30\%$**



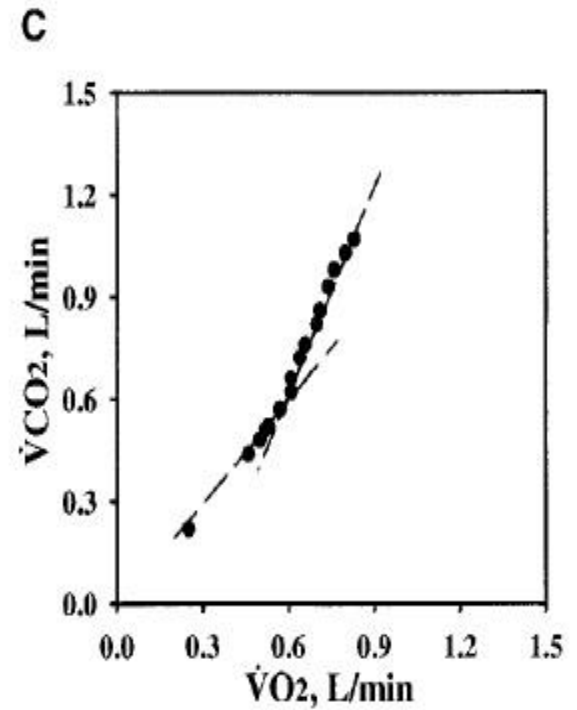
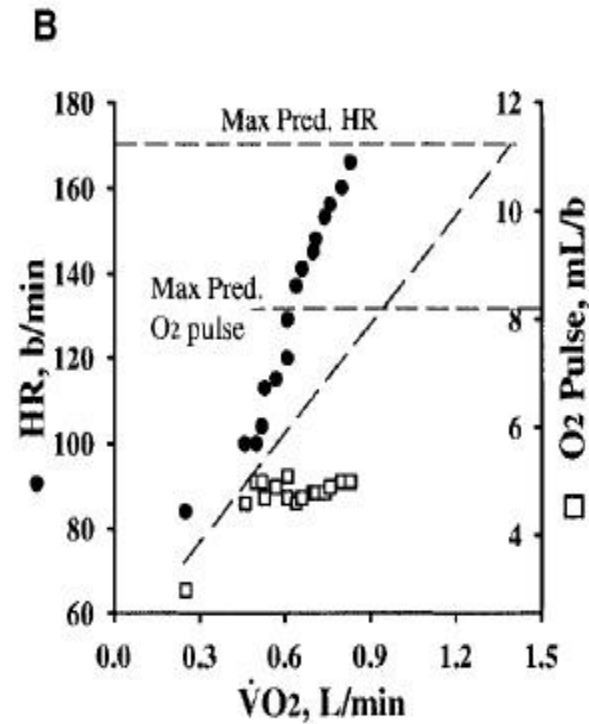
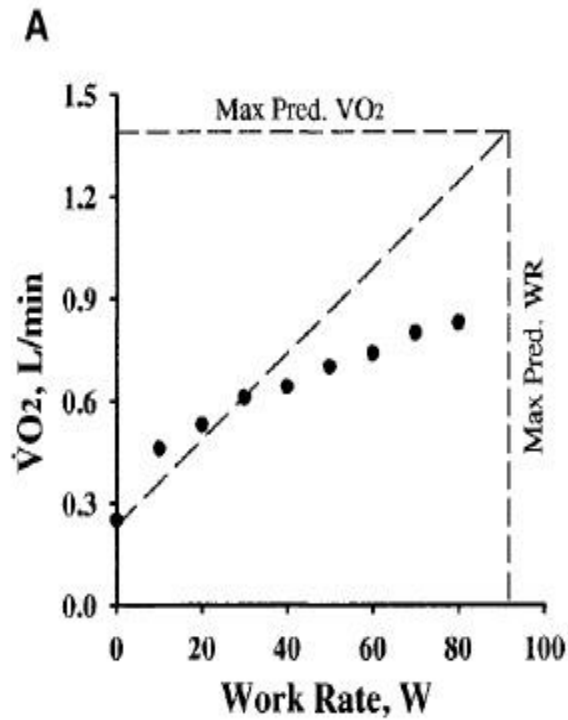
Interpretation: Other aspects

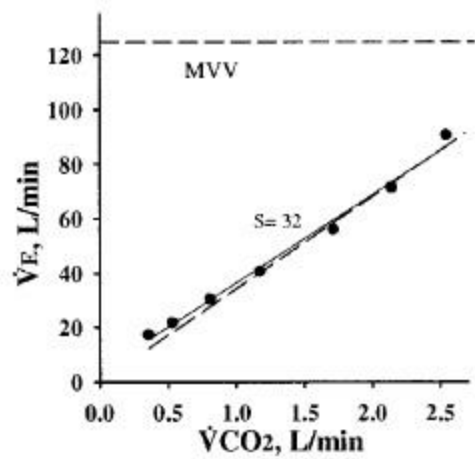
Criteria

- ❖ **ECG changes**
 - Arrhythmias
 - ST depression (2 mm flat or down sloping is diagnostic for CAD)
- ❖ **Blood Pressure response**
 - Systolic hypertension
 - Diastolic hypertension
 - Systolic hypotension
- ❖ **Oxygen desaturation (Sat 02%)**

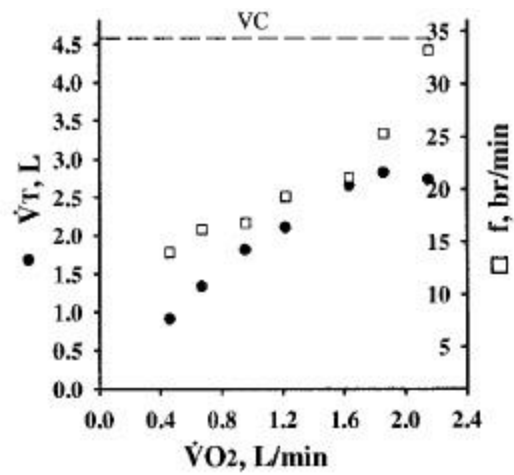


Graphic representation of the maximal, incremental, cardiopulmonary exercise response of a healthy aged person. These graphic data are averaged over an interval of 1 minute.

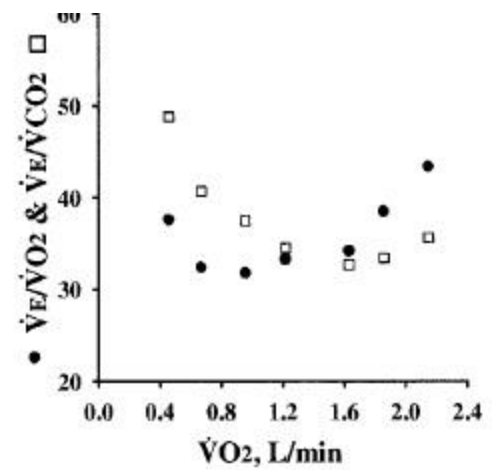




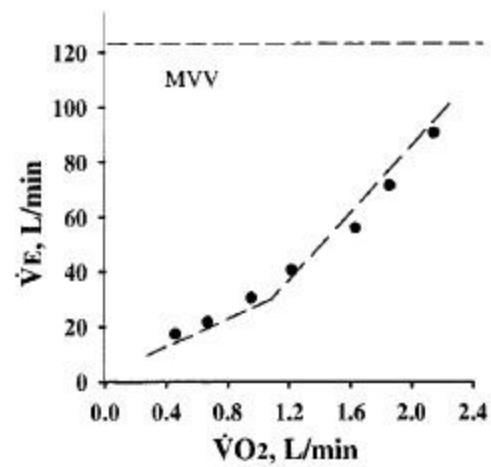
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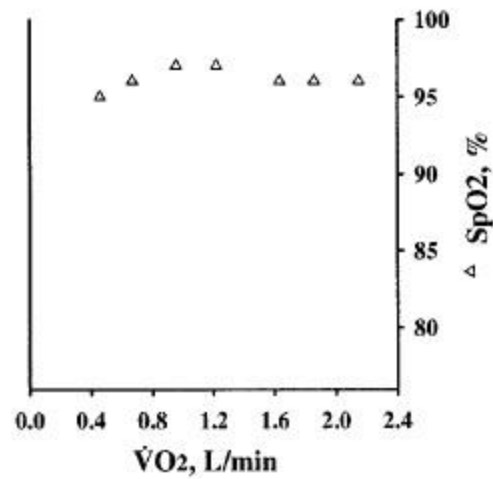
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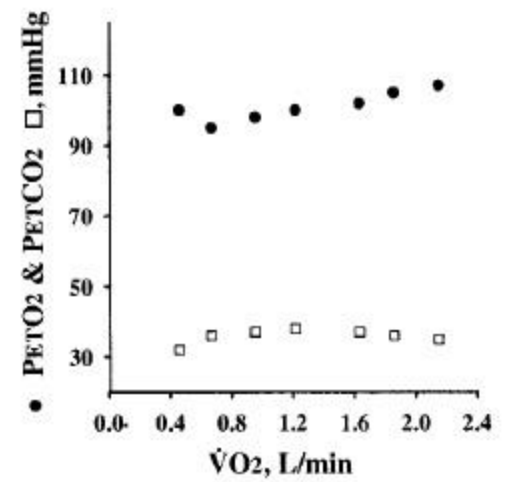
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