CARDIOPULMONARY EXERCISE TESTING

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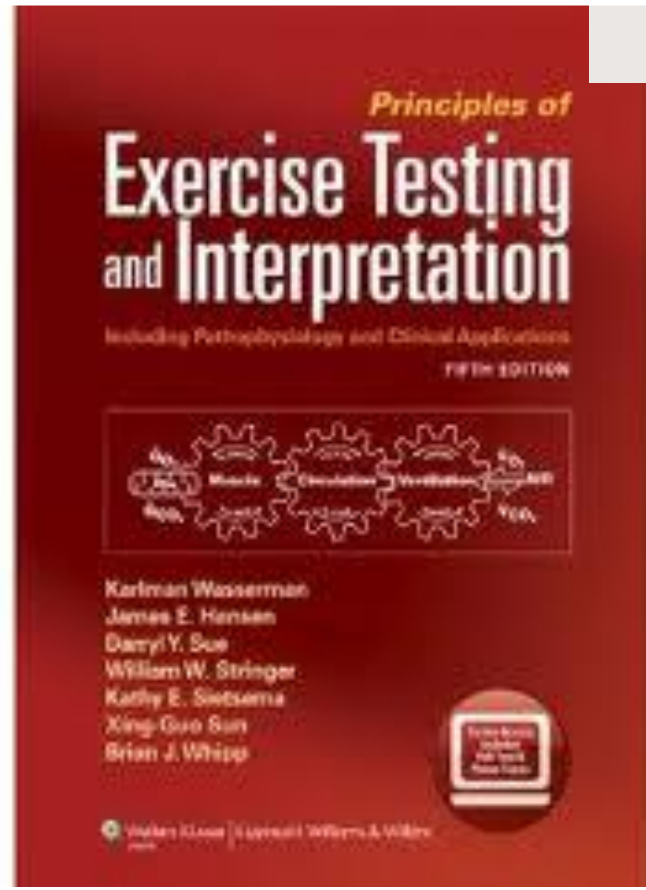
OUTLINE

- Description of CPET
- Who should and who should not get CPET
- When to terminate CPET
- Exercise physiology
- Define terms: respiratory exchange ratio, ventilatory equivalent, heart rate reserve, breathing reserve, oxygen pulse
- Patterns of CPET results

Karlman Wasserman, MD



SOURCES OF ENERGY FOR ATP

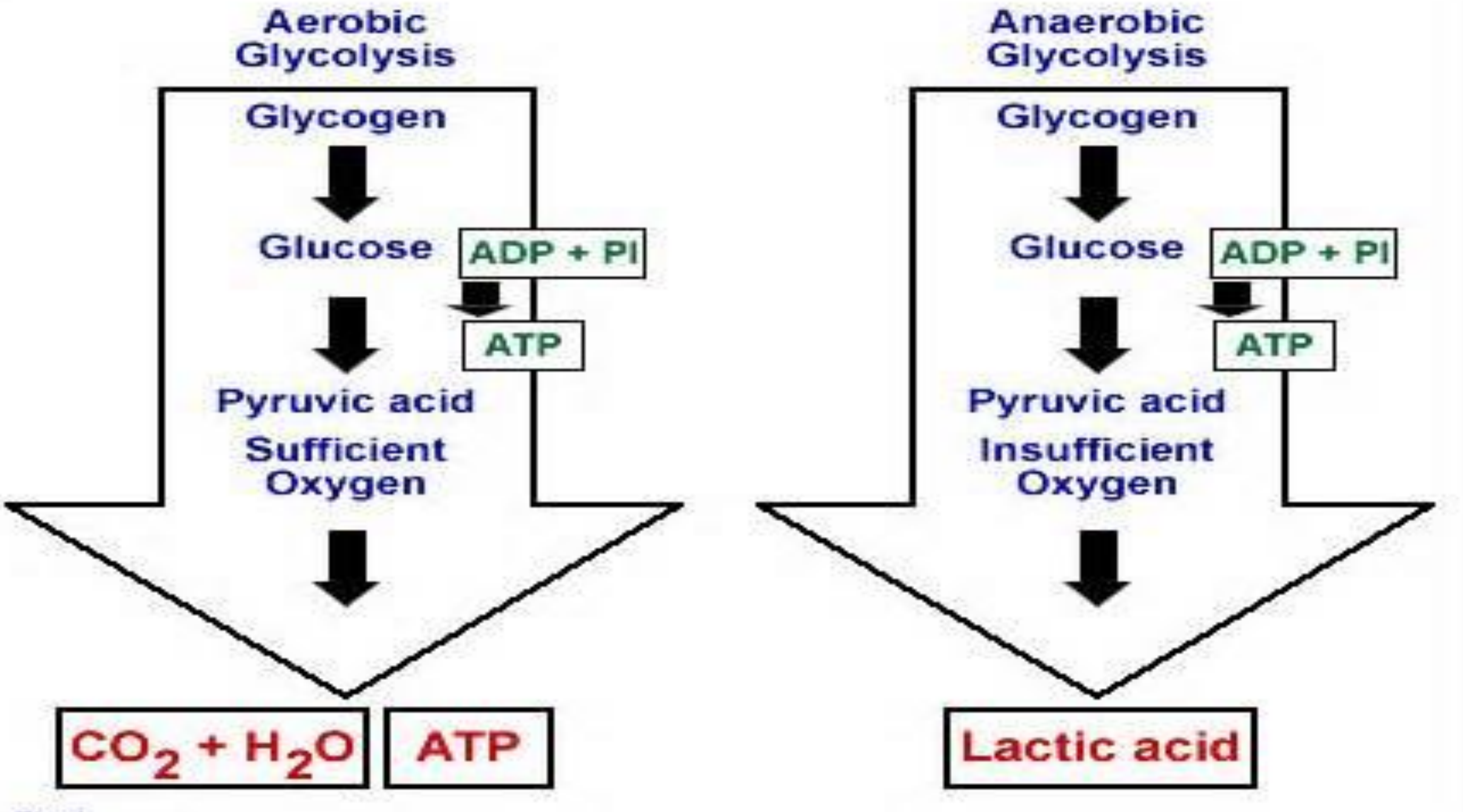
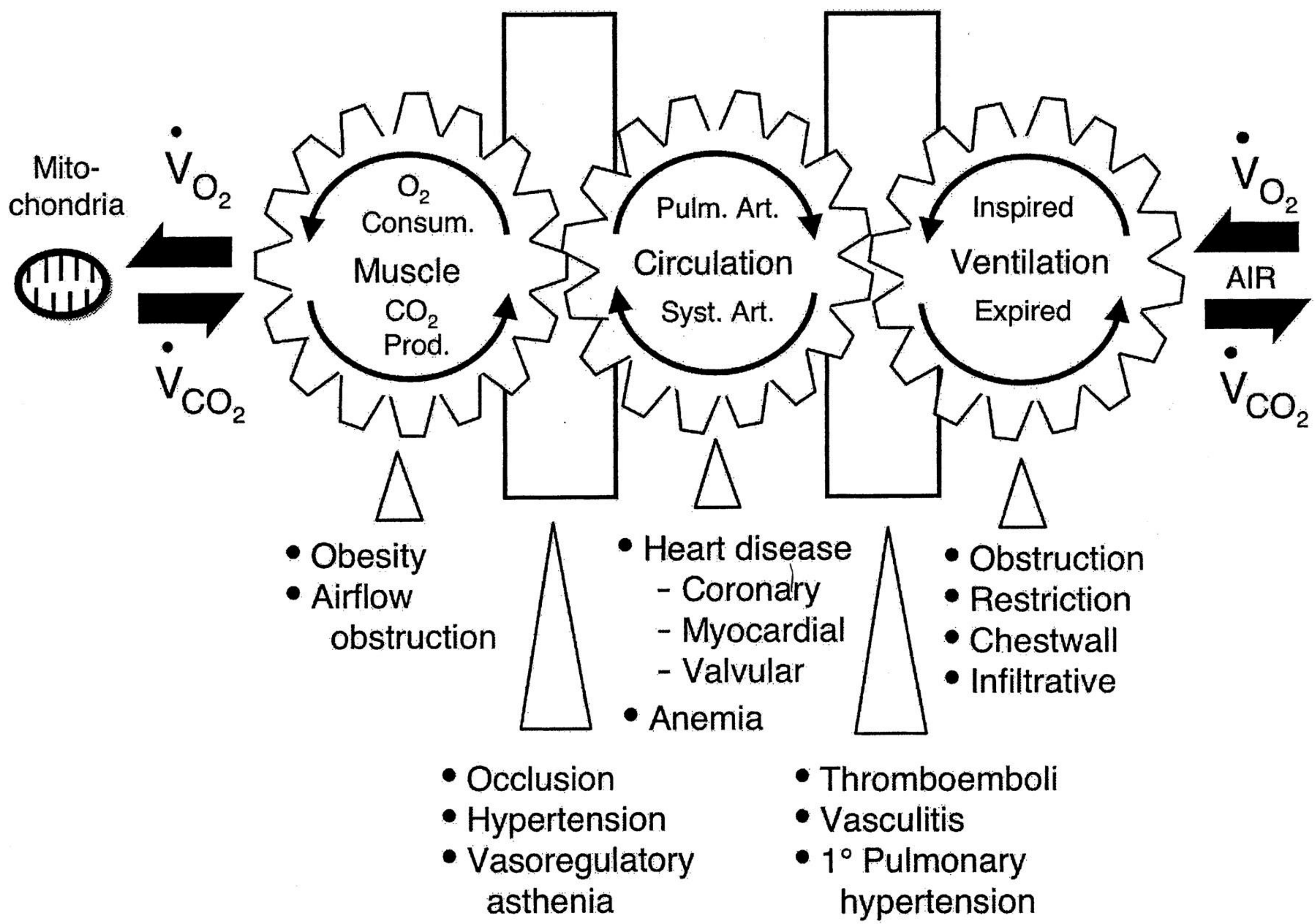


Fig. 1

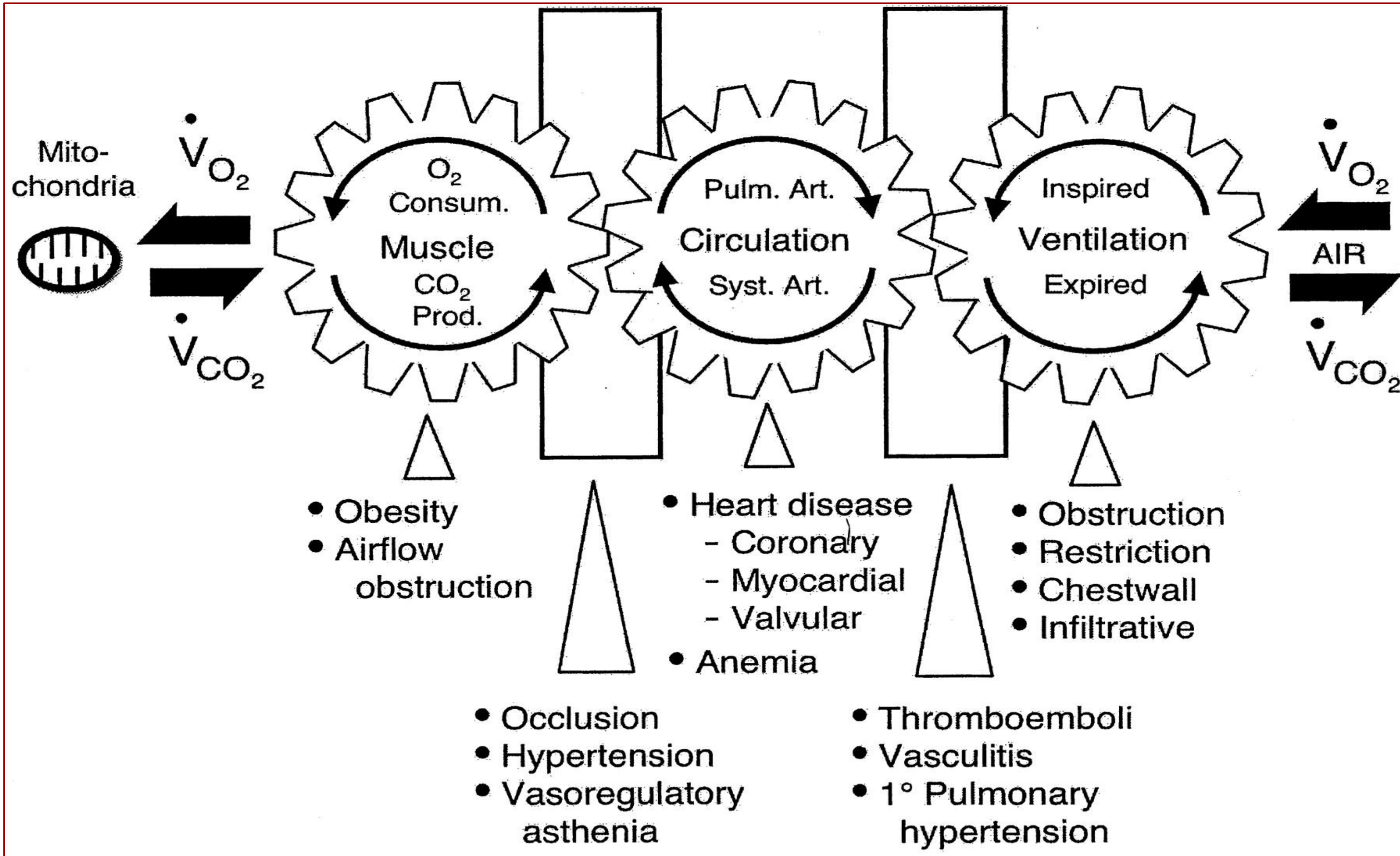
Derangements of gas exchange in disease.



Milani R V et al. Circulation. 2004;110:e27-e31

American Heart Association

Coupling of External Ventilation and Cellular Metabolism

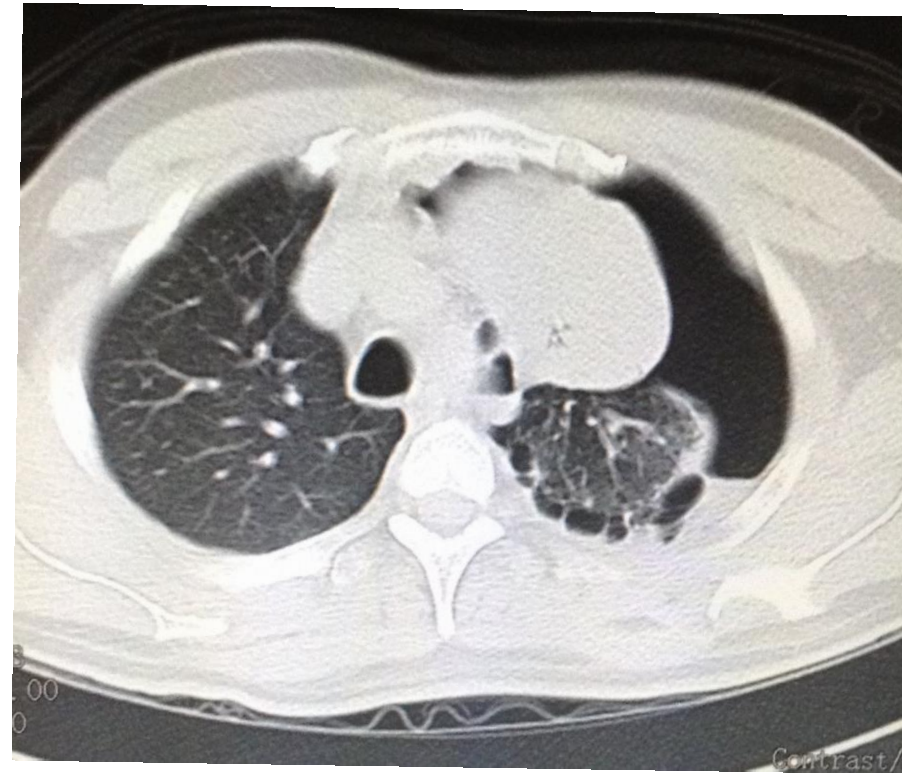


WHY EXERCISE ?

- ***The goal of CARDIO-PULMONARY exercise testing is to evaluate the physiologic response of the***
  - ***heart***
  - ***lungs and***
  - ***muscles to an increase in physical stress.***

CASE

- 50 year old, male, computer technician
- retired 10 years ago because of progressive dyspnea
- was a heavy cigarette smoker, but denies cough/phlegm/wheezing/chest pains
- recurrent pneumothorax secondary to multiple bullous disease



	Predicted	Measured	%Pred
FVC	4.84	1.88	39
FEV1	3.73	1.48	40

QUESTION 1:

- WOULD YOU CLEAR THIS PATIENT FOR PNEUMONECTOMY?
- A. YES
- B. NO

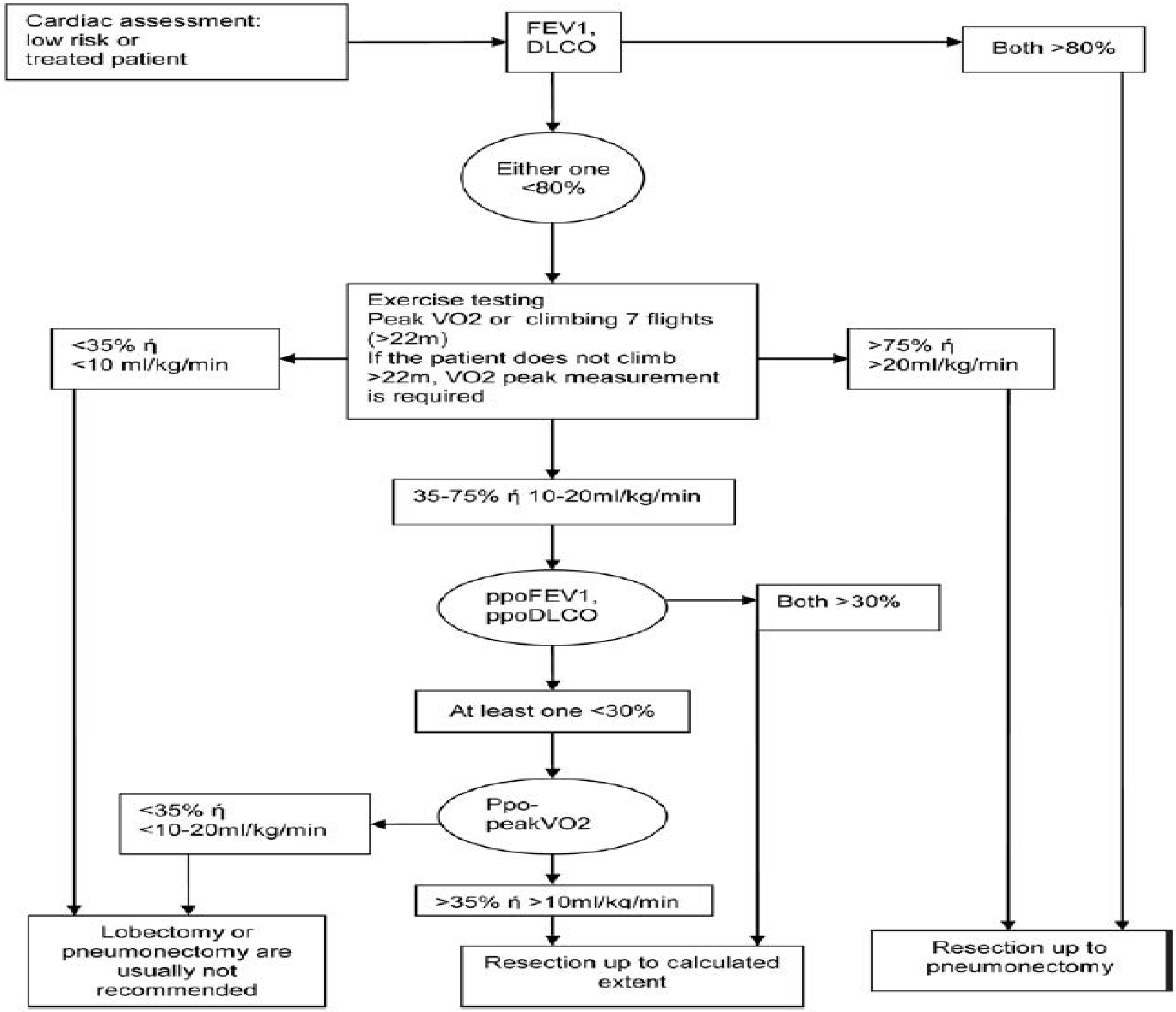


Figure 2. Algorithm for assessment of cardiopulmonary reserve before lung resection in patients with lung cancer

Predicted Post -Operative FEV1

PPO FEV1 = Pre-Op FEV1 x (1-a/b)

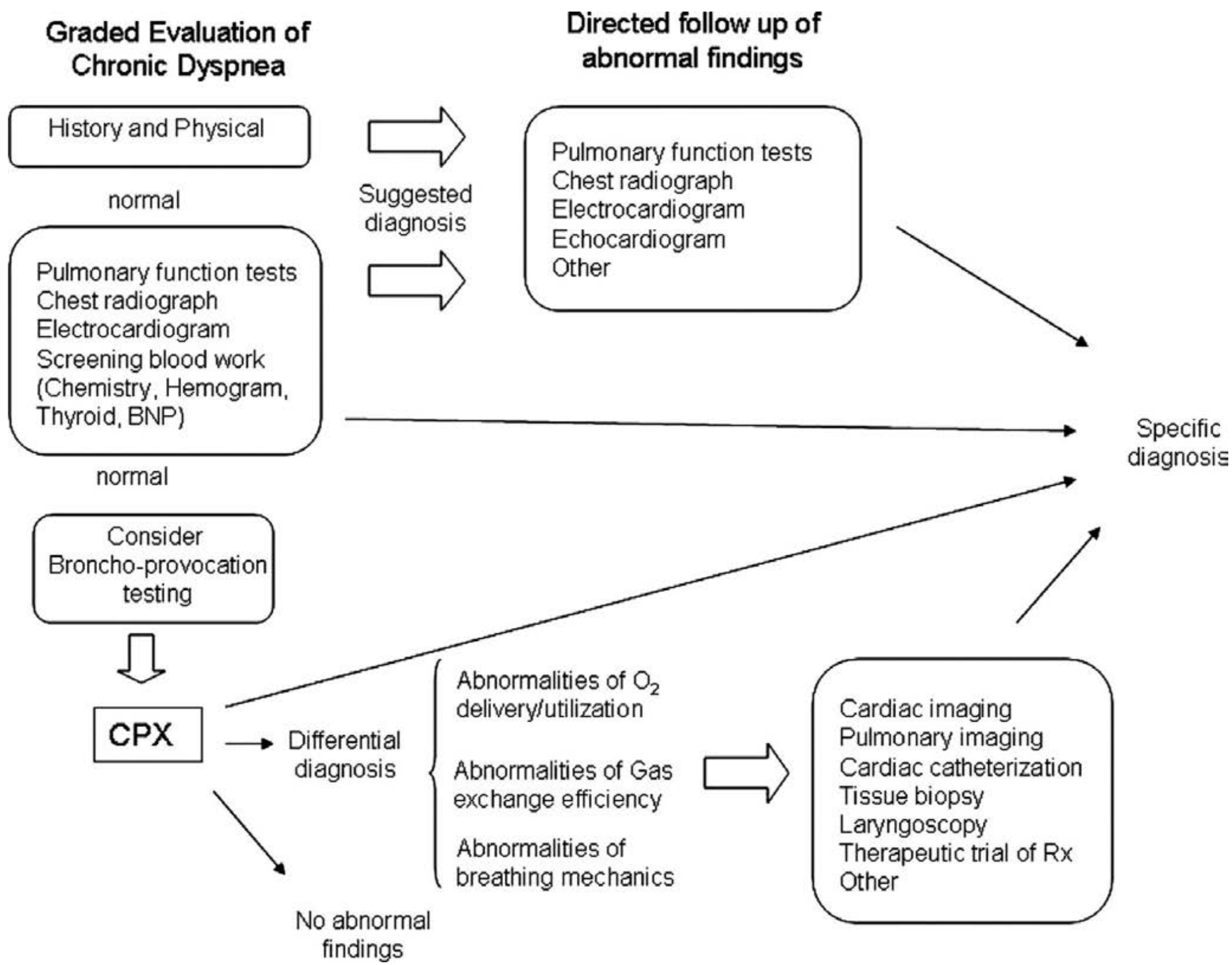
a= number of unobstructed segments to be removed
b= total number of unobstructed segments

PPO FEV1 = 1480 ml (1 - 9/19)
= 778 ml

QUESTION 2:

- WHAT IS THE NEXT MOST APPROPRIATE DIAGNOSTIC PROCEDURE TO CONFIRM WHETHER THIS PATIENY CAN UNDERGO PNEUMONECTOMY?
- A. STAIR CLIMBING
- B. DIFFUSION CAPACITY
- C. VENTILATION-PERFUSION SCANNING
- D. CARDIOPULMONARY EXERCISE TESTING

Use of CPX in the clinical evaluation of chronic dyspnea.



Balady G J et al. Circulation. 2010;122:191-225

American Heart Association

INDICATIONS FOR CPET

- Evaluation of dyspnea
  - distinguish cardiac vs pulmonary vs peripheral limitation vs others
  - detection of exercise-induced bronchoconstriction
  - detection of exertional desaturation
- Pulmonary rehabilitation
  - exercise intensity/prescription
  - response to participation
- Pre-op evaluation and risk stratification
- Prognostication of life expectancy

INDICATIONS …

- Disability determination
- Fitness evaluation
- Confirm the diagnosis
- Assess response to therapy

ABSOLUTE CONTRAINDICATIONS TO CPET

- Acute MI
- Unstable angina
- Unstable arrhythmia
- Acute endocarditis, myocarditis, pericarditis
- Syncope
- Severe, symptomatic Atrial Stenosis
- Uncontrolled CHF

ABSOLUTE CONTRA …

- **Acute PE, DVT**
- **Respiratory failure**
- **Uncontrolled asthma**
- **SpO_2 <88% on RA**
- **Acute significant non-cardiopulmonary disorder that may affect or be adversely affected by exercise**
- **Significant psychiatric/cognitive impairment limiting cooperation**

RELATIVE CONTRAINDICATIONS

- Left main or 3-V CAD
- Severe arterial HTN (>200/120)
- Significant pulmonary HTN
- Tachyarrhythmia, bradyarrhythmia
- High degree AV block

RELATIVE CONTRA …

- **Hypertrophic cardiomyopathy**
- **Electrolyte abnormality**
- **Moderate stenotic valvular heart disease**
- **Advanced or complicated pregnancy**
- **Orthopedic impairment**

INITIAL EVALUATION

- HISTORY: tobacco use, medications, tolerance to normal physical activities, any distress symptoms, contraindicated illnesses
- PHYSICAL EXAM: height, weight, assessment of heart, lungs, peripheral pulses, blood pressure
- EKG
- PULMONARY FUNCTION TESTS: spirometry, lung volumes, diffusing capacity, arterial blood gases

PRIOR TO THE TEST

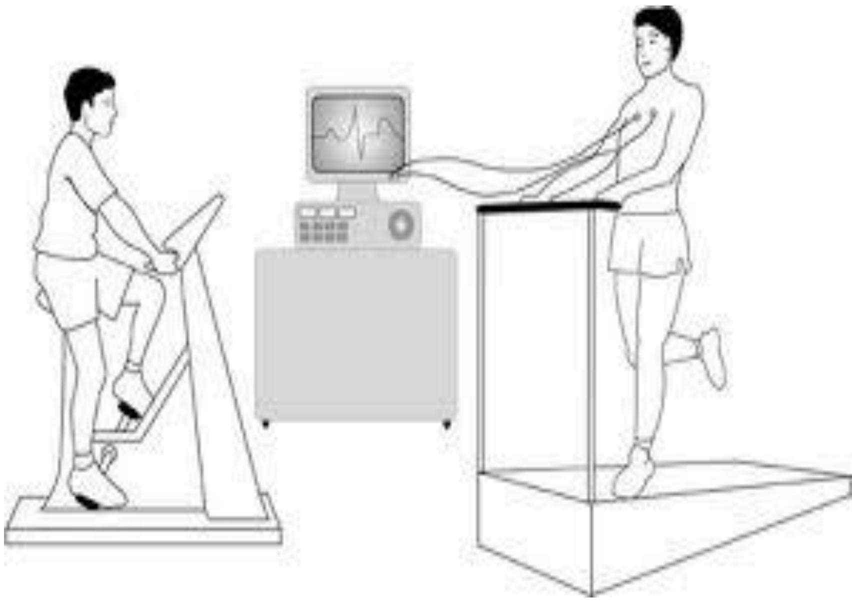
- Wear loose fitting clothes, low-heeled or athletic shoes
- Abstain from coffee and cigarettes at least 2 hours before the test
- Continue maintenance medications
- May eat a light meal at least 2 hours before the test

CARDIOPULMONARY EXERCISE TEST (CPET)

- symptom-limited exercise test
- measures airflow, SpO_2, and expired oxygen and carbon dioxide
- allows calculation of peak oxygen consumption, anaerobic threshold

EXERCISE MODALITIES

- Advantages of cycle ergometer
  - cheaper
  - safer
    - Less danger of fall/injury
    - Can stop anytime
  - direct power calculation
    - Independent of weight
    - Holding bars has no effect
  - little training needed
  - easier BP recording, blood draw
  - requires less space
  - less noise



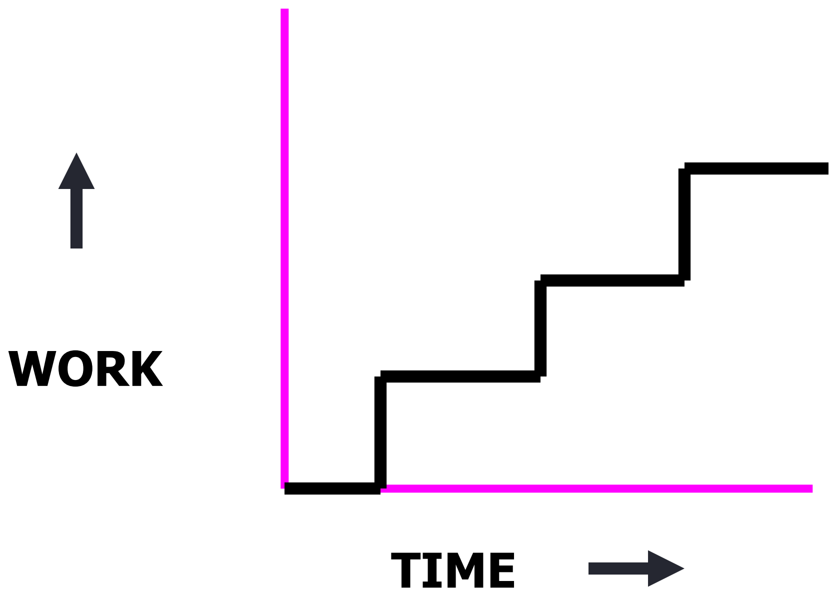
- Advantages of treadmill
  - attain higher VO_2
  - more functional

COMPARISON OF CYCLE VS TREADMILL

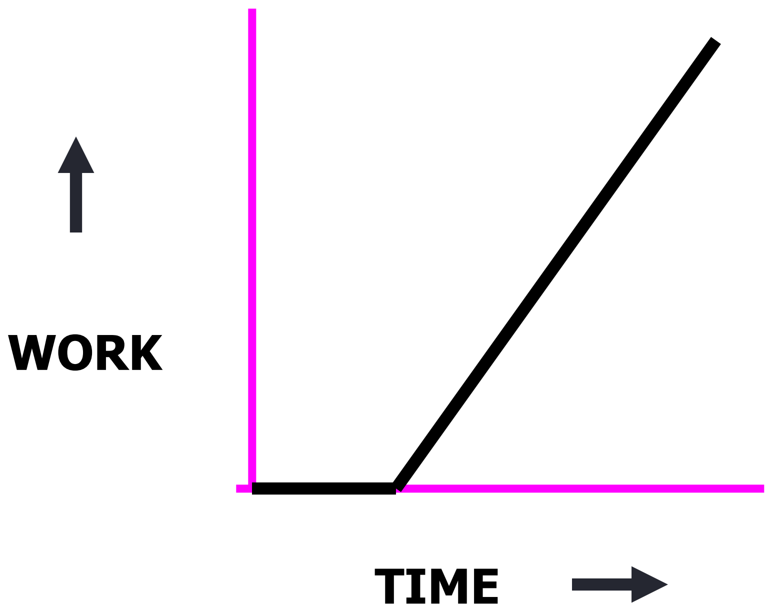
	CYCLE	TREADMILL
VO2 MAX	LOWER	HIGHR
LEG MUSCLE FATIGUE	OFTEN LIMITING	LESS LIMITING
WORK RATE QUANTIFICATION	YES	ESTIMATION
WEIGHT BEARING IN OBESE	LESS	MORE
NOISE & ARTIFACTS	LESS	MORE
SAFETY ISSUES	LESS	MORE

EXERCISE TEST PROTOCOLS

INCREMENTAL



RAMP



INDICATIONS TO EXERCISE TERMINATION

- **Patient's request: fatigue, dyspnea, pain**
- **Ischemic ECG changes**
  - **2 mm ST depression**
- **Chest pain suggestive of ischemia**
- **Significant ectopy**
- **2nd or 3rd degree heart block**
- **Bp_{sys} >240-250, Bp_{dias} >110-120**

INDICATIONS TO TERMINATION …

- **Fall in BP_{sys} >20 mmHg**
- **SpO_2 <81-85%**
- **Dizziness, faintness**
- **Onset of confusion**
- **Onset of pallor**

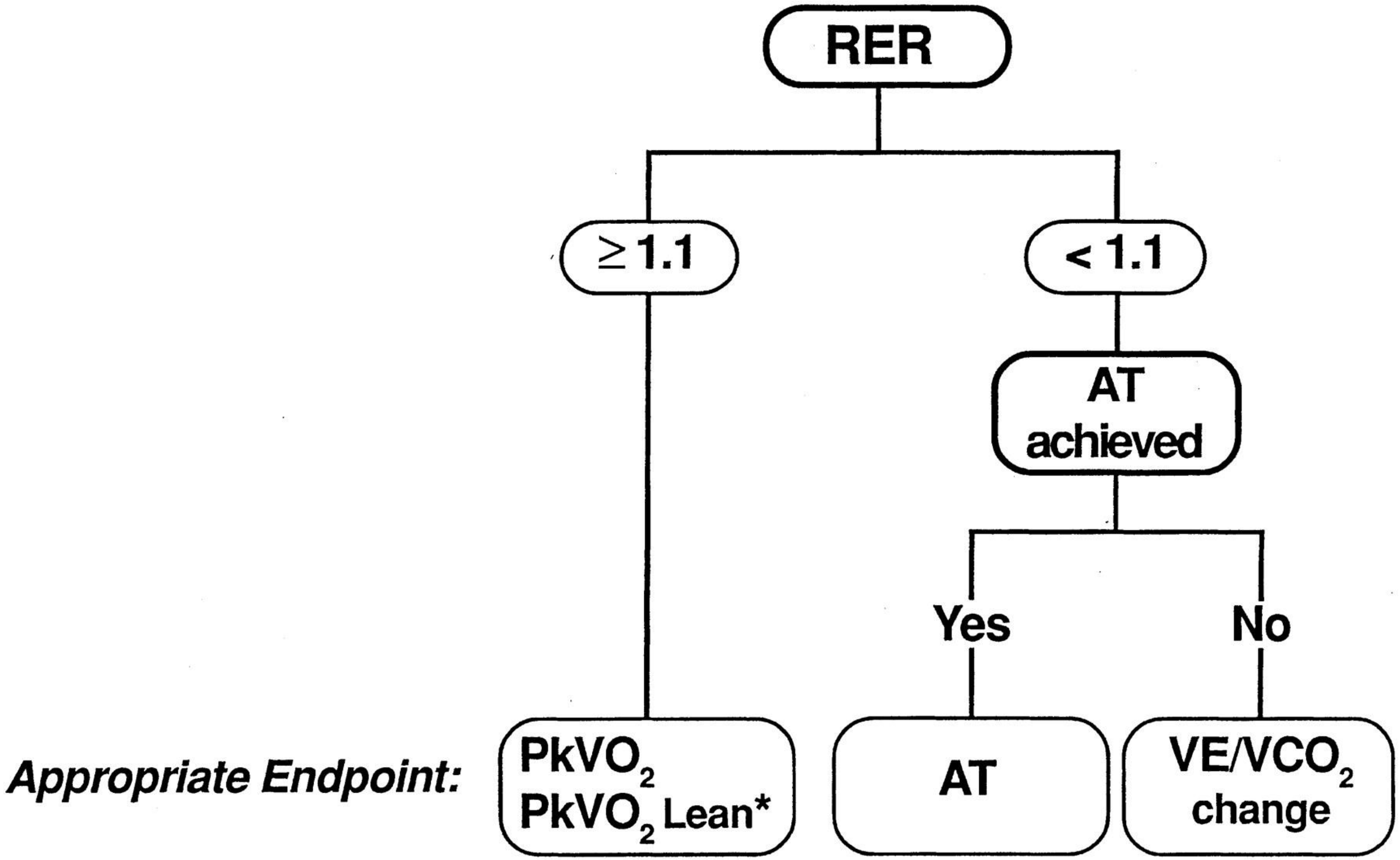
General Mechanisms of Exercise Limitation

- Pulmonary
  - Ventilatory impairment
  - Respiratory muscle dysfunction
  - Impaired gas exchange
- Cardiovascular
  - Reduced stroke volume
  - Abnormal HR response
  - Circulatory abnormality
  - Blood abnormality
- Peripheral
  - Inactivity
  - Atrophy
  - Neuromuscular dysfunction
  - Reduced oxidative capacity of skeletal muscle
  - Malnutrition
- Perceptual
- Motivational
- Environmental

CPET Measurements

- Work
- VO_2
- VCO_2
- AT
- HR
- ECG
- BP
- RR
- SpO_2
- ABG
- Lactate
- Dyspnea
- Leg fatigue

Metabolic endpoint to evaluate results of therapeutic interventions.



Milani R V et al. Circulation. 2004;110:e27-e31

PULMONARY PARAMETERS

- 1. MINUTE VENTILATION
  - NORMAL = 5 – 6 liters/ min
  - AT EXERCISE = 100 liters/min
  - increase is due to stimulation of the respiratory centers by brain motor cortex, joint propioceptors and chemoreceptors
  - ANAEROBIC THRESHOLD (AT) the minute ventilation increases more than the workload

PULMONARY …

- 2. TIDAL VOLUME
  - NORMAL = 500 ml
  - DURING EXERCISE = 2.3 – 3 liters
  - increases early in the exercise
  - increases ventilation

PULMONARY …

- 3. BREATHING RATE
  - NORMAL = 12 – 16 / min
  - AT EXERCISE = 40 – 50 / min
  - responsible for the increase in minute ventilation

PULMONARY …

- 4. DEAD SPACE / TIDAL VOLUME ratio
  - NORMAL = 0.20 – 0.40
  - AT EXERCISE = 0.04 – 0.20
  - decrease is due to increased tidal volume with constant dead space

PULMONARY …

- 5. PULMONARY CAPILLARY BLOOD TRANSIT TIME
  - NORMAL = 0.75 second
  - AT EXERCISE = 0.38 second
  - the decrease is due to increased cardiac output

- 6. ALVEOLAR-ARTERIAL OXYGEN DIFFERENCE
  - NORMAL = 10 mm Hg
  - AT EXERCISE = 20 – 30 mm Hg
  - changes very little until a heavy workload is achieved

PULMONARY …

- 7. OXYGEN TRANSPORT
  - increase in temperature, PCO_2 and relative acidosis in the muscles -> increase in release of Oxygen by blood for use by the tissues for metabolism

CARDIOVASCULAR PARAMETERS

- 1. CARDIAC OUTPUT
  - NORMAL = 4 – 6 liters / min
  - AT EXERCISE = 20 liters / min
  - increase is linear with increase in workload during exercise until the point of exhaustion
  - first half of exercise capacity, the increase is due to increase in Heart Rate and Stroke Volume
  - later, due to increase in Heart Rate alone

CARDIOVASCULAR…

- 2. STROKE VOLUME
  - NORMAL = 50 – 80 ml
  - AT EXERCISE = double
  - increase is linear with increase in workload
  - after a Heart Rate of > 120/ min, there is little increase in Stroke Volume

CARDIOVASCULAR…

- 3. HEART RATE
  - NORMAL = 60 – 100 /min
  - AT EXERCISE = 2.5 – 4 times the resting HR
  - HR max is achieved just prior to total exhaustion, physiologic endpoint of an individual

  - HR max = 220 – age
  - HR max = 210 – (0.65 x age)

CARDIOVASCULAR…

- 4. OXYGEN PULSE
  - NORMAL = 2.5 – 4 ml O_2 / heartbeat
  - AT EXERCISE = 10 – 15 ml
  - With increasing muscle work during exercise, each heart contraction must deliver a greater quantity of oxygen out to the body

  - O_2 PULSE = VO_2/ HR

CARDIOVASCULAR…

- 5. BLOOD PRESSURE
  - DURING EXERCISE:
    - Systolic BP increases (to 200 mm Hg)
    - Diastolic BP is relatively stable (up to 90 mmHg)
    - increase in Pulse Pressure (difference between Systolic and Diastolic pressures)

CARDIOVASCULAR…

- 5. ARTERIAL – VENOUS OXYGEN CONTENT DIFFERENCE
  - mL of O2 / 100 ml of blood
  - NORMAL = 5 vol %
  - AT EXERCISE = 2.5 – 3 times higher
  - the increase is due to the greater amounts of Oxygen that are extracted by the working muscle tissue

METABOLIC PARAMETERS

- 1. OXYGEN CONSUMPTION
  - NORMAL = 250 ml / min

    3.5 – 4 ml / min / kg
  - increases directly with the level of muscular work
  - increases until exhaustion occurs and until individual reaches ….
  - VO2max = maximum level of oxygen consumption

    definite indicator of muscular work capacity

    NORMAL RANGE = 1,700 – 5,800 ml / min

METABOLIC…

- 2. CARBON DIOXIDE PRODUCTION
  - NORMAL = 200 ml / min

    2.8 ml / min / kg
  - AT EXERCISE
    - initial phase, increases at same rate as VO2
    - once Anaerobic Threshold (AT) is reached, increases at a faster rate than VO2
    - increase is due to increased acid production

Lactic Acid is Buffered by Bicarbonate

Lactic acid $+ HCO_3 \rightarrow H_2CO_3 +$
Lactate

$$\downarrow$$

$$H_2O + CO_2$$

METABOLIC…

- 3. ANAEROBIC THERSHOLD (AT)
  - NORMAL: occurs at about 60% of VO2 max
  - followed by breathlessness, burning sensation begins in working muscles

METABOLIC…

- 4. RESPIRATORY QUOTIENT (RQ)
  - RESTING LEVEL = 0.8
  - AT = 1.0 or more
  - may exercise for a short time on 1.5

  - **RER = CO_2 produced / O_2 consumed**

    = VCO_2 / VO_2

- 5. BLOOD pH
  - relatively unchanged until AT is reached
  - the body becomes less able to buffer the excessive acid produced by anaerobic metabolism

INCREASES DURING EXERCISE

- **Heart rate**
- **Oxygen extraction**
- **Cardiac output**
- **Oxygen uptake**
- **Carbon dioxide output**
- **Arterial blood pressure**
- **Minute ventilation**
- **Alveolar ventilation**
- **Oxygen pulse**
- **RQ and RER**
- **METS**

DECREASES DURING EXERCISE

- During exercise, there are decreases in:
  - VD/ VT

Ventilatory Equivalents

- Ventilatory equivalent for carbon dioxide = Minute ventilation / VCO_2
  - Efficiency of ventilation
  - Liters of ventilation to eliminate 1 L of CO_2

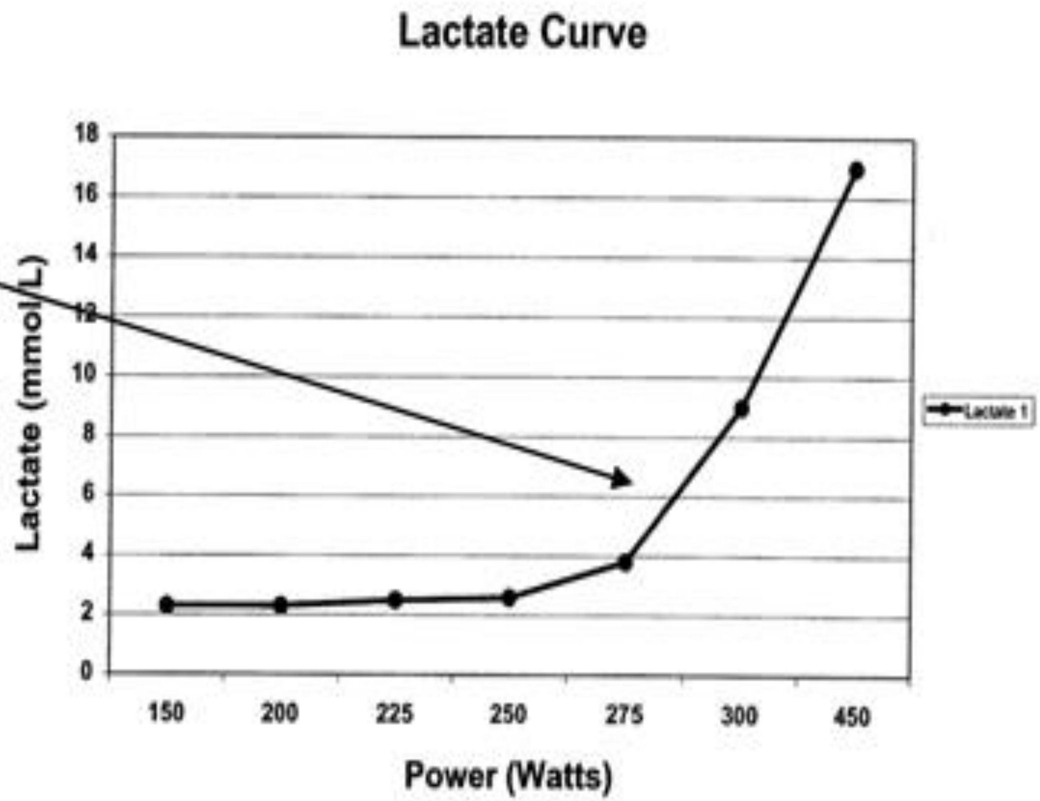
- Ventilatory equivalent for oxygen = Minute ventilation / VO_2
  - Liters of ventilation per L of oxygen uptake

Relationship of AT to RER and Ventilatory Equiv for O_2

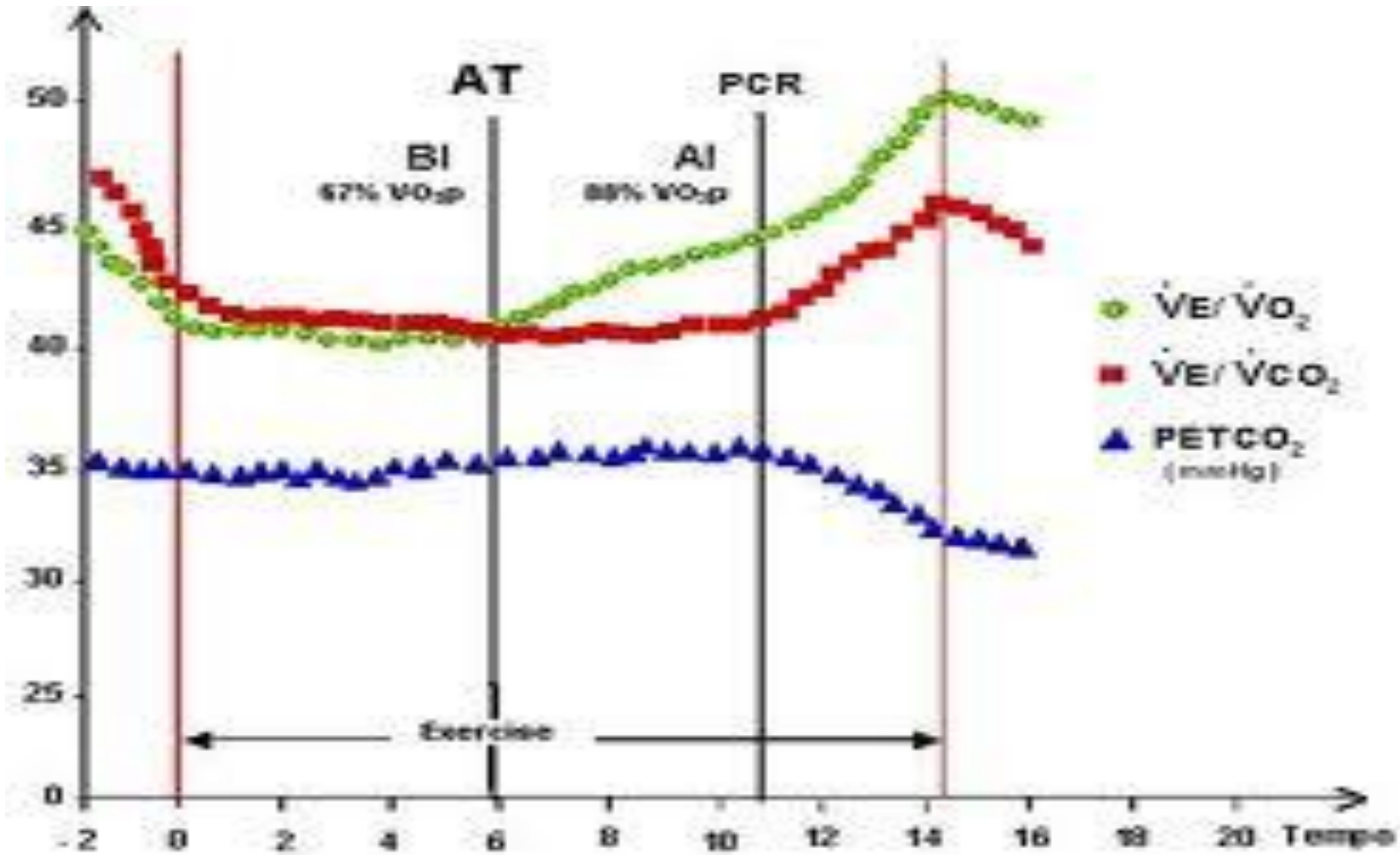
- Below the anaerobic threshold, with carbohydrate metabolism, RER=1 (CO_2 production = O_2 consumption).
- Above the anaerobic threshold, lactic acid is generated.
- Lactic acid is buffered by bicarbonate to produce lactate, water, and carbon dioxide.
- Above the anaerobic threshold, RER >1 (CO_2 production > O_2 consumption).
- Carbon dioxide regulates ventilation.
- Ventilation will disproportionately increase at lactate threshold to eliminate excess CO_2.
- Increase in ventilatory equivalent for oxygen demarcates the anaerobic threshold.

Lactate Threshold

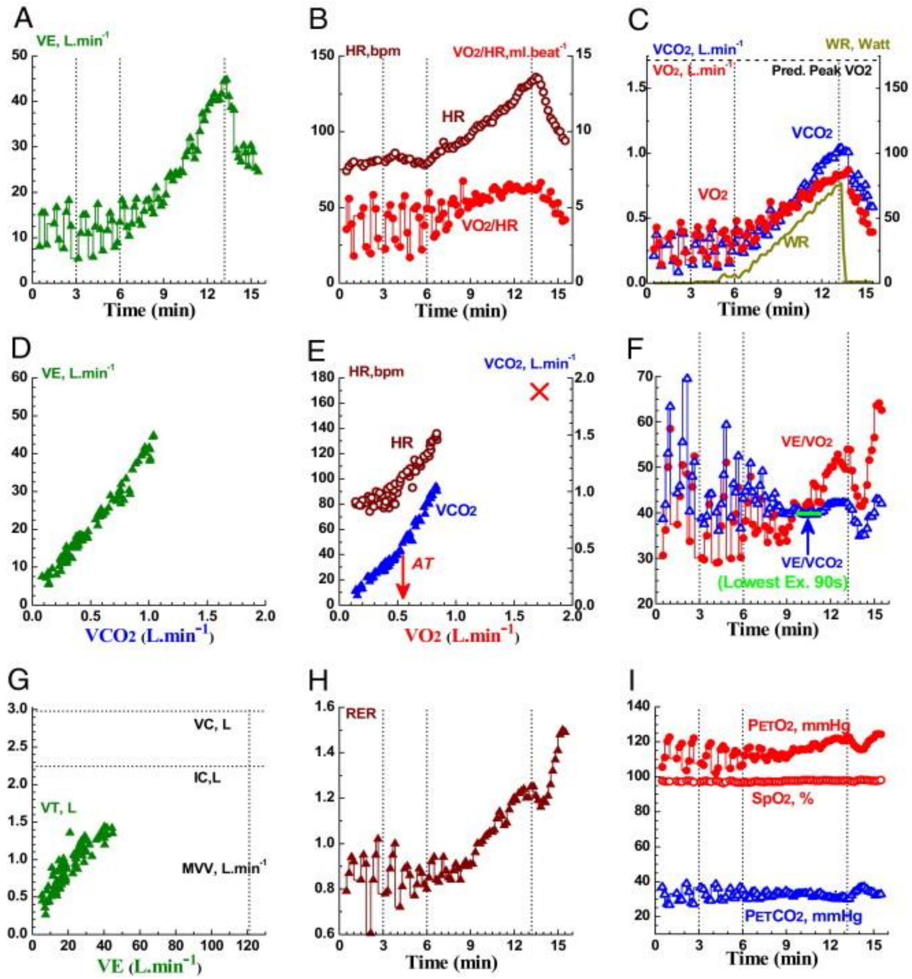
The lactate measurement shows the sudden increase in lactate



Determination of AT from Ventilatory Equivalent Plot



Wasserman 9-Panel Plot



Interpretation of CPET

- Peak oxygen consumption
- Peak HR
- Peak work
- Peak ventilation
- Anaerobic threshold
- Heart rate reserve
- Breathing reserve

Estimation of Predicted Peak HR

- 220 – age
  - For age 40: 220 - 40 = 180
  - For age 70: 220 - 70 = 150

- 210 – (age x 0.65)
  - For age 40: 210 - (40 x 0.65) = 184
  - For age 70: 210 - (70 x 0.65) = 164

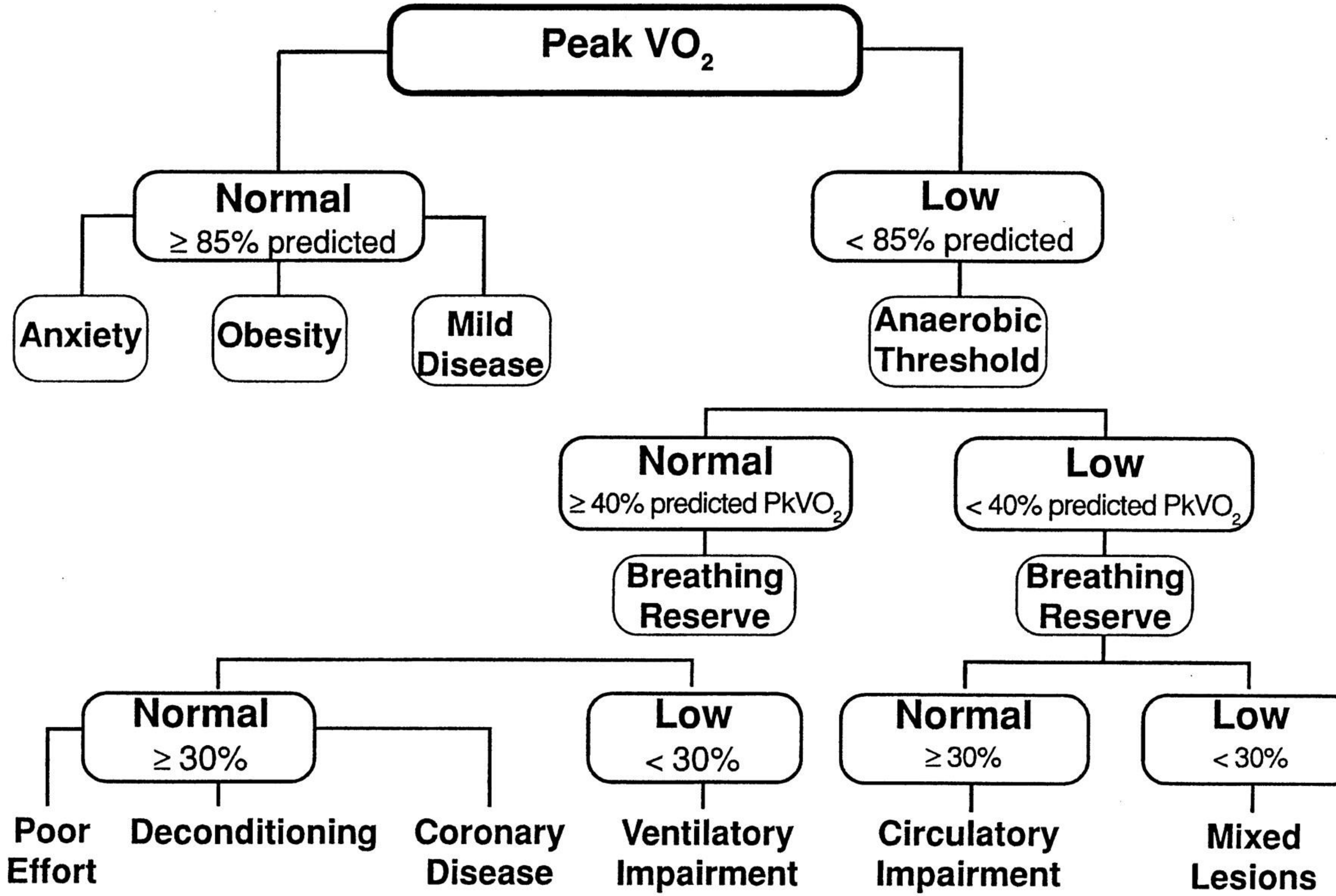
Heart Rate Reserve

- Comparison of actual peak HR and predicted peak HR

  = (1 – Actual/Predicted) x 100%

- Normal <15%

Flow chart for the differential diagnosis of exertional dyspnea and fatigue.



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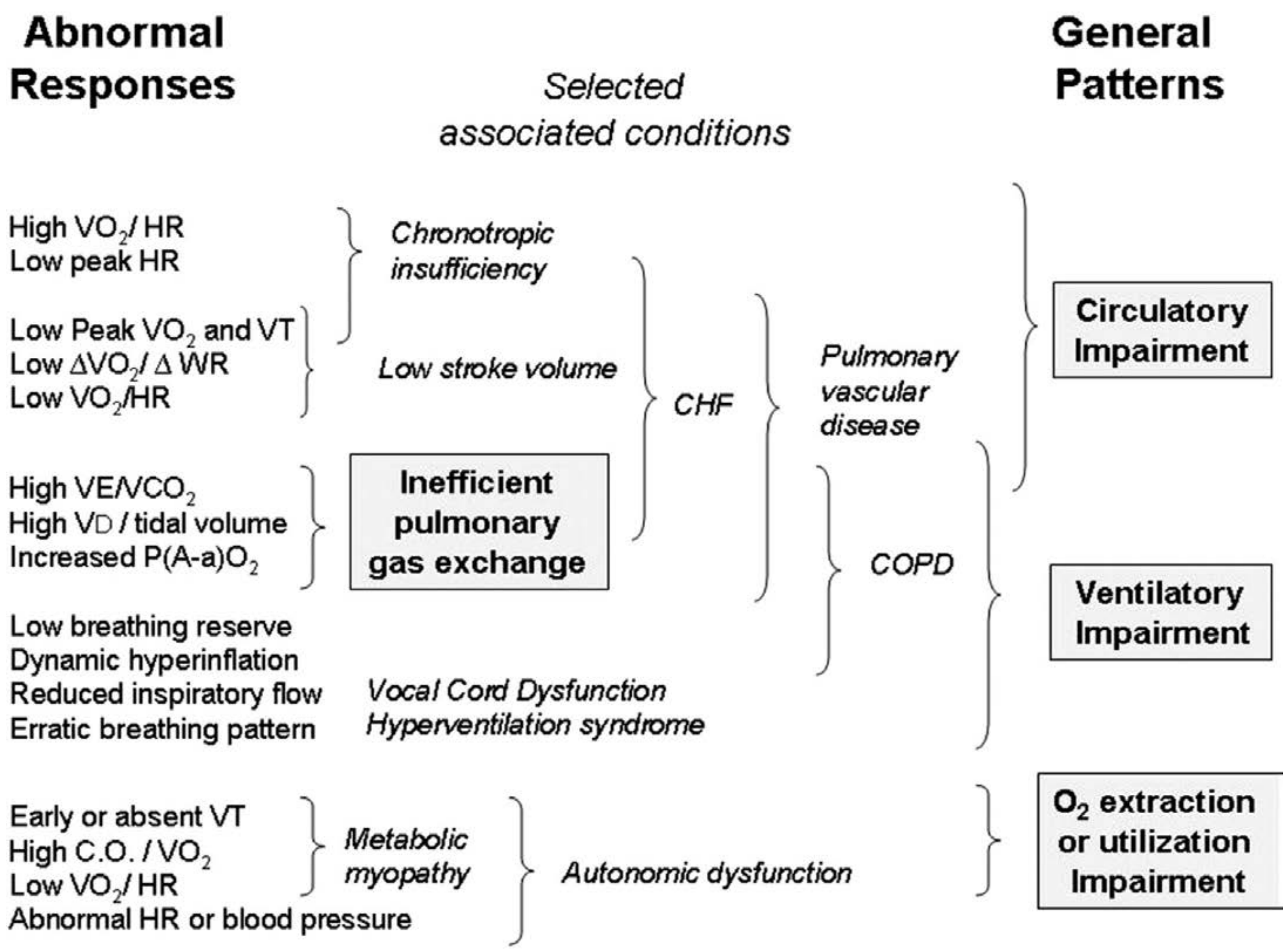
Abnormal patterns of responses from CPX characteristic of disorders that cause dyspnea



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Predicted and Normal Values for Test Parameters

Parameter	Predicted Value	Range
$VO_{2,max}$ (ml/min)	Based on gender, age, height	Lower limit of normal < 80% predicted
Resting VO_2 (ml/min)	150 + (6 X weight in kg)	250 -300 (larger in obese individuals)
Peak Heart Rate (bpm)	220- age or 210 – (0.65 X age)	90% predicted ± 15 bpm
Oxygen pulse (ml/beat)	(Predicted $VO_{2,max}$)÷ (predicted max HR)	80% predicted (~ 15 ml/beat in men; ~ 10 ml/beat in women)
Minute Ventilation (L/min)		Peak Exercise: 70-80% of MVV
Maximum Tidal Volume	60% of the FVC	
V_E/VCO_2 (early exercise)		25-35
V_E/VO_2 (early exercise)		25-35
V_D/V_T		0.25-0.35 at rest Should decrease with exercise
$P_{ET}CO_2$ (mm Hg)		38-42 (Should decline after ventilatory threshold)
$P_{ET}O_2$ (mm Hg)		95-100 (Should rise after ventilatory threshold)
A-a O_2 Difference (mm Hg)		Rest: 10-20 Peak Exercise: 15-30
S_aO_2 (%)		> 95% (Should remain constant with exercise)
Respiratory Exchange Ratio	Rest: 0.8 Peak Exercise: > 1.15	Rest: 0.6-1.0 Peak Exercise: 1.1-1.3

Note: Normal values based on data from Gold WM. "Clinical Exercise Testing" in Murray and Nadel's Textbook of Respiratory Medicine. Elsevier Saunders. Philadelphia

Table 1. Basic Patterns Observed On Cardiopulmonary Exercise Testing in Normals and Patients With Various Forms of Disease

	Disease Category				
Variable	**Normal Patient**	**Cardiovascular Disease**	**Obstructive Lung Disease**	**Pulmonary Vascular Disease /ILD #**	**Neuromuscular Disease**
$VO_{2,max}$	Normal *	Decreased	Decreased	Decreased	Decreased
Heart Rate Reserve	Absent to small reserve (< 20 bpm)	Absent to small reserve (< 20 bpm)	Large (> 30 bpm)	Small (< 20-30 bpm)	Large (> 30 bpm)
$V_{E,max}/MVV$ (Ventilatory Reserve)	< 0.8	< 0.8	> 0.8	< 0.8	< 0.8
Ventilatory Threshold	Present	Present	Absent	Present	Usually present
Dead Space (V_D/V_T)	Decreases	Decreases	Decreases	Remains stable or increases	Decreases
Oxygen Saturation	Stable	Stable	Decreases	Decreases	Stable
End-Tidal CO_2 (in late exercise)	Decrease	Decrease	Increase or stable	Decrease	Increase or stable
Reason for Stopping	Leg Fatigue	Leg Fatigue	Dyspnea	Dyspnea, leg fatigue	Fatigue

Note:
* "Normal" or "decreased" refers to how the variable changes relative to age, gender and size matched individuals.

Interstitial lung disease patients demonstrate a pattern very similar to the pulmonary vascular pattern and can only be differentiated based on their PFTs and chest imaging.

Variable	*Normal*	*Clinical Significance*
VO_2 max (peak)	>84%	Decreased in heart failure, COPD, ILD, obesity, pulmonary vascular disease, and deconditioned.
AT	>40% VO_2max	Decreased in heart failure, COPD, ILD, pulmonary vascular disease, and deconditioned. Normal in obesity.
Heart Rate Heart Rate Reserve	>90% <15 beats/min	Decreased in COPD, obesity, pulmonary vascular disease, and deconditioned. Normal in heart failure.
Oxygen Pulse	>80%	Decreased in heart failure, COPD, ILD, pulmonary vascular disease, and deconditioned. Normal in obesity.
V_E max Frequency Ventilatory or Breathing Reserve	70 – 80% <60 bpm 20 – 30%	Increased or normal in heart failure, COPD, ILD, obesity, pulmonary vascular disease, and deconditioned.

Variable	Normal	Clinical Significance
SaO_2	$\geq$95% $\leq$4% decrease	Decreased in ILD and pulmonary vascular disease. Normal in heart failure, obesity and deconditioned.
PaO_2	$\geq$80 mmHg $\leq$10 mmHg fall	Decreased in ILD and pulmonary vascular disease Normal in heart failure, obesity and deconditioned.
$P(A\text{-}a)O_2$	<35 mmHg	Increased in COPD, ILD, and pulmonary vascular disease. Normal in heart failure and deconditioned.
V_D/V_T	<0.28	Increased in heart failure, COPD, ILD, pulmonary vascular disease, and normal in obesity and deconditioned.
V_E/VCO_2 (at AT)	<34	Increased in heart failure, COPD, ILD, and pulmonary vascular disease. Normal in obesity and deconditioned.

Comparison CPET results

	Normal	CHF	COPD
Predicted Peak HR	150	150	150
Peak HR	150	140	120
MVV	100	100	50
Peak VO_2	2.0	1.2	1.2
AT	1.0	0.6	1.0
Peak VE	60	40	49
Breathing Reserve	40%	60%	2%
HR Reserve	0%	7%	20%
Borg Breathlessness	5	4	8
Borg Leg Discomfort	8	8	5

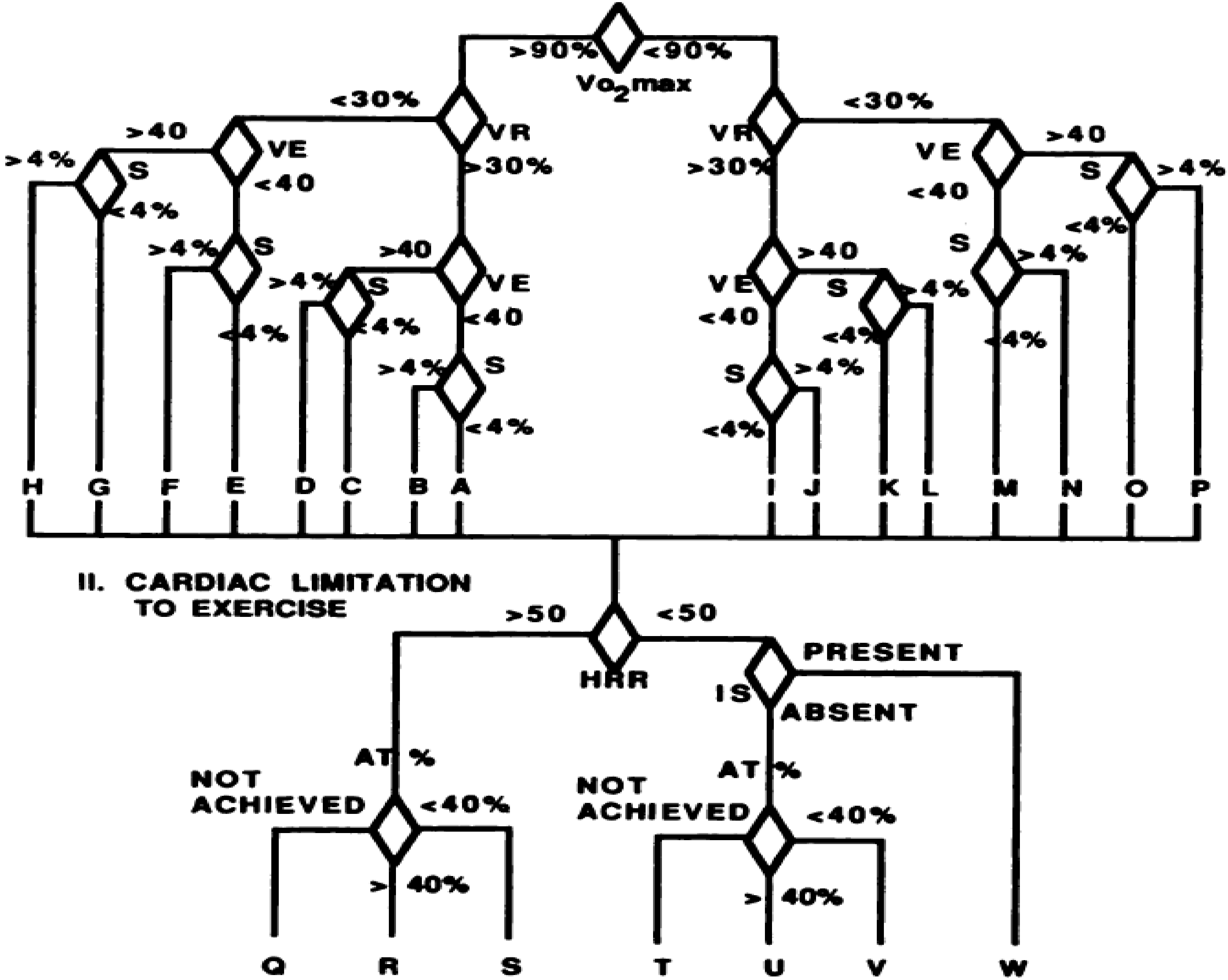
CPET Interpretation

	Peak VO_2	HRR	BR	AT/VO_2max	A-a
Normal	>80%	<15%	>30%	>40%	normal
Heart disease	<80%	<15%	>30%	<40%	normal
Pulm vasc dis	<80%	<15%	>30%	<40%	increased
Pulm mech dis	<80%	>15%	<30%	>40%	increased
Deconditioning	<80%	>15%	>30%	>40%	normal

Cardiac vs Pulmonary Limitation

- **Heart Disease**
  - Breathing reserve >30%
  - Heart rate reserve <15%

- **Pulmonary Disease**
  - Breathing reserve <30%
  - Heart rate reserve >15%



>90%
<90%
Vo2max
<30%
VR
>30%
>40
VE
<40
S
>4%
<4%
H
G
F
E
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II. CARDIAC LIMITATION TO EXERCISE
>50
<50
HRR
PRESENT
IS
ABSENT
AT %
NOT ACHIEVED
<40%
> 40%
Q
R
S
T
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V
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Peak Cardiovascular Responses	Predicted	Measured	% Predicted
VO2 (ml/kg/min)	38.3	24.0	(63)
VO2 (l/min)	2.938	1.517	(52)
VCO2 (l/min)		1.677	
Work (Watts)	205	250	122
Anaerobic Threshold (AT)(l/min)	>1.175	1.029	
AT (% Predicted Max VO2)	> 40%	35	
Heart Rate (bpm)	174	166	95
O2 Pulse (ml/beat)	15.2	9.1	(60)
Systolic Blood Pressure (Max)	179		
Diastolic Blood Pressure (Max)	85-105		
Heart Rate Reserve (bpm)	<15	174	
Peak Ventilatory Responses			
VE Max (l/min) BTPS	65.8	0.0	
Tidal Volume (VT) (L)	0.620	1.240	200
Respiratory Rate (RR)	<50	40	
Breathing Reserve (%)	20-40	100	
Gas-Exchange Responses			
End Tidal CO2 (Peak PetCO2)		40.7	
End Tidal O2 (Peak PetO2)		111.9	
VE/VO2 @ AT		31	
VE/VCO2 @ AT		31	
VD/VT (Est) @ Rest	0.30	0.12	(40)
VD/VT (Est) Peak	0.18	0.23	125
Respiratory Quotient (RQ)(Peak)	1.1-1.3	1.11	
SpO2 (O2 Sat--Pulse Ox) @ Peak	97	95	

QUESTION 3:

- WOULD YOU CLEAR THIS PATIENT FOR PNEUMONECTOMY?

- A. YES
- B. NO

CPET to Predict Risk of Lung Resection in Lung Cancer

Lim et al; Thorax 65:iii1, 2010

Alberts et al; Chest 132:1s, 2007

Balady et al; Circulation 122:191, 2010

- **Peak VO_2 >15 ml/kg/min**
  - **No significant increased risk of complications or death**
- **Peak VO_2 <15 ml/kg/min**
  - **Increased risk of complications and death**
- **Peak VO_2 <10 ml/kg/min**
  - **40-50% mortality**
  - **Consider non-surgical management**

SUMMARY

- Cardiopulmonary measurements obtained at rest may not estimate functional capacity reliably.
- CPET includes the measurement of expired oxygen and carbon dioxide.
- CPET may assist in pre-op evaluation and risk stratification, prognostication of life expectancy, and disability determination.
- **Cycle ergometer permits direct power calculation.**
- **Peak VO_2 is higher on treadmill than cycle ergometer**

SUMMARY…

- Peak VO_2 may be lower than VO_2max.
- Absolute contraindications to CPET include unstable cardiac disease and SpO_2 <88% on RA.
- Fall in BP_{sys} >20 mmHg is an indication to terminate CPET.
- 1 glucose yields 36 ATP in slow twitch fiber, and 2 ATP + 2 lactic acid in fast twitch fiber.
- RER= CO_2 produced / O_2 consumed

SUMMARY…

- Above the anaerobic threshold, CO_2 production exceeds O_2 consumption.
- Ventilation will disproportionately increase at lactate threshold to eliminate excess CO_2.
- AT may be determined graphically from V slope method or from ventilatory equivalent for CO_2.
- Derived from the Fick equation, Oxygen Pulse = VO_2 / HR, and is proportional to stroke volume.
- In pure heart disease, BR is >30% and HRR <15%.
- In pure pulmonary disease, BR is <30% and HRR >15%.

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Thank
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