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## PART II HRV Analysis Manual

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Electrode Placement
12 Lead and Lifeshirt

CHEST/ PRECORDIAL LEADS

V₁ Fourth intercostal space, Right sternal border
V₂ Fourth intercostal space, Left sternal border
V₃ Midway between V₂ and V₄
V₄ Fifth intercostal space midclavicular line
V₅ Level with V₄, anterior axillary line
V₆ Level with V₅, midaxillary line

LIMB LEADS

RA Right Arm aVR Midclavicular, Right superior pectoralis
LA Left Arm aVL Midclavicular, Left superior pectoralis
RL Right Leg Inline with V₄, Right lateral midabdomen (Ground: Eliminates electrical interference)
LF Left Leg aVF Left lateral midabdomen

LIFESHIRT LEADS

LF₁ Center of the Right pectoralis
LF₂ Center of the Left pectoralis
LF₃ Lower left abdomen on the margin of the external oblique
PREPARATION

ECG measures differences in electrical potential between two points. The skin conducts these electrical impulses, and therefore, a tight bond is necessary to reduce artifact. Body Hair, lotion, dirt, etc. must be removed prior to electrode placement.

– Alcohol swab each electrode site.

– Trim or shave body hair if necessary.

– Use sand paper to lightly sand the electrode sites.
  • This will “exfoliate” the skin providing a better surface for the electrode gel to adhere.

– Alcohol swab again

– Place electrodes as indicated

– Tape over all sides of the electrode to maximize adhesion

NOTE: Electrode placement may vary in respect to anatomical differences. Also it is important to avoid placing electrodes too close to the extremities. This will avoid noise created by movement, and possible friction with Lifeshirt instrumentation.
Attach the Leads to the Electrodes

Each lead is indicated with either ($V_1$, $V_2$, RA, etc.)

Squeeze the slides of the lead and press over the electrode

Release when fastened securely

Lifeshirt electrodes attach separately and will be connected after Cardiac Impedance electrode and lead placement.
Impedance Cardiography

Directions are printed on the electrode package

Each lead has a picture of where it attaches, and is direction sensitive

Depress the top of the lead with your index finger and press gently over the electrode

Release when securely seated

Electrodes are Inline
Impedance Cardiography

1st Visit

1. Start Monitor (Welcome Screen)
   a. Enter
      Subject I.D. #
      Last Name
      First Name
      Gender
      Height (Ft. and in) or (cm)
      Weight (lbs) or (Kg)
      Age

2. Electrode Placement
   a. Each Electrode package will have a placement diagram.
   b. Alcohol swap Electrode sites.
   c. Root of Neck (Vertical orientation, direction, sensitive placed on both sides).
   d. Xiphoid Process Level (Vertical orientation, direction sensitive, placed on both sides).

3. Attach Electrodes to the Impedance Leads.
   a. Each lead will have a diagram of where it attaches. (Two Leads per electrode pair, top and bottom/ left and right sensitive)
   b. Ensure that the Impedance leads do not interfere with the 12 lead or Lifeshirt Electrodes. This is vital for reducing artifact and maintaining a constant log of Lifeshirt data.

4. Place Blood Pressure Cuff on the Left Arm approximately 1 inch above the elbow joint on the Upper Arm with the bladder tube over the brachial artery.

5. With the Subject lying in the quiet supine position Hit [Start Monitor] to begin testing. Time the Subject’s rest to 7 minutes and record the time that Blood Pressure was taken.

2nd Visit

1. Start Monitor
   a. Hit [Stored Patient Info]
   b. Find the Subject’s name
   c. [Start Monitor] to begin Impedance.
SenseWear Arm Band Data Collection: Metabolic Demand and GSR

1. [Open Sensewear] (version depends on the Armband selected)

2. [Configure Armband & Display]

3. [Retrieve Configuration]

4. Enter Subject Information
   - Height (cm)
   - Weight (Kg)
   - Hand/Foot Dominance
   - Smoker/Non Smoker
   - Age

5. [Apply]

6. [OK]
Armband is ready for testing. Place the armband on the Lateral head of the Tricep. Right or Left placement varies depending on the model. Check to see if the Armband is labeled.

After Data Collection is Complete
1. Plug in the Sensewear Armband into the CPU via USB.
2. [Retrieve Armband Data]
3. Save Data
   a. File
   b. Save As: Name_yearMonth_date or subject I.D. #
   c. My Network Places
   d. Healthy Bones on Marlin
   e. Mito Project
   f. 14 Sensewear
4. File Close
   a. Generate Report
   b. Print for Subject file

5. Armband Maintenance
   a. Clear Data & Subject info

*You will press the armband before each activity within the protocol.
*Makes sure the dongle is in the CPU that you upload the data to.
Exercise Intolerance

Signs of exercise intolerance manifest when an individual is unable to participate in a level of activity that would be expected of a person of similar age or physical condition:

- Unusual breathlessness (dyspnea)
- Unusual muscle pain
- Muscle weakness that increases during exercise
- Severe headache during or after exercise
- Lightheadedness, dizziness, or nausea during or after exercise
- Decreasing endurance
- Extreme fatigue during or after exercise
- Sudden onset of muscle cramps, pain or discomfort in joints
- Profuse and uncontrollable sweating
- Lack of coordination
- Severe facial flushing
- Tingling in the extremities
- Chest pain or pressure
- Pain or achiness near the shoulder blades, pain in the shoulder area that may or may not radiate down the arms
- Pain in the neck or jaw

It is important to list at least 5 of these symptoms to each subject prior to graded maximal exercise. If you see anyone experiencing any of the above, have them slow down and stop exercising. In an emergency, call 911.
Cycle Ergometer Graded Maximal Exercise
Metabolic Cart Stress Test: 20 Watt/Step Protocol

1. Turn on the Cycle
   Power switch is located on the base of the Cycle.

2. Turn ON the Powervar 4.0 Pump and Computer
   1. Sign in as [Valued Customer]
   2. Allow 30 minutes for the system to warm-up prior to calibration.

3. Open Welch Allyn Cardio Perfect
   1. Welch must be opened before Breeze Suite to ensure that Welch will open on the left side monitor.

4. Open Breeze Suite
   1. The Login is [Admin]
   2. Leave the Password [Blank]
   3. Click [OK]

5. Calibrate the Pneumotach
   1. In Breeze on the RIGHT side Monitor Left click [Calibrate]
   2. Using the digital Thermometer, adjust the Temperature, Humidity, and Barometric Pressure located on the lower portion of the screen. The digital thermometer is used by all the exercise physiology labs and is generally located on the treadmill.
   3. Place the 3-Liter Syringe on a Sturdy Chair.
   4. Remove the Umbilical Clip from the Medgraphics Gas Analyzer and Insert the Clip into the Pneumotach.
      a. Align the Metal Probes from the Umbilical Clip with the holes of the Pneumotach. The Pneumotach has a TAB that will oppose the TAB side of the Umbilical Clip. (See Picture)
   5. Insert the Pneumotach into the 3-L Syringe Honeycomb side IN. Ensure the Umbilical clip cord is facing UP and the Pneumotach is seated evenly within the Syringe.
   6. In Breeze on the Right Side Monitor left Click [Zero Flow].
      a. Ensure that there is zero movement of the Syringe, Pneumotach, or umbilical clip.
   7. Manual Calibration
      a. Sit down on your Sturdy Chair and place the Syringe on your lap evenly. Ensure that the Umbilical Clip Cord is facing up and that the syringe is in a position on your lap that you are able to withdraw and inject the plunger without movement of the Syringe.
      b. Left Click [Start] or hit the Space Bar to begin calibration.
         1. You will be prompted to Withdraw and Inject the plunger 5 times.
2. Ensure that the entire volume of the Syringe in Injected and Withdrawn.
   3. Injections and withdrawals should be performed at different rates and mirror one another.
   4. If you receive the Green [Calibration Successful] message replace the Umbilical Clip into the Gas Analyzer. Left Click [OK] on the bottom right of the screen.
      c. Note: manual calibration is a skill and an art. This process may take several attempts and can get frustrating. Stay calm and ensure that there is no movement when Zeroing or Calibrating.

6. Automatic Calibration
   1. Left Click [GX Vac]
      a. Starts a 2 Minute timer that will change the [GX Vac] tab from Red to Green [GX Vac READY].
   2. Turn on the Gases
      a. Located behind the Cart. Open with at least two full Counter-Clockwise rotations.
      b. Open Before [GX Vac READY].
   3. Left Click [GX Auto Cal]
      a. The results of the test will be displayed as either [Calibration Successful] or [Calibration Failed].
      b. This test may take 1-6 attempts to successfully calibrate. Watch the acceptable error to see if adjustments need to be made to the gas mixture. Click [Retry] as necessary.
   4. Successful Calibration Message Turn off the Gases and Left Click [OK]

7. Create New File (This step may be performed at any time)
   1. Enter Personal Data
      Last Name    Sex
      First Name   Ethnicity
      I.D. #       
      D.O.B.
   2. Left Click [Add Visit]
      Height (in)
      Weight (lbs)
   3. [Save]
      a. Information should store, then project subject info onto the Welch Allyn ECG Monitor.

8. Left Click [Protocol Log] tab
   1. Change the Protocol to [Exercise FVL]
      a. This will prompt, “Changing the protocol will remove all stage markers from the visit log. Proceed anyway? Left Click [OK]
9. Left Click [GX] tab.
   1. Change the Script name to [C2 Bike].
   2. Remove the Blood Pressure from external devises.
   3. Change the Default Protocol to [20 Watt/Step]

10. Left Click the [Test] tab.

11. Plug in the ECG feed from the subject’s 12-lead into the Welch Allyn Fanny Pack located on the back of the Cart. Secure the fanny pack around the subject’s waist. Make sure it does not impede their natural cycling movement.

12. Using the Left side Monitor Click [Record] Without the mouthpiece and Pneumotach assembly in the subject’s mouth.
   1. While you are waiting for the ECG to record and Test Print insert Kim Wipes into the reservoir of the Pneumotach. Ensure that the tissues do not obstruct the Pneumotach. The wipes are used to prevent the Umbilical Clip with excessive saliva. Cap the reservoir.
   2. Insert the Pneumotach into the Mouthpiece Assembly.

13. Using the Left side monitor Click the [Exercise ECG] tab.
   1. Change the Exercise Protocol to [20 Watt Step]
   2. Print every 1-Minute

14. Insert the Pneumotach and Mouthpiece Assembly into the subject’s mouth allowing them to Warm-up for 5 minutes.
   1. Instruct the subject to maintain a pedal cadence between 60-65 RPM’s
   2. Adjust the seat as needed to ensure 25-30° of knee flexion
   3. Click [Start] on the Right side monitor to measure subject Gas Ex.

15. Click [Start] on the left side monitor to Begin Testing.

16. Once the Subject cannot maintain 60 RPM’s Click [Go to Recovery].

17. Allow the Subject to cool down for 5 minutes. Ensure that there is a tight seal around the Mouthpiece and that the subject keeps their head up throughout the cool down. After 5 minutes Click [Stop Test]
18. Click [Save] using Breeze on the Right side monitor.
19. Click [Gx Vac] to turn off the gas analyzer. Or you may be prompted with a message that asks if you wish to turn off the gas analyzers after stopping the test.
20. [Print] the results of the test using the Right side Monitor to add to their subject file.
21. Turn OFF the CPU, Pump, and Bike.
In Breeze on the Right side Monitor

1. Calibrate

2. Temp | Humidity | Barometric Pressure

3. 

4. 

4a

Tabs oppose

5. 

6. Zero Flow

Honeycomb side IN
Evenly spaced within the Syringe
Umbilical clip straight up
7. Manual Calibration
   a. Sit down and place the Syringe and Pneumotach assembly on your lap
   b. Or hit space bar

1. Withdraw and Inject the plunger 5 times
2. Inject and Withdraw the entire Syringe volume
3. Perform Withdrawals and Injections at different rates and mirror one another

4. If you Fail to Calibrate you first can restart the test by hitting start, or space bar.
   Repeat from step 6 on the previous page if you fail to calibrate within a few trials.

   Replace the Umbilical clip, and hit **OK**
6. Automatic Calibration

1. GX Vac

2. Turn ON the Gases (2 full CC rotations)

3. GX Auto Cal

4. Green Calibration Successful message
   Replace the Umbilical clip, and turn off the gases

   Retry

   As Necessary
Pneumotach and Mouth Piece Assembly

Insert 2-3 Kim wipes into the Reservoir of the Mouth Piece.

Cap the Reservoir

Ensure that the wipes do not obstruct air flow

Insert the Pneumotach into the Mouth Piece evenly with tab facing up
11. Plugging in the 12-Lead to the Welch Allyn ECG fanny pack

The leads are removed off of the cart before each subject is prepared.

Remove the leads from the Vivometrics fanny pack and plug the cable into the ECG fanny pack

Secure the fanny pack around the subject, making sure it doesn’t interfere with their movement
Resistance Protocol

**Purpose:**

1st Visit

10 and 5-RM Warm-up
Find Subject 1-RM within 4-6 single-set repetitions
Rest periods are kept to 60 seconds for all sets

2nd Visit

5 RM Warm-up
Find Subject 1-RM within 1-3 single-set repetitions
Perform as many repetitions at 60 % of 1-RM to failure, or until technique is compromised

**Key Points**

The purpose of the 1-RM is to see how much each subject can push, pull, or press with proper technique. Proper technique ensures test re-test reliability, validity, and that each subject will be able to safely complete both testing sessions within 1 week. The 1st Visit and 2nd visit 1-RM are used to find and validate the subject’s true 1-RM (± 5%). 1-RM is a direct measurement of maximum strength and can be used as a screening protocol for persons with moderate-to severe mitochondrial dysfunction.

Repetitions at 60% exposes the subject to a high glycolytic flux and measures local muscular endurance. This test will challenge the subjects ATP-PCr and Glycolytic systems, producing a high volume of metabolites that will cause vasodilation in active tissue. This test is used for prognostic purposes with persons with moderate-to severe mitochondria dysfunction. And Further, because all physiological data is measured pre and post, we can study effects of metabolite production on Autonomic Nervous System modulation of the heart period.
Seated Leg Press (Closed Chain)

1. Adjust the seat and record location

   Feet shoulder width apart, have the subject push through the feet to take the slack out of the pulley mechanism.

   Find 90-90° at the knee and ankle. Adjust as necessary

   Hip-Torso angle should be around 90° at full knee extension

2. Coaching Cues

   Back flat, chest up
   Drive though the heels
   Shoulders and head back on the pad
   Knees tracking with the feet (2\textsuperscript{nd} and 3\textsuperscript{rd} toe)
   Exhale as you Push
   Extend, but don’t forcefully “lock out”
Avoid:

1. Excessive toe-in or out
2. Heels coming off
3. Knee Varus or Vagus
4. Rounded back or forward head
5. Arched back (moderate-severe)
6. Slamming the weight stack
7. Locking out the knee forcefully
1. **Adjust the chest pad and record.**
   The subject should be able to reach the handles while the shoulders are protracted.

2. **Adjust the seat height and record.**
   The seat is only adjusted for height extremes.

3. **Coaching Cues.**
   - Back flat, chest up
   - Shoulders back, neutral head/chin
   - Squeeze the traps
   - Keep your elbows tight
   - Inhale, then exhale as they pull back on the handles. However, they may chose to HOLD their Breath until the Eccentric portion

   Place your hand slightly behind the subject’s torso to ensure they are breaking the plane with their elbow
Avoid:

1. The danger zone (abduction with internal rotation)
2. Internal rotation-forward roll
3. Rounded back
4. Chest coming off the pad
5. Forward head
6. Wrist Flexion
7. Momentum vs. Activation
Bench Press (Open-Chain)

1. Adjust the seat if necessary and record

2. Coaching Cues
   
   Heels flat on the floor
   
   Knees over the feet
   
   Handles are raised to Maxillary-line
   
   Shoulders back -activate the Traps
   
   Abs tight
   
   Activate the Glutes
Bench Press (part 2)

Press out forcefully **without protraction**

Elbows tight

Exhale as you push

Head and shoulders back

Handles tracking at shoulder height

(90 – 115° torso)

Use your hand as a guide to keep the

subject at the right height and distance
Avoid:

1. The **Danger Zone**: Shoulder abduction with external rotation “Elbows Tight”

2. Scapular protraction “Shoulders Back”

3. Shifting the heels “Activate the Glutes and Drive though the Heels”

4. Torso movement/back arch “Core Tight”

5. Shoulder elevation “Keep the Shoulders Away from the Ears”
HRV measures beat-to-beat fluctuations in heart period (R-R interval). HR and Systolic blood pressure are regulated tightly by the Autonomic Nervous System (ANS). The ANS is composed of two branches: (SNS) Sympathetic Nervous System and PNS Parasympathetic Nervous System. Discharge from the branches of the ANS alter a variety of physiologic functions, which intern, forms various feedback and forward loops. The network of feedback and discharge ensure that blood flow will be delivered to the active tissue and metabolic waste products will be removed.
Autonomic Nervous System (ANS)

- PNS (vagus nerve) releases ACh: controls resting metabolism, slows heart rate (HR), pupil constriction, facial expression, tear stimulation, increases saliva secretion.

- SNS (adrenal medulla) releases catecholamines EPI, NOREPI: Increases HR and contractility, Bronchiole dilation, vasoconstriction, thermoregulation.

- HRV is a non-invasive tool used to assess autonomic modulation of the Heart Period. It is described as variations in consecutive R-R intervals around its mean value. Reflects spontaneous oscillation of the heart period.

- Fluctuation of Heart Rate and Period are related to Three main Physiological factors:
  - Blood pressure control.
    - Related to Vagal mediated Baroreflex modulation of SNS efferent outflow.
      - SA node Na⁺ permeability decreases the pre-ejection period to increase HR to increase blood pressure (BP)
    - Respiration or Respiratory Sinus Arrhythmia (RSA)
      - Heart rate is synchronized with Ventilation. Vagal activity is stimulated during expiration and inhibited with inspiration.
  - Variable frequency oscillation due to thermal regulation.
    - SNS innervates sweat glands.
      - Skin conductance varies with level of perspiration (GSR Galvonic skin response).
Methods for Assessing HRV

• Pre-Ejection Period (PEP) a measure of time between the onset of left ventricular systole, and the onset of left ventricular contraction.
  – Reflects SNS β-adrenergic influence on myocardium contractility.
  – Norepinephrine binds to β-adrenergic receptors leading to a rise in cAMP, which then increases the duration of Na+ inward diffusion into the pacemaker cells in the SA node.
  – Elevations in cAMP also increases glycolytic flux.

• RSA magnitude is the difference in time between two consecutive R-R intervals. Reflects PNS Vagal influence on SA node action potential production rate.
  – Vagus nerve releases ACh, which binds to muscarinic receptors opening separate K+ channels decreasing membrane potential, and thus, action potential production rate.

• Linear methods use fast Fourier transformation of frequency and time domains to decompose Efferent Impulses to the SA node. ECG records the heart rhythm, time and frequency information is extracted.
  – Frequency Domain (Decomposition of the heart rate signal to the SA node)
  – Time domain (R-R)

• Three primary wave bands:
  – (HF) High frequency >0.15 Hz Vagal mediated respiratory (RSA) influence on the Heart Period.
  – (LF) Low frequency 0.04 -0.15 Hz Regarded as a marker of arterial BP control, having both PNS and SNS influence.
  – (VLF) Very Low Frequency <0.04 Hz Peripheral Vasomotor regulation

Vagal (RSA) Vagus nerve releases ACh, which binds to muscarinic receptors opening separate K⁺ channels slowing inward Na⁺

Adrenergic (PEP, LVET) Adrenal medulla releases Norepinephrine which binds to β-adrenergic receptors leading to a rise in cAMP increasing the duration of Na⁺ inward diffusion

1. Chronotropy: HR
   - SA node
     - Predominately PNS
   - (LVET) Left ventricle ejection time. Used as an index of SNS Chronotropic effects. Time it takes the LV to eject blood which corresponds to the opening and closing of the aortic valve.

2. Inotropy: Contractility
   - AV node
     - Minimal PNS influence under resting conditions
     - As SNS activity becomes greater vagal influence may decrease contractility substantially
   - (PEP) Pre-ejection period. An index of SNS Inotropic AND Dromotropic effects. ms of time between the onset of ventricular depolarization and the completion of LV blood ejection.

3. Dromotropy: Impulse Conduction Speed
   - AV junction
     - Increases with SNS stimulation
     - Decreases with PNS stimulation
     - Using animal models, Simultaneous maximal activation of both SNS and PNS outflow resulted in an almost zero net effect (Levy et. al 1996).
12 Lead Electrocardiogram (ECG)

Recording of electrical impulses generated within the sinoatrial (SA) node. This current is transferred from the skin to the electrodes. Depolarization travels from the SA node of the **Right** atria through the atrioventricular (AV) node. Here the impulse is delayed for about 0.1s, depending on ANS balance within this structure (Inotrophy/Contractility). Then relayed through the left and right bundle branches. Impulses finally reach the Purkinje fibers causing the Ventricles to contract.

**AP Impulse Conduction Sequence**

1. SA node
2. AV node
3. Left and Right Bundle Branches
4. Purkinje Fibers
5. Myocardium
6. Ventricles Contract

- **P Wave:** Atrial Depolarization
- **QRS Complex:** Ventricular depolarization
- **T Wave:** Ventricular repolarization

Fick Equation

Relationship between Cardiovascular function and Metabolism

\[
\text{VO}_2 = Q \times (HR \times SV) \times (a-v)\text{O}_2 \text{ diff}
\]

Rate of diffusion is higher when there is a large surface area.

Partial Pressure “driving force” is elevated.

Increases with Exercise Intensity
Resting Value ~5.6 vol % (ml O\(_2\) x 100 ml\(^{-1}\))
Max exercise ~ 16 vol %

Mitochondrial adaptation, increased capillary density, increased hemoglobin and myoglobin concentrations. Mitochondrial sensitivity is related to overall mitochondrial mass. Increased sensitivity to ADP activates oxidative phosphorylation at higher cellular energy charge. A higher cellular energy charge decreases the formation of metabolites that increase glycolytic flux. Higher glycolytic activity favors the conversion of pyruvate to lactate. This leads to an increased ADP/ATP and NADH/NAD\(^+\) (redox) charge, further increasing glycolytic rate. Dissociated H\(^+\) decreases muscle pH which ultimately inhibits mitochondrial respiration. Ventilatory threshold is reached once lactate formation exceeds removal.

Overall, there is only a slight increase in the (a-v)O₂ difference with training. This is because the adaptations that result from endurance training increase the oxidative phosphorylation rate and diffusion area. Increases to blood and plasma volume that follow with endurance training buffers significant increases to oxygen extraction.

EDV drops as ventricular filling time decreases. As HR increases toward maximum diastolic filling decreases. SV may increase as a result of Contractility, increased venous return or decreased after-load. Metabolic byproducts (H⁺, CO₂, ↓PO₂, and increased muscle temperature) increase vasodilatation in the active tissue thereby decreasing total peripheral resistance. Vasodilatation of the muscle increases capillary blood flow as SBP increases proportionately with exercise intensity. SNS discharge is regionally differentiated such that blood flow is redistributed to the source of greatest metabolic need. Initially SNS discharge to the skin causes vasoconstriction, decreases skin blood flow. However, as core temperature increases beyond threshold, vasodilatation of the skin increases Blood to the skin promoting heat exchange. Blood pressure increases capillary hydrostatic pressure, as metabolites accumulate intramuscular osmotic pressure increases thereby increasing capillary muscle diffusion.

Control Blood Acidity

Respiratory Center (hypothalamus)

Respiratory Period

Tidal Volume

Medullary Inspiratory Center

Medullary Expiratory Center

Apneustic Center (Pons)

Pneumotaxic Center (Pons)

Inspiratory-Expiratory Neurons are Reciprocally innervated

Medullary neurons Spontaneously generate AP’s

INCREASED phrenic (Lung) & intercostal nerve activity

INCREASED inspiratory muscle contraction strength

Control Blood Acidity

INCREASED phrenic (Lung) & intercostal nerve activity

INCREASED inspiratory muscle contraction strength

Ventral Medulla sensitive to H+ Concentration

Sensitive to Inc. Temp

Humoral (Chemical) input

Sensitve to Inc. Temp

Hypothalamus

Cerebellum

(Feed-Back) muscle contraction afferents

(Feed-Forward) Matches Ventilation with work rate.

Provides facilitatory input

General CNS arousal

Reticular Formation

Central Command Motor Cortex (Voluntary Breathing Control)

Central Command

Motor Cortex

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Exercise

Carotid Sinus & Glossopharyngeal nerves

Chemoreceptor

Aortic Bodies

Stimulated by decreased PaO2

Increased PaCO2

Decreased pH

Sensitive to PaO2, PaCO2, and pH

Vagus Nerve

Non Steady-State Exercise

PaO2 Fluctuates with arterial pulse wave

Decreased Arterial pH

The Motor Cortex may cause the Respiratory Center to be more sensitive to Input.

Ventilation Peripheral Input

Respiratory Center

Inhibits Inspiration

Increase Hr to Increase BP

Cardiovascular Response

Muscle Contraction

K+, dec. pH

III: Stretch-Deformation

IV: Chemical

Group III and IV nerve fibers

Muscle Metaboreceptors

Peripheral Mechanoreceptors (Chest-Lung)

Chest Expansion

Steady-State Exercise

PaO2 and PaCO2 are well maintained during steady-state exercise.

Cardiovascular Control Center (CVC)

- Blood O₂ and CO₂
- Central Command Cerebral Cortex
- Low PO₂
- Chemoreceptors
- Hypothalamus
- Baroreceptors
- Peripheral Afferents

TPR

Cardiac Output

Cerebral cortex
(Central Command)

Stimulates Cardioinhibitory Center of the Medulla

Decreases Vagal Outflow

Promotes SNS/PNS balance

Cardiovascular Control Center (CVC)

Myocardium contraction
Strength

Increased HR

Vasoconstriction

AP Conduction Velocity

Motor Unit Recruitment

Ventilatory Control

Na⁺/K⁺

Myocardial Ca²⁺
cAMP

Cardiovascular Control Center
Vasomotor Center (CVC) Medulla

Pressor Area
- Vasoconstriction
- Increases BP

Depressor Area
- Inhibits Vasoconstriction
- HR and BP decrease

Cardioacceleration center
- Activated by stimulation of the Pressor Area
- HR increases

Cardioinhibitory area
- Vagal discharge
- Decreases HR and Contractility

Cardiovascular Control Center (CVC)

Central Command
Cerebral Cortex

Peripheral Afferents

Chemoreceptors

Hypothalamus

Baroreceptors

Temperature Regulation

Dec. BP

Impulse rate to the CVC is Dec.

Inc. BP

Impulse rate to the CVC is Inc.

CVC increases SNS discharge to the skin

Vasodilation of the skin vessels

Impulse rate to the CVC is Inc.

CVC inc. BP

CVC dec. BP

CVC inc.

BP

Dec.

BP

Inc.

BP

Cardiovascular Control Center (CVC)

Baroreceptors

Central Command Cerebral Cortex

Peripheral Afferents

Muscle Contraction and Stretch

Metabolic Status

Impulses to CNS

Baroreceptors

Hypothalamus

Intense Exercise

Increases HR

Increases Contractility

Increases BP

Vasoconstriction

Chemoreceptors

Aortic Arch Carotid Bodies

↓PO₂, ↓pH, ↑PCO₂

Efferent Impulses to Pressor Area CVC

Increases vasoconstriction

Increases BP

**Total Peripheral Resistance**: Circulatory Resistance to blood flow. During exercise the CNS and CVC modulate ANS discharge to maintain Mean Arterial Pressure (MAP). Respiratory Sinus arrhythmia is the synchronization of heart rate with ventilation to maximize Gas Exchange. Baroreceptors relay set-point deviations to the CVC and modify Heart period within 1-6 Beats. Linear models of HR dynamics suggest that SNS discharge is dominant if not exclusive during exercise. However, RSA modifies Heart Period instantly by increasing the refractory period of the Heart. This then increases Ventricular filling, increasing PreLoad (Frank Starling), and subsequent Stroke Volume. Cardiac Output is increased, and depending on the sympathetic background, temperature, and metabolic vasodilation, Mean Arterial Pressure will be Maintained or raised. This will activate the Baroreceptors in a reverse fashion, decreasing SNS tonic discharge and decreasing Vagal inhibition. Accentuated antagonism has not been conclusively demonstrated in humans; However, this theory argues that Vagal influence is more potent in the presence of greater sympathetic background. Therefore, regardless of the ladder assumption, it can be contested that RSA and Vagal Discharge serve a substantial role in maintaining MAP during exercise.

Respiratory Sinus Arrhythmia (RSA): HR is synchronized with Ventilation to promote gas exchange.

Inspiration: (High $O_2$)

- 1. RA
- 2. RV
- 3. Lungs

Expiration: (Low $O_2$)

- 4. LA
- 5. LV

Heart rate increases when $O_2$ is high

Heart rate decreases when $O_2$ is low

Atropine is an ACH blocker that acts to block Vagal discharge.

Vagal discharge increases stroke volume by increasing the HR refractory period thus increasing Ventricular filling. Changes in Mean Arterial Pressure are buffered by increased SV.

Also, SV is lower at higher heart rates (filling-time).

Mean arterial pressure is significantly lower in non-treatment state. Highlights the cardiovascular dangers of increased SNS background.

Respiratory frequency decreases HR by increasing SV. Increased SV decreases tonic SNS discharge (Baroreceptors). As SNS discharge is slowed contractility decreases, which causes BP to drop and Increase SNS discharge to increase HR. (Feedback loop)

Cardiac Output is much higher with out Vagal influence. This is because HR is much higher, and fluctuates very little in period.
Pulmonary Ventilation increases with O$_2$ Consumption linearly until 50-60% VO$_2$.

Ex. Intensity

Pulmonary Minute Ventilation

- Tidal Volume
  - Increases
  - Plateaus: steady-state

- Frequency
  - Breathing Frequency Increases

- Peak Expiratory Flow rate is higher than Peak Inspiratory Flow rate
  - Inspiration

- SNS Contractility to Maintain MAP
  - Ca$^{++}$, Na$^+$/K$^+$
  - Tonic Vagal Discharge Decreases

- Net Inhibition of Vagal Discharge is Decreased

- Tidal Volume
  - HR Refractory Period

- Expiratory Time
  - Ventricular Filling

- Inspiratory Time
  - Stroke Volume

- Decrease Frequency

Conscious, Temporarily Voluntary...

- SV Maintains or Increases MAP

What Is the Exercise Intensity?

Cardiac Excitability

Motor Cortex Stimulation of Inspiratory Center

Central Command CVC Discharge

Regulation of SNS and PNS Discharge to maintain SBP

Gas Exchange

Bicarbonate Buffering

HCO$_3^-$

H$^+$

PCO$_2$

H$^+$

P$_i$

Temp

Metabolic Vasodilatation

SNS Vasoconstriction

Autoregulation Stretch-Contract

Central Command Baroreceptors Chemoreceptors Mechanoreceptors Hypothalamus

SA Node

ACH

K$^+$/Na$^+$

Cl$^-$

AV node

Ca$^+$

Increased HR Refractory Period

Venous Return

Frank Starling

Increased EDV

Increased SV

Cardiac Output

Baroreceptor Efferent Impulse Discharge rate

SNS Tonic discharge

Catecholamine Spill

Adenylate Cyclase / cAMP

Oxidative Phosphorylation

Exercise Intensity Muscle Mass Involved

Adenosine Charge

Glycolytic Flux

Central and Peripheral Input

Ventilation

Increased HR

Increased tidal volume

Respiratory Period

Inspiration Expiration
SBP Increases in Direct Proportion with $O_2$ Consumption

Does $O_2$ Consumption increase linearly with a 20 Watt/Step increase in Work load?

Motor Cortex relays increased recruitment of muscle mass and firing-rate

Metabolic status: Adenylate Charge drives Glycolytic flux and Oxidative Phosphorylation

Catecholamine Spill and (NO), $H^+$, $P_i$, $PCO_2$, Temp

Metabolic Vasodilation SNS Vasoconstriction

CVC/Respiratory Center Medulla Increase HR, Contractility, and TPR

Perceived Threat/RPE

Ventilatory Compensation

$O_2$ Gradient

BP and Hydrostatic Pressure in Capillary Beds

Baroreceptor Discharge Rate

$V_t$, $V_E$, Br / M MVV $T_i$ / $T_R$

Exercise Intensity

Untrained

Trained
Increased Preload can decrease PEP without SNS influence.
- Ventricular filling pre-stretches the myocardium, reflexively increasing myocardial contraction strength (Frank-Starling mechanism). Only active when there is a change to End Diastolic Volume EDV.

Increased Afterload increases PEP.
- Afterload increases the amount of time necessary for pressure to build-up within the ventricle needed to overcome aortic pressure. Therefore, peripheral resistance may increase PEP duration without β-adrenergic stimulation.

Increases in HR are accomplished by SNS drive and Inhibition Of Vagal discharge.
- During moderate to high-intensity exercise, regulatory feedback provided to the CVC (cardiovascular control center) causing inhibition of the cardioinhibitory area of the medulla.

A net reduction in Vagal discharge promotes the SNS balance within various structures of the heart.
- Tonic PNS and SNS Discharge rates influence SA node, AV node and AV junction function.
SNS β-Adrenergic Discharge

Adrenal Medulla releases Norepinephrine

AV node Na⁺/K⁺ balance
- Increases inward Na⁺ diffusion
- Contractility (Inotropy)

AV junction Na⁺/K⁺ balance
- Increases inward Na⁺ diffusion
- AP Conduction Speed (Dromotropy)

PEP is decreased:
HR and Contractility are increased to elevate or maintain SBP.
PEP Pre-Ejection Period: (Systolic time interval) noninvasive measure of beta- adrenergic (SNS) influence on myocardium contractility. PEP ms of time between the onset of ventricular DP and the completion of LV blood ejection.

Q-wave: Onset of ventricular DP

Opening of the Aorta, Initial LV blood ejection

PEP: Measures the Electrical and Mechanical duration prior to Ejection

1. EMD Electromechanical Delay between the onset of DP and beginning of Ventricular contraction

2. LV contraction time prior to the opening of the Aortic Valve
LVET: Left Ventricular Ejection Time

- Aortic Valve Opens
- Blood is Pumped from the LV
- ms of Time
- Aortic Valve Closes
Supine-to-Standing

Pooling of blood in the Lower Extremity (LE)

Decreased Central Blood Volume and EDV

SV is decreased

Cardiac Output is Decreased

\[ \text{BP} = \text{Q} \times \text{TPR} \]

Baroreceptors (Aortic arch, Carotid sinus)

Responds to Intrinsic Set-point deviation

CVC Discharge

SNS + PNS

HR, Contractility, TPR

Inhibits Vagal discharge promoting tonic SNS influence

Increase BP

Water Immersion Not COLD

Water exerts Pressure on the body

Increased Central Blood Volume and EDV

SV is increased

Increased Cardiac Output

BP increases

Decreases Baroreceptor discharge to the CVC

PNS discharge promoted/less inhibited
Cardiac Performance

Heart Rate
- B-adrenergic
- Epinephrine
- Adenylate cyclase
- cAMP
- Na+/K+
- Ca++ Released By SR

Focus on Stroke Volume
- Inhibition of Cardioinhibitory area
- Vagal Discharge rates
- Promotes SNS Balance

Preload
- SNS α-adrenergic
- Norepinephrine
- Vasoconstriction
- Central Blood Volume
- Ventricular Blood Volume

Afterload (TPR)
- SNS α-adrenergic
- Vasoconstriction
- Increases ventricular pressure need to overcome Aortic Pressure
- Increases Ventricular filling Decreases Ejection Fraction

Contractility
- Increases force of contraction
- Increases Amount of blood that is ejected

Cardiac Performance

Increase HR and Contractility

Max intensities
- Decrease Ventricular Filling Time
Cardiac Performance: **Preload** (Frank-Starling)

- **Stretch-Contraction characteristics** Respond to Changes in EDV.

- **Myocardial Stretch**
- **End Diastolic Volume** EDV

- **Body Position**
- **Atrial Contractility**
- **Intrathoracic Pressure**
- **Skeletal Muscle Pump**
- **Total Blood Volume**
- **Intrapericardial Pressure**
- **Total Peripheral Resistance**

Cardiac Performance: Stroke Volume (SV)

Cardiac Output = Stroke Volume \times Heart Rate (HR)

Preload
- Actin-Myosin Overlap, Myocardial Elasticity

Heart Rate
- LV filling time

Contractility
- SNS discharge

Afterload
- TPR

Cellular Energy Charge:

- **Glycolytic Flux** increases metabolic byproducts, which then serve to activate oxidative pathways.

- Oxidative Pathways and FFA utilization are inhibited from maximal production at **HIGHER Exercise Intensities**.

- Toward Maximal exercise, **Ca**++ Released from the **SR** and Spilled into the blood stream will serve as a potent stimulator of **FAST Glycolysis** (PDH complex, Phosphorylase_{ACTIVE}) and Muscle Glycogenolysis

- Maximal Glycolytic rates favor the adenyl kinase reaction. The AMP formed will decrease the availability of ADP, and reduce the concentration necessary to stimulate Oxidative Phosphorylation to its maximal capacity.

ATP, O$_2$, and H$^+$ Balance in Muscle: ADP influences Oxidative Capacity.

Cr Kinase Reaction: ATP is ultimately Shuttled from where it is produced to where it will be consumed by passing high energy phosphates.

Intracellular Creatine Shuttle: Cellular energy charge (ATP/ADP) is coupled with the CK reaction.

Near Equilibrium Hypothesis (Partial)
Redox Potential

Increases Oxidative Rate

Hydrogen Shuttle

Pyruvate

NADH

PDH

LDH

Lactate + H⁺

NAD⁺

Pyruvate + NADH + H⁺ ↔ lactate + NAD⁺

ADP, Cr/PCr, Ca⁺⁺, NADH/NAD⁺ stimulate Oxidative Phosphorylation

**Slow Glycolysis:** NADH shuttles Hydrogen and $e^-$ to the Mitochondria for ROBIC Oxidation.

**Fast Glycolysis:** (Lactate-Pyruvate ratio $\geq 10:1$) NADH passes its Hydrogen ion to pyruvate, which is *reduced* to lactate. This conversion is directed by LDH, which *oxidizes* NADH so that G3P has NAD$^+$ to support Glycolytic flux.

Muscle Contraction

\[ \text{ATP} \rightarrow \text{ADP} + P_i \]

ADP increases

PCr Depletion

- PCr decreases
- Cr increases
- P_i increases

CK_M Dissociation

Rate of Oxidative Phosphorylation

Pyruvate Dehydrogenase (PDH): Controls Glycolytic Flux to the Krebs Cycle (Slow Glycolysis)  
NADH⁺ is a cofactor of Glyceraldehyde 3-Phosphate Dehydrogenase (G3P)

Sustainable Work rate

At Muscle level ATPases (High Int.)
- High Exercise Intensities
- High Glycolytic Flux
- Inhibitory By-products Accumulate
  - Fatigue precedes ATP Decline

Ability to maintain ATP supply (Low-Moderate Int.)
- Muscle Contraction
- Glycolysis
  - ADP = (ATP)(Cr)/(PCr)(H+)
  - PCr Drops Until ADP levels rise enough to activate mitochondrial respiration
  - Oxidative Phosphorylation balances ATP supply with demand
  - PCr Breakdown reaches steady-state

Inhibition of Oxidative Phosphorylation
- ATP supply vs. demand
  - Pyruvate production exceeds removal.
  - pH drops
  - Failure to reach Metabolic Steady-State
  - ADP Availability Declines
  - Sustainable Power Output lower than at Capacity

~33.3 % of Max Power 30 -120 minutes: Limitations to Sustainable Power Output

- Steady-state Ex.
  - ADP Steady-state is lower than oxidative capacity
  - ADP fails to activate Mitochondrial respiration maximally
  - Intracellular pH
    - Rate of PCr recovery is lower with declining pH
      - Limits ADP
        - Oxidative Rates
          - ADP Concentration

- PCr is reduced to ½ at Maximal Steady-State Exercise
  - High Glycolytic Flux
    - Pyruvate production vs. clearance
      - Lactate + H⁺
        - Intracellular pH

Max Power Output > SHORT duration 2-5 seconds > PCr availability > ATP ActoMyosin crossbridge Availability

80% > 30 minutes

PCr declines > pH declines > $P_i$ > $H^+$

Decreased ADP Stimulation of Oxidation, Competitive Inhibition

Force Production Declines

Substrate level phosphorylation

Glycolytic rate exceeds pyruvate clearance

Accumulation of Inhibitory By-Products

Oxidative Phosphorylation operates SLOWER than maximal

Oxidative Phosphorylation cannot meet ATP supply with Demand

$VO_2_{max}$

$PO_2$ Declines

Perfusion Pressure-$O_2$ Gradient

$O_2$ Availability e- acceptor

Sustainable Work rate

Ability to maintain ATP supply (Sustained Power Output)

Inhibition of Oxidative Phosphorylation

At Muscle level ATPases (High-Power Output)

Glycolytic Flux

Glycolysis

oxidative phosphorylation

PCr Recycling, Oxidation of Glycolytic Products

ADP Concentration

Pyruvate Production Exceeds Clearance

Inhibitory By-Products Accumulate

Metabolic Acidosis-Competitive inhibition

Glycolysis

Lactate

H^+

ADP

PCR

ATP

P_i

H^+

Fatigue precedes a decline in ATP supply

20 Watt Increase in Power Output.

PCr levels drop to Increase ATP/ADP

Creatine Kinase Equilibrium

PCr + ADP + H⁺ ↔ ATP + Cr

Creatine Kinase

ADP + PCr → ATP + CR + P_i

Adenylate Kinase

ADP + ADP → ATP + AMP

Metabolic Steady-State? (NO)

Oxidative Supply Fails to meet ATP Demand

Increased Glycolytic Flux

Pyruvate/Lactate Clearance

Adenylate Kinase

ADP levels drop

Oxidative Activation

H⁺ Reduces pH

Complex Conscious Breathing patterns

- Frequency
  - Br/Min
  - (F) x Tidal Volume

- Volume
  - Avg. Volume/Breath
  - Pulmonary Minute Volume

Ventilation

- CO₂ O₂ Exchange
  - Pressure Gradient/Surface area
  - Inhalation-Expiration
  - Diffusion Time

- Control blood acidity
  - CO₂ in body fluids
  - CO₂ + H₂O ⇄ H₂CO₃ ⇄ H⁺ + HCO₃⁻

Oral Communication

- Oral Communication
  - Decreased ADP availability
  - Mito-Respiration
  - Glycolytic Flux
  - ΔpH
  - Pulmonary minute volume
  - Stimulates Inspiratory Center
  - H⁺
Peak Lactate is Not HIGHER between controls and subjects with disorders. Exercise Intensity and duration have not shown significant differences in desaturation among populations. Patients with Mitochondrial dysfunction have demonstrated Low Maximal Contractile Force. This is probably because the level of dysfunction can vary WIDELY among genetically defined patients with mitochondrial myopathy.

As demonstrated previously, Oxidative Capacity is ultimately inhibited by the products of metabolism. However, because of the differences among mitochondrial myopathy populations, local muscle fatigue may occur before there is significant glycogen depletion in the muscle. Thus, using the 20 Watt Step Protocol, where the onset of fatigue typically occurs within 15 minutes, substrate availability allows various populations to be able to complete the testing procedure.

Hormone Response 50-60% VO$_2$ Max

Catecholamine Release

**Epinephrine 80%**

A. α Adrenergic receptors
   1. Smooth Muscle Vasoconstriction

B. β Adrenergic receptors
   β$_1$ Heart function
   1. Activation of Adenylate cyclase
      a. Myocardial permeability to Na$^+$/ K$^+$
      b. Ca$^{++}$ Released from the SR
      c. Decreased Refractory period decreases Ca$^{++}$ resequestration time

β$_2$ Tissue metabolism

1. Muscle and Liver Glycogenolysis
2. FFA mobilization
3. Activation of adenylate cyclase in the active tissue
   Favors MyoKinase Reaction (ADP + ADP = AMP + ADP)
   Adenylate Charge: Drives Glycolytic Flux and Mito Respiration
      a. Increases TPR to balance muscle blood flow and pressure with metabolic induced Vasodilation.

**Norepinephrine 20%** Spill over results in 4-5:1 of circulating Norepinephrine

A. α-adrenergic receptors (mainly)
   1. Smooth Muscle Vasoconstriction: Increase TPR to increase Muscle bloodflow/Pressure to the active tissue. Balances Metabolic Vasodilation with Increased driving force.

**Cortisol:** Declining blood glucose levels, physical or emotional stress Stimulate the hypothalamus to release corticotropin-releasing factor (CRF) which then causes the anterior pituitary to secrete adrenocorticotropic (ACTH). The adrenal cortex then releases cortisol into the systemic circulation.

1. **Stimulates amino acid release from muscle (proteolysis)**
2. **Increases FFA mobilization from adipocytes**
3. **Increases hepatic gluconeogenesis**
4. **Provides negative regulatory feedback on its own secretion.**
5. **Influences glucose and glycogen replacement after exercise.**
   -ACTH stimulates adenylate cyclase activity in adrenocortical cells which causes the formation of cAMP.
Implications:

The ultimate goal of the cardiovascular system is to maintain BP so that the Brain is supplied with a continuous source of blood glucose. Numerous feedback sites: Baroreceptors, Chemoreceptors, Hypothalamus, Muscle efferents and Central Command send efferent impulses to the CNS and CVC where ANS discharge is balanced.

Maintaining blood flow to the brain requires close monitoring of Blood pressure via the aortic arch and carotid sinus. Deviations to the baroreceptor intrinsic set-point alter efferent impulse rates to the CVC causing Increased Sympathetic discharge and inhibition the cardioinhibitory area. Subsequently, tonic Vagal discharge is decreased. The Net result is increased heart rate and contractility in order to maintain BP.

RSA magnitude is the difference in time between consecutive R-R waves. Vagal discharge is either promoted (Expiration) or inhibited (Inspiration) during ventilation. Therefore, changes in breathing patterns resulting in differences in tidal volume may increase the refractory period of the heart (Depending on exercise intensity and necessary SNS tone). Increasing the refractory period of the heart increases ventricular filling, which may result in an increased EDV and SV. Increases to stroke volume then may result in greater cardiac output (depending on afterload:TPR) which will Increase BP and activate the baroreflex mechanism in a reverse fashion decreasing SNS discharge.

HRV research looks at beat-to-beat changes in HR. Specifically; we are investigating PEP, LVET and RSA under different stressors to determine ANS influence on each heart period. HRV is associated with greater recovery from exercise and reduced risk of all cause mortality and cardiac arrhythmias. Therefore, instead of simply looking at someone’s fitness in terms of a quantitative assessment such as VO$_2$ Max we are looking at someone in terms of how his or her ANS adapted, or failed to adapt, to a specific stimuli (Cardiovascular, Strength, Stroop, etc.) Further, graded maximal exercise tests are a relative experience and can be as difficult as an individual is able to endure before either their brain or body circum to the weighing pressures of central and peripheral feedback. Cycle ergometer tests, within healthy subjects, the major limiting factor is muscle acidosis leading to competitive inhibition within the crossbridge cycle causing the subject to reduce power output and fall below 60 RPM’s.
However, because each test is “relative,” individual subjects will have a different perceived threat for each exercise intensity. Ventilatory compensation will occur when the Motor Cortex relays increases in muscle mass recruitment. Ventilation is largely under involuntary control, and increased movement, or cycle resistance, is sensed by the motor cortex serving as a feedforward mechanism to stimulate the Inspiratory area of the Respiratory Center. (Ventilation rates tend to be higher in untrained vs. trained subjects). Thus, a disproportionate compensatory rise in Ventilation can be expected for subjects with a higher perceived threat (200W). This results in Hyperventilation (Increased $\text{PaCO}_2$) and will likely change the pH within the Cerebral Spinal Fluid causing an additive stimulus for Inspiration. Further, Hyperventilation will cause the Subjects’ SBP to drop, decreasing perfusion pressure within the capillary beds, thus, reducing gas exchange and $\text{H}^+$ buffering. In addition, the drop in SBP will activate the baroreflex mechanism and increase SNS discharge. SNS discharge will result in greater circulating catecholamine levels and influence cellular metabolism. Mitochondria and resulting Oxidative phosphorylation are sensitive to ADP concentrations and the Adenosine charge. (ATP/ADP AMP and $\text{P}_i$) As a result, the higher conversion of ADP to AMP decreases the available ADP needed to stimulate Oxidative phosphorylation maximally.

The subject’s ability to control glycolytic flux will determine the level of hormonal drive to support ATP utilization, uptake, and transport. However, this will also result in greater SNS influence on contractility. As the heart begins to beat more rapidly PEP (pre-ejection period) is shortened and there is less ventricular filling. The myocardium must then contract more forcefully to eject the same stroke volume. Further, as peripheral resistance increases, ventricular pressure must also increase in order to overcome the increased afterload. The above factors result in a challenge to cardiac output and will increase SNS discharge.
Stair tests can be more difficult than you may think...

MET is the resting metabolic rate, which can be expressed in terms of $O_2$ consumption.

$1 \text{ MET} = 3.5 \text{ ml } O_2/\text{kg/min}$ and is a caloric constant of $1 \text{ Kcal/kg/hr}$

Walking up stairs $\sim 8 \text{ METS}$

$8 \text{ METs} \times 3.5 = 28 \text{ ml } O_2/\text{kg/min}$

Average $VO_2 \text{ max}$ for ages 20-29
  female $= 36-40 \text{ ml/kg/min}$  7-77.7% $VO_2 \text{ max}$  
  male $= 40-49 \text{ ml/kg/min}$  57-70% $VO_2 \text{ max}$

145 lbs female
  $150 \text{ W} = 1840-2200 \text{ ml of } O_2/\text{min} \sim 27.9 - 33.4 \text{ ml/kg/min}$
  $200 \text{ W} = 2420-2770 \text{ ml of } O_2/\text{min} \sim 36 - 42 \text{ ml/kg/min}$
Therefore, it is clear that stairs may represent a significant challenge to average healthy adults.

Consider, the time of activity <30 seconds ATP is supplied through the ATP-PCr and fast glycolytic pathways.

Walking up the stairs you are storing potential energy. \( \Sigma F = ma \)

Overcoming gravitational force not only challenges your legs ability to produce force, it also increases resistance to blood flow.

Therefore, we have large muscle group multi-joint movement increasing blood flow to the active tissue in the lower extremity combined with an increase gravitational resistance to venous return. The result is pre-load and SV are decreased. Disruption of the baroreceptor set-point will inhibit vagal outflow and promote SNS discharge balance in order to increase peripheral resistance and myocardium contractility. Thus the ANS is promoting SNS discharge (as seen with a negative PEP inflection) such that more of the ESV volume can be ejected to maintain BP.

Lactate appearance increases at \(~ 40-50\% \text{ VO}_2\text{ max.} \) However, this lactate is cleared by oxidative fibers, the heart, mitochondria, and the liver (Cori cycle).

Blood lactate levels increase in a non-linear fashion after 60 % \text{ VO}_2\text{ max.}

Mitochondrial disorders are marked by increased lactate and \( P_1 \) accumulation. As exercise intensity increases beyond 40% \text{ VO}_2\text{ max} there may be significant lactate accumulation. This can lead to competitive inhibition within the acto-myosin crossbridge cycle and more importantly metabolic byproducts ultimately accelerate their own production. Or rather that there output will be sustained.

In fact, some mitochondrial myopathy populations will have a higher blood lactate concentration during rest. Further, elevated lactate accumulation and associated \( H^+ \) lead to increased formation of \( P_1 \), which contributes to a greater activation of fast (nonrobic) glycolysis. Therefore, during maximal exercise someone with mitochondrial disorder has an accelerated fast glycolytic rate paired with a decreased ability to clear pyruvate. Metabolic byproducts increase vasodilatation, which will ultimately stimulate the baroreceptors to alter ANS discharge.

It is important to understand that ANS balance is on a beat-to-beat basis and the baroreceptors influence HR within 1-6 beats. RSA is the synchronization of HR with ventilation and therefore influences HR instantly.

In conclusion, individual differences during exercises exists and it is essential to recognize the signs of exercise intolerance. Exercise is not necessarily something that EVERYONE should “Push Through.”