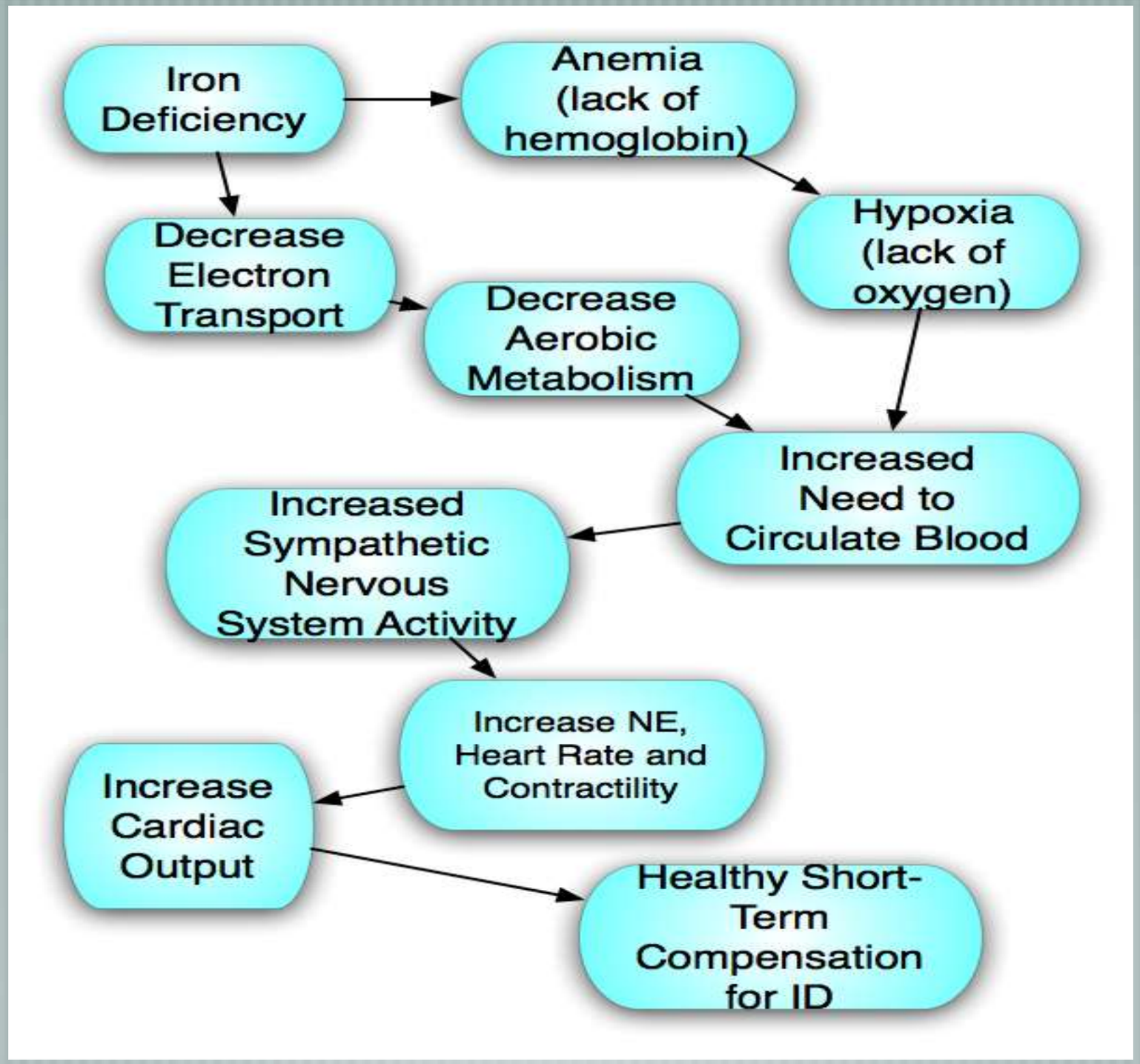
Positive Cardiac Adaptations to Iron Deficiency May be Reversible

Alix Boynton, Kelsey Dockter, Mario Arcadia, Adam Grasmick, Shayla Slaugh, Sami Wegner

Faculty Mentor: Bud Chew

Iron Deficiency (ID)



Healthy Consequences of ID

- Normally
  - Sympathetic Nervous System (SNS)
    - Short term stress; “fight or flight”
      - Norepinephrine (NE) released
  - Parasympathetic Nervous System (PNS)
    - Rest and repose
    - Conserve and replenish energy
- Iron Deficient
  - Chronic SNS activation
  - Constant NE release into bloodstream
  - Cardiac Hypertrophy

Working Hypothesis

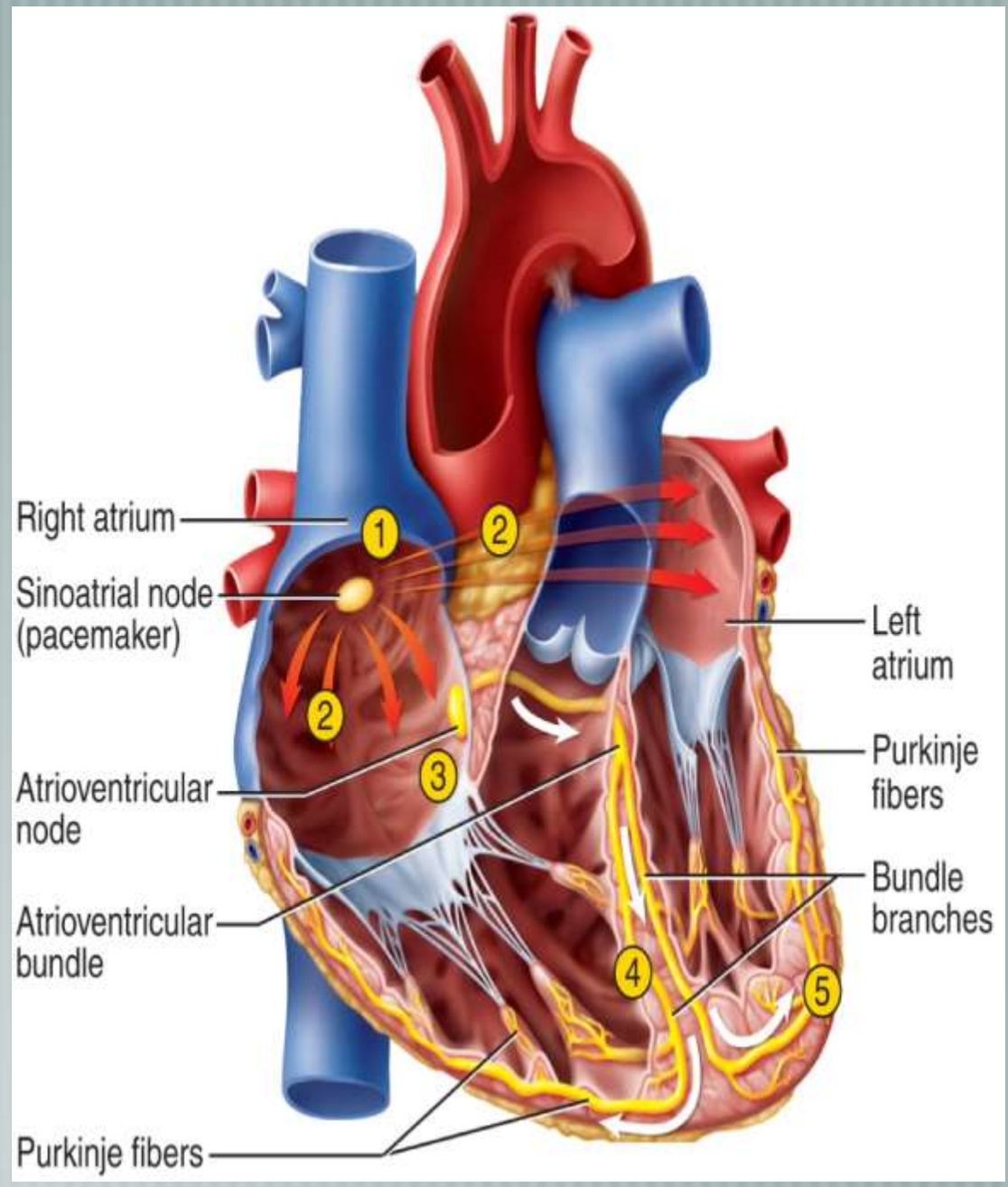
- Adaptive Hypertrophy
  - Initial adaptations to ID
    - Compensate for hypoxia
      - Increased contractility
- Pathological Hypertrophy
  - Chronic SNS activity depletes body’s resources
  - Decreased contractility
  - Indicates transition to pathological state

Physiological Adaptation Eventually Transitions to Pathology

- 2 Weeks of 
  - Anemia
  - Cardiac hypertrophy
  - Increased contractility
  - Increased LVP
- 4 Weeks of ID:
  - Severe anemia
  - Cardiac hypertrophy exacerbated
  - Decreased contractility
  - Decreased

Testing Heart Functionality

- Langendorff isolated heart perfusion
  - Allows heart to be tested outside the body
  - No SNS interference
- Autorhythmicity of the heart



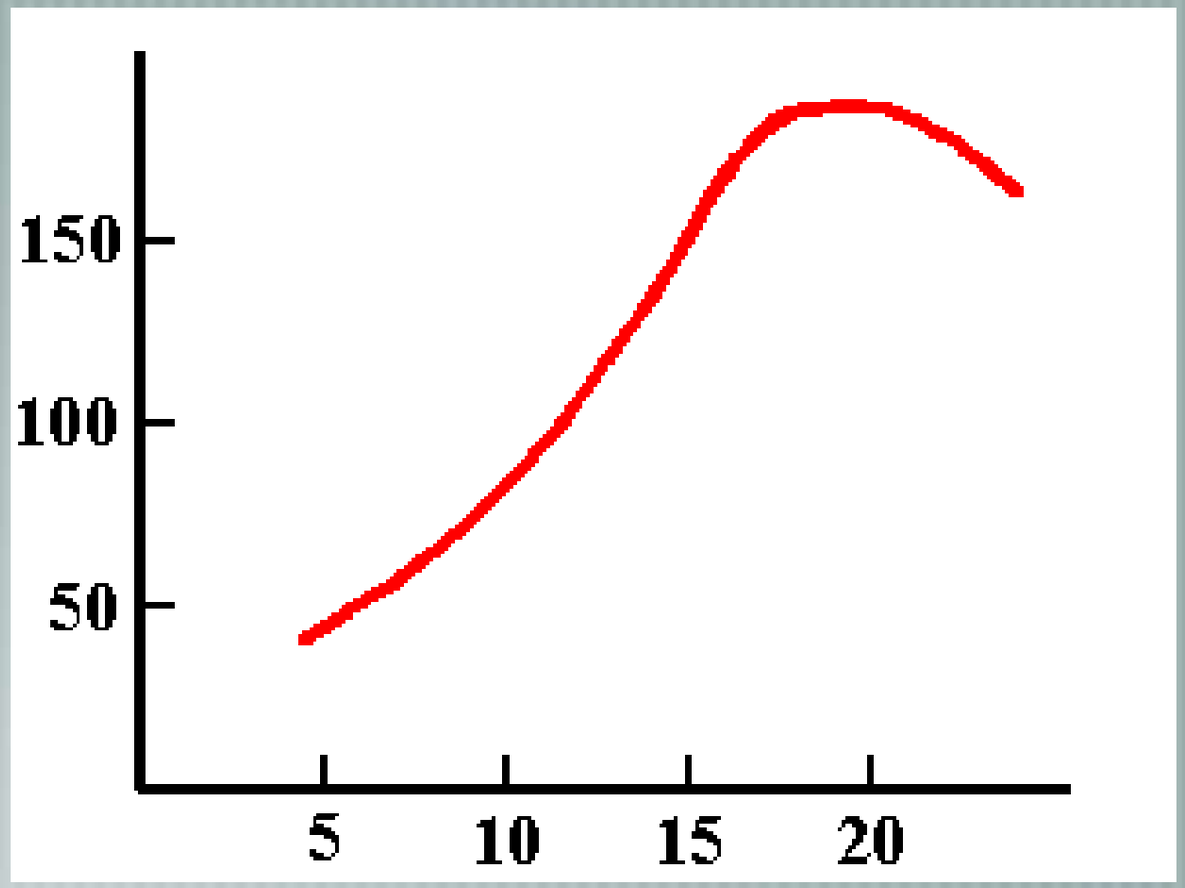
Methods

- Langendorff isolated heart perfusion
  - Heart excised from rat
  - Cannula inserted into aorta
  - Balloon catheter placed into left ventricle through left atrium
  - Range of perfusate flows
    - “Lang” solution mimics blood
    - Heart functionality data

QuickTime™ and a decompressor are needed to see this picture.

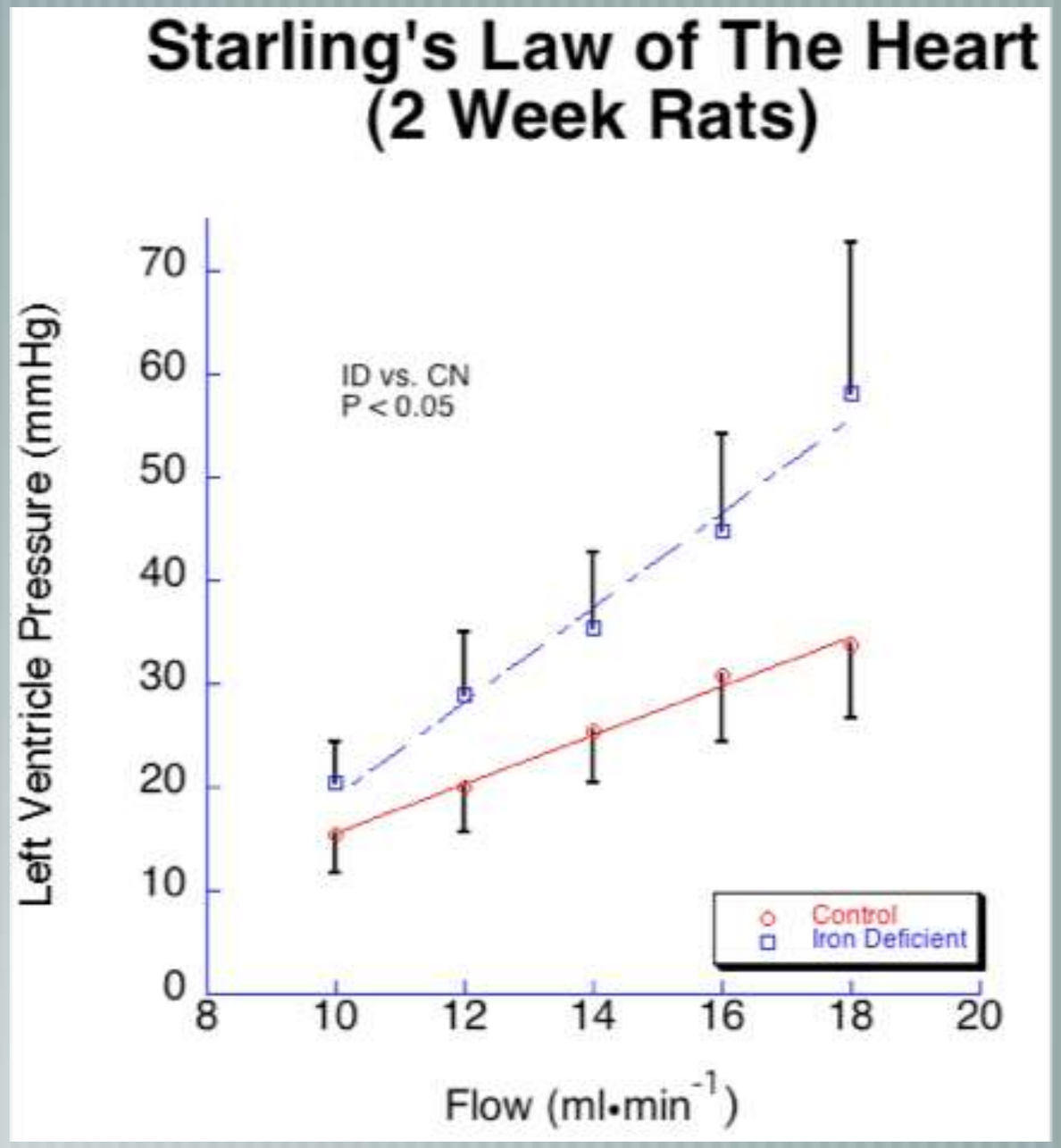
Frank-Starling's Law of the Heart

- As flow increases:
  - Muscle fibers stretch
    - Contractile force increases
- At extreme flows:
  - Fibers stretch too far
  - Contractile force drops off
- A range of flows
  - Generate Starling's Curves
  - Good indication of heart functionality



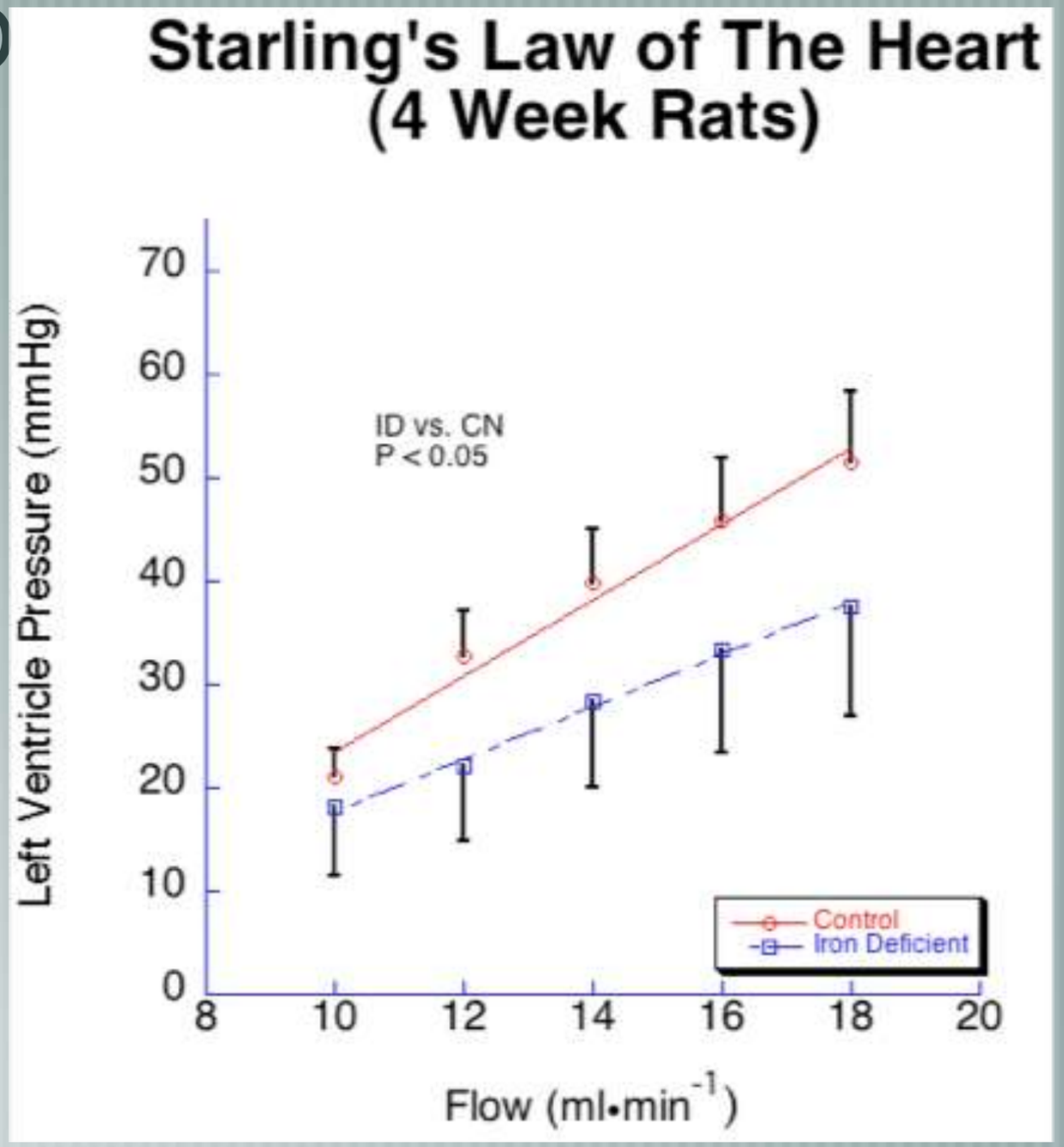
Previous Data

- After 2 weeks ID:
  - Anemia
  - Cardiac Hypertrophy
  - Increased left ventricular pressure (LVP)
  - Positive Adaptation



Previous Data

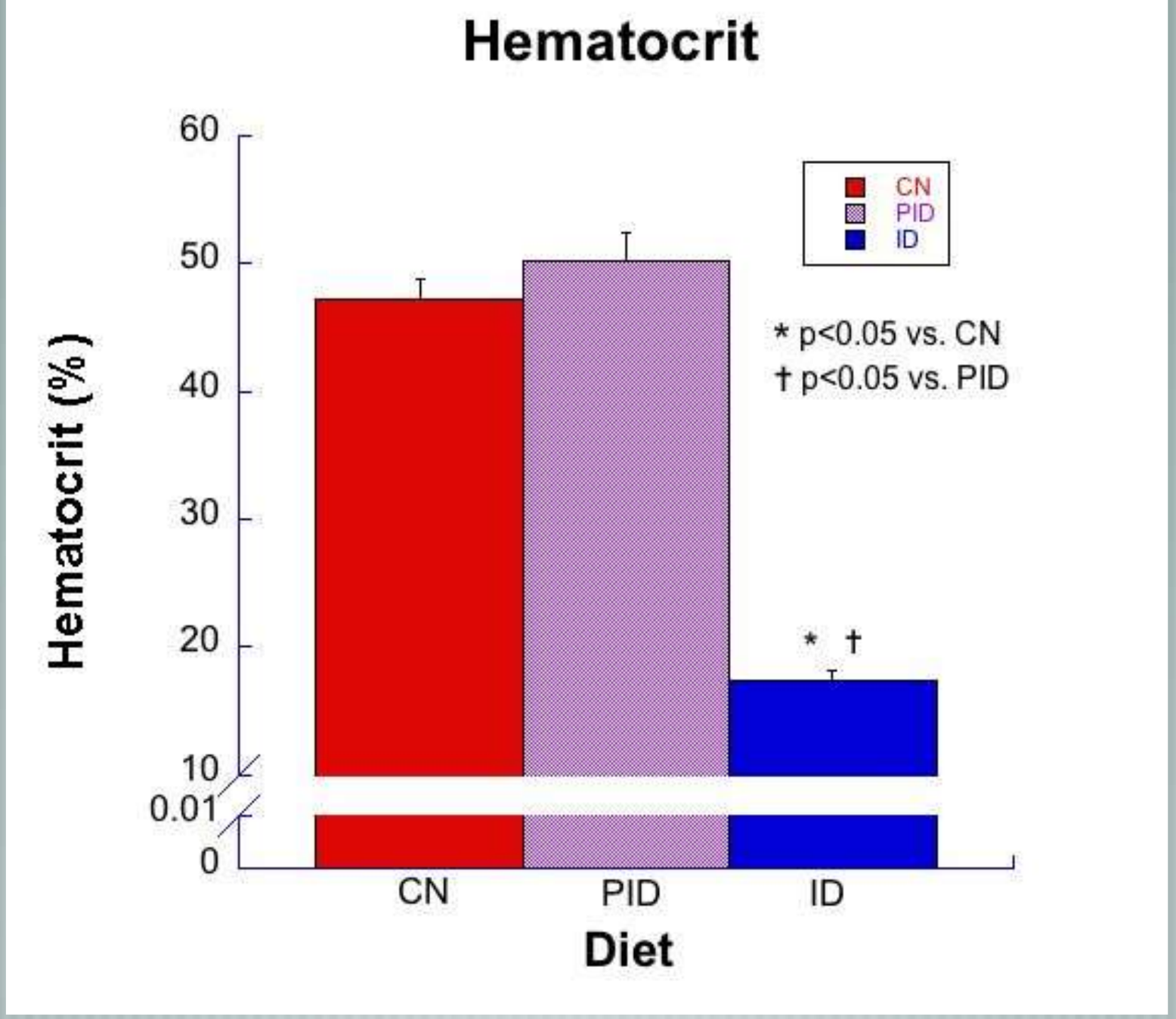
- After 4 weeks of ID
  - Severe Anemia
  - Cardiac Hypertrophy Exacerbated
  - Decreased LVP
  - Negative Adaptation



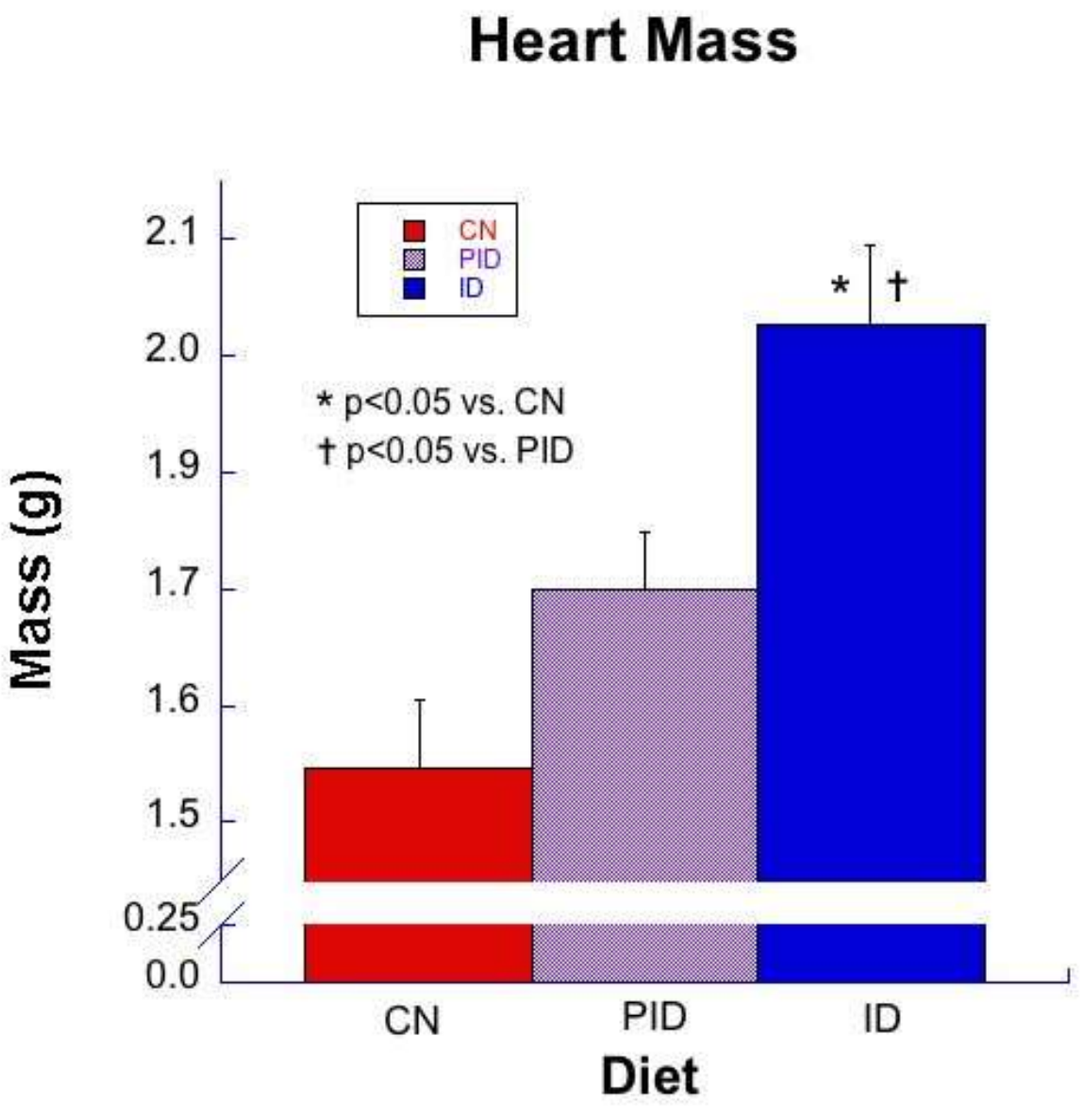
Current Hypotheses

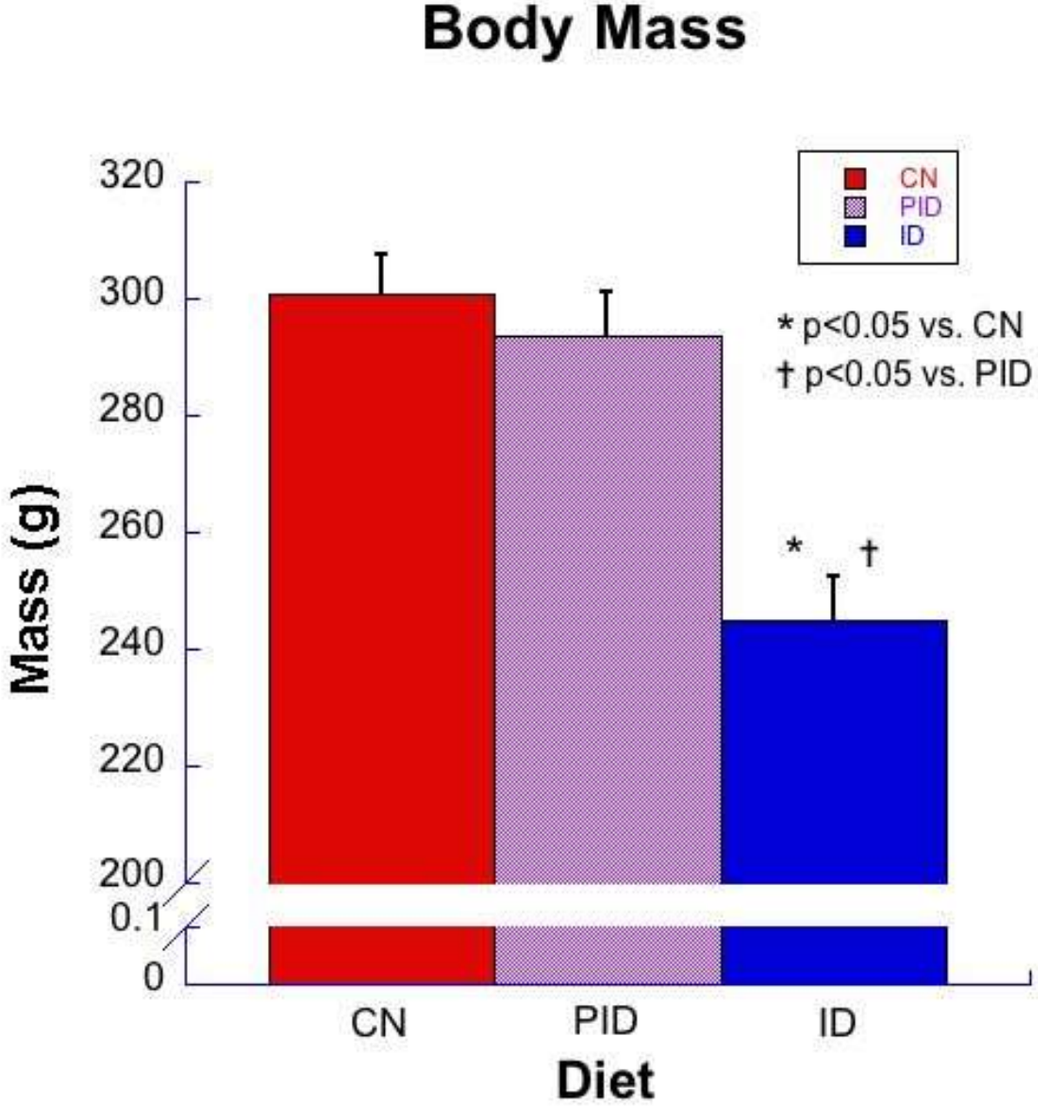
- Partial ID diet (PID)
  - 2 weeks ID, then 2 weeks control (CN) diet
  - LVP similar to CN
  - Morphology similar to CN

Hematocrit Establishes Anemia

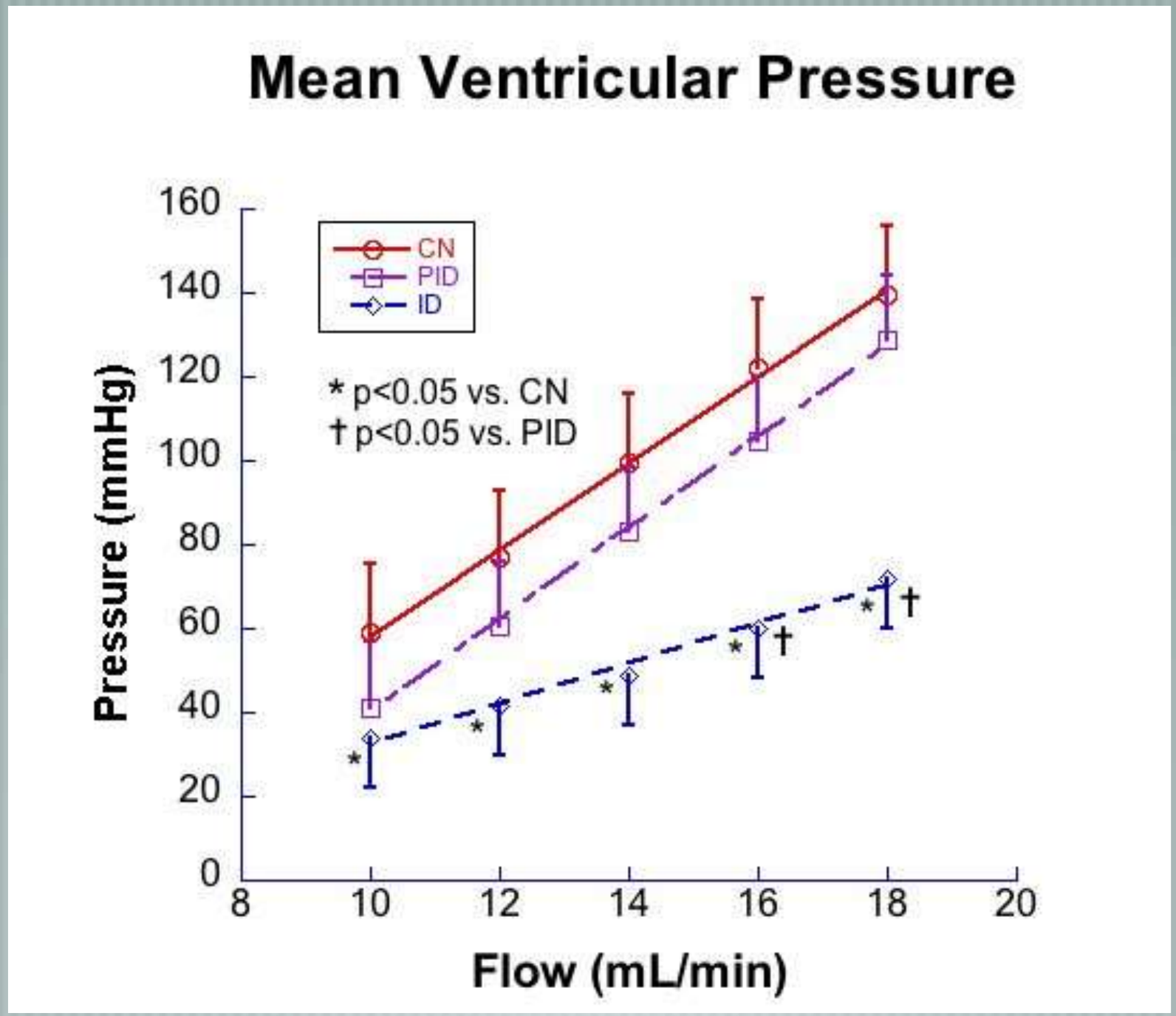


Heart Mass Establishes Hypertrophy

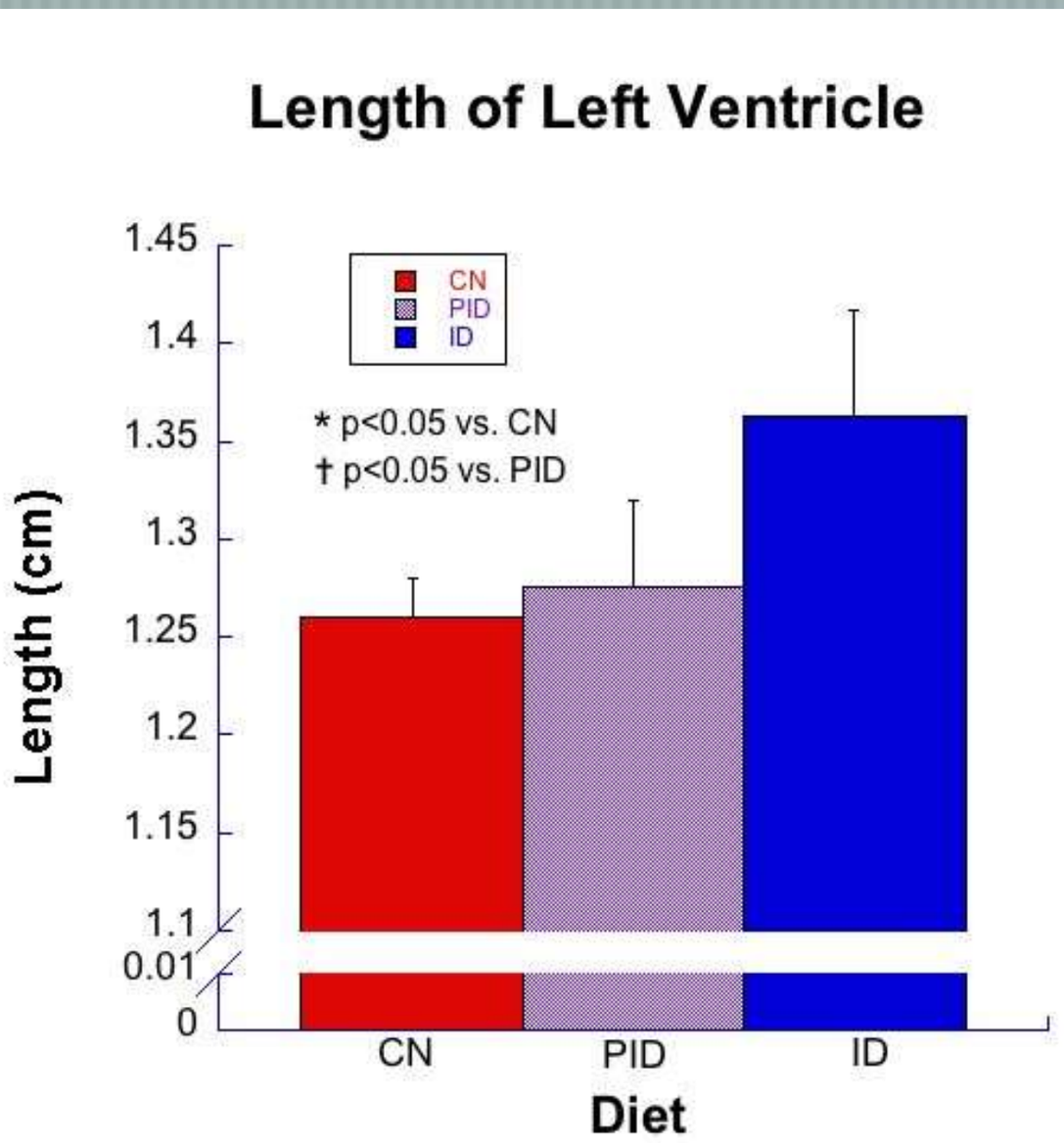


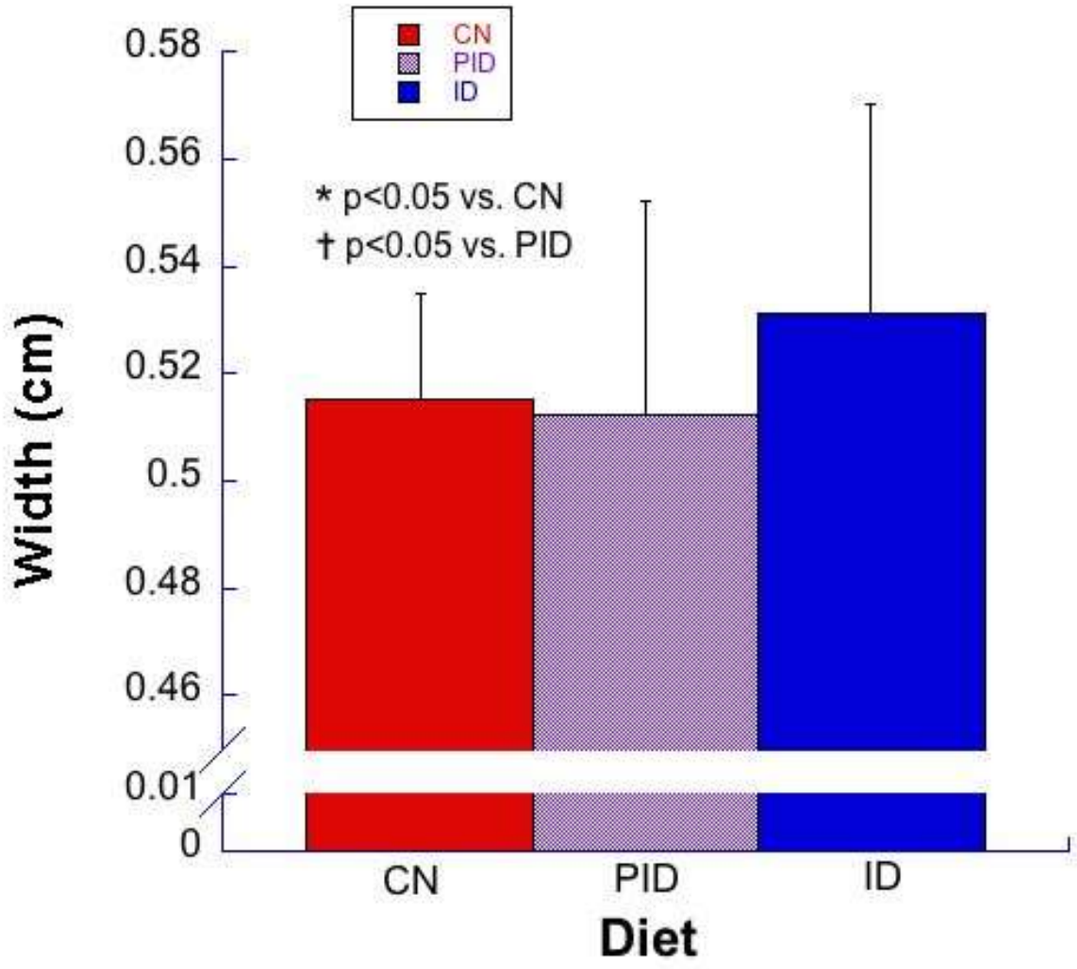


Partial ID Cardiac Functionality Normalized

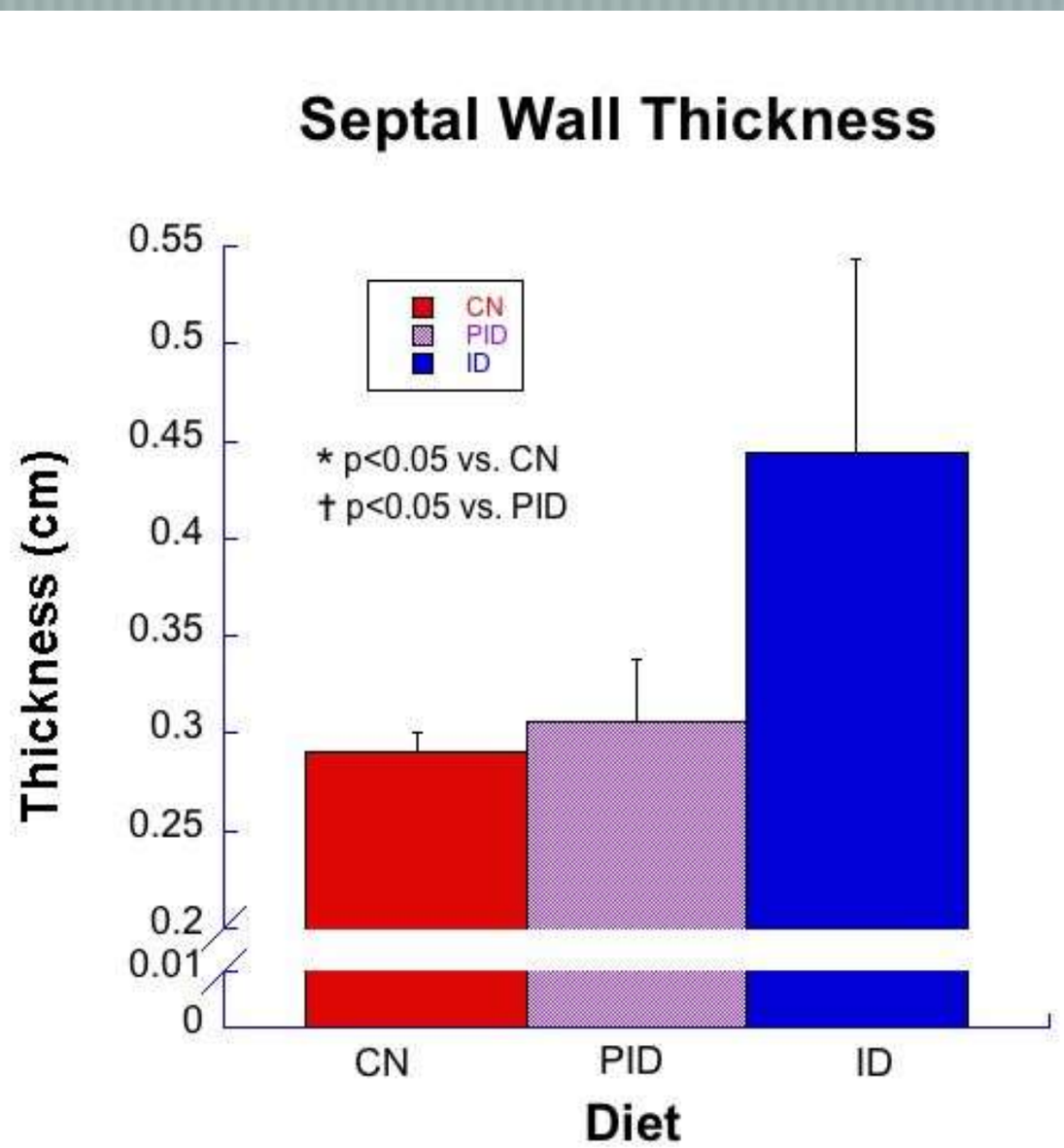


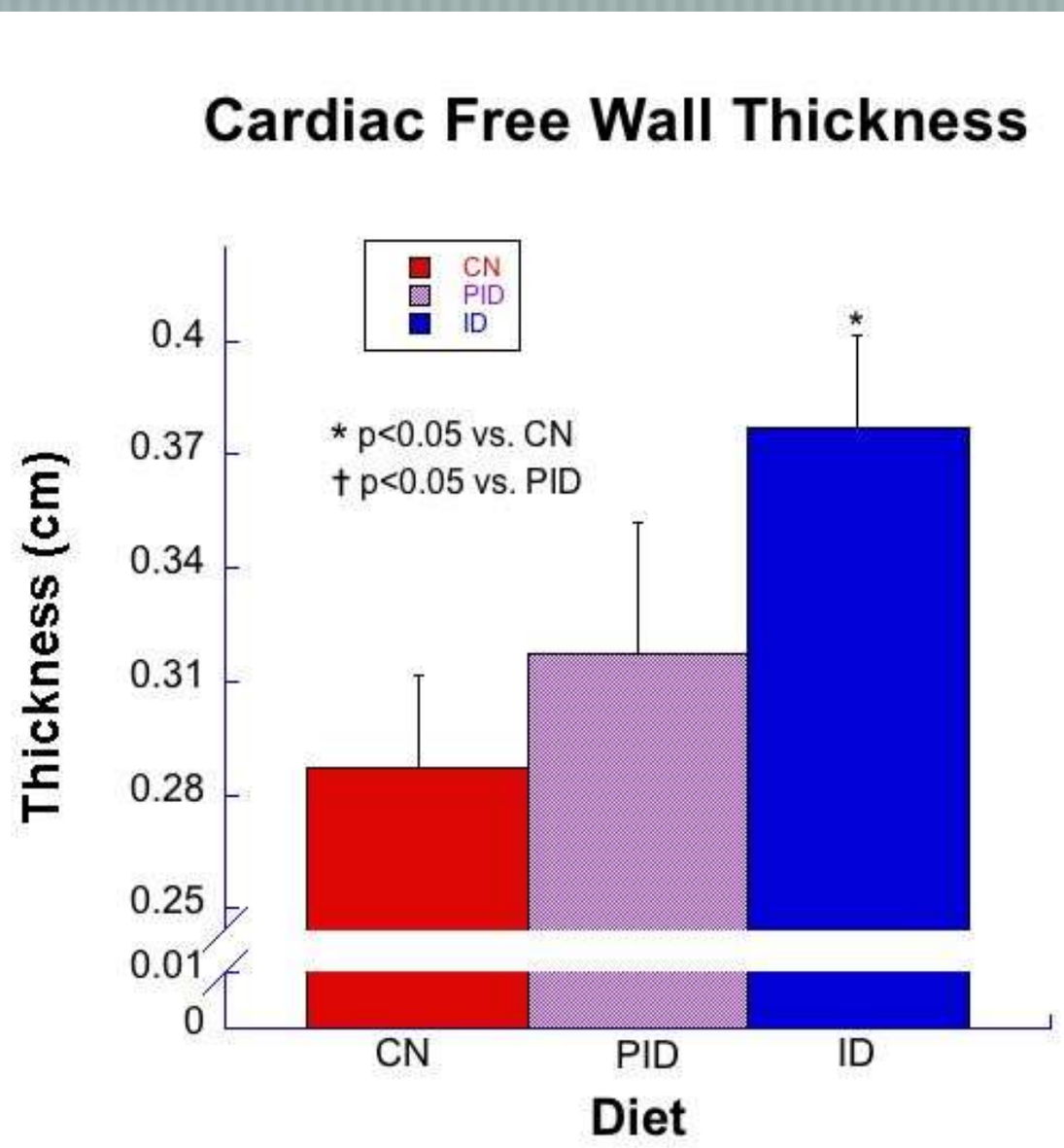
Partial ID Morphology Normalized





Partial ID Morphology Normalized





Take Home Message

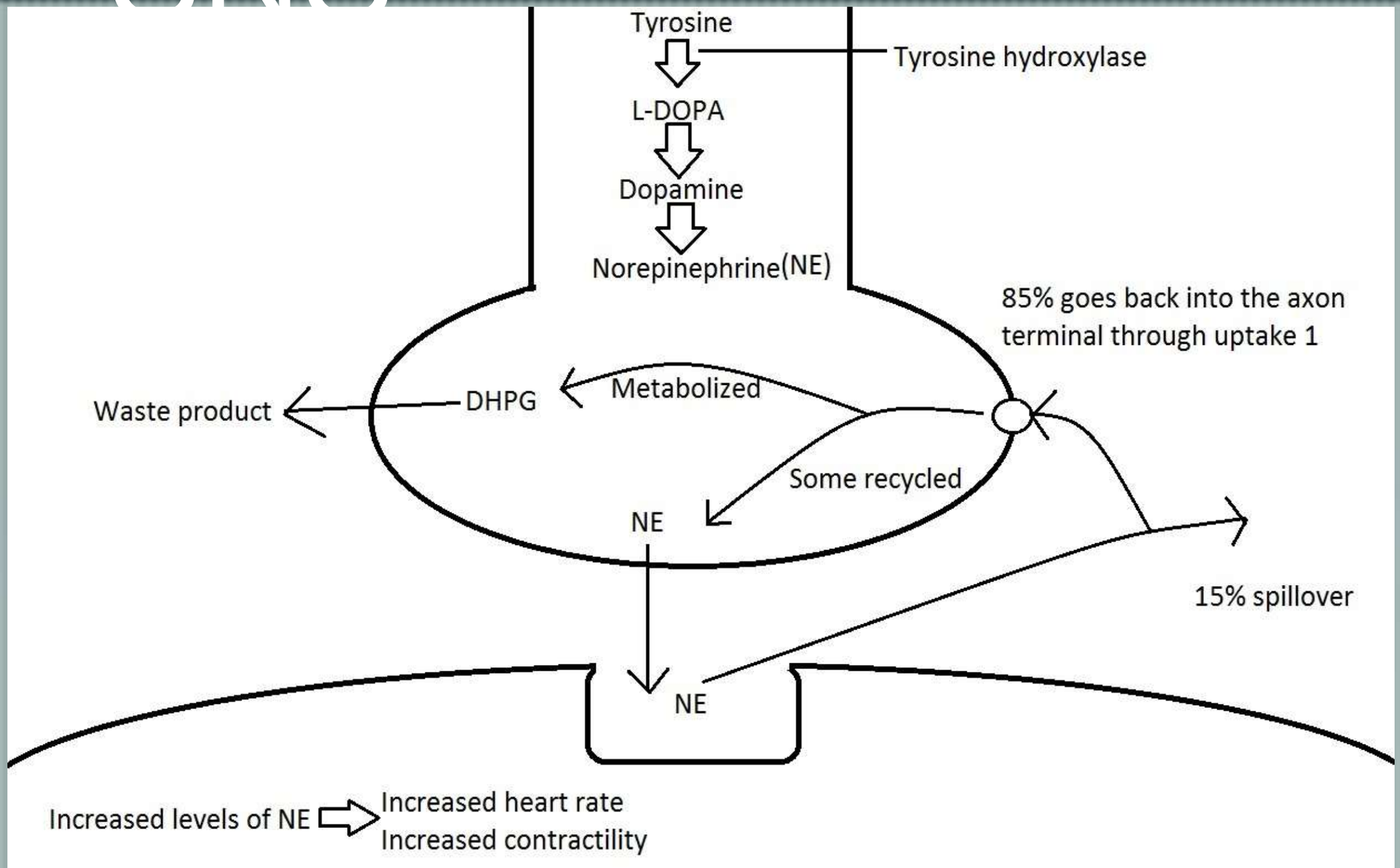
- 4 Weeks ID:
  - Decreased LVP
- Partial ID:
  - LVP similar to controls
  - Morphology similar to co

The Role of the SNS in Cardiac Hypertrophy Caused by Iron Deficiency

Quick Review

- Chronic stimulation of the SNS results from iron deficiency
  - Cardiac hypertrophy develops
  - Believed mediated by SNS
  - Norepinephrine (NE) is the neurotransmitter

Norepinephrine in SNS



Hypotheses

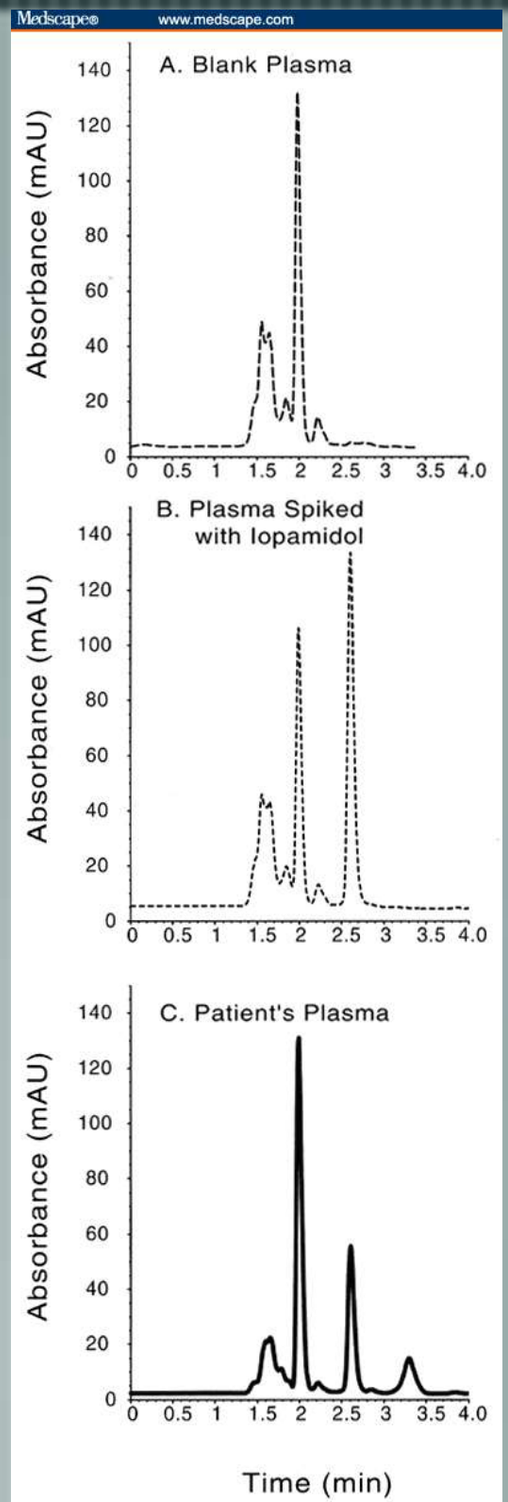
- NE stores in the axon terminal:
  - Normal at 2 weeks of ID
    - Adaptive hypertrophy
  - Depleted at 4 weeks of ID
    - Pathological Hypertrophy
  - Partial ID similar to CN at 4 weeks

Hypotheses

- NE in effluent:
  - Higher than normal at 2 weeks of ID
    - Drives higher LVP
  - Lower than normal at 4 weeks of ID
    - Results in lower LVP
  - Partial ID similar to CN at 4 weeks

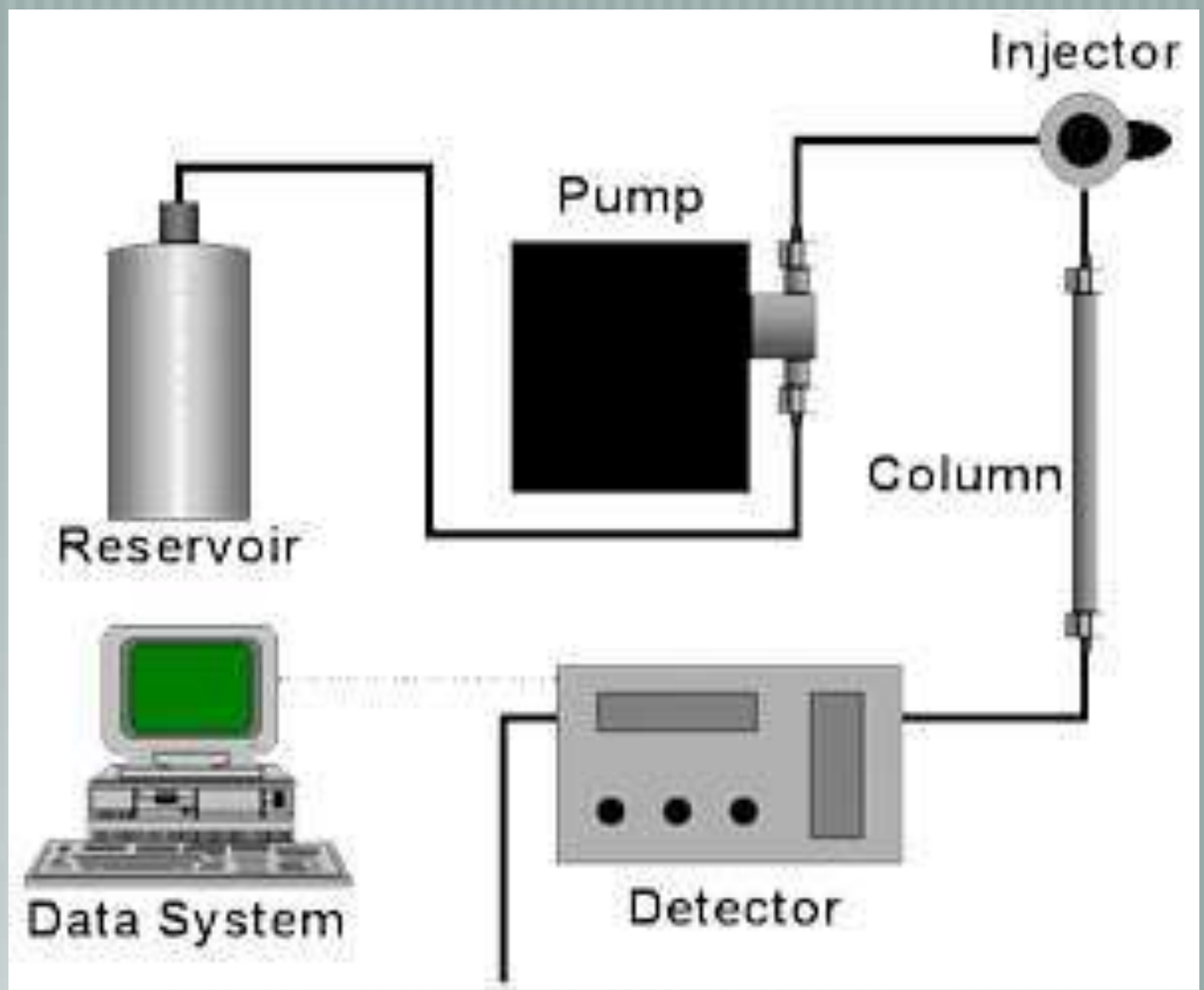
Methods

- Collected effluent during Langendorff Experiment
  - Freeze hearts and effluent for later analysis
- Catecholamines are extracted from samples
- Analyzed using High Performance Liquid Chromatography(HPLC)



How HPLC Works

- Physical separation technique in the liquid phase
- Pumped at a high pressure through a column
- Sample is injected into circulation
- Separated into its constituent components
- Electrochemical detector determines concentrations present
- Compared to internal



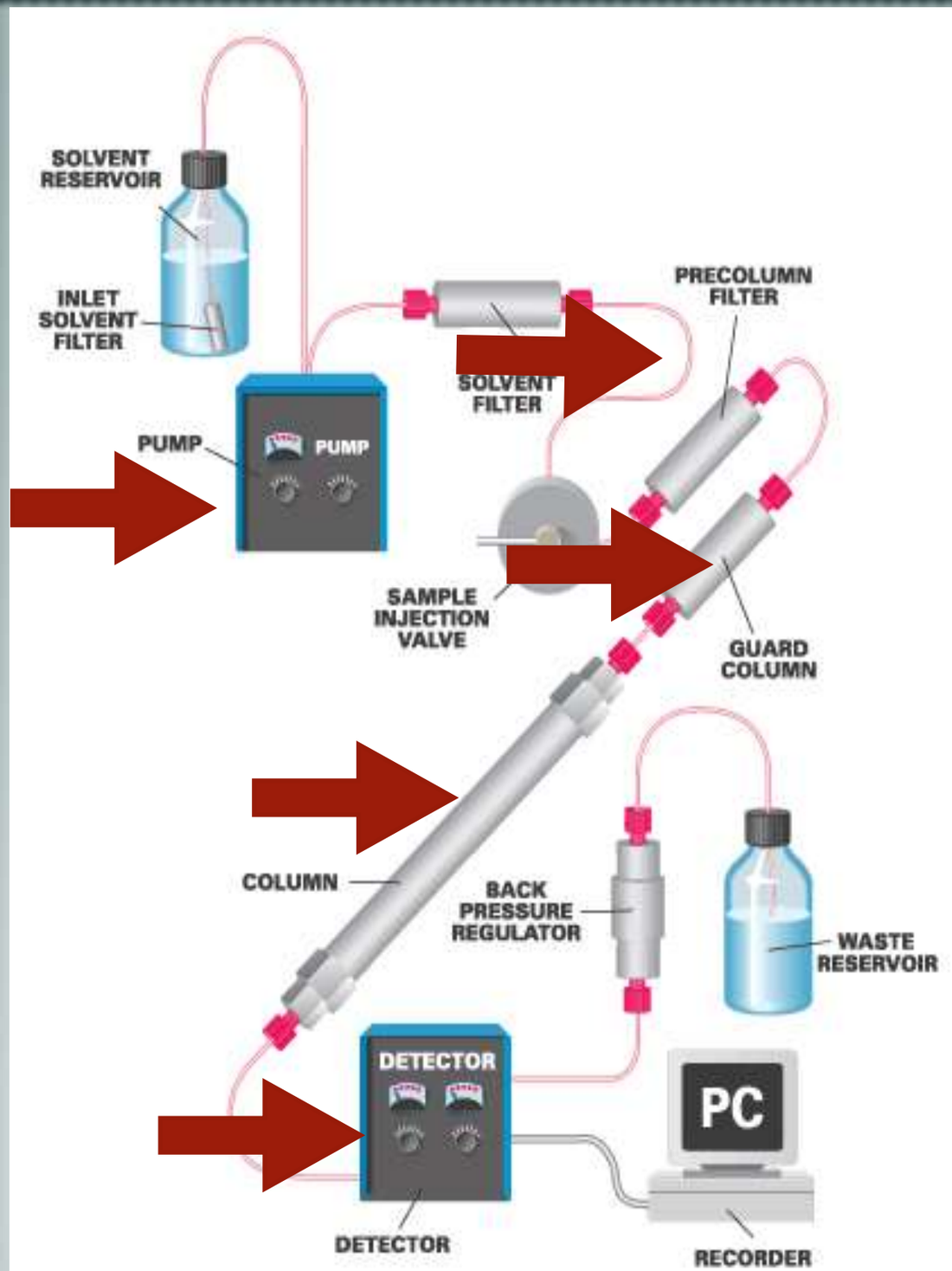
Catecholamine Extraction Procedure

- Effluent samples
- Catecholamines bond to Aluminum Oxide (Alumina)
- Remove supernatant from sample
- Wash with double distilled water
- $HCLO_4$ releases catecholamines from Alumina
- Inject into HPLC for separation

Achievements

Overhauled HPLC

- New seals, check valves, high pressure lines, column, guards and detector seal
- Perfecting extraction procedures 50% efficiency or better
- Internal standards are tested and ready
- Ready for data



Conclusions

- 4 weeks ID:
  - Decreased LVP
- Partial ID:
  - LVP similar to control
  - Morphology similar to control
- We hypothesize HPLC data will parallel Langendorff data

Special Thanks

Many thanks to NIH INBRE for funding this research