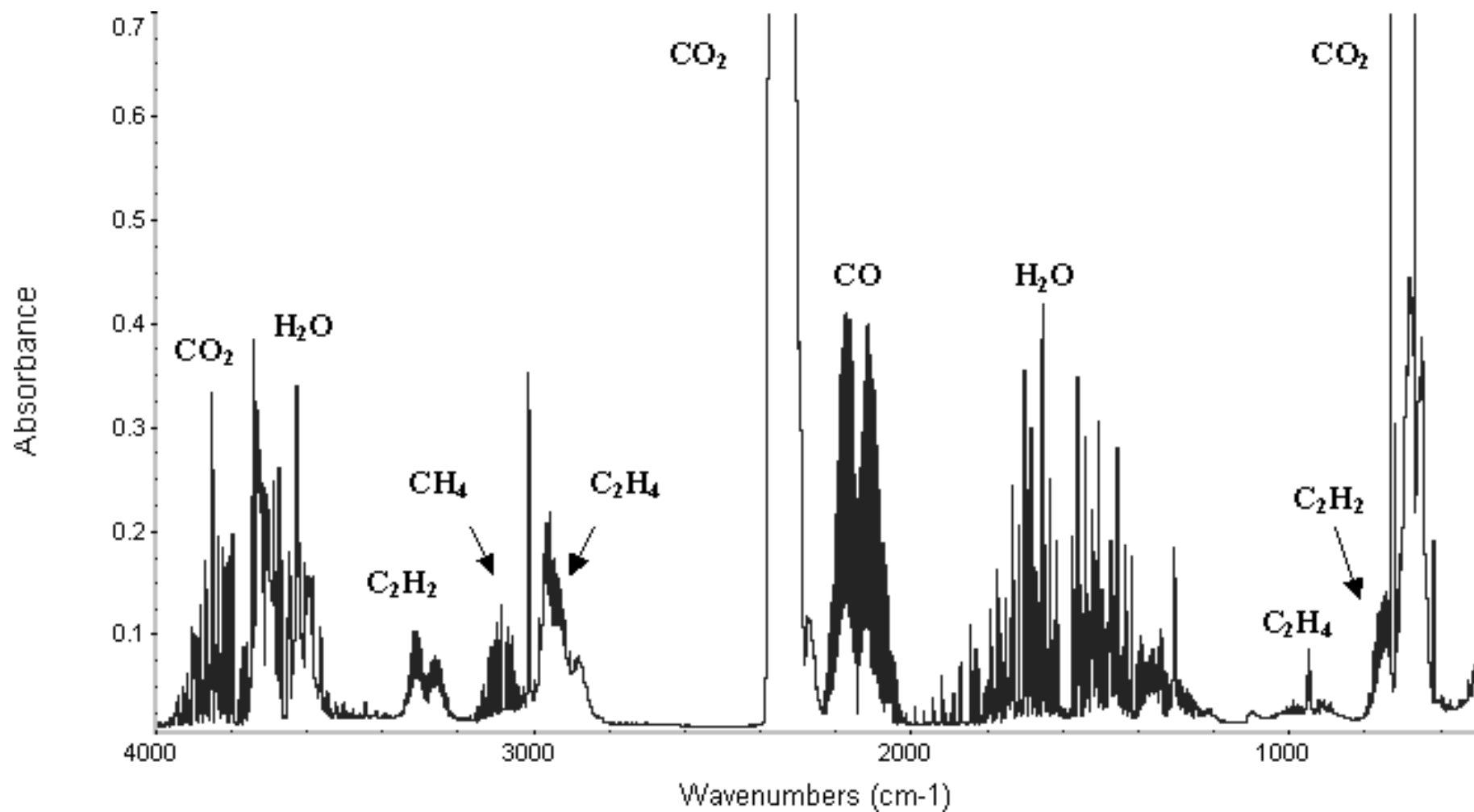


Exercise in Metabolic Myopathies

M.S. Riley



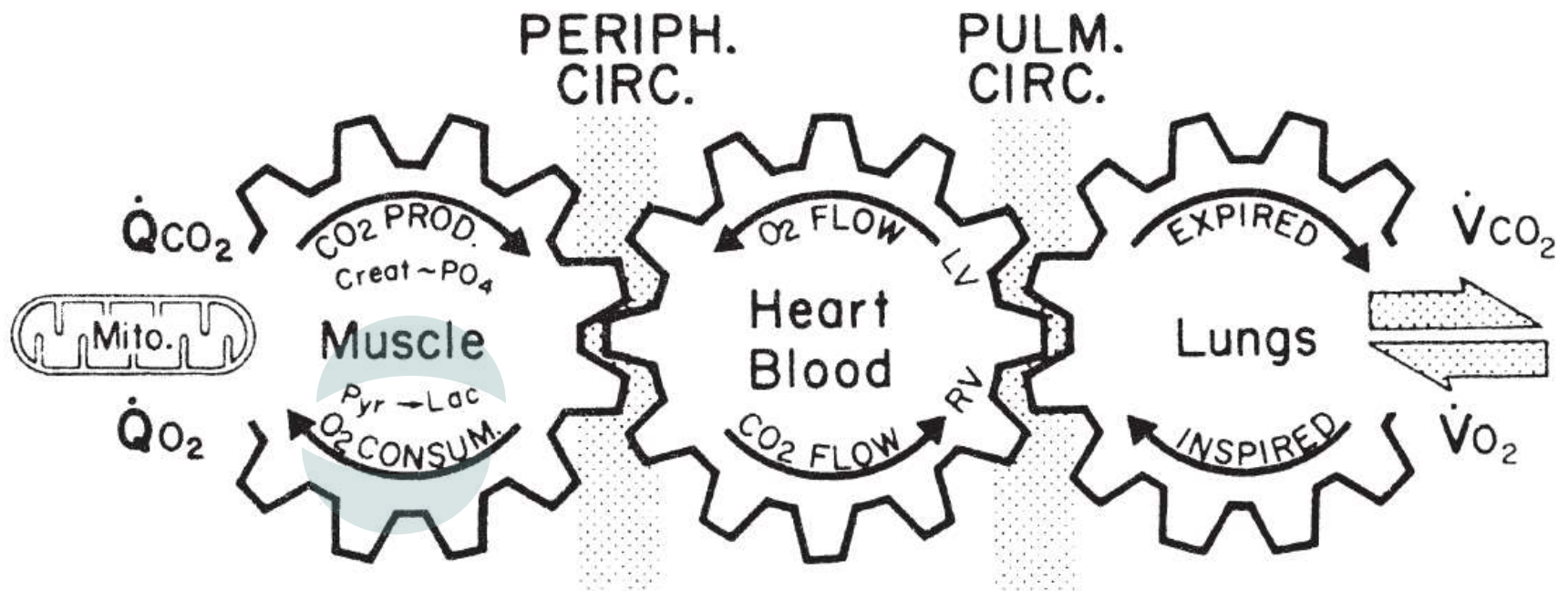


1942 Packard

MUSCLE
ACTIVITY

O_2 & CO_2
TRANSPORT

VENTILATION
($\dot{V}_A + \dot{V}_D = \dot{V}_E$)



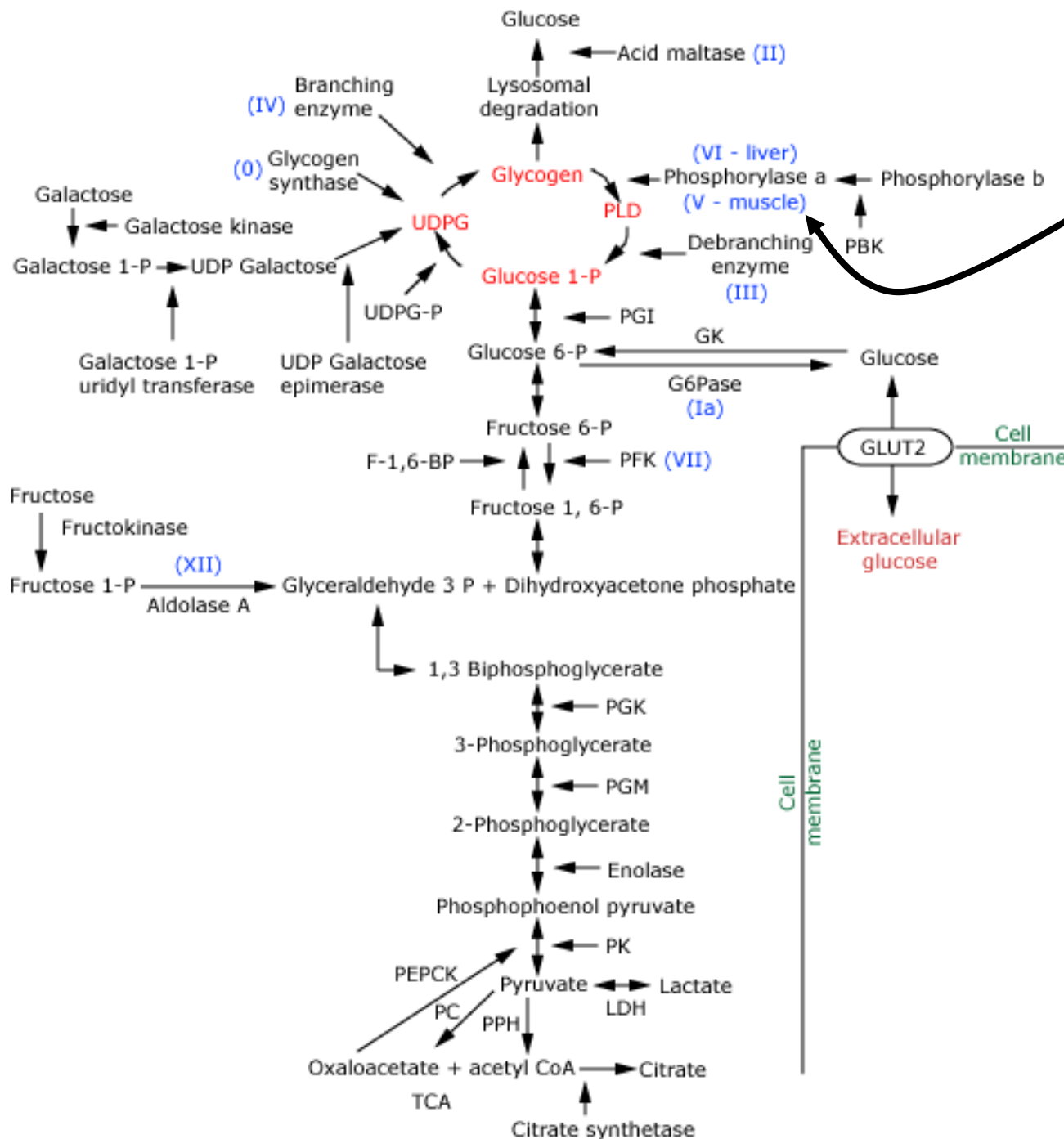
Measuring capacity at the metabolic level

Defects in Glycolysis

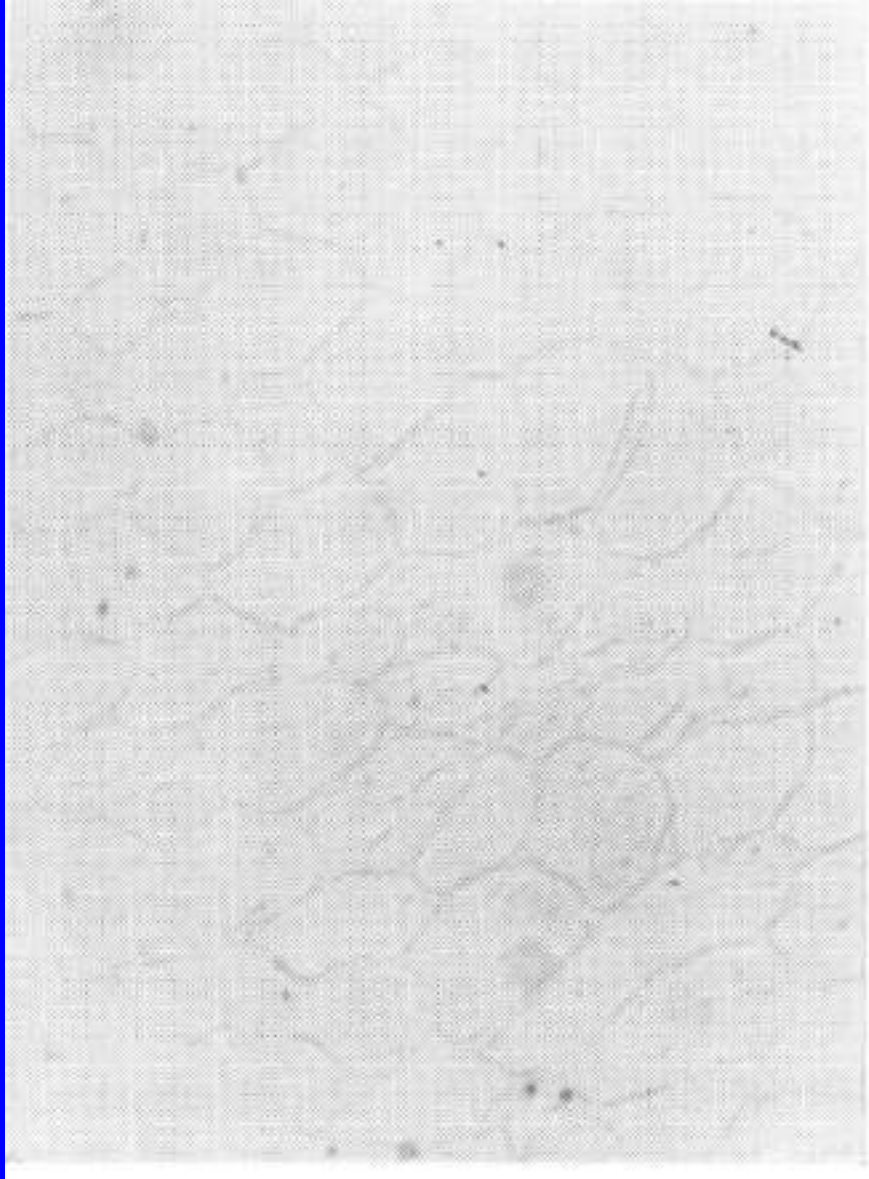


CPX International Inc.
formerly GSKB Inc.

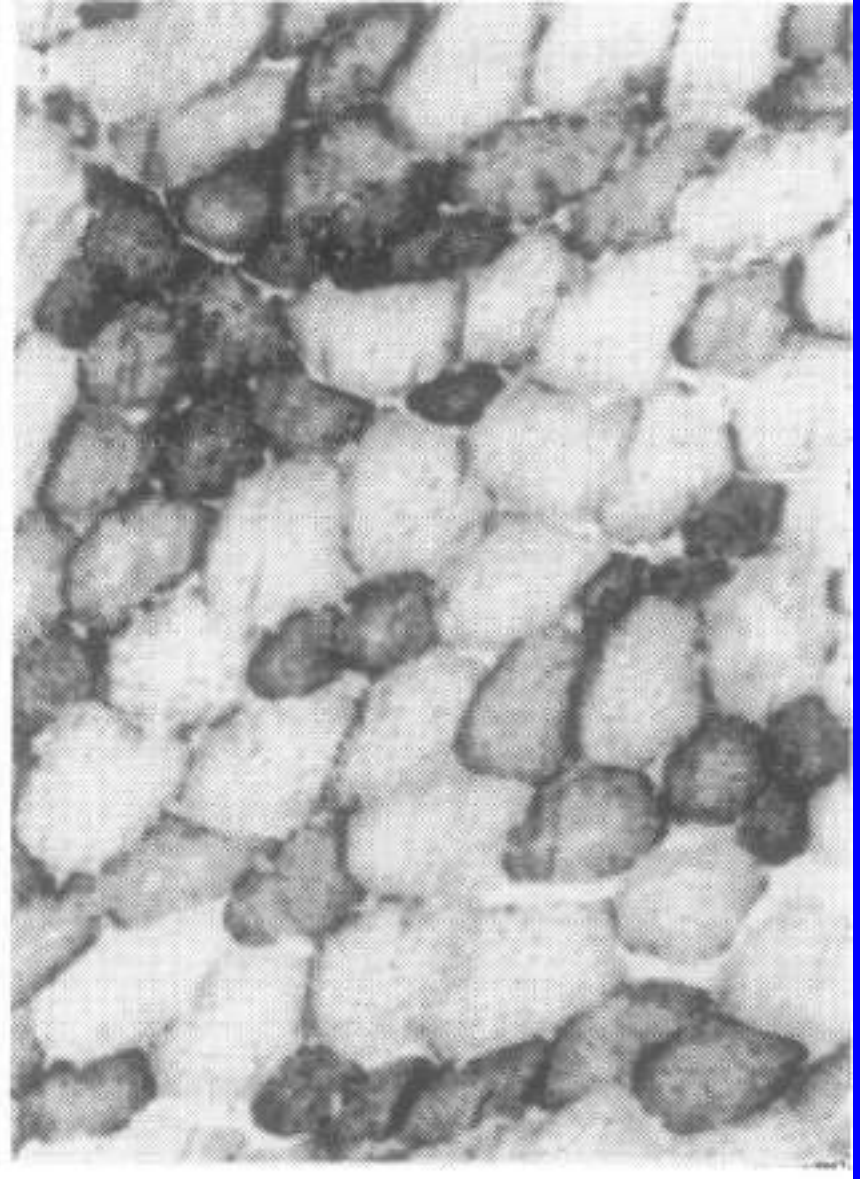
McArdle's disease



Phosphorylase stain



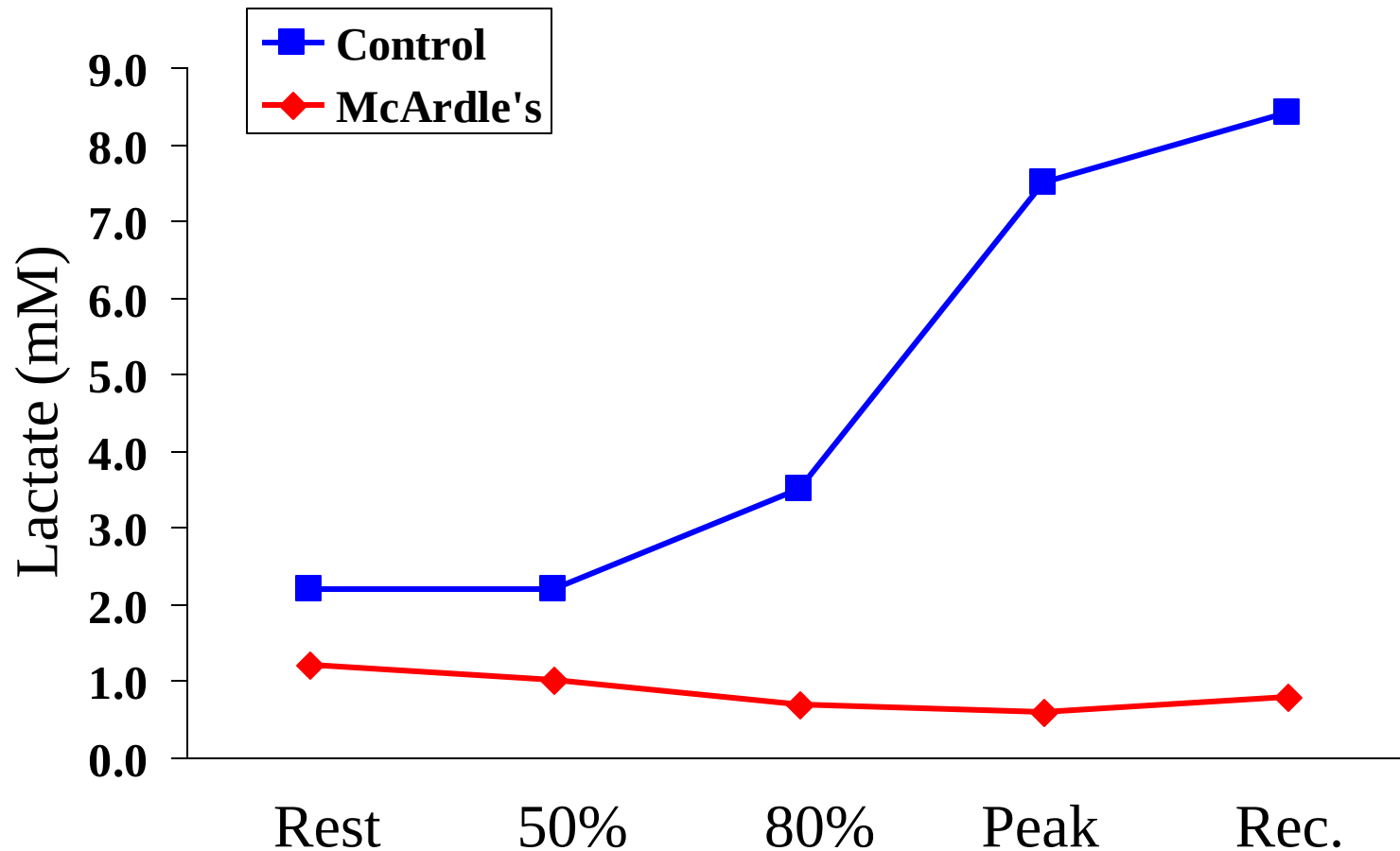
Glycogen stain

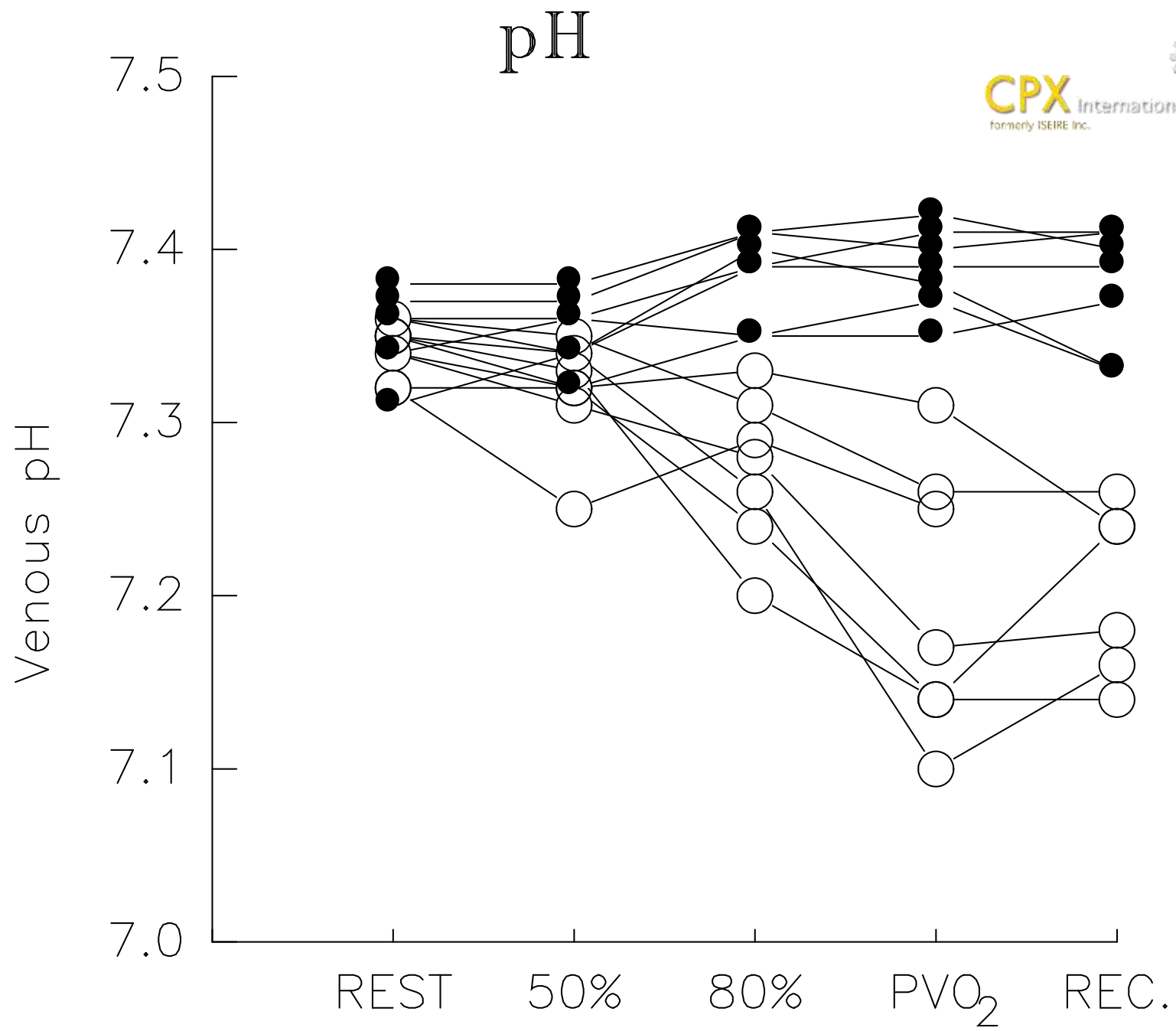


Symptoms

- Muscle cramps
- Fatigue
- Myoglobinuria

Lactate in McArdle's Disease



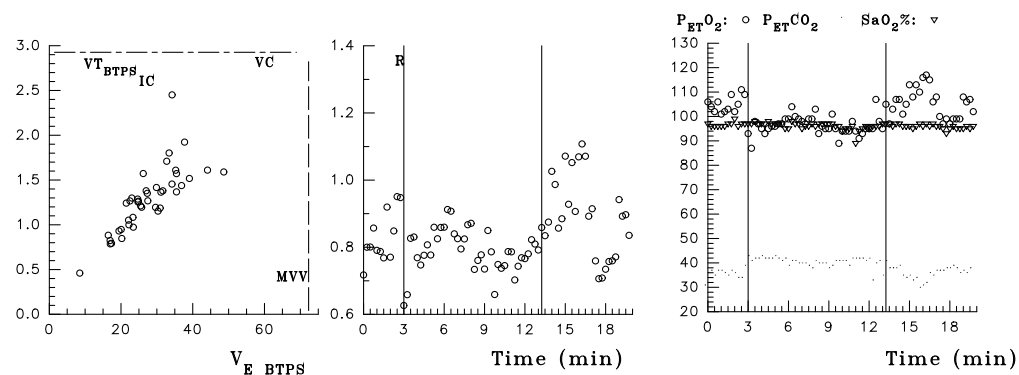
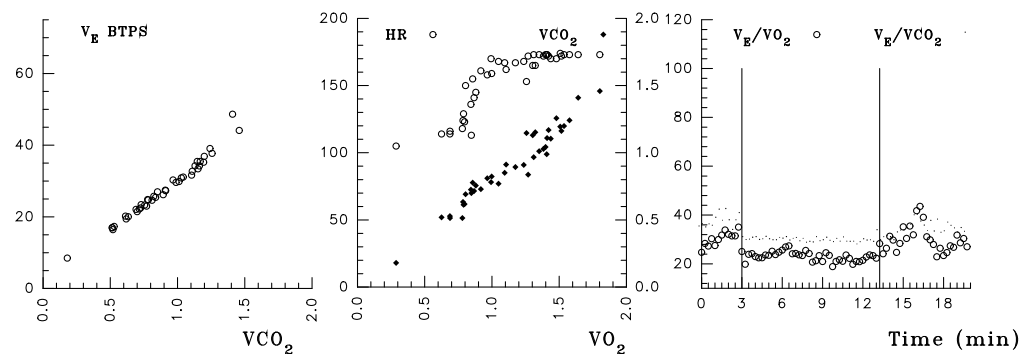
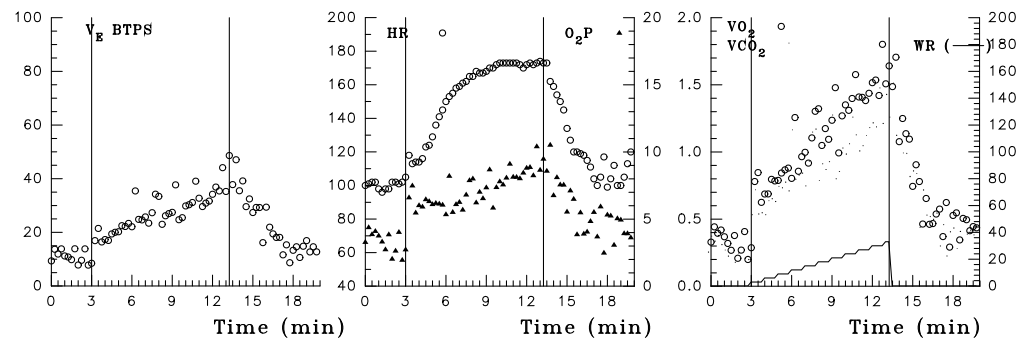


Subj: SB-McArdle's disease *EXERCISE PERFORMANCE REPORT*

Protocol: 5W min⁻¹ bicycle ramp

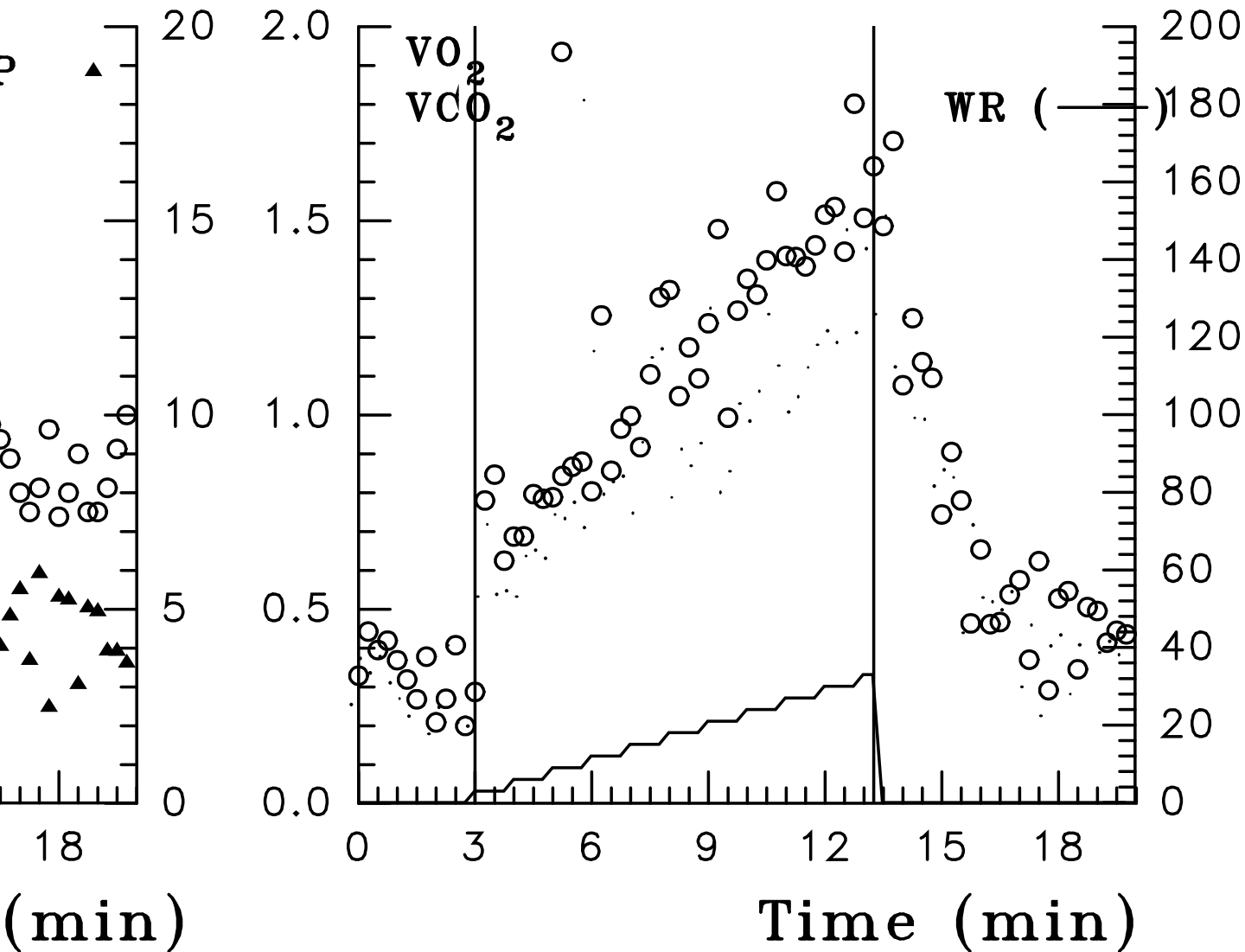
(10 sec average after second by second interpolation)

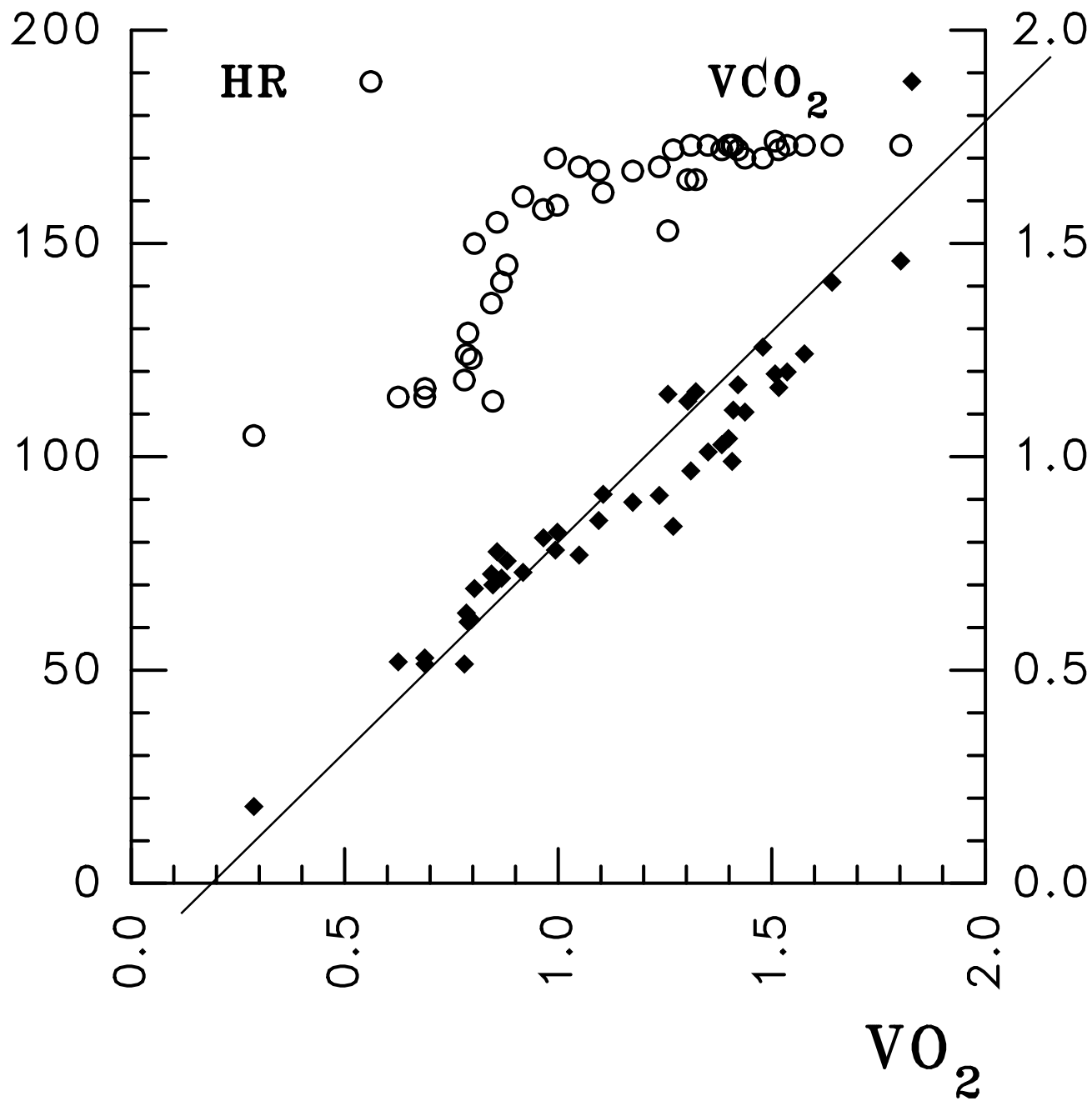
Gender: M Age: 36 Weight: 74kg Height: 1.73m Indication: McArdle's research



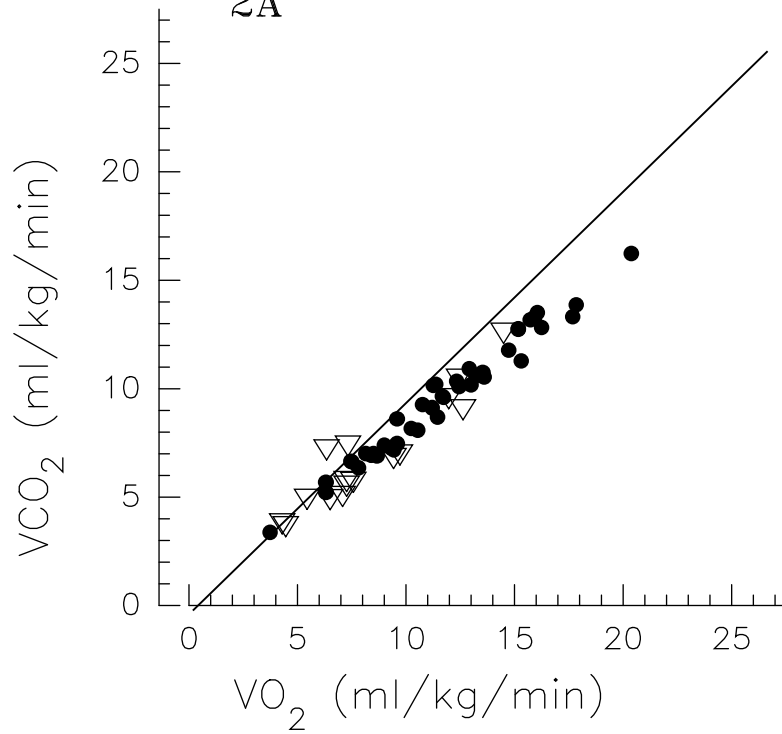
polation)

73m Indication: McArdle's research

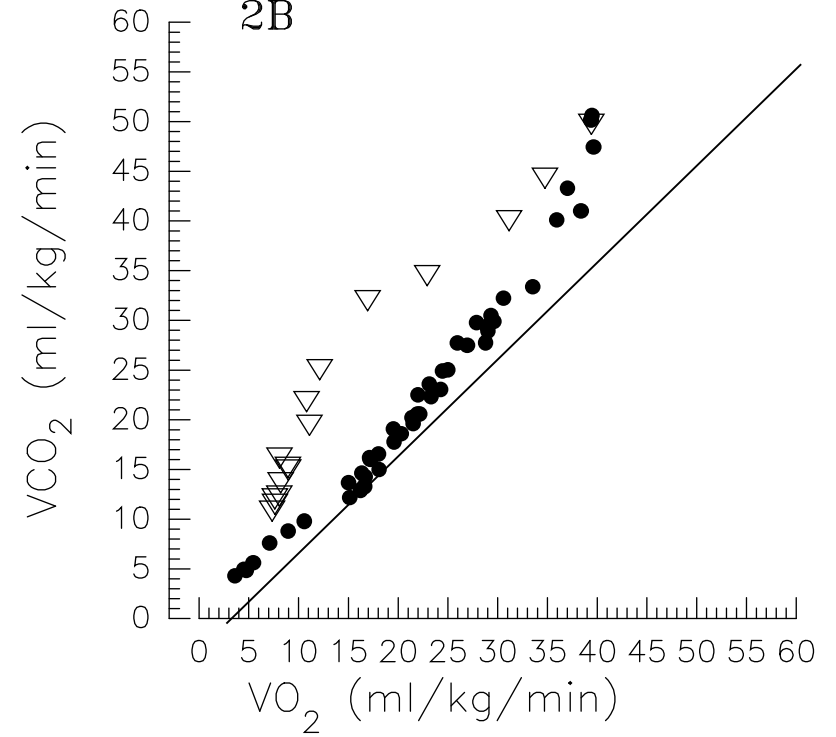




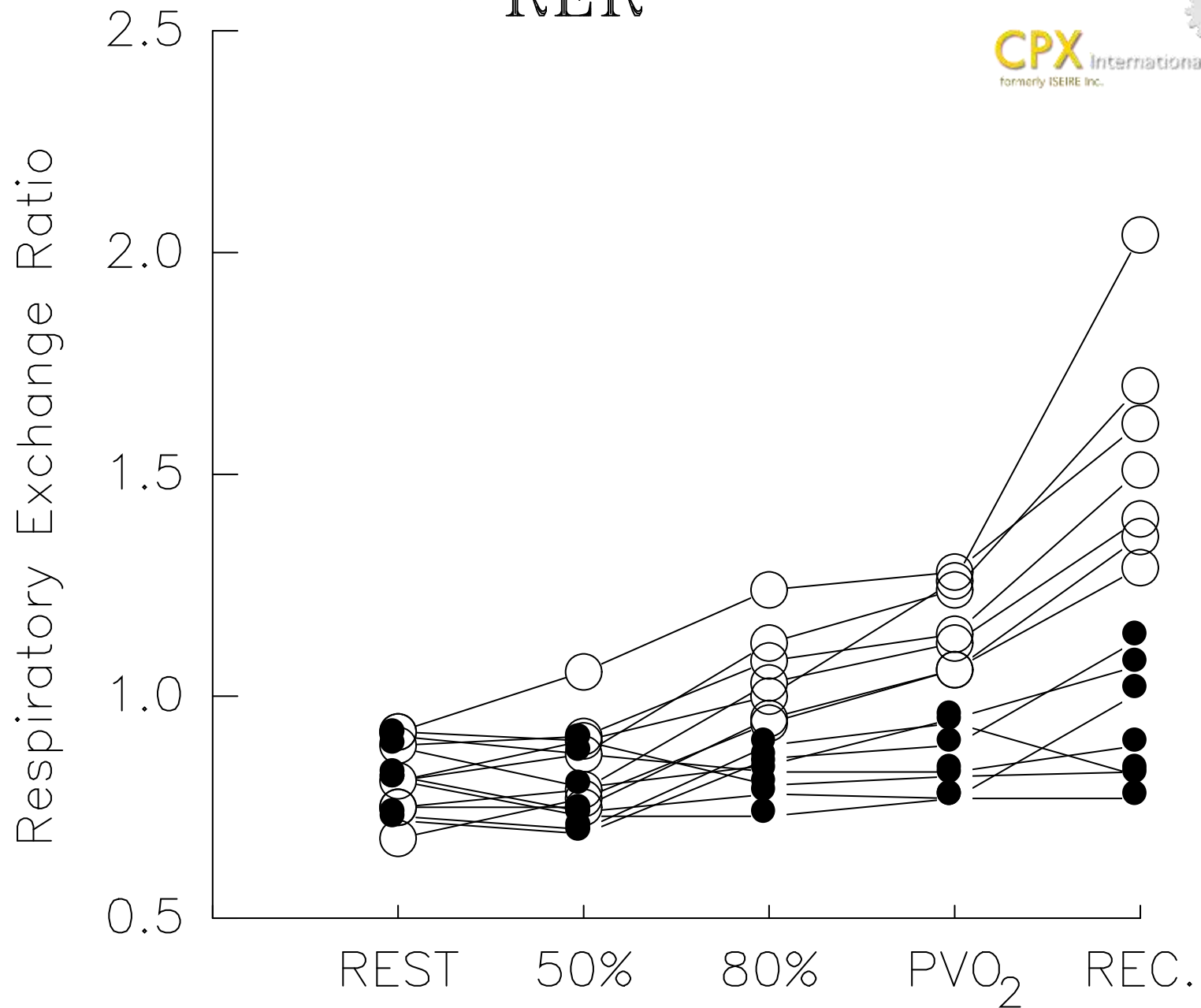
2A

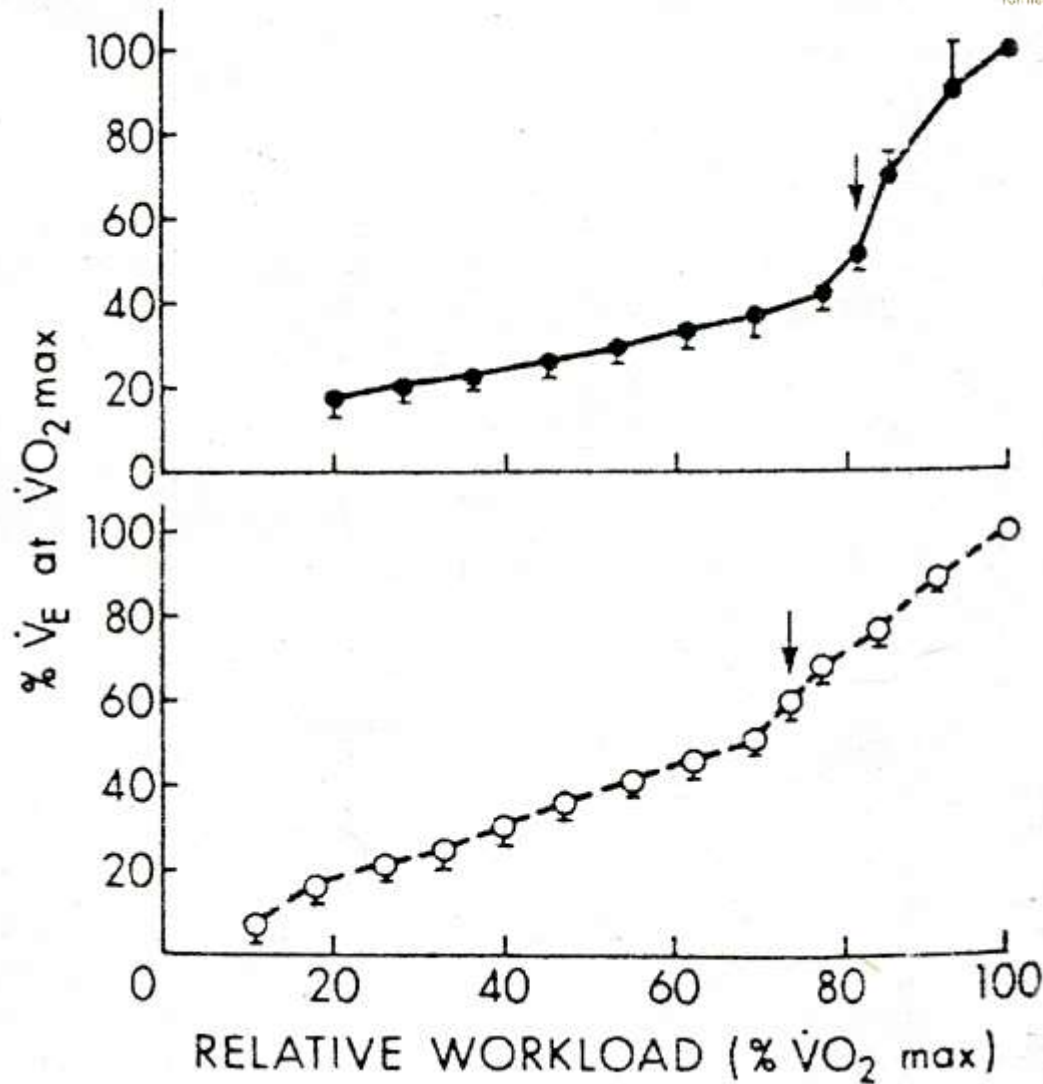


2B



RER

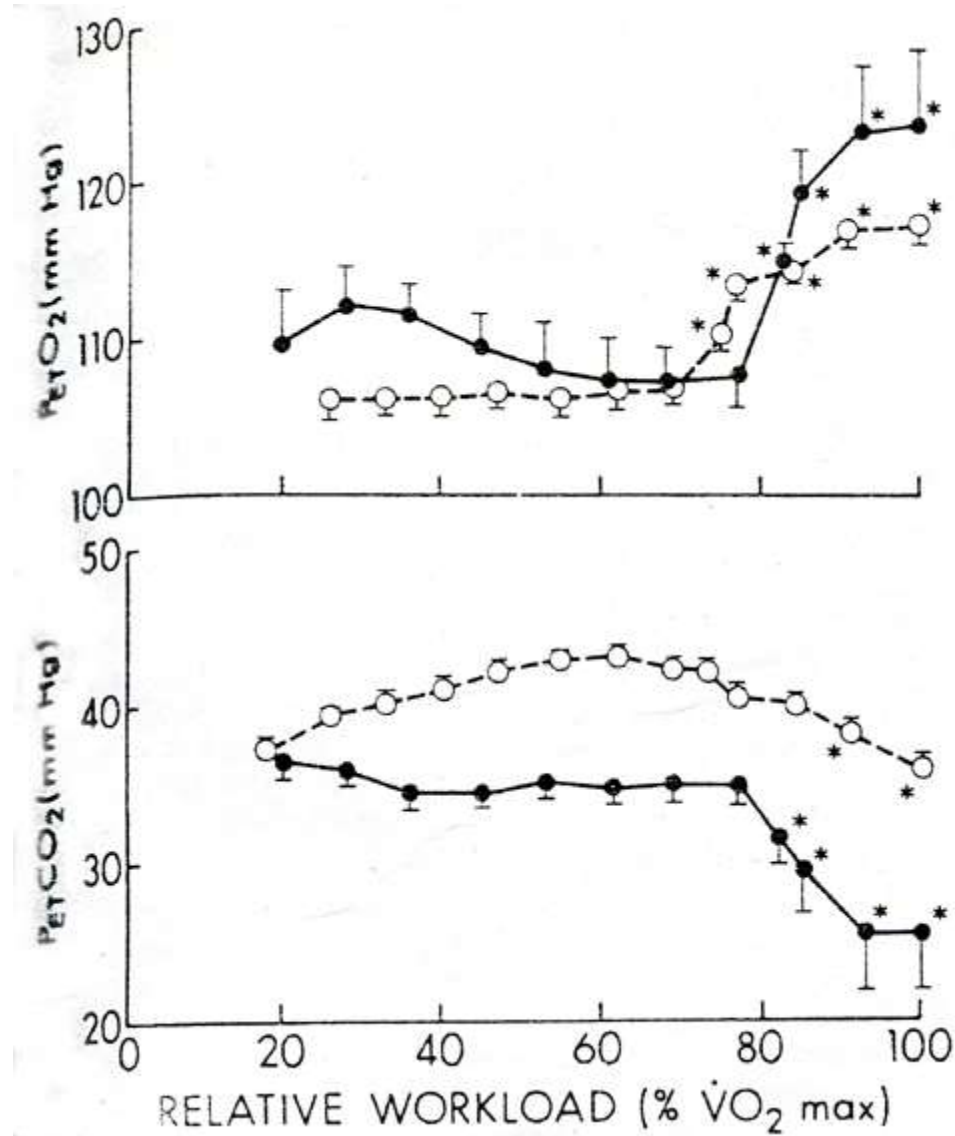




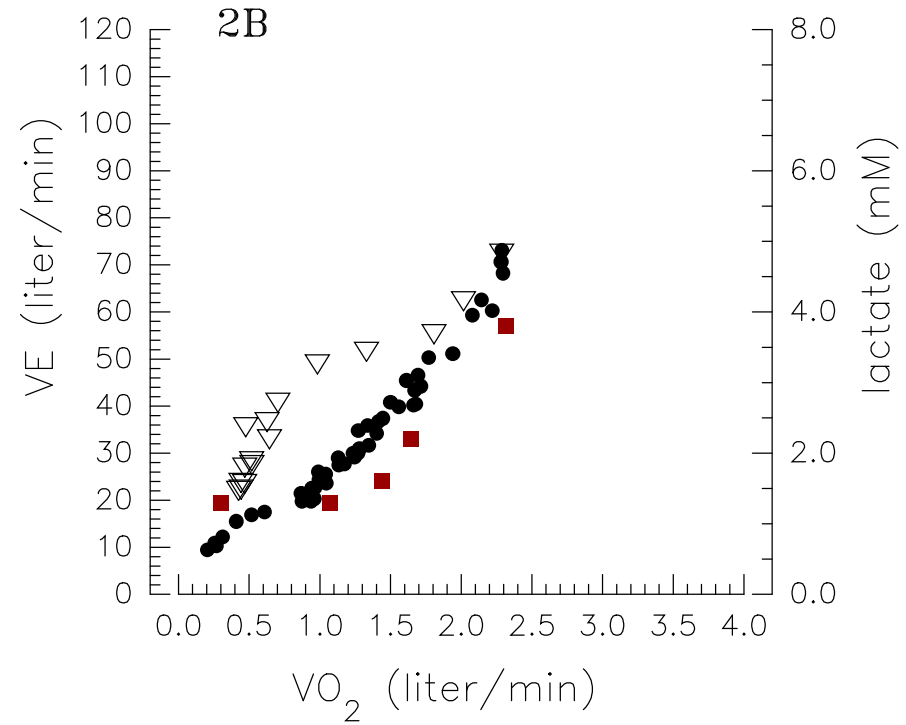
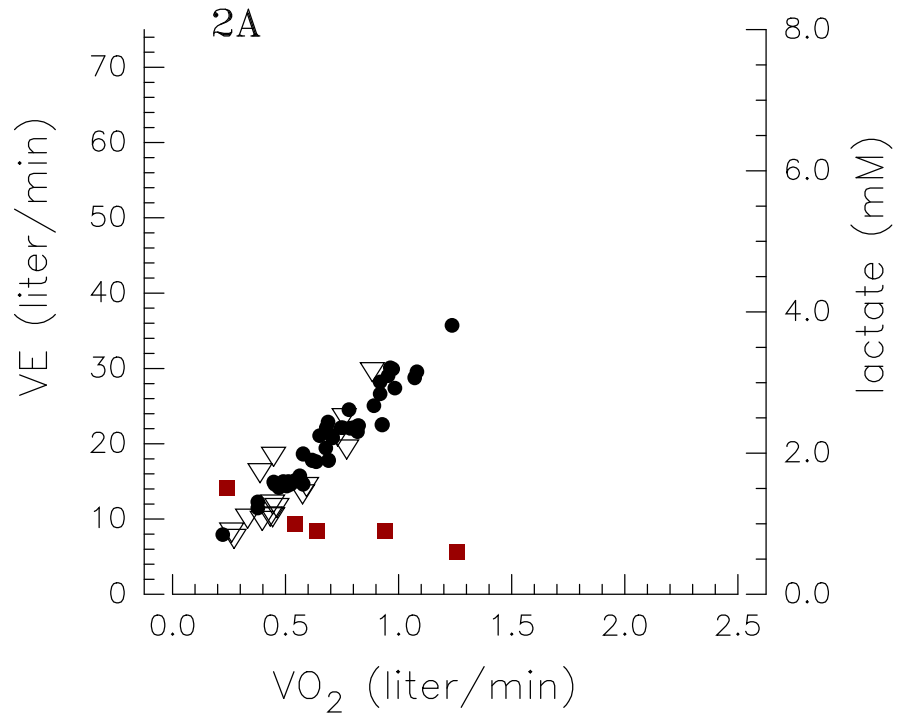
McArdle's

Controls

Hagberg et al. 1982



Hagberg et al. 1982



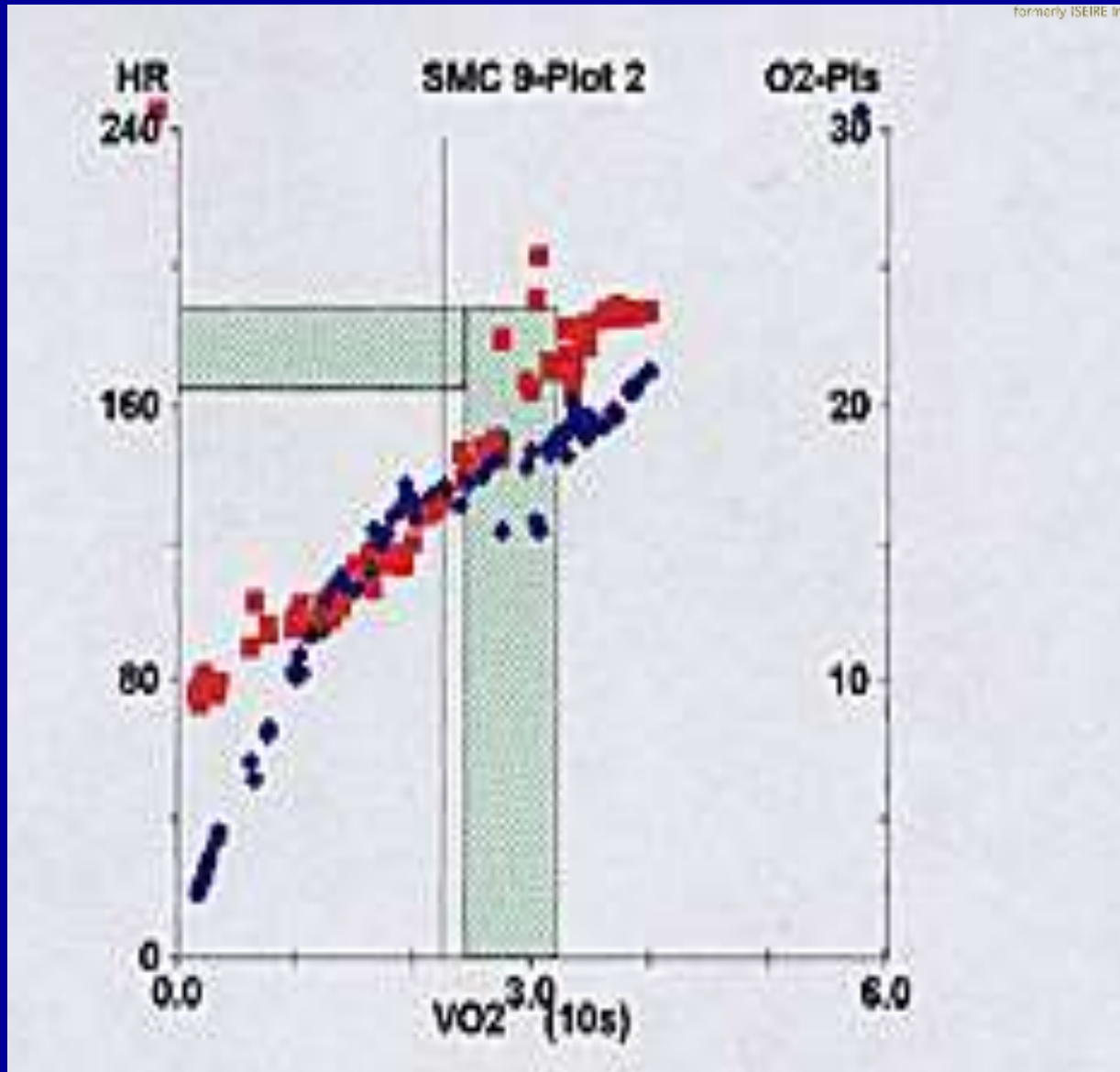
O₂-pulse ($\dot{V}O_2$ /HR)

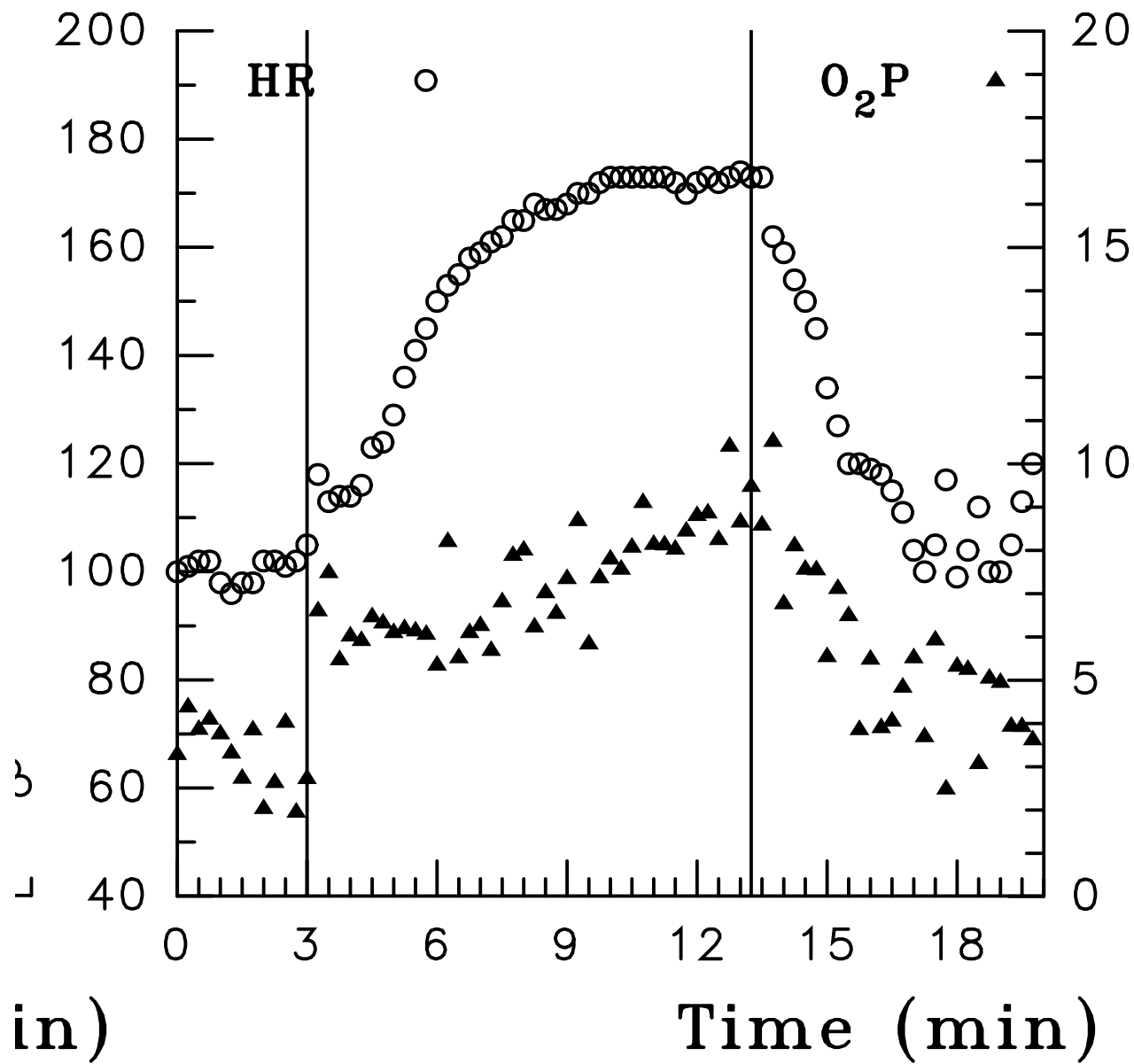
$$\dot{V}O_2 = \dot{Q} \times C(a-v)O_2$$

$$\dot{Q} = HR \times SV$$

$$\dot{V}O_2/HR = SV \times C(a-v)O_2$$

Normal O₂-pulse

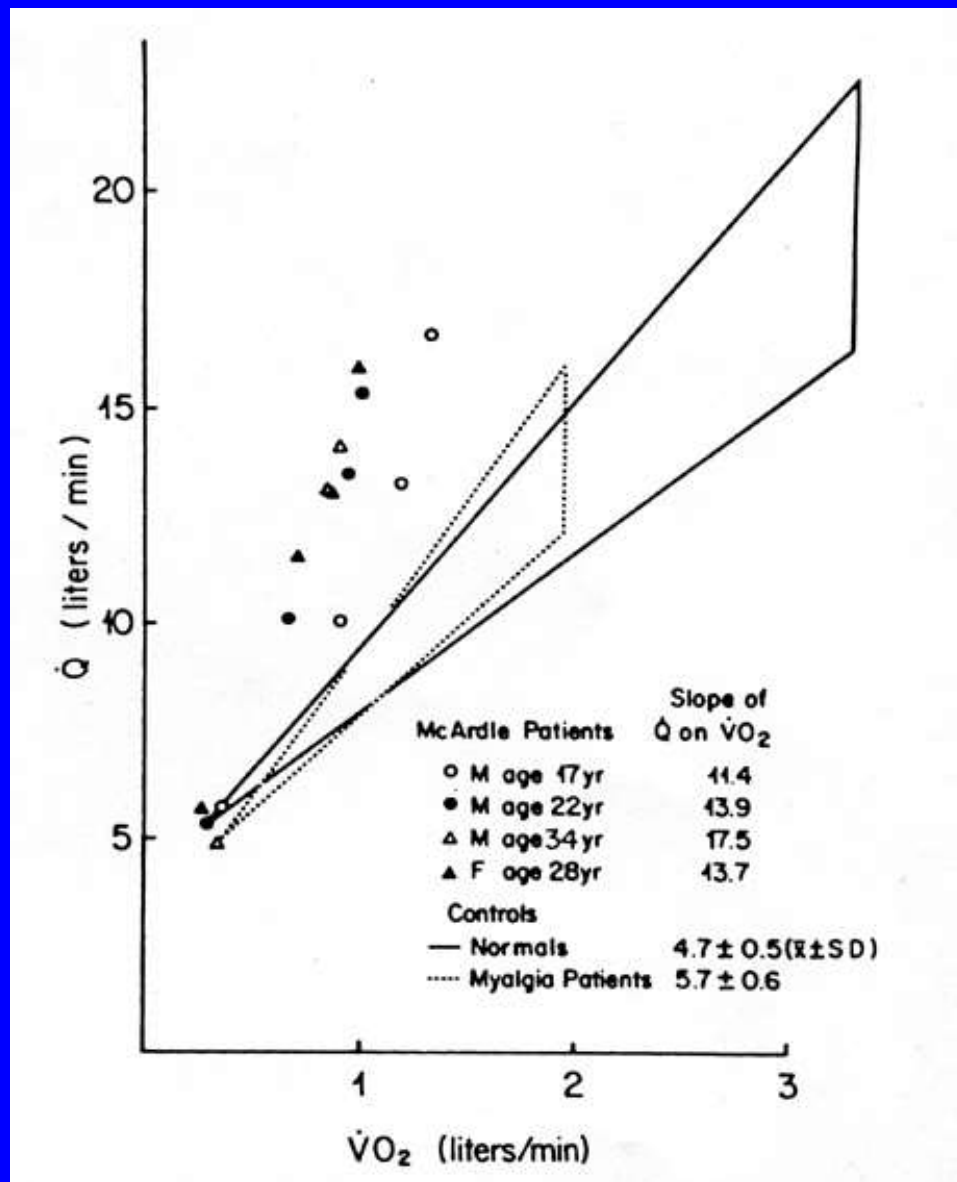


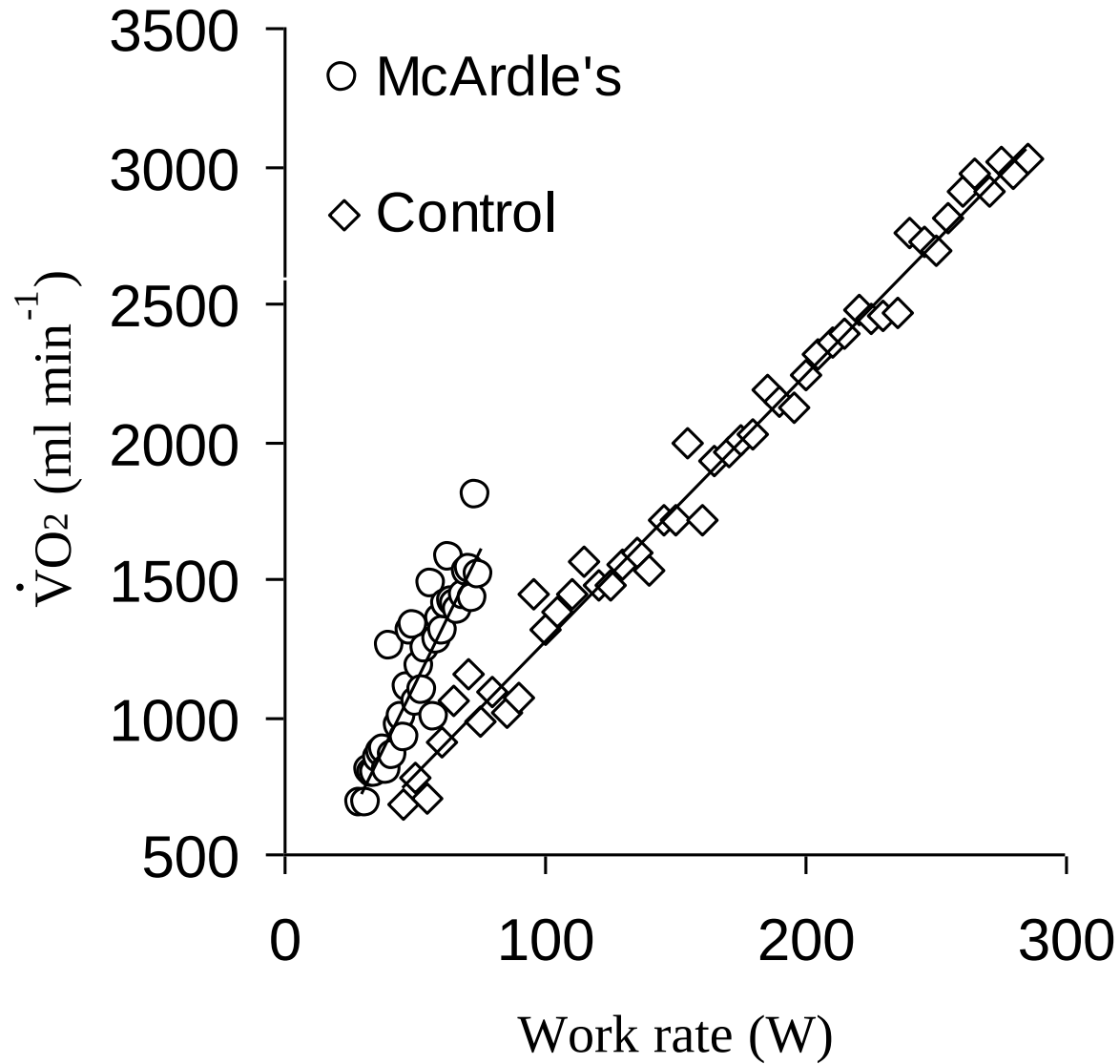


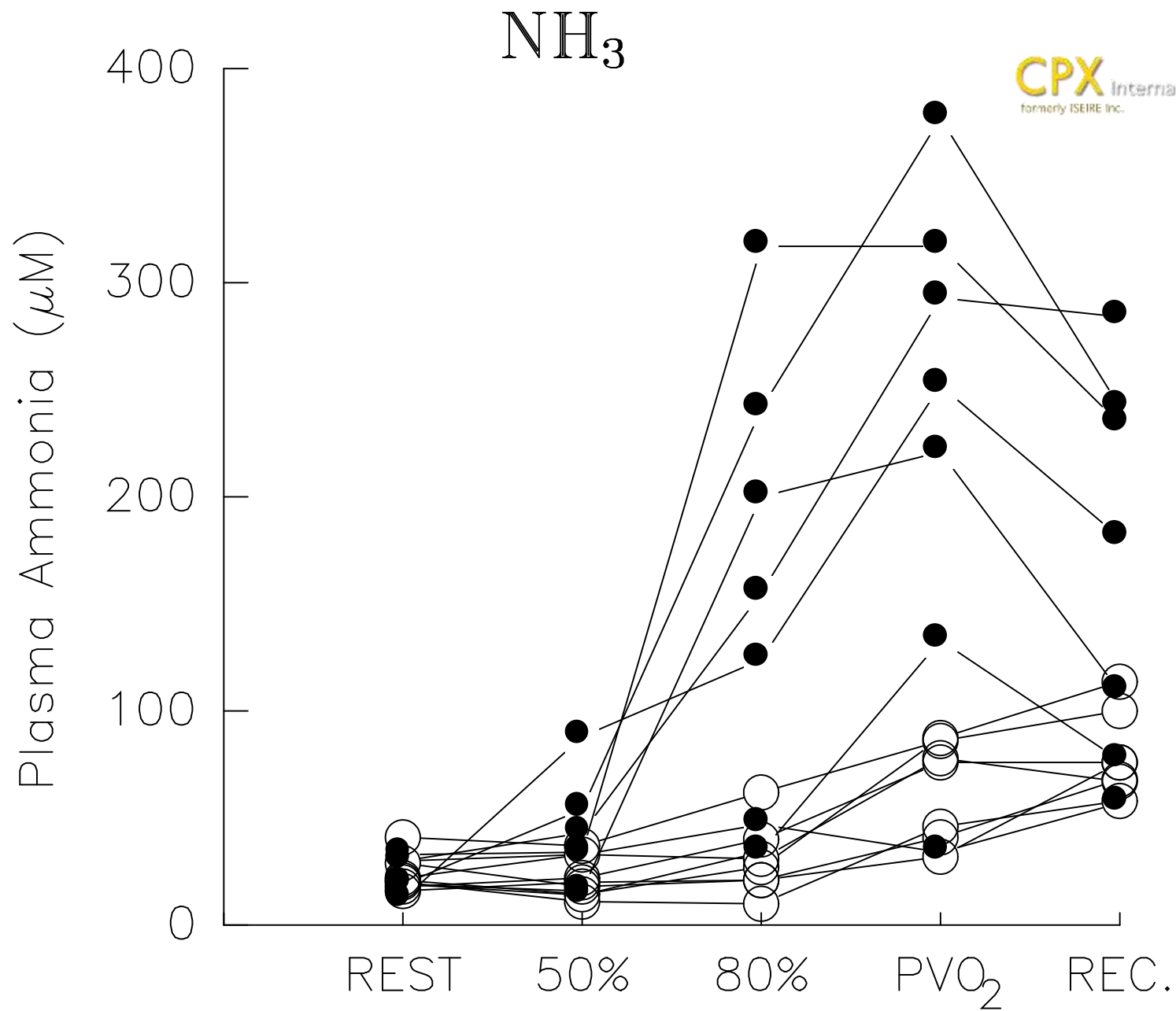
Arteriovenous O₂ difference (ml dl⁻¹)

	Rest	Maximum exercise
Normals (n=8)	5.3 ± 1.2	16.6 ± 1.4
McArdle's	4.9	6.5

$\dot{Q}$ - $\dot{V}O_2$ relationship in McArdle's







Source of ammonia during exercise

- ? • Myokinase Reaction



- Myoadenylate Deaminase Reaction

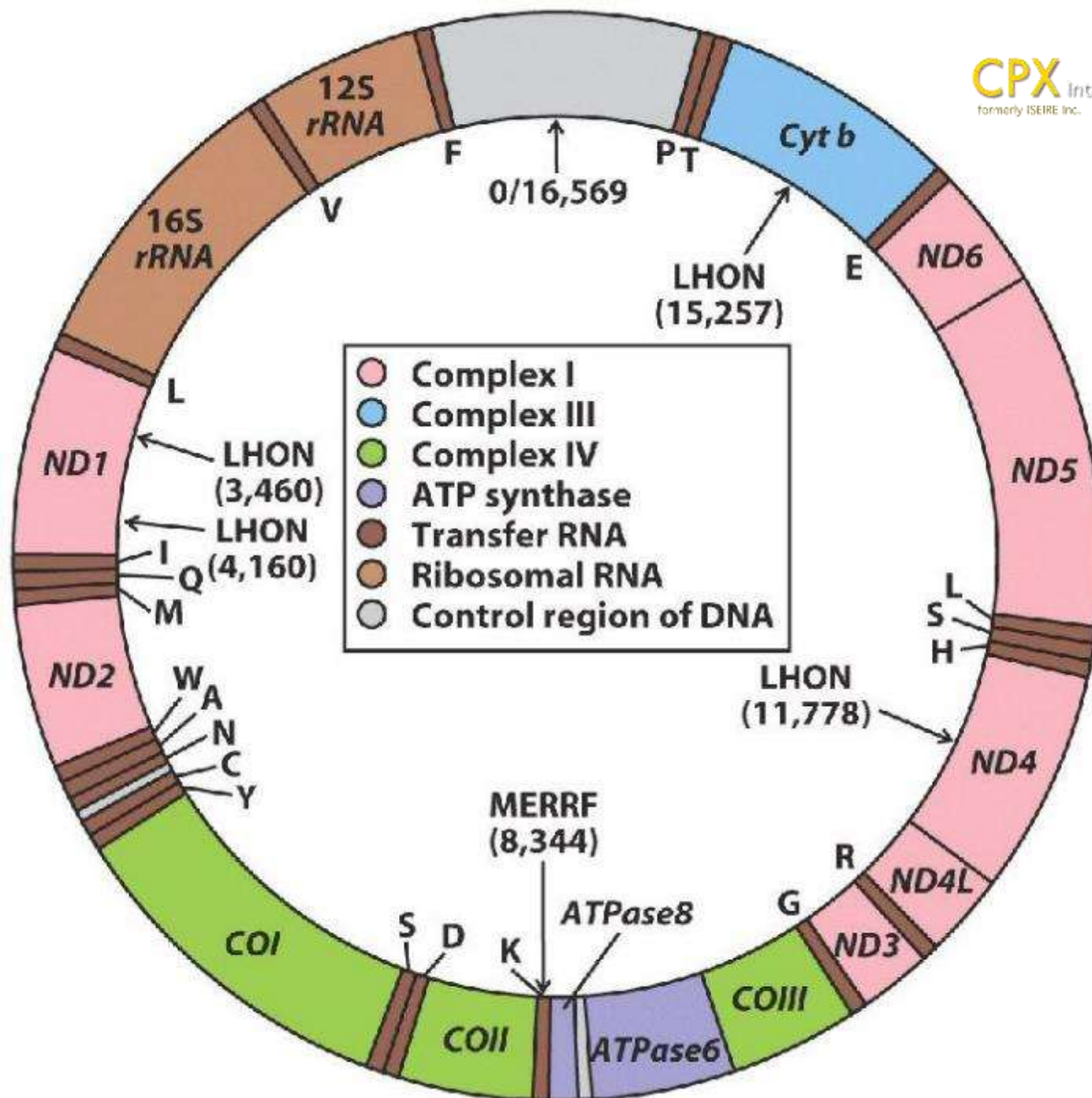


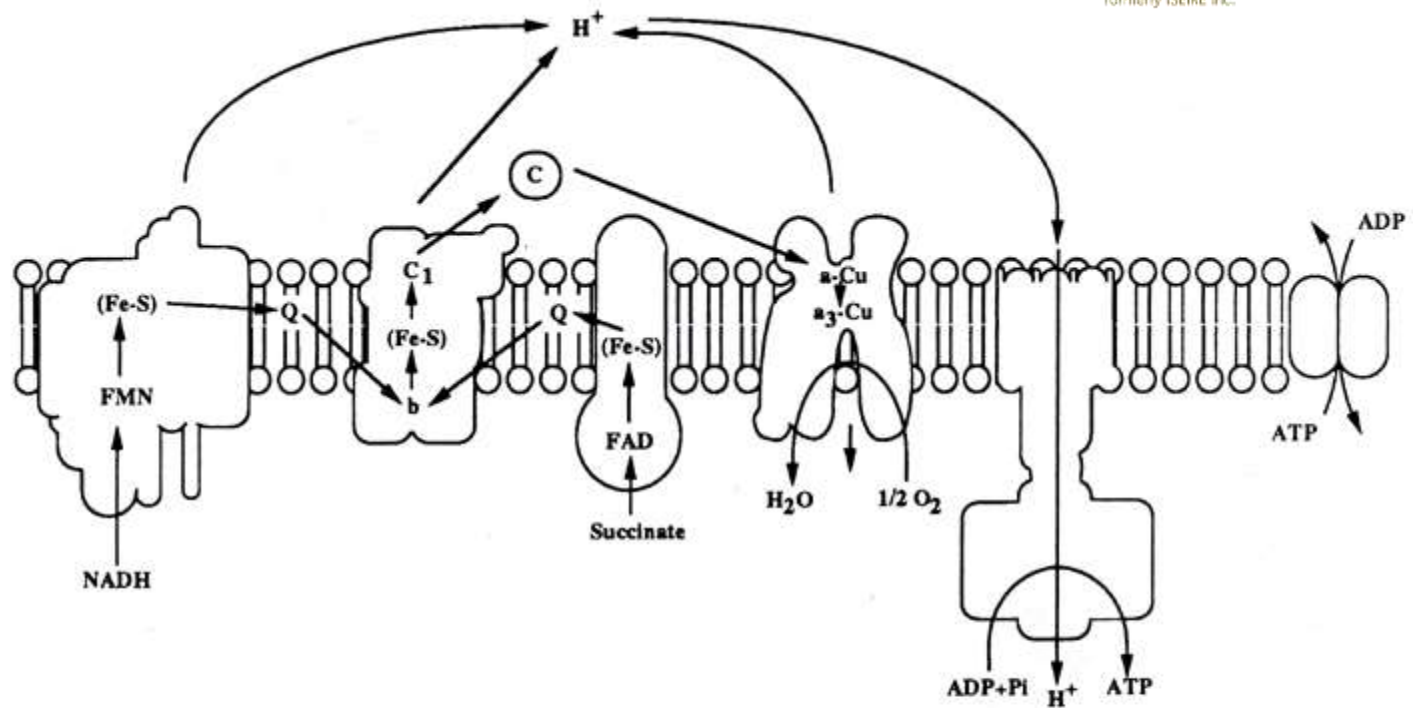
?gluconeogenesis with amino acid deamination

McArdle's Disease

- Low VO_2
- Low RER and absent LAT
- Brisk HR response with low O_2 pulse
- High $\text{Q} - \text{VO}_2$ and high $\text{VO}_2 - \text{WR}$ relationships
- Low lactate
- High ammonia

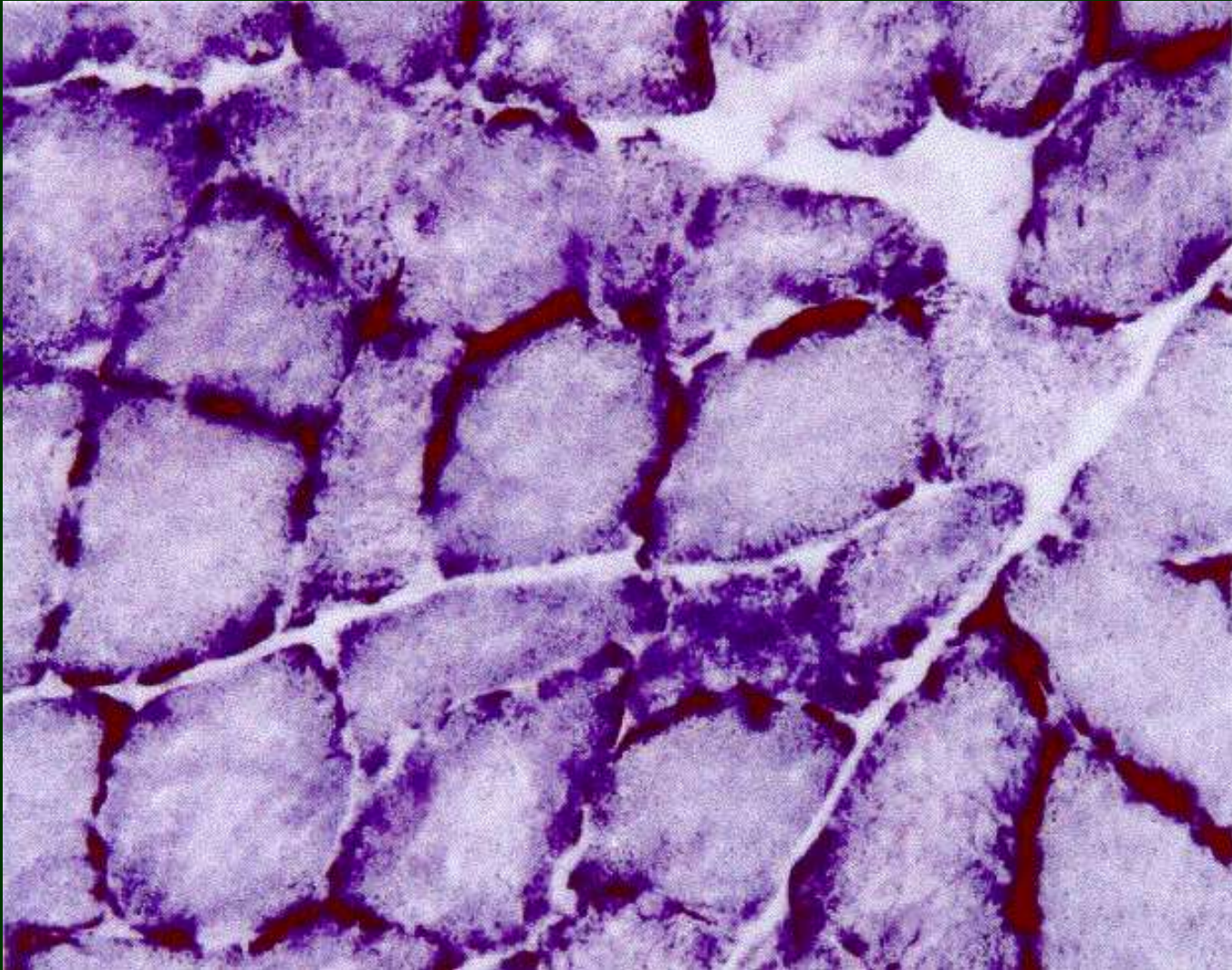
Mitochondrial myopathy



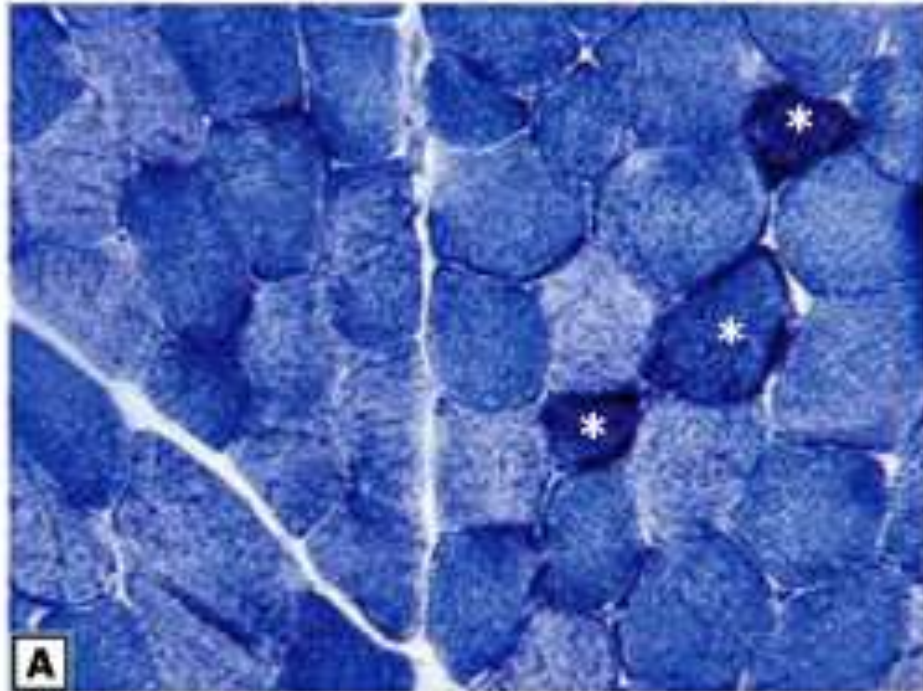


	Complex I NADH Ubiquinone Oxidoreductase	Complex III Ubiquinol Cytochrome c Oxidoreductase	Complex II Succinate Ubiquinone Oxidoreductase	Complex IV Cytochrome c Oxidase	Complex V ATP Synthase	ANT Adenine Nucleotide Translocator
SUBUNITS						
mtDNA	7	1	0	3	2	0
nDNA	~32	~9	4	10	10	1
TOTAL	~39	~10	4	13	12	1

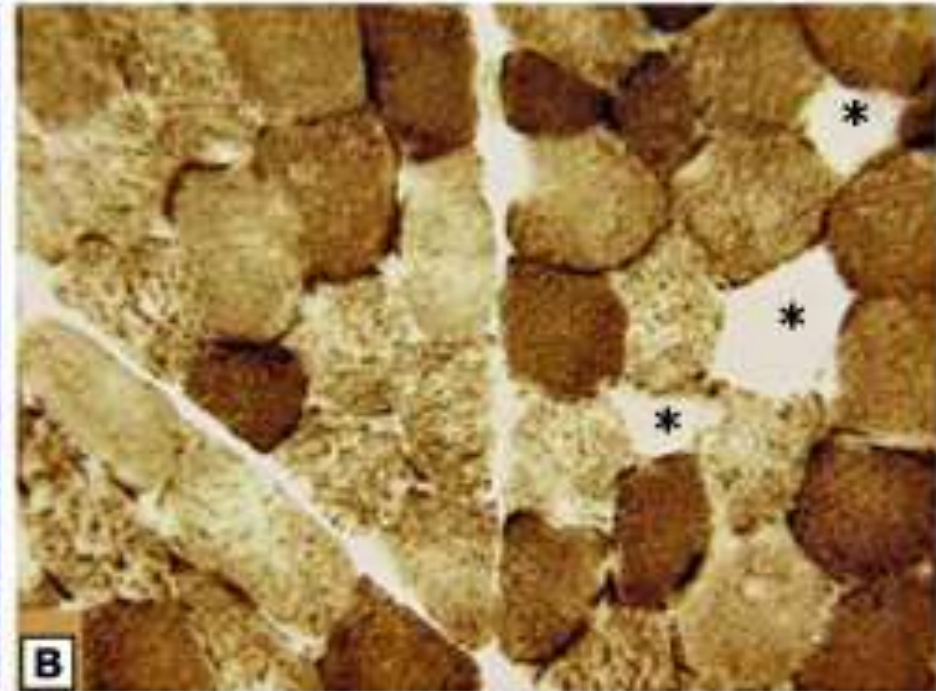
Ragged Red myopathy



Ragged red fibres



succinate dehydrogenase staining

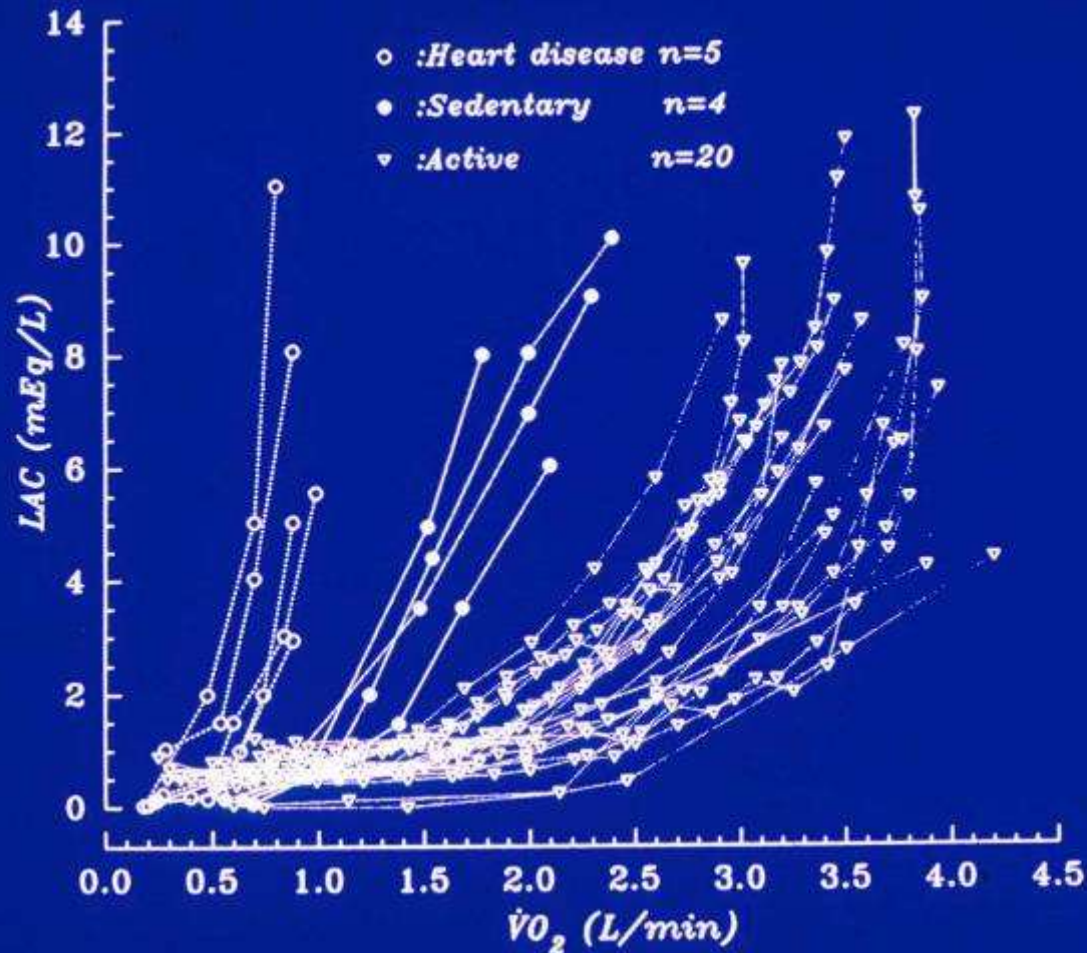


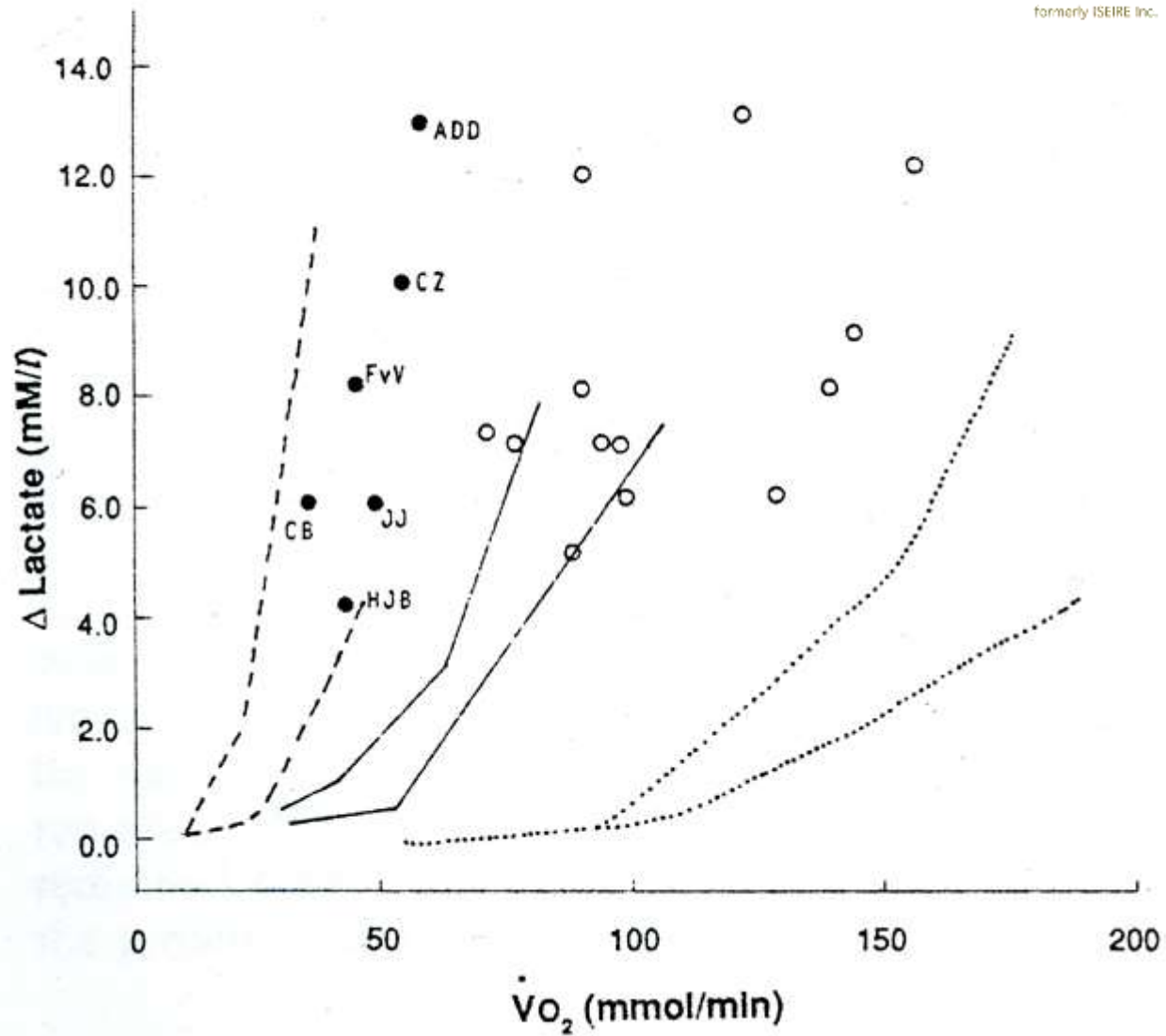
cytochrome c oxidase staining

Symptoms

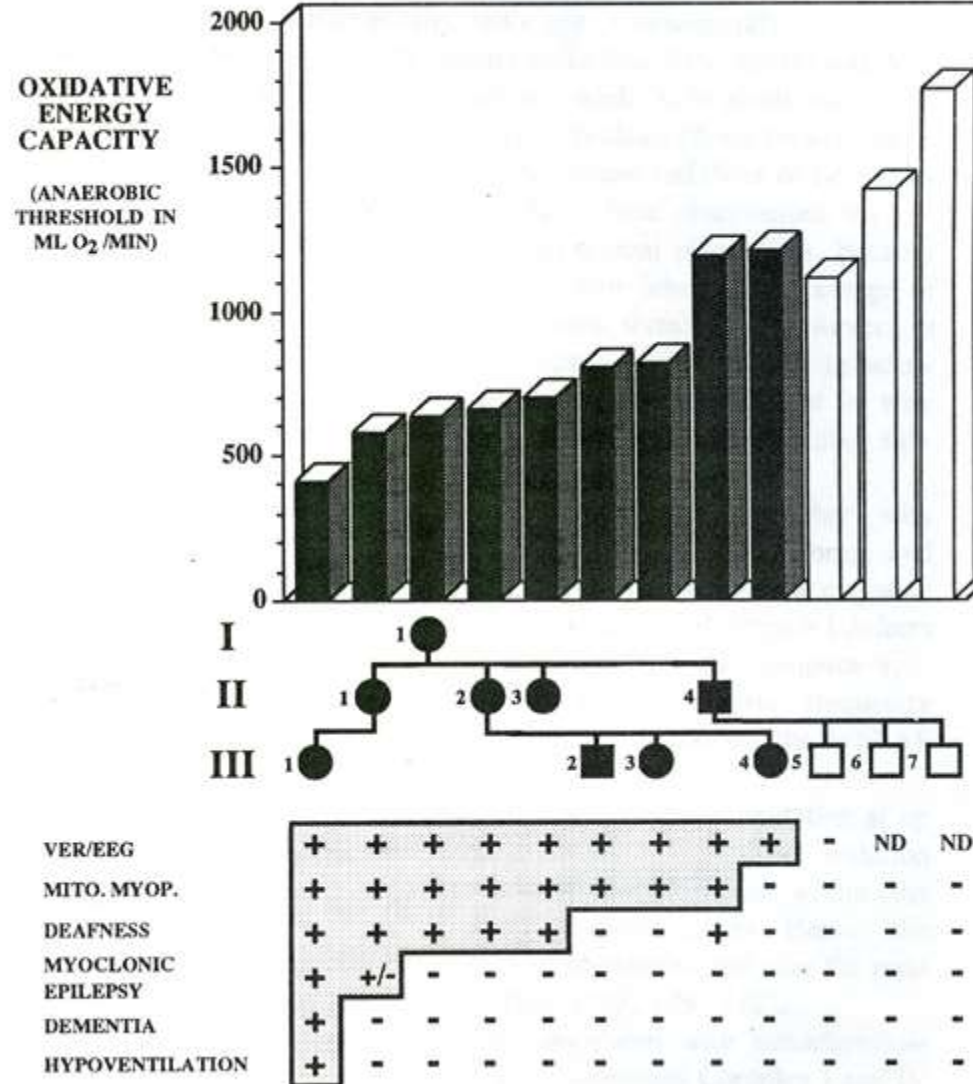
- Muscle cramps
- Fatigue
- Dyspnoea

Premature lactate accumulation in heart disease

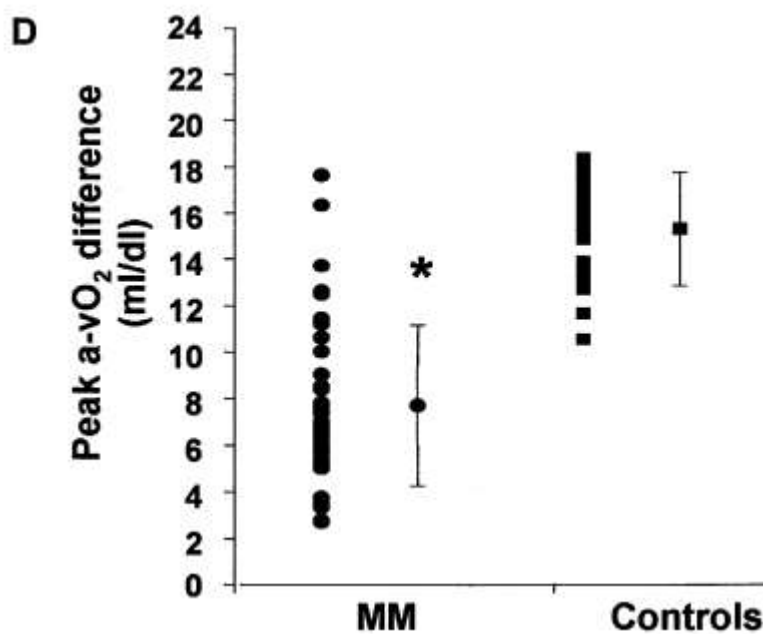
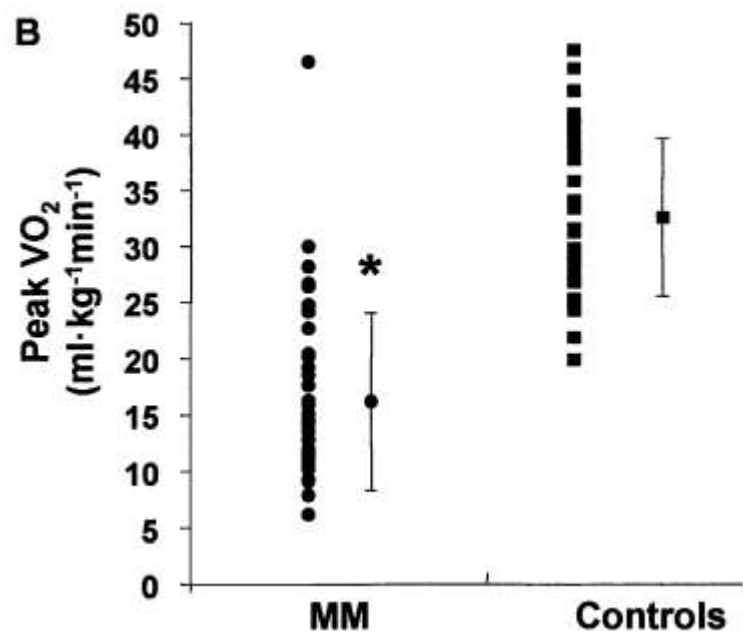
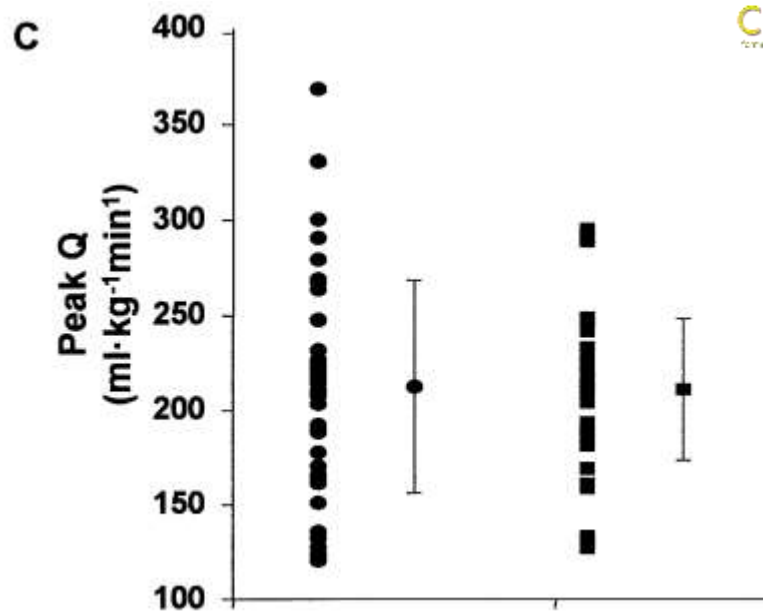
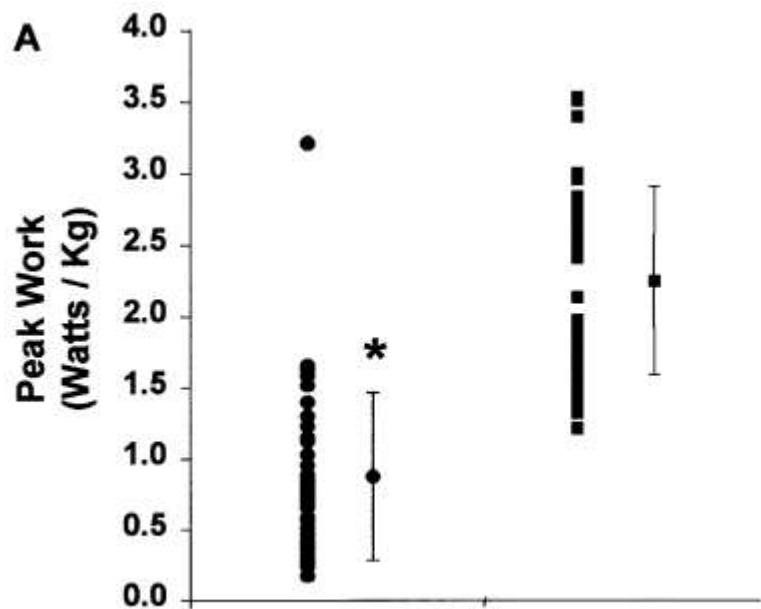




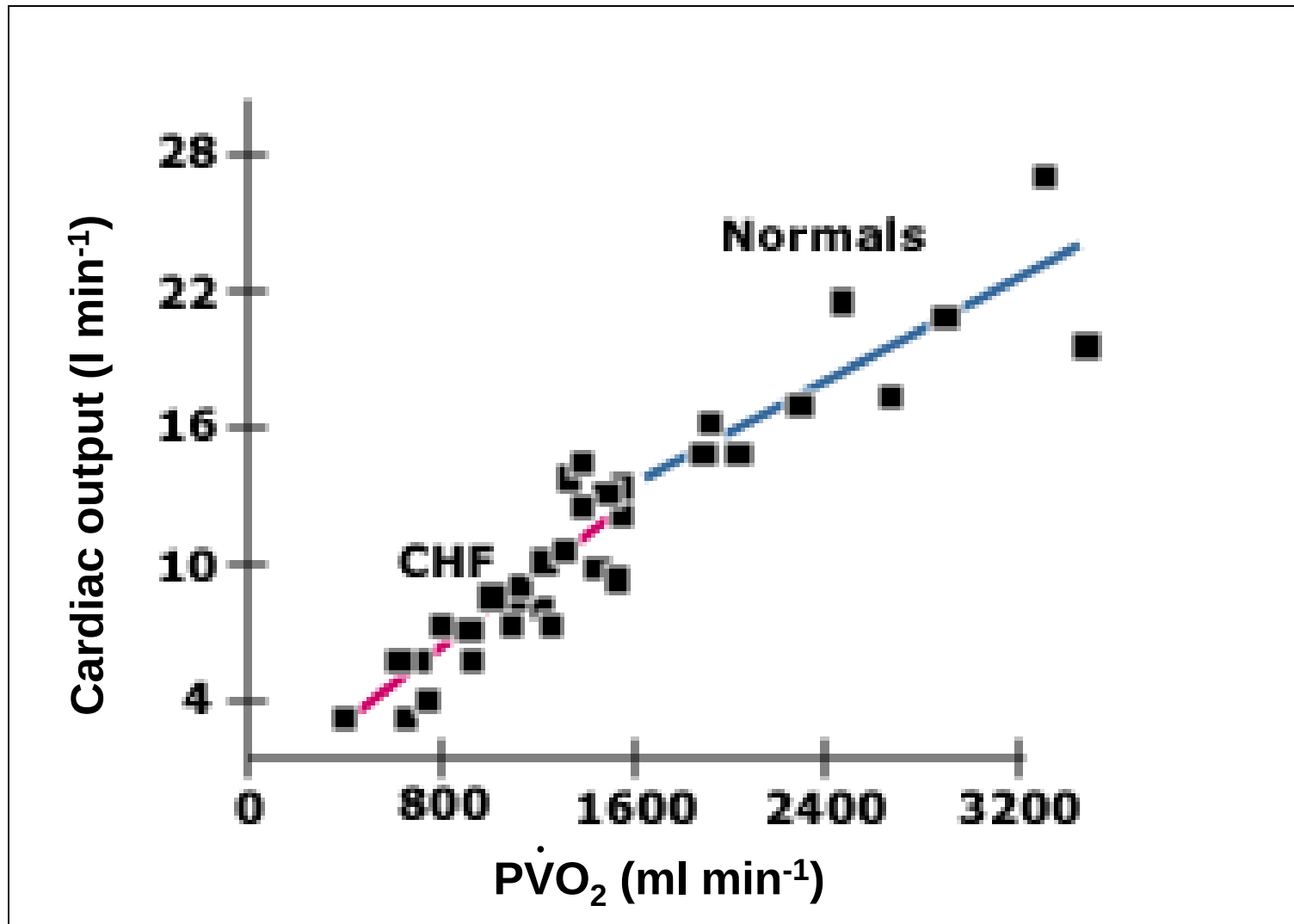
Bogaard et al. 1988



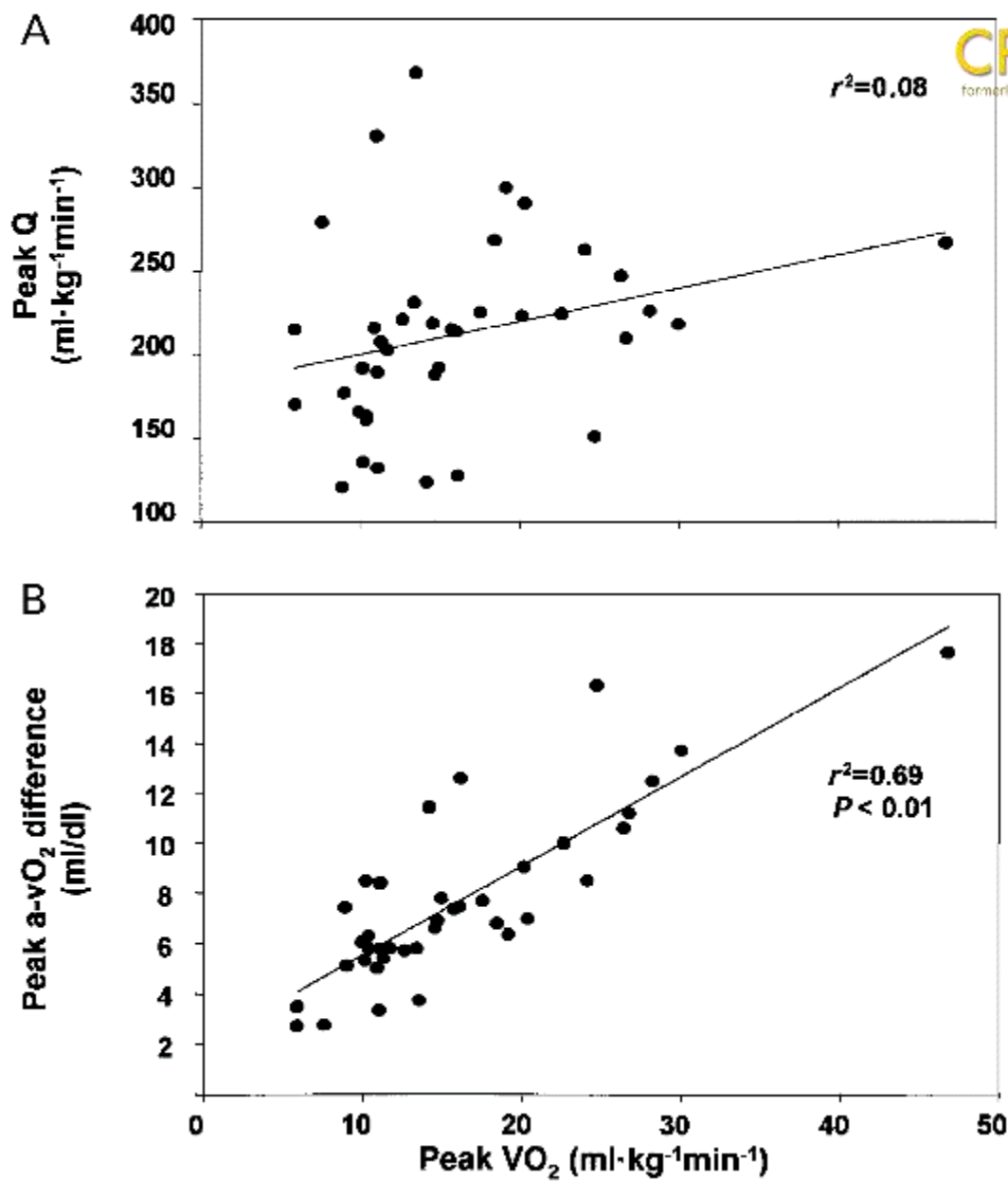
Wallace et al. 1988

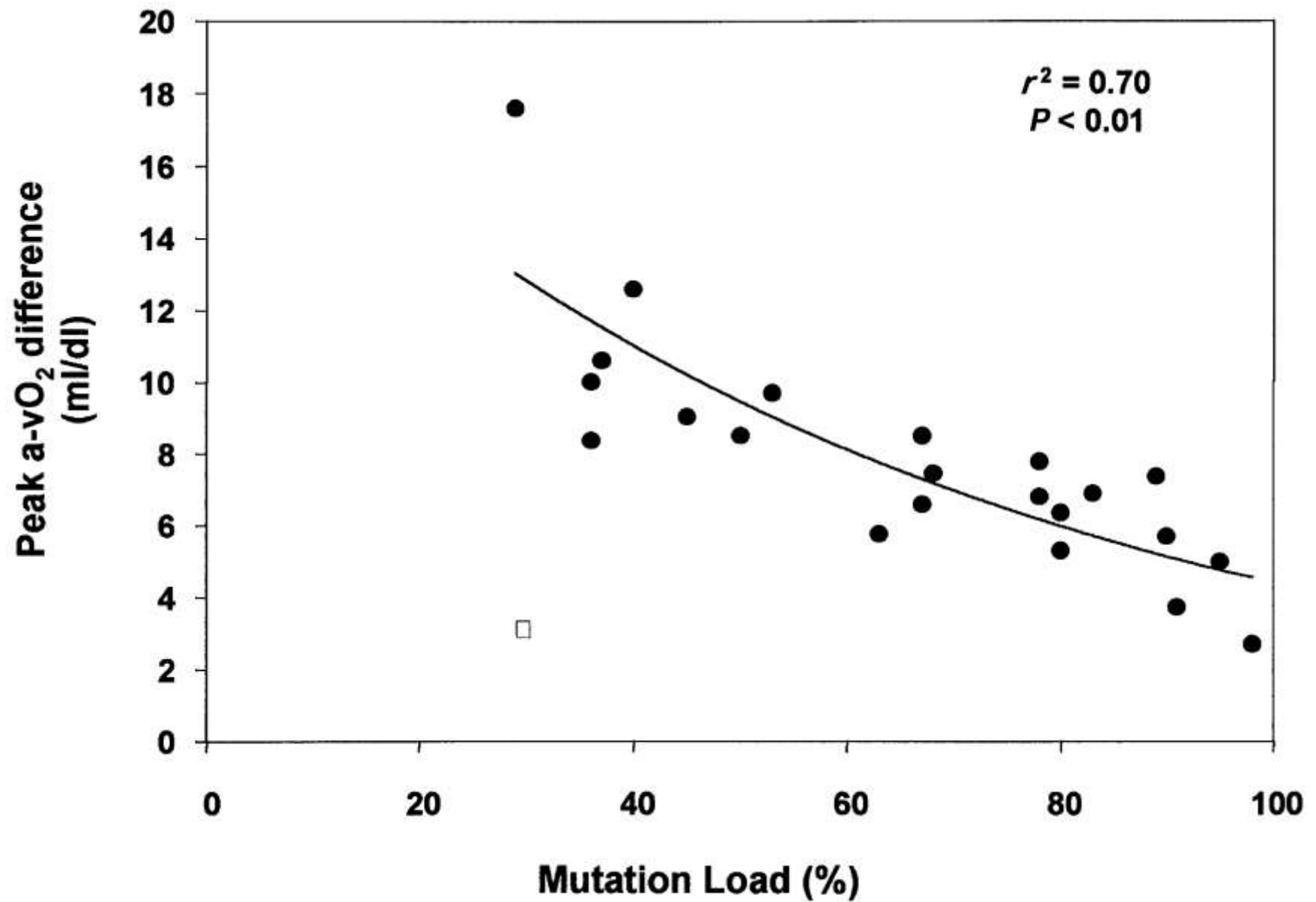


$$\dot{V}O_2 = CO \times \text{arteriovenous } O_2 \text{ difference}$$

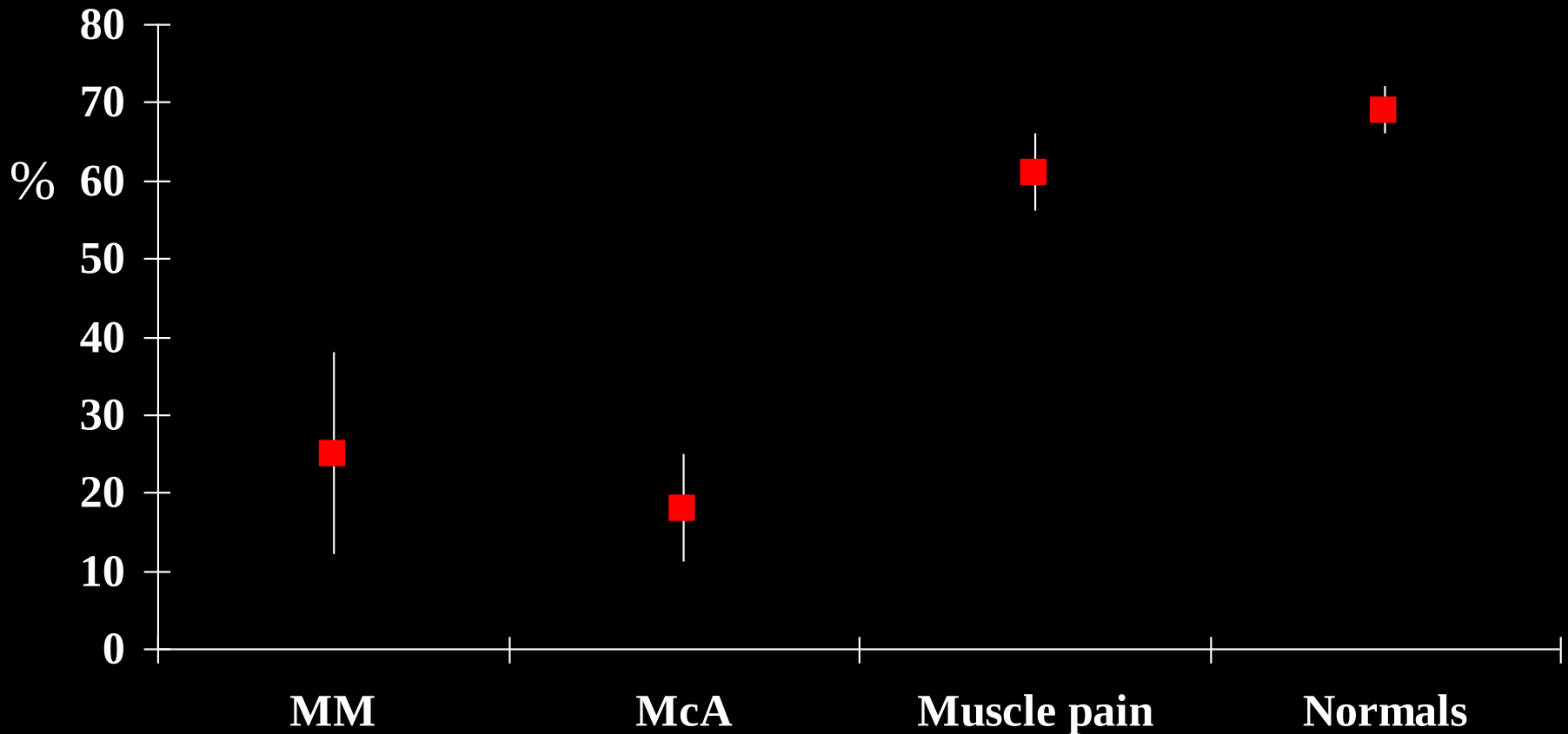


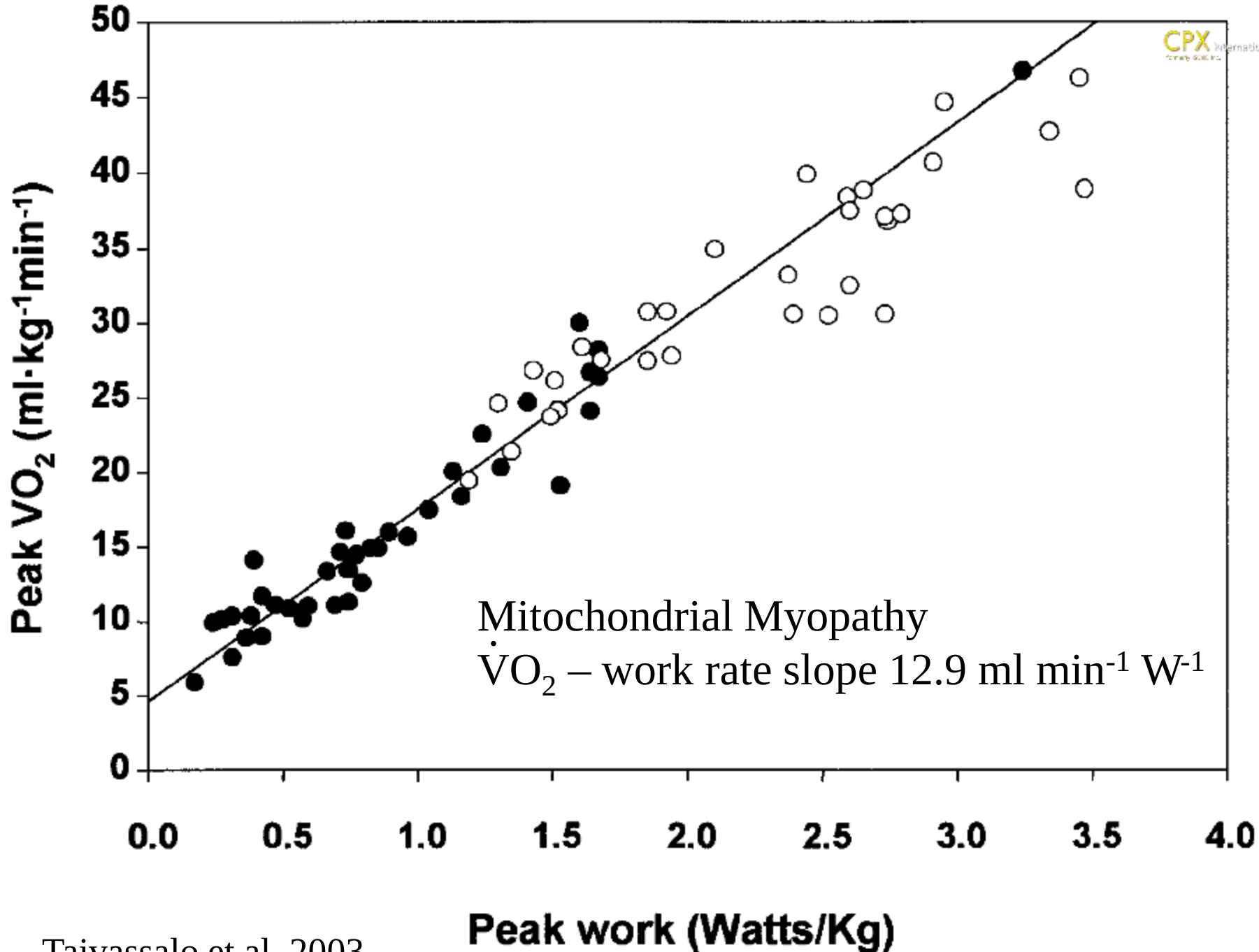
Sullivan et al. 1989





Near infra-red spectroscopy $\Delta(\text{deoxyHb})$ rest-peak





Ammonia

- 5 patients with MM and 5 patients with McArdle's disease
- McArdle's disease patients had very elevated ammonia, but MM patients had similar values to controls, but at lower $\dot{V}O_2$ (leftward shift)

Metabolic myopathies

- Muscle cramp/pain
- Low maximum VO_2
- Abnormalities of lactic acidosis threshold
- High VO_2 - work rate slope
- Low oxygen-pulse
- Elevated NH_3
- Elevated lactate
- Elevated creatine kinase