

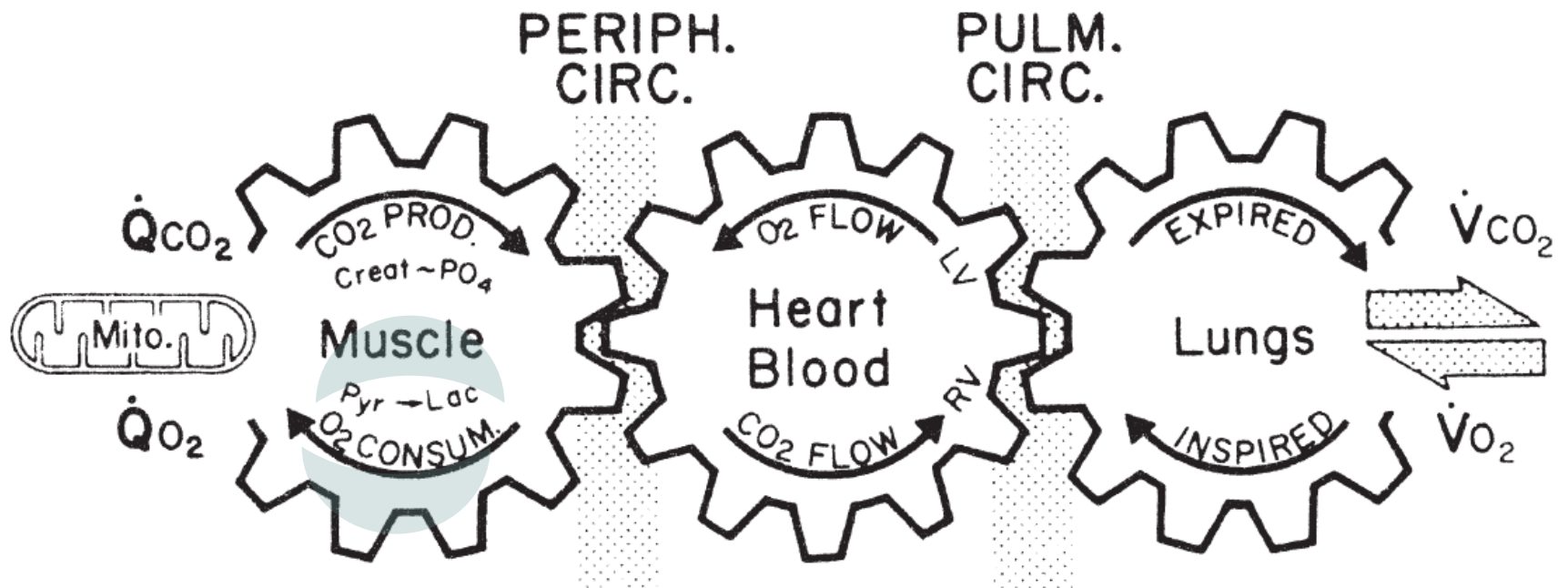
Gas Exchange Patterns in Metabolic Myopathies

M.S. Riley

MUSCLE
ACTIVITY

O_2 & CO_2
TRANSPORT

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

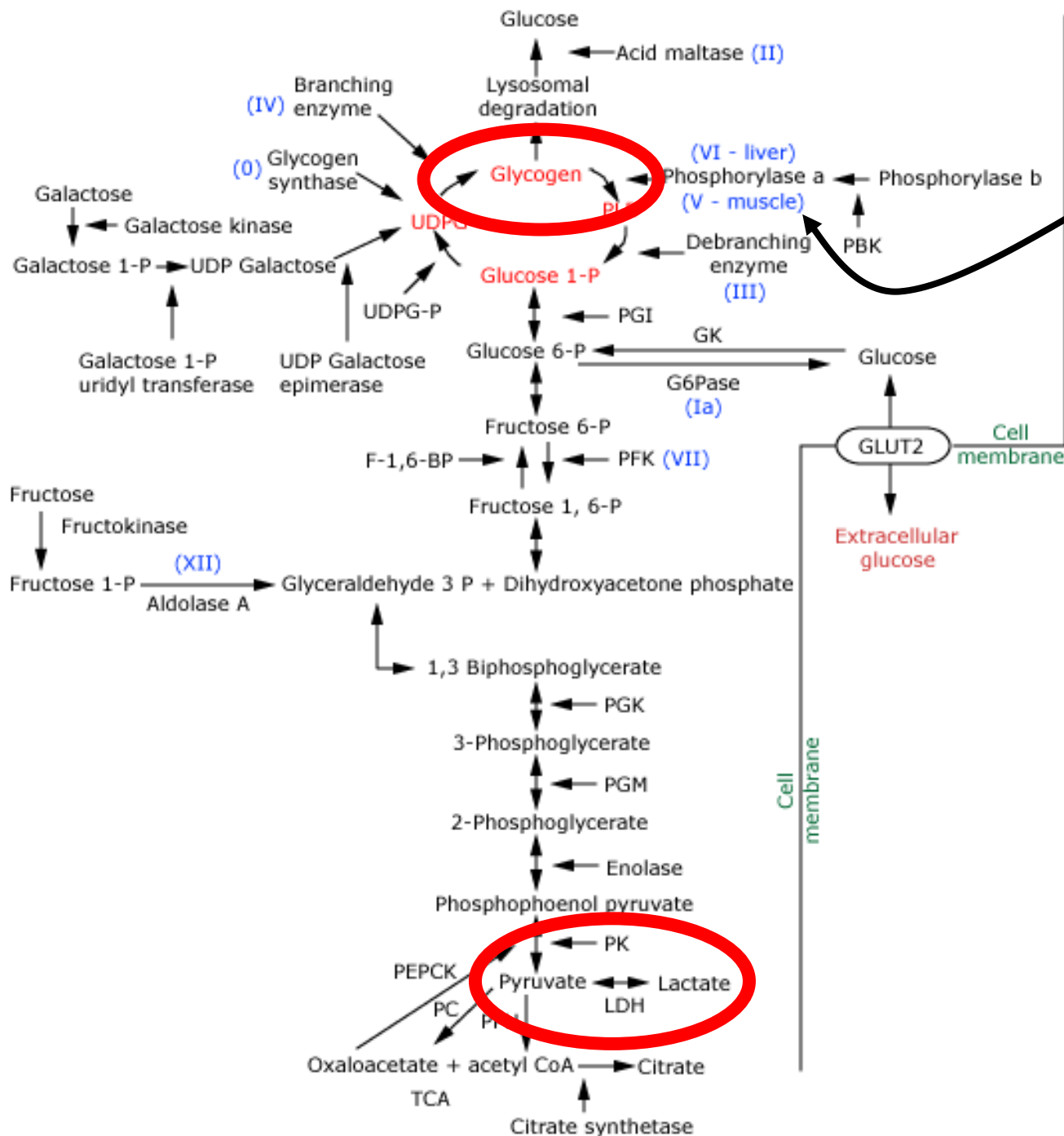


Metabolic Myopathies

Defective Cellular Energy Production

- Defects in glycolysis & glycogenolysis
- Defects in mitochondrial function
- Defects in lipid metabolism

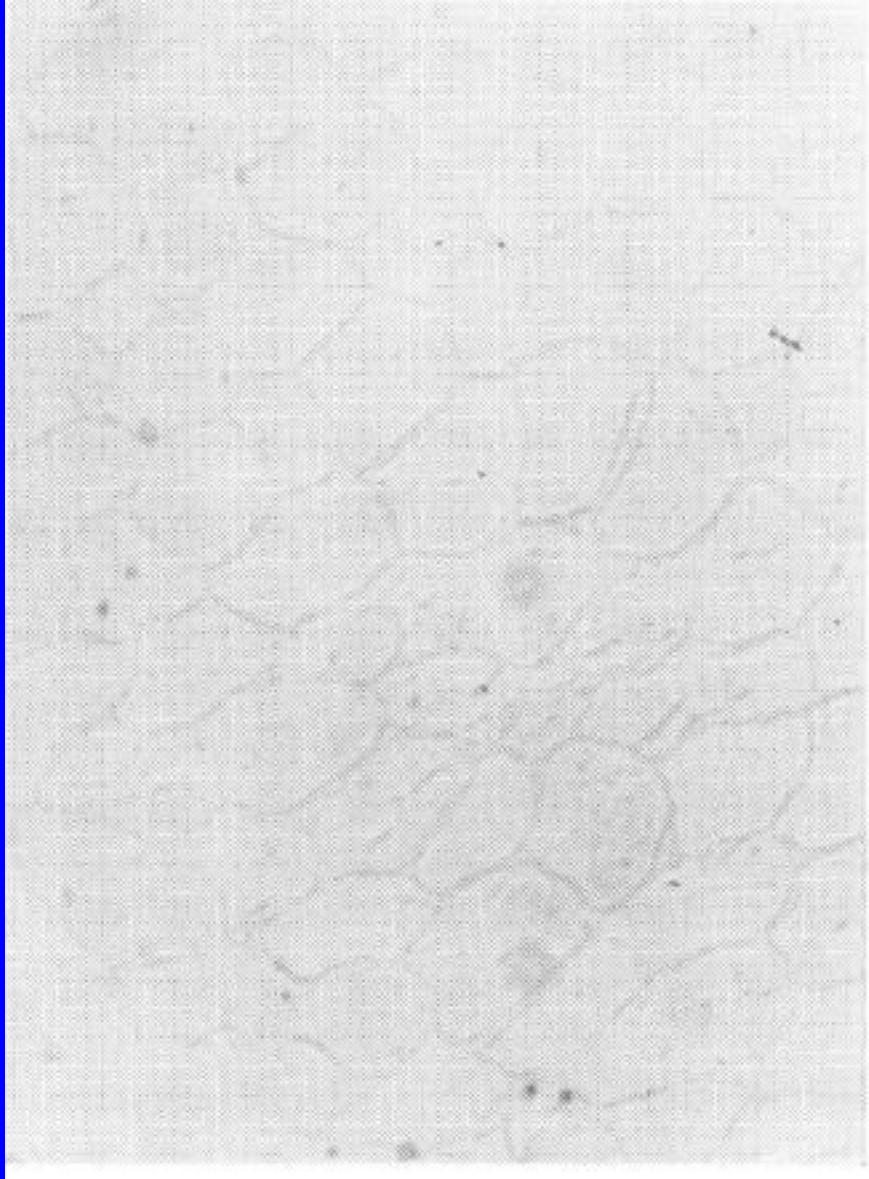
Defects in Glycolysis/Glycogenolysis



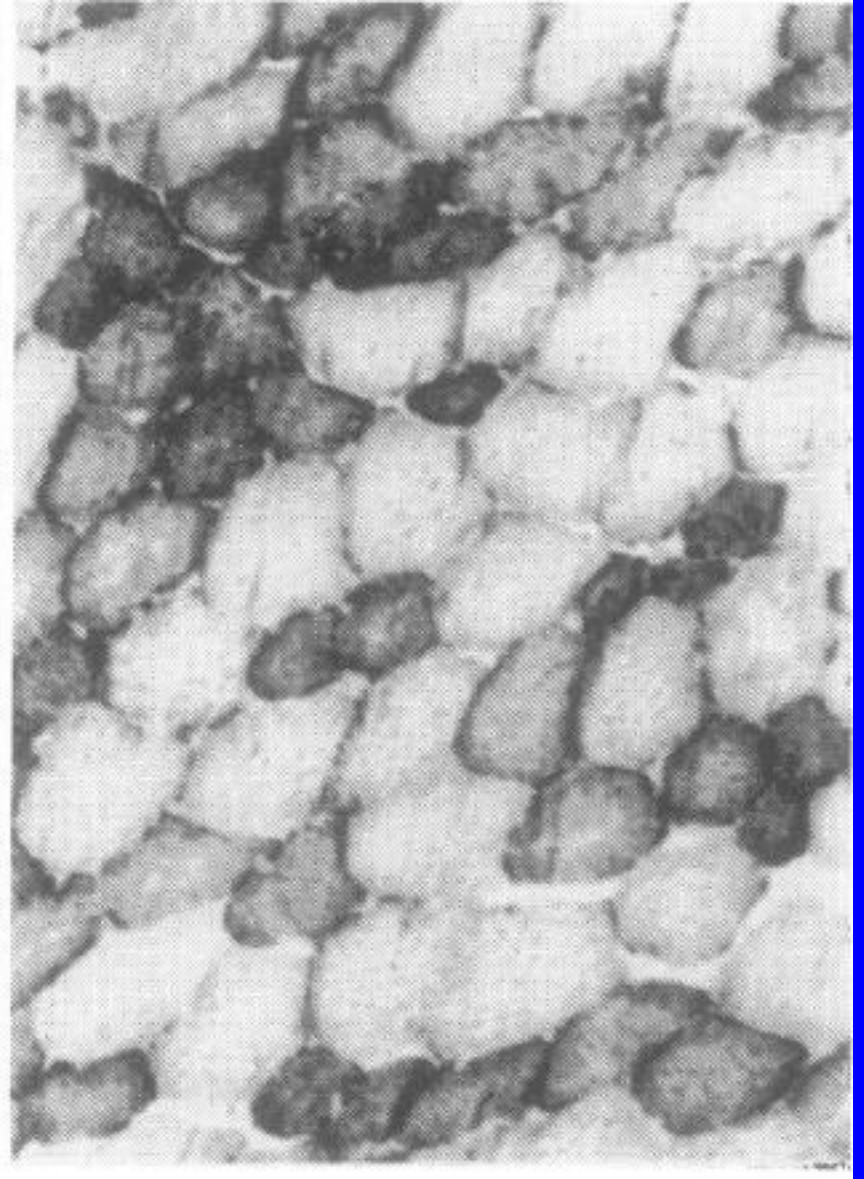
McArdle's disease

Glycolytic pathway

Phosphorylase stain



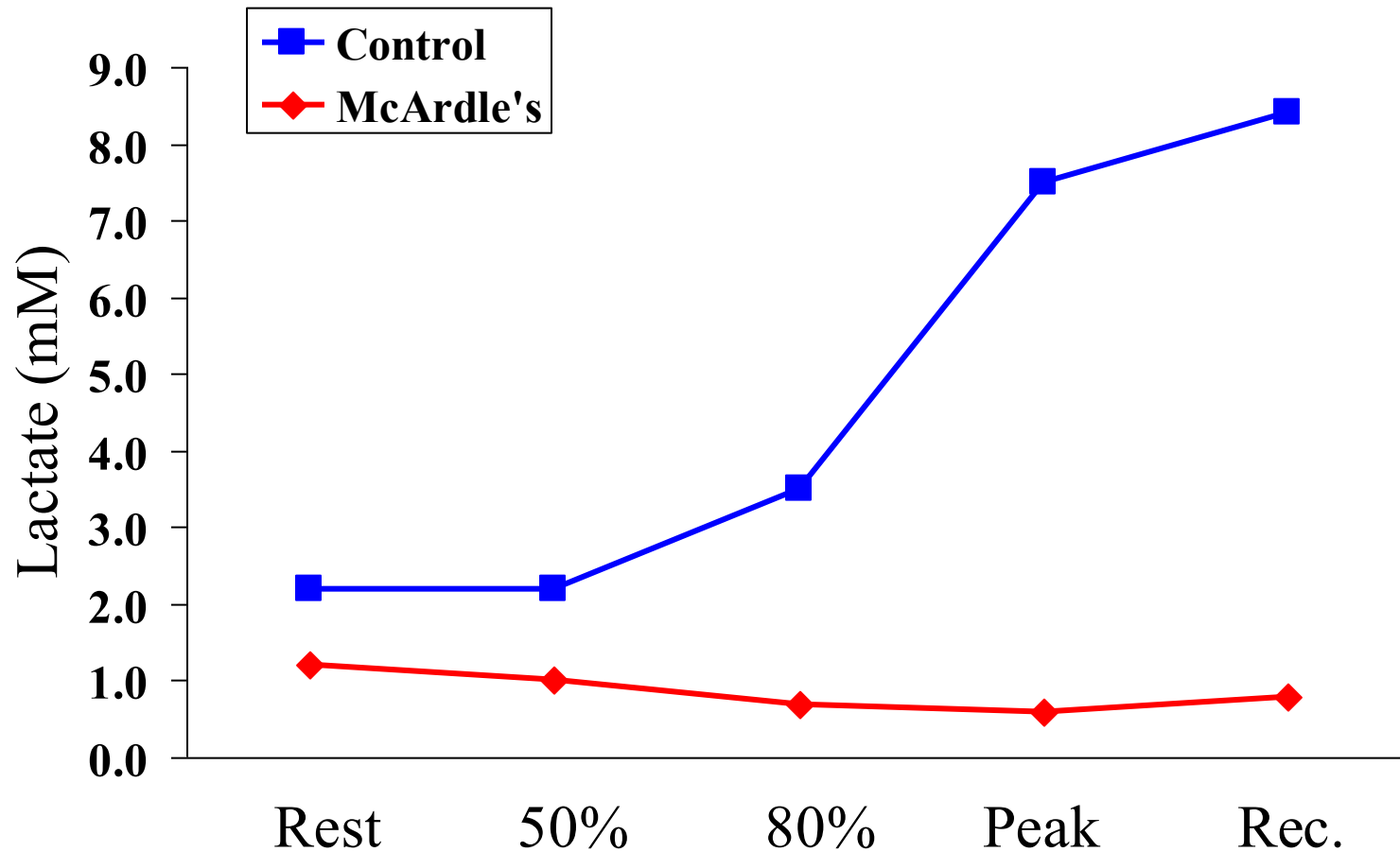
Glycogen stain



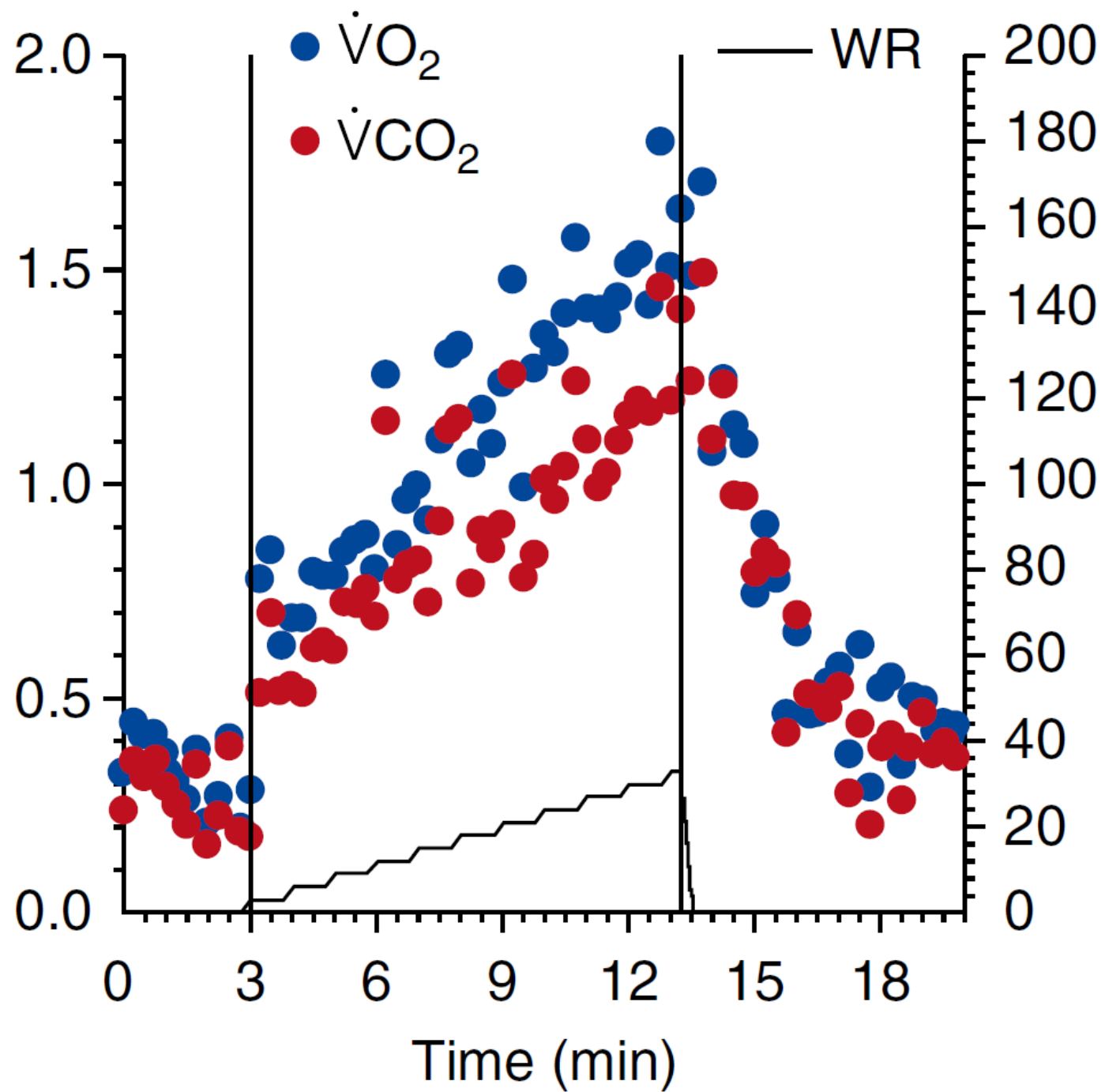
Features

- Muscle cramps
- Exertional fatigue
- Myoglobinuria
- High serum creatine kinase (CK)

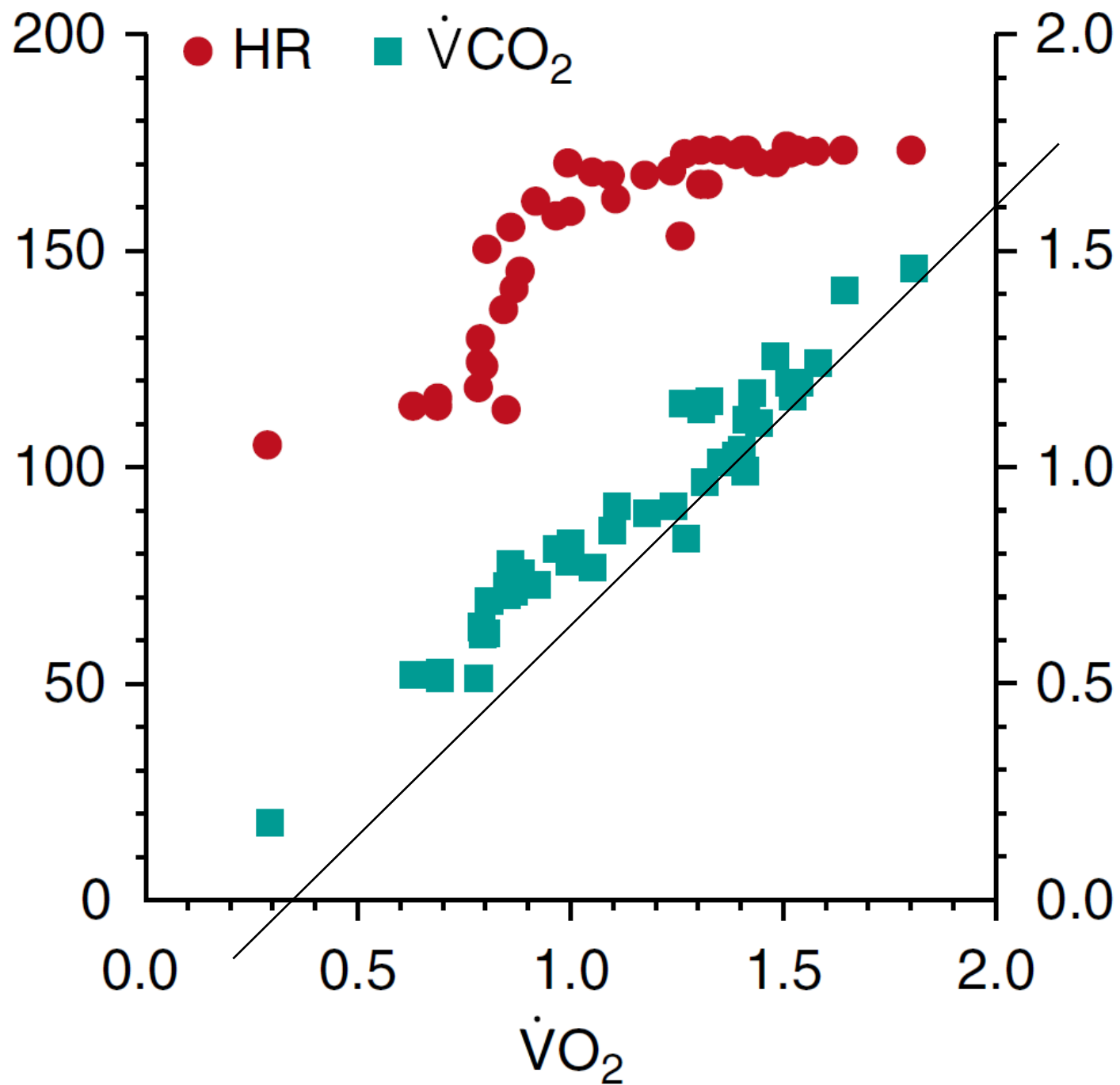
Lactate in McArdle's Disease



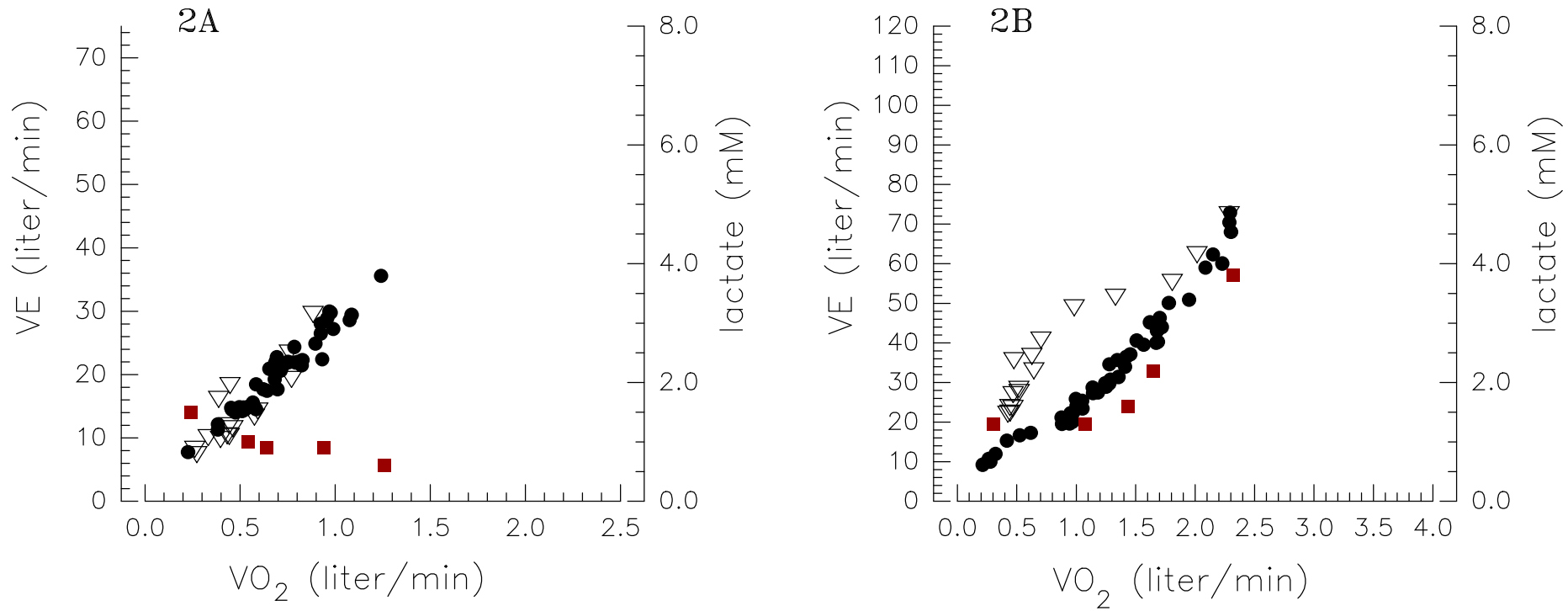
McArdle's
22 yr male



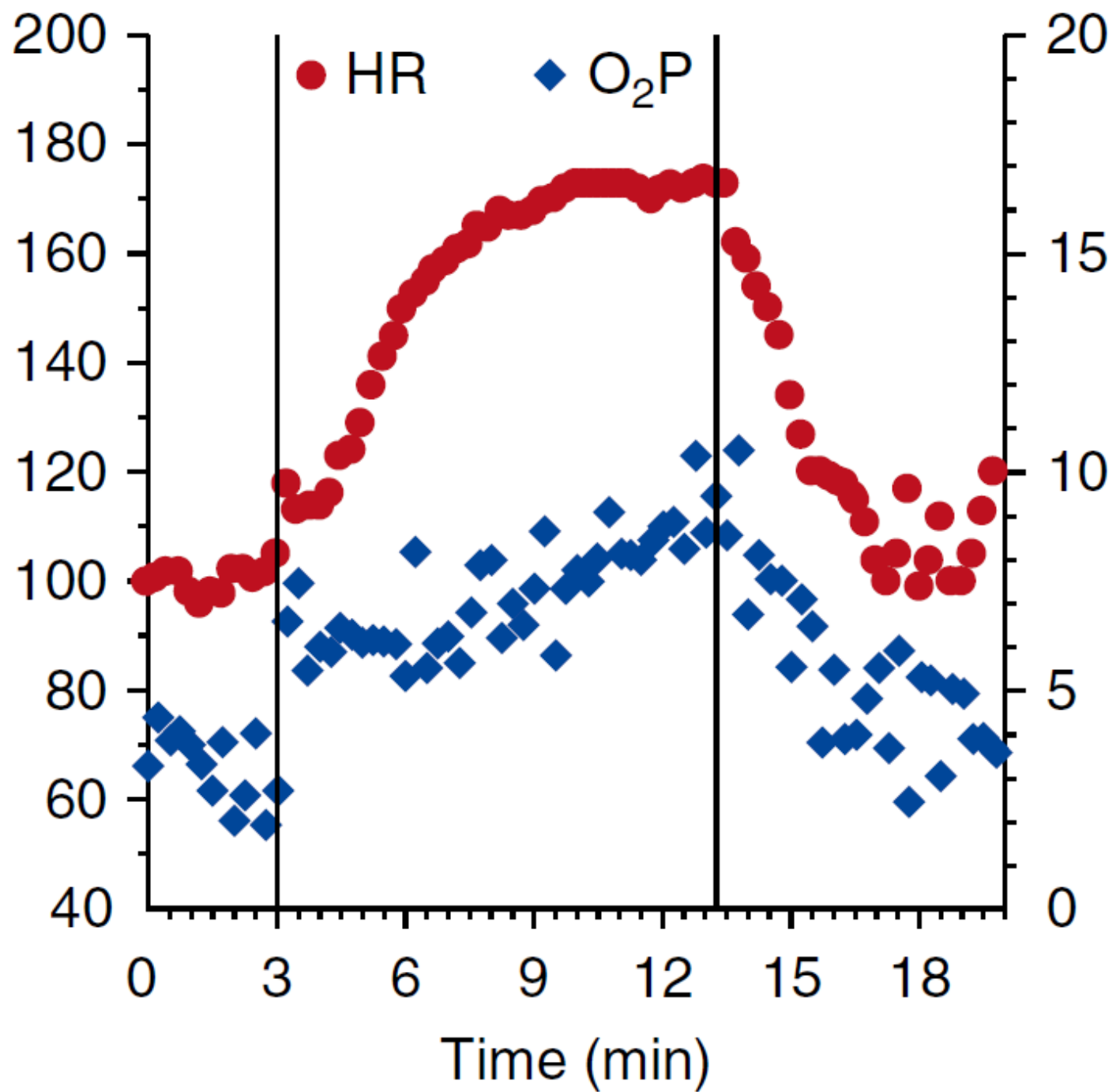
McArdle's
22 yr male



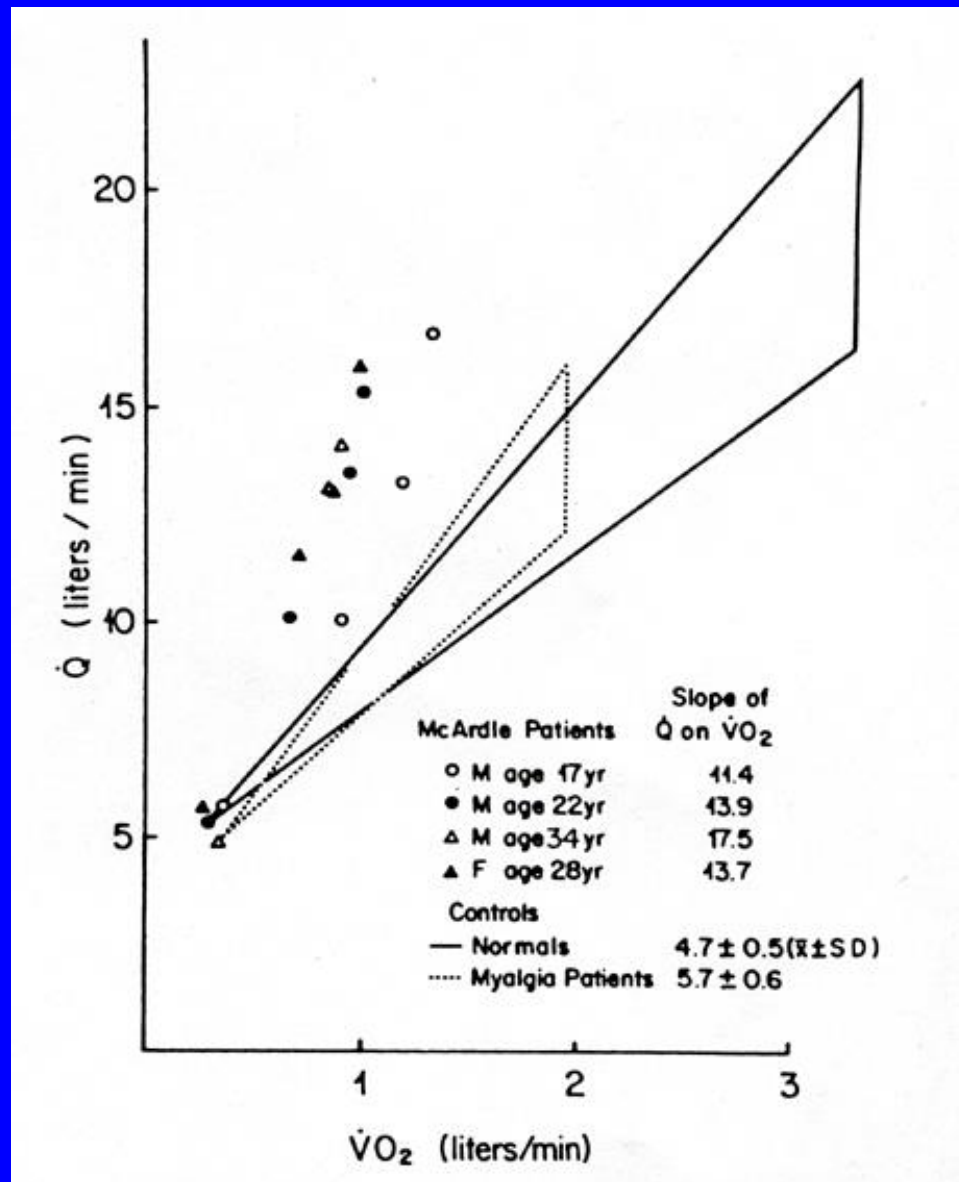
Ventilation in McArdle's disease 17 y/o female and control



McArdle's
22 yr male



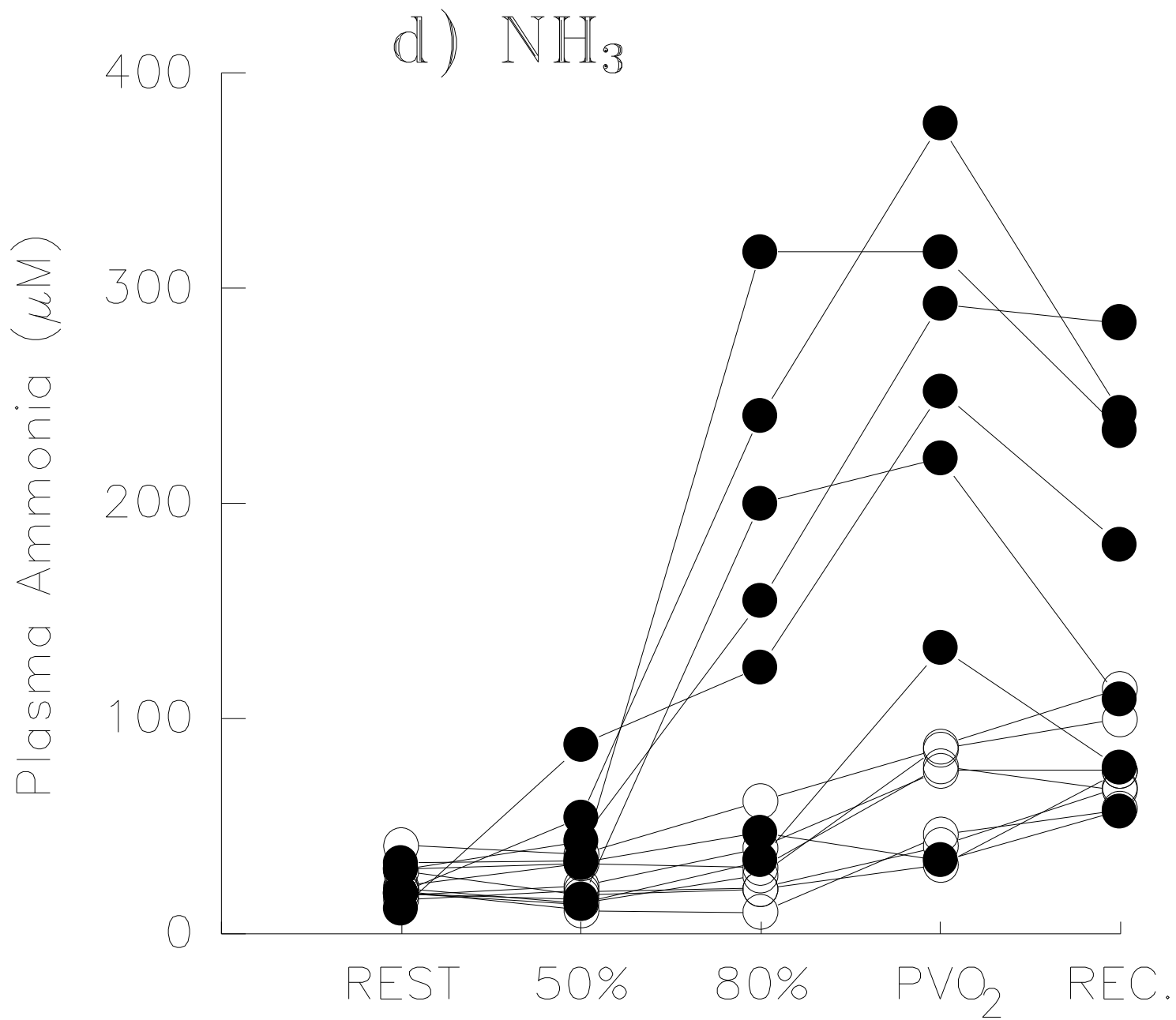
$\dot{Q}$ - $\dot{V}O_2$ relationship in McArdle's



McArdle's disease

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

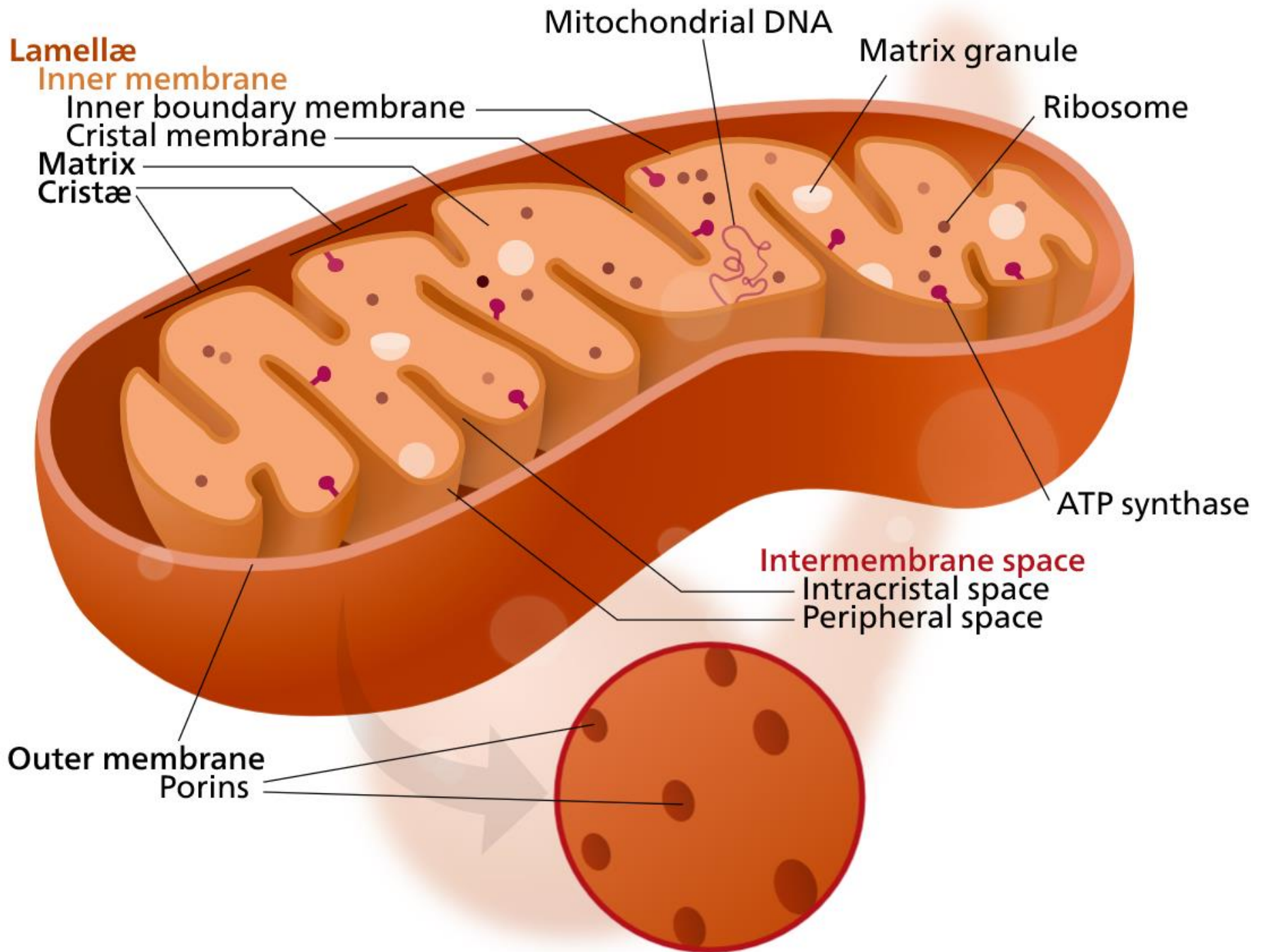


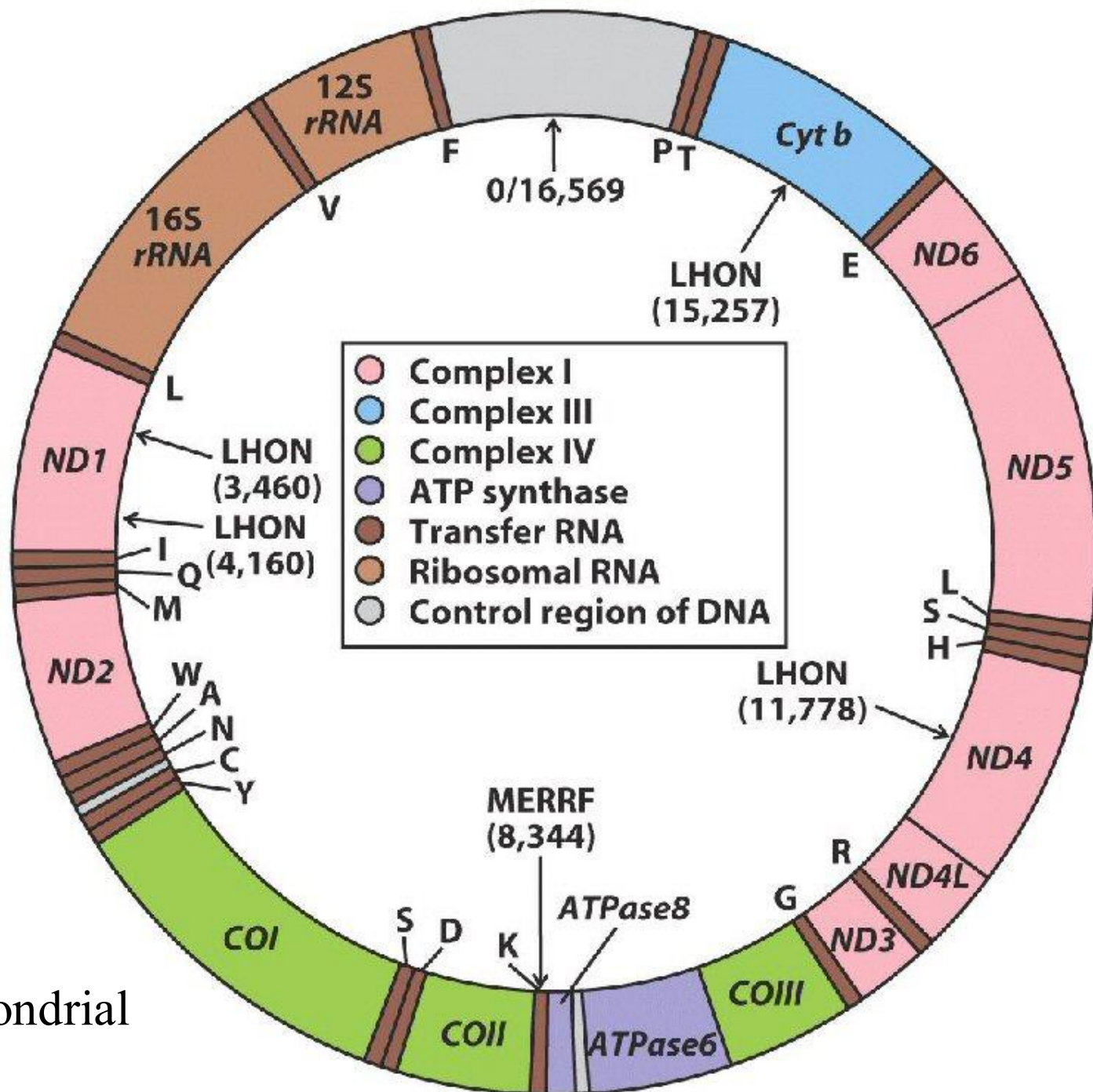
NH₃ production during exercise



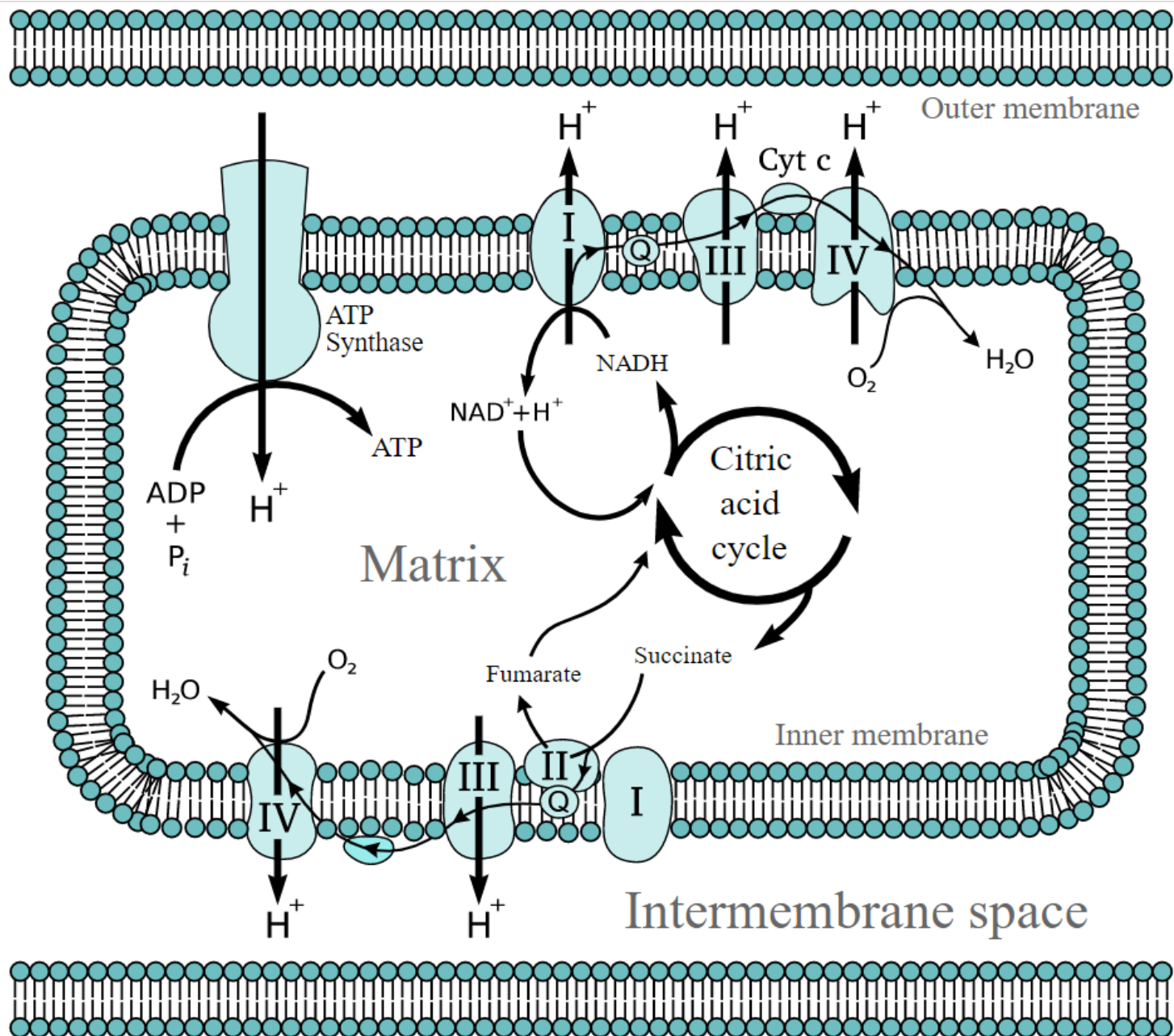
?gluconeogenesis

Mitochondrial myopathies

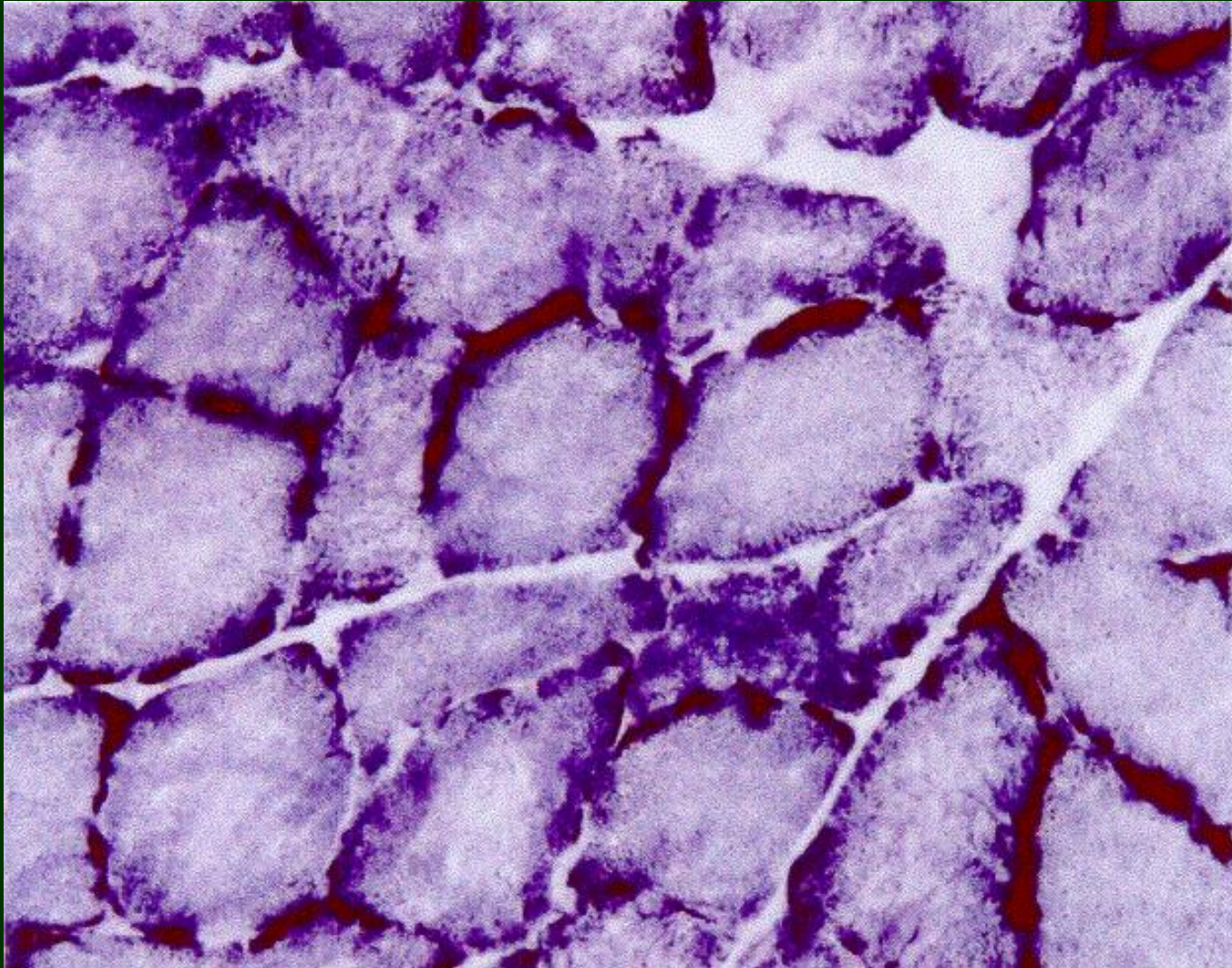




Mitochondrial
DNA



Ragged Red myopathy



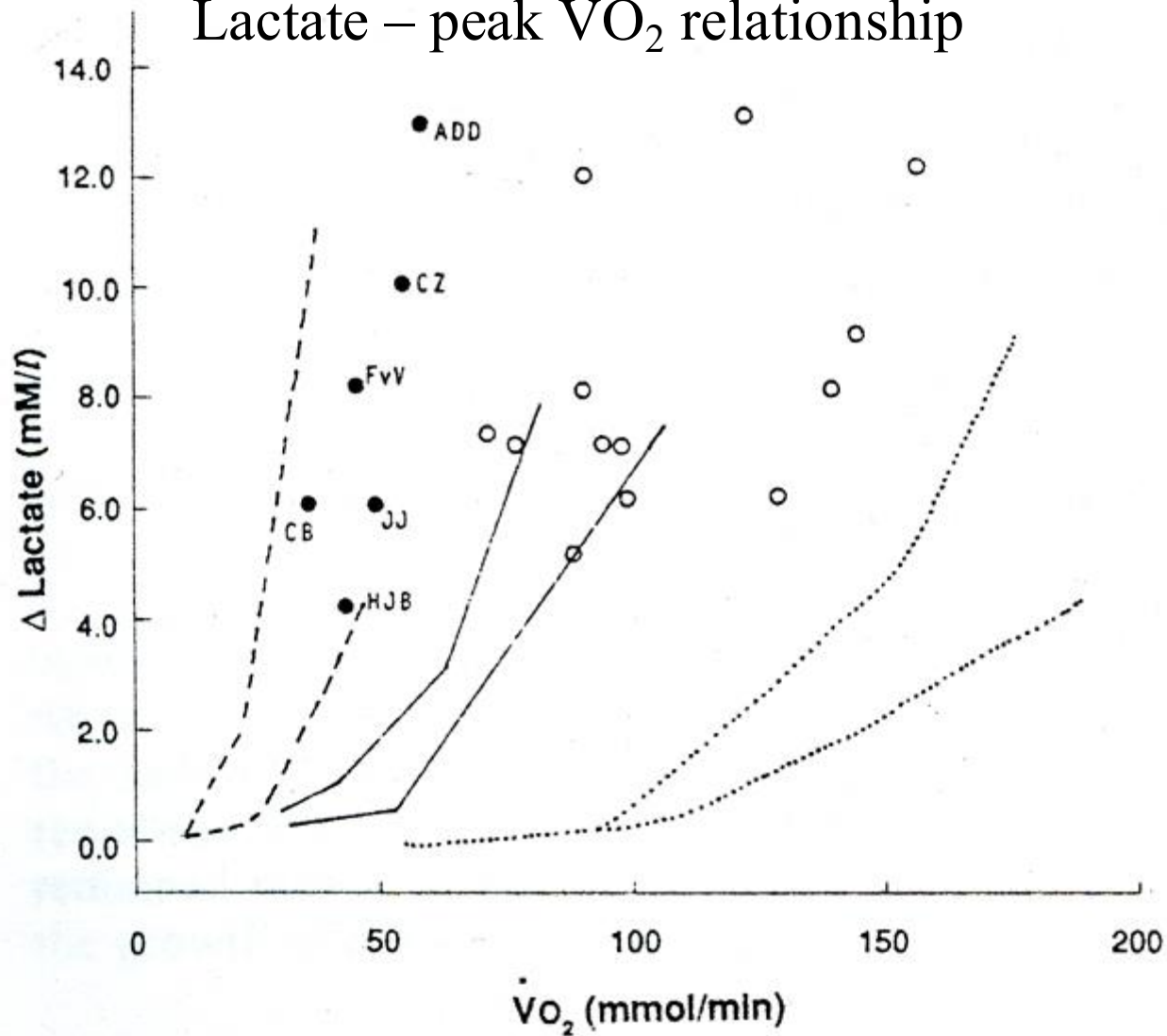
Mitochondrial Myopathy

Symptoms

- Muscle cramps
- Fatigue
- Dyspnoea

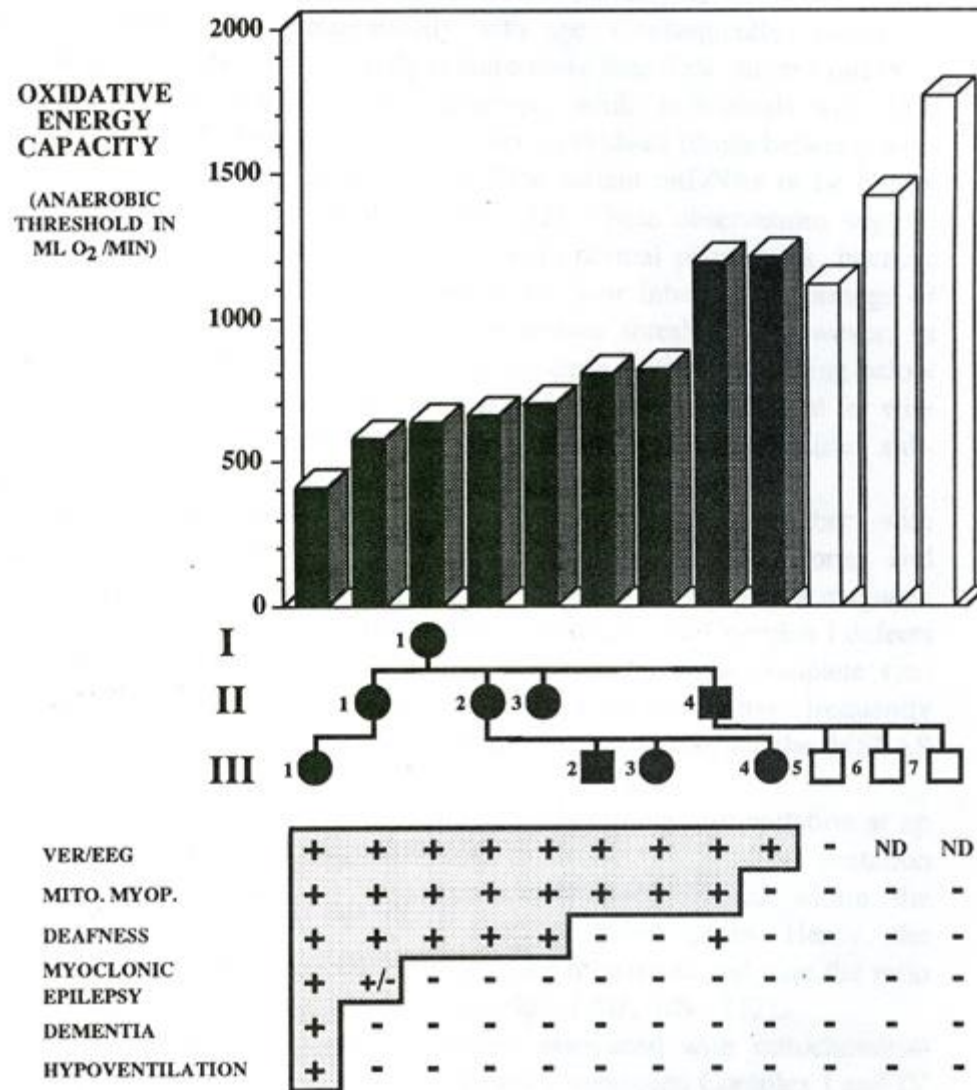
Mitochondrial myopathy

Lactate – peak $\dot{V}O_2$ relationship



Bogaard et al. 1988

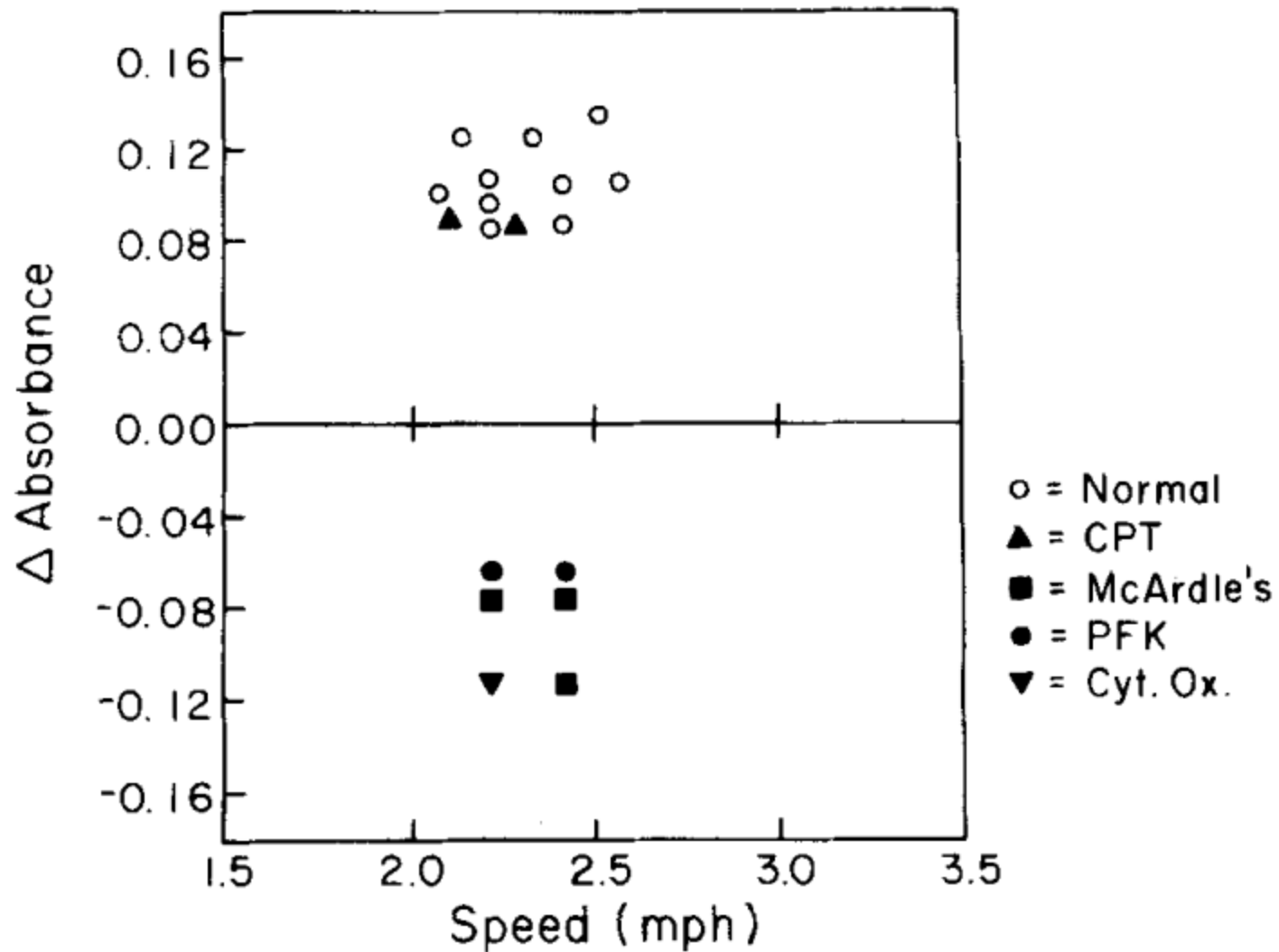
Mitochondrial myopathy



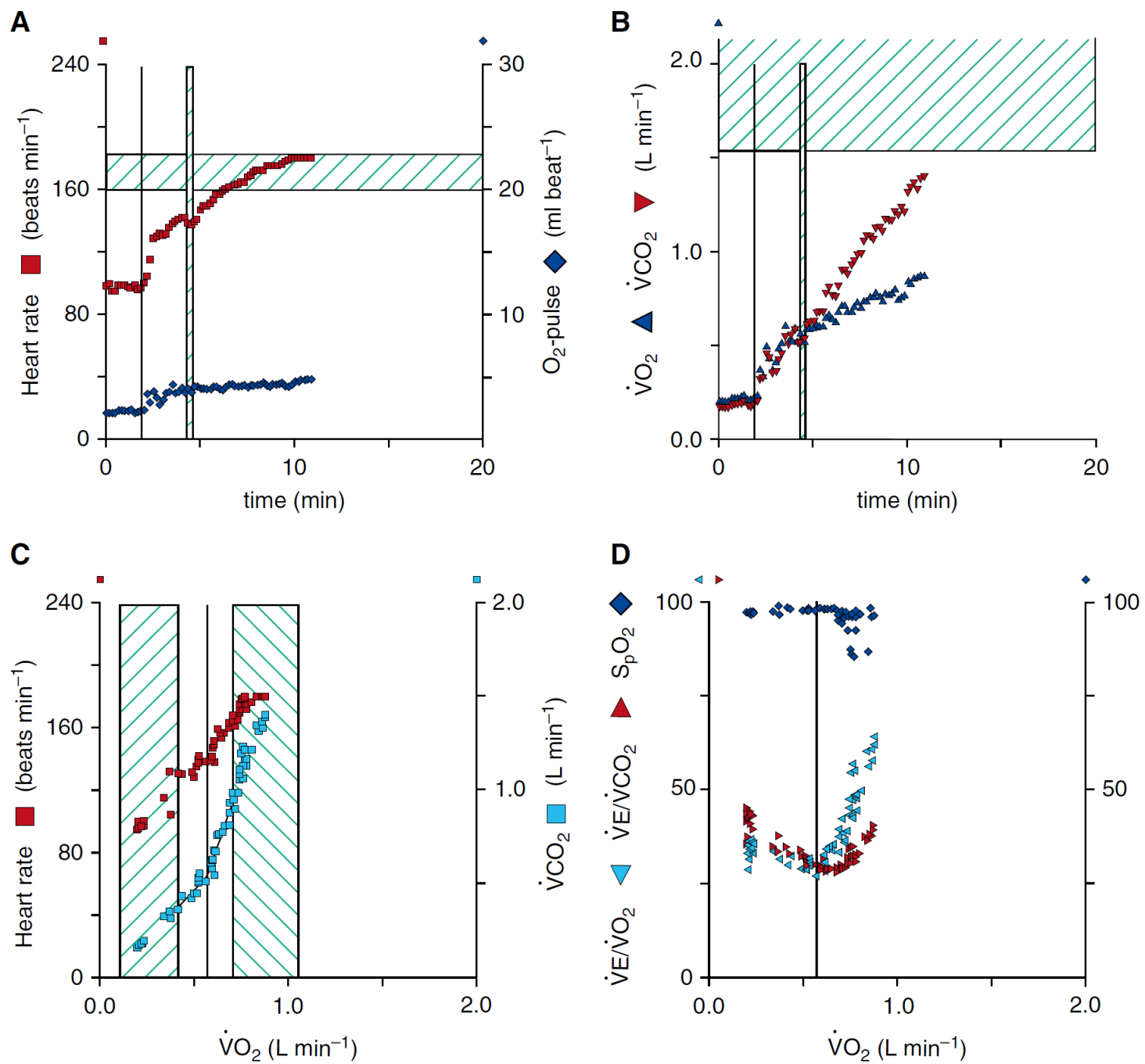
Wallace et al. 1988

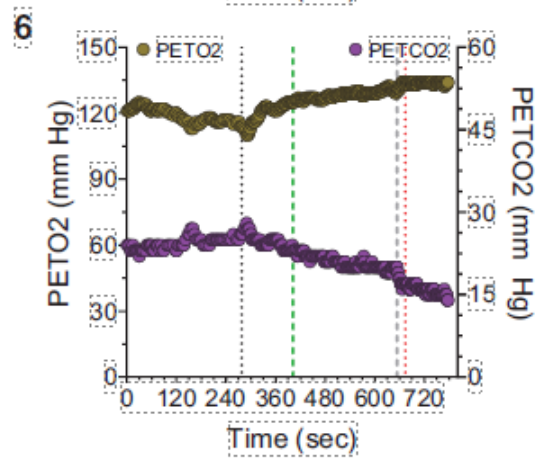
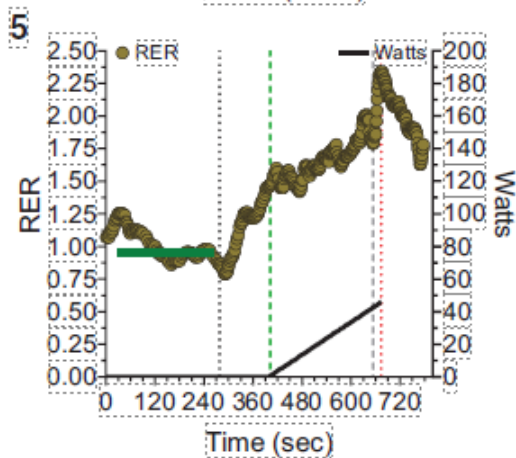
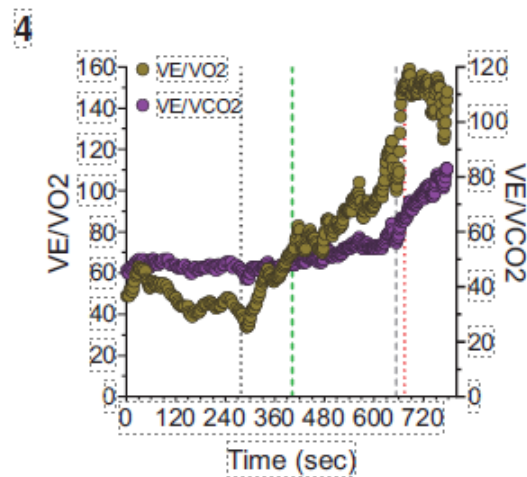
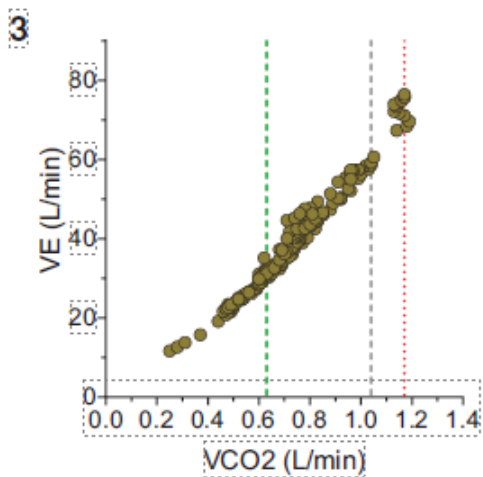
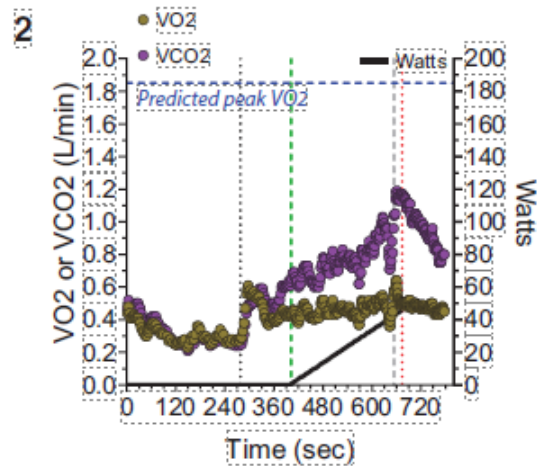
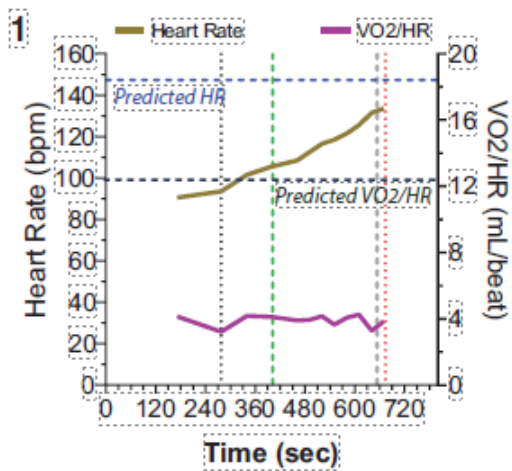
Mitochondrial myopathy

Mitochondrial myopathy near infra-red spectroscopy



Bank & Chance. Ann Neurol 1994;36:830-837.



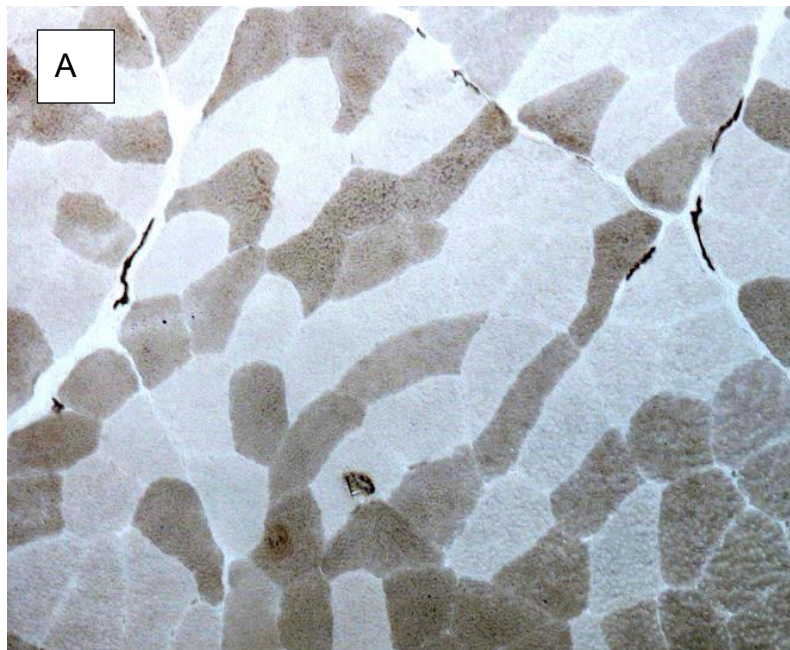


Martens et al. 2024

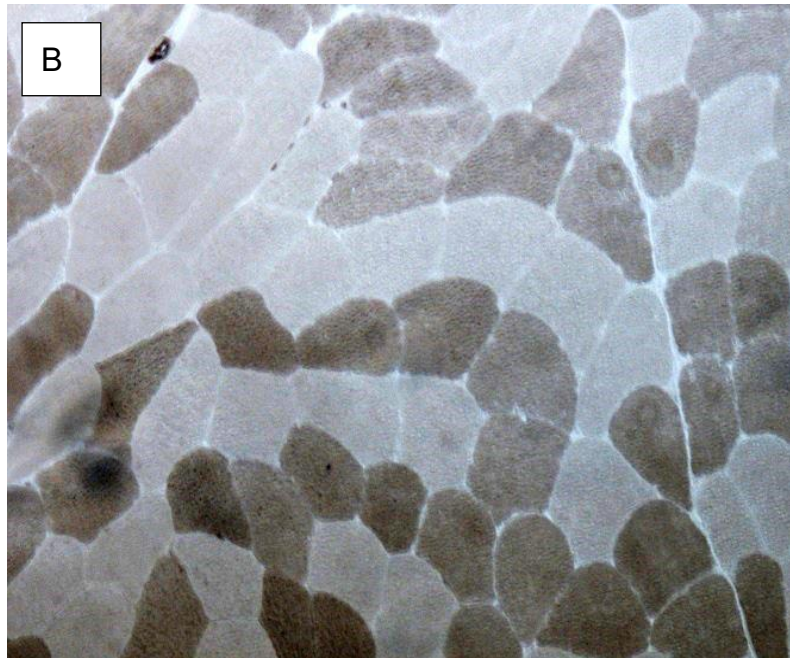
Some other causes of mitochondrial dysfunction

- Type II fibre predominance
- Chronically elevated CK
- Statins
- Chemotherapy

A

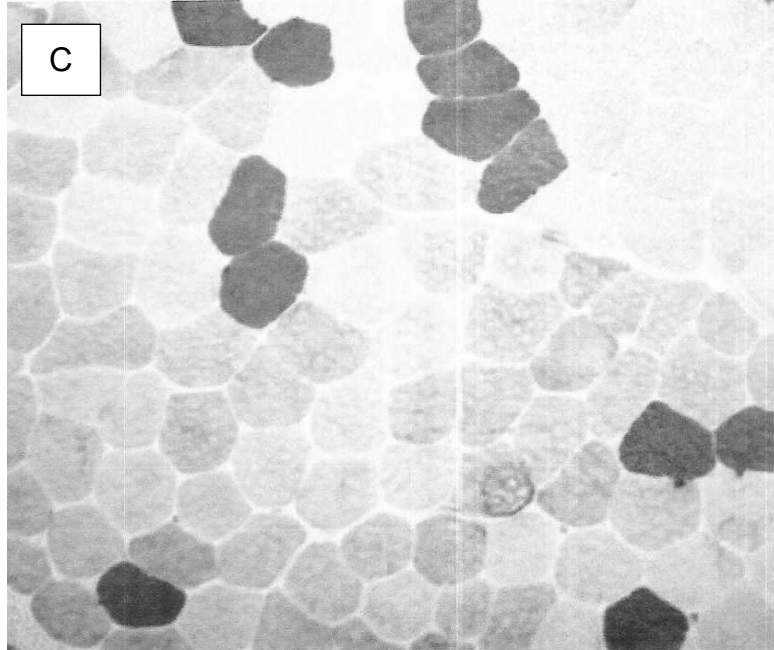


B

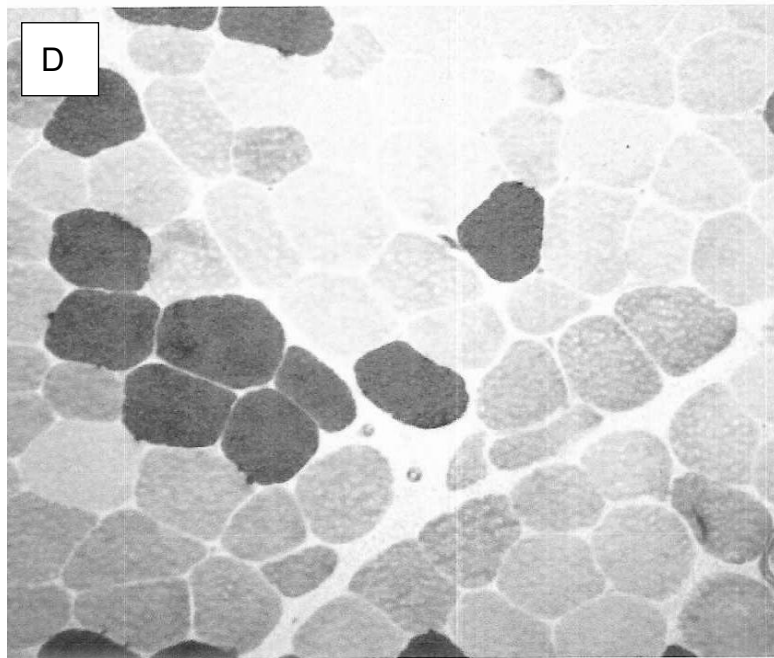


CONTROL

C



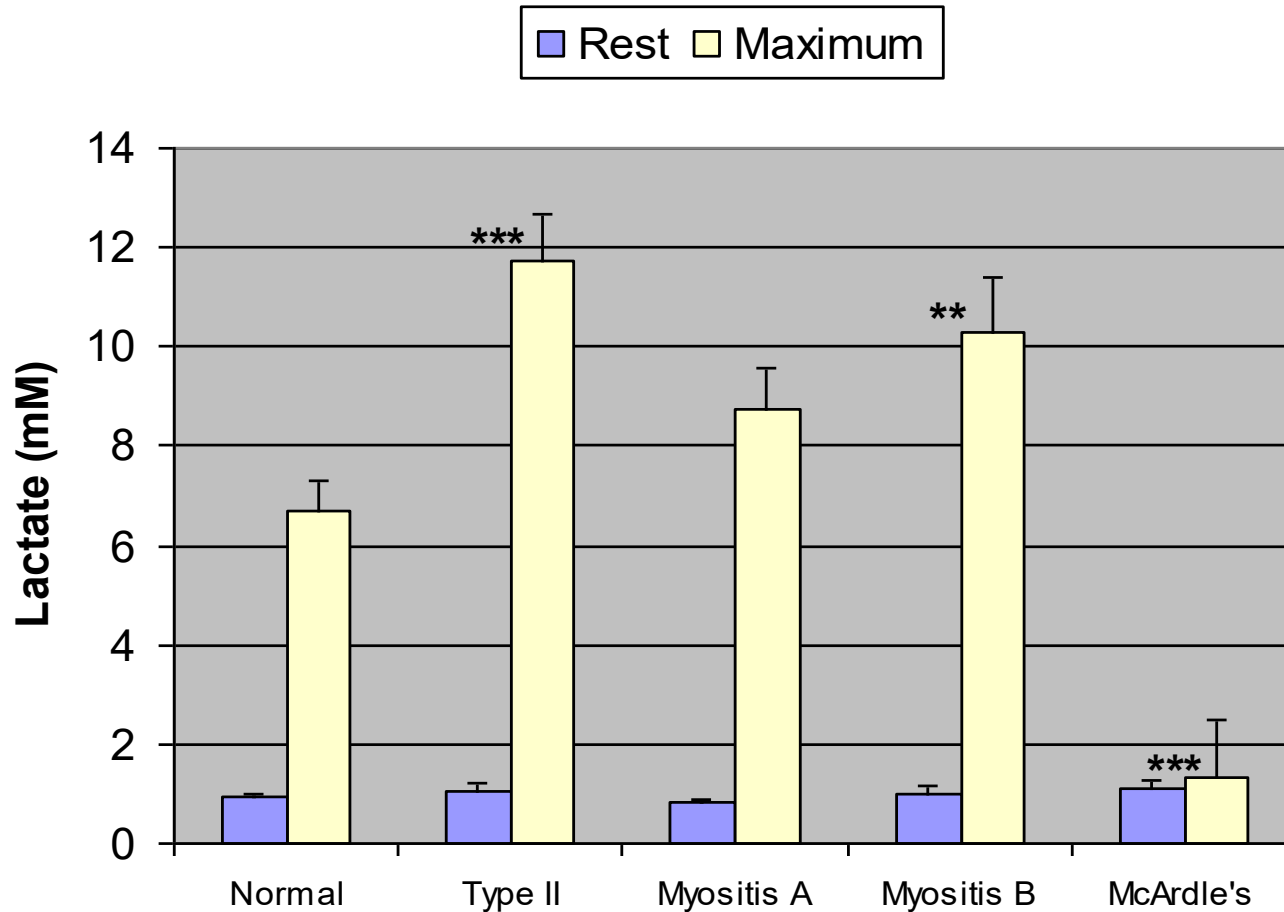
D



TYPE II PREDOMINANCE

Myosin-ATPase
stain at pH 4.60

Lactate increase with maximal exercise

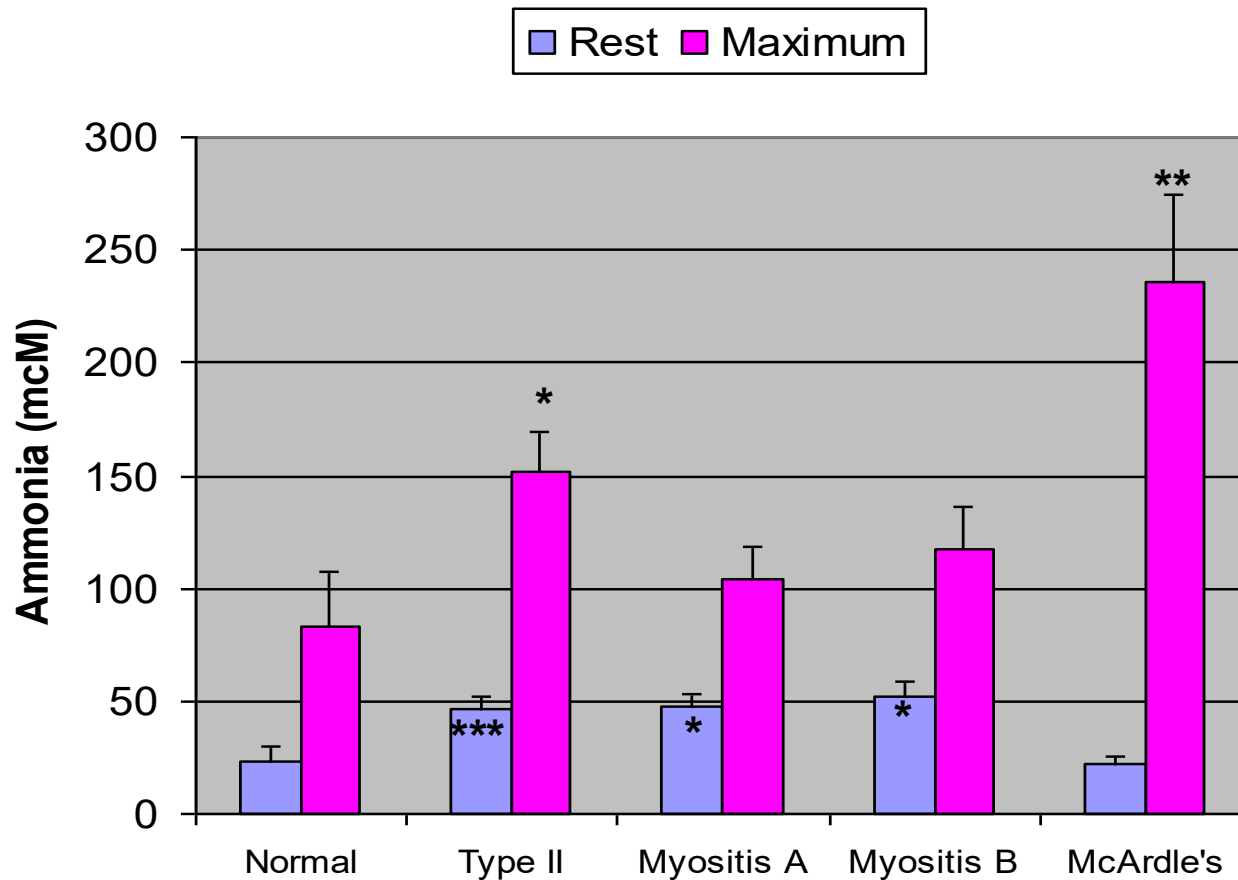


Cooper et al. Muscle & Nerve 2016

Different from normal: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Mixed effects model of level versus category with unstructured covariance matrix

Ammonia increase with maximal exercise



Cooper et al. Muscle & Nerve 2016

Different from normal: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Mixed effects model of level versus category with unstructured covariance matrix

Features of metabolic myopathies

- Low maximum $\dot{V}O_2$
- Abnormalities of lactic acidosis threshold
- Low oxygen-pulse
- Elevated NH_3 in some
- Lactate
- Elevated creatine kinase in some