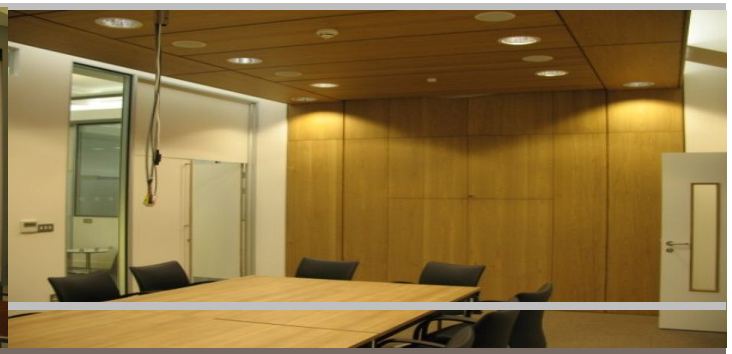
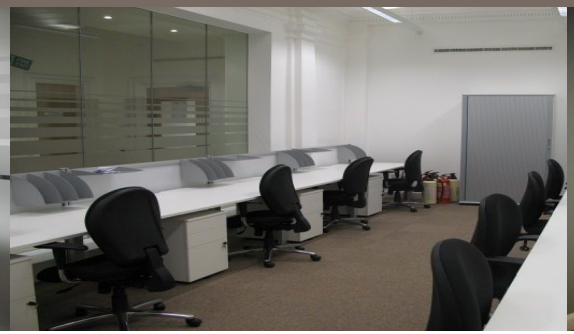
Queen Square Centre for Neuromuscular Diseases

NCG Diagnostic and Management Service for McArdle Disease and Related Disorders

Lead clinician: Dr Ros Quinlivan


McArdle disease

- Described 1951
- Autosomal recessive
- Myophosphorylase deficiency
- Frequency 1:100,000 – 1:350,000
  - 200-600 cases in UK
- Diagnosis
  - Ischaemic/non-ischaemic exercise test
  - Muscle phosphorylase
  - DNA testing of myophosphorylase gene (common mutation - R50X)

Anaerobic/aerobic exercise

Anaerobic

Sprinting, carrying heavy loads,

weight lifting, walking uphill,

tensing of muscles

Glycogen

↓

myophos phorylase

↓

Glucose

↓

Lactate, ATP

Aerobic

Jogging, cycling, walking

Fatty acids

↓

β-oxidation

↓

ATP

Symptoms

- Fatigue and pain within a few minutes of exercise
  - Muscle spasms, contractures
  - Myoglobinuria
  - Second wind (improvement of exercise performance after initial wekness)
  - Can lead to rhabdomyolysis
- Persistently increased CK
- Increased risk of gout

NCG service

- First discussions with NCG – 2003
- Service to cover
  - Any patient with a suspected **muscle** Glycogenolytic/ Glycolytic Disorder
  - Any patient with a confirmed **muscle** Glycogenolytic/ Glycolytic disorder
  - Include investigation & management

Diagnostic Service

- Diagnostic
  - Clinical evaluation/ diagnosis
  - DNA
  - Muscle biopsy

DNA

- R50X/ G205S Hot spot analysis
- Positive diagnosis in 70%, British Caucasians
- Heterozygosity in 95%, British Caucasians

- Birmingham Children's Hospital
- Sheffield Children's Hospital

Full gene Sequencing

- PYGM (Myophosphorylase)
- PFKM (Muscle phosphofructokinase)
- PHKA1 (Phosphorylase b kinase subunit A1)
- PHKB1 (Phosphorylase b kinase subunit B1)
- Direct access directly available via NCG form if clinically relevant

Muscle Histology/ Histochemistry

- Dr Janice Holton
- Pathology review biopsy slides
- Histochemical staining for phosphorylase and PFK
- MDT review of slides

Muscle Biochemistry

- Ralph Wigley Clinical Scientist
- Service is being set-up
- Not yet fully available
- Aim to identify rare glycolytic storage disorders e.g. muscle phosphorylase b kinase deficiency
- To double check conflicting results i.e. where muscle histochemistry is negative but no mutation on gene sequencing

Clinical Service

- Medical assessment and diagnosis of suspected cases
  - Patients presenting with exercise induced myalgia and /or rhabdomyolysis
- Investigation includes
  - Exercise assessment
  - Muscle and skin biopsy (including fatty acid oxidation defects and muscular dystrophy)
  - Genetic Studies (including fatty acid oxidation defects and muscular dystrophy)

Clinical service

- Aim
  - Provide information to patients on their condition
  - Encourage regular aerobic exercise
  - Reduce frequency of rhabdomyolysis episodes
  - Advice for management on acute rhabdomyolysis

Clinical service

- Management clinic
  - Walking assessment
  - Quality of life assessments
  - Motivational techniques to increase exercise capacity
  - Weight and dietary management
  - Psychological input to reduce anxiety
  - Exercise advice

Multi-Disciplinary Clinical team

- Dr Ros Quinlivan
  - Consultant in Neuromuscular Disease
- Miss Victoria Davies
  - Physiotherapist
- Mrs Andrea Beggs
  - Clinical Nurse Specialist
- Dr Jatin Pattni
  - Clinical Psychologist
- Dr Richard Godfrey
  - Exercise Physiologist
- Dr John Buckley
  - Exercise Physiologist
- Miss Heidi Chan
  - Dietician
- Ms Charle Maritz
  - Dietician
- Miss Charlotte Ellerslie
  - Dietician

Peer Support

- Andrew Wakelin, President AGSD present at clinics.
- Patients encouraged to meet one another
- Information about support group and their activities given

Providers

- Dr Ros Quinlivan
  - Queen Square Centre for Neuromuscular Disease
  - Dubowitz Neuromuscular Centre, GOSH
    - Dr Janice Holton
    - Institute of Neurology, Queen Square
- Dr Richard Kirk
  - Sheffield Children's Hospital
- Dr Sarah Ball (Mary Anne Preece)
  - Birmingham Children's Hospital
- Professor Simon Heales
  - Enzyme Laboratory GOSH

Developmental History

2003 First discussion with NCG

2007 Application submitted

2008 Decision by NCG deferred 1 yr

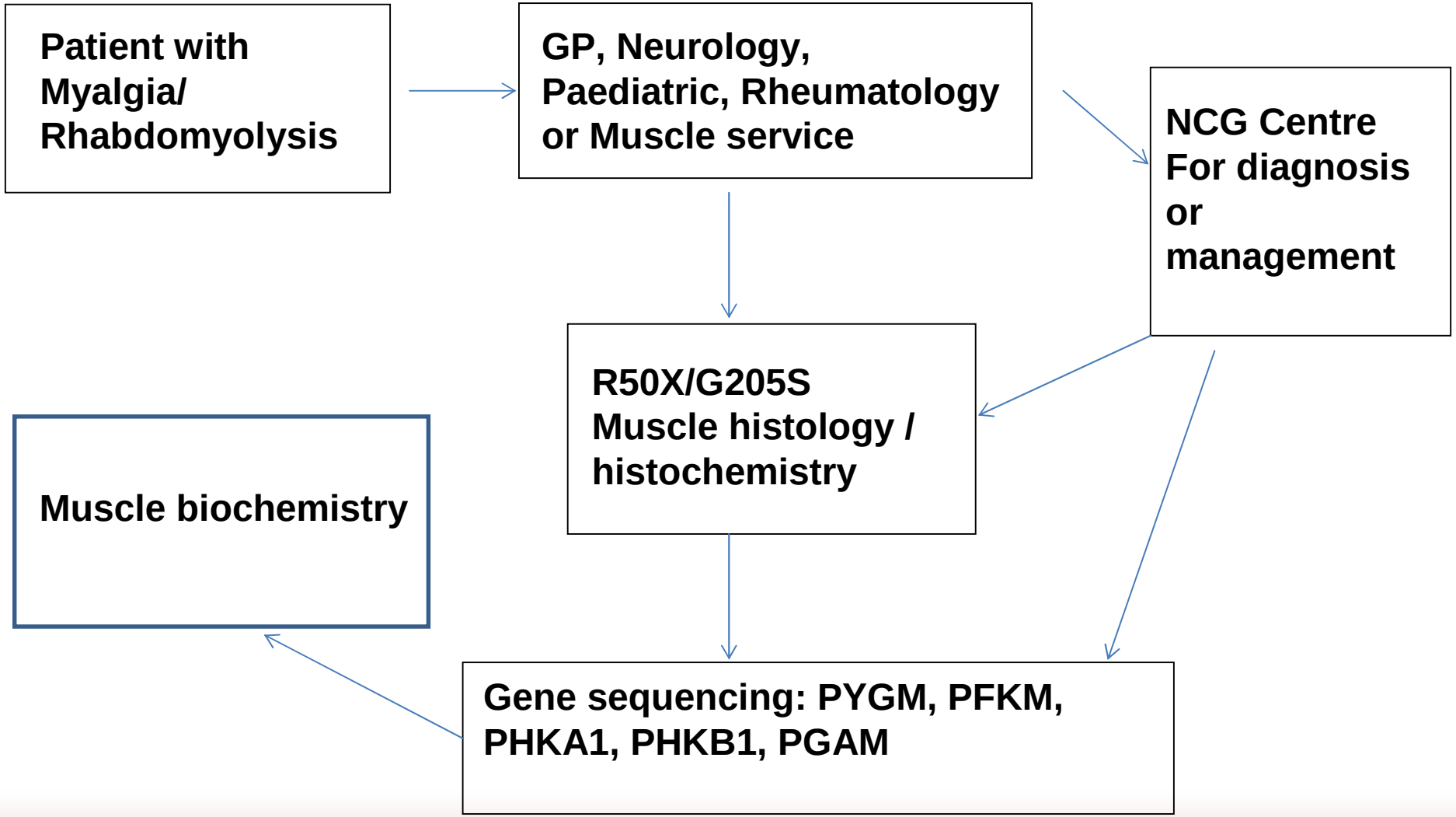
2009 NCG application approved

2010 Deferred 1 yr due to Dr Quinlivan's move

2011 Contract signed

2012 Physiotherapist and Nurse appointed

Service Pathway



Referrals

- For all referrals please send a completed form to the relevant provider
- For clinical/muscle biopsy assessment please send form electronically with a referral letter
- Contact numbers and NCG request forms can be downloaded from CNMD website

  http://www.cnmd.ac.uk/

UCL

THE NATIONAL HOSPITAL FOR NEUROLOGY AND NEUROSURGERY

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Acknowledgements:
National Commissioning Group
Association for Glycogen Storage Disorders
Muscular Dystrophy Campaign

Care and Research