British Inherited Metabolic Disease Group

Inherited Metabolic Disorders – A Service Vision for Setting Standards of Care and their Provision

Foreword

Following a Workshop in the autumn of 2002 in London it was agreed that it was important to set out a vision for how we should start to improve the provision of services for patients with inherited metabolic disorders. Continuing debate, through a number of draft documents, and discussion has meant a long gestation until we have arrived at this final version.

This document serves as a starting point and already other work is being considered to start to develop a more robust needs assessment of our services. This includes detailed work for commissioning services, for this individually rare, but collectively significant number of patients and conditions.

I would like to thank all those who have helped in preparation of this document and in particular Prof. James Leonard (London), Dr Phillip Lee (London) and Dr Anne Green (Birmingham).

Importantly I am grateful for comments and general support from various parent / patient support groups in preparing this text, in particular The Society for Mucopolysaccharide Diseases, CLIMB and The National Society for Phenylketonuria (UK).

Because of the changing nature of services it is inevitable that there may be some factual errors and can I apologise in advance. The general direction of travel and recommendations described in this document are intended to start to provide guidance for the further development of services to improve patient care and outcomes.

Dr Graham J Shortland
Chairman and on behalf of the BIMDG
Autumn 2004

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1. Summary of Service Development Requirements

The lack of a coordinated approach and appropriate services for patients with inherited metabolic disorders throughout the United Kingdom is of extreme concern to the professionals involved in these services, the patients and carers. These problems lead to inequity of service and are particularly acute because of;

- Advances in biochemical and genetic diagnoses
- Improved survival and increasing numbers of adult patients
- New treatments
- Developments in neonatal screening
- Excessive workloads

A clinical and laboratory network for patients with inherited metabolic disorders should be established to cover the whole of the United Kingdom. These will have:

- **Lead institutions** that will have more than one whole time equivalent consultant and provide a fully comprehensive service.
- **Regional centres** that would provide care by at least one specialist consultant.

All those in the **network**, would;

1.Provide core metabolic services

2.Share the workload and provide clinical cross cover as closely as possible.

3.Share outreach clinics for complex patients at Regional centres where there is no specialist and at district hospital for less complex ones.

4.Have regular joint meetings - research, teaching, clinical, audit and deaths enquiry

5.Have robust arrangements for shared care, particularly management of emergencies

6.Develop guidelines for management and protocols for investigation (these should be developed across the whole United Kingdom) including written information for parents and shared care.

7.All patients should have access to a clinical nurse specialist, specialised dietetic services and clinical psychology services.

To achieve this it will be necessary to:

- Establish a national database for these rare disorders as a resource for audit, research and evaluation of treatment
- Develop education and training packages
- Have National planning for training and consultant posts
- Recruit and train specialist dieticians, psychologists and specialist nurses
- Co-ordination of specialist Diagnostic Laboratory services including neonatal screening with the clinical service to form an integrated service
- Develop adolescent and adult services for each Lead centre and Regional centre

2. Introduction

Metabolic medicine and the treatment of patients with an inherited metabolic disease (IMD) is a small but highly specialised area of medicine. These disorders represent an important part of the growing number of genetic disorders with new diagnostic tests and new treatment possibilities.

Paediatric metabolic medicine is represented in the Royal College of Paediatrics and Child Health by the British Inherited Metabolic Disease Group and is a recognised sub-specialty of CESP (Confederation of European Specialists in Paediatrics, a section of UEMS). As the service is small and specialised, the United Kingdom needs to be considered as a whole. The organisation of the service should be based on the equity of the quality of the service and convenience, not historical geography. The historical development of services means that there is now an urgent need to create provision for a uniform and comprehensive multi-disciplinary service at a National level. The reasons for this concern are summarized as;

- Inequitable distribution of the service. Many children with metabolic disorders are under the care of district paediatricians with no specialist training.
- Many of the specialist consultants providing a service are single-handed.
- In a small specialty workforce planning is proving very difficult.
- Evidence based guidelines for investigation and management have been developed on a National basis for only a very small number of conditions.
- Information for patients, parents and health professionals is very limited.
- Specialist laboratory services have a major problem with inadequate numbers of clinical scientists and a looming crisis in succession, as many senior staff will retire in the next 5 years.
- Specialised adolescent and adult services for inborn errors are at best very limited and non-existent in some areas. Many adults are still looked after in paediatric units with others lost to follow up. Future development of neonatal screening programmes will impact on service provision for patients.

The service is almost entirely a tertiary one as these disorders are generally rare, most individual disorders having an incidence of less than 1 in 10,000 births. However so many disorders are now recognised that there is a considerable workload, which tends to be more concentrated in those areas with certain ethnic minorities because of genetic inheritance patterns.
The scope of any metabolic service is rapidly evolving with increasing recognition of inherited disease; increasing patient numbers, better survival, and an increasing expectation of health service delivery from the public. There is a constant development of new treatments for adult and

paediatric populations, including the recent development of enzyme replacement therapy for lysosomal storage disorders. Many are experimental and require close monitoring.

Many diseases are multi-system requiring a holistic approach and assessment by a wide range of specialist services including neonatal and paediatric intensive care, cardiology, neurology, nutritional teams and genetic services. These should be provided in a Regional centre. Shared care with local services is also very important as many of the patients may decompensate and need to be admitted locally. The patients may need other local services such as those for patients with disabilities.
In addition there is an increasing awareness of adult patients with inborn errors of metabolism and the need for services. These patients also present with a very wide spectrum of problems so that a broad range of resources is needed to provide comprehensive care and there is a considerable preventable morbidity and mortality.

3. Aims

The aim of the document is to provide outline advice for a structure and specifications for Health Care Purchasers for an integrated and multidisciplinary Metabolic Service encompassing Laboratory, Genetic, Dietetic, Paediatric and Adult Services. The agreement at a National Level with the Department of Health in England, Scotland, Wales and Northern Ireland, with Regional Health Authorities is necessary to agree a strategic framework for service provision. There is a particular need for discussion and development of consensus views because of considerable concern regarding the provision of appropriate manpower for all these services.

All patients throughout the United Kingdom with inherited metabolic disease should have access to specialist care of the highest quality.

4. Disease Definition

It is difficult to define the full scope of the service, as there is currently no nationally held data for the incidence and prevalence of different conditions. This requires the urgent development and funding of disease registers.

5. Review of Current provision and staffing for Services

5.1 Paediatric Consultant service

Seventeen consultants working at 10 centres provide current services in England (table 1). The service is patchy and inequitable. At present three units have more than two consultants (Great Ormond Street Hospital for Children, London, Royal Manchester Children's Hospital, Manchester and The Children's Hospital, Birmingham,). In all other units the consultants are single-handed. There is no local specialist in Bristol, Oxford, Southampton and Leeds. In Northern Ireland there is no recognised paediatric specialist and in the Republic of Ireland there is one centre based in Dublin. As a result many patients are still under the care of district paediatricians, only some being seen in outreach clinics.

The problems are clearly illustrated by a recent survey of Phenylketonuria, one of the most common disorders managed by this specialty (personal communication J Leonard). That showed that 104 units cared for a total of 2944 patients, some shared. Of these 77% attended centres that cared for more than 40 patients. However 75 centres look after less than 10 patients, some as few as one or two patients (table 2).

There are considerable obstacles in addressing these inequalities and providing a specialist service. Paediatric Metabolic Medicine is now recognised by the EU (UEMS). There is a syllabus for training programmes and plans are in progress to recognise training centres in Europe. However national workforce planning in the United Kingdom severely handicapped by lack of information about plans for appointment of consultants and lack of training posts. As there is a worldwide shortage of specialists in this field there is little hope of being able to recruit from abroad. There are two training posts in the UK but this will not meet the needs and the establishment of an additional training site is needed. Smaller Regional centers may be able to provide comprehensive training by rotation and networking through different centers.

To improve existing services networks should be established that would cover the whole country. There could be comprehensive outreach clinics and truly shared guidelines and protocols with a lead centre. The mechanics for funding of such managed networks would need to be clarified.

Table One. Current Staffing in Paediatric Metabolic Medicine

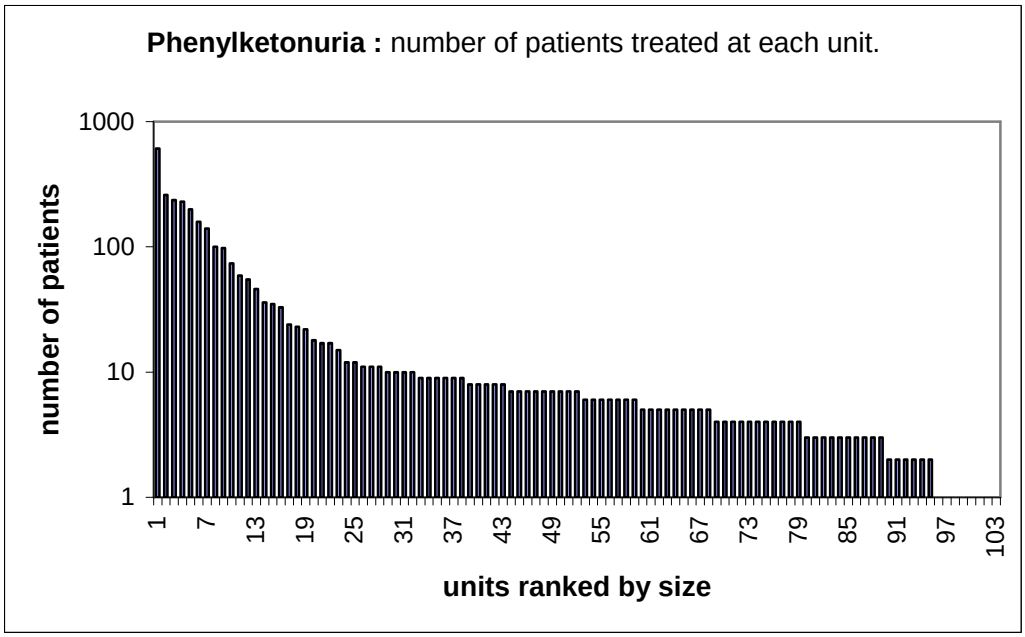
(Modified from original data provided by J Leonard)

Centre	Current Establishment	Vacancies	Retirements	Future posts
ENGLAND				
Newcastle	1	0	0	
Leeds	0	0	0	1
Manchester	3	0	0	
Sheffield	1	0	0	
Liverpool	1	0	2004	
Nottingham	0	0	0	
Leicester	0	0	0	
Birmingham	2	0	0	
Cambridge	1	0	0	
London QMC/London	0	0	0	
London Imperial/St Mary's, etc	0	0	0	
London UCL/ GOS	4 (+1)	0	2004/5	
London Guys	2	0	0	
London St George's	1	0	0	
Bristol	1(General paediatrician with interest)	0	0	
Oxford	0	0	0	
Southampton	0	0	0	
WALES				
Cardiff	1	0	0	
SCOTLAND				
Glasgow	1	0	0	
Edinburgh	1	(1)	0	
N.IRELAND				
Belfast	(1)	0	0	
EIRE				
Dublin	3	0	0	1

Table 2

PHENYLKETONURIA

A total of 2944 patients were identified who attending 104 units. 12 Units looked after more that 50 patients accounting for 75% of all patients but the remaining 721 patients attended 92 clinics, some of which looked after less than 5 patients.



Notes:

1. The logarithmic scale on the Y-axis.
2. Some of the units include adult patients whilst others do not.
3. No account has been taken of patients who may attend more than one unit.

5.2 Dietetic Service

In the treatment of IMD patients an experienced dietitian plays an important role in the multidisciplinary core team.

Dietitians hold a degree or postgraduate qualification in nutrition and dietetics. In order to practise in the NHS dietitians must be registered with their statutory regulatory body the Health Professions Council (HPC). The professional body is the British Dietetic Association (BDA). Both

these bodies consider specialist knowledge, such as the dietary management of IMD, should be obtained at post-graduate level.

Skills in the dietary management of IMD are mainly gained from workplace experience. As the specialty has grown there are more dietitians working single-handed in departments where there is little or no previous experience in IMD. Experience is generally only available in the major metabolic centres and dietitians at these centres provide advice, on an informal basis, to other dietitians for whom IMD management is not considered a specialty. Of major concern is the paucity of dietitians trained to deal with adult IMD patients. Paediatric dietitians at paediatric hospitals predominantly manage these.

There is only limited formal post-graduate training in the dietary management of paediatric IMD and at present there is no formal training established for dietitians working with adult IMD patients and this needs to be addressed.

The dietary management of IMD is complex. To provide a high quality service appropriately graded and numbers of dietetic staff are required. At present no published figures are available which estimate staffing levels to patient case load however a review of the North West service has recommended a figure of 1 WTE dietetic post to 140 patients with IMD (Service Framework For Children and Adults with Inherited Metabolic Disorders in the North West Region. March 2002). Currently there are 15 dietitians (13 paediatric, 2 adult) working across 15 centres in the UK. This equates to 14.5WTE and is inadequate to provide a comprehensive service to metabolic centres and the further advice to other smaller isolated units and district general hospitals. With the likelihood of more metabolic consultant appointments more specialist dietitians both paediatric and adult will be needed.

IMD is a small but highly specialised area and collaboration between large centres and with smaller units is essential to help facilitate training, production of protocols and resources. Networking via e-mail has just been established within the dietitians' sub-group of the BIMDG.

5.3 Clinical nurse specialists.

At present there are few clinical nurse specialists with very poor coverage of the United Kingdom. These are at Willink, Manchester (1), Great Ormond Street Hospital (2), Birmingham (1), Guys (1), Cardiff (1 part time funded) and University College London Hospitals (1).

5.4 Other Clinical Services

The considerable burden imposed on families with the diagnosis, poor cognitive outcome, long-term chronic illness and sometimes bereavement means there is a considerable need for the availability of clinical psychology services as part of a multidisciplinary service. For many of these disorders, neuropsychometric assessment is the main outcome measure and is normally obtained by clinical psychologists. This need is poorly provided for at present.

5.5 Adult Services

Only 6 adult IEM services are presently identified in the UK, although few provide a comprehensive service as seen in paediatric centres. In a European questionnaire survey of services 3,797 adult patients with IEM were identified amongst 41 different centres.

Improvements in screening programmes, diagnostic tests and therapeutic interventions have all led to increasing numbers of children with inherited metabolic diseases surviving through childhood into adolescence and adulthood. These individuals are often able to integrate into society, but many have complex, multi-system problems that require on-going care. Understanding of the long-term outcome of these disorders is scanty. Awareness of these conditions within the adult medical community is sadly limited and much of the good work of the paediatricians potentially could go to waste. This is often prevented by paediatricians remaining involved in patient care into the third decade and beyond. Appropriate resources to deal with the transition from the children's services to the adult sector are necessary, and appropriately trained medical and dietetic personnel are required to run these services. An adult inborn errors service needs to have close links with a feeding paediatric unit, as well as integrate with other adult medical and surgical specialties, and be supported by metabolic biochemical and molecular laboratories.

Training for Metabolic medicine had been agreed between the Royal College of Physicians and the Royal College of Pathology to include lipids, diabetic medicine, nutrition, calcium and bone and inherited metabolic disease. There are nine such accredited programmes currently approved in the UK with trainees in chemical pathology/ clinical biochemistry able to take this option. At present, just one adult internist is training in metabolic medicine. The IEM component of these programmes is relatively small but will hopefully attract some individuals who would wish to develop more expertise within this area. In addition medically trained biochemists should have a better appreciation of inherited metabolic disease.

5.6 Laboratory Services.

5.6.1 Current Provision Issues

The clinical service is crucially dependent on the specialist metabolic biochemistry laboratory service. In all centres with a clinical service there is a complementary laboratory with access to a full range of specialist testing and links to neonatal screening. There is acute concern about the vulnerability of some services because of the retirement of senior clinical scientists in the next 5 years. Planning for replacement these is an urgent issue.

Major advances in genetics and biochemical diagnosis have also highlighted the need for specialised laboratory services. Currently services are largely provided as part of (or closely allied to) Paediatric Clinical Chemistry Services and, generally though not exclusively, located in specialist children's hospitals where clinical scientists posts are frequently associated with the provision of Regional services for:

- Neonatal screening
- Inherited metabolic disorders

Some services are located in large teaching hospitals (clinical chemistry) where there is a substantial clinical paediatric component. Wherever they are located, they are usually linked with general Paediatric Clinical Biochemistry.

The need to recognise and develop specialist training for paediatric clinical biochemistry (including metabolic biochemistry) has been made and a proposal, supported by the Royal College of Pathologists and the Association of Clinical Biochemists, resulted in a recommendation to: -

- Designate Paediatric Metabolic Clinical Biochemistry as a sub-specialty of Clinical Biochemistry
- Create training posts for Paediatric Metabolic Biochemistry across the United Kingdom.

It is becoming increasingly clear that whilst a traditional background in clinical biochemistry or a traditional background in molecular genetics is extremely valuable neither on their own meet the requirements for the future. This need is being emphasised by the inclusion of the inherited metabolic disorders and neonatal screening services under genetic commissioners. Clinical scientists are needed to maintain the interpretative and clinical skills of the biochemist and yet have a thorough understanding of molecular diagnostic techniques and the genetic implications of the results. Training posts and programmes need to reflect these needs.

To facilitate these training and development needs a National Metabolic Biochemistry Laboratory Network has recently been established under the umbrella of GENCAG on a two-year project. The network is a focus for laboratory service provision across the whole of the UK. It gives a high priority to planning training, assessing risks and development needs. There has been significant progress in the past two years. The Department of Health for England agreed to fund eight higher specialist trainee (HST) posts and three whole time equivalent trainer posts dedicated to

Paediatric Metabolic Clinical Biochemistry. Appointments to all these posts were made during 2004. The HST appointments are for five years and the trainers have three year contracts. The challenge for the profession will be to identify funding to enable this level of training to continue into the future and match the needs identified by manpower assessments.
However, there remains an urgent requirement for the other countries of the UK to emulate this training provision.

5.6.2 Future Laboratory Developments

Current Screening Programme.
Newborn screening for Phenylketonuria within the United Kingdom is well established and successful. This condition has an incidence of approximately 1in 12000. Recommendations exist for the diagnostic concentrations of phenylalanine and standards of treatment and monitoring. The National Newborn Screening Centre came into being in April 2002 and followed on from the Medical Research Council /Department Of Health funded PKU register. It is a joint enterprise between Great Ormond Street Hospital for Children NHS Trust, the Institute of Child Health and the Institute of Education. The purpose is to oversee the quality of newborn screening in the United Kingdom.

Standards will be developed for the various stages in the Screening Process. These will help to pinpoint inequities of clinical support and opportunities for improvement.

It is acknowledged that there are problems in regional specialist commissioning arrangements for neonatal screening. This highlights that there was a disparity between what was advocated at national level and what was implemented at regional level.
Registers will be established for phenylketonuria and a number of problematic issues regarding consent and the use of residual neonatal blood spots have to addressed.

Extended Neonatal Screening.
New diagnostic technology in the form of tandem mass spectrometry (TMS) is being introduced throughout the United Kingdom and will change the practice of the specialty of metabolic medicine. This technology, using neonatal blood spots, leads to the possibility of more patients being diagnosed in the newborn period with extended screening. As a wide range of disorders may be detected, immediate specialist advice and counseling will need to be available throughout the United Kingdom. The most obvious candidate for inclusion was medium chain acyl CoA dehydrogenase deficiency (MCAD). A pilot screening programme was initiated by laboratories covering approximately half the births in the UK starting March 2004. The value for screening

other disorders e.g. urea cycle disorders and maple syrup urine disease is less clear. Each candidate disorder is being carefully considered on its merits. It is very likely that the profile of tests will increase in the next few years.
Introduction of screening impacts on the need for rapid diagnosis and management of IMD, which requires clinical, laboratory, nursing and dietetic services.

6. Conclusion

The lack of a coordinated approach and appropriate services for patients with inherited metabolic disorders throughout the United Kingdom is of extreme concern to the professionals involved in these services, the patients and carers. These problems lead to inequity of service.

A clinical and laboratory network for patients with inherited metabolic disorders should be established to cover the whole of the United Kingdom.

To achieve this it will be necessary to

- Establish a national database for these rare disorders as a resource for audit, research and evaluation of treatment
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This will require appropriate resources and recognition at National level that this is an important clinical service.