

**Inherited Metabolic Disorders (IMDs):
Needs Assessment and Service Review
Laboratory Services**

**National Metabolic Biochemistry
(Biochemical Genetics) Network
www.metbio.net**

September 1st 2005

**Anne Green
Lead Scientist
anne.green@bch.nhs.uk
metbionet@aol.com**

EXECUTIVE SUMMARY

CURRENT LABORATORY SERVICES FOR INHERITED METABOLIC DISORDERS ACROSS THE UK

1. Test Provision/Repertoire

Workload volumes for core tests relates to populations served by individual laboratories - there is no evidence of significant under or overprovision.

There is a deficiency of acyl carnitine services for some laboratories.

Some of the more specialist tests are vulnerable and a robust service is currently not provided. There are concerns about the potential impact of Foundation Hospitals on provision of the expensive very rare tests.

2. Turnaround Times

Turnaround times for routine core tests are significantly compromised in about 30% requests due to limited staff time and/or equipment failure.

3. Out of Hours Services

There are no formal arrangements for emergency out of hours work and *ad hoc* services are dependent on individuals being available and willing to help. There is a need for more formal back up arrangements between laboratories.

4. Accommodation for next 5 years

Accommodation needs for the future for laboratory services require addressing.

- 55% centres have inadequate laboratory accommodation
- 75% centres have inadequate office accommodation

5. Equipment

Urgent replacement is required for 30% of the amino acid analyzers (AAA) and replacement within 3 years is required for 50% of AAA and gas chromatographs.

6. Staffing/Manpower Planning

There are significant needs for additional scientists over the next five years to plan for retirements and new developments.

DIAGNOSES BY LABORATORIES

Data on diagnoses made by specialist laboratories in the UK suggests that between 550 - 570 IMD diagnoses are made per annum. These data exclude some disorders and therefore this is a minimum figure. The lack of databases means that this is an approximate figure.

Approximately 20% of diagnoses are in adults.

For many patients there are no specialist clinical services for the patients to be referred to.

RECOMMENDATIONS

1. Increased manpower resources are required to ensure the very specialist tests are provided, to improve turnaround times and to provide out-of-hours services on a more formalised basis.
2. A greater capital investment in expensive specialist equipment is needed for new and replacement equipment, i.e. not just reliant on individual Trust equipment programmes.
3. Continuation of investment in training for all health care scientists beyond the current 3 year plan from the DH Genetics monies is required.
4. There is a need to review accommodation needs in the context of the overall plan for IMD services and newborn screening developments across the UK.
5. There is a need for laboratories to record all IMD diagnoses as part of a formalised database to enable service planning, monitoring and audit.

ACKNOWLEDGEMENTS

The Lead Scientist would like to thank colleagues in all Stakeholder laboratories who have contributed to the provision of this data and to Mary Dowling, Network Administrator for compiling the report.

Stakeholder Laboratories Surveyed

Belfast	Royal Victoria Hospital
Birmingham	Birmingham Children's Hospital
Bristol	Bristol Royal Infirmary
Bristol	Southmead Hospital
Cambridge	Addenbrooke's Hospital
Cardiff	University Hospital of Wales
Edinburgh	Royal Hospital for Sick Children
Glasgow	Royal Hospital for Sick Children
Leeds	St. James' University Hospital
Liverpool	Royal Liverpool Children's Hospital
London	Guy's Hospital
London	Great Ormond Street Hospital
Manchester	Willink Biochemical Genetics Unit
Manchester *	Royal Manchester Children's Hospital
Newcastle	Royal Victoria Infirmary
Sheffield	Sheffield Children's Hospital
Southampton	Southampton General Hospital

* Specialist tests only - not included in core service analysis

ASSOCIATE LABORATORIES SURVEYED FOR THE SERVICE REVIEW

London	The National Hospital for Neurology and Neurosurgery
London	University College of London Hospitals
Oxford	Department of Biochemistry, University of Oxford

Others (Completed Service Review Questionnaire)

St. Helier Hospital, Carshalton - but not included in analysis as local service only (population approximately 500,000)

PROCESS

1. Service Provision

In October - December 2003 an assessment (by questionnaire) of laboratory services was undertaken to obtain information on : -

- Current workload patterns
- Development/future needs
- Robustness of service

There was a 100% response i.e. all 17 stakeholder laboratories responded (16 provide the core services). The survey provides data on manpower, equipment, accommodation and training. The data were compiled in February 2004. Selected summary data is provided in this document. A full report is available (metbionet@aol.com).

More extensive manpower data collection for the workforce review team was undertaken in May 2004.

2. Inherited Metabolic Disorders (IMD) Diagnoses

A second survey was undertaken by questionnaire in February 2005 to obtain data on IMD diagnoses. Data has been provided by 14 laboratories. There are no data on diagnoses from the Liverpool and Southampton laboratories.

INTRODUCTION/ROLE OF SPECIALIST LABORATORIES

The specialist laboratories provide services for a core group of tests to diagnose and manage patients with the following groups of disorders:

- Amino acids
- Organic acids
- Fat oxidation
- Urea cycle
- Carbohydrate

Some of the laboratories include services for other disorders:

- Peroxisomal
- Mitochondrial
- Lysosomal
- Purine & Pyrimidine

The tests are largely chemically based and include assays of metabolites and enzymes in body fluids and tissues. Some laboratories also provide selected molecular testing for IMDs to complement the other tests.

The laboratory role includes:

- Advice on testing
- Provision of specialist assays for diagnosis
- Interpretation of results and further testing
- Extended family testing
- Prenatal diagnosis
- Testing for management of the treatment and monitoring disease progression

Staffing comprises Consultant Medical and Consultant Scientists who lead, direct and manage the laboratory service. The services in most centres are intimately linked with the newborn screening service with shared accommodation, staff and equipment. The service is supported by highly specialised post doctoral clinical scientists (CS) who specialise in specific areas. They are responsible for method selection and development, the quality and reporting of results and clinical liaison. Clinical scientists also participate in outpatient clinics and ward rounds as part of the multidisciplinary IMD team. The clinical scientists are complemented by highly experienced Biomedical Scientists who undertake a large part of the specialist technical work. Both clinical scientists and biomedical scientists require specialist training and many years of experience before they are able to provide a clinical service.

RESULTS - Current Service Provision

Summary of laboratory size/population served (for 'core' tests) (n = 16)

Population	Number of labs
4 million or greater	5
3 - 3.9 million	2
2 - 2.9 million	6
1 - 1.9 million	3

Quality & Accreditation

15/16 laboratories are accredited with CPA UK Limited.

All laboratories participate in specialist External Quality assessment schemes (EQAs) where available; these are listed on the Metabolic Biochemistry website (www.metbio.net) against each laboratory entry.

A summary of EQAs schemes for specialist assays is provided on the Network website.

Stakeholder laboratories providing core tests (n = 16)

Ammonia	16
Amino Acids (plasma)	16
Amino Acids (urine)	16
Organic Acids	16
Acyl Carnitines	9
Free Fatty Acids/3-hydroxybutyrate	13
GAGs	14
Mono/Disaccharides	14

CONCLUSION: There is a deficiency in services for acyl carnitines in some areas. This is important because these tests are required urgently in some acute clinical situations.

WORKLOAD UNDERTAKEN BY STAKEHOLDER LABORATORIES

Requests per annum

Workload/annum Population Served (millions)	Amino Acids Urine	Amino Acids Plasma	Organic Acids	
1.4	-	-	648	
1.5	470	380	540	
1.6	560	840	492	
1.75	-	-	702	
2	800	650	1000	
2	1200	800 **	1800 *	* 4 million ** 3 million
2	820	415	820	
2.5	756	605	765	
4	-	-	1800	
4.5	1900	1000	2000	
4.5	1750	500	1800	
5.3	2163	687	2209	
> 5			3714	

CONCLUSION: The workloads correlate with the total populations served

SPECIALIST TEST REPERTOIRE (NON CORE)

For those tests which are non-core the survey showed the following:

- i. There are some redundant tests which could be dropped from the repertoire
- ii. There is some overprovision of specialist tests i.e too many laboratories for some tests
- iii. Many of the rarer tests not easily available in the UK i.e need to refer specimens outside the UK
- iv. There is a need for more molecular tests for IMD
- v. There is vulnerability for some specialist tests eg some enzyme assays are provided in one centre and/or are dependent on one or two individuals

The network is currently addressing these issues via:

- i. Enzyme working group - to advise on the specific areas which need improved provision
- ii. UKGTN for molecular tests - the network is inputting to the UKGTN

CONCLUSION: There is a need to invest in the provision of the very rare tests to ensure robust provision for the future.

TURNAROUND TIMES (TATS)/ROBUSTNESS OF SERVICE

Routine Assays

Acceptable TATS for routine analyses are not met for a significant number of laboratories.

Assay		Reason
Amino Acids	11/16	Batch size too small, equipment failure, CS time
Organic Acids	10/14	Equipment, CS time
Acyl Carnitines	5/8	CS time

For ~ 30% activity turnaround times are compromised because of equipment failure and/or staff availability.

Emergency Assays

TATs are not met as follows:-

		Reason
Amino acids	14/15	Equipment failure
Organic acids	12/14	Equipment failure, CS time

CONCLUSION: Some labs are unable to meet acceptable turnaround times for both routine and urgent assays due to instrument failures/ shortage and /or staff availability.

OUT OF HOURS SERVICES

Most labs did not offer a formal out of hours **analytical** service; however several provide an ad hoc service for some tests - by negotiation on a needs basis.

13 laboratories provide an out of hours advisory service:

formal duty biochemist	4
consultant service	7 (1:1 or 1:2)
ad hoc access	2

CONCLUSION: The out-of-hours advisory service is dependent on very few staff and goodwill. There are no formal arrangements in place

EQUIPMENT NEEDS

Several items of equipment are required in the next 3 years to meet service needs:

Amino acid analysers-

5 required urgently (30% rigor mortis!)

10 required in the next 3 years

Tandem Mass Spectrometers-

4 required in next 3 years

Gas chromatograph/Mass Spectrometer

9 required in the next 3 years

CONCLUSION: capital for equipment purchase (new and replacement) at Trust level is insufficient or not a priority!

ACCOMMODATION

Current position

Lab 12/14 - adequate

Office 8/14 - adequate

Future (next 5 years)

Lab 6/16 adequate & 1 with plans

Office 3/16 adequate & 1 with plans

CONCLUSION: For future needs:
 55% have inadequate laboratory accommodation
 75% have inadequate office space

This will be particularly important to address, together with the development plans for newborn screening.

STAFFING: CURRENT MANPOWER FOR THE LABORATORY IMD SERVICE (Clinical Scientists and Consultant Medical)

	Number of individuals (wte)		
	Consultants (Medical and scientists)	Principal Scientists	Senior Scientists
Belfast	1 (0.8)	1 (1.0)	
Birmingham	2 (1.5)	4 (3.0)	2 (2.0)
Bristol 1 (STHM)	1 (0.4)	1 (0.9)	
Bristol 2 (BRI)		2 (2.0)	
Cambridge	1 (1.0)	1 (1.0)	
Cardiff	1 (0.2)	1 (0.5)	1 (0.8)
Edinburgh	1 (0.5)	1 (0.25)	1 (0.25)
Glasgow	2 (0.9)		3 (2.4)
Leeds	1 (0.9)		
Liverpool	1 (0.5)	1 (1.0)	1 (1.0)
London (GOS)	1 (0.2)	2 (1.5)	2 (1.6)
London (Guys)	2 (1.2)	1 (0.5)	3 (3.0)
London (Guys) Enzymes	1 (1.0)	1 (1.0)	2 (2.0)
London (Guys) Purines	1(0.8)	1 (1.0)	2 (2.0)
Manchester	1 (1.0)	3 (3.0)	4 (3.05)
Newcastle	2 (1.0)	1 (0.4)	1 (0.9)
Sheffield	2 (1.2)	3 (2.8)	3 (2.7)
Southampton	1 (0.5)		
TOTAL	22 (13.6)	24 (19.85)	25 (21.7)
TOTAL NUMBER SCIENTISTS	71 (55.15)		

These data exclude contributions to neonatal screening where stated although the roles may often be shared/overlap.

The data exclude service contributions from trainees as this is difficult to assess. Specialist biomedical scientist staff not included.

Manpower Planning (for clinical scientists and biomedical scientists)

This was undertaken as a separate exercise for the Workforce Review team in May 2004 (separate report available). It includes planning for Newborn Screening developments.

Staff needs are estimated for the next 5 years for the UK (due to retirements and additional developments including newborn screening and training).

Manpower needs are

Clinical Scientist Consultants and Principal posts - 49
10 posts/year across the UK

Biomedical Scientists

Chief and Senior (Grade 3 and 4 posts) - 46

9 posts per years across the UK

These data assume 25% attrition rate and some individuals taking up posts in the less specialised centres.

TRAINING

Clinical Scientists

Clinical scientist staff function as consultants or principal scientists and require training to MRCPATH level **plus** higher specialist training (HST) in metabolic biochemistry. Until recently there were no training posts. With funding from DH Genetics additional trainee clinical scientists have been appointed to new HST posts - 11 individuals are in post across England. (Note that these plans cover England only). Although these current plans are addressing training needs there are concerns from within the profession that there will be a gap at the higher level for a few years whilst this present cohort of trainees complete their training. There are also no on-going plans for training posts.

BioMedical Scientists.(BMSs)

There is a need to establish training posts for BMSs to provide the specialist technical training required for the delivery of the service. This would ideally be linked with a vocational MSc module in Metabolic Biochemistry. Currently no such formalised training exists and it is 'on the job'.

Trainers

Insufficient trainer time was a major issue and has now been addressed via the Network with DH Genetics funding. A Lead Trainer and cluster trainers in three sites have been appointed across England with Genetics White Paper funding for 3 years.

There are also increased training demands on the labs arising from the specialist registrars in metabolic medicine and other health professionals eg Genetics .

Limited space for training purposes is also an issue for some laboratories.

CONCLUSIONS: There is a need to engage with the Workforce Development Directorate to plan manpower requirements beyond this first intake of additional clinical scientist trainees and specifically to plan and develop more formalised training for biochemical scientists

IMD DIAGNOSES

Data on the total diagnoses made by the specialist laboratories for their 'regional' population have been collated and related to the population served. There will be some bias because some laboratories have a special interest and specialise in certain tests.

	~Population (millions)	*Diagnoses /Million pop
Belfast	1.6	6.3
Birmingham	5.2	20.6
Bristol (BRI & Southmead)	3.8	8.4
Cambridge	1.0	10
Leeds	4.5	7.5
London (Guys)	4.0	8.5
London (GOS)	10.0	9.1
Manchester**	4.5	*
Newcastle	2.5	5.6
Sheffield	4.2	7.1
Cardiff	2.0	7.5
Glasgow	3.0	7.3
Edinburgh	2.2	7.7
TOTAL	44	~9.5 (Total no diagnoses 416 pa)

*Diagnoses are averaged over the last 2-4 year periods (i.e 2001-2004/5) where available. An estimate for PKU diagnosed from newborn screening has been added where not provided

** Data available for lysosomal disorders only - therefore not included

Total diagnoses across UK pro rata

*** ~ 550 per annum (over last 4 years)
 (***) Extrapolated to whole UK 58.8 million)

Total diagnoses reported by UK laboratories

2003/ 2004 573

These are cumulative total diagnoses not related to population for all laboratories providing data BUT excludes some data from:

- Northwest (Manchester & Liverpool)
- Wessex
- Oxford/Northampton/Berkshire

There are clearly problems in making such extrapolations:

- Likely to be some double counting i.e. for confirmatory tests sent away on same patient and some diagnoses not recorded.
- Diagnoses arising from newborn screening may not have been included in some returns
- Not all specialist laboratories have been included eg diagnoses not provided for
Porphyrias
Neurotransmitters
Oxalurias
Trace metal disorders
- Hyperlipidaemia diagnoses not included
- Will not have captured some diagnoses where the diagnosis is made by molecular tests eg Mitochondrial disorders

CONCLUSION: There is a need for laboratories to record diagnoses as part of a formal database to enable planning of services, monitoring and audit.

DIAGNOSES AND PREDICTED INCIDENCE FOR GROUPS OF DISORDERS

	Total no cases pa *	Estimated total UK cases pa	Estimated incidence
Amino acids	75	155	1:5000
Urea CD	12	25	1:32 000
Organic Acids	43	89	1:9000
Fat Oxidation	51	106	1:7500
Carbohydrate**	50	103	1:7500
LSD(pop 36.6 million)	67	108	1:7300
Perox***	30		
Mito ***	21		
Purine/Pyr***	15		

*average of 2002 & 2003 in 11 labs covering population of ~ 28 million

**includes GSD

***probably includes supra regional or national services so cannot extrapolate

AGE AT DIAGNOSIS

< 10year	72%
10-16y	7%
.>16y	21%

CONCLUSION: Although most cases diagnosed are in the paediatric age group, a significant number of (~20%) cases are diagnosed in adults.

REFERRAL OF DIAGNOSED PATIENTS BY LABORATORIES

Laboratories were asked to state where patients were referred to. Comments are as follows:

No adult service to refer to - some go to neurology, hepatology or stay in a renal clinic (Birmingham)

65% paediatric cases referred to a non metabolic paediatrician (Bristol)

25% non metabolic referral (Cambridge)

100% metabolic referral (Cardiff)

Leeds no data provided

100% metabolic referral (Newcastle)

All patients can be offered specialist paediatric or adult metabolic referral. Shared care arrangements often undertaken (Sheffield)

47% non metabolic referral (Glasgow)

29% referred to metabolic paediatrician - rest unknown. Some may have died; others single speciality referral (Edinburgh)

London (Guys) - no data provided

London (Purine lab) - 90% non metabolic referral

CONCLUSION: In many centres some patients diagnosed from laboratory testing are not able to be referred to specialist metabolic services for management of their condition.
(Birmingham, Bristol, Cambridge, Glasgow and Edinburgh)