National Steering Group for Specialist Children's Services

Endocrinology Project Group Report

Background

Paediatric Endocrinology is concerned with the diagnosis and management of children and young people with hormonal disorders (including growth and puberty problems). Whilst specialised endocrinology services are not available in every local is hospital, considerable support is provided to a number of District General Hospitals via outreach support, from Glasgow and Edinburgh Children's Hospitals.

The quality of care presently provided within the endocrine service is high and a number of referral pathways exist into specialist centres within Scotland and United Kingdom. However the challenge facing the service is the sustainability of an accessible service which does not require children and families to travel excessive distances for support.

With this in mind the review group focused on the following -

- Completion of a review of current patterns of endocrinology care for children and young people up to 16 years of age across Scotland.

- Completion of review of laboratory provision for endocrine services.

- Identification of potential solutions for the sustainability of quality care across Scotland

- Produce a report for consultation with relevant groups, including specialist and non-specialist teams in remote localities.

Summary of Process

The following activity was undertaken as part of the review process –

- Analysis of ISD available data
- A data gathering exercise involving all those involved in the provision of endocrine care across Scotland
- A review of laboratory services
- A literature review

The output of the process has been the production of this report and recommendations to ensure the sustainability of the service.

It should be noted that this review has been undertaken within an extremely short time and an not all aspects of the service have been fully explore, such as future workforce requirements. The recommendations, have taken this into consideration.

It should also be noted that due to work being progressed in relation to the Scottish Diabetes Framework: Action Plan, diabetic care for children and young people was not included in this review.

Incidence and prevalence

The gathering of reliable information has provided to be challenging, due to the various ways in which it is recorded. SMR 1 data collected by ISD was of little value as it did not adequately reflect the number of children seen as outpatients, which currently there is no way to clearly identify. However based on recommendations by the British Society for Paediatric Endocrinology and Diabetes (BSPED, www.bsped.org.uk) the following may be relevant for Scotland –

Condition	**Incidence**	**Project Number**
Short and Tall stature	1 in 40	23750
Delayed puberty	1 in 30	31666
Idiopathic central precocious puberty	1 in 20	47500
Congenital hypothyroidism	1 in 4000	238
Idiopathic growth hormone insufficiency	1 in 3000	316

The BSPED recommend that all of these conditions are suitable for management within district general hospitals with appropriately trained staff and access to support from a specialised centre.

Rare conditions, or conditions requiring complex support and follow up including for example, Turner Syndrome, Adrenal disorders (incl CAH), Thyrotoxicosis, rare endocrine tumours and hypopituitarism require more specialised input. Information on the incidence of some of these conditions is currently being gathered. Paediatric endocrinologists currently see and advise on a broad spectrum of disorders with differing prevalence/incidence which require a spectrum of investigative resources and specialist skills.

Information gathered by the group via the distribution of a questionnaire would suggest that the incidence levels and projected numbers would be an acceptable estimate for Scotland. The data gather provides an estimate but may not be 100% accurate at this stage. A summary of the gathered information is attached as an appendix.

Models of Care

There is a strong view that there requires to be common diagnostic, investigative, treatment protocols (including integrated care pathways where appropriate) and national clinical networks for rare conditions. To drive this forward it is felt that there requires to be a national network established bring together specialist centres, District General Hospitals and Rural General Hospitals. This network would be the co-ordinating mechanism responsible for the future development and sustainability of endocrine services across Scotland.

The nature of endocrine conditions requires, there to be a UK dimension to the development of models of care for rare conditions.

Specialist Links include

Similar to other specialist services, endocrine services require considerable linkage with other specialities, some of which are captured in the table below. Access to some of these services is often limited due to competing demands. It is essential however for the sustainability of a quality endocrine services within Scotland that access and support is easily available to the services mentioned below.

Clinical Psychology	Genetic Counselling	Neurooncology & Surgery
Bone Densitometry	Molecular Diagnostics	Adult Endocrine
Day Investigations Unit	Neuroradiology	Endocrine Tumour Genetics
Endocrine Lab	Radioiodine Therapy	Adult Diabetes
Adult Late Effects Clinic	Assisted Conception	Reconstructive Gynaecology
Adult Metabolic Bone		

Workforce Issues

Similar to other specialist areas workforce issues are the key to providing a sustainable service. Fortunately the Endocrine service currently has a good level of Consultants working within the service and in the short-term there shouldn't be any challenges to the services from this area. Unfortunately issues have been identified which highlight a need for more specialist nursing input and allied health professional input. This is an area which requires to be further investigated and the establishment of a national network group would allow this to be progressed further.

Laboratory Services

Questionnaires were sent via the Scottish Association for Clinical Biochemistry Audit Group to all laboratories in Scotland, to gather information regarding the provision of Endocrine testing. A detailed report is attached as an appendix.

The main conclusions from this work were:

- Paediatric requests form a relatively small proportion of the workload for most Endocrine tests in most laboratories.
- Referral patterns of Endocrine tests within and beyond Scotland are generally appropriate for workload, with some recent rationalisation of low-workload tests.
- Some specialised Endocrine tests are highly complex and demanding in terms of equipment, staffing and skills. Threats to maintenance of current levels of service include staff turnover and the demographic profile, with loss of many experienced staff expected over the next 5-10 years owing to retirement.
- Many laboratories do not provide age- and sex-appropriate Paediatric Reference (normal) Ranges on their reports, compromising interpretation of results, particularly for non-specialist clinical staff. Several laboratories see this as a weakness in their service and would welcome guidance in this area.

- The types of endocrine Dynamic Function Tests performed were generally appropriate to the paediatric service provided by the hospital (district general or tertiary referral), with written protocols and interpretative cut-offs available. Interpretative cut-offs were usually taken from the published literature.
- Most laboratories/clinical services had written protocols for investigating Hypoglycaemia, but the content varied. Many laboratories provided no interpretation of reported results.

The key recommendations from this work are:

- Robust procedures for equipment replacement, staff succession planning and training for biomedical and clinical scientist staff in Scotland.
- Development of formalised referral pathways for complex/specialised Endocrine testing at appropriate labs (see separate Review of Specialised Pathology and Laboratory Medicine Services in Scotland).
- Progression towards development and implementation of evidence-based, method-specific Paediatric Reference (normal) Ranges on a national basis.
- National agreement on Dynamic Function Test protocols and interpretative guidelines.
- National agreement on Hypoglycaemia investigation protocols and their interpretation.

Potential Risks

As part of the review process an number of risks were identified, these being –

- Issues linked to the unplanned nature of existing service development, impact of academic contracts and increasing numbers of chronically ill children and young people; all provide potentials risks to the future provision of a sustainable service.
- Introduction of MMC and lack of appropriately trained nursing and AHP staff will impact on the sustainability of service provision.
- Increasing number of patients e.g. diabetes, obesity related conditions and chronic illness, all of which are putting pressures on the services.
- Similar to other paediatric specialities there are often issues associated with the transition to adult services, which requires to be further investigated.
- NICE guidance has been produced for GH Therapy but has no formal status in Scotland, a national shared care protocol is available for GH and a number of other protocols are being produced nationally.

Whilst these are seen as risks it is felt that establishment of a national network will help to reduce these.

Recommendations

These recommendations are being put forward for consideration to the National Steering Group.

	Action	**By when**
1	Establishment of a National Managed Service Network for Paediatric Endocrinology services	March 2009
2	Review of Workforce demands, pressures on services leading to development of a workforce plan	March 2010
3	Develop pathways of care for key conditions	July 2009
4.	Progress key laboratory recommendations for endocrine services Robust procedures for equipment replacement, staff succession planning and training for biomedical and clinical scientist staff in Scotland. • Development of formalised referral pathways for complex/specialised Endocrine testing at appropriate labs (see separate Review of Specialised Pathology and Laboratory Medicine Services in Scotland). • Progression towards development and implementation of evidence-based, method-specific Paediatric Reference (normal) Ranges on a national basis. • National agreement on Dynamic Function Test protocols and interpretative guidelines. • National agreement on Hypoglycaemia investigation protocols and their interpretation.	March 2010
5	Develop national standards of care to cover all aspects of endocrine care	March 2010

Appendix 1

NATIONAL STEERING GROUP FOR SPECIALIST CHILDREN'S SERVICES

REVIEW OF PAEDIATRIC ENDOCRINOLOGY SERVICES

BASELINE QUESTIONNAIRE

Background

As part of the review of endocrine services commissioned by the National Steering Group for Specialist Children's Services, a baseline audit of existing service provision was under taken. Whilst this was not an extensive reviewed it aimed to provide some baseline data, to help in considering key issues facing the service, locally, regionally and nationally.

- Raigmore
- Wishaw General
- Dumfries and Galloway
- Aberdeen Children's Hospital
- RAH – Paisley
- Borders General
- Ninewells
- Dr Gray's
- Forth Valley
- Fife
- Sick Kids- Glasgow
- Sick Kids – Edinburgh

Total number of Hospitals providing an Endocrine/growth disorder service -

- The 12 list all provide a service , with a range of links to one of the specialist centres

Number of designated lead paeds

- 8 Services have a designated lead
- 4 services have no designated lead

Average number of sessions designated lead has per month -

- 4 sessions per month

List of those involved in care –

Profession	**Average Sessions per week**
Dieticians	**1 session**
Community Nursing	**1 session**
Specialist Nursing	**6 sessions**
Consultant Paediatricians	**Difficult to define**

Note

- The above figures are only apply to services that provide additional support – the majority do not have access to Specialist nursing or dietetic inputs.

Access to an electronic data bases

- 5 Services have access
- 7 Services do not have access

Formal links with biochemistry department

- 6 services do not have any Formal links
- 6 services have a formal link

Provision of Dynamic test

- 10 Services provide dynamic tests

Type of test

Test
Clonidine
Arginine
GNRH
Short Synacthen

In last year the following have been seen

Procedure/Condition	**Yes**	**No**
Complex Bone disease	8 Services	
Skeletal Disorders	6 services	
Endocrine Surgery	1 service	
Radio Iodine	2 services	

Note

- The majority of these services are provide on a shared care basis with support from either Children's Hospitals in Glasgow or Edinburgh

Transition Issues

- 7 Services have structured transition links with Adult services

Do you have local access to the following?

	Yes	**No**
Neuro-imaging (including MR)	**10 services**	
medical physics (including DEXA)	**7 services**	
clinical genetics	**11 services**	

Obesity Criteria

- 3 Services have obesity criteria

Appendix 2

SURVEY OF LABORATORY PAEDIATRIC ENDOCRINE SERVICE IN SCOTLAND
REPORT

Questionnaires were sent via the Scottish Association for Clinical Biochemistry Audit Group to all laboratories in Scotland in February 2007. A reminder was sent to non-responders in April 2007.

Responses were received from 11/21 laboratories (52%) – see Appendix for a summary of the responses to individual questions. Responders included both single site and multi-site clusters of laboratories, with a representative spread of tertiary paediatric referral hospitals, university hospitals and larger/smaller district general hospitals. All provided a paediatric service of some description, with most (with some exceptions) providing a service for neonates, dedicated children's ward(s), Accident & Emergency, Outpatients and GPs. Two provided a paediatric intensive care service (RHSCE, Yorkhill). About half provided a service for tests referred from other laboratories. For most of the non-responders, there is probably a relatively small paediatric component to their laboratory workload, although the hospitals they serve may have an on-site neonatal service (e.g. St John's) and/or provide a sizeable paediatric service with several consultant paediatricians in post (e.g. Borders, Crosshouse, Stirling).

1. Individual endocrine tests

1.1 Workload and assay provision

Test workload data were provided by all responders except Yorkhill. Some laboratories provided workload data only for those tests analysed within their own laboratories, not for those tests referred to other laboratories. The paediatric component of the workload varied according to laboratory and test. For both paediatric laboratories, the paediatric proportion of the workload was high for all tests, as expected.

Test workload was arbitrarily divided into very high (median annual workload >5,000), high (1,000 – 5,000), moderate (100 – 1,000), low (10 – 100) and very low (<10). Within each of these categories, there was a very large between-laboratory range of workloads, typically 50 to 100-fold. For most but not all tests, RHSCE had the smallest workload and the North Glasgow laboratory group had the largest, partly because it was a multi-site cluster and partly because Glasgow Royal Infirmary (GRI) accepts many referred samples from other laboratories.

Very high workload tests were HbA1c, microalbumin, FT4/TSH and LH/FSH. These were usually analysed by the local laboratory, except for RHSCE which referred all endocrine-related tests except HbA1c. The paediatric component of the workload was usually very small except for the paediatric laboratories themselves.

High workload tests were T3, PTH, cortisol, oestradiol, testosterone, and plasma/urine HCG. Most of these were also analysed by the local laboratory, although a few were referred to other laboratories. For most of these tests, the paediatric component of the workload was

usually very small, except for cortisol for which 5 laboratories reported a moderate or high paediatric component.

Moderate workload tests were thyroid peroxidase antibodies, ACTH, growth hormone, IGF-I, SHBG, aldosterone, 17a-hydroxyprogesterone (17aOHP, plasma), 25-hydroxyvitamin D (25OHD) and urinary free cortisol. These tests were provided by between 1 and 5 of the responders in their own laboratory, with the remainder being referred to more specialised laboratories. In addition to the paediatric laboratories, some other laboratories reported a moderate paediatric component to their workload for growth hormone, IGF-I and 17aOHP.

Low workload tests were insulin, C-peptide, anti-GAD antibodies, TSH receptor antibodies (TRABS), calcitonin, renin, 17aOHP (blood spot), androstenedione, DHAS and urine steroid profile. For some of these tests (insulin, C-peptide, anti-GAD, urine steroid profile), paediatric samples comprised a moderate or high proportion of the workload in several laboratories. These tests were provided by between 1 and 3 laboratories in Scotland, except for anti-GAD which was referred south of the border. From the figures provided, the total Scotland-wide annual workload could be calculated for the following tests: insulin (2094), C-peptide (682), calcitonin (315), renin (1824), aldosterone (1812), blood spot 17aOHP (170), and urine steroid profile (620). For urine steroid profiles, the relatively low numbers may give a misleading impression of the work involved. Each profile consists of at least 20 urinary steroid metabolites measured by gas chromatography/mass spectrometry after extensive sample work-up, and requires considerable staff time and expertise. Several laboratories neither analysed themselves nor referred samples for anti-GAD and blood spot 17aOHP, presumably either because of lack of clinical demand in their local hospital or because of other referral routes (e.g. via Immunology for anti-GAD, blood spots collected at home and posted directly to the paediatric laboratory for 17aOHP).

Very low workload tests were pancreatic islet cell antibodies, anti-insulin antibodies, dihydrotestosterone (DHT), $1,25(OH)_2$ vitamin D, salivary cortisol and IGFBP-3. Several laboratories neither analysed nor referred samples for the antibody tests, probably because of other referral routes via Immunology. Requests for anti-insulin antibody (together with anti-GAD) and DHT were referred south of the border. $1,25(OH)_2D$ and salivary cortisol assays were provided at a single site in Scotland (GRI) with annual Scotland-wide workloads of 430 and 380 respectively. The demand for salivary cortisol was currently from only 3 responding sites, including GRI itself. Two laboratories stated that they referred requests for IGFBP-3 to another laboratory in Scotland, with another referring south of the border. In reality, this test is not available in Scotland, as it is considered not to give useful additional information to the measurement of IGF-I except in certain very rare clinical situations, and few laboratories have any arrangements for referring IGFBP-3 requests.

Among responding laboratories, there were no requests recorded by responders for AMH and deoxycortisol. With regard to AMH, the Scottish service has only just started and the service-provider (GRI) confirms that approximately 10 samples per month from Yorkhill are now being analysed (M. Wallace, personal communication).

1.2 Paediatric reference ranges

The two paediatric laboratories both provided paediatric reference ranges for all endocrine tests. However, only half the responding laboratories overall quoted paediatric reference ranges for thyroid function tests, LH/FSH/oestradiol/testosterone/SHBG, renin/aldosterone

and androstenedione/DHAS, although paediatric reference ranges for these tests are all markedly different from those in adults and also change through infancy and childhood. For most laboratories that did not quote paediatric reference ranges for these tests, the paediatric component of their workload was very small, but for one laboratory it was moderate (for thyroid function tests, LH/FSH). The two laboratories that measured IGF-I (GRI and Aberdeen) and the single laboratory that measured 17aOHP (GRI) both quote paediatric reference ranges, and these were appropriately quoted on reports by all referring laboratories with two exceptions. Urine steroid profiles are analysed in a single laboratory in Scotland (GRI) and this laboratory's paediatric reference ranges were quoted by all referring laboratories.

Paediatric reference ranges, where quoted, came from a variety of sources, including within-laboratory/evidence-based, published literature for method, published literature for another method adapted for own method by regression, textbook, another laboratory and manufacturer. One laboratory did not answer this question.

2. Dynamic function tests

One laboratory (WGH) has no paediatric in-patients on site and left this section of the questionnaire blank. Two additional laboratories (North Glasgow and RIE) only have neonates on site although both provide a referral service for DFT samples referred from other hospitals. These three laboratories therefore have no DFT protocols of their own although North Glasgow does provide interpretative cut-off for some DFTs.

In response to the question 'Is this test carried out in children in your hospital' between 6 and 8 respondents answered 'yes' for the following DFTs: oral glucose tolerance (with insulin measurement), short Synacthen (standard dose), GnRH, TRH, HCG stimulation and water deprivation. Between 3 and 5 respondents answered 'yes' for the insulin hypoglycaemia (RHSCE, Yorkhill, Ninewells), clonidine, arginine and short Synacthen (low dose) tests. Two respondents answered 'yes' for the glucagon test (Yorkhill, Ninewells), and one each for the GHRH-arginine (Yorkhill), exercise (Dumfries) and IGF-I generation (RHSCE) tests.

Most laboratories had written protocols and interpretative cut-offs for most DTFs carried out in children on their site, with some exceptions (see Appendix for details). Although the exercise test for GH is now generally considered to be an obsolete test, a protocol was still reported to be available in Dumfries, with interpretative cut-offs quoted by both Dumfries and GRI laboratories. However, it is doubtful whether this test is still being carried out in clinical practice (C. Kelnar, personal communication).

DFTs are done by a wide range of ward staff. In 4 hospitals some or all are done by specialist nurses, and one other (Victoria hospital, Kirkcaldy) is planning to train a nurse practitioner to do them. If there are no specialist nurses, DFTs are often done by middle-grade medical staff (SpR/SHO). Some tests are done by staff nurses (Inverness: OGTT), F/G grade nursing staff (Ninewells: short Synacthen) or foundation doctors (Ninewells: clonidine, short Synacthen, GnRH, TRH, HCG stimulation).

There was no consensus regarding who interprets DFTs. For some, interpretation is done by a combination of laboratory and medical staff, for a few only medical staff interpret DFTs and one laboratory reported that only the laboratory interpreted DFTs.

Interpretative cut-offs for DFTs came mainly from the published literature or a textbook, although one laboratory had their own evidence-based cut-offs for most of their DFTs. One laboratory used DFT cut-offs from Great Ormond Street and one did not know the source of its cut-off for the arginine test. One laboratory that provided interpretative cut-offs for many DFTs did not give any information as to their source.

3. Endocrine responses to hypoglycaemia

Excluding the laboratory that had no paediatric in-patients on site, all except one responder indicated that a written protocol was available in the hospital for samples to be collected and tests to be done in a hypoglycaemic baby or child. In some cases, the protocol was held by the ward rather than by the laboratory.

There was a wide range of responses to the question regarding the content/priority order of the local hypoglycaemia investigation protocol. Most listed cortisol as first or second endocrine priority, whilst those with an on-site neonatal unit usually (but not always) listed insulin as high priority. However, some laboratories appeared to prioritise according to what tests were available locally, resulting in urea and electrolytes, liver function tests, calcium/magnesium and/or blood gases being prioritised over insulin. Some laboratories did not include laboratory confirmation of glucose in their protocol, although this may have been assumed.

Only 6/11 laboratories provided interpretative comments for endocrine responses to hypoglycaemia on their reports. Those that did not gave various reasons: one relied on the referral laboratory to make comments, one referral laboratory refrained from making comments because it rarely saw the full hypoglycaemia screen results, one laboratory rarely provided interpretative comments of any kind on its reports, one laboratory cited lack of confidence/competence among some of its staff and one laboratory gave no reason.

4. Suggestions for improvements to the paediatric endocrine service provided by own laboratory

There were several suggestions (see Appendix for details). The lack of paediatric reference ranges was a recurring theme, the constraint being the difficulty of obtaining such data. Three laboratories suggested that the laboratory should develop agreed protocols with paediatricians, the constraints being largely those of lack of time, also a recurring theme. Integration with paediatric-trained biochemists was seen as a solution by one laboratory, the constraint being separate site working. Two laboratories thought that there should be an improved turnaround of tests, the cited constraints being respectively staff availability and transport links for referred tests. One laboratory highlighted the need for an equipment renewal programme and for increasing the number of well-trained staff, with (lack of) finance the constraint for both.

5. Suggestions for improvements to the Scotland-wide paediatric endocrine service

The need for paediatric reference ranges and protocols was a recurring theme here as well (see Appendix for details). The difficulty is that paediatric samples form only a small proportion of the workload for many Scottish laboratories, are not necessarily seen as a priority and are swamped by much larger numbers of tests from adult patients. There are also different methods/analysers in use across Scotland, making it difficult to roll out reference

ranges developed in one centre to other laboratories. One laboratory thought it would be useful to have a directory of endocrine services available in Scottish laboratories. Two laboratories thought that some endocrine tests had a very slow turnaround (although the cited example of anti-GAD erroneously suggested that this was only available from a research lab). Underlying many of these concerns was the need on the part of many clinical biochemists for guidance in obtaining paediatric reference ranges, developing paediatric protocols and interpreting paediatric endocrine results.

6. Summary and Conclusions

1. *Endocrine test workload, repertoire and referral patterns*. Except for the two paediatric laboratories in Yorkhill and RHSCE, paediatric requests usually formed a relatively small proportion of the endocrine test workload, although a few tests had a higher paediatric component e.g. insulin, growth hormone, 17aOHP, urine steroid profile. The choice by a laboratory of whether to analyse an endocrine test on-site or refer it to another laboratory appeared to be largely determined by the test workload, and appeared to be appropriate in most cases. Several relatively low-workload tests were provided by between one and three laboratories in Scotland with appropriate expertise and equipment. Some very low workload tests (<500 per annum Scotland-wide) were analysed in a single Scottish laboratory, whilst some were referred south of the border. These centralisation and referral patterns appear appropriate on the whole. However, there is uncertainty regarding to which accredited laboratory in England samples for anti-GAD and anti-insulin antibodies should be referred in order to confirm type I diabetes in cases of diagnostic difficulty. There appears to be variation in diagnostic performance among laboratories and the most sensitive antibody test for type I diabetes, anti-IA2, does not appear to be available except in a research laboratory. There has been some rationalisation of other low-volume tests over the past few years, e.g. centralisation of calcitonin measurement to a single centre in Scotland, removal of IGFBP-3 from the repertoire and recent introduction of sensitive measurements of AMH, a diagnostically important test for disorders of sexual development. Some specialised endocrine tests are highly complex and require specialised equipment (e.g. urinary steroid profile) and are also demanding in terms of staff time and expertise (e.g. urinary steroid profile, renin activity). Many laboratories face difficulties in replacing or upgrading equipment, and staffing turnover makes it difficult to acquire and retain the necessary skills required for method development and trouble-shooting. Staffing shortages can impact on turnaround times for some assays. Many experienced staff are expected to retire in the next 5-10 years, making succession planning a priority. These problems are shared by all specialised areas of the laboratory service in Scotland and are not restricted to endocrinology.

2. *Paediatric reference ranges* may be markedly different from adult reference ranges for some endocrine tests, may be highly age and/or sex-dependent even within the paediatric age group, and are often method-specific. Currently, several laboratories reporting endocrine tests in children do not provide age-appropriate reference ranges on their reports, a major shortcoming and one recognised as such by the laboratories themselves. Approximately half the responding laboratories did not quote paediatric reference ranges for several endocrine tests that change markedly through the neonatal / infancy / childhood / adolescent / adult age range. Some of these may be of crucial diagnostic importance e.g. thyroid function tests in the neonatal period. Where quoted, paediatric

reference ranges came from a variety of different sources. The survey did not seek to evaluate whether laboratories' paediatric reference ranges were appropriate. Several laboratories commented on the difficulty of obtaining appropriate paediatric reference ranges. This is a world-wide issue that applies to many non-endocrine as well as endocrine tests. Paediatric laboratories have responded by searching the literature for paediatric reference ranges appropriate to their methods and/or by deriving their own ranges for their own population and methods through various strategies. There have been various efforts to collate published paediatric reference ranges from original studies of variable quality, most recently under the auspices of the American Association for Clinical Chemistry (reference 1). Manufacturers of immunoassay analysers and/or hormone assay kits have been slow to address the problem, although some initiatives are now underway in conjunction with paediatric hospitals (e.g. reference 2). There are also some national collaborative efforts in progress such as the Canadian Laboratory Initiative on Pediatric Reference Interval Database (CALIPER, reference 2) and the Pediatric Reference Interval Project being undertaken by a group of laboratories in the United States (reference 3).

3. *Dynamic function tests.* In most instances, the DFTs carried out were appropriate to the paediatric service provided by the hospital in which the laboratory was located. The insulin hypoglycaemia and glucagon tests, both of which are potentially dangerous, were performed only in tertiary paediatric referral centres where there was a consultant paediatric endocrinologist in post. However, it is of concern that a protocol for the exercise test for growth hormone stimulation is still held in one DGH, as this test is now generally considered to be obsolete. The tests were performed at ward level by a variety of staff types and grades generally appropriate to the DFT. Results were interpreted by either laboratory or medical staff, or both, presumably depending on local expertise. The great majority of responding laboratories had written protocols and interpretative cut-offs for the DFTs they carried out in children. Most interpretative cut-offs came from the published literature or a textbook, although one laboratory had derived its own cut-offs for several DFTs, one used protocols and cut-offs from Great Ormond Street and for two laboratories the source was unclear. The survey did not ask for details of individual protocols nor did it seek to evaluate whether the interpretative cut-offs used were appropriate.

4. *Hypoglycaemia investigation protocols.* It was gratifying that all except one responding laboratories providing an in-patient paediatric service had a written protocol for investigating hypoglycaemia in their hospital, in some cases held by the ward rather than the laboratory. Both metabolic and endocrine tests were included in all protocols but the range of tests and test priority order varied considerably. Some did not include a confirmatory plasma glucose (although this may have been assumed) and some appeared to prioritise tests in their own repertoire that were of little or no relevance to hypoglycaemia, instead of more appropriate tests that required referral to another laboratory e.g. insulin. Some laboratories had adopted the protocols from Yorkhill and RHSCE respectively. There is scope for greater harmonisation of hypoglycaemia investigation protocols across Scotland. Interpretation of endocrine responses to hypoglycaemia was a problem for many laboratories, with half reporting results without comment. The reasons were partly cultural (some laboratories rarely comment on results), partly lack of confidence/knowledge and partly reliance on someone else to interpret results. Interpretation may fall between multiple stools, with the laboratory relying on the

paediatrician, the paediatrician relying on the laboratory and laboratories relying on one another.

5. *Non-responders.* Most of these were laboratories serving district general hospitals in which the paediatric workload is probably a small component of the total workload. Nevertheless, many of the hospitals concerned do provide a neonatal or paediatric service, or both, with several consultant paediatricians in post. Indirect anecdotal evidence suggests that some of the non-responders do not provide paediatric reference ranges and may not provide appropriate guidance for hypoglycaemia investigation protocols and their interpretation.

7. References

1. Soldin SJ, Brugnara C, Wong EC (eds). Pediatric reference ranges. AACC Press, Washington. 4th ed 2003.
2. Khun Chan M, Seiden-Long I, Quinn F, Ambruster D, Adeli K. Canadian Laboratory Initiative on Pediatric Reference Interval Database (CALIPER): pediatric reference intervals for 8 endocrine hormones on Abbott ARCHITECT® $i2000_{SR}$. [Abstract] 17th IFCC-FESCC European Congress of Clinical Chemistry and Laboratory Medicine, 2007.
3. Pediatric Reference Interval Project. Children's Health Improvement through Laboratory Diagnostics. www.childx.org/

Recommendations

1. Laboratory endocrine test repertoire and referral patterns within Scotland currently appear to be appropriate for workload. The UK provision of an accredited laboratory service for anti-GAD, anti-insulin and anti-IA2 antibodies for type I diabetes in cases of diagnostic difficulty remains sub-optimal; however, this issue cannot presently be resolved within Scotland as the low workload probably does not justify a separate Scottish service. Future laboratory service provision for paediatric endocrinology in Scotland will depend on robust procedures for equipment replacement, staff succession planning and training, both for biomedical scientist and clinical scientist staff.

2. Grade B clinical scientist and chemical pathology specialist registrar training should include periods of secondment to one of the paediatric laboratories in Scotland. This is already occurring on an ad hoc basis for varying periods, and places a considerable burden on the paediatric laboratories. Such training requires to be appropriately resourced. Training should include paediatric endocrinology topics to improve interpretative skills.

3. There is a need for a Laboratory directory to include specialised endocrine tests. In this regard, it should be noted that there is currently a wider review of all laboratory services in Scotland in progress, chaired by Graham Beastall, with Mike Wallace responsible for the section on specialised Clinical Biochemistry, including specialised endocrinology. The review was set up by the Scottish Executive following a specific recommendation arising out of 'Delivering for Health' and is due to report this year. One of the outcomes will be a Directory of Scottish Specialised Laboratory tests. It will be important to keep the information up to date and a continually updated web-site would be the preferred option.

4. Obtaining robust evidence-based paediatric reference ranges is difficult and, in the longer term, may require active multi-centre collaboration among laboratories, paediatricians and manufacturers under the auspices of an appropriate professional association. Development of harmonised paediatric reference ranges is a challenging goal because there are considerable differences in hormone results obtained by different methods on different analysers. It would depend on instrument/method harmonisation, perhaps through a centralised procurement process, which must also involve consideration of suitability for paediatric samples. This long term goal may not be fully achievable. A shorter term partial solution would be to convene a working group, perhaps under the auspices of the Scottish Paediatric Endocrine Group (SPEG), to investigate what evidence-based endocrine paediatric reference ranges are available for the methods in use. Any identified gaps would require collaboration among laboratories, other organisations and the diagnostics industry to remedy. There are clear resource implications. All stakeholders would need to be signed up to the process and its implementation.

5. It would be desirable to develop a Scottish handbook of paediatric dynamic function test protocols, together with advice on interpretation, for use by both laboratories and paediatricians in Scotland. This could be achieved through the Scottish Paediatric Endocrine Group, with input from appropriate laboratories.

6. Infants and children may present with hypoglycaemia in or to a wide variety of hospital locations, including neonatal units, children's wards and Accident and Emergency.

Although neonatal units usually have a hypoglycaemia protocol, this may not always be true of other locations. Possible causes of hypoglycaemia include both endocrine and metabolic. It is recommended that the hypoglycaemia investigation protocols used by Yorkhill and RHSCE should be harmonised, together with interpretative guidelines, then rolled out to other laboratories and hospitals in Scotland.

P. Crofton, July 2007