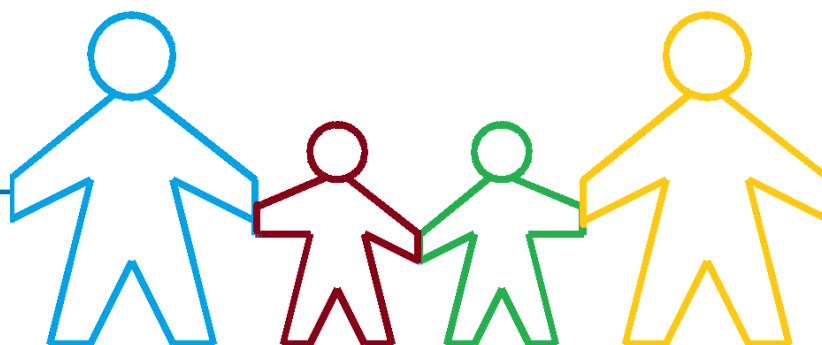


YORK TEACHING HOSPITALS

CLINICAL BIOCHEMISTRY

**P A E D I A T R I C
H A N D B O O K**

OCTOBR 2019, VERSION 5.0



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PAEDIATRIC CLINICAL BIOCHEMISTRY HANDBOOK

1. INTRODUCTION

This guide has been designed by the biochemistry department in consultation with the paediatric teams at York and Scarborough Hospitals. It is hoped that it will:

- Help you collect the correct specimen types for the tests you require
- Answer common questions about sample volumes and collection
- Prepare patients requiring specialist follow-up for referral to tertiary centres

If you have any remaining concerns or questions regarding sample volumes or types after reading this information, please contact the duty biochemist on extension 6366.

GENERAL INFORMATION

Biochemistry at York Hospital

The Laboratory Medicine Department reception is located on the ground floor at York Hospital with the departments on the first, second and third floors above. Our address is:

Laboratory Medicine Department,
York Hospital
Wigginton Road
YORK
YO31 8HE

The Laboratory Medicine Department is the block to the right of the main hospital entrance at Junction 2a. Biochemistry is situated on the second floor and is open from 08:30 to 17:30 Monday to Friday. Please see the 'contact details' section on page 4 for details regarding enquiries about results and specimens.

Biochemistry at Scarborough Hospital

The Laboratory Medicine Department is located in a purpose-built block at Scarborough Hospital and spans two storeys. From inside the hospital and the South and North entrances, follow the signs to Pathology.

Our address is:

Laboratory Medicine Department,
Scarborough Hospital
Woodlands Drive
Scarborough
YO12 6QL

The department is labelled as point F on the hospital plan below:



The Pathology office, stores, phlebotomy, blood sciences and blood transfusion are on the ground floor, microbiology is on the first floor. Access into the laboratory is restricted (electronically locked doors) and visitors are asked to report to the office reception. Please see the 'contact details' section below for details regarding enquiries about results and specimens.

CONTACT DETAILS

Please use the CPD reporting system whenever possible. This is available on the hospital network and is updated with completed results every 15 minutes.

For results & specimen enquiries:

YORK HOSPITAL

Blood Sciences Office, York (01904 72) 6802
 Available 09:00 – 18:30 Monday to Friday

SCARBOROUGH HOSPITAL

Scarborough Reception (01723 34) 2351

Note that the York office cannot provide copy reports or updates on samples that are live within the laboratory at Scarborough. For copy reports or results on samples collected <24 hours prior, please use the details provided for Scarborough.

Out of hours enquiries:

On-call Biomedical Scientist Bleep via switchboard

The department operates a shift system and there is a biomedical scientist (BMS) in the hospital at all times. Outside routine hours only one BMS is on duty and they are often extremely busy. Please be patient and only bleep when absolutely necessary.

For clinical advice, specialist testing and interpretation of results:

Duty Biochemist (01904 72) 6366
Available between 09:00 and 18:00 Monday to Friday

Out of hours clinical advice:

On-call Consultant Biochemist Contact via switchboard

Point of Care Testing:

Anne Penrice (01904 72) 5890

Point of Care Co-ordinator

Clinical Biochemists:

Alison Jones (01904 72) 5786

Consultant Clinical Biochemist and Lead Clinician

Alison.jones@york.nhs.uk

Dr. Deepak Chandrajay

(01904 72) 5670

Consultant Chemical Pathologist

Deepak.chandrajay@york.nhs.uk

Dr. Daniel Turnock

(01904 72) 1847

Consultant Clinical Biochemist

daniel.turnock@york.nhs.uk

Miss Claire Chapman

(01904 72) 6098

Principal Clinical Biochemist

claire.l.chapman@york.nhs.uk

Mrs Maria de Ferrars

(01904 72) 5599

Senior Clinical Biochemist

maria.flenley@york.nhs.uk

YORK HOSPITAL ONLY

For Phlebotomy and blood-taking enquiries:

Paediatric phlebotomy – Childrens' Assessment Unit (01904 72) 2018

For complaints and quality improvement:

Mrs Joanna Andrew

(01904 72) 5802

Head Biomedical Scientist - York

joanna.andrew@york.nhs.uk

SCARBOROUGH HOSPITAL ONLY

For Phlebotomy and blood-taking enquiries:

Charlotte Goodall / phlebotomy team (01723 34) 2652

Charlotte Goodall / phlebotomy team

Senior Phlebotomist - Scarborough

charlotte.goodall@york.nhs.uk

Scarborough Pathology Office:

Mrs Caroline Vipurs

(01723 34) 2356

Pathology Office Manager – Scarborough

caroline.vipurs@york.nhs.uk

For complaints and quality improvement:

Mr. Carl Burkinshaw

(01723 34) 2028

Operational Manager

carl.burkinshaw@york.nhs.uk

REQUESTS AND REPORTS

Any request form **must** display an **NHS number, date of birth, surname, and forename**, preferably printed in CAPITALS. Identifiers must be correctly spelt and complete, i.e. Initials are insufficient, as is an age of patient or just a year of birth.

Unlabelled samples are unfortunately not suitable for processing and will be discarded.

Where possible, please include all patient details including location, gender, and any relevant clinical information or drug history. This will ensure that results are delivered to the correct location with appropriate interpretive comments.

The table below shows the identifiers that may be included on the sample request form and sample tubes in order to process a request. The identifiers provided on the form and sample **MUST MATCH** e.g. samples should not be labeled 'Bob' if a form states the patient's name as 'Robert.'

	ESSENTIAL	Desirable	Optimal
Request Form	Tests required Surname Forename <u>AND</u> At least one of the following:- -NHS number - DOB -Hospital Number - A/E number	Essential details <u>AND</u> Requestor name Time and date collected Clinical Details Priority tests Urgency status* Risk status*	Essential and desirable details <u>AND</u> Patient's current location Patient's gender Patient's address Drug history Dose and Time for drug assays Consultant/GP contact details (essential for any immunology)
Sample Tube	Surname Forename <u>AND</u> At least one of the following:- -NHS number - DOB -Hospital Number - A/E number	Essential details <u>AND</u> Time and date collected Risk status**	Essential and desirable details <u>AND</u> Requestor name

*please see 'urgent or infectious samples' section overleaf for details.

URGENT OR INFECTIOUS SAMPLES

Urgent specimens should be taken by the doctor and hand-delivered to the laboratory immediately with a request form clearly marked URGENT. The laboratory must be informed by telephone of the imminent arrival of an urgent sample (**For York: 6802, for Scarborough: (01723 34) 2351, York or Scarborough out of hours: bleep on call biomedical scientist**).

Samples marked “urgent” for which there has been no telephone call will be treated as routine.

High Risk Samples are those collected from a patient that has (or is suspected of having) any disease classed as category 3 or above, and any of the following:

HIV TB CJDv HepB HepC

All samples high risk samples should be taken by medical staff, **clearly labelled as high risk of infection with a yellow sticker, and double bagged.**
These samples CAN NOT be transported using the vacuum tube system.

1) *Requests made by Ordercomms electronic requesting.*

The High Risk box must be ticked. This ensures a subtle format change to the request form which, along with the use of double bagging, provides all the labelling required. Samples must also be labelled with a high risk sticker.

2) *Other requests.*

Where no Ordercomms requesting is available the infection risk of the patient must be indicated on the request card, in addition to a sticker on the sample. Samples should be double bagged (placed inside a second request form bag).

Any queries regarding high risk samples should be directed to the on-call microbiologist (via switchboard). If Phlebotomists are asked to take blood from patients at high risk of infection or being barrier nursed, they must be informed of the situation.

Requesting further tests on samples already received in the laboratory

We keep most of the samples we receive for approximately 3 days before they are discarded. Some samples are kept longer depending on the tests requested. If you want to add further tests to a sample please use the add-on functionality in CPD. If the desired test is unavailable, please ring (01904 72) 6802 OPTION 1 in York or the laboratory on (10723 34) 2351 in Scarborough.

We will check if we still have the sample and then add the tests. Please note that some analytes are labile and deteriorate rapidly. In these cases we will tell you that the sample we have left is unsuitable and fresh sample will have to be taken.

Reports

Most reports are available to view on CPD and completed reports are uploaded electronically every 15 minutes for the hospital.

Reference Ranges

Age- and sex-related reference ranges are printed on the report forms alongside the result and listed in section 3 (table of sample requirements). Please contact the duty biochemist if you have any queries regarding paediatric reference ranges (772 6366).

PHLEBOTOMY (BLOOD TAKING)

YORK HOSPITAL ONLY

Paediatric blood samples are collected on the Childrens' Assessment Unit (CAU) on Ward 18, or by a qualified healthcare professional on the paediatric ward. To arrange an appointment for sample collection, please contact CAU (01904 72 2108). Note that phlebotomy do not provide a routine service for paediatric patients at York.

SCARBOROUGH HOSPITAL ONLY

The phlebotomy department on the ground floor of the pathology block next to reception will collect blood samples on children aged >4 years. To arrange an appointment please contact charlotte.goodall@york.nhs.uk at least 1 week in advance. Opening hours: 9am - 5pm, Monday to Friday.

To reach pathology, enter the hospital via the main entrance, turn right and follow straight down the corridor. At the end of this corridor turn right again and continue until you reach Pathology Reception, where you should hand in your request form.

PREPARATION

To avoid errors in sample collection, when bleeding paediatric patients, we ask that:

(1) You familiarise yourself with the requirements for your samples BEFORE bleeding a patient, using the information in section 3.

Please highlight any special requirements to the phlebotomist. If you remain unsure about sample requirements for your specific investigations, please phone the duty biochemist (01904 72 6366). You may be directed to other departments if your query relates to haematology or immunology tests.

In some cases, there may be special requirements for samples to be delivered to the lab within a specific timeframe or under special conditions (e.g. on ice, or with specialist paperwork). These are listed in the 'sample requirements' column in the tube type tables in section 3.

If these requirements are not met, the sample may not be processed.

(2) Any samples requiring ice or immediate delivery to the lab are taken to the specimen reception hatch by hand.

This is the only way to guarantee safe delivery – air tubes may be unsuitable for some sample types and may fail, causing samples to be lost or delayed.

(3) You consider test priorities carefully before proceeding with phlebotomy and indicate any tests that are a priority on the sample request form.

This is particularly crucial if there is a limited sample volume or specialist test.

Specialist tests may need to be transported to referral laboratories in other parts of the UK. Where large numbers of specialist investigations are being carried out, each needing to be sent to a different centre, the number of tubes required may add up very quickly!

(4) No more than 4 tests are ordered to a single paediatric tube - please provide an additional sample when ordering 4 or more routine tests on the same sample type.

If this is not possible, consider splitting the number of requests across separate phlebotomy episodes. Please also note that certain tests may require a separate sample, as indicated in section 3.0

(5) Adult sized tubes are used wherever possible – this avoids difficulties with sample volume and quality associated with using numerous small tubes.

2. TESTS AND TUBES

TURNAROUND TIMES AND TEST REPERTOIRE

We are able to measure over a hundred analytes in the laboratory. Most assays are performed daily, but some specialist tests are performed less frequently or sent away to other laboratories. Sending samples to other laboratories may prolong the time taken to obtain results and require collection of extra samples (see section 3).

Turnaround times are calculated from the time that the sample is received in the laboratory to the result becoming available to the user in electronic format. Exact turnaround times for any test can be supplied on request, however, as a guide:

Test Type	Examples	50% reported within	75% reported within	95% reported within
Routine, non-urgent chemistry	CRP Glucose	45 minutes	1 hour	2.5 - 3 hours
Urgent Samples	Glucose marked 'urgent' & lab informed	1 hour		
Endocrine Tests	TFT, FT3, B12, ferritin			24 hours
	LH, FSH, Oestradiol, Testosterone			3 days

Test Repertoire

For simplicity the following tests are grouped with other, related tests:

Test Group	Analytes Included as Standard
Bone Profile	Calcium, Phosphate, Albumin, ALP (Alkaline phosphatase)
Liver Function Tests (LFT)	Bilirubin, Total Protein, Albumin, ALP, ALT (ALT = Alanine amino transferase)
Urea and Electrolytes (U&E)	Sodium, Potassium, Urea, Creatinine (eGFR is not valid in patients <18 years of age)

If you only require a single test or selected tests from a group please indicate which tests are required by writing their names in the space below the request boxes.

THIS IS ESPECIALLY IMPORTANT WITH LOW-VOLUME PAEDIATRIC SAMPLES when there may be insufficient sample to perform all the requested tests. Please highlight any priorities during sample analysis to ensure that any crucial tests are performed first.

Blood gases and ionised calcium

YORK HOSPITAL

These are measured on the machines in SCBU. There are also machines in Delivery, CCU, AMU, ICU, and the Emergency Department. Samples from ward based patients are analysed by healthcare staff on one of these analysers.

SCARBOROUGH HOSPITAL

Machines are available in ITU, AAU, A&E and Bridlington Ward. Samples from ward based patients are analysed by healthcare staff on one of these analysers.

TUBE TYPES AND ORDERING

Sample Preservatives

All samples will deteriorate from the time they are collected but, with a few simple measures, this can be minimised. Samples collected in the hospital should be transported to the laboratory as soon as possible. For some tests special collection procedures should be followed. Please check the tables of sample requirements in section 3. The following types of samples are available for paediatrics:

Plain gel (serum): BROWN TOP →

Suitable for most routine biochemistry tests



Lithium Heparin (plasma): ORANGE TOP →

Suitable for most routine biochemistry tests
Mandatory for some metabolic tests
e.g. very long chain fatty acids, karyotyping



EDTA (plasma): RED TOP →

Required for routine haematology tests (e.g. FBC),
as well as PTH, microarray studies and some
specialist biochemistry e.g. lead analysis.



Fluoride Oxalate (plasma): YELLOW TOP →

Mandatory for measurement of glucose and lactate



Sodium Citrate (plasma): GREEN TOP →

Used within haematology for clotting studies. Not
routinely used for biochemistry tests.



Ordering Consumables

YORK HOSPITAL

There is a form for ordering consumables from Pathology Reception:
This form can be sent into the laboratory or faxed to 01904 726358.
Please order weekly and try not to keep large stocks of consumables
as some items deteriorate with time.



Consumables Order
Form.doc

SCARBOROUGH HOSPITAL

Consumables are ordered by filling in an order form, which can be obtained from Pathology stores (email below). The completed form should be scanned and emailed to pathologystores@york.nhs.uk or delivered by hand. Please allow 3-5 days for order processing. As some items deteriorate with time, we advise placing regular orders rather than keeping large stocks of consumables.

DYNAMIC FUNCTION TESTS (DFTs)

The most commonly performed dynamic function test in paediatric patients is the combined pituitary function test. Like all DFTs, this is complex in terms of patient preparation, sample collection and generation of reports in the laboratory.

As the samples collected are extremely precious, we recommend that you:

- (1) Perform the test in the morning. As the protocol takes 3 full hours to complete, afternoon testing results in samples reaching the laboratory at the busiest time of day (late afternoon/evening) and they may not be processed efficiently.
- (2) Familiarise yourself with the protocol and sample requirements before beginning the test. Collect and label all tubes required in advance.
- (3) Hand deliver samples to the lab – **do NOT use the air tube**
- (4) **Deliver all samples to the laboratory promptly once the final set has been collected from the patient (at 180 min)**. Handling DFT samples is typically complex and delivery of samples for more than one patient at the same time greatly increases the chance of human error in the laboratory.
- (5) Use the step-by step guide below when placing on order in CPD.

Ordering a Combined Pituitary Function Test in CPD

The combined pituitary function test MUST be carried out as specified in the protocols supplied by specialist healthcare professionals. This table provides an overview of the test and samples required:

Time Point	Test for	Tubes required
Preparation	Follow patient preparation instructions detailed in the clinical protocol. Collect and label any sample tubes required during the test.	
Baseline (0 mins)	ACTH	1 x EDTA (red top) Deliver to lab immediately (within 30 min)
	EITHER testosterone OR oestrogen	1 x brown top serum Specify whether oestrogen or testosterone is required
	TSH, FT4, LH, FSH, prolactin, GH, IGF-1, cortisol	Minimum of 2 x full tubes (brown top serum or orange lithium heparin) 1 x brown top serum for IGF-1
Give Glucagon as specified by clinical protocol		
30 mins	Cortisol, Growth Hormone	2 x full tubes (serum or lithium heparin)
60 mins	Cortisol, Growth Hormone	2 x full tubes (serum or lithium heparin)
90 mins	Cortisol, Growth Hormone	2 x full tubes (serum or lithium heparin)
120 mins	Cortisol, Growth Hormone	2 x full tubes (serum or lithium heparin)
150 mins	Cortisol, Growth Hormone	2 x full tubes (serum or lithium heparin)
180 mins	Cortisol, Growth Hormone	2 x full tubes (serum or lithium heparin)

To order in CPD:

- Go to the CPD "Place order" screen, select patient, consultant and enter clinical details as normal.
- Select BIOACTH from a list of pathology order items as you would for a normal blood test order.

- In the next field, select either BIOTES (testosterone) or BIOOES (oestradiol) depending on whether the patient is male or female.
- Click "Order sets" button and search "pituitary" to find the order set called "PITUITARY FUNCTION TEST – PA." This should add a list of items beginning with BIOPFT0 and ending with BIOPFT180. **If you can't find this order set, click the option for: "View sets I am not authorised to submit" and search again.**
- BEFORE clicking the "process order" button, the "Sample Sep" box on the right hand side should be ticked for each item on the list. This will ensure that 9 separate request forms are printed.
- Clicking 'process order' will bring up a prompt to send the ACTH sample to the laboratory immediately (all other samples can be stored on the ward).
- Once all forms are printed, collect the ACTH sample (red top) and handwrite the time of collection on the request form. Deliver this to the laboratory immediately by hand (must arrive within 30 minutes of sample collection).
- Follow the clinical protocol for collecting the rest of the samples. Label each sample taken during the test with the actual time of collection (e.g. 10:27 if sample collected at this time) AND the time in relation to the DFT (e.g. t = 0, t = 30 min etc). Store samples and forms on the ward until the end of the test.
- Once test is complete and all blood samples have been collected, CHECK ALL TIMES AND PATIENT INFORMATION on the samples and request forms to ensure that these match up. Send all seven samples down to the laboratory.

Please refer to the Endocrine Protocols or contact the duty biochemist (01904 726366) for further information or assistance.

SWEAT TESTING FOR CYSTIC FIBROSIS

This involves electrical stimulation of sweat glands near the skin surface and collection of a sweat sample by a trained member of laboratory staff. Patients should be >2 weeks of age (preferably >3 months), well hydrated and without systemic illness.

Sweat testing may need to be rescheduled:

- if an insufficient volume is collected (e.g. patient very young or dehydrated)
- if the collection site is eczematous
- if there is evidence of systemic illness or oedema
- in patients on topimarate, 9-alpha fludrocortisone, or open delivery oxygen systems

(Guidelines for the Performance of the Sweat Test for the Investigation of Cystic Fibrosis in the UK v.2)

To arrange an appointment for sweat testing:

YORK HOSPITAL

Please phone 5802 to arrange an appointment (WEEKDAYS and typically >7 days in advance).

SCARBOROUGH HOSPITAL

Contact the pathology office on (01723 34) 2356. As the office is not open at weekends, and the laboratory needs to ensure that a trained tester is available, we advise booking at the earliest possible opportunity. Although the majority of sweat tests take place in the pathology department during a dedicated outpatient appointment, testing can usually be arranged for inpatients,

CSF NEUROTRANSMITTERS

Monoamine metabolites, Pterins, Methyl Tetrahydrofolate and Pyridoxal-5-phosphate (Vitamin B6)

These are highly unstable analytes, which are collected by lumbar puncture into a special preservative, and must be collected onto ice by a member of laboratory staff at the patient bedside. If this investigation is planned, the laboratory should be contacted at the earliest possible opportunity so that specialist collection tubes can be ordered and arrangements made for a trained member of staff to be available.

Ideally, one of the consultant biochemists should be copied into the letter stating the date and time of the lumbar puncture appointment. This should be confirmed by contacting the duty biochemist on 6366 a week before the appointment takes place.

Failure to notify the laboratory promptly may result in appointment cancellation.

GENETIC TESTING

(Microarray, Karyotyping and Molecular Genetics)

Genetic test requests should generally be made through the Yorkshire Regional Genetics service. Referral to a clinical geneticist ensures that patients are appropriately counselled prior to testing, that a targeted test or panel of gene tests are carried out, and that relevant ethical guidance is followed.

Where necessary, samples may be referred to Leeds on behalf of the genetics team or an experienced specialist (usually a consultant). These requests **MUST** be accompanied by a fully completed genetics request card, which can be accessed using the links below.

- For **most molecular genetic or cytogenetic tests** (microarray, karyotyping, genes or gene panels):
<http://www.leedsth.nhs.uk/assets/Uploads/Referral-form-June-2016.pdf>

- For DNA testing in suspected **mitochondrial disorders**:
[http://www.mitochondrialncg.nhs.uk/documents/NCG Referral Form.pdf](http://www.mitochondrialncg.nhs.uk/documents/NCG%20Referral%20Form.pdf)

If testing for **MODY, Familial Hypercholesterolaemia, FHH** or **MEN-1**, please contact the duty biochemist on extension 6366 (these samples are referred elsewhere and also require a request form, which we will be able to provide you with).

DRIED BLOOD SPOT SCREENING FOR FABRY DISEASE IN FEMALE PATIENTS

Fabry disease is a lysosomal storage disorder, and can be detected on a white cell enzyme panel or using a dried bloodspot (a more targeted method if there is strong clinical suspicion of Fabry's).

If the dried bloodspot method is used, abnormal results in female patients are followed up using genetic testing.

For this reason, **ANY female patient undergoing Fabry's screening using the dried blood spot method should be made aware that genetic testing is a possibility and asked to provide consent at the outset.**

When consent has been obtained, this should be written onto the request form that comes with the sample i.e. "Consent for genetic testing obtained."

Failure to document that consent has been obtained may result in a delayed diagnosis as the referral laboratory that carries out testing for Fabry's disease will not proceed with genetic follow-up unless they have a clear, written statement of consent.

Consent is not necessary if a full white cell enzyme screen is being performed, as genetic testing for Fabry's does not form part of this screening procedure (any abnormal findings on the white cell enzyme screen can be followed up using more specific tests, such as the dried blood spot method. It is only at this point that the possibility of genetic testing will need to be considered).

GENERAL GUIDANCE FOR INTERPRETING BIOCHEMISTRY RESULTS IN PAEDIATRICS

This topic is the subject of an excellent review in the British Medical Journal (see <https://www.bmj.com/content/bmj/361/bmj.k1950.full.pdf> or click below to view pdf)



Biochemistry
Interpretation for Paed

Although the laboratory supplies paediatric reference ranges wherever possible, these are not available for every test offered by the laboratory. This may be because:

- Concentrations of an analyte in a particular age group have not been studied due to challenges in sampling and analysis (e.g. premature neonates)
- The evidence base for paediatric reference ranges in tests which have been recently been developed is poorly established (e.g. Faecal Calprotectin)
- Concentrations of an analyte vary over a huge range during early life and it is not practical to include a full list of paediatric ranges in tests which are more commonly requested in adults (e.g. sex hormones, gonadotrophins).

As such, you should be aware that tests results may sometimes be flagged as 'abnormal' in a child due to an adult range having been applied and interpret all values in the context of a patient's clinical presentation and developmental stage.

If you require assistance with result interpretation, please contact the Duty Biochemist on 01904 726366.

We will do our best to help you source an appropriate reference range, but please be aware that we are limited by what has been published in the scientific literature.

When ordering a specific test, it is essential to remember that you are committing to the responsibility of acting on the end result and should have a reasonable idea of how the result that is returned to you will influence patient management.

3. TABLES OF SAMPLE REQUIREMENTS

ROUTINE BIOCHEMICAL TESTS

The laboratory will make every attempt to ensure that the tests required are carried out on the sample volume provided, but **please be aware that additional tubes may be required if multiple tests are being requested. If possible, provide a second sample where there are 4 or more routine tests to perform. A new tube is also required for any tests requiring a 'separate sample' where this is indicated in the tables below.**

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE								
Alanine aminotransferase (ALT) Part of LFT profile Increases indicate liver cell damage.	Serum or Lithium Heparin	Daily	F = 0-34 IU/L M = 0-45 IU/L								
Albumin - Part of LFT and Bone Profiles Low levels reflect kidney/GI loss, infection, malnutrition, hemodilution or redistribution	Serum or Lithium Heparin	Daily	<1 year: 30-45 g/L 1-16 years: 30-50 g/L								
Alkaline Phosphatase (ALP) Part of LFT and Bone Profiles Elevated in bone and liver disease or benign transient hyperphosphatasia.	Serum or Lithium Heparin	Daily	Neonate: 70-380 U/L Child <16: 60-425 U/L >16 years: 30-130 U/L								
Alpha Fetoprotein (AFP) Produced by the foetal liver and yolk sac during gestation and up to 1 year of age. Used alongside other tests to diagnose and monitor hepatoblastoma, and in detection of interuterine disease	1mL blood in Serum or Lithium Heparin	Daily	>1 year-old: <7 kU/L Please contact the duty biochemist to discuss age-specific ranges in children <1 year old.								
Ammonia Investigation of suspected hyperammonaemia e.g. in encephalopathy, hyperventilation and acid base disturbances.	1mL in EDTA Samples must arrive within 30 minutes of collection.	Daily	<table style="width: 100%; border: none;"> <tr> <td style="text-align: right;">Group</td> <td style="text-align: right;">umol/L</td> </tr> <tr> <td>Sick/premature:</td> <td style="text-align: right;"><150</td> </tr> <tr> <td>Neonate:</td> <td style="text-align: right;"><100</td> </tr> <tr> <td>Child <16 years:</td> <td style="text-align: right;"><50</td> </tr> </table>	Group	umol/L	Sick/premature:	<150	Neonate:	<100	Child <16 years:	<50
Group	umol/L										
Sick/premature:	<150										
Neonate:	<100										
Child <16 years:	<50										
Aspartate aminotransferase (AST) Raised in liver and muscle damage. N.B. this is NOT included in the LFT profile.	Serum or Lithium Heparin	Daily	F = 0-31 IU/L M = 0-35 IU/L								
Bicarbonate (Total CO₂) Informative about acid/base status.	Serum 1.3mL	Daily	22-29 mmol/L								
Bilirubin - Part of LFT profile Total bilirubin may be raised for numerous reasons, including 'breast milk jaundice,' haemolysis, or hepatocellular dysfunction	Serum or Lithium Heparin Samples should be protected from light if possible.	Daily	14 days-16 years: <21 umol/L								
Bilirubin Split (Conjugated and Unconjugated) Differential diagnosis of jaundice. Unconjugated bilirubin predominates in haemolytic or 'breast milk' jaundice; conjugated bilirubinaemia indicates other causes (e.g. infection, biliary atresia, IMD).		Daily	Direct bilirubin >33% of total is generally considered conjugated hyperbilirubinaemia.								
Bone Profile Includes total and adjusted calcium, phosphate, albumin, total protein, ALP	Serum or Lithium Heparin	Daily	See individual analytes								

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Calcium (Total) - Part of Bone Profile Assessment of calcium homeostasis. Adjustment provides an estimate of free calcium, based on total calcium and albumin concentrations.	Serum or Lithium Heparin	Daily	Neonate: 2.0-2.7 mmol/L Child <16: 2.2-2.70 mmol/L
Ceruloplasmin Copper binding serum protein used to screen for Wilson's disease	Serum or Lithium Heparin Separate sample required.	Weekly	0.20-0.60 g/L
Chloride Note routinely reported, but may be useful in investigation of electrolyte imbalance and acid-base disorders.	Serum or Lithium Heparin	Daily	95-108 mmol/L
Cholesterol Diagnosis and monitoring of disorders of lipid metabolism, such as familial hypercholesterolaemia or diabetes.	Serum or Lithium Heparin	Daily	Levels >6.5 mmol/L in a child <16 years of age may be suggestive of FH.
LDL Cholesterol Calculated from total cholesterol and triglyceride in fasting sample.	Serum or Lithium Heparin	Daily	Levels >4.0 mmol/L in a child <16 years of age may be suggestive of FH.
C-reactive protein (CRP) Acute phase reactant, particularly increased in bacterial infection	Serum or Lithium Heparin	Daily	<5 mg/L
Creatinine Part of U&E profile Measurement of renal function. Affected by muscle mass, muscle breakdown and protein intake as well as glomerular function. For this reason, age-related ranges are a guide only.	Serum or Lithium Heparin Please specify if dopaminergic drugs or vitamin supplements are used.	Daily	Dependent on muscle mass, roughly (umol/L): Neonate: 22-90 Infant <1 yr: 11-34 Child <14 years: 21-65 Age>14 years: 49-104
Creatine kinase (CK) Non-specific indicator of muscle damage. Raised in inherited myopathies and neuromuscular disorders, such as Duchenne Muscular Dystrophy.	Serum or Lithium Heparin	Daily	No-specific paediatric range – as a guide, adult ranges are: F = 25-200 IU/L M = 40-320 IU/L
Gamma glutamyl transpeptidase (GGT) Sensitive indicator of liver disease. Increased after exposure to enzyme inducing drugs (e.g. ethanol) or hepatobiliary damage. N.B. this is NOT included in the LFT profile.	Serum or Lithium Heparin	Daily	F = <38 U/L M = <55 U/L
Glucose Diagnosis and monitoring of diabetes mellitus and hypoglycaemia.	Fluoride Oxalate	Daily	Fasting: 2.5-6.0 mmol/L
Glucose (CSF) Measured in bacterial meningitis	1 mL CSF in Fluoride Oxalate	Daily	0-2 years: 2.2-3.9 mmol/L >2 years: 3.3-4.4 mmol/L
Haemoglobin A1c Monitoring of glycaemic control in diabetes mellitus – NOT suitable for diagnosis of diabetes in children.	EDTA 1.3mL	Daily	20-42 mmol/mol

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Haptoglobins Decreased with <i>in vivo</i> haemolysis or ineffective erythropoiesis. Increased after corticosteroids and acute phase response.	Serum or Lithium Heparin Separate sample required.	Weekly	0.30-2.00 g/L
Iron Used in assessing iron toxicity. Ferritin is a better indicator of iron storage.	Serum or Lithium Heparin Please include details of any iron therapy.	Daily	0-2 years: 9-21 umol/L M >2 y: 12-30 umol/L F >2y: 9-27 umol/L
% Iron saturation Calculates % of transferrin bound to iron.		Daily	15-50%
Lactate (CSF) Increased in some inherited metabolic disorders (e.g. mitochondrial cytopathy) also bacterial and fungal meningitis	1 mL CSF in Fluoride Oxalate	Daily	1.1-2.4 mmol/L
Lactate (whole blood) Investigation of hypoglycaemia, inborn errors of metabolism or unexplained acidosis.	1mL in Fluoride Oxalate Patient should be resting.	Daily	0.6-2.5 mmol/L
Lactate Dehydrogenase (LDH) Measured in jaundice and suspected haemolysis. Also suitable for use in megaloblastic and pernicious anaemias, leukaemia, lymphomas, and liver disease	Serum or Lithium Heparin	Daily	<248 IU/L
Liver Function Tests (LFT) Includes ALT, ALP, Total Protein, Albumin, total bilirubin.	Serum or Lithium Heparin	Daily	See individual analytes
Magnesium Measured in hypocalcaemia (low Mg impairs PTH release), nutritional deficiency, GI losses (e.g. severe diarrhoea) and renal tubulopathy. Serum Mg levels are not a good indicator of body stores.	Serum or Lithium Heparin	Daily	Neonate: 0.6-1.0 mmo/L Child: 0.7-1.0 mmol/L
Osmolality (serum) Measurement of the total osmotically active particles in serum. Comparison with the calculated osmolarity can show if there is an "osmolar gap" due to unidentified substances in the serum (e.g. ketones).	Serum	Daily	275-295 mmol/kg (see specialist protocol for interpretation in water deprivation tests)
Phosphate Part of bone Profile Investigation of hyper- or hypo-phosphataemia, rickets, bone and renal disorders. Increases with standing or delayed separation from red cells	Serum or Lithium Heparin	Daily	Age mmol/L Neonate: 1.3-2.6 Infant <1 yr: 1.3-2.4 1-16 years: 0.9-1.8
Potassium Part of U&E Profile Monitored in renal disorders and infants requiring nutritional support. Old or haemolysed samples are not measured due to the spurious rise in potassium from the lysed red cells.	Serum or Lithium Heparin Samples MUST show a time of collection	Daily	Age mmol/L Neonate: 3.4 - 6.0 Infant <1 yr: 3.5 - 5.7 1-16 years: 3.5 - 5.0

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Protein (CSF) May be increased in meningitis and CNS tumours	Plain CSF	Daily	0-1 week: 0.45-1.09 g/L 1-4 weeks: 0.34-0.98 g/L 1-4 m: 0.19-0.71 g/L 4-6 m: 0.21-0.37 g/L 6m-1y: 0.13-0.41 g/L 1-16y: 0.12-0.32 g/L
Sodium (serum) - Part of U&E profile Main use is as a measure of the state of hydration of a patient.	Serum or Lithium Heparin	Daily	133-146 mmol/L
Transferrin Measured to estimate iron saturation in the investigation of iron overload and also as a marker of nutritional status	Serum or Lithium Heparin . Please include details of any iron therapy.	Daily	2.0-3.6 g/L
Triglycerides Diagnosis and monitoring of disorders of lipid metabolism, such as obesity and diabetes. Levels may be falsely raised due to contamination with glycerol in nappy creams or glycerol kinase deficiency.	Serum or Lithium Heparin Fasting sample preferred – please specify	Daily	<1.7 mmol/L
Urea and Electrolytes (U&E) Includes sodium, potassium, urea, creatinine. eGFR is not valid in patients under the age of 18 years old.	Serum or Lithium Heparin	Daily	See individual analytes
Urea - Part of U&E profile Measure of renal function (with creatinine) and degree of hydration (with sodium). Also affected by protein intake, GI bleeding and liver function.	Serum or Lithium Heparin	Daily	Neonate: 0.8-5.5 mmol/L Infant: 1.0-5.5 mmol/L 1-16 y: 2.5-6.5 mmol/L
Valproate Only useful to check compliance or possible overdose, little use for therapeutic monitoring (clinical effects more reliable).	Serum or Lithium Heparin collected before dose taken	Daily	No well-established range. As a rough guide: 50-100 mg/L
Zinc – Part of Trace Elements Profile Estimation of the zinc nutritional state of a patient. Must be interpreted with the serum albumin level (as some zinc is bound to albumin) and CRP (infection and inflammation decrease serum zinc).	Serum or Lithium Heparin Separate sample required.	Weekly	9.8 - 17.9 umol/L

IMMUNOASSAY AND ENDOCRINE TESTS

This includes most endocrine tests and haematinics. Please note that although plasma samples are now acceptable for the majority of these tests, testosterone remains an exception as different tube types can give significantly different results.

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Adrenocorticotrophin (ACTH) Second line test for adrenal & pituitary disorders.	1mL blood in EDTA MUST be put on ice and transported to the lab within 30 minutes of collection. Requires a separate sample to any other EDTA tests.	Sent away (Hull)	<47 ng/L Requires a paired cortisol for interpretation.
Aldosterone Investigation of hypokalaemia / hypertension	0.3mL Serum or Lithium Heparin Please include medication details. Requires a separate sample to any other tests.	Sent away (Leeds)	See report; interpreted in light of renin result
Androstenedione Measured with DHAS in adrenal androgen disorders.	Serum only Send separate sample to any other serum tests.	Sent away (Hull)	Pre-pubertal: <1.4 nmol/L
Cortisol (blood 9 a.m) Investigation of adrenal cortical function. Hydrocortisone and prednisolone interfere.	Serum or Lithium Heparin Please include details of any steroid medications or dynamic function tests and record TIME of collection.	Daily	150-650 nmol/L (a.m)
Dehydroepiandrosterone (DHAS) Measured with androstenedione in adrenal androgen disorders.	1.3mL Serum Send separate sample to any other serum tests.	Sent away (Hull)	Pre-pubertal: <1 umol/L
Ferritin To detect iron deficiency and iron overload (in rare cases). Increases in the acute phase, so CRP also measured.	Serum or Lithium Heparin Please specify if recently transfused or taking iron supplements.	Daily	M = 22-322 ng/mL F = 20-291 ng/mL
Folate (serum) Investigation of folate status.	Serum or Lithium Heparin	Daily	>3.4 ug/L
FSH Assessment of precocious or delayed puberty. Levels are best interpreted as part of stimulation or suppression tests.	Serum or Lithium Heparin	Daily	Pre-pubertal: <1 IU/L
Growth Hormone Investigation of hypoglycaemia, short stature and gigantism. Secretion is best assessed by stimulatory or suppression tests.	Serum or Lithium Heparin Please note that random levels provide little information, as secretion is pulsatile (i.e. low levels may be related to missed pulse). Separate sample ideally required.	Weekly	N/A – levels are best interpreted as part of stimulation or suppression tests – see individual protocols for further information.
17 Hydroxyprogesterone Diagnosis of CAH due to 21 hydroxylase deficiency in precocious puberty/hirsutism.	0.5 mL Serum Collect samples prior to dose if on treatment for CAH. Requires a separate sample	Sent away (Leeds)	0-5 days: 0-3 nmol/L 5 days -16y: 0-4 nmol/L

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Insulin (and C-peptide) Investigation of hypoglycaemia and newly-diagnosed diabetes. For hypoglycaemia, glucose must be measured simultaneously using the laboratory assay.	Serum only Samples must be transported ON ICE and arrive at the lab within half an hour of collection. Send separate sample to any other serum tests. Also send sample for glucose if screening for hypoglycaemia.	Sent away (Guildford)	See report – results are interpreted in light of blood glucose level at the time of sampling. Lab glucose must be <2.2 mmol/L for hypoglycaemia screening
Insulin-Like Growth Factor I (IGF-I) Useful in the investigation of growth disorders.	Serum only. Separate sample required to any other serum tests.	Sent away (Leeds)	See report for exact age-related range.
LH Assessment of precocious or delayed puberty. Levels are best interpreted as part of stimulation or suppression tests.	Serum or Lithium Heparin	Daily	Pre-pubertal: <2 IU/L
Oestradiol Assessment of delayed or precocious puberty in females and disorders of sexual development.	Serum or Lithium Heparin	Daily	Male: 0 – 206 pmol/L Female Pre-menstrual: 50-150 pmol/L Female Post-menarche: 150 -1500 pmol/L
Parathyroid Hormone (PTH) Useful in clarifying the cause of hyper- and hypo-calcaemia. Interpretation should be made in light of the serum calcium level.	EDTA Please send to the laboratory within 24 hours of calcium measurement. Separate sample preferred i.e. 2 EDTA samples for PTH and FBC.	Daily	Levels must be interpreted in context of serum calcium. For normal calcium: 1.2-8.5 pmol/L
Renin Measured in the investigation of causes of juvenile hypertension (suspected primary hyperaldosteronism)	Lithium Heparin Must be transported at room temperature and arrive at the lab within 30min. Please include medication details. Separate sample required.	Sent away (Leeds)	0.5-3.5 nmol/L/h random sample – interpret in the context of UE and aldosterone results.
Sex hormone binding globulin (SHBG) Assessment of free androgen index. Reduced in obesity and thyroid dysfunction.	Serum or Lithium Heparin	Daily	F = 18-114 nmol/L M = 10-57 nmol/L
T3 (free) Investigation of hyperthyroidism.	Serum or Lithium Heparin Please include details of thyroxine therapy and any other medication.	Daily	3.5-6.5 pmol/L
T4 (free) Investigation of possible hyper- or hypothyroidism in conjunction with TSH		Daily	9-23 pmol/L

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Testosterone Assessment of delayed or precocious puberty in males and disorders of sexual development.	Serum only Please ensure time of collection is included and aim to sample at 9am to avoid changes due to diurnal variation.	Daily	nmol/L F <12y: 0.07-0.69 TRF M <1y: 0.42-0.72 M 1-6y: 0.1-1.12 M 7-12y: 0.1-2.37 M 13-17y: 0.98-38.5
TSH Raised in primary hypothyroidism	Serum or Lithium Heparin Please include details of thyroxine therapy.	Daily	0.55 - 4.78 mU/L
TSH (Down Syndrome) Investigation of thyroid disorders in patients where venous sampling with a needle is not possible	Guthrie card (with special label) Finger prick blood spots, leave to dry for 4h before packaging.	Sent away (Leeds)	<5 mU/L
Urine steroid profile	Please see ' Urine Tests ' table on page 29		
Vitamin B12 Megaloblastic anaemia, dietary deficiency, malabsorption and some inherited metabolic disorders. Reference ranges are a guide, please interpret in the context of haematological / neurological findings	Serum or Lithium Heparin Please contact the duty biochemist to discuss testing if an inborn error of metabolism is suspected.	Daily	211-911 ng/L
Vitamin D Investigation of unexplained hypo- and hypercalcaemia, assessment of patients at risk of fat-soluble vitamin deficiencies.	Serum or Lithium Heparin	Daily	Deficiency: <30 nmol/L Insufficiency: 30-50 nmol/L

ALLERGY AND IMMUNOLOGY TESTS

This includes common requests in patients with symptoms of allergy, autoimmune disease or immunodeficiency. Further information on how to request individual allergy tests or test panels can be found in the text below this table.

ANALYTE (TEST SET)	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Alpha-1-antitrypsin Investigation of liver disease	2 mL Serum . Separate sample required to all other serum tests.	Weekly	See report. As a rough guide: Neonate: 0.9-2.2 g/L Infant: 0.8-2.0 g/L Child 1.1-2.2 g/L Adult 1.1-2.1 g/L
Cryoglobulin Investigation of suspected Raynaud's disease, pain and numbness in fingers and toes. ESSENTIAL that samples are kept at 37°C.	Serum only. Contact the duty biochemist (6366) to arrange testing. Blood MUST be collected into a warmed flask supplied by the laboratory between 9am - 2pm.	Daily	Negative
C1 Esterase inhibitor Investigation of angioedema and low C4 complement.	Serum only Send separate sample	Sent away (Hull)	0.21-0.39 g/L See report for further details
C3 and C4 Complement Low in diseases such as SLE, nephritis, vasculitis, rheumatism and hereditary angioedema.	Serum or Lithium Heparin. Separate sample required.	Weekly	C3: 0.90-1.8 g/L C4: 0.1-0.4 g/L
Electrophoresis (serum) Suspected immunodeficiency.	Serum only Please provide clinical details.	Daily	Normal pattern
Immunoglobulins Includes Ig A, Ig G, IgM Autoimmune disorders, chronic or recurrent infections	Serum or Lithium Heparin	Daily	Age related up to 9y for IgG and IgA and up to 6y for IgM. See report
Immunoglobulins IgG subclasses Persistent infection with apparently normal total immunoglobulin levels.	Serum or Lithium Heparin A separate tube is required for this test.	Sent away (Leeds)	Age related ranges. Please see report for range applicable to your age group.
Immunoglobulins IgE (Total and specific IgEs) Allergic and atopic diseases; please see text below for further information.	1 mL Serum If >8 tests are selected or any tests are NOT offered at York (see link on next page) please collect <u>an extra serum sample</u> . Please ensure that specific IgE tests are clearly and legibly written on request form in BLOCK CAPITALS.	Twice weekly	<1y 0 - 29 kU/L 1-2 y 0 - 49 kU/L 2-3 y 0 - 45 kU/L 3-9 y 0 - 52 kU/L >9y 0 - 87 kU/L
Tryptase Investigation of anaphylaxis (e.g. reactions to anaesthetic) Take blood on presentation, then at 3 and 24hrs post-reaction.	Serum samples taken on presentation and a 3 and 24-hours post-reaction. Samples should arrive within 1 hour of collection. Requires a separate sample.	Sent away (Leeds)	2-14 ng/mL

Allergy Testing and Specific IgE analysis

We test for most common allergens by measuring specific IgE to the suspected allergen. Panels are available in patients with typical allergy symptoms – these are listed below:

Panel	Tests Included
Inhalant	Timothy grass, alternaria alternata, Cladosporium herbarum, Birch and Mugwort. Please note this panel no longer includes HDM, cat and dog dander and cultivated rye grass.
Food	Milk, egg, cod, wheat, peanut and soybean.
Rodent	Guinea pig, Hamster, Rabbit, Rat and Mouse.
Nut	Hazel, Brazil, Almond, Peanut and Coconut.
Weed	Ox-eye daisy, dandelion, plantain, golden-rod and Lamb's quarters.
Tree	Alder, Birch, Hazelnut, Oak and Willow
Mould	Penicillium chrysogenum, Cladosporium Herbarum, Candida Albicans, Aspergillus fumigatus, Alternaria alternata and Setomelanomma rostrata
Fish	Cod, tuna, salmon, mussel and shrimp.
Feather	Goose, chicken, duck and turkey feathers.

A full lists of the tests offered at York and guide to interpretation can be found here:

<https://www.yorkhospitals.nhs.uk/our-services/a-z-of-services/lab-med/general-information/information-for-health-care-professionals1/advice-for-primary-or-secondary-care-clinical-biochemistry/>

Please note that vague requests for 'IgE' will result in a total Ig E result without any further allergy testing. If the patient's history suggests specific allergens, please request these individually by writing CLEARLY on the request form (e.g. WALNUT).

Alternatively, you can use the laboratory's dedicated allergy request form (click below or contact the Duty Biochemist):



CB-TEM-ALLERGYRE
Q v2.docx

Requests for less common allergens are sent to a reference laboratory, and a full range is available on request (please contact the duty biochemists on: 01904 72 6366).

In the event of any queries or requirement for clinical advice, please contact:

Dr Anna McHugh (Clinical Immunologist): 0113 39 25550

SPECIALIST AND METABOLIC INVESTIGATIONS

The table below lists investigations for patients with symptoms of an inherited metabolic disorder (e.g. hypoglycaemia, seizures, cardiomyopathy or global developmental delay), genetic disorder, renal calculi, nutritional deficiency, or heavy metal poisoning. Please see 'urine tests' for any urine analyte (including metals, citrate, oxalate, urine organic acids and amino acids).

If the test you require is not listed below, contact the duty biochemist (01904 726366).

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Amino Acids Diagnosis of disorders of amino acid metabolism. Please state whether a specific disorder is suspected.	0.2 mL in Serum or Lithium Heparin Separate sample required.	Sent away (Leeds)	See report for specific pattern and interpretation.
Beta hydroxybutyrate (ketones) and Free fatty acids. Investigation of hypoglycaemia, diabetic ketoacidosis.	0.5 mL in Fluoride Oxalate. Separate sample required.	Sent away (Sheffield)	Results are interpreted in light of glucose and free fatty acid concentrations.
Biotinidase Enzyme involved in recycling biotin (an essential co-factor in fat, carbohydrate and protein metabolism).	0.2 mL in Serum Samples must be delivered to laboratory immediately. Separate sample required.	Sent away (Leeds)	4.4-12.0 nmol/min/mL
Calculus (Renal Stone analysis) Identification of stone components	Dry renal stone specimen	Sent away (London)	N/A
Carnitine and acylcarnitine Co-factors involved in free fatty acid and acyl CoA transport across membranes. Deficient in some errors of fatty acid oxidation with hypoglycaemia and cardiomyopathy (e.g. MCADD)	2 dried blood spots on a Guthrie card (available from children's clinic, leave to dry for 4h before packaging.)	Sent away (Leeds)	See report - specific pattern of metabolites may be either normal or suggestive of a particular disease.
CSF Neurotransmitters* (Monoamine metabolites, pterins, Vitamin B6). Investigation of cyclical seizures, and neurological disorders.	Testing by appointment only. Contact the duty biochemist (6366) at least a week in advance of lumbar puncture to arrange for a member of staff to collect samples into liquid nitrogen.	Sent away (London)	See report for ranges and interpretation of specific metabolite pattern.
Free Fatty acids and beta hydroxybutyrate Investigation of hypoglycaemia and suspected fatty acid oxidation defects.	0.5 mL in Fluoride Oxalate. Separate sample required	Sent away (Sheffield)	Results are interpreted in light of glucose and free fatty acid concentrations.
Galactosaemia screening test Investigation of galactosaemia (inborn error of metabolism) and prolonged jaundice.	0.1 mL Lithium Heparin Send separate sample.	Sent away (Leeds)	See report. Please note, recent transfusion invalidates results.
Galactose-1-Phosphate Confirmatory test, which is only available to patients who have a positive galactosemia screen.	2mL Lithium Heparin Must be collected on Monday-Thursday ONLY. Separate sample required.	Sent away (Bristol)	See report <0.60 umol/g Hb for known galactosemia.

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
α-galactosidase / Fabry's screen For the diagnosis of Fabry's disease. Note that definitive diagnosis in females requires genetic testing. Consent should be obtained at the point of blood collection in any female patient.	0.5 mL EDTA or Lithium Heparin or dry blood spot on Guthrie card (leave 4h before packaging). A statement about consent for genetic testing should be handwritten on request forms i.e. 'genetic consent obtained/not obtained.' Send to lab as soon as possible.	Sent away (Willink)	6.3-47 pmol/punch/hr
α-1,4 glucosidase / Pompe Screen Investigation of Pompe's disease	5mL EDTA Samples MUST arrive at the laboratory Monday-Thursday to avoid delays in transport over the weekend. Separate sample required.	Sent away (Willink)	3 – 20 μ mol/g.h with acarbose
β-glucosidase / Gaucher Screen Investigation of Gaucher's disease		sent away (Willink)	1-5 μ mol/g.h in white cells
Homocysteine Diagnosis of classic hyperhomocysteinuria. Also a factor for atherosclerosis.	0.5mL EDTA Send to lab immediately (must be within 30min). Separate sample required.	Sent away (Leeds)	<18 μ mol/L
Karyotyping* Investigation of suspected aneuploidy and disorders of sexual development.	1-2 mL in Lithium Heparin Please include completed genetics form*. Separate sample required.	Sent away (Leeds)	See individual report.
Lead Suspected toxicity e.g. in PICA, anaemia, neurological disorders	1 mL in EDTA tube (a special tube is no longer required)	Sent away (Leeds)	<2.4 μ mol/L
Mercury (blood) Suspected overexposure	2mL whole blood in EDTA . Separate sample required.	Sent away (Guildford)	See report <30 nmol/L
Microarray* Investigation of learning or behavioural difficulties, delay, autism, seizures or dysmorphism.	1 mL in EDTA Please include completed genetics form*. Separate sample required.	Sent away (Leeds)	See individual report.
Mitochondrial Genes* Investigation of maternally inherited disorders presenting with myopathy, deafness, blindness, seizures and acidosis.	2-3 x 4.5mL in EDTA Please include completed mitochondrial request form*. Separate sample required.	Sent away (Newcastle)	See individual report.
Mucopolysaccharide screen Organic Acids	Plain random urine – please specify if particular disorder suspected		
Phenobarbitone Investigation of suspected toxicity or non-compliance.	0.5 mL serum . Requires a separate, pre-dose sample to arrive at the laboratory within 2 hours of collection.	Sent away (Leeds)	See individual report.
Porphyrin (red cells) Increased levels seen in erythropoietic protoporphyria, congenital erythropoietic porphyria, iron deficiency anaemia and lead poisoning	0.5mL in EDTA WITH Random Urine AND Faecal samples Samples MUST be protected from light (e.g. brown envelope, wrap in tinfoil) Send separate samples.	Sent away (Leeds)	Negative

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Selenium Included in Trace Elements Profile with copper and zinc. For assessment of nutritional deficits.	0.5mL Serum Separate sample required.	Sent away (Leeds)	<6 months: 0.4-0.7 umol/L 7m-6y : 0.6-1.2 umol/L >6 years: 0.8-2.0 umol/L
Sweat Test* Used in the diagnosis of cystic fibrosis	Testing by appointment only. Please phone the laboratory on 5802 to arrange an appointment for sweat collection	Twice weekly	Sweat Chloride (mmol/L) 0-6 months: <30 Over 6 months : <40
Trace Elements Includes copper, zinc and selenium Measured in patients at high risk of nutritional deficiency e.g. parenteral nutrition or highly restricted diet.	1mL Serum Send separate sample	Sent away (Leeds)	Selenium (umol/L): 0-6 months: 0.4 - 0.7 7m – 6 y: 0.6 - 1.2 >6 years: 0.8 - 2.0 Copper / Zinc: See report for age-dependent limits
Transferrin glycoforms (sialotransferrin) Investigation of congenital disorders of glycosylation (CDG).	1mL Serum Send separate sample	Sent away (London)	See report
Very long chain fatty acids (VLCFA) including phytanic acid Investigation of suspected adrenoleukodystrophy and adrenomyeloneuropathy (ALD and AMN).	1mL Lithium Heparin Send separate sample.	Sent away (Sheffield)	C22: 15-112 umol/L C24: 14-80 umol/L C26: 0.33-1.50 umol/L C24/22 ratio: 0.44-0.97 C26/22 ratio: 0.005-0.030
Vitamin A Measured as part of a nutritional screen in patients at risk of deficiencies of fat soluble vitamins (e.g. in cystic fibrosis)	2mL Serum or Lithium Heparin Send separate sample. Please protect from light if there is a delay in sending to the laboratory e.g. wrap securely in tinfoil or place in a brown paper envelope.	Sent away (Hull)	1.1-2.6 umol/L
Vitamin E As for vitamin A, above			12-42 umol/L
White Cell Enzymes A screen of enzyme activities which are associated with 17 different lysosomal storage diseases.	5mL EDTA Samples MUST arrive at the laboratory Monday-Thursday to avoid delays in transport over the weekend.	Sent away (Willink)	See individual enzymes. If 5mL blood unavailable, please state any enzymes / disorders which are a priority.
Zinc Protoporphyrin Investigation of suspected lead poisoning, anaemia and porphyria.	0.5mL EDTA Must be protected from light Send separate sample.	Sent away (Leeds)	5-55 ug/dL <2.0 ug/g haemoglobin

*** Further information on sweat testing, CSF Neurotransmitter collection and Genetic testing can be found on page 11**

URINE TESTS (ROUTINE AND SPECIALIST)

The table below lists all tests performed in urine, including common analyses, such as urine albumin, and specialist tests for oncology, endocrinology, neurology, urology and metabolic medicine. Please see 'Specialist and Metabolic Investigations' for identification of renal stone components (listed as 'calculus').

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
AASA – alpha amino adipic semi aldehyde Investigation of pyridoxine-responsive seizures.	5mL random urine	Sent Away (London)	See report
Amino Acids - Part of Metabolic Screen Diagnosis of disorders of amino acid metabolism; urine is particularly important for diagnosis of cystinuria, which can be missed using plasma only.	1.5 mL random urine Please state whether a specific disorder is suspected.	Weekly	See report for specific pattern of results and interpretation.
Albumin:creatinine ratio (ACR or urine microalbumin) An indicator of glomerular damage in patients with protein-losing renal disease.	2mL random urine in plain container. Early morning "first pass" urine is preferred.	Daily	<30 mg/mmol creatinine (non-diabetic)
Calcium:creatinine ratio Investigation of hyper- or hypocalcaemia, where a congenital renal cause is suspected (e.g. familial hypocalciuric hypercalcaemia). Investigation of renal stone formation.	2mL random urine in a plain container.	Daily	Calcium/Creatinine ratio Age (mmol/mmol) 0-1 yrs <1.50 1 - <2 <1.25 2 - <5 <1.00 5- <10 <0.70 10-18 <0.60
Catecholamines Diagnosis of Neuroblastoma. HMMA and VMA ratio to creatinine measured.	2mL random urine in plain container. Deliver to the lab immediately.	Sent away (Leeds)	See report (age related)
Chloride (urine) Only measured in some circumstances - contact laboratory if unsure.	2mL random urine in plain container or plain 24hr urine collection.	Daily	170-250 mmol/L OR 170-250 mmol/24hr
Copper (urine) Increased in Wilson's disease	24h urine	Sent away (Guildford)	<0.9 umol/24h
Citrate (urine) Investigation of renal tubular acidosis and renal stone disease.	2mL random urine in a plain container.	Weekly	0.11-1.75 mmol/mmol creatinine
Cortisol (urine free) Useful in the diagnosis of Cushing's syndrome	Plain 24h urine collection. Please list any medications.	Weekly	0-165 nmol/24h
Creatinine (urine) Used as a measure of renal function (creatinine clearance) and to correct for differences in urine concentration when making measurements in random urine.	2mL random urine in plain container or plain 24hr urine collection.	Daily	F = 8-13 mmol/24h M = 8-16 mmol/24h N.B. Age and muscle mass dependent.

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Creatinine clearance An approximate measurement of glomerular filtration rate	Plain 24h urine collection AND a serum sample drawn on the same day	Daily	Age related, see report
Cystine Renal stones, suspected cystinuria	2mL random urine. Deliver to the lab immediately.	Sent away (Leeds)	Child: <8 umol/mmol creat Adult: <15 umol/mmol creat
Drugs of Abuse Screen Investigation of passive or active drug exposure e.g. confirmation of opiate or methadone exposure in neonates with withdrawal symptoms, suspected drug ingestion in children or adolescents.	5mL random urine This is <u>NOT</u> a forensic service – use should be strictly confined to situations where drug detection will affect clinical management.	Daily	Positive result if above cut-off values. Samples positive for opiates require further testing to distinguish codeine and morphine. Please contact the duty biochemist (6366) if this is required.
Guanidinoacetate (urine) – Screen for Creatine Synthesis Disorders Investigation of suspected creatine biosynthesis disorders in children with seizures, intellectual disability and speech delay.	2mL random urine in a plain container & paired 1mL blood sample in lithium heparin tube. Deliver to lab within 2h of collection.	Sent away (Leeds)	See report for interpretation of metabolite patterns in blood and urine. Urine is essential for diagnosis of the commonest (X-linked) disorder, plasma rules out rarer forms of defect.
Magnesium (urine) Estimation of renal magnesium loss in deficiency states	2mL random urine in a plain container.	Daily	Magnesium/creatinine ratio: Age mmol/mmol <1 year <2.2 1-2years <1.7 2-18years 0.2-1.1
Mercury (urine) In suspected toxicity or exposure to inorganic mercury compounds	24h urine	Sent away (Guildford)	<50 nmol/24 hr
Metabolic Screen Includes urine amino acids, urine organic acids and urine sugar chromatography.	5mL random urine in a plain container. If glycosaminoglycans are required, please state.	Sent away (Leeds)	See individual analytes
Mucopolysaccharide screen One of the components of the metabolic screen test. Increased levels are seen in patients with mucopolysaccharidoses.	3mL random urine in a plain container.	Sent away (Leeds)	See report – pattern of results may be normal or suggestive of a specific disease.
Organic acids (urine) - Part of Metabolic Screen Detection of a wide variety of metabolic disorders.	5mL random urine in a plain container. Please state whether a specific disorder is suspected and list any medications.	Sent away (Leeds)	See report - pattern of results may be normal or suggestive of a specific disease.
Orotic Acid (urine) Suspected urea cycle disorders; X-linked ornithine transcarbomylase deficiency cannot be diagnosed using plasma or urine amino acids.	2mL random urine in a plain container.	Sent away (Leeds)	See report - pattern of results may be normal or suggestive of a specific disease.

ANALYTE	SAMPLE REQUIREMENTS	ANALYSED	REFERENCE RANGE
Osmolality (urine) Investigation of polyuria	2mL random urine in a plain container.	Daily	300-900 mmol/kg
Oxalate Investigation of renal stones	2mL random urine in a plain container. Deliver to the lab immediately.	Weekly	Oxalate/creatinine ratio Age (mmol/mmol) <5yrs <0.2 5-10yr <0.085 10-15yrs <0.06
Phosphate (urine) Investigation of abnormal calcium / phosphate levels or renal stones.	2mL random urine in a plain container.	Daily	See report or for age-related ranges
Porphobilinogen (urine) Screening test for acute porphyria.	2mL fresh random urine in a plain container – must be protected from light. Collect during an attack if possible. List relevant medication and history.	Sent away (Leeds)	See report for full details. N.B normal levels may be observed between acute attacks.
Porphyrin (urine) Quantitative test for more detailed investigation of porphyria. A full screen requires urine, stool and blood samples.	5mL fresh random urine in a plain container - must be protected from light. List medications and clinical / family history.	Sent away (Leeds)	See report for full details – specific pattern of metabolites may be normal or suggestive of a specific disease.
Potassium (urine) Estimation of potassium losses in potassium deficiency states	2mL random urine in a plain container AND a serum sample for U&E	Daily	30-125 mmol/L Interpret in light of serum potassium results.
Protein (urine) Estimate of renal protein losses in patients with renal failure and nephrotic syndrome	2mL random urine in a plain container or plain 24h urine collection.	Daily	As a guide only: <20 mg/mmol creatinine
Sodium (urine) Measure of sodium excretion in patients with electrolyte disturbances	2mL random urine in a plain container or plain 24h urine collection.	Daily	40-300 mmol/L OR 50-250 mmol/24 hr Interpret in light of serum sodium results.
Sugar Chromatography (urine) - Part of Metabolic Screen Investigating disorders of carbohydrate metabolism	2mL random urine in a plain container. Please provide clinical details.	Sent away (Leeds)	See report for full details – specific pattern of metabolites may be normal or suggestive of disease.
Steroid Profile (urine) Diagnosis and monitoring of congenital adrenal hyperplasia and other disorders of steroid metabolism	2mL random urine in a plain container OR plain 24h urine collection. Provide full clinical and medication details.	Sent away (London)	See report for full details and specific pattern of metabolites. This may be normal or suggestive of disease.
Stone screen Investigation of recurrent renal stone formation	5mL random urine in a plain container. Deliver to the lab immediately.	Screen includes calcium, phosphate, magnesium, citrate, oxalate, urate – see individual entries for details.	
Urate (urine) Measured in 24h urine as part of screen for renal stone disease.	2mL random urine in a plain container.	Daily	Urate/creatinine ratio Age (mmol/mmol) <2yr 0.7-1.4 2-6yrs 0.3-1.0 6-12yr 0.1-0.7 12-16yr 0.1-0.5

FAECAL (STOOL) TESTS

ANALYTE (TEST SET)	SAMPLE REQUIREMENTS	FREQUENCY OF ANALYSIS	REFERENCE RANGE
Calprotectin (faeces) Marker of inflammatory bowel disease	Fresh random faecal sample Samples should ideally be the size of a grape or small marble. Note that liquid stool samples are unsuitable for analysis, and blood staining may affect results.	Twice weekly	2-9 y: <166 ug/g faeces Adult: 0-50 ug/g faeces
Faecal elastase - Measure of exocrine pancreatic function		Weekly	>200 mg/g faeces
Porphyrin (faeces) Investigation of suspected porphyria, particularly if cutaneous symptoms present.	Fresh random faecal sample (10g - 15g) – must be protected from light. Please provide clinical details.	Sent away (Leeds)	See report for full details – specific pattern of metabolites may be normal or suggestive of a specific disease.

Faecal Reducing Substances are no longer tested at the laboratory. Due to problems with sample stability and the sensitivity and specificity of traditional test methods, an exclusion diet is now considered a better means of diagnosing lactose intolerance and other malabsorptive conditions.

3. INVESTIGATIONS BY CONDITION

The following protocols detail the specialist investigations that should be considered in infants with the following symptoms, provided all obvious causes, and those which can be diagnosed on the basis of clinical symptoms or history, have been ruled out. Protocols are Best Practice Guidelines formulated by an expert opinion group at MetBioNet (Metabolic Biochemistry Network). These are aimed at helping the local laboratory and clinical teams carry out the correct panel of investigations for a specific presentation of suspected metabolic origin. Further information is available via the Metabolic Biochemistry Network website:

<http://www.metbio.net/metbioGuidelines.asp>

HYPOGLYCAEMIA

Instructions and sampling kits for the investigation of hypoglycaemia in children are available in the following locations:

YORK HOSPITAL	SCARBOROUGH HOSPITAL
SCBU	SCBU
Ward 17	Duke of Kent Ward
Child Assessment Unit	Paediatric Outpatients

If you require a further kit, please ring Main Laboratory Reception on:

YORK HOSPITAL: 772 6542 (or contact the on-call BMS via switchboard out of hours)

SCARBOROUGH HOSPITAL: 771 2625 (or on-call BMS via switchboard out of hours)

A set of biochemistry tests is available to order as a panel in CPD (Hypoglycaemia screen – PA). The Hypoglycaemia screen in CPD requires the following samples:

Tests included in panel	Samples required
CALCIUM - ADJUSTED FOR ALBUMIN , LFT (LIVER FUNCTION TESTS) U&E INCLUDING EGFR	One full Serum or Lithium Heparin tube should be sufficient for UE, LFT and Calcium
ACYL CARNITINE and CARNITINE	Dried blood spot on Guthrie card
AMMONIA	Red EDTA (hand deliver to lab within 30 minutes of collection)
CORTISOL	Serum or Lithium Heparin
C PEPTIDE AND INSULIN	Serum tube (hand deliver to lab within 1 hour of collection)
GROWTH HORMONE	Serum or Lithium Heparin
LACTATE GLUCOSE	Yellow fluoride oxalate One full tube should be sufficient for Glucose and Lactate
AMINO ACIDS – URINE, MUCOPOLYSACCHARIDE SCREEN – URINE ORGANIC ACID SCREEN – URINE, SUGAR CHROMATOGRAPHY - URINE CREATININE – URINE	A minimum of 5mL random urine collected into a plain universal container (referred to Leeds)
DIPSTICK - URINE	Perform on fresh urine on the ward

Please note that this does not currently include beta-hydroxybutyrate and free fatty acids, so these will need to be requested separately.

<http://www.metbio.net/docs/MetBio-Guideline-GARU968012-23-01-2012.pdf>

SEIZURE DISORDERS

The following tests are available to order on CPD using the 'Seizure-PA' panel:

Tests included in panel	Samples required
BONE PROFILE	2 x full serum or Lithium Heparin tubes should be sufficient to carry out all of the necessary tests
CRP (C-REACTIVE PROTEIN) - SERUM	
GLUCOSE - SERUM (BROWN TUBE)	
MAGNESIUM - SERUM	
U&E INCLUDING EGFR - SERUM	

The guideline below provides further information on the metabolic investigations which should be performed in children with ongoing seizure disorders

<http://www.metbio.net/docs/MetBio-Guideline-NACU622286-23-07-2009.pdf>

HYPERAMMONAEMIA

The following guideline provides a framework for the metabolic investigation of neonates or children presenting with unexplained hyperammonaemia

<http://www.metbio.net/docs/MetBio-Guideline-UMUF338839-23-07-2013.pdf>

CARDIOMYOPATHY

The following guideline provides a framework for the metabolic investigation of neonates or children presenting with unexplained cardiomyopathy

<http://www.metbio.net/docs/MetBio-Guideline-NAFF997813-13-07-2012.pdf>

PROLONGED JAUNDICE

The following panel is available to order on CPD named 'Prolonged jaundice -PA':

Tests included in panel	Samples required
LFT (LIVER FUNCTION TESTS) - SERUM	Serum or Lithium Heparin tube
FULL BLOOD COUNT (PAEDIATRIC)	Red EDTA tube
G-6-PD SCREENING TEST	Contact haematology for details if required

The following guideline provides a framework for the metabolic investigation of neonates or children presenting with unexplained prolonged jaundice.

<http://www.metbio.net/docs/MetBio-Guideline-DUUM428158-28-01-2013.pdf>

GLOBAL DEVELOPMENTAL DELAY

A comprehensive set of tests for the investigation of developmental delay is available as an order set CPD (Developmental Delay – PA). This requires the following samples:

Tests included in panel	Samples required
AMINO ACIDS - SERUM	Orange lithium heparin tube or brown serum (referred to Leeds)
CALCIUM - ADJUSTED FOR ALBUMIN, CREATINE KINASE, LFT (LIVER FUNCTION TESTS), GAMMA GLUTAMYL TRANSFERASE (GGT), U&E INCLUDING EGFR URATE	2 x full serum or lithium heparin tubes should be sufficient to carry out all of these tests
LEAD - BLOOD	Red EDTA tube (referred to Leeds)
THYROID FUNCTION TEST (TSH AND FT4) FERRITIN	1 x full serum or lithium heparin tube should be sufficient
AMINO ACIDS – URINE, MUCOPOLYSACCHARIDE SCREEN – URINE ORGANIC ACID SCREEN – URINE, SUGAR CHROMATOGRAPHY - URINE CREATININE – URINE	A minimum of 5mL random urine collected into a plain universal container (referred to Leeds)
CHROMOSOME STUDIES - ST JAMES	Red EDTA tube and completed genetics request form (see page 13) - referred to Leeds
FULL BLOOD COUNT (PAEDIATRIC)	Red EDTA tube

N.B. The following tests are **NOT** included in the standard CPD panel but **should also be considered** in specific patient populations:

Tests	Inclusion Criteria	Samples required
Guanidinoacetate / creatine metabolites	Patients from families in which 2 or more males are affected by global developmental delay ANY patient with developmental delay and significant speech and language delay	Orange lithium heparin tube with 1mL paired random urine in a plain container (deliver within 2h of collection).
Total Homocysteine	Patients born outside the UK or within the UK BEFORE Jan 2015 (i.e. those who have NOT undergone expanded newborn screening). ANY patient with symptoms suggestive of homocystinuria i.e. myopia, lens abnormalities, abnormally long bones, FH of cardiovascular disease	Minimum of 0.5 mL plasma in a red EDTA tube – to be delivered to the lab immediately and arrive within 30 min of collection. Do not use the pod system.

<http://www.metbio.net/docs/MeiBio-Guideline-HURA100024-28-01-2013.pdf>

FACIAL DYSMORPHISM

The following guideline provides a framework for the metabolic investigation of neonates or children presenting with unexplained dysmorphic features

<http://www.metbio.net/docs/MetBio-Guideline-PEDE620597-28-01-2013.pdf>

SUDDEN UNEXPECTED DEATH IN INFANCY (SUDI)

Investigation of unexpected infant deaths requires careful collection and handling of a diverse range of sample types. To facilitate this process, **'SUDI boxes' are available** in the **resus rooms in the Emergency Department** at York and Scarborough Hospitals, and in the **mortuaries at both sites**.

These contain sample containers for collection of blood, urine/nappy and nasal swabs as well as a document for completion by the clinician dealing with the death. Completed samples and paperwork should be placed back into the SUDI box, sealed with a tamper-proof tag and sent urgently to the Laboratory Medicine for processing.

Please notify the duty biochemist on 1904 72 6366 (or the laboratory if calling out of hours) if a SUDI box is to be delivered to the laboratory. You will be asked to sign a chain of custody form on delivering the box, and should obtain a new, unused box in its place.

For further information on metabolic causes of SUDI, please refer to:

<http://www.metbio.net/docs/MetBio-Guideline-RASU337946-27-11-2010..pdf>



Olpin, S.

"The metabolic investigation of sudden infant death"
Ann Clin Biochem 2004, 41: 282-9.