Biochemistry Paediatric Handbook

No. of copies :	1.
Location of copies :	1. Intranet
	2.

Contents

Introduction

In this handbook you will find information concerning the services available for paediatrics through the Biochemistry department, relating to more specialised investigations that may help investigation and monitoring of child health problems. See also our general guide to Biochemistry Services. This guide is really a compilation of the appropriate information in one booklet, which we hope you will find useful.

Further information that is applicable for all pathology disciplines can be found on the website at:
http://www.therotherhamft.nhs.uk/Pathology/Pathology/

The Biochemistry Department

The Biochemistry department analyses blood and other body fluids to determine the homeostasis of the numerous metabolic processes of the body. Biochemistry forms part of the Blood Sciences Department which is situated within the Pathology Directorate on A floor of Rotherham NHS Foundation Trust.

Due to the large number of samples analysed daily, much of the analysis is automated enabling the small team of Biomedical Scientists to perform many thousands of tests per hour for patients from both within the hospital and from the local community.

The Biochemistry department offers a large repertoire of analytes, the majority of which are measured in-house to help to ensure the best possible service and turnaround times for our users. For the less common tests, these are referred to various specialist laboratories around the United Kingdom following the completion of the available in-house tests first. The department is accredited by the United Kingdom Accreditation Service (UKAS) (accredited to ISO 15189:2012, UKAS Medical accreditation number 9623). Our accreditation is limited to those activities described on our UKAS schedule of accreditation.

Link to the test repertoire table available on the following web page:
http://www.therotherhamft.nhs.uk/Pathology/Biochemistry/

Location of the Laboratory

The Biochemistry Laboratory is situated within Pathology on 'A' level (top floor). Following the signs for Pathology, at the T junction near the central lifts go down the corridor opposite the lifts and the Pathology department is first on the left double wooden doors. Pathology Reception is straight ahead.

Laboratory opening times

Normal Service:	Monday – Friday 0900 hrs - 1730 hrs
Limited service:	Saturday mornings 0900hrs - 1300 hrs
Out of Hours:	Please contact the on-call Biochemistry BMS on EXT: 4241

Postal Address

Biochemistry Department (Blood Sciences)
Level A
The Rotherham NHS Foundation Trust
Moorgate Road
Rotherham
S60 2UD

Contact numbers

Business and Service Manager	01709 42 4023
Quality Manager	01226 43 2289 / 01709 42 4008
Deputy Quality Manager	01709 42 4008 / 01226 43 2289
Direct Line to Biochemistry Laboratory	01709 42 4241
Extensions via Hospital Switchboard	01709 82 0000

Out of Hours: The Biochemistry BMS on-call can be contacted on EXT: 4241

Consultant Chemical Pathologist Direct Line	01709 42 4412
Secretary	01709 42 4051
Consultant Clinical Scientist (Biochemist)	01709 42 4103
Blood Sciences Manager	01709 42 7621 / 01226 432061
Lead Biochemistry BMS	01709 42 7714
Senior Biochemistry BMS	01709 42 7714
Enquiries for previous results	01709 42 7553

Specimen Reception

All samples arrive at the laboratory via the centralized specimen reception area. The specimen reception area also deals with initial result enquiries.

Specimen Reception contact numbers are as follows:

- Urgent requests: 7510
- Result enquiries 7553

Any queries regarding Specimen Reception should be directed to the Specimen Reception Manager on any of the above numbers.

Please ensure that specimens and correct request forms are clearly labelled (please include the NHS number where possible).

Requesting Tests

Specimens should always be in the appropriate container and accompanied by a request form. Details of specimen requirements are detailed in the Biochemistry Test Repertoire table available on the Biochemistry Website:

http://www.therotherhamft.nhs.uk/Pathology/Biochemistry/

Please use electronic test requesting where available. Requests should be made via the ICE or Meditech systems where possible, or in the event of electronic request failure or unavailability please use the manual request form or the reverse of the ICE paper.

Request form completion and labelling of sample

We cannot process samples unless we can be sure about the patient's identity, the test(s) required and where to send the result.

A minimum of three criteria should match on specimen and form for the sample to be accepted.

* Denotes mandatory requirement

SAMPLES MUST HAVE

- Patient's forename AND surname*
- Date of birth and/or hospital or NHS number*
- One of the following unique numerical identifiers*:
  - Hospital number
  - NHS number
  - GUM number
  - Full address and postcode (if unique numerical identifier cannot be provided)
- Date and time of sample

REQUEST FORMS MUST HAVE

- Patient's forename AND surname*
- Date of birth and/or hospital or NHS number*
- One of the following unique numerical identifiers*:
  - Hospital number
  - NHS number
  - GUM number
  - Full address and postcode (if unique numerical identifier cannot be provided)
- Location (ward, clinic or surgery, written in full)
- Consultant/GP /Requesting practitioner (written in full)
- Tests required
- Date and time of sample
- Relevant clinical information including current medication

Unless the sample is regarded as “precious” e.g. a CSF sample, the sample will not be processed if the minimum criteria rule is not met. We will endeavour to contact the sender within an appropriate time scale to inform them of this and request a repeat sample.

Specimens should always be in the appropriate container and accompanied by a request form.

Appropriate clinical details should be given including current medication.

Specimen Rejection

A sample **will not** be processed if the minimum criteria rule is not met. Where the information on request form and sample do not match, samples will not be tested. We will endeavour to contact the sender within an appropriate time scale to inform them of this and request a repeat sample. If a sample is regarded as “precious”/not repeatable e.g. a CSF sample or a sample from a dynamic function test, the user may be contacted to take full legal responsibility for the analysis of the sample.

Some unrepeatable samples (e.g. CSF, sterile fluids and blood cultures) are treated as precious samples and the sample will be tested even if inadequately labelled, however a comment will be added to the result that the specimen was unlabelled, and the sender should take responsibility for the validity of the result. The requestor may be asked to attend the laboratory to confirm the identity of any mislabelled precious sample and sign a precious sample form.

High risk specimens

These include samples from patients known or suspected of being infected with a Hazard Group 3 pathogen must have a “Danger of Infection” label placed on both request form and all specimens.

Samples from patients falling into the categories below should be regarded as high risk for the laboratory:-

- HIV antibody positive
- Hepatitis B surface antigen or E antigen positive
- Hepatitis C positive
- Patient being investigatedfor Blood Borne virus
- IV drug user (past/present)
- All samples from GU Med/CASH
- Covid-19 positive

Packaging

All specimens irrespective of mode of delivery should be placed in the appropriate container which must be securely fastened. The container should be sealed into the plastic compartment attached to the request form. Specimens should be transported to the laboratory as rapidly as possible after collection to ensure that no significant deterioration occurs before processing.

Transportation of specimens

Specimens for tests that are unstable (please see Samples with Specific Transportation Requirements) e.g. blood gas/CSF specimens, and for requests that are very urgent, should be taken directly to the specimen reception.

Samples taken within the community at GP practices are transported to the laboratory by Courier Logistics.

Hospital samples are delivered either via the air tube system or by hand to the Laboratory Specimen Reception Department.

- Serum samples should be processed (centrifuged and serum separated from the cells) within 5 hours of collection. Any delay can influence potassium and enzyme results.
- Serum Glucose – stable for up to 4 hours in a fluoride oxalate tube, 1 hour in a serum tube
- Extreme temperatures (hot or cold) can cause abnormal levels of some analytes – especially potassium.

Samples with Specific Transportation Requirements

Various samples can NOT be transported by the hospital air tube or require special collection conditions, this list is not exhaustive but gives the most frequently encountered tests:

- **ACTH – on ice,** deliver immediately to laboratory, do NOT send via POD
- **Aldosterone and renin,** deliver immediately to the laboratory
- **Ammonia** - deliver immediately to laboratory, do NOT send via POD
- **Blood gases** - arterial blood, cap to prevent air contact, deliver immediately to laboratory, do NOT send via POD
- **Calcitonin - on ice**, deliver immediately to laboratory, do NOT send via POD
- **Carboxyhaemoglobin** - arterial blood, cap to prevent air contact, deliver immediately to laboratory, do NOT send via POD
- **Methaemoglobin** - arterial blood, cap to prevent air contact, deliver immediately to laboratory, do NOT send via POD
- **CSF –Xanthochromia** - protect from light, do NOT send via POD, ensure LFTs checked in last 24hrs if unsure – SEND PAIRED SERUM FOR LFTs. Hand deliver immediately.
- **Homocysteine** –deliver immediately to laboratory, do NOT send via POD
- **Porphyria full screen/Porphyrins** - protect from light, do NOT send via POD
- **Vitamin A (Carotene) -** protect from light, do NOT send via POD
- **Vitamin B1 (Thiamine) -** protect from light, do NOT send via POD
- **Vitamin B6 -** protect from light, do NOT send via POD
- **Vitamin E -** protect from light, do NOT send via POD
- **Vitamin C (Ascorbic Acid)** - protect from light, do NOT send via POD

- **ALL High risk samples** – do NOT send via the POD

Additional test requests

The department does not recommend or encourage the use of 'add-on tests' but under specific circumstances tests may be added as shown below.

For tests not routinely performed within the Blood Sciences department refer to the specific analytes within the test repertoire table.

Routine Chemistry, Endocrine & Therapeutic Drug Monitoring – Stable for up to 2 days, samples are recapped after analysis and stored at 24°C for up to 24 hours before being transferred to 4°C.

With the exception of:

- Plasma Amino Acids, up to 4 hours
- Bicarbonate – stable for up to 2 hours
- BNP - stable for up to 24 hours
- Ca125 – stable for up to 24 hour
- Creatine Kinase (CK) – stable for up to 24 hour
- Serum Glucose – stable for up to 4 hours in a fluoride oxalate tube, 1 hour in a serum tube
- Lactate- must be Fl/oxalate sample, accept if 4C or -20 Stored
- Phosphate- accepted up to 24 h but may be unreliable
- PTH- accepted to 2 hours
- Hs Troponin I – stable for up to 24 hours in fridge, 8hrs room temp
- Urea & Electrolytes - stable for up to 24 hours – but not potassium
- Vitamins B1, B2,B6, A,E- accepted up to 4 h dependent on storage/light exposure
- Vitamin K- accepted to 24h

Paediatric samples may be unsuitable for additional requests. The volume of the sample will be checked prior to addition of any test and the Consultant Biochemist may be approached for advice.

Rotherham and Barnsley Labs: Add on tests will **not** be accepted for

- ACTH
- Ammonia
- Plasma metanephrines
- Aldosterone/renin
- Cysteine (plasma)
- Homocysteine
- C-peptide (but insulin accepted up to 4h, insulin must not be haemolysed even only slightly)
- AMH
- Vitamin C

Turn-around times

These are detailed in the Biochemistry handbook

Referred work

The Biochemistry Department provides a referral service for Vitamin analysis for other centres across the United Kingdom. For further details, please contact the laboratory using the contacts at the start of the handbook. Alternatively, information for users is available on the Biochemistry website:

http://www.therotherhamft.nhs.uk/Pathology/Biochemistry/

The Biochemistry Department maintains a list of names, addresses, tests sent and accreditation status of all laboratories to which work is routinely referred. These lists are available on request. The laboratory will seek to refer tests to UKAS accredited providers

Dynamic Function Tests

The Biochemistry laboratory processes samples from dynamic function tests which are required for the investigation of certain, usually endocrine, conditions.

Details of the Dynamic function tests and associated protocols are available from the Endocrinology and Paediatric department.

Factors known to affect biochemistry test results

If it is thought that a patient's results do not fit with the clinical picture, please phone the laboratory.

It is not practical to list all of the factors known to affect analyte concentration/assay performance but a few of the more common issues are listed below:

- Correct tube and blood draw order reduce the risk of interference – e.g. EDTA contamination with potassium, calcium and magnesium
- CSF samples for xanthochromia need to be protected from light
- Haemolysis, icteric and lipaemic samples can interfere with certain analytes. These are indicated as comments on the report and the sample should be repeated as the results will be unreliable. Common analytes affected include: sodium, potassium, bilirubin, magnesium, phosphate, AST, ALT, Troponin and hormones.
- Serum samples should be processed (centrifuged and serum separated from the cells within 12 hours of collection. Any delay can influence potassium and enzyme results.
- Extreme temperatures (hot or cold) can cause abnormal levels of some analytes – especially potassium.
- The use of the AIR TUBE can cause issues in certain analytes – see section on transportation of specimens.
- HbA1c is affected by any factor that affect red blood cell life span e.g. haemoglobinopathies
- Prolactin may be analytically elevated due to a benign condition such known as macroprolactin
- Time of taking a sample in relation to a person taking a drug will influence the concentrations and ability to interpret results for therapeutic drug monitoring.
- Sodium is affected by abnormal levels of protein and lipids. These can cause a falsely elevated reading in the laboratory and if there is any clinical suspicion a blood gas machine should be used to confirm – PLEASE SPEAK TO THE LABORATORY FIRST

- A high platelet and white blood cell count can cause a falsely elevated potassium (Pseudohyperkalaemia). It is recommended that a sample be taken in to a serum and a lithium heparin tube and sent immediately to the laboratory for confirmation.

Critical results

In the hospital, all results will be telephoned 24 hours a day if they meet the criteria stated. All GP results meeting the telephone criteria will be telephoned during the normal working day with selected results telephoned to the GP Out-of-hours service.
Please refer to Biochemistry laboratory Handbook for critical telephone limits:
http://www.therotherhamft.nhs.uk/Pathology/Biochemistry/

Paediatric reference ranges and sample requirements for Biochemistry

Blood Biochemistry
Specimen requirements are serum or plasma unless otherwise indicated
For neonates and small children the recommended tubes are Sarstedt Microtubes (approximately 1.3mL blood).
For older children Sarstedt *Monovette* may be useful, these hold approximately 4.5 mL of blood

Sarstedt Microtubes (*hold approximately 1.3mL blood).*

Serum is obtained from	**PLAIN cap tube**
Plasma is obtained from	ORANGE cap tube (lithium heparin as anticoagulant).
EDTA blood	Pink cap tube

For further information please see:
http://www.sarstedt.com/pdf/katalog/en/SARSTEDT_E_0409%2032.pdf

Sarstedt Monovette (*hold approximately 4.5 mL blood).*

Serum is obtained from	BROWN cap tube
Plasma is obtained from	ORANGE cap tube (lithium heparin as anticoagulant).
EDTA blood	Pink/purple cap tube
Fluoride/oxalate blood–	YELLOW cap tube

Heel/Finger-prick or venous samples?
Many assays can be analysed from finger prick samples rather than formal venepunctures. These are easier for the clinician to obtain and probably kinder for the child when only small quantities of blood are required. Finger prick samples are routinely used for estimation of Haemoglobin A1c in diabetic children and in children in whom it is impossible to obtain blood by other means. The process of massaging the pulp of the finger to increase the flow of blood results in a degree of tissue damage and the consequent release of extra vascular tissue fluid and cellular contents which invalidates the estimation of plasma electrolytes and enzymes e.g. AST & LDH.

How much blood sample is needed?
Minimum volumes of whole blood are described in Child Health document/minimum blood volumes. Below are absolute minimum volumes of plasma/serum required for analysis**.**

For whole blood (assuming haematocrit of 50%) **the minimum blood volume is approximately double these values.**

In addition, you need to consider the "dead volume" of our analysers (the extra sample volume required in order to introduce the sample for analysis, which is based on the volume to height relationship of the sample container). For our main biochemistry laboratory analyser (Siemens Atellica) this is 2mm of sample if no separator, and 7mm of sample if there is a separator. This should be <50uL but can be as high as 100uL for non-adult tubes.

To calculate how much plasma would be required, add the volume required for all analytes to the "dead volumes". Note that the Siemens Atellica can perform approximately 15 photometric chemistry tests from a sample volume of 50 uL and 3 electrolytes from a sample volume of 25 uL (Therefore a panel of 15 chemistry tests and 3 electrolytes plus dead volume = 125 uL). Endocrinology tests generally require larger samples e.g. TSH = 75 uL (plus 100 uL dead volume = 175 uL and free T4 requires 25 uL, so both free T4 and TSH could be assayed from a plasma volume of 200 uL. See table below:

In general for neonates it may be better to send blood as Li-Heparin Plasma (Orange Microtube) as more plasma sample can be harvested compared with serum, but for some assays it is NOT possible to use plasma samples (e.g. GH,). Please check the following listing to ascertain sample type before venepuncture.

Analyte	**Volume of Plasma Required (uL).** *Note this is NOT the volume of BLOOD: yield of plasma/serum from whole blood will be affected by haematocrit etc. SEE above*	**Notes**
Amino acids	100	assayed by SCH who specify 0.5mL blood
Bilirubin	*assayed with other LFTs*	Main Biochemistry Analyser *
U/E bicarb/chloride	150	Main Biochemistry Analyser *
LFT	100	Main Biochemistry Analyser *
Ca profile	100	Main Biochemistry Analyser *
Caffeine	*200*	assayed by SCH who specify 0.5mL blood
Glucose	100	requires Fl/oxalate preservative (yellow cap micro tube)
Ammonia	100	requires special handling, Li-Heparin tube
Cortisol	70	immunoassay analyser
CK	100	Main Biochemistry Analyser *
fT4 and TSH	200	immunoassay analyser
Lactate	100	can be assayed with glucose from Fl/oxalate sample
Osmolality	20	Main Biochemistry Analyser *
Uric acid		Main Biochemistry Analyser *

*Is it possible to analyse several 'routine' biochemistry tests from the same 100ul. Approximately two lots of the Main Biochemistry Analyser sets.

Hypoglycaemia Screen

If required urgently contact biochemistry lab 4241

These can be supplied as "pack" of microtubes (2 Yellow Fl/oxalate, 3 Orange LiHeparin, 1 White Serum and a Plain universal). Helps to ensure appropriate samples are collected at time of hypoglycaemia.

Glucose	Fl/oxalate preservative (yellow cap tube)
Lactate	Fl/oxalate preservative (yellow cap tube)
3-OH Butyrate and FFA	Fl/oxalate preservative (yellow cap tube)
Insulin	LiHeparin preservative (orange cap tube)
C-Peptide	LiHeparin preservative (orange cap tube)
Acyl Carnitines	LiHeparin preservative (orange cap tube)
Plasma Amino acids	LiHeparin preservative (orange cap tube)
Cortisol	Serum (white top)
	Also:
URINE organic acids	Universal Container

POCT investigations:

POCT glucose
POCT ketones
Blood gas

Additional Metabolic investigations:

Ammonia	sample volume 100 uL Li Heparin tube (please also send an empty tube)
Acyl Carnitines	Li-Heparin sample, ideally as a dried blood spot
Carnitine	sample volume *200* uL *assayed by SCH who specify 1.0 mL blood*

Other investigations:

eGFR: not validated for use in children. Where required please refer to the children's BNF – available online throughout the trust. The section on dose adjustment in renal impairment gives the formula that should be used.
Galactose-1-phosphate Uridyl Transferase (classical galactosaemia screen) *assayed by SCH who specify 0.5mL LiHep whole blood*
Galactose-1-phosphate (monitoring galactosaemia) *assayed by Birmingham Children's Hospital who specify two full orange microtubes (5 mL).*
17a-Hydroxyprogesterone *200* uL *assayed by Leeds steroid lab who specify 0.5 mL blood*
VLCFA *200* uL *assayed by SCH who specify 0.5 mL blood*
Toxicology for Specific Medication *Urine (plain universal container) if indicated by history (e.g. sulphonylurea OR if concern about factitious or induced illness)*

Reference ranges

The ranges for many analytes differ during childhood and adolescence from adult values. We do have problems for some analytes in obtaining age specific ranges such that only adult reference ranges are quoted. If in doubt refer to this handbook or contact the laboratory.

Creatinine reflects the mass of muscle and will therefore increase as a child grows; normal neonates have creatinine concentrations of about 20-30 mmol/L and these values increase to 70-120 mmol/L in the late 'teens in proportion to muscle development.

Alkaline phosphatase reflects bone growth. It has therefore relatively high concentration during the first year of life and then falls until the growth spurt during puberty. High concentrations will also occur after bony fractures (and during pregnancy).

Protein: Immunoglobulins change throughout childhood according to age and sex. Total protein increases by approximately 10% from infancy to adulthood.

Pathology Harmony 2011
The Association for Clinical Biochemistry, the Institute of Biomedical Science and Royal College of Pathologists support the process for common laboratory reference ranges (Department of Health supported: Pathology Harmony Group).

Agreed ranges for a number of adult & paediatric analytes are now available and have been included in this handbook.

ASSAY	**Specimen requirements are serum *or* plasma unless otherwise indicated** **See pages 1- 4 for recommended sample tube requirements**	**Source of ref ranges/ notes, etc.**
Acyl Carnitines Ideally Li-Heparin blood or Dried Blood Spot	Interpretation provided with report	Sheffield Children's Hospital (SCH)
Angiotensin Converting Enzyme (ACE)	**Paediatric** Serum also suitable Newborn children and children aged 4-18 have higher ACE (up to about 1.4 x adult value) with Ace activity staying at higher values for a longer time in boys compared with girls. *Adult* 0-20 yrs 29 - 112 U/L 20yrs + 20-70 U/L	Clin Chem 1990:**36**;344-346 Sheffield RHH

ACTH	**Requires EDTA blood sample, ideally on ice to lab within 20 minutes of collection** *Adult* *09:00h <46ng/L* *24:00 <15ng/L*	 Sheffield Teaching Hospitals (STH)
Albumin	**Paediatric** Plasma albumin concentration in neonates is lower by about 5 g/L. This rises over the first 3 weeks of life. Lower concentration in prematurity (correlates with gestational age) *28-43 (0-7days)* *30-43 (7-14d)* *27 – 44 (14 – 21d)* *31-44 (21-28d)* **Pathology Harmony** 2011 ranges: Neonate 30 - 45 g/L Infant 30 - 45 1 - 16y 30 - 50 *Adult (Pathology Harmony 2011)* *35-50 g/L*	Neonatology & Lab Medicine ACB Venture Publication 2017 Pathology Harmony
Alkaline Phosphatase (ALP)	**<u>Alkaline phosphatase is highly method dependent.</u>** **Paediatric** Up to ~3x the upper adult ref range (up to about 500 U/l) may be seen, especially during growth spurts in children. In neonates the ALP may be elevated in the first week due to *placental* ALP ($t_{1/2}$ = 3 days) Preterm concentrations higher and can be up to 700U/L in the absence of active rickets. **Pathology Harmony** 2011 ranges: Neonate 70 - 380 U/L Infant - 16y 60 - 425 Adult 30 – 130 *Adult (Pathology Harmony 2011)* *30 - 130 U/L*	Neonatology & Lab Medicine ACB Venture Publication 2017 Arch Dis Child Educ Pract Ed 2012;97:157-163 Acta Paediatrica 2008;97:407-413 Pathology Harmony

Alanine Aminotransaminase (ALT, SGPT)	**Paediatric** Adult values reached between the ages of 6-24 months. ACB neonatology book states up to 40u/L and may vary with method *Adult* *10-49u/L*	Soldin AACC paediatric pub 6th Ed 2007, method very different to ours so no figures quoted. Neonatology & Lab Medicine ACB Venture Publication 2017 *Siemens Atellica*
Aldosterone MUST be Li Heparin **Renin** PLASMA immediately to lab – NOT on ice	Of value in Bartters syndrome, assayed with renin Na intake 100-150mmol/day K intake 50-100mmol/day **Paediatric** Higher at birth and in infants Values can be very high (>5000pmol/L) in the neonate, but reduce rapidly. Adult ref. ranges are reached by age 10 yrs. *Adults aged 20-40yrs* *08.00h after overnight recumbency; 100-450pmol/L* *When taken randomly thro day with normal activities: 100-850 pmol/L* Values decrease significantly in the elderly >60yrs	Leeds Steroid lab In-house RIA – use literature derived paediatric ranges and in-house adult ranges.
Amino Acid Screen LiHeparin PLASMA Random URINE ***TO LAB ASAP***	Screen: 2D Thin layer chromatography If any abnormalities amino acids are quantitated Carnitine can usually be done on same sample 1mL microtube for plasma samples (EDTA and Fl/oxalate samples also acceptable)	Sheffield Children's Hospital (SCH)

Ammonia Li Heparin blood (ideally chilled) IMMEDIATELY TO LAB with prior contact if possible. Also send an empty (unfilled) tube at same time which lab uses to check for background ammonia level. EDTA sample (also acceptable): required for follow up/confirmation of raised levels (SCH assay)	**Paediatric** **Pathology Harmony** refers to Metbionet: Prem / sick neonate <150 umol/L Neonate <100 1 - 16y <40 Adult <40	Metbionet ranges
Amylase	**Paediatric** Amylase is low in infants for the first 2 months of life (about half adult values) and gradually increases to adult values by the end of the first year of life. *Adult* *30 - 118 U/L*	Tietz - Clinical Guide to Laboratory Tests, 1995 Clin Chem 1988;**34**:1622-1625 *Siemens Atellica*
Aminoadipic acid **α-aminoadipic semialdehyde (urine)** Fresh random Urine (min 10mL) before Thursdays Can also be assayed in CSF	Analysis of **α-aminoadipic semialdehyde** is an important tool in the diagnosis of antiquitin deficiency (pyridoxine-dependent epilepsy). Continuing use of this test has revealed that elevated urinary excretion of α-aminoadipic semialdehyde is not only found in patients with pyridoxine-dependent epilepsy but is also seen in patients with molybdenum cofactor deficiency and isolated sulphite oxidase deficiency. This should be taken into account when interpreting the laboratory data. Sulphite was shown to inhibit α-aminoadipic semialdehyde dehydrogenase in vitro	GOSHH
Androstenedione	**Paediatrics** In pre-pubertal children <1.4 nmol/L (Leeds take this from literature) *Adult* *Females without PCO, early follicular phase, 1.1-5.7nmol/L.* *Males 1.3-5.8 nmol/L*	Leeds steroid lab LC-MS/MS method since 2007

<table>
<tr><td>Aspartate amino Transaminase (AST, SGOT)</td><td colspan="3">Paediatric
The AST reference range is slightly higher for neonates and adult values are reached between the ages of 6-24 months.

Adult <60yrs
<34U/L</td><td>Soldin AACC paediatric pub 6th Ed 2007, method very different to ours so no figures quoted.

Siemens Atellica</td></tr>
<tr><td>Bicarbonate

MUST be Li Heparin PLASMA</td><td colspan="3">Applicable to all ages (child not significantly different from adult)

Pathology Harmony 2011 ranges:
19 - 28 mmol/L (plasma)
22-29 mmol/L (serum)</td><td>Pathology Harmony</td></tr>
<tr><td>Bilirubin</td><td colspan="3">Paediatric
Physiological jaundice may develop after 48h, normalising by day 10. Largely unconjugated.

Pathology Harmony 2011 ranges:
No range quoted for age less than 14d
14 day - 16 years <21 umol/L
Adult <21

Conjugated/Direct Bilirubin
Adult: <5.1 umol/L.</td><td>Pathology Harmony

Siemens Atellica</td></tr>
<tr><td>Biotinidase
Must be Li Heparin sample
Minimum volume 0.5mL plasma</td><td colspan="3">Child/adult 2.5-10.5 U/L</td><td>Sheffield Children’s Hospital</td></tr>
<tr><td rowspan="6">Blood Gases
requires special handling, use blood gas syringe
Do NOT use the air tube
Please ensure in laboratory within 15 minutes of venepuncture to ensure accuracy of results, with gentle agitation throughout transport.</td><td colspan="3">Children*</td><td rowspan="6">*Paediatric ranges not provided by manufacturer, Sheffield Children’s Hospital reference ranges are provided for comparison</td></tr>
<tr><td>H+</td><td>Newborn: 32 - 47
Neonate/Infant: 35 – 48
Child: as adult</td><td>mmol/L</td></tr>
<tr><td>pO2</td><td>Neonate: 6.7 – 12.0
Child: 11.0 – 13.5</td><td>KPa</td></tr>
<tr><td>pCO2</td><td>Neonate: 3.6 – 5.4
Infant: 3.5 – 5.5
Child: 4.4 – 6.1</td><td>KPa</td></tr>
<tr><td>Actual bicarbonate</td><td>Child: 17 - 27</td><td>mmol/L</td></tr>
<tr><td>Base excess</td><td>Newborn: -10 to -1
Infant: -7 to -1
Child: -4 to +2</td><td>mmol/L</td></tr>
</table>

<table>
<tr><td></td><td>Adult (arterial)<table>
<tr><td>H+</td><td>35.5 – 44.7</td><td>mmol/L</td></tr>
<tr><td>pH</td><td>7.35 - 7.45</td><td></td></tr>
<tr><td>pO2</td><td>11.0-14.4</td><td>KPa</td></tr>
<tr><td>pCO2 (male)</td><td>4.6 – 6.4</td><td>KPa</td></tr>
<tr><td>Actual bicarbonate</td><td>21 - 28</td><td>mmol/L</td></tr>
<tr><td>Base excess</td><td>-2 - +3</td><td>mmol/L</td></tr>
</table></td><td>Werfen GEM 5000 User Handbook</td></tr>
<tr><td>Caffeine
Must be Li Heparin sample
Sample assayed most days, need to be at SCH lab before 12:00</td><td>Child
10-35mg/L</td><td>Sheffield Children’s Hospital – as per BNF for children therapeutic range</td></tr>
<tr><td>Carboxyhaemoglobin
To lab ASAP</td><td>Treat as sample for blood gas analysis</td><td></td></tr>
<tr><td>Calprotectin
Fresh Faeces</td><td>Calprotectin is very high in infants and higher in children than adults
For children 2 – 9y expect normal values up to 166 mg/Kg.

Adults
<50ug/g suggests IBD not present
Results >50 regarded as positive
100 - 150 indicate bowel inflammation
>150 consistent with active IBD</td><td>Immundiagnostik IDK Calprotectin ELISA</td></tr>
<tr><td>Carotenoids / Beta Carotene
Light Sensitive - requires microtube immediately to lab serum or plasma are suitable
Minimum volume 0.2 mL
Avoid exposure to light at all times</td><td>B-carotene: 0.06 – 2.20 umol/L</td><td>Assayed by St Helier Hospital, Carsholton (HPLC technique for beta-carotene & other carotenoids).</td></tr>
</table>

Calcium blood serum/plasma	**Paediatric** *Concentrations fall after birth with lowest values at 24-48h, after which there is a slow rise to a constant level* **Pathology Harmony** 2011 ranges: Neonate 2.00 - 2.70 mmol/L Infant - 16yrs 2.20 - 2.70 (not adjusted for prevailing serum albumin concentration) *Adult* *2.20 - 2.60 mmol/L* *(use adjustment equation normalised to a mean calcium of 2.4mmol/L)*	*Neonatology & Lab Medicine ACB Venture Publication 2017* Pathology Harmony Pathology Harmony
Urine calcium	**Pathology Harmony** 2011 ranges: *Adult 2.5 - 7.5 mmol/24H* **Calcium/creatinine ratio: in 2nd morning urine** *Calcium:creatinine ratio falls from birth to an 'adult' range by 7 years of age* *< 6 months <2.42 mmol/mmol* *6-12 months 0.09-2.2* *1-2 years 0.07-1.5* *2-3 years 0.06-1.4* *3-5 years 0.05-1.1* *5-7 years 0.04-0.8* *> 7 years 0.04-0.7* *Adult* *Male 0.30 – 6.10 mmol/ g creatinine* *0.225-9.47mmol/* *Female 0.225 – 8.2 mmol/ g creatinine* *0.125-8.92 mmol/L* CO2 loss from specimen increases pH and decreases calcium	Pathology Harmony *J Pediatr 1997;131:252-257* TIETZ Guide to Lab Tests2006 4TH ed
Ionised calcium MUST be serum sample immediately to lab Analysed ASAP (within 1hr) Avoid haemolysis	**Paediatric** 0-1month: 1.10 – 1.50 mmol/L 1-6 months: 0.95 – 1.50 *Adult1.15 – 1.27 mmol/l*	Paediatric reference Intervals 6th ed . Edited by Soldin *et al.* AACC Press Werfen Gem 4000 Reference range

Carbamazepine (tegretol)	Target range: 4 – 12 mg/L for all ages	Pathology Harmony
Carbohydrate deficient glycoprotein (transferrin) (CDG) Serum sample only Minimum volume 250uL of serum	Test is unreliable in neonates younger than 3 weeks Interpretation provided with report	Institute of neurology, London
Carnitine ***See also acyl carnitines*** Preferred assay is ACYL CARNITINES – dried blood spot or Li Heparin Whole blood (can also do plasma (serum and fluoride oxalate)	Total: 23-60 umol/L Free: 15-53	Sheffield Children's Hospital
Catecholamines This is a URINE analysis Random urine / UCP urine immediately to lab or 24h collection into acid preserved urine container See also catecholamine metabolites: VMA, HVA	**Paediatric** Age related: expressed as excretion per creatinine nmol/mmol creatinine Age / Adrenaline / Noradrenaline / Dopamine <1yr <80 < 430 < 1950 1-3 <80 < 200 < 1450 3-5 <80 < 190 < 950 5-8 <80 < 180 < 850 8-11 <80 < 170 < 750 >11 <80 < 130 < 650 *Adult* *usually assayed as "Overnight Excretion" with metanephrines as first line test*	Fitzgibbon and Tormey Ann Clin Biochem (1994)**31**:1-11 In House Data
Chloride **Urine Chloride** **Please** *contact lab*	**Pathology Harmony** 2011 ranges: *Adult Plasma 95 - 108 mmol/L*	Pathology Harmony

Cholesterol	**Paediatric** See also FH Guidelines CG71 (NICE 2008) for child/young person. *Adult* *Primary prevention target: < 5.0 mmol/L* *The European guideline considers patients in terms of different levels of risk and targets reflect the different level of risk. The guidance states that '..in general, total plasma cholesterol should be <5 mmol/L, and LDL cholesterol should be <3 mmol/L. In subjects with higher CVD risk, the treatment goals should be lower*	Perk J et al. European Guidelines on cardiovascular disease prevention in clinical practice. European Heart Journal (2012) 33, 1635-1701
Cholinesterase EDTA tube needed	See pseudocholinesterase	
Copper Ideally "trace metal" vacutainer *alternative* Full serum microtube, or lithium heparin microtube.	**Paediatric** Copper and caeruloplasmin are low and rise in early weeks; adult levels by 2 years, but may not be complete until puberty. This makes the diagnosis of Wilson's disease difficult during the first six months. < 26weeks 5.9-16.3 umol/L > 26weeks 3.8-23.8 Female 1-<13yrs 11.0-27.2 Female 13-49yrs 11.0-38.9 Female >49yrs 11.0-27.2 Adult Male 11.0-27.2 *Copper concentrations which fail to rise above 5 umol/l after the first few weeks may indicate copper deficiency.* *Note that serum Cu raised by inflammatory response, injury, sepsis, steroids, pregnancy.*	Northern Gen Hospital, Sheffield (NGH) assay Reference ranges, data from 2015/16 Implied from data in J Trace Elem Biol Med 1997; 11: 92-98
Urine Copper 24H URINE COLLECTION RANDOM	no paediatric data *Adult 0.047 - 0.55 umol/24h* *0.068 - 0.19 umol/L*	Ann Clin Biochem 2000;37:289-297 NGH in house data Confirmed 24.2.17

Cortisol Ideally: serum sample	**Paediatric** There is considerable inter-individual variation in cortisol levels in childhood. Results in the lower part of the reference range do not exclude deficiency. Difficult to measure at birth due to cross-reacting steroids. Marked fall after 24h partly due to falling maternal cortisol. Can take a few months for diurnal rhythms to establish, appropriate dynamic function should be used instead 09:00 180-550nmol/L 8-10am 2hrs 34.4 822.2 nmol/L 7days 3.6 265.9 2wk-3mon 25.5 239.4 3m – 1yr 58.5 477.0 1 – 3yr 47.2 377.9 3-5yr 89.4 355.9 5-7yr 109.8 375.4 7-11yr 97.7 507.6 11-15yr 59.9 480.0 Serum [cortisol]: neonatal reference intervals are dependent on gestational age and time since delivery; 1–16 years (08.00 h) 200–700; (00.00h) <150 nmol/L Reference intervals (adults) Serum [cortisol]: 09.00 h, 171-536 nmol/L (Roche Elecsys); 00.00h <50 nmol/L. *Adult* *07:00-09:00am 140 – 500 nmol/L* *15:00-17:00pm 85 - 460 nmol/L* *Midnight <100 nmol/L*	ACB, Neonatology and Clinical Biochemistry, 2017 Sippell et al.1980 Paed Res 14 39-46 ACB Monograph http://www.acb.org.uk/docs/default-source/committees/scientific/amalc/cortisol.pdf J Clin Endo Metab 2008 93;1526- 24:00 from Local endocrine team advice by email Dr Franke 25.06.2020
Urine Cortisol 24H Urine collection	**Paediatric** In-house age related ranges not available (published literature data used for children) Random (<24h) ranges not available. *Adult* *10 – 147 nmol/24h*	Leeds Steroid Lab LC MS-MS since 2007 Leeds Steroid Lab LC MS-MS since 2007

Creatine **(see also GAA)** MUST be Li Heparin blood sample Random urine immediately to lab	Investigation of creatine disorders (e.g. *low* serum creatinine) Interpretation provided with report Fresh urine sample, with Li-heparin blood sample directly to lab	Assays available via Leeds St James and Camelia Botnar Lab GOSH.
Creatine kinase (CK, CPK)	**Paediatric** Beyond 1st year ref range ~ adult 0-90d 28 – 470 U/L 90d-1yr 24 – 240 1yr – 10yr 24 - 175 11y – 14y 30 – 170 15y – 18y 27 – 145 Adult 30 - 170 **Pathology Harmony** 2011 ranges: *Adult* *Caucasian M: 40 - 320 IU/L* *F: 25 – 250* *Higher values in black/Asian groups*	Sheffield Children's Hospital Handbook based on Paediatric reference Intervals 6th ed. Edited by Soldin *et al.* AACCPress Pathology Harmony

<table>
<tr>
<td>Creatinine</td>
<td>Paediatric

<table>
<tr><th></th><th>Male
Lower limit</th><th>Upper limit</th><th>Female
Lower limit</th><th>Up</th></tr>
<tr><td>0 - <14days</td><td>27</td><td>81</td><td>27</td><td>81</td></tr>
<tr><td>14d - <1yr</td><td>14</td><td>34</td><td>14</td><td>34</td></tr>
<tr><td>1 - <3yr</td><td>15</td><td>31</td><td>15</td><td>31</td></tr>
<tr><td>3 - <5yr</td><td>23</td><td>37</td><td>23</td><td>37</td></tr>
<tr><td>5 - <7yr</td><td>25</td><td>42</td><td>25</td><td>42</td></tr>
<tr><td>7 - <9yr</td><td>30</td><td>48</td><td>30</td><td>48</td></tr>
<tr><td>9 - <11yr</td><td>28</td><td>57</td><td>28</td><td>57</td></tr>
<tr><td>11yr</td><td>36</td><td>64</td><td>36</td><td>64</td></tr>
<tr><td>12yr</td><td>36</td><td>67</td><td>36</td><td>67</td></tr>
<tr><td>13yr</td><td>38</td><td>76</td><td>38</td><td>74</td></tr>
<tr><td>14yr</td><td>40</td><td>83</td><td>43</td><td>75</td></tr>
<tr><td>15yr</td><td>47</td><td>98</td><td>44</td><td>79</td></tr>
<tr><td>16yr</td><td>54</td><td>99</td><td>48</td><td>81</td></tr>
</table>

Adult
Male 53 – 97umol/L
Female 44 – 71 umol/L</td>
<td>https://www.thinkkidneys.nhs.uk/aki/wp-content/uploads/sites/2/2016/05/Guidance_for_paediatric_patients_FINAL.pdf

PaLMnet

Siemens Atellica</td>
</tr>
<tr>
<td>Cystine
plasma MUST be Li Heparin sample send to lab ASAP

Cystine in leucocytes/ White cell cysteine
MUST be Li Heparin sample
Absolute Minimum volume is 2x orange microtubes
Preferably 2mL whole blood in Orange Top Monovette</td>
<td>Part of amino acid analysis

Interpretation provided with report

Phone to arrange before venepuncture – needs rapid handling.

Normal up to 0.5 nmol ½ cystine / mg protein
Heterozygotes up to 1.0,
Cystinosis patients usually >2.0 nmol ½ cystine / mg protein</td>
<td>Sheffield Children’s Hospital

St James, Leeds</td>
</tr>
<tr>
<td>Cyclosporin (Ciclosporin)
MUST be EDTA sample</td>
<td>Child/adult
Trough levels approx. 100 – 400 ug/L</td>
<td>Sheffield Teaching Hospital</td>
</tr>
<tr>
<td>7-Dehydro Cholesterol
Lithium heparin or EDTA blood. Min volume is 0.2mL plasma</td>
<td>For Smith Lemli Opitz Syndrome diagnosis

Normally <2umol/L
In SLI usually >5umol/L</td>
<td>Sheffield Children’s Hospital</td>
</tr>
</table>

11-deoxy cortisol Lithium heparin plasma or serum	**No longer available**	
DHEAS	**Paediatric** Pre adrenarche <1 umol/L Age Range Females Males Post puberty – 24 y 2.7 – 11 3.6 – 13 25 – 34 y 2.1 – 10 2.9 – 12 35 – 49 y 1.3 – 8.5 1.7 – 10 50 – 59 y 1.0 – 7.0 1.0 – 8.0 60 – 69 y < 6.0 < 7.0 > 70 y < 5.0 < 6.0	Leeds Steroid Lab
Dihydrotestosterone (DHT)	Assayed with testosterone For investigation of 5-alpha reductase deficiency or to ascertain presence of testicular tissue Of most use as part of an hCG stimulation test **Paediatric** No ranges, interpretive comment added for hCG test. *Adult:* *Male 0.9 – 2.9 nmol/L* *Female 0.2 – 1.0*	Leeds steroid lab
Faecal Elastase (FE-1) Fresh to Lab, small faecal sample *Other faecal GI investigations:* See Calprotectin	Faecal elastase > 200 ug/g faeces - no indication of exocrine pancreatic insufficiency 100-200ug/g - moderate exocrine pancreatic insufficiency <100ug/g- severe exocrine pancreatic insufficiency	Bioserv Pancreatic Elastase ELISA

Ferritin Serum sample is best (plasma: li-heparin gives slightly higher results, EDTA slightly lower results)	**Paediatric** Ref interval not well defined for paediatrics Very high post birth, falls to maximum of about 400 ug/L by 8 weeks For ages 1 – 6years expect lower limit of *ca* 9 ug/L with lower upper limit ca 80. From age 6 similar to adult ranges. Infant range 110 – 503ug/L *Adult* *Male 22-322 ug/L* *Female 10 - 291 ug/L*	Paediatric reference Intervals 6th ed. Edited by Soldin *et al.* AACCPress Flynn et al., Arch Dis Child Fetal Neonatal Ed 2003 88: F124-F127 *Siemens Atellica*
Free T3 Serum samples also acceptable	**Paediatric** Age pmol/L 1-3d 2.32-8.11 4-30d 2.40-7.94 31-60d 2.48-7.78 61d-12m 2.72-7.30 1-5y 3.05-6.93 6-10y 3.30-6.79 11-14y 3.46-6.71 15-18y 3.57-6.65 *Adult* *3.5 – 6.5 pmol/L*	Clin Chem Lab Med 2002; 40(10):1040–1047 *Siemens Atellica*
Free T4	**Paediatric** Age pmol/L 1-3d 10.8-26.8 4-30d 10.9-25.5 31-60d 11.0-24.3 61d-12m 11.4-20.9 1-5y 11.4-19.0 6-10y 11.0-18.8 11-14y 10.8-18.7 15-18y 10.7-18.7 *Adult* *11.5 – 22.7 pmol/L*	Clin Chem Lab Med 2002; 40(10):1040–1047 *Siemens Atellica*

Folate	*Adult ng/ml* *Deficient 0.35 – 3.37* *Intermediate 3.38 – 5.38* *Normal >5.38*	*Siemens Atellica*
Follicle Stimulating Hormone (FSH)	**Paediatric** FSH is low at birth. In first 2 years it rises intermittently to adult (occasionally higher) levels. Then low until puberty: pre-pubertal children of both sexes tend to have FSH >LH with both levels <2 mIU/mL *Adult:* *Female* *Follicular phase 2.5 – 10.2 mIU/mL* *Mid-cycle 3.4 – 33.4 mIU/mL* *Luteal 1.5 – 9.1 mIU/mL* *Post-menopausal 23 – 116.3 mIU/mL* *Pregnant <0.3 mIU/mL* *Male 1.4 – 18.1 mIU/mL*	Leeds Steroid Laboratory *Siemens Atellica*
Free Fatty Acids MUST be Li Heparin sample	See **intermediary metabolites**	Sheffield Children's Hospital
Guanidinoacetate (GAA) (see also creatine) MUST be Li Heparin blood sample Random urine Minimum volume: 100uL both sample types immediately to lab	Investigation of creatine disorders (e.g. low serum creatinine) Commonest disorder is transporter defect (urine creatine) GAMT deficiency needs plasma assay.	Service provided by Leeds St James or Camelia Botnar Lab GOSH
Gabapentin Pre-dose (trough) level required Serum also suitable	No paediatric range *Adult:* *2-20 mg/L*	Nat Soc Epilepsy, Little Chalfont https://www.epilepsysociety.org.uk/sites/default/files/Therapeutic-Drug-Monitoring-of-Antiepileptic-Drugs-Table.pdf

<table>
<tr>
<td>Gamma Glutamyl Transferase (transpeptidase) (GGT)</td>
<td>Paediatric
<table>
<tr><td>Age</td><td>Male</td><td>Female</td></tr>
<tr><td>1 – 182d</td><td>12 – 122</td><td>15 – 132</td></tr>
<tr><td>183 – 365d</td><td>1 – 39</td><td>1 – 39</td></tr>
<tr><td>1 – 12y</td><td>3 – 22</td><td>4 – 22</td></tr>
<tr><td>13 – 18y</td><td>2 - 42</td><td>4 - 24</td></tr>
</table>
GGT in neonatal period (0-4w) is 5-7X higher than adult. Thereafter declines. Adult ref range for GGT applicable by 7 months, gender difference in ref range occurs from puberty

Adult
Male <73 U/L
Female <38 U/L</td>
<td>Ref ranges are method dependent

Paediatric reference Intervals 6th ed. Edited by Soldin et al. AACCPress

Ann Clin Biochem 2002;39:22-25,

Siemens Atellica</td>
</tr>
<tr>
<td>Glucose
Fluoride Oxalate tube</td>
<td>Plasma (Fasting)
Neonate 2.5 – 5.5 mmol/L
Child 3.0 – 6.5
Adult 2.5 - 6.0

Newborn 1d 2.2 - 3.3
1D-child 2.8 - 4.4
child 3.5 - 5.6
Adult 4.1 - 5.9

CSF
Child 3.3 – 4.4
Adult 2.2 – 3.9</td>
<td>TRFT

Siemens Atellica

Siemens Atellica</td>
</tr>
<tr>
<td>Galactosaemia screening test (Galactose 1 phosphate uridyl transferase in erythrocytes)

Orange microtube at least half full or Li Heparin (green) vacutainer immediately to lab. Assay requires at least 500 uL whole blood</td>
<td>Invalid (3months) if blood transfusion
Interpretation provided with report
Other investigations of neonatal galactosaemia:
Galactitol in urine
Galactokinase and epimerase lesions – in benign form no galactosaemia or galactosuria but in severe form similar to transferase deficiency
Please contact laboratory to arrange analysis as arrangements have to be made with external laboratories.</td>
<td>Assayed by Sheffield Children’s Hospital</td>
</tr>
</table>

Galactitol (urine) Random urine stable for a few days	Galactitol may be useful for investigating galactosaemia when there has been a recent blood transfusion. Interpretation provided with report It is not useful when LFT's are raised (will also raise galactitol)	Lewis Labs, Southmead, Bristol
Galactose 1 phosphate <u>Special sample requirement</u> Li heparin blood sample: At least 2 orange microtubes or Half full Li Heparin (green) vacutainer immediately to lab. **Please contact laboratory to arrange analysis as arrangements have to be made with external laboratories.**	Monitoring for dietary control by red cell galactose 1 phosphate: **Do not send after Wednesday**	Birmingham Children's
Glycine **CSF:Plasma ratio** Ideally Li Heparin plasma (EDTA or Fl/oxalate sample acceptable) CSF containing no additive (Fl/oxalate sample acceptable) Send samples immediately to lab	CSF must not be blood stained Interpretation provided with report	Sheffield Children's Hospital
Glycosaminoglycans Urine RANDOM or aliquot of 24h collection	See also sialic acids/oligosaccharides Interpretation provided with report	Routinely to Sheffield Children's Hosp. Follow up may be via Willink Lab, Manchester Univ Hospital.
Growth Hormone serum sample only (plain cap microtube or gold cap vacutainer)	GH now reported as mass units (ug/L) 0 – 7d 1-23 5 – 15d 1 – 15 15d – 11y <4.7 11y – 18y <11 18+y <4.3 Results are approx. one third of the old units (1ug/L = 3 mU/L).	The Royal Hallamshire Hospital Sheffield or Royal Surrey Hospital, Guildford.

HbA1c EDTA (Pink/purple) or dedicated capillary collection system (BioRad) product	Children: HbA1c target level of 48 mmol/mol (6.5%) or lower is ideal to minimise the risk of long-term complications	NICE guidelines ng18: August 2015 Diabetes (type 1 &2) in children and young people: diagnosis and Management
	Adults *Reported in IFCC units (mmol/mol)* *Normal range 20 - 42 mmol/mol* *In diabetics -* *< 48 mmol/mol indicates good glycaemic control* *If lifestyle+diet+1 drug(no hypo) then target 48 mmol/mol* *If on drug associated with hypo then target 53 mmol/mol* *Patient involved in target setting* *Consider relaxing the targets (individual) if elderly, frail, reduced life expectancy or at high risk of hypo* *Pregnant women – see specific guideline* *> 58 mmol/mol indicates abnormal control*	NICE guidelines ng28: updated May 2017 Type 2 diabetes in adults (Management)

HDL Cholesterol	Foetal plasma cholesterol levels are low and, much of the circulating cholesterol is present as HDL resulting in HDL levels close to those of adults. Plasma HDL is probably relatively constant in childhood. However, a decline occurs in males at puberty and the HDL levels do not rise again until in the 50s. In women there is no change in HDL during adolescence and from the age of 25 there is a progressive rise in HDL. *There is a marked negative assay bias on HDL with increased serum bilirubin concentrations so it may be better to use total cholesterol only for neonates etc.* *Adult* *Low undesirable high risk* *< 1.0 mmol/L* *High (desirable, low risk)* *>1.6 mmol/L*	Woollett LA, Heubi JE. Fetal and Neonatal Cholesterol Metabolism. [Updated 2020 Jan 4]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK395580 Paediatric reference Intervals 6th ed. Edited by Soldin *et al.* AACCPress *Siemens Atellica*
Homocysteine – requires special handling LiHeparin or EDTA sample **immediately** to lab **Urine test – *see amino acids***	*Adult* *0-18 umol/l male* *0-16 umol/l female*	Sheffield Children's Hospital
18-Hydroxy cortisol (18OH F, 18OHC) 0.5ml EDTA Plasma serum is also OK 24h Urine assay also available	Interpretation provided with report	Endocrine Unit, Southampton Gen Hospital 023 80 796707

17-*a* Hydroxy - progesterone	Rapid fall from very high values post birth; Maternally derived in first 24-48h. Inappropriate to assay at this time **Paediatrics** Neonates (>48h after birth) 5d: <3.0 nmol/L 0-16 yrs <4.0nmol/L Premature and stressed neonates may have 2-3x higher values than full term Adult Male <5.0nmol/L Female <5.0nmol/L may be higher in luteal phase	Leeds Steroid Lab LC-MSMS since April 2015
Homo vanillic acid (HVA) Catecholamine metabolite: This is a URINE analysis Random urine / UCP urine immediately to lab	**Paediatric** Age <1 year <25.0 umol/mmol creatinine 1-3 years <17.0 3-5 years <16.0 5-8 years <14.0 8-11 years <11.5 >11 years <7.0 For investigation/exclusion of neuroblastoma	Fitzgibbon and Tormey Ann Clin Biochem (1994) **31**;1-11
Iron MUST be serum sample	For toxicity measure at 4h post ingestion (best laboratory measure of severity since absorbed iron is rapidly cleared from the blood) Toxicity due to local and systemic effects Blood iron concentrations do not correlate well with symptoms < 55 umol/L mild toxicity 55-90 umol/L moderate toxicity >90 umol/L severe toxicity *Adult* *Male: 12 – 31 umol/L* *Female: 9 – 30* *Diurnal variation: lower later in day*	Toxbase/NPIS *Siemens Atellica* Am J Clin Pathol 2002;117:802-808
Insulin Serum also acceptable	Any degree of haemolysis invalidates insulin assay *Adult* *17.8 - 173 pmol/L* *Insulin/glucose ratio calculation discontinued from 2011 (found to be unreliable)*	Royal Hallamshire Hospital Sheffield

Intermediary metabolites requires special HANDLING Must be Fl/oxalate samples (Yellow microtube) See also hypoglycaemia screen	**3- OH Butyrate** **Free Fatty Acids** Interpretation provided with report	Assayed by Sheffield Children's Hospital
Lactate This requires special handling: Fl/oxalate (YELLOW MICROTUBE IMMED TO LAB) **CSF Lactate**	**Paediatric** **Pathology Harmony** 2011 ranges: No age related changes 0.6 - 2.5 mmol/L *Compare with plasma*	Pathology Harmony
LDH **Lactate dehydrogenase**	Higher than adult level: Up to 10x in neonates 2x in children *Adult* *120 - 246 U/L*	Paediatric reference Intervals 6th ed. Edited by Soldin *et al.* AACCPress *Siemens Atellica*
Luteinising Hormone (LH)	**Paediatric** In neonates up to 6months, LH can be measured as index of pituitary function (range similar to adult). Thereafter LH very low until puberty Children <0.1 – 6.0 *Adult Female (mIU/mL)* *Follicular phase* *1.9 – 12.5* *Mid-cycle* *8.7 – 76.3* *Luteal* *0.5 – 16.9* *Pregnant* *<0.1 – 1.5* *Post-menopausal* *15.9 – 54.0* *Contraceptives* *0.7 – 5.6* *Male 20 – 70y* *1.5 – 9.3* *Male > 70y* *3.1 – 34.6*	Tietz - Clinical Guide to Laboratory Tests, 2006 *Siemens Atellica*

Lead Whole heparinised blood Must be at least a full orange microtube	Whole blood: *Children: <5 ug/dL (if 1-2 µg/dL consider repeat based on clinical Hx/advice from UKHSA; if >2 µg/dL identify and remove source of lead; if ≥ 5 µg/dL reported to LEICSS at UKHSA)* Whole blood in general population: <5 µg/dL Occupational exposure : Males < 35 µg/dL; Women of reproductive capacity : < 20 µg/dL Urine : < 10 µg/24 hrs or < 4.5 µg/mmol creatinine	Sheffield Teaching Hospital
LDL - Cholesterol	Familial hypercholesterolaemia? For child/young person >4.0 mmol/L = FH possible (Simon Broome criteria: adopted by NICE 2008) Definite FH if TC/LDL-C criteria plus tendon xanthomas or evidence in 1st/2nd deg relatives, or if evidence of LDL receptor mutation. LDL-C >11.0 mmol/L = homozygous FH	
Lipase Serum also suitable	**Paediatric** From approx. 6 weeks levels may be lower up to 1+ years when compared with adult values *Adult:* *Serum 12-53 U/L*	Paediatric reference Intervals 6th ed. Edited by Soldin *et al.* AACCPress *Siemens Atellica*
Magnesium **Urine Magnesium**	**Paediatric** Infant child levels are similar but may be lower than adult **Pathology Harmony** 2011 ranges: Neonate 0.6 - 1.0 mmol/L Infant - 16y 0.7 - 1.0 *Adult* *0.7 – 1.0 mmol/L* 24 Hour 2.4 – 6.5 mmol/24hrs **2nd voided random urine Mg** Mg/creatinine ratio decreases from 2.2 to 0.6 mol/mol with increasing age from 1 month to 14y	Pathology Harmony Pathology Harmony (Matos et al J.Paed 1997)

<table>
<tr>
<td>Metanephrines
Urine assay

Random urine / UCP urine immediately to lab or overnight (or possibly 24h) collection into acid preserved urine container</td>
<td>Paediatric
Metanephrine present in neonatal urine on the first day of life. Remain low until the 10th month of life and then progressively increase.
In contrast normetanephrine levels are already high in the neonatal period and increase only beyond the 4th year of age.

Adult
Metanphrine < 0.30 umol / mmol creatinine
Normetanephrine < 0.35 umol / mmol creatinine</td>
<td>Eur J Clin Chem Clin Biochem 1997;35:533-537</td>
</tr>
<tr>
<td>Microalbumin (ACR)</td>
<td>Albumin/Creatinine Ratio (ACR) in early morning urine (EMU)
< 3 mg/mmol creatinine , Normal to mildly increased
3–30 mg/mmol, Moderately increased
>30 mg/mmol Severely increased</td>
<td>NICE guidelines (CG182)</td>
</tr>
<tr>
<td>Mucopolysaccharides
This requires FRESH URINE analysis.
Creatinine must be >1.0mmol/L for a valid result.</td>
<td>Glycosaminoglycan screened by DMB
Electrophoresis performed if abnormal screen
Age related reference ranges

<table>
<tr><th>Age</th><th>Range</th></tr>
<tr><td>0 – 4w</td><td>22.1 – 40.8</td></tr>
<tr><td>1 - 3m</td><td>9.2 – 38.8</td></tr>
<tr><td>3 – 6m</td><td>11.9 – 34.5</td></tr>
<tr><td>6m – 1y</td><td>4.2 – 30.5</td></tr>
<tr><td>1 – 2y</td><td>6.8 – 21.7</td></tr>
<tr><td>2 – 3y</td><td>9.7 – 19.5</td></tr>
<tr><td>3 – 5y</td><td>6.2 – 15.4</td></tr>
<tr><td>5 – 7y</td><td>6.2 – 12.1</td></tr>
<tr><td>7 – 9y</td><td>4.1 – 10.8</td></tr>
<tr><td>9 – 11y</td><td>4.5 – 10.8</td></tr>
<tr><td>11 – 13y</td><td>2.8 – 10.4</td></tr>
<tr><td>13 – 15y</td><td>2.0 – 7.6</td></tr>
<tr><td>>15</td><td>1.7 – 4.4</td></tr>
</table>

Interpretation provided with report

See also Sialic acids/oligosaccharides</td>
<td>Sheffield Children’s Hospital</td>
</tr>
</table>

Oestradiol (E2)	**Paediatric** Oestradiol is generally less than 60 pmol/l in both sexes. In females the levels start to rise around 11 years reflecting the onset of cyclical ovarian activity. Oestradiol also increases in the male during puberty largely reflecting peripheral aromatisation of testosterone. **Paediatrics** Prepubertal Children <30 pmol/L *(adult male <150 pmol/L* *Premenopausal female 200-2000 pmol/L* *Post-menopausal <150 pmol/L)* *(CV<10% at 25 pmol/l)* *From Age 16+y Siemens assay:* *Follicular 77.6 – 529.2 pmol/L* *Mid-cycle 234.5 – 1309.1 pmol/L* *Luteal 204.8 – 786.1 pmol/L* *Post-menopausal <118.2 pmol/L* *Adult Male <146.1 pmol/L*	Assayed locally, can also be assayed by LC-MSMS (more specific technique) Manchester labs or by extraction and RIA at Leeds Steroid Lab Leeds Steroid Lab *Siemens Atellica*
Oligosaccharides (and sialic acids) This requires FRESH Random urine. Send immediately to lab	Interpretation provided with report	Assayed by Leeds (also available via Willink lab, Manchester)
Orotic Acid Random urine immediately to lab or 24h collection	Infant/child/adult <3.5 umol/mmoL creatinine	Sheffield Children's Hospital
Osmolality	Plasma 275-295 mOsmol/kg Urine Varies	Athermistor Freezing point depression info.

Paracetamol	Therapeutic 10-30 **mg/l** Toxicity : 100 mg/l at 4 hours post ingestion 50 mg/l at 8 hours post ingestion 15 mg/l at 15 hours post ingestion () **Paracetamol Overdose** (see BNF) **Blood for paracetamol levels should be taken after 4 hours - before this time the drug is incompletely absorbed and a falsely low level may be reported**. The paracetamol level is plotted on a 'treatment line'. If the level falls above the line treatment is given.	*Cambridge Life Science Previously reported in nmol/ L units* MHRA Drug safety update Sept 2012 **Take care to ensure correct units when using "treatment line" nomogram e.g. in BNF** *(mmol/l x 151 = mg/l)* The decision whether to treat with N-acetylcysteine is based on the plasma paracetamol concentration at more than 4 hours post ingestion using nomogram
Phenobarbitone Serum /EDTA blood also acceptable	Children have shorter elimination half-life than adults **Pathology Harmony** 2011 ranges: *Adult* *10 - 40 mg/L*	Pathology Harmony
Phenytoin (Epanutin) Serum /EDTA blood also acceptable	**Pathology Harmony** 2011 ranges: *Adult* *5 - 20mg/L*	Pathology Harmony

Phosphate	**Paediatric** *Neonatal phosphate affected by type of milk feed* **Pathology Harmony** 2011 ranges: Neonate 1.3 - 2.6 mmol/L Infant 0.9 - 2.4 1 - 16y 0.9 - 1.8 *Adult Pathology Harmony* *0.8 - 1.5 mmol/L*	Pathology Harmony
Urine phosphate 2nd voided random urine	**Urine** 15 - 50 mmol/24h 2nd voided random urine phosphate/creatinine ratio decreases from 19.0 to 2.7 mmol/mmol with increasing age from 1 month to 14y.	Pathology Harmony Matos et al J.Paed 1997
TMP/GFR	**Paediatric** Children usually have higher values. Birth 1.43-3.43 mmol/L 3 months 1.48-3.30 mmol/L 6 months 1.15-2.60 mmol/L 2-15 yrs 1.15-2.44 mmol/L *Adult* Male 0.90 – 1.35 mmol/L Female 0.88 – 1.42 mmol/L	Payne (1998 Ann Clin Bio 35 201 – 206 Barth et al. (2000) Ann Clin Bio 37: 79-81
Potassium Plasma /Serum also suitable ***Spot Urine***	**Paediatric** **Pathology Harmony** 2011 ranges: Neonate 3.4 - 6.0 mmol/L Infant 3.5 - 5.7 1 - 16y 3.5 - 5.0 *Adult* *Plasma 3.5-5.3 mmol/L* *< 20 mmol/L or < 2mmol/mmol creatinine= extra renal loss*	Pathology Harmony Pathology Harmony *ACB monograph Potassium 2013*

<table>
<tr>
<td>Pipecolic Acid
Plasma – 1ml, Li Hep (EDTA also suitable)
CSF – 0.5ml, no preservative
Urine – 5ml, plain sample</td>
<td>Investigation of peroxisomal biogenesis disorders, pyridoxine responsive epilepsy

ENSURE lab informed if prev/current vit B6 Rx

Interpretation provided with report</td>
<td>Sheffield Children’s Hospital</td>
</tr>
<tr>
<td>Progesterone
Serum also suitable</td>
<td>Paediatric
Levels are low at birth and rise with Tanner Stage
Female ranges by tanner stage
<table>
<tr><th>Tanner stage</th><th>Range nmol/L</th></tr>
<tr><td>1</td><td>N/A</td></tr>
<tr><td>2</td><td><0.67 – 32.98</td></tr>
<tr><td>3</td><td><0.67 – 32.90</td></tr>
<tr><td>4</td><td><0.67 – 27.55</td></tr>
<tr><td>5</td><td><0.67 – 49.32</td></tr>
</table>
Adult
Follicular phase <4.45 nmol/L
Luteal phase 10.62 – 81.28
Mid-luteal 14.12 – 89.14
Post-menopausal <2.32 nmol/L
Adult Male 0.89 – 3.88

Pregnant female
First trimester 35.68 – 286.2 nmol/L
Second trimester 81.25 – 284.29
Third trimester 153.91 – 1343.55</td>
<td>Siemens Atellica

Siemens Atellica

Siemens Atellica</td>
</tr>
</table>

<table>
<tr>
<td>Prolactin</td>
<td>
Paediatric
Much higher than adult range in newborn – 1y
Childhood higher than adult, but not as pronounced as <1y

<table>
<tr><td>Age</td><td>Female</td><td>Male</td></tr>
<tr><td>0 – 30d</td><td colspan="2">667 – 5034</td></tr>
<tr><td>31 – 60d</td><td colspan="2">510 – 3136</td></tr>
<tr><td>61 – 90d</td><td colspan="2">108 – 211</td></tr>
<tr><td>3 – 5m</td><td colspan="2">80 – 2095</td></tr>
<tr><td>6 – 8m</td><td colspan="2">86 – 1647</td></tr>
<tr><td>9 – 12m</td><td colspan="2">106 – 820</td></tr>
<tr><td>1y</td><td>67 – 865</td><td>65 – 789</td></tr>
<tr><td>2 – 4y</td><td>56 – 640</td><td>57 – 717</td></tr>
<tr><td>5 – 8y</td><td>45 – 466</td><td>47 – 438</td></tr>
<tr><td>9 – 11y</td><td>44 – 548</td><td>40 – 555</td></tr>
<tr><td>12 – 16y</td><td>58 - 602</td><td>44 - 479</td></tr>
</table>

Adult
Females
Non-pregnant 59 – 619 mIU/L
Pregnant 206 – 4420
Post-menopausal 38 – 430

Male 45 - 375
</td>
<td>
Aitkenhead & Heales Ann Clin Bio 2013 50: 156-158

See S Heales p5O ACB (2013)

Siemens Atellica
</td>
</tr>
</table>

Protein **(total protein)** **Plasma**	**Paediatric** **Plasma** Term baby 54 – 70 g/L *Pre-term babies have lower values* Gradual increase from birth	*Neonatology & Lab Medicine ACB Venture Publication 2017*
Urine	**Urine** Protein/Creatinine ratio: up to 0.01 g/mmol in neonates and up to 0.02 g/mmol in infants and above (up to 20 mg/mmol in infants and above Note 0.02g is the same as 20mg)	Gattineni J. Highlights for the management of a child with proteinuria and hematuria. Int J Pediatr. 2012;2012:768142.
CSF	**CSF** Neonatal (< 8 weeks) CSF protein may be up to 1.2 g/L	*Neonatology & Lab Medicine ACB Venture Publication 2017*
	< 1 month: 0.2 – 0.8 g/L > 1 month: 0.15 - 0.4g/L	TIETZ Guide to Lab Tests 2006 4TH ed
	Adult *Plasma* *60-80 g/L Siemens state 57 – 82g/L*	Pathology Harmony
	Urine *< 0.1g/L or 0.1-0.14 g/L* *CSF* *0.15-0.45 g/L*	*Siemens Atellica* *Siemens Atellica*
	Serum 57-76 g/L	Lab derived due to assay performance change
	Urine < 140 mg/24 hrs or < 20 mg/mmol creatinine	TIETZ Guide to Lab Tests 2006 4TH ed

Pseudocholinesterase/ cholinesterase ***Sensitivity to suxamethonium*** Although Plasma (LiHep) or serum can be used for phenotyping it is recommended to use EDTA blood (for possible genotyping) Min volume 1mL *(BUT 4mL if genotyping also required)*	Interpretation provided with report	Lewis Lab, Southmead Hospital Bristol https://www.nbt.nhs.uk/severn-pathology/pathology-services/clinical-biochemistry/cholinesterase
Parathyroid hormone (PTH) Must be EDTA blood. .	No paediatric range available In cord blood PTH is very low, adult levels usually by 2y, but it is believed that children have lower limit compared with adults – so quoted range may not be applicable until puberty *Adult* *1.95 – 8.49 pmol/L*	*Siemens Atellica* *To convert ng/L to nmol/L divide by 9.43*
Pyruvate Requires special handling Contact laboratory to obtain special tube	Interpretation provided with report	
Reducing Substances Urine	Non-specific reaction: Salicylate, creatinine, urate, homogentisic acid & some drugs may give positive results. **Available as part of SCH Urine Amino acids screen.**	

Renin (PRA) **See also aldosterone** MUST be LiHeparin PLASMA immediately to lab	**Paediatric** The reference ranges for PRA are poorly defined in infants, but in the first few weeks of life values of up to 50 nmol/L/h have been reported. There is an initial rapid fall, followed by a slower decrease until normal adult levels are reached at about the age of 6 Affected by age, posture, state of hydration & electrolyte status. *Na intake 100 – 150, K intake 50 – 100 mmol/day* *Adult 20-40yr olds* *08:00 after O/N recumbency 1.1 – 2.7 nmol/L/h* *08:30 after 30min ambulant 2.8 – 4.5 nmol/L/h* *PRA random during day 0.5 - 3.5 nmol/L/h* *(Aldosterone and renin decrease with increasing age above 50 yrs*	Leeds Steroid Lab
Salicylate	*Toxic >300mg/L* *Reyes syndrome has been reported in association with therapeutic aspirin use in children; the risk of this syndrome from ingestion of salicylates in children is extremely small* *Mild poisoning <300 mg/L* *Moderate poisoning 300 – 700 mg/L* *Severe poisoning >700 mg/L*	*Siemens Atellica* *Previously reported as mmol/L units* *To convert mmol/l to mg/l multiply by 138* *TOXBASE*
Sex Hormone Binding Globulin (SHBG) Serum also suitable	**Paediatric** After the neonatal period reference ranges in children are very wide with higher values than adults seen in first 6 years. *Adult* *Male* *<50 yrs–14.55 – 94.64 nmol/L* *>50 yrs 21.63 – 113.13* *Female –* *10.84 - >180 nmol/L (premenopausal range)* *23.15 – 159.07 (postmenopausal)*	*Siemens Atellica*

<table>
<tr>
<td>Selenium
NB: negative acute phase reactant.</td>
<td>Serum sample

<table>
<tr><th>Age</th><th>Reference range</th></tr>
<tr><td>0 - <2 years</td><td>0.22 – 1.22 µmol/L</td></tr>
<tr><td>2 - <5 years</td><td>0.33 – 1.44 µmol/L</td></tr>
<tr><td>5 – <16 years</td><td>0.52 – 1.52 µmol/L</td></tr>
<tr><td>≥16 years</td><td>0.61 – 1.24 µmol/L</td></tr>
</table>

Adult
0.61 - 1.24 µmol/L</td>
<td>Sheffield TH Hospitals (Revised ranges: Locally derived. June 2016, in conjunction with SCH lab)</td>
</tr>
<tr>
<td>Sodium
Serum also suitable

Urine Sodium</td>
<td>Pathology Harmony
Adult 2011 ranges:
133 - 146 mmol/L
No age related differences

? May be lower in first week – some authors

Depends upon clinical status, hydration state and plasma sodium concentration.</td>
<td>Pathology Harmony</td>
</tr>
<tr>
<td>Sulphocysteine
Random fresh urine to lab ASAP</td>
<td>Contact laboratory to arrange before collecting urine.

Sulphocysteine replaces the urine sulphite test.

Ref range <10 µmol/mmol creatinine</td>
<td></td>
</tr>
<tr>
<td>Sialic acids/oligosaccharides
This requires FRESH URINE analysis</td>
<td>Interpretation provided with report</td>
<td>Willink Lab, Manchester Children’s Hosp Also available via Leeds St James</td>
</tr>
</table>

<table>
<tr>
<td>Testosterone
Serum also suitable</td>
<td>Paediatric
Neonatal male levels are high from day 1 (residual BhCG), then (usually after 1 week) fall, only to rise again in week 2 due to LH/FSH. By 2nd or 3rd month show “low adult values”, but fall to pre-pubertal values (by 6th month).
Male 6 months - 8yrs < 0.9 nmol/L
Female 0 - 8 yrs < 0.9 nmol/L

Adult: by Mass Spectrometry
Male 8 – 30 nmol/L
Female premenopausal <1.8 nmol/L

By routine local lab assay (Siemens immunoassay)
Male 9.3 – 32.2 nmol/L.

Female premenopausal0.42 – 2.06
Post-menopausal <0.24 – 1.70</td>
<td>Leeds Steroids Lab, (LC MS-MS since May 2004)

(Leeds, LC MS-MS assay)

J Clin Endocrinol Metab. 2017 Apr 1;102(4):1161-1173.
Not using data from IFU
Siemens Atellica</td>
</tr>
<tr>
<td>Theophylline
Serum also suitable</td>
<td>Pathology Harmony 2011

10-20 mg/L adults and age > 6months
(lower in neonates)
Therapeutic effect may be seen with levels as low as 5 mg/L in some patients.</td>
<td>Pathology Harmony</td>
</tr>
<tr>
<td>Triglyceride
Serum also suitable
Fasting blood Sample</td>
<td>Paediatric
Triglyceride levels are substantially lower in the newborn than in the adult. After birth triglyceride levels vary considerably. This may relate to different types of milk feeding or weaning. In early childhood triglycerides remain low. They rise in adolesence, particularly in males.

<table>
<tr><th>Age (d)</th><th>Male mmol/L</th><th>Female mmol/L</th></tr>
<tr><td>0-7</td><td>0.24-2.06</td><td>0.32-1.88</td></tr>
<tr><td>8-30</td><td>0.34-2.08</td><td>0.34-1.86</td></tr>
<tr><td>31-90</td><td>0.45-1.98</td><td>0.40-3.19</td></tr>
<tr><td>91-180</td><td>0.51-3.29</td><td>0.57-4.01</td></tr>
<tr><td>181-365</td><td>0.51-5.66</td><td>0.41-4.87</td></tr>
</table>

Cord blood 0.1 – 1.04 mmol/L

Adults
Normal <1.70 mmol/L
Borderline High 1.70 – 2.25 mmol/L
High 2.26 – 5.64 mmol/L
Very High >5.65 mmol/L</td>
<td>Paediatric reference Intervals 6th ed. Edited by Soldin et al. AACCPress
Non –fasting

Siemens Atellica</td>
</tr>
</table>

TMP/GFR	See **Phosphate & URINE tests**	
TSH **Thyrotropin** Serum also suitable	**Paediatric** Age mIU/L 1-3d 0.13-9.23 4-30d 0.16-8.48 31-60d 0.19-7.78 61d-12m 0.30-5.88 1-5y 0.42-4.79 6-10y 0.48-4.67 11-14y 0.53-4.58 15-18y 0.56-4.53 Premature babies with CHT, especially those born at <28w gestation have a delayed increase in TSH due to immaturity of the hypothalamic/pituitary axis and may not be detected at screening at 5 d (false negative), should be retested at 28d. TSH is high in first day of life (20-50mU/L), fall to normal levels (1-8mIU/L) by 5-7d. Before 7 –14 days levels > 10mIU/L (up to 35 mIU/L) may occur *Adult* *0.55 – 4.78* *For female TSH results for ages 16-50 yrs: aim for TSH level of 0.38-2.5 mIU/L in the preconception period and 1st trimester of pregnancy and a level of 0.38-3.0 in the 2nd and3rd trimesters* (Barnsley Local Endocrine Team)	Clin Chem Lab Med 2002; 40(10):1040–1047 ACB, Neonatology & Clinical Biochemistry, 2017 *Siemens Atellica*
Urea Serum also suitable	**Paediatric** Reference range for serum (plasma is slightly lower) Infants fed cow's milk have higher urea than breast-fed. **Pathology Harmony** 2011 ranges: Neonate 0.8 - 5.5 mmol/L Infant 1.0 - 5.5 1- 16y 2.5 - 6.5 *Adult* *Serum/Plasma 2.5-7.8 mmol/L* *Urine 0.43 – 0.71 mol/24hr*	ACB, Neonatology & Clinical Biochemistry, 2017 Pathology Harmony Pathology Harmony *Siemens Atellica*

Uric Acid **(Urate)**	**Paediatric** Serum/Plasma Neonate 120 - 470 umol/L Child < 10 yrs 160 - 390 umol/L Child > 10 yrs 160 - 500 umol/L Urine Neonate 0.3-1.7 mmol/mmol creatinine Infant 0.3-1.3 mmol/mmol creatinine Child 0.3-0.8 mmol/mmol creatinine ***Pathology Harmony*** *2011 ranges:* *Adult* *Male 200 - 430 umol/L* *Female 140 - 360 umol/L* *Urine 1.5 - 4.5 mmol/24H*	Sheffield Children's Hospital Sheffield Children's Hospital **Pathology Harmony**
Urine Screening Tests	**Paediatric** Reaction reported as negative or positive. Used to screen for presence of Nitrite (and leukocytes), pH, Protein, Glucose, Ketones, Urobilinogen, Bilirubin, Blood May suffer from non-specific reaction (eg drugs, vitamins, sugars) and lack of sensitivity Interpretation provided with report	Sheffield Children's Hospital
Valproate ***Sodium valproate***	Not a candidate for TDM in epilepsy (is of use in TDM for bipolar affective disorder) ***Pathology Harmony*** *2011 ranges:* No range should be quoted	Pathology Harmony
Vitamin A Sample must be sent immediately to lab, light protected Serum/plasma EDTA or li heparin acceptable	**Paediatric** Term neonates (>37wks) 0.63-1.75 umol/L Preterm neonates (<36.6wk) 0.46-1.61 <1 yr 0.5 – 1.5 umol/L 1-6 yrs 0.7-1.5 umol/L 7-12 yrs 0.9-1.7 umol/L 13-19 yrs 0.9-2.5 umol/L Plasma vitamin A is a negative acute phase reactant *Adult (> 18yrs)* *0.84-3.6 umol/L*	Nutr Res (1996):16, 191-6 {cord blood} TIETZ Guide to Lab Tests 2006 4TH ed *Laboratory data (1989)*– small study performed as part of FIMLS dissertation

Vitamin B1 (Thiamine) Must be EDTA or LiHeparin sample Sample must be sent immediately to lab, light protected	*Adult* *66.5 – 200nmol/L* Marginal deficiency at 40 nmol/L Overt deficiency suggested by 5nmol/L or less	Chromsystems IFU (10/2015 R4)
Vitamin B2 (Riboflavin) Must be EDTA or LiHeparin sample Sample must be sent immediately to lab, light protected. Light-sensitive; wrap in tin foil. Send by first class post within 72 hours. If delivery to Glasgow is >72 hours of sample collection, prepare red cells (minimum volume 300 µL) by removing plasma and buffy layer (mark clearly on tube that they are red cells) and store frozen until sending and then send by first class post (ice or dry ice not required).	*Adult* Red cell FAD: 1.0 to 3.4 nmol/g Hb (In-house, n = 126)Interpretation provided with report	Scottish Trace element and micronutrient diagnostic and research laboratory (STEMDRL)
Vitamin B6 (Pyridoxine) Ideally, EDTA or LiHeparin sample Sample must be sent immediately to lab, light protected	*Adult* *Whole blood (as PLP and pyridoxal) 35 - 110 nmol/L* <20 nmol/L whole blood PLP associated with high risk of deficiency Plasma (as PLP and pyridoxal) 20 – 121 nmol/L - is subject to negative acute phase response	Chromsystems data (09/2015 R3)
Vitamin C Must be LiHeparin sample ONLY Please contact lab to arrange for sample handling. Sample must be sent immediately to lab, light protected.	Laboratory stabilises the sample by treatment with metaphosphoric acid (MPS) *Adult* *26 - 85 umol/L* *Deficiency threshold < 11.1 umol/L* CRP should also be assayed since plasma vitamin C exhibits negative acute phase response.	Chromsystems (07/2015 R1) supported by local laboratory data

Vitamin D (25 OH Vitamin D)	**Paediatric** Adult Assayed as 25-OH vitamin D (= storage form) Exhibits seasonal variation: levels should be >50 nmol/L at all times Overt deficiency <30 nmol/L Moderate deficiency 30-50 nmol/L Sufficiency > 50 nmol/L Upper limit of normal typically 120 nmol/L, although higher values may be acceptable? > 200 nmol/L may be consistent with possible adverse effects.	Rotherham CCG http://www.rotherhamccg.nhs.uk/Downloads/Top%20Tips%20and%20Therapeutic%20Guidelines/Becky%20Top%20Tips/vitD%20adults%20RCCG.pdf#:~:text=NHS%20Rotherham%20CCG%20does%20not%20support%20prescribing%20of,products%20over%20the%20counter%20as%20part%20of%20Self-Care.

Vitamin E Ideally, EDTA or LiHeparin sample Sample must be sent immediately to lab.	0 - <1yr: 5-50 µmol/L 1-6 yrs: 7-21 µmol/L 7-12 yrs: 10-21 µmol/L 13-18 yrs: 14-23 µmol/L *Adult* *11.6-35.5 umol/L* Best expressed as molar ratio with plasma lipids: No molar ratio available for < 1 year 1-6 yrs 3-5umol/mmol lipids 7-12 yrs 2-5 13-19 yrs 2-4 *Adult* *3.9 – 5.9* For all ages Vitamin E/Lipid ratio <2.1 umol/mmol lipids suggests suboptimal status/possible deficiency.	CALIPER Clin Biochem (2014) 47(9):812-815 Clin Chem 1988 34(8) 1625-1628 Adult ONLY Laboratory data (1989) Reference: small study performed at RGH as part of FIMLS dissertation in 1989 Data compares favourably with: Hercberg S et al Int. J. Vit. Nutr. Res. (1994) 64, 220 In general many studies now support a range of 11.6 — 46.4 umol/L Clin Chem 1988 34(8) 1625-1628 Adult ONLY Laboratory data (1989) Reference: small study performed at RGH as part of FIMLS dissertation in 1989
Vitamin K Sample must be sent immediately to lab	Assayed as PIVKA II Functional marker of vitamin K1 status PIVKA Reference Range= <0.15AU http://www.guysandstthomas.nhs.uk/our-services/haemostasis-thrombosis/nutristasis-laboratory/overview.aspx#na	Assayed by haemostasis lab, St Thomas Hosp.

VLCFA **Very long chain fatty acids** LiHeparin or EDTA sample immediately to lab Minimum sample: at least half full microtube (100uL)	Note that plasma VLCFAs cannot completely exclude carrier status for x-linked Adrenoleukodystrophy (normal results in about 10% of carriers). Interpretation provided with report	Assayed by Sheffield Children's Hospital NGH lab/ Tietz Clinical Chemistry, 1995
Vanilyl Mandelic Acid (VMA / HMMA) Catecholamine metabolite Random urine / urine collection pad (UCP) urine immediately to lab	**Paediatric** <1 year <13.9 umol/mmol creatinine 1-3 years <11.0 3-5 years <10.5 5-8 years <10.0 8-11 years <7.5 >11 <7.0 See also: **HVA Homo vanillic acid** For investigation/exclusion phaeochromocytoma/neuroblastoma	Fitzgibbon and Tormey Ann. Clin Biochem (1994) **31**, 1-11
White Cell Enzymes (Lysosomal enzyme screen) EDTA sample Ideally 5mL <u>Absolute minimum is 3mL blood</u>, samples with less than this will be rejected by Willink Lab unless prior arrangement made with duty clinical scientist. Send to lab ASAP. (Avoid sending after Wednesdays)	Rejection of small samples: This is because 2015 audit data has shown small sample size to be associated with reduced (although not deficient) enzyme activity. Interpretation provided with report	Manchester Children's Hospital Willink Lab Follow up work may involve referral of samples to Camelia Botnar Enzyme Lab, GOSH. *See:* <u>http://www.labs.gosh.nhs.uk/laboratory-services/chemical-pathology</u>
Zinc ideally use trace metal tube, otherwise plain or LiHeparin microtube	*Adult* *7.20-20.43 umol/L*	Sheffield teaching Hospitals Data

Skin Biopsy Punch Skin Biopsy: samples should be 1-2mm diameter & 1mm depth (dermal tissue needed), taken from alcohol swabbed area.	**Contact Sheffield Children's Hospital** – Sterile saline may be used if media not available. If delay unavoidable store 4C prior to delivery to SCH, do not place in formalin. Interpretation provided with report	Protocol (tissue Culture medium & consent form) available from Sheffield Children's Hospital 0114-2717302

URINE ASSAYS

Analyte	Reference Ranges	Source
Amino Acids	Must be fresh sample immediately to lab Interpretation provided with report	
Biogenic Amines (catecholamine metabolites) Random urine / Urine collection pad (UCP) urine immediately to lab or contact lab if unsure.	Free Catecholamines & Metanephrines HVA VMA Ideally for investigation of neuroblastoma request HVA For phaeochromocytoma request metanephrines For early ages use "spot" urines immediately to lab Adults Not normally assayed Paediatrics (ranges in WinPath) umol/mmol creatinine Age HVA VMA < 1yr < 25 < 13.9 1-3 < 17 < 11 3-5 < 16 < 10.5 5-9 <14 < 10 8-12 < 11.5 < 7.5 > 11 < 7 < 7	Fitzgibbon and Tormey, Ann Clin Biochem (1994) 31, 1-11
Calcium	See entry above under Calcium	
Cortisol **Urine free cortisol (UFC)**	**Paediatric** In-house age related ranges not available (published literature data used for children) Random (<24h) ranges not available. *Adult* *10 – 147 nmol/24h*	Leeds Steroid Lab (LC MS-MS since 2007)

Galactitol Random urine to lab ASAP	Galactitol may be useful for investigating galactosaemia when there has been a recent blood transfusion. It is not useful when LFT s are raised (will also raise galactitol) www.nbt.nhs.uk/metabolic	Has to be shipped to Lewis Labs, Southmead Hospital. Avoid sending close to weekends.
Glycosaminoglycans (Mucopolysaccharidoses) RANDOM or aliquot of 24h collection	Interpretation provided with report	Sheffield Children's Hospital

HVA **Homovanillic acid** See also **Biogenic Amines** Random urine / UCP urine immediately to lab	**Paediatric** Age <1 year <25.0 umol/mmol creatinine 1-3 years <17.0 3-5 years <16.0 5-8 years <14.0 8-11 years <11.5 >11 years <7.0 For investigation/exclusion of neuroblastoma	Fitzgibbon and Tormey Ann. Clin Biochem (1994) **31**, 1-11
Microalbumin Albumin/Creatinine Ratio (ACR) in early morning urine (EMU)	Male <2.5 mg/mmol Female <3.5 mg/mmol Albumin Excretion Rate (AER) <20 ug/min	
Purines/pyrimidines Must be fresh sample immediately to lab	Interpretation provided with report	Purine Lab, London
Organic Acids Must be fresh sample immediately to lab	Interpretation provided with report	Sheffield Children's Hospital
Orotic Acid Random urine immediately to lab or 24h collection	Interpretation provided with report	Sheffield Children's Hospital
Sulphocysteine	Must be fresh sample immediately to lab	Sheffield Children's Hospital
Phosphate as TMP/GFR	**Paediatric** Children usually have higher values than adults. Birth 1.43-3.43 mmol/L 3 months 1.48-3.30 mmol/L 6 months 1.15-2.60 mmol/L 2-15 yrs 1.15-2.44 mmol/L *Adult* *0.8 – 1.35 mmol/L*	Ann Clin Biochem 1998;35:201-206
Uric Acid	Neonate 0.3-1.7 mmol/mmol creatinine Infant 0.3-1.3 mmol/mmol creatinine Child 0.3-0.8 mmol/mmol creatinine	Sheffield Children's Hospital

Vanilyl Mandelic Acid (VMA / HMMA) Catecholamine metabolite Random urine / urine collection pad (UCP) urine immediately to lab	**Paediatric** <1 year <13.9 umol/mmol creatinine 1-3 years <11.0 3-5 years <10.5 5-8 years <10.0 8-11 years <7.5 >11 <7.0 See also: **HVA Homo vanillic acid** For investigation/exclusion phaeochromocytoma/neuroblastoma	Fitzgibbon and Tormey Ann. Clin Biochem (1994) **31**, 1-11

Service Disruption

There are occasions where there may be an interruption to service or where turnaround times may be longer than anticipated. In such instances, users will be notified in advance where possible. Within the hospital this is via the Trust's Communication Team. Where unplanned disruption occurs, escalation will be made via the Pathology Business Contingency Plan (MP-PM-004).

Measurement Uncertainty

The laboratory makes regular estimates of measurement uncertainty for all analytes. Please contact the laboratory if further information is required.

Data Protection

Laboratory Medicine is committed to ensuring the confidentiality of all patient sensitive information. All data and information acquired while providing the services of the laboratory is handled in strict accordance with the Trust Confidentiality Policy. This ensures data is managed in compliance with all relevant legal obligations, standards and guidelines and professional codes of conduct. The requirements for preserving data integrity and patient and staff confidentiality are laid down in the Data Protection (2018) Act supported by the Trust IT policies. The department follows guidelines detailed in the Confidentiality and Data Protection Policy.

The Pathology Confidentiality Policy (MPL-PP-007) builds on the Trust's Confidentiality Policy in giving clear guidelines on the transmission of patients' Pathology results and reports.

Feedback and Complaints Procedure

Suggestions about our service may be raised by email, letter, phone call or by calling personally at the laboratory.
All complaints are dealt with in accordance with the Trust Complaints Policy and the departmental complaints and feedback policy. If you have any concerns about the services provided by the laboratory, please let us know using any of the contact options provided above.

Formal complaints can be made through the Trust Patient Experience Team
http://www.therotherhamft.nhs.uk/yourexperience/

See also the Laboratory Medicine website. http://www.therotherhamft.nhs.uk/Pathology/Pathology/