Division of Laboratory Medicine

Paediatric Biochemistry User Guide
(March 2021)

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Location of Laboratories

The Main Laboratory is located on the Ground Floor of the Pathology Clinical Sciences Centre CSB3, MRI.

The Specialist Biochemistry Laboratory is located on the first floor of the same building.

The Newborn Screening Laboratory (formerly the Hypothyroid Laboratory) is located within Genetic Medicine on Floor 6 of Tower 1 of the New St Mary's Development.

Telephone Numbers

Mrs. L.J. Tetlow, Consultant Clinical Scientist - Ext 11268 (office) or 15294(Lab)
Dr C Chaloner, Consultant Clinical Scientist - Ext 12752 (office) or 12250 (Lab)
Paediatric Duty Biochemist – Ext 12255
Paediatric Core Laboratory - Ext 12233
Newborn Screening Laboratory - Ext 12262

Laboratory Core Hours

Monday - Friday 09:00 – 17:00 hrs (Core Biochemistry) At other times, a shift-system for Continuous Pathology Processing (CPP) providing a near complete service is provided. The person on-call may be contacted via the appropriate hospital Switchboard.

0900 – 17:00 hrs (Specialist Biochemistry)

*** * * * * IMPORTANT NOTE:** Notification of an urgent request **must** be telephoned in advance to x12233 whether routine or CPP hours. *** * * * ***

Time limits for add-on analyses

Sometimes, a crucial investigation is missed from the original request. We are happy to add analyses to a current request provided we have an appropriate specimen and we receive a new ICE request form for the add-on.

However, some tests are adversely affected by a delay to analysis, in particular potassium, magnesium, phosphate, bicarbonate. These tests must be added before the specimen is 2 hours old and can not safely be performed in older samples.

Most other analytes are more robust, but we do not routinely store routine specimens for longer than 3 days and you should contact the laboratory on x12233 for specific advice.

Urgent Investigations

*** * * * * Telephone the laboratory first, x12233. * * * * ***

Urgent Requests during Normal Hours:

Some urgent tests can be sent in the Vacuum tube system. Some particularly precious and/or fragile samples require urgent Porter delivery. Sodexo help desk has the list of tests below for which a porter-response time of 5 minutes is targeted. These are termed 'Code Blue' tests. This form of words must be used when contacting the Sodexo helpdesk x4850.

Code Blue Samples = Specimens from New Royal Manchester Children's Hospital requiring rapid delivery and/or on ice:

Analyte	Maximum Acceptable Delay (minutes)
ACTH	15 on ice
Ammonia	15 on ice
Beta Hydroxybutyrate / FFA	20 on ice
Calcitonin	5 on ice
Chain-of-Custody medico-legal specimens	Discuss with lab on x12233
Gases, Capillary and Syringe	20 on ice
Gut Hormones	20 on ice
Jejunal Disaccharidases	Flash freeze in Liquid N2 at Theatres. Discuss
PTH	20
Renin / Aldosterone	30 **MUST NOT BE** on ice
Stool for Sugars chromatography	20, or freeze immediately at source and transport to lab frozen

The requesting clinician **MUST** contact the laboratory before the specimen is sent. The request form must be marked ‘URGENT’ otherwise the sample may not be identified as one requiring immediate attention. Failure to contact the laboratory will result in the sample being treated as non-urgent. **Ensure that the report form includes the name and bleep number of the doctor who should be contacted when the results are available**.

Outside core working hours:

The person "on-call" should be contacted via the hospital Switchboard. All core investigations are available without consultation with the on-call Consultant Biochemist with the exceptions of osmolality and caeruloplasmin. Specialist Biochemistry tests are not performed out of hours or weekends / Bank Holidays. If you are unsure whether a test is available please bleep the Biomedical Scientist on call via switch and specify ‘paediatric’.

For urgent requests, please contact the laboratory before sending a specimen. Arrangements for Vacuum tube and 'Code Blue' are as for the Core Day.

Key to specimen types and containers:

H : Lithium heparin, orange capped tube.

C : No anticoagulant, plain white-capped tube.

C/H : Either of above - heparinised sample will give better plasma volume yield on small samples.

F : Fluoride, yellow capped tube.

E : EDTA anticoagulant, pink-capped tube.

X : Special tube/container obtainable from laboratory by arrangement.

Where appropriate the MINIMUM volume of blood/sample is given in ml, therefore C 0.5 means clotted sample (no anticoagulant) and 0.5 ml blood required ASSUMING A NORMAL PACKED CELL VOLUME / HAEMATOCRIT (PCV / HCT). Where groups of tests are requested the individual volumes can be reduced i.e. 1.0 ml of blood in a lithium heparin tube is sufficient for U/E, LFT, calcium and phosphate.

It is helpful to number the requested analytes in order of priority especially in the case of small samples.

All blood samples should be venous / arterial except for gases, neonatal bilirubins, glucose, antibiotics, HbA1C, which may be collected from a capillary if a good blood flow is obtained. Other analytes may be affected if collected from capillaries and should be discussed with laboratory before collection. Please contact routine biochemistry if you are experiencing problems with capillary collection of above samples. (See Appendix 1). Capillary Specimens **MUST** be clearly marked on request form as such.

Completing Request forms on Integrated Clinical Environment (ICE)

It is recommended that you complete **all** fields in the ICE request window as completely as possible. The minimum data set for acceptance is forename, surname, date of birth and hospital number. However, we ask you to pay particular attention to the fields for bleep number (this is not necessarily YOUR bleep number, as it may be more appropriate to give a colleague's if you are going off duty, or are otherwise likely to be uncontactable) and also to ensure that you raise the request against the correct patient episode, particularly as some patients are seen at other locations (e.g. SMH).

Interferences from haemolysis, icterus and lipaemia

Analytical interference caused by pre-analytical factors is a significant source of error in clinical laboratory measurements. Analytical interference by haemolysis, bilirubin and lipids with laboratory assays is the most common concern in laboratory medicine. These altered results may lead to repeat tests, incorrect interpretation, wrong diagnosis, and potentially inappropriate intervention and unfavourable outcome for patients.

The table below details the impacts of haemolysis, icterus and lipaemia on laboratory tests:

Analyte	Effect of haemolysis	Effect of icterus		Effect of lipaemia
		Conjugated	Unconjugated	
Orosomucoid	-	-	-	↑
α1-antitrypsin	-	-	-	↑
Acetaminophen (Paracetamol)	Dependent on level of paracetamol (contact laboratory for information)			
Albumin				
Alkaline Phosphatase	↓	↓	-	-
ALT	↓↑	↓	↓	↓
Amikacin	↑	-	-	-
Ammonia	↓↑	↑	↓	↓
Amylase	↓	-	-	↓
AST	↑	-	-	↓
Bicarbonate	-	-	-	-
Bilirubin (Total)	-	N/A	N/A	-
Calcium	-	-	-	-
Caeruloplasmin	-	-	-	↑
Chloride	-	-	-	-
Cholesterol	↑	↓	↓	-
Creatine Kinase	↑	-	-	-
Creatinine	↓	↓	↓	↓
CRP	-	-	-	-
Gentamicin	-	-	-	↓
GGT	↓	-	↓	-
Glucose	-	-	-	↑
HDL	-	↓	-	-
Iron	↑	-	-	↓
Lactate	-	↓	-	-
LDH	↑	-	-	-

Direct LDL	-	-	-	↓
Magnesium	↑	-	-	-
Phenobarbital	-	-	-	-
Phenytoin	-	-	-	↓
Phosphate	↑	↑	-	↑
Potassium	↑	-	-	-
Salicylate	-	-	-	↓
Sodium	-	-	-	-
Theophylline	-	-	-	↓
Tobramycin	-	-	-	-
Total Protein	-	↓	↓	-
Triglycerides	↑	↓	↑	N/A
UIBC	↑	↓	-	↓
Urea	-	-	-	↓
Uric Acid	-	↓	↓	-
Valproate	-	-	-	↓
Vancomycin	-	-	-	↓

Data taken from the Roche global package inserts and application report, July 2013. Table shows the impacts of haemolysis, icterus and lipaemia on laboratory tests on the Roche c501, c311 and c502 analysers. (Serum/plasma samples only). ↓ under-recovery, ↑ over-recovery, ↓↑ variable recovery, - no significant impact.

Potential for Biotin interference in Immunoassays

The Biotin – Streptavidin couple is part of the assay design for many biomarker immunoassays. If patients are taking large doses of this Biotin / Vitamin B7, there is known potential for significant interference in immunoassays for a number of commonly requested tests in Biochemistry.

Although normal diets, and low dose multivitamin preparations are thought not to interfere, in recent times, health food enthusiasts have been recommending people take large doses of Biotin for healthy hair, skin and nails, and supplements up to 10mg per tablet are available over the counter in many health food stores and online. There are also a couple of ongoing clinical trials of megadoses (up to 300mg/d) of Biotin in Multiple Sclerosis.

If you have a test result that does not fit the clinical picture, you may wish to exclude possible biotin interference as a cause, by asking the patient / parent / carer about any over the counter supplements or checking for a biotin prescription.

Particular care should be taken in interpreting Troponin T or I levels, where appreciable concentrations of biotin may cause a negative interference and is therefore potentially falsely reassuring. Clinicians caring for patients being investigated for chest pain / ?AMI / ?ACS should ask about biotin supplements for all patients when a Troponin level is requested.

5-10 mg supplements are typical concentrations sold over the counter. Pharmacokinetic data extrapolation shows that these concentrations correspond to plasma concentrations of between 15.6-31.3 ng/ml.

High-dose biotin (100 mg) is sometimes used to treat metabolic diseases (isolated carboxylase defects and defects of biotin metabolism). A 100 mg biotin dose equates to 500 ng/mL plasma concentration. This concentration leads to gross analyte disturbance across all Roche assays

Yellow highlighting in the table below indicates the assays that may suffer from interference due to a 5-10 mg dose of biotin.

Analyte	Max plasma/serum biotin concentration cut-off concn nmol/L	Max plasma/serum biotin concentration cut-off concn ng/ml	Analyser	Type of assay	Will the interference increase or decrease the analyte level?
AFP	<246 nmol/L	<60.024	Cobas-Roche	sandwich	↓
AMH	≤143	≤34.892	Cobas-Roche	sandwich	↓
CA125	<143 nmol/L	<34.892	Cobas-Roche	sandwich	↓
CEA	<491	<119.804	Cobas-Roche	sandwich	↓
cortisol II	≤123	≤30.012	Cobas-Roche	competitive	↑

Analyte	Max plasma/serum biotin concentration cut-off concn nmol/L	Max plasma/serum biotin concentration cut-off concn ng/ml	Analyser	Type of assay	Will the interference increase or decrease the analyte level?
digoxin	<409 nmol/L	<99.796	Cobas-Roche	competitive	↑
Estradiol III	≤147	≤35.868	Cobas-Roche	competitive	↑
ferritin	<205 nmol/L	<50.02	Cobas-Roche	sandwich	↓
folate III	≤86.1 nmol/L	≤20.984	Cobas-Roche	competitive	↑
FSH	<246	<60.024	Cobas-Roche	sandwich	↓
FT3 III	<286 nmol/L	<69.784	Cobas-Roche	competitive	↑
FT4 II	< 81.8 nmol/L	<19.9592	Cobas-Roche	competitive	↑
HCG stat	<164 nmol/L	<40.016	Cobas-Roche	sandwich	↓
Calcitinonin	<163	<39.772	Cobas-Roche	sandwich	↓
LH	<205	<50.02	Cobas-Roche	sandwich	↓
NT-proBNP	<123	<30.012	Cobas-Roche	sandwich	↓
PLGF	<123	<30.012	Cobas-Roche	sandwich	↓
progesterone II	<82 nmol/L	<20.008	Cobas-Roche	competitive	↑
prolactin II	<164	<40.016	Cobas-Roche	sandwich	↓
PTH	<205 nmol/L	<50.02	Cobas-Roche	sandwich	↓
SFLT	<123	<30.012	Cobas-Roche	sandwich	↓
SHBG	<246	<60.024	Cobas-Roche	sandwich	↓
Testosterone	<123	<30.012	Cobas-Roche	competitive	↑
total PSA	<246 nmol/L	<60.024	Cobas-Roche	sandwich	↓
trop t HS	<82 nmol/L	<20.008	Cobas-Roche	sandwich	↓
TSH	<102 nmol/L	<24.888	Cobas-Roche	sandwich	↓
Vit B12 II	≤205 nmol/L	≤50.02	Cobas-Roche	competitive	↑
direct renin	<25 nmol/L	<6.1	IDS-iSYS	sandwich	↓
PINP	<300 nmol/L	<73.2	IDS-iSYS	sandwich	↓
hGH	<300 nmol/L	<73.2	IDS-iSYS	sandwich	↓
IGF-1	<300 nmol/L	<73.2	IDS-iSYS	sandwich	↓
IGF BP-3	<300 nmol/L	<73.2	IDS-iSYS	sandwich	↓

- Biotin is renally excreted – it is therefore likely that in CKD/AKI plasma/serum concentrations of biotin can be higher than expected.
- For microgram doses of biotin the drug half-life is 1.8 hr.
- For 100-300 mg dose biotin the drug half-life is 7.8-18.8 hr.

- Cobas-Roche state that samples should not be taken from patients receiving therapy with high biotin doses (i.e. > 5 mg/day) until at least 8 hours following the last biotin administration.

Requirements and Reference Ranges

DISCLAIMER

Adult reference ranges quoted within this Paediatric Biochemistry User Guide reflect historical practice and methodological principles. They are under ACTIVE REVIEW and are in some instances different from those given in the Adult Biochemistry User Guide. Please speak to a member of the Paediatric Biochemistry team if you have any queries.

Analyte	Specimen Type / volume	Patient Age	Reference Range
Acid Base (blood gases)	Pre-heparinised syringe, 0.5ml minimum or heparinised capillary tube (avoid air bubbles). Mix well immediately after collection to prevent clotting.		**Reference ranges apply to arterial specimens only** Please state if patient is on O_2
pH		0-28d (term) 1 to 5 months 6 to 11 months >=12 months	7.18 to 7.51 7.18 to 7.50 7.27 to 7.40 7.35 to 7.45
pCO2		0 to 28d 1-11 mo 12 mo to 17 y	3.6 to 5.3 kPa 3.6 to 5.5 kPa 4.3 to 6.4 kPa

pO2 (in room air) Arterial specimen only		1 to 24h	7.3 to 10.6 kPa
		24 to 48h	7.2 to 12.6 kPa
		>48h	11.1 to 14.4 kPa
Actual bicarbonate			19 to 28 mmol/L
Base excess		Newborn	-10 to -2 mmol/L
		Infant	-7 to -1 mmol/L
		Child	-4 to +2 mmol/L
		Adult male	-2.3 to +2.3 mmol/L
		Adult female	-3.0 to +1.6 mmol/L

*Send labelled sample **on ice** to the laboratory immediately after collection. **Inform the laboratory before you send a gas.** Capillary samples require proper collection technique to ensure reliable results, and are not recommended for the estimation of pO2.*

Alanine Aminotransferase (ALT)	H 1.0	0 to 1 mo	<90 IU/L
		Male >1mo	< 50 IU/L
		Female > 1mo	< 35 IU/L
Albumin	H 1.0	up to 1 mo	25 - 35 g/L
		2 - 6 mo	28 - 40 g/L
		7 mo - 17yrs	30 - 45 g/L

Alkaline phosphatase (ALP)	H 1.0		Female	Male
		0 – 7 d	75 – 300 IU/L	75 – 300 IU/L
		8 - 28 d	90 - 477	90 - 477
		29 – 90d	90 -540	90 - 540
		91 – 180d	77 - 540	77 - 540
		181 – 360d	87 - 382	87 - 382
		361 – 540d	69 - 434	69 - 434
		541d – 2 yrs	60 to 370	60 - 370
		2 – 8 yrs	60 – 320	

		2 – 10 yrs		60 - 300
		Pubertal	60 - 400	60 - 400
		Adult	30 - 130	30 - 130
Alpha Fetoprotein (AFP)	H 1.0		**Male and Female**	
		0 - 2 days	0 to 103990 kU/L	
		2 - 7 days	0 to 60750	
		7 - 14 days	0 to 48950	
		14 - 21 days	0 to 19000	
		21 - 28 days	0 to 5500	
		29d – 6 weeks	0 to 4750	
		6 – 8 weeks	0 to 1650	
		8 wk – 3 mo	0 to 850	
		3 mo – 4 mo	0 to 350	
		4 mo – 5mo	0 to 100	
Ammonia	X 1.3 **NOTE: PLASTIC EDTA TUBE**	Up to 14d	10 to 100 μmol/L	
		Others	5 to 50 μmol/L	

Note: May be higher in prematurity. Please arrange with laboratory before taking the sample which should be sent to the laboratory immediately in ice/water.

~~Amylase~~	~~H 1.0~~	~~child~~	~~less than 100IU/L~~

~~*Note: The normal distribution in adults is skewed with normal individuals occasionally producing levels up to 200 IU/l. A similar study has not yet been undertaken in children.*~~

No longer available – use Lipase instead

		Male and Female	
Aspartate Aminotransferase (AST)	H 1.0	0 to 14d	<169 IU/L
		14d to 1y	<78 IU/L
		1 to 7y	<55 IU/L
		7 to 12y	<48 IU/L
		>12y	<50 IU/L (<35 in females)
Bicarbonate	H 1.0		19 to 28 mmol/L
Bilirubin, total	H 1.0		0 to 21 μmol/L
		full term infant	Levels may rise from birth to

			approximately 150 µmol/l at 5 - 6 days and then fall to normal childhood levels by day ten. Refer to NICE CG98
Bilirubin, conjugated		0 to 28d 1 month to 18y	1 to 13 micromol/L 1 to 8 micromol/L
*Caeruloplasmin *(only in conjunction with copper)*	X 2.0 (Cu/Caer)	<2 months 2 months to 1 year 1 year to 18 years >18 years	45 - 213 mg/L 109 - 371 mg/L 181 - 416 mg/L 200 - 600 mg/L
Note: Copper and zinc can be assayed on the same sample.			
Calcium, whole blood, **ionized**	H 1.0 Syringe, balanced heparin	Independent of age	1.00 - 1.40 mmol/L
Calcium, plasma, total	H 1.0	premature 0 to 14d child >14d *Avoid venous stasis*	1.50 to 2.50 mmol/L 2.00 to 2.70 mmol/L 2.20 to 2.60 mmol/L
Chloride	H 1.0		95 to 108 mmol/L
Cholesterol, total	H 1.0	up to 1 month 1m - 2yrs	1.1 to 2.6 mmol/L 1.2 to 4.7 mmol/L
Copper	See above (Caeruloplasmin)	up to 1 month > 6 months	2 to 8 µmol/L 13 to 26 µmol/L
[Note: Zinc and Selenium may be estimated on same sample].			
Creatine Kinase (CK) *[Note: adult levels reached ~2 y]*	H 1.0	0 to 90 d 3mo to 1 year adult male adult female	<475 IU/L <250 IU/L 40 to 320 IU/L 25 to 200 IU/L
Creatinine	H 1.0	0 - <14days 14d - <1yr 1 - <3yr 3 - <5yr	M 27 – 81; f 27 – 81 µmol/L M 14 – 34; f 14 - 34 M 15 – 31; f 15 - 31 M 23 – 37; f 23 - 37

		5 - <7yr	M 25 – 42; f 25 - 42
		7 - <9yr	M 30 – 48; f 30 - 48
		9 - <11yr	M 28 – 57; f 28 - 57
		11yr	M 36 – 64; f 36 - 64
		12yr	M 36 – 67; f 36 - 67
		13yr	M 38 – 76; f 38 - 74
		14yr	M 40 – 83; f 43 - 75
		15yr	M 47 – 98; f 44 - 79
		16yr	M 54 – 99; f 48 - 81
		>16 years to adult	55 – 104 (males) 45 – 84 (females)
eGfR (Estimated GfR) **This test is for use with Gentamicin levels only. 51Cr-EDTA test or Creatinine Clearance should be used for dosing with other potentially nephrotoxic drugs.**	Calculated as part of a U&E [eGfR = 40 x height in cm /plasma creatinine]		> 90 ml/min/1.73m2 Seek renal opinion for values below 90ml/min/1.73m2
C-Reactive Protein (CRP)	H 1.0		0.3 to 5 mg/L
Cystatin C	H 1.0	0 to 28d 29d to 12mo 13mo to 17y 18 to 50y >50y	0.80 to 2.30 mg/L 0.70 to 1.50 0.56 to 1.30 0.56 to 0.98 0.61 to 1.40
Fat absorption	H 1.0	Fasting rise in triglycerides and 2 hours post dose	> 0.45 mmol/L
Gamma Glutamyl Transferase (GGT)	H 1.0	0-4wks 1 - 2 mths	10 to 270 IU/L 10 to 155 IU/L

		3 to 4 mo >5 mo Male >5 mo Female	10 to 93 IU/L 10 - 71 IU/L 6 - 42 IU/L
Glucose (fasting)	F 0.5	0 to 1d 1 to 7d >7d	2.0 to 6.1 mmol/L 2.6 to 6.1 mmol/L 3.0 to 6.5 mmol/L
Iron	H 1.0	0 to 14y 14 to 18y	5 to 25 µmol/L Male 8 to 31 µmol/L Female 6 to 31 µmol/L
Note: there is diurnal variation in iron levels, so please sample at 9am.			
Iron Binding Capacity (IBC)	as above	1 month 1 year child adult	20 - 60 µmol/L 35 - 65 µmol/L 40 - 70 µmol/L 45 - 75 µmol/L
Lactate	F 0.5 **Sample must be < 2hrs old**	fasting	0.6 to 2.5 mmol/L
Lactate Dehydrogenase	H/ C 1.0	0 to 14d 15d to 1y 1 to 9y 10 to 14y 10 to 14y >=15y	303 to 1143 IU/L 169 to 435 IU/L 196 to 314 IU/L Male 175 to 279 IU/L Female 163 to 269 IU/L 139 to 249 IU/L
Lipase	H 1.0	All ages	13 to 60 IU/L
Lipid Profile incl *TG, LDL, HDL (*if fasting)	H 1.0		referral lab provides interpretation
Magnesium	H 1.0		0.70 to 1.0 mmol/L
Orosomucoid	H 1.0		300 to 1200 mg/L
Osmolality	H 1.0		275 to 295 mOsmol/kg

	Not done routinely. Can be calculated from plasma electrolytes		
Phosphate	H 1.0	1 month 2 mo - 1 year 2 – 3 years 4 - 12 years 13 - 15 years 16 yrs to adult	1.4 to 2.8 mmol/L 1.2 to 2.2 mmol/L 1.1 to 2.0 mmol/L 1.0 to 1.8 mmol/L 0.95 to 1.5 mmol/L 0.8 to 1.40 mmol/L
Potassium (serum) Potassium (plasma)	C 1.0 H 1.0	All ages Up to 1 month 2 mo – 17 yrs	3.5 to 5.5 mmol/L 3.4 to 6.0 mmol/L 3.5 to 5.0 mmol/L
Protein, total	H 1.0	0 to 14d 15d to 1 yr >1 yr to adult	55 to 83 g/L 46 to 72 g/L 60 to 80 g/L
Retinol (Vitamin A) **Protect from light** [To convert µmol/L to mg/L x 0.286]	C 1.0		0.7 to 2.8 µmol/L
Sodium	H 1.0	0 to 7d 7 to 31d >31d to 17y	131 to 144 mmol/L 132 to 142 mmol/L 133 to 146 mmol/L
Thiopurine Methyl Transferase	E 1.0	Deficient activity Low activity Normal activity Additional infomation:	less than 10 mU/L 20 - 85 mU/L 86 - 185 mU/L Recent blood transfusion may mask a deficient result
Tocopherol (Vitamin E) To convert µmol/L to mg/L x 0.431	C 1.0		11.6 – 34.8 µmol/L *lower in neonates*

Triglycerides, fasting	C 1.0	Up to 1 month 2 mo - 1 yr 2 yrs to adult	0.1 to 0.9 mmol/L 0.4 to 1.4 mmol/L 0 to 1.7 mmol/L
Urate	H 1.0	**Male** 0 - 14 days 15d - <1 yr 1 - <12 yrs 12 - <19 yrs **Female** 0 - 14 days 15d - <1 yr 1 - <12 yrs 12 - <19 yrs	 158 to 748 µmol/L 88 to 370 µmol/L 100 to 282 µmol/L 150 to 446 µmol/L 158 to 748 µmol/L 88 to 370 µmol/L 100 to 282 µmol/L 147 to 342 µmol/L
Urea	H 1.0	Up to 1 month 2mo - 1 year 2 – 12 years 13 - 17 years	2.0 to 5.0 mmol/L 2.5 to 6.0 mmol/L 2.5 to 6.5 mmol/L 3.0 to 7.5 mmol/L
Vitamin A (see Retinol)			
Vitamin E (see Tocopherol)			
Zinc *serum levels decrease shortly after birth and regain childhood levels at a few months. Copper can be assayed on same sample.*	X 4.0 Plain **plastic** 4ml tube	1 month child adult	10 - 22 µmol/L 10 - 18 µmol/L 10 - 22 µmol/L

CSF

Glucose	F 0.3	40% - 80% plasma level plasma level also required.
Lactate	F 0.3	1.1 - 2.4 mmol/L plasma level also required

Protein	* 0.3 **2ml plain ('clotted') container*	Up to 7 days 0.4 - 1.1 g/L 1 to 4 weeks 0.4 - 0.8 g/L 1 – 3 months 0.2 – 0.7 g/L 3 months – adult 0.05 - 0.45 g/L

Biopsies

Disaccharidases	Jejunal mucosa (min wt. 2mg.) wrap biopsy in silver foil, place in 2ml screwcap tube, place on ice immediately	Maltase 12 - 45 IU/g wet wt Sucrase 4 - 15 IU/g wet wt Lactase 2 - 12 IU/g wet wt

Drug Overdose

Analyte	Specimen Type / Volume	Time post ingestion	Toxic Level
Paracetamol	H 1.0	4 hours	200 mg/L
		8 hours	100 mg/L
		12 hours	50 mg/L

NB These levels are for guidance only. Lower levels may be toxic in patients at "high risk" and when chronic poisoning is suspected. For further information consult the nomogram in the A&E Department.

Salicylate	H 1.0	6 hours*	300 mg/L

** Due to variable absorption salicylate should be measured on admission, or with paracetamol, and repeated at 6 hours if detected in the first sample.*

Other Toxicology

Admission of Drowsy, Semi-comatose and Comatose Patients

When a patient is admitted it is not unusual for the clinician subsequently to query drug toxicity. The request may be indicated after it is too late to obtain the necessary specimens from the patient as the drug may have been metabolised and/or excreted.

On admission it is essential routinely to collect:

1. At least 20 mL of urine in a plastic container with no preservative (many drugs can only be detected in urine with current methodologies)

2. At least 2mL of clotted blood.

These specimens can be kept overnight refrigerated at 4^{o}C on the ward and sent to the laboratory the following day with a request form containing all relevant clinical information.

Where the result of laboratory investigations may be used as evidence in cases of non-accidental injury, the Chain-of-Custody procedure described below must be followed.
CONTACT THE LABORATORY FOR COPIES OF THE APPROPRIATE DOCUMENTATION

Procedure for requesting laboratory investigations in cases of suspected non-accidental injury

- A completed Chain-of-Custody form must accompany the request. These forms are available ONLY from the Biochemistry Department. These forms have an allocated "chain of custody" number. **On no account may they be photocopied**. All hospital staff taking or handling these samples must sign the Chain-of-Custody form.
- Take samples as soon as possible after admission, preferably with witnesses and handled by as few staff as possible.
- Care should be taken to ensure that specimen containers are correctly labelled and that the accompanying "normal" laboratory request forms are completed in full. The form must detail suspected drugs/time of ingestion also therapeutic drugs administered and clinical details.
- All containers must have the tops sealed on the ward with sellotape and then be carefully sealed in the bag of a routine Biochemistry request form. The person who collected the specimen must sign the sellotape seal.
- The samples must be taken directly to the Biochemistry Department, ideally by the person who has collected the specimens or alternatively by a member of the ward staff. Do not use the air tube or any other means of delivering specimens.
- Specimens must be delivered to a member of the laboratory technical, scientific or medical staff.

For further information regarding availability or interpretation of TDM or toxicology requests, contact either;

Mrs. L.J. Tetlow, Consultant Clinical Scientist ext. 11268 (Office) ext. 12255 (Lab)
or bleep via switchboard

Dr C Chaloner, Consultant Clinical Scientist ext 12752 (Office), 12255 (Lab) or via Switch

Serum / Plasma Therapeutic Drug Monitoring

Analyte	Specimen Type / volume	Optimal Range
Busulfan PK	E 1.0 **[always contact the laboratory first on x64719 / 64699]**	SEE REPORT
Carbamazepine	H/C 1.0	4 - 12 mg/L trough level
Cyclosporin A (CyA)	E 1.0	**12 hours post dose** - state dose and timings.
Digoxin	H/C 1.0	0.6 – 1.2 µg/L NB Sample must be taken at least **6** hours post dose.
Lamotrigine	H/C 1.0	3 - 15 mg/L
Phenobarbitone	H/C 1.0	trough 10 -40 mg/L
Phenytoin	H/C 1.0	trough 5 - 20 mg/L
Tacrolimus	E 1.0	**12 hours post dose** - state dose and timings. Trough 5 - 20 µg/L
Theophylline	H/C 1.0	asthma 10 - 20 mg/L apnoea 7 - 12 mg/L
Valproate	H/C 1.0	sample peak level 2 - 4 hrs post dose. trough 60 - 100 mg/L

Note : Contact the laboratory on 12243 for further information on sample requirements

Serum / Plasma Antibiotic Levels

Please refer to the Trust Antibiotic and Pharmacy guidelines.

Venous samples are preferred, though a finger prick (capillary sample) may be performed. Minimum volumes of 0.5 ml per specimen **must** be provided.

Target Concentrations For extended interval (single daily) dosing Gentamicin regimen, a single specimen between 12 and 24 hrs post dose must be provided. The timing of the specimen in relation to dose **MUST** be recorded and this information provided to the laboratory. For interpretation, refer to the nomogram in the document link below.

Extended interval gentamicin in paediatrics: dosing policy

For multiple daily dosing regimens, pre-dose concentrations are an indicator of accumulation and relate to toxicity. Post-dose level are an indicator of distribution in the body and relate to efficacy. The target concentrations will vary according to the clinical condition of the patient for example cystic fibrosis and brochiectasis patients require higher concentrations as their bodies remove the drugs faster. In most clinical situations, eg, post-operative, febrile neutropaenia, the standard concentration ranges given below are usually sufficient.

Standard Treatment:

	Specimen Type/Volume	**Pre-dose conc (mg/L)**	**Post-dose conc (mg/L) EXACTLY ONE HOUR POST-DOSE**
Amikacin **(Multiple Daily Dosing)**	H 1.0	Less than 5 (Less than 10)	(25-50) (25-35 MDRTB)
Gentamicin	H 1.0	Less than 1 (ideally less than 2)	5-10
Tobramycin	H 1.0	Less than 2 (ideally less than 1)	5-10

Cystic Fibrosis and Bronchiectasis:

	Specimen Type/Volume	Pre-dose conc (mg/l)	Post-dose conc (mg/L)
Amikacin	H 1.0	Less than 10 (ideally 2-5)	25-30
Gentamicin **Multiple Daily Dosing**	H 1.0	Less than 2 (ideally less than 1)	8-10
Tobramycin	H 1.0	Less than 2	8-10

		(ideally less than 1)	
Vancomycin	H 1.0	10 -15 (15-20 deep-seated infection)	Post dose monitoring is no longer recommended

IMPORTANT
If concentrations are outside of these ranges, please ensure that you have sought pharmacist advice.

Pharmacist Advice

Detailed guidelines have been drawn up to ensure continuity of advice given by the pharmacists and in many cases a pharmacist will request further information when contacting wards.

When a dose adjustment is necessary, the responsible pharmacist will contact a doctor responsible for the care of the patient to ensure agreement with respect of the advice given. Messages will not be left with nursing staff unless there are exceptional circumstances.

Endocrine Tests

Analyte	**Specimen Type / volume**	**Reference Range**	
Cortisol *Diurnal variation established at about 3 months of age; Normal response post-Synacthen 30 minutes > 430 nmol / litre*	H 1.0	9am 133 - 537 nmol/l Late pm up to 100 nmol/l	
Gonadatrophins (LH/ FSH)	H/C 1.0		
Follicle stimulating Hormone (FSH)	H/C 1.0	Pre-pubertal	Varies with age and Tanner stage. See DFT Protocol

			handbook
		Post pubertal Males	1.5 – 12.4 IU/L
		Post pubertal Females	Follicular: 3.5-12.5 IU/L Mid cycle: 4.7-21.5 IU/L
:			
Luteinising hormone (LH)	H/C 1.0	Pre-pubertal:	Varies with age and Tanner stage. See DFT Protocol handbook
Insulin & C-Peptide	H 1.0	2-10 years (prepubertal) <0.3 U/L Post pubertal Male 1.7 – 8.6 IU/L Post pubertal Female Follicular phase: 2.4-12.6 IU/L Mid cycle: 14 – 95.6 IU/L Luteal phase: 1.0-11.4 IU/L Fasting samples with normal glucose	
Note : A fluoride sample for glucose taken at the same time is required. IF INVESTIGATING HYPOGLYCAEMIA, SAMPLES MUST BE OBTAINED AT THE TIME OF THE HYPOGLYCAEMIC EPISODE. **The samples must be received in the**		Insulin 12-150 pmol/L	

Biochemistry laboratory within 2.5hrs of collection. Out of hours, the person on-call must be contacted prior to collecting the sample.		
Insulin-like Growth Factor (IGF-1)	C 1.0	C-Peptide 350-1800 pmol/l
Insulin-like Growth Factor – Binding Protein type 3 (IGF-BP3)	H/C 1.0	
Growth Hormone	C 1.0	Age and gender specific reference ranges. Please see report
17 alpha hydroxyprogesterone	H 0.5	Age and gender specific reference ranges. Please see report For interpretation please refer to paediatric DFT Handbook Neonatal samples should not be taken in first 48 hours

Full term infant 0 -

			nmol/l
Parathyroid Hormone (PTH)	E 1.0	Premature infant 0 - 40 nmol/l Children & Adults 0 - 6 nmol/l	
Note : Change of sample type and reference interval from 14th June 2010. Samples must be sent immediately to the laboratory. Bleep BMS out of hours			
Procollagen Type 1 Amino Terminal Peptide (P1NP)	H 1.0		
Renin (concentration)	E 1.0	27-128 µg/L <1 week <312 mU/L 1 wk to 1 yr 31.2 - 109.2 mU/L 1 to 2 yrs 32.4 - 93.6 mU/L 2 to 10 yrs 22.8 - 62.4 mU/L	>10 yrs 12.0 – 3 mU/L
Note : Levels higher in infants and early childhood. Sample must be sent to laboratory immediately.			
Thyroid Function Tests Thyroid Stimulating Hormone (TSH)	H 1.0 <1 month up to 10 mu/l		
Free Thyroxine (FT4)		Child & adult 0.2 - 5.0 mu/l <1 month 15-34 pmol/l	

Urine Catecholamines

Child & a
- 24 pmo

Analyte	Sample
Dopamine	A 24 hour urine collected into acid, container supplied by laboratory is the preferred specimen, for which reference ranges have been established. In infants in whom it is difficult to obtain 24 hour specimens, shorter collections or random urine may be used. Send sample to laboratory immediately if not collected into acid See individual report for reference ranges.
HMMA (VMA)	
HVA	
Noradrenaline	

Urine - other

Analyte	Specimen Type / volume	Reference Range
Albumin/Creatinine Ratio	1st urine of the day	< 2.1mg/mmol creatinine
Albumin Excretion Rate	Timed collection, usually overnight	< 10µg/min

Calcium **Note** : Special container from laboratory	24 hour	Child < 0.1 mmol/kg/24hrs Adult 2.5 - 7.5 mmol/24hrs	
Calcium/Creatinine Ratio	10 ml of the 2nd urine of the morning. Alternatively post prandial. FRESH URINE SPECIMEN MUST BE SENT TO THE LABORATORY IMMEDIATELY	up to 0.56 mol/mol creatinine	
Copper	24 hour Plain container, no preservative	<1.0 μmol/24h	Low probability of Wilson's Disease
		>6.0 μmol/24h	Consistent with a diagnosis of Wilson's Disease
		1.0 - 6.0 μmol/24h	Equivocal, probably due to Chronic Liver Disease
Cortisol	24 hour	less than 165 nmol/24hrs	
Creatinine Clearance *Note : A 24 hour urine sample and coincident 0.5 ml heparin blood sample is required. please indicate*	up to 1 month 1 - 3 months	29 - 69 ml/min/1.73m2 31 - 91 ml/min/1.73m2	Creatinine Clearance *Note : A 24 hour urine sample and coincident 0.5 ml heparin blood sample is*

patient height and weight ***This test is NOT the same as eGfR***			*required. please indicate patient height and weight* ***This test is NOT the same as eGfR***
	3 - 6 months	44 - 109 ml/min/1.73m2	
	6 - 12 months	51 - 165 ml/min/1.73m2	
	12 - 18 months	65 - 200 ml/min/1.73m2	
	2 - 12 years	90 - 173 ml/min/1.73m2	
	adult male		90 - 182 ml/min/1.73m2
	adult female	90 - 155 ml/min/1.73m2	
Osmolality - usually early morning urine - discuss with lab.			
Oxalate - 24 hour *Note: Special container from laboratory.*	up to 13 years		< 0.35 mmol/24hrs
	adult male		0.19 - 0.48mmol/24hrs
	female		0.27 - 0.52mmol/24hrs
Phosphate Excretion Index			contact laboratory
Porphyrins			contact laboratory
Protein /creatinine ratio *early am preferred*	5 ml urine		< 20 mg/mmol
Reducing Substances	freshly voided urine		individualised

		report
within laboratory hours	***NB**: if specimen cannot be sent to lab in core hours, freeze immediately and send frozen*	
Faeces		
~~Occult Blood~~	~~dietary restrictions apply~~	**FOBTest no longer available**
Reducing Substances	Specimen must be less than 20 minutes old, or frozen while fresh.	

APPENDIX 1: CHANGE ARCHIVE

Changes in March 2021 review:

- Header updated to match version number in QPulse.

Changes in April 2019 review:

- Further minor changes to reference intervals following traceability review. All paediatric Reference Intervals are now traceable to studies in the literature and / or other documented evidence for example in-house validation studies. Full details are available on request.
- Tests affected
    - AFP units updated to kIU/L
    - Amylase no longer available, use lipase instead
    - AST in plasma
    - Base excess in whole blood
    - ALT in plasma
    - Bicarbonate in plasma
    - Calcium in plasma
    - Calcium (ionized) in whole blood
    - Chloride in plasma
    - LDH (plasma)
    - Lipase Ref Range added
    - Thiopurine Methyl Transferase activity whole blood

Changes in November 2018 review:

- Further minor changes to reference intervals following traceability review. All paediatric Reference Intervals are now traceable to studies in the literature and / or

other documented evidence for example in-house validation studies. Full details are available on request.

- Tests affected
  - Bicarbonate in plasma
  - Calcium (Adjusted)
  - Creatine Kinase (adult ref values)
  - Digoxin
  - Lactate (CSF)
  - Parathyroid Hormone

Changes in October 2018 review:

- Multiple minor changes to reference intervals following traceability review. All paediatric Reference Intervals are now traceable to studies in the literature and / or other documented evidence for example in-house validation studies. Full details are available on request.
- Tests affected
  - Acid base (pH, pCO2, pO2 only) (Whole blood)
  - AST (plasma)
  - Bilirubin Direct (plasma)
  - Caeruloplasmin (plasma)
  - Calcium (adjusted) (plasma)
  - CK (plasma)
  - Glucose Fasting (plasma)
  - Iron (plasma)
  - LDH (plasma)
  - Potassium (serum or plasma)
  - Protein Total (plasma)
  - Sodium (plasma)
  - Urate (plasma)

Changes in April 2018 review:

- Pages 12 and 13: Addition of table of information on interference by supraphysiologic doses of Biotin, either prescribed or self-administered

Changes in August 2017 review:

- Page 28: Urine free cortisol reference range changed from <240 μmol/24h to 165 μmol/24h

Changes in February 2017 review:

- Page 21: CSF Protein upper limit 3 was incorrect. Now corrected to match the value in APEX that goes out with results

Changes in February 2017 review:

- Page 6: insulin and C-peptide removed from code blue list
- Page 25: cortisol reference range and synacthen limit updated.
- Page 25: LH & FSH Ranges updated.
- Page 26: Insulin units now pmol/L. Fasting range 12 to 150 pmol/L. New transport instructions for insulin and C-peptide: must be received in the lab within 2.5 hours of collection (no need to send on ice).
- Page 26: GH - refer to DFT protocol book for interpretation. Level of 5.8 ug/L not used anymore.
- Page 27: no longer require special tube from lab for renin

Changes in January 2017(2) review:

- Laboratory core opening hours and CPP further updated - page 5, 6 and 7

- Interpretation of urine Na – page 8

Changes in January 2017 review:

- Laboratory core opening hours and CPP updated - page 5

Changes in December 2016 review:

- Antibiotics target ranges updated to match new Trust Antibiotics policy - pages 24&25

Changes in October 2016 review:

- In response to users' comments, change archive moved to end of document as an appendix
- IGF-BP3 added – page 26

Changes in November 2015 review:

- Busulfan Pharmacokinetics (BuPK) service – page 23

Changes in September 2015 review:

- Renin is now reported in concentration units (mU/L) – page 27
- Aldosterone now done in house – page 25

Changes in May 2015 review:

- Harmonised paediatric creatinine reference intervals – page 17
- Cystatin C reference Intervals – page 17

Changes in April 2015 review:

- Addition of table highlighting effects of interference by Haemolysis, Icterus and Lipaemia - page 10
- New TPMT service – page 19
- Drugs reference ranges - page 22 and 23
- Carbamazepine Epoxide now available only as a send away test - page 22

Changes in April 2014 Reference Range review:

- Numerous minor changes

Changes in April 2014 review:

- Paediatric Duty Biochemist Extension number – page 5
- P1NP information added – page 23
- IGF-1 information added – page 22

Changes in October 2013 review:

- Samples for Retinol should be protected from light – page 15.
- Units for Retinol and Tocopherol, reference intervals and conversion factors updated – page 15
- Adult Zinc lower limit changed to 10 from 12 μmol/L – page 16
- Alkaline phosphatase reference intervals updated: pathology harmony values for adults, new ranges from local data for babies 0 to 18 months – pages 9 and 10

Changes in September 2012 review:

- All Pages: Document Control header and footer updated.
- Location of laboratories updated – page 3

- New 'phone extension for paediatric duty biochemist 17594 – page 4
- Removed Vitamin D from 'Code Blue' table – page 5
- Stool for sugars chromatography: info from p21 now matches that in 'code blue' table – page 5
- Sample type for lipids is now Heparinised blood – page 14
- Digoxin can be either heparinised or clotted specimen – page 18
- Re Antibiotics TDM, lab no longer contacts pharmacist to alert to abnormal levels – page 18
- Insulin and C-Peptide Reference Intervals updated – P20
- Faecal Occult Blood test no longer available – page 23

Changes in May 2012 review:

- Page 10: Schwartz equation error - corrected.