Harmonisation of Reference Intervals

In recent times it has become clear to the users and commissioners of hospital diagnostic services that there are differences in reference intervals and units of measurement between laboratories. We, in the profession, recognise that there are sometimes genuine scientific reasons for these differences, for example differences in local populations or analytical methodology. However, it is important to differentiate those analytes for which there is no clearly identifiable reason for a difference. It is these analytes that have been considered by the Pathology Harmony group. This is a professionally led group supported by a grant from the Department of Health.

The identification of harmonisable analytes has been achieved through a process of consensus involving a large number of laboratory scientists supported by professional bodies. Clearly many analytes, particularly those measured by immunoassay, cannot be easily harmonised. This has been recognised by Pathology Harmony and further work will be necessary. In addition, this group has made recommendations on units of measurement that should be used to minimise possibility of confusion.

The Association for Clinical Biochemistry, the Institute of Biomedical Science and Royal College of Pathologists support this process and believe that the introduction of common reference ranges and units of measurement will improve patient safety.

We recommend that our members should introduce these changes and would hope that this can be achieved by April 2011.

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The Association for Clinical Biochemistry

IBMS

The Royal College of Pathologists
Pathology: the science behind the cure

Agreed Adult Clinical Biochemistry Reference Intervals

Test Name	Units	Range low	Range high	Comments
Sodium	mmol/L	133	146	
Potassium	mmol/L	3.5	5.3	
Urea	mmol/L	2.5	7.8	
Chloride	mmol/L	95	108	
Bicarbonate	mmol/L	22	29	
Phosphate	mmol/L	0.8	1.5	
Magnesium	mmol/L	0.7	1.0	
Albumin	g/L	35	50	
Total Protein	g/L	60	80	
Osmolality	mmol/kg	275	295	
Alkaline Phosphatase (ALP)	U/L	30	130	IFCC candidate method p-NPP using AMP buffer
Creatine Kinase (CK)	U/L	40 25	320 (M) 200 (F)	Ranges are for white Caucasian only; other ethnic groups may have higher values
Bilirubin (total)	µmol/L		<21	
Adjusted Calcium	mmol/L	2.2	2.6	Use adjustment equations normalised to mean calcium of 2.4 mmol/L
Urate	µmol/L	200 140	430(M) 360(F)	
Carbamazepine	mg/L	4	12	
Phenobarbitone	mg/L	10	40	
Phenytoin	mg/L	5	20	
Theophylline	mg/L	10	20	
Valproate	mg/L			No range should be quoted
Paracetamol	mg/L			
Salicylate	mg/L			
Methotrexate	µmol/L			
Lithium	mmol/L	0.4	1.0	Complies with NPSA guidance
Digoxin	µg/L	0.5	1.0	
Tacrolimus	µg/L			
25OH Vitamin D (including separately measured D2 & D3)	nmol/L			No ranges recommended
PTH	pmol/L			Method dependent
BNP/NTproBNP	ng/L			
Troponin I	ng/L			Method dependent
Troponin T	ng/L			
24 h Urine Calcium	mmol/24h	2.5	7.5	
24 h Urine Urate	mmol/24h	1.5	4.5	
24 h Urine Phosphate	mmol/24h	15	50	
24 h Urine Magnesium	mmol/24h	2.4	6.5	

Agreed Paediatric Clinical Biochemistry Reference Intervals

Test Name	Age	Units	Range low	Range high	Comments
Sodium	No age-related differences	mmol/L	133	146	
Plasma Potassium	Neonate	mmol/L	3.4	6.0	
	Infant	mmol/L	3.5	5.7	
	1-16 yrs	mmol/L	3.5	5.0	
Urea	Neonate	mmol/L	0.8	5.5	
	Infant	mmol/L	1.0	5.5	
	1-16 yrs	mmol/L	2.5	6.5	
Magnesium	Neonate	mmol/L	0.6	1.0	
	Infant - 16 yrs	mmol/L	0.7	1.0	
Plasma lactate	No age-related differences	mmol/L	0.6	2.5	Enzymatic method only
Bilirubin (total)	14 days - 16 yrs	µmol/L		<21	
Albumin	Neonate	g/L	30	45	
	Infant	g/L	30	45	
	1-16 yrs	g/L	30	50	
Calcium	Neonate	mmol/L	2.0	2.7	Actual not adjusted
	Infant - 16 yrs	mmol/L	2.2	2.7	
Phosphate	Neonate	mmol/L	1.3	2.6	
	Infant	mmol/L	1.3	2.4	
	1-16 yrs	mmol/L	0.9	1.8	
Alkaline Phosphatase (ALP)	Neonate	U/L	70	380	p-NPP using AMP buffer
	Infant - 16 yrs	U/L	60	425	
Ammonia	Sick or premature	µmol/L		<150	Follow metbio.net guidance
	Neonate	µmol/L		<100	
	Infant - 16 yrs	µmol/L		<50	
Plasma Bicarbonate	No age-related differences	mmol/L	19	28	

Definitions: Neonate <4 weeks; Infant 4 weeks – 1 year

What Happens Next . . .

The Pathology Harmony project was conceived as an action learning set in the West Midlands SHA and more recently has received support from Dr Ian Barnes and the Department of Health. In Phase II of the project laboratory staff were joined by representatives from the Royal College of Pathologists, Association for Clinical Biochemistry and Institute of Biomedical Science.

The results of Phase I and II of the project have culminated in recommendations that have been widely consulted on, including consideration by professional groups. Phase II of this work included studies in Immunology and Haematology but here we present just the harmonised reference intervals and units in Clinical Biochemistry.

Details of the members of Pathology Harmony group and approaches taken and background information behind the decisions that are presented here can be found on the Pathology Harmony website.

What Next?

Early in 2011 the Pathology Harmony group will be meeting to consider how to take forward new areas of activity. If you have comments or suggestions then you can contact Pathology Harmony by emailing: secretary@pathologyharmony.co.uk