

# Pathology news

April 2011 – Referral Labs Edition

## Salivary Drugs Screening

**The use of saliva to screen for illicit drug use is becoming more widespread.**

Saliva offers several distinct advantages over other matrices: it is easier to obtain, there are fewer clinical waste issues, and it can determine if someone is currently taking an illicit drug, rather than historic use whereby a urine sample may be preferable. The window of detection for illicit drugs in saliva is typically <1 day, and so repeat or random sampling may have to be performed to ascertain a true pattern of drug misuse.

We have been working on methods for salivary drugs of abuse screening and these are now evaluated and ready for use. A minimum of 0.5mL of neat oral fluid sample is required. The laboratory can provide specimen collection devices and advice leaflets. We can screen for

the following drug groups:

Drug	Detection cut-off (ng/mL)
Amphetamine	50
Benzodiazepines	10
Buprenorphine	5
Cannabis	1
Cocaine	5
Metamphetamine	40
Methadone	50
Opiates	10

Further details from Robyn Shea,  
Email: [robyn@cityassays.org.uk](mailto:robyn@cityassays.org.uk)  
or from Steve George,  
Email: [steve@cityassays.org.uk](mailto:steve@cityassays.org.uk)



Robyn Shea and Steve George, on the salivary drugs screening section.

### PDF Email Results

We are now able to send results as PDF files attached to an email to NHS.Net email addresses. This is a powerful tool for speedy return of results while we have not yet got full electronic results.

It works like this:

- **Our End:** Once work is authorised. Our pathology computer is programmed to send an email containing the PDF report to you.
- **Your End:** You need to have an NHS.NET email account that you use for result return and a robust system in place to check the account several times a day and print off the report forms.

Key benefits include cost and time savings in posting results and reducing the risk that report forms are lost.

For further details please contact Rajvinder Garcha, Email: [raj@cityassays.org.uk](mailto:raj@cityassays.org.uk).

### Reduced Prices

We've held the price of most tests for 2011, and reduced the price of several, including:

**Vitamin D** was £16.50, now £10

**TPMT** was £29.00, now £26

Full details on page 4.

### see inside for

	page
MoM hips: Chromium & Cobalt	2
Caffeine misuse	2
New TPMT test	2
Thipurine metabolites service	3
Blood spot 25-Hydroxyvitamin D	3
Faecal Calprotectin	3
Renal stone service	3
Assay prices and contacts	4

# Chromium and Cobalt in Patients with MoM Hip Replacements

Some individuals with replacement hip joints and similar prostheses may show elevated blood concentrations of some of the metallic elements of which these devices are composed. Chromium, cobalt, nickel, molybdenum, vanadium and titanium have all been investigated in this context. Recently, in response to concern in a small number of patients with poorly-performing metal-on-metal (MoM) hip replacements, the MHRA issued a Medical Devices Alert (MDA/2010/033). Certain categories of patient with MoM hip replacement should be considered for the measurement of blood chromium and cobalt. In these



cases, if the result for either of the elements is above seven parts per billion (7ppb; 135 nmol/L chromium, 120 nmol/L cobalt), a second measurement is to be performed three months after the first.

It should be noted that, while elevated blood chromium and cobalt concentrations reflect varying degrees of wear to the hip implant, it is not currently possible to interpret these results in respect of potential toxicity to the patient.

## Analysis

Analysis is performed by inductively-coupled plasma mass spectrometry (ICP-MS). Typical between-batch variation is 5.6% for chromium at 130 nmol/L and 7.2 % for cobalt at 80 nmol/L.

For our information leaflet on MoM monitoring please visit: [www.cityassays.org.uk](http://www.cityassays.org.uk)

## New TPMT Test Well Received

Our TPMT workload has continued to increase, reflecting a greater awareness of the importance of testing prior to thiopurine drug use. We have also taken on work from several new Trusts around the country.

In August 2010, we successfully changed to a new method, reporting TPMT as mU/L of whole blood. As well as overcoming misleading high results in some patients with anaemia, this simplification of the assay has allowed us to reduce the price significantly.

Our target turn round time remains 1-2 working days for TPMT phenotyping. Follow-on TPMT genotyping is performed where relevant, at no extra charge.

### TPMT Stability Study

A common question from users concerns TPMT stability. Recent studies by us confirm whole blood TPMT activity is stable for samples to be transported as follows:

- 1st class post within the UK, even over holiday periods (up to 19 days at 5 °C and 6 days at 23°C).
- Chilled, following accidental freezing (stable for 3 days at 5°C and <1 day at 23°C).

For further details on any aspect of our TPMT service, contact Nicola Barlow, Email: [nicola@cityassays.org.co.uk](mailto:nicola@cityassays.org.co.uk)

### Performance audit 2010/11

Total number of requests:	22,581
Number of Hospitals served:	183
Number of TPMT deficient:	52
Number of low TPMT results	2155
Number of normal TPMT results:	19,613
Number of high TPMT results:	761

## Caffeine Misuse

Caffeine is the world's favourite psychoactive substance.

There is currently an explosive growth in the sales of caffeine-based energy drinks and mounting concern that these can be abused, particularly by children, leading to adverse side-effects such as tachycardia, flushing, insomnia and anxiety. Chronic users will also experience caffeine withdrawal side-effects.

We have studied caffeine and metabolite levels in the serum and urine of an adult reference population to determine reference intervals for 'normal', 'high' and 'very high' caffeine, using this data to assess the caffeine levels in children and in individuals attending drug rehabilitation clinics. We found a significant number of the latter had 'very high' caffeine levels, while a small but significant number of children had 'high' and 'very high' levels, higher than most adults.

Caffeine abuse is generally thought to be under-recognised. Caffeine measurement can be useful in patients who present with symptoms such as insomnia, headache, tachycardia and anxiety, to determine whether caffeine consumption is a contributory factor.

An information leaflet is available from: [www.cityassays.org.uk](http://www.cityassays.org.uk).



*Kirsty Hedges, responsible for our caffeine research programme, with a few of the brands of high caffeine drinks available in local supermarkets.*

# Thiopurine Metabolites Service

Our national referral service has seen a marked increase in thiopurine metabolites requests over the last year. We now receive samples from over 50 NHS Trusts.

A recent audit has demonstrated that 6TGN monitoring can successfully titrate thiopurine drug doses into the therapeutic range. Of 1,043 6TGN requests from 596 patients:

- 57% were outside the therapeutic range, 26% above, 31% below.
- 219 (37%) patients had more than one sample with 42% (93)

of these showing 6TGN moving towards the therapeutic range upon repeat testing.

Since January 2010 we have offered 6-methylmercaptopurine nucleotides (6MMPN) in addition to 6-thioguanine nucleotides (6TGN) as part of our routine service with no increase in test cost. The ratio of 6MMPN:6TGN may be useful in non-responders to distinguish under-dosing or non-compliance from resistance to therapy, where 6MMPN is produced in preference to 6TGN.

## 6MMPN Audit

424 thiopurine metabolite results:

- 28 (6.6 %) had a high 6MMPN associated with increased risk of hepatotoxicity.
- In 54% of these, 6TGN was within the suggested therapeutic range and 21% below; providing no indication of risk of toxicity

For further details of our thiopurine metabolites assay service, please email Nicola Barlow on: [nicola@cityassays.org.uk](mailto:nicola@cityassays.org.uk).

# Hitting the 'spot' with 25-Hydroxyvitamin D!

**With 25-hydroxyvitamin D never out of the news, demand for this test remains high.**

Over the last year, we have focused on making this test more accessible and have spent considerable time developing a new LC-MS/MS assay capable of measuring 25-hydroxyvitamin D<sub>2</sub> and D<sub>3</sub> from a single 3mm dried blood spot – equivalent to <math>3\mu\text{L}</math> of serum!

One of the most challenging aspects of developing this new test was calibration and control. We have created our own whole dried blood spot calibrators and controls, standardised against our conventional LC-MS/MS plasma/serum 25-hydroxyvitamin D assay. As a result, whole dried blood spot 25-hydroxyvitamin D<sub>2</sub> and D<sub>3</sub> results are directly comparable to plasma/serum levels and the same

reference intervals apply.

We can use both Whatman 903 (GE Healthcare) or Ahlstrom 226 (ID Biological Systems) based devices. Whole dried blood spots are stable for up to 8 months for Vitamin D stored dry at room temperature.

This test is ideal for paediatric settings, testing in the community and population studies.

The turn round time for results is the same as our conventional assay – 2-3 working days – and if you supply the collection card the price is the same as our conventional plasma/serum 25-hydroxyvitamin D assay: £16 for NHS contracts, £20 for others.

We are currently working on CE marking a blood spot collection pack.

**Read more about our blood spot 25-hydroxyvitamin D assay at: [www.cityassays.org.uk](http://www.cityassays.org.uk).**

## Faecal Calprotectin

Calprotectin is an important marker for the differentiation of Inflammatory Bowel Disease (IBD) from Irritable Bowel Syndrome (IBS). We now have a highly sensitive quantitative ELISA technique to detect this calcium binding protein.

For further information, please contact Pervaz Mohammed, Email: [pervaz@cityassays.org.uk](mailto:pervaz@cityassays.org.uk)

## Renal Stone Service

Over the past five years our renal stone service has grown to serve over 50 laboratories from across the UK. The workload has seen a growth of 8% over the last 12 months. To continue the quality service and maintain our five day turn round we have invested in a second FT-IR system.

A recent audit of turn round time looked at 1,500 samples and identified that >99% of samples were analysed and reported within five days with 68% of the samples analysed and reported the next working day.



# Specialist Assays

Prices and turn round targets\* offered to NHS Contracts

Biochemistry	Turn round	Cost
ACE	3 days	£14
Bile Acids	1 day	£14
Caeruloplasmin	2 days	£6
Carotenes	5 days	£32
Faecal Calprotectin	3 days	£40
Faecal elastase-1	3 days	£31
Fructosamine	1 day	£14
Gilberts Syndrome (UGT1A1*28)	3 days	£30
Stone Analysis	5 days	£25
Thioguanine Nucleotides	3 days	£29
TPMT Service (Enzyme activity and relevant DNA)	2 days	£26

Fat soluble vitamins	Turn round	Cost
25-hydroxyvitamin D <sub>2</sub> & D <sub>3</sub> Serum/Plasma	2-3 days	£10
Vitamin A	2-3 days	£13
Vitamin E	2-3 days	£13

Blood spot analysis	Turn round	Cost
25-hydroxyvitamin D <sub>2</sub> & D <sub>3</sub>	2-3 days	£16
Lithium	Available Soon	
Blood Spot Pack		£6

Stone service	Turn round	Cost
Stone Analysis	5 days	£25
Urine Citrate	5 days	£15
Urine Oxalate	5 days	£15
Urine stone screen (calcium, phosphate, citrate, oxalate, magnesium, urate)	5 days	£50

Therapeutic drugs	Turn round	Cost
Caffeine	1-2 days	£20
Clozapine & Norclozapine	2-3 days	£16.50
Lamotrigine	2-3 days	£16.50
Lithium	1 day	£6
Olanzapine	3 days	£31

Toxicology	Turn round	Cost
Caffeine & Paraxanthine	1-2 days	£20
Ethanol	1-2 hours	£30
Ethylene/Diethylene Glycol	1-2 hours	£130
Methanol (methyl alcohol)	1-2 hours	£40
Plasma Quinine	1-2 hours	£130
Plasma Thiopental	2-3 hours	£100
Sulphonyl Urea, Antidiabetic Drug Screen	2-3 hours	£80
Tricyclic Antidepressants (Total) by Immunoassay	1-2 hours	£60
Unknown Drug Screen	2-3 hours	£250
Urine Diuretic Screen	1-2 days	£80
Urine Laxative Screen	2-3 days	£80
Urine Naltrexone	1-2 days	£26
B-Hydroxy-Butyrate (BHB)	2-3 days	£70
G-Hydroxy-Butyrate (GHB)	2-3 days	£70

Drugs of abuse screen	Turn round	Cost
Saliva Collection Device (pack of 10)		£20
Saliva Screen	1 day	£15
Saliva Confirmation	1 day	£20
Urine Screen	1 day	£15
Urine Confirmation	1 day	£20

Drugs of abuse confirmation	Turn round	Cost
Amphetamine ratio (resolution of D, L isomers)	1 day	£33
Amfetamines	1 day	£26
Barbiturates	1 day	£26
Benzodiazepines	1 day	£26
Buprenorphine	1 day	£26
BZP-Benzylpiperazine (includes TFMPP)	1 day	£26
Cocaine and Metabolites	1 day	£26
Cyclizine	1 day	£26
Dihydrocodeine	1 day	£26
Dipipanone	1 day	£26
Ephedrine/Pseudoephedrine	1 day	£26
Ketamine	1 day	£26
Khat (Qat)	1 day	£26
MDMA (Ecstasy) and related drugs	1 day	£26
Mephedrone	1 day	£26
Methadone+Metabolite (EDDP)	1 day	£26
Nalbuphine	1 day	£26
Naltrexone	1 day	£26
Opiates	1 day	£26
Phencyclidine (PCP)	1 day	£26
Zopiclone	1 day	£26

Trace Elements	Turn round	Cost
Aluminium Plasma	5 days	£25
Arsenic Blood & Urine (inorganic)	5 days	£40
Arsenic Blood & Urine (total)	5 days	£30
Blood Spot Lithium	available soon	
Cadmium Blood & Urine	5 days	£30
Chromium	2-3 days	£30
Cobalt	2-3 days	£30
Chromium & Cobalt	2-3 days	£50
Copper Urine	2-5 days	£30
Lead Blood	2-5 days	£17
Manganese Blood	2-3 days	£30
Mercury Blood & Urine	2-5 days	£30
Nickel	2-3 days	£30
Selenium Copper & Zinc any two	2-3 days	£30
all three	2-3 days	£40
Toxic Metals Screen (blood & urine)	2-5 days	£75
Other Metals	2-5 days	£30

\*Where days are given these are working days.

## Contact Point

### General Enquiries

info@cityassays.org.uk  
Tel: 0121 507 5162

### Trace Elements

elements@cityassays.org.uk  
Tel: 0121 507 4137

### Toxicology

toxicology@cityassays.org.uk  
Tel: 0121 507 4135

## cityassays.org.uk

Our website gives basic details for many of the tests that we offer.

This includes:

- Downloadable PDF files of user information leaflets
- Relevant information and background details
- Up to date details on the turn round time for the tests that we offer.



## IBMS Congress Birmingham

26 – 28 September 2011

We will be having a stand at the IBMS congress again this year. We hope to be able to meet many of our users for our referred in tests. We take working with you very seriously and gaining feedback and ideas on how we can work even better together is very important to us.

