

Pathology news

IBMS Congress Special – September 2017

Specialist Services Sorted!

It is great to attend the IBMS Congress again this year, where we look forward to meeting many of the users of our referred in testing services. Since 2003 our approach has been to take forward new developments in the clinical laboratory that can make a real difference to patient care. We then introduce relevant services that others can make use off. Clearly this has been a successful approach and we now work for around five-hundred health care providers, including nearly every NHS Trust in the United Kingdom.

Key to what we do is focussing on being an 'extension of your laboratory'. Our aim is to offer our users a 'service' rather than just a 'result'. So, if we are privileged enough to receive your work we expect you to demand not only timely services at the right price, but also the added value of consultant support and test development. This is seen from areas as diverse as our approach to modern toxicology, where we have pioneered routine services for the many new drugs being misused in society, through to new tests for pharmacogenomics. We have stepped up to the challenge of metal-on-metal hip monitoring in our Trace Elements service. For tests such as faecal elastase and faecal calprotectin we offer levels of service that only a high throughput laboratory can attain.

Pricing is very important in all Pathology environments. We are the only referral service prepared to publish our prices in the United Kingdom. There is always someone around the corner who will offer to undercut on price, but overall our prices are seen as excellent value for the services we provide.



Brenda Blundell getting ready to do her daily run of the serology blood spots.

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Serology Blood Spots Down in Price

One area that we are very excited about is our blood spot testing service. Our in-house testing device offers significant advantages over commercial products with its enclosed drying meaning samples do not have to be left lying around.

The growth in the serology blood spot testing service has been remarkable. From September 2017, due to economy of scale, we are able to reduce the price from £35 to £25 including provision of a test pack and reply paid service. See article on page 2 for full details.

The Institute of Biomedical Science
IBMS CONGRESS 2017
24-27 SEPT - BIRMINGHAM, UK

Come and meet us on Stand R15

Dried Blood Spot Serology Testing



Early detection of Blood Borne Viruses (BBVs), particularly Hepatitis C, is important for improved patient outcome and preventing disease transmission especially in closed communities such as prisons. The rapid turnover of prisoners requires a simple and convenient approach to screen quickly with minimal risks of sharp injuries. Conventional screening with venepuncture is simply not viable. Organisations such as Public Health England, NHS England and the National Offender Management Service recommend adopting Dried Blood Spot Testing to improve the uptake of screening in secure units.

Training front of house staff is vital

We provide training sessions for health care assistants, nurses and doctors using laboratory trained staff in every new location. The sessions include site visits with an introduction covering the background of dried blood spot technology. After a practical demonstration of correct sample collection techniques staff perform the blood spot sampling on each other. Even the completion of the request form is demonstrated as this is a major area of problems in the laboratory. At the end of the session

a training guide containing key information on collection and contact details is provided.

Test packs easy to use

Blood spot collection packs are provided in bulk. Individually wrapped packs contain all components required for testing a single patient, including request form, instruction leaflet detailing the testing procedure and return envelope. Our 'in-house' blood spot

collection card can be sealed as soon as the blood spots have been collected as it has been designed to enable enclosed drying. This offers significant safety and practical advantages over other devices where the blood spots are left out to dry before being sealed. Our requirement of a maximum of four blood spots also offers significant advantages.

Laboratory analysis

In the laboratory each card is first visually examined to ensure the blood spots are of a acceptable quality. A single disc is used to test for the presence of HIV antigen/antibody, Hepatitis B surface antigen and Hepatitis C antibody using HIV Ag/Ab Combo, HBsAg Qualitative II and anti-HCV assays. Our service is led by a Consultant Microbiologist who helps with result interpretation and clinical advice.

Electronic return of results

After analysis and interpretation of results, electronic PDF reports are issued to secure email addresses. Encryption requiring entry of a password is used for email addresses considered non-secure. The turn round target for the service is 2-3 working days.

What difference does it make?

One of our prison sites sent us a total of 1222 patient samples (see Fig 1). The number of samples

Fig 1. Results from the prison

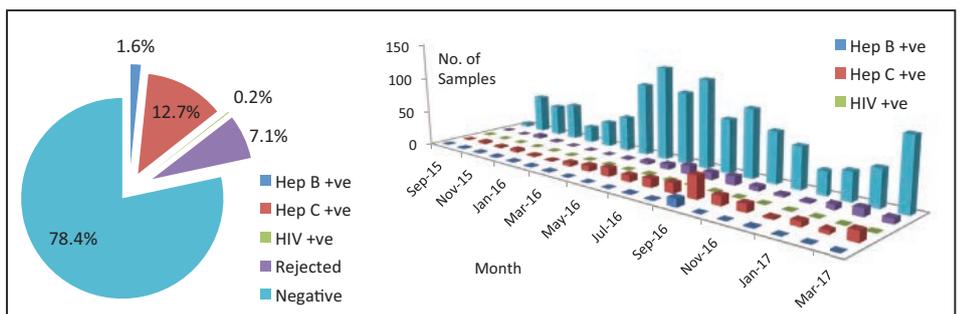
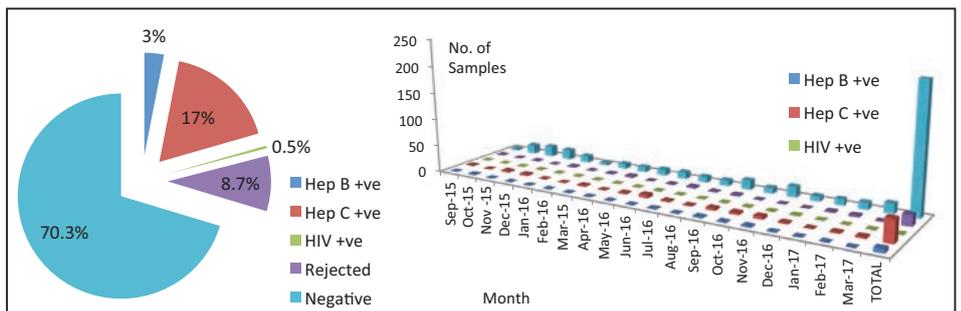


Fig 2. Results from the drug misuse centre



testing reactive for HIV Ag/Ab, HBsAg and anti-HCV were 2 (0.16%), 20 (1.64%) and 155 (12.68%) respectively.

The number of samples received each month for the prison, range from 22 – 133 with a mean of 64.

A drug misuse centre, 229 samples collected (see Fig 2). The number of samples reactive to HIV Ag/Ab, HBsAg and anti-HCV were 1 (0.5%), 7 (3%) and 40 (17.5%) respectively.

The numbers of samples received per month for the same time frame for the drug recovery misuse; range from 4 – 19 with a mean of 11.7.

Regarding the ease of use, the failure rate for our method of testing was 7.12% for the prison and 8.7% for the drug misuse centre.

The main reason for rejecting samples on receipt was due to either incomplete patient request forms or less commonly due to the poor quality of blood spots being received.

Undiagnosed Disease Revealed

Diagnosing a total of 195 new patients with Hepatitis C and 60 with Hepatitis B, emphasises the importance of screening 'high prevalence' populations. Detecting three new patients for HIV provides compelling evidence of the usefulness of easy access serology testing using blood spots.

Service Level Agreements for UKAS

We offer all our users a two way Service Level Agreement (SLA). This is designed to comply with key UKAS requirements and to make things nice and simple for both us as the specialist laboratory and those that refer to us.

In particular, there is no need to update this every year as our SLA refers to our annual Pathology News to referral laboratories which acts as the updated appendix of the agreement.

Metal on Metal Hip Service

New guidance was issued by the MHRA in July on the follow-up of patients with metal-on-metal (MoM) hip replacements, to help the early detection of soft tissue reactions.

Annual Monitoring

The key change is the recommendation to monitor blood Cobalt and Chromium (Co&Cr) on all patients with MoM hip replacements, regardless of the size of the implant or whether the patient is symptomatic. Annual monitoring is recommended for most groups with less frequent monitoring in low risk groups.

The cut-off of $\geq 7 \mu\text{g/L}$ ($\geq 120 \text{ nmol/L}$ Co, $\geq 135 \text{ nmol/L}$ Cr) remains in use to indicate increased risk of soft tissue reactions and need for follow-up and imaging. The guidance points out that in some patients, metal ion concentrations $< 7 \mu\text{g/L}$ may be associated with wear and this has been the focus of several publications and consensus guidelines, with a particular interest in Co levels of 2–7 $\mu\text{g/L}$.

June 2017 snapshot audit

Of 350 Co&Cr requests, 50.6% of patients were female. The age range was 20 to 90 years.

What concentrations did we measure?

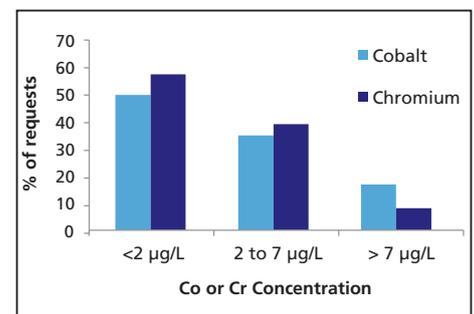
Approximately half of patients had Co&Cr below 2 $\mu\text{g/L}$. While only a

small percentage of requests exceeded the MHRA threshold, a significant proportion had concentrations in the 2-7 $\mu\text{g/L}$ range.

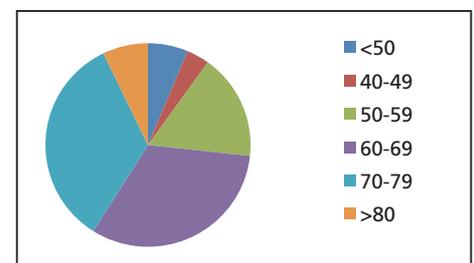
Co&Cr ($\mu\text{g/L}$)	% of all requests
Co & Cr ≥ 7	6.0
Co $\geq 7 \mu\text{g/L}$ but Cr < 7	9.7
Cr $\geq 7 \mu\text{g/L}$ but Co < 7	1.7

Cobalt is raised over the MHRA threshold more commonly than Cr and accordingly raised Co independent of raised Cr is observed more frequently than the reverse scenario.

Concentrations of blood Co and Cr



Age of patients with Co and Cr requests



UKAS Accreditation

All our laboratories were inspected by UKAS to check compliance with ISO 15189 quality system in spring 2017. Non compliances that were identified by our inspectors all had recommendations sent in to the UKAS deadline. We await feedback from this.

Specialist Assays

Prices and turn round targets* offered

Biochemistry	Turn round	Cost
ACE	3 days	£15
Bile Acids	1 day	£15
Caeruloplasmin	2 days	£15
Carotenes	5 days	£35
Faecal Calprotectin	3 days	£26
Faecal Elastase	3 days	£36
Fructosamine	1 day	£15
Gilberts Syndrome	3 days	£40
HFE	3 days	£40
Cholinesterase	within 24 hours	£15
RBC Cholinesterase	within 24 hours	£50
Xanthochromia	2 hours	£35

Pharmacogenomics	Turn round	Cost
Thioguanine Nucleotides	2 days	£30
TPMT Service	1 day	£22
Serum Infliximab	5 days	£25
Anti Infliximab Antibodies	7 days	£35
Adalimumab	5 days	£25
Adalimumab Antibodies	7 days	£35

Fat soluble vitamins	Turn round	Cost
25-hydroxyvitamin D ₂ & D ₃ 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 ₂ & D ₃	2-3 days	£16
Serology BBV Screening	2-3 days	£25

Stone service	Turn round	Cost
Stone Analysis	5 days	£28
Urine Citrate	5 days	£15
Urine Oxalate	5 days	£15
Urine Stone Screen	5 days	£50
(calcium, phosphate, citrate, oxalate, magnesium, urate)		

Trace elements	Turn round	Cost
Aluminium (plasma or water)	2-5 days	£25
Arsenic (blood or urine)	2-5 days	£25
Cadmium (blood or urine)	2-5 days	£25
Chromium (blood)	1-2 days	£15
Chromium (urine)	2-5 days	£20
Cobalt (blood)	1-2 days	£15
Cobalt (urine)	2-5 days	£20
Chromium & Cobalt (blood)	1-2 days	£25
Chromium & Cobalt (synovial fluid)	7 days	£40
Copper (urine)	2-3 days	£20
Lead (blood)	2-3 days	£20
Lead HB ZPP	2-3 days	£35
Manganese (blood)	2-3 days	£20
Mercury (blood or urine)	2-5 days	£25
Nickel (blood, serum or urine)	2-5 days	£30
Selenium, Copper & Zinc (serum)	1-2 days	£10 each or for all three £25
Toxic Metals Screen (blood & urine or powders)	1-2 days	£100
Bromide (serum)	2-3 days	£40

Thalium (blood or urine)	5 days	£40
Other Metals (£ per element) (e.g Urine: lead, iron, manganese, bismuth, barium, antimony, selenium, tellurium, silver, gallium, indium. Blood: Bismuth, barium, boron, strontium.)	2-5 days	£40

Therapeutic drugs	Turn round	Cost
Amitriptyline & Nortriptyline	5 days	£22
Caffeine	1-2 days	£20
Clozapine & Norclozapine	2 days	£22
Lamotrigine	2 days	£22
Lithium	1 day	£10
Olanzapine	5 days	£22
Levetiracetam	5 days	£22
Quetiapine	5 days	£22

Toxicology	Turn round	Cost
Caffeine & Paraxanthine	1-2 hours	£20
Ethanol (urine & blood)	1 day	£30
Ethylene/Diethylene Glycol	1-2 hours	£200
		Out of hours: £400
Methanol (methyl alcohol)	1-2 hours	£100
		Out of hours: £200
Sulphonyl Urea, Antidiabetic Drug Screen	2-3 hours	£90
Unknown Drug Screen	3 days	£155
LC-QTOF Screen (urine, blood, stubs, powders, pills, tobacco & paper)	4 hours	£100
Paraquat & Diaquat	1 day	£90
Rohypnol (Flunitrazepam)	5 days	£85
Urine Diuretic Screen	1-2 days	£90
Urine Laxative Screen	2-3 days	£90
γ-Hydroxy-Butyrate (GHB)	2-3 days	£90
Spiked Drink Screen	5 days	£240

Medico-legal work	Turn round	Cost
Medico-legal kits & screen	24hrs	£100

Drugs of abuse screening kits	Cost
Oral fluid collection device without pre-paid postage – pack of 20	£30
Urine & oral fluid reply paid kits – each	£7

Drugs of abuse screen	Turn round	Cost
Oral Fluid (incl Cannabis)	1-2 days	£25
Urine (incl Cannabis)	1-2 days	£25

Current drugs of abuse panel includes 26 classic drugs and common legal highs.

Other drugs of abuse screening	Turn round	Cost
Amphetamine ratio (resolution of D, L isomers)	3 days	£50

Immunology	Turn round	Cost
ANCA abs	1-2 days	£10
Anti-C1INH abs	up to 28 days	£180
Anti-nuclear antibodies	1-3 days	£10
Anti-nuclear antibodies titration	1-3 days	£11.50
Aspergillus IgG	3-7 days	£11
Avian IgG - budgie	3-7 days	£13

Avian IgG - pigeon	3-7 days	£13
Beta 2 Microglobulin	3-7 days	£7
CCP abs	3-5 days	£10
Complement C3	1-2 days	£10
Complement C4	1-2 days	£10
Double Stranded dsDNA screen	1-3 days	£7.50
Double stranded DNA quantitation abs	1-7 days	£11
Endomysial (IgA) abs	3-5 days	£13.50
ENA Screen	3-7 days	£10
ENA Profile	10-14 days	£22
Epidermal abs	3-7 days	£12
GAD abs	10-20 days	£16
Gastric Parietal cell abs	3-5 days	£10
Glomerular Basement Membrane (GBM) abs	3-5 days	£12
IHIB abs	10-14 days	£10.50
IgG/IgM Cardiolipin abs screen	3-7 days	£14
IgG Cardiolipin abs	3-7 days	£6
IgM Cardiolipin abs	3-7 days	£6
Intrinsic Factor abs	3-7 days	£10
ISAC (Specific IgE allergen component panel)	14-21 days	£180
Liver Kidney Microsomal abs	3-5 days	£10
Mitochondrial abs	3-5 days	£10
Mitochondrial abs quantitation	3-7 days	£15
Myeloperoxidase (MPO) abs & Proteinase 3 (PR3) abs	3-7 days	£30
Pneumococcal ABS	10-14 days	£13
Rheumatoid factor	1-2 days	£6
Smooth Muscle abs	3-5 days	£10
Smooth Muscle abs quantitation	3-7 days	£15
Specific IgE single common allergen	3-5 days	£14
Specific IgE single rare allergen	3-5 days	£15
Specific IgE Bee Venom Apim1	3-5 days	£15
Specific IgE Birch, rBetv1	3-5 days	£15
Specific IgE Egg Gald1	3-5 days	£15
Specific IgE Grass – rPhl p7,p12	3-5 days	£15
Specific IgE Hazelnut – Cora1/Cora8	3-5 days	£22
Specific IgE Latex HevB1, B3, B5, B6.01, B6.02, B8	3-5 days	£65
Specific IgE Mixed panel	3-5 days	£15.50
Specific IgE to Mixed Food	3-5 days	£18.50
Specific IgE Peanut Arah1,2,3,8, 9	3-5 days	£55
Specific IgE Wasp Vesv5	3-5 days	£15
Specific IgE Wheat Omega5 gliadin	3-5 days	£15
Tetanus abs	10-14 days	£10.50
Tissue Transglutaminase (IgA) abs	2-4 days	£10
Total IgE	3-5 days	£13
Tryptase	3-5 days	£20
Thyroid Peroxidase abs (TPO)	3-7 days	£10
T spot	24 hours after sample receipt	£75

*Where days are given these are working days.



Changing Trends in Street Drugs

Substance misuse is constantly changing, and in order for our clinical toxicology service to remain effective it is important we reflect this in the services we offer.

For drugs of abuse screening (urine and oral fluid) we use tandem mass spectrometry (UPLC-MS/MS). This testing strategy means we get the right results first time, with no requirement for separate confirmation testing. Another major advantage is we can decide which compounds to include in our drug screening panel. This enables us to detect new psychoactive substances (NPS) as well as prescription and over-the-counter medication.

In October 2017 we will be making changes to our routine drugs of abuse UPLC-MS/MS screening panel by introducing not only more stringent positive cut-offs for classic drugs of abuse, but also inclusion of new tests as shown in Table 1.

Diversion and Illicit Supply of Medicines (DISM)

In December 2016 the Advisory Council of Drug Misuse (ACDM) issued a report on the diversion and illicit supply of medicines (DISM) in response to a request from the Home Secretary in 2013 to explore

the potential for medical and social harms arising from the illicit supply of medicine. Highlighted in the report were several drugs including antihistamines such as promethazine, the antidepressant mirtazapine and antipsychotic quetiapine.

Using time of flight (UPLC-MS/TOF) we can screen for a more extensive panel of compounds in a single analysis, currently over 1300 drugs and metabolites, including over-the-counter and prescription medications. The results of UPLC-MS/TOF screening of different population groups for DISM compounds is summarised in Table 2. The highest % positive for all DISM compounds was found for the prison group (highlighted grey on table). Inclusion of DISM tests in our routine drug screening panel should not only help increase awareness of potential for abuse, but also help our users better enforce the NICE Guidelines on the Safe Use and Management of Controlled Drugs.

Fentanyl

Fentanyl is a short acting pain killer 50 to 100 times more potent than morphine, which the UK National Crime Agency (NCA) have found there have been 60 drug related deaths reported in the UK since

December 2016. Inclusion of this opioid in our drug screening panel will serve as a vigilance system to determine the extent of its use in UK, as well as alerting clinicians to

Table 1. UPLC-MS/MS drug screening panel and positive cut-off thresholds. To be introduced in October 2017.

Drug	Current cut-off	Proposed cut-off
Opiates		
Morphine	5 ng/mL	5 ng/mL
DHC	300 ng/mL	50 ng/mL
Codeine	300 ng/mL	50 ng/mL
6-MAM	10 ng/mL	5 ng/mL
Opioids		
Buprenorphine	5 ng/mL	2 ng/mL
Nor-buprenorphine	5 ng/mL	2 ng/mL
Methadone	250 ng/mL	250 ng/mL
EDDP	250 ng/mL	75 ng/mL
Fentanyl	-	2 ng/mL
Amphetamines		
Amphetamine	200 ng/mL	100 ng/mL
Methamphetamine	200 ng/mL	100 ng/mL
MDMA	200 ng/mL	100 ng/mL
Mephedrone (Meow, Meow)	10 ng/mL	5 ng/mL
Cocaine		
Benzoylcegonine	150 ng/mL	80 ng/mL
Benzodiazepines & Z drugs		
Diazepam	5 ng/mL	2 ng/mL
Nordiazepam	5 ng/mL	2 ng/mL
Temazepam	5 ng/mL	2 ng/mL
Oxazepam	5 ng/mL	2 ng/mL
Lorazepam	5 ng/mL	2 ng/mL
Clonazepam	-	2 ng/mL
Zopiclone	-	2 ng/mL
Other Drugs		
Ketamine	10 ng/mL	5 ng/mL
Tramadol	10 ng/mL	5 ng/mL
Thebaine	2 ng/mL	2 ng/mL
DISM		
Quetiapine	-	5 ng/mL
Mirtazapine	-	5 ng/mL
Pregabalin	-	100 ng/mL
Gabapentin	-	100 ng/mL
Promethazine	-	5 ng/mL



TPMT Genetic Testing Confirmation

To help take our service forward we will now be clearly reporting these results to our users. If we reflex to a genetic TPMT test this will be reported to you and an additional charge of £30 made for the genetic results. Up until now we have managed to offer the genetic part of the TPMT service free of charge but increased use of our genetic TPMT service does require that we cover the cost. Genetic testing is only undertaken on a very small part of our overall TPMT service and for most users the financial impact is negligible.

For queries about this contact Rachel Griffiths, TPMT Laboratory Clinical Scientist Lead, email: rachellouisejones@nhs.net.



Table 2. Results of UPLC-MS/TOF Screening from 2014 to 2016 for different population groups for DISM compounds (6479 urine samples)

Requesting Source	Total requests	% positive				
		Pregabalin	Gabapentin	Mirtazapine	Promethazine	Quetiapine
All	6479	4.0	2.5	6.9	2.5	5.6
A&E	631	3.2	2.1	6.8	2.4	5.5
In-patients*	1676	5.4	3.6	9.2	2.4	6.8
Other hospital	2216	2.1	2.1	4.5	2.5	3.8
Mental Health	1493	3.0	0.8	3.9	2.6	5.6
Prison	463	13.0	6.5	19.8	3.0	9.9

*Applies to requests from Sandwell & Birmingham Hospital NHS Trust, only (patients admitted to West Birmingham Poisons Units & Coronary and intensive care).

Table 3. Summary compounds detected for 59 suspect herb materials screened for NOIDS by UPLC-MS/TOF

Year	Synthetic cannabinoid detected								
	AKB-48	5F-AKB48	5F-PB22	AB-CHMINACA	MDMB-CHMICA	MAB-CHMINACA	MAB-CHMINACA	AMB-FUBINACA	5F-ADB
2014	1	11	2	11	0	0	0	0	0
2015	0	12	1	13	3	10	0	0	0
2016	0	12	0	10	1	2	1	5	1
2017	0	0	1	0	0	0	1	3	8
Total	1	35	4	34	4	12	2	8	9

*NOID materials were found on patients either admitted to West Birmingham Poisons Units & Coronary and intensive care at Sandwell & Birmingham Hospital NHS Trust or Birmingham & Solihull mental health Trust

potential users at risk of significant harm.

Update on NOIDS

Synthetic Cannabinoids (NOIDS) are new psychoactive substances (NPS) which act at the CB1 receptors as the main psychoactive ingredient in cannabis (THC) but are structurally different and usually far more potent. As of December 2015 the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) recognised over 160 NOID compounds, and this list continues to grow.

In a recent audit of NOID material collected from clinical users and tested by UPLC-MS/TOF, we have noticed new types of chemical which may explain the very profound

clinical effects which have been reported as 'Zombie like' subjects (Table 3). Images in the media have shown individuals stumbling around in a zombie like state after smoking these NOID products.

Screening for NPS presents a challenge to the testing laboratory. This is especially the case with NOIDS. Using the latest equipment such as time of flight (UPLC-MS/TOF) to test actual materials means we have been able to follow the changing trends in NPS use and develop new screening tests. Currently we are working on new screening methods for these ultra-potent NOIDS and these services will be available to those that use our screening services in the coming months.

Electronic IT Links

Getting full electronic two way communication for specialist referral testing is increasingly important in an efficient and effective pathology environment. We now have two ways we can help:

- **PDF Email Reporting** Very established using SQL download from our Pathology LIMS. We have over 60 users in place and this process is a convenient low cost and secure way of receiving electronic results.
- **NPEX** We are seeing increased numbers of users linked into our NPEX service. So if you have this facility do consider this as a way forward.

To discuss installing electronic links for your results service please contact Jo Murray, Email joseph.murray@nhs.net for NPEX or Raj Garcha, Email rajvinder.garcha@nhs.net for PDF reporting.

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Our website gives basic details for many of our tests.



This includes:

- Downloadable PDF files of user information leaflets
- Relevant information and background details
- Up to date turn round times

