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Doctors' Newsletter

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CEO Message

Dr Shaun Donovan
BMedSci, MBBS (Hons), FRCPA, GAICD
CEO Diagnostic Services Pty Ltd (DSPL)
Hobart, Launceston and North West Pathology

I have great pleasure in introducing the last Doctors' Newsletter for 2019

Firstly, I would like to welcome two new pathologists to our ranks. Dr Andrea Cretney is a histopathologist who commenced with us in the middle of the year and will be based in our Hobart Laboratory and Dr. Dylan Close, a general pathologist who has been filling a locum role this year in our Histopathology Department in Hobart, will commence a permanent role in 2020 predominantly in Histopathology and Biochemistry.

In this newsletter, there is an article on pharmacogenomics testing, a new test offered by Sonic Genetics, which enables personalisation of a patient's medication according to genetic makeup. Dr Roslyn Malley has provided an article on therapeutic drug monitoring and Dr Alistair McGregor a measles update. I would especially like to thank Ros and Alistair on the many articles they have provided for our Doctors Newsletters this year.

Finally, I would like to take this opportunity to wish all our referrers a happy and safe Christmas and New Year.

Welcome Pathologists

Dr Andrea Cretney
MBBS(Hons) FRCPA
Anatomical Pathologist

Andrea completed her medical degree at Monash University and completed her Fellowship in Anatomical Pathology in Melbourne in 2007.

Since that time she has worked in the public system in Victoria, with a particular interest in gynaecologic and placental pathology.

She has recently relocated with her family from Melbourne to Hobart.

Dr Dylan Close
MBBS(Hons) FRCPA
General Pathologist

Dylan grew up on the north west coast of Tasmania, before completing his medical degree at Monash University in Melbourne.

He trained in General Pathology in Geelong and Melbourne, completing his fellowship in 2016 working as a General Pathologist at Cabrini Hospital in Melbourne until 2019.

Dylan is very happy to have returned home to Tasmania and will be working in the anatomical pathology and clinical biochemistry departments at Hobart Pathology from 2020.

Pharmacogenomics

Pharmacogenomic (PGx) testing allows you to personalise your patient's medication according to their genetic variation. This has been shown to improve clinical outcomes by enhancing therapeutic efficacy and improving clinical safety.[1,2]

The Sonic PGx Panel is a 10-gene pharmacogenomic test that provides guidance on medication and dose across common therapeutic areas, including cardiology, gastroenterology, pain management, and psychiatry and addiction medicine.

Sonic PGx Panel is most useful for patients:

Experiencing unwelcome side-effects or not responding to medication; or
About to commence medications where PGx has been shown to influence clinical outcomes.

Arranging a Sonic PGx Panel

1. Complete a Pharmacogenomic (PGx) Panel Request Form or request the 'Sonic PGx Panel' using your local pathology request form.
2. Send your patient to any Hobart, Launceston or North West Pathology collection centre for a blood test.

Sonic PGx Panel reports are delivered via Sonic Dx or courier, usually within 10 business days following receipt of the sample in our laboratory.

The report includes:

Prescribing recommendations for current or proposed medications
Genotypes, predicted metaboliser/activity status and potential drug-gene interactions
The evidence level supporting the PGx guidance

Cost

Medicare does not cover the cost of the Sonic PGx Panel and your patient will receive an invoice. Please refer to the Sonic Genetics website, www.sonicgenetics.com.au/pgx, for current pricing.

References
1. Caudle K, et al. Incorporation of pharmacogenomics into routine clinical practice: the Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline development process. Curr Drug Metab. 2014; 15(2):209–217
2. Swen J, et al. Pharmacogenetics: From bench to byte an update of guidelines. Clin Pharmacol Ther. 2011; 89(5):662–673

Therapeutic Drug Monitoring

Therapeutic Drug Monitoring (TDM) is used to assess drug toxicity, dosing and monitoring especially when physical state or other medications have changed. Noting the dosing regime, time of blood collection, time of last dose and when next dose is due will allow the laboratory to assess the significance of the drug level. Trough levels refer to a drug level taken just prior to the next due dose.

Drug and TDM measurement	Metabolism/excretion, toxicity and other associations and considerations when monitoring
Carbamazepine[1] Trough level.	*Hepatic. Influenced by P450 inhibitors/inducers.* Toxicity: Visual, nystagmus, drowsiness, ataxia to coma. Tachycardia. Anticholinergic symptoms. Other: Hyponatremia (SIADH), decreases fT4/normal TSH, high GGT & mild neutropenia/eosinophilia. Rare aplastic anaemia. Stevens-Johnson Syndrome (SJS) more common with some HLA alleles. *Monitor: FBC, UEC and LFTs.*
Cyclosporin[2] Trough and/or 2 hours post dose. **Tacrolimus**[2] Trough level.	*Hepatic. Liver disease prolongs elimination. Influenced by P450 inhibitors/inducers.* Toxicity: Hepatoxicity, hypertension, nephrotoxicity, tremors, headache, tinnitus, blurred vision, weakness, seizures (+ HTN). Other: Hyperuricaemia, hyperkalaemia and hypomagnesaemia, dyslipidaemia and insulin resistance can occur. *Monitor: LFTs & UEC, Ca^{2+}, Mg^{2+}, PO_4, uric acid, fasting lipids/glucose.*
Digoxin[3] At least 8 hours post last dose.	*Mainly renal. Liver disease not significant. Gastrointestinal. Thyroid disease alters metabolism.* Toxicity: Weakness, headache, confusion & visual colour changes. GIT upset. Hypo-kalaemia/magnesemia increase risk of toxicity/arrhythmias. New/worsening arrhythmia. In acute toxicity hyperkalaemia. Digibind can be used in high risk toxicity cases. *Monitor: UEC, Ca^{2+}, Mg^{2+}, PO_4 and TFTs.*
Lithium[4] 12 hours post last dose.	*Renal. Renal impairment, dehydration & sodium depletion increase levels.* Toxicity: Nausea, vomiting, diarrhoea & anorexia, blurred vision, muscle weakness, coarse tremor, ataxia, dysarthria, drowsiness, confusion and seizures. Other: Polyuria (decreases renal response to ADH). Risk of hypothyroidism and hyperparathyroidism & renal disease. *Monitor: UEC, Ca^{2+} +/- PTH, Mg^{2+}, PO_4 and TFTs.*
Phenytoin (Dilantin)[1] Trough level.	*Hepatic & renal.* Toxicity: double vision, nystagmus, confusion, slurred speech & ataxia. Nausea, vomiting and anorexia. Other: Gingival hyperplasia & hirsutism. SJS more common with some HLA alleles. Hepatitis may occur. Folate deficiency due to reduced absorption. Low bone mineral density by increasing vitamin D catabolism. *Monitor: FBC, LFTs, 25(OH)D3 & folate.*
Sodium Valproate[1] Trough level.	*Hepatic. Dose adjustments required in liver disease.* Toxicity: Hepatotoxicity. Encephalopathy including lethargy, seizures, rarely coma. Other: Nausea, vomiting, pancreatitis, thrombocytopenia, hyperammoniaemic encephalopathy. May alter lipid metabolism. Insulin resistance can also occur. *Monitor: LFTs, FBC (platelets), fasting lipids/glucose. Ammonia if encephalopathic/increased seizures.*
Thiopurines[5] Measure: 6 –TG and/or 6-MMP Trough level preferred.	Includes: Azathioprine, Mercaptopurine, 6 thioguanine (6 –TG) *Metabolised by thiopurine methyl transferase (TPMT). TPMT phenotype and TPMT genotype can be evaluated.* Toxicity: Low and high levels of TPMT can cause severe cytopenias and hepatotoxicity respectively. *Monitor: FBC and LFTs.*

References
1. Schachter SC et al. Antiseizure drugs: Mechanism of action, pharmacology and adverse effects. UpToDate: Sept 2019; 2. Hardinger K et al. Pharmacology of cyclosporine and tacrolimus. UpToDate: April 2018; 3. Giardina E et al. Treatment with digoxin: Initial dosing, monitoring, and dose modification. UpToDate: June 2018; 4. Janiacak PG et al. Bipolar disorder in adults and lithium: Pharmacology, administration, and management of side effects. UpToDate: Feb 2019; 5. A-Rahim Yousif et al. Overview of azathioprine and mercapto-purine use in Inflammatory bowel disease. UpToDate: May 2019;

GP Management of Measles

Measles is an acute, highly communicable viral illness, transmitted via respiratory secretions.

Typically there is a prodromal phase of 2–4 days, with fever, coryza and conjunctivitis. The characteristic maculopapular rash appears 2 – 7 days after the prodrome, begins on the face and upper neck, spreads to the trunk and extremities and lasts for up to one week.

People with measles are generally very unwell, and other symptoms may include diarrhea, anorexia and generalised lymph-adenopathy. Possible complications include otitis media, pneumonia and encephalitis.[1]

While measles is rare it is a serious and highly infectious illness. As such, it requires a prompt and intensive public health response that aims to limit spread and prevent further cases.

There have been 5 cases of measles in Tasmania since 2015, but no sustained transmission. Most cases of measles in Australia occur in people who have recently travelled to countries where measles is circulating, or were infected by such a traveller, and have not had two documented doses of a measles-containing vaccine.

In assessing the likelihood of measles, it is useful to consider the clinical picture, possible exposure to the virus (i.e. history of travel and exposure to unwell contacts) and susceptibility to measles (i.e. vaccine history).

Management of patients with suspected measles

1. **Isolate** – Suspected cases should be isolated in a single room and asked to wear a mask. Alternatively, suspected cases can be seen in their homes or at the end of the day. Staff interacting with a suspected case of measles should also take airborne precautions.
2. **Notify** – In Tasmania, inform the Communicable Disease Prevention Unit (CDPU) of Public Health Services immediately on suspicion of measles by calling 1800 671 738. Do this before initiating any investigations.
3. **Test** – If the CDPU agree that there is a possibility of measles they will liaise with the Royal Hobart Hospital to arrange urgent molecular testing. The appropriate specimens for PCR testing are
    a. A throat and / or nasopharyngeal swab (collected with a "flocked" swab)
    b. A first pass urine

In addition, blood should be taken for measles serology (IgG and IgM).

Ideally, to avoid the additional exposures inherent in referring an infectious case to a Collection Centre, patients who present to their GP should have specimens collected at the time of consultation.

- If referral to a collection centre is unavoidable, an appointment MUST be made. This is to prevent contact with other, possibly susceptible, patients attending the collection centre.
- Mark the tests requested as URGENT.

Suspected cases should also be excluded from work, school, early childhood education and care services whilst awaiting laboratory results.

Please seek support from CDPU on 1800 671 738 for advice regarding defining susceptible contacts , appropriate contact management and the need for other measures, such as post-exposure prophylaxis.

We are grateful to Dr Miriam Paul at DHM Pathology
and the Tasmania Communicable Diseases Prevention Unit in compiling this article.

References
[1] Kyle C [ed]. Measles - Sonic Pathology Handbook: A guide to the interpretation of pathology tests. 1st ed. Sydney: Sonic Healthcare, 2014. pp. 573-574

To subscribe for updates in pathology and our Doctors' Newsletter, please email clientservices@dspl.com.au

Dr Daniel Owens
BMedSci, MBBS (Hons), FRCPA, FRACP, GAICD
State Medical Director

Hobart Pathology 2-4 Kirksway Pl Hobart TAS 7000 | PO Box 1535 Hobart TAS 7001
P: 03 6223 1955 F: 03 6224 1509 | www.hobartpath.com.au
Consultant Pathology Services Pty Ltd T/A Hobart Pathology ABN 64 009 581 159
A subsidiary of Sonic Healthcare Ltd ABN 24 004 196 909

Launceston Pathology 71 Frederick St Launceston TAS 7250 | PO Box 906 Launceston TAS 7250
P: 03 6334 3636 F: 03 6334 2273 | www.launcestonpath.com.au
Consultant Pathology Services Pty Ltd T/A Launceston Pathology ABN 64 009 581 159
A subsidiary of Sonic Healthcare Ltd ABN 24 004 196 909

North West Pathology 21 Brickport Rd Burnie TAS 7320 | PO Box 1080 Burnie TAS 7320
P: 03 6432 8800 F: 03 6432 8885 | www.northwestpath.com.au
Consultant Pathology Services Pty Ltd T/A North West Pathology ABN 64 009 581 159
A subsidiary of Sonic Healthcare Ltd ABN 24 004 196 909