

SA
PATHOLOGY

Newsletter

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Mt Gambier

59
YEARS

Wallaroo

54
YEARS

Port Augusta

45
YEARS

Berri

46
YEARS

We're part of your community

Gawler

35
YEARS

Port Pirie

29
YEARS

Murray Bridge

41
YEARS

Victor Harbor

27
YEARS

Port Lincoln

47
YEARS

Whyalla

50
YEARS

From the inside

From the Executive Director



FEW BUSINESSES TODAY are unaffected by technological change; and this will be keenly felt in health. SA Pathology in particular is in the process of radical change, which is both daunting and exciting as significant change like this occurs once every few generations.

I consider myself privileged to be here at this point in time, as we step into a new future as part of a wider healthcare revolution.

At SA Pathology we are implementing a new electronic pathology laboratory information system (EPLIS), and are about to implement a new track and

robotics technology, which will all work together with the new patient administration system (EPAS) being introduced across our SA hospitals.

The convergence and integration of technologies puts us under pressure to achieve time lines and agreed service benchmarks, but also presents opportunities to embrace change for better patient outcomes.

We now have a chance to improve on the best diagnostic support for all South Australians, ensuring we are there at the right time for the right clinical reason, and to support healthcare professionals making their decisions and tasks easier, resulting in improved care for our patients and the population.

Far from altering our vision, these changes mean we confirm our commitment to enhanced healthcare using tomorrow's tools, including genetic testing and sequencing for personalised care, and in partnerships which will improve delivery of quality pathology services to clinicians.

SA Pathology is investing in the future and we will be there to take our place in the new RAH as it starts to support patients, clinicians and our other hospitals across the state.

Mr Ken Barr

SA Pathology on mobile

Have you used your mobile phone or tablet to visit the SA Pathology web site lately? If you're looking for a test in the Pathology Guide or for a nearby Patient Centre you'll find the site much easier to navigate following our recent upgrade for mobile devices. Visit www.sapathology.sa.gov.au next time you need to know.



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TFT or TSH

When considering thyroid testing consider whether you should request a TFT or a TSH?

A request for TFT allows us to provide you with a fT4 test where the TSH is abnormal or the tests are performed:

- for the purpose of monitoring thyroid disease in the patient; or
- to investigate the sick euthyroid syndrome if the patient is an admitted patient; or
- to investigate dementia or psychiatric illness of the patient; or
- to investigate amenorrhoea or infertility of the patient; or
- you suspect your patient has a pituitary dysfunction or
- your patient is on drugs that interfere with thyroid hormone metabolism or function.

Please include the relevant clinical notes on your request form.

DHEA or DHEA-S

Testing DHEA or its sulphated analogue DHEA-S is conducted to assess adrenal gland function in a variety of conditions including hirsutism in women, adrenal dysfunction and the investigation of adrenal tumours. DHEA-S is more stable than DHEA and can be used interchangeably with DHEA for most clinical situations.

SA Pathology provides routine DHEA-S testing for screening which is covered under the MBS. DHEA screening is not covered under the MBS and will attract an upfront patient fee of \$28.23.

Unless specifically noted all DHEA screening requests will be processed as DHEA-S. ■



Improved detection of maternal GBS

On 6th October we replaced the current culture test for Group B Streptococcus (GBS) with a Nucleic Acid Test (NAT) which detects up to 10% more GBS infections than traditional culture.

What to collect

- Vaginal, rectal and combined swabs are suitable.
- Place swabs in liquid Amies and request GBS NAT screen.

If additional bacteriological testing is required (e.g. because of premature rupture of membranes, maternal fever) the same swab can be used but please also;

- request MCS and
- include clinical information.

Why change?

Two thirds of neonatal GBS infections occur in mothers who tested negative for GBS before delivery. Current laboratory methods lack sensitivity for GBS detection, resulting in a risk to some infants. GBS NAT, a more sensitive test, will improve detection and reduce infection in newborn children.

Sensitivity testing

Prevention of perinatal GBS infection involves administration of IV benzyl-

penicillin/amoxycillin during labour, if GBS is detected. Susceptibility testing is only required for patients with *severe and immediate IgE-mediated allergy* such as anaphylaxis – *please indicate this on the request form.*

Further information

For further information please contact the On Call Microbiologist on (08) 8222 3000. ■

Sterilising equipment safety

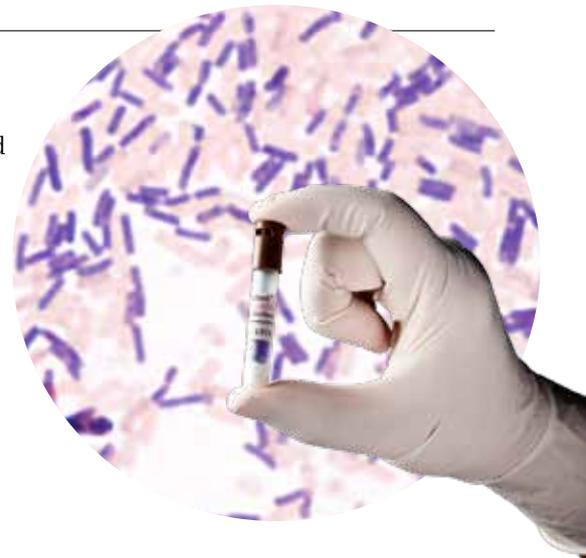
SA Pathology's Food and Environmental Laboratory offers rapid biological indicators (RBI's) to monitor steam units and autoclaves, providing evidence of the proper operation of sterilisation equipment.

Self-contained RBI's contain bacterial spores resistant to the mode of sterilisation being measured. *Geobacillus stearothermophilus* is the highly-resistant spore used to monitor steam, hydrogen peroxide

gas plasma and ozone sterilisation processes. We have recently upgraded our test to provide faster results, in most cases next day.

If you own or operate sterilisation equipment we can help provide the confidence you need to ensure its safe operation.

For more information visit www.sapathology.sa.gov.au/foodlab or phone the laboratory on 8222 3363. ■



New Patient Centres

North Adelaide

Recently relocated to
55 O'Connell Street
Monday to Friday 7:30am to 4:30pm
Saturday 8:00am to 12 noon

Maitland

69 Robert Street, Maitland
Monday to Friday 8:30am to 12 noon

Modbury

Modbury GP Plus
77 Smart Road, Modbury
Monday to Friday 8:30am to 12:30pm

Kensington Park

Specialises in paediatrics
360 Magill Road, Kensington Park
Monday, Tuesday and Thursday
8:30am to 12.30pm

Yorketown

23 Waterloo Bay Road
Monday to Friday 8:30am to 11:30am

Rose Park

24 Kensington Road, Rose Park
Monday, Wednesday & Thursday
8:30am to 12:30pm

Angaston

3-7 Fife Street, Angaston
Monday to Friday 8:00am to 12:30pm
Saturday 8:30am to 11:30am

SA Pathology Patient Centre hours are correct at time of publication.

Please check the website
for the latest updates
www.sapathology.sa.gov.au

New genetics technology improves diagnosis

A significant number of us will be affected by genetically determined diseases in our lives. 2 to 3% of the population will be identified at birth and, by the age of 25, up to 5.5% of the population will have developed a genetic disorder. Later in life, up to 60% of the population is affected by a condition such as cardiovascular disease or cancer in which genetics plays a role.

The diagnostic challenge

Diagnosis of genetic disorders has, to date, been hampered by a number of factors leading to some families experiencing years of delay in diagnosis, the so-called 'diagnostic odyssey'. There are literally thousands of rare genetic disorders, each individually affecting only a small number of people. This means that genetics health professionals may see few or even no cases of some conditions in their working life. A second major challenge has been the vast number of genes potentially involved in a given condition. This often results in the need for consecutive rounds of gene prioritisation and testing, each time excluding another possible cause.

Next-Generation Sequencing

Advances in sequencing technology are now transforming the way genetic disorders are diagnosed. Next-Generation Sequencing (NGS) describes the process by which DNA is fragmented, selectively targeted and sequenced in a massively parallel fashion, producing millions of short fragments which are then reassembled to identify variants in a patient's DNA. The technology breakthrough is the ability to scale this process, so that a full human exome, the full coding sequence of a patient's DNA, can be sequenced in a single run at a cost comparable to that of testing a single gene using traditional technology.

This unprecedented change in processing capacity has resulted in significant advances in genetic pathology. All candidate genes can now be tested at once, significantly reducing the time to diagnosis. Depending on the clinical phenotype, gene analysis can be broad, eliminating the need for health professionals to prioritise a select group of genes for testing. This is a paradigm shift as, for the first time, genetic testing may precede early attempts at clinical diagnosis.

Diagnostic testing

Targeted testing

SA Pathology is also accredited for targeted gene panel analysis using NGS. For conditions with few genetic causes, testing a subset of genes or 'panels' is appropriate, as only the genes known to be associated with a disorder need be tested.

We offer targeted gene panel testing for a number of defined disease phenotypes, including familial cancer, cardiomyopathy and inborn errors of metabolism.

Whole-exome sequencing

SA Pathology has effectively applied whole-exome sequencing to severe paediatric cases including multiple congenital abnormalities, complex neurological and metabolic disorders, developmental delay and intellectual disability.

While many rare genetic conditions don't have an effective treatment or cure, it is often possible to alleviate symptoms with new therapies and help people better manage their disorders. Test results provide information on risk of recurrence in families and can help plan future pregnancies. But for genetically complex conditions, testing the whole exome is appropriate as it avoids the problem of prioritising individual gene targets, and repeat testing if the results are negative.

Past obstacles, new breakthroughs

In the past, challenges for genetic diagnosis included the turnaround time, high cost and the anxiety for patients and families seeking quick answers to complex diagnostic questions.

Genetic testing may now precede early attempts at clinical diagnosis

With NGS, genetic tests can take months, not years, and reduce patient uncertainty as the diagnostic detection rate is much higher than that of traditional testing. With an average 20% increase in genetic tests requests per year, investment in technology and improving throughput has been crucial to meeting clinical need. It also ensures that testing remains accessible to all patients in need.

Collaborative research

SA Pathology is the first laboratory in Australia to receive NATA accreditation for whole-exome sequencing. This achievement resulted from intense collaboration by scientists, technology experts, bio-informaticians, pathologists and geneticists, together with research staff from the Centre for Cancer Biology (CCB) including the CCB's ACRF (Australian Cancer Research Foundation Cancer Genomics Facility), UniSA and Adelaide University. Support for these activities came from eResearchSA and grants from the ACRF and Therapeutic Innovation Australia (TIA).

Referral

Referral for genetic testing is mainly via clinical geneticists, with other medical specialists increasingly requesting access to testing. Given the potential impact of genetic test results on other family members we recommend referral to SA Pathology's South Australian Clinical Genetics Service at the Women's and Children's Hospital in the first instance. ■



SA Pathology in the new RAH

SA Pathology's integration into the new Royal Adelaide Hospital represents generational change that will have significant benefits for patients and health professionals alike.

Not since 1954, when our laboratory functions were extended at the Queen Elizabeth Hospital and established in Mount Gambier and other regional centres, has the expansion of services been so important for our patients and the South Australian population.

SA Pathology's operations will be fully assimilated into the patient care facilities of the new RAH. Allocated 3,500 square metres of laboratory space on Level 3, we will move most of our critical patient care tests to the new site, with features including leading-edge laboratory information systems, automated specimen tracks and robotic technology.

Easily accessed, SA Pathology is located at street level, immediately to the left of the hospital's main entrance. Centrally positioned in the heart of the new hospital, our laboratories sit directly below the array of technical suites (operating theatres) and close to lifts where priority airlifted patients will be brought into specialist treatment areas.

This places SA Pathology operations at the epicentre of hospital activity and highlights the critical role pathology plays in fast diagnosis and timely treatment. The synergy between co-located pathology and hospital personnel, allied with fully integrated analysers and interconnected information systems, will provide a collaborative patient focused service that can supply rapid answers to demanding clinical questions.

SA Pathology has embraced the opportunity to be part of South Australia's major future health initiative.



Senior staff at an early planning session for SA Pathology's new RAH laboratories

Haemoglobinopathy on the increase?

ADRIAN GRIFFITHS

In South Australia in the 60s, 70s and 80s haemoglobinopathy (thalassaemia or variant haemoglobins) was predominantly a condition associated with people of Greek or Italian origin. Awareness in these communities of the risk of having an affected child (and appropriate prenatal testing) resulted in a dramatic reduction in children being born with more severe forms of haemoglobinopathy.

In recent times, due to increasing immigration of other ethnic groups, there has been a re-emergence of the more severe forms. In 2008 the World Health Organisation in its bulletin "Global epidemiology of haemoglobin disorders and derived service indicators" estimated that in Australia and New Zealand the number of pregnancies at risk of disease was 351 per annum, (approximately 20 in South Australia). Data from the Australian Bureau of statistics show a sustained increase in permanent migration to SA of people from areas with higher rates of haemoglobinopathy.

Haemoglobinopathies

Thalassaemias and variant haemoglobins are inherited disorders. Some result in decreased synthesis of globin chains, and these are termed 'thalassaemic'; others, the variant haemoglobins, have altered physicochemical properties the best-known example being HbS, which is associated with sickling crises in the homozygous (HbSS) form or, if co-inherited, with beta (β) thalassaemia or HbC.

The most severe syndromes occur when all α -globin genes are mutated (hydrops fetalis) or both β -globin genes (thalassaemia major). In general, the inheritance of multiple mutations in the same gene family results in more severe syndromes (like sickle cell disease or beta thalassaemia intermedia or major), whereas the co-inheritance of α and β mutations together often results in a less severe condition than either mutation on its own.

Laboratory testing

Complete blood examination (CBE)

The marker of most interest to the laboratory, when considering thalassaemia, is the mean corpuscular haemoglobin (MCH). Generally thalassaemia is associated with a low MCH and often, but not always, a low mean corpuscular volume (microcytosis). The mean corpuscular haemoglobin concentration (MCHC), is an indicator of hypochromasia, and is generally normal in thalassaemia unless there is a co-existing iron deficiency or chronic inflammatory disease.

Usually the red cell parameters are normal for patients with sickle trait and in some cases with sickle disease, however, sickle cells may be observed on the blood film.

Haemoglobin studies

SA Pathology currently uses High Performance Liquid Chromatography (HPLC) to detect and quantify normal and variant forms of haemoglobin. Total haemoglobin consists of three main components Hb A, HbA₂ and HbF. At birth the proportions of haemoglobins A, A₂, and F are approximately 29-34%, 1-1.5% and 65-70% respectively (Figure 1a).

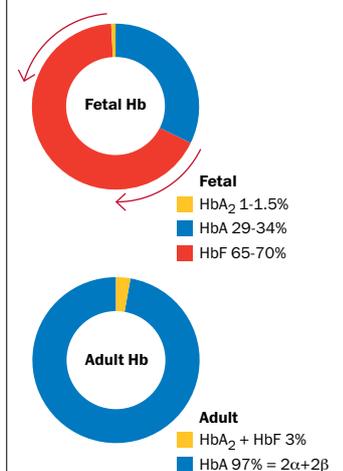
CBE is an important screening tool and often, but not always, provides a clue to diagnosis

Table 1 Top 10 source countries SA 2012-2013

Birth country	Born here	Born overseas	Total
United Kingdom	911	1732	2643
India*	922	921	1843
China*	512	917	1429
Philippines*	399	508	907
New Zealand	41	252	693
Sri Lanka*	229	273	502
Iran*	190	302	492
Malaysia*	0	470	470
South Africa	217	201	418
Afghanistan*	134	284	418
Other	1849	3204	5053
Total	5880	9064	14944

*regions where haemoglobinopathies are endemic

Figure 1 HbF to HbA conversion



HbF starts converting to HbA shortly prior to birth and normally reaches adult levels at around 9 months of age

The switch from fetal to adult haemoglobin starts in the perinatal period and approaches adult levels at around 9 months of age (Figure 1b). For this reason detecting beta thalassaemia and beta haemoglobin variants before the age of 9 months may not be possible.

Haemoglobin variants

Common β -globin variants S, E, C and D and some rare α -globin variants such as Constant Spring are detectable using HPLC.

HbS (sickle cell) is endemic in West Africa and in Afro-Caribbean populations around the world (Figure 2). S is also seen in people of Arabic ethnicity. HbE trait is common in South-East Asia but is clinically insignificant and even in the homozygous state (HbEE) it tends to be mild. It is of more concern when co-inherited with β thalassaemia. HbC is another variant that can cause significant disease when co-inherited with HbS or beta thalassaemia. Whilst less common than S or E, it is more frequent in populations from western Africa, Oman and Thailand.

Thalassaemia

Thalassaemia is more difficult to diagnose than the variant haemoglobins.

Beta thalassaemia

Most carriers of β thalassaemia trait will have increased HbA₂, but there are rare situations where the HbA₂ is normal, these include severe iron deficiency and hypothyroidism. Beta thalassaemia is common around the Mediterranean (southern Europe and North Africa), on the Indian subcontinent and amongst populations from Africa and South East Asia.

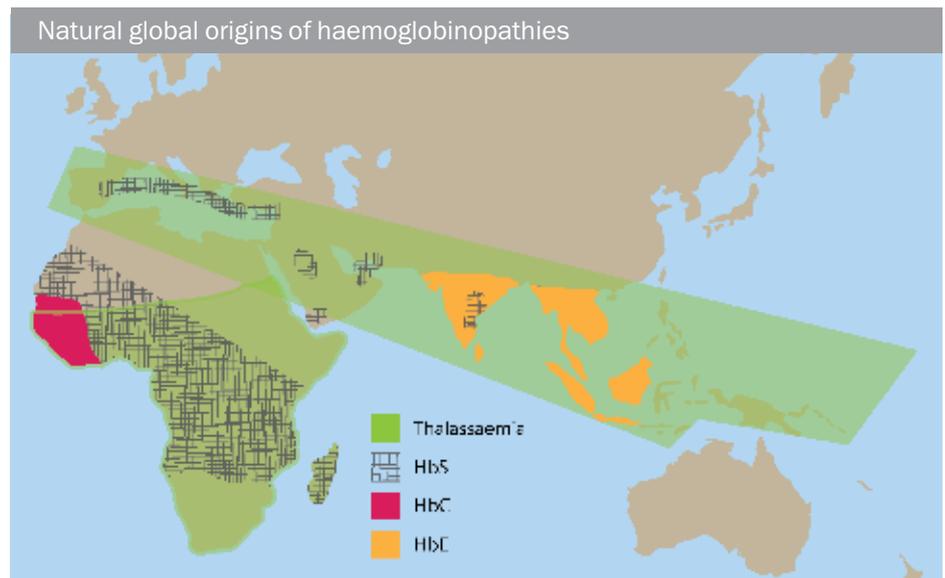
Did you know?

Hyperthyroidism, particularly in those with Grave's disease, can mimic beta thalassaemia trait.

Alpha thalassaemia

The severity of α thalassaemia depends on the number of genes deleted. HPLC is usually normal

Figure 2 The 'malaria belt'



in α thalassaemia which in most cases requires genetic testing for diagnosis and is mostly reserved for prenatal/antenatal testing.

4 gene deletion (hydrops fetalis) is associated with spontaneous miscarriages and fetal death. If a fetus does survive to delivery it invariably dies shortly after birth.

3 gene deletion (HbH disease) produces a syndrome of varying severity, depending on the specific mutations. Severe cases may be transfusion-dependent, but most have milder degrees of anaemia.

2 gene deletion (thalassaemia trait) is benign, with microcytosis, but has no clinical consequences for the carrier. Its importance lies in the risk of a more severe syndrome in children of a carrier.

1 gene deletion can be associated with normal red cell indices.

When to screen?

Screening is recommended in the following situations.

- Women planning pregnancy or currently pregnant with:
 - low MCH (with or without microcytosis)
 - family history/partner history of haemoglobinopathy

- familial origin/partner familial origin from a region where haemoglobinopathy is endemic.

Partner testing is highly recommended if screen positive or suggestive of haemoglobinopathy.

- All other patients with unexplained persisting low MCH (with or without microcytosis) i.e. iron replete, normal thyroid functions and no evidence of chronic disease.

What to request

CBE, iron studies (if the status is unknown – this information is very important to the laboratory when interpreting results) and haemoglobin variant analysis.

Clinical notes are always important when requesting any pathology test and particularly so for haemoglobinopathy, *please include partner history*. ■

Did you know?

➔ A patient with recently resolved iron deficiency may have a microcytic, hypochromic blood picture for up to four months after starting iron therapy. Red cell indices gradually return to normal as circulating microcytic cells are replaced by normocytic red cells. Unless there is some urgency (e.g. in pregnancy) it is better to delay haemoglobinopathy testing for several months after correction of iron deficiency.

Vitamin B12 Deficiency:

Active B12 Assay

DR MOHAMED SALEEM

Vitamin B12, also called cobalamin, plays a fundamental role in the formation of blood and the normal functioning of the brain and nervous system. The true prevalence of B12 deficiency in the Australian population is unknown, although studies suggest that it may be as high as 23%. The incidence appears to increase with age (>65 years) and also with the ubiquitous use of gastric acid-blocking agents. Symptoms of deficiency may be ill defined and a high index of suspicion is required for testing.

Symptoms

B12 deficiency can interrupt key biochemical pathways disturbing DNA synthesis resulting in megaloblastic anaemia and adverse effects on the nervous system and other organs.

A full blood count which shows anaemia and macrocytosis has traditionally prompted investigations for B12 deficiency. The presence of oval macrocytes and hypersegmented neutrophils (figure 2) has been considered to be of high diagnostic accuracy although there are other non-specific causes for this finding (e.g. iron deficiency anaemia). If untreated, deficiency may lead to severe anaemia and a broad range of neurological symptoms including peripheral neuropathy, irritability, tiredness and mild deterioration of memory and cognitive ability.

Importantly, B12 deficiency may present without any haematological abnormalities at all. Severe deficiency causes subacute combined degeneration of the spinal cord. In pregnancy, maternal B12 deficiency is associated with neural tube defects in infants and deficiency in childhood is associated with developmental delay and failure to thrive.

Impaired DNA synthesis may also affect other rapidly dividing cells causing glossitis, gastrointestinal symptoms and infertility.

Causes

Absorption of B12 requires:

- adequate gastric acid
- intrinsic factor
- and a functional terminal ileum.

Deficiency is most commonly seen in:

- pernicious anaemia where autoimmune destruction of gastric parietal cells causes a concurrent loss of intrinsic factor
- total or subtotal gastrectomy and gastric bypass procedures
- exocrine pancreatic failure
- loss or disease of the terminal ileum (impedes absorption of B12)
- intestinal bacterial overgrowth (may consume B12).

Deficiency may also occur at times of increased requirement such as in pregnancy and during lactation.

Who to test?

Patients with symptoms or signs of B12 deficiency including anaemia (macrocytic anaemia or macrocytosis) and patients with suspected neuropsychiatric abnormalities should be tested for B12 deficiency.

Other groups where testing may be considered include the elderly, long-term vegans, patients who abuse alcohol, people on drugs that interfere with B12 absorption (such as long-term H2 receptor antagonists, proton pump inhibitors or metformin) and patients with inflammatory bowel disease, gastric or small intestine resection.

Up to 30% of patients with B12 deficiency may show total serum B12 levels in the lower normal range

B12 deficiency due to poor nutrition is rare, particularly given the small daily requirement (1-5 mg/day) and its abundant presence in animal products. Populations at risk for nutritional deficiency include the elderly with a poor intake of meat and dairy products, chronic alcoholics and strict vegans.

Laboratory testing

Serum B12 is bound to two major carrier proteins;

- 1 Transcobalamin I, also called Haptocorrin (HC) binds to the major portion of plasma B12. This complex is *not active* in delivering B12 to cells.

2 Transcobalamin II binds to B12 forming a complex called holotranscobalamin (holoTC, commonly referred to as active B12). This complex is *active* in delivering B12 to cells. (Figure 1)

Serum B12

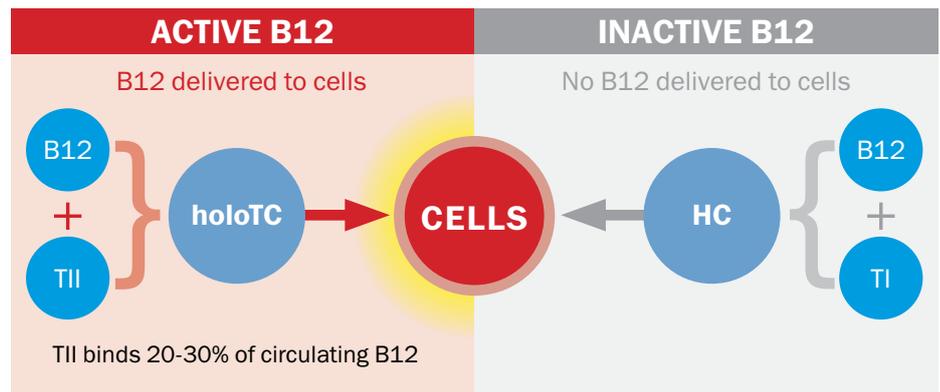
Total Serum B12 is the most common test of B12 status and measures the sum of inactive (HC) and active B12 (HoloTc). In clinical situations where there is a significant change in the inactive fraction total serum B12 may not reflect tissue status. Inactive B12 is decreased in pregnancy and oestrogen therapy but may be increased in renal failure and haematological malignancies. Therefore tissue deficiency (of active B12) may occur despite apparently normal serum total B12 levels and vice versa. Up to 30% of patients with B12 deficiency may show total serum B12 levels in the lower normal range.

Active B12

Active B12 levels give a better indication of the B12 available for tissue use. Levels ≤ 30 pmol/L are considered to be deficient; in a minority of patients levels above this may still be associated with tissue deficiency. Patients in whom there is clinical suspicion of deficiency may benefit from homocysteine or methylmalonic acid analysis.

To assist diagnosis within the low-normal total serum B12 group, SA Pathology will automatically perform an active B12 on all samples with total B12 levels < 260 pmol/L.

Figure 1 B12 binding



Active B12 levels give a better indication of B12 status

True deficiency is very unlikely above this level.

Intrinsic Factor and Parietal Cell Antibodies

Intrinsic Factor Antibodies (IFA) and Parietal cell antibodies may be helpful in supporting a diagnosis of pernicious anaemia. Whilst the presence of IFA is virtually diagnostic of pernicious anaemia, they are detected in only about 50% of cases and B12 treatment can cause false IFA negatives.

Homocysteine

A normal plasma homocysteine makes B12 deficiency unlikely; however it has limited specificity because elevations occur in inherited and acquired disorders, including folate and pyridoxine (B6) deficiency and particularly in patients with chronic kidney disease.

Poor conversion of homocysteine to methionine in B12 deficiency may cause an elevated fasting plasma homocysteine level.

Methylmalonic acid (MMA)

Like homocysteine, MMA also has poor specificity as elevations may occur in rare inherited disorders and in chronic kidney disease.

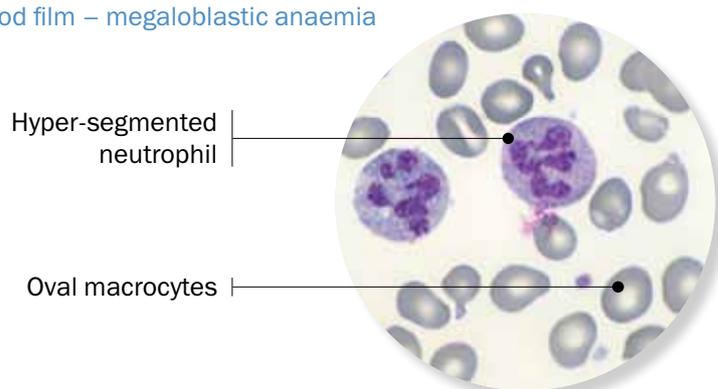
Poor conversion of methylmalonyl Coenzyme A to succinyl Coenzyme A in B12 deficiency may cause an elevated serum level of MMA.

In the absence of these conditions a significantly elevated MMA strongly supports B12 deficiency.

Summary

- B12 deficiency is common.
- Symptoms may be ill-defined and a high index of suspicion is necessary to test.
- B12 exists as *active* and *inactive* forms in the blood.
- Total serum B12 assay measures active and inactive forms and is thus prone to false positives and negatives.
- An active B12 assay measures only the active form and is superior for detecting deficiency.
- SA Pathology uses active B12 to confirm deficiency when the total serum B12 result is in the borderline low range. ■

Figure 2 Blood film – megaloblastic anaemia



Multi-drug resistant aspergillosis infection

Globally, the number of life-threatening fungal infections and the death toll associated with them is just as high as for tuberculosis or malaria. *Aspergillus fumigatus* is the most common species of fungus to cause disease in individuals with an immunodeficiency. Multi-triazole resistant aspergillosis has been emerging in Europe, Africa, and Asia over the past decade but until this study had not been reported in Australia.

The importance of SA Pathology's National Mycology Reference Centre research was highlighted for international delegates at a recent conference on fungal infections in Melbourne. Dr Sarah Kidd published the work of her team in the journal *Mycoses*, describing how strains of the common opportunistic fungus *Aspergillus fumigatus* that are resistant to first-line treatments such as triazole antifungal drugs, have been identified for the first time in Australia.

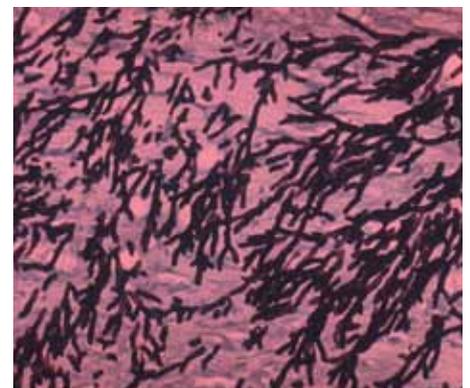
The resistance has been attributed to a range of point mutations in the *cyp51A* gene of the fungus, leading to amino acid substitutions in the protein targeted by the triazoles. Mutations have been identified in environmental isolates as well as those from azole-naïve patients.

European researchers believe that the high rate of drug-resistant strains has evolved in the environment in response to the extensive use of fungicidal sprays used in agriculture. For example, the bulbs of tulips grown commercially in Holland for export are dipped in fungicides to preserve them.

Other point mutations have also been characterised in clinical *A. fumigatus* isolates, however their relationship to agricultural fungicides is yet to be clarified.

The Australian picture

In 2009, a 12-month prospective international surveillance study, which included one Melbourne tertiary hospital, found no evidence for triazole resistant *A. fumigatus* in that hospital. However, one isolate of *Neosartorya pseudofischeri*,

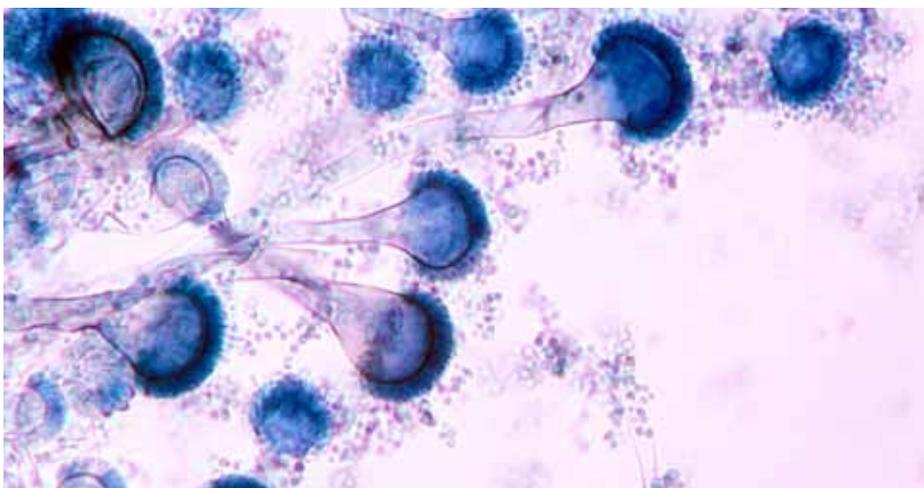


Aspergillus fumigatus

a closely-related, morphologically similar, 'sibling species' with inherent resistance to the triazoles, was identified.

More recently a retrospective examination by the National Mycology Reference Centre of *A. fumigatus* species antifungal susceptibility data, collected between 2000 and 2013 identified thirteen isolates with an elevated minimum inhibitory concentration to one or more of voriconazole, posaconazole, or itraconazole. Further analysis of these isolates revealed two that carried the same fungicide-associated *cyp51A* resistance mutations seen in Europe.

These two isolates were from invasive aspergillosis patients from Sydney in 2004 and Melbourne in 2012. The 2004 case had no known travel history and almost 8 years of exposure to itraconazole prior to *A. fumigatus* isolation, while the 2012 case had recently travelled to Europe.



Photomicrograph of *Aspergillus* infection in human tissue

Four isolates had other mutations conferring triazole resistance. Three isolates had no resistance-associated *cyp51A* mutations and resistance was presumably mediated by as yet undiscovered mechanisms. Another four isolates were definitively identified as *A. lentulus*, another closely related triazole-resistant member of the *A. fumigatus* complex.

Nation-wide prospective surveillance for triazole-resistant *A. fumigatus*, including environmental surveillance, is lacking, but will be important to accurately assess the scale of the triazole resistance problem in Australia.

Australia does use triazole-based pesticides in agriculture and is not immune to the antifungal resistance problems encountered in other parts of the world. Given that triazole resistant isolates are associated with mortality rates up to 88% higher than susceptible isolates, Australian clinical practice needs to take this into account.

Request antifungal susceptibility testing for all clinically significant *Aspergillus* isolates

Who's at risk?

People most at risk of infection include those with weakened or compromised immune systems, transplants patients or those suffering from various types of cancer. *Aspergillus fumigatus* is the most prevalent cause of invasive mould infections in the haematology and solid organ transplant setting. Australian treatment guidelines recommend the use of triazole antifungals, particularly voriconazole, for first-line treatment of invasive aspergillosis.

Dr Kidd's recent research has discovered some aspergillosis infections are caused by strains resistant to the whole class of drugs usually used to treat them.

Recommendations

Based on increasing identification of triazole resistant *A. fumigatus* globally, and coupled with this new evidence for both local and a probably imported fungicide-associated aspergillosis case, we recommend Australian clinicians be alert to the possibility of infection with triazole-resistant *Aspergillus* species including inherently resistant sibling species such as *A. lentulus* and *N. pseudofischeri*.

Definitive species identification and antifungal susceptibility testing is recommended for all *Aspergillus* isolates from patients at risk for invasive fungal diseases, especially in cases where the patient has recently travelled overseas or has been taking antifungal drugs for long periods. ▣

RURAL ROUNDUP

50 years in Whyalla

With its state-wide network of laboratories SA Pathology has a long history of supporting and working in regional South Australian communities. In August we celebrated 50 years of service to the people of the west coast from our Whyalla laboratory.

During the 1950's and 60's, regional centres in SA saw hospital services boosted to cater for the influx of new workers, and in response IMVS (now SA Pathology) established a laboratory in Whyalla in 1965.

Originally operating from a room in the nurses' home, it was run by a handful of staff, analysing a few thousand samples annually. Within five years the lab was processing over 40,000 tests a year.

Much has changed over fifty years and SA Pathology took the opportunity to reflect on the achievements of staff past and present at a recent local celebratory dinner. What has remained constant is the commitment of SA Pathology and its staff to both the population and the medical community of the west coast.

Today two out of every three tests are performed in Whyalla itself ensuring results are readily and rapidly available, with the remaining third conducted in our main laboratories in Adelaide. Speaking at the dinner, past Director of both IMVS and Whyalla Hospital Professor Brendon Kearney said it was this level of crucial clinical support that made possible services like the hospital's cancer hub.

Whyalla joins our Wallaroo and Mt Gambier laboratories with 50 years of regional service.

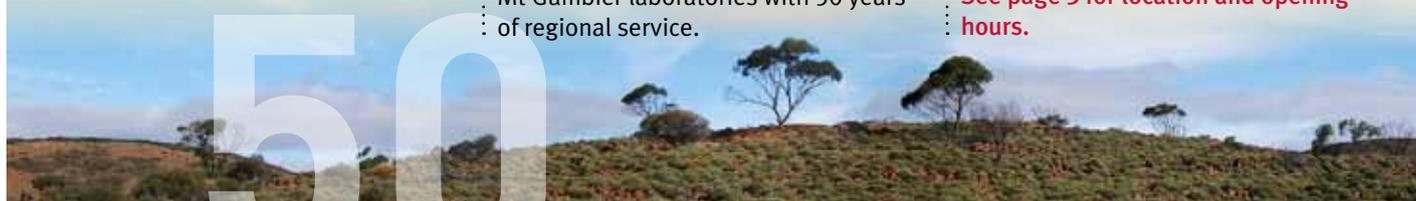
Field Days

The Yorke Peninsula Field Days at Paskeville are always a big event on the country calendar, in fact it is the largest regular agricultural event in the nation, and SA Pathology was there.



Maitland

Maitland has a new patient centre. See page 3 for location and opening hours.



Influenza and other Respiratory Pathogens

update

The winter of 2015 saw yet another big influenza season here in South Australia with the unprecedented dominance of the Influenza B virus.

The latest *Australian Influenza Surveillance Report* states that, whilst remaining within the range of previous seasons, influenza-like illness activity is increasing.

Influenza notification rates have been highest among those aged between 5 and 9 and over 85 years with a secondary peak in those aged 40 to 44 years.

Several other respiratory pathogens have also been active including Respiratory Syncytial Virus (RSV), Parainfluenza, Rhinovirus, Metapneumovirus, Adenovirus and *Bordetella pertussis*. Table 1 lists all respiratory viral activity reported by SA Pathology (including *Mycoplasma pneumoniae* and *Bordetella pertussis*) both in the recent week and year to date.

Figure 1 Australia Influenza typing data (WHO Influenza Centre)

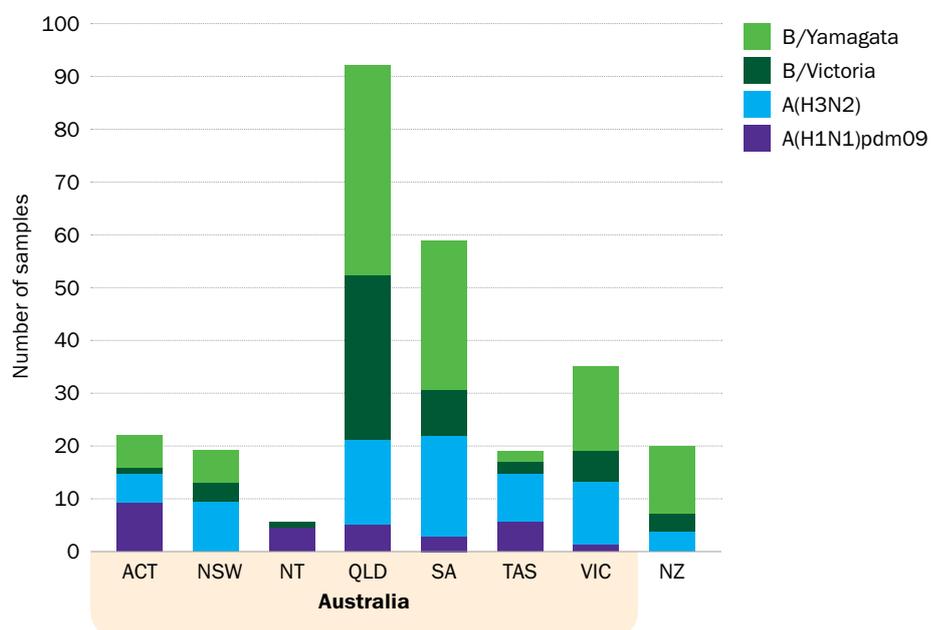


Table 1 Respiratory viral and bacterial pathogens

Respiratory pathogen	Week ending 04/10/15	Year to date 2015
Influenza A	218	4127
Influenza B	156	5033
RSV	37	4156
Parainfluenza 1	1	38
Parainfluenza 2	2	319
Parainfluenza 3	83	1533
Adenovirus	61	1429
Metapneumovirus	140	1886
Rhinovirus	261	9263
<i>M pneumoniae</i>	47	642
<i>B pertussis</i>	10	292

VACCINATIONS

The seasonal influenza vaccines for 2015 appear to be a good match for the circulating strains. However approximately one-quarter of influenza B viruses tested are due to a lineage not contained in the trivalent seasonal vaccine (TIV).

The WHO recommended the following vaccine compositions for the southern hemisphere winter of 2015.

Trivalent vaccines:

- an A/California/7/2009 (H1N1)-like virus
- an A/Switzerland/9715293/2013 (H3N2)-like virus
- a B/Phuket/3073/2013-like virus (Yamagata lineage)

In addition to the above Quadrivalent vaccines contained a B/Brisbane/60/2008-like virus (Victoria lineage).

SA Pathology enquiries

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