



PathWay

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA



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Issue #015

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Welcome to the June edition of ePathWay

It's the flu season and Dr David Smith tells us why the influenza virus still demands respect. Dr Penny Coates outlines the correct use for tumour markers, while Dr Raymond Chan and Dr David Ellis cover some of the behind-the-scenes activities that Pathologists participate in to make sure they are delivering the safest and most comprehensive service possible.

Pathology is an 'invisible' activity to the majority of people, yet it reaches in to so many lives. The pathology result that is presented to patients by their treating doctor is actually the product of a quality assured process delivered by highly trained Pathologists. In fact, the behind the scenes work of Pathologists astonished a film producer in the US, and Dr David Ellis explains why!

We welcome your feedback about the stories covered in ePathWay and hope you find it an invaluable way of being kept up to date about pathology in Australasia.

Interesting Facts

50 million

The approximate number of deaths worldwide from the 1918-1919 Spanish flu pandemic, compared with the worldwide total of about 10 million military personnel and seven million civilians killed during World War I (1914-1918)

2 million

The approximate number of deaths worldwide from the 1957-1958 Asian flu pandemic

Influenza viruses still command R.E.S.P.E.C.T



Influenza is an acute infectious disease caused by several closely related influenza viruses. It kills between 250,000 to 500,000 people worldwide each year, many more in pandemic years, and when people develop immunity to a particular strain it can then 'drift' to a different strain. No wonder the medical community treats these viruses with respect.

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1 million

The approximate number of deaths worldwide from the 1968-1970 Hong Kong flu pandemic

Sources: Australian Government Department of Health and Ageing; Wikipedia

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Look who's talking!

Medicine can seem like a segmented profession to patients. They might see their primary clinician at one place, have their x-ray someplace else, and go to yet another room to have a pathology test. And throughout this process they might only see one doctor face-to-face. What they don't see are the Multidisciplinary Case Conferences (MDCCs) that happen regularly amongst the medical profession where teams of doctors meet to discuss complex medical cases.



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Australia's pathology laboratories process millions of pathology tests each year. Most of these tests are processed in accredited laboratories which have quality assurance (QA) processes in place that are studied and copied around the world. In short, we're simply the best when it comes to laboratory QA.



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"Influenza is the most serious respiratory virus disease in the world and causes more deaths and illnesses than any of the other respiratory viruses," explains Dr David Smith, Pathologist and Clinical Microbiologist at PathWest Laboratories in Western Australia. "And the nature of the influenza virus means it changes regularly so we never really become immune to it."

These changes, or mutations, make the virus a moving target for Pathologists to track and classify, although they do have worthy victories.

"When the 2009 Swine Flu pandemic happened in the US and Mexico, we knew the sequence of the virus, which tests we would need to test for it, and we had a new test ready to go within two weeks of being sent the information about the virus. This meant we were ready to detect that virus before it even got here."

So how does influenza spread itself around?

Dr Smith says the influenza virus is typically spread by coughs and sneezes when droplets of infected fluid are sprayed through the air. It can also spread by people touching surfaces infected with droplets of infected fluid which then gets onto their hands and eventually finds its way into their respiratory tract. Once a person has influenza they can become very sick.

"People often the say they have 'the flu' when they probably have a milder respiratory illness, because influenza typically causes high fever, sore throat, cough and aches. That's when people start to say things like they 'feel like death warmed up'."

Another aspect of the influenza virus is its ability to worsen preexisting conditions such as heart disease, respiratory disease, diabetes and other chronic illnesses, so that patients are more likely to become seriously ill or die. It can also lead to bacterial pneumonia by damaging the lung's defences.

Dr Smith says testing for influenza is essential to control its spread in the community and in hospitals, such as isolating those with the virus, and to help guide decisions about

early treatment with antiviral medications. Testing for the virus is also a vital part of the World Health Organization (WHO) program to monitor how the virus changes, and to decide how the vaccines need to change.

"Pathologists can run tests to detect the influenza virus, tell which type it is, and then determine if it is a strain of an existing circulating virus or a new strain," he says.

The major types of the influenza viruses are A, B and C, though influenza C is a minor player compared with the other two. Influenza A viruses are usually the most virulent and are also classified into subtypes differentiated on the basis of two surface proteins (antigens) called haemagglutinin (H) and neuraminidase (N). For example, H1N1 caused the Spanish Flu in 1918 and the Swine Flu in 2009, while H5N1 caused the Bird Flu in 2004.

While pandemics happen occasionally, the annual threat from influenza should not be sneezed at. It is constantly monitored by the WHO and is the only respiratory virus to have its own medical therapies - the influenza vaccine¹ and antiviral drugs. And since it is capable of constantly changing, rapidly spreading and still leads to death and serious illness, everyone should treat influenza and the 'flu season' with caution and respect.

¹ How the flu brew is made http://epathway.rcpa.edu.au/previous/003_0511.pdf

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Associate Professor David Ellis, Anatomical Pathologist at the Flinders Medical Centre in Adelaide, says MDCCs ensure the lines of communication remain open amongst doctors, and that everyone is 'on the same page' with regards to the diagnosis and treatment of a patient with a major disease. It is also an opportunity for the primary clinician to closely examine the pathological and radiological evidence.

"These are dynamic meetings which are very important for patient care," he explains. "What people should know is that there is a lot of work happening in the background where multidisciplinary teams of specialists review cases and think very hard as a group to bring each patient into sharp focus with regards to the diagnosis and possible treatment paths."

A/Prof Ellis says Pathologists are key players in these meetings and spend a lot of time reviewing and preparing cases for them. This usually involves some hours of preparatory work and an hour or so at the MDCC for which there is limited remuneration.

"Often, as we sit in these meetings, I find myself wondering if the patients have any idea of the thought and discussion which is going on behind the scenes."

A/Prof Ellis says MDCCs are also an important part of the quality assurance (QA) process because it's usually a different Pathologist who reviews and prepares the cases for these meetings from the one who performed the initial work. Once the MDCCs are in progress, he says Pathologists' input is especially important when reviewing cancer cases since they provide the critical information including the type of tumour, the grade or aggressiveness of the tumour and the extent of spread or stage of the tumour. In short, the Pathologist provides the 'diagnosis' which then determines the best treatment for the patient.

"There is a famous soft tissue Pathologist in America who was involved in a filmed documentary about a patient with a soft tissue sarcoma," recalls A/Prof Ellis. "The producer and crew were filming the MDCC while the patient's pathology and diagnosis were being discussed by this leading Pathologist. In the middle of the meeting the film producer exclaimed to him: 'Oh my God! Pathologists are the ones that actually make the diagnosis!'"

A/Prof Ellis says this anecdote illustrates the importance of the 'unseen' role of Pathologists in medicine.

"Not many people realise that an anatomical pathology examination of a pathology specimen is actually a medical consultation where the Pathologist is consulted by another doctor. They give the Pathologist clinical information and the Pathologist interprets the many pathology findings in light of the clinical history and other information. The Pathologist then works out the likely disease process and formulates a diagnosis," he explains.

"Obtaining the correct clinical and imaging information about a patient is absolutely essential if we are to make the right conclusions and get the diagnosis right. MDCCs are especially important because on rare occasions a review of the clinical findings and imaging results in conjunction with the pathology can lead to a completely revised diagnosis and treatment pathway."

Patients don't usually see Pathologists in the course of their treatment, and other medical professionals deliver the results of their expertise to patients, but when groups of doctors gather in MDCCs it's very clear who's talking, and that medicine IS pathology.

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Tumour markers seem to be one of those tests where the expectation exceeds the reality. When considered alone they are not enough to show a cancer is present because they can also be elevated by non-cancerous diseases. The question is what are they good for?

"Tumour markers are best used to monitor a known diagnosis of cancer, especially if the marker was high at the time of diagnosis," explains Dr Penny Coates, Chemical Pathologist at IMVS in South Australia. "Unfortunately people seem to think they can ask for these tests to detect something early but this isn't the case."

Tumour markers are substances that can be found in the body when a cancer is present. They are usually a protein released by the tumour that can be detected in the blood. However, Dr Coates says they are not an effective screening test because the same or similar proteins can also be produced by normal tissue.

"They are useful tests for following up a known disease such as cancer but not for screening for that disease."

Dr Coates says there are two issues to consider with tumour markers: how sensitive they are and the interpretation or specificity of the tests.

"Tumour markers only pick up about 80% of cancers so it's possible to be falsely reassured or falsely alarmed. Sometimes they only become elevated quite late in the course of a disease," she explains. "If the result is positive then is it cancer or some other non-cancerous condition? For example, CA125 is used to monitor ovarian cancer but it can also be elevated due to ovarian cysts or ascites [fluid collected in the belly]. So this doesn't help to distinguish a cancerous condition from a non-cancerous condition."

Dr Coates says the most commonly used tumour markers are:

- Carcinoembryonic antigen (CEA) for colorectal cancer
- CA125 for ovarian cancer
- CA19.9 for gastric/pancreatic or stomach cancer
- CA15.3 for breast cancer.

To test for a tumour marker a blood sample is usually sent to the pathology laboratory for analysis. Tumour markers can also be present in urine or other body fluids which can also analysed at the pathology laboratory. When the pathology result confirms these markers are elevated, they must also be considered along with the patient's history, physical examination and other laboratory and/or imaging tests.

"It's important to remember they are useful tests for following up a known disease, such as cancer, but are not useful tests for screening," reiterates Dr Coates. "A negative result does not necessarily rule out disease as some tumours don't release markers and some don't do so until very late in the course of the illness."

When tumour markers are used correctly they are less likely to suffer from the great expectations currently attributed to them, and can take their rightful place as useful tests to monitor a known diagnosis of cancer.

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Dr Raymond Chan, Pathologist and Clinical Microbiologist at the Royal Prince Alfred Hospital

Australia's pathology laboratories process millions of pathology tests each year. Most of these tests are processed in accredited laboratories which have quality assurance (QA) processes in place that are studied and copied around the world. In short, we're simply the best when it comes to laboratory QA.

"There is an assumption that pathology tests and reports are always correct but I don't think many people give much thought to how this happens," says Dr Raymond Chan, Pathologist and Clinical Microbiologist at the Royal Prince Alfred Hospital. "However, they should be aware that there is a system of controls in place to ensure the quality of the testing and the results are as good as they can be."

Dr Chan says Australian pathology laboratories must adhere to a legislative framework to be reimbursed by Medicare for performing pathology tests. This framework includes the requirement that the laboratory is accredited by the National Association of Testing Authorities (NATA)¹ and the Royal College of Pathologists of Australasia (RCPA) who jointly inspect and review individual laboratories every three years.

"If they think there is a problem then NATA/RCPA may insist on additional requirements inside of that three year time frame," he says.

Pathology laboratories must also have a quality system in place that demonstrates how key elements that may impact on the quality of the whole pathology-testing pathway have been actively reviewed and any deficiencies addressed. But the QA requirements don't end there.

"Laboratories must also participate in external quality assurance processes² where samples are blinded to participating laboratories. They process these samples and the results are checked across all laboratories to monitor the entire accredited laboratory system," explains Dr Chan.

The key word when it comes to quality standards is 'accreditation.' This is because pathology laboratories which don't expect to be reimbursed by Medicare for their tests are not required to participate in any accreditation or quality assurance procedures. So how do you know which labs are accredited?

"Look for the NATA and RCPA logos on the laboratory documentation, or in the collection rooms, or just ask the laboratory staff. They will usually display their accreditation

status because it is considered a 'badge of honour'," advises Dr Chan.

Another way to check a laboratory's status is to go to the NATA website (www.nata.com.au) which lists currently accredited medical testing laboratories (under the Facilities and Labs tab).

"Australia is recognised as a world leader in the area of laboratory quality assurance," says Dr Chan. "If a person has a pathology sample tested at an accredited Australian laboratory, then they can be confident it will be a good result in terms of quality."

¹ International Accreditation New Zealand (IANZ) accredits laboratories in the same fashion as NATA in Australia. For more information go to www.ianz.govt.nz.

² RCPA Quality Assurance Programs (RCPA QAP Pty Ltd) offer a broad range of external quality assurance programs across all disciplines of pathology to support the scientific and medical communities in Australia, New Zealand and overseas countries.

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