



PathWay

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA



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Issue #030

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Introduction

Congratulations to Dr Annabelle Farnsworth who has received an Honorary Fellowship to the Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Our story on Dr Farnsworth highlights why this honour is well deserved.

We have also noted two important events – Haemophilia Awareness Week (13-19 October) and Be Medicinewise Week (14-20 October) – with articles on haemophilia and the importance of monitoring digoxin medicine levels.

Our final article gives a round up of botulism in the wake of the botulism scare that happened in New Zealand earlier this year (and we haven't left Botox out of the story!).

We would also like to thank outgoing RCPA president Professor Yee Khong for his valuable contribution to the college in this important role over the past two years, and welcome incoming president Professor Peter Stewart.

Thankyou to all of the people who have 'liked' our Facebook page – we've reached 200 likes. If you haven't done so yet, or want to join the online pathology community, then go to www.facebook.com/TheRoyalCollegeOfPathologistsOfAustralasia, or follow our CEO Dr Debra Graves (@DebraJGraves) or the College (@PathologyRCPA) on Twitter.

Interesting Facts

3,792,517

The number of Australian women who had a Pap smear between 2009-2010

RCPA Fellow's significant contribution to womens' health recognised by RANZCOG

20,104

The number of Australian women in the target age range (20-69) with high-grade abnormalities detected by the National Cervical Screening Program

40 percent

The reduction in the incidence of cervical cancer in New Zealand since the National Cervical Screening Programme was established in 1990

Sources: Australian Government Department of Health and Ageing, New Zealand Ministry of Health



Dr Annabelle Farnsworth's invaluable contribution to gynaecological pathology, and in particular gynaecological cytology, as well as her commitment to improving the health of all women in Australasia have been recognised with an Honorary Fellowship of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG).

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Being medicine wise is important when you are dealing with Deadmen's bells

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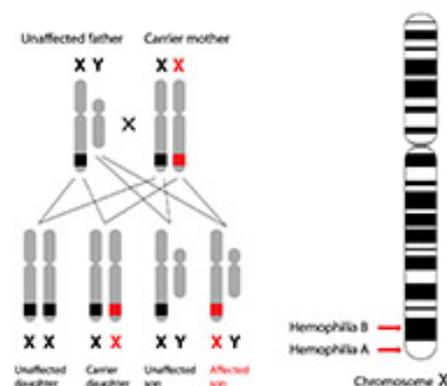
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Haemophilia Awareness Week promotes awareness and busts myths about bleeding disorders

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A recent botulism scare in New Zealand focused attention on this rare but potentially fatal disease. The issue arose when 38 tonnes of whey protein (destined for products such as infant milk formula) produced by a dairy co-operative was suspected of being contaminated by the bacterium that causes botulism. Tests have since confirmed the contaminant was a different bacterium, but what is botulism, and how is it related to Botox?



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- Bladder cancer on the agenda at important scientific meeting
- 'Stay in bed day' raises awareness about mitochondrial disease
- Look out for 'surprises' lurking at the bottom of the

Introduction

We've seen the anti smoking ads, heard the slogans and know that smoking is a health nightmare. But just when you think there's nothing more to learn about it, we asked Dr Andrew Dettrick to give us a run down on the effects of smoking from a pathologist's point of view. It's not a light read!

If you need a rest after reading the smoking article you're in luck. September 22 is 'Stay in Bed Day' which concludes Global Mitochondrial Disease Awareness Week. You can find out more about this disease in this edition.

If staying in bed all day isn't really for you, then you might head

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"I had great pleasure in nominating Dr Farnsworth for an Honorary Fellowship with RANZCOG," says Professor Gabrielle Casper, Chairman of the RANZCOG NSW Regional Committee. "Her knowledge and expertise is highly regarded and internationally respected. Dr Farnsworth has also successfully bridged the gap between pathology and gynaecology which is a consequence of her enthusiasm and ability to communicate comprehensible pathology to clinicians."

Dr Farnsworth, cytopathologist, Medical Director at Douglass Hanly Moir Pathology and Director of their cytopathology department, says she has a strong relationship with many gynaecologists who often seek her advice, especially for difficult cases.

"Pathology often goes under the radar but the gynaecologists we are associated with value not just my expertise, but the expertise of the whole Gynaepath team," she says. "Pathology is certainly an integral part of the whole clinical process."

One of Dr Farnsworth's notable contributions has been in the area of Quality Assurance in Gynaecological Cytology and

quality processes in pathology generally. She was a member of the original working group on Quality Assurance for the Organised Approach to Cervical Screening set up in 1994, and later chaired the review of these standards. These quality standards and performance measures significantly increased the quality of gynaecological cytology in Australia, and contributed to the success of the Cervical Screening Program in Australia.

Dr Farnsworth was also involved with a review of Pap smears from the Gisborne region in New Zealand in 1999 and 2000. This led to major recommendations to improve quality standards in New Zealand.

“I have been working in gynaecological cytology for my entire career,” says Dr Farnsworth. “I was therefore delighted to receive an Honorary Fellowship from RANZCOG.”

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Being medicine wise is important when you are dealing with Deadmen's bells



It's Medicinewise Week (14-20 October) and this year's theme highlighted how older people can become wiser about their health and medicines. There are many aspects to taking medicines wisely including monitoring medicine concentration levels in the body. We've chosen digoxin, an infamous medicine sometimes prescribed for various heart conditions including heart failure and atrial fibrillation, to highlight why monitoring is important.

Digoxin is derived from a medicinal plant called *digitalis purpurea*, also commonly known as Foxglove. *Digitalis* has been used therapeutically for about 200 years, and is one of the most famous and most dangerous of medicinal plants. It's also known as Deadmen's or Witch's bells, and has been used with homicidal intent in fictional stories by Mary Webb, Dorothy Sayers and Agatha Christie, and in real life alleged homicides as well.

Perhaps the most famous historical case involved painter Vincent Van Gogh who was thought to have exhibited a form of digoxin toxicity because he used foxglove plants to treat his epilepsy. His yellow period (yellow vision), missing ear (he allegedly cut it off due to ototoxicity from digoxin which caused ringing ear) and inclination for painting halos around landscape objects (halo vision) are often attributed to digoxin toxicity. Monitoring digoxin is therefore important because it can reach dangerous levels and cause side effects!

Dr Graham Jones, chemical pathologist at SydPath in Sydney, says several aspects of the timing of the blood test are important to ensure the pathology test result accurately reflects the active level of digoxin in the body.

“To correctly measure digoxin levels, the blood sample should be taken at least six hours after the last dose was taken,” he explains. “If the test is taken less than six hours afterwards, the result can look higher than it really is because the medicine hasn’t had time to be distributed evenly throughout the body.”

Dr Jones says when a person first starts taking digoxin, or their dose is changed, they must wait seven days for it to reach a ‘steady state’ in their body before it is measured. It should also be measured when a situation occurs that may change the effect of the medicine such as a higher or lower dose.

“Digoxin is a drug that requires monitoring because different people have different rates of digoxin absorption and metabolism,” explains Dr Jones. “There are other factors to consider as well such as electrolyte levels and renal (kidney) function because digoxin is a medicine that is excreted via the kidneys.”

Understanding the relationship between digoxin and other risk factors is important because digoxin toxicity is more likely to occur in various situations such as when there are low levels of potassium in the body.

There is also the risk of acute digoxin toxicity if too much of the medicine is taken at one time. Dr Jones says this can be life threatening and the patient may require hospitalisation.

“When a person has suspected acute digoxin toxicity, the blood test should be done as soon as possible, although repeat testing may be required if a large overdose has just been taken and the drug is still being absorbed from the gut,” he says. “Symptoms can include abdominal pain, nausea, diarrhoea, abnormal heart beats and confusion.”

Dr Jones also says that when writing down any pathology result, such as a digoxin level, it is important to note the unit of measurement as well as the number. This is because different laboratories use different units of measure in their tests.^[1]

From different units of measurement to risk factors that can facilitate toxicity, it’s clear that being medicine wise involves more than taking medicines as prescribed. Correct monitoring is also important for some medicines to ensure they are working to their optimal level for the best health outcome

[1] Different units of measurement is covered in [ePathWay Issue 019](#)

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Today (October 18) is the final day of Haemophilia Awareness Week^[1] which highlighted haemophilia, von Willebrand disorder and related inherited bleeding disorders. Since pathology is integral to the diagnosis and management of these conditions, we've chosen to shine a spotlight on the most common bleeding disorder – haemophilia.

“Haemophilia is an inherited condition and occurs when a person’s blood doesn’t have enough specific clotting factor to form clots and stop bleeding,” says Dr John Rowell, Haematologist at the Queensland Haemophilia Centre located at the Royal Brisbane and Women’s Hospital. “Clotting factors are proteins in the blood, and deficiencies in two different clotting factors cause two different types of haemophilia.”

Haemophilia A is the most common and is caused by reduced levels of clotting factor (8) VIII. Haemophilia B is caused by reduced levels of clotting factor (9) IX. Both affect significantly more males than females because the genes that encode factors VIII and IX are located on the X chromosome (termed X-linked). Females have two X chromosomes which means there is a healthy spare able to produce these clotting factors. Males only have one X chromosome, and if it’s affected they don’t have a spare. Although it’s a male dominated disorder, Dr Rowell says women can still have symptoms associated with haemophilia if they carry the abnormal gene.

Since haemophilia has a genetic basis, genetic tests can identify carriers of the disorder within a family and look for specific

genetic mutations.

“Genetic tests allow us to not only find carriers of the disorder, but to also assess the impact of treatment, including predicting if a person has a higher than normal chance of developing an antibody to the treatment based on their specific genetic mutation,” explains Dr Rowell. “We can also test 10 to 12 week old foetus’s to determine if they are male and have the disorder, or female and a carrier of the disorder.”

Dr Rowell says pathology tests are valuable to help diagnose haemophilia, classify it as mild, moderate or severe, monitor clotting factor levels over a person’s lifetime or when they have surgery or trauma, and monitor complications such as developing antibodies to the prophylactic (preventative) treatment.

“People with severe haemophilia need prophylactic treatment with factor VIII or IX two to three times a week given intravenously,” he explains. “Sometimes they develop antibodies to these proteins which makes their treatment ineffective. If an antibody develops, treatment with high doses of the clotting factor over a prolonged period of time can eradicate the antibody in 70 percent of cases.”

Prophylactic treatment once involved administering clotting factor concentrates derived from blood plasma donations. Doctors have now moved to recombinant therapy - clotting factor produced artificially without the use of blood products - although Dr Rowell says developing countries may rely on blood plasma therapy.

Another development on the horizon is gene therapy. Although it’s about 10 years away from becoming mainstream, Dr Rowell says gene therapy can convert persons with severe haemophilia who produce less than one percent of clotting factor VIII or IX to being able to produce a little bit more. And a little bit goes a long way.

“If a person produces less than one percent of factor eight or nine then they are committed to regular prophylactic treatment for the rest of their life. If gene therapy can increase their production up to even two or three percent, then they only need prophylactic treatment for surgery or trauma,” says Dr Rowell.

“This means that only being a little bit better at producing the required clotting factor has a major clinical impact. They are also less likely to suffer side effects such as arthritis at an early age from repeated bleeds into joints.”

Haemophilia is a lifelong condition that can’t be cured, but it can be controlled. However, it is still the subject of mythology such as persons with haemophilia can bleed to death from a cut or wound (they can’t), they bleed faster (they don’t), they can’t play sport (they can) and it’s a contagious disease (it’s not). This is why it’s important to raise the profile of bleeding disorders by supporting events such as Haemophilia Awareness Week.

[1] <http://www.haemophilia.org.au/red-cake-day>

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A recent botulism scare in New Zealand focused attention on this rare but potentially fatal disease. The issue arose when 38 tonnes of whey protein (destined for products such as infant milk formula) produced by a dairy co-operative was suspected of being contaminated by the bacterium that causes botulism. Tests have since confirmed the contaminant was a different bacterium, but what is botulism, and how is it related to Botox?

Dr Sally Roberts, clinical microbiologist at Auckland Hospital, says botulism is a life threatening disease caused by the anaerobic bacterium^[1] *Clostridium botulinum*. This bacterium, commonly found in soil, forms spores and can persist in the environment for many years. Spore forming bacteria can revert to vegetative or active bacteria in the right environment, and it is during this active growth phase that they produce botulinum toxin.

“Botulinum toxin is a neurotoxin, and is also the most poisonous toxin known in the world. A lethal dose is very, very small,” explains Dr Roberts. “The neurotoxin causes muscular paralysis resulting in respiratory failure.”

Dr Roberts says there are two types of botulism – adult and infant.

Adult botulism usually develops from ingesting food contaminated with *C. botulinum* toxin, often due to the food being improperly processed or sterilised. This allows the bacteria to grow and produce the botulinum toxin which causes the symptoms of botulism.

“Symptoms of adult botulism include descending paralysis from the eyes to the legs which is often very rapid. People often die from not being able to breathe because their respiratory muscles become paralysed,” says Dr Roberts.

Infant botulism develops when a baby (less than six months of age) ingests *C. botulism* spores from sources such as contaminated milk powder. Their immature gastrointestinal tracts are susceptible to overgrowth by invading bacteria which enables the ingested botulism spores to turn into growing (or vegetative) bacteria. This bacteria then produces botulinum toxins in the infant’s gut.

“These babies basically ingest the bacteria that make the toxin. They become constipated because their gut is paralysed, they become ‘floppy’, and eventually develop the same paralysis as adults.”

Pathology tests for botulism use various techniques to look for the botulinum toxin in a patient’s stool sample. Dr Roberts says it’s a rare disease so testing capabilities and medical expertise are quite limited.

While botulism may be rare, it’s alter ego is less so. *Clostridium botulinum* is the same bacterium that is used to produce Botox.

“Botox is produced from the botulinum toxin and is used medically in people with torticollis (abnormal, asymmetrical head or neck position), muscle spasms and other muscular related conditions,” says Dr Roberts. “But it’s probably best known for its cosmetic use.”

She says Botox is used cosmetically to relax muscles which ‘removes’ wrinkles.

“If muscles can’t move then they can’t cause wrinkles. You know if someone has had Botox for cosmetic reasons when they can’t raise their eyebrows. This is because the muscles that do this are basically paralysed.”

From wrinkle free brows to international food scares, Botox and botulism has a broad reach. And while the recent botulism scare in New Zealand raised eyebrows around the world, it was fortunate it turned out to be a false alarm because botulinum toxins are one of the most lethal known substances in the world.

[1] [Anaerobic bacteria can only grow in the absence of oxygen](#)

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