



PathWay

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA



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Issue #029

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Interesting Facts

More
than 5
million

The number of people globally who die from smoking every year

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 outside for some spring gardening. Gardens are living ecosystems where a variety of bugs can grow, so we've outlined a few of the more troublesome ones to look out for.

And finally, it may not be in the same headline-grabbing league as cancers related to smoking, but bladder cancer is an important topic on the agenda at the New Zealand Society of Pathologists Annual Scientific Meeting 2013 (September 27 to 29). Internationally renowned Professor John Srigley will deliver two talks on bladder cancer at this meeting, and we've included a round up of this disease in this edition.

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Smokers' lives are defined by 'pack years'

More than 600,000

The number of people globally who are non-smokers and who die from being exposed to second-hand smoke every year

100 million

The number of deaths from tobacco use in the 20th century. If current trends continue, it may cause one billion deaths in the 21st century

16

The percentage of people in the world protected by comprehensive national smoke free laws

Source: World Health Organization

Important Message



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You've probably seen those grisly pictures on cigarette packets where gangrenous feet, cancerous tongues, diseased lungs and other images of the consequences of smoking are depicted in full horrific detail. If you find those images difficult to look at for more than few moments, then spare a thought for pathologists. They are the doctors who examine and diagnose many of the effects of smoking - including almost every cancer case.

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Bladder cancer on the agenda at important scientific meeting

Bladder cancer doesn't hit the headlines much, even though it's the fifth most common cancer in men. It is however on the agenda at this month's New Zealand Society of Pathologists Annual Scientific Meeting^[1] (NZ ASM 2013) where Professor John Srigley, urological pathologist from McMaster University in Canada, will share his expertise with his Australasian colleagues. It is therefore a good time to have a general look at bladder cancer.



Prof Srigley

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'Stay in bed day' raises awareness about mitochondrial disease

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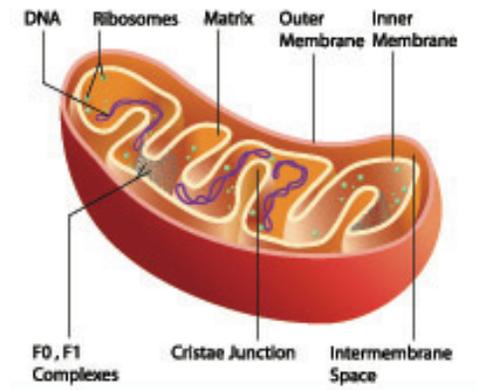
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For some a 'stay in bed day' is a luxury. For those with mitochondrial disease it can be a sad fact of life. Mito, as it's commonly known, is a debilitating and incurable genetic disorder that robs the body's cells of energy. Sufferers often stay in bed for most of the day to harness enough energy to perform the most basic tasks. Mitochondrial disease is also notoriously difficult to diagnose.



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Look out for 'surprises' lurking at the bottom of the garden

If the crowds flocking to nurseries to buy seedlings and plants are any indication, a lot of people are spending time tending their garden. While there are numerous health benefits associated with gardening, Dr Robert Norton, microbiologist and Director of Pathology at Townsville Hospital, says there are some soil and garden infections to look out for.



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Smokers' lives are defined by 'pack years'



You've probably seen those grisly pictures on cigarette packets where gangrenous feet, cancerous tongues, diseased lungs and other images of the consequences of smoking are depicted in full horrific detail. If you find those images difficult to look at for more than a few moments, then spare a thought for pathologists. They are the doctors who examine and diagnose many of the effects of smoking - including almost every cancer case.

"We see the smoke or black tar, which is a carbon pigment, on the lungs of smokers," explains Dr Andrew Dettrick, anatomical pathologist and A/Director of Pathology Queensland at The Prince Charles Hospital. "Normal lungs are pink, but smokers' lungs really are black."

He says the lungs' alveolar walls, where oxygen exchange takes place when you breathe, also start to disappear in smokers, and the cellular makeup of the tissue lining the lungs changes.

"The most common type of lung cancer in smokers is squamous cell carcinoma. This is interesting because there are no squamous cells in healthy lung tissue which means smoking causes quite a significant change at a cellular level."

Dr Dettrick also stresses that smoking causes more than just lung cancer. He says it affects your whole body including the

mouth, larynx (voice box), pancreas, kidneys and heart – the list goes on. The extent of damage to the body from smoking is also related to ‘dose and duration’.

“Every cigarette smoked really is doing you damage,” he says. “It’s a linear function in terms of the more you smoke, the more your risk of disease goes up.”

Dr Detrick says pathologists measure the dose and duration of a person’s smoking habit in ‘pack years’. For example, 20 cigarettes smoked every day for one year is called ‘one pack year’, while 40 cigarettes smoked every day for one year is ‘two pack years’, and so on.

“I have seen a person who had 213 pack years which was simply amazing. He couldn’t have done anything all day except smoke cigarettes!”

‘Pack years’ date back to the 1950s when cigarettes came in packs of 20. Even though they now come in different pack sizes, smoking is still defined in this way.

“Other unfortunate facts for smokers are that lung cancer related to smoking has an overall five-year survival rate of about 15 percent, and three quarters of lung cancers have already spread beyond the lungs at diagnosis,” explains Dr Detrick.

“Pathologists are critical in this process because we make the diagnosis and are then involved in planning the treatment based on the type and stage of the cancer.”

The health risks start to decrease when a person gives up smoking, but Dr Detrick says it takes about 10 years for them to significantly decline and even then they never really go away. If the graphic pictures on cigarette packets are anything to go by, then it would be hard to breathe easy if your life was, or still is, defined by ‘pack years’.

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Professor Brett Delahunt, Professor of Pathology and Molecular Medicine at the Wellington School of Medicine and Health Sciences (University of Otago) and Adjunct Professor of Biological Sciences at Victoria University (Wellington), says the most common symptom of bladder cancer is painless haematuria (blood in the urine).

"Haematuria can be associated with a number of conditions such as cystitis (bladder infection), but it is also a sign of bladder cancer. If people notice they have haematuria they should have it investigated by their doctor."



Prof Delahunt

Over 90% of bladder cancers originate in the cells of the bladder's innermost lining called the urothelium. These are called urothelial carcinomas or transitional cell carcinomas. Because these cells line the bladder they come into contact with waste products in the urine that can cause cancer such as chemicals found in cigarette smoke.

"Cigarette smoking is a significant risk factor for bladder cancer," says Prof Delahunt. "Another is exposure to dyes in the plastics industry. People who work in this industry undergo routine screening for bladder cancer."

While bladder cancers start in the urothelium, it is important to know at diagnosis if the cancer has also spread into the muscle layer of the bladder or beyond.

"Pathologists examine bladder tissue biopsies and report on the type, stage and grade of the cancer including whether it has spread into the muscle," says Prof Delahunt. "This information is important because the treatments for muscle invasive versus non muscle invasive bladder cancers are quite different."

Prof Delahunt says the ideals of treatment include maintaining bladder function for as long as possible, and to try to avoid removing part or all of the bladder (cystectomy).

"If the cancer has invaded the muscle layer then the treatment often involves a cystectomy," he says. "It's also important to know that some types of superficial non-invasive bladder cancers can recur so regular medical checks are important."

Diagnosis, staging and grading of bladder cancer is clearly vital in terms of prognosis and treatment. It is also important to understand the different types of bladder cancers - including rare types - which can occur. Prof Strigley will present information on these subjects to his colleagues at the NZ ASM 2013, but it is the general population who ultimately benefits from these events in terms of an informed and up-to-date pathology profession.

[1] <http://www.rcpa.edu.au/Continuing/NZASM2013.htm>

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- RCPA embraces social media to spread the pathology message
- Pathology is the gold standard for cancer diagnosis and the foundation for personalised therapy
- Vaccine is in progress for group A streptococcus

Introduction

There's change in the air and it's not just seasonal. The Royal College of Pathologists of Australasia (RCPA) have a growing presence in cyber-space thanks to their new Facebook and Twitter social media platforms. An article this month explains how this vision happened and why.

Changes are also happening with cancer diagnosis and reporting which is particularly notable since today is Daffodil Day. Pathologists from the RCPA helped initiate changes to the way cancer is reported and their project is now global. Our article outlines how this happened, and looks at other transformations in the cancer-pathology journey including a name change!

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'Stay in bed day' raises awareness about mitochondrial disease



For some a 'stay in bed day' is a luxury. For those with mitochondrial disease it can be a sad fact of life. Mito, as it's commonly known, is a debilitating and incurable genetic disorder that robs the body's cells of energy. Sufferers often stay in bed for most of the day to harness enough energy to perform the most basic tasks. Mitochondrial disease is also notoriously difficult to diagnose.

"There is no blood test specifically for mitochondrial disease but research is active in this area," says Dr Janice Brewer, anatomical pathologist and senior staff specialist at Royal North Shore Hospital.

"Although mitochondrial disease is a genetic disorder, you can't screen for it because the current genetic tests are expensive and time-consuming. Also, a single mitochondrion is made up of about 1,400 genes. The 'right' gene to test must be selected making the chance of a positive genetic test result quite low."

Mitochondria are our cells' 'batteries' providing them with energy to function. They are present in almost every cell in our body (the exception is red blood cells) and can therefore cause problems in a single organ or across many organs. Symptoms are

very broad and non-specific, but there are a few clues.

“Mitochondrial disease can present with muscle weakness and lethargy which is where anatomical pathologists enter the diagnostic picture,” explains Dr Brewer. “If a doctor is suspicious that a person has mitochondrial disease they will often take a biopsy of muscle tissue for us to examine. We look for evidence of muscle disease such as muscle cell degeneration or muscle fibre regeneration where damaged muscle fibres have tried to repair themselves.”

Dr Brewer says biopsies for mitochondrial disease must be sent to the laboratory fresh as opposed to preserved in formalin (although some of the tissue is still preserved this way), and frozen almost straight away to preserve the muscle’s enzymatic activity. The pathologist then looks for evidence of mitochondrial disease such as ‘ragged red’ fibres - so called because that is what the damaged muscle fibres look like under a microscope once they are stained.

“Even if the pathologist finds these markers for mitochondrial disease, they may be due to the normal ageing process. On the other hand, the biopsy sample may not contain any damaged fibres. If the initial biopsy results are negative, and there is still a strong suspicion of this disease, then the pathologist will look at the tissue under an electron microscope to view the actual mitochondria.”

The pathologist looks for abnormal-looking mitochondria and checks to see if they are increased in number. When defective mitochondria are struggling to provide enough energy, they multiply to try to compensate.

Although there are known markers, Dr Brewer says diagnosing mitochondrial disease can be like trying to find a needle in a haystack. It can affect many organs, display a wide range of symptoms and affect people of any age. There is also no cure.

To raise the profile of this disease and raise funds for research, a worldwide ‘stay in bed day’^[1] is organised for September 22. Research estimates that mitochondrial mutations are present in at least 1 in 250 people, and at least 1 in 5,000 will develop serious illness. That’s a lot of people who may have to stay in bed until a breakthrough with this disease occurs.

[1] For more information on Mitochondrial Disease, including Stay in Bed Day, go to www.amdf.org.au

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Look out for 'surprises' lurking at the bottom of the garden



If the crowds flocking to nurseries to buy seedlings and plants are any indication, a lot of people are spending time tending their garden. While there are numerous health benefits associated with gardening, Dr Robert Norton, microbiologist and Director of Pathology at Townsville Hospital, says there are some soil and garden infections to look out for.

"People in northern Australia (above Mackay) should look out for melioidosis," says Dr Norton. "This bacteria sits in the soil during the dry season and comes to the surface during the wet season. It lives and breeds in surface water and soil, and can be inhaled through dust or droplets of water, or acquired through cuts on the skin."

Melioidosis symptoms depend on the site of the infection, but most commonly start as a chest infection with shortness of breath, productive cough and fever. People most at risk include those with compromised immune systems, diabetes, heavy alcohol intake, kidney disease and lung disease.

Another nasty surprise can be Q Fever. Traditionally associated with cattle and in people who work at abattoirs, Dr Norton says he has seen patients with Q Fever who have had no contact with cattle.

"Q Fever can be present in the droppings of mammals such as wallabies, kangaroos, possums and bandicoots. When these

animals leave droppings on the grass of homes that verge onto their habitat, such as acreage blocks, spores from these droppings are sprayed into the air when the grass is mowed. These spores can then be inhaled.”

Dr Norton says Q Fever is a resistant organism that can lie dormant in soil during very dry conditions. People can then inhale the dormant bacteria in the dust. Most infected people have no or few symptoms. Those who become ill typically experience a high fever, chills, headache, extreme fatigue, muscle and joint pain and severe sweats.

Next on the list is *Legionella longbeachae*. Normally associated with water in cooling systems, it has been found in potting mix for about 30 years.

“*Legionella longbeachae* is the most prevalent form of disease that you can acquire from big piles of potting mix,” explains Dr Norton. “It gets very hot in the middle of these piles and this is where the organism multiplies. The heat actually selects out the *Legionella longbeachae* to grow because it tolerates high temperatures. People then inhale the organism when they start digging into the potting mix, and this can lead to pneumonia in rare cases.”

If this information causes you to look at your small bags of potting mix with increased suspicion - don't worry. Dr Norton says you need a big pile of the stuff to generate enough heat for *Legionella longbeachae* to multiply. Symptoms of infection include fever, cough, chest pain, breathlessness and diarrhoea.

Next on the list are direct puncture wounds which can admit organisms such as *Nocardia* or atypical mycobacteria. These organisms are found everywhere in soil and can enter the body through cuts on hands or feet, or via wounds from rose thorns.

“Healthy people usually get a localised reaction, but if a person has a compromised immune system then the bacteria can get into their system. They are also quite common infections in people who garden in bare feet or who perhaps stab themselves with a pitchfork!”

Nocardia infections affect the lungs, brain or skin. Symptoms of atypical mycobacterial diseases depend on the infecting organism.

Last but not least are (relatively uncommon) allergies to fungal spores which can produce an asthma-like illness in some people, depending on their predisposition for allergic reactions. They can also cause allergic alveolitis (inflamed alveoli within the lung) in people with compromised immune systems as well as (rarely) fungal pneumonia if inhaled.

Gardens are living ecosystems, and the fact that they harbour various bugs shouldn't prompt people to put their mowers and potting mix away and avoid the great outdoors. It's just useful to know what surprises might be lurking at the bottom of the garden.

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