



# PathWay

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA



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Issue #058

## In This Issue

- NZ pips Australia as melanoma capital of the world
- Safety is a key factor for medicinal cannabis use in Australia
- There's more to hepatitis than A, B and C
- Precision medicine for diabetes is not science fiction

## Welcome to the May edition of ePathWay

Medicine is a dynamic discipline that necessarily responds to new research and epidemiologic changes. Pathology is a key player in this equation since pathologists diagnose more than 70% of diseases, and in many cases, inform and guide treatment. With this in mind, this month's edition reflects some changes that have happened, or will happen, in the medical arena. They cover:

- Why New Zealand now has the highest incidence of invasive melanoma in the world.
- The importance of safety as medicinal cannabis edges closer to an approved medical framework.
- Why hepatitis is a syndrome and not a diagnosis.
- A new gene that will help personalise diabetic management.

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## Interesting Facts

### Over 4000

The number of New Zealanders diagnosed with melanoma each year.

### Around 300

The number of New Zealanders who die of melanoma each year.

## NZ pips Australia as melanoma capital of the world

## Over 50

The age when most cases of melanoma occur.

Source: *Melanoma New Zealand*

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A [study](#) has found New Zealand now has the highest per capita rates of invasive melanoma in the world, knocking Australia out of the top spot in the process. It wasn't a two horse race either. Six populations<sup>[1]</sup> were studied over a 30-year period from 1982 to 2011, with Australia the only population where melanoma rates had begun to fall overall.

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## Safety is a key factor for medicinal cannabis use in Australia

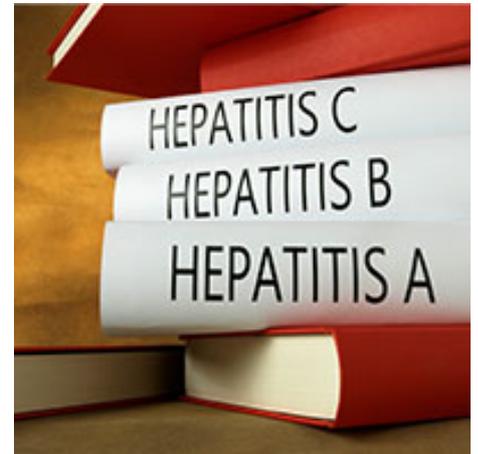
Growing cannabis for medicinal use is one step closer thanks to the [Narcotic Drugs Amendment Bill 2016](#) passed by the Australian Parliament in February. But if you think this is a green light to grow your own 'pot' plant then you're in for a reality check. Its supply and use will be strictly regulated, and rightly so.



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## There's more to hepatitis than A, B and C

Hepatitis has become a medical mononym alongside conditions such as cancer, diabetes, dementia and pneumonia. This hasn't helped the wider community understand its many types and causes, so we asked expert virologist Professor William Rawlinson to shine some light on this disorder.

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## Precision medicine for diabetes is not science fiction

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Associate Professor Sof Andrikopoulos and his team discovered Abcc8 which is a gene that directly causes defective insulin secretion resulting in the high blood sugar levels of type 2 diabetes.

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## Previous Editions



**APRIL 2016 | PUBLISHED BY RCPA** **ISSUE #057**

### IN THIS ISSUE

- The next chapter for NIPT shows it has scope outside of the prenatal setting
- Can gene therapy cure sickle cell anaemia and thalassaemia?
- The 'resistance movement' could send us back to the future

### Welcome to the April edition of ePathWay

This month's edition spotlights talks given at Pathology Update 2016, and while they cover different topics there is also a common thread – they all look towards the future. The articles cover:

- The next chapter for non-invasive prenatal testing.
- The search for a cure for two debilitating blood disorders.
- A possible new approach to diagnosing food allergies in children.
- Infection control in the 21st century.

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2016

[055 - February 2016](#)

[056 - March 2016](#)

[057 - April 2016](#)

## 2015

[044 - February 2015](#)

[045 - March 2015](#)

[046 - April 2015](#)

[047 - May 2015](#)

[048 - June 2015](#)

[049 - July 2015](#)

[050 - August 2015](#)

[051 - September 2015](#)

[052 - October 2015](#)

[053 - November 2015](#)

[054 - Dec 2015/Jan 2016](#)

## 2014

[033 - February 2014](#)

[034 - March 2014](#)

[035 - April 2014](#)

[036 - May 2014](#)

[037 - June 2014](#)

[038 - July 2014](#)

[039 - August 2014](#)

[040 - September 2014](#)

[041 - October 2014](#)

[042 - November 2014](#)

[043 - Dec 2014/Jan 2015](#)

## 2013

[022 - February 2013](#)

[023 - March 2013](#)

[024 - April 2013](#)

[025 - May 2013](#)

[026 - June 2013](#)

[027 - July 2013](#)

[028 - August 2013](#)

[029 - September 2013](#)

[030 - October 2013](#)

[031 - November 2013](#)

[032 - Dec 2013/Jan 2014](#)

## 2012

[010 - Dec 2011/Jan 2012](#)

[011 - February 2012](#)

[012 - March 2012](#)

[013 - April 2012](#)

[014 - May 2012](#)

[015 - June 2012](#)

[016 - July 2012](#)

[017 - August 2012](#)

[018 - September 2012](#)

[019 - October 2012](#)

[020 - November 2012](#)

[021 - December 2012](#)

## 2011

[001 - March 2011](#)

[002 - April 2011](#)

[003 - May 2011](#)

[004 - June 2011](#)

[005 - July 2011](#)

[006 - August 2011](#)

[007 - September 2011](#)

[008 - October 2011](#)

[009 - November 2011](#)

[« Back to Home Page](#)

---

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## NZ pips Australia as melanoma capital of the world



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According to Dr Patrick Emanuel, Consultant Pathologist at the Auckland District Health Board and Honorary Associate Professor at the University of Auckland, there are probably multiple factors why New Zealand is now in the hot seat.

"New Zealand doesn't have as rigorous sun awareness campaigns as Australia, and we have been slow to act on things such as sunbeds and hats in schools. There are possible biological factors as well such as cell mutations related to sun exposure leading to melanoma, and the UV Index rating in New Zealand which can be very high."

The UV Index (UVI) is a standard measure of sunburn-causing UV intensity. The peak UVI in New Zealand is about 40% greater than at comparable latitudes in the Northern Hemisphere because of differences in ozone, sun-earth separation and pollution. This is a key point, especially since Dr Emanuel suspects there is a perception that New Zealand doesn't have a skin cancer 'problem' because it is seen as a cold southern country.

"It's important to understand that New Zealand clearly has high rates of melanoma. We also have a higher UV Index rating in the Southern Hemisphere meaning the sun is much more damaging on the skin compared to the sun in the Northern Hemisphere," he explains.

"Research<sup>[2]</sup> that I was involved with also found melanoma mutations were different between New Zealand's South Island and North Island. The only reasons for this anomaly are the UV Index and habits related to sun exposure."

It's not all doom and gloom for the land of the long white cloud. The study also notes that New Zealand's melanoma rates are expected to start declining from about 2017 onwards, while the rates in the other populations studied – with the exception of

Australia – are predicted to keep increasing until at least 2022.

Sunscreen, shirt and hat anyone?

[1] Populations studied were Australia, New Zealand, the United Kingdom, Norway, Sweden and the Caucasian population of the United States.

[2] Dr Emanuel is a co-author of a paper titled [NRAS and EPHB6 mutation rates differ in metastatic melanomas of patients in the North Island versus South Island of New Zealand](#) published in the journal Oncotarget this month.

[« Back to Home Page](#)

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## Safety is a key factor for medicinal cannabis use in Australia



Growing cannabis for medicinal use is one step closer thanks to the [Narcotic Drugs Amendment Bill 2016](#) passed by the Australian Parliament in February. But if you think this is a green light to grow your own 'pot' plant then you're in for a reality check. Its supply and use will be strictly regulated, and rightly so.

The Bill provides a national licencing scheme to ensure cannabis is safely cultivated for use in medicinal cannabis products. This means groups already sourcing cannabis for medical reasons will have access to products that are safe and of appropriate quality. But cannabis will continue to be an illegal recreational drug, so who will benefit from its use in a medical sense? Before we answer this question, it might be useful to briefly review this drug.

Cannabis comes from the *Cannabis sativa* plant. Marijuana is its most common product and refers to the plant's dried leaves and flowers. Other cannabis products include hashish (dried resins from the plant compressed into small blocks), and cannabis oil extracted from hashish. Extracts of the plant contain a large number of compounds, only some of which may have useful medicinal properties.

Despite its reputation as a 'party drug', cannabis is actually a hallucinogen and depressant drug. This means it slows down brain functions and the ability of a person to respond to the external environment. Knowing this effect puts its medicinal use into perspective.

"Medicinal cannabis can be helpful as a treatment for people with certain serious medical conditions. For example, it may be used for conditions that cause severe muscle spasms and pain such as multiple sclerosis, or for people with severe nausea and vomiting, including during treatment for AIDS," explains A/Prof Morris Odell, Head of the Clinical Forensic Medicine Service at the Victorian Institute of Forensic Medicine.

"Medicinal cannabis can also be used to treat seizures when other treatments have not been effective, and to assist pain management during palliative care."

A/Prof Odell says the RCPA supports the use of medicinal cannabis, provided it is prescribed under the oversight of an expert committee that includes appropriate medical specialists and the relevant state or territory health authority, and is approved for use on a case-by-case basis. He says there are potential issues to be aware of as well.

“The use of medicinal cannabis may interfere with legitimate drug screening such as those associated with occupational drug testing or traffic drug testing. This must be taken into consideration in the occasional case where this could cause problems. Its approved medicinal form must also take into account the potential for it to be diverted for illegal non-medicinal uses.”

Despite these concerns, A/Prof Odell says they are unlikely to become major issues. This is because people prescribed medicinal cannabis are often very ill and unlikely to require drug screening for occupational, medical or forensic reasons.

“In terms of diverting its use, there are only a couple of substances in cannabis that have a therapeutic value, and these will probably be of little interest to recreational drug users. Having said that, the drug shouldn’t be available as a crude plant extract because its composition can’t be as easily controlled in that form.”

A/Prof Odell says the effects of cannabis are not related to blood levels so there will be no need for routine pathology tests to check body fluid levels of the drug. If such a test is required for any reason it will most likely be performed at a forensic testing laboratory to access the required expertise.

Medical expertise is a key component in this debate as cannabis prepares to take a legitimate place within a medical framework. This necessarily comes with quality assurance to ensure patient and community safety. A reliable and safe supply of the drug from farm to pharmacy is critical to ensuring there is a balance among patient access, community protection, expert oversight and appropriate medical supervision.

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Hepatitis has become a medical mononym alongside conditions such as cancer, diabetes, dementia and pneumonia. This hasn't helped the wider community understand its many types and causes, so we asked expert virologist Professor William Rawlinson to shine some light on this disorder.

"Hepatitis simply means 'inflammation of the liver' which means it is not a diagnosis or even a single disease. It's really a syndrome that requires further investigation to find out why the liver is inflamed, and this could be due to a number of causes," he explains.

"It might be from drugs, an existing illness, alcohol, connective tissue diseases or from a virus. We know that more than 10 viruses infect and damage liver cells, including viruses such as cytomegalovirus (CMV) and Epstein-Barr virus (EBV) which are better known for causing other problems such as infectious mononucleosis (glandular fever)."

Prof Rawlinson says many cases of hepatitis are now found through biochemistry blood tests that simply point to a hepatitis syndrome. This flags there is a problem and informs the direction for further investigation to find the cause, make a diagnosis and provide treatment.

"When people have an abnormal blood result that indicates their liver is inflamed we call it biochemical hepatitis, and that test, along with the patient's history and presenting symptoms, guides the diagnostic process."

One type of hepatitis is caused by hepatitis viruses, and discussing them is like sipping alphabet soup - especially since there are more types than the commonly known A, B and C. There are also types D, and E, and researchers are looking for the other elusive letters.

Hepatitis viruses are traditionally divided into blood borne (also known as parenteral), and faeco-oral types. Blood borne types (HBV, HCV and HDV) are acquired through direct exposure to infected blood or other body fluids such as by sharing needles or having unprotected sex. Faeco-oral types (HAV and HEV) are acquired by ingesting pathogens excreted in the stool of an

infected person or animal, such as by drinking infected water or eating infected food.

In terms of prevalence, Prof Rawlinson says the hepatitis types spread faeco-orally are the most common types in the world, occurring mainly in developing countries.

“Almost everyone in countries such as in South East Asia has had HAV and HEV, usually as a child, and once they have the virus they have immunity. In the past we would test for HEV in Australia if people presented with hepatitis symptoms and they had travelled overseas to countries where it is endemic. An outbreak in Australia in 2013 traced to a pork products highlighted that the virus is probably also circulating in Australia, although at much lower rates than in developing countries.”

Diagnostic lines are also drawn between acute viral hepatitis and chronic hepatitis.

“HAV, HEV, EBV, CMV and human herpesvirus 6 (HHV6) cause acute viral hepatitis, while HBV, HCV and HDV can cause chronic hepatitis. However, the recently described ‘hepatitis viruses’ HGV and transfusion-transmitted virus (TTV) don’t cause hepatitis at all.”

It’s pretty clear that there’s more to hepatitis than A, B and C. The other point to note (again) is that it’s perfectly clear hepatitis isn’t a single disease, but a syndrome that hoists a red flag to indicate that the liver is inflamed and should be investigated.

Prof Rawlinson is the Senior Medical Virologist at South Eastern Area Laboratory Services (SEALS) Pathology & UNSW, Director of SAVID (Serology & Virology Division) and the Director of a NSW State Reference Laboratory for HIV/AIDS.

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Associate Professor Sof Andrikopoulos and his team discovered Abcc8 which is a gene that directly causes defective insulin secretion resulting in the high blood sugar levels of type 2 diabetes.

"We used the Polygenic New Zealand Obese Mouse that is a model of type 2 diabetes to look at a number of genes and found a very specific point on a particular chromosome associated with high blood sugar levels that also harbours the Abcc8 gene."

A/Prof Andrikopoulos says this discovery will help researchers improve insulin secretion in a targeted and specific manner with the durability required to treat diabetes over the long term without causing cell damage.

This is an important consequence because current therapies for type 2 diabetes do not specifically fix the underlying cause of the disease and in fact some may even contribute to progressive deterioration of beta-cell ( $\beta$ -cell) function through unregulated secretion of insulin.

$\beta$ -cells are a type of cell unique to the pancreas. They produce, store and release the hormone insulin, which regulates the level of glucose in the blood, directly into the bloodstream. When a person has type 2 diabetes, their  $\beta$ -cells are unable to produce enough insulin to control their blood sugar levels.

"We know there is a strong genetic component underlying glucose tolerance and drug response. Understanding the mechanics of how this gene affects insulin secretion will facilitate targeted therapeutics to be developed that will significantly correct the defect," he says.

A/Prof Andrikopoulos is now looking to take his research to the next level and identify other genes that contribute to diabetes.

"We hope to discover multiple genetic defects so that we can develop even more specific, effective and durable therapies for diabetes," he says. "This is important because diabetes is a life long disease."

A/Prof Sof Andrikopoulos is head of the Diabetes Laboratory at the University of Melbourne Department of Medicine at the Austin Hospital, President of the Australian Diabetes Society, and Editor-In-Chief for the Journal of Endocrinology and Journal of Molecular Endocrinology.

He delivered a talk titled *What mice teach us about diabetes* on Friday 26 February at Pathology Update 2016 held at the Melbourne Convention Centre.

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