



PathWay

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA



MAY 2019 | PUBLISHED BY RCPA

ISSUE #091

IN THIS ISSUE

- Measles: the importance of highly vaccinated population
- *Candida auris*, an emerging global health threat
- Allergies and asthma, a serious public health issue
- Precision medicine through cancer proteomics

INTERESTING FACTS

50,000

the number of samples that ProCan aims to analyse over the next 5-7 years.

80%

the rough percentage of people with asthma who also test positive for allergies.

613

the number of confirmed cases of *Candida auris* in the US, as at 30 April 2019.

Source:

[1] <https://www.cmiri.org.au/ProCan>

Welcome to the May issue of ePathWay

ePathway is an e-magazine designed for anyone interested in their health and wellbeing and the integral role pathology plays in the diagnosis, treatment and management of diseases.

This month's issue of *ePathway* looks at the following:

- Measles: the importance of highly vaccinated population
- *Candida auris*, an emerging global health threat
- Allergies and asthma, a serious public health issue
- Precision medicine through cancer proteomics

Measles is a highly contagious viral illness which can cause serious, sometimes fatal complications. With the number of measles cases increasing in recent years, and a number of countries experiencing severe and prolonged measles outbreaks^[1], we spoke to Professor William Rawlinson who explained the importance of maintaining a highly vaccinated population.

Recent reports have identified an emerging global health threat which has been causing severe illness in hospitalised patients. *Candida auris* (*C. auris*) is a new, uncommon fungus which causes invasive, life-threatening bloodstream infections and is often resistant to multiple antifungal medications. Doctor Michael Thomas took the time to speak with us to provide a more detailed background on this new health threat.

The rapid increase of allergic diseases over the past few decades has become a serious public health issue in Australia and New Zealand. To coincide with asthma awareness week, we spoke with Doctor Daman Langguth to discuss the impact that allergies can have on asthma. Many of those people diagnosed with asthma, have also tested positive for allergies, and so in order to treat asthma effectively, it is important that the allergy is also considered.

Finally, we spoke to Professor Roger Reddel to learn more about his research into proteomics. Proteomics is referred to as the newest frontier of medical research and refers to the study of proteomes – the entire sum of proteins that is or can be expressed by a cell, tissue, or organism. ProCan will analyse thousands of proteins in 50,000 cancers of all types over the next 5-7 years and aims to help scientists all over the world studying cancer through a vast, publicly-available database.

[2] <https://www.nationalasthma.org.au/living-with-asthma/resources/patients-carers/brochures/asthma-allergy>

[3] <https://www.cdc.gov/fungal/candida-auris/index.html>

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Measles: the importance of highly vaccinated population



The number of measles cases worldwide has increased substantially in very recent years, with a number of countries currently experiencing severe and prolonged measles outbreaks^[1]. We spoke to Professor William Rawlinson, Senior Medical Virologist, Director of Serology, Virology and OTDS Laboratories (SAViD) at NSW Health Pathology Randwick, to discuss the importance of maintaining a highly vaccinated population to prevent this highly contagious viral illness which can cause serious, sometimes fatal complications.

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Candida auris, an emerging global health threat

Candida auris (*C. auris*) is a new, uncommon fungus which has emerged as a serious global health threat, largely due to the fact that it is multidrug-resistant. First recognised in

Japan, *C. auris* has since been reported by healthcare facilities in a number of countries, causing severe illness in hospitalized patients. We spoke to Dr Michael Thomas, microbiologist at Pathology Queensland Gold Coast, to discuss this relatively new threat.



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Allergies and asthma, a serious public health issue

Allergies and asthma are very common in Australia and New Zealand, with one in five people developing allergies at some time in their life^[1]. To coincide with asthma awareness week which took place this month, we spoke with Doctor Daman Langguth, Head of the Immunology Department at Sullivan Nicolaides Pathology, Brisbane to discuss the effect that allergies can have on asthma.



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Precision medicine through cancer proteomics

We spoke to Professor Roger Reddel to discuss his presentation at this year's Pathology Update 2019, 'Diagnoses through cancer proteomics – PROCAN.' Prof Reddel has been Director of Children's Medical Research Institute (CMRI), and the Sir Lorimer Dods Professor, Sydney Medical School, University of Sydney, since 2007. He is also Head of CMRI's



Cancer Research Unit, Director of CellBank Australia and Co-Director of ProCan®.

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Measles: the importance of highly vaccinated population



The number of measles cases worldwide has increased substantially in very recent years, with a number of countries currently experiencing severe and prolonged measles outbreaks [\[1\]](#). We spoke to Professor William Rawlinson, Senior Medical Virologist, Director of Serology, Virology and OTDS Laboratories (SAViD) at NSW Health Pathology Randwick, to discuss the importance of maintaining a highly vaccinated population to prevent this highly contagious viral illness which can cause serious, sometimes fatal complications.

“Measles is an extremely infectious disease which is caused by the morbilli (‘measles’) virus and is seen in unvaccinated or previously unexposed people from countries with low vaccination rates. Symptoms begin with a fever, a runny nose, cough, and conjunctivitis, which usually appear around 7-14 days after a person is infected. Around four days after these symptoms begin, the infected person usually develops a rash which classically begins at the head and spreads to the rest of the body.

“The majority of cases in Australia and New Zealand are due to unvaccinated people either arriving from, or becoming infected whilst travelling to, countries where measles is common because of low vaccination rates. It is spread by droplets, either by coming into contact with someone, or by breathing those droplets in. If you are not vaccinated, and come into contact with someone with measles, then you can contract this virus pretty quickly,” said Prof Rawlinson.

It is critical to diagnose measles to allow prompt public health follow-up and contact tracing to reduce further spread. Presumptive diagnosis can be done based on the

symptoms and signs, which may include distinctive 'Koplik's spots' on the inside of the cheek. However, often the signs such as the rash are not typical, and more classical signs such as Koplik's spots are missed, not present, or not seen at the time of clinical examination. Laboratory testing is therefore required to confirm the infection, either through detection of the virus using molecular testing (often with PCR), or detection of antibodies (particularly specific IgM) in the blood. People who are diagnosed are advised to rest, avoid contact with susceptible people, drink plenty of fluids, and take paracetamol for the fever. There is currently no antiviral treatment for measles.

"Vaccines are the best way of preventing infectious diseases such as measles and should be given by a GP/health provider when they are due, which for measles is at 12 months age and again at 18 months of age. If children don't get them on time because they are ill or because they are travelling, then they can have them 1-2 months later. If parents choose not to vaccinate their children, they are putting them at risk of problems such as otitis or pneumonia, or potentially encephalitis with long-term neurological damage. Being highly contagious, the infected person is at risk of infecting others, such as pregnant women where infection can be more severe, including causing maternal pneumonia, or stillbirth or congenital measles in the infant. The risks of the vaccine are very low, and the vaccine is very effective - protecting people for life. Governments continue to recognise this, and the benefits of protecting at-risk children from potentially deadly diseases. In states such as NSW, about \$130 million has been invested in the 2018-19 Immunisation Program, providing free vaccines to protect people, in most of these vaccines thereby providing protection for life.

"Transmission of measles between large numbers in Australia and New Zealand had, until recently, largely stopped since the late 1990's, however it is still surprising how many times measles is now raised as a possibility in the person with a rash. On average, we probably see the issue raised at least once every week in our laboratory. And although only about 5% of the tests we do are positive, it is still often brought up as an issue around someone with a fever and rash, particularly who has travelled, or who has travelled with a child back from a country where endemic measles still occurs. In 95% of the tests that we do, the rash is due to something else but because everyone is quite rightly worried about measles, we do the test frequently.

"Overall measles is trending down, but this last year particularly we and others have seen much larger numbers and we're not sure why. This could be associated with people reducing their vaccination rates from anti-vaccination or other influences, due to more travel resulting in an increase in imported measles or heightened awareness, or perhaps all of these. What we're relying on is our ability to identify infections where they occur, having continuing excellent public health response, and to continue to have a vaccinated population," said Prof Rawlinson.

Those people who believe they have been in contact with measles should continue to look for symptoms until 18 days after their last contact. If symptoms of measles begin to develop then it is important not to attend any public places, use the telephone to be in touch initially with your health provider/GP, and to contact a health professional such as your GP as soon as possible. It is important to continue to spread the word about the enormous benefits of vaccination to improving personal and community health.

References:

[1] <https://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-measles-outbreaks-2019.htm>

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- Call to end freeze on Medicare rebates for pathology testing
- Increasing testing for Familial Hypercholesterolemia (FH)
- Pathology, it's in the blood: Dr Julie Lokan and Dr Anand Murugasu
- Diagnosing and treating Haemophilia

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The Royal College of Pathologists of Australasia (RCPA) has called on the Government to end the freeze on Medicare rebates for pathology testing.

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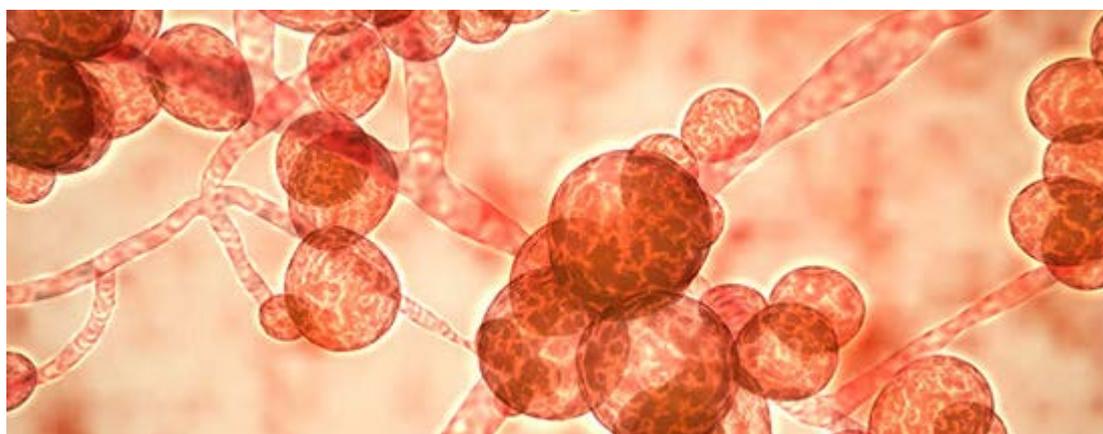
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Candida auris, an emerging global health threat



Candida auris (*C. auris*) is a new, uncommon fungus which has emerged as a serious global health threat, largely due to the fact that it is multidrug-resistant. First recognised in Japan, *C. auris* has since been reported by healthcare facilities in a number of countries, causing severe illness in hospitalized patients. We spoke to Dr Michael Thomas, microbiologist at Pathology Queensland Gold Coast, to discuss this relatively new threat.

“*Candida* species are single-celled fungi (yeasts). Other *Candida* species are well known as the cause of vaginal and oral thrush, infections which are very often mild and easy to treat. *Candida auris* is a new species which often does not respond to commonly used antifungal drugs, making infections more difficult and expensive to treat,” said Dr Thomas.

Candida auris was first identified as a new species after it was grown from the ear canal of a 70-year-old hospitalised woman in Japan in 2008^[1] (*auris* is Latin for “of the ear”). When grown in the laboratory, *C. auris* closely resembles other *Candida* and specialised techniques are required to differentiate it from these other species.

C. auris causes invasive, life-threatening bloodstream infections and is often resistant to multiple antifungal medications - even in people who have never previously been treated with antifungals^{[2][3]}. Unlike most other yeasts, it has also caused outbreaks in hospitals^[3]. It has been grown from many body sites, including the skin, genitals and urinary system, and respiratory system (mouth to lungs)^[4]. It is likely that the organism lives on these sites unsuspected until some breach of the body surfaces occurs and facilitates invasion, a situation termed “colonisation”.

“Healthy people may be colonised by *C. auris* but are unlikely to become seriously ill. Those most at risk of severe illness are people with impaired immune systems, for example people receiving cancer chemotherapy. Patients who have been admitted to an intensive care unit are also at risk, especially those who require broad-spectrum antibiotics, invasive procedures or breathing assistance with a mechanical ventilator. Both children and adults have been affected,” said Dr Thomas.

Unless there is an outbreak, the treating doctor is unlikely to have any obvious prior clues that *C. auris* is involved. In terms of diagnosis, *C. auris* will initially be grown (“isolated”) from the affected body part using routine microbiological culture techniques. “As it is a relatively newly-recognised species, *C. auris* may be misidentified, especially if a laboratory only uses traditional methods of yeast identification. Fortunately, awareness of this organism and the ability to identify the organism is high among Australian microbiologists,” said Dr Thomas.

A finding of an usual species and/or unexpected antifungal resistance is likely to trigger further testing. Reliable identification methods and procedures have now been established and most automated identification databases have been updated to include *C. auris*^{[2][5]}. Furthermore, many laboratories now use mass spectrometry for routine yeast identification. This method analyses yeast proteins directly and is both rapid and reliable. Misidentification with mass spectrometry is still possible, however, and since it is still a relatively rare organism, suspected *C. auris* isolates should be definitively identified using DNA sequencing or a similar method^[6].

The US Centers for Disease Control and Prevention (CDC) keep a monthly running total of cases in the United States, with 613 confirmed and 30 probable infections noted as at 30 April 2019^[3].

In Australia, a 65-year-old man was diagnosed in Perth^[7] in 2015. The patient had an infection of the sternum (breastbone) which he acquired after a 3-month admission to a Kenyan intensive care unit (ICU) in 2012. A second case report has recently been published^[2], describing an isolate grown from urine in July 2018 (possibly imported from the United Kingdom). Given the increasingly common discovery of this organism worldwide, more cases are expected to follow.

Public health authorities do not require mandatory notification of *C. auris* infections, however the high importance of this organism makes it is likely that they would be involved in Australian cases.

“If *C. auris* infection or colonisation is suspected, it is useful to inform the microbiologist before sending samples. Treatment success is more likely the earlier antifungal results are obtained from the microbiology laboratory, especially if advanced testing is required. Colonisation before and after an infection is common, as antifungal drugs do not easily reach the surface of intact skin where the yeasts may be located. Management of *C. auris* therefore includes removing invasive medical devices and following infection control practices to prevent its spread to others,” said Dr Thomas.

Within hospitals, the spread of *C. auris* may be controlled by “screening”, i.e. searching actively for colonisation of close contacts to a known case. This may be done easily by swabbing the groin and armpits, as well as sending urine or other samples as appropriate, to the microbiology laboratory^[4].

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[1] Satoh K, Makimura K, Hasumi Y, et al. *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. *Microbiology and immunology* 2009; 53: 41-44.

[2] Chew SM, Sweeney N, Kidd SE, et al. *Candida auris* arriving on our shores: an Australian microbiology laboratory's experience. *Pathology* 2019.

[3] US Centers for Disease Control and Prevention. *Candida auris*, <https://www.cdc.gov/fungal/candida-auris/index.html> (2019).

[4] Queensland Health. Infection Prevention and Control of *Candida auris*, https://www.health.qld.gov.au/_data/assets/pdf_file/0028/722827/Candida-auris-guideline.pdf (2019).

[5] National Center for Emerging and Zoonotic Infectious Diseases. Algorithm to identify *Candida auris* based on phenotypic laboratory method and initial species identification, <https://www.cdc.gov/fungal/diseases/candidiasis/pdf/Testing-algorithm-by-Method-temp.pdf> (2018).

[6] US Centers for Disease Control and Prevention. Identification of *Candida auris*, <https://www.cdc.gov/fungal/candida-auris/recommendations.html> (2019).

[7] Heath CH, Dyer JR, Pang S, et al. *Candida auris* sternal osteomyelitis in a man from Kenya visiting Australia, 2015. *Emerging infectious diseases* 2019; 25: 192.

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Allergies and asthma, a serious public health issue



Allergies and asthma are very common in Australia and New Zealand, with one in five people developing allergies at some time in their life^[1]. To coincide with asthma awareness week which took place this month, we spoke with Doctor Daman Langguth, Head of the Immunology Department at Sullivan Nicolaides Pathology, Brisbane to discuss the effect that allergies can have on asthma.

“Most commonly, allergy is an overreaction of the body’s immune system to a natural substance which should ideally be ignored. An allergy leads the body to react and present symptoms or signs such as hay fever, asthma or food allergy. Overall, allergy has increased significantly over the last 40 years which appears to have a “hygiene-hypothesis” background,” said Dr Langguth.

The hygiene-hypothesis is the idea that exposure to germs and infection helps to build the immune system, therefore protecting against allergies and asthma. The rapid increase of allergic diseases over the past few decades has become a serious public health issue in Australia and New Zealand. Allergy plays an important role in asthma, with around 80% of those people diagnosed with asthma also having positive allergy results.

“Asthma is hyperreactivity of the airways, referred to as inappropriate bronchoconstriction. It’s a wheezy chronic illness which in a significant number of people, has a significant allergic component. Around 40-60 people die each year from asthma – it’s not huge numbers but those are all preventable deaths. If you also look at the number of hospitalisations for asthma, it is quite significant. Probably around 50% of those admissions would be easily preventable if the patient saw their GP and took their medications.

“There are still a lot of people that don’t have that allergic component, however in those people that do, it is important to control both the asthma and the allergy. It is quite common that people will only treat one, and you may find that a patient is more likely to have uncontrolled asthma if they also have hay fever. This is because people usually find it difficult to treat more than one thing at once. Asthma has a chronic element to it, so removing the allergens does not mean that the asthma would go away.

“It is not necessarily obvious if there is an allergy playing a role in someone’s asthma. For example, if someone has continued exposure to something that they are allergic to, perhaps in their home, then the symptoms would be persistent therefore making it difficult to pinpoint. Once again, those people who have more than one allergic disease are the people that really need to be targeted or pay attention,” said Dr Langguth.

A skin prick test or blood test may be performed to find out if an allergy is playing a role in asthma. Once it has been established if an allergy is involved then treatment should be sought, or preventive action should be taken to minimise exposure. This will lead to an improvement in asthma symptoms.

“A large number of people with significant allergy don’t do much about it. It is important to be aware that those people with asthma that also have an unrecognised, or poorly managed food allergy, are at a very high risk of death. The asthmatic component of an acute reaction is much harder to control, and often you can get rid of the signs of anaphylaxis, but the persistent severe wheezing can actually lead to a person’s demise,” said Dr Langguth.

There is currently no cure for asthma, however there are a number of treatments available meaning that it can usually be well controlled. Most people with asthma are therefore able to have an active and healthy life.

“There are a whole host of treatments available for asthma, from those who only need intermittent treatment, to the majority of people who need it every day. The base line for treatment is inhaled corticosteroids, then there are a number of other agents which can be prescribed as additional treatments, such as long acting bronchodilators – which make the lungs open up. We now also have medications for life threatening severe asthma available on the PBS, which are very effective,” concluded Dr Langguth.

References:

[1] <https://www.allergy.org.au/patients/about-allergy/common-myths-about-allergy-and-asthma-exposed>

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Precision medicine through cancer proteomics



We spoke to Professor Roger Reddel to discuss his presentation at this year's Pathology Update 2019, 'Diagnoses through cancer proteomics – PROCAN.' Prof Reddel has been Director of Children's Medical Research Institute (CMRI), and the Sir Lorimer Dods Professor, Sydney Medical School, University of Sydney, since 2007. He is also Head of CMRI's Cancer Research Unit, Director of CellBank Australia and Co-Director of ProCan®.

"A proteome refers to the sum total of proteins expressed by a cell, tissue or organism, and we are near the beginning of a major, multi-year project to look at the proteome of cancer. By creating a large-scale database of cancer proteomes, we aim to increase the precision of cancer diagnosis and help predict the best currently available treatment to target an individual patient's cancer," said Prof Reddel.

ProCan is a new, international centre located within CMRI which was developed by Professors Phil Robinson and Roger Reddel. Launched in September 2016, it is a world-first initiative which aims to significantly improve the speed and precision of cancer diagnosis and provide personalised treatment. The information generated by ProCan will help scientists all over the world studying cancer through a large, publicly-available database.

Established with a \$10 million grant from the Australian Cancer Research Foundation (ACRF), ProCan aims to analyse thousands of proteins in 50,000 cancers of all types over the next 5 years, using technology called mass spectrometry. Widely used to analyse biological samples, mass spectrometry has evolved into an indispensable tool for proteomics research. "One of the difficulties in finding effective treatments for cancer is the fact that every cancer is unique. The reason for this is that one of the

characteristics of cancers is that they undergo mutations at an abnormally high rate. A lot of these changes are random, and sometimes it's hard to work out which changes are important, and which are not. But the net result is that each cancer ends up being different on a molecular level from other cancers.

“By generating data on this scale, we want to make it possible to match a cancer in a newly-diagnosed patient to the most similar cancers anywhere in the world, keeping in mind that no two will ever be exactly the same. By storing information regarding the treatments that had or had not been successful for those patients, the database could then be used to predict in a relevant clinical time-frame what treatment is most likely to be effective for that individual cancer. We have set ourselves a goal of being able to do this whole process within 36 hours of receiving the cancer sample,” said Prof Reddel.

ProCan is the only proteomic centre of this scale in the world dedicated to cancer research and is acting in partnership with cancer researchers, clinicians, tumour banks, and technology experts. The database will mean clinicians can effectively narrow down the best type of currently available treatment to target a cancer patient's individual diagnosis, without having to waste time trialling medications that won't effectively treat the disease.

“In the past, it hasn't been technically possible to do this on a large scale. What we're attempting to do is to look across all cancer types, examining tens of thousands of samples of cancer, representing virtually every type of cancer, from childhood through to adulthood. And we are using the same technology every time so that we can do massive cross comparisons of the proteome of all cancer types.

“In order to create a database with such analytical capacity, we need to identify effective methodologies, determine the computational requirements for dealing with data on such a large scale and bring in teams of technical and scientific experts such as software engineers and data scientists. Our aim is to do about 10,000 samples per year, and we are now quite close to achieving that rate.

“We want this to be not just a stand-alone project, but the start of a database that grows continuously. As new treatments come online, they would be reflected in the database so that it continues to grow as large as possible, continually increasing its statistical power,” concluded Prof Reddel.

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