

ISSUE #092

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- Influenza 2019: why has this season been particularly bad?
- An insight into Neuroendocrine Tumours (NETs)
- Testing for hereditary haemochromatosis, what's new?
- Pathology as a true lifeline for survival

INTERESTING FACTS

200

1 in 200 Caucasian Australian and New Zealand people have a genetic predisposition to Hereditary Haemochromatosis (HH)^{[1][2]}

65

Anyone aged 65 years or over is at high risk of severe influenza

3-4

The incidence of NETs in Australia per 100,000 people^[3]

Welcome to the June 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:

- Influenza 2019: why has this season been particularly bad?
- An insight into Neuroendocrine Tumours (NETs)
- Testing for hereditary haemochromatosis, what's new?
- Pathology as a true lifeline for survival

This month, more than 1,000 outstanding Australians have been recognised in the Queen's Birthday Honours List. Please join us in congratulating distinguished Fellows, Prof Jane Dahlstrom (OAM, FRCPA, FSc, FFOP), A/Prof Alex Forrest (AO, FOMP) and Prof Andrew Biankin (AO, FSc) who were all named in this year's list. All recipients have made significant contributions to pathology, medical education and research in their respective fields. The RCPA congratulates them all on this well-deserved recognition.

Influenza is notoriously difficult to predict, and this year's season is no different. With many reports that year has been a "killer" flu season, we speak to Professor David Smith to understand if and why this year has been particularly bad, and what we can do to prevent the spread of infection. Prof Smith explains the importance of receiving the vaccine, and encourages everyone to get vaccinated well ahead of each year's season.

We speak with Professor Anthony Gill to find out more about Neuroendocrine tumours (NETs), a group of low-grade cancers which develop from neuroendocrine cells. Unlike most cancers, NETs are normally slow growing but can spread to other parts of the body. NETs are being diagnosed more commonly, but this is probably not due to a true increase in incidence, rather it is due to better detection and more accurate diagnosis.

Hereditary haemochromatosis (HH) is an autosomal recessive disorder of iron absorption and is thought to be one of the most common genetic diseases in people of northern European descent. This year, with World Haemochromatosis Week taking place between 3-9 June, a worldwide

campaign to raise awareness of this, we speak with Dr Samuel Vasikaran to discuss this disease.

Since the age of 9 months old, Louisa di Pietro has received regular treatment for haemoglobinopathy, a term referring to a range of conditions which affects haemoglobin. Like many others, Louisa has received life-saving pathology services on a regular basis for most of her life. We speak to Louisa to discover how pathology is not behind the scenes for her, but rather a way of life.

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Influenza 2019 - Professor David Smith



With many reporting that this year is a "killer" flu season, we spoke to Clinical Professor David Smith, Clinical Microbiologist/Virologist in the Division of Microbiology, and Director of the National Influenza Centre at PathWest QEII Medical Centre, to discuss if and why the 2019 flu season has been particularly bad, and what we can do to prevent the spread of infection.

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An insight into Neuroendocrine Tumours (NETs)

The term neuroendocrine tumour (NET) refers to a group of low-grade cancers that develop from neuroendocrine cells scattered throughout the body. As these secretory cells have traits of both nerve cells and hormone -producing cells, and release hormones into the blood, NETs can also produce hormones. We spoke to Professor Anthony Gill, Professor of Surgical Pathology at University of Sydney and



Senior Staff Specialist, Department of Anatomical Pathology at Royal North Shore Hospital to discuss these tumours which arise most commonly in the gastrointestinal tract or lung.

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Testing for Haemochromatosis; what's new?

Hereditary Haemochromatosis (HH) is thought to be one of the most common genetic diseases in people of northern European descent. Around one in 200 Caucasian Australian people have a genetic predisposition to this disease, with the incidence also the same in New Zealand. This year, World Haemochromatosis Week took place between 3-9 June, a worldwide campaign to raise awareness of this disorder which causes the body to

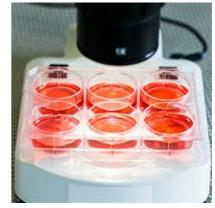


absorb too much iron, leading to iron overload. We spoke with Dr Samuel Vasikaran to discuss this disease.

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Pathology as a true lifeline for survival

Pathology is the foundation for the clinical practice of medicine, paving the way to the appropriate diagnosis, management and treatment of diseases. In reality, every person relies on the work of a pathologist at some point in their life however, more often than not, patients don't know how closely involved a pathologist is in



their healthcare and the diagnosis and treatments of their conditions. For some however, pathology is

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Influenza 2019 - Professor David Smith



With many reporting that this year is a "killer" flu season, we spoke to Clinical Professor David Smith, Clinical Microbiologist/Virologist in the Division of Microbiology, and Director of the National Influenza Centre at PathWest QEII Medical Centre, to discuss if and why the 2019 flu season has been particularly bad, and what we can do to prevent the spread of infection.

"Influenza is notoriously difficult to predict. The 2019 season has started badly with a high number of cases and many people seeking medical treatment, going to hospital or dying. We saw that the season started earlier than usual with a high circulation of two viruses which are causing problems; an influenza A/H3N2 strain and an influenza B strain. However, we won't really know how bad the season will be until later when we know how big the peak of the season is and how long it lasts.

"On average between 10-30% of the population will get infected and around 2,500 people will die due to influenza infection each year, most of whom will be aged 65 or over. It is important that people get vaccinated each year *before* the influenza season starts. We can't be sure whether a season is going to be mild, moderate or severe, so if people wait until we know how bad it is going to be, then their vaccination will be too late to give them protection throughout the season. So just go and get vaccinated every year!"

Influenza virus is a respiratory virus, meaning it mainly causes infections involving the lungs, airways, nose and throat. Infections are usually mild, however high fevers, aches and pains, cough, and a sore throat are common, and people are often off work or school for a few days. Sometimes, and especially in pregnant women, young children, older people and people with chronic illness, the virus causes pneumonia. Rarely, it can

also spread to involve the heart, brain or muscles. Influenza infection also increases the likelihood of bacterial infections, ranging from middle ear and sinus infections, right through to fatal bacterial pneumonia.

There are two main types of influenza viruses that cause infections each year; influenza A and influenza B, both of which are found worldwide. Influenza A is the most serious of these and is found in both humans and animals, though the human and animal subtypes are different. It is also the type that causes pandemics when a completely new subtype spreads from animals to humans and adapts to become a human strain. The influenza A/H1N1, influenza A/H3N2 and influenza B viruses that are currently circulating in humans continually change their surface proteins, so they are not affected by the protection we have built up from previous infections or vaccinations. This is why we can get multiple infections in our lifetime, why the vaccine has to be changed each year, and why we have to get the vaccine every year.

"There has been a lot of discussion about why it is likely that this year will be a severe season, and whether or not this is linked to last year's mild winter season, or the increase in influenza cases across the summer. The thinking behind this is that because there was so little influenza last year, very few people got a boost to their immunity from being exposed to influenza. This idea, however, needs some research to prove that is the case, which would be valuable in getting a better understanding of the virus and its prevention.

"The single best preventive measure against influenza is to get vaccinated 1-2 months before the beginning of the season. Everyone will benefit from vaccination, but it is particularly important in those who are at high risk of severe influenza. These include pregnant women, anyone aged 65 years or over (even if they are healthy), aboriginal and Torres Strait Islander populations aged 15 years or over, children under 5 years-old, and people with any chronic illnesses including heart disease, respiratory disease, diabetes, neurological diseases or any other illness requiring regular doctor visits or admission to hospital; the very obese; and people with a poor immune system due to a disease or treatments that depresses the immune response.

"Vaccination of pregnant women is particularly important not just to protect the mother and baby while it is still in the uterus, but also to protect the baby in the first few months of life. They rely on antibodies that have crossed the placenta from the mother to protect them. Of course, good personal hygiene practices are always recommended to help reduce your risk of getting or spreading influenza and other respiratory viruses.

"Influenza imposes a huge health, social and economic burden on communities each year, and those who choose not to be vaccinated magnify that burden. There is the obvious personal health risk of being unvaccinated, especially those who are vulnerable to severe influenza, but also the lost work time and income, caring for sick children, and also exposing others to influenza. Vaccination reduces the number of people attending medical practices and Emergency Departments, and preserves that capacity for those that need it. The vaccination is safe and there are very few scientifically valid reasons for people not to get vaccinated."

If a doctor is confident that influenza is present, then testing may not be necessary. Otherwise, influenza is usually diagnosed by taking swabs from inside the nose on both sides, and from the back of the throat. For young children and people who are in hospital, other samples may also be collected.

"Most testing is now done through methods which detect the genetic material of the virus and show which influenza type is present. Those results usually take a few days to come back, so your doctor will decide on the best treatment before those results are available. Antiviral drugs are now available, the commonest of which is a tablet called oseltamivir which can reduce the illness and lower the risk of complications like middle ear infections and pneumonia. However, this needs to be started as soon as possible, and no later than 48 hours after symptoms begin."

If testing is done, we use the information about the specific influenza virus to assist treatment decisions and to determine the risk of spreading the infection. This information will also be used to assess how effective the vaccination program has been. A selection

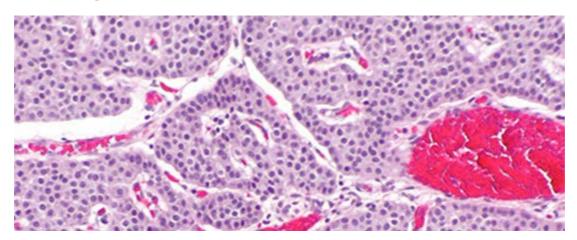
of these viruses is also sent to the World Health Organization laboratories where they are analysed, and the information is used to select strains for future vaccines.				
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An insight into Neuroendocrine Tumours (NETs)



The term neuroendocrine tumour (NET) refers to a group of low-grade cancers that develop from neuroendocrine cells scattered throughout the body. As these secretory cells have traits of both nerve cells and hormone -producing cells, and release hormones into the blood, NETs can also produce hormones [1]. We spoke to Professor Anthony Gill, Professor of Surgical Pathology at University of Sydney and Senior Staff Specialist, Department of Anatomical Pathology at Royal North Shore Hospital to discuss these tumours which arise most commonly in the gastrointestinal tract or lung.

"NETs are uncommon but not rare. They account for less than 0.5% of all malignancies, and the estimated incidence is 3 to 4 per 100 000 each year, which is about as common as testicular cancer or Hodgkin Lymphoma. NETs are being diagnosed more commonly, but this is probably not due to a true increase in incidence, rather it is due to better detection and more accurate diagnosis," said Prof Gill.

Unlike most cancers, NETs are normally slow growing tumours but can spread to other parts of the body. Some patients will develop symptoms due to the hormones secreted by the NET's such as flushing, wheezing or diarrhoea, but most patients will present like other cancers with vague symptoms, perhaps due to a mass which may involve and damage organs.

"There are some rare syndromes including hereditary syndromes, which place people at an increased risk of developing NETs, including multiple endocrine neoplasia (MEN) or von Hippel Lindau syndrome (VHL), but the overwhelming majority of NETs occur sporadically for no known reason. Like all tumours they are more common in the elderly, but they can occur at any age and, compared to other cancers, are relatively more common in young people.

"The main role of the pathologist is to diagnose NETs on a biopsy and to separate them from high grade cancers which are much more common but require very different treatment. Importantly, the pathologist can also try to predict how quickly a neuroendocrine tumour will grow, and one way of doing this is to perform a Ki67 index – a test which estimates how quickly the cancer cells are growing," said Prof Gill.

A multidisciplinary team is important for those people with NETs, working together to create an overall treatment plan for a patient by combining different types of treatments. These care teams generally consist of doctors (surgeons, oncologists, endocrinologists, pathologists, radiologists) and allied health professionals (nurses, dieticians, physiotherapists). Treatment options can depend on a number of different factors, including the type of NET, the stage and grade, possible side effects, and the patient's preferences and overall health [2].

"The prognosis depends on the grade, i.e. how quickly the pathologist thinks the tumour is growing, and the stage i.e. how big the tumour is and whether it has spread. For example, almost all patients with microscopic tumours in the appendix will be cured by simple appendicectomy with no further treatment. However, once the tumour has spread widely it is difficult to cure but could be controlled by treatments for many years - much longer than most tumours - and many patients live longer than 5 years even when the tumour has spread throughout the body.

"It is important that patients with NETs are treated in specialty units so they can access new treatments. For example, there are a lot of new treatments available for those tumours which have spread, including a class of drugs known as 'somatostatin analogues' which work by stopping the tumour cells excreting hormones and slowing their growth. Another new treatment becoming available for NETs is peptide receptor radionuclide therapy (PRRT), where radioactive tracer material is injected into the blood stream. This radioactive material binds to the tumour (but not normal cells) and can either kill the tumour cells or slow their growth," said Prof Gill.

References:

[1] https://rarediseases.info.nih.gov/diseases/13445/neuroendocrine-tumor

[2] https://www.cancer.net/cancer-types/neuroendocrine-tumors/types-treatment

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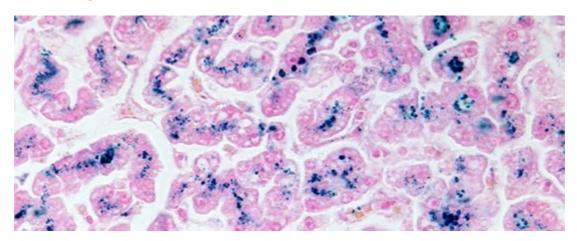
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Testing for Haemochromatosis; what's new?



Hereditary Haemochromatosis (HH) is thought to be one of the most common genetic diseases in people of northern European descent. Around one in 200 Caucasian Australian people have a genetic predisposition to this disease [1], with the incidence also the same in New Zealand [2]. This year, World Haemochromatosis Week took place between 3-9 June, a worldwide campaign to raise awareness of this disorder which causes the body to absorb too much iron, leading to iron overload. We spoke with Dr Samuel Vasikaran to discuss this disease.

"Haemochromatosis is an autosomal recessive disorder of iron absorption, with progressively increasing tissue iron deposition and organ damage. Not all patients with detectable common genetic abnormalities may be symptomatic, but they remain at risk for cirrhosis and other end organ damage.

"HH is most commonly caused by mutations in a gene called HFE. The two main mutations causing HH are referred to as C282Y and H63D. The C282Y mutation is associated with most cases of HH, and those with the mutation are at risk of developing iron overload. However, it should be noted that many individuals with HFE mutations will not have clinical iron overload as disease penetrance is low," said Dr Vasikaran."

Testing for haemochromotosis should be performed in patients with;

- clinical signs or symptoms suggestive of diseases associated with iron overload [such as lethargy, fatigue, unexplained chronic liver disease, cardiomyopathy, type 2 diabetes mellitus, male hypogonadism, increased skin hyperpigmentation, certain arthropathies and porphyria cutanea tarda], or
- 2. laboratory findings such as unexplained liver function test abnormalities, a high

serum ferritin or transferrin saturation, and

3. in first- or second-degree relatives of those diagnosed with HH.

Haemochromatosis tends to be under-diagnosed and, in many cases, there are no symptoms, especially in children and young adults. When symptoms do arise, they are often vague and can be similar to those caused by a range of other illnesses. Early diagnosis and treatment can prevent complications and results in normal life expectancy. Professor John Olynyk, Professor of Translational Medicine at the School of Medical and Health Sciences, Edith Cowan University, explains the testing involved for haemochromotosis:

"The most common blood test used to diagnose haemochromotosis is measurement of serum iron studies, which includes serum transferrin saturation and ferritin. Recently we have also shown that you can identify people at high risk of hemochromatosis using information presented in the results of a full blood count. This is something that we have built into the GP health pathways here in WA. There are a range of other blood tests, including liver biochemistry, testing for diabetes – arthritis test which can also determine if clinical problems are due to hemochromatosis or whether they are just occurring coincidentally.

"Full blood counts are done routinely in Australia, there are about 12 million done every year. Out of these blood counts that are being done often, if the results for Haemoglobin, white cell count and platelet count are normal – people tend to ignore the remaining parameters. However, if you pay attention to the mean cell volume (MCV) and mean cell haemoglobin (MCH), you can identify subgroups at substantially increased probability of having HH," said Professor Olynyk

Professor Olynyk's research team determined the sensitivity, specificity and clinical utility of erythrocyte parameters in 144 HH subjects with (n = 122) or without (n = 22) clinical and/or biochemical expression of iron overload. These results were compared with the general population and subgroups with chronic diseases. For both expressing and non-expressing HH subjects, the mean pre- and post-phlebotomy values of MCV and MCH were always significantly higher when compared to all other groups and demonstrated excellent diagnostic utility for detection of HH in men and women $^{[3]}$.

"What I now recommend in addition to the currently accepted guidelines for screening for HH is that those individuals of northern European ancestry with MCV greater than 94 fL or MCH greater than 32 pg also investigated for HH. If you are actually diagnosed early with the condition, before you have any end organ damage, then your survival and longevity is identical to everyone else of similar age and gender in our population. It is a completely treatable and controllable situation," said Professor Olynyk.

References:

[1] https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/haemochromatosis?viewAsPdf=true

[2] https://www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/iron-overload-haemochromatosis

[3] https://www.sciencedirect.com/science/article/pii/S1079979618303127?via%3Dihub

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Pathology as a true lifeline for survival



Pathology is the foundation for the clinical practice of medicine, paving the way to the appropriate diagnosis, management and treatment of diseases. In reality, every person relies on the work of a pathologist at some point in their life however, more often than not, patients don't know how closely involved a pathologist is in their healthcare and the diagnosis and treatments of their conditions. For some however, pathology is something which has become an integral part of their everyday lives and a true lifeline for survival.

Like many others, Louisa Di Pietro has received life-saving pathology services on a regular basis for most of her life. For her, pathology is not behind the scenes, but rather a way of life:

"I have a very different perspective from those people who enter the health system once or twice in their life. My reference point is that I have a whole of life pathology services awarded to me as my human right in Australia. From my perspective, and from a life with a chronic genetic blood disorder where I received my first treatment at 9 months old, my entire life revolves around pathology services," said Louisa.

Since the age of 9 months old, Louisa has received regular treatment for haemoglobinopathy, a term referring to a range of conditions which affects haemoglobin. This can include α -thalassaemia and β -thalassaemia, sickle cell disease and other abnormal haemoglobins, such as haemoglobin E (HbE). In Louisa's case, her genetic condition is β -thalassaemia major, meaning her body does not produce sufficient haemoglobin. She therefore requires regular blood transfusions, ranging anywhere between once every three weeks to even weekly if she is acutely unwell.

"I receive a blood transfusion every three weeks, so if you consider the process of

transfusion medicine for me then you will see that it is incredible. Prior to receiving the blood, I need to go to a pathology services, either in the hospital or in the community. I have a full blood assessment, including having my haemoglobin levels tested, and then I have blood taken for cross matching purposes, where a blood sample of mine and one from the donor are compared to try and get the best likeness possible. This has been the case for 49 years."

"In addition, I need to receive safe blood which is not only matched to my blood type, but which also does not have any antibodies which can be very destructive. For me, what the RCPA and the health system provide around pathology, and specifically the protocols around blood transfusion medicine which require pre and post testing, is an absolute lifeline. They not only keep me alive but also they keep me healthy due to the processes which are in place to ensure I am getting a reliable, safe source of blood."

Health service organisations have systems in place for the safe and appropriate prescribing and clinical use of blood and blood products. These National Safety and Quality Health Service (NSQHS) Standards were developed by the Australian Commission on Safety and Quality in Health Care (the Commission) in consultation and collaboration with jurisdictions, technical experts and a wide range of other organisations and individuals, including health professionals and patients. The primary aims of the NSQHS Standards are to protect the public from harm and to improve the quality of care provided by health service organisations.

There are a range of different conditions which depend on regular blood transfusions, including anaemia, cancer, haemophilia, kidney disease, liver disease, sickle cell disease and thrombocytopenia. For these people, pathology becomes a part of their day to day life, and many of these people owe their health and well-being to the hard work of pathologists.

""I belong to just one group of conditions – if you think of people with ongoing cancers, or leukemia, or the haemophilia group, it's a huge population. These are all people with a chronic condition, an acute health condition where pathology is first line medicine. For those who are chronically ill, who have life-long conditions – pathology is a lifeline and is the one service that they rely on the most. It gives them the information needed to treat, and to provide health and wellbeing as safely as possible."

"What we have in Australia is gold. I am aware of the gaps in services and I am aware there is unmet need for many of those engaged continuously with the health system, but in comparison to other OECD countries, we still have it very good. I believe that if you take an interest in your healthcare, and the processes around your healthcare, and learn that you have to manage it, then you realise that the system is not broken, the system is not horrible, it isn't all bad and so much is delivered to us as part of our national health care system."

In 2017, Louisa was inducted in the Lifetime Achievement Honour Roll at the 2017 Victorian Disability Awards. The achievement recognises Louisa's decades-long advocacy for those with genetic conditions and rare diseases. She is the former Group Leader of the Genetic Support Network of Victoria (GSNV) and currently holds the education and advocacy strategy advice portfolio. Louisa is actively involved in professional and community engagement and sits on numerous professional boards and advisory groups within the genetic health space, and employs her professional and 'lived' experience/knowledge of managing a genetic condition to assist in the continuum of care delivered to Australians and in linking them in with specialised support/services and assisting advocacy efforts. [2]

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[2] https://www.gsnv.org.au/about-gsnv/our-team.aspx

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- Precision medicine throug

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Measles is a highly contagious viral illness which can cause serious

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