ePathWay
THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

JUNE 2018 | PUBLISHED BY RCPA ISSUE #081

IN THIS ISSUE

- The lifesaving gift of blood
- National Diabetes Week
- Testing for inherited iron overload
- Landmark funding gives hope of a cure for young people with genetic heart disease

INTERESTING FACTS

1,700,000

The number of Australians who have been diagnosed with diabetes[1]. In New Zealand, there are over 240,000 people who have been diagnosed with diabetes[2].

22

The number of different medical treatments that donated blood can be made into[3].

12

One Australian dies of cardiovascular disease every 12 minutes[4]. In New Zealand

Welcome to the June 2018 edition of ePathWay

This month's issue of ePathway will look at the following:

- The lifesaving gift of blood
- The importance of early detection and treatment for all types of diabetes
- Haemochromatosis, one of the most common genetic disorders in Australia; and
- Landmark funding gives hope of a cure for young people with genetic heart disease

Blood is essential to life. It carries essential substances such as oxygen and nutrients to the body's cells and transports metabolic waste products away from these cells. To coincide with World Blood Donor Day, this issue will discuss the importance of donating blood.

But with respect to blood and the iron from which it is made, can there be too much of a good thing? We also explore hereditary haemochromatosis, a disorder which causes the body to absorb too much iron from the diet.

Ahead of National Diabetes Week, which will take place in July, we spoke to an expert on the importance of early detection and treatment for all types of diabetes.

We will also discuss the impact on forensic and genetic pathology of recent funding announcements for cardiology research in New South Wales.

Remember to follow us on Facebook (@TheRoyalCollegeofPathologistsofAustralasia), Twitter (@PathologyRCPA) or on Instagram (@the_rcpa). CEO, Dr Debra Graves can be followed on Twitter too (@DebraJGraves).

The lifesaving gift of blood

one person dies every 90 minutes from heart disease[5].

Source:

[1] https://www.diabetesaustralia.com.au/about-diabetes

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

[3] https://www.donateblood.com.au/

[4] https://www.heartfoundation.org.au/about-us/what-we-do/heart-disease-in-australia

[5] https://www.heartfoundation.org.nz/

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On World Blood Donor Day, 14 June 2018, we spoke with Dr Peter Flanagan, National Medical Director at New Zealand Blood Service, about the importance of donating.

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National Diabetes Week

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Testing for inherited iron overload

We spoke to Dr Kym Mina, Director of Genetics at Douglass Hanly Moir Pathology, earlier this month during Haemochromatosis Awareness Week

(4-10 June 2018) to find out about inherited iron overload.

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Landmark funding gives hope of a cure for young people with genetic heart disease

Professor Chris Semsarian is an internationally renowned cardiologist and scientist studying genetic heart disease and sudden death, and the management of individuals and families with, or at risk of, inherited cardiac disorders. He is the Director of the Genetic Heart Disease and Hypertrophic Cardiomyopathy Clinic at Royal Prince Alfred Hospital, Sydney, and Director of the Australian Genetic Heart Disease Registry.

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The lifesaving gift of blood

On World Blood Donor Day, 14 June 2018, we spoke with Dr Peter Flanagan, National Medical Director at New Zealand Blood Service, about the importance of donating.

The World Health Organisation, the International Society of Blood Transfusion, the International Federation of Blood Donor Organisations and the International Federation of Red Cross and Red Crescent Societies initiated World Blood Donor Day in 2004. It provides an opportunity for a national and global celebration on a day that has particular significance: it's the birthday of Karl Landsteiner, the Nobel Prize winner who discovered the ABO blood group system.

Dr Peter Flanagan says,

"Blood donation is important because the availability of sufficient safe blood components underpins modern health service provision. World Blood Donor Day is our opportunity to celebrate those selfless individuals in Australia and the 110,000 in New Zealand, and all of those around the world who, on a regular basis, give blood to help other people have the health treatment that they require, with no immediate benefit to themselves. It also provides a very powerful tool for advocacy to government to ensure that appropriate resources are directed towards the development and maintenance of the transfusion service.

"Having blood available is essential, and it's worth remembering that not everybody can give blood. So, I think that those that are able to do so, perhaps it's their civic responsibility to try to give blood when they can."

The NZ Blood Service[1] and the Australian Red Cross[2], have a quiz on their websites which reveals whether you are eligible to donate blood in these countries.

"The criteria for giving blood in Australia and New Zealand are pretty well aligned, but it's worth checking the blood services website in your country to see if you are able to donate. There are a significant proportion of individuals who, for a range of reasons, will not be able to donate blood. They won't meet the very strict criteria that the blood services have, and in New Zealand at least, somewhere in the order of one in seven to one in ten first time blood donors will be found ineligible for one reason or another, so we're talking about a significant number of people being excluded.

"Additionally, there are also many other people who would meet our criteria, but, for a range of reasons either believe that they aren't eligible, i.e. we haven't properly raised awareness of what the criteria are, or they may have some fears associated with donating blood. Historically, there have been fears that it's painful, it's dangerous, or it can impact on their own health. Fortunately, the reality is that in developed countries such as Australia and New Zealand, blood donation is a very safe and controlled process. The likelihood of individuals coming to harm as a consequence of giving blood is very low indeed but I think we need to better communicate that message to people.

"If you look at the modern world blood services, certainly in New Zealand, we have a marketing team that relies heavily on social media to get our message across. We're constantly communicating with donors. With those who have already donated, we like to encourage them to come back when we need them and, of course, we're always managing that very careful balance between collecting enough blood and not too much. We always aim to avoid collecting more than is needed as we wouldn't want to waste that precious gift.

"The amount of blood that we collect is a reflection of the demand placed on us by hospitals around the country. Undeniably, over the last 10 to 12 years there's been a changed perspective of the role of transfusion in patient care and I think that's a good thing. We now allow haemoglobin to fall to lower levels than would have been the case say, ten years ago. This comes from research that demonstrates the so called restrictive transfusion trigger of 70 grams per litre, in an otherwise healthy individual, is quite safe and isn't associated with any adverse outcomes. Previously, we used a haemoglobin figure of 90 to 100 grams per litre and if a patient's haemoglobin fell below that, we would transfuse them. As a result, we collect significantly less whole blood today, perhaps 25% less, than we did a decade ago," says Dr Flanagan.

There are about five litres of blood in the human body and it's made up of several useful components. People may be eligible to donate whole blood, plasma or platelets. Each type of blood donation is used for different medical treatments, and the individual's blood type determines the best donation that they can make. [2]

"In Australia and New Zealand, the driver for collection now is plasma, which is used for the production of immunoglobulin. In both countries the demand for immunoglobulin is increasing and, with that demand, plasma. So, over the last decade, the pattern of blood product use has changed and, therefore, the blood collection services have changed accordingly so that plasma collections have increased. Whole blood collection has plateaued; however, I would expect that a slow gradual increase, linked to population growth and an ageing population, will occur over the next several years.

"If you look at many of the developments in clinical care over the last fifty years, they bring with them a requirement for access to safe and effective blood components. For example, the modern treatment of patients with leukaemia by chemotherapy and bone marrow transplantation wouldn't be possible without access to transfusion. This is the case if you look at cardiac surgery and in fact most forms of major surgery today. We may have used less blood in 2018 than we did 10 years ago, but nonetheless, the availability of that blood when it is required is absolutely pivotal to enable healthcare to move forward.

"As we move into winter, which is classically a time where there is illness in the community - coughs, colds, ill heath associated with winter – it can be more difficult to maintain blood inventories. We encourage all individuals who are capable of donating blood to contemplate giving this lifesaving gift," says Dr Flanagan.

[1] https://www.nzblood.co.nz/give-blood/donating/am-i-eligible/

[2] https://www.donateblood.com.au/eligibility

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National Diabetes Week

National Diabetes Week runs from 8 July to 14 July 2018. This year it aims to raise awareness of the importance of early detection and treatment of all types of diabetes as part of the 'It's About Time' campaign. The campaign's main message is that many Australians with either type 1 or type 2 diabetes are diagnosed late: a delay which can put them at risk of life threatening health issues.

The total annual cost of diabetes in Australia is estimated at AUD 14.6 billion. Around 1.7 million Australians have diabetes, including all types of diagnosed diabetes (1.2 million known and registered) and silent, undiagnosed type 2 diabetes (up to an estimated 500,000 individuals). 280 Australians develop diabetes every day. That's one person every five minutes. [1]

Associate Professor, Graham Jones, a specialist in Chemical Pathology at St Vincent's Hospital SydPath discussed diabetes with us.

"These are quite extraordinary statistics, particularly when considering that all of these diagnoses are absolutely reliant on laboratory tests. Once a diabetes diagnosis has been made, it will then hopefully lead to a change in a person's life, encouraging them to respond to the results by making improvements in their lifestyle."

Diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar; therefore, when an individual has diabetes, their body can't maintain healthy levels of glucose in the blood. There are three main types of diabetes: type 1, type 2 and gestational diabetes.

"Type 2 diabetes is by far the most common type of diabetes and is increasing at the

fastest rate. The main things that put someone at risk are being overweight, central adiposity, a lack of exercise, and too much of the wrong kind of food.

"You could describe diabetes as a definitional disease as it's defined by pathology results. The only way that someone can be diagnosed with diabetes is either through one or more glucose tests, which need to be done in a formal laboratory, or by another laboratory test called HbA1c. Without those tests, it's not possible to diagnose diabetes. Additionally, the key to monitoring whether the treatment is working is by the use of pathology tests.

"The type of diabetes that an individual has affects the methods of testing. With the most common type, type 2 diabetes, individuals might be expected to have a test called HbA1c, which is a blood test that reflects the average blood sugar over a period of one or two months. Individuals might need to have that test perhaps twice a year. Every year or so, or in some cases more frequently, they will also have their urine tested for protein. Individuals with type 1 diabetes will generally test themselves for blood glucose four or more times every day. They also have their HbA1c tested perhaps four times a year and will be monitored for potential damage to their kidneys by means of urine albumin. Other routine tests include blood tests to identify reduction in kidney function, and also for lipids like cholesterol, HDL cholesterol and triglycerides to ensure that they're not otherwise at risk of vascular disease," says A/Prof Jones.

The potential complications of diabetes are the same for type 1 and type 2 diabetes. They include heart attacks, blindness, kidney failure, amputations, and can affect a person's mental health by causing depression and anxiety. [2]

"We know if the HbA1c is lower than the appropriate level, then it can indicate overtreatment. It's very important to monitor HbA1c to reduce complications like heart disease, heart attack, vascular disease, kidney disease and eye disease. We know that if there's a response to treatment then those complications can be reduced."

Whilst there is no known cure for diabetes, steps can be taken to control blood sugar levels, therefore slowing down the advance of the condition.

"With type 2, if you can reverse the things that might have caused the diabetes in the first place, then the severity tends to be markedly reduced. That means reducing excess weight, eating an appropriate diet and exercising. That can be hard, and often oral medications may be prescribed, which should be taken regularly. If type 2 diabetes becomes more severe, then these patients may need treatment in the form of a little injection under the skin with subcutaneous insulin one or more times a day. In addition, because one of the main ways that diabetes causes ill health is in the vascular system, then attention is placed on things like blood pressure, cholesterol and other lipids. Making sure that the individual is not smoking and is getting exercise is also very important.

"In pathology, most of the effort is focused on doing the basic things very well. For instance, the quality of results for things like HbA1c, blood glucose and urine albumin in Australia is very, very high. Patients can have confidence that the results are the same from different labs and can be relied on to monitor their treatment.

"Some areas of improvement in relation to diabetes are more in therapeutics. There are new medicines coming out, and also for type 1 there are newer monitoring techniques with continuous blood glucose monitors improving all the time. But essentially, what pathologists are doing in the laboratory is absolutely the mainstay for diagnosis and also for monitoring the treatment of diabetes," says A/Prof Jones.

[1] Diabetes in Australia - https://www.diabetesaustralia.com.au/diabetes-in-australia

[2] Diabetes Australia, Preventing Complications - https://www.diabetesaustralia.com.au/preventing-complications

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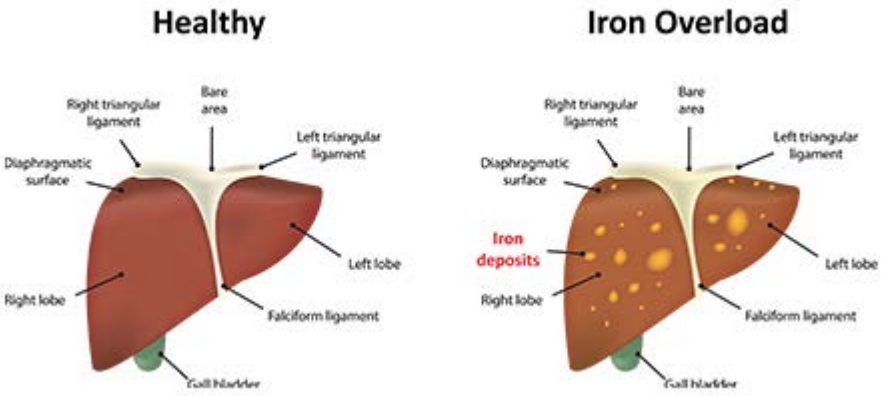
Testing for inherited iron overload



We spoke to Dr Kym Mina, Director of Genetics at Douglass Hanly Moir Pathology, earlier this month during Haemochromatosis Awareness Week (4-10 June 2018) to find out about inherited iron overload.

“Hereditary haemochromatosis is a disorder which causes the body to absorb too much iron from the diet. If we take in too much iron, the body doesn’t have a way of increasing the amount of iron that it removes and therefore we accumulate iron in our tissues and organs and this can cause damage to those organs.”

Inherited disorders are caused by specific genes that have changed or mutated and been passed down through generations. While several mutations to the gene that governs iron absorption have been discovered, C282Y and H63D are the two main mutations that cause hereditary haemochromatosis. [1]

"Haemochromatosis is most commonly caused by the C282Y mutation in a gene called HFE. Those with the mutation are at risk of developing iron overload. It is estimated that 1 in 200 Caucasians are homozygous (have two copies of the same gene abnormality) for that mutation."

For the condition to be passed on, mother and father must each have one copy of the abnormal HFE gene.

“Whilst there might be 1 in 200 people who are homozygous for that mutation, not everybody that has the mutation will actually develop iron overload and clinical features of haemochromatosis. It’s estimated that in females about 1% of those with the mutation will actually develop clinical features, although it’s higher for males (about 28%), so men are more commonly affected than women by this disorder,” says Dr Mina.

“Haemochromatosis caused by the C282Y mutation is an adult onset disorder, so you might expect to see it in males between the ages of 40 and 60 years of age. Typically, it is seen in females after menopause, which is due to the fact that they stop menstruating so they’re no longer losing iron in that way.”

Chronic fatigue and joint pain are the most common complaints of people with haemochromatosis. Patients often complain of lack of energy, abdominal pain, memory fog, loss of sex drive, heart flutters and irregular heartbeat. [2]

“Early symptoms can be non-specific but, as iron accumulates in tissues, individuals may begin to experience joint pain and stiffness. A serious consequence that we associate with haemochromatosis is liver cirrhosis, which is fibrosis and scarring of the liver. Other major features we see include diabetes, heart abnormalities and skin discolouration. Whether these features develop is also affected by environmental factors, for example alcohol consumption increases the load on the liver and therefore the risk of developing cirrhosis,” explains Dr Mina.

“Pathology plays a critical role in the diagnosis of haemochromatosis. It’s detected by laboratory iron studies, in particular by ferritin and transferrin levels. This provides us with a measure of how much iron you have in your body. If the levels of those are high, this might alert your doctor to the fact that you may be iron overloaded. From there, a number of tests can be done, including a DNA test to look for the C282Y mutation in the HFE gene to see if the iron overload is genetically caused, or if it is a result of other non-genetic causes.

“Many people who have the mutation don’t ever require treatment because they don’t go on to develop iron overload. However, for those who do develop overload, the recommended treatment is therapeutic blood donation. This involves a schedule of blood donation and, during the course of that, iron levels are monitored. Once iron returns to a normal level, some patients can stop donating blood, but most will need to continue to do so less frequently.

“Genetic testing is recommended for anyone who has repeatedly elevated iron levels, or a first degree blood relative that has haemochromatosis or is known to have the mutation. Testing is available on Medicare under those circumstances.

"It’s very important to diagnose someone who has hereditary haemochromatosis early because you can prevent some of the end organ damage caused by iron accumulation. Once a patient has developed cirrhosis, they are then at risk of other complications, including liver cancer and complete liver failure, so it’s better to identify these people before that kind of damage occurs. Pathology and genetic testing play a key role,” says Dr Mina.

[1] Haemochromatosis Australia, https://haemochromatosis.org.au/genetics/

[2] Haemochromatosis, https://www.hemochromatosis.org/welcome-2#symptoms

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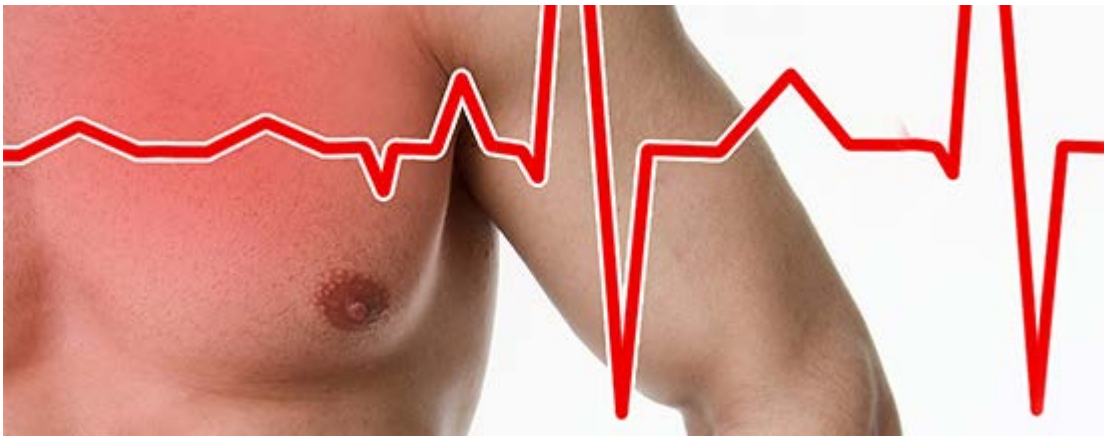
Landmark funding gives hope of a cure for young people with genetic heart disease



Professor Chris Semsarian is an internationally renowned cardiologist and scientist studying genetic heart disease and sudden death, and the management of individuals and families with, or at risk of, inherited cardiac disorders. He is the Director of the Genetic Heart Disease and Hypertrophic Cardiomyopathy Clinic at Royal Prince Alfred Hospital, Sydney, and Director of the Australian Genetic Heart Disease Registry.

Professor Semsarian also became an Honorary Fellow of the Royal College of Pathologists of Australasia (RCPA) in 2017, acknowledging two of his ground-breaking studies into sudden cardiac death in the young across Australia and New Zealand. This prestigious RCPA award recognised Professor Semsarian's important work as a clinician and researcher working in close collaboration with forensic and other pathologists, with the ultimate goal of preventing sudden cardiac death in our communities. Professor Semsarian has also presented at Pathology Update in 2006, 2009, 2011, 2014 and 2017 in both the forensic and genetic pathology scientific streams.

Following recent funding announcements for cardiology research in New South Wales, we spoke to him about what this means for research and areas of innovation in this field.

Professor Semsarian says,

"In order to do research we need funding, and without research we really have no answers. Research is absolutely vital if we're going to improve the management and diagnosis, and hopefully prevent the occurrence, of cardiovascular disease in our communities. There have been two big announcements for funding in cardiovascular research recently: The Heart Foundation [1] and the NSW Government [2].

“My research is in the area of young people with heart disease. This area of cardiology is not in relation to coronary heart disease, blood pressure, smoking or cholesterol, but in young people who have a fault in a gene that they’re born with that leads to heart conditions, such as cardiomyopathy and rhythm problems of the heart.

“A particular complication of all of those genetic heart diseases is sudden death. This tends to be the young person that goes onto a soccer field, basketball court or rugby field and dies suddenly or is found deceased at home. The Heart Foundation and other organisations have helped us to fund a lot of the research we do, which looks at identifying why young people die suddenly.

“Specifically, The Heart Foundation has supported a study where we’ve looked at sudden deaths across all of Australia and New Zealand. Of the many findings, there are two key aspects. Firstly, for approximately 40% of young people who die suddenly in Australia and New Zealand under the age of 35, no cause is found after a post mortem examination. The second aspect is that we can now do a molecular autopsy, where we can take a blood sample from the post mortem of the individual who died suddenly and unexpectedly (where nothing was found at post mortem), and do a whole genetic profile to see if there was a faulty gene that caused the sudden death,” says Professor Semsarian.

Genetic testing is a growing discipline which diagnoses genetic diseases by overseeing the testing of patient samples for mutations. Genetic testing is available to identify the cause of a family’s heart disease and can also help to determine which specific relatives are at risk of developing this condition for which pathology testing is integral.

“The benefit of that is, firstly, it gives the parents a bit of closure as to why their son or daughter died suddenly, but secondly, and very excitingly, we can use that genetic information for other relatives in the family – other children, siblings, parents and cousins. If we identify someone at risk who is carrying these gene abnormalities, we can do a lot of things to stop people from dying suddenly. So it’s a very proactive process. I guess that’s one example of where the research funding that’s been announced by the Heart Foundation is helping us to do projects like this - to investigate why young people die suddenly.

“No project that we ever do in research is solely funded by one organisation because it’s just too expensive. The Heart Foundation funds a particular aspect of the study. The current funding was related to following up with these families over time to see how many develop diagnoses, how many sudden deaths were prevented in the family relatives, that sort of thing.

“In addition, I was recently part of the NSW Government’s $150 million initiative[2]. I was part of a team that lobbied the government for 18 months. They announced that the new funding aims to reduce the number of Australians dying from heart disease over the next decade. The NSW Government Premier Gladys Berejiklian, Treasurer Dominic Perrottet and Health Minister Brad Hazzard announced the landmark funding in the NSW Budget 2018,” says Professor Semsarian.

At the time of the announcement, Premier Gladys Berejiklian said,

“Heart disease remains Australia’s number one killer but with greater investment, researchers can predict, prevent and treat it more accurately.”

Professor Semsarian says, “This input of $150 million over 10 years, specifically into cardiovascular disease in New South Wales, will be broken down into funding for actual research, but also for people for fellowship funding - for young career researchers who often struggle to get their fellowship. It will bring bright and talented people back to New South Wales so we can make New South Wales the premier state in terms of cardiovascular research. To my knowledge, this is the biggest injection of research funds ever at a government level, specifically into cardiovascular research.”

“It’s calculated that every 12 minutes one Australian dies of cardiovascular disease, which is a horrific statistic - one death every 12 minutes. In the genetic heart diseases that lead to a heart condition, it occurs in up to 1 in 200 people, so it’s quite a common

occurrence. One in three Australians have evidence of heart disease," says Professor Semsarian.

"There are some big issues in cardiovascular disease at the moment. The obvious ones are things like the obesity and diabetes epidemic and coronary artery disease, but there's also a lack of emphasis on younger people with heart disease, such as genetic heart diseases and congenital heart disease, when babies are born with a holes in the heart or with half a heart. This funding will cover everything from birth onwards.

"We know that these genetic heart diseases are caused by a mistake in a gene. For the heart gene that has a mistake in it, we now have technologies called genome editing, or the other term is CRISPR. This technology provides the ability to correct the genetic mistake and essentially cure disease."

CRISPR (Clustered Regularity Interspaced Short Palindromic Repeats) technology is a powerful tool for editing genomes, allowing researchers to alter DNA sequences and modify gene function. Professor Semsarian has been working with this technology to find potential treatment and cures for heart disease.

"At this stage, we've done most of our work in a dish, so we've corrected the disease in heart cells that have a genetic mutation. We've used CRISPR and returned the gene back to normal so it's a bit like a spellcheck autocorrect scenario. We've done it in cells in a dish but the obvious challenge is how we do it in a human. I think research gives hope to patients that one day there will be not just better treatment but, in this instance, potential cures. To me, probably the biggest, most exciting thing is genetic editing in order to correct genetic mutations that kids are born with," says Professor Semsarian.

[1] https://www.heartfoundation.org.au/news/3.8-million-boost-to-heart-disease-research-in-nsw

[2] http://www.health.nsw.gov.au/news/Pages/20180603_00.aspx

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