



ePathWay

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

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Issue #018

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- Vaccine research coughs up some surprises
- Syphilis is still standing after all these years
- Holy cow! Scientists surprised by TB case in New Zealand

Interesting Facts

50
percent

The number of people with diabetes who die of cardiovascular disease (primarily heart disease and stroke)

Welcome to the September edition of ePathWay

When it comes to medicine the truth is often stranger than fiction. But it was still a surprise when a cow turned up in New Zealand with an unusual strain of tuberculosis (TB) and an even more unusual source of the infection. A scientist from AgResearch filled us in on this case, and it's an eye opener.

We also take a closer look at syphilis which is springing up again, and report on why research into the current whooping cough vaccine is causing a bit of a stir. And finally, we look at why our own advocates are putting together the medical case to use an existing pathology test to help diagnose diabetes early.

We welcome your feedback about the stories covered in ePathWay, and hope you find it an invaluable way of being kept up to date about pathology in Australasia.

Experts make their position clear on early detection of diabetes

50 percent

The number of people who have damage to nerves (known as diabetic neuropathy) as a result of diabetes

15 years

The time it takes for about two percent of people with diabetes to become blind, while about 10 percent develop severe visual impairment

Source: World Health Organization Fact Sheet No. 312



Who would have thought the 'pleasant new spice' called sugar, which was discovered by western Europeans in the 11th century, would contribute to a disease that boasts its very own United Nations General Assembly Resolution! Diabetes is a worldwide epidemic and significantly impacts on both individual health and national productivity levels. Early detection is important to significantly reduce the risk of developing complications, and a simpler regime that may catch the early diagnoses that currently 'get away' has been put forward by an expert panel.

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Vaccine research coughs up some surprises

Whooping cough has gone 'viral' thanks to a study ^[1] which found that children vaccinated with the current vaccine were more likely to develop this highly contagious respiratory infection than those who received the earlier vaccine type. The study's results, which have spread around the world, could partly explain the resurgence of whooping cough in Australia and America.



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Syphilis is still standing after all these years

What do King Henry VIII, Ivan the Terrible, Christopher Columbus, George Washington, Napoleon Bonaparte, Adolf Hitler, Al Capone,



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Vincent Van Gogh, Leo Tolstoy and Oscar Wilde have in common? They all allegedly suffered from syphilis. This bunch probably weren't thrilled about this footnote in history, but privacy laws prevent this type of information being shared today. People are diagnosed and treated discretely which is fortunate because syphilis is still standing and notifications are on the rise – again.



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Holy cow! Scientists surprised by TB case in New Zealand

There are some situations where it takes a while to get your head around the details, and this is one of them. An 11-year-old dairy cow sent to slaughter in New Zealand last year was found to have an unusual lesion in a lymph node during a routine meat inspection. The lesion was caused by tuberculosis (TB), but the next bit surprised everyone. Once the TB organisms were further investigated at the genetic level, and the history of the farm and its workers were carefully investigated, it became clear that the cow had caught a very unusual TB species from a human.



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Experts make their position clear on early detection of diabetes



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The Royal College of Pathologists of Australasia (RCPA), Australian Diabetes Society and the Australasian Association of Clinical Biochemists (AACB) have produced a joint position statement^[1] addressing the importance of detecting diabetes early. They propose using a simple blood test called a glycated haemoglobin (HbA1c) which measures the average amount of sugar in the blood over a two-month period.

The HbA1c is currently included on the Medicare Schedule to monitor people with a known diagnosis of diabetes. The experts think it has more potential and are seeking reimbursement to also use it as a diagnostic test. The earliest this may occur would be early to mid 2013.

"In 2011 the World Health Organization (WHO)^[2] issued a position statement supporting the use of HbA1c as a diagnostic test," explains Dr Graham Jones, Chemical Pathologist at St Vincent's Hospital in Sydney and one of the authors of the joint

position statement. "We have now made the first step towards getting it approved as a diagnostic test with our position statement, especially for Type 2 diabetes, and we are following it up with a document outlining the evidence-based medical case."

While this case is being assembled, there is another benefit associated with the HbA1c test.

"During a consultation a doctor would assess who is at risk of diabetes and request diagnostic tests such as a plasma glucose blood test. The problem is that the patient should be fasting for this test so some people do not follow through with it," explains Dr Jones. "People in an indeterminate range may also be asked to have an oral glucose tolerance test (OGTT) which requires an appointment and takes a few hours to complete. And this means we lose more people again who don't show up for this test."

Dr Jones says that every step in a diagnostic process where the patient has to come back means more people are 'lost' along the way. The benefit of the HbA1c test is that it doesn't require any special preparation but it needs to be on the Medicare schedule so it can be rebated for diagnostic purposes. This process has been started in Australia, while New Zealand has already approved the HbA1c test for diagnosing diabetes.

"All of Australia's other diagnostic tests for diabetes are based on plasma glucose and are in line with WHO recommendations, and once a person is diagnosed with diabetes they have a HbA1c blood test anyway to see where their disease is up to."

So while the pleasant new spice discovered more than 1000 years ago may be an integral part of our food culture, a group of concerned experts are committed to finding the best methods to diagnose its nemesis - diabetes. And that boils down to including the HbA1c test on the Medicare Schedule as another diagnostic tool that may catch the early diagnoses that currently get away.

[1] [d'Emden MC, Shaw JE, Colman PG, Colagiuri S, Twigg SM, Jones GRD, Goodall I, Schneider HG, Cheung NW. The role of HbA1c in the diagnosis of diabetes mellitus in Australia. Med J Aust 2012; 197 \(4\): 220-221.](#)

[2] [Use of Glycated Haemoglobin \(HbA1c\) in the Diagnosis of Diabetes Mellitus](#)

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Whooping cough has gone ‘viral’ thanks to a study^[1] which found that children vaccinated with the current vaccine were more likely to develop this highly contagious respiratory infection than those who received the earlier vaccine type. The study’s results, which have spread around the world, could partly explain the resurgence of whooping cough in Australia and America.

Whooping cough, or pertussis, is a highly contagious bacterial disease caused by *Bordetella pertussis*. It starts out with mild symptoms and develops into severe coughing fits which produce the signature high-pitched “whoop” sound in infected babies and children when they breathe in after coughing. The infection is generally milder in adults, but can be life threatening to babies.

The study looked at more than 40,000 Queensland children born in 1998 who were vaccinated against whooping cough. The current acellular vaccine^[2] (diphtheria-tetanus-acellular pertussis [DTaP]) became available in Queensland in 1996 and replaced the whole cell vaccine^[3] (DTwP) for publicly funded primary course immunisations delivered at ages two months, four months and six months in March 1999. This means the study’s cohort may have received a primary course consisting of only DTwP, only DTaP, or a mixed schedule of the two.

“The new vaccine used in Australia was an acellular mix made up of three separate pertussis antigens which were deemed

the most important to produce antibodies against this disease,” says Professor Lyn Gilbert, Director of the Centre for Infectious Diseases and Microbiology - Public Health at Westmead Hospital. “The reason it was changed was due to the high rate of local reactions, fever, convulsions and other transient neurological occurrences in response to the whole cell vaccine which understandably made people anxious.”

Prof Gilbert says the original studies on the new acellular vaccine did not suggest it would be less effective than the one it replaced. It also had the benefit of being suitable for adults and older children in response to emerging evidence, based on notification data in Australia, that immunised older children had higher rates of whooping cough due to waning protection. This vaccine provided the opportunity to give them a booster.

“It is a difficult situation to sort out because other factors affect rates of notification such as different diagnostic techniques, and whether whooping cough is in the news which means it will be at the front of a doctor’s mind when they are investigating their patient’s symptoms,” she explains. “It is not an unreasonable assumption that the acellular vaccine loses its potency sooner than the whole cell vaccine, but there are other factors to consider.”

Prof Gilbert is involved in research which has shown different strains of the pertussis antigens to those used in the vaccine are circulating in the community.

“The significance of this finding is in dispute although we are looking prospectively at children with whooping cough and the strains they have to sort it out. The real issue is what to do with the information when we get it.”

Prof Gilbert says a new vaccine containing different strains of the bacteria may be on the cards, but this is a slow and expensive process. In the mean time she stresses the current vaccine (DTaP) still provides protection for many years.

“People should continue to be immunised, and have their boosters, and be aware that no vaccine against whooping cough will be one hundred percent effective because the pertussis organism is just too complicated. But older children and adults may be reservoirs of this disease for young babies, so we have to protect them from the burden of this disease with immunisations.”

[1] Sheridan SL, Ware RS, Grimwood K, Lambert SB. Number and Order of Whole Cell Pertussis Vaccines in Infancy and Disease Protection. *JAMA*. 2012;308(5):454-456.

[2] An acellular vaccine is composed of only those antigens of bacterial cells that are best suited to stimulating a strong immune response. The number of antigens (3-component or 5-component) depends on the brand of the vaccine.

[3] A whole cell vaccine is composed of suspensions of whole bacterial cells that have been killed.

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Syphilis is still standing after all these years



What do King Henry VIII, Ivan the Terrible, Christopher Columbus, George Washington, Napoleon Bonaparte, Adolf Hitler, Al Capone, Vincent Van Gogh, Leo Tolstoy and Oscar Wilde have in common? They all allegedly suffered from syphilis. This bunch probably weren't thrilled about this footnote in history, but privacy laws prevent this type of information being shared today. People are diagnosed and treated discretely which is fortunate because syphilis is still standing and notifications are on the rise – again.

Once known as the great pox, syphilis is caused by the spirochaete bacterium *Treponema pallidum*. It is a sexually transmitted infection passed from person to person through direct contact with a syphilis sore (chancre). These mostly occur on the external genitals, vagina, anus or in the rectum, but can also appear on the lips and in the mouth. The bacterium is transmitted during vaginal, anal or oral sex and through kissing, while pregnant women with the disease can also pass it onto their babies.

Syphilis is also known as the great imitator because its symptoms can mimic those of other diseases such as tuberculosis or the measles. Once you've been infected you are not immune to re-infection either, but it is easily treated.

"Syphilis is extremely sensitive to penicillin and even the most advanced cases can have a one hundred percent bacterial cure rate," explains Dr David Leslie, Medical Microbiologist at Victorian Infectious Diseases Reference Laboratory (VIDRL). "It is having another resurgence at the moment and we don't know why, but it is turning up unexpectedly."

Dr Leslie says syphilis infections mostly occur in the gay community and in people from developing countries. He has seen

one patient with Human Immunodeficiency Virus (HIV) infected five times with syphilis, while he says immigrants and sex tourists may also be a source of infections. The signs and symptoms depend on which phase the infection is in – primary, secondary, latent and tertiary – and diagnosis is usually via a blood test.

“Pathologists can test blood for an immune response to the infecting organism, and they can also measure what stage the disease is up to and monitor treatment. A test called a polymerase chain reaction (PCR) is also becoming increasingly available to diagnose syphilis from a swab, biopsy or cerebrospinal fluid.”

An important point to note about syphilis is that it will ‘cure’ itself at each stage, but the infection remains in the body in a latent form. It can stay like this for many years, and without treatment can spread to the brain, blood vessels, heart, eyes, liver, bones and joints with dreadful consequences such as syphilis madness (when it invades the brain).

There is no need to get this far down the path in the 21st century. Diagnosis can be confirmed via pathology tests and treatment is straightforward and effective. And if the famous bunch above had access to modern diagnostic and treatment methods, and were protected by our privacy laws, they would only be renowned for their exploits and not their ‘sexploits’ as well.

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“The cow was infected with *Mycobacterium orygis* which was surprising as this was the last thing you would expect to find in New Zealand,” explains Dr Des Collins, Scientist at AgResearch in New Zealand and coauthor of a scientific paper^[1] on this case.

“It turned out that a young lady had come to New Zealand from India with untreated clinical tuberculosis before the cow was born, and also while she was responsible for nurturing the cow when it was a calf ten years before it was found to be infected. This was a clear cut case of a human infecting an animal which is rare in developed countries.”

This finding also raised further questions related to this case.

“The species *M. orygis* has traditionally been associated with a few infections in animals in the Middle East and North Africa and has only very recently been reported from humans in India,” says Dr Collins.

“This might mean that this particular species is more common in people that we previously knew, especially in India where they usually only identify whether a person has TB or not and don’t further investigate the TB organisms. This is because TB is a huge problem there and virtually all the resources available are used to diagnose and treat TB. Identifying particular species and strains of TB is rarely possible.”

The strain *M. orygis* was originally called the oryx bacillus and occasionally isolated from members of the *Bovidae* family such as oryxes, gazelles, deer, antelope and buffalo. Until now, Dr Collins says this strain has been an oddity without much research behind it and of little significance to human TB, but this recent case may change that. In short, it might be more common in people than previously thought and could be spread from human to human.

The fallout from this case so far involves staff from New Zealand’s Animal Health Board developing appropriate ongoing surveillance of the remaining dairy herd, and the New Zealand Ministry of Health investigating the potential public health risks. And while these processes are underway, it gives everyone a chance to digest the fact that a strain of TB common in the Middle East and North Africa was contracted by a young lady in India who subsequently infected a dairy cow in New Zealand. As we said before, there are some situations where it takes a while to get your head around the details, and this is one of them.

[1] Dawson KL, Bell A, Kawakami RP, Coley K, Yates G, Collins D. Transmission of *Mycobacterium orygis* (*M. tuberculosis* Complex Species) from a Tuberculosis Patient to a Dairy Cow in New Zealand. *J. Clin. Microbiology*. 2012, 50(9): 3136-3138.

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