



PathWay

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA



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IN THIS ISSUE

- Testing for and diagnosing kidney disease early – the silent disease
- What is a renal (kidney) biopsy?
- Treating kidney disease in the Indigenous communities
- Taking a detailed look at kidney disease through the electron microscope

INTERESTING FACTS

90

The percentage of kidney function that can be lost without experiencing any symptoms¹

10

The percentage of people in Australia who may already have kidney disease but are unaware.²

5

The number of stages of chronic kidney disease.³

Source:

Welcome to the April 2018 edition of ePathWay

The kidneys are essential to our general health and wellbeing, providing a complex waste disposal system that cleans our blood, but they are often undervalued. Many people are unaware of the vital role the kidneys play, the symptoms of kidney disease and the risk factors which contribute to its development.

Kidney disease can often go undetected until the later stages, when serious damage has already occurred. Diagnosing kidney disease early is essential for timely treatment and prevention of further damage.

The role of pathology is crucial in the diagnosis, monitoring and treatment of kidney disease.

In this month's issue of ePathway, we will look at

- Testing for and diagnosing kidney disease early - the silent disease
- What is a renal (kidney) biopsy?
- Treating kidney disease in the Indigenous communities
- Taking a detailed look at kidney disease through the electron microscope

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Testing for and diagnosing kidney disease early – the silent disease

[1] www.betterhealth.vic.gov.au/health/conditionsandtreatments/kidney-failure

[2] http://kidney.org.au/cms_uploads/docs/kidney-fast-facts-fact-sheet.pdf

[3] <http://kidney.org.au/your-kidneys/detect/kidney-disease/stages-of-chronic-kidney-disease-787>

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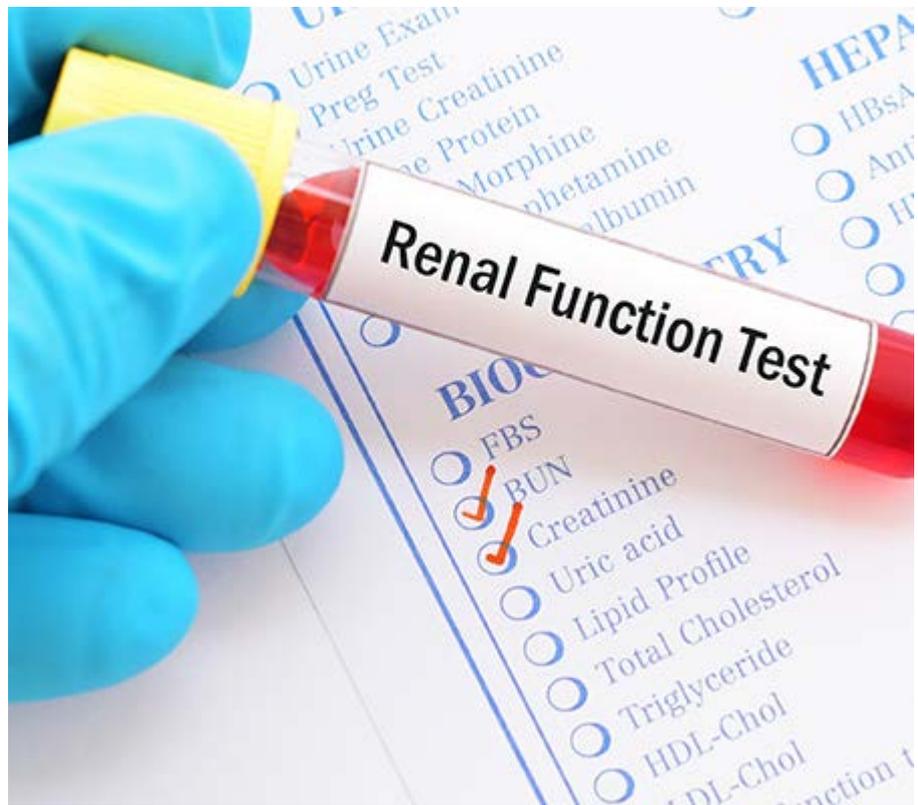
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Diagnosing kidney disease early is crucial, particularly considering it's not uncommon for people to lose up to 90 percent of their kidney function before experiencing any symptoms. Chronic kidney disease (CKD) is called a 'silent disease' as there are often no warning signs.

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What is a renal (kidney) biopsy?

A renal (kidney) biopsy is a medical procedure that collects a tissue sample from the kidney so it can be examined under a microscope. It can provide doctors with a comprehensive understanding of a patient's kidney disease and the best treatment.



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Treating kidney disease in the Indigenous communities

Associate Professor Rob Baird,

Director of Pathology, Territory Pathology and Infectious Diseases Physician at Royal Darwin Hospital, discusses the complexities of treating kidney disease effectively in remote rural communities.



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Taking a detailed look at kidney disease through the electron microscope

In the 1970's and 1980's, the electron microscope had a very major diagnostic role in tumour diagnosis. Nowadays, that role has largely been replaced by alternative measures. As a result, the electron microscope is now almost wholly reserved for medical diagnostic problems in renal, muscle and other ultrastructural studies which include cilia analysis of the respiratory tract. In terms of the workload of the electron microscopy unit, renal biopsies account for approximately 80% of the unit's workload.



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Testing for and diagnosing kidney disease early – the silent disease



Diagnosing kidney disease early is crucial, particularly considering it's not uncommon for people to lose up to 90 percent of their kidney function before experiencing any symptoms. Chronic kidney disease (CKD) is called a 'silent disease' as there are often no warning signs.

According to Kidney Health Australia, some symptoms and signs may indicate reduced kidney function and it's important to take note of them. These can include high blood pressure; changes in the amount and number of times urine is passed; changes in the appearance of urine; blood in urine; puffiness in legs, ankles or around the eyes; pain in the kidney area; tiredness; loss of appetite; difficulty sleeping; headaches; lack of concentration; itching; shortness of breath; nausea and vomiting; bad breath and a metallic taste; muscle cramps; and pins and needles.

Clinical Professor John Burnett, Consultant Chemical Pathologist at PathWest Laboratory Medicine, Royal Perth Hospital says, "These symptoms and signs are non-specific and could easily be attributed to stress or something else. As a result, there are an estimated 10% of Australians who already have kidney disease, but are unaware of this silent disease."

"Unfortunately, once individuals begin to experience symptoms, they may already have end-stage kidney disease (ESKD). This is the most severe form of CKD; therefore, it's important for people to be aware if they are susceptible to developing the disease," says Professor Burnett.

CKD is categorised into 5 stages^[1], with each stage related to the level of kidney

function and kidney damage. For individuals with ESKD, kidney replacement therapy in the form of dialysis or kidney transplantation is usually required for survival.

“A third of adult Australians are at an increased risk of kidney disease due to other pre-existing conditions, such as high blood pressure, cardiovascular disease, diabetes or a family history of kidney failure. Obesity and smoking are also risk factors which impact the rates of kidney disease. It’s much more common in the elderly and is overrepresented amongst Aboriginal and Torres Strait Islander persons. In each of these cases, a GP should test the kidney function of these individuals more regularly.”

Chemical Pathologists can identify the first warning signs that something is wrong, using a simple blood test called the eGFR (estimated glomerular filtration rate) which picks up decreased kidney function.

“It’s not until an individual has a blood test or a urine test that a person will know if they have kidney disease. The eGFR is a means of looking at how well the kidney is functioning and excreting waste products. An eGFR that is greater than 60 is regarded as normal; however, if it’s less than 60, then you have kidney disease. Individuals who have levels of less than 15 may need to go onto dialysis or possibly have a transplant. A urine test can also be used to measure the urine albumin to creatinine ratio. Having higher than normal levels can be a sign of early kidney disease.”

Albumin is a protein that is present in large amounts in the blood. When kidneys are functioning properly, only a tiny amount of albumin leaks through into the urine, less than 30 mg/day. In kidney failure, large amounts of protein spill into the urine.

“Early detection of kidney disease is very important. People at increased risk for kidney disease should get tested, as early treatment with lifestyle measures and medications can benefit those with CKD,” says Professor Burnett.

[1] <http://kidney.org.au/your-kidneys/detect/kidney-disease/stages-of-chronic-kidney-disease-787>

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What is a renal (kidney) biopsy?



A renal (kidney) biopsy is a medical procedure that collects a tissue sample from the kidney so it can be examined under a microscope. It can provide doctors with a comprehensive understanding of a patient's kidney disease and the best treatment.

Reasons to do a kidney biopsy include blood or protein found in the urine; abnormal blood test results; acute or chronic kidney disease with no clear cause; nephrotic syndrome and other glomerular disease (which happens when the filtering units of the kidney are damaged).

Dr Jonathan Zwi, Histopathology Department, LabPLUS in Auckland, explains that nearly all kidney biopsies are percutaneous (through the skin).

“A needle is placed through the skin and is guided to the right place in the kidney, usually with the help of an ultrasound” says Dr Zwi.

A kidney biopsy can assess a patient's type of kidney disease, what caused the disease, how severe it is, what treatment is necessary, whether it might run in the family, if the disease is getting better or worse with treatment, and why a transplanted kidney is not working well. A kidney biopsy can also help to identify lesions seen on imaging, which could be cysts or benign or malignant tumours.

Dr Zwi explains that pathology plays a crucial role not only in the diagnosis of kidney disease, but also in the recommendation of therapies and subsequent monitoring.

“Part of what we do here is not only diagnosing the condition but also grading the severity of it. We assess how much permanent damage is present in the kidney, for example scarring. If the kidney is too scarred then, even if you've got the diagnosis, it

may not be worth treating. If the disease has significantly and permanently damaged the kidney, then a transplant is necessary.

“After a transplant, biopsies are also done at set times to monitor the progress, but also at any time if the kidney starts to not function properly. A biopsy is done to see if there is rejection or a viral disease of the kidney, which can happen in immunocompromised patients. That evaluation very much guides the therapies of a patient, particularly anti-rejection therapy.”

Dr Zwi says that, in addition to biopsies, blood tests offer further insights in relation to the cause of the disease. As well as the more common causes of kidney disease, such as diabetes and high blood pressure, a number of other factors can affect the glomerulus, which is the kidney’s filtering unit.

“Quite often, kidney disease is diagnosed as a result of a blood or urine test. The laboratory plays a crucial role in picking up blood and or protein that may be present in the urine. Sometimes the disease is identified quite late when patients are really presenting renal failure with anaemia and lethargy,” says Dr Zwi.

“Blood tests are used to determine some of the main causes of renal impairment. For example, a blood test may identify lupus (systemic lupus erythematosus), which is an auto-immune disease that is quite common in causing renal impairment, or diabetic renal disease. Other diseases that could be identified include, post infectious glomerulonephritis, which usually occurs in children after a sore throat or skin infection with streptococci, and IgA nephropathy, which is a primary disease of the kidney. There are also diseases that are a consequence of treatment with medications. These are quite important to diagnose because, if caught early, they are treatable. The role of the laboratory is crucial in diagnosing and monitoring kidney disease, offering a range of information in order to treat the patient effectively,” says Dr Zwi.

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Treating kidney disease in the Indigenous communities



Associate Professor Rob Baird, Director of Pathology, Territory Pathology and Infectious Diseases Physician at Royal Darwin Hospital, discusses the complexities of treating kidney disease effectively in remote rural communities.

“I’m located in the Northern Territory. I would estimate that chronic kidney disease (CKD) and end-stage kidney disease (ESKD) are at least ten times more prevalent in the Indigenous community, in comparison to the non-Indigenous population. Providing effective treatment and monitoring kidney disease can pose its own set of complications in the remote Indigenous communities, as dialysis treatment or undergoing a renal transplant often requires extensive travel.

“Currently, there are not dialysis units in every small community, the dialysis units are centralised; and if a patient is on dialysis and needs to be dialysed three times per week, a roundtrip from a remote community is a long way. Therefore, families usually move off their homeland and come to town for dialysis treatment. Consequently, communities can be left without elder leadership, and community culture is weakened. Patients suffer from isolation and depression, restricted by a dialysis machine for their foreseeable future,” says A/Prof Baird.

In 2014, a survey of around 3,300 Aboriginal and Torres Strait Island adults (aged 18 years and over) across Australia, revealed that nearly one in five (17.9%) had chronic kidney disease. When compared with those in urban areas, Aboriginal and Torres Strait Islander adults in remote areas were two and a half times as likely to have signs of chronic kidney disease (33.6% compared with 13.1%). When compared with the non-

Indigenous population, Aboriginal and Torres Strait Islander people were twice as likely to have signs of chronic kidney disease (rate ratio of 2:1)^[1]. In 2011–13, care involving dialysis was the leading cause of hospitalisation (45%) for Indigenous Australians. Hospitalisation for dialysis was 10 times the non-Indigenous rate.^[2]

“In some cases, a patient may not seek out a level of medical intervention if the result is moving away from their community and land. The option to move to a large city to seek treatment might even be rejected by the patient, even when the reality of that decision means the patient won’t survive. When health services are available locally, there can still be complexities to providing these services, due to socio economic factors, such as housing, education, unemployment and poverty.

“The issues are well recognised and, looking forward, solutions may include mobile dialysis units (<https://www.westerndesertdialysis.com/communities/the-purple-truck>), changing the funding models for regional dialysis centres and, in the future, technology improvements may advance to the level that portable dialysis machines can be offered to patients. However, the best current option is successful renal transplantation.

“Kidney transplants are fantastic - a patient’s whole life changes for the better. The patient’s overall wellbeing improves, as they’re off dialysis and mobile again. A/Prof Baird explains that there has been a shortage of organs in the Indigenous communities. “Ideally you want a good tissue match, but that’s not quite as important as it once was due to improved drugs”.

Unfortunately, the rates of renal transplantation in Indigenous patients are far lower than in other groups. Kidneys for transplantation are largely from deceased donors, as there are very few living kidney donors in Aboriginal and Torres Strait Islander communities.

According to an article in the Australian Medical Association^[3], the reasons for poor access to transplantation experienced by Aboriginal and Torres Strait Islander Australians are complex. Some of those can be attributed to

- The greater burden of comorbid illness amongst Aboriginal and Torres Strait Islander dialysis patients, leading to fewer patients being judged medically suitable;
- The shortage of living and deceased donors from within Aboriginal and Torres Strait Islander communities;
- The challenges in delivering appropriate health services to people living in remote areas who might also have low health literacy and not speak English as a first language;
- The dislocation that follows from moving to transplant centres in distant capital cities; and
- The high complication rate, particularly in terms of early infectious complications leading to poor transplant outcomes, including substantially higher death and graft loss rates.

“Prior to transplantation, significant work up tests and assessments require visits to major centres. After transplantation there is the prospect of a post-operative stay and side effects away from home and supports. The number of medications usually increases, and there is an increased risk of infections and cancers. In summary, this is a highly challenging area with much still to be done,” says A/Prof Baird.

[1] Australian Bureau of Statistics. Australian Aboriginal and Torres Strait Islander Health Survey: Biomedical Results, 2012-13. 2014. Report No.: 4727.0.55.003, Canberra

[2] Australian Government. Department of the Prime Minister and Cabinet. Aboriginal and Torres Strait Islander Health Performance Framework 2014 Report

[3] Australian Medical Association. Unacceptable kidney transplant rate for Indigenous Australians

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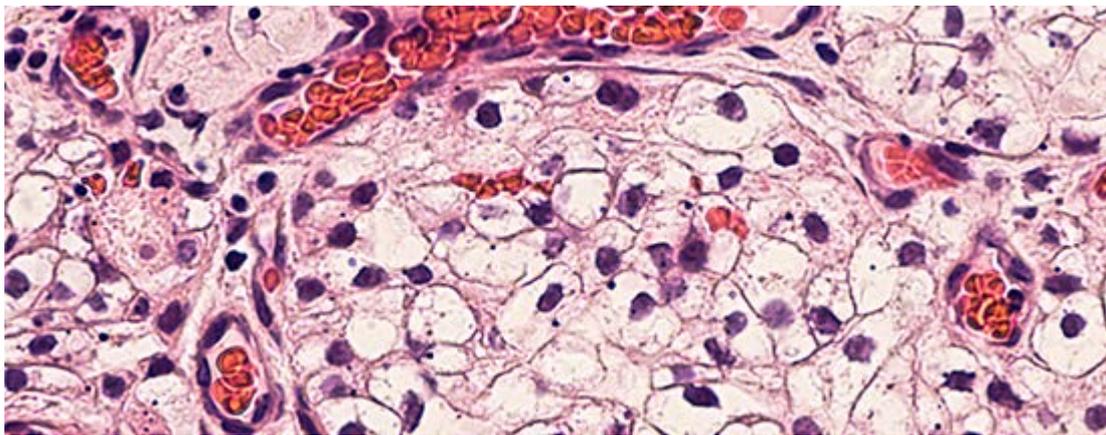
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Taking a detailed look at kidney disease through the electron microscope



In the 1970's and 1980's, the electron microscope had a very major diagnostic role in tumour diagnosis. Nowadays, that role has largely been replaced by alternative measures. As a result, the electron microscope is now almost wholly reserved for medical diagnostic problems in renal, muscle and other ultrastructural studies which include cilia analysis of the respiratory tract. In terms of the workload of the electron microscopy unit, renal biopsies account for approximately 80% of the unit's workload.

Dr Julie Fletcher, Anatomical Pathologist, explains that there are four electron microscope units in New South Wales. Two machines are located at Concord General Hospital where she works.

"The unit at Concord takes referrals from a number of other institutions within New South Wales, elsewhere in Australia, New Zealand and some of the Pacific Islands. In addition to our unit, St Vincent's Hospital, Westmead Hospital and Liverpool Hospital have electron microscopy units to process in-house hospital work."

"With an electron microscope, we examine ultra-thin tissue sections stained with a heavy metal compound that allows the machine to focus an electron beam through the tissue. This provides high magnification, high resolution images at a subcellular or ultrastructural level. It is therefore quite a different form of tissue examination to the light microscope, allowing examination at a much higher level of detail."

At Concord Hospital, Dr Fletcher explains that both machines are fully utilised supporting a busy diagnostic unit, where up to 80% of the workload is composed of renal biopsies. These biopsies include native kidney biopsies (when a patient's own kidney is biopsied)

or a transplant renal biopsy (a biopsy of a donor kidney transplanted into a recipient).

“Up to 80% of all kidney biopsies in Australia, or possibly even more, have electron microscopy studies as an integral part of the biopsy examination. In up to 30% of these cases, electron microscopy findings are either diagnostic beyond the light microscopy findings or add significantly to the light microscopy findings, thus influencing clinical treatment.”

“In the scenario of transplant biopsy examination, electron microscopy studies have become an integral part of the diagnostic classification for rejection of the graft (transplant), which is invaluable. Early diagnosis of graft rejection by electron microscopy can allow institution of added anti-rejection treatment and ultimately prolong the life of the graft. In Australia there is a very high referral rate of renal transplant biopsies for electron microscopy examination, which is possibly one of the reasons that Australia has one of the best overall renal graft survival rates globally.”

Dr Fletcher goes on to discuss the future of electron microscopy.

“Currently, there is no alternative technology available that has the degree of resolution that an electron microscope offers. For the foreseeable future, there are no alternative diagnostic tools that are going to fulfil this significant role in the diagnosis of the difficult cases which depend on EM to clarify the diagnosis.”

Dr Fletcher explains that the electron microscope is an expensive process and is labour intensive.

“In our institution, we are only able to charge about \$180 for one of these cases and it costs us between \$700 and \$800 to actually examine one of the specimens. So we absorb the financial load for a lot of these referring institutions. The microscopes require specialised scientific staff to prepare biopsy material for examination, work both of the machines, recognise the ultrastructural changes and take the photographs. They require pathologists who have an understanding of electron microscopy to report the cases together with the scientific staff. Training in medical electron microscopy is not formal in any university, requiring training on the job training for all new personnel.”

“Replacement of a machine comes at a cost of around \$700,000-\$900,000. Fundraising and grants have contributed significantly to procurement of machines at Concord in the past. The availability of this important diagnostic test, which has a vital role in the diagnosis and evaluation of kidney disease in Australia, particularly for transplantation, should remain a priority for the Health Department.”

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