



PathWay

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA



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Issue #016

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Interesting Facts

10

The number of lives that can be saved or enhanced by one organ, eye and tissue donor

Welcome to the July edition of ePathWay

What do you like to do on your holidays? Relax, catch up on a good book or visit relatives? What about making your way to a developing country to help them instigate life saving procedures through pathology? Well, that sort of 'break' is high on the agenda for two members of the pathology fraternity and our story on their work in Bhutan is inspiring.

This edition also covers the importance of pathology when it comes to transplants and why Pathologists don't take 'rejection' lightly. There is also a wrap up of two relatively common conditions – thyroid disease and Systemic Lupus Erythematosus.

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.

Two Aussies help save Bhutan's women through pathology

1296

The number of transplanted organs donated in Australia in 2011

186

The number of transplanted organs donated in New Zealand in 2011

Sources: Australia and New Zealand Organ Donation Registry; Donate Life (Australia)



There is a saying that we should be the change we want to see in the world. Mrs Marilyn Betchley and Dr Andrew Field are putting this philosophy into practice by giving their expertise to the country of Bhutan to help save women's lives from both cervical and breast cancers. And since they are putting these words into action, it is time to put their actions into words.

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Important Message



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Pathologists don't take rejection lightly

Our bodies are territorial. They won't accept the transplantation of cells, tissues or organs unless a complex set of criteria is met. The main 'gatekeeper' is the immune system which has elaborate and effective mechanisms to combat foreign agents including transplanted material. It's the role of Pathologists to ensure the transplanted material has the best chance of being accepted by the body's immune system to minimise the chances of rejection.



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The lowdown on lupus

When it comes to Systemic Lupus



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You have to admire the human body. When something goes wrong it usually leaves clues that point to the problem. Often these clues are so subtle it takes skill – and pathology tests - to figure them out, especially when it comes to thyroid disease. But as Physician Sir Arthur Conan Doyle had his famous character Sherlock Holmes say in most of his books: “Eliminate all other factors, and the one which remains must be the truth.” Well that is certainly the case with thyroid disease.

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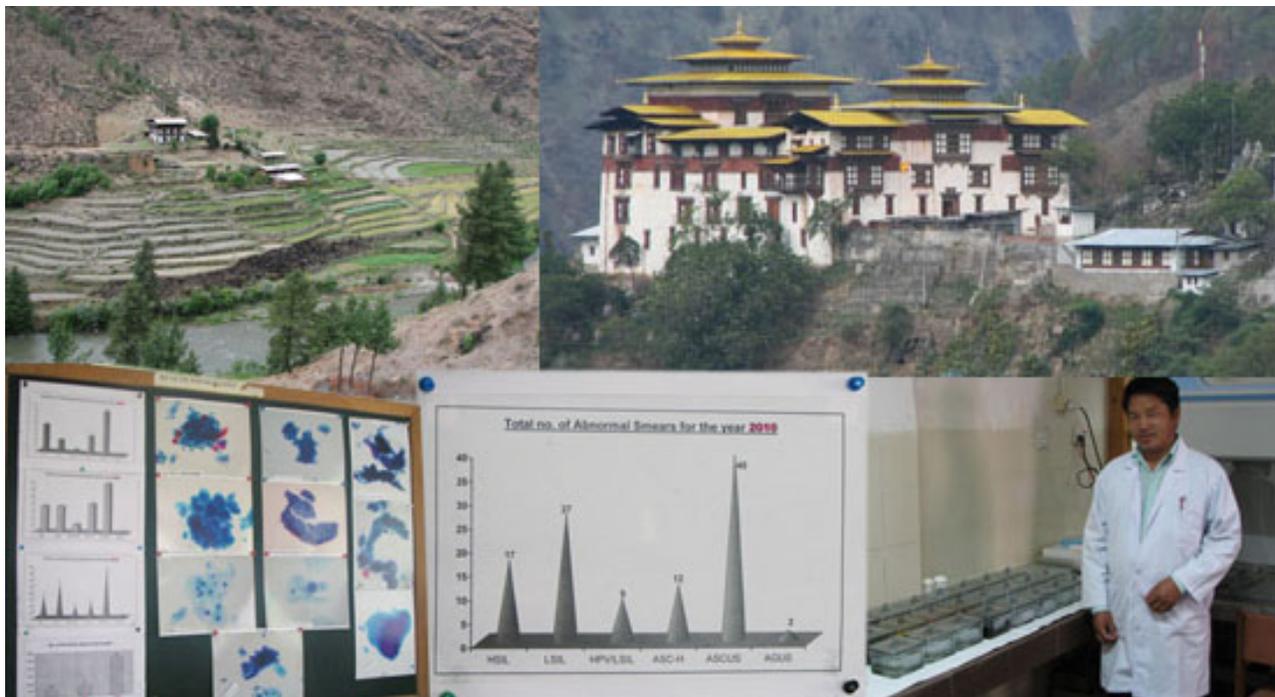
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We'll start with Mrs Betchley, Senior Cytotechnologist at Adelaide Pathology Partners, who first visited Bhutan in 2006 at the invitation of The Ministry of Health and the American-based not-for-profit organisation Pathologists Overseas. Her brief was to assess the Pap smear¹ program and offer further education to the Cytotechnologists.

"The Medical Director in Bhutan said to me 'please help save our mothers' which had a huge impact on me," explains Mrs Betchley. "During my initial three month visit I travelled the Kingdom visiting the laboratories and started to look at ways to solve some basic problems."

Mrs Betchley first noted the method used to collect a Pap smear was substandard and resulted in up to 75 percent of smears

being unsatisfactory. Her advice was to replace their 'cotton wool wrapped around a bamboo stick' implement with spatulas, and improve the fixative so the collected cervical cells were well fixed for the best possible analysis.

"I sourced a company in Australia which donated 200 fine spray bottles. These were posted to Bhutan through a donation from the Australian Society of Cytology as the ingredients for the fixative were available in Bhutan, but not these types of bottles. The Cytotechnicians then prepared the fixative in their labs. Pathologists Overseas donated 100,000 spatulas, so the next step was to retrain the nurses throughout the country to use the spatula and spray fixative."

These simple changes were augmented with improved education for 11 Cytotechnicians in 'reading' the Pap smears which resulted in a higher standard of interpretation and more confident diagnoses. However, sometimes the opportunity to even have a Pap smear is challenging in Bhutan because of the geography of this mountainous country.

"Pap camps' are set up to ensure women in remote areas also benefit from having a health check and a Pap smear. The women walk for days to reach these camps, and the medical teams also walk for days from where the road ends carrying generators, microscopes, stains and other equipment. Word gets out pretty fast so lots of women attend them."

Mrs Betchley has been to Bhutan five times during her annual holiday breaks and receives no remuneration for her work. But she has been bestowed with the title 'Mother of Cytology' in Bhutan, and also has the satisfaction of knowing the cervical cancer rate for women is starting to decrease due to her efforts.

Dr Andrew Field, Senior Consultant Pathologist at St Vincent's Hospital in Sydney, also donates his time and pays his own way to countries to teach Cytopathology. Over the past 12 years he has taught at the annual joint meeting of the Thai and Japanese Societies of Clinical Cytology, and was asked to join a review of cytology services and teaching in Bhutan by the Director General of Public Health.

"I travelled for six days with the Thai delegation in Bhutan meeting senior Government Ministers, Administrators, Pathologists and Cytotechnologists and visited basic hospital units, small laboratories, regional hospitals and their referral hospital," he explains. "We then wrote a draft report for the Department of Medical Services of the Thai Ministry of Public Health, which also went to the Ministries of Bhutan."

Dr Field firmly believes in change through education and has actively taught Pathologists and Cytotechnicians in cervical and fine needle biopsy cytology for breast and other cancers in many developing countries.

"Bhutan is a country of 700,000 people where cervical cancer is still the most prevalent cancer for women, as it is in most developing countries. My goal is to concentrate on training people in their countries where they work so they can provide a better cytology service and provide teaching for their junior colleagues. I also plan to continue training Pathologists to perform and interpret fine needle biopsies."

The positive changes achieved in Bhutan through the work of these two Australians include assisting to train 16 Cytotechnicians, adequate equipment to collect Pap smears and fine needle biopsies and other appropriate equipment to analyse and report on the tests, while at the last count 22,000 women were given a Pap smear in 2010². This illustrates what can happen when people such as Mrs Betchley and Dr Field implement the change we want to see in the world, which in their case means saving women's lives through pathology.

¹ Pap smears are covered in ePathWay issue 008 http://epathway.rcpa.edu.au/previous/008_1011.pdf

² The total number of Pap smears taken between 2000 and 2011 is 142,500 which meets Bhutan's target for this health check.

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According to Dr Brian Tait, Senior Research Fellow from the National Transplant Services section of the Australian Red Cross Blood Service, it is essential to match the tissue type – or pattern of Human Leukocyte Antigens (HLAs) - between the transplant recipient and donor to reduce the prospect of rejection. HLAs are proteins located on the surface of white blood cells and other tissues in the body. This HLA matching process is performed on a blood sample.

Dr Tait says there are two types of transplant rejection: cellular and humoral. Cellular rejection occurs when cytotoxic T cells recognise the transplanted material as foreign and attack it. Humoral rejection (also known as antibody-mediated rejection) is an indirect recognition of the transplanted organ when the immune system's B cells recognise 'foreign' HLA proteins on the cells of the transplant and produce new antibodies against those cells, tissue or organ. Long lasting memory B cells are also formed which can be activated in the future when confronted with the same 'foreign' HLA antigen. This also enables the immune system to 'recall' previous events.

“There is now an increased understanding of the importance of antibodies and in the past there were quite a few unexplained rejections. We can now define the patient’s antibody profile more accurately and also determine the reason for the rejection. We tend to see both types of rejection, but cellular rejection is more easily controlled while humoral rejection can be more damaging.”

Dr Tait says people waiting for an organ transplant are also screened to determine their HLA antibody profile. There is a large pool of people waiting for a kidney and they are often transplanted on a non-urgent basis which allows the Pathologist time to determine the most suitably matched recipient for a particular donor. However, Dr Tait says finding a good HLA match may ‘go out the window’ when it comes to heart, lung and liver transplants.

“These are often based on an individual’s clinical urgency and the pool of people on the waiting list is also smaller compared to kidney transplants. However, we try to ensure the antibody component is as close a match as possible because, as you can imagine, having a heart transplant rejection is very serious.”

Bone marrow (or haematopoietic stem cell¹) transplants are another story because there is little room for error.

“Matching HLA types is critical to avoid Graft-versus-host disease where the newly transplanted material attacks the transplant recipient’s body. This reaction can be fatal, and sometimes we can’t find the perfect match even though there are in excess of 19 million HLA-typed individuals on bone marrow donor registries² worldwide.”

Dr Tait says the pathology component is vital when it comes to the transplantation of any material, and the future is looking brighter with the development of new genetic techniques.

“We extract DNA and use gene sequencing methods to determine HLA types and there are also more sensitive techniques available to detect low levels of circulating antibodies.”

While these new techniques mean Pathologists are more likely to accurately define ideal HLA matches between recipient and donor, at the end of the day we’re fortunate that they are such skilled matchmakers who don’t take rejection lightly.

¹ Stem cells are covered in ePathWay issue 014 (<http://epathway.rcpa.edu.au/index.html>)

² More information on bone marrow donor registries can be found at www.abmdr.org.au (Australian Bone Marrow Donor Registry) and www.bonemarrow.org.nz (New Zealand Bone Marrow Donor Registry)

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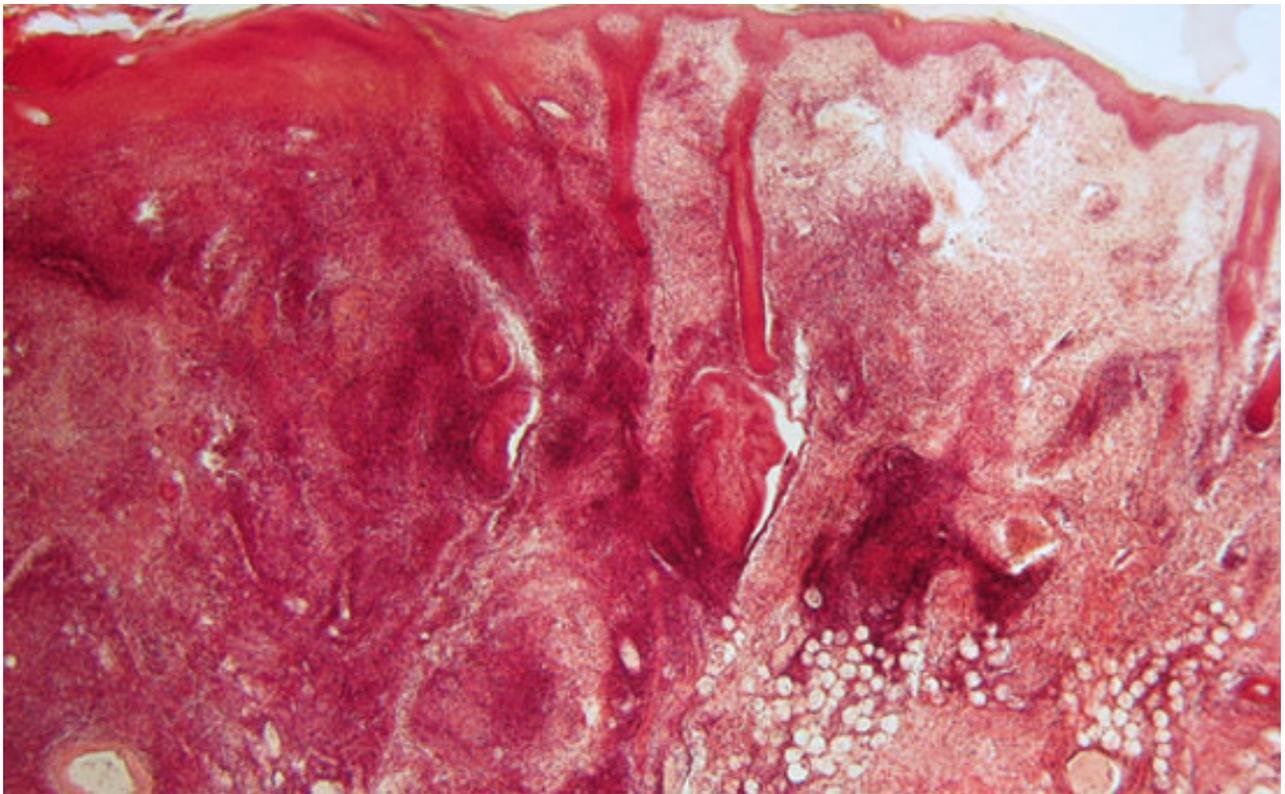
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The lowdown on lupus



When it comes to Systemic Lupus Erythematosus (SLE) there is good news and there is bad news. The good news is that this disease is the subject of a lot of research, while the bad news is that it is a lifelong condition. However, the effects of lupus can be monitored through pathology tests which makes its diagnosis and management a much smoother path to tread.

“There is a lot of research happening on the pathogenesis or mechanism that causes the disease and on its multigenic* origin,” explains Dr Roger Garsia, Pathologist and Immunologist at the Royal Prince Alfred Hospital in Sydney. “Researchers are also looking at the potential of new therapies to reduce relapse rates and give more sustained control of serious stages of this disease. Monitoring of these processes involves pathology tests.”

Systemic Lupus Erythematosus is quite a mouthful to say which is why it is often abbreviated to either lupus or SLE. It is an

autoimmune disorder where people produce abnormal antibodies (known as autoantibodies) that target their own body's tissue rather than foreign infectious agents.

"SLE can affect diverse sites around the body including the skin, joints, muscles and internal organs. It usually has a long early onset or prodromal phase with negligible or mild symptoms, while some people can have an explosive onset and a destructive process which can occur within weeks. Most people have exacerbations and partial remissions during the course of the disease."

Diagnosing SLE can be difficult because there is no single diagnostic marker. It must be identified through a combination of clinical and laboratory criteria. The laboratory component usually involves blood tests to measure levels of autoantibodies in the blood including anti-nuclear constituents (autoantibodies directed against certain components found in the nucleus of a cell), while the occasional tissue biopsy may also be required.

Once the diagnosis is established, pathology tests are vital to monitor the progress of the disease and the effectiveness of treatment.

"SLE is a lifelong condition, and once the diagnosis is made people may need immunosuppressive therapy to reduce the transition rate from low grade to active via drug therapy," Dr Garsia explains. "It is also a disease that predominantly affects females of childbearing age so enhanced monitoring may be needed pre-conception and in pregnancy."

Researchers are looking closely at the link between females in this demographic and SLE, but until a breakthrough happens, those with this disease can at least be effectively monitored through pathology tests to assess its activity. And that's good news from a 'glass half-full' perspective!

* an inherited characteristic that is specified by a combination of multiple genes

More information on SLE and its associated pathology tests can be found at www.labtestsonline.com.au

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Diagnosing thyroid disease can be elementary with pathology tests



You have to admire the human body. When something goes wrong it usually leaves clues that point to the problem. Often these clues are so subtle it takes skill – and pathology tests - to figure them out, especially when it comes to thyroid disease. But as Physician Sir Arthur Conan Doyle had his famous character Sherlock Holmes say in most of his books: “Eliminate all other factors, and the one which remains must be the truth.” Well that is certainly the case with thyroid disease.

“Various disease states can affect the thyroid gland, including states of under or over-activity as well as nodules and various grades of malignancy,” explains Associate Professor Chris Florkowski, Chemical Pathologist at Canterbury Health Laboratories in New Zealand.

“Some studies have suggested that as many as 10 percent of the Australasian population over the age of 50 have recognised

thyroid disease, and that many more in this age group have unrecognised thyroid disease. It is also sufficiently common in the older age groups to warrant clinical vigilance and, where appropriate, laboratory testing.”

The thyroid gland is found in the neck below the thyroid cartilage. It controls the rate of metabolism (how quickly the body uses energy and how sensitive the body is to other hormones) and secretes thyroid hormones which regulate the function of many other organ systems in the body.

“In addition to their important role in regulating the rate of metabolism, thyroid hormones also play a particularly crucial role in brain maturation during foetal development. Lack of thyroid hormones can have serious consequences for the growth and development of the neonate, as well as for adult health,” says A/Prof Florkowski.

“The pathology laboratory plays a vital part in the diagnosis of thyroid disease as the symptoms of thyroid disease are often subtle and not recognised by clinicians as being due to a thyroid cause. For example, in two studies of over 3000 unselected patients assessed by both clinical and laboratory criteria, thyroid disorder was not suspected in over 90 percent who tested positive, even when clinical features were apparent in retrospect.”

Pathology tests can measure the levels of thyroid hormones as well as thyroid stimulating hormone (TSH) from the pituitary gland (a pea-sized gland located at the base of the skull which controls thyroid gland activity). A/Prof Florkowski says the pattern of results enable Pathologists to work out the type of thyroid disease present, and if antibody levels are also measured, to also determine if there is an autoimmune response.

“In the case of thyroid nodules, a critical part of the diagnosis rests with fine needle aspiration and the examination of tissue under the microscope, and there is also an emerging role for molecular diagnostics. These all happen under the umbrella of the pathology laboratory,” explains A/Prof Florkowski. “When treatment is started for thyroid disease, such as drug therapy, it is also possible to use pathology tests to monitor the responses and determine whether adjustments are needed.”

Thyroid disease causes a huge array of symptoms depending on the disease process. For example, hyperthyroidism (an overproduction of the thyroid hormones) is commonly due to autoimmune disease and causes protruding eyes, swelling in the neck (goitre), palpitations, sweating, diarrhoea, weight loss and heat intolerance. Hypothyroidism (underproduction of the thyroid hormones) is often the result of multiple causes and may result in weight gain, tiredness, cold intolerance and slow heart rate.

And if Sherlock Holmes was asked to solve a case of thyroid disease, he would probably request the relevant pathology tests, declare the case solved once the test results were known and proclaim that diagnosing and monitoring thyroid disease can be elementary with pathology tests.

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