ePathWay
THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

OCTOBER 2017 | PUBLISHED BY RCPA ISSUE #074

IN THIS ISSUE

- Lupus is usually only skin deep
- Diagnosing systemic lupus erythematosus is as complex as the disease itself
- Anatomical pathology provides a roadmap for lupus patients
- Blood tests give kidney matches the best chance of success

INTERESTING FACTS

More than 20,000

The estimated number of people in Australia and New Zealand with systemic lupus erythematosus (SLE).

About 50%

The percentage of people with SLE who experience joint pain and swelling.

5 to 1

The ratio of the number of females with discoid lupus

Welcome to the October 2017 edition of ePathWay

Singer Selena Gomez made world headlines when she had a kidney transplant as a result of the effects of systemic lupus erythematosus (SLE). Lupus erythematosus (LE) is actually a group of diverse autoimmune inflammatory diseases, and SLE is just one type. It is also the underlying theme of this edition, including what happens when SLE leads to a kidney transplant. Our articles cover:

- Discoid lupus erythematosus
- Systemic lupus erythematosus (including lupus nephritis)
- Kidney transplant histology
- Tissue typing for a kidney transplant.

As always, check in to our Facebook page, or review the latest tweets from our CEO Dr Debra Graves (@DebraJGraves) or the College (@PathologyRCPA), to keep up to date with the RCPA and news about pathology.

Lupus is usually only skin deep

erythematosus (DLE) to the number of males with this disease.

Source: ASCIA, DermNet New Zealand

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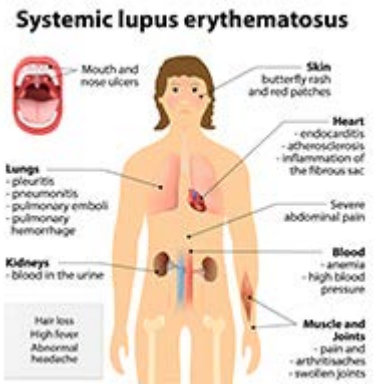
Anatomical pathology provides a roadmap for lupus patients



Systemic lupus erythematosus (SLE) can be difficult to diagnose because of its wide range of symptoms. It is an autoimmune disease in which a person's immune system attacks their body's own cells. It can affect the skin and many internal organs including the brain, joints and blood vessels. Anatomical Pathologists examine biopsies to identify which of these are affected and how severely. They then monitor this often-elusive disease that can ultimately require a kidney transplant, as in the case of singer Selena Gomez.

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Blood tests give kidney matches the best chance of success

When singer Selena Gomez posted pictures of herself on social media post-kidney transplant, systemic lupus erythematosus (SLE) and kidney transplants started trending. Gomez has been open about her diagnosis of SLE and her struggle with this autoimmune disease. When it affects the kidneys it's known as lupus nephritis and sometimes leads to a kidney transplant.

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Previous Editions

2017

066 - February 2017 | 067 - March 2017 | 068 - April 2017

069 - May 2017 | 070 - June 2017 | 071 - July 2017

072 - August 2017 | 073 - September 2017

2016

055 - February 2016 | 056 - March 2016 | 057 - April 2016

058 - May 2016 | 059 - June 2016 | 060 - July 2016

061 - August 2016 | 062 - September 2016 | 063 - October 2016

064 - November 2016 | 065 - Dec 2016/Jan 2017

2015

044 - February 2015 | 045 - March 2015 | 046 - April 2015

047 - May 2015 | 048 - June 2015 | 049 - July 2015

050 - August 2015 | 051 - September 2015 | 052 - October 2015

053 - November 2015 | 054 - Dec 2015/Jan 2016

2014

033 - February 2014 | 034 - March 2014 | 035 - April 2014

036 - May 2014 | 037 - June 2014 | 038 - July 2014

039 - August 2014 | 040 - September 2014 | 041 - October 2014

042 - November 2014 | 043 - Dec 2014/Jan 2015

2013

022 - February 2013 | 023 - March 2013 | 024 - April 2013

025 - May 2013 | 026 - June 2013 | 027 - July 2013

028 - August 2013 | 029 - September 2013 | 030 - October 2013

031 - November 2013 | 032 - Dec 2013/Jan 2014

2012

010 - Dec 2011/Jan 2012 | 011 - February 2012 | 012 - March 2012

013 - April 2012 | 014 - May 2012 | 015 - June 2012

016 - July 2012 | 017 - August 2012 | 018 - September 2012

019 - October 2012 | 020 - November 2012 | 021 - December 2012

2011

001 - March 2011 | 002 - April 2011 | 003 - May 2011

004 - June 2011 | 005 - July 2011 | 006 - August 2011

007 - September 2011 | 008 - October 2011 | 009 - November 2011

« Back to Home Page

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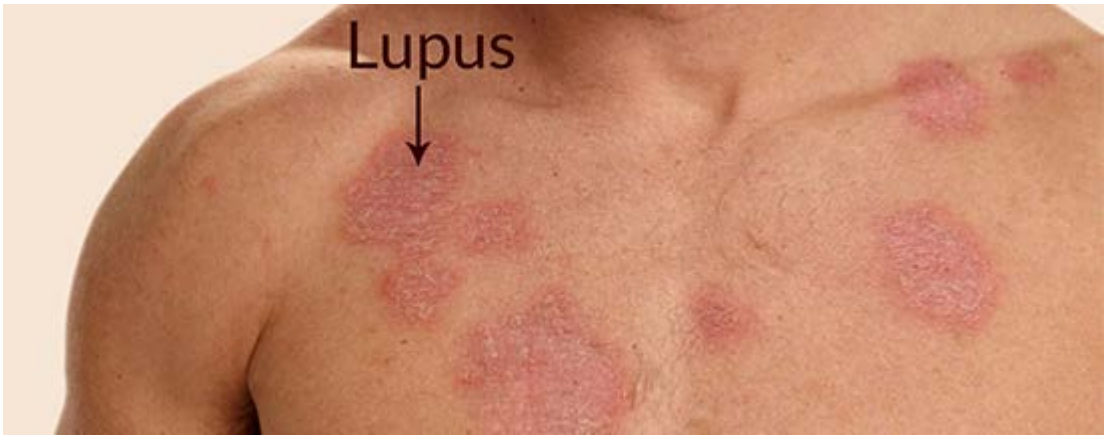

When we think of lupus erythematosus we normally think of systemic disease (SLE). More prevalent though is cutaneous lupus erythematosus (CLE) which specifically involves the skin. We've focused on the most common chronic form of CLE called discoid lupus erythematosus (DLE) which affected the singer Seal.

DLE is more common than its systemic cousin, and usually more straightforward to diagnose. Dr Rod O'Keefe, Dermatologist in private practice, Dermatopathologist at Melbourne Skin Pathology, and Director of Pathology at Skin and Cancer Foundation Inc., said DLE usually presents with characteristic clinical signs.

"Early lesions are red scaly patches or plaques in the head and neck region, typically involving ears, cheeks and nose as well as the scalp. More established lesions show plugs of keratin within hair follicles and scarring with loss of pigment and atrophy (skin thinning). There may be increased pigment at the edges of the lesions, and scalp lesions may lead to permanent hair loss due to scarring."

Dr O'Keefe said the diagnosis may be confirmed on skin biopsy with the key histologic feature being an interface (lichenoid) dermatitis."

"If a person has only DLE then the risk of developing SLE is between five and 10 per cent. In some studies the risk is put as high as 25 per cent, but I believe it is closer to five per cent in adults with a higher risk in the rarer childhood cases. Those patients who have more disseminated skin disease with lesions on the trunk and limbs seem to be at greater risk of progression to SLE."

Dr O'Keefe said cigarette smoking has been associated with DLE. Sun exposure may also be a predisposing factor in some people, along with a genetic predisposition to the

disease. Although DLE is a chronic condition persisting for years, he said DLE can sometimes ‘burn itself out’ and the disease may eventually become inactive. Early diagnosis and treatment is important in preventing progression to disfiguring scarring and pigmentary change and permanent hair loss.

A few more DLE facts

- It is more common than SLE.
- It is 5 times more common in females than males.
- It can affect anyone at any age although onset is usually between 20 and 40 years of age.
- It is more common and a more severe disease in people who smoke.

« Back to Home Page

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Diagnosing the chronic autoimmune disease systemic lupus erythematosus (SLE) is complex. Symptoms vary according to which tissues are attacked, and are common enough to be attributed to many other conditions. Its incidence also alters according to ethnicity and gender. Where do you start?

Dr Daman Langguth, Clinical Immunologist and Immunopathologist at Sullivan Nicolaides Pathology, said there isn't one pathology test that confirms a diagnosis of SLE. If it is suspected then an antinuclear antibody (ANA) test is usually the first pathology investigation requested. This test doesn't confirm the diagnosis. It flags that an autoimmune disease may be present. Most people with a positive ANA do not have an autoimmune disease.

"If the ANA test is positive then subsequent pathology investigations might include an anti-double stranded DNA test (anti-dsDNA) that specifically targets the genetic material found in the nucleus of cells, an ENA (Extractable Nuclear Antigen Antibodies) Panel, and a test for complement proteins," he explained.

An ENA Panel detects the presence of one or more specific autoantibodies in the blood and the resulting pattern of positive and negative results helps diagnose different autoimmune disorders. Complement proteins are a part of the immune system, and their levels can be used to help diagnosis or monitor disease activity. Presenting symptoms are also investigated, including investigating which organs, tissues and joints are affected.

"SLE is a true protean multisystem disorder. It can affect every organ except the liver,

and we don't know why this is the case. It can also affect the skin, eyes and joints, and cause diseases such as pleurisy and pancreatitis. Between 10 and 30% of patients have kidney involvement and this is called lupus nephritis. If this is suspected, then pathology tests may be requested to check the kidneys' function," said Dr Langguth.

SLE can affect anyone at any age, but it has a known risk profile. About nine in 10 people affected are pre-menopausal women, mostly between 15 and 45 years of age. Post menopause the incidence becomes equal for men and women.

"The male and female disease profile is also different. Men usually experience sudden severe episodes while women tend to have it simmering in the background all of the time," explained Dr Langguth.

He also said a person's ethnicity is also a risk factor.

"African Americans have the highest risk with an incidence of one in 70. But people of African ethnicity don't have a high incidence if they reside in Africa. This is because of the genetic relationship between cerebral malaria and SLE. The genes that protect people from this type of malaria also promote developing SLE. When people of African ethnicity live in a malaria-free country such as North America, their incidence of SLE increases."

Other ethnicities at greater risk are non-Caucasian populations such as Aboriginals, Hispanics/Latinos, Asians, Native Americans, Native Hawaiians and Pacific Islanders. It is also more prevalent in some families.

Dr Langguth said SLE is still relatively poorly understood but responsible for a significant degree of disability in the community. It is also a disease for life. Early diagnosis can prevent serious downstream complications, but that's not as simple as it sounds. It takes about seven years from onset of disease to measureable symptoms, and there is no single pathology test for it. That's part of the reason why diagnosing SLE is often as complex as the disease itself.

« Back to Home Page

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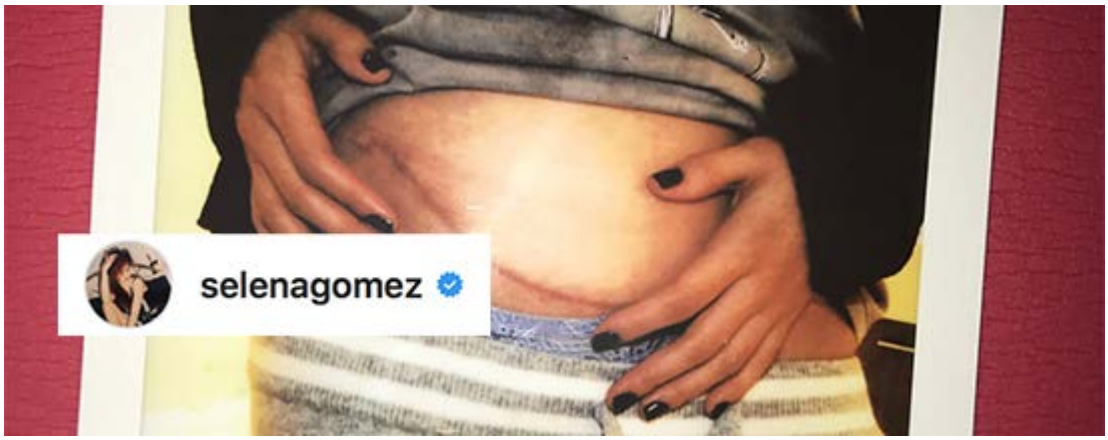

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When lupus affects the kidneys it's called lupus nephritis. This is a type of glomerulonephritis where the glomeruli (clusters of small blood vessels that form the kidney's basic filtration unit) become inflamed.

"Diagnosis of lupus nephritis is confirmed by a renal biopsy where an anatomical pathologist makes the diagnosis and then stages the disease. Further biopsies are then needed to monitor the progress of the disease, plan the patient's treatment, and follow up the progress of the kidney after treatment," explained Dr Tony Landgren, Anatomical Pathologist at the Royal Melbourne Hospital and Australian Clinical Labs.

He said lupus nephritis is staged into five classes ranging from Class 1 minimal disease to Class 2 mild disease and Classes 3-5, more severe disease. Progression of the kidney disease can lead to dialysis and potentially a kidney transplant.

"In many cases lupus nephritis can be kept under control for long periods of time with treatment. Other times the deterioration is very fast. Often teenagers and young adults are diagnosed with lupus, and if their kidneys are involved they can progress to dialysis

and potentially a kidney transplant very quickly. It's devastating for them," Dr Landgren explained.

"It's also very important not to assume that signs of kidney disease in a person diagnosed with lupus are automatically deemed to be lupus nephritis. Kidney disease can result from other causes such as vascular disease or IgA nephropathy, or it might be from more than one disease process occurring at the same time such as lupus. This is why examining the kidney tissue to accurately diagnose the cause of kidney disease is important."

Dr Landgren said once a patient has a kidney transplant, protocol biopsies at designated intervals are used to check the new kidney's status. If there are signs of a problem developing then an indication biopsy will be requested to find out why. Problems might include organ rejection, infection, blood vessel disease, drug toxicity and recurrence of lupus nephritis in the new kidney.

Although Selena Gomez now has a new kidney, lupus is a disease for life. This means monitoring the disease is for life as well. Much of this process falls under the watch of Anatomical Pathologists who provide a valuable roadmap into the future for every lupus patient.

« Back to Home Page

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Blood tests give kidney matches the best chance of success

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Regardless of the reason why a kidney transplant is needed, Dr Heather Dunckley, Clinical Scientist and ASHI Director, Tissue Typing, at the New Zealand Blood Service, said pathology tests to find the best donor kidney match are the same for everyone. These include four key blood tests that determine if the kidney recipient and donor are a suitable match before the transplant.

ABO blood grouping is carried out and donor-recipient compatibility is assessed following the same rules as for blood transfusion. For example, if the recipient's blood type is A, they can receive a kidney from donors with the blood types A and O. If the donor's and recipient's blood types are compatible then three more blood tests follow - tissue typing, antibody screening and cross matching.

Despite the name, tissue typing is a blood test for human leukocyte antigens (HLA). "We extract the DNA from the recipient's and donor's blood sample to identify the major HLA genes and the corresponding proteins (antigens) that are found on most cells in the body," explained Dr Dunckley.

These proteins, or markers, are inherited from our parents and are a unique signature. They help the body's immune system discriminate between a person's own cells ('self')

and those that are foreign or ‘non-self’. The cells recognised as ‘non-self’ can trigger an immune response, and this is why it’s important to match these HLA proteins as closely as possible between the donor and transplant recipient.

“If the donor and recipient have the same HLA types then the immune system of the recipient is less likely to initiate an immune response against the transplanted kidney. We also perform an antibody screen on the recipient to check they have no anti-HLA antibodies against the donor,” said Dr Dunckley.

The fourth test is a crossmatch.

“This is where we isolate the lymphocytes from the donor’s blood and incubate them with the recipient’s serum (a component of blood) and look for a reaction. If there is a positive reaction then it can stop the transplant from taking place. This is because there is a factor in the recipient’s serum that can react against the donor kidney cells as the blood goes through the kidney, potentially causing rejection. We won’t always know why the crossmatch test is positive, only that there is a reaction that could cause a problem,” she explained.

Dr Dunckley said blood tests to monitor for anti-HLA antibodies after the kidney transplant are performed at scheduled intervals.

“An HLA antibody test will usually be immediately requested if there are any signs of the transplanted kidney being rejected. The patient’s clinician may also request additional tests including a kidney biopsy to assess the condition of the kidney’s cells.”

Kidney donors can be deceased or living donors related or unrelated to the recipient.

“In the case of an unrelated living donor, they may be a friend or they may be an anonymous altruistic donor unknown to the patient who has decided they would like to donate a kidney to a patient in need. The tissue typing and matching process is the same whether the donor is deceased, related or unrelated. In the case of an altruistic donor, they will donate to the best-matched patient on the kidney waiting list,” said Dr Dunckley.

Despite all human kidneys being anatomically similar, they can’t be successfully transplanted into other people without the information collected from these key blood tests. While not every recipient receives a perfect kidney match, the blood test’s information provides the vital road map for the greatest transplant success.

« Back to Home Page

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