This is a summary from the First IgA nephropathy patient information day, held on Saturday 8th March 2014 at the National Space Centre, Leicester. The day was organised by a team of scientists, patients and clinicians, and was kindly sponsored by Kidney Research UK and the British Kidney Patients Association.

**Dr Karen Molyneux**, Senior Research Scientist, University of Leicester, gave an introduction to the day. Dr Molyneux, with Dr Jonathan Barratt, leads the IgA nephropathy (IgAN) research group at the University of Leicester. The group is focused on ways that kidney damage occurs in IgAN. Karen introduced the organising committee, Tricia Higgins, Barbara Fentum, Chee Kay Cheung, and Phil Smith, who has been heavily involved in securing funding for the day. There were three overall aims to the day: to provide information to patients, to allow patients to share their own experiences, and lastly to provide feedback to funding bodies about research priorities from the terms of patients. The agenda was organised after feedback from patients at registration.

The audience and speakers were then divided into three groups to share their background, experience of and interest in IgAN. Stories of ‘good things’ that had happened over the last year (ranging from births, holidays, starting new businesses, retiring from work and even swimming with dolphins!) were swapped between patients who had been diagnosed with IgAN as recently as 3 months ago to 30 years ago.

**Professor John Feehally**, Professor of Renal Medicine, University of Leicester, gave us an overview of IgAN (originally known as Berger’s disease). He explained that patients with IgAN are usually identified after the finding of blood in the urine (haematuria), which may be visible – often coinciding with a sore throat, gastrointestinal upset, or exercise, (blood in the urine can resemble Coca-Cola), or non-visible, for example identified after a urine test performed for screening tests. There may also be protein in the urine, called proteinuria. Other ways patients may be identified are through tests for high blood pressure or reduced kidney function. However, he stressed that IgAN can only be diagnosed by renal biopsy where a small piece of kidney tissue is taken and examined under the microscope. Kidneys consist of millions of filters called glomeruli. IgAN occurs when IgA gets stuck in the filters. IgA is a type of antibody and is part of the natural defence mechanisms of the immune system. Sometimes, but not always, IgA getting stuck leads to inflammation then scarring of the filters, which stops the kidney working properly.

IgAN is a highly variable condition, with some people progressing to need dialysis, while others will be completely unaware they have the condition and their kidney will work normally in the long term. The disease can go away, can stay the same, patients may slowly lose kidney function, the kidneys may fail completely, and IgAN may recur after kidney transplantation. Those with non-visible haematuria only have a very low risk of disease progression. Attacks of visible haematuria can occur (more often in teenagers and young adults), but do not indicate a worse outcome. Proteinuria, high blood pressure and reduced kidney function are associated with disease progression. Steps to reduce high blood pressure and proteinuria are therefore important for managing IgAN.
As IgAN is so variable, and there is currently no reliable way of predicting how the disease will progress in any one individual, it is important to ‘get on with life!’ One patient has competed for Team GB at the Olympics a few years after diagnosis!

Kidney biopsies in IgAN are now ‘scored’ using an internationally agreed set of criteria known as the ‘Oxford classification’. On biopsy, predictors for progression include how inflamed the glomeruli are, whether there is scarring, and whether there is damage to the rest of the kidney as well as the filters. We can predict the risk of progression by the kidney biopsy in combination with the clinical signs of high blood pressure and proteinuria, as well as the level of kidney function. These predictions become more accurate as time goes on, but predictions are always an estimate.

The cause of IgAN remains unknown. IgA molecules in IgAN have small but important differences in their structure and there are subtle differences in the immune system that produces IgA. We still don’t know exactly why IgA sticks in the glomeruli, why it causes more damage in some people than others, why it is more common in males, and why it is more common in some parts of the world.

In terms of treatment, if the kidneys deteriorate, general advice includes a healthy diet and lifestyle, and to consider medication in certain cases. There are no specific treatments currently to stop IgA sticking to the kidney filters. Steroids (prednisolone), and a medication to suppress the immune system called mycophenolate mofetil have been used occasionally to reduce the inflammation seen in IgAN. Which patients are treated, when, and for how long all remain controversial. Clinical trials are ongoing to try to answer these questions. The treatments of proven benefit include controlling blood pressure, which not only involves taking blood pressure lowering medication, but also exercise, reaching an ideal weight, medications, and, importantly, reduction of salt in the diet. The other treatment of proven benefit is to reduce proteinuria. This is usually done by using one of two types of specific blood pressure lowering medications – angiotensin converting enzyme inhibitors (usually known as ACE inhibitors) or angiotensin receptor blockers (ARBs).

Rarely IgAN can run in a family, but this is so uncommon that screening of family members is not usually recommended. Flu jabs are safe in IgAN. The evidence behind taking fish oil remain uncertain – there was one trial that suggested benefit 20 years ago which involved taking 12 fish oil capsules daily over 2 years, but others trials were negative. There is currently not enough evidence to recommend their use.

Next Dr Emma Watson, exercise physiologist and post-doctoral researcher with the Leicester Kidney Exercise Team, gave a talk on Exercise and Chronic kidney disease: time for action. She pointed out that humans were not designed to be sedentary, and have evolved from hunter-gatherers. In fact the health benefits of exercise have been recommended since the time of Hippocrates in 460 BC! She stressed that ‘exercise’ does not have to mean daily trips to the gym or running a marathon! Exercise should be regular and can be as simple as gardening or walking the dog. The risk of cardiovascular disease, which includes heart disease and stroke, are increased in people with kidney disease. There are many potential health benefits of exercise, such as reduction of this risk, weight control, control of blood pressure, reduction of cholesterol, control of diabetes and improvement of bone density.
Patients with more advanced kidney disease may also suffer from muscle wasting, which can lead to weakness and fatigue. Muscle wasting can be due to age-related changes or lack of use but is also associated with the toxin build-up that occurs advanced kidney disease. Dialysis is also known to induce muscle wastage and loss. It’s important to maintain muscle mass, as muscles help to control glucose levels, and use up fat.

She recommended that we all aim for 30 minutes of moderate-intensity exercise 5 times a week. Moderate-intensity exercise will raise your heart rate and make you breathe faster and feel warmer. One way to tell if you're working at a moderate intensity is if you can still talk, but you can't sing the words to a song. These 30 minutes can be taken in one block or with breaks, for example in 3 blocks of 10 minutes. Try to include some strength exercises 2 days a week. If you have any concerns about exercise, discuss these with your doctor, especially if you have heart disease, liver disease or diabetes.

**Aileen Case**, Senior Renal Dietician at the John Walls Renal Unit, Leicester General Hospital, gave us a talk on Diet and IgAN: food for thought. Diet can help reduce the risk of cardiovascular disease, control blood pressure and help to protect the kidneys. The Eatwell plate ([http://www.nhs.uk/Livewell/Goodfood/Pages/eatwell-plate.aspx](http://www.nhs.uk/Livewell/Goodfood/Pages/eatwell-plate.aspx)) was recommended which advises that your daily diet is made up of a balance of starchy food, dairy, fruit and vegetables, and protein (meat, fish, eggs and/or beans). Watch out for your sugar intake – the average person consumes 700g sugar per week, which is equivalent to 140 teaspoons! Be ‘food aware’ and read the food labels so you know what is contained in the food that you are eating. Swap fats for lower fat options, for example low fat spreads instead of butter. It's recommended that everyone has five portions fruit or vegetables per day.

Salt is very important to be aware of as eating too much can increase your blood pressure and damage your kidneys. High quantities can be found in ready meals. It’s recommended that people have a maximum of 6g salt per day, although average salt consumption in the UK is 9g per day. When looking at the salt content of foods remember that ‘sodium’ is only a part of salt. To convert the amount of sodium to the amount of salt multiply by 2.5. There is no difference between ordinary table salt, rock salt, or sea salt – it’s all salt! Be careful of ‘lo-salt’ which is potassium based and may be a problem for those on a potassium restricted diet – this is more common in people with advanced kidney disease. Know your recommended alcohol limits - 3-4 units/day for men, and 2-3 units/day for women.

Helpful ways to help change your food habits include using fitness and diet apps, national resources available on websites, cook books, making changes together with family members or friends, and asking to see your local dietician. She stressed that as a patient with IgAN, your dietary needs will vary depending on the stage of your disease

Next, **Dr Peter Topham**, Consultant Renal Physician and Honorary Senior Lecturer, University of Leicester, talked on kidney transplantation in IgAN. A kidney transplant is usually placed in the lower abdomen in a place called the iliac fossa. The patient’s own kidneys are usually not removed. There are two main sources of kidneys – from live donors, and deceased donors. Despite efforts to increase the numbers of donors,
there remains a shortage of kidneys available for transplant. The average waiting time remains around 3 years.

A kidney transplant is the best treatment for end stage renal disease with IgAN. Compared to dialysis, kidney transplantation is associated with improved patient survival and improved quality of life. There are significant cost benefits to the NHS also when comparing transplantation to dialysis.

There is limited evidence that after transplantation, between 21-58% of patients who underwent a renal biopsy had evidence of recurrent deposition of IgA on their kidney transplant, but this does not always result in kidney dysfunction. Recurrence of IgA deposition is more likely if the kidney has come from a living donor, if there is a better tissue type match or if the recipient has a higher serum IgA concentration. However, there is no way of predicting or preventing recurrence. Patients with recurrent IgA deposits on the transplant often present in a similar fashion to their original disease course. There remain no specific treatments for the recurrence of IgAN after transplantation.

There is approximately a 10% risk of loss of the kidney transplant due to recurrence of IgAN. However the overall 10 year survival of the kidney transplant is similar to that of patients with kidney diseases that are not IgAN. Chronic transplant rejection or death are more common causes of loss of the transplant. When asked about the potential risk to a live donor he stressed that when donating a kidney, the donor is evaluated very thoroughly for their own health and ability to donate before the procedure is approved. Kidneys are now removed from live donors by laparoscopic ‘keyhole’ surgery resulting in smaller scars than in the past.

Dr Jonathan Barratt, Consultant Renal Physician and Reader of Nephrology, University of Leicester, talked on how research can help and what is currently going on in the UK. Current research in Leicester is focused on why some people with IgAN do well and others develop progressive kidney disease. We need your help to research IgAN, and to help think about new treatments and developments. Research works best as a collaborative effort, and we have been involved in organising the UK IgAN research consortium, and also share ideas with colleagues in Europe, North America, China and Japan via the International IgAN network.

As well as looking in the clinic at blood pressure, protein in the urine, and creatinine, we are trying to develop new biomarkers of progression. Two research projects in Leicester were described. Firstly, how does the structure of the IgA antibody change in IgAN? We are trying to visualise proteins – which for comparison are 100 million times smaller than an egg! IgA is purified from blood samples taken from patients with IgAN and sent to Oxford (the Rutherford Appleton laboratory), and the ISIS SANS lab in Grenoble for detailed analysis. The aim of this project is to work out whether differences in the shape of the IgA molecule may make it more sticky, and therefore stick to the filters of kidney in IgAN. This project is funded by Kidney Research UK. The second project, funded by the Medical Research Council and the National Institute for Health Research, is to investigate whether there are changes in the genes of patients with IgAN. Samples of DNA have been taken from 500 patients with IgAN. We have already looked at genes associated with the disease. The current
aim is to look at clinical data, and to take further blood samples, to see whether
certain genes can predict people who will have progressive kidney disease in IgAN.

We face challenges to attract further funding to research in IgAN in terms of national
priorities. Dr Barratt emphasised the importance of patient involvement in research,
not only by providing vital clinical samples for laboratory work, but also to provide
input into clinical trial design and to speak to funders about the importance of
research in IgAN.

Lastly Dr Frederick Tam, Consultant Renal Physician and Reader of Nephrology,
Imperial College London, talked about clinical trials in IgAN. Progress in converting
laboratory findings to bedside treatments has been slow, so collaboration with the
pharmaceutical industry to facilitate this is vital. The current mainstay of treatment is
control of blood pressure, often by angiotensin blockers, and, in specific cases,
treatments to suppress the immune system, which often are associated with side
effects. There are currently two large ongoing trials in IgAN to look at the role of
steroids in treating IgAN – the Supportive versus immunosuppressive Therapy Of
Progressive (STOP) IgAN trial (which has finished recruitment) and the Therapeutic
evaluation of STeroids in IgAN Global (TESTING) trial.

Dr Tam described an exciting new drug, which is an inhibitor of spleen tyrosine
kinase (Syk). This molecule is involved in inflammatory signalling pathways. Dr Tam
showed data that Syk is increased in IgAN compared to other kidney diseases such as
minimal change nephropathy. Work in the laboratory using cells from human kidneys
has shown that IgA extracted from the serum of patients with IgAN activates Syk
within the kidney cells leading to the release of inflammatory proteins from the cells.
In the presence of the active component of a drug called fostamatinib, which inhibits
the activity of Syk, the production of these proteins is inhibited. Work on pre-clinical
models of IgAN also showed that fostamatinib reduced haematuria and proteinuria
and reversed kidney damage.

Fostamatinib can be taken orally and has already been used in large clinical trials for
Rheumatoid Arthritis, so its safety record and side effect profile is well documented.
It will now be tested for its effectiveness in patients with IgAN in a clinical trial
across centres in Europe and Asia, starting in the near future. The trial will be
coordinated by Rigel pharmaceuticals (who make fostamatinib) and Kidney Research
UK.

Four patients with varied experiences of IgAN then spoke candidly about their disease
and the impact that it has had on their lives.

PS was identified after investigations into high blood pressure, where a blood test
indicated that he had impairment of his kidney function. He underwent a kidney
biopsy and was diagnosed with IgAN. He now has approximately 25% kidney
function, although this has been stable over the past few years. He leads a healthy
lifestyle - he doesn’t smoke or drink alcohol, he goes to the gym three times per week,
and sticks to a low salt diet. In fact he thinks he leads a healthier lifestyle compared to
before being diagnosed, and describes being diagnosed with IgAN as having had a
positive impact on his life.
ST was diagnosed after screening tests for life insurance showed that he had protein in his urine. He had no other symptoms. He was referred to a kidney specialist and had a kidney biopsy that showed that he had IgAN. He underwent treatment with prednisolone, cyclophosphamide, and then azathioprine, but suffered from insomnia and poor concentration so had to stop these. His kidney function is now stable. He finds Renal Patient View (a website that allows patients to check their own blood results) very useful in aiding interaction with his consultant. He is also on a Facebook forum for IgAN.

LK was travelling in South America for 14 months, when he developed severe headaches and had to be hospitalised, where he was found to have severe kidney disease. He had a kidney biopsy in Brazil, and had another biopsy in the UK. These showed that he had IgAN and that the disease was advanced. He had a trial of steroids but had to start dialysis in 2012. Other than the headaches, he had no other symptoms of being unwell. The hardest thing to deal with was having to adjust from feeling well on a beach in Brazil to being in a hospital in Stoke. It was a massively difficult thing to come to terms with. He is now on haemodialysis and initially found this very restrictive. He has now changed to doing nocturnal haemodialysis 6 nights per week. This has given him more freedom, in that he can go to the gym every day, and his diet is less restricted. However, he is less free to travel now, which was something that he really enjoyed doing before. His friend has volunteered to donate kidney, and the transplant operation is due to take place next month, after going into the paired exchange programme. His biggest concern is the disease coming back after the transplant, as well as all the new medications that he will have to take.

MB had no symptoms of ill health, until she was found to have a high blood pressure, and subsequent tests including a kidney biopsy showed that she had IgAN. Her kidney function fell from 65% to 30% in under one year, and she was told to expect to start dialysis in 6 months. She was given aggressive treatment with blood pressure medications, prednisolone and mycophenolate. Thankfully her kidney function stabilised, and her level of proteinuria reduced. She wanted to reinforce what had already been said about ‘the wonderful’ Renal Patient View – she can see what is happening with her kidney function and what the trend is. She also checks her own urine dipsticks every week. She has never been ill before. She enjoys an active lifestyle, and enjoys golf, walking and racquetball.

Finally questions were put to a panel of experts at the end of the day, including:

**How do you organise travel insurance with having IgAN?**
Please see the National Kidney Federation and British Kidney Patients Association websites for more advice about this.

**How do you access Renal Patient View?**
Please contact your consultant or renal department about this.

**How can we organise a patient support group for future meetings?**
Please email philsmith_55@hotmail.com for further details

We would like to thank all the speakers, and participants for coming to the day.

Chee Kay Cheung
Theresa Page