



# Insulin Dependent Diabetes Trust

Kidneys and Diabetes

Updated December 2008

Registered Company Number 3148360  
Registered Charity No 1058284



## Contents

Healthy Kidneys  
Kidney disease and diabetes  
The use of ACE Inhibitors  
Kidney failure  
Useful organisations  
Research

## Facts

- Diabetes is the single most common cause of end-stage renal disease [ESRD] in Europe and the US.
- Between 30 and 50 % of people with diabetes are at risk of kidney disease.
- People with type 2 diabetes often have microalbuminuria and overt nephropathy shortly after the diagnosis of their diabetes, because diabetes is often present many years before diagnosis.
- The key to preventing kidney damage is early detection of the excretion of protein in the urine and early intervention with treatment.
- People with kidney disease are at higher risk of heart disease. Therefore attention should be given to lowering blood pressure and cholesterol, taking exercise and not smoking

## Healthy Kidneys

The healthy balance of our body's chemistry is largely due to the work of our two kidneys that are about the size of a fist and are shaped like beans. They are situated just above the waist in your back and are partly protected by the ribs. You can live a healthy life with only one kidney.

### What do normal kidneys do?

- The kidneys get rid of the body's waste products and excess water as urine. The waste products form from the breakdown of the protein we eat and from normal muscle activity.
- The kidneys also produce hormones that help in the production of red blood cells, build strong bones and help to keep blood pressure under control.

### What causes kidneys to stop working?

- Diabetes
- High blood pressure
- Chronic kidney infections
- Severe injury or birth defects
- Certain drugs and other kidney disease

Inside each kidney there are about one million tiny units called **nephrons** that filter and remove excess fluid and waste products from the blood. The entire body's blood supply circulates through the kidneys every two minutes. The waste products and the fluid that are filtered out are excreted as **urine**. The urine travels through tubes, the **ureters**, into the bladder where it is stored and eventually passes out of the body through another tube called the **urethra**. If the kidneys fail then the harmful waste products build up in the blood, called **uremia**, and you feel ill. Some of the signs and symptoms of kidney failure are:

- Extreme tiredness
- Nausea and vomiting

- Shortness of breath
- Difficulty sleeping
- Swelling of hands, feet and face
- High blood pressure
- Itchiness
- Loss of appetite

### The kidneys and blood pressure

One of the most important functions of the kidneys is the control of blood pressure. High blood pressure, hypertension, is very common in people with kidney failure and can occur from the early stages of kidney damage. But it is a 'chicken and egg' situation - high blood pressure can cause kidney failure but kidney failure can cause high blood pressure. As people with kidney disease have a significantly increased risk of heart disease compared to the general population, it is important that high blood pressure is treated.

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## Kidney disease and diabetes

One of the long-term complications of diabetes can be kidney disease and most of us are aware that prevention of the development of kidney disease is one of the reasons that we need to keep good blood glucose control. Aggressive treatment of blood pressure and stopping smoking, are also methods by which kidney disease can be either prevented or treated.

### Definition of kidney disease or nephropathy [its medical name]

Diabetes at Your Fingertips, a very useful book, defines it as:

*"In the first instance nephropathy makes the kidney more leaky so that protein [albumin] appears in the urine. At a later stage it may affect the function of the kidney and in severe cases leads to kidney failure."*

## What are the ways in which diabetes can affect the kidneys?

- If there is a lot of sugar in the urine, because you are running high for whatever reason, then this can lead to infection that can spread from the bladder to the kidneys. Chronic kidney infections do not always produce symptoms and may only show up on routine clinic tests.
- In both longstanding and poorly controlled diabetes the kidneys have to work hard to get rid of the excess sugar and the small blood vessels in the kidneys can be damaged, in the same way as those supplying the eyes and causing retinopathy. If both diabetes and high blood pressure are present the risk to the kidneys is greater.

## Does kidney damage produce symptoms?

- In the early stages there are no symptoms and any kidney damage should be picked up in the urine tests carried out at your normal clinic visit when albumin levels are measured.
- If large amounts of urine are lost then this leads to frothing of the urine and a build up of fluid in the body with swelling of the ankles [oedema] but this should be spotted in the routine clinic urine tests.

## What is microalbuminuria?

This is the name for the condition described above where abnormal amounts of protein [albumin] leak from the kidneys into the urine. It is the first sign that kidney disease may be developing. If kidney damage progresses then there are increased amounts of protein excreted in the urine and this is called macroalbuminuria.

The presence of microalbuminuria is detected by testing all the urine collected during a 24hour period. The test carried out in the laboratory checks the ratio of albumin to creatinine, another substance that if higher than normal is a good predictor of kidney damage. Creatinine is a waste product produced as a result of muscle activity. The albumin/creatinine ratio is measured in micrograms per milligram. Someone without diabetes normally excretes less than 25 µg/mg per day although this 'normal' figure is less in men [18µg/mg] than in women

[25µg/mg].

## Understanding the results

From personal experience, when my daughter was given the results of her first 24 hour urine collection, we knew they were high but did not know how high. The actual figures were meaningless to us because we didn't know the normal range and how high they can go. For example a figure of 29 sounds dreadful but not if you look at the worst possible figures! So that other people are able to understand their results and maybe not worry quite so much, with the permission of Diabetes Interview we are printing their table of ranges of albumin/creatinine ratios:

	Male	Female
Normal albuminuria	17µg/mg or less	25µg/mg or less
Low microalbuminuria	18-65µg/mg	26-29µg/mg
High microalbuminuria	66-250µg/mg	93-355µg/mg
Proteinuria	More than 250µg/mg	More than 355µg/mg

**Note - Don't panic at one high result!** Results of urine tests for protein can be high for various reasons - for example it could be due to infections of the kidney, bladder or urethra or if you had been exercising vigorously around the time of the test. If subsequent tests are consistently higher than expected then your doctor should carry out further tests and, if necessary, treatment.

Obviously your doctor will decide when and if you should receive treatment for microalbuminuria. The key to preventing kidney damage is early detection of the excretion of protein in the urine and early intervention with treatment to slow down the progression of microalbuminuria to prevent further kidney damage. Microalbuminuria can progress to renal failure if left untreated.

## The use of ACE inhibitors

ACE inhibitors, are drugs normally used for the treatment of high blood pressure. This is a category of drugs called Angio-Converting Enzyme inhibitors – ACE for short. ACE is an enzyme found in our bodies which activates a hormone called angiotensin causing the blood vessels to constrict, so raising blood pressure and putting pressure on the heart. ACE inhibitors prevent the action of angiotensin resulting in a lowering of blood pressure.

However, there is now evidence showing that the use of ACE inhibitors in people who start to show small amounts of protein in the urine, helps to reduce the progression to macroalbuminuria. In other words the use of ACE inhibitors has a protective effect on the kidneys, even in people whose blood pressure is normal.

### What does the research show?

A meta-analysis [Ann Intern Med 2001 March ; 134[5] 370-9] was published on this subject. This is an analysis of selected studies and it provides better evidence than just looking at individual studies. In this case, the studies were selected on the following basis:

1. they included at least 10 people with Type 1 diabetes who had microalbuminuria and normal blood pressure
2. they had a control group who were not treated with ACE inhibitors [placebo group]
3. they had follow up results at least a year later.

12 studies were selected with a total of 698 patients. The results showed:

- the progression to macroalbuminuria was reduced in patients receiving ACE inhibitors
- After two years the albumin excretion rate was 50.5% lower in treated patients than in those receiving a placebo [no treatment].
- For patients with normal blood pressure, Type 1 diabetes and microalbuminuria, ACE inhibitors significantly reduced progression

to macroalbuminuria and also increased the chances of regression back to normal where no proteins were found in the urine.

- The beneficial effects of ACE inhibitors were weaker at lower levels of protein excretion.

This has led to some debate amongst the medical profession about when ACE inhibitors should be prescribed and to whom.

- In a 1995 issue of The Lancet researchers issued a consensus statement recommending the use of ACE inhibitors irrespective of blood pressure, once microalbuminuria has been diagnosed.
- The American Diabetes Association [ADA] Position Statement dated January 2001, recommends the use of ACE inhibitors in people with microalbuminuria who have high blood pressure and those who have normal blood pressure.
- The National Kidney Foundation in the US recommends their use in people with diabetes at risk of kidney disease who have normal blood pressure.
- In Diabetes Interview, April 2001, Dr Alan Marcus, California says “Some physicians feel that having diabetes is reason enough to use ACE inhibitors, while others wait until certain levels of proteinuria are reached.”

**Note** – ACE inhibitors can have fairly mild side effects, the common one being an irritating cough. They are not suitable for everyone so this needs to be discussed with your doctor and they are not recommended for pregnant women.

While there are differing views on the use of ACE inhibitors to protect the kidneys, it is clear that early detection and early intervention is the way to prevent, treat and even regress problems with protein in the urine. The debate appears to be centred around whether or not people with diabetes should start taking low dose ACE inhibitors before there is any sign of protein in the urine or raised blood pressure to try to prevent the development of microalbuminuria. If people who are at risk of developing kidney disease can be identified, then there appears to be a case for prescribing ACE inhibitors for these people.

## Kidney Failure

Each kidney contains about 1 million nephrons to carry out the filtration of the waste products. If the number of nephrons is reduced by damage to the kidneys then the remaining nephrons work harder and the overall kidney function is maintained. However, once a certain amount of kidney tissue has been damaged the surviving nephrons are under increased pressure, become damaged and the kidney function declines.

### What can be done if my kidneys fail?

If your kidneys fail then you will be treated like any other kidney patient.

- Dialysis. There are two forms of dialysis which remove extra water from the body and the waste products that have built up in the blood. This keeps you fit and well while you are waiting for a transplant.
- Kidney transplantation replaces the lost kidney function. It is a treatment not a cure. For many people it provides the optimum method of treatment because it removes the constraints of dialysis and restores a 'normal' lifestyle. There are two barriers to widespread successful kidney transplantations – a shortage of donor organs and rejection after surgery by the body's immune system.
- Dietetic advice on what foods can help to make you feel better.
- Medications from your doctor to help other problems such as blood pressure and water removal.

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## Useful organisations for more information

The British Kidney Patient Association  
Bordon  
Hants  
GU35 9JZ

tel: 0142 472021/2

The National Kidney Research Fund  
Kings Chambers  
Priestgate  
Peterborough  
PE1 1FG

helpline: 0845 300 1499

website: [www.nkrf.org.uk](http://www.nkrf.org.uk)

### Another useful website:

[www.kidneyoptions.com](http://www.kidneyoptions.com)

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## Research

### The influence of age of onset of Type 1 diabetes on the development of diabetic nephropathy.

This study carried out in 1999, used a population-based diabetes register to identify everyone with diabetes that was diagnosed between 1960 and 1982, resident in a particular catchment area. They were divided into groups according to the age at diagnosis 0-4, 5-9, 10-14 and compared with a control group who were diagnosed between the ages of 20-25 with similar durations of diabetes. Information about the state of their kidneys was obtained for 86% of the people. The results showed that all the children's groups had worse renal outcomes than the adult onset group and the proportion with protein in the urine was greater the younger the age at diagnosis. 73%, 47% and 48% respectively in the young age groups compared to 28% in the adult onset group. However the time taken to the stage of showing protein in the urine was similar for all age groups including the adult onset group – 27, 28, 27 and 31 years respectively.

The researchers conclude that renal outcome in Type 1 diabetes is related to the age of diagnosis with a marked difference between adult and childhood onset patients.

Abstract A111, Annual Professional Meeting, Diabetes UK, April 2001

### **Diagnosis of Type 1 diabetes before or at puberty increases the risk of kidney disease**

Research looking at 459 people showed that age of diagnosis and HbA1c levels were factors in determining whether a person would develop microalbuminuria. Young people diagnosed before or during puberty were more at risk than those diagnosed after puberty. Researchers suggest that the difficulty in maintaining blood glucose control during the teenage years can cause temporary injuries to the kidneys which can accumulate and contribute to a higher risk of kidney disease.

*Diabetes Care, Dec 2000*

### **No correlation between raised protein in the urine and high blood pressure in children with type 1 diabetes**

A study was carried out in the UK to look at whether blood pressure was raised in children with Type 1 diabetes before microalbuminuria was detected in the urine. The researchers compared 63 children who developed microalbuminuria during one or more annual tests with a control group of children of the same sex and age at diagnosis. The results showed that there was no significant difference in blood pressure between the groups before microalbuminuria developed. The researchers concluded that a rise in blood pressure should not be used as the first indicator of impending kidney disease in children with Type 1 diabetes.

*Diabetes Care, March 2001*

### **Fish protein reduces the risk of microalbuminuria**

Researchers in Sweden looked at 1150 people that whose duration of diabetes was more than 5 years and identified 75 who had higher than normal albumin excretion rates. They compared this group of 75 with a control group of 225 with diabetes for the same length of time but with normal protein levels in the urine. By means of a

questionnaire to all 300 people they studied their eating habits for 12 months. They found there was little difference in their consumption of protein, meat or vegetables but the people who ate more fish protein [an average of about an ounce or 9.35gms a day] were less likely to have microalbuminuria compared to those who ate less fish protein. This applied to 12 people in the group with microalbuminuria at the outset and 63 in the control group. The researchers suggest that fish protein may reduce the amount of work the kidneys have to do so reducing the risk of the development of kidney disease.

*Diabetes Care, May 2001*

### **Low protein diets are not needed in chronic renal failure.**

For many years the part of the treatment for chronic renal [kidney] failure has been low protein diets. But recent research has shown that these have little beneficial effect. The authors of this study also say that there is little evidence in the journals to show the role of low protein diets in people with diabetes. They also maintain that the nutritional safety of these diets is suspect because patients with chronic renal failure have low energy intakes, which is further reduced by these diets. In the Modification of Diet in Renal Disease Study even nutritionally sound, non-diabetic patients developed sub-clinical signs of malnutrition and the malnutrition could have been worse with a longer follow-up time. The final point that they make is that these diets are difficult to follow, and the people need a lot of support from the dietician. They conclude that low protein diets are not necessary in chronic renal failure.

*Ref 1 Miner Electrolyte Metab 1999 Dec;25(4-6):311-316*

**Insulin Dependent Diabetes Trust**

PO Box 294  
Northampton  
NN1 4XS

tel: 01604 622837

fax: 01604 622838

e-mail: [support@iddtinternational.org](mailto:support@iddtinternational.org)

website: [www.iddtinternational.org](http://www.iddtinternational.org)