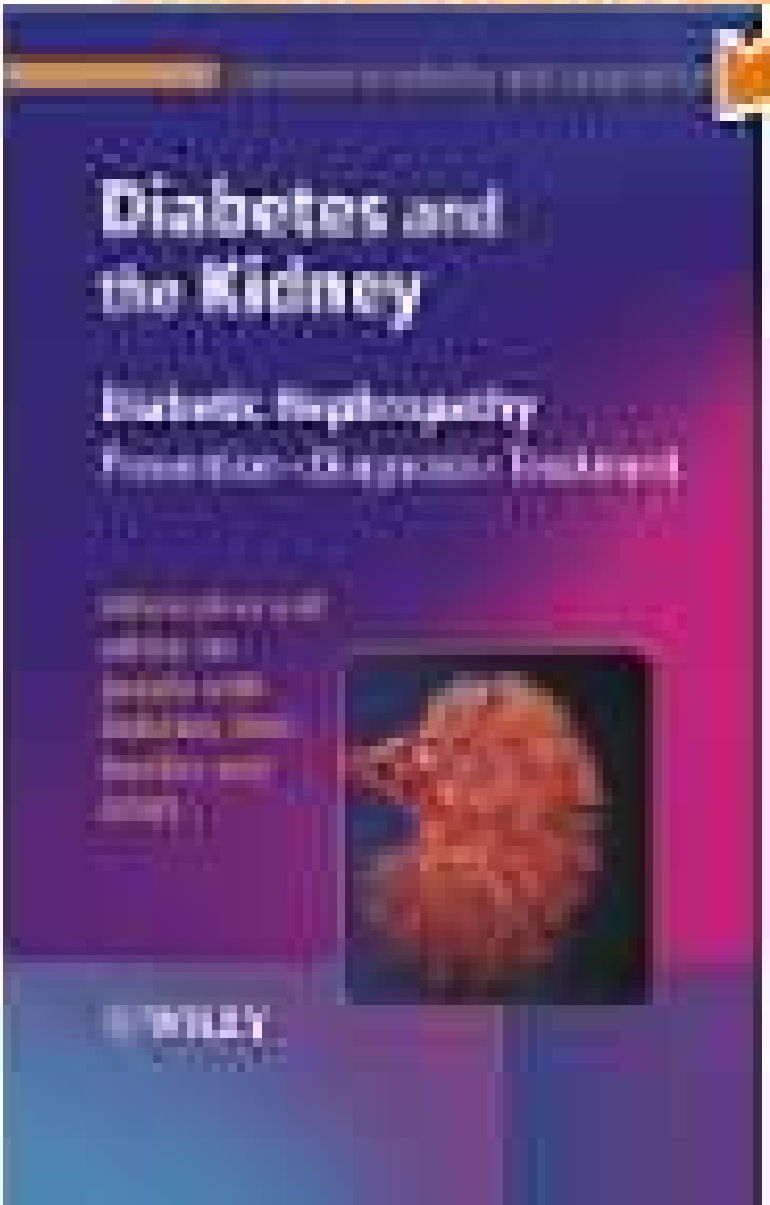

Diabetes and the Kidney

Diabetes and the Kidney (English edition) by Christoph Hasslacher and Sonja Böhm
 ISBN 0 470 021158 6

Diabetes and the Kidney

Christoph Hasslacher
and
Sonja Böhm

Diabetic Nephropathy

Prevention Diagnosis Treatment

Information and advice for people with diabetes,
their families and carers

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Contents

The treatment of diabetes mellitus has improved markedly over the past two decades. With different education programmes, very precise meters for measuring blood sugar levels and blood pressure in the clinic and at home, new drugs, new insulins, and simple injection devices (pens), doctors and patients today have many methods of controlling blood glucose concentrations. In recent years, this has undoubtedly led to a better quality of life and prognosis for people with diabetes.

The problem of the typical complicating conditions that accompany diabetes has, however, not yet been solved. The St Vincent Declaration, which was adopted by many countries in 1989, stated that the rate of diabetic complications would be reduced through intensive treatment, but this has not been achieved. The goal was to reduce diabetes-associated kidney damage and to decrease the number of diabetic patients needing dialysis by one-third. Unfortunately, the opposite is the case: today, diabetic nephropathy is one of the most frequent causes of kidney replacement therapy in the Western world.

How can we explain such a development?

There are many causes: on the one hand, the longer life expectancy and the growing number of patients with diabetes certainly contribute to the higher number of dialysis patients. On the other hand, the risk of developing diabetes-associated kidney disease was certainly underestimated.

Ten or 15 years ago, diabetic nephropathy was viewed almost exclusively as a complication of Type 1 diabetes. Today, we know

that patients with Type 2 diabetes, who are far more numerous, face the same risk of suffering kidney failure. Now, most patients who develop kidney damage and need to undergo dialysis have Type 2 diabetes.

What can we do about it?

We know a lot about the course of diabetic kidney disease and about the factors that influence it. If we could combine that knowledge with the therapeutic opportunities currently available, diabetic nephropathy would soon cease to be a threat. Diabetic patients can do much for themselves. To say this even more clearly: without the participation of patients, we will not be able to fight nephropathy.

This book is primarily for people with diabetes, their families and carers. It describes the development of nephropathy and shows the possibilities for prevention, for early diagnosis and, of course, for the treatment of this complication. It also contains abundant information about 'Diabetes and the Kidney'. We hope that this book will help motivate many patients to take responsibility for the prevention and treatment of their disease.

Sonja Böhm
Weinheim

Christoph Hasslacher
Heidelberg

Patient Interview

Diabetic Nephropathy

– 'a fairly horrible experience'

'I was never a model diabetic patient,' says Marcus Merz[1] of himself. The 43-year-old has suffered from Type 1 diabetes since he was seven. During his childhood, his parents did everything they could to keep their son's blood sugar level under control and allow him to grow up as unaffected as possible. The dilemma began when Marcus was 15 years old and outgrew the care of his parents and his childhood doctor. 'My diabetes didn't interest me very much at that time,' reports Marcus. 'I no longer controlled my blood sugar, I ate and drank what I wanted, and simply let everything go! I was too frivolous,' he sees today. 'I believed then that I didn't need to bother because in a few years there would be a cure for diabetes.'

But this view was too optimistic, which soon became clear to the young man. When he finished school he trained as a dental technician. By his mid-20s, the consequences of the years of neglect of his illness began to show. He was reading the newspaper when he realized for the first time that he could no longer see as well. Then, on the way home from a skiing holiday, 'Suddenly, a cloud formed in front of my right eye – it was as though someone put a drop of ink in a glass of water and it slowly spread out.' At the eye clinic in Heidelberg, he was diagnosed as having advanced damage to the retina at the back of the eye, caused by chronic high blood sugar levels. The 'cloud' was due to a haemorrhage from one of the broken blood vessels in the eye.

'That was the beginning of the end,' Marcus acknowledges with hindsight. 'If I hadn't done so much sport as a young man, it would probably have caught me much earlier!' Meanwhile, he had started studying dentistry but, after another haemorrhage in the eye, which

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[1] The name has been changed.

occurred during a lecture and produced a 'thick mist' in front of his eye within 15 minutes, an operation was necessary. This was not a success and Marcus became blind in his right eye. The other eye was also suffering. Despite laser treatment and removal of the vitreous humour, the doctors at a specialist clinic could not save it and Marcus now has only 3% vision in this eye. 'That's enough, in good light, to see someone opposite me as a dark shape.'

A career as a dentist was out of the question under these conditions, but the 30-year-old did not give up hope. 'I was angered by the poor results of the operations, but I did not despair.' He was helped by his large circle of friends, but also by continued sporting activity. Marcus says, not without pride, that three years ago he went on a diving holiday in the Red Sea. 'With the help of a diving instructor, physical handicap can be overcome.'

He has achieved much more. After a three-year break, Marcus began to study law. He had to go to court to win the money to finance this, since at the rehabilitation clinic they tried to make him study information technology – a subject he didn't like. He wanted a job that would give him contact with other people. Of course, a student cannot avoid using computers. He repeats the material from lectures using a computer system that reads him pages scanned in from textbooks. Marcus says that he has also been helped through his studies by the many contacts that he made by joining a student club.

Meanwhile, he has also involved himself much more actively in the management of his diabetes. Some time ago, he started intensive insulin therapy. He measures his blood sugar level at least five or six times a day and is content if his HbA1c concentration is about 6.5%.

Sadly, however, his efforts came too late in another area as well. By his early 20s, Marcus's blood pressure had begun to rise and the hypertension gradually got worse with lack of proper treatment. The high blood pressure accelerated the damage to his eyes and also affected his kidneys. Over the years, there were ever-clearer signs of failing kidney function.

As early as May 1992, patient and doctors together decided to try for a transplant. Marcus's own kidneys were not yet fully destroyed, but the prospect of a new, fully functional additional kidney, that would be transplanted with a new pancreas, which would also help to combat the diabetes, seemed the optimal solution to all those involved. 'I dreamt about a trouble-free existence, with a better quality of life and no more need to inject myself,' says Marcus. But luck was not with him this time either: within two weeks of the

transplant there were problems and both new organs had to be removed.

Until one and a half years ago, his own kidneys could still cope but then they broke down completely. The ongoing diabetic nephropathy made kidney replacement therapy necessary and since then Marcus has been going three times a week to the dialysis centre for blood purification. The start of dialysis has made the greatest impact on his life up to this time and has been 'a fairly horrible experience,' he explains. 'Just the time: Mondays, Wednesdays and Fridays, each time having to lie there from 7.15 am to 1.30 pm with two thick needles in my arm and with six other people in the room.' For lively single people, the restrictions imposed by the dialysis on everyday activities are very disturbing. 'I love life – eating and drinking.' The limitations are particularly hard with respect to drinking: being allowed only water, apple juice, white coffee and an occasional beer badly affects his quality of life.

Of course, the visual impairment is also terrible, adds Marcus, but he has learned to live with that. In contrast, 10 years of dialysis seem unimaginable and he doesn't plan to put up with it. He is already on the waiting list for a new kidney transplant. This time the operation will be combined with the insertion of pancreatic islet cells. A very promising procedure has been developed in Canada which gives a relatively good chance that the islet cells are not destroyed by the recipient's own immune defence system. This Canadian method is being used in Giessen in Germany and Marcus will have his next operation there.

So for the moment he is optimistic, even though he has to put up with dialysis and the restrictions it imposes. He has completed his law studies and is starting as a junior barrister. After that, he wants to set up as an independent lawyer with two friends. He also has plans for his personal life: 'I can imagine a wife and two or three children.'

1 Your fate is in your hands

As the story of Marcus Merz demonstrates, in the long term diabetes can lead to problems with many different organ systems, particularly when blood sugar levels are allowed to remain high over several years. Typical diabetes-associated complications are:

- Damage to the small blood vessels (microangiopathy).
- Damage to the eyes (diabetic retinopathy), even leading to blindness.
- Damage to the kidneys (diabetic nephropathy) that can make dialysis or a kidney transplant necessary.
- Arteriosclerosis of the large blood vessels, commonly known as thickening of the arteries, with an increased risk of a heart attack and other circulatory problems, particularly in older patients.
- Damage to the nervous system (diabetic neuropathy), with possible consequences including foot ulcers and amputation, itching and pain in the legs, impotence, a weak bladder and incontinence.

This list sounds dramatic and the possibility of suffering from such complications naturally causes worry and anxiety. What will happen to me? Will I become blind or have to undergo dialysis? These are questions that some people may ask themselves. Such concerns and anxieties in the first stages after diagnosis with diabetes are understandable. However, a deciding factor in life with diabetes is how one copes with these fears – you can be positive!

What we mean is that, as a diabetic, you can take care yourself that your diabetes is kept well controlled. There are various options at your disposal: a formal diabetes education is an indispensable basis.

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The risk of nephropathy is equally high for Type 1 and Type 2 diabetes

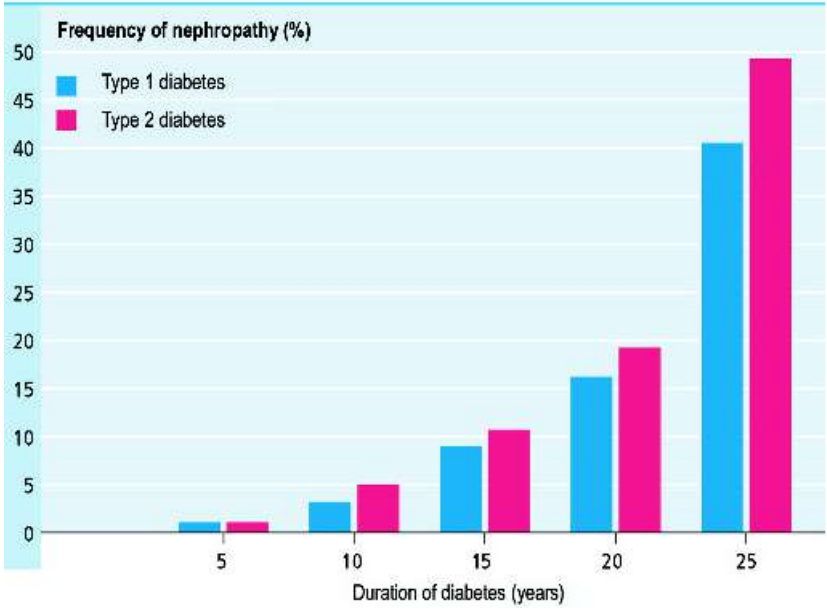

Figure 1.1 The risk of kidney damage increases with the duration of diabetes. After 25 years, it is between 40% and 50%. [1]

You can also make use of books, newspapers, the Internet, self-help groups and diabetes organizations.

You should not allow the (unnecessary) concerns and anxieties to become so great that you feel 'crippled' by them and can no longer look after your diabetes appropriately. The urge to say 'It won't

What you should know:

- Diabetic kidney disease does not affect every person with diabetes.
- Diabetic kidney disease does not occur overnight – it takes years to develop.
- Doctors today have the ways and means to detect kidney disease early and to treat it adequately at every stage.
- As someone with diabetes, you can join in the management of your diabetes and thereby minimize the risk of renal complications.

happen to me' is not helpful (see the example of Marcus Merz) – such behaviour can easily lead straight to difficulties with the eyes or the kidneys. As someone with diabetes, you must address the problem of the typical complications associated with this disease. It therefore makes sense to acquaint yourself with the facts. If protein is repeatedly found in the urine (proteinuria), that is the first sign that diabetic kidney disease is developing. However, even with diabetes of long duration, not everyone experiences protein in the urine but 'only' every second or third person with diabetes. And it occurs as often in Type 2 diabetes, which develops at a later stage in life, as in Type 1 diabetes, where metabolic disturbances arise in childhood or adolescence (Figure 1.1).

This is alarming – particularly when one considers that the number of diabetics with kidney disease (above all those with Type 2 diabetes) continues to rise. Of course, this is partly due to the ever-improving life expectancy of the population. But that is not the only cause: an equally valid reason for this worrying situation is that the risk of developing kidney disease has, until now, been underestimated in the largest patient group, those with Type 2 diabetes. And not only by the patients (how were they supposed to know?) but also by the doctors who treat them.

Much has changed in the field of diabetes care in recent years. One of the most important things to be recognized is that even older patients with Type 2 diabetes need much more intensive treatment and management than was customary a few years ago.

Better therapies have reduced the risk in recent years

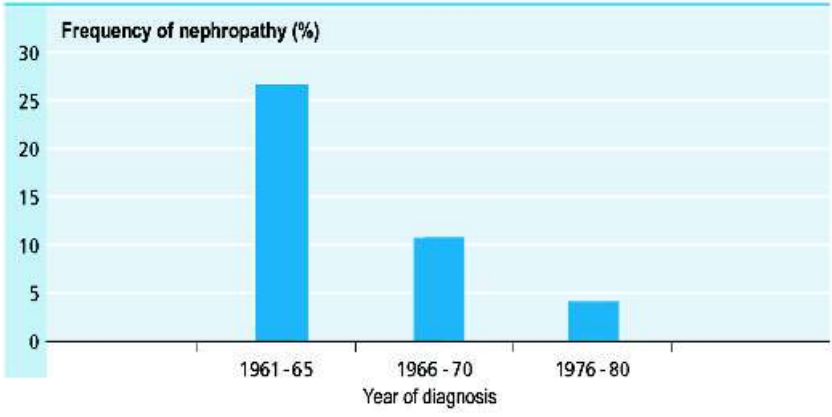

Figure 1.2 People who were diagnosed with diabetes between 1961 and 1965 had a much higher risk of nephropathy than those who were diagnosed between 1976 and 1980. [2]

Today, diabetic nephropathy is the most common reason for dialysis

Today, even a 70-year-old wants to live the most active and healthy life possible. The diagnostic and therapeutic means exist but not all doctors apply them. Patients today have to take much more responsibility for themselves and take a much more active part in the management of their condition. This book should help.

Finally, to show that such efforts can work, let us consider the example of the Scandinavian countries. In recent years, they have achieved a dramatic reduction in the frequency of kidney damage in patients with Type 1 diabetes, through intensive management by doctors and increased cooperation by the patients (Figure 1.2).

2 Diabetic kidney disease – what is it?

The kidney: an organ with many functions

People have two kidneys which lie on the right and left sides of the abdomen, well protected by the back musculature (Figure 2.1). In adults, each kidney is about 12 cm long and 5–7 cm wide and weighs between 150 and 200 grams.

The kidneys have many tasks and functions to fulfil. Amongst other things, they clear the blood of waste products that arise from the metabolic processes of various cell types. They also excrete toxins that are taken in with food, as well as breaking down and excreting drugs. In addition to this function as a 'clearing house', the kidneys regulate the water content of the body and the composition of the blood salts, namely the concentrations of sodium, potassium, calcium and phosphorus. Finally, the kidneys make hormones, which are essential for certain bodily functions, e.g. renin, which regulates the blood pressure, and erythropoietin ('Epo'), which is needed to make new blood cells.

For all these tasks to be fulfilled, a good blood supply is essential. The renal arteries, which carry the blood to the kidneys, arise as thick branches directly from the body's largest artery. A person's entire blood content passes through the kidneys every 20 minutes. After passage through the kidneys, the blood is returned to the circulation through a large collecting vessel, the renal vein.

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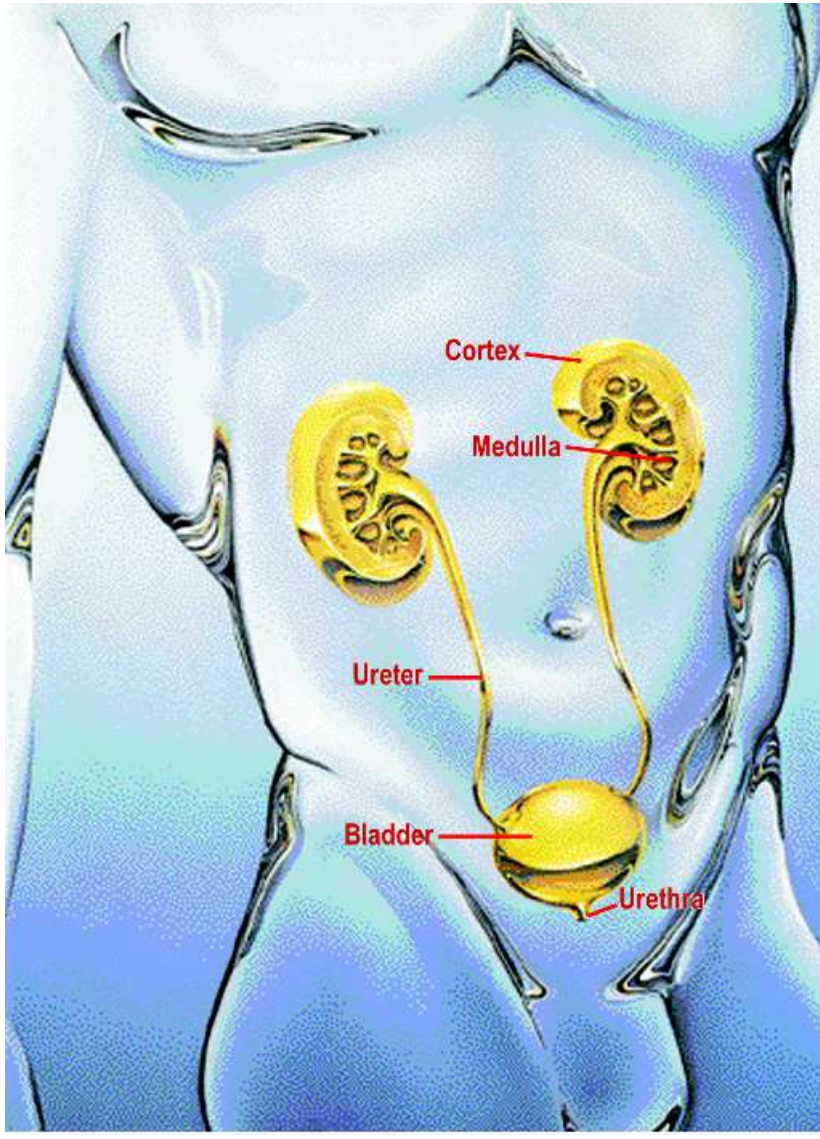

Figure 2.1 The kidneys are important organs in the detoxification of the body. The primary urine is transported via the ureter to the bladder and from there it is excreted via the urethra.

How do the kidneys perform their functions?

The essential tasks of blood cleansing and water excretion are done by the glomeruli, of which each kidney has about one million. Each glomerulus consists of a ball of tiny blood vessels (capillaries) (Figure 2.2). The unpurified blood flows through an incoming arteriole into the ball, where it is filtered. The filtered blood is then led back into the circulation through another blood vessel. The incoming and outgoing vessels have special properties: they can regulate the flow of blood very precisely by narrowing or widening. This is particularly important for two reasons:

- First, it is essential to have exactly the right blood pressure in the glomeruli for the blood cleansing to occur. This is known as the filtration pressure and in a healthy kidney it is regulated automatically.

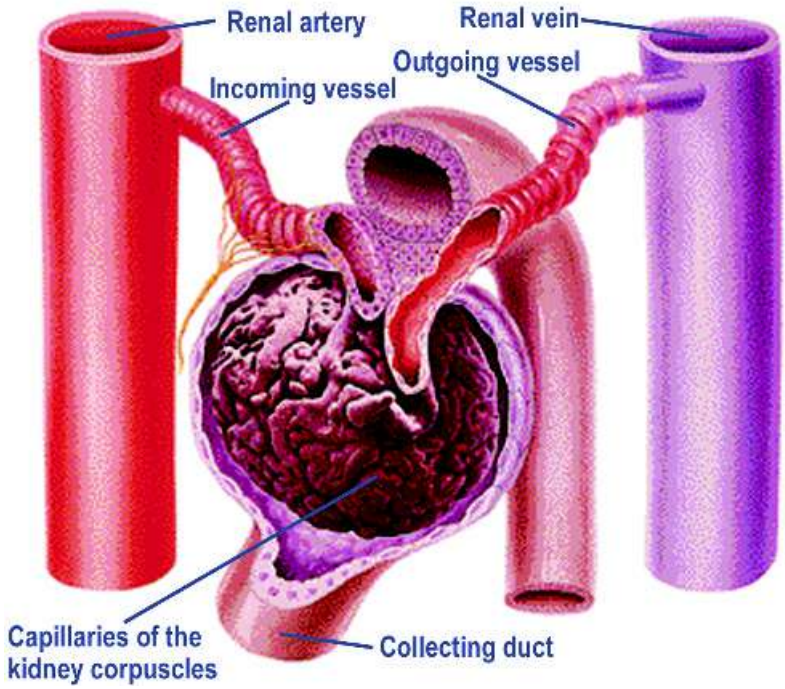

Figure 2.2 In the kidney corpuscles, the blood is filtered and the urine is formed. The blood flows through the incoming vessel into the capillary bed in the kidney corpuscles where filtration occurs. It passes through the outgoing vessel back into the circulation. The urine is collected and flows into the kidney collecting ducts for further processing.

- Second, it gives the glomeruli the ability to protect themselves when the circulatory blood pressure is too high. The incoming vessel is narrowed, reducing the blood flow, and the renal cells are thereby guarded against excessive pressure. If the circulatory blood pressure falls, the kidney can expand the incoming vessel and narrow the outgoing one to maintain the required filtration pressure.

The actual blood purification occurs via the basal membrane in the capillaries (Figure 2.3). This contains small pores and acts as a filter: cells and large protein fragments that will be needed again are held back in the blood; water, salts and metabolic waste products pass through the membrane.

The filtered liquid accumulates in a capsule that surrounds the glomeruli and is then led through the kidney tubules. 180 litres of this so-called 'primary urine' pass through the filter every day. So that not too much fluid is lost from the body, the filtered liquid is built up again: water and salts are taken back by the kidney and returned to the body. Only a small percentage of the original filtered urine ends up in the kidney collecting duct, from where it is passed through the ureter and excreted as urine (see Figure 2.1).

How is kidney function measured?

When the kidneys are no longer working efficiently, tell-tale signs appear in the blood and the urine – but not until a certain stage. In the

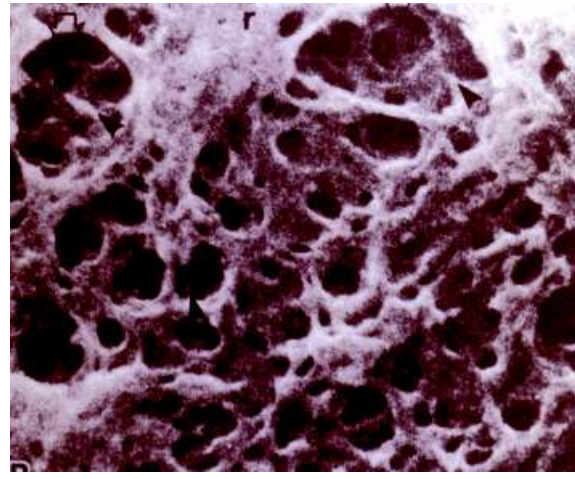

Figure 2.3 Scanning electron microscopy shows the various large pores in the basal membrane, through which the blood is filtered. [3]

blood, for example, creatine and urea accumulate. Creatine is a waste product of muscle metabolism that is normally excreted through the kidneys. Healthy people (Table 2.1) have a creatine serum concentration of between 0.6 and 1.2 mg/100 ml. The normal value in an individual depends on the muscle mass. In someone with less muscle, it is lower; in 'muscle men', it is higher. If kidney function fails, the creatine concentration in the blood gradually rises.

Generally, though, mild kidney impairment does not lead to a noticeable change in serum creatine concentration. It rises only when kidney function has decreased by more than half. In people with little musculature, the low starting point for the creatine concentration can mean that it stays within the normal range for a long time, even when kidney function is seriously compromised.

A more exact picture of kidney function is given by the so-called creatine clearance rate. To measure this, the urine must be collected for 24 hours or overnight, then the creatine concentration in the blood and in the urine is determined. A formula can then be used to calculate the filtration rate and thereby the activity of the kidney. However, a precise value is obtained only when all the urine is collected. In practice, this is where mistakes can easily be made.

Table 2.1
These blood parameters give information about the activity of the kidney

Parameter	Normal range
Creatine	0.6–1.1 mg/dl 53–106 mmol/l
Creatine clearance	80–140 ml/min
Urine	Less than 45 mg/dl Less than 7 mmol/l
Calcium	8.8–10.5 mg/dl 2.2–26 mmol/l
Phosphorus	2.6–4.5 mg/dl 0.84–1.45 mmol/l
Potassium	3.6–4.8 mmol/l
Uric acid	Less than 7 mg/dl Less than 415 µmol/l

Warning: the normal values vary according to the laboratory method used to measure them and are partially dependent on age and sex.

A simpler and faster method is to calculate the creatine clearance using a formula based on serum creatine concentration, body weight and age (see the example on page 119). This gives reasonable values for a wide range of kidney function. Normally, the rate of creatine clearance lies between 80 and 140 ml/min.

Urea is the end product of protein metabolism and is excreted through the kidneys. In healthy people, the concentration of urea in the blood is less than 45 mg/100 ml. As

kidney function fails, the amount of urea in the blood rises. This occurs particularly when a person eats a lot of protein. The concentrations of the blood salts, potassium, calcium and phosphorus, as well as that of uric acid, can also give information about the state of the kidneys.

In the urine, the most important marker for impaired renal function is protein excretion. Normally, only a very small amount of albumin, a special blood protein, is found in the urine – less than 20 mg/l, which is too little for the standard tests to detect. If the albumin concentration rises above a certain threshold, this can be one of the first signs of kidney failure. Protein may occur in the urine as a result of other circumstances, such as after major bodily damage, infection, pressure on the kidneys or low temperatures.

Examination of the urine composition can also give clues regarding the state of the kidneys. Usually, no red or white blood cells should be visible in the urine under a microscope. If they are present, it is an indication that something is wrong with the kidney–bladder system. Such a finding should be the starting point for further investigations.

How does diabetes affect the kidneys?

Generally, the changes produced in the kidneys by diabetes occur very slowly, taking place over years (Table 2.2, Figure 2.4). If they are recognized early, they can – with the right treatments – be reversed.

The changes start, at the onset of diabetes, with an increase in the size of the kidneys and in the amount of blood passing through them. This first, early stage is known as 'the hypertrophy and hyperfunction stage' (stage 1) because of the enlarged kidneys, enriched in blood. Even at this stage, a rise in the amount of protein in the urine is often observed. If the diabetes is properly controlled, these changes can usually be reversed within weeks or months. The protein also disappears from the urine.

The progression of these changes in the kidneys depends strongly on the state of the body's metabolism. If the blood composition is good – that is, if the haemoglobin A1c (HbA1c) concentration is near-normal, namely between 6% and 7%, the diabetes will barely affect the kidneys in the ensuing years. But if the blood sugar level (as assessed by the HbA1c concentration) remains too high over years, this leads to damage to the basal membrane, which filters the blood. Such damage is initially detectable only through laboratory

Table 2.2 Stages of the development of nephropathy and typical findings

Stage	Time	Characteristic symptoms
1. Increase in size and activity of the kidney	At diabetes diagnosis	Enlarged kidney, higher blood flow and rate of filtration
2. First changes to the kidney tissue	2–5 years	Thickening of the basal membrane
3. Onset of nephropathy	5–15 years	Microalbuminuria, rise in blood pressure
4. Clinical manifestation of nephropathy	10–25 years	Macroalbuminuria, falling blood flow and filtration rate, high blood pressure in 60–80% of patients
5. Renal insufficiency	15–30 years	Rise in serum creatine concentration, near-permanent hypertension

investigations of the blood and urine. However, if you could remove a small piece of the kidney and examine it under a microscope, you would be able to see a marked thickening of the basal membrane – stage 2 of kidney damage.

If the blood sugar level is still not brought under control, the filtration ability of the basal membrane gradually falls. It becomes permeable to proteins, which are normally retained within the circulation. The blood protein albumin is found at slightly higher concentrations in the urine. Because only a small amount of albumin is excreted, this stage is known as 'microalbuminuria'. The presence of albumin in the urine makes it plain to both the doctor and the patient that the diabetes has led to kidney damage and therefore that nephropathy has begun (stage 3).

If even greater damage to the basal membrane is not prevented by taking the appropriate measures, the filtration capacity is further compromised. Large amounts of albumin and other proteins pass through the membrane and are excreted in the urine. When the albumin concentration in the urine exceeds 200 mg/l, this is called 'macroalbuminuria', which means 'high albumin excretion'. This is stage 4; it represents clinical nephropathy.

The onset of macroalbuminuria makes it clear that the filtration apparatus of the kidneys is already seriously damaged. But the increased amounts of protein in the urine don't just act as markers of

Kidney function decreases as protein excretion increases

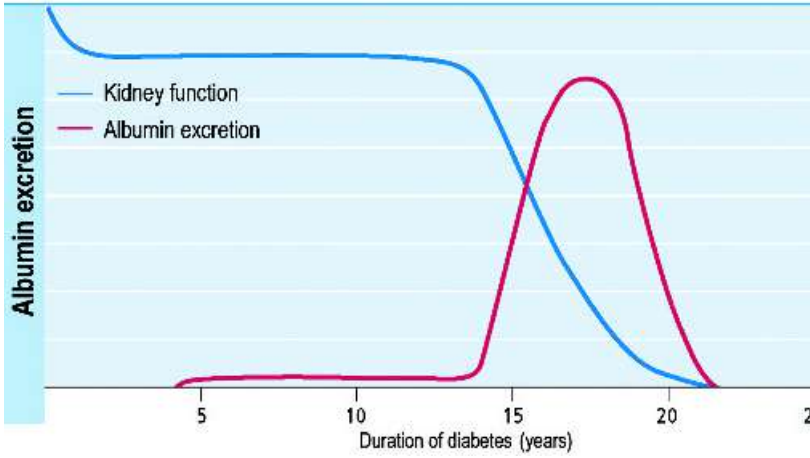

Figure 2.4 If the amount of albumin excreted into the urine increases with the duration of diabetes, this has bad consequences for kidney function.

renal impairment – albumin and other proteins also contribute to further damage. They get stuck between the small blood vessels (capillaries) and block the kidney corpuscles. Without blood flow through the corpuscles, these can no longer operate (Figure 2.5).

This process can be accelerated by another detrimental factor – high blood pressure (hypertension). Because the kidneys are involved in the regulation of blood pressure, many patients develop hypertension during the stages of micro- and macroalbuminuria. When not properly treated, this can damage the kidney corpuscles directly and indirectly. Since the incoming vessels can no longer be narrowed protectively, the high blood pressure impacts unhindered on the corpuscles and contributes to their destruction. The filtration pressure also rises and more proteins are excreted, which leads to further blockage of the corpuscles.

If nothing is done at this stage either, more and more corpuscles cease to function and finally creatine and urea concentrations in the

What you should know:

Even at this stage, kidney damage can be stopped! Blood sugar levels and blood pressure must be lowered. The protein damage should be reduced, for example by drug treatment.

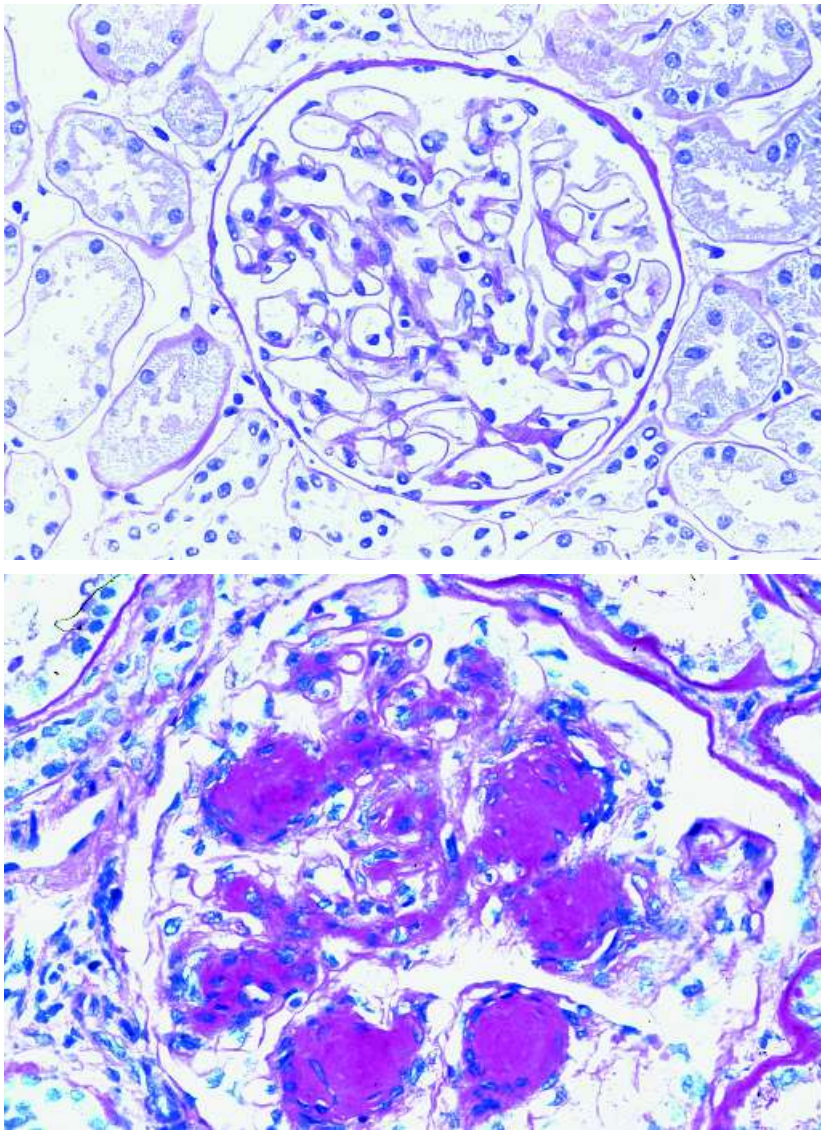

Figure 2.5 Kidney corpuscles magnified 20-fold. Compared with a healthy kidney (top panel), the corpuscles in someone who has had diabetes for many years are totally blocked with protein deposits and are no longer functional (bottom panel).

blood rise as a sign of the ongoing kidney failure. This is stage 5. At this point, a vicious circle often develops. The surviving kidney corpuscles must take over the function of those that have been destroyed. They have to work harder, which means more wear and

Figure 2.6 Children from families with diabetes in which a member already has kidney disease have a much higher inherent risk of developing nephropathy.

tear, which means that they are destroyed more rapidly (Figure 2.7). So the rate of kidney failure accelerates continuously. Only two or three decades ago, when the therapeutic options for hypertension and diabetes were still limited, it was often only a few months before the kidneys failed completely and dialysis became necessary. Today, the vicious circle can be slowed or even broken for a time by good management of blood pressure and diabetes. The need for dialysis can be postponed for years or even decades.

Factors that influence the development of nephropathy

Whether nephropathy ever develops and how rapidly it progresses vary immensely from patient to patient. For some, the risk of kidney damage increases with the duration of diabetes, but the risk does fall when the diabetes is continuously well controlled. For others, however, hereditary factors are also important. Even among those who have high blood sugar levels for years, there are some people who never develop nephropathy. On the other hand, there are people with fairly good diabetes control who nevertheless develop kidney damage. We know that children from families with diabetes in which one member already has a renal problem have a much higher risk, from the onset, of developing nephropathy. Unfortunately, there is as yet no definite known marker in the blood or the urine that can predict the risk of developing nephropathy for an individual patient. This would naturally be a great help, as patients at higher risk could then be managed much more intensively.

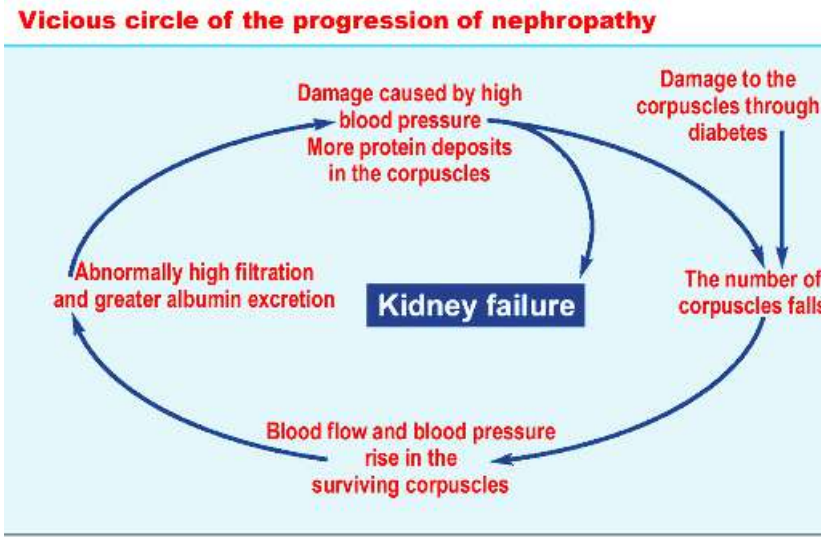

Figure 2.7 If the kidney corpuscles are damaged through diabetes, a vicious circle develops: ever fewer corpuscles have to do ever more work; higher rates of protein deposition and higher blood pressure lead to the corpuscles being destroyed more rapidly.

Since this is not yet possible, patients and doctors must all try to reduce, or at least to retard, kidney damage via the factors that we can influence. The most important is good blood sugar control and good management of high blood pressure. Sometimes, it is helpful to eat less protein. If that is not enough, protein excretion in the urine and its detrimental effects can be treated with special medicines. Levels of blood fats should not be too high and intensive management of the diabetes should be started as soon as possible. Another factor that increases the risk of kidney damage is smoking, so giving up is a helpful step to take.

Signs and symptoms of nephropathy

Like other complications of diabetes, diabetic kidney damage does not usually cause overt signs for a long time. This 'secret' progression means that an advanced stage of kidney impairment has often been reached by the time the first symptoms appear.

These symptoms are frequently caused by increased water retention:

- Feet and ankles swell, shoes pinch, socks cause blisters; you can sometimes make an indent in the lower thigh by pressing with the

What you can do for yourself:

You can reduce the risk of nephropathy by:

- **Good control of your diabetes.**
- **Regular monitoring of your blood pressure.**
- **Having your urine tested for excreted protein.**
- **Not eating too much protein.**
- **Giving up smoking.**
- **Monitoring your blood lipid levels.**
- **Starting intensive diabetes management early.**

thumb. These symptoms are known as 'oedema' and are often present only in the evening. In the morning, after a night's rest, they disappear again.

Other signs or symptoms, which may appear in parallel or individually, are:

- Breathlessness, which arises at first only during exercise but later also when at rest.
- High blood pressure, with values greater than 140/90 mmHg.
- General symptoms that are not specific to kidney failure, such as headache, tiredness, bodily weakness, loss of concentration.

If these symptoms prompt you to go to the doctor, he or she will usually establish that there is already a marked increase in protein excretion (macroalbuminuria), that the markers of kidney function are bad and that blood pressure is high. Kidney damage may already have reached stage 4 or stage 5.

At this point, an eye examination will often reveal diabetes-induced damage to the retina, which is complicated by high blood pressure. The heart may also, at this advanced stage of kidney failure, show the first signs of damage.

What you should know:

Kidney failure is not inevitable.
Have regular urine checks to detect kidney damage at the early stages.
Catch it while the process is still reversible.

3 Early diagnosis of diabetic nephropathy

Diabetic nephropathy doesn't affect everyone. 50–70% of people with diabetes never develop kidney damage. Of those who do, for some it is due to their genetic inheritance, for others it is due to factors such as how well their blood sugar levels and blood pressure are controlled. So far, there is no way of telling who is at risk of developing diabetic nephropathy on the basis of their genetic make-up. If this were possible, it would be the ideal situation as then doctors and patients would be able to initiate intensive management of the diabetes of those at greatest risk. At present, we can only keep a look out for early signs of nascent kidney damage in order to be able to treat it promptly.

What you should know:

Nephropathy doesn't hurt!

Nephropathy is not detected through symptoms such as problems with urinating, tiredness or headache. Even blood parameters that give information about kidney function, such as creatine concentration, may stay normal for years, including after the diabetes has begun to damage the kidneys.

The earliest sign of diabetes-associated kidney damage is the appearance of microalbuminuria. Even before the filtration capacity of the kidney corpuscles has been compromised, proteins such as albumin, which otherwise never appear in the urine or

What you should know:

Microalbuminuria is not a harmless sign. There may be underlying kidney damage. Early detection is essential, in order to be able to treat it promptly.

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only at very low concentrations, may be excreted. This is a warning signal. An albumin concentration in the urine of 20–200 mg/l is a sign of 'microalbuminuria' (literally, 'little albumin in the urine') (Table 3.1). If the rate of albumin excretion rises, this is known as 'macroalbuminuria' (literally, 'much albumin in the urine').

Detection of microalbuminuria

There are many different, fast tests available for establishing the presence of microalbuminuria. These can determine within a few minutes whether there are tiny amounts of albumin in the urine (Figure 3.1). Such tests may be performed in any doctor's surgery. If protein is detected, the result of the quick test should be confirmed by a more exact measurement of the urine albumin concentration in a laboratory analysis.

Table 3.1 Albumin concentration in the urine

Normal range	Less than 20 mg/l
Microalbuminuria	20–200 mg/l
Macroalbuminuria	More than 200 mg/l

Measurement of the albumin concentration is often imprecise because it depends on the amount of urine as well as the amount of excreted albumin. For example, in people who have drunk a lot of liquid before giving a urine sample, there will be a dilution effect, such that the measured albumin concentration will be too low. To compensate for this, the albumin concentration can be compared with the amount of creatine excreted in the urine.

Table 3.2 Microalbuminuria is present at the following values

According to the time of urine collection:	
(a) Collection over a fixed time, e.g. overnight	20–200 μg/min
(b) Collection over 24 hours	30–300 mg/24 h
According to the rate of creatine excretion:	
For women	20–300 mg/g urinary creatine
	2.5–35 mg/mmol urinary creatine
For men	20–200 mg/g urinary creatine
	2.5–25 mg/mmol urinary creatine

The best method, however, is to calculate the *rate* of albumin excretion. For this, the urine has to be collected over a given time (24 hours or overnight) and the amount of albumin excreted is divided by the set time. The range of microalbuminuria measured using different urine collection methods and time periods is shown in Table 3.2.

What you should know:

Not every case of microalbuminuria means the onset of nephropathy. A 'positive' test should be repeated.

It is not only diabetes-associated damage that causes the kidneys to excrete albumin. Protein may also be found in the urine during physical stress, urinary tract infection, hypertension or fever. Once these conditions are resolved, the albumin usually disappears from the urine. Therefore, to be sure that microalbuminuria truly indicates the onset of diabetic nephropathy, the test should be repeated after a gap of two to four weeks. If the test is still 'positive', it is probably a sign of the start of kidney damage.

What's more, microalbuminuria is not just a sign of nephropathy. Studies have shown that people with microalbuminuria have a much higher risk of circulatory problems or a heart attack than does the general population.

Microalbuminuria testing: when and by whom?

In fact, urine collected at any time of day may be tested. However, early morning urine is usually taken, since constant conditions have generally applied during the night before collection.

For people with Type 1 diabetes, the experts recommend that an annual microalbuminuria test is performed starting five years after

Table 3.3 Who should be tested for microalbinuria

Patients with Type 1 diabetes:	
Children	**From puberty**
Adults	**From five years after diagnosis of diabetes**
Patients with Type 2 diabetes:	
	From the diagnosis of diabetes

How to test urine for microalbuminuria

Dip test strip in the urine

Lie the test strip on the glass

Compare the colour of the strip with the calibration chart after 30 seconds

diagnosis of the diabetes. In children, the annual test is usually initiated at the onset of puberty (Table 3.3).

For people with Type 2 diabetes, the tests are best begun at the time of diagnosis of the diabetes, because many of these patients have already had high blood sugar levels for years, without knowing about it (Table 3.3).

What you can do for yourself:

Remind your doctor about your annual microalbuminuria test. After all, you send your car for a regular check-up. If you have a diabetes clinic, the test can be done there. If albumin is found in the urine, management of your blood sugar and blood pressure levels must be stepped up immediately.

4 Management of diabetic kidney disease

4.1 The benefits of good blood sugar control

Although the risk of developing diabetic kidney disease is partially determined by your genetic make-up, the onset of the disease can be prevented or at least postponed for a long time by good blood sugar control. This was demonstrated for patients with both Type 1 and Type 2 diabetes by two major trials that were published in the 1990s.

The Diabetes Control and Complications Trial (DCCT) involved about 1400 patients with Type 1 diabetes. They were divided into two treatment groups. One half received 'intensive' treatment with intensive education. These patients were injected several times a day with insulin or put on an insulin pump. They tested their blood sugar levels themselves at least four times a day and adjusted the insulin dose accordingly. They also went to see the doctor every four weeks.

The other group were treated 'conventionally'. They received a single session of dietary advice. They injected an insulin mixture only once or twice a day, measured their blood sugar levels only occasionally and visited the doctor only once a quarter.

As expected, the intensively treated group managed their blood sugar much better. Their HbA1c concentration, which indicates how well the diabetes was controlled in the preceding months, was on average a relatively good 7%. In the conventionally treated group, on the other hand, the average value was 8.9% – which expert opinion today considers to be far too high.

The trials showed that good diabetes management markedly reduced the risk of kidney damage. The risk of developing microalbuminuria was at least 34% (about one-third) lower in

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What do we mean by 'intensive' diabetes management?

- Completing a special programme of diabetes education.
- Keeping the blood sugar concentration as normal as possible:
  - (a) For those with Type 1 diabetes, by applying intensive therapy (injecting insulin at every mealtime and, in addition, a basal insulin once or twice a day).
  - (b) For those with Type 2 diabetes, through dietary control, blood sugar-lowering drugs or with the help of insulin.
- Joining an experienced diabetes clinic.
- Regular screening for typical diabetes-associated complications.
- Management of co-morbidities such as high blood pressure and poor lipid metabolism.
- Repetition of the education programme at regular intervals.

those patients with better metabolic control than in those treated conventionally (Figure 4.1). What's more, the beneficial effect of good metabolic control on the risk of nephropathy becomes noticeable only after several years of intensive therapy. So people have to persevere for some time to see the real advantages.

With good blood sugar control, microalbuminuria seldom arises

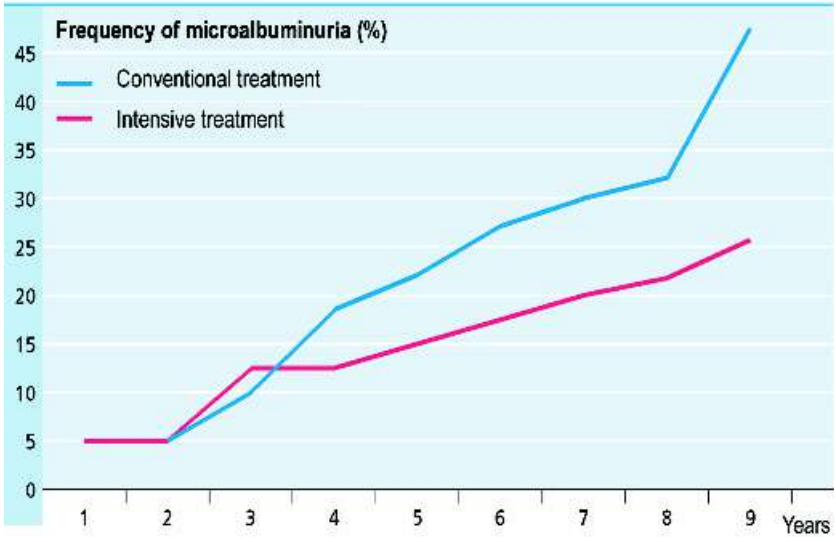


Figure 4.1 In the DCCT study, intensive diabetes therapy delayed the development of microalbuminuria: after nine years protein was detectable in the urine in only 25% of the intensively treated group compared with 40% in the conventionally treated group. [4]

There were some patients in the intensive group in the trial who, despite all efforts, did not achieve good blood sugar control (the HbA1c value of 7% was an average taken over the nine years of observation). This explains why diabetic kidney disease did develop in this group.

A similar study in the United Kingdom showed that what is true for Type 1 diabetes is also true for Type 2. The UK Prospective Diabetes Study (UKPDS) involved nearly 4000 patients with newly-diagnosed Type 2 diabetes, who were allocated to either 'intensive' or 'conventional' treatment. For the group on intensive therapy, the goal was a fasting blood sugar level of less than 110 mg/dl. For the conventionally treated group, much higher levels (up to 275 mg/dl) were allowed. Various drugs were used to lower blood sugar concentrations, as well as insulin.

In both treatment groups, the blood sugar control became progressively worse over the years. However, the average HbA1c concentration was always about 1% better in the intensively managed group. The risk of developing diabetic kidney disease was about one-third lower. It made no difference whether the better metabolic control was achieved using drugs or insulin.

Is there a threshold, above which the risk noticeably increases?

This question is of great practical interest for patients and doctors. To put it another way, 'How well must I manage my diabetes for the risk of nephropathy to be minimized? Do I have to reach an HbA1c concentration of 6% or 7% or will 8% be enough?'

The answer is: the lower the HbA1c concentration, the lower the risk of microalbuminuria! Neither the DCCT nor the UKPDS could establish a threshold at which the risk either rose or fell significantly. This relationship was the same for both groups, whether treated intensively or conventionally. This means that someone who can achieve good blood sugar control by conventional treatment is equally well protected as someone who is treated intensively (see Figure 4.2).

Naturally, another question arises: how low should the blood sugar level be? Is a very low concentration actually dangerous? In the patients treated intensively with insulin, there was a risk of hypoglycaemia (dangerously low blood sugar). In the DCCT, particular attention was paid to the 'danger' of intensive therapy. Patients undergoing such therapy did in fact experience hypoglycaemia more frequently than those treated conventionally. Considering the poor metabolic control observed in the conventionally treated group, this is hardly surprising.

In any case, the results of the last few years have shown that good metabolic control can be achieved without greatly increasing the risk

As the HbA1c concentration falls, so does the risk of microalbuminuria

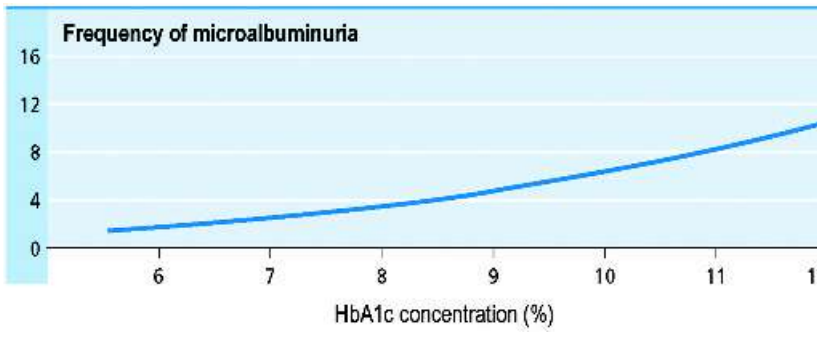


Figure 4.2 The lower the HbA1c concentration, the lower the risk of microalbuminuria. There is no lower threshold for this. [5]

of hypoglycaemia (dangerously low blood sugar). This is particularly true when people with diabetes are well educated about their condition, check their blood sugar regularly and generally participate in the management of their diabetes.

With nephropathy, is there a 'point of no return'?

Another important question is whether there is any benefit of good blood sugar control once the signs of kidney failure, either micro- or even macroalbuminuria, have appeared. This was disputed for a long time. The opinion was that there was a point of no return, after which there could be no reversing the course of the disease – it would progress inexorably until dialysis was necessary, regardless of how well controlled the blood sugar level was.

But the studies of recent years have shown clearly that good blood sugar control brings benefits, even at this stage. The progression of the nephropathy can be prevented, or at least delayed, by good management. This is true for both Type 1 and Type 2 diabetes.

What you should know:

Those who can achieve normal metabolism at the stage of microalbuminuria will benefit from it more than those who don't achieve good control until the appearance of macroalbuminuria.

We should add, however, that the beneficial effect of good metabolic control on the course of nephropathy is greater, the lower the pre-existing damage.

This was proved to be equally true for Type 1 diabetes as for Type 2 diabetes by two studies. People with Type 1 diabetes who had already developed microalbuminuria and who were treated intensively, as in the DCCT, showed a significant delay in the progress to macroalbuminuria. Kidney function deteriorated in only 8% of these, whereas it worsened in 31% of the conventionally treated group. The same result was obtained in the Kumamoto Trial, which enrolled people with Type 2 diabetes and microalbuminuria. Good blood sugar control reduced the risk of kidney damage progressing from 32% to 12% (Figure 4.4).

The more advanced the kidney damage is, the smaller the effect that blood sugar control can exert on its progression. However, the

With good diabetes control, nephropathy progresses more slowly

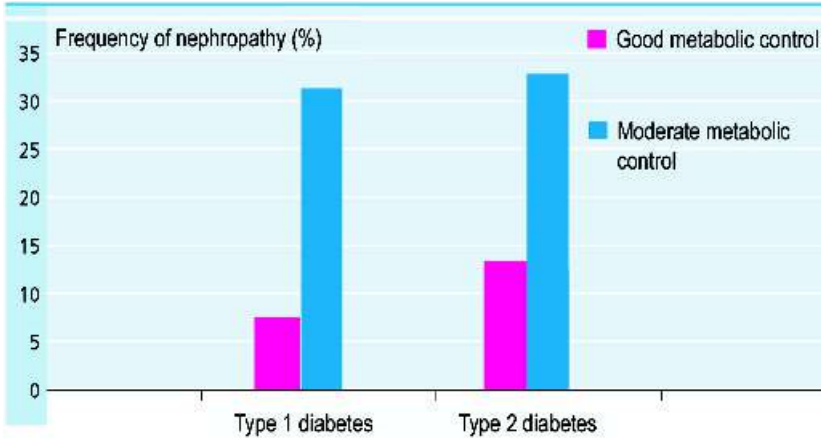
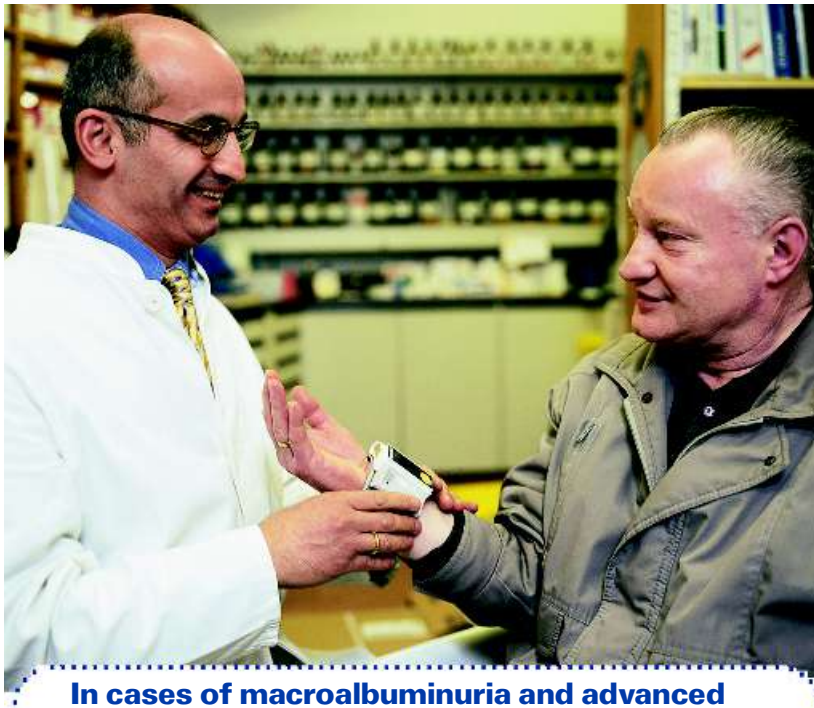


Figure 4.4 Those who achieve good blood sugar control can thereby hold off the development of micro- and macroalbuminuria and thus the progression of kidney damage. [6, 7]

impact of another factor that can be influenced grows – blood pressure. Once macroalbuminuria or even renal insufficiency has developed, high blood pressure plays a deciding role in the progression of the disease. For the patient and doctor, this means:



In cases of macroalbuminuria and advanced kidney disease, you should watch not only your blood sugar level but also your blood pressure, and significantly reduce this.

How failing kidney function affects diabetes management

To achieve good blood sugar control in the presence of failing kidney function is a difficult task for patient and doctor. There are various reasons for this.

In some people with diabetes the insulin sensitivity changes, for reasons that are often unclear: the tissues no longer respond as well to insulin. This can lead to a worsening of the diabetes.

Insulin – whether made by the body or injected as a drug – is partly broken down in the kidneys. When the kidneys are not functioning properly, less insulin is metabolized, so that the effect of the insulin is

prolonged. This partially compensates for the reduced insulin sensitivity mentioned above, but can also result in hypoglycaemia – dangerously low blood sugar.

Someone who has advanced nephropathy often also suffers from other complications of diabetes. These may include damage to the nerves that regulate the gastrointestinal tract. Then food is no longer digested and absorbed properly. Typical signs are bloating, feeling full, irregular bowel movements, diarrhoea, nausea and vomiting. The irregular absorption of food can cause the blood sugar levels to swing violently.

Additionally, remember that many drugs, including those that reduce blood pressure, are excreted via the kidneys. If kidney function deteriorates and excretion does not occur properly, these drugs may persist in the circulation. This means that their effects are heightened and prolonged, which can lead to hypoglycaemia or other complications. Therefore, not all drugs are suitable for the treatment of people with impaired kidney function.

The drugs that should not be given include the biguanides, the most common of which is metformin. It is excreted exclusively via the kidneys and accumulates even in cases of mild kidney impairment. If the dose is too high, it can lead to life-threatening acidosis.

Many of the heavily prescribed sulphonylurea drugs are excreted via the kidneys, although in very different amounts. For nearly all preparations, the dose should be reduced (in consultation with a doctor) to avoid hypoglycaemia. An exception is gliquidone (Glurenorm®), of which only a small fraction is excreted by the kidneys.

There is a new generation of blood-lowering substances that includes repaglinide (NovoNor®) and nateglinide (Starlix®). These drugs are taken only at mealtimes and cause a short burst of insulin secretion that prevents a rise in blood sugar levels after eating. The drugs persist for only a short time in the blood. Repaglinide is broken down and excreted mainly (up to 92%) by the liver. Thus, it may be given to patients with impaired kidney function, as demonstrated in a recent study. Even in the presence of advanced kidney damage, blood sugar can be well controlled without an increased risk of hypoglycaemia. Nateglinide is also metabolized mainly in the liver and may therefore be given to patients with kidney failure. However, there are no large studies and no great experience with this drug as yet.

The newly introduced insulin-sensitizers, rosiglitazone (Avandia®) and pioglitazone (Actos®) improve diabetes control by making the tissues more responsive to insulin, so that the hormone works better.

What you can do for yourself:

Do everything you can, from diagnosis onwards, to keep your diabetes under control.

For people with Type 1 diabetes, this means that after the appropriate diabetes education, start intensive insulin therapy to keep your blood sugar level as normal as possible. It is advisable to join an experienced diabetes clinic. The state of the diabetes should be monitored regularly, including tests for typical diabetes complications. Repeat the diabetes education programme at regular intervals.

For people with Type 2 diabetes, the recommendations are specific to the individual because the disease expresses itself variably and alters with age. Naturally, in this case education and the effort to maintain blood sugar as near as possible to normal levels are still the most important. But the measures that need to be taken can vary:
a change in diet and lifestyle (for example, more exercise), blood sugar-lowering drugs or – and this shouldn't be put off too long – insulin injections. People with Type 2 diabetes should also be familiar with methods of self-management of blood sugar. Joining an experienced diabetes clinic for supervision and regular checking for diabetes complications is very important. In this case too, education should not be a one-off event.

When kidney function weakens, the diabetes worsens. A good diabetes education programme that covers the specific details pertaining to kidney impairment, as well as regular check-ups at the doctor's, mean that good metabolic control can be maintained – and this will help maintain your quality of life.

These drugs are broken down mainly in the liver; the resulting compounds are then excreted via the kidneys. Studies, admittedly on only a few patients, have shown that the drug profile does not rise in the presence of kidney failure.

People who inject insulin must also adjust their dose as soon as kidney function is impaired, because about half of insulin is metabolized in the kidneys. When these organs no longer work properly, insulin action is prolonged and the danger of hypoglycaemia rises. In patients with kidney damage, the most rapid-acting insulin possible should be used, because its effects can be controlled more easily.

4.2 The benefits of good blood pressure control

Whether diabetic kidney disease develops quickly or slowly depends on the level of the blood pressure as well as on the level of the blood sugar. Low blood pressure can prevent or at least postpone the appearance and also the further development of kidney damage.

The methods for attaining normal blood pressure have improved continually in recent years. There are now many medicines available for the management of high blood pressure, whose effectiveness and also tolerability become better all the time. Patients can assess the success of the treatment themselves at home, using a blood pressure meter. Measuring your blood pressure over 24 hours provides a profile for the whole day and also the night, so that unwanted fluctuations can be discovered and targeted for treatment. Monitoring your own blood pressure is today a 'must' in the management of hypertension. As with blood sugar management, a high degree of self-responsibility is required of patients for therapy to be successful. But regular testing of your blood pressure and blood sugar level and taking tablets are worth the effort.

What is normal blood pressure?

The normal values for blood pressure are usually depicted as two numbers, such as 140/80, but what do these numbers actually mean?

- The higher, systolic value describes the pressure in the circulation when the heart muscle contracts and pumps the blood into the arteries.
- The lower, diastolic value provides information about the pressure in the body when the heart muscle is relaxed and the heart is filling with blood.

The systolic pressure therefore reflects the 'peak pressure' for the heart and blood vessels, while the diastolic pressure represents the ongoing pressure. Both values are equally important when talking about the development of complications caused by hypertension.

The blood pressure varies considerably during the course of the day and night. Physical and emotional stress, sadness or happiness cause it to rise or fall (Figure 4.6). During the night, the blood pressure is usually lower than during the day. The World Health Organization (WHO) recently set the boundary between normal and high blood

pressure as 140/90 mmHg. If these values are exceeded over several measurements, hypertension is present: the reasons for this need to be examined and treated. As well as the 'normal' threshold, the WHO also defined a state of 'high normal' blood pressure (systolic value 130–139 mmHg, diastolic value 85–89 mmHg). In people with illnesses that increase the risk of cardiovascular disease – and diabetes is one of these – blood-lowering treatments are recommended even in the range of 'high normal'. According to the WHO, the optimal value is below 120/80 mmHg (Table 4.1).

The results of epidemiological studies have allowed us to calculate the increased risk of a cardiovascular event for each extra unit of high

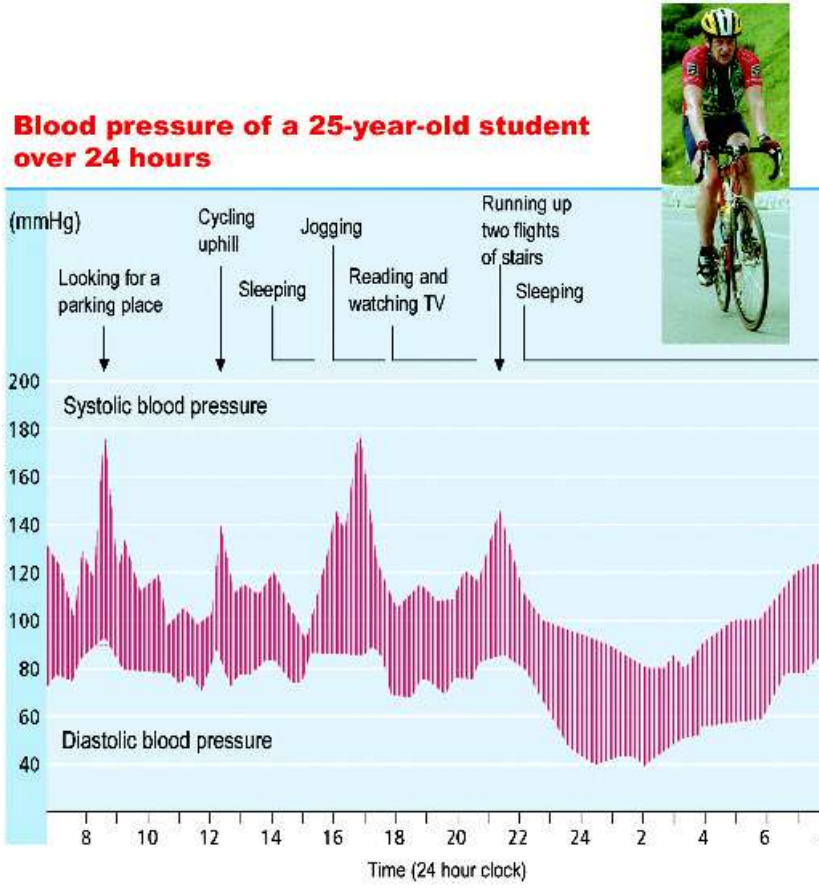


Figure 4.6 Even in healthy people the blood pressure can fluctuate markedly during the course of the day: stress and physical activity cause it to rise, while it falls during sleep.

Table 4.1 Classification of blood pressure values*

Classification	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)
Optimal	Under 120	and	Under 80
Normal	Under 130	and	Under 85
High normal	130–139	or	85–89
Classification of hypertension			
Mild	140–159	or	90–99
Moderate	160–179	or	100–109
Severe	180 or over	or	110 or over

*In 1999, the World Health Organization published a new classification of blood pressure values.

blood pressure. For patients with diabetes and associated nephropathy, this risk – regardless of the degree of hypertension – is always considered to be 'very high'. This means that the probability of having a severe cardiovascular event, such as a heart attack or stroke, within the next 10 years is at least 30%.

Therefore, people with diabetes and signs of kidney damage should not wait until they have hypertension, but should start drug therapy as soon as they have 'high normal' blood pressure.

Many people today already own a blood pressure meter – but it is important that they know how to use it correctly (see page 41).

When your blood pressure is too high . . .

You should not think that you have hypertension after obtaining a high result from a single test of your blood pressure. Normal blood pressure fluctuates much too much for this to be the case (see Figure 4.6). Therefore, control measurements should be made. You need to have at least two more readings over 140/90 mmHg before you can be considered to have hypertension. These control measurements should be made on different days and, where possible, in different places – not just at the doctor's surgery but also at home or at work. This is because there are some people who always give a high blood pressure reading at the hospital or at the clinic, owing to stress or excitement. This is known by doctors and nurses as the 'white coat

effect'. The phenomenon is quite common and seems to occur particularly frequently in people with diabetes.

The white coat effect can be excluded by measuring your blood pressure yourself at home or, better, by a 24-hour measurement. Hypertension in the surgery often resolves itself as soon as you are back in familiar surroundings. Someone who has only white coat hypertension does not need medical therapy, according to current knowledge.

Rules for correct measurement of blood pressure

- The blood pressure should be measured while sitting down. Measurement while lying or standing gives different values and is done only during special medical investigations.
- The upper arm should be uncovered when the pressure cuff is applied. Measurement through the shirtsleeve or other clothing gives incorrect readings.
- The pressure cuff must be the right size: this depends on the size of the upper arm. If the cuff is too small, the reading is likely to be too high (see the Appendix for appropriate sizes).
- Rushing gives a false reading. Before taking the measurement, you should sit quietly for a few minutes and relax.
- If you have a new wrist monitor, at first you should compare the values obtained with this with those taken using your old device on the upper arm.

When blood pressure is too high in people with diabetes

In people with Type 1 diabetes, blood pressure usually rises only as a result of kidney damage. Whereas previously mainly normal blood pressure readings were obtained, as soon as microalbuminuria appears, the blood pressure begins to rise, although at first it may stay in the normal range. For example, if under normal albuminuria it was 125/80 mmHg, after the onset of microalbuminuria it might rise to 130/85 mmHg, then later to 135/90 mmHg. This is why there is no 'official' value for hypertension, but a rise in blood pressure compared with earlier values indicates increased stress for the heart, kidneys and blood vessels. Should macroalbuminuria then develop, or even renal failure, the blood pressure rises sharply if it is not treated promptly.

As well as people with Type 1 diabetes, every second or third person with Type 2 diabetes shows raised blood pressure as soon as metabolic disease begins. Because there is often no visible cause for the high blood pressure, people talk about 'essential hypertension'. In those with Type 2 diabetes, the blood pressure also begins to rise as soon as kidney function is impaired. In practice, all patients with renal damage have high blood pressure.

The lower the blood pressure, the less frequent is the occurrence of kidney or eye damage

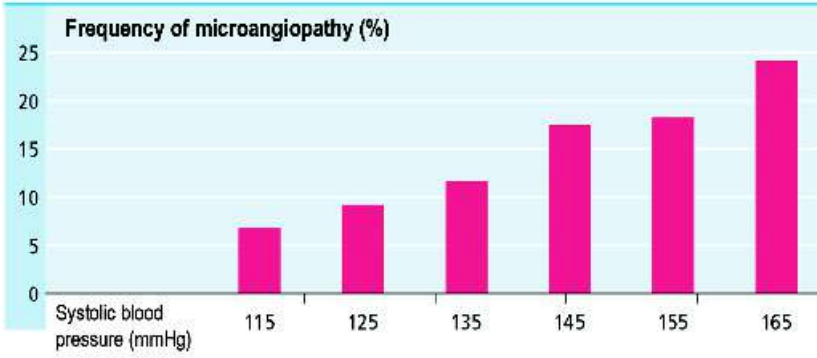


Figure 4.7 Damage to the small blood vessels (microangiopathy) is responsible for diabetic complications in the kidney and in the eye. When the blood pressure is low, the risk of such complications is greatly reduced. [8]

How blood pressure affects the development of kidney damage

This is most important for people with Type 2 diabetes because, in their case, the blood pressure is often already high when the diabetes is diagnosed. A large trial has recently shown a significant relationship between the value of the systolic blood pressure and the onset of kidney disease: the lower the systolic pressure, the less frequent is the occurrence of kidney disease (Figure 4.7). But, as with blood sugar, there is no threshold for blood pressure below which one is definitely protected from kidney failure.

When nephropathy already exists

The more developed the kidney disease is, the more relevant is the degree of high blood pressure for the progression of the disease. If

appropriate treatment can keep the blood pressure in the normal range at the stage of micro- or macroalbuminuria, the chances are good that the kidney damage will not proceed or will at least be delayed. This has been demonstrated in several studies. Figure 4.8 shows, as an example, the course of kidney disease in a patient who already had macroalbuminuria as a sign of advanced kidney damage and in whom the blood pressure was at first not well managed. At this time, the kidney function deteriorated fairly rapidly. However, it was possible, through good management of the blood pressure, to arrest the downwards trend after several months and to stabilize kidney function at a lower level.

Management of high blood pressure stabilizes kidney function

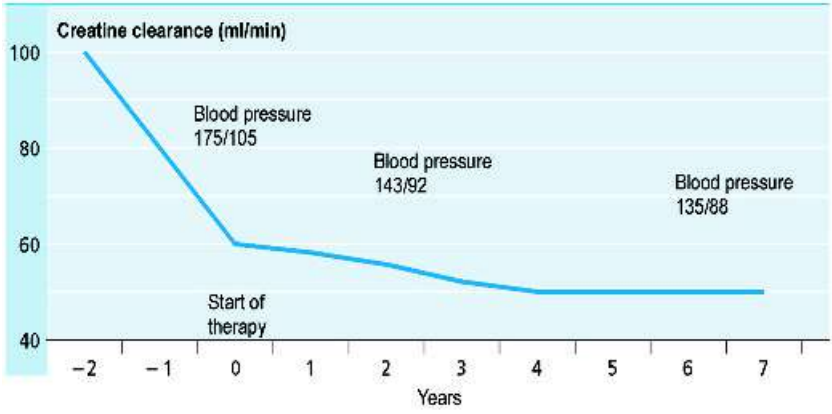


Figure 4.8 The course of kidney failure in a 46-year-old with Type 1 diabetes and nephropathy. As long as the blood pressure remains high, kidney function decreases rapidly. Successful management of the hypertension allows kidney function to be stabilized, albeit at a lower level.

Why did high blood pressure have such a strong effect in this patient? At this stage, the corpuscles in the already damaged kidney have often lost their ability to regulate the blood pressure themselves through narrowing of the incoming vessels. Thus, the high circulatory pressure impacts unhindered on the corpuscles and causes further damage.

How low should the blood pressure go?

From what has been said so far, it is clear that the earlier you start treatment and the lower you take the blood pressure, the better it is.

ACE inhibitors arrest kidney damage – even at normal blood pressures

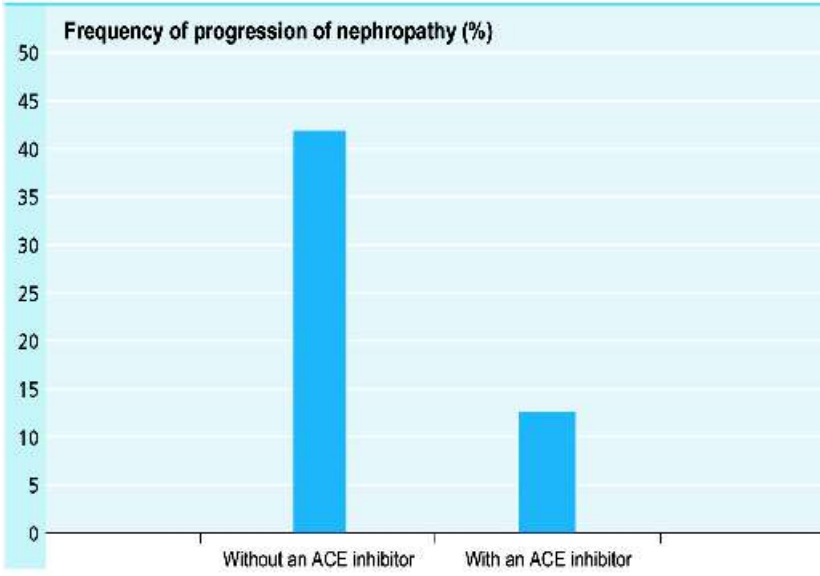


Figure 4.9 In people with Type 2 diabetes who already have microalbuminuria but no hypertension, treatment with an ACE inhibitor delays the frequency of progression of nephropathy from about 40% to 10%. [9]

Many people with Type 1 diabetes start with a normal blood pressure, which slowly rises over weeks and months with the development of kidney damage. It helps to treat the rising blood pressure in these patients even while it remains in the normal range, as shown in several trials. In one of these studies, 93 people with Type 2 diabetes and microalbuminuria but no hypertension were treated with a blood pressure-lowering drug from the class of ACE inhibitors (see the Appendix). The progress of kidney damage was arrested in nearly all the patients (Figure 4.9). During the following five years, only 12% developed macroalbuminuria, compared with 42% in the untreated group.

This and other studies have led to the opinion that in every patient with the first signs of kidney failure, be it micro- or macroalbuminuria, the blood pressure should be reduced, even if no actual hypertension is present. If the blood pressure is already over 140/90 mmHg, treatment must of course be started straight away, even if the kidneys are functioning normally.

Obviously, there are lower boundaries for the reduction in blood pressure. If it falls too far, unpleasant side-effects appear, such as

fainting, tiredness or other complications. Care must be taken regarding concurrent illnesses, such as circulatory problems in the legs or brain, since a low blood pressure can aggravate these conditions. The target value for blood pressure management therefore varies from patient to patient and should always be determined individually. The experts have set a value of 130/80 mmHg as a guideline.

What you should know:

Target blood pressure: no more than 130/80 mmHg.

Such target values are ideals and will not be achievable by everyone. The aim of blood pressure therapy should be to get as close as possible to the target. This will not happen overnight – on the contrary, the reduction of high blood pressure should be managed cautiously, since a too-rapid fall in blood pressure can cause problems with balance and often leads to side-effects.

There are more than 100 blood pressure-lowering drugs – which are the best?

There are various classes of hypotensive drugs which differ in the first instance in their mechanism of action (see page 120). Because the cause of the hypertension is not known for most people, it is not so simple to determine the most suitable treatment for each individual. Often it is simply a case of testing which drugs reduce the blood pressure most effectively and are also well tolerated.

There is not such a wide choice of suitable drugs for people with diabetes. For this special group, the so-called ACE inhibitors have established themselves as key players. This is because they don't just reduce the pressure in the general circulation, but act particularly in the kidney corpuscles. Thus, they have a special renoprotective effect. ACE inhibitors are therefore usually given to patients with microalbuminuria, even when the blood pressure is still in the normal range. Their use is also recommended in people with advanced kidney disease (macroalbuminuria), because they reduce protein excretion in the urine more effectively than other hypotensive drugs.

For patients who cannot tolerate ACE inhibitors – for example, a certain percentage of people develop a cough – the alternative is a new class of blood pressure-lowering drugs called the AT1 receptor

blockers (also known as angiotensin-II receptor antagonists). They act in a similar way to the ACE inhibitors to reduce blood pressure and have the same advantage of protecting the kidneys. This has been demonstrated recently in three large trials of people with diabetes with early and advanced nephropathy.

Other drugs that lower blood pressure are the calcium channel antagonists and the beta blockers. The latter are used when there are accompanying circulatory problems with the heart (coronary artery disease) because they also have a protective effect there.

If a hypotensive drug alone is not sufficient, a combination of different drugs is often given. The drugs preferred for use in combination, particularly with the ACE inhibitors, are diuretics. These lower blood pressure by increasing the excretion of sodium (salt) and water from the body. If there is water retention, as in advanced kidney failure, especially in the legs (oedema), strong-acting diuretics are used to resolve this.

In addition to those already mentioned, there are other hypotensive drugs that are not among the first choice of therapies because of their side-effect profiles (see page 123).

It is important to manage your blood pressure yourself

Today, everyone who has high blood pressure should regularly test the effectiveness of their treatment themselves. There are many measuring devices available that can be used at home to determine the blood pressure in the upper arm or wrist without any problem.

An important instrument for assessing blood pressure is the long-term or ambulatory blood pressure meter. This measures and records the blood pressure at certain intervals over 24 hours. These intervals are usually 20 minutes during the day and 30 minutes during the night. Blood pressure measurement at night can be irritating, but it provides important information concerning the behaviour of the circulatory system. In some people, and particularly those with diabetes, the blood pressure does not fall overnight in the normal way, which imposes a much higher burden on the body. This phenomenon occurs especially often in people with kidney disease. In some, the blood pressure even rises overnight, instead of falling

In someone with Type 2 diabetes, the blood pressure can rise at night instead of falling

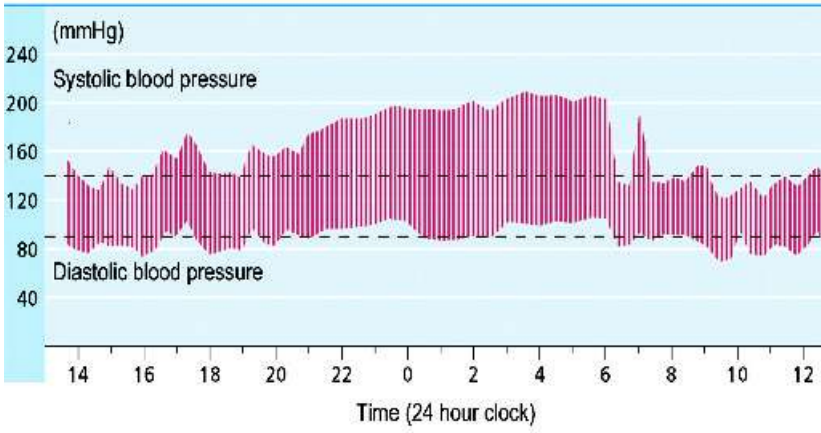


Figure 4.10 Ambulatory 24-hour blood pressure monitoring of a 58-year-old with Type 2 diabetes and microalbuminuria. Because of the hypotensive treatment, during the day the blood pressure stays within an acceptable range but at night it climbs steeply – which over the long term causes organ damage, including to the kidneys.

(Figure 4.10). Detecting this and initiating the right treatment to correct it can be a deciding factor in successfully delaying the progression of nephropathy. Therefore, the ambulatory blood pressure should be measured repeatedly at regular intervals in patients with renal failure.

Measurement is not the only part of blood pressure management: blood tests are also required to monitor for side-effects of the drugs. The treatment is very complicated, especially when several drugs are given concurrently. It is therefore usually not a good idea for patients to change their medication or even the dose of individual drugs themselves. Self-responsibility for the patient resides in controlling his or her blood pressure and in knowing about the medicines being taken, both of which can be learned during an appropriate course of education in diabetes and hypertension.

Practical tips for before you start managing your blood pressure yourself:

- Have the operation of your blood pressure meter explained clearly when you are relaxed and able to concentrate, for example at the hospital, pharmacy or clinic.
- Test whether your blood pressure is the same in both arms. Differences of up to 15 or 20 mmHg in the systolic value are normal. You should always measure the arm with the highest value.
- To be able to compare the values, you should try to take the readings at the same time of day, such as in the morning, after getting up, and in the evening before supper – preferably before taking your blood-lowering drugs. You may of course test your blood pressure more often.
- During the measurement, follow the rules given above (page 35).
- Write the measured values down straight away. Your doctor can give you good advice only on the basis of good documentation.

4.3 Eating correctly – it's all about protein and salt!

The kidneys and protein – what is the connection?

Every time that we eat something rich in protein, such as a large piece of meat, our kidneys get work to do, because they have to excrete the end-product of protein metabolism, urea. If someone eats a lot of protein, their kidneys have to deal with a large amount of urea. After you have eaten a steak, for example, the blood flow through the kidney corpuscles and the pressure there increase temporarily via a mechanism that is not fully understood. A healthy kidney copes with this without a problem. But you can imagine that a kidney that is already damaged by long-standing, poorly controlled diabetes, for example, is very sensitive to the increased pressure after a protein-rich meal. If too much urea is produced, it can no longer be completely excreted through the kidneys and begins to accumulate in the blood.

Not all protein is the same

Protein is an indispensable part of our diet. The building blocks of proteins, the amino acids, are used to make all our body's cells, many of our hormones and components of the blood. There are 20 amino acids in total, of which the body can make 12 itself. The others have to be taken in through foodstuffs; they are therefore known as 'essential' amino acids.

Both animals and plants can be the source of our dietary protein. Animal protein is consumed as meat, cheese, dairy products, eggs and fish: vegetable proteins are found in legumes, soya, cereals, vegetables, potatoes and in a small amount in fruits. These two types of protein differ in several ways.

Animal protein has a very similar amino acid composition to human protein. It can therefore be used by human organs without any special changes to the chemical structure. However, a distinct disadvantage is that animal protein is nearly always found closely associated with fat. Because 1 gram of fat contains twice as many calories, and therefore twice as much energy, as 1 gram of carbohydrate or 1 gram of protein, eating animal protein usually results in the consumption of a lot of calories and a lot of fatty acids.

This can lead to overweight and a rise in the levels of fatty acids in the blood. It also seems that animal proteins in particular stimulate blood flow through the kidneys.

In this respect, vegetable protein is much healthier. It is often found associated with fibrous substances that cannot be broken down by the human digestive system, which are good for the health of the intestinal tract. Their fat content is usually low and they impose less of a burden on the kidneys.

How much protein do you need?

It has been calculated that a person needs about 0.8 gram of protein per kilogram (g/kg) of bodyweight each day to provide the body with the necessary amino acids. Thus, a person who weighs 70 kg needs about 56 g of protein every day. That is not very much – if you eat a piece of chicken for lunch, for example, you have already consumed about 36 g of protein, which is two-thirds of your daily requirement. If you then eat two slices of Emmental cheese for supper, the body has already had enough protein. Any more that you take in through milk, bread or vegetables is extra.

The risk of eating too little protein is very small. Dietary studies have shown that each of us consumes on average about 1.6 g of protein per kg of bodyweight per day, which is twice as much as is necessary. People with diabetes often consume a lot of protein because it used to be recommended that they should eat more protein instead of carbohydrate, to help control the blood sugar level. According to current opinion, this is wrong. A healthy diet – and this holds true for those with diabetes as well as for everyone else – should consist mainly of carbohydrate (about 50–60% of total calorie intake), with about 30% coming from fat and only about 15% from protein. The food pyramid is the easiest way of demonstrating this (see Figure 4.11).

What you should know:

Nutritionists recommend obtaining half your protein requirement through animal protein and half through vegetable protein. This helps the body to use the proteins most efficiently.

What happens when you eat too much protein?

Healthy kidneys can cope with us eating too much protein, but if they are already damaged, the additional protein burden over a long time is not good. The reasons for this have already been explained – too much protein in the diet leads to a rise in the amount of urea and an increase in the blood flow through the kidney corpuscles, which damages them. What is completely wrong in this situation is an old dietary recommendation that is still heard sometimes – that if someone is losing a lot of protein through his or her urine because of kidney damage, he or she should consume more protein to compensate. The opposite is true!

If you want to compile a picture of your protein consumption, you should complete a food diary for a day, listing all the things you have

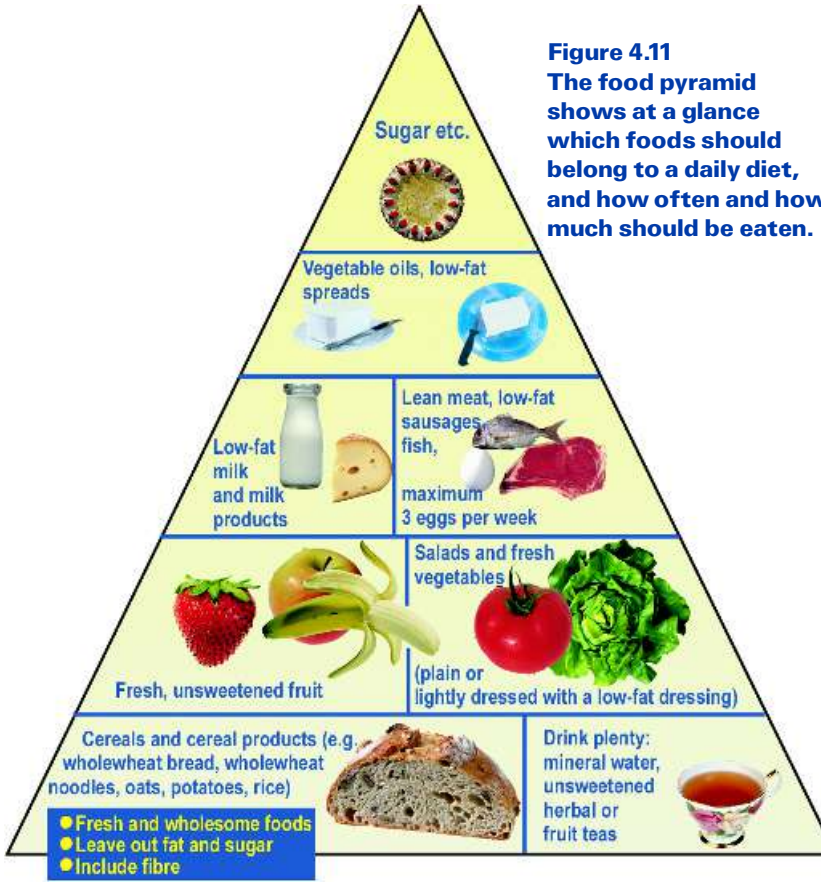


Figure 4.11
The food pyramid shows at a glance which foods should belong to a daily diet, and how often and how much should be eaten.

A healthy diet – and this holds true for those with diabetes as well as for everyone else – should consist mainly of carbohydrate (about 50–60% of total calorie intake), with about 30% coming from fat and only about 15% from protein.

eaten. You can then discuss this with a dietician. They can calculate the average protein content of animal and vegetable proteins. They may also suggest ways in which you can modify your protein consumption. But the goal is not that every person should eat 0.8 g of protein per kg of bodyweight per day or even less. For many of us, that would mean a serious change in our lifestyle and it has not yet been proved scientifically that this would be beneficial in the long term. Each small reduction in a significantly high rate of protein consumption, however, can reduce the burden on the kidneys.

What you should know:

People who have known kidney damage, as shown by macroalbuminuria or a high creatine concentration, should not eat too much protein.

There are situations in which a protein-poor diet, with less than 0.8 g of protein per kg of bodyweight per day, is actually necessary. If there is already some kidney damage and this gets worse very quickly, the amount of urea in the blood can rise steeply. A protein-poor diet allows the urea concentration to fall again, thereby avoiding kidney toxicity. Such treatment is usually undertaken in the clinic.

Salt and the kidneys

Cooking salt (which chemically is sodium chloride) belongs to the list of nutrients that are essential for the body. It is used, amongst other things, to maintain the function of the nerves, muscles, glands and circulation. The kidneys play a key role in the regulation of the salt content of the body. If the amount is too high, the kidneys intervene and excessive salt is excreted; on the other hand, if the intake is too low, the urgently required mineral is held back in the body.

If the kidneys are damaged, such that they can no longer perform this function efficiently, then the salt content of the body rises. Because salt exists in the body in its dissolved form, a higher salt content leads to water retention and thereby to higher blood pressure. This rise in blood pressure is highly detrimental for the kidneys.

Six grams of salt a day are enough

On average, each of us consumes about 9 grams of salt a day. Someone who likes to season their food can easily consume up to 12 or 15 grams a day! Nutritionists, on the other hand, recommend only 6 grams per day. This amount is absorbed by the body from a mixed diet through the natural salt content of the foodstuffs, without the need for adding more salt. You should remember that the salt content of food is highly variable, so that it is easy to exceed the target amount. See Table 4.2 for a list of examples.

Table 4.2 Salt content of foods

Low salt content (up to 120 mg sodium, equivalent to 0.3 g cooking salt/100 g food)	Medium salt content (120–400 mg sodium, equivalent to 0.3–1 g cooking salt/100 g food)	High salt content (more than 400 mg sodium, equivalent to more than 1 g cooking salt/100 g food)
Suitable*	Suitable in small amounts	Generally unsuitable (except in very small portions)
	**Meat**	
All fresh meat, minced meat, fresh poultry, game	Roast beef	All sausage products, preserved meats, salted meat, ham (raw or smoked)
	**Fish and fish products**	
All fresh fish	Kippers, smoked mackerel, tinned smoked crab, tuna fish in oil	Salted and other types of preserved herring, eels, smoked fish, fish salad, sardines in oil, smoked salmon
	**Fats and oils**	
Low-fat margarine, unsalted fats	Garlic butter	Mayonnaise, lard
	**Milk and dairy products**	
Low-fat milk, buttermilk, diet yoghurt	French cheese, Swiss cheese	Hard cheeses (Edam, Gouda), soft cheeses (Tilsiter, Brie, Limburg, Camembert), processed cheese

Bread, pasta, pastry

Cereals, semolina, noodles, spaghetti, rice, shortcrust pastry

Butterbiscuits, white bread, rusks

Rolls, pumperknickel bread, cornflakes, crisps, sodabread, crackers

Vegetables, salads, mushrooms and potatoes

All types of fresh or deep-frozen vegetables

Vegetables in tins, vegetables boiled without salt, potato dumplings, beetroot

Pickled vegetables, olives, capers, conserved mushrooms, gherkins, sauerkraut, salad dressings

Fruit

All fresh fruits, conserved fruits, fruit juices

Special products, ready-made meals

Ready-made soups, ready-made meals (deep-frozen or in tins), ready-made sauces

Herbs, spices and flavourings

All fresh, dried or deep-frozen herbs, all pure spices, salt-free curries and sauces

Cooking salt, curry, stock cubes, spice mixtures, soup and meat extracts, all ready-made sauces and marinades, mustard, ketchup

*Suitable with respect to their salt content. In practice, the cholesterol and fatty acid content must also be taken into consideration.

What you can do for yourself:

It is tedious to calculate your exact daily salt intake and generally impractical. You should therefore follow these rules: avoid adding salt to meals and avoid the consumption of very salty foods, such as salted pork, salted nuts, ready-made soups, smoked meats and preserved foods. Herbs and spices can greatly improve the taste of meals that are low in salt. Don't worry, after 4–6 weeks 'acclimatization', even the most low-salt meal will taste just as good as one containing a lot of salt used to do.

You should avoid the so-called 'salt replacements' or 'diabetic salts' that are available in pharmacies or health food shops because these often contain large amounts of potassium. This is particularly unhealthy for people with impaired kidney function (see Chapter 9). If you want to use these products as a 'bridge' for a short time, you should discuss this with your doctor.

Many people with diabetes can lower their blood pressure significantly just by avoiding cooking salt. Specific blood-lowering drugs, the diuretics, can be used to protect the kidneys further by causing the excretion of excessive salt and water from the body. Diuretics are especially useful in patients who suffer from water retention in the tissues, a condition known as oedema.

4.4 Smoking – a particularly dangerous habit for diabetics

There are many good reasons not to smoke. For people with diabetes there are more such reasons than for other people, whose main risk is lung cancer. For someone with diabetes who smokes, the risk of developing circulatory problems in the legs or in the heart (such as an infarct or heart attack) is about two or three times higher than for smokers who do not have diabetes.

Since the 1980s, we have known that smoking damages not only the major blood vessels but also the capillaries, particularly those in the kidneys.

Trials involving thousands of participants have shown that smokers develop micro- and macroalbuminuria as signs of kidney failure more often than do non-smokers – even when they do not have diabetes. For people with diabetes, this relationship is plainer still. In a study of 800 people with Type 2 diabetes, more than twice as many smokers as non-smokers developed macroalbuminuria within the four-year observation period. There was also a significant relationship with the number of cigarettes smoked. The heaviest smokers were the most at risk of developing diabetic nephropathy (Figure 4.13). Smoking not only favoured the appearance of kidney failure, but also aggravated its condition.

The risk of nephropathy rises with the number of cigarettes smoked

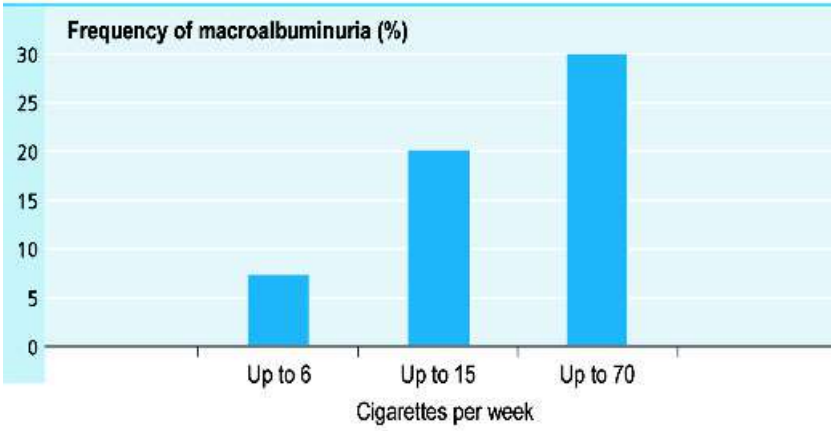


Figure 4.13 The more cigarettes a person smokes, the earlier he or she excretes protein in the urine. Smoking 10 cigarettes a day increases the frequency of macroalbuminuria by more than 30%. [11]

The reasons why cigarette smoking is so bad for the kidneys are not known exactly. We know that blood pressure increases during smoking. In addition, there are many detrimental effects on the walls of the blood vessels.

Motivation for smokers to give up or at least to cut down the number of cigarettes comes from observations on ex-smokers. When someone quits smoking, their risk of nephropathy falls (Figure 4.14).

It is not only the risk of nephropathy that increases with smoking, but also the risk for other complications relating to blood vessels. Numerous studies have shown that patients with hypertension – which includes nearly all diabetics with nephropathy – reduce their risk of a myocardial infarction or heart attack by nearly a half when they give up smoking. Such success is very hard to achieve by medical therapy!

We all know that it is very hard to break the smoking habit. But you should try, because the health benefit is huge. Today there are many methods available to help you give up cigarettes, such as nicotine patches or nicotine chewing gum to provide support in the first few weeks; no-smoking programmes, usually run in groups led by an expert; and relaxation exercises, which can help you continue to do without cigarettes.

Smoking accelerates the onset and course of kidney failure

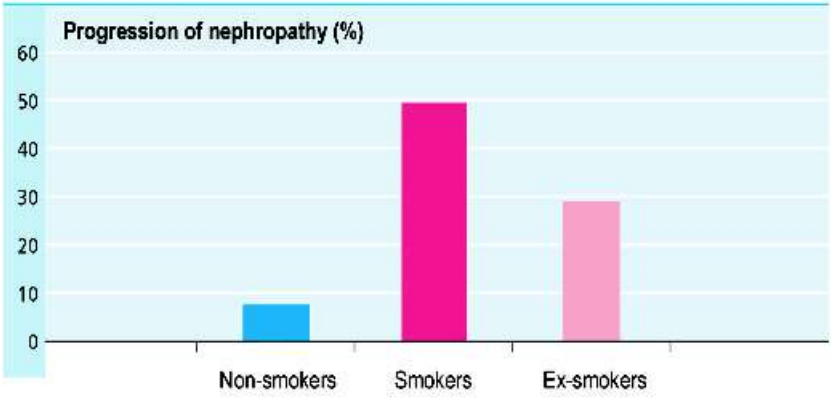


Figure 4.14 Someone who stops smoking can reduce his or her risk of developing kidney disease. [12]

A serious attempt is worth the effort, in any case. Succeed or fail, you should not despair straightaway. Most ex-smokers have on average taken three attempts to break the habit successfully (Figure 4.15).

Figure 4.15 Smoking? No thank you!

4.5 High levels of fatty acids in the blood – bad news in every case

For many patients, ongoing nephropathy leads to a disturbance of the fatty acid metabolism, with the result that the concentrations of triglycerides and cholesterol in the blood increase (Figure 4.16). From animal experiments, there is evidence that these elevated blood fats accelerate the progress of kidney disease. Whether this also occurs in people has not yet been demonstrated convincingly. Some studies have shown that in patients with advanced nephropathy, the loss of kidney function was less when, for example, the level of cholesterol was reduced by medical therapy (Figure 4.17).

Regardless of any possible detrimental influence on the course of nephropathy, a raised blood fatty acid profile, particularly of cholesterol, leads to the development of atherosclerosis. The consequences are circulatory problems in the heart, the brain and the legs. People with diabetes and concomitant kidney damage are especially at risk from arteriosclerotic complications of the blood vessels. It is therefore important for them to monitor the fatty acid profile in their blood.

Not all fat is the same

The best-known fat risk factor for arteriosclerosis is cholesterol. It is one of the most important components of the body, needed in many places, for example for making cell walls, for the immune system which guards the body against infection, and as starting material for the synthesis of many hormones. In addition, cholesterol forms the initial building block for the bile acids, which are essential for normal fat digestion in the small intestine.

Cholesterol can be made in the body, primarily in the liver. It is also obtained from the diet, almost exclusively from foods of animal origin.

Cholesterol occurs in different forms. The two most important are LDL (low density lipoprotein) cholesterol and HDL (high density lipoprotein) cholesterol. LDL makes up the major part of the total cholesterol and is known as the ‘bad’ cholesterol, because it is deposited along the walls of the blood vessels, leading to arteriosclerosis. HDL cholesterol, on the other hand, has a protective effect on blood vessels: it is able to absorb cholesterol from deposits on the

Triglyceride and cholesterol profile in the blood in patients with nephropathy

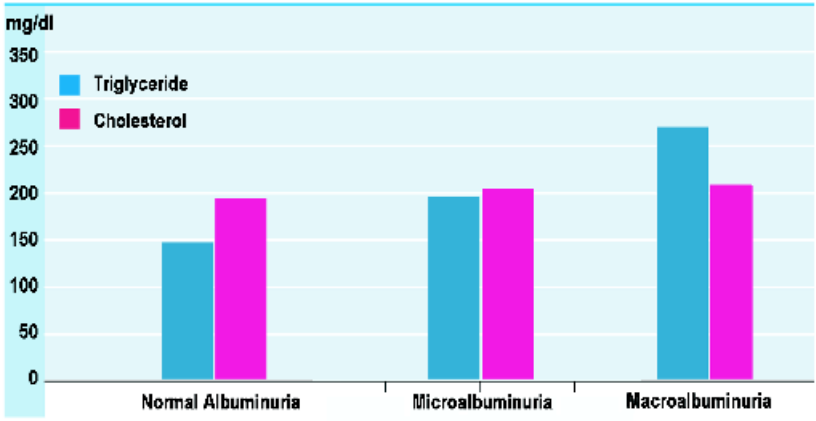


Figure 4.16 Blood concentrations of fatty acids rise with progressive stages of nephropathy.

vessel walls and transport it to the liver. There, the cholesterol is broken down and excreted via the bile. It is therefore known as 'good' cholesterol.

LDL and HDL cholesterol can be measured in the blood. In order to assess your risk of developing arteriosclerosis, it is important to know the concentrations of both types. The best situation is when the level of LDL cholesterol is as low as possible and the level of HDL is as high as possible.

Loss of kidney function is less during statin therapy

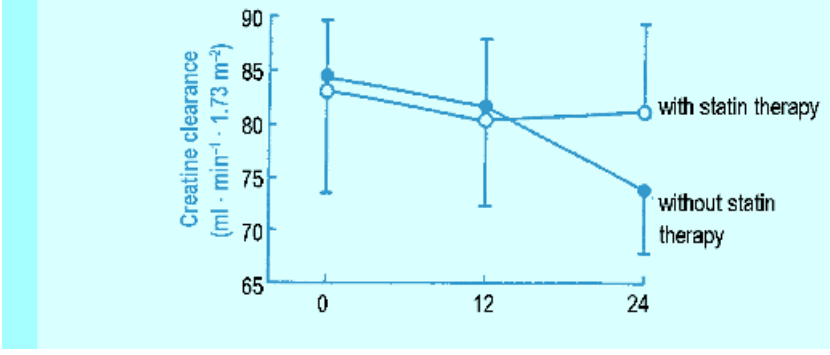


Figure 4.17 Patients who are treated with a statin show a smaller decrease in kidney function after two years of therapy. [9]

The experts have set recommended cholesterol targets for people who have kidney damage and a concomitant increased risk of arteriosclerosis.

Target values for patients with nephropathy:

Total cholesterol under 200 mg/dl.
LDL cholesterol under 100 mg/dl.
HDL cholesterol over 35 mg/dl.

After cholesterol, the triglycerides are the second-most important lipid in the body. They are the most important storage compound for fats. Triglycerides are obtained mainly from the diet, but can be made and broken down in organs such as the liver or fat cells (adipose tissue). Normal levels of triglycerides in the blood are less than 200 mg/dl. A high concentration of triglyceride is often associated with a low concentration of HDL cholesterol and therefore has a bad influence on the development of arteriosclerosis. But this is low in comparison with the effect of LDL cholesterol. In the presence of very high levels of triglycerides, e.g. over 500 mg/dl, the blood serum, which is normally clear, becomes cloudy. This affects the fluid properties of the blood and, in the presence of pre-existing narrowing of the arteries, for example in the heart or brain, can be very unhealthy. Very high concentrations of triglycerides can also cause inflammation of the pancreas.

What can you do about high blood fat levels?

The first step to combat raised levels of LDL cholesterol should be to examine your dietary habits, i.e. assess your daily intake of fat. This is important and independent of whether you are going to start taking lipid-lowering drugs because, on the one hand, a small rise in the lipid profile can be treated with a change in the diet alone, while on the other hand, the effect of lipid-lowering drugs can be reduced or even blocked by the wrong food!

The goal of any change in the diet should be to reduce the high proportion of fat in your food, particularly fats of animal origin. This

can be done without having a major impact on your normal eating behaviour. You just need to increase the amount of suitable food in your diet by a small amount and reduce the unsuitable foods. You also need to follow low-fat methods of preparing foods, as shown in Table 4.3. It is not enough simply to forgo your breakfast egg!

You can also have a beneficial effect on your cholesterol profile by increasing your physical activity. Regular physical training increases the amount of 'good' HDL cholesterol. The best activities are those that promote endurance, such as walking briskly, jogging, cycling, swimming or even skiing. It is important that these activities are performed regularly, i.e. at least three times a week for about 30 minutes each time. A short daily programme is better than a mammoth programme at the weekend.

The changes required to your lifestyle and eating pattern are not that great. You should be able to achieve some of them, at least in part, to back up your medical therapy.

Here, we must mention smoking again. Smoking cigarettes decreases the level of 'good' HDL cholesterol. Therefore, giving up smoking will help prevent arteriosclerosis by enhancing protective factors.

If you cannot get your cholesterol profile into the required range through changes in diet and lifestyle, you need to start medical therapy. The most effective drugs for lipid lowering are the cholesterol synthesis inhibitors, the statins (see page 123). They block the synthesis of new cholesterol in the liver and thereby lower the concentration of 'bad' LDL cholesterol particularly effectively. The importance of this reduction in LDL cholesterol for the development of coronary artery disease in people with diabetes was shown in the Scandinavian 4S trial. The risk of suffering a second myocardial infarct after an initial one was 42% lower in patients who received the statin, simvastatin, than in those who did not.

If the above dietary measures are taken, the triglyceride profile will also improve. An important factor here is excess alcohol consumption, which sharply raises the triglyceride concentration in many people. How much alcohol is allowed has to be determined for each individual. We know that alcohol, in moderate amounts, can have

beneficial effects on the blood vessels. Drinking about 20–30 g per day, which is about ¼ litre of wine or ½ litre of beer, raises the concentration of the 'good' HDL cholesterol.

If the triglyceride concentrations cannot be lowered sufficiently through dietary control and statin therapy, fibrates or other drugs can be added to the treatment regime. Combination therapy with statins and fibrates has possible side-effects and should be initiated only under close medical supervision.

Some practical tips

The relationship between diet and blood lipid profile has been known for a long time. The goal of any change in diet is, first, to reduce the proportion of fat in the diet, particularly animal fat. This is easy to achieve if you follow some simple ground rules, as shown in Table 4.3.

Fats can also be reduced by preparing food in their absence or with only a little. Good methods are boiling, grilling or steaming. When baking or stewing, the amount of fat can be minimized by using special pans and baking foil.

It is not only the total amount of fat in the diet but also the type of fat that determines your lipid profile. There is a difference between saturated and unsaturated fatty acids. The saturated fats are the dangerous ones, because they prevent the uptake of LDL cholesterol into cells. They occur mainly in animal fats: meat, cheese, butter, eggs, cream, full milk and its products. Chocolate and cooking fats also contain predominantly saturated fats.

Unsaturated fats count as healthy fats because they lower the concentration of LDL cholesterol. These types of fats occur mainly in vegetable matter: vegetable oils, rice, oats or millet. Fish also contain large quantities of unsaturated fatty acids.

The dietary changes described above will lead automatically to a decrease in cholesterol absorption. Some foods contain significant amounts of cholesterol and should therefore be avoided; egg yolk, all offal, crustaceans and shellfish. An egg yolk contains a full day's portion of cholesterol (250–300 mg)!

Table 4.3 Practical tips for reducing the amount of fat in your diet

Choose	Avoid
Meat	
Lean meat – without visible fat – either pork, beef, veal (fillet, schnitzel, roast beef). The meat should be cooked in only a small amount of fat	Fat meat (visible fat), e.g. minced meat, offal (liver, heart, kidney, brain)
Poultry	
Chicken, turkey, pigeon, pheasant	Duck and goose
Sausage products	
Lean ham, low-fat sausages, corned beef	All-fat sausages, bacon, brawn
Fish	
Halibut, perch, salmon, cod, trout, pike, sole, plaice, shellfish, tench, mackerel	Eel, caviar, sardines in oil, lobster, oysters, mussels, crabs, prawns
Fats, oils, mayonnaise	
Vegetable margarines and vegetable oils with a high proportion of unsaturated fats, e.g. sunflower oil; diet mayonnaise	Butter, cream, mayonnaise, remoulade, dripping, lard, margarine and oils with a low proportion of unsaturated fats, cocoa butter
Eggs	
Egg white	Yolk. Remember that egg yolk is present in cakes, omelettes and pasta
Milk and dairy products	
Skimmed milk, low-fat yoghurt, cheese with less than 30% fat, buttermilk	Full-cream milk, condensed milk, cream, normal yoghurt, ice cream, cheese with over 30% fat
Bread and pastry	
All types of bread, cakes in small amounts. Spread with only diet margarines or oils. When baking, use only the egg white	Cakes made with butter, cream or egg yolk; biscuits
Sweets	
Only in small amounts	Sugar, chocolate, marzipan, nougat, pralines, sweets













Table 4.3 Practical tips for reducing the amount of fat in your diet *(continued)*

Choose	Avoid
Fruits and vegetables	
All types. Vegetables should be steamed or prepared in vegetable oil Potatoes: baked, mashed, as dumplings or salad with diet mayonnaise	Chips, fried potatoes, crisps, croquettes
Drinks	
Tea (without sugar, use sweeteners), mineral water, fruit juice, alcohol in small amounts (wine, beer, champagne), skimmed milk	Full-cream milk, lemonade, cola, iced coffee, liqueurs, dessert wines

5 Diabetics with kidney failure are threatened in other ways

Chronic exposure to abnormally high blood sugar levels and hypertension doesn't just damage the kidneys. In other parts of the body, organs and blood vessels are also affected. When microalbuminuria appears as a sign of the onset of kidney failure, it is high time to check for other complications. Patients with diabetes and microalbuminuria frequently show changes to the back of the eye, so-called 'retinopathy', as well as signs of cardiovascular disease and problems with the circulation to the brain or the legs.

What you should know:

Every patient with kidney damage should undergo a careful examination of their other organ systems.

5.1 How diabetes can affect your sight

People with diabetes should undergo an eye examination at least once a year (Figure 5.1). This does not just look at vision and the blood pressure in the eye, but also examines the retina at the back of the eye, paying close attention to the capillaries. If these tiny blood vessels become damaged by the blood pressure being too high, your visual ability may be seriously compromised. This is because the image seen by the eye falls onto the retina, where it is converted by special cells into nerve impulses that travel along the optic nerve to

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You should have your vision checked at least once a year.

the brain (Figure 5.2). In the worst cases, diabetes can cause total blindness.

Just like nephropathy, diabetes-associated damage to the eye, known as retinopathy, does not develop overnight but gradually over years. This means that with early diagnosis, we can use this time to halt the progress of the retinopathy by giving the appropriate therapy and prevent the onset of blindness.

At first, diabetic retinopathy does not produce any symptoms. Only an ophthalmologist or optician can detect small swellings in the capillaries, called microaneurysms, during a routine examination (Figure 5.3). The first minor haemorrhages (bleeding) in the capillaries in the retina may even occur without affecting the vision. These early changes are known as non-proliferative diabetic retinopathy (Figure 5.4) and can be reversed by good management of blood sugar levels and blood pressure. But if these two factors cannot be controlled, they may lead to damage and destruction of the capillaries and from there to major bleeding in the retina.

The eye tries to combat this by growing new capillaries to deliver blood to its cells correctly. This stage is called proliferative retinopathy (Figure 5.5). The new capillaries, however, are brittle

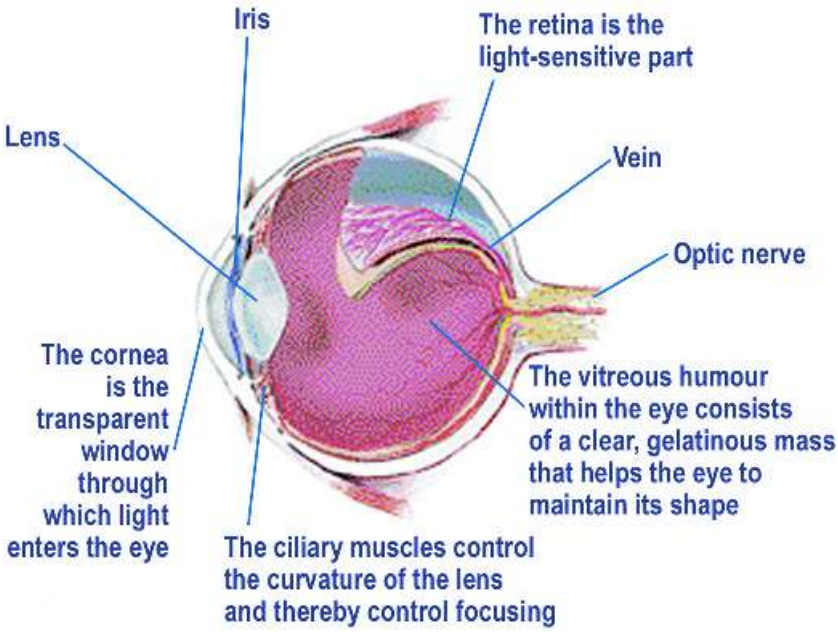


Figure 5.2 Cross-section through a human eye.

and bleed easily. Once the majority of the retina is covered with blood from this bleeding, there is acute loss of vision. Bleeding in the vitreous humour is particularly damaging. The vitreous humour is a clear, gelatinous mass that fills most of the eye and helps it to maintain its shape. The blood that leaks from the capillaries is broken down but leaves fragments and scars that seriously impair vision.

In people with diabetes, kidney and eye damage often develop in parallel. For both these complications, the blood sugar level plays a decisive role: the lower the blood sugar, the less likely is the development of retinopathy or nephropathy. The blood pressure has a similar effect – and in this case, low values can protect against ongoing damage, as shown by the major trials in people with Type 1 and Type 2 diabetes (DCCT and UKPDS; see Chapter 4).

What you should know:

The eyes of patients with kidney failure are especially at risk, because they often suffer from difficult to manage hypertension and the state of their diabetes is usually most advanced.

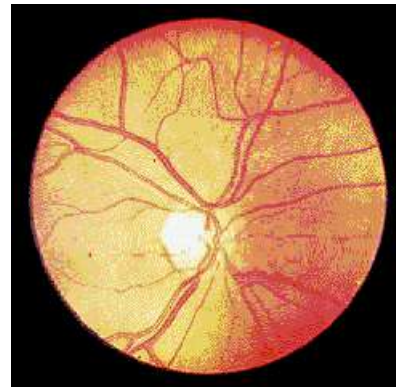


Figure 5.3 The appearance of the retina of a healthy human eye.

Figure 5.4 At the onset of retinopathy, small haemorrhages appear in the retina.

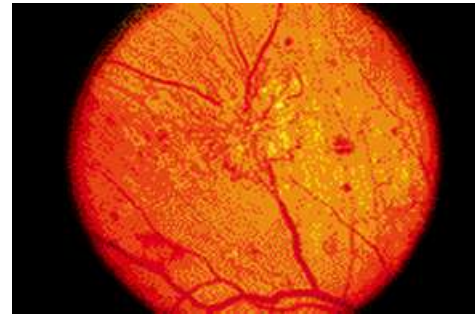


Figure 5.5 By the stage of proliferative retinopathy, new capillaries start to grow; these are brittle and can lead to further bleeding.

Intensive control of diabetes and blood pressure delays damage to the eye

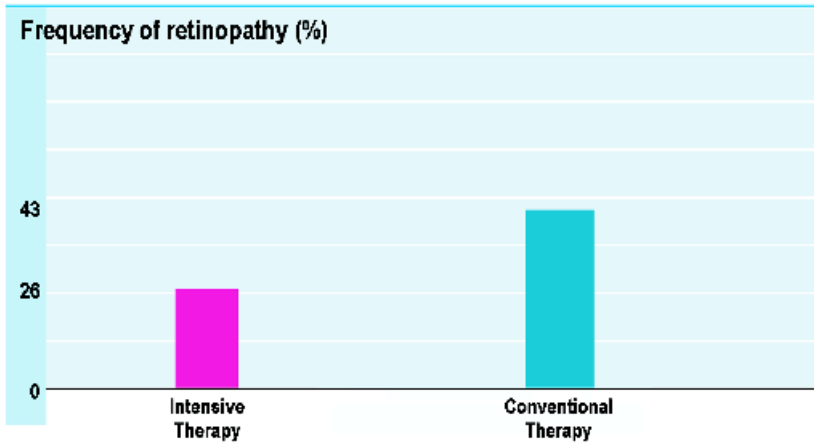


Figure 5.6 The progress of retinopathy in people with Type 2 diabetes and kidney impairment can be delayed through good diabetes management (target HbA1c under 6.5%), good blood pressure control (target under 140/85 mmHg) using ACE inhibitors, normalization of blood fatty acid profiles and treatment with aspirin. [10]

Sadly, blindness and dialysis used to be a common fate for people with diabetes. Today, this is not the case. By intensive management of the blood sugar level and blood pressure, we can delay or prevent the onset and further progression of retinopathy in patients with nephropathy, as shown in the large Swedish study (Figure 5.6). As with nephropathy, the ACE inhibitors have a significant beneficial effect on retinopathy. It is important that patients with kidney failure, who are therefore at high risk of damage to their vision, have their eyes examined by an ophthalmologist at least every six months and eventually even more frequently.

Fortunately, the treatment of diabetic retinopathy has made great progress in recent years. Laser therapy and surgical treatment of the retina and vitreous humour can often prevent the worse case scenario, blindness. The prospects, as with diabetic nephropathy, are better when the damage is detected early and the blood sugar level and blood pressure are reduced.

5.2 Kidney failure also endangers the heart

It has been known for a long time that people with diabetes have a much higher risk of a heart attack or a serious cardiac arrhythmia (abnormal heartbeat) than do people with normal metabolism. The Framingham study in the USA showed that in men this cardiac risk is 3.8 times higher and in women it is 3.5 times higher. The risk is particularly high in people with diabetes who already have kidney damage. Many studies have shown that for people with Type 1 diabetes there is a significant increase in the frequency of heart attack, especially once macroalbuminuria is present. For people with Type 2 diabetes, the risk is much higher from the start, but still increases further once micro- or macroalbuminuria becomes detectable (Figure 5.7).

The main reason for this is that in these people, a host of risk factors for blocked arteries come together: diabetes, hypertension, lipid metabolism disorders and smoking all increase the chances of coronary artery disease. In addition, narrowing or malfunction of the capillaries in the heart plays an important role, leading to disruption of heart muscle function. Many patients with nephropathy have suffered damage to their autonomic nervous system, which prevents regulation of the filtration pressure in the kidneys. This also adversely

Coronary artery disease is particularly common in people with diabetes and neuropathy

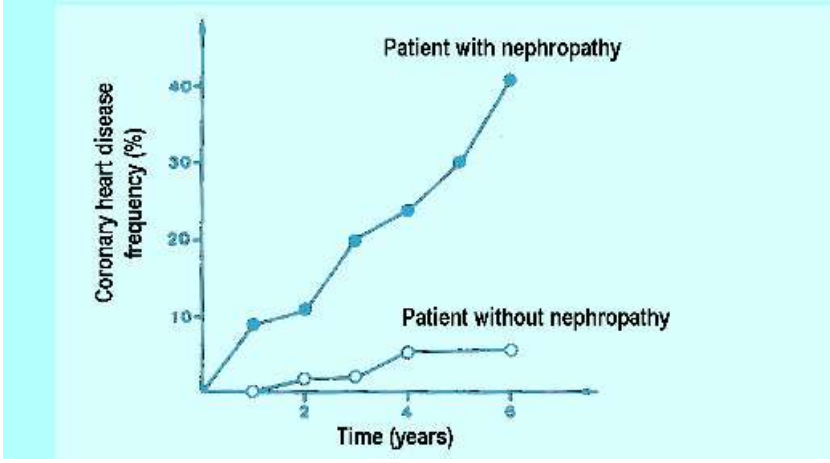


Figure 5.7 The risk of coronary artery disease and a consequent heart attack increases rapidly in people with diabetes as soon as the diabetes leads to increased albumin excretion.

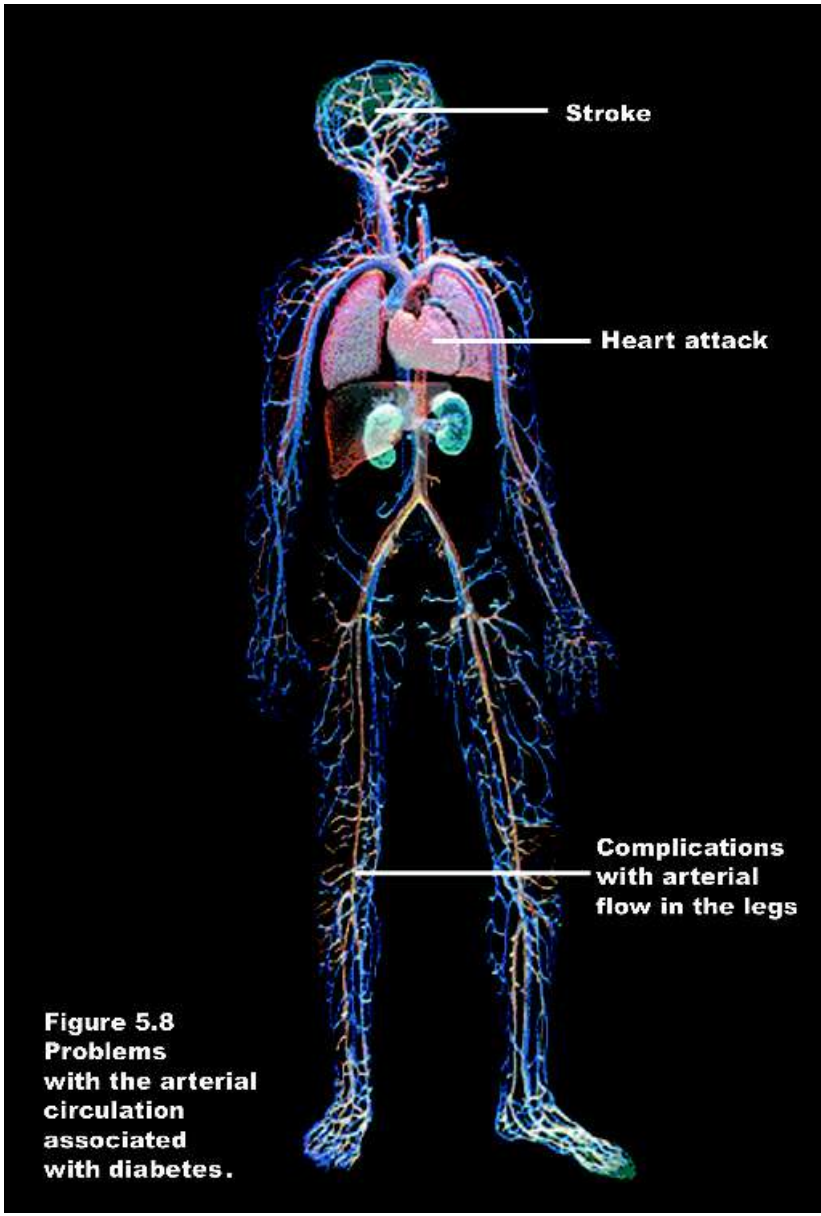


Figure 5.8 Problems with the arterial circulation associated with diabetes.

affects the heart. It leads to an increased risk of cardiac arrhythmia and eventually atrial fibrillation. It has also been established that the blood platelets of people with diabetes are 'stickier' than those in other people. Consequently, they form clots more readily; these can

then stick to the walls of the coronary blood vessels, which have already been damaged by arteriosclerosis, to form plaques, leading to blockage of these vessels.

Arteriosclerosis of the coronary arteries, which in the end results in a heart attack, is a slow process that often goes undetected for many years. Is is therefore very important to pay attention to the first symptoms that indicate the heart muscle is not receiving sufficient oxygen because the blood vessels that supply the muscle have become blocked with plaque.

The best known method of investigation is electrocardiography (ECG). This is usually performed both when the person is at rest and after exercise. It detects changes in the circulation which can be interpreted by the doctor or nurse. If circulatory disturbances or alterations in the heartbeat are seen, further cardiological investigations must be undertaken, such as angiography. This can reveal where the arteries are blocked. The constricted regions may be dilated again by balloon angioplasty or by insertion of a coronary stent. Sometimes, a heart bypass operation may be necessary.

Signs of arteriosclerosis of the coronary arteries:

- **Pressure or constriction in the chest.**
- **Chest pain or heart cramps, which may extend to the arms, the shoulders, the throat, jaw or stomach.**
- **Breathlessness.**
- **Atrial fibrillation.**

The symptoms may appear when you are at rest or engaged in physical activity. They may also appear when the temperature is low, when leaving a warm building in winter or when swimming in cold water.

What you should know:

If you experience any of these symptoms, you should visit your doctor at once. In people with diabetes, however, these warning signals may be missed because the nerves that transmit the signals from the heart have been damaged. This is why, even if you don't have any symptoms, you should have your heart examined once a year.

Echocardiography is another very useful method of investigation, especially for patients with kidney failure and hypertension. This uses ultrasound to determine the state of the chambers in the heart, the heart muscle and the heart valves. It provides information concerning the burden on the cardiac muscle and its capability. The echocardiogram can show whether the heart muscle has enlarged in response to the high blood pressure, a condition known as cardiac hypertrophy. This is a bad prognosis: the thickened heart muscle is particularly sensitive to circulatory disturbances, because it is poorly provided with oxygen but actually has a higher than normal need for oxygen. The inner wall of the left ventricle (the main chamber in the heart) is the most sensitive, since it is poorly supplied with blood vessels but exerts the greatest pressure. The heart muscle here can die off continuously, totally undetected, and be replaced by connective tissue. The ability of the heart to pump blood around the body fades gradually. This can be recognized early by echocardiography. One of the first noticeable symptoms for such changes is breathlessness during physical activity.

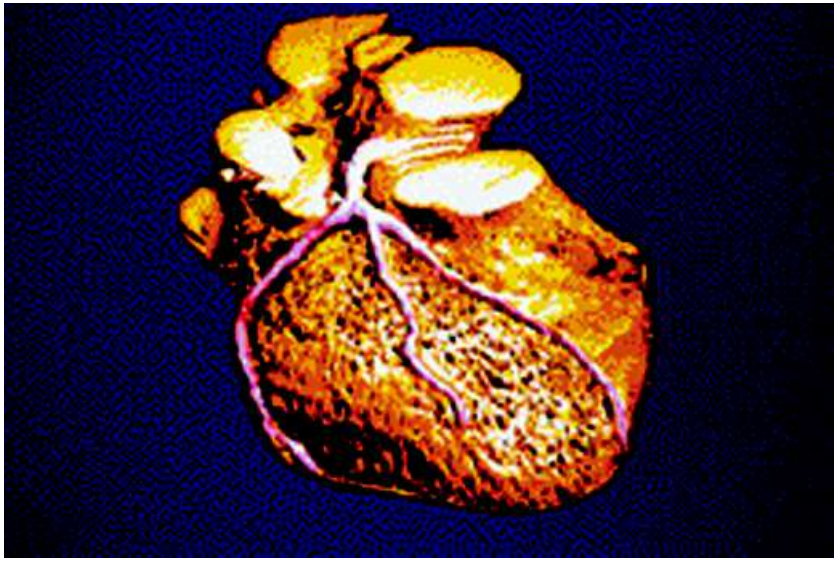


Figure 5.9 The tissues of the heart are nourished via the coronary arteries. If these arteries are damaged, there is an infarct and heart tissue dies.

Examination by echocardiography should also be performed regularly for people with diabetic nephropathy. This provides information on the activity of the heart but also on the quality of the blood pressure management. If the thickness of the heart does not decrease, but continues to increase, then the blood-lowering treatment needs to be improved. A special technique, called stress echocardiography, can nowadays give information on circulatory disturbances in the heart, which then indicate the need for further investigation.

Echocardiography is an important method of examination for patients with pre-existing kidney failure. These patients should avoid angiography because the contrast materials required for this technique are excreted via the kidneys and would impose an additional burden on these already overstressed organs.

What you can do for yourself:

To avoid heart problems, you must reduce all the risk factors for arteriosclerosis, such as high levels of sugar and cholesterol in the blood and hypertension. Giving up smoking is also important. Many studies have shown that taking these steps definitely helps to prevent a heart attack. Think about a regular examination of your heart and look out for the early warning signs.

5.3 The brain also suffers from arteriosclerosis

As the central control station for all bodily functions, the brain is of enormous importance. The brain cells require lots of energy and a plentiful supply of oxygen for their activities. Clear access through the many blood vessels that carry oxygen and nutrients to the brain is therefore a high priority (Figure 5.10).

When people with diabetes get arteriosclerosis, these cerebral vessels are frequently also affected. The walls of the arteries change – often over years, without being noticed – until finally the vessel narrows, with the result that the brain no longer receives enough blood. If such a shortage of blood supply occurs suddenly, it is known as a stroke. How much damage such an event causes in the brain depends above all on how big the affected blood vessel is and which nerve cells it supplies.

Warning signs of a threatening stroke:

- Feeling deaf or paralysis in the arms or legs.
- Drooping of the mouth.
- Speech problems, such as the sudden inability to speak or slurred speech.
- Visual disturbances, such as brief blindness in one eye – often perceived as a curtain that suddenly falls in front of the eye – or double vision.
- Unsteady gait: even in familiar surroundings you may suddenly bump into things or fall without any reason.
- Difficulties in swallowing.

The symptoms may last for seconds or minutes or even several hours. This is called a transient ischaemic attack. It may occur in a cerebral blood vessel that is already partially blocked. The most common cause is that a plaque that has developed on the internal wall of a blood vessel breaks off and passes along the circulation until it becomes trapped in a narrow vessel, preventing the flow of blood.

A stroke does not always manifest itself as a transient ischaemic attack. In order to start treatment at the right time, it is advisable for people with diabetes to have a regular examination of the major

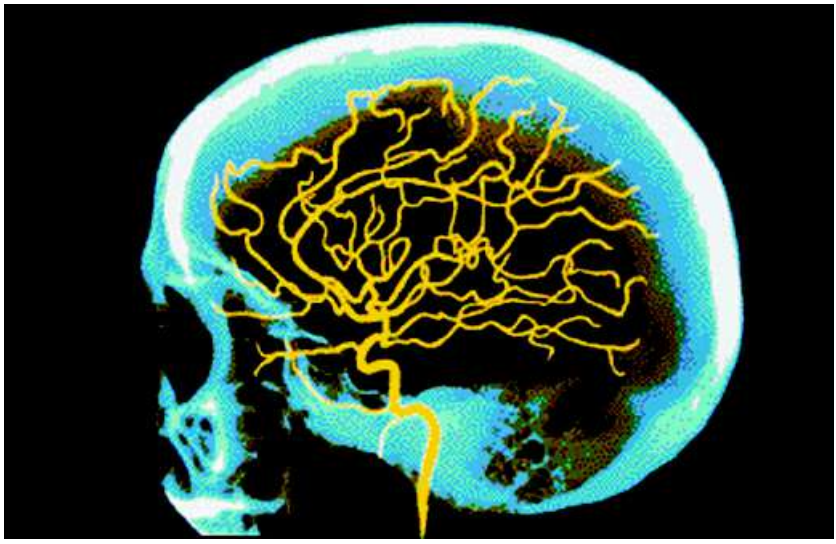


Figure 5.10 The brain is provided with blood and oxygen predominantly by the carotid artery.

blood vessels feeding the brain. Nowadays, this can be done very easily and precisely using ultrasound. This shows not only the state of the blood flow but also whether the vessel walls already have plaques forming, indicative of the start of arteriosclerosis.

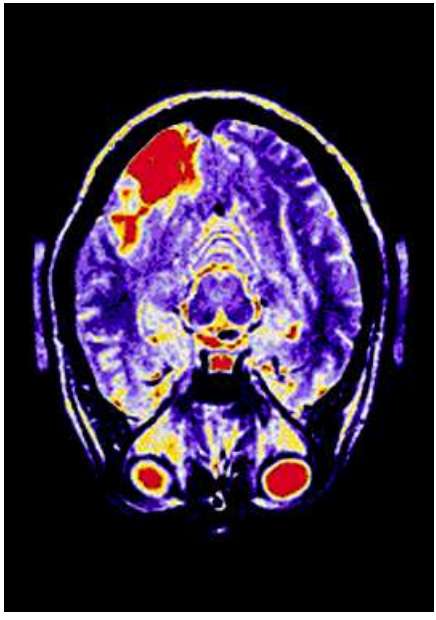


Figure 5.11 Haemorrhage (bleeding) in the left half of the brain after a stroke.

What you can do for yourself:

Participate in the management of the known risk factors for arteriosclerosis, particularly hypertension. Have an ultrasound investigation of your cerebral arteries and look out especially for the early signs of an impending stroke – as described above.

Once there is evidence that the blood vessels are becoming blocked, there are several options at our disposal. On the one hand, it is important to tackle the risk factors for arteriosclerosis. On the other hand, the 'stickiness' of the blood platelets can be reduced by drug treatment, which reduces the risk that a blood clot will form and block one of the narrow vessels. The best known drugs for this are aspirin (acetyl salicylic acid) and clopidogrel. If the cerebral arteries that serve the brain are already dangerously affected, it may be necessary to widen the partially blocked vessel or even to bypass it by a surgical procedure.

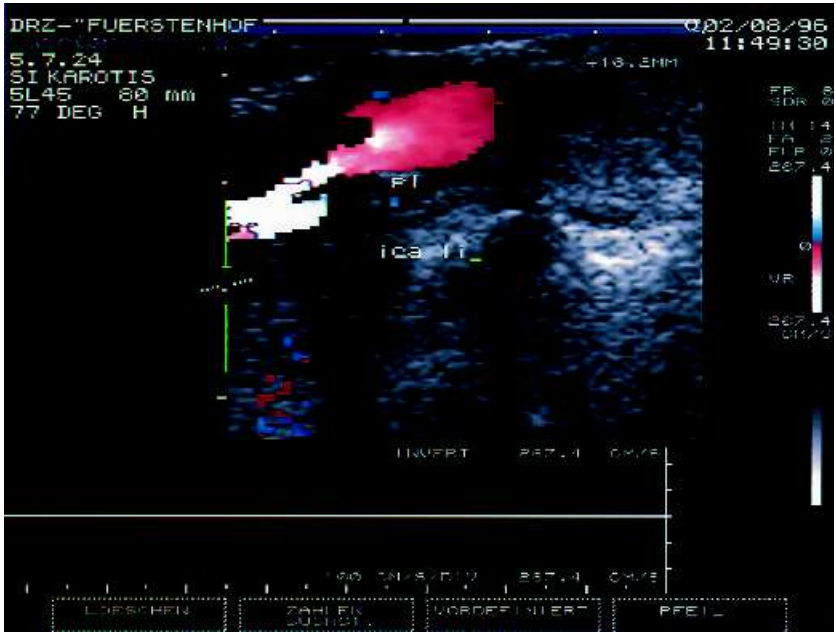


Figure 5.12 Colour duplex scan of the left carotid artery showing a constriction, recognizable by a change in colour from red to white. This indicates the patient is at risk of a stroke.

5.4 A common problem – poor circulation in the legs

Another very common problem in people with diabetes and accompanying nephropathy, particularly those who smoke, is circulatory problems in the legs. In this case as well, the cause is a narrowing of the blood vessels as a result of arteriosclerosis. This complication is commonly known as 'peripheral arterial disease'. Like other circulatory problems in diabetes, it develops gradually, often remaining undetected for years, and only causes damage when it is already well advanced (Table 5.1).

The symptoms are very characteristic: the legs start to hurt after walking even a short distance. The problem usually arises in the calf muscles, more seldom in the thigh, bottom or foot. As soon as you stand still, the pain ceases and you can proceed, until it starts again and you have to stop once more (Figure 5.13).

The cause of the pain is a shortage of oxygen. The narrow atherosclerotic blood vessels cannot supply enough blood and therefore oxygen to the tissues to meet the increased demand during walking. The working muscles react to this shortage with a sensation of pain. People with diabetes who already have nerve damage do not experience these symptoms as painfully or even at all.

If the thickening of the vessel walls proceeds, the circulation gradually gets worse and the pain starts to occur even at rest, especially when the legs are horizontal, such as at night. The leg becomes pale and feels cool to the touch. Because of the poor oxygen supply, small wounds heal badly and tissues can be permanently

Table 5.1 Stages of arterial disease (after Fontaine)

Stage I	**Evidence of narrowing of the vessels but no damage**
Stage II	**Pain when walking**
Stage IIa	**Maximum distance that can be walked more than 200 m**
Stage IIb	**Maximum distance that can be walked less than 200 m**
Stage III	**Pain while at rest**
Stage IV	**Tissue death caused by lack of circulation**

Figure 5.13 'Window-shopping disease': patients with poor circulation and pain in their legs often stop frequently when walking and look as though they are window shopping.

damaged. Infections are hard to treat, even with antibiotics. If large amounts of tissue die, in the worst cases amputation may be necessary.

One indication of damage to the circulation is when the pulse in the legs and feet becomes barely detectable. A more exact method is to use ultrasound to compare the blood flow and blood pressure in the upper and lower thigh. If these are low, there is probably a blockage

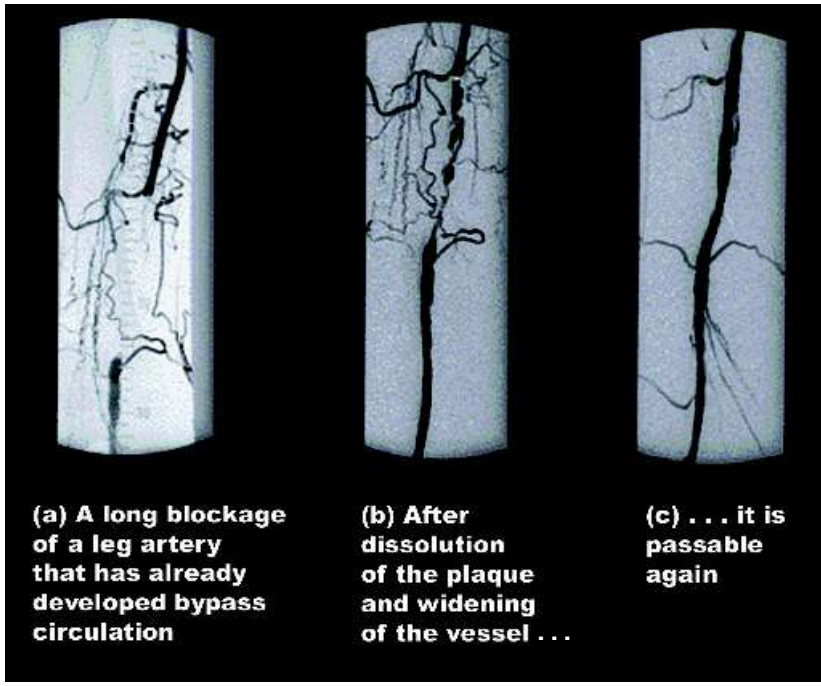


Figure 5.14 Re-opening of a blocked section of blood vessel by dissolving the clot and balloon dilatation.

in one of the blood vessels. This should usually be confirmed by angiography. If the condition is not too far advanced, the patient can be helped with medical therapy and walking exercises. Today, aspirin (acetyl salicylic acid) is prescribed to treat peripheral arterial disease.

If a serious or even total blockage occurs, interventions to improve the blood flow should be considered (Figure 5.14). There are several proven techniques available:

- Dissolving the clot that is blocking the vessel.
- Widening the constricted vessel using a balloon (Figure 5.15).
- Surgically removing the atherosclerotic plaque from large vessels, for example in the pelvis.
- A bypass operation, in which a diversion is constructed around the blockage.

By these methods, it is now possible to avoid amputations in many patients.

What you should know:

If circulatory problems are detected early, amputation can be avoided.

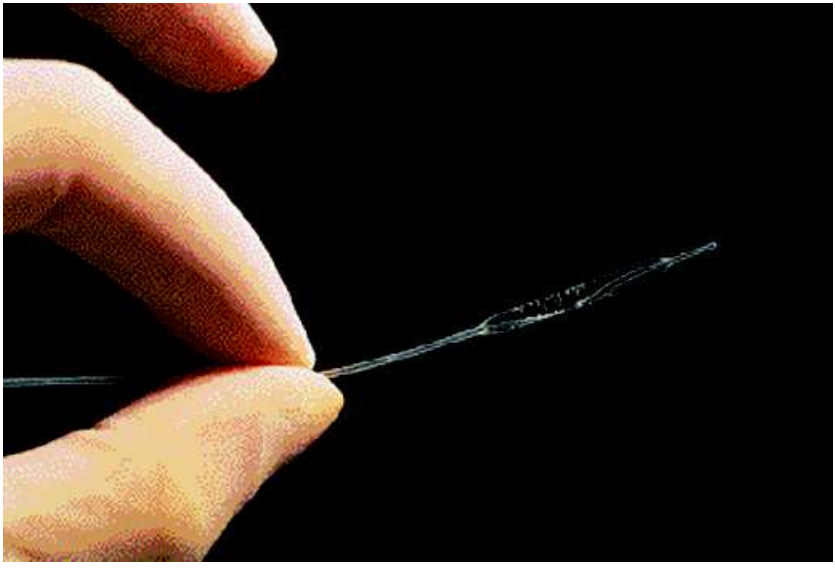


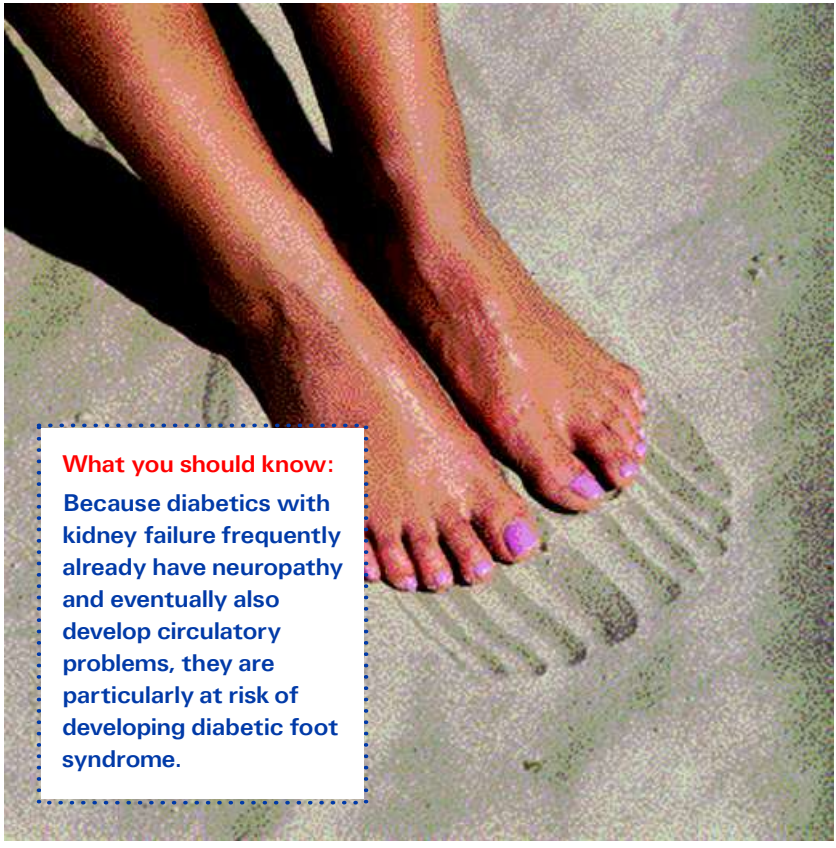
Figure 5.15 Narrow or blocked vessels can be reopened by dissolving the clot and widening the vessel using a balloon. The balloon is attached to a wire and inserted into the closed region, then inflated at high pressure, forcing the vessel to open.

What you can do for yourself:

Tackling the risk factors for arteriosclerosis takes priority. Look out for the early signs of problems with the circulation in your legs and have your foot pulse tested every year.

5.5 The diabetic foot – how to avoid amputation

Each year in the UK, around 5000 lower limb amputations are performed for vascular disease alone. It is not just problems with the circulation that cause this high risk of amputation. The so-called 'diabetic foot syndrome' is mostly the result of an unholy alliance between diabetes-induced nerve damage (neuropathy) and perturbed circulation. It often begins with a seemingly harmless foot injury, due to pinching shoes, poor foot care or walking in bare feet. Because of the nerve damage, the wound isn't noticed, the foot is not protected or looked after properly, it becomes infected and – especially when there is also poor circulation – the tissue starts to die. If this is not handled correctly, large, deep wounds develop, which may involve



What you should know:

Because diabetics with kidney failure frequently already have neuropathy and eventually also develop circulatory problems, they are particularly at risk of developing diabetic foot syndrome.

Typical signs of neuropathy:

- **Do you feel little pain from wounds that should hurt?**
- **Do you occasionally get a feeling of numbness or itchy feet?**
- **Do you get cold feelings in your feet even though they are warm to touch?**
- **Do you sometimes feel unsteady when walking?**
- **Do you have pain when you 'put your feet up' and is this particularly bad at night?**
- **Is the skin on your legs dry or even cracked?**
- **Do you have calluses at pressure points on your feet?**

If you answer Yes to one or more of these questions, there is possible nerve damage. Your doctor can check this using simple tests such as a tuning fork or a filament, or by testing your leg reflexes.

If, despite all precautions, diabetic foot syndrome develops, an expert, targeted treatment is urgently required to prevent even more serious consequences.

the bone and are very hard to treat. Amputation of the affected toes or other part of the foot is then unavoidable in order to prevent further damage, which may eventually make it necessary to amputate the whole leg.

But – as with all the other complications of diabetes – it is ultimately up to the person with diabetes to take responsibility for his or her own health and to take the right precautions. An important aspect is proper foot care. Following the basic rules outlined in Table 5.2 (page 82) can prevent the development of large, dangerous wounds that are difficult to treat.

You can determine for yourself whether you have neuropathy and thus whether you need to pay extra care to your feet.

Some patients are able to attend special diabetic foot clinics. These are often managed by a team including diabetologists, radiologists and surgeons. They may also work with special orthopaedic shoe manufacturers who can make shoes to fit individuals to help them after the treatment and reduce the risk of regression.

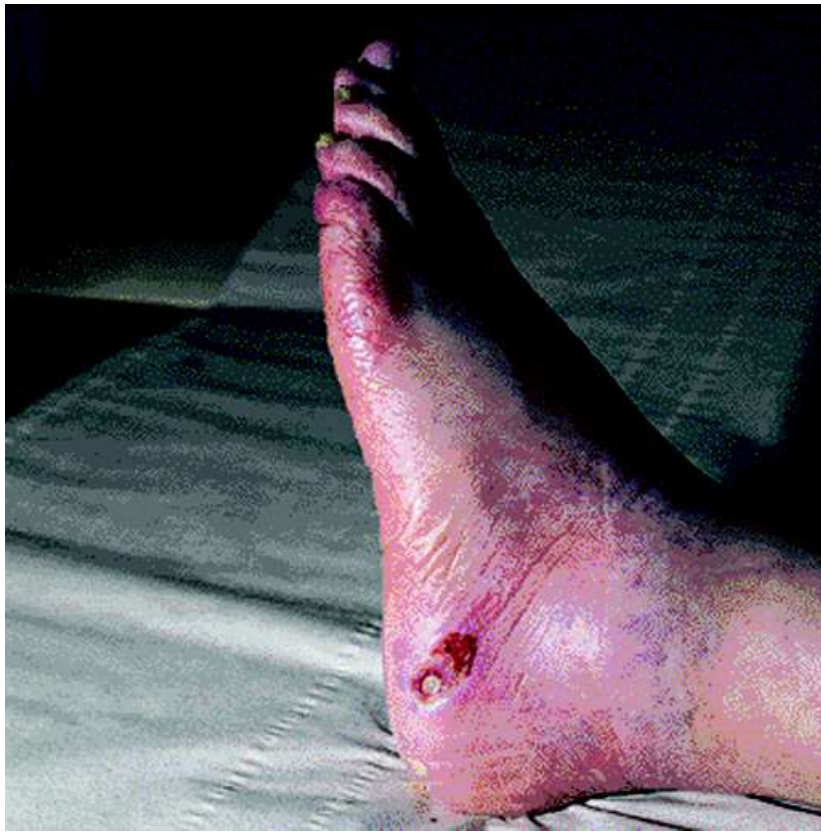


Figure 5.16 Wounds on the feet of people with diabetes often heal badly because of diabetes-associated nerve damage and problems with the circulation, leading to amputation in the worst cases.

Recognized treatment principles for diabetic foot syndrome:

- Protect the affected limb, preferably with bed rest.
- Improve the circulation and blood flow using appropriate measures.
- In cases of infection, take antibiotics.
- Maintain good blood sugar control.
- Treat the wound promptly and properly.

What you can do for yourself:

Examine your feet every day, including the soles, the toes and between the toes. If you are no longer so flexible, use a mirror to see the parts that are out of reach or ask your partner to look for you. Take proper care of your feet, especially when neuropathy is already apparent. Look after cuts and blisters: don't wait – go to the doctor straight away.

Table 5.2 A dozen tips for good foot care

Watch out: Examine your feet every day for redness, pressure points or wounds, with the help of a mirror if necessary. No pain is not a reliable sign of no injury!

Wash: Clean your feet every day with warm water (up to 37°C). Check the temperature of the water with a thermometer. Don't trust the temperature sensitivity of your feet, since this may have been destroyed by the neuropathy. The feet should be soaked for three to five minutes, but this is not recommended when there are open wounds.

Dry: Use a soft towel and dry your feet carefully, including between the toes and the creases in the toes.

Care: For dry skin, daily application of a cream or salve is recommended. Don't put cream between the toes as this can lead to crumbs or irritation of the skin. Oils or zinc paste, which dry out, are not suitable.

Toe nails: Use a file to keep your nails short. Round off the corners so that they don't press on the adjacent toe. Don't use pointed or sharp instruments to care for your nails. Ingrowing nails should be managed by a diabetes-educated chiropodist.

Corns: Do not use corn plasters, salves or tinctures because these contain substances that can damage your skin. Corns should be treated by an experienced chiropodist.

Calluses: These can be removed by carefully using a pumice stone. It is better to undergo subsequent management in a medical foot care practice. Calluses are evidence of raised pressure, so your footwear should be examined.

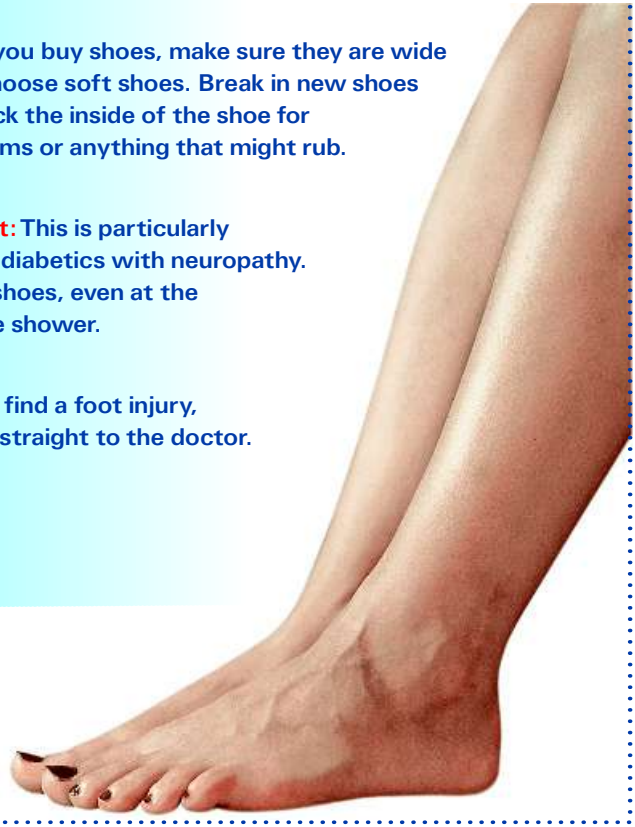
Skin and nail fungi: Fungal infections in people with diabetes should be treated by a doctor because they are entry points for germs and may lead to more serious infections.

Socks and stockings: Wear only soft socks or stockings made from natural materials (with a high proportion of cotton). Don't wear tight socks because these can block the circulation. Take care that there are no creases which may cause blisters.

Shoes: When you buy shoes, make sure they are wide enough and choose soft shoes. Break in new shoes carefully. Check the inside of the shoe for prominent seams or anything that might rub.

Going barefoot: This is particularly dangerous for diabetics with neuropathy. Always wear shoes, even at the beach or in the shower.

Injuries: If you find a foot injury, it's best to go straight to the doctor.



6 What else to consider

6.1 Urinary tract infection – particularly common in women with diabetes

Many women with diabetes suffer especially frequently from urinary tract infections. These are 2–4 times more common than in women without diabetes. For men with diabetes there seems to be no such increased risk for this type of infection.

Some urinary tract infections are not noticeable; they are detected by the doctor during a routine check for bacteria in the urine. This form is known as 'asymptomatic bacteriuria'. Frequently, however, the typical pains associated with such an infection are felt.

While it is not clear whether it is worth treating asymptomatic bacteriuria with antibiotics, as soon as symptoms are noticed – or if the infection reaches the kidneys – a course of antibiotics should be taken. This is particularly important when the kidney has already suffered some damage. At the end of the treatment, the urine should be tested again, to be certain that the infection has been cleared successfully.

Characteristic symptoms of a urinary tract infection:

- **Permanent need to urinate without much urine being passed.**
- **A feeling of burning when urinating.**
- **Pain in the bladder region.**
- **If there is additional fever or pain in the region of the kidneys, you should suspect that the upper urinary tract and the kidneys may also be infected.**

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If the infection continually reappears, at intervals of several weeks, the underlying cause should be sought: this might be bladder or kidney stones, an anatomical defect of the urinary tract or pockets in the bladder where urine might accumulate.

Diabetic neuropathy may also be a cause of frequent infections, if the damage means that the bladder is not emptied properly and residual urine is retained, which acts as a breeding ground for bacteria. The urine may even back up into the kidneys, adversely affecting their function. Because the concurrent nerve damage leads to loss of sensation and therefore no feelings of pain, the patient may remain unaware of all this for some time.

A urological examination should be undertaken to determine whether there is any obstruction of the urinary flow, such as an enlarged prostate or narrowing of the urethra. If these are excluded, one can try to empty the bladder through regular urination 'by the clock', i.e. every 3–4 hours, and to train it to empty properly again through tightening of the abdominal muscles. A class of drugs that acts on the autonomic nerves controlling the bladder, the parasympathetic mimetics, can help. If the bladder function cannot be fully restored by these methods, eventually a catheter must be inserted or the patient has to undergo an operation.

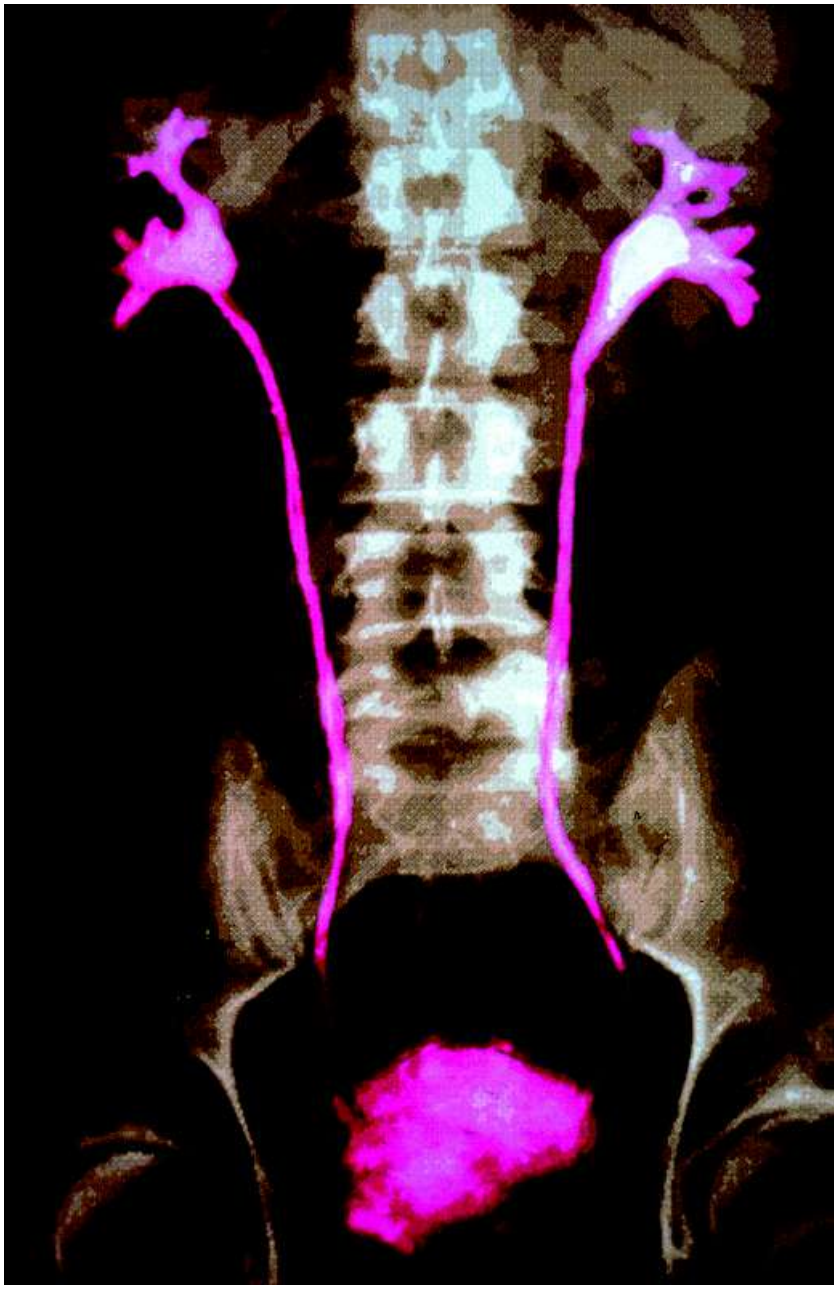

Figure 6.1 An X-ray image: the ureters connect the kidneys (top) with the bladder (below).

6.2 X-ray examinations – contrast agents may be dangerous in patients with kidney failure

Today, to make a given organ, such as the intestine or urinary tract, more clearly visible using X-rays, people are often given a contrast agent. But in people who already have kidney impairment, these diagnostic materials should be used only reluctantly because of the danger that the contrast agents will cause additional damage to the kidneys. A worsening of kidney function after administration of such contrast agents can be detected by a rise in the amount of creatine and urea in the serum. This rise is usually transient and after a few days kidney activity has returned to its normal value. Sometimes, however, these blood parameters stay high, which indicates that more permanent damage has been done to the kidneys.

Precautions to be taken during X-ray examinations

The first priority is to ask whether an examination using a contrast agent is absolutely necessary or whether another less stressful diagnostic method, such as ultrasound, could be used.

If the use of a contrast agent cannot be avoided, care should be taken that the body is at no time dehydrated. If insufficient fluid is available in the body, this will lead to concentration of the contrast agent in the kidneys, which increases the detrimental effect. You should therefore drink a lot before and after such an examination. The fluid reservoir of the body can be replaced via a saline infusion.

High blood sugar levels have a dehydrating effect on the body as it tries to remove the excess sugar by excretion through the kidneys. Before an examination using contrast agents, you should therefore pay extra attention to controlling your blood sugar. It has also proved beneficial to stop taking ACE inhibitors and possibly other types of medication (such as antirheumatic drugs). These may be started again one or two days after the examination. Biguanides (metformin) should also be stopped two days before the examination. This is a precaution, so that if the contrast agent does cause kidney damage, the concentration of the biguanide in the body does not increase, leading to a dangerous acidosis (see Chapter 4).

If an X-ray examination with a contrast agent is necessary, even in the presence of marked kidney impairment, it is advisable to remove the contrast agent by dialysis as quickly as possible after the examination.

6.3 Dental problems in people with nephropathy

Inflammation of the gums (gingivitis) and surrounding areas (parodontitis) is widespread in the population. Young adults already have, on average, 17 teeth with decay and fillings; only half still possess all their teeth! The main causes are poor oral hygiene and bad tooth-brushing technique, through which the bases of the teeth are exposed. This makes it easy for bacteria to attack the roots of the teeth. By middle age, 40–80% of people already have caries in the roots of their teeth!

Figure 6.2 Good care of your mouth and teeth can prevent complications.

Statistically, people with diabetes do not do well in terms of dental health. Problems with the teeth and gums are three times more frequent than in people of the same age with normal metabolism; decay appears earlier and is more pronounced. Harmful bacteria are often found in pockets in the gums, especially at times of poor metabolic control.

What do teeth have to do with the kidneys?

It has been known for a long time that pus in the roots of the teeth can be a forerunner of various illnesses or complaints: fever, pain in the joints, changes in the blood composition, and inflammation in other organs infected by the bacteria, including the kidneys. Infection of the kidneys is indicated by the presence of red and white blood cells in the urine, as well as protein in the urine and other specialized changes. It is not known how often this occurs. When there is frequent oral infection, the risk to the kidneys is certainly considerable, particularly when the kidneys are already damaged and therefore more susceptible. Exposure to this additional risk is totally unnecessary, since it can easily be avoided by good mouth and dental care – something that is not difficult to achieve.

Another point worth noting concerns fillings made from amalgam. The pros and cons of materials containing mercury have been debated since these compounds were first used and do not need to be repeated here. If you have impaired kidney function and thus a reduced ability to remove toxins from your body, you should ask whether any amalgam fillings can be replaced with those made from other materials.

7 Prospects yesterday and today

Just a few decades ago, the diagnosis of nephropathy was a reason to be very concerned about the future. People who were found to have a high level of protein excretion in the urine (macroalbuminuria) in the 1960s or 1970s could count on needing to start dialysis within months or at most one year. On average, they would lose 15–30% of their remaining kidney function every year (Figure 7.1).

Thanks to modern management techniques the progression of nephropathy can be arrested

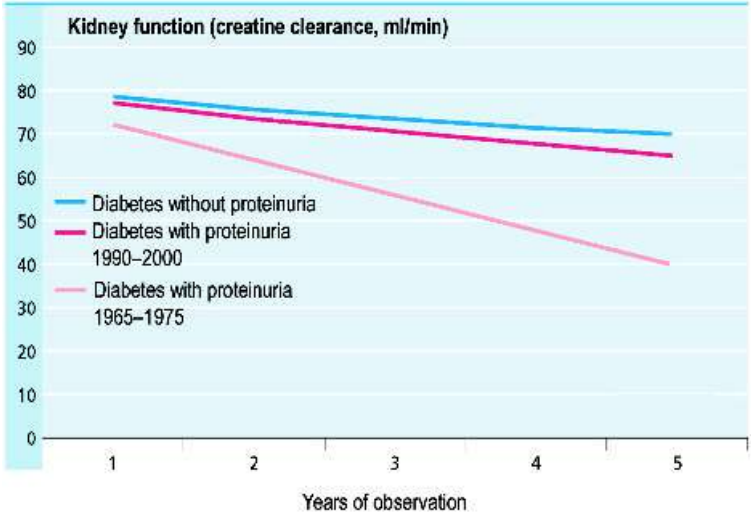

Figure 7.1 In the 1960s and 1970s kidney function generally deteriorated rapidly after the first appearance of protein in the urine. In the 1990s this was no longer the case: the reduction in kidney function over the years was almost comparable to that observed during normal ageing. [14]

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Today, not only is kidney impairment detected much earlier – at the stage of microalbuminuria – but the outlook for those affected is much brighter. Over the last 20 years, the prospects for people with nephropathy have improved more than for almost any other illness. This has been possible because in that time we have learned so much about how nephropathy develops and progresses and, above all, how we can control it. Nowadays, there is intensive diabetes management, more and better drugs are available to lower blood pressure and the options for dialysis are markedly improved. The pleasing consequences are shown by the results of a comparative study. In the 1960s and 1970s, two-thirds of 28 patients observed after they were found to have increased protein excretion died within five years. The most frequent cause of death was cardiovascular disease, such as a heart attack or stroke, and kidney failure, because at that time there were barely any opportunities for dialysis. In the 1990s, all of a similar cohort of 23 patients survived the six-year observation period, without the need for dialysis (Figure 7.2).

Patients and doctors today have many means at their disposal to recognize diabetic nephropathy early and to ensure good control of blood sugar levels and blood pressure – the two most important influencing factors. If these opportunities are taken, it is possible,

The life expectancy of people with Type 2 diabetes and nephropathy has increased

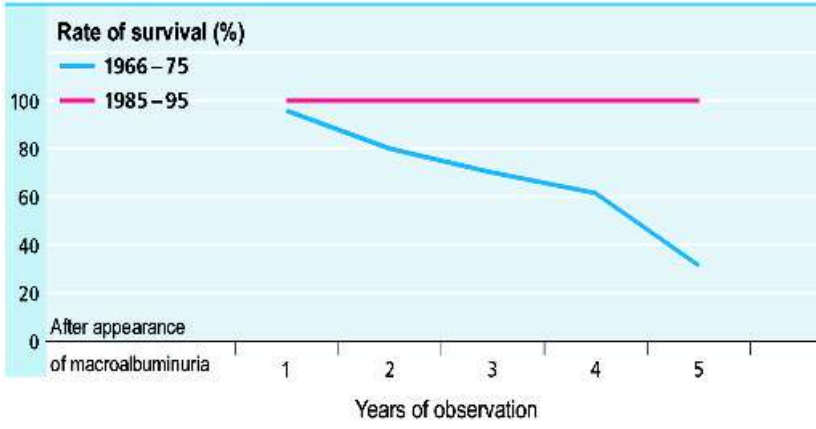

Figure 7.2 In the 1960s and 1970s two-thirds of patients were dead within five years of diagnosis with macroalbuminuria. In the 1980s and 1990s the management outcomes were greatly improved: in this study all the patients survived the first six years of follow-up. [14]

The course of typical diabetic complications can best be described by comparison with a large tanker at full speed at sea – it takes many miles and a long time to stop it.

even when microalbuminuria is already present, to reduce the loss of kidney function to the appropriate rate for that age (see Figure 7.1). For long life expectancy, additional factors come into play, such as better options for intensive cardiological therapy – the mortality rate from heart attacks has fallen over recent decades – and the improved opportunities for managing metabolic or blood-clotting disorders.

To benefit from all this progress, you have to make use of all these possibilities over the long term. As a patient you have an important role to play – with your doctors and nurses – in the management of your diabetes. You must take a high degree of responsibility for your condition. For this, participating in a good diabetes education programme is essential; not just once, but repeatedly during the lifetime of your diabetes.

8 Special situations

8.1 Pregnancy and diabetic nephropathy

Today, it is just as possible for a woman with Type 1 diabetes to become pregnant and have a healthy baby as for someone without diabetes. This was not always the case. Previously, because there were fewer methods for achieving good blood sugar control, women with diabetes not only risked increased complications during their pregnancy and labour, but their children were frequently susceptible to deformities and health problems after birth. The fact that this risk no longer exists for diabetic women is, above all, thanks to the possibility of intensive diabetes management before and during the pregnancy, as well as better observation and treatment during and after the birth.

What to do before getting pregnant

- Diabetes control should already be optimal. Then the risk of a birth defect, which may arise during the first few weeks of pregnancy when the blood sugar level is high, can mostly be avoided. This means, however, that the timing of the pregnancy should be planned as accurately as possible, so that sufficient time is available to establish good blood sugar control through intensive therapy.
- The retina in the eye should be examined. If there are no signs of retinopathy (see Section 5.1), checks every three months are sufficient. If retinopathy is already present, this gets worse in half of such affected women during pregnancy. Sometimes, early laser treatment of the damaged eye before or even during the pregnancy

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may be advisable. The development of the eye damage should be closely monitored by an ophthalmologist.

- Protein excretion and blood pressure should be tested before and at the start of the pregnancy.

What to do during the pregnancy

- Blood sugar levels must be tightly controlled, to keep the risk to mother and child as low as possible. For pregnant women, the limits are particularly strict: the blood sugar level should stay just below 90 mg/dl and if possible should not exceed 120 mg/dl after eating.
- Blood pressure, urine (tests for protein excretion and for urinary tract infections) and blood should be monitored regularly. Body weight is also important. If this increases very rapidly and by too much, it may be evidence of a dangerous complication that threatens both mother and child, known as EPH syndrome. EPH stands for oedema ('edema' in American English; water retention in the tissues), proteinuria (increased protein excretion in the urine) and hypertension (high blood pressure).
- The development of the baby should be monitored regularly using ultrasound.

What you should know:

The priority for the successful outcome of your pregnancy is that you are motivated and prepared to take part in the management of your diabetes and ready to take on a high degree of responsibility yourself. To achieve this, you need to participate in a good diabetes education programme that includes detailed information relevant to pregnancy. At this time, you must work closely with your diabetologist, obstetrician and midwife.

When diabetic nephropathy is already present

Even when a woman already has diabetes-induced kidney damage, a successful pregnancy and the birth of a healthy child are still possible. In principle, the same rules for management should be followed as for all other women with Type 1 diabetes, but the presence of diabetic nephropathy can complicate the pregnancy and endanger both the mother and child.

If micro- or macroalbuminuria is present before the start, protein excretion will usually increase during the pregnancy. Rises of four-fold or more are possible – but in most cases this should not be a reason to worry. After the pregnancy, the rate of protein excretion nearly always falls again. It is important, however, to test the rate of albumin excretion regularly during the pregnancy because an unusually high value may warn of the onset of the feared complication, EPH syndrome. A woman who has microalbuminuria before her pregnancy has a 12% greater risk of developing EPH. If this is not recognized early or is not treated, it can be life-threatening for the mother and her baby.

Blood pressure also rises significantly in most pregnant women who have impaired kidney function – if it wasn't already high because of the nephropathy. It must be lowered again and today there are many drugs available to achieve this. ACE inhibitors, which are usually the first choice drugs for patients with nephropathy, may not be given during pregnancy. This is because they may have adverse effects on the organ development of the child. The same is true for calcium antagonists. Thus, a woman who has been taking any of these drugs should change her regime before getting pregnant. Of course, it is particularly important to measure your blood pressure yourself at home, every day during your pregnancy. Long-term (24-hour or overnight) measurements are also advisable.

What you can do for yourself:

Women with diabetes today are able to have a child if they so wish, even when they already have micro- or macroalbuminuria. As long as kidney function stays in the normal range, there is no great risk for either the mother or child. It is, however, very important for women with diabetes (with or without nephropathy) to plan the pregnancy carefully and make adequate preparations. The preparatory phase should be used for special education and for optimizing your blood sugar and blood pressure control. Go to see a specialist doctor or attend a specialist centre. With good management and plenty of cooperation from yourself, the chances of having a healthy child are just as good as for all other women.

What happens to kidney function during pregnancy?

This is a very important question. As a woman with diabetes who already has early kidney impairment, must I count on having to undergo dialysis after the birth? Up to now, very few studies have addressed this. They have shown that in about half of women there is no worsening of kidney function during pregnancy. In the other half, kidney function deteriorates but improves again after labour. Which group you belong to is strongly dependent on the state of your kidneys before the pregnancy:

- If your kidney function is only lightly impaired, with a serum creatine concentration of less than 2 mg/dl, the risk of it worsening seems to be slight.
- If you already have significant kidney damage, you must expect further impairment, which may even continue after the pregnancy. In a study from the 1980s and 1990s, one in four women with diabetic nephropathy needed dialysis within three years of giving birth.

Children of women with diabetic nephropathy often develop more slowly during the pregnancy and have a lower birth weight. The degree of growth retardation depends above all on the kidney function of the mother. To avoid threatening complications in women with diabetic nephropathy, labour is often induced early or the child is born by Caesarean section. Although these babies more frequently need to be kept in intensive care, the survival rates in specialized centres are today just as good as for children of non-diabetic mothers.

8.2 Sport and diabetic nephropathy

Physical activity has always been one of the pillars of diabetes therapy. This is not only because of its beneficial effects on lowering blood pressure and improving the blood lipid profile, but also because of its action of promoting a general sense of well-being. Sport and physical activity are fun, they demand strength and endurance and thereby increase your self-confidence. In addition, people who are overweight find it easier to lose weight when they undertake regular exercise.

People with diabetic nephropathy usually have hypertension as well as diabetes. Physical activity causes a rise in blood pressure in everyone, which is steeper when hypertension is already present. This obviously depends on the type of exercise. It is well known that blood pressure rises much more during strength and speed training, such as lifting weights or a short fast run, than during endurance training, such as cycling, jogging or swimming. Sports that lead to short-term high stress are not suitable for people with hypertension because of this peaking in blood pressure, and should be avoided. On the other hand, endurance training, also known as cardiovascular training, has long-term beneficial effects on blood pressure. After several weeks of regular training the resting blood pressure falls by about 5–10 mmHg; the rise in blood pressure under stress also becomes much smaller. The following pages show some good types of exercise for people with diabetic nephropathy and some that are not recommended.

Rules for exercising with hypertension and nephropathy

The resting blood pressure should be less than 140/90 mmHg. Because the increase that will occur during an exercise programme cannot be predicted, it is best to undergo an ergometric examination by a doctor beforehand. This might be walking on a treadmill or cycling on an exercise bike. This enables the doctor to measure the rise in your blood pressure and your pulse rate under controlled conditions.

For healthy men and women, the upper limit for the normal rise in blood pressure under stress is 200/100 mmHg. If the blood pressure rises above 250/120 mmHg, the exercise should be stopped.

Recommended sports for people with high blood pressure:

- Jogging
- Running
- Cycling
- Swimming
- Riding an exercise bike
- Social rowing or canoeing
- Gentle hill-walking
- Golf
- Cross-country skiing on the flat

Sports permitted for young people with well-controlled diabetes after discussion with their doctor:

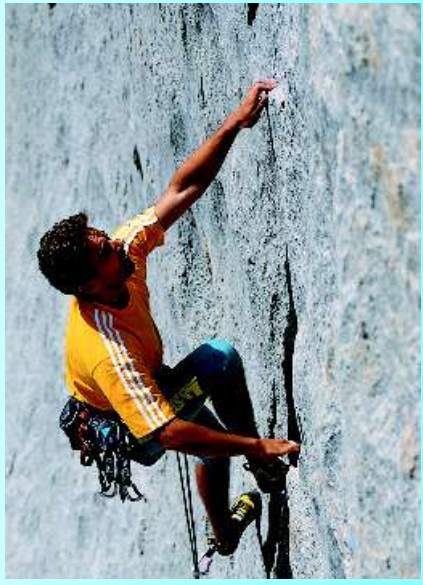
- Football
- Handball
- Basketball
- Volleyball
- Tennis
- Table tennis
- Badminton
- Surfing
- Horse riding
- More strenuous hill-walking
- Ice skating

Less suitable sports or gym exercises:

- Squash
- Knee bends
- Bench pressing
- Downhill skiing or snowboarding
- Mountain biking

Sports not recommended for people with hypertension:

- Weightlifting
- Wrestling
- Boxing
- Gymnastics using apparatus
- Bodybuilding
- Ten-pin bowling
- Rock climbing
- Diving
- White-water canoeing or rafting



For patients with nephropathy, there is at present no 'official' guideline for the rise in blood pressure under stress. This must be considered individually. For example, if someone has only microalbuminuria and no further heart or circulatory complications, they should be able to follow the values given for healthy people. If, however, macroalbuminuria is present and the person is also known to have retinopathy or coronary artery disease, such peak blood pressure values are certainly too high. Before starting a training programme, it is best to get your blood pressure under better control and to start exercising very carefully. After all, it is no problem today to measure your blood pressure yourself at any time and any place – so why not when exercising?

Another frequently used method to guide the intensity of your training is to measure your pulse rate.

As a rule of thumb, the optimal pulse rate during exercise is: 180 minus your age (in years).

The calculated pulse rate should be reached during endurance training but not exceeded. Something to watch is that beta blockers and some calcium antagonists that are used to treat hypertension can slow the pulse rate. The optimal pulse rate during exercise should then be about 15–20% lower than as calculated above.

Figure 8.1 It is advisable to discuss your planned sporting activities with your doctor and to join a sports group. There are clubs, adult classes or other facilities in most towns that offer special exercise programmes for people with diabetes or hypertension.

9 When kidney function fails . . .

Typical problems

When the kidneys stop working properly, the body can no longer clear itself of toxins and excess water. The typical symptoms of kidney failure then appear – earlier in some people, later in others:

- As water excretion falls, so does the volume of the urine. Water is retained in the body in a condition known as oedema. This usually occurs first in the ankles: they swell and it is easy to make a 'thumbprint' in them. Later the whole leg may become swollen. If there is also water retention in the lungs, breathlessness occurs and this is a warning sign of renal failure.
- The skin is pale, because the density of the red blood cells falls. This is because the kidneys can no longer make enough erythropoietin, a hormone that is needed to make red blood cells in the bone marrow.
- The calcium profile may rise: in some people this leads to cramps and muscle weakness in the legs. A very high calcium profile can cause life-threatening disturbances to the heart rhythm (cardiac arrhythmias); it should therefore be monitored regularly.
- One consequence of kidney failure is that the concentrations of calcium and phosphorus in the blood change. This can lead to changes in the bones, known as renal osteopathy. These develop because the kidneys are an important source of vitamin D, which is

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needed to help absorb calcium from the food in sufficient quantities and to strengthen bone. In addition, the low calcium concentration in the blood stimulates the body to produce more parathyroid hormone, which pulls calcium out of the bones and thereby contributes further to skeletal weakening.

- Phosphorus metabolism is also disturbed. Phosphorus is found in the bones and, like calcium, is an important component of enzymes and cellular proteins. It is taken up in food and excreted via the kidneys. When kidney function is impaired, the amount of phosphorus in the blood rises. This high phosphate profile lowers the calcium profile and thereby triggers an automatic increase in the release of parathyroid hormone, which controls phosphorus excretion via the kidneys. But this induces more calcium to be resorbed from bone, which over time leads to softening of the bones. This can manifest itself as bone pain and spontaneous breaks. These changes in mineral content are responsible for a variety of other symptoms in people with kidney failure, including itching, chalky deposits in the joints and muscle weakness.
- The rising concentrations of urea and toxins, which are no longer excreted properly, result in frequent tiredness followed by apathy. You experience disturbed sleep and loss of concentration, you lose your appetite and may suffer from nausea and vomiting. Women experience problems with menstruation, often missing periods completely. In men, a possible consequence is impotence.
- The toxins in the body may give rise to nerve damage, leading to burning sensations in the soles of the feet, pain in the legs, particularly at night, or muscle weakness. The technical term for this is ‘uraemic polyneuropathy’.

What you can do about these problems

The amount of urea in the blood can be reduced by eating less protein. The water content of the body can be reduced by cutting your salt intake, as explained in Section 4.3. These dietary modifications are particularly important at the stage of terminal renal insufficiency.

In addition, you should take care not to consume too much phosphorus in your diet. This is not easy, because phosphorus is

present in almost all foodstuffs. Foods particularly rich in phosphorus are those comprising mainly protein, such as meat, milk and dairy products, as well as nuts, especially almonds, and ready-made meals. Dietary measures are usually not enough to normalize the phosphorus concentration in the blood. Drugs known as phosphate binders have to be taken with meals. These bind to phosphate in the food and prevent it being absorbed by the body; instead it is excreted in the faeces.

So that the calcium profile does not rise too high, you should not eat too much calcium in your diet. Calcium-rich foods include vegetable and fruit juices, dried fruits, nuts, mushrooms and precooked potato products.

Although these recommendations may sound complicated at first, in practice it is not that difficult to follow them. If you combine different foodstuffs, it is still possible to prepare varied and tasty meals. There are plenty of special cookbooks that can help and you could also obtain special education about nutrition.

The lack of red blood cells, known as anaemia, is today easily treated by administration of artificially produced erythropoietin. The water retention can be combatted with diuretics, which stimulate urination.

By these methods, the complaints caused by terminal renal insufficiency can be at least partially improved. All the same, the appearance of these symptoms is clear evidence that the kidneys can no longer perform their allotted functions themselves but need help – kidney replacement therapy.

It is understandable that many people try to postpone starting dialysis for as long as possible, but that does not do any good. Although there are no general guidelines for the exact time at which to start replacement therapy, it should not be delayed for too long. Personal well-being and the success of the dialysis treatment are both better when the patient has not lost too much weight by waiting too long and become totally discouraged by the unpleasant symptoms of kidney failure.

9.1 The different possibilities for kidney replacement therapy

On the one hand, you can take the phrase 'kidney replacement' literally: some people do actually receive, via transplantation, a new, well-functioning kidney. More often, sometimes only temporarily while a person waits for a suitable organ to be found, kidney replacement means dialysis. This process removes toxins and excess water from the blood. Two different types of dialysis are relevant: peritoneal and haemodialysis.

Peritoneal dialysis

In peritoneal dialysis, the lining of the patient's own abdominal wall is used as the filter. Clean dialysis fluid is passed into the abdominal cavity through a narrow tube or catheter that is permanently fixed in the abdominal wall during a surgical procedure. Toxic substances and excess water gradually, over several hours, pass from the blood into this dialysis fluid. Once these waste products have accumulated in the dialysis fluid, this can be removed via the catheter and replaced with clean fluid. Such a procedure needs to be performed three or four times a day, each time for half an hour. Overnight the dialysis fluid can stay longer in the abdomen (Figure 9.1).

This type of peritoneal dialysis is called CAPD (continuous ambulatory peritoneal dialysis). An alternative is APD (automatic peritoneal dialysis), in which abdominal dialysis is performed only overnight by a machine operating automatically. This has the advantage that you are not hindered during the day.

Peritoneal dialysis has both advantages and disadvantages. The main advantage is that you remain mobile. You can undergo dialysis by yourself at home, at work, on holiday, on long journeys or even in an aeroplane. Obviously, it is essential to have proper education and training by a specialized care team. Travel domestically and abroad is possible, without particular problems. You just have to ensure that sufficient supplies of key materials, especially the dialysis fluid, are available or send them ahead. A good dialysis centre will usually have addresses and contact details for dialysis centres near your holiday resort.

Problems may arise with peritoneal dialysis through infection and inflammation of the abdominal wall or at the site of insertion of the

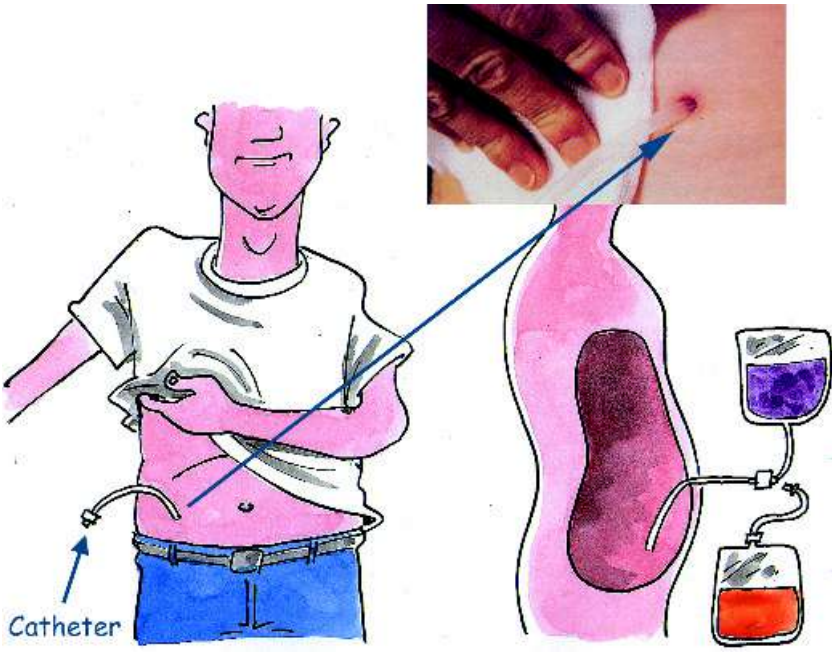

Figure 9.1 In peritoneal dialysis the abdominal wall is used as a filter. The dialysis fluid is passed through a plastic tube (catheter) into the abdominal cavity. This catheter is inserted in the abdominal wall during a small operation. About 15 cm of the tube stays outside the body and this is attached to the bag containing the dialysis fluid. Dialysis takes place as long as the dialysis fluid remains in the abdomen. Water and waste products pass from the blood through the abdominal wall into the dialysis fluid, which is changed after a few hours.

catheter. It is important to recognize such problems early and report them to a doctor immediately. Most infections can be treated at home with antibiotics. If there are no particular problems, it is sufficient for a patient on peritoneal dialysis to visit the dialysis centre only once a month, to have the blood parameters and general health checked.

Is peritoneal dialysis suitable for you?

There are several illnesses that are not compatible with peritoneal dialysis. These include seriously overstretched lungs, because the fluid in the abdominal cavity can hamper breathing. In addition, patients who have suffered ruptures, for example to the stomach wall, or have

What you should know:

Under both types of dialysis the dietary measures described here may be partially relaxed. You should undergo a personal dietary assessment. Insulin therapy must also be adjusted to the dialysis regime, that is, the number and duration of dialysis sessions and the type of dialysis fluid. Renewed diabetes education is necessary here as well.

scars in their abdominal cavity from operations or who have intestinal disease are not suited to this type of dialysis.

Haemodialysis

During haemodialysis, the toxins and excess water are removed from the blood through a filter that is outside the body, inside a dialysis machine. The blood is pumped into the machine from a large vein, purified there, then returned to the body.

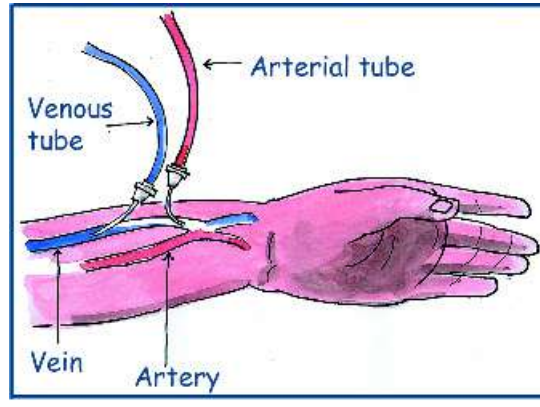

Figure 9.2 Before haemodialysis can be performed, a small blood entry point has to be created surgically. The surgeon links a vein and an artery in the lower arm together. During haemodialysis blood flows out of the body through the arterial needle into the dialysis machine. It is then cleaned and finally returned to the body via the venous needle. At any one time, only a small amount of blood is outside the body. After the treatment, both needles are removed and a plaster placed over the insertion point.

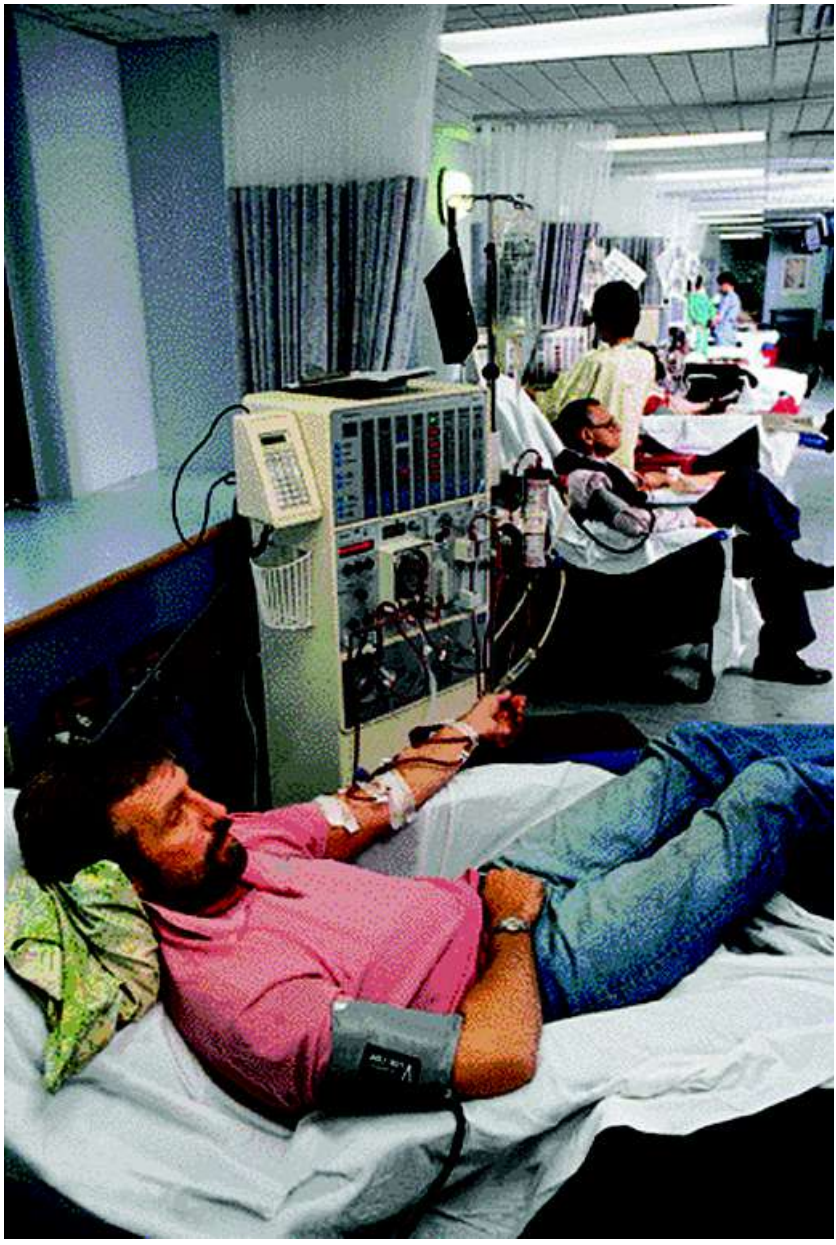

Figure 9.3 Haemodialysis in a dialysis centre.

For haemodialysis to be possible over a long period, a good entry point to the circulation must be maintained. Veins all have very soft walls which would give way and close themselves if you tried to keep them permanently open for dialysis. Therefore, a small operation is performed to create an artificial opening (Figure 9.2). For this, a vein in the wrist is usually linked to an artery, creating a shunt. The blood, which is under high pressure in the artery, then flows directly into the vein and widens it. In this way, sufficient blood flow for the dialysis is ensured. In the machine, the blood is purified over a filter. Toxins and excess water pass across the filter membrane into the dialysis fluid and are thus removed from the body.

The dialysis is usually performed three times a week for 4–6 hours. The patient either travels to a dialysis centre or has a machine at home for his or her own use (Figure 9.3).

Haemodialysis patients may also travel, because there are dialysis centres in major towns in all countries, where you can make an appointment in advance.

What to look out for

People with diabetes often have hard vessels in their arms. It is therefore important that a shunt is created early, perhaps even months before dialysis is started. This allows the vessel entry point to establish itself firmly.

Dialysis patients are taught to take care of the vessel entry point. If it is necessary to draw blood, this should be taken from the other arm; the blood pressure should also be measured only in the other arm. When gardening or exercising, it is important to make sure that no pressure is exerted on the shunt and that it is not damaged.

Two main problems may arise with the blood entry point: clots may form or it may become infected. The blood flow in the region of the shunt must be checked daily. The patient can do this by probing the shunt: if the blood flow is good, a buzz will be felt. You can also listen to the blood flow using a stethoscope.

Skin infections can result from wounds or scratching with the fingernails. Thorough cleaning is therefore essential. Every patch of redness or dampness or other sign of infection should be reported to your doctor as quickly as possible.

Transplantation

Today, kidney transplantation, eventually combined with transplantation of a pancreas or just islet cells, is undoubtedly the best form of kidney replacement therapy. The new kidney is usually implanted in the pelvic region; the pancreas may be put into the pelvis or the abdomen.

One problem when an entire pancreas is transplanted is that this organ produces not just insulin and other hormones but also pancreatic enzymes that are usually secreted into the intestine. With a newly transplanted pancreas, these enzymes have to be directed into the intestine or the bladder. A combined kidney and pancreas transplant is relatively rare: about 700–800 such operations are performed worldwide each year, almost exclusively in people with Type 1 diabetes. If it is successful, the patient is relieved of the need for dialysis and his or her diabetes is also cured, so that there is no longer a need to inject insulin.

The success of combined kidney and pancreas transplants has improved over the last 10 years. In the first year after transplantation, about 80–85% of patients are insulin-independent; this falls to about 63–75% of patients after five years. The life expectancy is much better after a transplant than on dialysis. However, the recipients do

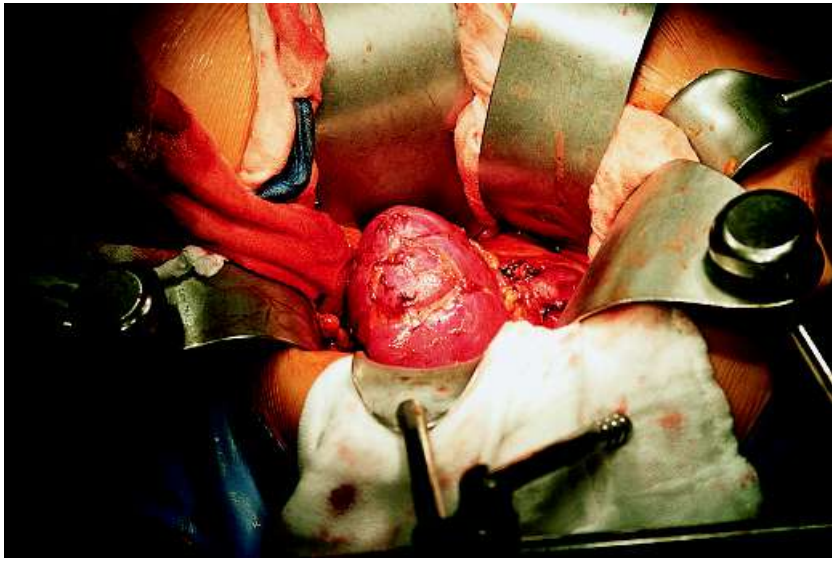

Figure 9.4 Pancreas and kidney transplantation.

have to take immunosuppressant drugs for the rest of their lives to prevent rejection of the new organs.

There is currently much less experience with the transplantation of islet cells than with an entire pancreas. In principle, this is the ideal procedure, because only the islet cells that make the insulin – the so-called beta cells – are transplanted. The advantage is that there is no extra production of digestive enzymes. In addition, the method is very simple because the isolated islet cells can be injected into the hepatic vein. They attach there and grow, making insulin that passes directly into the circulation, where it is needed.

Unfortunately, the long-term results with this procedure are not yet very good. The islet cells are often destroyed again and the insulin produced by them is often not sufficient to cure the diabetes, so that the patient has to continue to inject insulin. There is a promising new development. In Canada, they have succeeded in preventing the rejection of the islet cells with new immunosuppressant drugs and thereby greatly improved the outcome of islet cell transplantation. This method is being tested in studies worldwide.

Is a transplant suitable for you?

A transplant is not suitable for everyone. Intensive tests are required to see who has a good chance of successfully coming through such major surgery. People who suffer from other accompanying diseases, and in whom the heart may be damaged, may not withstand the stress of the operation and the consequent suppression of the body's defence system, the immune system. Which form of kidney replacement therapy is best for an individual must be considered very carefully, in consultation with the nephrologist, the surgeon and the diabetologist.

What you can do for yourself:

Kidney replacement therapy makes it possible today for people with diabetes to enjoy an almost undiminished quality of life, even when their kidneys are seriously damaged. But starting such therapy makes a major impact on your lifestyle at the time. This can be reduced by various means.

First, it is important to plan the replacement therapy in good time with your nephrologist. That is the only way to decide on the procedure most suitable for you in relative peace.

Second, you should learn as much as possible about the condition. Only someone who understands the basis of dietary recommendations, drugs and dialysis procedures can take responsibility for their own treatment. This helps you to accept your new lifestyle and it will soon become routine.

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Calculation of creatine clearance by age, body weight and serum creatine concentration

The formula is:

$$\text{Creatine clearance (ml/min)} = \frac{(140 - \text{age}) \times \text{body weight (kg)}}{72 \times \text{serum creatine concentration (mg/dl)}}$$

Because of the different muscle mass of men and women, the calculated value must be multiplied by 0.85 for women.

This is not so complicated, as shown by the following example:

You are 60 years old and weigh 76 kg. Your serum creatine concentration is 1.2 mg/dl:

$$\text{Creatine clearance (ml/min)} = \frac{(140 - 60) \times 76}{72 \times 1.2}$$

$$= \frac{6080}{86.4}$$

$$= 70.3$$

Thus, the creatine clearance rate for a man is 70.3 ml/min. For a woman, the value must be multiplied by 0.85:

$$70.3 \times 0.85 = 59.7$$

Therefore, the creatine clearance rate for a woman with these characteristics is 59.7 ml/min.

A creatine clearance rate of 70.3 ml/min for the man indicates mild impairment of kidney function. For the woman, a rate of 59.7 ml/min

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Table A1 Cuff sizes for the measurement of upper arm blood pressure in adults

Upper arm circumference (cm)	Rubber portion of the cuff width × length (cm)*
Less than 35	12–13 ×24
33–41	15×30
More than 41	18×36

*The lengths given are minimum sizes.

shows that there is already considerable damage to the kidneys (see Table 2.1, page 9).

Blood pressure-lowering drugs

These can be divided into different classes, according to their mode of action.

ACE inhibitors

ACE inhibitors (angiotensin-converting enzyme inhibitors) block the action of an enzyme that produces angiotensin II. This is a hormone that narrows the blood vessels and thereby raises the blood pressure. People treated with an ACE inhibitor make less angiotensin II and their blood pressure falls.

There are several ACE inhibitors, which differ mainly in their duration of action. Captopril, the first to be used, works for only a short time and must usually be taken three times a day. The other ACE inhibitors work for longer and therefore have to be taken only once or twice a day.

All ACE inhibitors are well tolerated; however, care should be taken when they are given in the presence of serious kidney damage. The most frequent side-effect is a dry cough, that is often transient. If the cough persists, an alternative treatment to the ACE inhibitors is to give one of the so-called angiotensin 1 (AT1) receptor blockers (also known as angiotensin II receptor antagonists).

Table A2 List of the ACE inhibitors available in the UK

Generic name	Brand names
Captopril	Acepril, Acezide, Capoten, Capozide
Cilazapril	Vascace
Enalapril	Innovace, Innozide
Fosinopril	Staril
Lisinopril	Carace, Zestoretic, Zestril
Moexipril	Perdix
Perindopril	Coversyl
Quinapril	Accupro, Accuretic
Ramipril	Triapin, Tritace
Trandolapril	Gopten, Odrik, Tarka

AT1 receptor blockers/angiotensin II receptor antagonists

Angiotensin II exerts its blood-raising effect via a receptor, the AT1 receptor in the muscle cells of the blood vessel wall. The AT1 receptor blockers, also known as angiotensin II antagonists, prevent angiotensin II binding to its receptor. This causes the blood pressure to fall. These drugs are often given when ACE inhibitors cannot be tolerated by the patient.

Diuretics

These drugs cause sodium and water to be excreted from the body, which leads to a fall in blood pressure. If they are taken for a long time, the resistance of the blood vessel walls decreases, which means that the fall in blood pressure lasts for longer.

The most frequent side-effects of diuretics are a fall in the potassium concentration in the blood and a rise in the amount of uric acid in the blood. These values must therefore be monitored carefully.

A special class of diuretics are the so-called 'potassium-sparing' diuretics. Their action is weaker but the body does not excrete as much potassium. Potassium-sparing diuretics cannot be given when the kidneys are badly damaged. The most important side-effect is an increase in the amount of potassium in the blood.

Table A3 List of the AT1 receptor blockers/angiotensin II receptor antagonists available in the UK

Generic name	Brand name
Candesartan	Amias
Eprosartan	Teveten
Irbesartan*	Aprovel, CoAprovel
Losartan*	Cozaar
Telmisartan	Micardis
Valsartan	Diovan

*These substances have been shown in clinical trials to have special kidney-protecting effects in people with diabetes.

Beta blockers

Beta blockers lower blood pressure by acting on the autonomic nervous system. This is the part of our nervous system that is not under conscious control. It operates 'automatically' and regulates various bodily functions. In the circulation, activation of the sympathetic nervous system raises the blood pressure: the heart rate increases and the blood vessels are narrowed. Beta blockers restrict these effects of the sympathetic nervous system: the heart rate slows down and the constricted blood vessels relax. This allows the blood pressure to fall.

The beta blockers can be divided into those that act primarily on the heart (cardioselective) and those that act chiefly on other bodily functions – they affect organs such as the lungs or processes such as metabolism. Diabetics should be treated with cardioselective beta blockers in the first instance. This is also true for the treatment of coronary heart disease. The beta blockers act for between 12 and 24 hours and therefore must be taken usually once or twice a day.

Beta blockers are not suitable for patients who have a slow heart rate (less than 60 beats/minute) or a lung condition, such as asthma. Before beta blockers are prescribed, the patient should have an ECG (electrocardiogram) to make sure that there are no problems with cardiac excitation. Apart from slowing of the heart rate, the most important side-effects are tiredness, cold feet and sleep disturbances;

for men there is also a risk of impotence. These side-effects are generally dose-dependent and rarely appear at the standard doses.

When someone is taking a beta blocker, there is a risk that the symptoms of hypoglycaemia will change. Patients should understand this, but it is not a reason not to take a beta blocker. If you have to stop taking a beta blocker, the dose should be reduced slowly, to prevent the sympathetic nervous system overreacting.

Calcium antagonists

Calcium antagonists reduce the amount of calcium in the muscle cells of the blood vessels. Because calcium is necessary for muscle tension, loss of calcium leads to relaxation and widening of the blood vessels and thereby lowers blood pressure. Calcium antagonists are very well tolerated and are prescribed often. The various antagonists differ in their duration of action. It is better to take a long-acting drug, so that you don't have to think about it several times a day.

The most important side-effect of these antagonists is an abnormally strong heartbeat and hot flushes; sometimes there is also mild water retention in the legs (oedema). Usually, these side-effects disappear after a few days.

Table A4 List of the cholesterol synthesis inhibitors available in the UK

Generic name	Brand name
Atorvastatin	Lipitor
Fluvastatin	Lescol
Pravastatin	Lipostat
Rosuvastatin	Crestor
Simvastatin	Zocor (also available as generic product)

Table A5 List of the fibrates available in the UK

Generic name	Brand name
Bezafibrate	Bezalip, Zimbacol
Ciprofibrate	Modalim
Fenofibrate	Fenogal, Lipantil, Supralip (also available as generic product)
Gemfibrozil	Lopid (also available as generic product)

Other substances

If the blood pressure-lowering drugs described above are not successful, there are other drugs that can be used. These are not among the first choice treatments because of their side-effects. They include dihydralazine, which works on the small blood vessels. The main side-effect is an increase in heart rate and the drug is therefore often combined with a beta blocker. Another drug is clonidine. This acts on the brain and sympathetic nervous system to reduce blood pressure. The main side-effects are a dry mouth and tiredness. This drug is therefore usually given at night so that these effects can be 'slept away'.

Diabetes and kidney organizations

Diabetes UK

Diabetes UK is the largest organization in the UK working for people with diabetes as well as professionals involved in their care. Their website provides almost all the information you need to know about living with diabetes in the UK.

Office: 10 Parkway, London NW1 7AA, UK
Tel: 020 7424 1000
Fax: 020 7424 1001
E-mail: info@diabetes.org.uk
Website: www.diabetes.org.uk

Diabetes Research and Wellness Foundation

This is an organization of diabetes patients, their families and friends who work together to help anyone who has diabetes to lead a healthy life.

Office: 101–102, Northney Marina,
Hayling Island, Hampshire PO11 0NH, UK
Tel: 023 9263 7808
Fax: 023 9263 6137
E-mail: drwf@diabeteswellnessnet.org.uk
Website: www.diabeteswellnessnet.org.uk

Diabetic Exercise and Sports Association

This US-based association provides information on many different kinds of exercise, how much you can and should do, and whether there are any limitations because of diabetes. You will also find other people who share your interests.

Office: 8001 Montcastle Drive, Nashville, TN 37221, USA
Tel: 001 800 898 4322
Fax: 001 615 673 2077
E-mail: desa@diabetes-exercise.org
Website: www.diabetes-exercise.org

The Diabetes Travel Information Website

This site is run by the staff at the Diabetes Centre in the Western General Hospital in Edinburgh. It is for people who enjoy travelling and have diabetes treated with insulin or those who are travelling with someone who has insulin-dependent diabetes. It is intended to provide tips and information to make your journey enjoyable and trouble-free.

Website: www.diabetes-travel.co.uk

National Kidney Federation

The Federation is a UK charity run by kidney patients for kidney patients. Its aim is to promote the welfare of persons suffering from kidney disease or renal failure and those relatives and friends who care for them.

Website: www.kidney.org.uk

The British Kidney Patient Association

The Association works to help meet the material and physical needs of the patients and their relatives and to lobby for more and improved facilities and increased Governmental funding, so that all patients may benefit from improvements in technology and pharmaceutical achievements. It also uses the media to raise awareness of the need for kidney donors and all problems resulting from the lack of them.

Office: BKPA, Bordon, Hampshire GU35 9JZ, UK
Tel: 01420 472021/2
Fax: 01420 475831
Website: www.britishkidney-pa.co.uk

The National Kidney Research Fund

The mission of the Fund is to improve the health and well-being of individuals living with kidney and related diseases, through funding research into improving the understanding of kidney and related diseases, their causes, treatment and management; working towards the relief of people with kidney and related diseases; and raising the awareness of kidney disease amongst the general public and healthcare professionals.

Office: Kings Chambers, Priestgate, Peterborough PE1 1FG, UK
Tel: 01733 704650
Fax: 01733 704699
E-mail: enquiries@nkrf.org.uk
Website: www.nkrf.org.uk

General Health Websites

NHS Direct Online

This provides on-line health care information and advice. Its health encyclopaedia covers many conditions and plenty of information about diabetes. The service is also available in Welsh.

Website: www.nhsdirect.nhs.uk

National Electronic Library for Health

This electronic library provides healthcare professionals and the public with knowledge and information to support healthcare-related decisions. The site has an extensive diabetes section.

Website: www.nelh.nhs.uk

MedicAlert

MedicAlert is a registered charity that provides identification jewellery for people with hidden medical conditions and allergies. They provide a 24-hour emergency telephone number that can be used to access the wearer's details from anywhere in the world in over 100 languages.

Office: 1 Bridge Wharf, 156 Caledonian Road,
London N1 9UU, UK
Freephone: 0800 581420
Tel: 020 7833 3034
Fax: 020 7278 0647
E-mail: info@medicalert.org.uk
Website: wwww.medicalert.co.uk

The National Institute for Clinical Excellence (NICE)

NICE is part of the UK's National Health Service. Its role is to provide patients and healthcare professionals with authoritative and reliable guidance on current best practice in diabetes care.

Website: www.NICE.org.uk

Diabetes information websites in other languages

French: www.diabetenet.com
German: www.diabetes-deutschland.de
Italian: www.publinet.it/diabete
Korean: www.diabetes.or.kr
Russian: www.diabet.ru
Spanish: www.feaed.org

Bengali, Cantonese, Gujarati, Hindi, Punjabi, Urdu and Welsh: the Diabetes UK site provides information in all these languages: www.diabetes.org.uk/risk/index.html

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