

CKD - Stage 4 (kidney function 15% - 29%)

Stage 4 is the stage of kidney disease where the estimated GFR is 15-29mL/min and the serum creatinine may range up to around 800µmol/L. People with this level of kidney function may have symptoms varying from almost unnoticeable to quite severe, often depending on the underlying cause of kidney failure and associated illnesses. The biochemistry shows typical changes of kidney failure: the serum potassium tends to rise and the blood becomes more acidic. In this stage, there is a greater risk of further rises in serum potassium from some 'potassium sparing' diuretics and blood pressure medications. There is a wide range of abnormalities of hormonal levels as well as routinely measured biochemistry. Anaemia has usually (but not always) appeared and may become quite severe, requiring treatment.

Anaemia results when there are not enough red blood cells. Anaemia is caused by a reduction in the hormone erythropoietin, which is normally produced by healthy kidneys and stimulates the production of red blood cells in the bone marrow. Red blood cells carry oxygen and so a shortage will cause tiredness, weakness and shortness of breath. Anaemia can now be treated by the use of erythropoietin-like drugs that stimulate the bone marrow to produce red blood cells and reduce the symptoms of anaemia.

Continued reduction of kidney function causes further rises in blood pressure, so good blood pressure control is very important to reduce the risk of cardiovascular diseases, including heart attacks and strokes. Treatment to prevent bone disease, usually with medications, is also very important at this time.

CKD - Stage 5 (kidney function less than 15%)

This is the stage of chronic kidney disease where kidney function is severely impaired. Estimated GFR is reduced to 15% of normal or less and serum creatinine can be above 800µmol/L. The need for dialysis is approaching very fast.

Symptoms during this stage may still be almost negligible or be quite severe. They can include itch, nausea, loss of appetite, tiredness, pins and needles in the hands or feet and, at a late stage, chest pain due to pericarditis, which is inflammation of the lining around the outside of the heart. Bleeding and bruising become more prominent. Patients are often prone to infection and develop fluid retention with ankle swelling and shortness of breath. The aim is to commence dialysis before symptoms necessitating

hospitalisation arise and well before patients develop such severe symptoms. There is now a trend to start dialysis earlier e.g. at 10-15% of kidney function rather than 5-10% of kidney function.

Dialysis improves many of the symptoms of kidney failure, but some problems including hypertension, anaemia and itch often require additional drug treatments as well.

Other Observations

1. The *rate of progress* from one stage to the next may be unpredictable. Not all patients who lose some kidney function will progress to eventual loss of all kidney function. Progressive loss of function often depends on the extent of damage when a patient is first seen; for instance, the damage from an acute attack of glomerulonephritis, longstanding hypertension, from analgesics etc. Even in disorders where progression is usually inexorable, good blood pressure and biochemical control can delay the process, sometimes for years. Conversely, acute events such as severe infection, dehydration from vomiting or very high blood pressure can accelerate the progression of renal failure.
2. *Medications* should always be checked with your doctor if you have abnormal renal function. Some drugs directly harm kidney function and for some others, the level of kidney function may determine whether or not ordinary doses of medication might become toxic. Some common drugs or substances that require extra caution include antibiotics (such as tetracycline), some pain relieving drugs, some drugs used for the treatment of hypertension, diuretic (fluid) drugs, some oral treatments for diabetes, digoxin, potassium containing or sparing drugs and the dye (or contrast) used for X-ray tests that require an intravenous injection. These safety concerns generally increase the worse kidney function becomes.

Understanding Chronic Kidney Disease

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Causes of Chronic Kidney Disease

Most causes of chronic kidney failure are diseases that are not usually accompanied by symptoms until late in the progress of the disease.

1. Glomerulonephritis (inflammation of kidney filters)
2. Diabetic nephropathy (kidney damage resulting from 'sugar' diabetes)
3. Reflux nephropathy (kidney damage caused by a leaking valve in the bladder allowing urine to flow back into the kidney)
4. Hypertension (high blood pressure)
5. Polycystic kidney disease (cysts in both kidneys, not detectable until adolescence, and often familial)

In some people, the exact cause of chronic kidney disease remains unknown. The kidneys may already be too damaged to reveal the underlying cause.

Symptoms of Chronic Kidney Disease

Sometimes, there are no symptoms of chronic kidney disease until kidney failure is severe and problems, which contribute to progressive kidney disease, often have no symptoms. These include high blood pressure, raised cholesterol and sometimes urinary tract obstruction (blockage) or urinary tract infection. Regular check-ups are essential to detect these problems and monitoring with blood tests can assist in determining whether kidney function is stable or worsening.

Important clues to the presence of kidney disease and kidney failure are abnormal urine tests, high blood pressure and reduced kidney function, confirmed by a blood test. Due to the reduced ability of the kidney to form concentrated urine during the night, impaired kidney function can result in the need to pass urine several times during the night (nocturia).

Measurement of Kidney Function

The progression of kidney damage is marked by rises in two important chemical substances in the blood - creatinine and urea. Creatinine is produced from muscles and is excreted through the kidneys with other waste products. Urea is a waste product from dietary protein and is also filtered into the urine by the kidneys.

Thus, progressive kidney damage, with loss of kidney filtration and less excretion of wastes, results in

accumulation of both creatinine and urea in the blood. The normal level for creatinine in a blood sample is up to $110\mu\text{mol/L}$ for males (0.11mmol/L) and $90\mu\text{mol/L}$ (0.09mmol/L) for females. Males have higher serum creatinine levels than females because males have greater muscle mass. As kidney function declines, creatinine and urea accumulate in the blood. The higher the blood levels, the worse the kidney function. However, neither creatinine nor urea is directly toxic – these are just substances used to measure kidney function.

Calculations based on the serum creatinine, the age and sex of the patient are used to estimate more precisely the degree of kidney function. Sometimes a 24 hour urine collection and blood test together are used to measure the kidney's removal (or clearance) of creatinine from the body. These results are known as creatinine clearance or Glomerular Filtration Rate (GFR).

Calculated or measured GFR or creatinine clearance has a normal range of 90-120 ml/min. For convenience, this is referred to as 100% of kidney function. For example, if GFR is 15ml/min, that is said to represent approximately 15% of kidney function. GFR (or creatinine clearance) varies with age. There is generally a slow decrease of about 1% of GFR/year from the mid thirties. So at age 70 years, GFR on average is often only 60-70% of the normal.

As kidney function declines, other waste products such as potassium, uric acid and phosphate accumulate. A high blood uric acid level may lead to gout and retention of phosphate may lead to parathyroid overactivity and bone disease.

Progress of Chronic Kidney Disease (CKD)

The stages of kidney failure may be conveniently divided into five levels of severity.

CKD - Stage 1 (kidney function 90-100 %)

In Stage 1, the estimated GFR is usually $> 90\text{mL/min}$ and the serum creatinine level is usually normal. Overall kidney function is good but the kidneys show other signs of disease. This may be protein loss into the urine or structural damage seen on an X-ray or ultrasound. People with this level of kidney function commonly have no symptoms and the other blood tests are normal. However, their kidneys are susceptible to dehydration or toxicity by drugs such as antibiotics, non-steroidal anti-inflammatory pain-killers and high levels of some drugs normally removed by the

kidneys can build up in the blood; an example is digoxin. Older patients may have renal artery disease, making them susceptible to further renal impairment by some anti-hypertension drugs, such as 'ACE inhibitors' and 'Angiotensin Receptor Blockers'. Concerns about the suitability of some medications can be addressed by consulting a renal physician. Good blood pressure control and possibly some dietary modification will usually delay and sometimes prevent progression to the next stages. Cardiovascular risk factors such as diabetes, high cholesterol, vascular disease, obesity and smoking should be modified as much as possible.

CKD - Stage 2 (kidney function 60%-89%)

Kidney damage is mild with a slight drop in estimated GFR to 60-89mL/min. The serum creatinine level is generally around the upper normal limit ($110\mu\text{mol/L}$) or slightly higher. Generally, most other blood test results are normal. Patients may have no symptoms but nocturia may be present. At this stage, blood pressure may be elevated and urine abnormalities can be present. Good blood pressure control and possibly some dietary modification will usually delay and sometimes prevent progression to the next stages. Such measures can also help to reduce the risk of cardiovascular disease. Cardiovascular risk factors such as diabetes, high cholesterol, vascular disease, obesity and smoking should be modified as much as possible.

CKD - Stage 3 (kidney function 30%-59%)

The estimated GFR is further reduced to 30-59mL/min. This degree of impaired function implies that both kidneys are damaged. The serum creatinine is elevated, generally up to around $400\mu\text{mol/L}$ and there are more widespread abnormalities in blood tests, including increases in levels of uric acid, phosphate and acidity. Symptoms of kidney failure may become apparent, including nocturia, mild symptoms of malaise, lethargy, oedema (generally swelling of the ankles) and sometimes a loss of appetite. Blood pressure is often elevated unless there is a tendency to lose salt in the urine.

Increased medication may be required to control blood pressure and serum levels of phosphate and acid. The practical aspects of starting dialysis should be arranged, e.g., education about dialysis and transplantation, vascular access (making a blood vessel available) for haemodialysis and assessment of suitability for kidney transplant surgery. Referral to a specialist renal physician should have been arranged by this stage, if not sooner.