

## Assessing renal function

The kidney has several functions, including the excretion of water, soluble waste (eg, urea and creatinine) and foreign materials (eg, drugs). It is responsible for the composition and volume of circulating fluids with respect to water and electrolyte balance and acid-base status. It has an endocrine function playing a part in the production of vitamin D and erythropoietin and as part of the renin/angiotensin/aldosterone axis.

## Assessment of renal function

Measurements of renal function rely on measuring, in various ways the degree to which the kidney is successful in these roles.

An assessment of renal function may be required for several reasons:

- To identify renal impairment.
- To monitor disease progress.
- To assess baseline measurements prior to starting treatment with certain drugs.
- To monitor disease progress.
- The type of measurement of kidney function performed will be determined by the reason for assessing renal activity.

## Investigations<sup>[1]</sup>

### Urinalysis

See also the separate article on [Urine Dipstick Analysis](#).

- Appearance - blood, colour, turbidity.
- Specific gravity - sticks measure ionic particles only, not glucose.
- pH - normally acidic, except after a meal.

- Glucose – the presence of glucose in urine may indicate increased blood glucose, or tubular disorder.
- **Proteinuria** – the presence of protein in the urine may be caused by glomerular leak, raised serum low-molecular weight proteins, Bence Jones' proteins, myoglobin, or protein of renal origin. National Institute for Health and Care Excellence (NICE) guidance highlights the importance of proteinuria as a marker for **chronic kidney disease (CKD)** which may be as significant as glomerular filtration rate (GFR), particularly in terms of determining the development of cardiovascular complications.<sup>[2]</sup>
- Microscopy – urinary tract infection will show polymorphs with no casts; acute glomerulonephritis will show cells and casts; chronic glomerulonephritis shows little sediment.

### Estimated GFR

Estimated glomerular filtration rate (eGFR) is the most frequent test of renal function. GFR varies as a function of normal physiology as well as disease. Its measurement is based on determining the volume of plasma from which a substance is removed by glomerular filtration during its passage through the kidney – in other words, the 'clearance' of that substance.

$$\text{Clearance} = (U \times V) / P$$

Where U = urinary concentration of X; V = rate of urine formation (ml/min); P = plasma concentration of X

- **Creatinine clearance** is often used as a rough measurement of GFR, with a timed urine collection (often 24 hours) and a blood sample taken to measure plasma creatinine during that time period. It is limited by problems of accurate urine collection and tends to overestimate the GFR. It is also time-consuming.
- **Inulin GFR** is the gold standard for measurement but is a complex procedure used only when a more accurate result is important.
- **Isotopic GFR** is also sometimes performed using radioactive isotopes.

- **eGFR:**<sup>[1]</sup>
  - The plasma creatinine concentration (alone) is only a very rough guide to renal function.
  - Creatinine is produced by the muscles at a relatively constant level by the body and the plasma concentration therefore depends on the rate of excretion by the kidneys.
  - Levels are, however, affected by age, gender, ethnic group, muscle bulk, ingestion of cooked meat, malnutrition and after use of some drugs – eg, trimethoprim.

Different equations for assessing renal function include:<sup>[3]</sup> <sup>[4]</sup>

- Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation:
  - Uses serum creatinine, age, gender and race.
- 4-item Modification of Diet in Renal Disease (MDRD) equation:
  - Uses serum creatinine, age, gender and race
  - Tends to underestimate normal or near-normal function – slightly low values should not be over-interpreted. It is not valid in those aged under 18.
- 6-item MDRD equation:
  - Uses serum creatinine and albumin, blood urea nitrogen, and also age, gender and race
- Cockcroft and Gault equation:
  - Uses serum creatinine, age, weight and gender
- Counahan-Barrat method: used for those under 18 years.<sup>[5]</sup>

The eGFR can then be used to assess the severity of the **CKD**.

NICE recommends the CKD-EPI creatinine equation because it is more accurate than the MDRD Study equation, is less biased at a GFR of more than 60 ml/min/1.73 m<sup>2</sup> and performs better in people aged 75 years and over.

## NICE recommendations<sup>[1]</sup>

Creatinine-based estimate of glomerular filtration rate:

- Whenever a request for serum creatinine measurement is made, clinical laboratories should report an estimate of (eGFR<sub>creatinine</sub>) in addition to reporting the serum creatinine result.
- eGFR<sub>creatinine</sub> may be less reliable in certain situations (eg, acute kidney injury, pregnancy, oedematous states, muscle wasting disorders, and in adults who are malnourished, who have higher muscle mass or use protein supplements, or who have had an amputation) and has not been well validated in certain ethnic groups (eg, black, Asian and other minority ethnic groups with CKD living in the UK).
- Clinical laboratories should use the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation to estimate GFR<sub>creatinine</sub> for adults
- Interpret eGFR<sub>creatinine</sub> with caution in adults with extremes of muscle mass – eg, in bodybuilders, people who have had an amputation or people with muscle-wasting disorders. Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR.
- Advise adults not to eat any meat in the 12 hours before having a blood test for eGFR<sub>creatinine</sub>. Avoid delaying the despatch of blood samples to ensure that they are received and processed by the laboratory within 12 hours of venepuncture.

Reporting and interpreting GFR values:

- Clinical laboratories should report eGFR either as a whole number if it is 90 ml/min/1.73 m<sup>2</sup> or less, or as 'greater than 90 ml/min/1.73 m<sup>2</sup>'.
- If eGFR is greater than 90 ml/min/1.73 m<sup>2</sup>, use an increase in serum creatinine concentration of more than 20% to infer significant reduction in kidney function.

- Interpret eGFR values of 60 ml/min/1.73 m<sup>2</sup> or more with caution, bearing in mind that estimates of GFR become less accurate as the true GFR increases. Confirm an eGFR result of less than 60 ml/min/1.73 m<sup>2</sup> in an adult not previously tested by repeating the test within two weeks. Allow for variability of serum creatinine ( $\pm 5\%$ ) when interpreting changes in eGFR.
- If a highly accurate measure of GFR is needed - eg, during monitoring of chemotherapy and in the evaluation of kidney function in potential living donors, consider a reference standard measure (inulin, 51Cr-EDTA, 125I-iothalamate or iohexol).

### **Stages of Chronic Kidney Disease**

Use the suffix (p) to denote the presence of proteinuria when staging chronic kidney disease (CKD).

<b>Stage</b>	<b>Glomerular Filtration Rate</b> Values are normalised to an average surface area (size) of 1.73 m <sup>2</sup>	<b>Description</b>	<b>Management</b>
I	90+	Normal renal function (but urinalysis, structural abnormalities or genetic factors indicate renal disease).	Observation and control of blood pressure.
II	60-89	Mildly reduced renal function (Stage 2 CKD should not be diagnosed on GFR alone - but urinalysis, structural abnormalities or genetic factors indicate renal disease.)	Observation, control of blood pressure and cardiovascular risk factors.
IIIa	45-59	Moderate decrease in renal function, with or without other evidence of kidney damage.	Observation, control of blood pressure and cardiovascular risk factors.
IIIb	30-44	Moderate decrease in renal function, with or without other evidence of kidney damage.	Observation, control of blood pressure and cardiovascular risk factors.
IV	15-29	Severely reduced renal function.	Planning for end-stage kidney disease.

V	<15	Very severe (end-stage) kidney disease.	Transplant or dialysis.
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## Cystatin C

This is a small protein produced at a relatively constant rate which is reabsorbed in the proximal tubule. One study found that it was superior to MDRD and Cockcroft-Gault formulae in estimating the GFR rate in renal allografts.<sup>[6]</sup>

Cystatin C-based estimate of GFR should be used for the diagnosis of CKD at initial diagnosis in people with:<sup>[1]</sup>

- An eGFR creatinine of 45–59 ml/min/1.73 m<sup>2</sup>, sustained for at least 90 days; and
- No proteinuria (albumin:creatinine ratio (ACR) less than 3 mg/mmol) or other marker of kidney disease.

## Iohexol<sup>[7]</sup>

Being a single injection (plasma) clearance technique, this affords an accurate measure of GFR. Iohexol is an exogenous marker that is comparable to inulin and (51)Cr-EDTA and can be measured by high-performance liquid chromatography. Iohexol can accurately measure GFR using a four-point plasma disappearance curve (10, 30, 120 and 300 min) or, in most cases, a two-point disappearance time (120 and 300 min).

## Current developments in renal function<sup>[8]</sup>

It is recognised that using eGFR levels as a proxy for renal function has its limitations.<sup>[9]</sup> Work is ongoing to develop a new method of staging CKD centred on its progression to end-stage kidney disease.<sup>[10]</sup>

In particular, the current methods for estimating kidney function are not easy to apply in older age groups and there is a need to develop new methods for assessing renal function for the elderly.<sup>[11]</sup>

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