What is creatinine?

Creatinine is a chemical waste molecule that is generated from muscle metabolism. Creatinine is produced from creatine, a molecule of major importance for energy production in muscles. Approximately 2% of the body's creatine is converted to creatinine every day. Creatinine is transported through the bloodstream to the kidneys. The kidneys filter out most of the creatinine and dispose of it in the urine. Creatinine is mainly filtered by the kidney, though a small amount is actively secreted. There is little-to-no tubular reabsorption of creatinine. If the filtering of the kidney is deficient, blood levels rise. As a result, creatinine levels in blood and urine may be used to calculate creatinine clearance (ClCr), which reflects the glomerular filtration rate (GFR). The GFR is clinically important because it is a measurement of renal function. However, in cases of severe renal dysfunction, the creatinine clearance rate will be overestimated because the active secretion of creatinine will account for a larger fraction of the total creatinine cleared. (In the absence of secretion, creatinine behaves like inulin.)

A more complete estimation of renal function can be made when interpreting the blood (plasma) concentration of creatinine along with that of urea. In the USA, urea concentration is given as blood urea nitrogen (BUN), in mg/dL. In other countries, including those of Europe, urea concentration is measured and quoted in mmol/L.

The ratio of urea to creatinine can indicate other problems besides those intrinsic to the kidney. For example, a urea level raised out of proportion to the creatinine may indicate a pre-renal problem such as dehydration.

Men tend to have higher levels of creatinine because they have more skeletal muscle than women. Vegetarians tend to have lower creatinine levels, because vegetables contain no creatinine.

The kidneys maintain the blood creatinine in a normal range. Creatinine has been found to be a fairly reliable indicator of kidney function.
function. As the kidneys become impaired the creatinine level in the blood will rise. Abnormally high levels of creatinine thus warn of possible malfunction or failure of the kidneys, sometimes even before a patient reports any symptoms. It is for this reason that standard blood and urine tests routinely check the amount of creatinine in the blood.

*What are ‘normal’ blood creatinine levels?*

Normal levels of creatinine in the blood are approximately 0.6 to 1.2 milligrams (mg) per deciliter (dl) in adult males and 0.5 to 1.1 milligrams per deciliter in adult females. (In the metric system, a milligram is a unit of weight equal to one-thousandth of a gram, and a deciliter is a unit of volume equal to one-tenth of a liter.)

Muscular young or middle-aged adults may have more creatinine in their blood than the norm for the general population. Elderly persons, on the other hand, may have less creatinine in their blood than the norm. Infants have normal levels of about 0.2 or more, depending on their muscle development. A person with only one kidney may have a normal level of about 1.8 or 1.9. Creatinine levels that reach 2.0 or more in babies and 10.0 or more in adults may indicate the need for a dialysis machine to remove wastes from the blood. Having a low level of blood creatinine indicates nothing more than an efficient and effective pair of kidneys.

A further test of kidney function is to collect all the urine passed over a period of twenty-four hours and then to compare the amount of creatinine in the blood to the level in the blood stream (creatinine clearance test). This can look at the efficiency of the kidneys and is only usually done if there is an indication of a problem with renal function. In normally functioning kidneys, the level of creatinine in the urine compared to the blood should be high as it is being passed out efficiently. Conversely, if the level in the urine is low, with a high blood creatinine level, this in an indication of a problem, for which a
consultant physician is usually involved. I hope that this information helps you understand the significance of a low creatinine level.

**Creatinine and Creatinine Clearance**

Creatinine and creatinine clearance tests measure the level of the waste product creatinine in your blood and urine. These tests tell how well your kidneys are working. The substance creatine is formed when food is changed into energy through a process called metabolism. Creatine is broken down into another substance called creatinine, which is taken out of your blood by the kidneys and then passed out of your body in urine. See an illustration of the kidneys.

Creatinine is made at a steady rate and is not affected by diet or by normal physical activities. If your kidneys are damaged and cannot work normally, the amount of creatinine in your urine goes down while its level in your blood goes up.

*Three types of tests on creatinine can be done:*

**Blood creatinine level**
The blood creatinine level shows how well your kidneys are working. A high creatinine level may mean your kidneys are not working properly. The amount of creatinine in the blood depends partly on the amount of muscle tissue you have; men generally have higher creatinine levels than women.

**Creatinine clearance test**
A creatinine clearance test measures how well creatinine is removed from your blood by your kidneys. A creatinine clearance test gives better information than a blood creatinine test on how well your kidneys are working. A creatinine clearance test is done on both a blood sample and on a sample of urine collected over 24 hours (24-hour urine sample).

**Blood urea nitrogen-to-creatinine ratio (BUN: creatinine)**
The levels of blood creatinine and blood urea nitrogen (BUN) can be used to find the BUN-to-creatinine ratio. A BUN-to-creatinine ratio
can help your doctor check for problems, such as dehydration, that may cause abnormal BUN and creatinine levels.

Urea is a waste product made when protein is broken down in your body. Urea is made in the liver and passed out of your body in the urine. A blood urea nitrogen (BUN) test measures the amount of urea in your blood. Like creatinine, it can help your doctor see how well your kidneys are working.

**Estimating GFR**

Glomerular filtration rate (GFR) can be calculated by measuring any chemical that has a steady level in the blood, and is freely filtered but neither reabsorbed nor secreted by the kidneys.

Creatinine is used because it fulfills these requirements (though not perfectly) and it is produced naturally by the body (creatinine is a metabolite of creatine, which is found in muscle). It is actively secreted by the kidneys such that creatinine clearance overestimates actual GFR by 10-20%. This margin of error is acceptable considering the ease with which creatinine clearance is measured. Other more precise GFR measurements involve constant infusions of inulin or another compound, to maintain a steady state in the blood. Since creatinine is already at a steady-state concentration in the blood, measuring creatinine clearance is much less cumbersome.

The result of this test is an important gauge used in assessing excretory function of the kidneys. For example grading of chronic renal insufficiency and dosage of drugs that are primarily excreted via urine are based on GFR (creatinine clearance).

It is commonly believed to be the amount of liquid filtered out of the blood that gets processed by the kidneys. Physiologically, these quantities (volumetric blood flow and mass removal) are only related loosely. Clearance is a ratio of the mass generation and concentration at a steady state.
Calculation

Creatinine clearance \( (C_{Cr}) \) can be calculated if values for creatinine’s urine concentration \( (U_{Cr}) \), urine flow rate \( (V) \), and creatinine’s plasma concentration \( (P_{Cr}) \) are known. Since the product of urine concentration and urine flow rate yields creatine’s excretion rate, creatinine clearance is also said to be its excretion rate \( (U_{Cr} \times V) \) divided by its plasma concentration. This is commonly represented mathematically as

\[
C_{Cr} = \frac{U_{Cr} \times V}{P_{Cr}}
\]

For example, a normal individual with a plasma creatinine concentration of 1 mg/dL, urine creatinine concentration of 60 mg/dL, and urine flow rate of 0.5 dL/h, would have a creatinine clearance given by

\[
C_{Cr} = \frac{60 \text{ mg/dL} \times 0.5 \text{ dL/h}}{1 \text{ mg/dL}}
\]

which yields 30 dL/h. Thus, 30 dL of blood are cleared of creatinine per hour.

Cockcroft-Gault approximation

More often, the creatinine clearance is estimated using the Cockcroft-Gault formula:

The following equation applies to men. For women deduct 15%. For obese individuals estimation of \( C_{cr} (ml / min) \) will be more correct if lean body weight is used to calculate \( S_{cr} \).

If \( S_{cr} \) is measured in mg/dL:

\[
C_{cr} (ml/min) = \frac{(140 \text{ - Age years}) \times \text{weight (in kilograms)}}{72 \times S_{cr} \text{(in mg/dL)}}
\]
If $S_{cr}$ is measured in mmol/L:

$$Cr\ Cl = \frac{(140 - \text{age}) \times \text{weight (in kilograms)}}{812 \times S_{Cr} \ (in \ mmol/L)}$$

An online Cockcroft-Gault calculator is at http://www.intmed.mcw.edu/clincalc/creatinine.html.

Reference ranges

Normal reference ranges for creatinine clearance are:

<table>
<thead>
<tr>
<th>Gender</th>
<th>Low</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>male</td>
<td>55</td>
<td>146</td>
</tr>
<tr>
<td>female</td>
<td>52</td>
<td>134</td>
</tr>
</tbody>
</table>

Units: ml/minute/1.73 m2

Why It Is Done

A blood creatinine level or a creatinine clearance test is done to:

- See if your kidneys are working normally.
- See if your kidney disease is changing.
- See how well the kidneys work in people who take medicines that can cause kidney damage.
- See if severe dehydration is present.

Dehydration generally causes BUN levels to rise more than creatinine levels. This causes a high BUN-to-creatinine ratio. Kidney disease or blockage of the flow of urine from your kidney causes both BUN and creatinine levels to rise.

Results

Creatinine and creatinine clearance tests measure creatinine levels in your blood and urine to give information about how well your kidneys are working. The creatinine clearance value is found from the
amounts of creatinine in the urine and blood and from the amount of urine you pass in 24 hours. This value is the amount of blood cleared of creatinine per minute, based on your body size.

*Normal*

Normal results may vary from lab to lab.

<table>
<thead>
<tr>
<th>Blood creatinine and creatinine clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood creatinine:</strong></td>
</tr>
<tr>
<td>Men 0.6–1.2 milligrams per deciliter (mg/dL) or 53-106 micromoles/L (mcmol/L)</td>
</tr>
<tr>
<td>Women 0.5–1.1 mg/dL or 44–97 mcmol/L</td>
</tr>
<tr>
<td>Teen 0.5–1.0 mg/dL</td>
</tr>
<tr>
<td>Child 0.3–0.7 mg/dL</td>
</tr>
<tr>
<td>Newborn 0.3–1.2 mg/dL</td>
</tr>
<tr>
<td><strong>Creatinine clearance:</strong></td>
</tr>
<tr>
<td>Men 90–140 milliliters per minute (mL/min) or 1.78–2.32 milliliters per second (mL/sec)</td>
</tr>
<tr>
<td>Women 87–107 mL/min or 1.45-1.78 mL/sec</td>
</tr>
</tbody>
</table>

Creatinine clearance values normally go up as you get older (normal values go down by 6.5 mL/min for every 10 years past the age of 20).

<table>
<thead>
<tr>
<th>BUN-to-creatinine ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 12 months of age:</td>
</tr>
<tr>
<td>Infants less than 12 months of age:</td>
</tr>
</tbody>
</table>
High values

**High creatinine blood levels.** High creatinine blood levels can mean serious kidney damage or disease is present. Kidney damage can be caused by a life-threatening infection, shock, cancer, or low blood flow to the kidneys. Other conditions that can cause high blood creatinine levels include blockage of the urinary tract (such as by a kidney stone), heart failure, dehydration, excessive blood loss that causes shock, gout, or muscle conditions (such as rhabdomyolysis, gigantism, acromegaly, myasthenia gravis, muscular dystrophy, and polymyositis). Usually a high blood creatinine level means that the creatinine clearance value is lower than normal.

**High creatinine clearance.** High creatinine clearance values can be caused by strenuous exercise, muscle injury (especially crushing injuries), burns, carbon monoxide poisoning, hypothyroidism, and pregnancy.

**High BUN-to-creatinine ratio.** High BUN-to-creatinine ratios occur with sudden (acute) kidney failure, which may be caused by shock or severe dehydration. A blockage in the urinary tract (such as a kidney stone) can cause a high BUN-to-creatinine ratio. A very high BUN-to-creatinine ratio may be caused by bleeding in the digestive tract or respiratory tract.

Low values

**Low blood creatinine levels.** Low blood creatinine levels can mean lower muscle mass caused by a disease, such as muscular dystrophy, or by aging. Low levels can also mean some types of severe liver disease or a diet very low in protein. Pregnancy can also cause low blood creatinine levels.

**Low creatinine clearance.** Low creatinine clearance levels can mean serious kidney damage is present. Kidney damage can be from conditions such as a life-threatening infection, shock, cancer,
low blood flow to the kidneys, or urinary tract blockage. Other conditions, such as heart failure, dehydration, and liver disease (cirrhosis), can also cause low creatinine clearance levels.

**Low BUN-to-creatinine ratio.** A low BUN-to-creatinine ratio may be associated with a diet low in protein, a severe muscle injury called rhabdomyolysis, pregnancy, cirrhosis, or syndrome of inappropriate antidiuretic hormone secretion (SIADH). SIADH sometimes occurs with lung disease, cancer, diseases of the central nervous system, and the use of certain medications.

*What Affects the Test*

Certain drugs can sometimes cause abnormally elevated creatinine levels. Other reasons you may not be able to have the test or why the results may not be helpful include:

- Taking medicines, such as methyldopa (Aldomet), trimethoprim (Proloprim, Trimpex), cimetidine (Tagamet), some diuretics, and cephalosporin antibiotics, especially cefoxitin (Mefoxin). These affect the blood creatinine levels.
- Taking medicines, such as vitamin C (ascorbic acid), phenytoin (Dilantin), some cephalosporin antibiotics, captopril, aminoglycosides (Garamycin), trimethoprim (Proloprim, Trimpex), quinine, quinidine (Cardioquin, Quinaglute, Quinidex), procainamide (Procan, Pronestyl), and the antifungal medication amphotericin B. These affect the creatinine clearance levels.
- Taking medicines, such as cimetidine (Tagamet), steroids, and tetracycline antibiotics. These can affect the BUN-to-creatinine ratio.
- Doing strenuous exercise 2 days before creatinine clearance test.
- Eating more than meat, especially beef, in the 24 hours before a blood creatinine test and during a creatinine clearance urine test.
• Ketoacids, cimetidine, and trimethoprim reduce creatinine tubular secretion and therefore increase the accuracy of the GFR estimate, particularly in severe renal dysfunction.

• It is important to drink enough fluids during the 24-hour urine collection but do not drink coffee and tea. These are diuretics that cause your body to pass more urine.

What to Think About

• A high blood creatinine level is generally seen with a low creatinine clearance level because creatinine in the blood is removed by the kidneys. If the kidneys are not able to remove creatinine (low creatinine clearance), levels of creatinine in the blood go up (high blood creatinine level).

• If you are pregnant, your doctor can check the amount of creatinine in amniotic fluid to see how developed, or mature, your baby’s kidneys are. This can be helpful if there is a chance your baby will be delivered early. A baby who has mature kidneys will make more creatinine than a baby whose kidneys are still developing.

• A normal blood creatinine level does not rule out kidney disease. To help see whether kidney damage may be present, a BUN level is also measured. Other tests may also be done to check for kidney disease.

• Creatinine levels increase more slowly than blood urea nitrogen (BUN) levels, so an increase in creatinine may mean chronic kidney problems.

• A glomerular filtration rate may be done for people with chronic kidney disease to regularly check how well the kidneys are working.

• Diabetes experts recommend that blood creatinine levels be done every year for people with diabetes. The creatinine level is used to find the glomerular filtration rate, which shows how well the kidneys are working.
• The amount of creatinine in the blood depends partly on the amount of muscle tissue; blood creatinine levels are generally higher in men than in women. Also, people who have large muscles, such as athletes, normally have above-average blood creatinine levels.

• The creatinine level is usually measured before performing a contrast-enhanced Computed tomography (CT) scan. In a small proportion of patients the administration of iodine based contrast can cause kidney damage. This may be more likely or severe in patients with an elevated baseline serum creatinine level and, again, in rare cases may require temporary or permanent dialysis. The risk can be reduced somewhat in higher-risk patients by choosing a low-osmolality contrast medium.

A one-time urine sample to measure urine creatinine and sodium is sometimes done along with blood creatinine and sodium levels to help find the fractional excretion of sodium (FENA). This test can help your doctor see whether a problem with blood flow to the kidneys is caused by dehydration or shock or by damage to the kidneys themselves.