

Review

Overview of Urea and Creatinine

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Urea, commonly referred to as blood urea nitrogen (BUN) when measured in the blood, is a product of protein metabolism. BUN is considered a non-protein nitrogenous (NPN) waste product. Amino acids derived from the breakdown of protein are deaminated to produce ammonia. Ammonia is then converted to urea via liver enzymes. Therefore, the concentration of urea is dependent on protein intake, the body's capacity to catabolize protein, and adequate excretion of urea by the renal system.¹

Urea accounts for the majority (up to 80%-90%) of the NPNs excreted by the body. The body's dependency on the renal system to excrete urea makes it a useful analyte to evaluate renal function. An increase in BUN can be the result of a diet that is high in protein content or decreased renal excretion.

Creatinine, also a NPN waste product, is produced from the breakdown of creatine and phosphocreatine and can also serve as an indicator of renal function.² Creatine is synthesized in the liver, pancreas, and kidneys from the transamination of the amino acids arginine, glycine, and methionine. Creatine then circulates throughout the body and is converted to phosphocreatine by the process of phosphorylation in the skeletal muscle and brain. The

majority of the creatinine is produced in the muscle. As a result, the concentration of plasma creatinine is influenced by the patient's muscle mass. Compared to BUN, creatinine is less affected by diet and more suitable as an indicator of renal function.

Clinical Significance

The measurement of creatinine concentrations in plasma and urine samples illustrates the filtration capacity of the glomerulus, also known as the glomerular filtration rate (GFR.) Creatinine is produced endogenously within the body and is freely filtered by the glomerulus. These characteristics make creatinine a useful endogenous marker for creatinine clearance. If the GFR is decreased, as is in renal disease, creatinine clearance via the renal system is compromised. The reduced GFR will then lead to an increase in plasma creatinine concentration. The measurement of plasma alone should not be used to assess renal function. Plasma creatinine levels may not be affected until significant renal damage has occurred. In addition, a plasma creatinine level that is within normal reference range does not equate to a normal functioning renal system.³

Although not as specific as creatinine, BUN can also be used as an indicator of renal function. BUN is not the preferred marker for clearance because it is influenced by factors such as a high protein diet, variables in protein synthesis, and patient hydration status. Alone BUN is not the ideal marker for GFR. Combined with plasma creatinine as a creatinine/BUN ratio, BUN can be a useful analyte in differentiating pre or post renal increase of plasma NPNs.⁴

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Abbreviations

BUN, blood urea nitrogen; NPN, non-protein nitrogenous; GFR, glomerular filtration rate

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Specimen Requirements

Creatinine may be measured using serum, plasma, or urine specimens. Additives such as fluoride and ammonium heparin should not be used due to interference with the

method of measurement. Measuring creatinine clearance requires the collection of a 24-hour timed urine specimen and a plasma sample collecting within the 24-hour urine collection period.

Serum or plasma may be tested for BUN. Additives such as fluoride and citrate should not be used due interference with the method of measurement.¹

Testing Methods

Creatinine may be measured either chemically or enzymatically. The chemical method known as the Jaffe reaction involves creatinine reacting with picric acid in an alkaline environment to produce an orange-red colored compound. The disadvantage to this method is that the reaction is non-specific for creatinine. Other sources in the patient sample such as ascorbic acid, acetone, or cephalosporins may erroneously produce an orange-red color as they react with the picric acid. The chemical method is time consuming and not widely used in automated instruments.⁵

Creatinine may be also measured enzymatically. Multiple enzymatic methods utilizing creatinase have been used to measure creatinine. These enzymatic methods employ the

use of a spectrophotometer to measure NADH to NAD⁺ or H₂O₂ to H₂O.

BUN is most frequently measured using enzymatic methods. The first step involves the enzyme urease to hydrolyze urea, thereby producing ammonium. The second step involves the quantitative measurement of ammonium using a variety of methods to determine the amount of urea in the sample. The various methods include the glutamate dehydrogenase (GLDH) method which measures NADH to NAD⁺, measurement of ammonium ion conductivity, or an indicator dye that reacts with ammonium ions.⁶ **LM**

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