# EXCRETION OF WASTES AND PATHOPHYSIOLOGY

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**Keywords:** Creatinine, urea, acute renal failure, chronic renal failure, uremia, renal insufficiency, anuria, oliguria, polyuria, proteinuria, anemia.

## Contents





## Summary

The kidneys are the major site for water and ion excretion and the non-volatile waste products produced by metabolism. The kidneys also have other important functions. They synthesize various biologically active molecules like erythropoeitin and angiotensin II. They are involved in hormonal regulations, sometimes as the effector organs, as in the case of natriuretic peptide function, or they metabolize hormones such as leptin and insulin. Measurement of the excretory changes offers the most practical and simple tool to evaluate renal function. From this point of view, creatinine, the end product of creatine metabolism in muscle, and urea, the end product of protein metabolism, are the most important molecules. Since the excretion of these molecules by the kidneys depends on free glomerular filtration, their plasma levels and/or their renal clearance characterize the renal function. Creatinine is not only freely filtered by the glomerulus, but it is also secreted by the proximal tubule. Under normal conditions this secretion accounts for 5 to 10% of the total excreted ceratinine. Thus the GFR calculated from the excreted creatinine may overestimate the real value by 5 to 10%. In patients where the GFR is low and the creatinine level is high, this discrepancy can be even higher.

Various diseases can lead to disturbance in renal function. A*cute renal failure* is the rapid decrease in GFR. Chronic progression of functional and morphological damages

in the kidneys ultimately manifest as end stage renal failure or uremia. This chronic condition is characterized by progressive kidney damage with uremia as its final stage.

## 1. Introduction

Aquatic animals have little problem in excretion of wastes as they have a lot of water around. Terrestrial animals must take care of their water balance, when they excrete non-volatile waste ions and compounds.

Urine and bile are the main routes of waste excretion. In both cases the primary products of excretion are highly processed. The lipophilic waste compounds are usually extensively reabsorbed, as the processing surface areas are large, both in the kidneys and in the gut. In brief, the task division between urinary and biliary excretion is as follows: high molecular weight waste compounds are excreted into bile and smaller molecules are excreted in urine.

In both cases the lipophilic compounds must be transformed into hydrophilic conjugates of e.g. glucuronic and/or sulphuric acids. Those compounds excreted into bile may, after the bacterial metabolism be reabsorbed and then finally be excreted into the urine. This explains why urine is yellowish, as some of the bile pigments are excreted by the kidneys after an enteric phase. Practically all urea entering the gut is hydrolyzed by the microflora, and thus produced ammonium ions are reabsorbed and reconverted into urea in the liver (see *Intestinal Microflora*). Urea is finally excreted from the body by the kidneys.

The liver is one of the main organs of biotransformation e.g. in detoxification of organic xenobiotics like drugs (see *Biotransformation of Xenobiotics and Hormones*). The kidneys also significantly contribute to this process since the blood circulation through the kidneys is very high and they have a high content of cytochrome P-450.

Urine is the main route for excretion of salts. Kidneys especially take care of nitrogen-containing wastes i.e. urea, uric acid and creatinine. Some ammonium ions are also excreted as the kidneys balance the hydrogen ion excretion by producing ammonium ions and keep the urine pH at 4.5 or above. The main emphasis of this short overview is paid to the excretion of nitrogen wastes.

Analysis of urine provides a lot of important information on body homeostasis. Urinary samples are easy to collect, but one must remember that the diurnal variations of urine chemistry are great, as reflected by its color and density. Testing urine glucose and protein levels as well as blood content are of great value in practical medicine. The evaluation of many parameters requires the collection of daily (24 hour) urine.

In this case one must take care of the inhibition of bacterial growth during collection. Renal infections are rather common, especially in females. We may encounter red and white blood cells or bacteria in urine. It must be remembered that these elements do not necessarily originate from the kidneys; they may come from the urinary bladder, the urinary ducts, prostate or even in females they may arise from the genital organs.

## 2. Excretion of Creatinine

Creatine in muscle originates in part from dietary meat, and partly it is synthesized in the body. Metabolism of creatine in muscle gives rise to creatinine. Cooking meat also converts some of the creatine to creatinine, which is absorbed and enters the creatinine pool. Therefore, creatinine generation depends on muscle metabolism and to a lesser extent, on the amount of meat intake. Women, children, the elderly, malnourished individuals, and those with restricted meat intake show lower serum creatinine levels. In these groups, serum creatinine may remain normal despite a reduction in renal creatinine clearance. Therefore, in detecting a reduction in GFR, an elevated serum creatinine is a less-sensitive indicator than a reduced creatinine clearance.

## 3. Excretion of Urea

Urea is freely filtered by the glomerulus. Some 30 to 60% of the filtered urea is reabsorbed back to plasma by the proximal and the distal tubules. Thus urea clearance is lower than the creatinine clearance and this difference is increased when the reabsorbtion of urea is facilitated by the low tubular fluid flow rate and increased contact time in the tubule during low renal perfusion pressure due to hypotension, or internal renal circulatory problems.

Urea is the end product of protein catabolism and is synthesized primarily by the liver. Approximately one quarter of synthesized urea is metabolized in the intestine to carbon dioxide and ammonia. The ammonia thus generated returns to the liver where it is reconverted to urea. In the steady state, the level of blood urea nitrogen (BUN) is an index of urea generation.

Dietary protein intake is the principal determinant of urea generation. A high dietary protein intake raises the BUN and consequently the BUN/creatinine ratio. Other factors that increase urea generation include accelerated catabolism of endogenous protein, as occurs during febrile illnesses, trauma, gastrointestinal bleeding, tumor lysis or therapy with tetracyclines or corticosteroids. On the other hand, urea generation may be reduced in liver disease.

## 4. Renal Failure

Various diseases can lead to the impairment of renal function. This impairment can take a very rapid course leading to decreased GFR, a condition referred to as *acute renal failure*. In other cases, kidney diseases can lead to a chronic progression of functional and morphological damages in the kidneys, which ultimately manifest as end stage renal failure (uremia). This is a chronic condition characterized by progressive deterioration in function and morphology with uremia as its final stage in *chronic renal failure* (CRF) due to a non-functioning kidney tissue.

### 4.1. Acute Renal Failure (ARF)

ARF is defined as an abrupt and often reversible reduction of glomerular filtration rate (GFR) within hours or days. Many conditions can cause ARF, classified mainly in three

groups: pre-renal (e.g. severe plasma volume depletion, hypotension), renal (e.g. toxic damage, intra-renal hemodynamic disturbances), post-renal (e.g. prostate cancer). Pre-renal and post-renal causes will ultimately extend into the kidneys and involve the parenchyme.

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