Diagnostic Evaluation of the Patient with Acute Renal Failure

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Acute renal failure (ARF) is abrupt deterioration of renal function sufficient to result in failure of urinary elimination of nitrogenous waste products (urea nitrogen and creatinine). This deterioration of renal function results in elevations of blood urea nitrogen and serum creatinine concentrations. While there is no disagreement about the general definition of ARF, there are substantial differences in diagnostic criteria various clinicians use to define ARF (*eg*, magnitude of rise of serum creatinine concentration). From a clinical perspective, for persons with normal renal function and serum creatinine concentration, glomerular filtration rate must be dramatically reduced to result in even modest increments (*eg*, 0.1 to 0.3 mg/dL) in serum creatinine concentration. Moreover, several studies demonstrate a direct relationship between the magnitude of serum creatinine increase and mortality from ARF. Thus, the clinician must carefully evaluate all cases of rising serum creatinine.

The process of urine formation begins with delivery of blood to the glomerulus, filtration of the blood at the glomerulus, further processing of the filtrate by the renal tubules, and elimination of the formed urine by the renal collecting system. A derangement of any of these processes can result in the clinical picture of rapidly deteriorating renal function and ARF. As the causes of ARF are multiple and since subsequent treatment of ARF depends on a clear delineation of the cause, prompt diagnostic evaluation of each case of ARF is necessary.

CHAPTER 12

RATIONALE FOR ORGANIZED APPROACH TO ACUTE RENAL FAILURE

- Common
  - Present in 1%–2% of hospital admissions
  - Develops after admission in 1%–5% of noncritically ill patients
  - Develops in 5%–20% after admission to an intensive care unit
- Multiple causes
  - Prerenal
  - Postrenal
  - Renal
- Therapy dependent upon diagnosing cause
  - Prerenal: improve renal perfusion
  - Postrenal: relieve obstruction
  - Renal: identify and treat specific cause
- Poor outcomes
  - Twofold increased length of stay
  - Two- to eightfold increased mortality
  - Substantial morbidity

FIGURE 12-1

Rationale for an organized approach to acute renal failure (ARF). An organized approach to the patient with ARF is necessary, as this disorder is common and is caused by several insults that operate via numerous mechanisms. Successful amelioration of the renal failure state depends on early identification and treatment of the cause of the disorder [1–7]. If not diagnosed and treated and reversed quickly, it can lead to substantial morbidity and mortality.

PRESENTING FEATURES OF ACUTE RENAL FAILURE

- Common
  - Rising BUN or creatinine
  - Oligoanuria
- Less common
  - Symptoms of uremia
  - Characteristic laboratory abnormalities

FIGURE 12-2

Presenting features of acute renal failure (ARF). ARF usually comes to clinical attention by the finding of either elevated (or rising) blood urea nitrogen (BUN) or serum creatinine concentration. Less commonly, decreased urine output (less than 20 mL per hour) heralds the presence of ARF. It is important to acknowledge, however, that at least half of all cases of ARF are nonoliguric [2–6]. Thus, healthy urine output does not ensure normal renal function. Rarely, ARF comes to the attention of the clinician because of symptoms of uremia (*eg*, anorexia, nausea, vomiting, confusion, pruritus) or laboratory findings compatible with renal failure (metabolic acidosis, hyperkalemia, hyperphosphatemia, hypocalcemia, hyperuricemia, hypermagnesemia, anemia).

Blood Urea Nitrogen, Creatinine, and Renal Failure

OVERVIEW OF BLOOD UREA NITROGEN AND SERUM CREATININE

	Blood Urea Nitrogen	Serum Creatinine
Source	Protein that can be of exogenous or endogenous origin	Nonenzymatic hydrolysis of creatine released from skeletal muscle
Constancy of production	Variable	More stable
Renal handling	Completely filtered; significant tubular reabsorption	Completely filtered; some tubular secretion
Value as marker for glomerular filtration rate	Modest	Good in steady state
Correlation with uremic symptoms	Good	Poor

FIGURE 12-3

Overview of blood urea nitrogen (BUN) and serum creatinine. Given the central role of BUN and serum creatinine in determining the presence of renal failure, an understanding of the metabolism of these substances is needed. Urea nitrogen derives from the breakdown of proteins that are delivered to the liver. Thus, the urea nitrogen production rate can vary with exogenous protein intake and endogenous protein catabolism. Urea nitrogen is a small, uncharged molecule that is not protein bound, and as such, it is readily filtered at the renal glomerulus. Urea nitrogen undergoes renal tubular reabsorption by specific transporters. This tubular reabsorption limits the value of BUN as a marker for glomerular filtration. However, the BUN usually correlates with the symptoms of uremia. By contrast, the production of creatinine is usually more constant unless there has been a marked reduction of skeletal muscle mass (*eg*, loss of a limb, prolonged starvation) or diffuse muscle injury. Although creatinine undergoes secretion into renal tubular fluid, this is very modest in degree. Thus, a steady-stable serum creatinine concentration is usually a relatively good marker of glomerular filtration rate as noted in Figure 12-5.

BLOOD UREA NITROGEN (BUN)-CREATININE RATIO

> 10	< 10
Increased protein intake	Starvation
Catabolic state	Advanced liver disease
Fever	Postdialysis state
Sepsis	Drugs that impair tubular secretion
Trauma	Cimetidine
Corticosteroids	Trimethoprim
Tissue necrosis	Rhabdomyolysis
Tetracyclines	
Diminished urine flow	
Prerenal state	
Postrenal state	

FIGURE 12-4

The blood urea nitrogen (BUN)-creatinine ratio. Based on the information in Figure 12-3, the BUN-creatinine ratio often deviates from the usual value of about 10:1. These deviations may have modest diagnostic implications. As an example, for reasons as yet unclear, tubular reabsorption of urea nitrogen is enhanced in low-urine flow states. Thus, a high BUN-creatinine ratio often occurs in prerenal and postrenal (*see* Fig. 12-6) forms of renal failure. Similarly, enhanced delivery of amino acids to the liver (as with catabolism, corticosteroids, etc.) can enhance urea nitrogen formation and increase the BUN-creatinine ratio. A BUN-creatinine ratio lower than 10:1 can occur because of decreased urea nitrogen formation (*eg*, in protein malnutrition, advanced liver disease), enhanced creatinine formation (*eg*, with rhabdomyolysis), impaired tubular secretion of creatinine (*eg*, secondary to trimethoprim, cimetidine), or relatively enhanced removal of the small substance urea nitrogen by dialysis.

CORRELATION OF STEADY-STATE SERUM CREATININE CONCENTRATION AND GLOMERULAR FILTRATION RATE (GFR)

Creatinine (mg/dL)	GFR (mL/min)
1	100
2	50
4	25
8	12.5
16	6.25

FIGURE 12-5

Correlation of steady-state serum creatinine concentration and glomerular filtration rate (GFR).

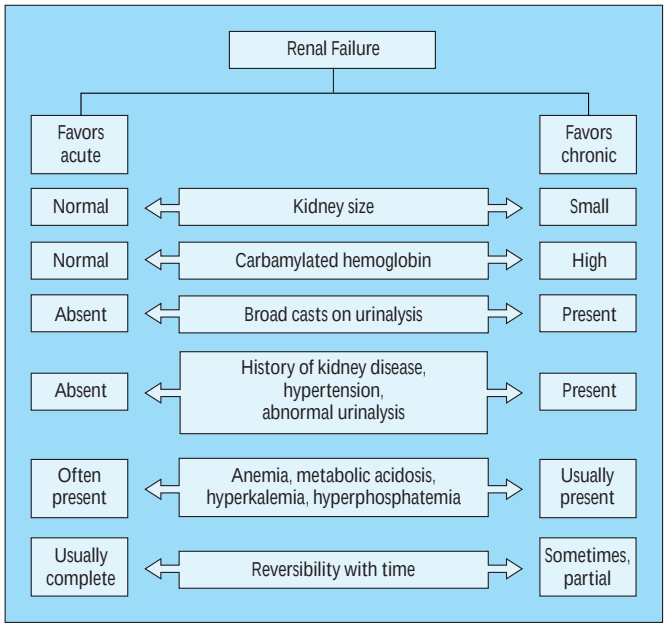

FIGURE 12-6

Categories of renal failure. Once the presence of renal failure is ascertained by elevated blood urea nitrogen (BUN) or serum creatinine value, the clinician must decide whether it is acute or chronic. When previous values are available for review, this judgment is made relatively easily. In the absence of such values, the factors depicted here may be helpful. Hemoglobin potentially undergoes nonenzymatic carbamylation of its terminal valine [8]. Thus, similar to the hemoglobin A1C value as an index of blood sugar control, the level of carbamylated hemoglobin is an indicator of the degree and duration of elevated BUN, but, this test is not yet widely available. The presence of small kidneys strongly suggests that renal failure is at least in part chronic. From a practical standpoint, because even chronic renal failure often is partially reversible, the clinician should assume and evaluate for the presence of acute reversible factors in all cases of acute renal failure.