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).

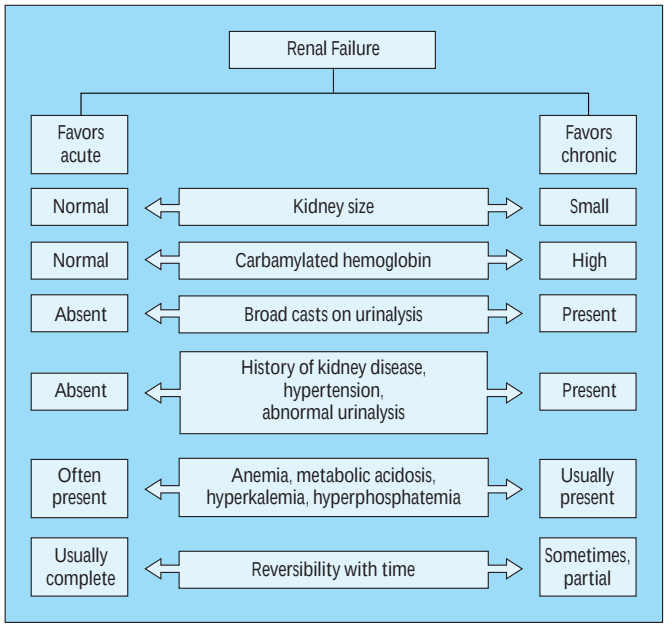

FIGURE 12-6

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.

Categorization of Causes of Acute Renal Failure

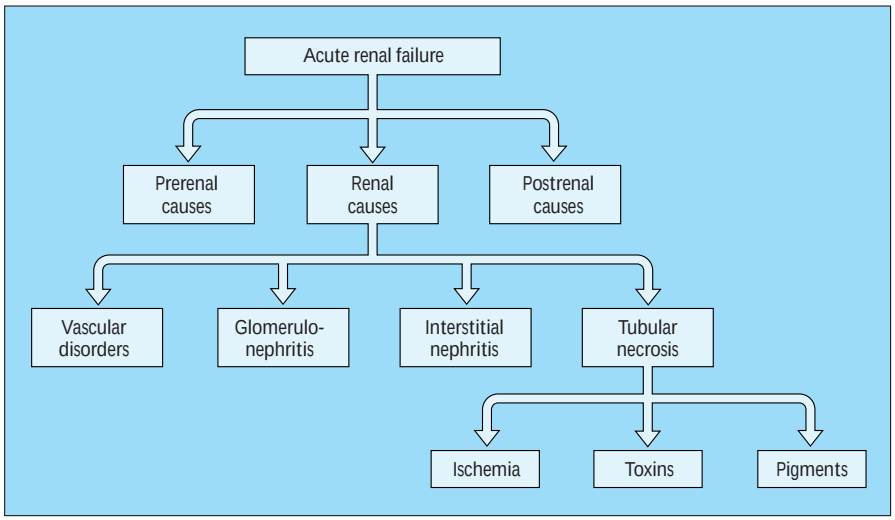

FIGURE 12-7

Acute renal failure (ARF). This figure depicts the most commonly used schema to classify and diagnostically approach the patient with ARF [1, 6, 9]. The most common general cause of ARF (60% to 70% of cases) is prerenal factors. Prerenal causes include those secondary to renal hypoperfusion, which occurs in the setting of extracellular fluid loss (*eg*, with vomiting, nasogastric suctioning, gastrointestinal hemorrhage, diarrhea, burns, heat stroke, diuretics, glucosuria), sequestration of extracellular fluid (*eg*, with pancreatitis, abdominal surgery, muscle crush injury, early sepsis), or impaired cardiac output. In most prerenal forms of ARF, one or more of the vasomotor mechanisms noted in Figure 12-8 is operative. The diagnostic criteria for prerenal ARF are delineated in Figure 12-9. Once prerenal forms of ARF have been ruled out, postrenal forms (*ie*, obstruction to urine flow) should be considered. Obstruction to urine flow is a less common (5% to 15% of cases) cause of ARF but is nearly always amenable to therapy. The site of obstruction can be intrarenal (*eg*, crystals or proteins obstructing the terminal collecting tubules) or extrarenal (*eg*, blockade of the renal pelvis, ureters, bladder, or urethra). The diagnosis of postrenal forms of ARF is supported by data outlined in Figure 12-10. After pre- and postrenal forms of ARF have been considered, attention should focus on the kidney. When considering renal forms of ARF, it is helpful to think in terms of renal anatomic compartments (vasculature, glomeruli, interstitium, and tubules). Acute disorders involving any of these compartments can lead to ARF.

VASOMOTOR MECHANISMS CONTRIBUTING TO ACUTE RENAL FAILURE

Decreased Renal Perfusion Pressure	Afferent Arteriolar Constriction	Efferent Arteriolar Dilation
Extracellular fluid volume loss or sequestration	Sepsis	Converting enzyme inhibitors
Impaired cardiac output	Medications (NSAIDs, cyclosporine, contrast medium, amphotericin, alpha-adrenergic agonists)	Angiotensin II receptor antagonists
Antihypertensive medications	Hypercalcemia	
Sepsis	Postoperative state	
	Hepatorenal syndrome	

FIGURE 12-8

Vasomotor mechanisms contributing to acute renal failure (ARF). Most prerenal forms of ARF have operational one or more of the vasomotor mechanisms depicted here [6]. Collectively, these factors lead to diminished glomerular filtration and ARF. NSAIDs—nonsteroidal anti-inflammatory drugs.

DIAGNOSIS OF POSSIBLE PRERENAL CAUSES OF ACUTE RENAL FAILURE

History	Examination	Laboratory/Other
Extracellular fluid loss or sequestration from skin, gastrointestinal and/or renal source (*see* Fig. 12-15)	Orthostatic hypotension and tachycardia	Normal urinalysis
Orthostatic lightheadedness	Dry mucous membranes	Urinary indices compatible with normal tubular function (*see* Fig. 12-14)
Thirst	No axillary moisture	Elevated BUN-creatinine ratio
Oliguria	Decreased skin turgor	Improved renal function with correction of the underlying cause
Symptoms of heart failure	Evidence of congestive heart failure	Rarely, chest radiography, cardiac ultrasound, gated blood pool scan, central venous and/or Swan-Ganz wedge pressure recordings
Edema	Presence of edema	

FIGURE 12-9
Diagnosis of possible prerenal causes of acute renal failure (ARF). Prerenal events are the most common factors that lead to contemporary ARF. The historical, physical examination, and laboratory and other investigations involved in identifying a prerenal form of ARF are outlined here [1]. BUN—blood urea nitrogen.

DIAGNOSIS OF POSSIBLE POSTRENAL CAUSES OF ACUTE RENAL FAILURE

History	Examination	Laboratory/Other
Very young or very old age	Distended bladder	Abnormal urinalysis
Nocturia	Enlarged prostate	Elevated BUN-creatinine ratio
Decreased size or force of urine stream	Abnormal pelvic examination	Elevated postvoiding residual volume
Anticholinergic or alpha-adrenergic agonist medications		Abnormal renal ultrasound, CT or MRI findings
Bladder, prostate, pelvic, or intra-abdominal cancer		Improvement after drainage
Fluctuating urine volume		
Oligoanuria		
Suprapubic pain		
Urolithiasis		
Medication known to produce crystalluria (sulfonamides, acyclovir, methotrexate, protease inhibitors)		

FIGURE 12-10
Diagnosis of possible postrenal causes of acute renal failure (ARF). Postrenal causes of ARF are less common (5% to 15% of ARF population) but are nearly always amenable to therapy. This figure depicts the historical, physical examination and tests that can lead to an intrarenal (crystal deposition) or extrarenal (blockade of the collecting system) form of obstructive uropathy [1, 6, 9, 10]. BUN—blood urea nitrogen; CT—computed tomography; MRI—magnetic resonance imaging.

POSTOPERATIVE ACUTE RENAL FAILURE

Frequency	Predisposing Factors	Preventive Strategies
Elective surgery 1%–5%	Comorbidity results in decreased renal reserve	Avoid nephrotoxins
Emergent or vascular surgery 5%–10%	The surgical experience decreases renal function (volume shifts, vasoconstriction)	Minimize hospital-acquired infections (invasive equipment)
	A second insult usually occurs (sepsis, reoperation, nephrotoxin, volume/cardiac issue)	Selective use of volume expansion, vasodilators, inotropes
		Preoperative hemodynamic optimization in selected cases
		Increase tissue oxygenation delivery to supranormal levels in selected cases

FIGURE 12-11
Postoperative acute renal failure (ARF). The postoperative setting of ARF is very common. This figure depicts data on the frequency, predisposing factors, and potential strategies for preventing postoperative ARF [11, 12].

Diagnostic Steps in Evaluating Acute Renal Failure

STEPWISE APPROACH TO DIAGNOSIS OF ACUTE RENAL FAILURE

Step 1	Step 2	Step 3	Step 4
History Record review Physical examination Urinary bladder catherization (if oligoanuric) Urinalysis (*see* Fig. 12-15)	Consider urinary diagnostic indices (*see* Fig. 12-16) Consider need for further evaluation to exclude urinary tract obstruction Consider need for more data to assess intravascular volume or cardiac output status Consider need for additional blood tests Consider need for evaluation of renal vascular status	Consider selected therapeutic trials	Consider renal biopsy Consider empiric therapy for suspected diagnosis

FIGURE 12-12

Stepwise approach to diagnosis of acute renal failure (ARF). The multiple causes, predisposing factors, and clinical settings demand a logical, sequential approach to each case of ARF. This figure presents a four-step approach to assessing ARF patients in an effort to delineate the cause in a timely and cost-effective manner. Step 1 involves a focused history, record review, and examination. The salient features of these analyses are noted in more detail in Figure 12-13. In many cases, a single bladder catheterization is needed to assess the degree of residual volume, which should be less than 30 to 50 mL. Urinalysis is a critical part of the initial evaluation of all patients with ARF. Generally, a relatively normal urinalysis suggests either a prerenal or postrenal cause, whereas a urinalysis containing cells and casts is most compatible with a renal cause. A detailed schema of urinalysis interpretation in the setting of ARF is depicted in Figure 12-15. Usually, after Step 1 the clinician has a reasonably good idea of the likely cause of the ARF. Sometimes, the information noted under Step 2 is needed to ascertain definitively the cause of the ARF. More details of Step 2 are depicted in Figure 12-14. Oftentimes, urinary diagnostic indices (*see* Fig. 12-16), are helpful in differentiating between prerenal (intact tubular function) and acute tubular necrosis (impaired tubular function) as the cause of renal failure. Sometimes, further evaluation (usually ultrasonography, less commonly computed tomography or magnetic resonance imaging) is needed to exclude the possibility of bilateral ureteric obstruction (or single ureteric obstruction in patients with a single kidney). Occasionally, additional studies such as central venous pressure or left ventricular filling pressure determinations are needed to better assess whether prerenal factors are contributing to the ARF. When the cause of the ARF continues to be difficult to ascertain and renal vascular disorders (*see* Fig. 12-17 and 12-18), glomerulonephritis (*see* Fig. 12-19) or acute interstitial nephritis (*see* Fig. 12-20) remain possibilities, additional blood analyses and other tests described in Figures 12-18 through 12-20 may be indicated. Sometimes, selected therapeutic trials (*eg*, volume expansion, maneuvers to increase cardiac index, ureteric stent or nephrostomy tube relief of obstruction) are necessary to document the cause of ARF definitively. Empiric therapy (*eg*, corticosteroids for suspected acute allergic interstitial nephritis) is given as both a diagnostic and a therapeutic maneuver in selected cases. Rarely, despite all efforts, the cause of the ARF remains unknown and renal biopsy is necessary to establish a definitive diagnosis.

FIRST STEP IN EVALUATION OF ACUTE RENAL FAILURE

History
- Disorders that suggest or predispose to renal failure: hypertension, diabetes mellitus, human immunodeficiency virus, vascular disease, abnormal urinalyses, family history of renal disease, medication use, toxin or environmental exposure, infection, heart failure, vasculitis, cancer
- Disorders that suggest or predispose to volume depletion: vomiting, diarrhea, pancreatitis, gastrointestinal bleeding, burns, heat stroke, fever, uncontrolled diabetes mellitus, diuretic use, orthostatic hypotension, nothing-by-mouth status, nasogastric suctioning
- Disorders that suggest or predispose to obstruction: stream abnormalities, nocturia, anticholingeric medications, stones, urinary tract infections, bladder or prostate disease, intra-abnominal malignancy, suprapubic or flank pain, anuria, fluctuating urine volumes
- Symptoms of renal failure: anorexia, vomiting, reversed sleep pattern, puritus

Record review
- Recent events (procedures, surgery)
- Medications (*see* Fig. 12-22)
- Vital signs
- Intake and output
- Body weights
- Blood chemistries and hemogram

Physical examination
- Skin: rash suggestive of allergy, palpable purpura of vasculitis, livedo reticularis and digital infarctions suggesting atheroemboli
- Eyes: hypertension, diabetes mellitus, Hollenhorst plaques, vasculitis, candidemia
- Lungs: rales, rubs
- Heart: evidence of heart failure, pericardial disease, jugular venous pressure
- Vascular system: bruits, pulses, abdominal aortic aneurysm
- Abdomen: flank or suprapubic masses, ascites, costovertebral angle pain
- Extremities: edema, pulses, compartment syndromes
- Nervous system: focal findings, asterixis, mini-mental status examination
- Consider bladder catheterization
- Urinalysis (*see* Fig. 12-13)

FIGURE 12-13
First step in evaluation of acute renal failure.

SECOND STEP IN EVALUATION OF ACUTE RENAL FAILURE

- Urine diagnostic indices (*see* Fig. 12-16)
- Consider need for further evaluation for obstruction
  - Ultrasonography, computed tomography, or magnetic resonance imaging
- Consider need for additional blood tests
  - Vasculitis/glomerulopathy: human immunodeficiency virus infections, antineutrophilic cytoplasmic antibodies, antinuclear antibodies, serologic tests for hepatitis, systemic bacterial endocarditis and streptococcal infections, rheumatoid factor, complement, cryoglobins
  - Plasma cell disorders: urine for light chains, serum analysis for abnormal proteins
  - Drug screen/level, additional chemical tests
- Consider need for evaluation of renal vascular supply
  - Isotope scans, Doppler sonography, angiography
- Consider need for more data to assess volume and cardiac status
  - Swan-Ganz catheterization

FIGURE 12-14
Second step in evaluation of acute renal failure.

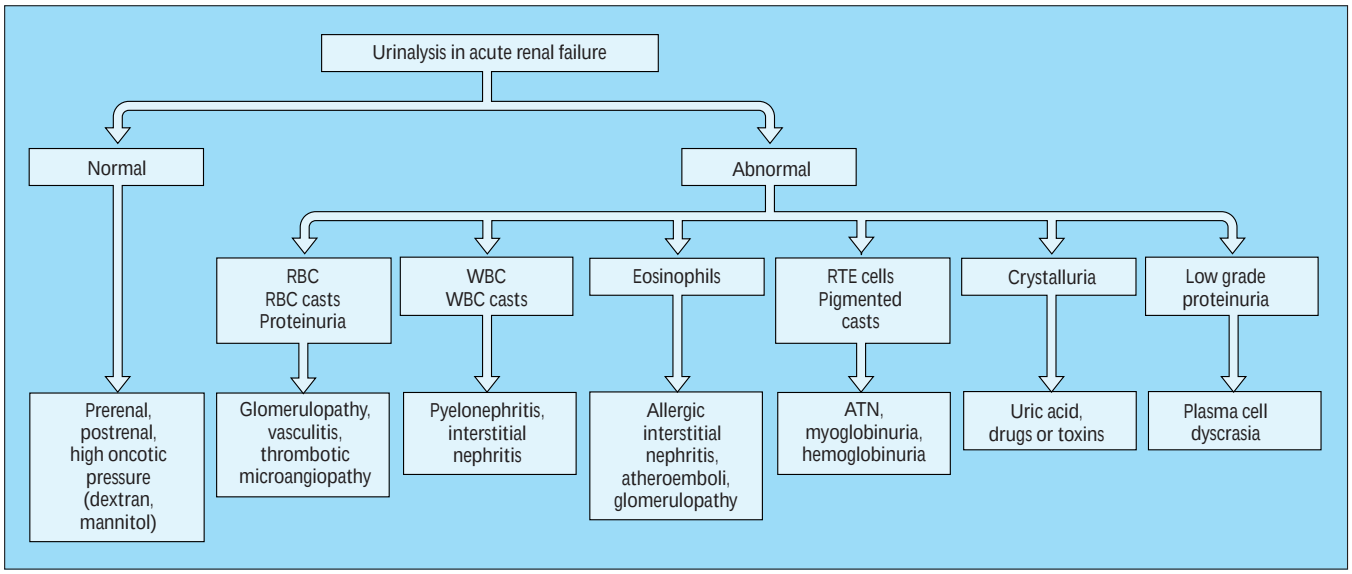

FIGURE 12-15

Urinalysis in acute renal failure (ARF). A normal urinalysis suggests a prerenal or postrenal form of ARF; however, many patients with ARF of postrenal causes have some cellular elements on urinalysis. Relatively uncommon causes of ARF that usually present with oliguria and a normal urinalysis are mannitol toxicity and large doses of dextran infusion. In these disorders, a "hyperoncotic state" occurs in which glomerular capillary oncotic pressure, combined with the intratubular hydrostatic pressure, exceeds the glomerular capillary hydrostatic pressure and stop glomerular filtration. Red blood cells (RBCs) can be seen with all renal forms of ARF. When RBC casts are present, glomerulonephritis or vasculitis is most likely. White blood cells (WBCs) can also be present in small numbers in the urine of patients with ARF. Large numbers of WBCs and WBC casts strongly suggest the presence of either pyelonephritis or acute interstitial nephritis. Eosinolphiluria (Hansel's stain) is often present in either allergic interstitial nephritis or atheroembolic disease [13, 14]. Renal tubular epithelial (RTE) cells and casts and pigmented granular casts typically are present in pigmenturia-associated ARF (*see* Fig. 12-21) and in established acute tubular necrosis (ATN). The presence of large numbers of crystals on urinalysis, in conjunction with the clinical history, may suggest uric acid, sulfonamides, or protease inhibitors as a cause of the renal failure.

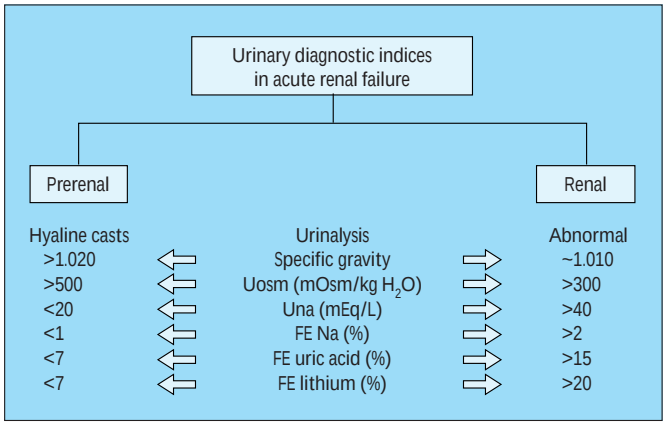

FIGURE 12-16

Urinary diagnostic indices in acute renal failure (ARF). These indices have traditionally been used in the setting of oliguria, to help differentiate between prerenal (intact tubular function) and acute tubular necrosis (ATN, impaired tubular function). Several caveats to interpretation of these indices are in order [1]. First, none of these is completely sensitive or specific in differentiating the prerenal from the ATN form of ARF. Second, often a continuum exists between early prerenal conditions and late prerenal conditions that lead to ischemic ATN. Most of the data depicted here are derived from patients relatively late in the progress of ARF when the serum creatinine concentrations were 3 to 5 mg/dL. Third, there is often a relatively large "gray area," in which the various indices do not give definitive results. Finally, some of the indices (*eg*, fractional excretion of endogenous lithium [FE lithium]) are not readily available in the clinical setting. The fractional excretion (FE) of a substance is determined by the formula: U/P substance ÷ U/P creatinine × 100. U/P—urine-plasma ratio.

Vascular Mechanisms Involved in Acute Renal Failure

VASCULAR CAUSES OF ACUTE RENAL FAILURE

Arterial	Venous
Large vessels	Occlusion
Renal artery stenosis	Clot
Thrombosis	Tumor
Cross-clamping	
Emboli	
Atheroemboli	
Endocarditis	
Atrial fibrillation	
Mural thrombus	
Tumor	
Small vessels	
Cortical necrosis malignant hypertension	
Scleroderma	
Vasculitis	
Antiphospholipid syndrome	
Thrombotic microangiopathies	
Hemolytic-uremic syndrome	
Thrombotic thrombocytopenic purpura	
Postpartum	
Medications (mitomycin C, cyclosporine, tacrolimus)	

FIGURE 12-17

Vascular causes of acute renal failure (ARF). Once prerenal and postrenal causes of ARF have been excluded, attention should be focused on the kidney. One useful means of classifying renal causes of ARF is to consider the anatomic compartments of the kidney. Thus, disorders of the renal vasculature (*see* Fig. 12-18), glomerulus (*see* Fig. 12-19), interstitium (*see* Fig. 12-20) and tubules can all result in identical clinical pictures of ARF [1]. This figure depicts the disorders of the renal arterial and venous systems that can result in ARF [15].

DIAGNOSIS OF POSSIBLE VASCULAR CAUSE OF ACUTE RENAL FAILURE

History	Examination	Laboratory/Other
Factors that predispose to vascular disease (smoking, hypertension, diabetes mellitus, hyperlipidemia)	Marked hypertension	Thrombocytopenia
Claudication, stroke, myocardial infarction	Atrial fibrillation	Microangiopathic hemolysis
Surgical procedure on aorta	Scleroderma	Coagulopathy
Catheterization procedure involving aorta	Palpable purpura	Urinalysis with hematuria and low-grade proteinuria
Selected clinical states (scleroderma, pregnancy)	Abdominal aortic aneurysm	Abnormal renal isotope scan and/or Doppler ultrasonography
Selected medications, toxins (cyclosporine, mitomycin C, cocaine, tacrolimus)	Diminished pulses	Renal angiography
Constitutional symptoms	Infarcted toes	Renal or extrarenal tissue analysis
	Hollendhorst plaques	
	Vascular bruits	
	Stigmata of bacterial endocarditis	
	Illeus	

FIGURE 12-18

Diagnosis of a possible vascular cause of acute renal failure (ARF). This figure depicts the historical, physical examination, and testing procedures that often lead to diagnosis of a "vascular cause" of ARF [1, 15, 16].

Acute Glomerulonephritis

DIAGNOSIS OF A POSSIBLE ACUTE GLOMERULAR PROCESS AS THE CAUSE OF ACUTE RENAL FAILURE

History	Examination	Laboratory/Other
Recent infection	Hypertension	Urinalysis with hematuria, red cell casts, and proteinuria
Sudden onset of edema, dyspnea	Edema	Serologic or culture evidence of recent infection
Systemic disorder (*eg*, lupus erythematosus, Wegener's granulomatosis, Goodpasture's syndrome)	Rash	Laboratory evidence of immune-mediated process (low complement, cryoglobulinemia, antinuclear antibody, anti-DNA, rheumatoid factor, anti–glomerular basement membrane antibody, antineutrophilic cytoplasmic antibody)
No evidence of other causes of renal failure	Arthropathy	Renal tissue examination
	Prominent pulmonary findings	
	Stigmata of bacterial endocarditis or visceral abscess	

FIGURE 12-19

Diagnosis of a possible acute glomerular process as the cause of acute renal failure (ARF). Acute glomerulonephritis is a relatively rare cause of ARF in adults. In the pediatric age group, acute glomerulonephritis and a disorder of small renal arteries (hemolytic-uremic syndrome) are relatively common causes. This figure depicts the historical, examination, and laboratory findings that collectively may support a diagnosis of acute glomerulonephritis as the cause of ARF [16, 17].

Interstitial Nephritis

DIAGNOSIS OF POSSIBLE ACUTE INTERSTITIAL NEPHRITIS AS THE CAUSE OF ACUTE RENAL FAILURE

History	Examination	Laboratory/Other
Medication exposure	Fever	Abnormal urinalysis (white blood cells or cell casts, eosinophils, eosinophilic casts, low-grade proteinuria, sometimes hematuria)
Severe pyelonephritis	Rash	Eosinophilia
Systemic infection	Back or flank pain	Urinary diagnositc indices compatible with a renal cause of renal failure (*see* Fig. 12-16)
		Uptake on gallium or indium scan
		Renal biopsy

FIGURE 12-20

Diagnosis of possible acute interstitial nephritis as the cause of acute renal failure (ARF). This figure outlines the historical, physical examination and other investigative methods that can lead to identification of acute interstitial nephritis as the cause of ARF [18].

Acute Tubular Necrosis

DIAGNOSIS OF POSSIBLE PIGMENT-ASSOCIATED FORMS OF ACUTE RENAL FAILURE

Myoglobinuria			Hemoglobinuria		
History	**Examination**	**Laboratory**	**History**	**Examination**	**Laboratory**
Trauma to muscles Condition known to predispose to nontraumatic rhabdomyolysis Muscle pain or stiffness Dark urine	Can be normal Muscle edema, weakness, pain Neurovascular entrapment or compartment syndromes in severe cases Flank pain	Serum creatinine disproportionately elevated related to BUN Elevated (10-fold) enzymes (CK, SGOT, LDH, adolase) Elevations of plasma potassium, uric acid, phosphorus, and hypocalcemia Urinalysis with pigmented granular casts, (+) stick reaction for blood in the absence of hematuria, and myoglobin test if available Clear plasma	Condition associated with intravascular hemolysis (red cell trauma, antibody-mediated hemolysis, direct red cell toxicity, sickle cell disease)	Can be normal Pallor Flank pain	Normocytic anemia High red cell LDH fraction Reticulocytosis Low haptoglobin Urinalysis with pigmented granular casts, (+) stick reaction for blood in absence of hematuria and reddish brown or pink plasma

FIGURE 12-21

Diagnosis of possible pigment-associated forms of acute renal failure (ARF). Once prerenal and postrenal forms of ARF have been ruled out and renal vascular, glomerular, and interstitial processes seem unlikely, a diagnosis of acute tubular necrosis (ATN) is probable. A diagnosis of ATN is thus one of exclusion (of other causes of ARF). In the majority of cases when ATN is present, one or more of the three predisposing conditions have been identified to be operational. These conditions include renal ischemia due to a prolonged prerenal state, nephrotoxin exposure, and sometimes pigmenturia. A diagnosis of ATN is supported by the absence of other causes of ARF, the presence of one or more predisposing factors, and the presence of urinary diagnostic indices and urinalysis suggested of ATN (*see* Figs. 12-15 and 12-16). A pigmenturic disorder (myloglobinuria or hemoglobinuria) can predispose to ARF. This figure depicts the historical, physical examination, and supporting diagnostic tests that often lead to a diagnosis of pigment-associated ARF [19]. BUN—blood urea nitrogen; CK—creatinine kinase; SGOT—serum glutamic-oxaloacetic transaminase; LDH—lactic dehydrogenase.

Nephrotoxin Acute Renal Failure

NEPHROTOXIC ACUTE RENAL FAILURE

Prerenal
- Diuretics
- Interleukin 2
- CEIs
- Antihypertensive agents

Tubular toxicity
- Aminoglyosides
- Cisplatin
- Vancomycin
- Foscarnet
- Pentamidine
- Radiocontrast
- Amphotercin
- Heavy metals

Vasoconstriction
- NSAIDs
- Radiocontrast agents
- Cyclosporine
- Tacrolimus
- Amphotericin

Endothelial injury
- Cyclosporine
- Mitomycin C
- Tacrolimus
- Cocaine
- Conjugated estrogens
- Quinine

Crystalluria
- Sulfonamides
- Methotrexate
- Acyclovir
- Triamterene
- Ethylene glycol
- Protease inhibitors

Glomerulopathy
- Gold
- Penicillamine
- NSAIDs

Interstitial nephritis
- Multiple

FIGURE 12-22

Nephrotoxin acute renal failure (ARF). A variety of nephrotoxins have been implicated in causing 20% to 30% of all cases of ARF. These potential nephrotoxins can act through a variety of mechanisms to induce renal dysfunction [6, 20, 21]. CEI—converting enzyme inhibitor; NSAID—nonsteroidal anti-inflammatory drugs.

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