Role of the Laboratory in Management of Acute and Chronic Renal Failure*

FRANCESCO DEL GRECO, M.D. and FRANK A. KRUMLOVSKY, M.D.

Section of Nephrology/Hypertension, Department of Medicine, Northwestern University Medical School, and
Clinical Research Center, Northwestern Memorial Hospital, Chicago, IL 60611

ABSTRACT

The initial assessment and differential diagnosis of acute renal failure is greatly facilitated by laboratory procedures of varying sensitivity and specificity; these are reviewed in detail. Patients with chronic renal failure receiving maintenance dialysis exhibit many laboratory abnormalities which may differ significantly between patients treated with hemodialysis and those receiving peritoneal dialysis. These are also reviewed.

Introduction

The role of the laboratory in acute and chronic renal failure is extremely important, both from the standpoint of differential diagnosis and management. It seems appropriate to discuss acute and chronic renal failure separately since, although there are many overlapping areas, the clinical and laboratory approaches to these syndromes are generally different.

Acute Renal Failure

Acute renal failure is usually first suspected by observing an increase in serum blood urea nitrogen (BUN) and/or creatinine concentration (Cr), or by a decrease in urine volume. Frequently, the patients have experienced acute hypotension or hypovolemia secondary to trauma, surgery, sepsis, myocardial infarction, or unrecognized dehydration, or have been exposed to a potentially nephrotoxic drug. Less commonly, acute renal failure presents as the manifestation of a systemic collagen-vascular disorder, in association with hemolysis or rhabdomyolysis, or is secondary to acute or chronic obstruction of the urinary tract. Rarely, acute glomerulo-nephritis is the cause of acute renal failure.

Prerenal Azotemia

Initially, the physician should attempt to classify acute renal failure as owing to prerenal, postrenal, or intrarenal mechanisms. This is of critical importance, since diagnostic and therapeutic procedures for reversing its course depend upon recogni-
tion of etiologic and pathogenic mechanisms. Prerenal azotemia develops as a result of decreased effective renal blood flow with resultant renal hypoperfusion almost always due to hypotension or intravascular hypovolemia. These, in turn, may be related to such diverse clinical events as dehydration, hemorrhage, reduced cardiac output secondary to myocardial infarction, congestive heart failure, or cardiac tamponade, sepsis, burns, adrenal insufficiency, or excessive doses of antihypertensive drugs.

Macro or microvascular disease resulting from renal artery stenosis or embolus, systemic or drug related vasculitis, or malignant hypertensive nephrosclerosis may all decrease renal blood flow and produce the picture of prerenal azotemia. The term, prerenal azotemia, implies lack of structural damage to the renal parenchyma itself. Thus, if the cause is corrected, renal function should return promptly to normal. Prerenal azotemia owing to hypotension or hypovolemia may, however, progress to acute tubular necrosis, which is not immediately reversible upon correction of prerenal factors and which may lead to permanent renal structural damage. For this reason, prompt recognition and appropriate management of prerenal azotemia is of critical importance.

**POSTRENAL AZOTEMIA**

Postrenal azotemia refers to obstruction of the urinary tract at any point along its course. It is important to emphasize that renal failure in presence of a normal urine output does not rule out obstructive uropathy as the cause, since incomplete obstruction may present as apparent acute renal failure with severe azotemia and a normal urine volume. Therefore, it is imperative to rule out obstruction in any patient with acute renal failure in whom prompt recovery of function does not occur following correction of prerenal factors.

**INTRARENAL AZOTEMIA**

Intrarenal causes of acute renal failure can be divided into several categories. Acute tubular necrosis is by far the most common and is usually subdivided into ischemic and nephrotoxic categories. Ischemic acute tubular necrosis is usually due to persistent or severe renal hypoperfusion consequent to the same causes outlined previously for prerenal azotemia. In many cases, a continuous spectrum progressing from prerenal azotemia to ischemic acute tubular necrosis may exist, depending upon duration and severity of renal hypoperfusion. Nephrotoxic acute tubular necrosis may result from exposure to a vast number of potentially nephrotoxic agents. The most commonly encountered clinically are nephrotoxic antibiotics, in particular those of the aminoglycoside group.

A variety of other drugs, organic solvents, heavy metals, and other agents may also produce acute tubular necrosis. Endogenous toxins, such as hemoglobinuria resulting from intravascular hemolysis owing to endotoxemia, mismatched transfusions, the hemolytic-uremic syndrome, or fresh water drowning, or myoglobinuria secondary to crush injury, heat stroke, deep burns, excessive exercise, hypokalemia, or primary myopathy, may also result in acute tubular necrosis. Other endogenous toxins include myeloma protein, acute urate nephropathy, and occasionally hypercalcemia. Finally, acute renal failure secondary to administration of iodinated contrast material may occur, owing either to direct tubular toxicity of the contrast agent or to acute urate nephropathy secondary to the uricosuric effect of the drug.

Other intrarenal causes of acute renal failure, in addition to tubular necrosis, include the whole spectrum of acute nephritides (a discussion of which is beyond the scope of this presentation), acute cortical necrosis, usually secondary to renal microvascular or macrovascular disease, and
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Acute interstitial nephritis. Other potential causes of acute renal failure of more diverse or less well understood mechanism include obstetrical events, such as toxemia, abruptio placentae, acute postpartum renal failure, and the hepatorenal syndrome.

The clinician's approach will require careful assessment of history, physical examination and, in particular, of laboratory studies for differential diagnosis and management. Determination of date of onset and rate of progression is especially helpful to correlate with possible etiologic factors. Physical examination will emphasize evaluation of state of hydration, with assessment of jugular venous filling, orthostatic hypotension or tachycardia, and presence of edema, rales, ascites, cool extremities, or signs of congestive heart failure. A recent change in weight, intake vs. output, or blood pressure may provide valuable clues.

Laboratory Evaluations

Examination of the urine is usually the first laboratory evaluation performed. Presence of red blood cells in the sediment is of particular importance in suggesting probable presence of either lower urinary tract bleeding, or acute glomerulonephritis, or vasculitis. Red blood cell casts indicate glomerular hematuria and will confirm a diagnosis of glomerulitis or vasculitis. Myoglobin casts may be seen in patients with acute myoglobinuria. White blood cells imbedded within a hyaline cast will help differentiate lower urinary tract infection from renal parenchymal infection. Bile stained casts may be seen in conditions such as carbon tetrachloride or mercury poisoning and in the hepatorenal syndrome. The presence of renal tubular epithelial cell casts, especially of a characteristic dirty brown color, is consistent with a diagnosis of acute tubular necrosis. The urine sediment in prerenal azotemia is generally unremarkable. Likewise, the urine sediment may be entirely normal in acute interstitial nephritis, although on occasion eosinophils may be seen. Crystals in the urine, in particular uric acid, oxalate, or sulfonamide, may provide valuable clues as to etiology of the acute renal failure.

After the initial assessment, the nephrologist will usually turn to laboratory parameters which will assist in differentiating prerenal, postrenal, and intrarenal causes of acute renal failure (table I). These studies, including determination of urine and plasma urea nitrogen and creatinine, urine osmolality (UOsm), urine sodium (UNa), renal failure index \( \frac{\text{UNa}}{\text{UCr}/\text{PCr}} \), and fractional excretion of filtered sodium

\[
\% \text{FNa} = \frac{\text{UNa}/\text{PNa}}{\text{UCr}/\text{PCr}} \times 100
\]

should be obtained before any therapeutic intervention if possible. Results can be rendered uninterpretable by several therapeutic measures, particularly with the administration of mannitol or furosemide. It is not necessary to obtain a timed (12 or 24 hour) urine collection, since the patient with acute renal failure is unable to vary his UNa concentration or UOsm significantly from hour to hour. A random sample will provide information of comparable validity to that obtained from a longer timed collection, and results can be made available almost immediately.

In prerenal azotemia, urinary findings are consistent with renal hypoperfusion and well preserved tubular function (table I). Urine specific gravity will be high, generally greater than 1.018; UOsm will also be high, > 400 mOsm per liter. Since the kidney with normal tubular function responds to hypoperfusion by conserving sodium and water, UNa will generally be low (< 30 mEq per L), urine to plasma osmolality ratio will be above 1.2, urine to plasma Cr ratio greater than 40, and urine to plasma urea nitrogen ratio greater than...
TABLE I
Laboratory Tests to Differentiate Pre-Renal Azotemia and Acute Tubular Necrosis (ATN)

<table>
<thead>
<tr>
<th>Urine and/or Serum Values</th>
<th>Pre-Renal</th>
<th>ATN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Na, mEq/L</td>
<td>&lt; 30</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>Urine specific gravity</td>
<td>&gt; 1.018</td>
<td>&lt; 1.018</td>
</tr>
<tr>
<td>Urine osmolality</td>
<td>&gt; 400</td>
<td>&lt; 400</td>
</tr>
<tr>
<td>U/P osmolality ratio</td>
<td>1.2 - 3.0</td>
<td>0.9 - 1.2</td>
</tr>
<tr>
<td>U/P urea nitrogen ratio</td>
<td>&gt; 10</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>U/P creatinine ratio</td>
<td>&gt; 30</td>
<td>&lt; 30</td>
</tr>
<tr>
<td>Renal failure index</td>
<td>&lt; 1.0</td>
<td>&gt; 1.0</td>
</tr>
<tr>
<td>BUN: creatinine ratio</td>
<td>&gt; 10:1</td>
<td>10:1</td>
</tr>
<tr>
<td>FENa</td>
<td>&lt; 1.0</td>
<td>&gt; 1.0</td>
</tr>
</tbody>
</table>

U/P = Urine/plasma.
Renal failure index = U/P creatinine
FENa = fractional excretion of sodium = 

\[
\frac{(U/P \text{ Na} \times 100)}{(U/P \text{ Cr})}
\]

10. The fractional excretion of filtered sodium, percent of FNa, will be less than 1 percent and the "renal failure index" will be less than 1.0. The BUN to serum Cr ratio in prerenal azotemia will usually be > 10:1. Heavy proteinuria (greater than 1 g per 24 hrs) is unusual.

In acute tubular necrosis, ability to conserve Na and water is diminished, resulting in a high UNa, usually > 30 to 40 mEq per L. UOsm approximates that of plasma, and the UOsm to P0sm ratio will be about 1.0. The urine specific gravity will approximate 1.010. The UCr to PCr ratio will usually be less than 20, and the urine:plasma urea ratio less than 10, and frequently less than 5. Filtered sodium will be greater than one percent, and the "renal failure index" will be greater than 1.0. The BUN:serum Cr ratio will approach the normal value of 10:1. Low grade proteinuria is frequently seen (less than 1 to 1.5 g per 24 hrs). Similar results from these indices will be obtained from both oliguric and nonoliguric forms of acute tubular necrosis.

Diagnostic features for other types of acute renal failure are less characteristic. In general, patients with acute glomerulonephritis will exhibit urinary indices similar to those observed with prerenal azotemia, and patients with urinary tract obstruction findings will exhibit indices similar to those with acute tubular necrosis.3

Discriminant analysis of the above parameters in 87 patients with acute renal failure (22 with acute oliguric tubular necrosis, 18 with acute nonoliguric tubular necrosis, 12 with acute urinary tract obstruction, 14 with acute glomerulonephritis, and 21 with prerenal azotemia) demonstrated a correct diagnostic classification in 86 of 87 patients using percent of FNa and only 46, 60, and 65 correct using UOsm, UNa, and UCr to PCr ratio, respectively.4 In this study, percent of FNa was identified as the most reliable noninvasive test for the differential diagnosis of acute renal failure. A value of more than one percent was consistent with oliguric or nonoliguric acute tubular necrosis or urinary tract obstruction, and less than one percent with prerenal azotemia or acute glomerulonephritis.

Other diagnostic studies are applicable in specific circumstances of a particular type of acute renal failure. Renal ultrasonography is most useful in ruling out presence of obstruction and in determining renal size. The procedure is safe and applicable to any level of renal function, since renal function is not required for visualization. Parenchymal abnormalities can, however, be evaluated only grossly by this technique. Radioisotopic examinations with Technetium-99m/SN/diethylene-triamine-pentaacetic acid (DTPA), Technetium-99m/ SN/dimercaptosuccinic acid (DMSA), and iodohippurate can be utilized to evaluate, in a somewhat imprecise but still clinically useful manner, renal anatomy, tubular function, and renal plasma flow.13 DTPA is excreted by glomerular filtration, can be used to assess renal blood flow and glomerular filtration rate, and is often referred to as an isotope arteriogram, although far inferior to standard renal arteriography. The isotope, DMSA, can likewise be used to determine gross renal anatomy and renal blood flow and, with computer techniques, to estimate selective renal plasma flow. The iodohippurate study can be utilized in a
somewhat crude manner to assess renal blood flow and tubular secretion, as well as possible obstruction. Intravenous urography is useful in determining renal anatomy, but it is not helpful in assessing renal function, except in a gross manner. Renal angiography may be indicated if renal artery stenosis, polyarteritis nodosa, arteriovenous malformation, or a mass lesion of the kidney exists or is suspected. Renal venography may be indicated to rule out renal vein thrombosis, and retrograde pyelography will definitively rule out urinary tract obstruction or further evaluate mass lesions.

If acute glomerulonephritis is suspected as a cause of acute renal failure, such studies as antinuclear antibody, antistreptolysin 0 titer, and serum complement may be indicated, as well as measurement of circulating immune complexes and antiglomerular basement membrane antibodies. Glomerulonephritis secondary to hepatitis B virus is being seen with increasing frequency and a determination of hepatitis-associated antigen has become part of the routine evaluation of patients presenting with acute glomerulonephritis. Occult malignancy must be ruled out in patients presenting with the nephrotic syndrome and renal failure. Serum and urine protein electrophoresis, examination of the urine for Bence Jones protein, and bone marrow examination may be indicated if multiple myeloma is clinically suspected. Urinary myoglobin determination is appropriate if myoglobinuria is suspected.

Disseminated intravascular coagulation or thrombotic thrombocytopenic purpura are observed not infrequently as causes of acute renal failure, and evaluation of coagulation profile as well as peripheral smear for presence of schistocytes will be appropriate in these cases. Hypercalcemia and hyperuricemia should be ruled out if clinically suspected. A serum chloride to phosphate ratio of greater than 33:1 in the presence of hypercalcemia suggests hyperparathyroidism. The possibility of acute allergic interstitial nephritis as a cause of acute renal failure can be evaluated by searching for eosinophilia in the peripheral blood or urine. Cryoglobulinemia, lymphoma, and macroglobulinemia may be associated with acute renal failure, and appropriate studies should be performed if clinically suspected.

Hypokalemia or hypophosphatemia may result in rhabdomyolysis with acute renal failure and, thus, determination of these electrolytes is routinely indicated. Acute urate nephropathy is usually associated with a uric acid:creatinine concentration ratio on a random urine sample of greater than 1.0, while patients with other types of acute renal failure will characteristically have a ratio of less than 1.0. As previously indicated, a vast number of drugs, heavy metals, solvents, and other substances are potentially nephrotoxic and may be the cause of acute renal failure. If there is anything in the clinical history of presentation to suggest a possible role for such agents, appropriate toxicologic studies should be performed. Finally, renal biopsy is occasionally indicated for diagnostic or prognostic purposes.

The laboratory management of the patient with acute renal failure, once dialysis has been instituted, is in many respects similar to that of the chronic dialysis patient, and will be discussed in the following section.

Chronic Renal Failure and Maintenance Dialysis

The initial assessment and evaluation of the patient who presents with chronic renal failure is, in many respects, simpler and more straightforward than the patient with acute renal failure; however, long-term management may be considerably more difficult. In most patients with chronic renal failure, the diagnosis will already have been determined or will be readily apparent. Careful evaluation must be made for any potentially reversible cause such as obstruction, infection, ingestion of nephrotoxic drugs, interstitial nephritis secondary to hypercalcemia,
hyperuricemia, hyperoxaluria, or heavy metal exposure. Other reversible causes include collagen vascular disease such as systemic lupus erythematosus or polyarteritis nodosa, Wegener’s granulomatosis, multiple myeloma, or membranous nephropathy secondary to occult lymphoma or other occult malignancy. As indicated previously, interstitial nephritis is characterized by bland urinalysis in the face of impaired renal function, which is associated with the inability to concentrate or dilute urine which may result in polyuria. Renal salt wasting is common, and hypertension relatively uncommon. Patients with primary glomerular disease, on the other hand, will frequently present with proteinuria greater than 2 g per 24 hrs, a more active urine sediment frequently containing red cells and casts, hypertension, and oliguria.

Once correctable or reversible factors have been ruled out, a decision must be made regarding institution of dialysis. In the patient with acute renal failure, this decision will be made based upon several criteria: sodium and volume overload, metabolic acidosis, or hyperkalemia not controllable by medical management; the development of uremic pericarditis; or an elevation of BUN above 100 to 120 mg per dl, especially if the rate of rise is rapid. Patients with acute renal failure are generally dialyzed frequently, and management of fluid, electrolyte, and acid base status is monitored by frequent laboratory determinations.

Institution of dialysis in chronic renal failure is based in many cases on criteria similar to those previously outlined; however, other criteria may also apply. In general, chronic dialysis is instituted when the creatinine clearance falls below 7 to 8 ml per min. This may reduce risk of development of peripheral neuropathy, renal osteodystrophy, uremic cardiomyopathy, and uremic pericarditis. Chronic dialysis may also be instituted when the patient becomes clinically uremic, usually manifest by such symptoms as anorexia, nausea, or vomiting.

**Dialysis Monitoring**

Adequacy of chronic dialysis must be monitored by several clinical and laboratory parameters. Hyponatremia may develop, usually on a dilutional basis. Hyperkalemia is a frequent problem, owing to both failure of excretion and excessive ingestion, or acute acidosis. Metabolic acidosis is almost universal in chronic dialysis patients and can usually be monitored adequately by serum bicarbonate levels. Endogenous production of fixed acids requiring renal excretion approximates 1 mEq per kg per day. Since the renal route of excretion of this acid load is lost in renal failure, it must be buffered by bone salts, which may contribute to renal osteodystrophy. Acidosis is controlled primarily by dialysis, utilizing dialysate containing either acetate or bicarbonate.

Bicarbonate dialysis is more physiologic and will directly elevate serum bicarbonate concentrations. Because of solubility problems when bicarbonate dialysate is used, acetate is widely used. Acetate diffuses into the patient during dialysis and will ultimately be metabolized to bicarbonate. However, in the early stages of each dialysis, acetate diffuses into the patient, while bicarbonate diffuses out, resulting in a temporary worsening of the already present metabolic acidosis. This combination of increased metabolic acidosis and elevated serum acetate level may result in peripheral vasodilation, decreased cardiac output, hypotension, and cardiac arrhythmias. Thus, currently there is an increasing tendency to use bicarbonate containing dialysate, especially in patients who are unstable cardiovascularly.

Calcium and phosphorus metabolism in the chronic dialysis patient are extremely important. Phosphorus excretion becomes impaired in the very early stages of renal failure. This phosphate retention re-
It is of interest to mention that in acute renal failure secondary to rhabdomyolysis, hypocalcemia is common as calcium deposits in injured muscle. During the recovery phase, this calcium may be mobilized, resulting in hypercalcemia.

Serum magnesium levels are usually within normal limits or only slightly elevated even in patients with severe renal failure. Fractional excretion of magnesium has been shown to increase as renal failure progresses. Most hypermagnesemia seen in patients with chronic renal failure results from excessive dietary ingestion, including magnesium containing antacids.

Although hyperuricemia is common in acute and chronic dialysis patients, the risk of urate nephropathy is minimal, since such patients are usually unable to concentrate or acidify their urine maximally. Allopurinol therapy is therefore usually not indicated, unless serum uric acid level exceeds 14 or 15 mg per dl, or symptoms of acute gout supervene.

Anemia is almost universal in chronic dialysis patients owing to reduced erythrocyte life span, reduced erythropoietin production, and possibly circulating factors that inhibit bone marrow response to erythropoietin. Iron deficiency is also relatively common as a result of decreased dietary intake and intestinal absorption, small but recurring blood losses owing to blood sampling, and residual blood in the dialyzer after each treatment. This can be readily assessed by determination of serum ferritin levels and, if necessary, by bone marrow aspiration for iron determination. Serum ferritin levels are widely used as an indication for exogenous iron administration if reduced. If adequate iron stores are present, administration of androgens is frequently undertaken in an attempt to increase erythropoiesis. Folic acid levels are measured routinely, since folic acid is a dialyzable water soluble vitamin. If levels are low, folic acid supplementation is administered. However, all of these measures may fail to

results in chelation of calcium ion, with resultant tendency towards hypocalcemia and development of secondary hyperparathyroidism. This permits maintenance of normal serum phosphorus until creatinine clearance falls below 20 to 25 ml per min. At this level of renal function, secondary hyperparathyroidism is no longer adequate to maintain adequate phosphaturia, and serum phosphorus begins to rise. Serum calcium concentration likewise usually remains within the normal range until creatinine clearance falls below 20 to 25 ml per min. The development of hypocalcemia, characteristic of chronic renal failure, is largely due to failure of the kidney to metabolize vitamin D to its biologically active metabolite, 1,25-dihydroxycholecalciferol.

In addition, there is evidence that bone becomes resistant to the action of parathyroid hormone. Although hypocalcemia is commonly seen in renal failure, tetany is rare, probably owing to metabolic acidosis increasing the ionized fraction of plasma calcium. On occasion, especially in patients with acute renal failure, administration of sodium bicarbonate may produce tetany owing to an abrupt decrease in the ionized fraction of plasma calcium.

Increased calcium phosphorus product in the chronic dialysis patient is managed by a combination of dietary phosphate restriction, oral phosphate binders, phosphate free dialysate, and relatively high calcium containing dialysate, in an attempt to maintain normocalcemia and suppress hyperparathyroidism. Administration of oral calcium supplements, frequently in association with vitamin D analogues such as Hytakerol or 1,25-dihydroxycholecalciferol, are usually recommended. Most chronic dialysis patients demonstrate elevated levels of parathyroid hormone. Owing to the variety of assays available, it still is difficult to correlate changes in serum parathyroid hormone levels with patient’s symptoms or radiographic changes.
maintain a satisfactory hematocrit level, and periodic blood transfusions must be instituted. Some patients may require administration of two units of packed red blood cells every three to four weeks. Physicians are becoming increasingly aware of the potential problem of iron overload in such patients. With increasing life expectancy on dialysis, this may become an increasingly frequent and serious problem.

Leukopenia and thrombocytopenia in chronic dialysis patients are usually a result of congestive hypersplenism. Platelet dysfunction is also seen in acute renal failure and chronic dialysis, manifested by reduced platelet factor 3 and decreased platelet aggregation. Increased levels of beta-thromboglobulin are seen in chronic renal failure, which increase further after hemodialysis, probably reflecting increased platelet consumption as well as decreased renal excretion of beta-thromboglobulin.

A prospective study recently completed by us compared maintenance hemodialysis to maintenance peritoneal dialysis in 32 carefully paired patients utilizing a variety of clinical and laboratory parameters. The peritoneal dialysis group demonstrated significantly lower values for blood urea nitrogen, potassium, total protein and albumin (probably reflecting peritoneal losses), and calcium (consistent with lower serum albumin); significantly higher values were demonstrated for bicarbonate, hematocrit, and hemoglobin. Lipid profiling demonstrated significantly increased triglycerides in both groups, with the peritoneal dialysis patients somewhat more elevated, decreased lipoprotein lipase activity in both groups, and significantly reduced high density lipoprotein cholesterol in hemodialysis but not peritoneal dialysis patients. Laboratory profiles of patients maintained on continuous ambulatory peritoneal dialysis have recently been reviewed by Nolph et al. Sexual dysfunction is common in chronic dialysis patients and is associated with a number of endocrinologic abnormalities. Serum-testosterone levels are low in most patients, suggesting interstitial (Leydig) cell dysfunction; even elevated luteinizing hormone levels were unable to restore testosterone production to normal. It is also possible that luteinizing hormone levels may not be appropriately elevated for the decreased testosterone levels, suggesting hypothalamic inhibition as well. Testicular hyporesponsiveness to luteinizing hormone probably results from cellular toxicity of retained uremic toxins. Pituitary function, however, appears relatively well preserved, since testosterone administration has been shown to suppress the elevated levels of luteinizing hormone. Early luteinizing hormone response to luteinizing hormone releasing hormone has been found to be normal or increased.

Spermatogenesis is impaired in chronic renal failure, ranging from mild impairment to germinal cell aplasia. This defect also appears to lie at the testicular level, since plasma levels of follicle stimulating hormone have been found to increase in parallel with damage to spermatogenesis. This suggests that the feedback relationship between seminiferous tubule epithelium and secretion of follicle stimulating hormone by the pituitary gland remains intact. Again, however, levels of follicle stimulating hormone may not be appropriately elevated, suggesting a hypothalamic defect in addition. Prolactin levels are elevated in chronic renal failure, probably related to impaired degradation resulting from decreased renal mass. Lowering prolactin levels with bromocriptine may restore gonadal function to normal, and favorable response to bromocriptine in chronic dialysis patients with impotence has been described.

Decreased plasma zinc levels have been reported in patients on chronic dialysis. Zinc deficiency has been shown
to cause growth retardation and testicular atrophy in laboratory animals, as well as delayed sexual development in humans. Dialytic administration of zinc has been shown to increase plasma testosterone levels and improve potency in chronic dialysis patients, although others have reported no beneficial effect.

Thyroid metabolism is quite complex in chronic dialysis patients. The response of thyroid stimulating hormone (TSH) to thyrotropin releasing hormone (TRH) is delayed and prolonged, probably owing to both hypothalamic-hypophyseal abnormalities and impaired renal degradation of TSH. Thyroid stimulating hormone, thyroid binding globulin (TBG), and T4 levels are usually normal, but T3 levels are reduced, owing to impaired peripheral conversion of T4 to T3. Chronic dialysis patients are clinically euthyroid, however, as measured by basal metabolic rate. Many other endocrinologic abnormalities are also frequently observed in patients with chronic renal failure.

Space does not permit discussion of numerous other laboratory abnormalities associated with chronic renal failure. Many of these are discussed in references included in this review.

References