Q&A CURRENT MANAGEMENT OF RENAL FAILURE

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Renal failure can be hard to treat because of its many diverse causes and the complications that arise from it.

What forms can renal failure take?

Renal failure, which manifests as azotemia, takes three forms: prerenal, renal, and postrenal. Prerenal azotemia results from anomalies that occur before blood is filtered by the kidney. The renal form is due to disease of the kidney itself. Finally, there can be impairments in postrenal processes.

What is prerenal azotemia, and how is it detected?

Prerenal azotemia is a reflection of decreased renal function due to reduction in arterial flow to the kidney. There is a spectrum of renal injury, from readily reversible to permanent failure, depending on the magnitude and duration of the insult. Causes of prerenal insufficiency are presented in *Table 1*. The diagnostic tests for prerenal failure are listed in *Table 2*.

In renal failure, there are always some nephrons that are dead (primarily cortical nephrons); some that have sustained damage (acute tubular necrosis); some that are not working but may recover; and, finally, some that would function if they were supplied with greater renal blood flow (prerenal failure). ➤

"In my day, I didn't need the Internet to tell me how my stocks were doing. I could feel it in my bones."

Table 1. Causes of Prerenal Azotemia

Blood loss: Gastrointestinal hemorrhage, trauma, and hemolytic anemia

Endocrine: Diabetes mellitus, diabetes insipidus, Addison's disease

Fluid loss: Diarrhea, vomiting, nasogastric suctioning, sweating, burns, diuretics, laxatives

Cardiac: Acute myocardial infarction, congestive heart failure, valvular heart disease, pericardial tamponade, constrictive pericarditis

The tests in *Table 2* aid in detecting a reversible component caused by reduced renal blood flow or volume contraction, such that, with volume repletion, renal function would improve. These indices should only be used when the patient is oliguric.

The definition of oliguria is derived from an understanding of the kidney's ability to concentrate and dilute. If the maximum urinary osmolality is 1200 mOsm/L and the normal daily waste solute is 600 mOsm/L, then the smallest urine volume that can excrete the daily waste is 600/1200 or 500 mL of urine daily. Thus, if the patient is excreting <500 mL of urine per 24 hours, the patient is in oliguric renal failure. Each of the indices listed in *Table 2* gives some indication of whether the kidney is still functioning. A urinary sodium index <10 mEq/L indicates that the kidney is recognizing the presence of volume contraction and is maximally reabsorbing sodium to expand the plasma volume. Thus, the kidney has not "failed." On the other hand, a high urinary sodium (>10 mEq/L) implies that the kidney is not responding appropriately to volume contraction and is "failing." All of the indices in *Table 2* operate on this same principle. The fractional excretion of sodium (FENA) is the most commonly used of these indices, as it tries not only to account for sodium avidity (urinary-to-plasma sodium) but also indexes this to the clearance of creatinine (i.e., renal function). Unfortunately, these ratios are not highly predictive of the individual patient's ability to respond to volume expansion.

In patients with prerenal failure, time is critical. The longer the nephrons are exposed to reduced blood flow (volume depletion), the more likely they are to become damaged or die. Thus, all patients with oliguric renal failure warrant an acute trial of volume expansion without waiting for the results of these flawed indices of prerenal failure.

How can the patient's volume be safely expanded?

Patients with renal failure are often older and have multiple other disabilities, including heart disease, making volume expansion more difficult—especially since the amount of fluid required to expand the plasma volume acutely is on the order of 2-4 L of 0.9 percent saline over a two- to four-hour period. In the hypotensive patient with a known source of volume depletion, such as diarrhea and vomiting, it is reasonable to give large amounts of intravenous fluids.

If, however, the clinical examination does not yield a definite result showing whether the patient is hypovolemic, or if there is history of heart disease, ➤

Table 2. Diagnostic Urinary Indices in Prerenal Azotemia

Urine Indices	Prerenal Azotemia	Renal Failure
Urine sodium index	<10 mEq/L	>10 mEq/L
Urine osmolality	>600 mOsm/L	<600 mOsm/L
Urinary/plasma BUN	>8	<8
Renal failure index urine sodium ÷ (urine creatinine/plasma creatinine)	<1	>3
Fractional excretion of sodium (FENA) (urine sodium/plasma sodium) ÷ (urine creatinine/plasma creatinine)	<1	>3

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A Clinical Case: Excess Painkiller Use and Fatigue

The patient, Mr. H, is a 45-year-old man who presented with loss of appetite and fatigue for the past eight months. During the last year, he had become hypertensive, and he is now taking methyldopa and hydrochlorothiazide. Most of his previous contacts with medical care involved visits to the doctor and to the emergency room for headaches. He has been on multiple medications for his headaches, most recently acetaminophen, ibuprofen, and sumatriptan. Review of his records, including ER visits, reveals that his serum creatinine was 1.0 mg/dL 13 years ago, 1.3 mg/dL 10 years ago, 2.3 mg/dL six years ago, and 6.1 mg/dL six months prior to this visit.

The patient's current medications include hydrochlorothiazide 50 mg/day, methyldopa 250 mg b.i.d., and Fiortal (50 mg butalbital, 325 mg aspirin, and 40 mg caffeine) p.r.n. At examination, Mr. H's blood pressure was 170/100 mm Hg sitting and 160/100 standing. Fundi showed group 1 Keith-Wagener-Barker changes of hypertension. A 2/6 systolic ejection murmur was noted at the upper left sternal border. There was no organomegaly, abdominal mass or ascites, or peripheral edema. Peripheral arterial pulse was normal. His electrolytes were unremarkable. Blood urea nitrogen was 73 mg/dL, and serum creatinine was 6.1 mg/dL. Urinalysis showed occasional white and red blood cells, but no casts. A 24-hr urine revealed 210 mg protein and a creatinine clearance of 12 mL/min. Ultrasound showed 7.1-cm kidneys with thin cortices. There was no hydronephrosis. The patient had analgesic nephropathy and chronic interstitial renal failure.

Mr. H has no history of collagen vascular diseases, renal stones, infections, antibiotic usage, diabetes mellitus, prostatism, abnormal voiding patterns, proteinuria, or illicit drug use. Asking about insurance, employment, or school athletic physicals can uncover this information. Proteinuria, hematuria, and hypertension may be discovered at these times and knowing whether the patient passed these examinations can help establish the time course of the renal disease. Almost all drugs can cause renal failure, so a good review of medications is important. A list of the most common drugs known to cause renal failure appears in *Table 3*. Mr. H has been taking analgesic medications to relieve chronic headaches for many years, and his serum creatinine has been rising over a period of 13 years. Finally, he does have hypertension but has only had it in the last year after he had developed significant renal failure, as indicated by serum creatinine >4mg/dL and thus an estimated creatinine clearance of <30 mL/min.

there are two options: One is to give fluids and carefully monitor the patient at 15-minute intervals for signs and symptoms of volume overload or nonresponsiveness to volume expansion. However, this approach requires a lot of time, and even the most astute clinician will only have excluded prerenal failure by volume-overloading the patient while increasing the need for emergent dialysis, since the patient with renal failure due to kidney disease is not likely to respond to diuretics.

A more practical approach is to place an IV monitoring line, such as a central venous catheter or Swan-Ganz pulmonary artery catheter, to monitor volume status minute by minute. As the volume challenge is administered, the filling pressures of the heart can be measured and the urine output observed. Rising filling pressures without the concomitant rise in urine volumes will allow the physician to reassess the appropriateness of the volume challenge and stop it before there is clinically significant volume overload. The catheter should be required for <48 hours, reducing the risk of catheter-related complications. For patients with known severe heart disease and low cardiac output, this approach allows volume expansion by maximizing cardiac output with such agents as dobutamine or angiotensin-converting enzyme inhibitors. The resultant rise in cardiac output will increase renal blood flow and urinary volumes, leading to renal recovery from prerenal failure.

Is furosemide effective for converting the patient from oliguric to nonoliguric renal failure?

Several protocols in the literature center around administration of the potent loop diuretic furosemide in the patient with oliguric renal failure. The hope is that by increasing urinary sodium and water excretion, the patient's chances of combating renal failure will improve. Of the many dosing regimens in the literature, one of the most aggressive is from Cantarovich (*Postgrad Med J* 47:13, ➤

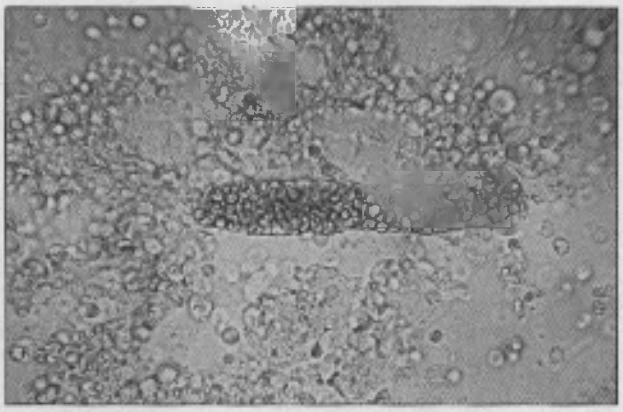

Figure 1. A classic red blood cell cast.

1971), who recommends a progressive dosing schedule from 100 to as much as 3200 mg of IV furosemide daily. Although this protocol was associated with a significant increase in the number of patients who converted from oliguric to nonoliguric acute renal failure, the number of patients who recovered renal function and the patients' overall survival were not improved. The primary side effect in this series was deafness due to furosemide ototoxicity. With the easy availability of dialysis support for renal failure, I do not recommend furosemide or other potent loop diuretics to convert oliguric to nonoliguric renal failure. As an aside, similar data have been seen for low-dose (1-3 mg/kg/min) infusions of dopamine. Despite its potential to improve renal blood flow when used in nonpressor doses such as these, dopamine does not seem to improve either renal function or patient survival.

What causes intrinsic renal failure?

The causes of intrinsic renal failure involve dysfunction of the kidney due to disease of the kidney structure itself. There is a long list of diseases that can cause this type of renal failure. They may be characterized as conditions involving one of the three types of tissue in the kidney: vascular, glomerular, and interstitial. By obtaining four pieces of information, physicians can identify which structure is involved and causing the renal failure.

Begin with a urinalysis in the office; urinalyses performed in most clinical labs are not as accurate, since they are done in batches, and by the time the urine is examined, the casts have disintegrated. There are two significant findings in the urinalysis: the presence of either red blood cell (RBC) casts (*Figure 1*) or oval fat bodies and fatty casts (*Figure 2*). All the other casts reported in the urinalysis (hyaline, waxy, ropy) and the presence of hematuria or pyuria indicate only that renal disease is present. Note that RBC casts are seen with glomerular problems (glomerulonephritis) and vascular problems (vasculitis) but not with interstitial disease.

The second important diagnostic test is the 24-hr urine for protein excretion. Glomerular disease is defined by proteinuria of >3.5 g/24 hr/1.73 m^2 body surface area. Vasculitis of the kidney produces proteinuria but in lesser amounts, rarely more than 3 g/24 hr. Interstitial disease stands out again by yielding only modest amounts of protein (<2g/24 hr), usually tubular in origin.

The third component to assess is the presence of hypertension. Approximately 50 percent of patients who present with glomerular disease are also hypertensive. Most vasculitides of the kidney are accompanied by hypertension at the time of diagnosis. Patients with interstitial disease rarely present with hypertension; when it does occur, it usually does so only after significant renal failure (serum creatinine >3 mg/dl) has developed.

The fourth finding that is helpful in differentiating the tissue involved in renal failure is the time course of the illness. Glomerular disease patients most commonly develop progressive renal failure over a period of one to 15 years. Vasculitis of the kidney is a much more aggressive illness, with significant renal failure or end-stage renal disease developing in less than one year's time. Interstitial disease, with the exception of acute allergic interstitial nephritis from reactions to penicillin or nonsteroidal anti-inflammatory drugs, takes ➤

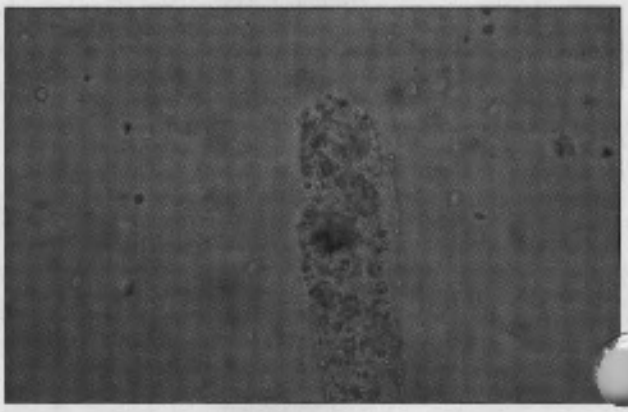

Figure 2. Fatty casts contain small refractile fat globules.

10-20 years or more to cause significant renal failure. The most common causes of glomerular, vascular, and interstitial renal failure are shown in *Table 3*.

Table 3. Causes of Intrinsic Renal Disease

Glomerular Disease	Vascular Disease	Interstitial Disease
Diabetes mellitus	Systemic lupus erythematosus	Sickle cell anemia
Idiopathic glomerulonephritis	Atheroemboli	Hypokalemia
Postinfection glomerulonephritis	Endocarditis	Acute tubular necrosis
Hepatitis B	Wegener's granulomatosis	Medications
Streptococcal infection	Goodpasture's syndrome	Analgesics
Endocarditis		Penicillin and its homologs
Medications		NSAIDs
Gold		Aminoglycosides
Penicillamine		Amphotericin B
NSAIDs		Acyclovir
		Cisplatin
		Radiocontrast media
		Most antibiotics

NSAIDs = nonsteroidal anti-inflammatory drugs

What postrenal processes cause renal failure?

There are only two exits from the kidney, the renal vein or the ureter. Renal failure can result from obstruction of either of these two structures. Renal vein thrombosis is uncommon, presenting with the classic triad of flank pain, gross hematuria, and acute renal failure. In adults, the condition is most commonly associated with hypercoagulable states and especially with metastatic malignancies. Adult renal vein thrombosis is also seen with acute glomerulonephritis. Renal vein thrombosis is more common in children, in whom the underlying etiology is marked dehydration.

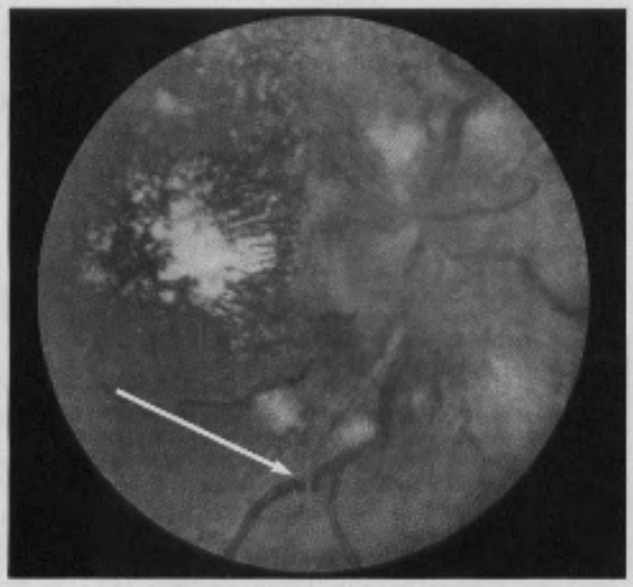

Figure 3. Group 4 Keith-Wagener-Barker classification or "malignant hypertension." At 7 o'clock from the fundus is a classic arteriovenous crossing deformity (*arrow*).

Obstructive uropathy is the most common form of postrenal failure and also the most readily reversible form. There are two types of obstruction: intrinsic and extrinsic. The intrinsic forms of obstructive uropathy include ureteral stone, blood clot, tumor, papillary necrosis, and stricture formation following instrumentation. Intrinsic obstruction may also be the result of a hypotonic neurogenic bladder, as is seen in patients with diabetes mellitus. In such cases, the obstruction is due to the elevated hydrostatic pressure of the enlarged and incompletely emptying bladder.

Extrinsic obstruction stems from compression of the ureter by structures in the retroperitoneal space, including lymphoma, idiopathic retroperitoneal fibrosis, and metastatic tumor to retroperitoneal nodes; medication (methysergide, ergot alkaloids, bromocriptine, tolcapone); radiation-induced retroperitoneal fibrosis; surgical trauma (unintentional ligation); and prostatic hypertrophy.

What clues in the history and physical exam suggest obstructive uropathy?

The classic history for obstructive uropathy is a sudden onset of anuria or markedly fluctuating urinary volumes as is seen with a ball-valving ureteral ➤

stone or with incomplete bladder outlet obstruction. On the physical exam, one should always feel for the presence of the bladder and check for correct anatomic placement of the Foley catheter if one is present. Numerous cases of "renal failure" have resulted from placement of a Foley in the vagina or within the prostatic urethra. Repositioning results in red-faced staff and a shorter-than-usual consult note. Historic evidence of methysergide use or previous malignancy should also increase one's suspicion for the presence of obstructive uropathy.

How does hypertension lead to renal failure?

Hypertension causes injury to the internal organs by damaging the small blood vessels. Looking at the eye grounds is the only noninvasive way to evaluate small blood vessels and to estimate the amount of ongoing hypertension-induced small-vessel damage. The characterization of funduscopic changes in patients with varying degrees of hypertension was made by Keith, Wagener, and Barker, Mayo Clinic ophthalmologists during the 1930s and 1940s (prior to the treatment of hypertension). The changes are grouped 1 through 4. Group 1 and 2 changes refer to the amounts of arteriolar sclerosis ("arteriovenous nicking") and arteriolar constriction seen in the retinal arterioles. Group 3 changes describe the presence of hypertensive exudates and hemorrhages in addition to arteriolar constriction and sclerosis. A group 4 change is the presence of papilledema (*Figure 3*), which is due to severe hypertension with increased intracranial pressure. Keith, Wagener, and Barker found that patients with group 4 fundi had a six-year survival of one percent. Since the six-year survival of many cancers at the time was also one percent, they coined the phrase "malignant hypertension," meaning that untreated hypertension which produced papilledema was just as fatal as cancer.

Hypertension causes damage to the small blood vessels.

What are the critical parts of the physical exam in the patient with renal disease?

The single most important part of the physical examination in the patient with renal failure is the assessment of volume status. The best way to evaluate volume contraction is to measure the blood pressure (BP) and heart rate while the patient is lying down and then after he or she stands. A fall in systolic BP of >20 mm Hg with standing is indicative of a 10-15 percent contraction of plasma volume. A fall in BP of <20 mm Hg accompanied by a marked increase in pulse (> 20 beats per minute) suggests a 5-10 percent decrease in plasma volume. Supine hypotension predicts a >20 percent loss of plasma volume.

Other physical findings used to establish volume status include the condition of the internal jugular vein; presence of rales or pulmonary effusion by percussion or auscultation; and presence of a third heart sound, ascites, or lower-extremity edema. Auscultation for an abdominal bruit (renovascular disease), palpation for abdominal masses (polycystic renal disease), palpation for an enlarged bladder, and evaluation of the joints for acute effusion (collagen vascular disease) also help in the diagnosis of renal failure.

Evaluation should begin with an in-house urinalysis and a 24-h urine for protein and creatinine clearance. Basic chemistries, including electrolytes, blood urea nitrogen, serum creatinine, glucose, calcium, phosphorus, and complete blood count, help in determining how quickly the diagnostic process must proceed. Low calcium, high phosphorus, and the presence of anemia speak to a more chronic process. When suggested by the history and physical, additional testing for connective tissue diseases and vasculitis may be necessary.

Imaging of the kidneys is best done with ultrasound so as to avoid the use of potentially nephrotoxic radiocontrast agents. Visualizing the kidney is helpful for a number of reasons. First and most important is to look for obstructive uropathy. The next step is to use Doppler interrogation of the renal arteries to look for renal artery stenosis as a cause of renal failure. Soft signs, such as increased cortical echogenicity and increased renal arteriolar resistance, suggest a chronic primary renal process. Finally, the size of the kidneys is very helpful. Large kidneys (>13 cm on ultrasound) indicate a number of specific differential diagnoses, including acute glomerulonephritis; ob-

Table 4. Suggested Reasons for Nephrology Consultation

Oliguric acute renal failure
Unexplained renal failure
Serum creatinine >2 mg/dL or creatinine clearance <50mL/min
Rapidly rising serum creatinine (Increasing by >1 mg/dL every two months)
Presence of nephrotic range proteinuria (>3.5 g protein/24 hr/ 1.73 m^2)

struction; amyloidosis; diabetes mellitus; polycystic renal disease; and infiltrative diseases of the kidney, such as multiple myeloma, leukemia, and lymphoma. Several of these are treatable, and thus, the presence of large kidneys is an important finding. Small kidney size (<7 cm) on ultrasound indicates chronic renal illness, which is irreversible.

When should the patient be referred to a nephrologist?

For most patients with renal failure, a nephrology consultation is helpful in devising a long-term treatment plan. Aggressive BP management to a goal level of <125/75, dietitian evaluation, control of diabetes, and education about end-stage renal disease and the patient's options can be beneficial to the patient and referring physician. It is important to realize that these approaches may markedly delay or arrest the progression of the renal failure and avoid dialysis. A list of reasons for early referral for nephrologic consultation is presented in *Table 4*.

"I've read your performance review, and you're toast."

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HIGHLIGHTS

Lotion Recommendations for Atopic Dermatitis

The use of mild, nonalkaline soaps and frequent use of emollients are important elements in the long-term management of atopic dermatitis. Because moisture evaporating off the skin can trigger flares, bathing is sometimes discouraged. A better approach is the prompt application of an emollient, such as petrolatum, (finishing within three minutes of the end of the bath), which can serve to seal the moisture from the bath. Products containing hydroxy acids, phenol, or urea can reduce dryness and scaling, but these can sting inflamed skin and should therefore be used with caution.

Eliminating Environmental Triggers Will Reduce Flares

The lifetime prevalence of atopic dermatitis, a chronic inflammatory dermatosis, is estimated to be 30 percent of the population.[1,2] The expression of atopic dermatitis is a complex integration of environmental, immunologic, and genetic factors. Because it can be quickly exacerbated by environmental factors[3] (wool, lanolin, and harsh detergents are particularly irritating) and because even emotional stress can lead to flares, reduction of these triggers, avoidance of occupations that require contact with them (e.g., hairdressing, nursing, and construction), and dealing with the root causes of stress are important steps to take in the treatment of atopic dermatitis. For example, cotton clothing, washed to remove finishing (which often releases formaldehyde), is preferable to wool or synthetics.

1. Laughter D, Istvan JA, Tofte SJ, et al. The prevalence of atopic dermatitis in Oregon schoolchildren. J Am Acad Dermatol *43:649, 2000.*

2. Foley P, Zuo Y, Plunkett A, et al. The frequency of common skin conditions in preschool-age children in Australia: atopic dermatitis. Arch Dermatol *137:293, 2001.*

3. Wollenberg A, Kraft S, Oppel T, et al. Atopic dermatitis: pathogenetic mechanisms. Clin Exp Dermatol *25:530, 2000.*

Vary the Steroid Therapy with the Dermatitis

Topical corticosteroids are a mainstay of therapy for atopic dermatitis. Application immediately after bathing improves cutaneous penetration. Lowering the risk of side effects with less potent preparations must be balanced against gaining control of a flare quickly with more potent preparations. However, long-term application of inadequately potent topical corticosteroids may pose a greater risk of adverse effects than brief use of more potent agents followed by a rapid taper to bland emollients. Because the risk of steroid-induced cutaneous atrophy is greater on the face, in intertriginous areas (e.g., groin, axillae, and inframammary folds), and under diapers, less potent steroids (e.g., hydrocortisone and desonide) should be applied in these areas, and they should be used with particular caution. For the remainder of the body, midpotency preparations, such as 0.1 percent triamcinolone acetonide, are helpful. More potent ointments, such as fluocinonide and desoximetasone, are helpful for lichenified plaques. Flurandrenolide tape is beneficial for nodular prurigo (so-called picker's nodules) ➤