Case 1

A 32-year-old man with chronic renal failure (from IgA nephropathy) being treated with maintenance hemodialysis began to take his phosphate-binding medications irregularly, and swelling of the right shoulder developed over a period of two months. The calcium-phosphate product (in milligrams per deciliter) was more than 90, and the serum N-terminal parathyroid hormone level was elevated. A biopsy showed that the shoulder mass consisted of hydroxyapatite. The patient underwent subtotal parathyroidectomy and was referred for renal transplantation. [NEJM 329: 695, 1993]

Case 2

A 47 y.o. man presents with chest pain and exertional dyspnea. The patient has end-stage renal disease from chronic glomerulonephritis. He has been on hemodialysis for the past 2 years but with shortened dialysis times due to frequent dialysis hypotension. He has chronic anemia with hematocrit 31-33% until 4 months ago when it fell to 27% and recombinant human erythropoietin (rHuEPO) was started. The anemia did not improve, however, despite increasing doses of rHuEPO and intravenous iron. On examination there is a pericardial friction rub. Chest x-ray shows an enlarged cardiac shadow with a water-bottle contour. The hematocrit is 25% with low transferrin saturation and high serum ferritin. C-reactive protein is markedly elevated. [Nephrol Dial Transplant 12: 1051, 1997]

Case 3

62 year old man with type 2 diabetes mellitus was diagnosed with diabetic nephropathy 4 years ago because of proteinuria at 6.8 g/d. At that time serum creatinine was 1.0 mg/dl. Two years later serum creatinine was 2.3 mg/dl and an angiotensin converting enzyme inhibitor was started. Now, serum creatinine is 3.5 mg/dl. Why was an ACE inhibitor started? Is it working? [Shayman's *Renal Pathophysiology* 1995]

1. **What are the roles of the kidney in the maintenance of systemic homeostasis and what are the consequences of loss of renal function?**

Systemic Effects of Kidney Failure

Loss of fluid & electrolyte balance	Loss of erythropoietin production	Effects of uremic toxins
Volume overload (Na & H_2O retention) Hypertension Edema (systemic & pulmonary) Congestive heart failure Hyperkalemia → cardiac arrhythmias Hyperphosphatemia Tissue calcium phosphate deposits Hypocalcemia (also due to low activated Vit D) Secondary hyperparathyroidism Renal osteodystrophy Metabolic acidosis Fluid & electrolyte and acid-base disorders probably contribute to altered cell membrane potentials and neurologic symptoms	Hypoproliferative anemia Fatigue & low physical capacity High cardiac output LVH / High O_2 demand Poor cognitive function Depression Sleep disturbance	Chronic pro-inflammatory state Gastritis, esophagitis, colitis Serositis (uremic pericarditis) Anorexia/ Nausea & vomiting Insulin resistance Catabolic state Cellular toxicity (inhibition NaKATPase?) Neuromuscular dysfunction Encephalopathy (seizures/ coma) Peripheral neuropathy Myopathy Platelet dysfunction →Bleeding diathesis WBC dysfunction → infections Itching Restless legs

2. **How do we assess loss of renal function clinically?**
   a. Glomerular filtration rate (GFR) as a reflection of functioning renal mass
   b. Azotemia: Relationship of BUN and serum creatinine to GFR
3. **What are the mechanisms of decreased GFR and renal failure?**
   a. Acute renal failure as sudden change in the physiologic determinants of GFR
      $GFR = K_f(\Delta P - \Delta\pi) = LpS\ [(P_{GC}-P_T)-\sigma(\pi_{GC}-\pi_T)]$
   b. Classic paradigm for diagnosing the cause of acute renal failure (ARF):
      Prerenal azotemia / Post-renal (acute obstruction) /Intrinsic renal disease
   c. Classification of intrinsic renal disease by primary targets of injury
      Vascular disease / Glomerular disease / Tubulointerstitial disease
   d. Chronic kidney disease as progressive loss of nephrons leading to end stage renal disease (ESRD)
   e. Mechanisms of progression of chronic kidney disease
      i. "Adaptive" glomerular and tubular changes in residual intact nephrons
      ii. Beyond the initial insult: Effects of glomerular hyperfiltration, systemic hypertension, proteinuria & interdependence of renal compartments
4. **What are the therapeutic options for ESRD?**
   a. Dialysis (hemodialysis and peritoneal dialysis) b. Kidney transplantation
5. **What is the outcome for patients with ESRD?**