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NEPHROLOGY BOARD REVIEW MANUAL

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Anemia of Chronic Renal Failure

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Anemia of Chronic Renal Failure

Anemia substantially influences the quality of life, morbidity, and survival of patients with advanced renal failure. The modern history of anemia and chronic renal failure (CRF) began in 1957 when Jacobson et al demonstrated that erythropoietin, the hormone that regulates erythropoiesis, is produced by the kidneys.¹ Since that discovery, human urinary erythropoietin has been purified, the gene for human erythropoietin has been isolated and cloned,² and recombinant human erythropoietin (r-HuEPO) has been synthesized and approved for treatment.^{3,4} r-HuEPO is now used worldwide in patients with CRF and end-stage renal disease (ESRD). This manual reviews the nature and pathophysiology of the anemia that accompanies CRF, emphasizing its treatment with r-HuEPO and supplemental iron.

PATHOPHYSIOLOGY AND CLINICAL MANIFESTATIONS

CASE PATIENT PRESENTATION

During a follow-up visit to her nephrologist, a 62-year-old woman reports worsening of her previously stable angina pectoris over the previous 2 months and increasing symptoms of fatigue, anorexia, and dyspnea on exertion.

History

The patient has a history significant for long-standing type 2 diabetes mellitus and chronic renal insufficiency. In addition, she has had hypertension for many years, which has been treated with furosemide, tenormin, and captopril. The patient was hospitalized 2 years ago with congestive heart failure and is known to have diabetic retinopathy.

Physical Examination

Physical examination reveals a pale-appearing wo-

man with a blood pressure of 130/70 mm Hg and a pulse of 100 bpm. Ear, nose, and throat examination is negative. Lung examination reveals basilar crackles, and cardiac examination reveals a normal S₁ and S₂ as well as an S₄. Abdominal examination is negative. A test for fecal occult blood is negative. Neurologic examination is unremarkable, and there is no asterixis.

Laboratory Testing

Laboratory studies reveal the following: blood glucose, 210 mg/dL; hematocrit (Hct), 24%; hemoglobin (Hb), 7.8 mg/dL; blood urea nitrogen (BUN), 70 mg/dL; and serum creatinine, 6.0 mg/dL. The BUN and serum creatinine levels are unchanged from values obtained 4 months ago. Electrolytes and liver function tests are unremarkable. The mean corpuscular volume (MCV) is 90 fL, with a mean corpuscular Hb concentration (MCHC) of 34 g/dL. Urinalysis reveals 3+ protein with a few hyaline and granular casts. A 24-hour urine collection demonstrates 6.2 g protein and a creatinine clearance of 14 mL/min. Echocardiography reveals well-preserved systolic function with left ventricular hypertrophy (LVH).

- What are the most important factors contributing to this patient's anemia?

PATHOPHYSIOLOGY OF THE ANEMIA OF CRF

The kidneys produce 85% to 90% of the body's erythropoietin, with most of the remainder produced by the liver. Renal production of erythropoietin decreases as kidney function declines. In most patients, anemia develops after the glomerular filtration rate decreases below 30 to 45 mL/min, but in patients with polycystic kidney disease, erythropoiesis tends to be better preserved than in patients with other causes of ESRD.

Erythropoietin production is stimulated by the reduced oxygen carrying capacity of blood delivered to pericapillary, fibroblast-like interstitial cells in the kidneys. Hypoxia-inducible factor, a protein produced in