recombinant form of this hormone is revolutionizing treatment of this form of anemia.
Most patients tolerate chronic anemia fairly well. In an otherwise healthy patient with chronic renal failure, a hematocrit of approximately 25% is typical. The presence of other medical problems, particularly heart and lung disease, can decrease a patient’s ability to tolerate a lower blood count. Patients who have undergone bilateral kidney removal (nephrectomies) often have hematocrits which are significantly lower, probably because they cannot make any erythropoietin at all. Patients whose kidney failure is a result of polycystic kidney disease generally do not have anemia.

The treatment of the anemia of chronic renal failure has changed dramatically in recent years. Until recently, the principal treatments were transfusion of red blood cells and administration of the hormone testosterone. Although transfusions will rapidly correct a low blood count, repeated transfusions are associated with some problems, including iron overload, the development of certain antibodies, and the possibility of viral infections. Testosterone may stimulate red blood cell production by the bone marrow, but the effect is generally small, and its use is often associated with virilizing side effects.

In 1983, the gene for erythropoietin was isolated, then cloned. Subsequently this led to the mass production of erythropoietin and finally to its use in renal failure patients in 1990 (see Chapter 20). It is administered either intravenously at dialysis or subcutaneously. In anemic patients with chronic renal failure, treatment with erythropoietin is now standard practice and has dramatically reduced the need for blood transfusions. The increase in hematocrit seen with patients treated with erythropoietin has generally resulted in improvement in exercise tolerance and overall sense of well-being. It is important to monitor the iron status of treated patients, as iron deficient patients will not respond appropriately to administration of erythropoietin. The use of erythropoietin is constrained by the extremely high cost of this hormone and the reimbursement policies of insurance companies and Medicare.

To summarize, anemia is a universal complication of chronic renal failure. It has multiple causes, the most important of which is decreased production of erythropoietin by the kidney. The availability of the
constituents of blood which aid in blood clotting, do not work normally in uremia. The defective blood clotting seen in uremia makes bleeding more common. Rapid bleeding—from an ulcer in the gastrointestinal tract, for example—causes a rapid decrease in the hematocrit and is a medical emergency. Very slow loss of blood can also cause anemia by depleting the body’s stores of iron, which the bone marrow uses to produce blood cells.

Excessive destruction of red blood cells is also seen in advanced renal failure. Normally, red blood cells survive for about four months before being destroyed. This life span is reduced in renal failure, probably because of chemical effects of uremia and decreased flexibility of the red blood cells. This hemolysis is usually mild and a person with a normal bone marrow could easily compensate for it by increasing red blood cell production. However, in renal failure, the bone marrow’s capacity to compensate is diminished.

What is the role of hemodialysis in the anemia of chronic renal failure? The effectiveness of dialysis in reversing any complication of uremia depends on the nature of that complication. Those disturbances which are due to accumulation of a uremic toxin may be reversible if that toxin is dialyzable and if the removal rate by dialysis outstrips its generation rate. Some improvement in red blood production is seen with initiation of dialysis, probably by decreasing the toxic effect of uremia on the marrow. Dialysis, however, does not replace the hormone producing functions of the kidney and therefore does not by itself correct the main cause of anemia, namely deficient production of erythropoietin. Dialysis does correct the bleeding tendency seen in uremia, but not to normal.

Dialysis itself may also contribute to the anemia. Iron deficiency can result from unavoidable dialyzer blood loss, clotted dialysis membranes, and frequent blood sampling. Hemolysis may occur if there are problems with the dialysate (temperature problems, contamination with aluminum, fluoride, copper, chlorine, or chloramine). Folate, a water soluble vitamin necessary for normal red blood cell production, is dialyzable. Generally, dialysis patients are given oral supplementation with folic acid in case their normal diet does not supply them with sufficient folate to keep up with its loss through dialysis.
Anemia is defined as a reduction in the oxygen carrying capacity of blood, measured in the laboratory as a low hemoglobin concentration, or a low hematocrit (the percentage of the blood volume that is occupied by red blood cells or erythrocytes). In a normal person, the hemoglobin is approximately 13 grams per deciliter and the hematocrit is approximately 40%.

Anemia is not a disease per se, but a reflection of some other problem. It occurs when the balance between the normal rates of blood loss and blood production is disturbed. There are three basic mechanisms by which this occurs: (1) blood loss, (2) excessive destruction of red blood cells (hemolysis), and (3) abnormally low production of red blood cells by the bone marrow.

In a person with normal renal function, the finding of anemia on routine blood analysis would prompt a work-up to determine the ultimate cause. In chronic renal failure, anemia is almost always present, and can be a result of any of the mechanisms listed above. However, the typical “anemia of chronic renal insufficiency” is a result of a decreased production of red blood cells by the bone marrow.

This defect in red blood cell production is largely explained by the inability of the failing kidneys to secrete the hormone erythropoietin. This hormone is a necessary stimulus for normal bone marrow to produce red blood cells. In addition, other factors associated with renal failure, including the accumulation of so-called uremic toxins, may play a role in depressing bone marrow function. Excess stores of aluminum may accumulate in the bone marrow of long term dialysis patients and can contribute to anemia as well.

Blood loss and red blood cell destruction also frequently contribute to the anemia in patients with renal failure. Platelets, which are small