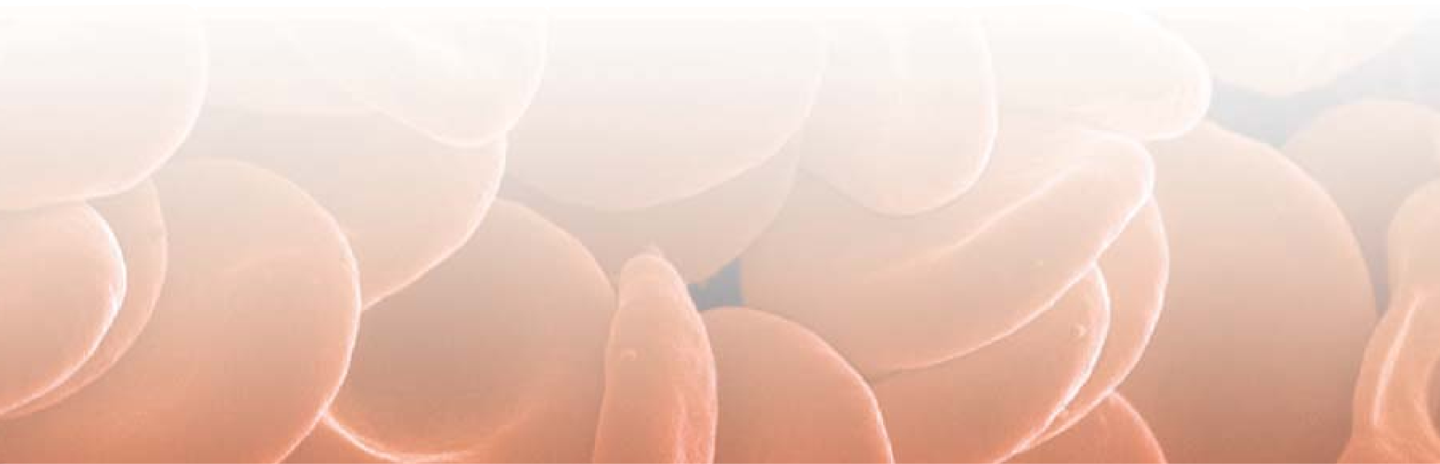
"The first step to be taken with the anemic patient is to establish the presence of the problem early enough to do something about it…"

X Anemia & Surgery

Key Points

- One-third to one-half of surgical patients may be anemic preoperatively because of conditions for which they require surgery.
- Postoperative anemia may occur in up to 90% of patients, probably due to a blunted erythropoietic response.
- In surgical patients, anemia has been linked to increased postoperative morbidity and mortality, and decreased quality of life.
- Treatment of perioperative anemia has been shown to decrease the need for transfusion, and improve patient outcomes and quality of life.



Multiple Causes of Anemia in Surgical Patients

Anemia is a concern for the surgical patient in two phases of treatment: before surgery and in the immediate perioperative period, which includes both the surgery itself and the time spent in the hospital during postoperative recovery. Surgery patients may develop preoperative anemia from acute or chronic blood loss (eg, trauma or peptic ulcer oozing), iron deficiency caused by poor nutrition or menstrual bleeding, renal insufficiency, malignancy, or chronic disease (eg, rheumatoid arthritis or inflammatory bowel disease).[1,2]

Catastrophic bleeding during surgery may occur, but this is uncommon and usually can be controlled before significant anemia develops. Coagulation defects, either congenital or acquired, such as trauma-induced disseminated intravascular coagulation, may lead to anemia. Frequent phlebotomies and untreated bleeding episodes can also cause blood loss and contribute to anemia during surgery and recovery.[2] Furthermore, after surgery, the erythropoietic response may be severely blunted in anemic patients because of diminished iron availability and the inhibitory actions of inflammatory cytokines.[1] Reduced red cell life span and occult gastrointestinal bleeding may also contribute to anemia in surgical patients.

Anemia Prevalence Varies in Surgical Patients

It is difficult to estimate an overall prevalence of anemia in surgery patients, in part because of variations among patients undergoing different types of surgery as well as the variability in investigators' anemia definitions. A recent review of the literature found 10 studies

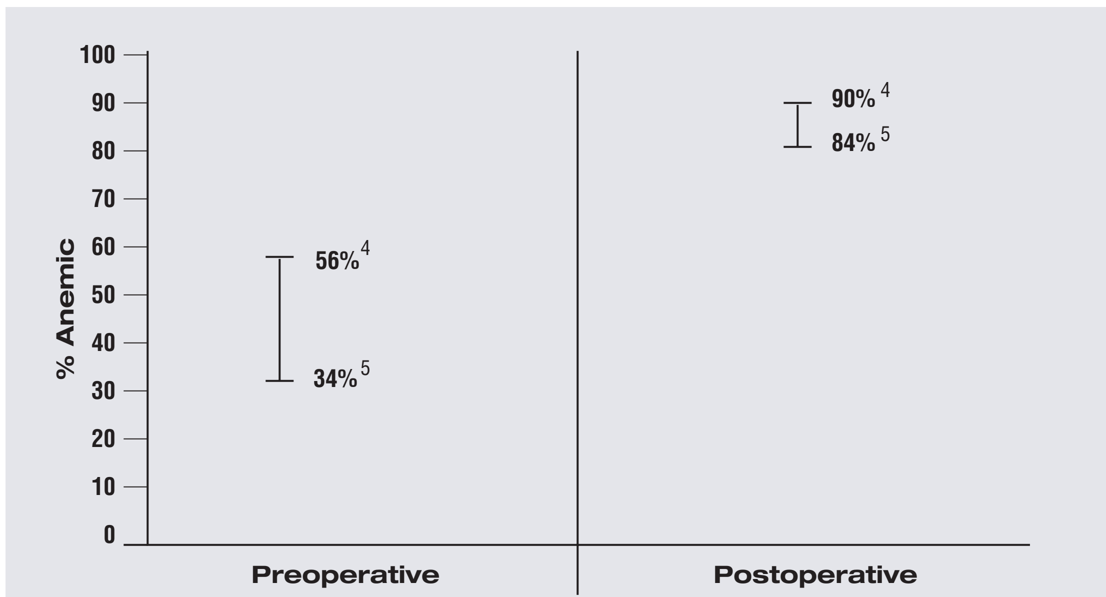


Figure 10-1. Preoperative anemia is common, and prevalence dramatically increases postoperatively.[4,5]

reporting the prevalence of anemia among surgery patients.[3] In these studies, the prevalence ranged from a low of 5% (in female geriatric hip fracture patients) to almost 76% (in patients with Dukes' stage D colon cancer). Clemens and Spivak found that 56% (49% of the women and 63% of the men) in a group of 84 elective surgery patients were anemic before surgery. Moreover, 66% of the women and 88% of the men were anemic after surgery. On postoperative day 5, the anemia frequency increased to 90% (80% of the women and all of the men), probably due to a blunted erythropoietic response.[4] Dunne and colleagues recently reported that 33.9% of 6,301 patients scheduled for noncardiac surgery were anemic before surgery and 84.1% were anemic in the postoperative period.[5]

Some patients may be more susceptible than others to perioperative anemia. Clemens and Spivak reported that female or African American patients were more susceptible to surgery-induced suppression of erythropoiesis.[4] In a study of nearly 7,000 patients undergoing coronary artery bypass graft (CABG) surgery, DeFoe and colleagues found that female patients and those with smaller body surface area were at increased risk of anemia compared to males and larger patients.[6] Gruson and colleagues found that 180 of 395 patients (45.6%) who entered their hospital for repair of a hip fracture were anemic, suggesting that recent blood loss from a hip fracture may be superimposed on chronic anemia.[7]

Increased Postoperative Risk of Anemia

Findings of several studies suggest that perioperative anemia may increase the risk of postoperative morbidity and mortality.[8-10] However, the exact relationships among preoperative, intraoperative, and postoperative factors and how to measure anemia remain unclear. Below-normal preoperative Hb levels may or may not be a deciding factor.

Carson and colleagues demonstrated that the degree of anemia as measured by Hb and Hct values was associated with postoperative mortality in the nontransfused patient.[11] However, in the same patients the research group showed that the amount of surgical blood loss was more important than preoperative Hb or Hct value.[12] Upon analysis of a larger patient population, these researchers found that among patients with low preoperative Hb (<6 g/dL), the risk of death was more pronounced in those with cardiovascular disease than in those without (interaction $P < 0.03$).[13] Subsequent analyses have called into question the validity of preoperative Hb and Hct values as predictors of outcome other than an increased need for transfusion.[14-16]

Other researchers have shown that preoperative Hb and Hct values can be used as predictors of outcome for specific types of patients, namely those undergoing CABG or orthopedic surgery.[17,18] The Northern New England Cardiovascular Disease Study Group has shown an association between nadir Hct during cardiopulmonary bypass and postoperative morbidity and mortality in 6,980 patients who underwent CABG.[6] Female patients and those with a smaller body size were most susceptible to low intraoperative Hct, suggesting that excessive hemodilution may contribute to this problem. This same group previously showed that hemorrhage leading

to re-exploration after CABG was associated with increased mortality, as one would expect.[19] The findings of another study, which involved nearly 1,000 patients undergoing CABG, revealed that a measure combining age and red blood cell volume was an important determinant of postoperative morbidity, as indicated by either serious complications or increased length of hospital stay. The researchers concluded that older patients with preoperative anemia, low blood volume, and comorbidities were at increased risk for postoperative complications.[8]

Dunne and colleagues point out the clinical significance of perisurgical anemia by demonstrating a statistical relationship between anemia and increased morbidity, mortality, and length of stay.[5] Overall length of stay and mortality up to 12 months after surgery were higher in the anemic group of patients in Gruson and colleagues' study of hip fracture patients.[7]

In addition to influencing survival and morbidity in surgical patients, perioperative anemia may adversely affect quality of life (QOL), especially because of its contribution to fatigue.[20,21]

Of particular relevance to surgery patients is the relationship between lowered Hb levels and the safety of general anesthesia. Some patients with lower perioperative Hb levels may be at increased risk of hypoxemia; therefore, the issue of safety should be considered in anemic patients undergoing anesthesia.[22] Anemia might also be one of several factors that can contribute to delirium during surgery.[23] In addition, red blood cells might play an important role as a supplier of phospholipids in the blood coagulation pathway; thus, anemia could represent a risk factor for hemorrhagic tendency.[24]

Presurgical Strategies to Correct Anemia

Multiple strategies can be used to correct perioperative anemia. These include allogeneic blood transfusion, the use of single transfusion alternatives, or combinations of the alternatives.[25,26] Allogeneic blood transfusion should be avoided whenever possible, not only because of associated risks but also because transfusion has not been proven to improve postoperative outcomes.[27] Transfusion risks include reactions, disease transmission, and immunomodulation.[28,29] Transfusion decisions must focus on patient characteristics, not Hb or Hct values alone.[30]

The simplest approach is to avoid transfusion regardless of the level of preoperative anemia. This may be necessary in emergency cases or in patients who refuse transfusion. Ott and Cooley's landmark report of successful cardiac surgery without blood transfusion in 542 Jehovah's Witness patients was the first demonstration that surgery could be done using this strategy without excessive blood loss or mortality.[31] The *sine qua non* of success using this approach is meticulous surgery to eliminate or reduce operative blood loss. This strategy entails accepting a lowered transfusion threshold, or trigger, and has been proven to be safe by several surgical groups.[25,32,33] The use of autologous blood either through preoperative donation or autotransfusion to return shed blood is also helpful.[28,29]

In surgeries with an expected high

blood loss (>1,000 mL), one of the major anesthetic techniques for avoiding allogeneic blood use is acute normovolemic hemodilution (ANH). ANH is a procedure that reduces the patient's red blood cell mass by the controlled removal of whole blood and the simultaneous replacement with colloid, crystalloid, or both to maintain essential adequate circulatory volume. The purpose of ANH is to avoid allogeneic blood transfusions during and after surgery. ANH is a point-of-care technique that results in acute anemia, decreased blood viscosity, and preserved tissue perfusion.[34]

While ANH is one cornerstone, other necessary blood conservation practices are pharmaceuticals (primarily erythropoietin plus iron) for enhancing Hb production, preoperative autologous donation, minimally invasive surgical techniques, new techniques for hemostasis, the staging of difficult surgical procedures, and intraoperative cell salvage. These are used selectively or in combination. Along with these specific techniques, a reasoned approach is necessary for a greater understanding of the implications of tolerating acute anemia.

Preoperative anemia often goes unrecognized and untreated unless the surgeon makes a particular effort to order Hb and Hct tests for review in advance of a planned operation. Therefore, the first step to be taken with the anemic patient is to establish the presence of the problem early enough to do something about it, if the risk is to be decreased by avoiding allogeneic blood.

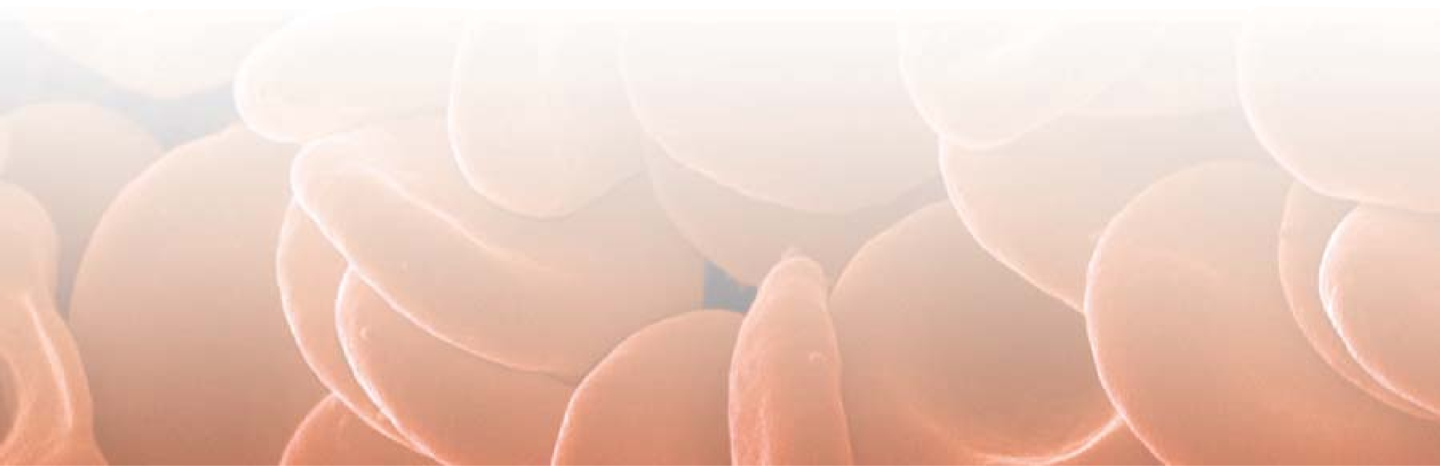
Although alternative therapies have their own risks, these are typically minimal when compared to transfusion. Autologous predonation can be very effective in reducing reliance on allogeneic blood, but it has been shown to increase overall exposure to transfusion and to increase the chance of perioperative anemia.[28,29,35] This problem can be avoided by the use of iron replenishment and erythropoietin to facilitate autologous blood procurement before surgery.[36-38]

Use of erythropoietin alone may eliminate the need for transfusion in some surgical patients, but when transfusion is indicated, the most effective approach may be to combine preoperative erythropoietin administration with procurement of autologous blood by methods such as ANH.[39]

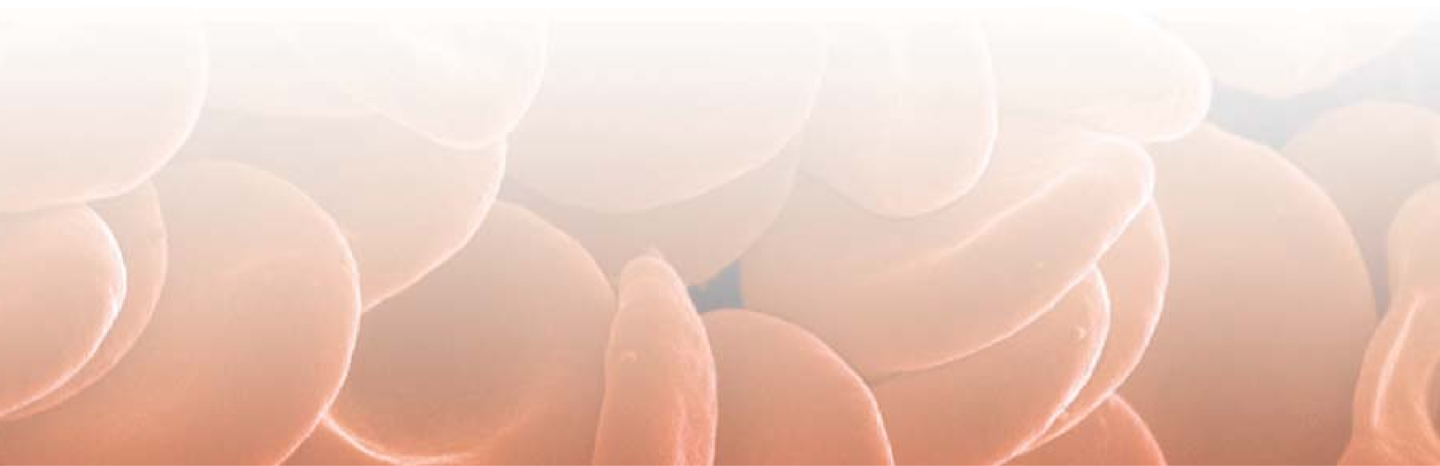
Erythropoietin use is also helpful in the postoperative period because it accelerates Hct recovery.[40] Erythropoietin has also been used in bloodless surgery, protecting patients from the possible hazards of allogeneic blood transfusion.[1,21,41,42] In addition to reducing the need for transfusion, management of anemia with erythropoietin has been shown to accelerate erythropoiesis and to enhance QOL in surgery patients.[43,44]

Beneficial Effects of Anemia Management

Early recognition of anemia allows the surgeon to offer patients proven, safe alternatives to allogeneic blood, thereby reducing risk. Blood transfusion has not been shown to reduce morbidity and mortality in surgical patients, but alternatives such as erythropoietin have. Sound management of anemia with combinations of alternatives avoids risk and appears to provide better outcomes.



References



1. Kulier A, Gombotz H. Perioperative anemia. *Anaesthesist.* 2001;50:73-86.
2. Eckardt KU. Anemia in critical illness. *Wien Klin Wochenschr.* 2001;113:84-89.
3. Zynx Health Incorporated. *The Prevalence and Impact of Anemia: A Systematic Review of the Published Medical Literature.* Zynx Health Incorporated; Los Angeles, CA;2001;59-61. Available at: http://www.anemia.org.
4. Clemens J, Spivak JL. Serum immunoreactive erythropoietin during the perioperative period. *Surgery.* 1994;115:510-515.
5. Dunne JR, Malone D, Tracy JK, et al. Perioperative anemia: an independent risk factor for infection, mortality, and resource utilization in surgery. *J Surg Res.* 2002;102:237-244.
6. DeFoe GR, Ross CS, Olmstead EM, et al, for the Northern New England Cardiovascular Disease Study Group. Lowest hematocrit on bypass and adverse outcomes associated with coronary artery bypass grafting. *Ann Thorac Surg.* 2001;71:769-776.
7. Gruson KI, Aharonoff GB, Egol KA, et al. The relationship between admission hemoglobin level and outcome after hip fracture. *J Orthop Trauma.* 2002;16:39-44.
8. Ferraris VA, Ferraris SP. Risk factors for postoperative morbidity. *J Thorac Cardiovasc Surg.* 1996;111:731-738;discussion 738-741.
9. Niibayashi H, Tamura K, Fujiwara M, et al. Survival factors in digital replantation: significance of postoperative anaemia. *J Hand Surg [Br].* 2000;25:512-515.
10. Diamond PT. Severe anaemia: implications for functional recovery during rehabilitation. *Disabil Rehabil.* 2000;22:574-576.
11. Carson JL, Poses RM, Spence RK, et al. Severity of anaemia and operative mortality and morbidity. *Lancet*. 1988;1:727-729.
12. Spence RK, Costabile JP, Young GS, et al. Is hemoglobin level alone a reliable predictor of outcome in the severely anemic surgical patient? *Am Surg.* 1992;58:92-95.
13. Carson JL, Duff A, Poses RM, et al. Effect of anaemia and cardiovascular disease on surgical mortality and morbidity. *Lancet.* 1996;348:1055-1060.
14. Faris PM, Spence RK, Larholt KM, et al. The predictive power of baseline hemoglobin for transfusion risk in surgery patients. *Orthopedics*. 1999;22(suppl):S135-S140.
15. Cordts PR, LaMorte WW, Fisher JB, et al. Poor predictive value of hematocrit and hemodynamic parameters for erythrocyte deficits after extensive elective vascular operations. *Surg Gynecol Obstet.* 1992;175:243-248.
16. Dougenis D, Patrinou V, Filos KS, et al. Blood use in lung resection for carcinoma: perioperative elective anaemia does not compromise the early outcome. *Eur J Cardiothorac Surg.* 2001;20:372-377.
17. Rady MY, Ryan T, Starr NJ. Perioperative determinants of morbidity and mortality in elderly patients undergoing cardiac surgery. *Crit Care Med.* 1998;26:225-235.
18. Magovern JA, Sakert T, Magovern GJ, et al. A model that predicts morbidity and mortality after coronary artery bypass graft surgery. *J Am Coll Cardiol.* 1996;28:1147-1153.
19. Dacey LJ, Munoz JJ, Baribeau YR, et al, for the Northern New England Cardiovascular Disease Study Group. Reexploration for hemorrhage following coronary artery bypass grafting: incidence and risk factors. *Arch Surg.* 1998;133:442-447.
20. Rock WA, Jr., Meeks GR. Managing anemia and blood loss in elective gynecologic surgery patients. *J Reprod Med.* 2001;46(suppl):507-514.
21. Bachmann GA. Epoetin alfa use in gynecology: past, present and future. *J Reprod Med.* 2001;46(suppl):539-544.
22. Gunawardana RH, Gunasekara SW, Weerasinghe JU. Anesthesia and surgery in pediatric patients with low hemoglobin values. *Indian J Pediatr.* 1999;66:523-526.
23. Aldemir M, Ozen S, Kara IH, et al. Predisposing factors for delirium in the surgical intensive care unit. *Crit Care.* 2001;5:265-270.
24. Sagesaka T, Juen H, Kaibara M. Anemia as a risk factor of hemorrhagic tendency during surgery. *J Obstet Gynaecol Res.* 2000;26:103-109.
25. Spence RK. Practice policies for surgical red blood cell transfusion: surgical transfusion policies. *Semin Hematol.* 1996;33(suppl 1):19-22.

26. Spence RK. Surgical red blood cell transfusion practice policies. *Am J Surg.* 1995;170(suppl):3S-15S.
27. Spence RK. Anemia in the patient undergoing surgery and the transfusion decision: a review. *Clin Orthop*. 1998:19-29.
28. Goodnough LT, Brecher ME, Kanter MH, et al. Transfusion medicine, I: blood transfusion. *N Engl J Med.* 1999;340:438-447.
29. Goodnough LT, Brecher ME, Kanter MH, et al. Transfusion medicine, II: blood conservation. *N Engl J Med.* 1999;340:525-533.
30. Carson JL, Chen AY. In search of the transfusion trigger. *Clin Orthop.* 1998:30-35.
31. Ott DA, Cooley DA. Cardiovascular surgery in Jehovah's Witnesses: report of 542 operations without blood transfusion. *JAMA.* 1977;238:1256-1258.
32. Bracey AW, Radovancevic R, Riggs SA, et al. Lowering the hemoglobin threshold for transfusion in coronary artery bypass procedures: effect on patient outcome. *Transfusion.* 1999;39:1070-1077.
33. Rosengart TK, Helm RE, DeBois WJ, et al. Open heart operations without transfusion using a multimodality blood conservation strategy in 50 Jehovah's Witness patients: implications for a "bloodless" surgical technique. *J Am Coll Surg.* 1997;184:618-629.
34. Messmer K. Hemodilution. *Surg Clin North Am.* 1975;55:659-678.
35. Cha CW, Deible C, Muzzonigro T, et al. Allogeneic transfusion requirements after autologous donations in posterior lumbar surgeries. *Spine.* 2002;27:99-104.
36. Earnshaw P. Blood conservation in orthopaedic surgery: the role of epoetin alfa. *Int Orthop.* 2001;25:273-278.
37. Goodnough LT, Monk TG. Erythropoietin therapy in the perioperative setting. *Clin Orthop.* 1998:82-88.
38. Adamson JW. Epoetin alfa as an adjunct to autologous blood donation in patients with a low hematocrit scheduled for elective orthopedic surgery. *Semin Hematol.* 1996;33(suppl 2):15-16; discussion 17.
39. Goodnough LT, Monk TG, Andriole GL. Erythropoietin therapy. *N Engl J Med.* 1997;336:933-938.
40. Atabek U, Alvarez R, Pello MJ, et al. Erythropoetin accelerates hematocrit recovery in post-surgical anemia. *Am Surg*. 1995;61:74-77.
41. Helm RE, Gold JP, Rosengart TK, et al. Erythropoietin in cardiac surgery. *J Card Surg.* 1993;8:579-606.
42. Trovarelli T, Kahn B, Vernon S. Transfusion-free surgery is a treatment plan for all patients. *AORN J.* 1998;68:773-778, 780-774.
43. Yazicioglu L, Eryilmaz S, Sirlak M, et al. Recombinant human erythropoietin administration in cardiac surgery. *J Thorac Cardiovasc Surg.* 2001;122:741-745.
44. Braga M, Gianotti L, Gentilini O, et al. Erythropoiesis after therapy with recombinant human erythropoietin: a dose-response study in anemic cancer surgery patients. *Vox Sang.* 1999;76:38-42.