CME CREDIT

Preoperative autologous blood donation: clinical, economic, and ethical issues

RONALD E. DOMEN, MD

SUMMARY Many patients are donating their own blood before surgery to avoid blood-borne infections, often on the advice of their physicians. But autologous blood transfusion, while safer than allogeneic transfusion, is not completely risk-free. It is also expensive, its benefits are difficult to assess, and its increasing popularity raises many difficult ethical issues, such as whether the benefit of allogeneic transfusion supports its additional expense.

KEY POINTS Record-keeping, collection, and transfusion errors are occasional risks of autologous transfusions. In addition, risks associated with blood donation, from mild dizziness to precipitation of angina, should be considered when high-risk patients are referred for autologous collection. Only approximately half of autologous units collected are actually used, and the cost per quality-adjusted year of life saved may be as high as $1 million, depending on the type of surgical procedure. Although recombinant human erythropoietin can stimulate red blood cell production before autologous donation and decrease the need for transfusion, it is not clear whether this strategy, which can cost thousands of dollars per patient, will be cost-effective. Perioperative hemodilution may become an important component in efforts to reduce patient exposure to allogeneic blood, but its use remains controversial.

INDEX TERMS: BLOOD TRANSFUSION, AUTOLOGOUS
CLEVE CLIN J MED 1996; 63:295–300

From the Department of Clinical Pathology, Section of Blood Banking and Transfusion Medicine, The Cleveland Clinic Foundation.

Address reprint requests to R.E.D., Section of Blood Banking and Transfusion Medicine, L20, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.

ALLOGENEIC BLOOD transfusions can have a number of possible adverse effects, including hemolytic transfusion reactions and transmission of infectious diseases.[1,2] Autologous transfusions, which are safer, are increasing in popularity, along with other efforts to decrease the adverse effects of allogeneic transfusion.[3–5] In 1980 only about 10% of hospitals in the United States had autologous blood collection programs.[4] Since then, autologous transfusion has grown almost exponentially and now accounts for approximately 8.1% of all blood collections and 4.1% of all transfusions in the United States.[6–9] This tremendous growth raises many medical, economic, and ethical issues.

Nevertheless, the benefits of autologous blood donation and transfusion are not always easy to measure,[10] and prospective and comprehensive data are needed.

Many patients undergoing major surgery today receive little or no allogeneic blood. Various ways

TABLE 1
MARKERS OF INFECTIOUS DISEASE
IN AUTOLOGOUS BLOOD COLLECTED AT THE CLEVELAND CLINIC

Disease marker	No. of positive* units	
	1993 (n = 1883)	1994 (n = 2104)
Hepatitis C virus antibody	41 (2.2%)	51 (2.4%)
Human immunodeficiency virus antibody	1 (0.05%)	2 (0.1%)
Hepatitis B surface antigen	7 (0.4%)	6 (0.3%)
Human t-lymphocyte lymphotropic virus-I antibody	1 (0.05%)	10 (0.5%)
Elevated alanine aminotransferase concentration, hepatitis B core antibody, or positive serologic test for syphilis	167 (8.9%)	195 (9.3%)
One or more infectious disease markers	217 (11.5%)	264 (12.5%)

*Positive (reactive) on initial screening tests but not necessarily confirmed positive with supplementary or confirmatory assays

to decrease the need for allogeneic blood have been studied over the past decade.[11] Preoperative autologous blood collection, perioperative blood salvage, perioperative hemodilution, recombinant human erythropoietin (EPO) therapy, and combinations of these approaches have all been advocated.

Physicians affect patient decisions

As physicians counsel patients about the use of autologous donation, they must take into account behavioral, emotional, clinical, and educational issues,[12–17] and the influence that physicians have on their patients' decisions. In a recent Cleveland Clinic survey, when we asked 110 patients why they opted for autologous blood, only 20% cited fear of infection, but 68% said their physicians had recommended it.[18]

CLINICAL ISSUES

Even though autologous blood is safer than allogeneic blood, it is not necessarily 100% safe.[2,19] Physicians and patients considering autologous blood donation need to understand the problems of transfusion errors, transfusion reactions, the rare adverse reactions to blood donation, and infections when weighing the cost and benefits.

Transfusion errors are rare, but do occur

The College of American Pathologists surveyed 3852 transfusion services in 1992 and found that 34 (0.9%) of the services had reported incidents of autologous blood being issued to the wrong patient in the preceding year, and in 20 of the 34 services, autologous blood was actually transfused to the wrong patient before the mistake was caught.[20] In another study, the New York State Department of Health found that of 124 601 autologous units collected before surgery and 64 500 units salvaged during surgery, four patients received blood from another patient (4 of 189 101 or 0.0021%), and three patients received allogeneic blood when autologous blood was available.[19] It is not known if the errors were associated with any significant morbidity or mortality.

Autologous blood can cause transfusion reactions

Bacterial contamination of autologous blood during collection and storage can cause a transfusion reaction, just as it can with allogeneic blood. In theory, the incidence of bacterial infection should be similar in both types of transfusions; in practice, clinicians should be alert to this possibility and treat transfusion reactions as such regardless of the source of the blood.[2]

Adverse reactions to giving blood are rare, but do occur

Several studies have addressed the safety of autologous blood donation.[21–25] The incidence of adverse reactions during blood donation is probably no higher (approximately 2.7% to 4.3% of patients) in autologous than in allogeneic donors, even though autologous donors tend to be older and sicker. Adverse reactions can range from mild dizziness and light-headedness (common) to the precipitation of angina and cardiac arrest (rare). In properly supervised and structured programs, autologous donation has proved safe in children, pregnant women, cardiovascular patients, and other high-risk patients.[24–29]

In 11 studies performed between 1974 and 1994 in cardiovascular patients, adverse effects occurred during the drawing of 42 (2.8%) of 2647 autologous units from 1526 patients.[22–25,29] Of the complica-

tions, 23 were mild, seven were moderate, and 12 were severe. Some of the severe reactions noted in two studies were in patients taking isosorbide dinitrate,[22,23] who may require special attention.[23]

Autologous donors have a higher prevalence of infectious diseases

Most studies of blood donors have found higher rates of infectious disease in autologous donors than in allogeneic donors, and intermediate rates in directed donors.[30–33] However, these studies are not always easy to compare.[30] For example, the prevalence is higher if first-time donors (known to have a higher rate of infectious disease) are included. The prevalence also varies depending on whether individual units or individual donors are analyzed.

Table 1 lists the prevalence of infectious disease markers in autologous units collected at the Cleveland Clinic in 1993 and 1994. The one autologous donor found to have antibodies to human immunodeficiency virus (HIV) by enzyme-linked immunosorbent assay (ELISA) in 1993 was confirmed HIV-positive on subsequent Western blot testing; the two patients found to have HIV antibodies in 1994 were subsequently found not to have them on Western blot testing.

Because autologous donors rarely meet all the standard donor requirements for allogeneic blood donation, unused autologous units are almost never given to other patients. We follow this policy at the Cleveland Clinic. Keeping track of the few units that would meet all acceptable criteria would not be worth the additional paperwork, expense, and time.

Other unresolved clinical issues surrounding allogeneic transfusion (eg, a possible association with cancer recurrence) may continue to encourage, support, and refine the indications for autologous donation and transfusion, at least under certain circumstances.[34,35]

ECONOMIC ISSUES

Autologous transfusion is expensive

Approximately half of the autologous blood collected in the United States is not used. At the Cleveland Clinic in 1994 we collected, or acquired from outside sources, 3490 units of autologous red blood cells for our preoperative patients. Of these, we actually used 1703 units (ie, the discard rate was 51.2%). Recent papers have addressed the cost-effectiveness of autologous blood programs,[7,36–38] an issue that is far from resolved.[12,39,40] There does seem to be general agreement, however, that such programs are expensive and that cost-cutting strategies should be pursued.[7,12,38–42]

Birkmeyer et al[36] found that autologous blood donation cost more than $300 000 per quality-adjusted year of life saved in unilateral hip replacement—and $1 147 000 in unilateral knee replacement. In coronary artery bypass grafting, the cost ranged from $508 000 to $909 000 per quality-adjusted year of life saved, but was as low as $158 000 in younger patients.[37] Etchason et al[38] found the added cost of substituting an autologous unit for an allogeneic unit in several surgical procedures ranged from $68 to $4783, and the cost per quality-adjusted year of life saved ranged from $235 000 to more than $23 000 000. These studies tested different strategies to reduce the cost of autologous transfusions, but the results were highly variable and questionable.[36–38]

Cost-cutting strategies

One way to cut costs is to use less blood. Guidelines for autologous blood use have general appeal as an effort to decrease the overcollection of red blood cells.[7,41] One strategy is for hospitals to develop a "maximum surgical blood order schedule" for autologous blood, similar to those currently used by surgeons and blood banks to guide how many units of blood to crossmatch before any particular surgical procedure. More controversial cost-cutting measures include not testing autologous donors and blood units for infectious diseases, not separating whole blood into specialized components, and holding patients responsible for the additional costs of collecting and storing their own blood.[7] Eliminating infectious-disease testing, for example, could save millions of dollars each year in the United States.

Not separating whole blood into specialized components may also save money, but individual institutions should assess the needs of their physicians and patients before doing so. In March 1994, Gerald A. Hoeltge, MD and I surveyed the 42 staff physicians who order most of the autologous transfusions at our hospital and asked them to choose one of three options for preparing autologous blood. Thirty-three physicians (79%) responded. Most (30, 91%) preferred the current policy of providing both red blood cells and fresh frozen plasma, often commenting that adequate levels of coagulation factors were an important clinical consideration (factors V and VIII are lost if plasma is not fresh frozen). At other hospi-

TABLE 2
ADVANTAGES AND DISADVANTAGES OF PERIOPERATIVE HEMODILUTION*

Possible advantages
Provides fresh whole blood
Platelets are viable and functional
Reduces clerical errors
Decreases allogeneic blood use and exposure
Decreases blood viscosity with potential improvement in tissue perfusion
Patient carefully monitored during blood collection
Functional coagulation factors preserved
Possible disadvantages
Adverse effects due to acute anemia
Increased edema due to crystalloids
Potential adverse effects on wound healing or lung function
Increased tissue hypoxia
Increased risk of perioperative myocardial ischemia and infarction
Patient starts operation with a relatively low hemoglobin and hematocrit
Actual clinical use is limited

*Based on Stehling and Zauder, reference 66; and Gillon, reference 67

tals, the need for autologous fresh frozen plasma may not be as important, and another autologous component (eg, whole blood) may be preferred for the types of surgery performed.

Whether any of these measures would actually make autologous collection more cost-effective, however, remains questionable and unproven.[38–40]

Of interest, in the survey of autologous donors at the Cleveland Clinic cited above,[18] 79% of those surveyed felt their health insurance should pay for autologous donation, but 18% indicated they would be willing to pay up to $100 per unit of autologous blood collected.

ERYTHROPOIETIN AND TRANSFUSION

Recent studies have examined the use of EPO to increase the number of units of blood that a patient can donate before surgery and to decrease the need for allogeneic blood transfusions.[43–58] This drug appears to be safe and to cause few serious side effects when used in autologous donors.[59,60] Goodnough[60] analyzed two published studies and found that thrombosis, a major complication, occurred in four (2.5%) of 163 autologous blood donors—but two of them had received EPO and the other two had received placebo. Less-serious adverse effects, including dizziness and hypertension, occur more frequently, in approximately 14% of patients in one study.[61] It is not clear whether EPO itself causes such symptoms or if blood-volume changes are responsible.[61] Additional clinical trials are needed in order to assess adverse reactions to EPO adequately.

Cost—approximately $10 per 1000 units of EPO, not including pharmacy charges, nursing costs, administrative costs, syringes, and needles—is one of the major drawbacks to using EPO more widely. Doses needed to enhance preoperative autologous blood donation or to decrease allogeneic blood transfusion in the perioperative period could cost thousands of dollars for a single patient.[62]

The use of EPO should be reassessed as the rate of infectious disease transmission from allogeneic blood decreases, blood-conservation programs are implemented, and the use of perioperative transfusion in general decreases. At present, apart from its use in chronic renal failure, EPO has yet to find its clinical niche in transfusion medicine. Questions related to dosage, efficacy in specific patient groups, adverse effects, and cost-effectiveness still require further study. Until more data are obtained, wider use of EPO in transfusion medicine is still investigational.[63-65]

PERIOPERATIVE HEMODILUTION

Perioperative hemodilution, or acute normovolemic hemodilution, is a variation of preoperative autologous donation. This procedure consists of removing blood either immediately before or shortly after induction of anesthesia. The blood volume is simultaneously maintained with intravenous crystalloid or colloid solutions. Often, enough blood is removed to achieve a predetermined hematocrit (eg, 28%).

Perioperative hemodilution remains somewhat controversial, having advantages and disadvantages (*Table 2*).[66,67] Cost-effectiveness studies have not been performed, but since perioperative hemodilution does not require such additional expenses as infectious-disease testing, storage, shipping, or crossmatching, it may prove more cost-effective than routine autologous donation. Ultimately, perioperative hemodilution may become one component of a multifaceted approach to decreasing exposure to allogeneic blood.[66–68]

ETHICAL ISSUES

In the absence of good data analyzing the cost and utility of autologous transfusion, a number of difficult ethical issues remain. Is it ethical to apply cost-effectiveness analysis to this aspect of patient care?[69] Does the benefit of autologous blood transfusion support its additional expense, especially since the risk appears to be minimal? Should patient fears and emotions that run counter to scientific and clinical data be considered during the decision-making process? Should certain groups automatically be denied participation in preoperative autologous blood collection programs because of underlying infectious diseases (eg, HIV, hepatitis B virus, or hepatitis C virus)?[70,71] Is it ethical to require autologous donors to undergo infectious-disease testing at all, when all surgical patients are not required to undergo the same testing, and the tests are expensive?[7,72,73]

It will not be easy to determine in which surgical procedures autologous donation is justified, especially when patient emotions and desires can be strong motivating factors. I know of otherwise-healthy teenagers who made autologous blood donations for elective tonsillectomies. Would it be ethical to adhere to a surgical blood order schedule and deny autologous blood donation for operative procedures that generally require blood transfusion in fewer than 5% of cases—or 10% or 15%? Likewise, should elderly patients with underlying high-risk medical conditions be encouraged to set aside their own blood regardless of their potential need for a blood transfusion? Should the patient's age be a criterion for participation in preoperative autologous blood donation?

These and other ethical questions will continue to arise in the years ahead, especially in light of efforts to control the cost of surgical procedures. It is important that additional data be collected and that these issues undergo careful scrutiny so that patient care is not jeopardized.

REFERENCES

1. **Dodd RY.** The risk of transfusion-transmitted infection. N Engl J Med 1992; **327:**419–420.
2. **Linden JV, Kaplan HS.** Transfusion errors: causes and effects. Transfus Med Rev 1994; **8:**169–183.
3. **Council on Scientific Affairs of the American Medical Association.** Autologous blood transfusions. JAMA 1986; **256:**2378–2380.
4. **Surgenor DM.** The patient's blood is the safest blood. N Engl J Med 1987; **316:**542–544.
5. **Toy PTCY, Strauss RG, Stehling LC, et al.** Predeposited autologous blood for elective surgery: a national multicenter study. N Engl J Med 1987; **316:**517–520.
6. **Renner SW, Howanitz PJ, Bachner P.** Preoperative autologous blood donation in 612 hospitals: a College of American Pathologists' Q-Probes study of quality issues in transfusion medicine. Arch Pathol Lab Med 1992; **116:**613–619.
7. **Kruskall MS, Yomtovian R, Dzik WH, Friedman KD, Umlas J.** On improving the cost-effectiveness of autologous blood transfusion practices. Transfusion 1994; **34:**259–264.
8. **Forbes JM, Laurie ML.** Blood collections by community blood centers, 1988 through 1992. Transfusion 1994; **34:**392–395.
9. **Wallace EL, Churchill WH, Surgenor DM, et al.** Collection and transfusion of blood and blood components in the United States, 1992. Transfusion 1995; **35:**802–812.
10. **Toy PTCY.** Continuous quality improvement: autologous blood donations. Arch Pathol Lab Med 1992; **116:**611–612.
11. **Ereth MH, Oliver WC, Santrach PJ.** Perioperative interventions to decrease transfusion of allogeneic blood products. Mayo Clin Proc 1994; **69:**575–586.
12. **Goldfinger D, Haimowitz M.** Is autologous blood transfusion worth the cost? Pro. Transfusion 1994; **34:**75–78.
13. **Strauss RG, Ferguson KJ, Stone GG, et al.** Surgeon's knowledge, attitude, and use of preoperative autologous blood donation. Transfusion 1990; **30:**418–422.
14. **Yomtovian R, Ceynar J, Kepner JL, Buhl M.** Predeposit autologous blood transfusion: an analysis of donor attitudes and attributes. Quality Review Bulletin 1987; **13:**45–50.
15. **AuBuchon JP, Gettinger A, Littenberg B.** Determinants of physician ordering of preoperative autologous donations. Vox Sang 1994; **66:**176–181.
16. **Ferguson KJ, Strauss RG, Toy PT.** Physician recommendation as the key factor in patients' decisions to participate in preoperative autologous blood donation programs: Preoperative Autologous Blood Donation Study Group. Am J Surg 1994; **168:**2–5.
17. **Randels MJ, Ferguson K, Strauss RG, Daniels M, Stehling L, Toy P.** Preoperative autologous donation: surgery clinic staff knowledge/attitudes. J Clin Apheresis 1994; **9:**168–170.
18. **Domen RE, Rybicki LA, Hoeltge GA.** An analysis of autologous blood donor motivational factors. Vox Sang 1995; **69:**110–113.
19. **Linden JV.** Autologous blood errors and incidents. Transfusion 1994; **34:**28S. Abstract.
20. **Shulman IA.** Comprehensive Transfusion Medicine Survey, Set J-C 1992. College of American Pathologists, Northfield, IL 60093.
21. **McVay PA, Andrews A, Kaplan EB, et al.** Donation reactions among autologous donors. Transfusion 1990; **30:**249–252.
22. **AuBuchon JP, Popovsky MA.** The safety of preoperative autologous blood donation in the nonhospital setting. Transfusion 1991; **31:**513–517.
23. **Domen RE, Hnat H, Panasiuk M.** Autologous blood donation by patients with cardiovascular disease. Vox Sang 1992; **63:**137. Letter.
24. **Hillyer CD, Hart KK, Lackey DA 3rd, Lin LS, Bryan JA.** Comparable safety of blood collection in "high-risk" autologous donors versus non-high-risk autologous and directed donors in a hospital setting. Am J Clin Pathol 1994; **102:**275–277.
25. **Adegboyega PA, Patten ED.** A review of presurgical autologous blood donation by high-risk patients. Transfus Med Rev 1994; **8:**200–209.
26. **Tasaki T, Ohto H, Noguchi M, Abe R, Kikuchi S, Hoshino S.** Autologous blood donation elective surgery in children. Vox Sang 1994; **66:**188–193.
27. **Kruskall MS.** The safety and utility of autologous donations by pregnant patients: pro. Transfusion 1990; **30:**168–171.
28. **Sayers MH.** Autologous blood donation in pregnancy: con. Transfusion 1990; **30:**172–174.
29. **Dzik WH, Fleisher AG, Ciavarella D, Karlson KJ, Reed GE, Berger RL.** Safety and efficacy of autologous blood donation before elective aortic valve operation. Ann Thorac Surg 1992; **54:**1177–1181.

30. **AuBuchon JP, Dodd RY.** Analysis of the relative safety of autologous units available for transfusion to homologous recipients. Transfusion 1988; **28:**403–405.
31. **Starkey JM, MacPherson JL, Bolgiano DC, Simon ER, Zuck TF, Sayers MH.** Markers for transfusion-transmitted disease in different groups of blood donors. JAMA 1989; **262:**3452–3454.
32. **Kruskall MS, Popovsky MA, Pacini DG, Donovan LM, Ransil BJ.** Autologous versus homologous donors. Evaluation of markers for infectious disease. Transfusion 1988; **28:**286–288.
33. **Pink J, Thomson A, Wylie B.** Infectious disease markers in autologous and directed donations. Transfusion Medicine 1994; **4:**135–138.
34. **Busch ORC, Hop WCJ, Hoynck van Papendrecht MAW, Marquet RL, Jekeel J.** Blood transfusions and prognosis in colorectal cancer. N Engl J Med 1993; **328:**1372–1376.
35. **Peller S, Sayfan J, Levy Y, et al.** Immunological profile changes following perioperative autologous vs homologous blood transfusion in oncologic patients. J Surg Oncol 1994; **56:**98–101.
36. **Birkmeyer JD, Goodnough LT, AuBuchon JP, Noordsij PG, Littenbeg B.** The cost-effectiveness of preoperative autologous blood donation in total hip and knee replacement. Transfusion 1993; **33:**544–551.
37. **Birkmeyer JD, AuBuchon JP, Littenberg B, et al.** Cost-effectiveness of preoperative autologous donation in coronary artery bypass grafting. Ann Thorac Surg 1994; **57:**161–169.
38. **Etchason J, Petz L, Keeler E, et al.** The cost effectiveness of preoperative autologous blood donations. N Engl J Med 1995; **332:**719–724.
39. **AuBuchon JP, Birkmeyer JD.** Is autologous blood transfusion worth the cost? Con. Transfusion 1994; **34:**79–83.
40. **Rutherford CJ, Kaplan HS.** Autologous blood donation—can we bank on it? N Engl J Med 1995; **332:**740–742.
41. **Axelrod FB, Pepkowitz SH, Goldfinger D.** Establishment of a schedule of optimal preoperative collection of autologous blood. Transfusion 1989; **29:**677–680.
42. **Goodnough LT.** The implications of cost-effectiveness for autologous blood procurement. Arch Pathol Lab Med 1994; **118:**333–334.
43. **Spivak JL.** Recombinant human erythropoietin and its role in transfusion medicine. Transfusion 1994; **34:**1–4.
44. **AuBuchon JP.** Minimizing donor exposure in hemotherapy. Arch Pathol Lab Med 1994; **118:**380–391.
45. **Goodnough LT.** Clinical application of recombinant erythropoietin in the perioperative period. Hematol Oncol Clin North Am 1994; **8:**1011–1020.
46. **Huch R, Huch A.** Erythropoietin in obstetrics. Hematol Oncol Clin North Am 1994; **8:**1021–1040.
47. **Konishi T, Ohbayashi T, Kaneko T, Ohki T, Saitou Y, Yamato Y.** Preoperative use of erythropoietin for cardiovascular operations in anemia. Ann Thorac Surg 1993; **56:**101–103.
48. **Mercuriali F, Adamson JW.** Recombinant human erythropoietin enhances blood donation for autologous use and reduces exposure to homologous blood during elective surgery. Semin Hematol 1993; **30:**17–21.
49. **Biesma DH, Marx JJM, Kraaijenhagen RJ, Franke W, Messinger D, van de Wiel A.** Lower homologous blood requirement in autologous blood donors after treatment with recombinant human erythropoietin. Lancet 1994; **344:**367–370.
50. **Shannon KM, Keith JF 3rd, Mentzer WC, Lonnqvist B, Wennberg L.** Recombinant human erythropoietin stimulates erythropoiesis and reduces erythrocyte transfusions in very low birth weight preterm infants. Pediatrics 1995; **95:**1–8.
51. **Klaesson S, Ringden O, Ljungman P, et al.** Reduced blood transfusions requirements after allogeneic bone marrow transplantation: results of a randomised, double-blind study with high-dose erythropoietin. Bone Marrow Transplant 1994; **13:**397–402.
52. **Canadian Orthopedic Perioperative Erythropoietin Study Group.** Effectiveness of perioperative recombinant human erythropoietin in elective hip replacement. Lancet 1993; **341:**1227–1232.
53. **Levine EA, Gould SA, Rosen AL, et al.** Perioperative recombinant human erythropoietin. Surgery 1989; **106:**432–438.
54. **Goodnough LT, Rudnick S, Price TH, et al.** Increased preoperative collection of autologous blood with recombinant human erythropoietin therapy. N Engl J Med 1989; **321:**1163–1168.
55. **Kyo S, Omoto R, Hirashima K, Eguchi S, Fujita T.** Effect of human recombinant erythropoietin on reduction of homologous blood transfusion in open-heart surgery. A Japanese multicenter study. Circulation 1992; **86(Suppl II):**II-413–II-418.
56. **Goodnough LT.** Toward bloodless surgery: erythropoietin therapy in the surgical setting. Semin Oncol 1992; **19(Suppl 8):**19–24.
57. **Schlaeppi B, Gunter P, Nydegger UE.** Enhancing the efficacy of preoperative autologous blood donation by erythropoietin. Transfusion Science 1994; **15:**171–177.
58. **Watanabe Y, Fuse K, Konishi T, et al.** Autologous blood transfusion with recombinant human erythropoietin in heart operations. Ann Thorac Surg 1991; **51:**767–772.
59. **Biesma DH, Bronkhorst PJH, deGroot PG, et al.** The effect of recombinant human erythropoietin on hemostasis, fibrinolysis, and blood rheology in autologous blood donors. J Lab Clin Med 1994; **124:**42–47.
60. **Goodnough LT.** The safety of recombinant human erythropoietin therapy in autologous blood donors. J Lab Clin Med 1994; **124:**17–18.
61. **Goodnough LT, Price TH, Friedman KD, et al.** A phase III trial of recombinant human erythropoietin therapy in nonanemic orthopedic patients subjected to aggressive removal of blood for autologous use: dose, response, toxicity, and efficacy. Transfusion 1994; **34:**66–71.
62. **Domen RE.** Commentary: Recombinant erythropoietin reduced the need for homologous blood transfusion. Ann Intern Med 1995; **122(Suppl 2):**36.
63. **Domen RE.** Commentary: Perioperative recombinant human erythropoietin in hip replacement. Ann Intern Med 1993; **46 (Suppl 2):**119.
64. **Wilimas JA, Crist WM.** Erythropoietin—not yet a standard treatment for anemia of prematurity. Pediatrics 1995; **95:**9–10.
65. **Shireman TI, Hilsenrath PE, Strauss RG, Widness JA, Mutnick AH.** Recombinant human erythropoietin vs transfusions in the treatment of anemia of prematurity. A cost-benefit analysis. Arch Pediatr Adolesc Med 1994; **148:**582–588.
66. **Stehling L, Zauder HL.** Perioperative hemodilution: pro. Transfusion 1994; **34:**265–268.
67. **Gillon J.** Acute normovolemic hemodilution in elective major surgery: con. Transfusion 1994; **34:**269–271.
68. **Spence RK.** Hemodilution in vascular surgery. Semin Vasc Surg 1994; **7:**85–88.
69. **Williams A.** Cost-effectiveness analysis: is it ethical? J Med Ethics 1992; **18:**7–11.
70. **Mintz PD.** Participation of HIV-infected patients in autologous blood programs. JAMA 1993; **269:**2892–2894.
71. **Popovsky MA, Hoff RG, Petz LD, Kleinman S.** HIV-infected patients participating in autologous blood programs. JAMA 1993; **270:**2181. Letter.
72. **American Association of Blood Banks.** BPAC discusses source plasma, autologous donations, and stem cells. Blood Bank Week 1994; **11:**2–3.
73. **Domen RE.** Infectious disease marker testing of the autologous blood donor. A case study in clinical ethics. Arch Pathol Lab Med 1995; **119:**807–810