Transfusion of buffy coat-depleted blood components and risk of postoperative infection in orthopedic patients

P. Innerhofer, C. Walleczek, G. Luz, P. Hobisch-Hagen, A. Benzer, B. Stöckl, G. Hessenberger, W. Nussbaumer, and W. Schobersberger

BACKGROUND: Allogeneic blood transfusions have been reported to increase susceptibility to postoperative infection, but the findings were inconclusive. This study was designed to investigate the effect of buffy coat-depleted allogeneic and autologous transfusion on postoperative infection in patients undergoing orthopedic surgery.

STUDY DESIGN AND METHODS: Patients (n = 385) undergoing elective orthopedic surgery (primary and revision joint replacement, spinal, or pelvic surgery) were included in a prospective observational study of the incidence of postoperative infection between April and December 1996. Infection rates in patients who received allogeneic buffy coat-depleted blood transfusions were compared with those in patients who received no transfusion or only autologous (buffy coat-depleted) blood.

RESULTS: Patients without exposure to allogeneic blood (no blood or only autologous blood) had an infection rate of 3.9 percent, as compared to a rate of 12.2 percent for those with exposure to allogeneic blood (allogeneic blood, autologous plus allogeneic blood) (odds ratio 3.442; 95% CI, 1.349-10.40; p = 0.006). Of the 385 study patients, 309 underwent primary hip or knee replacement surgery. In this homogeneous subgroup, the postoperative infection rate was 4.6 percent after no transfusion or autologous transfusion and 11.9 percent after allogeneic transfusion (odds ratio 2.827; 95% CI 1.059-8.799; p = 0.036). Multivariate regression analysis confirmed buffy coat-depleted allogeneic blood transfusion as an independent variable associated with high risk for postoperative infection.

CONCLUSION: Buffy coat-depleted allogeneic blood transfusion increases the incidence of postoperative infection in patients undergoing uncontaminated orthopedic surgery.

Since the early work of Opelz et al. in 1973,[1] allogeneic blood transfusions have been known to downregulate the recipient's immune system. This immunosuppression might be beneficial for allograft survival, but there are also reports of increased tumor recurrence and postoperative infection rate after allogeneic blood transfusion.[2] The results of retrospectively and prospectively randomized clinical trials on this topic are conflicting, and at present it remains unclear whether allogeneic blood transfusions per se—and what amount of transfused allogeneic white cells (WBCs)—are critical to clinically relevant immunosuppression, which increases perioperative morbidity.[3,4] It is generally accepted that the immunosuppressive effect of allogeneic blood transfusion results from donor WBCs and possibly plasma, pyrogens, and cytokines, the last two of which are released during storage of blood components.[5-10] Although the idea of a critical threshold below which donor WBCs provoke almost no immunosuppression is not approved, the degree of immunosuppression following blood transfusion supposedly depends on blood component preparation. Whole blood contains a substantial amount of WBCs (5-9 × 10^9/unit), while packed red cells (RBCs) contain fewer WBCs (2-3 × 10^9/unit) and little residual plasma. Further reduction of recipient exposure to allogeneic WBCs can be provided by removal of the buffy coat (<1.2 × 10^9 WBCs/unit). Since 1992, buffy coat-depleted (BCD)-RBCs have been the standard

ABBREVIATIONS: BCD = buffy coat-depleted; FFP = fresh-frozen plasma; Hct = hematocrit; RBC(s) = red cell(s); WBC(s) = white cell(s).

From the Departments of Anesthesia, Intensive Care Medicine, Orthopedic, Biostatistics, and Transfusion Medicine, Leopold-Franzens University of Innsbruck, Innsbruck, Austria.

Address reprint requests to: Petra Innerhofer, MD, The Leopold-Franzens University, Anichstrasse 35, A-6020 Innsbruck, Austria; e-mail: Petra.Innerhofer@uibk.ac.at.

Received for publication June 20, 1998; revision received and accepted October 26, 1998.

TRANSFUSION 1999;39:625-632.

preparation at our institution for autologous and allogeneic blood transfusion, whereas WBC-filtered preparations are used for special indications only. However, the general use of WBC-filtered blood components is now under discussion, as some authors suggest a WBC-reduction threshold of 10^7 WBCs per unit or less to prevent WBC-mediated adverse reactions.[10]

Two reports[11,12] found higher postoperative infection rates in orthopedic patients after transfusion of allogeneic blood than after that of autologous blood, whereas two other studies[13,14] found no association between allogeneic transfusion and postoperative infection. Moreover, packed RBCs or whole blood was used for those transfusion regimens, which prompts the question of whether BCD-blood components exhibit the presumed immunosuppressive effect.

To estimate the immunosuppressive potential of currently used allogeneic components, with moderate WBC contamination, we compared the impact of allogeneic BCD-transfusions and of autologous BCD-transfusions on the incidence of postoperative infection in patients undergoing uncontaminated orthopedic surgery in which conditions in surgery and after surgery were standardized.

MATERIALS AND METHODS

Selection of patients

A total of 385 consecutive patients who decided on preoperative autologous blood donation for elective orthopedic surgery (primary and revision joint replacement, spinal, and pelvic surgery) at Innsbruck University Hospital (Innsbruck, Austria) were enrolled in our present prospective observational study between April and December 1996. Given the risks of allogeneic transfusion, random assignment to an autologous or allogeneic transfusion regimen is unacceptable for ethical reasons. Therefore, patients were divided into two groups (donors and nondonors of autologous blood) at time of admission, according to their own decision to provide autologous blood or not. Patients with coexisting diseases that prevented the treating physicians from consenting to autologous blood donation were not included in the study. Reasons for not donating autologous blood were personal refusal, difficulties reaching the Department of Transfusion Medicine at Innsbruck University Hospital, too little time for blood donation, and unsuccessful venipuncture.

Clinical experience shows that about 30 percent of autologous blood donors require additional allogeneic transfusion, while about 20 percent of autologous blood nondonors need no perioperative transfusion at all. A retrospective scrutiny of actual transfusion regimen was therefore necessary. Accordingly, at discharge, patients were divided into four groups according to the actual type of perioperative transfusion received (autologous, allogeneic, both, none) and into two further groups (any allogeneic transfusion, no allogeneic transfusion). Data were obtained from patients' records and interviews (preoperative blood donation, reasons for no preoperative blood donation, history of chronic systemic illness, current medication). Patients were observed from the beginning of their hospital stay until discharge.

Clinical data

Data collected from medical records include age, sex, body mass index (BMI, kg/m^2), admission hematocrit (Hct), WBC count, surgical procedure, type of anesthesia, estimated blood loss (blood collected intraoperatively by suction device plus blood loss on the floor, in sponges; postoperative loss into surgical drains), duration of surgery, number and type of transfused RBCs (including intraoperative and postoperative autologous blood collection), units of transfused fresh-frozen plasma (FFP), therapeutic use of antibiotics, and length of hospital stay.

Perioperative management

All patients received standard general or regional anesthesia. General anesthesia was induced by use of thiopental sodium, fentanyl, and vecuronium bromide and maintained with inhalation of isoflurane in a nitrous oxide and oxygen mixture and additional bolus doses of fentanyl and vecuronium bromide given intravenously. Regional anesthesia was performed as spinal or combined spinal-epidural anesthesia, using plain bupivacaine at 0.5 percent. All patients were actively warmed by the use of fluid warmers (Biegler, Biotest Pharmazeutika, Vienna, Austria) and a convective warming system (Bair Hugger, Augustine Medical, Eden Prairie, MN). Monitoring during surgical intervention included blood pressure measurement, electrocardiogram, pulse oximetry, capnometry, and urine output measurement. Intraoperatively, a cell-saver system (Haemonetics 3, Haemonetics Corp., Braintree, MA) was used for salvage and processing of RBCs. Postoperative autotransfusion of shed blood was performed in all patients undergoing revision joint surgery, knee replacement surgery, and cementless hip replacement surgery. Postoperative analgesia was performed by intermittent intravenous application of piritramide or patient-controlled analgesia (intravenous piritramide or epidural bupivacaine-fentanyl-adrenaline).

Each patient received second-generation cephalosporin on the day of surgery. A Foley urinary catheter was inserted before surgery and usually removed on the morning of the second postoperative day. All patients underwent thrombosis prophylaxis with enoxaparin 12 hours preoperatively, and this was followed by daily postoperative administration until the third postoperative day and further oral anticoagulation with acenocoumarol.

Preparation of blood components

Autologous and allogeneic blood transfusions, provided by the Department of Transfusion Medicine of Innsbruck University Hospital, were prepared in the same manner: 450 mL ± 10 percent of whole blood was collected in top and bottom bags (Gerätezentrale Österreichisches Rotes Kreuz, Eugendorf, Austria) using automatic mixing and weighing devices (Biotrans GmbH, Dreieich, Germany). Anticoagulation was performed with CPDA-1. Within 16 hours of storage at 20°C, the whole blood was centrifuged at 3550 × *g* for 10 minutes. BCD-RBCs in additive solution (100 mL saline-adenine-glucose-mannitol) were separated by using an automatic system for blood component preparation (Compomat, NPBI, Amsterdam, Netherlands) and kept in the blood bank at 4°C. Plasma was frozen within 1 hour after separation (–30°C core temperature) and stored at –30°C. Residual WBC counts in BCD-RBCs were analyzed with an automatic cell counter (STKS, Coulter, Miami, FL) in 1 percent of the produced units with regard to the Austrian regulations and guidelines for quality control. The median residual WBC count was 1.1×10^9 per unit (range, 0.42-1.93 × 10^9/unit).

All intraoperative or postoperative transfusions of RBCs were given according to the hemodynamic status of the individual patient. For all perioperative transfusions, fluid warmers (Biegler, Biotest Pharmazeutika) and 40-µm blood filters (Microtrapper, Miramed, Mirandola, Italy) were used. In the autologous transfusion group, autologous FFP was used for volume replacement. Allogeneic FFP was transfused to patients with severe coagulopathy only.

In all patients, urine samples were taken at the time of removal of the urinary catheter for microbiologic cultures, while other microbiologic specimens were ordered only if signs of infection were clinically apparent. In-hospital infections were identified by positive results of microbiologic cultures, and antibiotics were consequently administered. Patients with positive preoperative cultures were not classified as developing postoperative infection if the same pathogens were also observed postoperatively. The diagnosis of pneumonia was established when the classic clinical signs (fever, leukocytosis, and chest infiltrate) were observed, and a purulent exudate was adequate evidence of wound infection.

Statistical analysis

Kruskal-Wallis and Mann-Whitney U tests were used 1) to determine variation in infection rates among the four transfusion groups (autologous, allogeneic, both, none); 2) to compare the infection rates in patients who did not receive allogeneic transfusions (autologous only, none) with rates in patients who received allogeneic transfusions (allogeneic only, autologous plus allogeneic); and 3) to perform univariate analysis of continuous variables associated with postoperative infection. Fisher's exact test (odds ratio) was used to estimate the influence of categorical variables on the relative risk for development of postoperative infection.

Further analysis was limited to patients undergoing primary hip and knee replacement surgery only (n = 309; 80.3% of patients). Univariate (odds ratio, Fisher's exact test; mean values, Mann-Whitney U test) and multivariate logistic regression analysis was performed to determine which of the independent variables associated with allogeneic transfusion accounted for the development of postoperative infection. Variables that had significantly contributed to the development of infection in univariate analysis were forced into multivariate logistic regression analysis. Variables that predicted only the need for allogeneic blood were replaced with allogeneic BCD-RBCs. Values are reported as mean ± SD, and the relative risk estimate is given with a 95% CI.

RESULTS

Patient characteristics, admission Hct, WBC count, and type of elective orthopedic surgery are listed in Table 1. Of 385 patients, 188 (48.8%) underwent preoperative autologous blood donation (1-6 units depending on type of surgery; mean, 2.7 autologous units; total, 501 units), while 197 (51.2%) did not. Patients who did not participate in preoperative blood donation were significantly older and predominately female and had a higher admission Hct and WBC count than those in the autologous blood donor group.

Rate of in-hospital infection, length of hospital stay, transfusion regimen, and type of anesthesia are shown in Table 2. Of the 188 autologous donor patients, 150 (79.8%) received their autologous BCD-RBCs, while 68 (36.7%) patients additionally needed allogeneic BCD-RBC transfu-

TABLE 1. Patient characteristics at admission and type of planned surgery in 385 orthopedic patients (continuous variables as mean ± SD)

	Autologous blood donors (n = 188)	Nondonors of autologous blood (n = 197)	p value
Characteristics			
Female/Male (%)	52.6/47.3	71.1/28.9	<0.001
Age (years)	62.4 ± 14.6	68.3 ± 14.6	<0.001
Weight (kg)	75.0 ± 14.0	71.0 ± 14.0	0.003
Height (cm)	167 ± 9.0	164 ± 9.0	<0.001
Admission Hct (%)	37.4 ± 3.4	40.8 ± 4.3	<0.001
Admission WBC count (×10^9/L)	6.7 ± 1.7	7.2 ± 2.0	0.008
Surgery			
Primary hip and knee replacement (%)	85.1	75.6	
Revision hip and knee replacement (%)	6.9	18.8	0.04
Spinal surgery (%)	7.4	4.6	
Pelvic surgery (%)	0.5	1.0	

TABLE 2. Rate of postoperative infection, length of hospital stay, transfusion regimen, and type of anesthesia in 385 patients who did (n = 188) and did not (n = 197) preoperatively donate autologous blood (continuous variables as mean ± SD)

	Autologous blood donors	Nondonors of autologous blood	p value
Postoperative infection (%)	4.3	13.2	0.002
Length of hospital stay (days)	14.6 ± 3.0	15.4 ± 3.7	0.013
Total BCD-RBCs (units)	3.6 ± 2.44	3.3 ± 2.7	0.048
Total FFP (units)	2.5 ± 1.3	0.5 ± 1.8	0.017
Intraoperative blood salvage (%)	47.9	43.1	NS
Postoperative blood salvage (%)	45.7	41.1	NS
Regional anesthesia (%)	48.9	44.2	NS
General anesthesia (%)	51.1	55.8	NS

sions (mean, 3.4 units) and 6 patients (3.2%) also received allogeneic FFP (mean, 2.7 FFP). Of 197 patients who did not participate in preoperative autologous blood donation, 36 (18.3%) did not receive any blood transfusion, whereas 162 (81.7%) received allogeneic BCD-RBCs and 18 (9.1%) needed allogeneic FFP. Patients without available autologous blood had a significantly greater postoperative infection rate and longer hospital stay than did the autologous donor group. Total numbers of BCD-RBC units transfused (autologous and allogeneic) and of FFP (autologous) were higher in the autologous donor group and can be explained by the lower admission Hct in autologous donor patients and our institutional agreement to use autologous FFP for volume replacement (81.9% of autologous blood donors received their autologous FFP).

Of 385 patients, 34 (8.8%) developed postoperative infections; two of these were wound infections, but the rest had no connection to operation site (Table 3). Although our patients received prophylactic antibiotics, most (29/34) diagnosed infections were culture-proven, with the exception of purulent conjunctivitis, pneumonia, and tracheobronchitis. All diagnosed infections were considered clinically relevant, and antibiotic therapy was consequently administered by the treating physicians.

All patients were divided into four groups according to perioperative transfusion regimen. The incidence of infections in patients receiving no blood was 4.7 percent (2/42 patients), that in autologous blood recipients was 3.5 percent (4/113 patients), that in allogeneic blood recipients 14.8 percent (24/162 patients), and that in patients receiving autologous and allogeneic transfusions 5.9 percent (4/68 patients). The difference between the groups' infection rates was significant (Kruskal-Wallis test, p = 0.005), and allogeneic blood recipients had significantly more infections than did autologous blood recipients (Mann-Whitney U test, p = 0.002). Patients receiving both autologous and allogeneic BCD-RBCs showed a trend toward lower infection rates than did those who received only allogeneic blood (Mann-Whitney U test, p = 0.059), while no difference was seen in relation to patients who received only autologous blood or no blood (Mann-Whitney U test, p = 0.459; p = 0.802) (Fig. 1).

TABLE 3. Type of postoperative infections (n = 34) in 385 patients after elective orthopedic procedures between April and December 1996

Infection	Number of patients
Urinary tract	27
Tracheobronchitis	1
Pneumonia	2
Wound	2
Purulent conjunctivitis	2

Further comparison of infection rates in patients with exposure to any allogeneic BCD-RBCs (allogeneic BCD-RBCs, autologous plus allogeneic BCD-RBCs) and in those without such exposure (no transfusion or autologous BCD-RBCs only) revealed a postoperative infection rate of 12.2 percent (28/230) after any allogeneic BCD-RBC transfusion versus 3.9 percent (6/155) without allogeneic BCD-RBC transfusion (odds ratio 3.442; 95% CI, 1.349-10.40; p = 0.006), a difference that is significant (Fig. 2).

Univariate analysis of potential variables predicting postoperative infection identified transfusion of allogeneic BCD-RBCs, advanced age, female sex, low body weight and height, and small numbers of transfused allogeneic FFP as significant factors associated with postoperative infection (Table 4). Infection rates increased significantly with in-

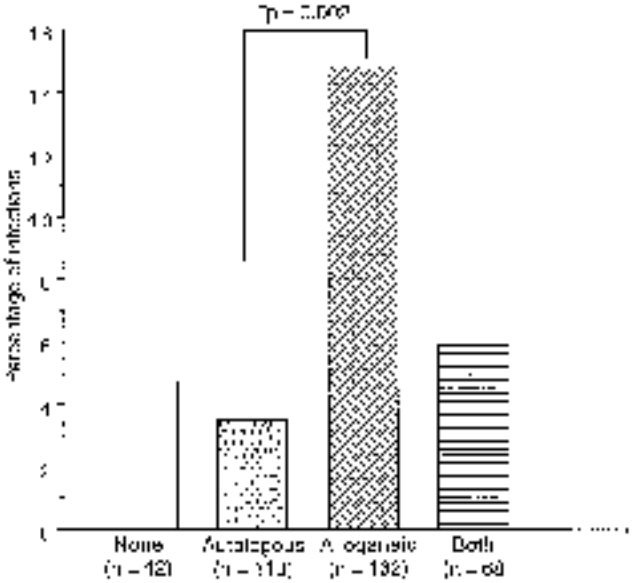

Fig.1. Dependence of postoperative infection frequency on type of transfusion regimen in 385 patients. A significant difference was found after transfusion of allogeneic or autologous BCD-RBCs (p = 0.002). Patients receiving both autologous and allogeneic transfusions showed a trend toward lower infection rates than did recipients of allogeneic transfusions (p = 0.059).

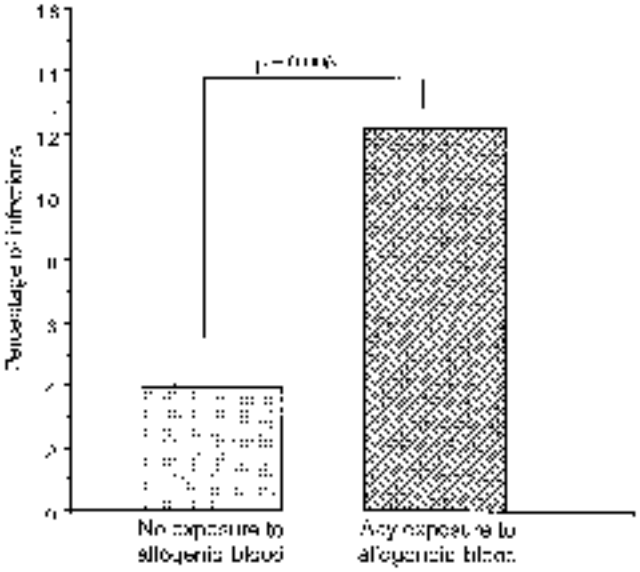

Fig. 2. Postoperative infection rate after any exposure to allogeneic transfusion of BCD-RBCs as compared to that after no exposure (no transfusions or only autologous transfusion) (p = 0.006).

creasing numbers of allogeneic transfusions (Fig. 3A), but not with the total number (autologous and allogeneic) of transfused BCD-RBCs (Fig. 3B).

Although blood loss, duration of surgery, and use of intraoperative and postoperative blood salvage were variables without statistical significance for increased infection rate in all 385 patients, clinical experience shows that the extent of intraoperative trauma is dependent on the type of surgery and might be related to postoperative infection rate. Therefore, further statistical analysis was performed for a more homogeneous study group of 309 patients undergoing exclusively primary hip and knee replacement surgery (80.3% of all enrolled patients), of which 27 developed postoperative infections. The infection rate was 11.9 percent (21/177 patients) after transfusion of allogeneic BCD-RBCs and 4.6 percent (6/132 patients) after the transfusion of autologous BCD-RBCs only or no transfusion (odds ratio 2.827; 95% CI, 1.059-8.799; p = 0.036). Univariate and multivariate analysis of variables confirmed transfusion of allogeneic BCD-RBCs as an independent variable predicting postoperative infection. Patients with postoperative infection were also older and predominately female, and they received more antibiotics. Increasing total numbers of transfused BCD-RBCs, small numbers of transfused FFP, smaller body mass index, and female sex were associated with the need for allogeneic transfusion (Table 5).

TABLE 4. Potential variables predicting postoperative infection in 385 orthopedic patients undergoing elective surgery

Variables	p value
Exposure to allogeneic BCD-RBCs	0.006
Numbers of allogeneic BCD-RBCs	0.003
Total numbers of BCD-RBCs	NS
Transfusion of autologous FFP	0.001
Total numbers of FFP	0.017
Age	0.002
Sex	0.013
Weight	0.008
Height	0.014
Admission Hct	NS
Admission WBC count	NS
Blood loss	NS
Intraoperative autologous blood recovery	NS
Postoperative transfusion of shed blood	NS
Duration of surgery	NS
Length of hospital stay	NS

DISCUSSION

The present study demonstrates a greater risk for postoperative infection in patients exposed to allogeneic BCD-RBCs than in patients receiving only autologous BCD-RBCs or no perioperative transfusions. This result implies that buffy coat removal is not a sufficient processing method in cases where transfusion-induced immunosuppression is a concern.

The present study was prospective but not randomized (for ethical reasons) and was conducted in a homogeneous population of patients; much effort was made to guarantee uniform perioperative clinical management. The influence of potentially confounding variables on the outcome for transfused patients was shown to distort results for postoperative infection after allogeneic transfusion.[15] In contrast to the retrospective study of Vamvakas et al.[15] and the other clinical trials comparing postoperative infection after autologous or allogeneic transfusions,[11-14,16,17] this study excluded possible effects of nonstandard perioperative conditions on the occurrence of postoperative infection, as in this single-center study, the intraoperative anesthesia management, the use of Foley urinary catheters, the application of postoperative analgesia, and the use of intraoperative and postoperative autologous blood salvage were similar for patients with and without available autologous BCD-RBCs. In addition, the duration of surgery and blood loss proved to be nonsignificant for the development of postoperative infection. Moreover, autologous and allogeneic blood components were prepared in the same manner as BCD components. Thus, in our study, the main difference between the perioperative management of the transfusion groups was the presence or absence of allogeneic BCD-RBCs and autologous FFP.

However, the findings that patients with infections were also older, were predominately female, had low body weight and height, and received only small numbers of FFP demand some explanation. These characteristics describe patients belonging to the group that did not donate autologous blood, 81.7 percent of whom received allogeneic BCD-RBCs, but only 9.1 percent of whom received FFP. Therefore,

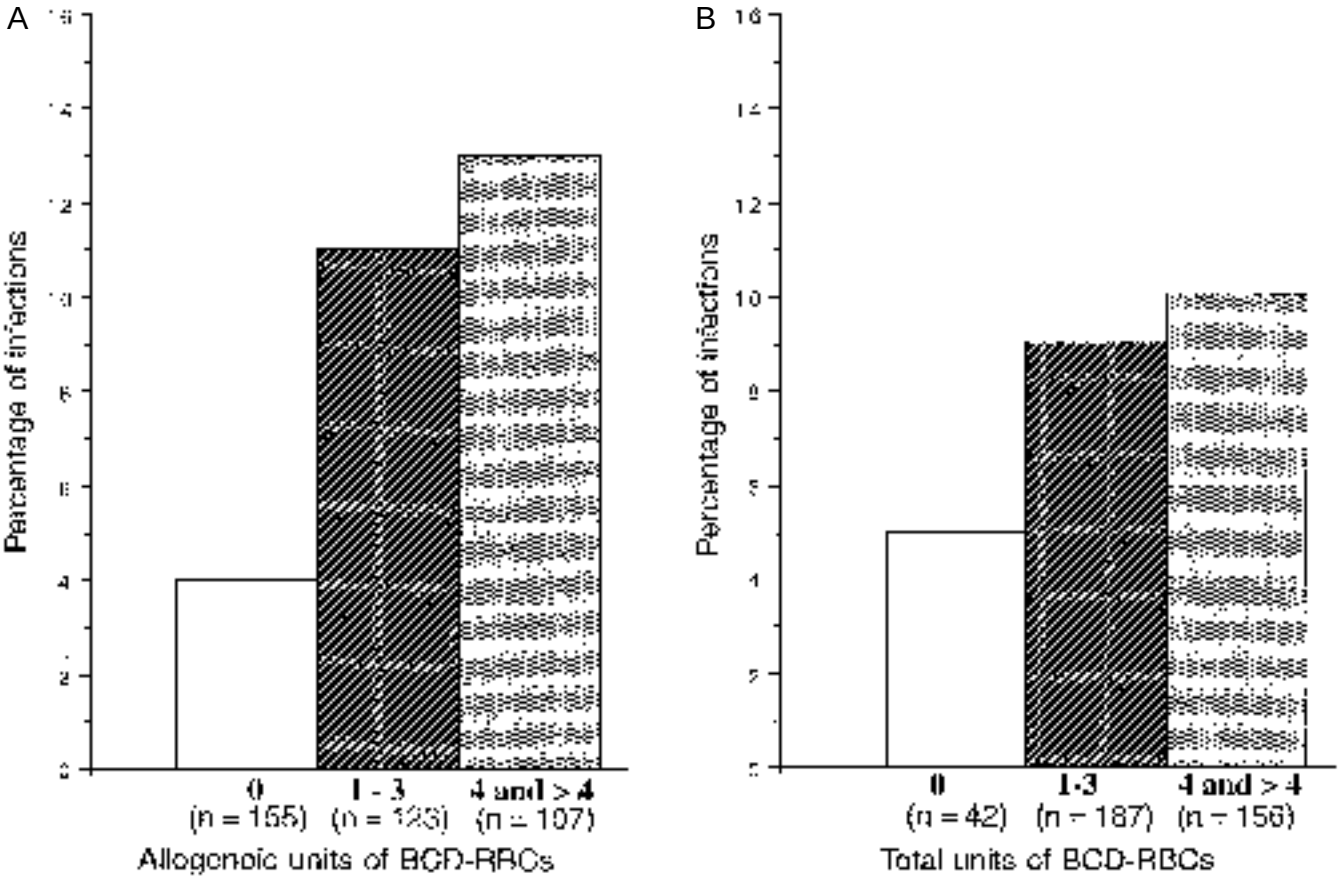

Fig. 3. A) In 385 orthopedic patients, a dose-response relationship between postoperative infection and number of transfused BCD-RBCs was found for allogeneic transfusion only (p = 0.017). B) In 385 orthopedic patients, no dose-response relationship between postoperative infection and the total number of transfused BCD-RBCs (autologous and allogeneic) was observed (p = 0.529).

these variables indicate the need for allogeneic transfusion rather than a contribution to an increased infection rate. This suggestion was also confirmed by results of multivariate analysis in a subgroup of patients undergoing primary endoprosthetic surgery.

TABLE 5. Analysis of potential variables predictive for allogeneic transfusion and development of postoperative infection in 27 of 309 patients undergoing primary hip and knee replacement surgery

	Univariate analysis		Multivariate analysis	
Categorical and continuous variables	Allogeneic transfusion	Postoperative infection	Allogeneic transfusion	Postoperative infection
Exposure to allogeneic BCD-RBCs		0.036		<0.001
Total numbers of BCD-RBCs	<0.001	NS	<0.001	
Total numbers of FFP	<0.001	0.011	<0.001	
Age	<0.001	0.001	NS	<0.001
Antibiotics	NS	<0.001		<0.001
Body mass index	0.002	NS	NS	
Sex	<0.001	0.011	NS*	
Intraoperative blood recovery	NS	NS		
Postoperative blood recovery	<0.001	NS	NS	
Admission Hct	NS*	NS	NS	
Anesthesia	NS	NS		
Operation (hip vs knee)	NS	NS		

* p = 0.064

Our findings of a threefold increase in postoperative infection rates due to allogeneic transfusion are in agreement with the findings of others. Triluzi et al.[11] reported a fivefold infection rate in orthopedic patients who were exposed to allogeneic transfusion when undergoing spinal surgery. The inclusion of patients with neuromuscular scoliosis, who are known to be at high risk for postoperative infection, and the use of autologous whole blood and allogeneic RBCs might explain the more pronounced difference between study groups. Murphy et al.[12] even found a 10-fold rate of postoperative infection after allogeneic transfusion than after autologous transfusion, patients, but only a few patients with diagnosed infection who had received allogeneic blood had positive bacterial cultures. One could argue that results were influenced by soft criteria for diagnosis of infection, but in patients undergoing prophylactic antibiotic therapy, cul-

ture data used as sole criteria may lead to false-negative diagnosis.

Nevertheless, controversial results were reported by Fernandez et al.[13] and Vamvakas et al.[14] Neither study was able to detect an association between allogeneic transfusion and the rate of postoperative infection. The definition of diagnosed infection was similar to that in our study, and both those studies and ours involved comparable numbers of orthopedic patients. However, those retrospective reviews included patients in several local hospitals. In contrast to our results, multivariate analysis yielded more surgical variables, such as duration of operation and blood loss, that were associated with postoperative infection. The insignificant influence of these variables in our study may be due to our prospective single-center approach and strictly standardized intraoperative anesthesiologic management, including active warming of patients with the intention to prevent hypothermia, which can be accompanied by adverse effects on coagulation, blood loss, and even resistance to infection.[18,19] Besides, we did not include posthospital infections in the present analysis, because differing posthospital conditions can uncontrollably influence the incidence of infection. We additionally investigated the relationship between allogeneic BCD-RBC transfusion and postoperative infection in a subgroup of patients undergoing primary hip or knee replacement. From a clinical point of view, surgical trauma, blood loss, time of surgery, and expected postoperative infection rate are homogeneous and comparable in these patients. We verify here that allogeneic transfusion is an independent variable associated with increased postoperative infection.

We found an 8.8-percent overall incidence of in-hospital infection (mainly, urinary tract infections), a rate that is slightly higher than that in other studies of orthopedic patients. The predominance of infections unrelated to wound site is also reported by others.[11-14] This might be the consequence of systemic immunosuppression following allogeneic transfusions, which leads to an increased susceptibility to nosocomial infections, whereas wound infections largely depend on surgical factors and hospital setting. As reported by these other investigators,[11-14] diagnosed infections were not clinically severe, and no deaths occurred, but allogeneic blood recipients received more antibiotic therapy and had a longer hospital stay. Although prolongation of hospital stay was moderate in our study, which included otherwise healthy patients, a much greater effect of infection on length of hospital stay has been reported in patients undergoing abdominal cancer surgery.[20, 21] The incidence of deep operative-site infections, which are deleterious in elective joint replacement surgery, is known to be below 1 percent at our institution (0.5% in the present study), while that in other reports on wound infection rates is 2.0, 7.1, 1.6, and 3.1 percent, respectively.[11-14] The fact that only two patients developed wound infection may be due to meticulous aseptic strategy (including preoperative management on the ward) and the use of laminar flow in primary endoprosthetic surgery.

All the previous studies comparing on infection rates after allogeneic and autologous transfusions used packed RBCs or whole-blood preparations that contained different amounts of WBCs per unit and plasma. Because either factor may influence the degree of immunosuppression, a comparison of patients receiving autologous whole blood with those receiving allogeneic RBCs seems difficult.[4,11-14,16,17] In our study, all transfused patients received BCD-RBCs, but the postoperative infection rate was associated only with allogeneic transfusions. These findings, as well as the results of four single-center studies on the effect of WBC reduction,[22-25] suggest that, in fact, exposure to allogeneic blood components, containing even moderate numbers of WBCs, causes observed immunosuppression. It is not yet clear, however, which WBC proteins are involved and whether transfused WBCs have to be viable to produce this effect. It is interesting that, in a recently published study comparing the outcome after allogeneic BCD or WBC-reduced transfusions, no difference was observed whether blood was filtered freshly or after storage.[25] Nevertheless, a large multicenter trial showed no differences between transfusion groups (BCD vs. WBC-reduced), but transfusion per se proved to be an independent variable predicting an increased postoperative infection rate.[26]

However, in the present single-center study with strictly standardized perioperative management, infection rates increased significantly with increasing numbers of allogeneic transfusions, but not with the total number (autologous and allogeneic) of transfused BCD-RBCs. Furthermore, total numbers of BCD-RBCs as well as FFP transfused were significantly higher in the autologous donor group, but the infection rate was significantly higher in the nondonor group. This indicates that, under standardized conditions, the exposure to allogeneic BCD-RBCs, rather than the need for or the effect of transfusion per se, might be the reason for increased postoperative infection. It interesting that we also found lower infection rates in patients receiving both autologous and allogeneic blood than in recipients of exclusively allogeneic BCD-RBCs. This supports the suggestion that autologous blood may offer some active protection against postoperative infection, as suggested by Heiss et al.,[16] and contradicts the hypothesis that RBC transfusions engage the reticuloendothelial system, which impairs the clearance of bacteria by phagocytic cells, and so leads to transfusion-associated postoperative infections.[26]

One of the potential limitations of our study is that it was not randomized, for ethical reasons. In addition, patients in the group that did not donate autologous blood were predominately female and older, which are clinical variables that in part proved to be associated with the need for allogeneic transfusion.

In conclusion, we found a significantly higher rate of postoperative infection in patients after allogeneic BCD-

RBC transfusion than in patients who received either no blood or only autologous blood. The rate of infection increased with the number of transfused allogeneic units, even when identically prepared blood components having moderate WBC counts were used. Although the precise mechanism(s) of immunosuppression after allogeneic blood transfusion are not yet clear, our results support the concept of an immunosuppressive potential of allogeneic blood transfusions and reveal buffy coat depletion to be an insufficient processing method for preventing transfusion-induced immunosuppression. We thus conclude that the universal WBC filtration of blood for transfusion must be considered to prevent any adverse effects of this important therapy.[20]

REFERENCES

1. Opelz G, Sengar DP, Mickey MR, Terasaki PI. Effect of blood transfusions on subsequent kidney transplants. Transplant Proc 1973;5:253-9.
2. Blumberg N, Triulzi DJ, Heal JM. Transfusion-induced immunomodulation and its clinical consequences. Transfus Med Rev 1990;4(4 Suppl 1):24-35.
3. Vamvakas EC. Transfusion-associated cancer recurrence and postoperative infection: meta-analysis of randomized, controlled clinical trials. Transfusion 1996;36:175-85.
4. Blajchman MA. Allogeneic blood transfusions, immunomodulation, and postoperative bacterial infection: Do we have the answer yet? (editorial) Transfusion 1997;37:121-5.
5. Meryman HT. Transfusion-induced alloimmunization and immunosuppression and the effects of leukocyte depletion. Transfus Med Rev 1989;3:180-93.
6. Nielsen HJ. Detrimental effects of perioperative blood transfusion. Br J Surg 1995;82:582-7.
7. Nielsen HJ, Reimert C, Pedersen AN, et al. Leucocyte-derived bioactive substances in fresh frozen plasma. Br J Anaesth 1997;78:548-52.
8. Marsh J, Donnan PT, Hamer-Hodges DW. Association between transfusion with plasma and the recurrence of colorectal carcinoma. Br J Surg 1990;77:623-6.
9. Busund R, Straume B, Revhaug A. Fatal course in severe meningococcemia: clinical predictors and effect of transfusion therapy. Crit Care Med 1993;21:1699-705.
10. Dzik WH. Effects on recipients of exposure to allogeneic donor leukocytes. J Clin Apheresis 1994;9:135-8.
11. Triulzi DJ, Vanek K, Ryan DH, Blumberg N. A clinical and immunologic study of blood transfusion and postoperative bacterial infection in spinal surgery. Transfusion 1992;6:517-24.
12. Murphy P, Heal JM, Blumberg N. Infection or suspected infection after hip replacement surgery with autologous or homologous blood transfusions. Transfusion 1991;31:212-7.
13. Fernandez MC, Gottlieb M, Menitove JE. Blood transfusion and postoperative infection in orthopedic patients. Transfusion 1992;32:318-22.
14. Vamvakas EC, Moore SB, Cabanela M. Blood transfusion and septic complications after hip replacement surgery. Transfusion 1995;2:150-6.
15. Vamvakas EC, Carven JH, Hibberd PL. Blood transfusion and infection after colorectal cancer surgery. Transfusion 1996;36:1000-8.
16. Heiss MM, Mempel W, Jauch KW, et al. Beneficial effect of autologous blood transfusion on infectious complications after colorectal cancer surgery. Lancet 1993;342:1328-33.
17. Busch OR, Hop WC, Hoynck MA, et al. Blood transfusion and prognosis in colorectal cancer. N Engl J Med 1993;328:1372-6.
18. Sheffield CW, Sessler DI, Hunt TK. Mild hypothermia during isoflurane anesthesia decreases resistance *to E. coli* dermal infection in guinea pigs. Acta Anaesthesiol Scand 1994;38:201-5.
19. Schmied H, Kurz A, Sessler DI, et al. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. Lancet 1996;347:289-92.
20. Blumberg N, Heal J. Blood transfusion immunomodulation. the silent epidemic (editorial). Arch Pathol Lab Med 1998;122:117-9.
21. Vamvakas EC, Carven JH. Allogeneic blood transfusion, hospital charges, and length of hospitalization: a study of 487 consecutive patients undergoing colorectal cancer resection. Arch Pathol Lab Med 1998;122:145-51.
22. Jensen LS, Andersen AJ, Christiansen PM, et al. Postoperative infection and natural killer cell function following blood transfusion in patients undergoing elective colorectal surgery. Br J Surg 1992;79:513-6.
23. Jensen LS, Kissmeyer-Nielsen P, Wolff B, Qvist N. Randomised comparison of leucocyte-depleted versus buffy coat-poor blood transfusion and complications after colorectal surgery. Lancet 1996;348:841-5.
24. Jensen LS, Hokland M, Nielsen HJ. A randomized controlled study of the effect of bedside leucocyte depletion on the immunosuppressive effect of whole blood transfusion in patients undergoing elective colorectal surgery. Br J Surg 1996;83:973-7.
25. Van de Watering LM, Hermans J, Houbiers JG, et al. Beneficial effects of leukocyte depletion of transfused blood on postoperative complications in patients undergoing cardiac surgery: a randomized clinical trial. Circulation 1998;97:562-8.
26. Houbiers JG, van der Velde CJ, van de Watering LM, et al. Transfusion of red cells is associated with increased incidence of bacterial infection after colorectal surgery: a prospective study. Transfusion 1997;37:126-34.