OBJECTIVES: To determine whether transfused colorectal surgery patients were at increased risk for postoperative infections in a tertiary care teaching hospital and whether transfusion alone was the only significant risk factor.

DESIGN: A retrospective study.

SETTING: A single tertiary care teaching hospital.

PATIENTS: All patients admitted to St. Boniface General Hospital, Winnipeg, for colorectal surgery during the period Apr. 1, 1995, through Mar. 31, 1996, were studied (N = 154).

RESULTS: The overall infection rate was 17%: nontransfused patients, 13%, and transfused patients, 28% (p < 0.038). Patients who received albumin perioperatively had a significantly higher infection rate (38%) than those who did not (13%) (p < 0.001). Stepwise logistic regression analysis identified transfusion and albumin administration as the only independent risk factors for postoperative infection.

CONCLUSION: Perioperative transfusion or albumin administration significantly increases the risk of postoperative infection in colorectal surgery patients.
Postoperative infection contributes significantly to prolonged hospital stay, which is necessitated by wound care, antibiotic and other treatments. In already debilitated patients, wound, intra-abdominal and respiratory infections can result in significant associated morbidity. Infections with highly pathogenic organisms, especially in these patients, can lead to septicemia and, occasionally, death. Postoperative infections, therefore, prolong patient recovery and lead to significant additional costs to the health care system.

The health factors associated with postoperative infection include advanced age, carcinoma, malnutrition and contaminated surgical fields such as occur in colorectal surgery. Recently, perioperative blood transfusion has been marked as an additional factor contributing to the risk of postoperative infection, prolonged hospital stay and higher hospital costs. It is believed that transfused allogeneic leukocytes have a detrimental effect on the recipient’s immune system, weakening the host response to infection. Other studies, both case-controlled and cohort, have shown that transfusion-risk studies may have not compensated for other confounding factors, including chronic illnesses, type of anesthesia and clinical intravenous catheterization, and hence question the causal relationship between transfusion and postoperative infection. A number of blood filters that prevent the transfusion of passenger donor leukocytes with the packed red blood cell units are currently available. The marketing information quotes significant reduction in postsurgical infection rates and increased health care savings (Pall Inc., East Hills, NY).

In an effort to determine whether these leukocyte filters would be beneficial for patients who must undergo colorectal surgery, at St. Boniface General Hospital in Winnipeg we carried out a preliminary retrospective study. We focused on 2 questions: are transfused patients at increased risk for postoperative infections and is transfusion alone the only significant risk factor? If this study should provide sufficient evidence for increased risk of postoperative infections in transfused patients, a randomized prospective leukocyte filtration study could be considered.

**Method**

All patients admitted to St Boniface General Hospital for colorectal surgery during the period Apr. 1, 1995, through Mar. 31, 1996, were identified using the computerized hospital information system (HIS). Colorectal surgery was defined using the clinical modification of the International Classification of Diseases, 9th revision (ICD-9-CM) codes of 45.71 to 45.8 (partial and total colectomy) inclusive and 48.41 to 48.69 (partial and total rectal resection) inclusive.

Postoperative infections were identified according to US Centers for Disease Control and Prevention criteria for nosocomial pneumonia or surgical site infections (SSIs), including superficial or deep incisional and organ or space infections. Blood transfusions (packed red blood cells) were recorded by the HIS as number of units infused. The Canadian Red Cross provided all red blood cell units, and these contain nonviable donor leukocytes (approximately 10^7/unit). No leukocyte-depleted blood was used for any patient requiring transfusion. The HIS was also used to identify patients who had clinically documented infections during their postsurgical hospital stay and provided all other medical information including age, diagnoses, surgical procedures, American Society of Anesthesiologists (ASA) rating of operative risk, administration of human serum albumin, total surgical procedure time, time in the recovery room, disease severity group, total length of hospital stay and on-admission probability of death.

There were 154 patients in the study group. A random 33% sample of all charts was examined manually to confirm agreement of the computer data with the chart information. Charts of patients who received more than 25 g of albumin were reviewed to determine the reason for albumin administration (e.g., total parenteral nutrition supplement, vascular instability). All statistics were calculated using SPSS for Windows version 7.5 (Statistical Package for the Social Sciences, Chicago, IL). Risk factors for the development of postoperative infections were analysed using univariate and multiple regression analyses. Cross-tabulation statistics were performed with Pearson’s test or the χ^2 test and outlier testing with Grubb’s test. A probability value of less than 0.05 was considered significant. Findings are reported as mean (and standard deviation). ASA coding is reported as a median.

**Results**

The overall infection rate was 17% (26 of 154, Table I). The infection rate in nontransfused patients was 13% and in transfused patients was 28%. Cross-tabular analysis showed a significant difference in infection rates between the 2 groups (p < 0.038). Pneumonia was present in 36% (4 of 11) of infections in transfused patients but in only 7% (1 of 15) infections in the nontransfused patient (p > 0.08). One patient in the nontransfused group had an organ/ space SSI. The remainder were incisional infections. Colorectal surgery patients who had postoperative infections stayed in hospital an average of 5 days longer than their noninfected counterparts (Table II), and transfused patients stayed in hospital 4 days longer than nontransfused patients. Nontransfused patients all had their surgery within 24 hours of admis-
There was no difference between the transfused, noninfected patients with respect to age (67 [20] years versus 66 [17] years), ASA code (3 [1] versus 3 [1]), probability of death (8.6% [20%] versus 4.0% [5%]), total procedure time (270 [70] minutes versus 280 [90] minutes), time spent in the recovery room (115 [60] minutes versus 90 [40] minutes) and disease severity index (2.2 [0.9] versus 2.0 [0.6]) (p > 0.05).

There was no difference in the total number of patients with neoplasia in any group or in the organ resected. Similarly, there was no difference in the mean total number of packed cell units received between transfused patients with or without postoperative infection (5 [3] units versus 4 [2] units) (p > 0.05).

Cross-tabular testing showed a significantly higher infection rate in the patients who received human serum albumin perioperatively (38% versus 13%) (p < 0.05) (Table III). Of the 14 patients receiving 50 mL or more of albumin, 2 received it as a supplement to intravenous nutrition. All other patients were given albumin to expand blood volume. Higher infection rates occurred in patients who received albumin, with or without transfusion (Table IV).

Stepwise logistic regression analysis identified transfusion and albumin administration as independent risk factors for postoperative infection. Age, procedure time, recovery room time, disease severity group, probability of death and ASA code were not identified as independent risk factors.

**DISCUSSION**

Many factors increase the occurrence of surgical complications, including postoperative wound, intra-abdominal and respiratory infections. Older patients are at higher risk for infections resulting from poor circulation, prolonged inactivity, less adequate nutritional status, and other pre-existing medical conditions such as diabetes. This is particularly the case in colorectal surgery where there is inevitably contamination of the surgical field from pathogenic bowel organisms. Intraoperative technical difficulties often extend the length of the procedure, thus increasing anesthesia time, which is a factor in the development of respiratory complications. The creation of an ostomy or placement of exteriorized surgical drains present some higher risks for infection of any nearby surgical wounds. In the present study of patients who underwent colorectal surgery, the risk factors analysed for the development of postoperative infections included age, ASA code, type of surgical procedure, procedure length and time spent in the recovery room, disease severity and assessed risk of death. Statistical analysis did not demonstrate that any of these or any combination of them was a significant risk factor for the development of postoperative infection.

The results from this retrospective study show that both the administra-
tion of human serum albumin and blood transfusions result in an increased rate of postoperative infection. This is the first report suggesting that albumin may play a role in these complications. In 1993, the Canadian Red Cross recommended that the use of albumin be restricted to blood volume expansion and maintenance of colloid osmotic pressure. In St. Boniface General Hospital, human serum albumin was occasionally also administered in combination with total parenteral nutrition to some patients with severe hypoalbuminemia resulting from malnutrition. Human serum albumin is a plasma fractionation product and is specifically treated to prevent the transmission of live viruses from donors. The transmission of hepatitis or human immunodeficiency virus from human serum albumin has not been detected. There are no reports of human serum albumin being associated with changes in immune function except in situations of specific allergic reactions. H owever, heat-stable proteins and other small antigenic molecules (including prions, the causative agents in Creutzfeldt-Jacob disease, and peptide fragments) could be transmitted.

Red cells administered to the patients in this study were provided exclusively by the Canadian Red Cross in Winnipeg. These units were prepared by centrifugation of whole blood followed by removal of the supernatant plasma. None of the patients studied received leukocyte-depleted red blood cells. Leukocyte filters were not used in red blood cell administration in our hospital. As a result, the transfused patient would have received between $10^8$ and $10^{10}$ allogeneic leukocytes per unit transfused. High-efficiency leukocyte filters can reduce the number of leukocytes infused to below $10^7$/unit. The leukocytes contained in the red blood cell units were (or should have been) the major component affecting the recipient's immune system. This is a reasonable explanation since the only major noncompatible antigens found in erythrocyte-matched blood products would be the major histocompatibility complexes found especially on mononuclear cells. The immunomodulating effects of blood transfusions have been documented and are often used to initially suppress rejection of allogeneic solid organ grafts.

In colorectal surgery, the postoperative infection rates found in both transfused (24% to 35%) and nontransfused (15% to 20%) patients in the published studies correspond well with the infection rates found in this study. However, the infection rates in nontransfused patients calculated by Jensen and associates and quoted in some leukocyte-filter marketing material (Pall Inc.), demonstrated that filtration of the blood through leukocyte-depleting filters reduced the rate of infection in transfused patients to that of nontransfused patients. The studies by Vignali and colleagues showed that the risk of postoperative infection was increased by receipt of only a single unit of allogeneic blood. Vamvakas and colleagues showed that by adjusting the statistics for confounding variables, there was no increase in infection rates (for all types of infections combined) in transfused patients after colorectal surgery. However, they did find that transfusion was a risk factor for the development of wound infection, increased hospital stay and hospital costs and that of all the variables included in their analysis, transfusion was the most significant predictor of infection. In a study of spinal surgery patients, transfusion resulted in increased postoperative infection rates (21% versus 4%). Studies of other surgical patients (trauma, burns and cardiovascular) found similar increases, suggesting that this transfusion effect is not specific to colorectal surgery patients. None of these studies investigated the use of albumin as it related to infection rates in their patient groups.
fluid collections or abscesses or repair of leaking anastomoses. Treating respiratory infections would mandate the use of antibiotics and possibly respiratory physiotherapy. Any of these infections can lead to clinically significant septicemia, with higher morbidity and mortality especially in debilitated cancer patients. If the leukocyte filters could lower the infection rate in the transfused population to the level of non-transfused patients, the annual cost saving in our hospital would be approximately Can$30,000 (based on a per diem cost of Can$1000, and antibiotic treatment cost of Can$500 per patient). The cost of the leukocyte filter is approximately Can$25 per unit transfused. Since it would not be known in advance which patients requiring transfusion might be at risk for infection, all colorectal surgery patients receiving blood transfusion would require filtration of each unit administered. The total annual cost for the filters would be Can$4500. From this cursory financial model, it appears that use of the filters could be cost-effective. Cost savings would be much larger if the complications associated with these infections (such as intensive care stay, reoperation and prolonged rehabilitation time) were included in our cost analysis.

Conclusions

Transfusion of packed red blood cells and the administration of human serum albumin were found to be independent predictors of postoperative infection in patients who had colorectal surgery. Filtration of red blood cell units with leukocyte-specific filters may reduce or prevent this transfusion effect. It is not known how the administration of albumin relates to the development of these infections. A randomized prospective trial should be undertaken using the blood filters to determine their effectiveness in reducing the postoperative infection rates in these patients.

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References