^b*Department of Cardiovascular
Surgery
Diyarbakir Military Hospital
Ankara, Turkey*

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Reply to the Editor:

Our thanks to Durukan and colleagues for their positive comments about our meta-analysis on bleeding after cardiopulmonary bypass (CPB).¹ We agree that it is important to consider the role of albumin in preserving coagulation system function among patients undergoing CPB. In particular, CPB places these patients at risk for acquired transient platelet dysfunction attended by diffuse nonsurgical postoperative bleeding.

A protective effect against hemorrhage is suggested by observations in cardiac surgical patients with albumin deficiency. In a prospective study of 5168 consecutive patients undergoing coronary artery bypass grafting, preoperative hypoalbuminemia (serum albumin <25 g · L⁻¹) was an independent risk factor of reexploration for bleeding, with an odds ratio (OR) of 1.4 (95% confidence interval [CI], 1.0-2.1; *P* = .04) after adjustment for 17 other variables.² Preoperative hypoalbuminemia was also an independent risk factor for mortality in that study (OR, 2.0; 95% CI, 1.3-3.0; *P* = .002).

In a meta-analysis of 21 controlled clinical trials with 1346 total patients, extracorporeal circuit priming with albumin maintained on-bypass platelet

counts at a significantly higher level than that seen with crystalloid alone.³ Furthermore, albumin priming was significantly associated with postoperative reductions in thrombocytopenia, blood loss, and reoperations for bleeding relative to crystalloid-alone priming in a retrospective study of 377 patients undergoing CPB. In a randomized trial, addition of albumin to a priming solution containing artificial colloid (dextran 70) also resulted in significantly higher platelet counts as long as 48 h after CPB, with significantly less blood loss from the mediastinal drains.

Albumin is capable of modulating platelet activity through biologically specific mechanisms. Platelet aggregability can be modulated both by complexes of fatty acids bound to albumin and by nitric oxide-albumin adduct. Albumin also binds with high affinity to platelet-activating factor, thereby reducing its activity, and this binding occurs exclusively in domain II of the albumin molecule extending from polypeptide chain amino acid position 240 to 386.

As Lange and coauthors⁴ acknowledge, it is accepted that albumin does not interfere with coagulation, other than possibly by hemodilution. Those authors nevertheless cite two pieces of contrary evidence, neither concerned with cardiac surgery. First, after in vitro dilution of blood samples from patients scheduled for elective general surgery, albumin impaired thromboelastographically assessed coagulation to a greater extent than normal saline solution or hydroxyethyl starch 450/0.7. However, in 3 randomized trials of colloid use in vivo among patients undergoing CPB, 1 involving pump priming and the other 2 involving postoperative volume expansion, albumin significantly improved clotting as measured by thromboelastography compared with hydroxyethyl starch 120/0.7, 130/0.4, 200/0.5, or 450/0.7.¹

Second, in a subgroup analysis of data from the SAFE (Saline versus

Albumin Fluid Evaluation) study, activated partial thromboplastin time on day 2 increased by 7% in patients receiving albumin while decreasing 2% in recipients of normal saline solution.⁵ The SAFE study investigators conceded that this difference was “small and thus of questionable clinical importance.”⁵ Furthermore, the difference can be readily explained by greater hemodilution in the albumin group. Thus the ratio of saline solution to albumin infused during the first 2 days of the SAFE study was only 1.4, whereas in a randomized trial of patients undergoing CPB, the ratio needed for equivalent plasma volume expansion was 5.8.

From a physiologic perspective, it appears highly unlikely that albumin, the most abundant protein in plasma, would specifically interfere with coagulation. The components of the coagulation system have evolved to function under constant exposure to serum albumin concentrations of approximately 35 to 50 g · L⁻¹ during normal conditions.

Albumin remains the criterion standard for fluid management in cardiac surgery. A chief advantage, either for extracorporeal circuit priming or perioperative volume expansion, is maintenance of a competent coagulation system.

*Roberta J. Navickis, PhD^a
Gary R. Haynes, MD, PhD^b
Mahlon M. Wilkes, PhD^a*

^a*Hygeia Associates
Grass Valley, Calif*

^b*Department of Anesthesiology and
Critical Care
Saint Louis University School of
Medicine
St Louis, Mo*

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AORTIC ARCH INTERRUPTION WITHOUT DUCTUS ARTERIOSUS AND NO VENTRICULAR SEPTAL DEFECT

To the Editor:

We read the interesting case report by Cazavet and associates¹ on “an infant with a previously unrecorded type of aortic arch interruption.” However, similar types of aortic arch interruption without ductus arteriosus and without ventricular septal defect, although rare, have been previously described since 1964.²⁻⁶ The common features of these unusual patients were the longevity up to adolescence with no severe symptoms and the presence of extensive collateral circulation supplying the descending aorta.²⁻⁶ Surgical treatment was also reported in relation to the various anatomic patterns.²⁻⁶ In the field of pediatric cardiology, sometimes some old scientific papers can represent important sources of knowledge.

The interesting new aspect described by Cazavet and associates¹ is the association with del 22q11 and the relative embryogenetic implications that expand the spectrum of cardiovascular defects of this syndrome.

Carolina Putotto, MD
Marta Unolt, MD
Dario Marino, MD
Department of Pediatrics
“La Sapienza” University
Rome, Italy

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RECOGNITION AND MANAGEMENT OF HEPARIN-INDUCED THROMBOCYTOPENIA IN PATIENTS AFTER CARDIAC SURGERY

To the Editor:

In a recent publication, Demma, Paciullo, and Levy¹ evaluated the recognition and treatment of heparin-induced thrombocytopenia (HIT) in patients after cardiothoracic surgery using the direct thrombin inhibitor (DTI) argatroban. We agree that the detection and management of HIT in patients who have had cardiac surgery is of clinical importance, and we have

used a similar method of HIT identification and treatment with the DTI bivalirudin.

Our familiarity with the use of bivalirudin was heightened after our participation in the CHOOSE-ON trial published in 2007, which evaluated the use of this DTI during cardiopulmonary bypass in patients having cardiac surgery.² Since then, we have standardized our method of identifying HIT patients postoperatively and treating them with bivalirudin. To detect HIT, we use a method similar to that of Demma, Paciullo, and Levy¹ in which patients who score in the moderate range on the 4-Ts schema³ are subjected to a platelet factor 4/heparin immunoassay. Occasionally, we will also confirm the diagnosis with a serotonin release assay. To then distinguish HIT from hemodilution or other causes of thrombocytopenia, we also categorize the patterns of platelet counts as outlined by Poupard and colleagues.⁴

Our standardization of detection methods did not alter the number of patients who received a diagnosis of HIT (14.5% compared with 15.1% before 2007). However, we did see an increased rate in the use of bivalirudin to treat thrombocytopenia (23.1% compared with 17.5%) (Table 1). This suggests that our standardization procedures may have resulted in earlier identification and medical management of HIT.

TABLE 1. Characteristics of patients treated with bivalirudin after cardiac surgery

	Before (2004-2006)	After (2007-2010)
Thrombocytopenia	15.1% 463/3065	14.5% 476/3288
DTI use in patients with thrombocytopenia	17.5% 81/463	23.1% 110/476
HITS (per decreased platelets)	4.3% 20/463	5.5% 26/476
HITS (per total adult patients)	0.7% 20/3065	0.8% 26/3288
HITS mortality	60.0% 12/20	23.0% 6/26

Thrombocytopenia is defined as a 50% decrease in platelets from preoperative baseline by 24 hours after cardiopulmonary bypass. Mortality is defined as death within index admission. DTI, Direct thrombin inhibitor; HITS, heparin-induced thrombocytopenia and thrombosis syndrome.