able amounts of radiolabeled dextran in the plasma protein fraction [15]. Consequently, we do not think this mechanism plays a substantial role in producing the lower than expected dextran concentrations seen in the present study.

The dextran we used had a mean molecular mass of 70,000 Da. Thus, some quantity of lower-molecular-mass dextran could have leaked out of the vascular space and distributed into the interstitial fluid, accounting for the increase in distribution volume. The decrease in dextran concentration could also be the product of hemodilution caused by the large quantities of fluids administered after the HSD. Hematocrit values agreed closely with the volume of fluid infused ($r = 0.60, n = 13, P < 0.05$) but not with the dextran concentrations ($r = 0.22, n = 13, P = 0.46$). Factors other than hemodilution from the administration of additional fluids must further decrease dextran. Thus, the lower concentrations of plasma dextran observed in trauma patients could be the product of a variety of factors and warrant further study to possibly improve the efficacy of HSD.

Importantly, the dextran concentrations observed in these trauma patients are much lower than those previously observed to adversely affect blood typing or coagulation [19, 20]. In vitro, a 1:5 ratio of HSD to erythrocytes did not affect blood typing but did slightly increase prothrombin time and decrease platelet aggregation. This ratio is about twice the concentration expected if an adult lost half of his or her blood volume and received 250 mL of HSD. Generally, prolonged bleeding or clotting times or adverse effects on blood typing have been associated with dextran concentrations of greater than 150,000 Da or after administration of large doses (>1.5 g/kg) of dextrans of >60,000 Da [19, 20]. No adverse effects on blood typing or coagulation were observed in the large clinical trials [3, 10]. Consequently, therapeutic use of HSD should carry minimal risk.

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Direct Measurement of LDL Cholesterol

To the Editor:

Recently, a new immunosorption method for directly measuring low-density lipoprotein cholesterol (LDL-C) in serum was introduced. Several abstracts addressing the analytical parameters of this methodology were presented at the AACC annual meeting in Anaheim [1-4], and scientific articles have appeared in this journal [5] and others [6, 7] evaluating this method. There is dispute over the analytical accuracy of the method in comparison with the beta-quantification (ultracentrifugation) Reference Method [2, 4], especially for measuring very low plasma concentrations of LDL-C. The consensus of the articles is that the immunosorption method appears more accurate than the Friedewald et al. calculation [8] for determining LDL-C from fresh unfrozen serum independently of triglyceride concentrations. The articles also agree that the Friedewald et al. calculation is accurate at lower triglyceride concentrations (<4 g/L). Because the first report of the National Cholesterol Education Program (NCEP) suggested that decisions to treat high blood cholesterol concentrations should be predicated on the LDL-C concentration [9], these articles suggest that the direct LDL-C measurement is clinically useful [5-7].

Although Jialal et al. [6] observed a significant difference between fasting and nonfasting samples with the direct LDL test, the difference was small and should rarely affect clinical decision-making. Thus, this test offers flexibility for scheduling patients, since fasting is not required. Even though this assay methodology is apparently accurate for measuring LDL-C from patients having a wide range of triglyceride concentrations [5, 6], widespread use for screening
and evaluation of coronary heart disease risk may result in failure to identify a number of patients at risk due to dyslipidemia. A more common dyslipidemia than an increased LDL-C concentration among patients with coronary heart disease is the "atherogenic lipoprotein phenotype" [10, 11]. This presents as a constellation of moderately increased triglyceride (>1.4 g/L), decreased high-density lipoprotein cholesterol (HDL-C), (<0.4 g/L), and normal LDL-C concentrations, with smaller than average sized LDL particles (LDL subclass pattern B) [11]. An estimated 15–20% of the US population has this genetically influenced phenotype [10, 11]. Measurement of serum LDL-C by the new immunoseparation method will not identify subjects with the atherogenic lipoprotein phenotype. In fact, a recent review suggests that if direct LDL-C methods are "widely used they will perpetuate the inappropriate emphasis on LDL cholesterol alone" [10].

Besides LDL, intermediate-density lipoproteins (IDL) are atherogenic. The measurement of LDL-C by both beta-quantification and the Friedewald formula, when the triglyceride concentration is <4 g/L, includes the concentration of cholesterol in IDL, whereas the direct measurement of LDL-C by immunoseparation does not measure the cholesterol in IDL [7]. This may explain why in one study, several samples assayed by the immunoseparation method, many of which were hypertriglyceremic (i.e., IDL might have been increased), showed a relatively large absolute bias from the beta-quantification method [5].

The NCEP guidelines are based on interventional trials, which in general have used the Friedewald-estimated LDL-C and, in cases of high concentrations of triglycerides, beta-quantification-measured LDL-C. Abandoning this method seems ill advised. Although lowering LDL-C still remains the primary goal of intervention, both the NIH consensus conference on triglycerides [12] and the summary of the second report of the NCEP [13] recommend including HDL-C and triglycerides in risk assessment. Furthermore, the consensus conference recommends treating triglycerides when levels exceed 5 g/L [12].

In our opinion, the best method currently for evaluating risk of coronary heart disease and tracking lipid-lowering interventions is the fasting lipid profile (total cholesterol, HDL-C, triglycerides, and LDL-C). The scope of usage for the direct LDL-C measurement is fairly limited. Owing to the much greater cost of the immunoseparation method for measuring LDL-C, calculated LDL-C seems preferable for patients with triglycerides <4 g/L and the majority of patients with the atherogenic lipoprotein phenotype fasting triglycerides between 1.5 and 2.5 g/L. The direct immunoseparation method for measuring LDL-C could be useful for monitoring those relatively few patients whose fasting triglyceride concentrations exceed 4 g/L, when ultracentrifugation is not available. As suggested by Jialal et al. [6], it may also have clinical utility in subjects with the rare type III hyperlipidemia (dysbetahyperlipoproteinemia). Further insight into these issues can be obtained from a recent editorial in the Archives of Pathology and Laboratory Medicine [4], which outlined and corroborated many of the same issues and concerns expressed here.

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References

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Troponin T and Troponin I After Coronary Artery Bypass Grafting: Discordant Results in Patients with Renal Failure

To the Editor:

Diagnosis of perioperative myocardial infarction (MI) in cardiac surgery remains an important task. Both clinical symptoms and electrocardiogram findings have inherent limitations. Release of enzymes such as creatinine kinase (CK) and CK-MB isoenzyme from noncardiac tissues during the surgical procedure makes it difficult or impossible to distinguish their increases caused by myocardial injury from those caused by skeletal muscle injury. The measurement of cardiac-specific marker proteins such as the troponins are claimed to eliminate the many falsely positive results produced by CK-MB [1]. However, even in patients without perioperative MI, both troponin T and troponin I are increased after cardiac surgery from their preoper-