Reply to the Editor:

My colleagues and I thank Drs. Sakakibara and Mitsui for their interest in our work and for raising the important question of the effluent return to the systemic circulation.

Undoubtedly, the venous effluent of limbs reperfused after several hours of complete ischemia contains greater amounts of myoglobin, free hemoglobin, creatine kinase, and potassium than do control limbs. After complete ischemia, this has been shown in experimental¹ and clinical² studies. To a lesser degree, this increase was also measurable after revascularization for incomplete ischemia.³

These components in the venous effluent are a consequence of the severe local damage of skeletal muscle (rhabdomyolysis, edema) and are the cause for systemic complications (hyperkalemia, myoglobinemia, acute renal failure, acidosis, multiorgan failure, and death) following revascularization after prolonged periods of limb ischemia.

Our limb reperfusion strategy has been developed to decrease the skeletal muscle reperfusion injury after revascularizations for prolonged ischemia. Less local damage will result in reduced concentrations of potassium, creatine kinase, and hydrogen ions in the venous effluent, which could be demonstrated in an experimental study.¹ Nevertheless, the venous effluent, even after controlled limb reperfusion, still contains significant amounts of end products of the rhabdomyolysis, which can only be prevented from entering the systemic circulation by discarding the venous effluent. Simply discarding the venous effluent is not possible because of the large amount of blood that would be lost. The same is true for any filtering process. The only possibility is to separately cannulate the femoral arteries and veins and use an extracorporeal circulation including oxygenator and roller pumps. This approach was recently described by Vogt and coworkers² from the Zürich group in a patient with complete ischemia for 24 hours.

The concentrations of myoglobin, potassium, and creatine kinase in the venous effluent are related to the severity of ischemia (complete/incomplete) (1/3) and the duration of ischemia (2/4). The more severe the ischemic insult, the more pronounced is the reperfusion damage, resulting in higher concentrations in the venous effluent. In our three-center study,⁴ we were able to reduce the concentrations of myoglobin, potassium, and creatine kinase to a level that did not produce systemic hyperkalemia or renal failure. However, Vogt and coworkers² have used a complete extracorporeal circuit (including an oxygenator) for a patient with complete ischemia for 24 hours and achieved excellent results with this approach. In patients with complete ischemia exceeding 24 to 36 hours, it might very well be necessary to discard the venous effluent and use an extracorporeal circuit to prevent severe systemic side effects. In our study with a mean ischemic time of 26 hours (range 6 to 39 hours), we did see systemic increases in potassium, creatine kinase, creatinine, and blood urea nitrogen; however, this did not produce remote organ failure. Even though we did not measure myoglobin concentrations in our patients, the fact that none had severe renal failure shows that there was no major renal tubular dysfunction.

Ideally, future refinements in the technique of controlled limb reperfusion will elucidate criteria, identify which patients will need controlled limb reperfusion without complete extracorporeal circulation, and define those patients who need controlled reperfusion with venous effluent discardment.

Friedhelm Beyersdorf, MD
Department of Cardiovascular Surgery
Albert-Ludwigs-Universität Freiburg
79106 Freiburg, Germany

REFERENCES

1. Mitrev Z, Beyersdorf F, Hallmann R, Poloczek Y, Ihnken K, Herold H, et al. Reperfusion injury in skeletal muscle: controlled limb reperfusion reduces local and systemic complications after prolonged ischemia. *Cardiovasc Surg* 1994;2:737-48.
2. Vogt PR, von Segesser LK, Pagotto E, Lijovic T, Turina MI. Simplified controlled limb reperfusion and simultaneous revascularization for acute aortic occlusion. *J Vasc Surg* 1996; 23:730-3.
3. Ihnken K, Beyersdorf F, Mitrev Z, Unkelbach U, Poloczek Y, Hallmann R, et al. Controlled reperfusion reduces reperfusion injury in skeletal muscle after incomplete limb ischemia. *Vasc Surg* 1994;28:241-60.
4. Beyersdorf F, Mitrev Z, Ihnken K, Schmiedt W, Sarai K, Eckel L, et al. Controlled limb reperfusion in patients having cardiac operations. *J Thorac Cardiovasc Surg* 1996;111:873-81.

12/8/77666

Failure of devices used for the closure of atrial septal defects

To the Editor:

I read with interest the report of Agarwal, Ghosh, and Mittal¹ on the surgical management of unsuccessful atrial septal defect (ASD) closures with the AngelWings device (Microventa Corp., White-Bear Lake, Minn.). These closures were performed by me as a part of the International ASD Closure Trial, which is being organized by the University of Minnesota to evaluate the feasibility, safety, and efficacy of a new percutaneous device² developed at the University of Minnesota. Our preliminary clinical experience in the first 100 patients (including the six reported by Agarwal, Ghosh, and Mittal¹) has been submitted for publication. The overall procedural success rate is 90%. We have learned a large number of lessons in the clinical use of this device from the more than 100 patients who have undergone this procedure.

The reason for emergency surgery for retrieval of errant devices has been the difficulty in retrieving the device, which is made of a nitinol alloy framework with a high tensile strength. Although we have demonstrated our ability to retrieve the device with snares in animal models,² the stiff wire can potentially perforate cardiac chambers and systemic veins. The overriding concern in the clinical trials has been that of patient safety and hence the adoption of a policy of surgical removal of unsuccessfully deployed devices and closure of defects. We have concurrently developed a system for retrieving these devices safely. Once this is made available to participating centers,

the procedural success rate will be much higher than at present and the need for emergency surgery minimized.

In these initial cases, we¹ used device sizes twice the balloon-sized diameter.² With experience, we have determined that we can successfully use ratios between 1.2 and 1.5, and, so long as the conjoint suture ring diameter² is as large as the anatomic diameter of the ASD, residual shunts are uncommon. The transient complete heart block (which did not require temporary pacing) was probably related to the large-sized device used.

Percutaneous closure of ASDs in human beings, who have thin compliant atrial septa and great variability of the size and position of the defects, is more difficult than the closure of experimentally created circular defects in the thick muscular atrial septa of dogs.² This device is self-centering and hence the anatomic criteria for selection of suitable candidates for this device is being actively investigated.

Surgical closure is the "gold standard" for the closure of ASDs. All three patients who needed emergency surgery in the series reported by Agarwal, Ghosh, and Mittal¹ were adults. In a surgical series of 166 adult patients with ASDs, Horvath and associates³ reported an early mortality rate of only 1.2% but a perioperative complication rate of 13%. The complications included arrhythmias necessitating cardioversion, reoperation for bleeding, air embolism, tamponade, congestive heart failure, cerebrovascular accident, transient ischemic attack, complete heart block, and respiratory failure. Obviously these two reports cannot be directly compared. In the next phase of the U.S. arm of the trials we will be formally comparing device closure and surgical closure in patients with identical entry criteria.

We hope that with greater experience in the use of this device, careful long-term follow-up, and comparison with surgical closure in a structured clinical trial, we will be able to determine the role of this new investigational device for the percutaneous closure of ASDs.

Gladwin S. Das, MD
Cardiovascular Division
University of Minnesota Hospital and Clinic
Minneapolis, MN 55455

REFERENCES

1. Agarwal SK, Ghosh PK, Mittal PK. Failure of devices used for closure of atrial septal defects: mechanisms and management. *J Thorac Cardiovascular Surg* 1996;112:21-6.
2. Das GS, Voss G, Jarvis G, Wyche K, Gunther R, Wilson RF. Experimental atrial septal defect closure with a new transcatheter, self-centering device. *Circulation* 1993;88(Suppl):1754-64.
3. Horvath KA, Burke RP, Collins JJ, Cohn LH. Surgical treatment of adult atrial septal defect: early and Long term results. *J Am Coll Cardiol* 1992;20:1156-9.

12/8/77709

Reply to the Editor:

The response of Dr. Das has aptly focused on the current deficiencies of atrial septal defect (ASD) closure devices and the limitations of extrapolating data from animal trials to therapeutic use in human beings. It was in

this perspective that we proposed the currently relevant indications for the use of ASD closure devices. We shall not play Nostradamus. When Dr. Das's newer trial with a lower device/defect ratio and new retrieval system becomes reproducibly effective, it may change the therapeutic approach to closure of ASDs.

Probal K. Ghosh, MCh, FRCSE
Surendra K. Agarwal, MCh
Pramod K. Mittal, MCh

Department of Cardiovascular and Thoracic Surgery
Sanjay Gandhi PG Institute of Medical Science
Lucknow 226 014, India
12/8/78554

Purulent pericarditis

To the Editor:

We are very interested in the article by Mann-Segal and associates,¹ concerning successful treatment of purulent pericarditis by irrigation of fibrinolytics, and we fully support this technique. We² previously reported the use of intrapericardial urokinase to dissolve pericardial fibrin layers in three patients, and the drug was well tolerated in these patients. Mann-Segal did not mention laboratory tests in his report; in our patients no changes occurred either in hemodynamic or in coagulation parameters during the period of intrapericardial fibrinolytic therapy. Our safety measures included echocardiography during instillation to detect iatrogenic right heart compression and warming of the irrigation fluid to prevent arrhythmias.

We used urokinase for the lysis of pericardial fibrin deposits because urokinase has equal fibrinolytic potency but less antigenic potency than streptokinase.³ The efficacy of urokinase in dissolving extravascular fibrin has been demonstrated especially in the pleural cavity by intrapleural administration.^{4,5}

Fibrinolytic pericardial irrigation with urokinase as well as streptokinase seems to be a promising treatment of exudative fibrinous pericarditis, which can prevent constrictive pericarditis without surgical intervention. The ideal dose and treatment regimen, however, remain to be defined.

W.-B. Winkler, MD
R. Karnik, MD
J. Slany, MD

Department of Internal Medicine II
Krankenanstalt Rudolfstiftung
A-1030 Wien, Austria

REFERENCES

1. Mann-Segal DDM, Shanahan EA, Jones B, Ramasamy D. Purulent pericarditis: rediscovery of an old remedy. *J Thorac Cardiovasc Surg* 1996;111:487-8.
2. Winkler WB, Karnik R, Slany J. Treatment of exudative fibrinous pericarditis with intrapericardial urokinase. *Lancet* 1994;344:1541-42.
3. Collen D, Verstraete M. Pharmacology of thrombolytic agents. In: Schlant RC, Alexander RW, O'Rourke RA, Roberts R, Sonnenblick EH, editors: *Hurst's the heart*. New York: McGraw-Hill, 1994:1327-37.
4. Moulton JS, Moore PT, Mencini RA. Treatment of loculated