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Reply to the Editor:

My colleagues and I thank Lange and colleagues for pointing out that we omitted mentioning the importance of volatile anesthetics and ischemic preconditioning (IPC) in a number of animal models and possibly human beings. For example, Kersten and coworkers¹ showed that halothane preconditioning in barbiturate-anesthetized dogs led to a profound infarct size reduction ($25.3\% \pm 2.9\%$ to $11.8\% \pm 2.7\%$) and that this reduction

was as effective as IPC ($9.6\% \pm 2.0\%$). We were remiss in not discussing these results and their importance to IPC. Lange and colleagues also stated, "Anesthetic preconditioning significantly reduces arrhythmias after ischemic periods." The antiarrhythmic effect of volatile anesthetics is more problematic. Recently Owczuk and associates² discussed how desflurane can prolong the QTc interval and may result in lethal cardiac arrhythmias. Huneke and coworkers³ also reported that halothane, and to a lesser extent isoflurane and sevoflurane, may lead to ventricular arrhythmias by shortening the refractory period. In addition, volatile anesthetics are known to inhibit a number of voltage-gated potassium ion channels, which could further increase the risk of ventricular tachycardia in predisposed patients.³ It is unfortunate that most animal studies investigating volatile anesthetics and IPC rarely report the incidence and duration of arrhythmias during ischemia-reperfusion. On the other hand, we reported that pretreating the heart with an intravenous solution of the adenosine A1 receptor agonist 2-chloro-N6-cyclopentyladenosine and sodium ion fast-channel modulator lidocaine (AIL) administered 5 minutes before and during 30 minutes of acute regional ischemia in the rat in vivo resulted in no deaths, virtually no severe ventricular arrhythmias and an infarct size equivalent to that seen with IPC.⁴ Finally, Lange and colleagues believe it is unlikely that the administration of a selective A1 agonist plus a volatile anesthetic could further enhance cardioprotection. However, we believe the combination may reduce the amount of each agent needed to exert cardioprotection; that is, the A1 receptor agonist may reduce the effective therapeutic threshold of the volatile anesthetic agent. This concept was recently reported by Chiari and colleagues,⁵ in whose study postconditioning during early reperfusion reduced the concentration of isoflurane necessary to exert cardioprotection. Because the underlying mechanisms of volatile anesthetics and the AIL combination are not fully understood, the synergistic effects of volatile anesthetics and A1 analogs (or AIL) remain to be determined. Moreover, modulating cardiac voltage-gated sodium ion fast channels with local anesthetics has received surprisingly little attention in IPC strategies, despite the resetting of the resting membrane potential toward a

more depolarized state during ischemic injury.³ To quote nineteenth century essayist and politician Benjamin Disraeli, "What we anticipate seldom occurs; what we least expected generally happens."⁵ Importantly, our work has shown that it is the combination of A1 agonist (or adenosine) and lidocaine administration that confers functional, electrical, and metabolic protection during myocardial ischemia-reperfusion.³ It would be of interest to study the effects of volatile anesthetics in the presence of the combination of A1 agonist (or adenosine) and lidocaine during and after acute myocardial ischemia in clinically relevant experimental models.⁶

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Management of pediatric airway obstruction

To the Editor:

We read with interest Vinograd and colleagues' article¹ on the management of airway obstruction in children by using self-expandable metal stents (SEMS). We commend the authors on a thorough and detailed description of the difficulties encountered in treating children with this complex problem.

The options available to treat pediatric airway obstruction include surgical resection and anastomosis (including slide tracheoplasty), silicone (eg, Dumon) stents, Montgomery T-tubes, and SEMS. Recently, there has been a disturbing trend of using SEMS as the first option in treating benign tracheobronchial pathology, primarily because of the ease of deployment and the dramatic relief of obstruction in the short term.² We feel that it needs to be reiterated strongly that SEMS should remain the last resort in patients with benign stenosis or those with a surgically correctable airway obstruction. SEMS have a number of complications that are difficult to treat long-term. The ideal indication for SEMS is a patient with terminal malignancy with airway obstruction in whom the expected low survival from the primary malignancy precludes the occurrence of stent-related complications. SEMS cause intense granulation tissue, which often causes the same symptoms for which the stent was deployed; subsequent attempts to alleviate this problem with laser, electrocautery, and so on usually have disappointing results. Moreover, contrary to the authors' views, removal of these stents is difficult and fraught with danger. Single and short-segment tracheal stenosis should be treated by primary surgery in centers experienced in pediatric tracheal surgery. Stenting should be reserved for patients in an acute situation (where silicone stents may be deployed as a temporary measure) before referral to a center specializing in tracheal surgery.

Although not practical in infants and very small children, Dumon stents and Montgomery T-tubes are invaluable in stenting lesions that are too long for safe reconstruction.³ More often than not, the stent stabilizes the airway, and decannulation is possible in most cases.⁴ Moreover, the ease with which silicon stents can be removed if definitive surgery is being considered makes it an attractive option to tide over an acute situation. The pediatrician, pulmonologist, or thoracic surgeon involved in managing complex airway problems needs to be aware of the basic underlying pathology and intelligently apply the right solution to a specific problem.

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Reply to the Editor:

In my article I emphasized that the use of intratracheal stents in children is dangerous and carries the risk of severe complications.

With regard to the use of self-expandable metallic stents (SEMS), I completely agree that their use should be avoided. There are enough data in the literature to support this.¹ The SEMS in this study were made from nitinol, an alloy with a "shape memory effect." In animal studies, this stent, because of its unique biochemical property, could be fixed and removed easily, even in very small airways.² In children, their use was associated with an excessive granulation, and although the extraction proved to be easy and smooth, their application is currently suspended.

Currently available silicone or Dumon stents have an external diameter that prevents their use in infants and small children.

The Montgomery and I-tubes could be an option in tracheal strictures, but they are not practical in bronchial or distal airway problems.

I would like to thank Mr Pramesh for his remarks.

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Molecular changes occurring with aneurysm formation: Possible impact of sampling error

To the Editor:

We congratulate Cotrufo and colleagues¹ for exploring messenger RNA expression and extracellular matrix protein content in the ascending aorta associated with bicuspid aortic valves (BAVs), with particular attention to differences between the inner and outer curvatures. Our laboratory is also exploring the molecular changes occurring with aneurysm formation, and we have been concerned about the potential impact of sampling error on experimental results.

Cotrufo and colleagues¹ demonstrated differences in levels of collagens I, III, and IV, as well as fibronectin and laminin protein, by western blot analysis when comparing samples taken from the concave and convex portions of dilated aortas resected from patients with BAV. Additionally, they reported differences between patients with functionally regurgitant versus stenotic valves. Importantly, Cotrufo and colleagues¹ also reported significant differences in protein levels between dilated aortas (regardless of functional valve pathology) and normal control aortas. Indeed, these differences were as striking as those observed between concavity and convexity or between stenotic and regurgitant specimens.

We too are intrigued by the observations made on aneurysmal tissues, but we urge caution in interpreting the comparisons made between dilated aortas and the control group. A marked difference in age may have profoundly impacted results. Cotrufo and colleagues¹ reported mean ages for the regurgitation, stenosis, and control groups as 56 ± 9 , 59 ± 12 , and 33 ± 8 years, respectively. The 95% confidence intervals for these groups (from data provided in the article's on-line Table E1¹) were 51.2-61.4, 50.9-66.4, and 24.6-41.4 years, respectively. The difference in collagen expression led Cotrufo and colleagues¹ to conclude that "collagen degradation by proteinases could prevail over collagen synthesis" and that smooth muscle cells "could react differently to different types and degrees of mechanical stress and could favor, in turn, a predominant production of either ECM [extracellular matrix] proteins or proteolytic enzymes." An alternative hypothesis