Different Vasoactive Mechanisms of Various Pulmonary Vasodilators

To the Editor:

We read with appreciation and interest the ACCP Consensus Statement "Primary Pulmonary Hypertension" by Rubin, which appeared in the July 1993 issue of Chest. In the section of therapy, the author states that many vasodilators such as prostacyclin, calcium channel blockers, nitrates, and others are currently available for treatment of primary pulmonary hypertension. About a fourth of patients, however, are felt to have "fixed" vascular disease, and vasodilator therapy is contraindicated. He also mentioned the advantage of prostacyclin to determine the potential and magnitude of vasoreactivity and the use of prostaglandin E1 (PGE1) as an alternative in this setting. It is a comprehensive and useful guideline. Nevertheless, the vasoactive mechanisms of these various agents on pulmonary arteries (PA) are not discussed. Are they all acting on the same site and through the same mechanism? Or do they cause the same degree of vasodilation?

Recently, we have conducted a series of investigations to study the direct vasoactive effects of various agents on isolated rabbit PAs. We used vessel rings precontracted with either norepinephrine or potassium chloride to determine the vasodilatory mechanism. Is it the result of the effect of Ca++ flux across the cellular membrane or release/reuptake of Ca++ from the sarcoplasmic reticulum (SR)? At the concentration of 10-6 M, norepinephrine-precontracted PA rings, PGE1 caused about 26 percent relaxation, nitroprusside (NTP) 70 percent, diltiazem (DTZ) 12 percent, and verapamil (VPM) 4 percent. On KCl-precontracted vessels, PGE1 produced 3 percent relaxation, NTP 20 percent, DTZ 55 percent, and VPM 22 percent. In summary, we have found that PGE1 and NTP act more on inhibiting Ca++ release from SR whereas DTZ and VPM on blocking Ca++ influx as expected. They cause different magnitude of vasodilation, which may be affected by the baseline sympathetic tone.

Is there any advantage in combined therapy? Should we base on prostacyclin only to determine the vasoreactivity? Before we can effectively and comfortably treat pulmonary hypertension, we need more information about the pharmacology of these pulmonary vasodilators.

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To the Editor:

Dr. Lee’s letter raises several important issues relating to the management of patients with primary pulmonary hypertension which warrant elaboration.

Although the mechanisms responsible for the vasodilator actions of the agents currently used to treat pulmonary hypertension are of great importance, the committee thought that a detailed discussion of this subject was beyond the scope of this clinical consensus statement. It is generally agreed, however, that the vasodilators that are commonly used to treat pulmonary hypertension do not work either at the same site or through a common mechanism, nor do they produce the same degree of vasodilation in the clinical setting. While the calcium channel blockers are generally regarded as first line vasodilator therapy for primary pulmonary hypertension both because of the convenience of oral administration and the sustained hemodynamic and symptomatic benefit manifested by responsive patients, Dr. Lee is correct in his statement that only a minority of patients will experience these optimal responses. Recent experience suggests that continuous intravenous infusion of prostacyclin may produce hemodynamic and symptomatic improvement even in patients who are unresponsive or intolerant of calcium channel blocker therapy. Additionally, the absence of a vasodilator response to prostacyclin administered acutely does not preclude the possibility of a beneficial response to chronic therapy. This raises the possibility that the chronic effects of continuous infusion prostacyclin may have less to do with its vasodilator properties than with other effects, such as altering the remodeling process in the pulmonary vascular bed. Combined therapy with oral vasodilator agents and continuous infusion prostacyclin has been used, and this approach may be beneficial for some patients.

Studies such as the one by Lee et al (Crit Care Med 1993; 21:5209, 5203) have provided us with a greater understanding of the cellular mechanisms of calcium handling and vasoactivity in pulmonary vascular smooth muscle cells. We agree that the optimal approach to medical therapy of primary pulmonary hypertension, however, will await the clarification of the cellular mechanisms responsible for the pathogenesis of this disease. Nevertheless, clinical investigation in this area has yielded several useful treatment options for patients with this heretofore untreatable disease; these treatment options are available at the present time to the majority of patients with primary pulmonary hypertension, and we need not wait until the pathogenesis is clarified to treat patients with this disease.

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Tracheal Occlusion

To the Editor:

We read with interest the case report on tracheal occlusion by Anderson et al., which appeared in the February 1993 issue of Chest. We describe a similar case at our institution and offer an additional report of airway obstruction after esophagogastrectomy.

In August of 1991, a 68-year-old woman came to us with a 2-month history of subternal pressure and progressive dysphagia. Esophagoscopy and computerized tomography (CT) revealed a tumor of the middle third of the esophagus, which was found to be squamous cell carcinoma on biopsy. She underwent right thoracotomy with Ivor Lewis esophagectomy, esophagogastrostomy, and pyloromyotomy. Her postoperative course was complicated by atrial fibrillation, urinary tract infection, and prolonged ventilator dependence. She required a tracheostomy on postoperative day 12.

Over the next 2 weeks, she was weaned from ventilator support and her nasogastric tube was then removed. About 12 h later, she was found in respiratory distress. She was ventilated via the tracheostomy tube with improvement. A chest roentgenogram revealed marked dilatation of the intrathoracic stomach. A CT scan of the chest (Fig 1) showed severe compression of the trachea and right mainstem bronchus by the dilated intrathoracic stomach. The patient was successfully weaned from mechanical ventilation after decompression of the intrathoracic stomach by a nasogastric tube. A barium swallow subsequently revealed minimal passage of barium through a markedly constricted pylorus.

The patient was returned to the operating room where pyloroplasty was performed. Postoperatively, she made remarkable progress and was weaned from ventilator support within 72 h. Enteral feedings were administered through a postpyloric feeding tube, and nasogastric suction was maintained for gastric decompression. One week after pyloroplasty, she was able to eat and had no further respiratory difficulty. A repeat barium study was performed, demonstrating free flow of barium through a widely patent pylorus. She was discharged after removal of the tracheostomy tube.

An additional case of airway obstruction from an intrathoracic stomach was reported by Santoscoy et al. in 1992. In their patient, partial airway obstruction occurred 6 months after transhiatal esophagogastrectomy. Barium swallow revealed delayed gastric emptying, and balloon dilatation of the pylorus successfully alleviated further respiratory symptoms.

Clearly, tracheal obstruction from gastric distention must be considered in patients developing respiratory distress after esophagogastrectomy. Several studies1-3 to date have suggested that pyloroplasty improved gastric emptying compared with control patients who did not undergo the procedure. However, there was no statistically relevant difference in symptoms between the two groups. Interestingly, none of the three patients described with airway obstruction after esophagogastrectomy had initially undergone pyloroplasty, although ours had undergone pyloromyotomy. Two of the three patients eventually required gastric drainage procedures to relieve tracheal compression.

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To the Editor:

Drs. Leite, Jones, and Panasuk describe a case of high grade, large airway occlusion due to extrinsic compression of the membranous trachea by a massively dilated intrathoracic stomach 26 days after esophagogastrectomy. In the case they describe, prolonged ventilator dependence requiring tracheostomy placement complicated the initial postoperative course. It is not clear if airway compromise from a distended intrathoracic stomach contributed to the initial difficulty in weaning. On the 26th postoperative day (14 days after tracheostomy placement), the patient was finally weaned from mechanical ventilation, and her nasogastric tube, presumably positioned proximal to the pylorus, was removed. Twelve hours later, the patient was in significant respiratory distress requiring reintroduction of positive pressure ventilation. After this sequence of events, we hear the first description of a markedly dilated intrathoracic stomach. The patient’s intrathoracic stomach was decompressed with a nasogastric tube, her symptoms subsided, and she was rapidly weaned from the ventilator. A barium swallow showed significant gastric outlet obstruction. She returned to surgery, pyloroplasty was performed, she did well, and she eventually left the hospital. Leite et al describe an additional case reported by Santoscoy et al., describing a similar partial large airway occlusion occurring 6

Figure 1. The CT scan reveals compression of the membranous trachea at the level of the tracheal carina by the dilated intrathoracic stomach. The stomach also displaces the right lung.