Letters to the Editor

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Inhaled prostacyclin is safe, effective, and affordable in patients with pulmonary hypertension, right-heart dysfunction, and refractory hypoxemia after cardiothoracic surgery

To the Editor:

We read with interest the elegant article by De Wet and associates,¹ who demonstrated that inhaled prostacyclin (PGI₂) prevents pulmonary hypertension, right-heart dysfunction, and refractory hypoxemia after cardiothoracic surgery. We would like to add some observations regarding the mechanisms of action that might be of interest and of possible value in the further clinical implementation of inhalational PGI₂.

First, pulmonary hypertension is associated with increased superoxide (O₂⁻) formation that is largely mediated by an upregulation of intravascular reduced nicotinamide adenine dinucleotide phosphate (NADPH) oxidase.²⁻⁵ O₂⁻ reacts with endogenous nitric oxide (NO) to form reactive nitrogen species, which effectively reduces NO bioavailability.² Because NO is a vasodilator and an inhibitor of inflammation, the reduction of NO formation is considered axiomatic in pulmonary hypertension.²

O₂⁻ also reduces endogenous vascular PGI₂ formation.³ We recently demonstrated that the PGI₂ analogue iloprost is a potent inhibitor of NADPH oxidase expression and activity in porcine pulmonary arteries and therefore of O₂⁻ formation.³ Therefore by reducing O₂⁻ formation, PGI₂ protects and enhances NO formation, which itself inhibits NADPH oxidase.⁴ The reduction of O₂⁻ also prevents the formation of isoprostanes, which are vasoconstrictors and promoters of NADPH oxidase expression.³

One interesting facet of the effect of inhalational PGI₂ reported by De Wet and associates¹ was that it prevented refractory hypoxemia. We found that hypoxia promotes the expression of NADPH oxidase in porcine pulmonary arteries.⁵ Hypoxemia, by promoting O₂⁻ formation, would create a self-perpetuating cascade that would worsen hypertension and further augment hypoxemia. PGI₂, by blocking the expression of NADPH

oxidase, might break this cycle and protect the pulmonary vasculature during surgical intervention through this antioxidant mechanism. Inhalational PGI₂ might also prevent perioperative and postoperative intrapulmonary inflammation because PGI₂ prevents the adhesion of leukocytes and platelets to vascular walls.⁶ Similarly, the preservation of intrapulmonary NO-forming capacity would also afford protection against inflammation because NO has similar anti-inflammatory properties to PGI₂.⁷ This is of importance because leukocytes and platelets release vasoconstrictors and inflammogens, including thromboxane A₂ and cytokines, all of which upregulate the expression of NADPH oxidase and the formation of O₂⁻.²⁻⁴

The beneficial effect of inhalational PGI₂ on left ventricular function reported by De Wet and associates¹ could be related to its antioxidative effect on the lungs. There is substantial evidence that reactive oxygen species, including O₂⁻ and peroxynitrite, impair left ventricular function.⁸ Thus it is reasonable to suggest that the suppression of intrapulmonary oxygen free radical formation by PGI₂ might contribute to the beneficial downstream protective effect of the prostanoide on the left ventricle.

Finally, in a broader context the administration of the stable analogue iloprost in cardiac surgery might be indicated for other more long-term conditions. In particular, PGI₂ has been shown to inhibit vascular smooth muscle cell proliferation and migration, platelet and leukocyte adhesion, and metalloproteinase expression,⁶ all key components of vein graft disease. As such, iloprost might be useful in preventing vein graft failure.

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Henry T. Bahnson, Hopkins, and harmonica

To the Editor:

Like many of Henry T. Bahnson's surgical peers at Johns Hopkins who were cited in the in memoriam article by Griffith,¹ I was privileged to be a close cardiology colleague of Hank at Hopkins. My association with Hank was primarily through my work in the cardiac catheterization laboratory at Hopkins. At that time, the cardiac catheterization laboratory was under the department of surgery because the laboratory was considered as a preoperative diagnostic facility before

Acoustical and physical dynamics of the diatonic harmonica

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The harmonica is arguably the most widely played instrument in the world, yet there is a surprising paucity of published studies of its acoustics or physical dynamics. The typical diatonic harmonica and the physical forces involved in its natural function are described, and simple observations of the harp's functions are reported. The speaking of the reeds, naturally, when producing a bend, and when speaking as an overblow or overdraw is discussed and investigated by simple stopping of the reeds, by videostroboscopic analysis, and by recording vibration of the reeds with displacement gauges. The reeds of the ten hole harmonica can be made to vibrate at varying frequencies depending on the size and shape of the player's vocal tract. Three different modes of speaking from each hole and its pair of reeds are revealed and studied: first, naturally in a closing mode, either blown or drawn; second, as a bend, either blown or drawn, with pitch in the interval between the two notes in the hole; and third, as an overblow or overdraw in an opening mode with a pitch outside the interval between the two natural notes of the hole. This dynamic interaction allows the player to speak with the instrument perhaps as with no other. © 1998 Acoustical Society of America. [S0001-4966(98)02404-7]

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INTRODUCTION

The name, *Harmonica*, has been used to designate many instruments over the years, some being reed instruments related to the instrument under discussion, and others seemingly unrelated, such as the glass harmonica attributed to Benjamin Franklin, which consisted of a set of glasses of varying size, tuned by varying the amount of water within.

activated by positive pressure in the comb (i.e., blowing), is fastened to the top side of the comb with the reeds inside. A second plate of reeds, the *draw reeds*, which are activated by negative pressure, is fastened to the bottom side of the comb with the reeds outside. The reed slots on the blow- and draw-reed plates are arranged to coincide with each other on opposite sides of the chambers of the comb. Thin metal covers

Figure 1. Top portion of the first page of the article on the harmonica by Bahnson, Antaki, and Beery³ published 3 years before his death. My initials are T.O., commonly used by my colleagues at Hopkins. (From Bahnson HT, Antaki JF, Beery QC. Acoustical and physical dynamics of the diatonic harmonica. *J Acoust Soc Am.* 1998;103:2134-44. Published with the permission of the *Journal of the Acoustical Society of America*, American Institute of Physics.)

patients, young and old, were operated on for their congenital and acquired heart diseases by Blalock and associates. I was a fellow in the respiratory laboratory of the late Dr Richard L. Riley, who arranged with Blalock to let me work 1 day a week in the cardiac catheterization laboratory because Riley knew of my interest in cardiac catheterization. I still remember the few times that I needed some advice from Hank during cardiac catheterization of babies. I asked the nurse to page H.T.B. for me. She immediately tried to correct me by saying, "Do you mean H.B.T.?" H.B.T. stood for Helen B. Taussig, of the Blalock-Taussig operation, and H.T.B. stood for Henry T. Bahnson. Because the patient was a baby, it was natural for the nurse to think I wanted to speak to Helen B. Taussig rather than to Henry T. Bahnson.

Because Griffith's article began and ended with a reference to Bahnson's har-

monica, I wish to amplify a bit on Hank's association with this musical instrument. As Griffith¹ mentioned, *The Wall Street Journal* in 1999 published an article titled "Of artificial hearts and artificial harps in a Pittsburgh laboratory," with the subtitle "Cardiac surgeon and bioengineer study a harmonica virtuoso from inside his mouth."² The reporter mentioned Hank's application of his artificial heart experience to that of artificial harps, more commonly known as the harmonica. Because many of your readers might not be familiar with publication number 250 in Hank's bibliography mentioned in Griffith's article, I wish to mention that the article by Hank was published in the *Journal of the Acoustical Society of America* (Figure 1).³ I suggest that everyone read the entire article to understand the history, physics, and physiology of the harmonica. As Hank said at the end of his article, "This helps keep the harmonica interesting, and indeed has

To T.O.
It was fond
memories of our
days together
at Hopkins
Henry T. Bahnson