hypertension, was probably the main factor responsible for the abnormalities that they observed.

The authors showed that the patients, who had primary pulmonary hypertension, worked more slowly, did less work and recovered more slowly than normal subjects. Inhaling nitric oxide reduced the patients’ pulmonary arterial pressures, but changed none of the above abnormal measurements. This made it difficult to claim that the pulmonary hypertension was the cause of the abnormal measurements. The decrease of pulmonary artery pressure after inhalation of nitric oxide and possible, but underestimated, increase of blood flow resembled Wilson and Ferraro’s (4) study using hydralazine. This showed that hydralazine decreased arterial pressure and increased cardiac output during exercise in heart failure, but did not influence exercise oxygen consumption or peak lactate concentration or oxygen debt (4). Dilating blood vessels, reducing intravascular pressures and increasing blood flow did not correct the important abnormalities in either situation.

A new clue concerning pulmonary hypertension is in the report of Driss et al. (5) of producing tiny left ventricular infarcts that did not change left ventricular hemodynamics or size, but caused pulmonary hypertension. Riley et al. (1) should extend their studies into the field of neurohumoral and other signaling to improve our understanding of primary pulmonary hypertension.

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REPLY

We thank Dr. Krohn for his thoughtful comments. The mechanism for the desaturation seen in some elite athletes is likely to be related to the high cardiac output leaving insufficient time for equilibration of oxygen tensions between the alveolus and alveolar capillaries. Oxymyoglobin desaturation in response to maximal exercise is a very unusual finding in normal adults performing exercise near sea level (1). Cardiac output at peak exercise is low in patients with primary pulmonary hypertension (PPH). Desaturation is unlikely to be due to the same mechanism as that occurring in elite athletes. Arterial oxymyoglobin desaturation is not a feature of circulatory diseases or deconditioning.

We found that nitric oxide (NO) reduced right ventricular systolic pressure (RVSP) at rest in our patients with PPH, but failed to alter exercise responses. Several factors may have been responsible: 1) Nitric oxide may not have improved cardiac output, despite causing a fall in pulmonary vascular resistance; NO may adversely affect the positive inotropic response to beta-adrenergic stimulation in left ventricular dysfunction (2) resulting in reduced cardiac contractility. 2) Hemodynamic improvement present at rest may not have been sustained during exercise; our study was noninvasive and we could not be sure that NO improved either RVSP or cardiac output during exercise. 3) As proposed by Dr. Krohn, peripheral factors may have limited the benefit of any rise in cardiac output with NO. In patients with chronic left ventricular failure, Wilson et al. (3,4) found an increase in cardiac output with the acute administration of hydralazine or isosorbide dinitrate during submaximal exercise or dobutamine during maximal exercise. However, none of these drugs improved total oxygen consumption, oxygen uptake across the exercising leg or venous lactate. This paradox was attributed to a failure of “nutritive” flow to increase in the exercising muscle. Even though peripheral oxygen extraction is high in patients with PPH (5), it is possible that the peripheral circulation may not have been able to distribute appropriately any additional acute increase in cardiac output caused by NO inhalation.

We agree that the study of neurohumoral mechanisms in PPH may prove fruitful. Endothelin is known to be elevated in patients with PPH (6) and may be important in promoting vascular remodeling. At present it is unclear whether abnormalities of other vasoactive hormones also occur. However, even if neurohumoral abnormalities occur under conditions of circulatory stress, the matter of discerning cause and effect will remain.

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