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In reply: Prough and Johnston raise several important points. They state correctly that the dose of oleic acid (0.8 ml/kg) reported in our recent study[1] is in excess of that usually employed to produce canine lung injury.[2-4] The dose of oleic acid as recorded in the text was incorrect. We used 0.08 ml/kg, not 0.8 ml/kg, and we would like to thank Prough and Johnston for bringing this error to our attention. Numerous investigators have studied acute cardiopulmonary effects of oleic acid, and the reported doses range from 0.035 ml/kg to 0.1 ml/kg.[1,2,4-8] Clearly 0.8 ml/kg is markedly in excess of other studies and such a high dose rapidly results in death of the animal.[2]

Prough and Johnston compared the cardiovascular status of the dogs in our study with other studies and point out that, while cardiac output (CO) usually decreases[2-4] after oleic acid, it increased in ours. They attributed the difference to volume expansion, we agree. As stated under methods, during initial preparation, "about 500 ml of normal saline and 500 ml of 6% dextran were infused." Also, saline infusion was "continued throughout the study to maintain pulmonary capillary wedge pressure (PCWP) approximately 6 mmHg." Also, note that while CO was numerically increased from baseline at 1.5 h after oleic acid, the difference was only 14% and was not significant. We also note that their reference number two does not support their statement that oleic acid reduces CO. In that study, mean cardiac index remained constant or increased 1 and 2 h after oleic acid.

Prough and Johnston raise the possibility "that augmentation of CO with volume administration increased Qs/Qt before the administration of hydralazine, and therefore attenuated any increase in Qs/Qt, produced by the drug. The effects of hydralazine in animals that have not been volume expanded would be of considerable interest." In response to this possibility, we note that the mean CO 1.5 h after oleic acid was 3.65 $l \cdot min^{-1}$ and the standard deviation was 1.3. Prior to hydralazine, in one dog CO was 2.4 $l \cdot min^{-1}$ and in another it was 2.6 $l \cdot min^{-1}$. In both of these dogs, Qs/Qt remained constant, and Pa_{O_2} increased when CO increased with hydralazine. These data do not support the speculation that a high baseline CO would have attenuated an increase in Qs/Qt with hydralazine. Most importantly, in a recent study of canine oleic acid edema,[8] we compared, in the same dogs, acute effects of different doses of nitroprusside and hydralazine. In that study, CO decreased with lung injury and 90 min after oleic acid, mean CO was 2.9 $l \cdot min^{-1}$. Our larger dose of nitroprusside decreased ($P < 0.05$) blood pressure and systemic vascular resistance and increased ($P < 0.05$) CO from 2.9 to 3.4 $l \cdot min^{-1}$. Corresponding to that change in CO, mixed venous O_2 tension (Pv_{O_2}) increased ($P < 0.05$) from 46 to 50 mmHg, Qs/Qt increased ($P < 0.05$) from 28 to 37%, and arterial O_2 tension decreased ($P < 0.05$). In contrast, despite an increase ($P < 0.01$) in CO from 2.4 to 4 $l \cdot min^{-1}$ and an increase ($P < 0.01$) in Pv_{O_2} from 43 to 56 mmHg, Qs/Qt remained constant and arterial O_2 tension increased ($P < 0.05$) with hydralazine. Mean right to left shunt was 27% before and 28% after hydralazine.

Results of this latter study, confirm previous work[1] and demonstrate that in diffuse lung disease, Qs/Qt may not increase when CO and Pv_{O_2} increase with hydralazine.

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