Our own findings indicate an increase in Vc/Dm ratio as the most characteristic abnormality in patients with mitral valve disease. In the accompanying figure Vc has been plotted against Dm in different clinical situations including 19 patients with mitral valve disease. Isopleths of DLco which follow a rectangular hyperbole have been constructed assuming $1/\theta = 1.263$. Eighteen of the 19 patients with mitral valve disease have a ratio > 3 which is more than the ratio in all the 18 normal subjects. These estimations were performed by a steady state technique, the details of which have been described earlier.[6]

J. N. Pande
S. P. Gupta
J. S. Guleria
All India Institute of Medical Sciences
New Delhi, India

References

1. Burgess JH: Pulmonary diffusing capacity in disorders of the pulmonary circulation. Circulation **49:** 541, 1974
2. McCreddie RM: The pulmonary capillary bed in various forms of pulmonary hypertension. Circulation **33:** 854, 1966
3. Yuba K: A study on the pulmonary functions and the pulmonary circulation in cardiopulmonary diseases. (1) Pulmonary diffusing capacity in cardiopulmonary diseases. Jap Circ J **35:** 1391, 1971
4. Daly WJ, Giammona ST, Ross JC, Feigenbaum J: Effects of pulmonary vascular congestion on postural changes in the perfusion and filling of the pulmonary vascular bed. J Clin Invest **43:** 68, 1964
5. Flatley FJ, Constantine H, McCreddie RM, Yu PN: Pulmonary diffusing capacity and pulmonary capillary blood volume in normal subjects and in cardiac patients. Am Heart J **64:** 159, 1964
6. Jain BP, Pande JN, Guleria JS: Membrane diffusing capacity and pulmonary capillary blood volume in chronic obstructive lung disease. Am Rev Resp Dis **105:** 900, 1972

The author replies:

To the Editor:

The observations of Drs. Pande, Gupta and Guleria are limited to measurements of the subdivisions of the diffusing capacity in patients with mitral valve disease. This is a minor point of my article. Estimations of Dm and Vc are based on the measurement of Dco at different inspired oxygen tensions and the graphical solution of Roughton and Forster's equation. As a result, values obtained for these subdivisions are considerably less reliable than the total Dco. One should not draw conclusions from variations in Dm and Vc when the Dco is normal. An increase in inspired oxygen tension in patients with mitral valve disease probably produces physiological changes in the pulmonary capillary bed. This casts further doubt on the interpretation of Dm and Vc.

The major point of the above letter is their finding of a low Dm and therefore increased Dm/Vc ratio in patients with mitral valve disease. However, Dm is a less reliable measurement than Vc, especially when the pulmonary capillary blood volume is small.[1] In the latter case the slope of the line for the graphical solution for Dm and Vc is steep. The intercept on the y axis is then less certain and Dm varies widely. It may approach infinity when Vc is very low indicating that the capillary resistance to diffusion predominates. This explains the rather high values for Dm that I reported.

Dco measurements are clinically useful in patients with mitral valve disease and other pulmonary circulatory disorders. Measurements of the subdivisions do not provide further information of clinical value. For the reasons stated above, I do not believe that values obtained for Dm in these patients are very meaningful physiologically. Conclusions regarding capillary geometry based on changes in Dm and a Vc/Dm ratio in patients are unreliable. The subdivisions of the Dco are conceptually useful, but interpretation of the total Dco is on much firmer ground.

J. H. Burgess, M.D.
Montreal General Hospital
Montreal, Quebec, Canada

Reference

1. Burgess JH, Bishop JM: Pulmonary diffusing capacity and its subdivisions in polycythemia vera. J Clin Invest **42:** 997, 1963

Sleep and Ventricular Premature Beats

To the Editor:

We were pleased by the results reported by Lown and his colleagues (Circulation **48:** 691, 1973) regarding the importance of neural mechanisms to the ventricular ectopic activity seen in some patients. Their suggestion that neural events might trigger ventricular extrasystoles in patients is substantiated by experimental studies in animals. We as well as others[1] have shown that electrical stimulation of brain centers will produce a variety of cardiac arrhythmias. The same is true when peripheral autonomic nerves are stimulated.[2] Furthermore, circumstances that give rise to arrhythmias such as digitalis administration and experimental myocardial infarction produce generalized excitation of brain stem nuclei.[1, 3] Depression of these brain sites by neurodepressant drugs or surgical removal delays and even corrects these arrhythmias.[1, 3]

The animal data suggest that enhanced sympathetic tone is the causative factor in disrupting cardiac rhythm. But as pointed out by Lown and colleagues, "it is hard to account for the failure of large doses of propranolol to reduce VPBs in three patients, though such a result was observed with sleep alone." This seeming paradox becomes clear when one considers the results of Randall and colleagues.[2] They have shown that electrical stimulation of cardiac sympathetic nerves produces arrhythmias which cannot be prevented by pretreating animals with propranolol. Additionally, it was shown that the arrhythmias could not be blocked by atropine. Thus, arrhythmogenic stimuli from the CNS may travel to the heart through nerves whose neuroeffector junctions are not amenable to blockade by conventionally employed antagonists.

Lown and colleagues put forward the view that "the pharmacologic focus should be in restraining the neurophysiologic trigger rather than in attempting to protect the cardiac target." This is an approach that we have been advocating for several years. For example, we have found that several of the drugs currently in use for treating arrhythmias possess neurodepressant actions.[1] Furthermore,