

minant of the contractile state of the heart in the presence of altered ventricular preload, therefore, is not established.

It seems that the authors erred in their quote of Wilken *et al.*, when they stated that  $\dot{Q}_{\max}$  was little affected by changes in afterload. Wilken and associates actually showed that  $\dot{Q}_{\max}$  uniformly diminished when afterload increased, and  $\dot{Q}_{\max}$  increased following a sudden reduction in afterload (Circ. Res. 14: 283-293, 1964).  $\dot{Q}_{\max}$  is merely one index of the performance of the heart as a pump, as is cardiac output, and is dependent upon many peripheral factors, including preload, afterload, contractile state of the myocardium, and heart rate. It is not related to the intrinsic contractile properties of the heart. Obviously, therefore, changes in  $\dot{Q}_{\max}$  during cyclopropane and halothane anesthesia cannot be related to the directional change in left ventricular myocardial contractility in a simple manner.

Rusy *et al.* stated that, in contrast to their findings, Price *et al.* (J. Clin. Invest. 41: 604-610, 1962) and Etsten and Shimamoto (Clin. Anesth. 3: 55-78, 1964) found little or no change in myocardial contractility during cyclopropane. This was based upon the interpretation that the ventricular function curve (the relationship between the ventricular end-diastolic pressure and external useful stroke work) is rendered complex when the aortic pressure is elevated, as during cyclopropane anesthesia. However, they failed to refer to other published data which showed that the heart still operates upon the same ventricular function curve when the mean aortic pressure (afterload) is experimentally elevated during both cyclopropane and halothane anesthesia (Etsten and Shimamoto: Acta Anaesth. Scand. 23: 242-247, 1966).

The effects of anesthetics upon myocardial contractility are primarily determined by  $V_{\max}$ , derived from intraventricular pressure and its time-rate of change (dp/dt). Unlike  $\dot{Q}_{\max}$ ,  $V_{\max}$  is independent of changes in preload and afterload. When the effect of cyclopropane on myocardial contractility was evaluated by means of  $V_{\max}$ , it was found that arterial cyclopropane concentrations of  $19 \pm 1$  mg/100 ml caused no significant change in  $V_{\max}$  in intact dogs. In addition, we recently reported that cyclopropane anes-

thesia (arterial blood concentrations ranging from 9 to 46 mg/100 ml) does not cause any significant change in either shape or position of the force-velocity curves. The average change in  $V_{\max}$  was -6 per cent ( $P > 0.2$ ). These data confirm our previous findings of unchanged left and right ventricular function curves during cyclopropane anesthesia in the intact dog. It is interesting that in the same animals  $\dot{Q}_{\max}$  was reduced by cyclopropane  $50.2 \pm 6.3$  per cent ( $P < 0.01$ ), agreeing with findings of Rusy *et al.* (Shimamoto, Shanks and Etsten: ANESTHESIOLOGY 33: 497-502, 1970).

It should also be emphasized that the tension-time index (TTI), the product of the mean systolic pressure and the duration of systole, is unreliable as an index of myocardial oxygen consumption when the contractile state of the myocardium or  $V_{\max}$  is altered (Sonnenblick *et al.*: Amer. J. Physiol. 209: 919-927, 1965). The major determinants of myocardial oxygen consumption are preload, afterload, contractile state of the myocardium, and heart rate. The afterload is determined by a variety of closely interrelated factors, including ventricular volume and wall thickness, the impedance to ejection, and the shortening characteristics of the myocardial fibers. Therefore, their findings of increased TTI for cyclopropane and decreased TTI for halothane, with accompanying changes in afterload, must be evaluated conservatively.

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*To the Editor:*—Doctors Shimamoto and Etsten have questioned the appropriateness of using the variable,  $\dot{Q}_{\max}$  as an index of change in myocardial contractility.

Noble and associates (Circ. Res. 19: 139-147, 1966) claim that  $\dot{Q}_{\max}$  is sensitive to changes in inotropic state but not to changes in initial fiber length. These authors have clearly demonstrated that  $\dot{Q}_{\max}$  is markedly changed by interventions which undoubtedly

alter the contractile state of the myocardium, *e.g.*, the intracoronary arterial injection of isoproterenol. While their claim of insensitivity of  $\dot{Q}_{\max}$  to initial fiber-length change is based upon indirect evidence, *i.e.*, upon the observation that  $\dot{Q}_{\max}$  remains constant during postural change, it should be pointed out that changes in end-diastolic volume accompanying postural change have been well documented by Rushmer (Handbook of Physiology, Circulation 1: 533, 1962). It should also be mentioned that the postural changes of Noble's dogs were accompanied by large changes in stroke volume, which almost certainly indicates that changes in end-diastolic volume actually did occur.

Regarding the effect of changing afterload on  $\dot{Q}_{\max}$ , we stated that  $\dot{Q}_{\max}$  was little affected by changes in this variable, basing our statement on the published data of Wileken *et al.* (Circ. Res. 14: 283-293, 1964) which showed that  $\dot{Q}_{\max}$  increased less than 10 per cent, for a beat-to-beat change in peak ventricular pressure of approximately 180 to 140 mm Hg.

Concerning ventricular function curves (VFC), we stated that their use to determine contractile state was not valid unless one took into account the fact that stroke work was a function not only of contractile state, but of afterload as well (Sonnenblick and Downing: Amer. J. Physiol. 204: 604-610, 1963). This dependence of stroke work on afterload has been mentioned by Shimamoto *et al.* (ANESTHESIOLOGY 29: 538-549, 1968). Doctors Shimamoto and Etsten now state that "the heart still operates on the same VFC when the mean aortic pressure (afterload) is experimentally elevated during both cyclopropane and halothane anesthesia." We feel that this probably indicates that myocardial depression was induced by both of these agents, since Sonnenblick and Downing found that stroke work was insensitive to increasing afterload only in the failing myocardium.

Our employment of  $\dot{Q}_{\max}$  was based upon our statement that it correlates well with the contractile state of the ventricle. We made no attempt to justify its use on the basis of some conceptual relationship between it and intrinsic contractile element activity. Con-

sidering the present state of knowledge about cardiac muscle, we feel that there are probably a number of indices which can, at best, be said only to correlate with myocardial contractility. It may not be surprising that different indexes are affected somewhat differently by anesthesia.

The basic concern of our study was to examine the effects of cyclopropane and halothane on the mechanical aspects of myocardial function which have been shown to correlate well with myocardial oxygen consumption ( $\dot{M}\dot{V}_{O_2}$ ). To date, there has been much concern about the effects of anesthetics on myocardial contractility, while the very important aspect of myocardial energetics has received scant attention. In our article we stressed the fact that both the contractile state and some measure of cumulative wall tension, *e.g.*, the tension-time index (TTI), are important determinants of  $\dot{M}\dot{V}_{O_2}$ . In deriving the TTI, we pointed out that consideration of ventricular size, as well as pressure, was involved. While we did not measure heart size in the study, we referred to independent observations of ours which showed that ventricular volume, derived by cineradiography, was increased by halothane and was increased more by cyclopropane. If these observations were considered, the actual TTI's would be greater than those reported.

Finally, we stated that the effects of halothane and cyclopropane on contractile state and TTI suggested that  $\dot{M}\dot{V}_{O_2}$  was decreased with halothane and increased with cyclopropane. The analysis for cyclopropane was somewhat complex, since one of the determinants of  $\dot{M}\dot{V}_{O_2}$  (contractile state measured in terms of  $\dot{Q}_{\max}$ ) was decreased, while the other (TTI) was increased. If, however, contractile state were not decreased by cyclopropane, as is stated by Doctors Shimamoto and Etsten, then  $\dot{M}\dot{V}_{O_2}$  would be increased to an even greater extent by this agent.

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