Correspondence

Isovolemic Intraventricular Pressure

To the Editor:—In the article, "Isovolemic Intraventricular Pressure Change: An Index of Myocardial Contractility during Anesthesia" (ANESTHESIOLOGY 31: 327, 1969), Dr. Shimosato presents a method for evaluating myocardial contractility by calculating V_{max} of the contractile element (CE V_{max}) from a high-fidelity pressure measurement in the left ventricle. Unfortunately, the validity of the V_{max} technique as an index of contractility is being seriously challenged by current reports. Moreover, in applying the V_{max} technique to the intact ventricle, Dr. Shimosato employs several questionable analytical processes and assumtions.

The validity of the V_{max} technique as an index of contractility is premised on the independence of CE V_{max} from fiber length. But it has recently been demonstrated that CE V_{max} is in fact markedly dependent upon fiber length (Pollack, Circ. Res. 26: 111, 1970). Furthermore, data recently obtained by Noble and his colleagues (Circ. Res. 24: 821, 1969) indicate that V_{max} of cardiac muscle as a whole is also dependent upon fiber length. Since fiber length *independence* of CE V_{max} is crucial to the validity of the V_{max} technique, it appears that the conclusions drawn by Dr. Shimosato in applying this technique may not be reliable.

Moreover, the calculation of CE V_{max} from ventricular pressure and its time derivative as performed by Dr. Shimosato assumes that the modulus of elasticity of the series elastic element is linearly related to the stress on the muscle as in:

$$dT/dl = KT \qquad (1)$$

where

T = muscle stress
l = muscle fiber length
K = a constant

But if equation 1 were correct, at zero stress $T = 0$) the elastic modulus of the series elastic element, dT/dl, would be zero, an assumption which measurements have clearly shown to be incorrect. Instead, recent experimental determinations (Parmley and Sonnenblick, Circ. Res. 20: 112, 1967; Yeatman *et al.*, Am J. Physiol. 217: 1030, 1969) have shown that the series elastic element is characterized by the following relationship:

$$dT/dl = KT + C \qquad (2)$$

where C is a constant.

The constant, C, may not be ignored when attempting to calculate *CE* V_{max}. By neglecting C, Dr. Shimosato arrived at the following relationship:

$$V_{CE} = \frac{dP/dt}{KP} \qquad (3)$$

where

P = instantaneous isovolumic pressure
V_{CE} = contractile element velocity
t = time

Through use of equation 3, *CE* V_{max} was shown to be independent of fiber length. However equation 2, the correct formulation for the elastic modulus of the series elastic element, yields the following expression for V_{CE}:

$$V_{CE} = \frac{dP/dt}{KP + 2hC/r} \qquad (4)$$

where

h = ventricular wall thickness
r = ventricular radius

When this equation is applied to Dr. Shimosato's data, the extrapolations of the V_{CE} curves to zero pressure do not give a *CE* V_{max} independent of fiber length, but instead result in a *CE* V_{max} which *increases with end-diastolic radius.* In fact, application of this equation shows that there is a 100 per cent increase of *CE* V_{max} for a 5 per cent increase of end-diastolic radius!* Thus, Dr. Shimosato's data, properly interpreted, indicate that $CE\ V_{max}$ is markedly sensitive to ventricular and diastolic fiber length and therefore that it cannot uniquely reflect the inotropic state of the muscle. In other words the data show, contrary to his own conclusion, that $CE\ V_{max}$ is not a valid index of cardiac muscle contractility.

Dr Shimosato's reliance upon the *two*-element Hill model for his analysis also leads to erroneous conclusions. Modern studies agree that at least *three* elements are necessary in a model of cardiac muscle. Although some have assumed that a three-element model may be reduced to a two-element model during isovolumic contraction, it can be shown that this assumption is invalid when calculating $CE\ V_{max}$ of cardiac muscle (Pollack, *ibid*).

Finally, certain geometric assumptions which are implicit in Dr. Shimosato's analysis should be drawn to the attention of the reader. His application of the "Law of Laplace" to his data presupposes that:

1. The ventricle is spherically shaped;
2. It has a thin wall; this generally means that the wall thickness must be less than 10 per cent of the radius if reasonable accuracy is desired;
3. The wall is homogeneous and isotropic, *i.e.*, the fibers are arranged *uniformly* around the sphere and their contractile properties in all tangential directions are identical;
4. The sphere does not change shape during isovolumic contraction.

Thus, even if one disregards the earlier-mentioned reservations, Dr. Shimosato's calculation of $CE\ V_{max}$ would be valid only to the extent that these four assumptions are valid.

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To the Editor:—Dr. Gerald H. Pollack's letter suggests that the validity of the maximal intrinsic velocity (V_{max}) as an index of myocardial contractility is being seriously challenged. Unfortunately, this statement was made without established evidence. Certain comments in his criticism are appreciated; however, most of the points are minor and do not relate the the fundamental basis for the concept of force–velocity relations as a reliable and accurate index for evaluation of changes in myocardial contractility owing to anesthetics.

Several important points relevant to Doctor Pollack's comments need clarification.

1) There has been no scientific evidence indicating that the use of maximal intrinsic velocity (V_{max}) as an index of contractility is invalid. On the contrary, most cardiovascular researchers use the concept of V_{max} as the index of contractility (Henderson *et al.*, Am. J. Physiol. 217: 1273, 1969; Parmley, Brutsaert and Sonnenblick, Circulation 22: 521, 1969; Gault, Ross and Braunwald, Circulation 22: 451, 1968; Siegel, ANESTHESIOLOGY 30: 519, 1969).

2) Evidence that V_{max} is dependent upon fiber length is not conclusive. Data reported by Noble *et al.* (Circ. Res. 24: 821, 1969) only suggests that the shape of the quick-release force–velocity curves is dependent upon muscle length. However, the quick-release method itself has been criticized on the grounds that any change in muscle strain (release or stretch) tends to promote relaxation (*CE* uncoupling) (Brady, Physiol. Rev. 48: 570, 1968). On the other hand, it has been well demonstrated that V_{max} is independent of muscle length in isotonically-contracting cardiac muscle (Sonnenblick, Am. J. Physiol. 202: 931, 1962).

It has also been shown that cardiac muscle, unlike skeletal muscle, has a slow onset and decay of the active state, and that the quick-release method for obtaining an instantaneous force–velocity relation inherits the problem of uncertainty in determining the maximal velocity (Brady, Physiol. Rev. 48: 570, 1968). Noble *et al.* demonstrated that the quick-release method for the assessment of V_{max} was not precise when the myocardial fiber length was varied.

3) Stiffness of the series elastic element (SE) increases as a linear function of load (Sonnen-

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* This is easily calculated by choosing typical values for K and C from Yeatman *et al.* (*ibid.*), selecting two values for r, calculating corresponding values for h (assuming myocardial-wall volume remains constant), and estimating (from the literature) two values of initial dP/dt corresponding to the two different radii. Substitution of these two sets of parameters into equation 4, letting P approach zero in each case, generates the two values of $CE\ V_{max}$.