

Braunwald E. Control of myocardial oxygen consumption: physiologic and clinical considerations. *Amer. J. Cardiol.* 27:416-32, 1971.

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This paper summarizes experiments carried out in the dog heart and cat papillary muscle designed to elucidate the determinants of the heart's requirements for O_2 . The basal O_2 consumption of the heart and the O_2 cost of depolarization were relatively small. The oxygen cost of 'pressure work' was found to be far greater than 'flow work,' and a close relation was found between the area beneath the left ventricular pressure curve and myocardial oxygen consumption. Myocardial contractility, as reflected in the maximal velocity of isotonic shortening, and heart rate were found to be additional major determinants of myocardial oxygen consumption. [The *SCI*® indicates that this paper has been cited in over 455 publications since 1971.]

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"This paper represents the culmination of experimental work which my colleagues and I carried out during a 13-year period at the National Institutes of Health, begun during my postdoctoral fellowship in S.J. Sarnoff's laboratory and continued in my own laboratory. This effort involved many talented scientists, including Sarnoff, R.B. Case, Ross, and E.H. Sonnenblick.

"The experiments summarized in this paper depended on the development of techniques for independently regulating aortic pressure, stroke volume, and heart rate. The preparation employed was an isolated heart from which the coronary venous return was directed to the jugular veins of a second (support) dog, which renewed the isolated heart circuit with fresh arterialized blood, permitting the preparation to exhibit stable performance for hours. We found that the myocardial oxygen consumption MVO_2 per beat was closely related to what we termed the tension-time index, i.e., the area under the left ventricular pressure curve. Thus, it is not possible to estimate the energy needs of the heart from the external work when the latter is calculated as the product of developed pressure and stroke volume. External myocardial efficiency, i.e., the ratio of external work performed to the oxygen consumed, varies widely depending on the

hemodynamic conditions. In addition to the tension-time index, heart rate emerged as a second major determinant of MVO_2 . In closely related studies, we found that MVO_2 is a major determinant of coronary blood flow.²

"Six years after the completion of these experiments, we were working on the technique of paired electrical pacing³ by which we hoped to slow heart rate and thereby reduce MVO_2 . To our surprise, paired pacing increased, not reduced, MVO_2 , even though the heart rate decreased. Since paired pacing increases contractility, we reasoned that in addition to the tension-time index and heart rate, myocardial contractility must be another major determinant of MVO_2 . This was soon confirmed using other interventions which stimulated or depressed contractility while heart rate and tension-time index were held constant.⁴

"Subsequently, we used the results in a long series of experiments—still ongoing—designed to reduce the size of myocardial infarction following coronary occlusion.⁵ Since myocardial ischemia and ultimately myocardial necrosis depend on an imbalance between myocardial O_2 supply and demand, interventions which reduce demand (by lowering the tension-time index, heart rate, and/or contractility) reduce infarct size. It was found that they do so in experimental animals and in patients as well, if MVO_2 can be reduced immediately following coronary occlusion.

"This paper has been widely quoted because it was published at a time when interest in the treatment of myocardial ischemia became intense. Manipulations to reduce MVO_2 , such as beta adrenergic blockade and balloon counterpulsation, were becoming available for clinical use. Methods to challenge coronary reserve, such as electrical stimulation of heart rate, were being used in cardiac diagnostic laboratories. An understanding of the mechanism of producing myocardial ischemia in the face of a restricted coronary vascular reserve, of the amelioration of ischemia, and of the prevention of necrosis all require knowledge of the factors that regulate MVO_2 ; these factors and their relative importance and interactions were summarized in this paper. Early in 1983, I reviewed more recent experimental work on the determinants of myocardial oxygen consumption, and related the results of these physiological studies to clinical problems in ischemic heart disease.⁶

"This work on MVO_2 resulted in my receiving the Research Achievement Award of the American Heart Association in 1972."

1. Sarnoff S J, Braunwald E, Welch G H, Jr., Case R B, Stainsby W N & Macruz R Hemodynamic determinants of oxygen consumption of the heart with special reference to the tension-time index. *Amer. J. Physiol.* 192:148-56, 1958. (Cited 1,140 times since 1958.)
2. Braunwald E, Sarnoff S J, Case R B, Stainsby W N & Welch G H, Jr. Hemodynamic determinants of coronary flow: effect of changes in aortic pressure and cardiac output on the relationship between myocardial oxygen consumption and coronary flow. *Amer. J. Physiol.* 192:157-63, 1958.
3. Braunwald E, Ross J, Jr., Frommer P L, William J F, Jr., Sonnenblick E H & Gault J H. Clinical observations on paired electrical stimulation of the heart: effects on ventricular performance and heart rate. *Amer. J. Med.* 37:700-11, 1964.
4. Sonnenblick E H, Ross J, Jr., Covell J W, Kaiser G A & Braunwald E. Velocity of contraction as a determinant of myocardial oxygen consumption. *Amer. J. Physiol.* 209:919-27, 1965. (Cited 325 times.)
5. Rude R E, Muller J E & Braunwald E. Efforts to limit the size of myocardial infarcts. *Ann. Intern. Med.* 95:736-61, 1981.
6. Braunwald E & Sobel B E. Control of myocardial oxygen consumption. (Braunwald E, ed.) *Heart disease*. Philadelphia: W. B. Saunders, 1983. p. 1235-57.