

Neely J R, Liebermeister H, Battersby E J & Morgan H E. Effect of pressure development on oxygen consumption by isolated rat heart.  
*Amer. J. Physiol.* 212:804-14, 1967.  
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This paper describes the first published technique for perfusing isolated hearts of small animals under conditions where they perform external mechanical work. It also describes the contributions of pressure and volume work on total rates of oxygen consumption by rat hearts. [The SCI® indicates that this paper has been cited in over 590 publications.]

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April 17, 1987

In 1895 O. Langendorff published his very classic paper<sup>1</sup> on the perfusion of isolated hearts by antigrade flow of a physiological salt solution down the cannulated aorta. Various modifications of this procedure are still in use, and they are commonly referred to simply as the "Langendorff procedure," the meaning of which is clearly understood by investigators of cardiac metabolism. This isolated heart preparation continued to beat but was assumed to be nonworking because no provision was made for flow of fluid into the ventricles; therefore no fluid was pumped out by the left ventricle.

In the mid-1960s, James R. Neely started working as a graduate student in the laboratory of Howard E. Morgan of

the Department of Physiology at Vanderbilt University. Morgan perceived the experimental need for a system that allowed perfusion of isolated hearts from small animals under conditions where they performed physiologically relevant mechanical work. At the time, experiments on cardiac function, or studies relating mechanical function to cardiac metabolism, were usually performed in dogs, an expensive and time-consuming procedure. Morgan designed, and he and Neely worked through, many modifications of an isolated working heart preparation for rat hearts. The final design that was published allowed heart rate, ventricular preload and afterload, and cardiac output to be accurately controlled and varied over a wide range. Because it is an isolated tissue that is perfused with a physiological salt solution, the availability of substrates, hormones, oxygen, and drugs can be precisely controlled, and the cells receive these compounds from their own capillary beds. This preparation has proven to be a highly useful tool for studies on alterations of mechanical function of the heart,<sup>2</sup> the relation between mechanical function and metabolism,<sup>3,4</sup> and the effects of various pathological conditions,<sup>5</sup> hormones, drugs, and other agents on cardiac function and metabolism.

When first submitted to the *American Journal of Physiology*, the paper was not accepted for publication. After two attempts, the reviewers were finally convinced that the paper might make a contribution. The technique is currently in use by several investigators around the world and in many cases is referred to only as "the isolated working heart."

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3. Morgan H E, Chua B H L, Fuller E O & Siehl D. Regulation of protein synthesis and degradation during *in vitro* cardiac work. *Amer. J. Physiol.* 238:E431-E442, 1980. (Cited 55 times.)
4. Kobayashi K & Neely J R. Mechanism of pyruvate dehydrogenase activation by increased cardiac work. *J. Mol. Cell. Cardiol.* 15:369-82, 1983.
5. Rovetto M J, Whitmer J T & Neely J R. Comparison of the effects of anoxia and whole heart ischemia on carbohydrate utilization in isolated, working rat heart. *Circ. Res.* 32:699-711, 1973. (Cited 255 times.)