

This Week's Citation Classic™

Ople L H. Metabolism of the heart in health and disease. Part I.

Amer. Heart J. 76:685-98, 1968.

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The major fuels for the normal human heart are free fatty acids in the fasted state and glucose in the fed state. During hypoxia, glucose metabolism is accelerated with the production of lactate (anaerobic glycolysis). When lactate accumulates or when the intracellular pH falls, glycolysis may be limited. During hypoxia, products of lipid metabolism, such as triglycerides, accumulate and these might have harmful effects. The state of oxygenation therefore profoundly affects myocardial metabolism. [The SCI® indicates that this paper has been cited in over 220 publications since 1968.]

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"My interest in myocardial metabolism was awakened by Sir John McMichael, previous director of the department of medicine at the Hamersmith Royal Postgraduate Medical School, in 1959. He pointed out: 'When the heart fails, the anatomy looks the same, but something has gone wrong with the chemistry.' In a flash of enthusiasm I realized that not only congestive heart failure, but drug action and many clinical aspects of heart function were ultimately going to be explained by myocardial metabolism. I avidly began to read about the subject but could find no suitable review reference material except for two: Olson and Schwartz reviewed basic science in *Medicine* in 1951,¹ and Richard Bing described human heart metabolism in *Circulation* in 1955.² The field was clearly developing, as shown by Bing's Harverian Oration to the New York Academy of Sciences in 1946, so it seemed to me before any extensive research work should be undertaken that existing knowledge required gathering and analysis. That decision was made in 1960 when I was a research fellow at Harvard Medical School.

"The review took much longer to write than I had anticipated, and it only began to look like something reasonable in 1966 while I was working with Sir Hans Krebs in biochemistry at Oxford University, England. However, Sir Hans pointed out that the review was still not ready and required even more work. Consequently, I had grave doubts about the academic quality of the proposed publication, which was not completed until I was working with Sir Ernst Chain (like Krebs, also a refugee from Nazi Germany and, like Krebs, also a Nobel prizewinner). By now the review was becoming more solid and Chain encouraged me to proceed. The *American Heart Journal* accepted it at once.

"I believe the article was a success for four reasons. First, my article was among those which led clinical cardiologists to see, as Sir John had emphasized, that the way the heart muscle functioned was more important than the way it looked. Secondly, it was written at a time when there was an enormous amount of new work in the area of human heart metabolism (Bing at Detroit)² and in glucose and fatty acid metabolism of the heart, coming especially from the units of Howard Morgan³ at Nashville and Philip Randle⁴ at Cambridge. Thirdly, because of the very high standards of Krebs and Chain, I had to go to great lengths to establish that the article was of the highest possible academic standard. The ultimate product was therefore accepted not only by cardiologists but also by biochemists and physiologists as a standard reference. I should add a fourth reason for the success of the article—namely, that the *American Heart Journal* had the foresight to publish what was basically an *avant-garde* subject at that time and thereby brought the subject of myocardial metabolism to the attention of the cardiological community as a whole.

"My interest in myocardial metabolism has served as a basis for my forthcoming book entitled *The Heart: Physiology, Metabolism and Pharmacology*.⁵ The fascinating relationship between cardiac metabolism and mechanics is well explored in the book *Cardiac Metabolism*,⁶ edited by Angela Drake-Holland and Mark Noble. Myocardial metabolism is now largely concerned with the regulation of calcium ion movements and, therefore, with contractility; hence, it is a subject that continues to be fundamental to modern cardiology."

1. Olson R E & Schwartz W B. Myocardial metabolism in congestive heart failure. *Medicine* 30:21-41, 1951.
2. Bing R J. Metabolism of the human heart. *Circulation* 12:635-47, 1955.
3. Morgan H E, Henderson M J, Regan D M & Park C R. Regulation of glucose uptake in muscle. *J. Biol. Chem.* 236:253-61, 1961. (Cited 510 times.)
4. Randle P J, Newsholme E A & Garland P B. Regulation of glucose uptake by muscle. *Biochemical J.* 93:652-65, 1964. (Cited 260 times.)
5. Ople L H. *The heart: physiology, metabolism and pharmacology*. New York: Grune & Stratton. To be published, 1984.
6. Drake-Holland A J & Noble M I M, eds. *Cardiac metabolism*. New York: Wiley, 1983. 544 p.