

This Week's Citation Classic

Oliver M F, Kurien V A & Greenwood T W. Relation between serum-free-fatty-acids and arrhythmias and death after acute myocardial infarction. *Lancet* 1:710-15, 1968. [Depts. Cardiology and Clinical Chemistry and Coronary Care Unit, Royal Infirmary, Edinburgh, Scotland]

Elevation of serum-free-fatty-acids (FFA) occurs during acute myocardial ischemia and, when marked, is associated with ventricular arrhythmias. This elevation results from catecholamine-induced lipolysis. Myocardial lipolysis is also increased. Metabolism of excess FFA may increase oxygen consumption in an already ischemic myocardium. [The *SCJ*[®] indicates that this paper has been cited over 250 times since 1968.]

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"There were two origins to the hypothesis that an excess of free-fatty-acids (FFA) might be one of the causes of ventricular arrhythmias during acute myocardial ischemia.

"A laboratory observation made when working in the University of Edinburgh with George Boyd in the middle-1950s on paper electrophoresis of serum lipoproteins was of a fast moving, lipid-rich peak, related to the mobility of albumen, which contained no cholesterol or phospholipid. This was frequently present in patients with acute myocardial infarction (MI) and never in those with previous MI or angina pectoris. A conceptual question which later interested me was what is the relationship between available myocardial energy and the intrinsic development of ventricular arrhythmias? One possibility was that the ionic disequilibrium initiating VF is entirely related to reduced coronary blood flow and is independent of substrate availability—the arrhythmia, once

initiated, would rapidly use up substrate to the point of exhaustion. The other, which formed the basis of the hypothesis, was that potentially lethal ven-tricular arrhythmias might be initiated and perpetuated by an uneconomic excess of one or more of the sources of myocardial energy. The obvious choice, in a situation where there is an excess of catecholamines, such as a heart attack, was FFA.

"In 1965, Abraham Kurien, who had in-dependently been measuring 'lip-albumen,' and I showed¹ that serum FFA levels were significantly higher in patients with acute MI compared with those with acute renal colic and those with cerebral thrombosis. It was then a simple step to examine the relationship of raised serum FFA with the in-cidence of serious ventricular arrhythmias during an acute heart attack. The observa-tion that arrhythmias were significantly more frequent and that there are more deaths when plasma FFA exceed a 2:1 molar binding ratio with albumen (approximately 1200 u eq/l) is the subject of this *Citation Classic*.

"I believe that the 1968 paper has been frequently cited because it was the first that provided factual evidence pointing to a fun-damental metabolic disturbance during acute myocardial ischemia in man. It also provided the basis for the subsequent hypothesis² that an excess of peripheral and myocardial FFA can lead to increased myocardial oxygen requirements (subse-quently demonstrated)³ and that an acute energy crisis in the ischemic myocardium can lead to the development of lethal re-entry arrhythmias. Later, we showed that pharmacologic⁴ reduction of peripheral and myocardial lipolysis decreased the inci-dence of ventricular arrhythmias in patients with MI. Lipid-free albumen reduces experi-mental ischemia⁵ and anti-lipolytic treatment reduces the extent of myocardial ischemia in patients."⁶

1. **Oliver M F & Kurien V A.** Serum-free-fatty-acids after acute myocardial infarction and cerebral vascular occlusion. *Lancet* 2:122-7, 1966.
2. **Kurien V A & Oliver M F.** A metabolic cause for arrhythmias during acute myocardial hypoxia. *Lancet* 1:813-15, 1970.
3. **Mjøs O D.** Effect of free fatty acids on myocardial function and oxygen consumption in intact dogs. *J. Clin. Invest.* 50:1386-9, 1971.
4. **Rowe M J, Neilson J M M & Oliver M F.** Control of ventricular arrhythmias during myocardial infarction by antilipolytic treatment using a nicotinic-acid analogue. *Lancet* 1:295-300, 1975.
5. **Miller N E, Mjøs O D & Oliver M F.** Relationship of epicardial ST segment elevation to the plasma free fatty acid/albumin ratio during coronary occlusion in dogs. *Clin. Sci. Mol. Med.* 51:209-13, 1976.
6. **Russell D C & Oliver M F.** Effect of antilipolytic therapy on ST segment elevation during myocardial ischaemia in man. *Brit. Heart J.* 40:117-23, 1978.