This Week's Citation Classic®

Schamroth L, Krikler D M & Garrett C. Immediate effects of intravenous verapamil in cardiac arrhythmias. *Brit. Med. J.* 1:660-2, 1972.
[Baragwanath Hospital and University of the Witwatersrand, Johannesburg, South Africa and Cardiac Department, Prince of Wales's Hospital, London, England]

One hundred eighty-one patients with cardiac arrhythmias received verapamil by intravenous injection. No adverse clinical side effects were noted. Favourable responses occurred in some patients. [The *SCI*® indicates that this paper has been cited in over 305 publications.]

Leo Schamroth
Department of Medicine
University of the Witwatersrand
Johannesburg 2192
South Africa

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In 1969 the director of Knoll Pharmaceutical Company in Johannesburg invited me to do a clinical research trial on verapamil, which was designated as another beta-blocking agent. At that stage I had already completed three such trials with different beta-blocking agents and was reluctant to embark upon another. However, he doggedly persisted with his request so that after three months I reluctantly agreed to test verapamil.

The trial was designed to test the immediate effects of intravenous verapamil on patients with atrial fibrillation. After I tested three patients, it became abundantly clear that verapamil was not a beta-blocking agent but a different class of drug. Verapamil displayed some notable differences from beta-blocking agents, among which were the following: (1) the blocking effect on the atrioventricular (A-V) node was exceptionally powerful, (2) in addition to slowing the ventricular response in atrial fibrillation, it also tended to regularize the ventricular rhythm, (3) the side effects were different from those of a beta-blocking agent, and (4) in a few cases where the verapamil was administered to patients with sinus rhythm, the bradycardic effect was not nearly as marked as that which occurred with beta-blocking agents; in fact it was barely noticeable at most times.

A pilot study of 20 patients with atrial fibrillation was carried out. This confirmed the profound effect of verapamil in blocking the A-V node. It was, in fact, the strongest A-V blocking effect I had yet encountered. This prompted me to test the drug in a few cases of reciprocating tachycardia due to the Wolff-Parkinson-White syndrome, again with remarkable effect. The tachycardia was aborted before the intravenous injection of verapamil had been completed.

The original paper was submitted to *Diseases of the Chest* (now called *Chest*) and would have been the first paper published in the North American literature on a calcium channel blocking agent. The paper was, however, rejected by the referee on the following grounds: (1) there is no such thing as a calcium channel blocking agent, and (2) digitalis acts in precisely the same manner—this, despite the fact that all 20 of the original cases were fully digitalised, and the effect was clearly over and above that of digitalis.

The eventual publication of the paper in *Cardiovascular Research*[1] stimulated another, more comprehensive trial that became the *Citation Classic*. This heralded a new therapeutic era with numerous studies of verapamil in many clinical conditions. Verapamil is now of major importance in the treatment of hypertension, angina pectoris, any arrhythmia where a blocking effect on the A-V node is desired (atrial flutter and fibrillation reciprocating tachycardia), and hypertrophic cardiomyopathy.

[See reference #2 for a recent review in this field.]

1. **Schamroth L.** Immediate effects of intravenous verapamil on atrial fibrillation. *Cardiovasc. Res.* 5:419-24, 1971. (Cited 115 times.)
2. **Nayler W G & Dillon J S.** Calcium-antagonists and their mode of action. An historical overview. *Brit. J. Clin. Pharmacol.* 21:S97-107, 1986.

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