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This Week's Citation Classic™

Wolfson S, Heinle R A, Herman M V, Kemp H G, Sullivan J M & Gorlin R.
Propranolol and angina pectoris. *Amer. J. Cardiol.* **18**:345-53, 1966.
[Cardiovascular Res. Lab., Dept. Medicine, Harvard Med. Sch. and Peter Bent Brigham Hosp., Boston, MA]

Propranolol was administered orally to 37 patients with severe angina pectoris, producing a favorable clinical response in 81 percent. The mechanism of action of the drug was studied at the time of diagnostic catheterization in 13 patients. Propranolol induced reductions in heart rate and indices of left ventricular mechanics, with an accompanying reduction in coronary blood flow and myocardial oxygen consumption. No clinical effect was demonstrable when propranolol was given orally to patients with noncoronary chest pain syndromes. [The *SCI*® indicates that this paper has been cited in over 190 publications since 1966.]

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"The cited paper reported the first study in the US of a beta-adrenergic blocking agent as an antianginal drug. It presented a combination of a clinical study and a basic evaluation of the effects of intravenous propranolol upon hemodynamics, coronary flow, and myocardial oxygen consumption in patients during the course of cardiac catheterization. These data were then integrated into a hypothesis which attempted to explain how such agents might be of benefit to patients with coronary artery disease.

"This paper laid the groundwork for much of the subsequent work both with adrenergic blocking agents and other approaches to angina pectoris by the avenue of decreasing myocardial oxygen demand. A recent review has discussed the extension of this approach to the prevention of infarction.[1] The study was successful because of a combination of hard work, the foresight of my mentor, Richard Gorlin, and the timing of the first international symposium on propranolol in November 1965. I arrived in Gorlin's laboratory as a cardiology fellow in July 1965, with the background of having performed a study of pronetholol (a precursor of propranolol) for the treatment of cardiac arrhythmias during my internship and junior residency.[2] The Gorlin laboratory had in the years previous to this developed techniques for studying coronary blood flow, hemodynamics, and myocardial metabolism.[3] Gorlin foresaw the utility of the beta-adrenergic blocking agents for the treatment of angina pectoris, and saw in me a trainee with great reserves of energy. July and August 1965 became a blur of activity. Nearly every patient catheterized for diagnostic purposes received propranolol as an investigative tool. As a result, when an invitation was received to present data at the symposium in November, to be held in Great Britain, we had already accumulated a considerable amount of clinical and basic data. These were then included in a symposium issue of the *American Journal of Cardiology* the following year.

"The work was the result of an effort coordinated by Gorlin which included the fellowship cadre at that time, the entire laboratory staff, and even extended to my family. One question which we considered was the possibility that propranolol, which had local anesthetic properties, might ameliorate anginal symptoms because of analgesic effects. When discussing this question at home one evening, my wife suggested that we try the drug in patients who had pain syndromes that were not related to coronary artery disease. As I brought this suggestion to Gorlin the following morning, his reply was to set up a controlled trial in patients with chest pain syndromes but normal coronary arteries. The group of subjects became known in the laboratory as the 'Susan Wolfson Series.' The results were edifying because the great majority of patients with coronary artery disease encountered relief of their anginal symptoms with the drug. Very few of the patients with chest pain syndromes and normal coronary arteries had any clinical effect from propranolol.

"As I look back on the two years that I spent with Gorlin, they glow in recollection. He was a stimulating, exciting, coordinating force in directing our research and our education. I have seldom met a more dedicated, brilliant, supportive, and cooperative group of men than my fellow trainees in that laboratory. These factors and the good fortune which dictated that they came together at the right time led, I believe, to the development of a *Citation Classic*."

1. **Braunwald E, Muller J E,*Kloner R A & Maroko P R.** Role of beta-adrenergic blockade in the therapy of patients with myocardial infarction. *Amer. J. Med.* **74**:113-23, 1983.
2. **Wolfson S, Robbins S I & Krasnow N.** Treatment of cardiac arrhythmias with beta-adrenergic blocking agents. *Amer. Heart J.* **72**:177-87, 1966.
3. **Krasnow N, Neill W A, Messer J V & Gorlin R.** Myocardial lactate and pyruvate metabolism. *J. Clin. Invest.* **41**:2075-83, 1962. (Cited 135 times.)

