

# The Wild Ride: Cardiology and Clinical Pharmacy 1967–2005

Larry M Lopez

It was Spring 1985, during my fifth year as a University of Florida College of Pharmacy faculty member, when an editorial was published that turned my world upside down.<sup>1</sup> It was entitled “Are  $\beta$ -Adrenergic Blocking Drugs Useful in the Treatment of Dilated Cardiomyopathy?” and it contradicted everything I taught and had been taught about the pharmacology of  $\beta$ -blockers and the pathogenesis of heart failure. It was widely known and accepted then that a  $\beta$ -blocker was contraindicated in patients with dilated cardiomyopathy as a consequence of its well-known negative inotropic effects. The editorial suggested quite the opposite, however, and after reading it, I remember thinking, “This could actually work!!” The rest, as they say, is history.

The results of the US Carvedilol Heart Failure Trials Program were published in 1996,<sup>2</sup> followed shortly thereafter by comparable clinical trials documenting the usefulness of metoprolol and bisoprolol in the management of heart failure. The results of these trials, together with those of the DIG (Digitalis Investigation Group) trial<sup>3</sup> and the numerous angiotensin-converting enzyme (ACE) inhibitor trials,<sup>4,5</sup> resulted in a profound change in how these patients were managed with pharmacotherapy.

This editorial was published when *The Annals*, at that time, *Drug Intelligence and Clinical Pharmacy*, was 18 years old, founded in 1967—the same year that propranolol was approved by the Food and Drug Administration as the first  $\beta$ -adrenergic blocking agent. When I reflect now on how far we have come since the first issue of *Drug Intelligence* was published, I am humbled and astounded.

What was the state of the art of cardiology in 1967 as it related to clinical pharmacy practice? Considering that there really was no clinical pharmacy practice then, any relation to cardiology would have to be considered a fairy tale. What about cardiovascular pharmacotherapy itself? At that time, use of nitroglycerin in the setting of acute

myocardial infarction was considered contraindicated due to the associated reflex tachycardia. Reduction of elevated blood pressure was still not universally accepted as beneficial, since the first of the landmark Veterans Affairs clinical trials documenting these benefits was still 3 years in the future. When a patient was treated for hypertension, (s)he might receive chlorothiazide, methyldopa, or a combination product such as hydrochlorothiazide/ spironolactone or reserpine/hydralazine/hydrochlorothiazide. By 1985, at least there were guidelines for use of anticoagulants and management of hypertension, and the choice of medications to manage hypertension had expanded to include ACE inhibitors and calcium antagonists.

Today there are guidelines for treating stable angina, heart failure, atrial fibrillation, acute coronary syndrome, acute myocardial infarction, and hyperlipidemia, in addition to those for managing hypertension and anticoagulation. The necessity for this plethora of guidelines was due, at least in part, to the profound increase in the number and types of cardiovascular agents that have been developed over the past 40 years. A partial list of these includes the antiplatelet agents (ticlopidine, clopidogrel, the glycoprotein IIb/IIIa inhibitors), low-molecular-weight heparins, thrombolytic agents, direct thrombin inhibitors, and finally, low-dose aspirin, which emerged as a cornerstone of both prophylaxis and treatment of coronary artery disease.

What about the future? I urge readers to proceed with care, given that I previously predicted that carvedilol would never be approved for management of heart failure. Nevertheless, a few tentative predictions seem reasonable. First, I believe that cardiovascular pharmacotherapy will continue to expand both outwardly and inwardly. Outwardly, both new agents and “me-too” ones will continue to be released as our understanding of the pathogenesis of cardiovascular disorders continues to advance. A good example of this phenomenon is the recent development of levosimendan, which is based, in part, on an expanded understanding of the physiology of calcium in the failing myocardium.

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Author information provided at the end of the text.

Inwardly, our ability to individualize pharmacotherapy of cardiovascular disorders will very likely be enhanced by advances in the infant field of pharmacogenomics. With the recent characterization of the human genome, it has been estimated that upwards of 4000 new drug entities will result, and it is likely that new cardiovascular agents will represent a prominent proportion of these. In addition, the role of pharmacists in management of cardiovascular disorders will continue to grow. In my view, this increased role of pharmacy practice in the care of patients with cardiovascular disorders will be borne predominantly by community pharmacists, some with specialized training, and all of whom will be reimbursed for their care of these patients by virtue of their having earned provider status. Finally, self management of cardiovascular disorders by patients will grow, driven largely by pharmacoeconomic forces. Of necessity, however, the number of patients who self manage their cardiovascular problems will likely remain small, especially when compared with the overall population of patients with these disorders.

If the changes in cardiovascular clinical pharmacy over the past 40 years are in any way indicative of the pace of changes for the next 40 years, those of you who will be a

part of this are in for some exciting times. My advice to you is to hang on and enjoy the ride.

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