

EDITOR'S PAGE



## PCSK9: Is it Fluoride for Cardiology?



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When I first came to Emory in the 1960s, we had a medical school and a dental school. Now there is just the medical school. What happened to the dental school? The Emory Dental School, along with several others across the country, closed because of a reduced demand for dentists. Why? Fluoride! The bread and butter of dentistry when I was a child was filling cavities. With the introduction of fluoridation in the water and in the toothpaste, there was a dramatic reduction in dental cavities and in the need for dentists to fill them. Is there a lesson in this for cardiology, and especially for interventional cardiology?

At the European Society of Cardiology meeting in Barcelona, there were many interesting trials, although the number of true practice-changing developments was few. Perhaps there was 1 big development in heart failure. The thing that caught my attention, however, was not the interventional trials, but was the updates on the continuing evolution of the various monoclonal antibodies to PCSK9. This class of drug produces marked reductions of low-density lipoprotein (LDL) in addition to aggressive statin therapy. The studies reported were phase II mechanistic and safety studies, but they consistently showed almost 60% LDL reduction, with increases in high-density lipoprotein and a significant reduction in lipoprotein(a). Whether these efforts will translate into clinical benefit is now being investigated in 3 large phase III trials by 3 different pharmaceutical companies. It is interesting in the context of the recent American College of Cardiology/American Heart Association guidelines, in which the LDL value is not emphasized but rather the use of moderate- to high-dose statins determined by the patient's risk profile. These recommendations, developed from the hard clinical trial data, contrast sharply with the European Society of Cardiology approach, which is still placing emphasis on obtaining LDL targets. Much of

the discussion at the European Society of Cardiology meeting focused on how low these targets should be, but with the addition of agents acting on PCSK9, very low targets are possible even for patients with familial hypercholesterolemia. The phase II trials seem to point to very few adverse effects of this aggressive approach. There was understandable excitement about these agents, even though they have to be given by injection twice or perhaps only once a month. But, have we seen this movie before? When statins were introduced, Brown and Goldstein predicted the demise of atherosclerosis. When torcetrapib raised the protective high-density lipoprotein to stratospheric levels, we thought it would be the demise of the lipid-laden plaque. Statins have indeed reduced cardiovascular events, but torcetrapib was a flop. Will a return to primordial lipid values stabilize atherosclerosis and eliminate cardiovascular events? I have no idea, but it strikes me that interventional cardiologists must pay close attention to whether advances in medical therapy may make cardiac events rare, therefore making interventions to prevent those events rarely needed as well. Is "fluoridation" for cardiology on the way? Will interventional cardiologists be out of work? Will as many need to be trained? What happened to our dental colleagues? Well, as those of you who have been to the dentist lately have seen, they do not seem to be suffering much. True, they do not need to fill all of those cavities, but there is plenty for them to do even if much of it is cosmetic. I do not think cosmetic angioplasty is going to work for us (although we are accused of it by some). But, before we close our interventional training programs, we might reflect on what is going on in our catheterization laboratories. Perhaps Emory University Hospital is not representative, but one-half of the cases performed last year were not coronary cases. When interventional cardiology boards were developed 16 years ago, we were working hard

to justify a few questions on structural heart disease, and peripheral vascular questions were prohibited. For fellows-in-training now, structural and peripheral cardiovascular disease issues are prominent. This is indeed an exciting time, as it takes me full circle back to my catheterization laboratory training, which was entirely composed of cases of congenital heart disease, rheumatic heart disease, and acquired adult structural and myocardial disease. Coronary arteriography was indeed in its infancy.

In this issue of *JACC: Cardiovascular Interventions*, you will see 5 important papers on structural heart disease: 1 each on transcatheter aortic valve replacement (1), patent foramen ovale closure (2), alcohol ablation for hypertrophic cardiomyopathy (3), atrial appendage closure (4), and percutaneous pulmonary valve implantation (5). Interventional cardiologists

are evolving into a new breed. Do I really believe that coronary artery disease will be cured and cardiac events will be eliminated? Of course not. We will cheer for improvements in medical therapy and, as they occur, interventions for those conditions will decrease. At least they will decrease if age-adjusted, but with the aging population, do not expect this reduction to be dramatic. Meanwhile, we must evolve with the technology that enables minimally-invasive approaches to structural heart disease. New therapies for mitral regurgitation are on the cusp, and those for heart failure are not far behind.

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