

**Foreword****From the editor: Lessons from the East**

A momentous study presented at the recent American Heart Association meeting in Chicago, Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention trial (REDUCE-IT), showed 25% reduction of major cardiovascular events among approximately 8000 statin-treated patients with high triglycerides and LDL cholesterol under 100 mg/dL.<sup>1</sup> This result might impress us as the first solid evidence for an effective lipid treatment strategy targeting something other than LDL. After some prominent failures over the past 10 years, it feels good to celebrate success. But we should not think that REDUCE-IT provides the first positive evidence. The drug employed in REDUCE-IT, purified ethyl esters of eicosapentaenoic acid (EPA ethyl esters, now with a new name of icosapent ethyl), already had achieved success when results of Japan EPA Lipid Intervention study (JELIS) were published in 2007.<sup>2</sup> JELIS was a mixed primary and secondary prevention trial among 18,645 subjects all taking low dose statins. Major coronary events were reduced significantly by 19%.

JELIS was led from Kobe, Japan. Another discovery, lest we forget, happened during the 1970s in Tokyo. Akira Endo isolated the first statin, now called mevastatin, from the culture broth of one of approximately 6000 microbial strains.<sup>3</sup> In the late 1960s, Endo had traveled across the globe to gain experience in cholesterol biochemistry, spending 2 years as a research associate at the Albert Einstein College of Medicine in New York City. Today the Akira Endo Award of the Foundation of the NLA is given triennially to “to recognize those responsible for the development of new therapies documented to prevent cardiovascular disease and atherosclerosis.” Recipients in 2018 were Jonathan Cohen from UT Southwestern in Dallas and Nabila Seidah of the Clinical Research Institute of Montreal, both for elucidating PCSK9.

Let us reflect on the fact that prevention of atherosclerotic cardiovascular disease is a worldwide collaborative effort. As international barriers ratchet up in several ways today, medical research still transcends borders with an ethic of collegiality to the benefit of all. Broad international contributions to this journal will be obvious if you simply scan through the articles.

In this issue, the Roundtable and a review focus on lipoprotein(a), a proven atherosclerotic risk factor that might soon become amenable to effective pharmacologic

therapy.<sup>4,5</sup> Blackett, George, and Wilson provide a road-map that combines lipid management with 6 other metrics to implement cardiovascular prevention in pediatric practice.<sup>6</sup> Sniderman et al show how apolipoprotein B measurement combined with a regular lipid panel can diagnose type III hyperlipoproteinemia. They suggest that screening by this method could expand the number of type III cases identified—an important concept because remnant particles in type III are considered more atherogenic and differently responsive to treatment compared to VLDL and LDL in routine combined hyperlipidemia.<sup>7</sup> Steffen et al draw a surprising conclusion from analysis of plasma phospholipid fatty acids in the Multi-Ethnic Study of Atherosclerosis. Higher levels of oleic acid were associated with increased risks of heart failure and total mortality. The authors caution that their results require confirmation in other population groups and, importantly, should not be extrapolated to impugn dietary intake of oleic acid.<sup>8</sup> Antioxidant activity of HDL has been studied up to now only with isolated lipoprotein fractions. Swertfeger et al asked whether antioxidant activity of HDL can be studied in the presence of blood plasma, akin to the use of apolipoprotein B-depleted plasma to assess HDL-mediated cholesterol efflux. They find that other plasma antioxidants including albumin and other proteins, uric acid, and ascorbic acid overwhelm the contribution of HDL, which is only 1%–2% of total plasma antioxidant activity. These results will need to be considered whenever HDL is viewed as an antioxidant.<sup>9</sup>

One more word about Japan. Begin today your plans for a 2021 trip to the next International Symposium on Atherosclerosis in Kyoto!

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