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Oxidative Stress: Introduction

IN THIS SYMPOSIUM we have heard about a number of issues regarding oxidative stress. These include: (1) How is it measured? (2) How is it related to glycosylation and glycemia? (3) Do different types of therapy have differential effects on oxidative stress?

The answers to these questions are: (1) In several ways (Betteridge); (2) Both to chronic glycemia (advanced glycosylation end products, Brownlee) and acute increases in glycemia (Ceriello); (3) Yes (Noda, Renier, and Jennings).

These answers are found in reviews presented in this symposium. A more central issue, however, is do we need "oxidative stress" given the recent advances in therapy in diabetes for lipid reduction in the Scandinavian Simvastatin Survival Study (4S),[1] glycemic control in the United Kingdom Prospective Diabetes Study (UKPDS),[2,3] and blood pressure reduction in the UKPDS.[4,5] Nevertheless, there are a number of reasons to avoid complacency and to seek to examine possible new interventions. In middle-aged, diabetic subjects without vascular disease, the rate of coronary heart disease is similar to nondiabetic subjects with vascular disease.[6] In the recently published follow-up of the National Health And Nutrition Examination Survey (NHANES) in the United States (Fig 1),[7] while coronary artery disease decreased in nondiabetic subjects, there was no decrease in diabetic subjects and perhaps even an increase in coronary heart disease (CHD) in diabetic women. Even the most successful intervention for CHD in diabetic subjects (lipid reduction in the 4S study[1]) reduced CHD only by approximately 50%. The benefits of glycemic control on CHD were more modest and may be dependent on the type of hypoglycemic agent used.[2,3]

Strategies to reduce oxidized low-density lipoproteins (LDL) would appear to be a promising target. Oxidized LDL is increased in subjects with diabetes[8,9] and oxidized LDL has been shown to enter the arterial wall although "native" (or unmodified) LDL does not. A detailed review of the problem of oxidative stress is the focus of this symposium.

Steven M. Haffner, MD
Professor of Medicine
University of Texas Health Science Center
San Antonio, TX
Guest Editor

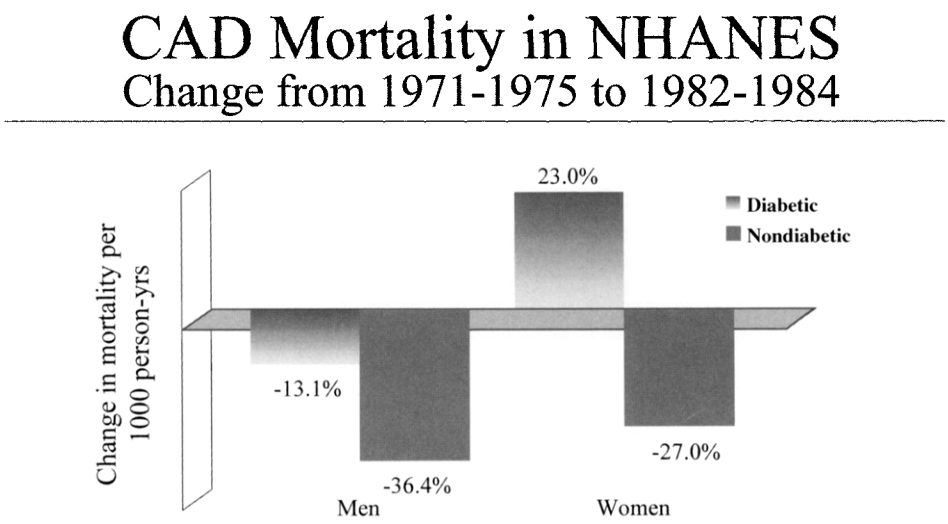

Fig 1. Coronary artery mortality in the NHANES. Modified and reprinted with permission.[7]

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