Glycation and Oxidation in Age-related Diseases

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The processes of glycation and oxidation have been shown to be closely linked and contribute to the ageing process. Glucose initially reacts with protein to form reversible early glycation products. Glycoxidation is the later stage of glycation in which the reversible Schiff base proceeds to stable covalently bonded Amadori rearrangement products. Amardori products then undergo further rearrangement reactions to produce a heterogeneous group of protein bound moieties called advanced glycation endproducts (AGE). The formation of AGE is accelerated by oxidative stress and by decreased renal clearance of these products. The accumulation of AGE on tissue proteins has been implicated in the ageing of proteins and the progression of chronic, age-related diseases, such as atherosclerosis, diabetes mellitus, chronic renal failure and Alzheimer's disease. The formation and accumulation of AGE on long-lived proteins affects the structure and function of proteins, enhances cytokine production and activates transcription factors via binding to specific receptors (eg. the receptor for AGE).

Hyperglycaemia significantly increases the formation of AGE. Elevated serum concentration of AGE in patients with type 2 diabetes mellitus is associated with endothelial dysfunction independent of other cardiovascular risk factors and contributes to the pathogenesis of diabetic complications. To determine whether increased oxidative stress is also associated with enhanced formation of AGE, serum AGE concentration has been determined in a group of patients with obstuctive sleep apnea (OSA), a condition associated with increased oxidative stress. The repeated episodes of upper airway obstruction during sleep lead to significant hypoxia and the hypoxia/reoxygenation leads to alteration in oxidative balance through the induction of excess oxygen free radicals. Serum concentration of AGE in patients with OSA was intermediate between that of a group of healthy age-matched controls and that of a group of type 2 diabetic patients. Serum concentration of AGE correlated with respiratory disturbance index, suggesting that increased oxidative stress in patients with OSA might also increase the formation of AGE.