

## Review Article

### Below the Radar:

### Advanced Glycation End Products that Detour “around the side”

*Is HbA<sub>1c</sub> not an accurate enough predictor of long term progression and glycaemic control in diabetes?*

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#### **Abstract**

Advanced glycation is the irreversible attachment of reducing sugars onto the free amino groups of proteins. Its physiological roles are thought to include the identification of senescent proteins and hence there is a time dependent accumulation of advanced glycation end products (AGEs). AGE labelled proteins are catabolised by cells into low molecular weight peptides and amino acids and excreted primarily via the kidneys. This process appears to be tightly controlled by AGE clearance receptor complexes containing AGE-R1, AGE-R2 and AGE-R3 and scavenger receptors such as CD36, SR-AII and SR-BI. Conditions such as diabetes, however, which have a metabolic overload of reducing sugars, rapidly accelerate AGE formation. In addition, advanced glycation is facilitated by oxidative stress and renal disease even in the absence of increases in reducing sugar concentrations. As part of our western diet, we also ingest AGEs of which approximately 50-80% are absorbed, catabolised and excreted over a period of two days. As AGE levels rise during diabetes, interruption of normal function occurs via three distinct mechanisms, namely AGE induced cross-linking of extracellular matrices, stiffening elastic fibres, disturbing cellular adhesion and preventing turnover. The second is by intracellular formation of AGEs, which causes generalised cellular dysfunction. The third is via the chronic activation of specific receptors such as RAGE, the receptor for advanced glycation end products, which produces excesses in inflammatory molecule production. Due to the range of dysfunction produced by the accumulation of AGEs in diabetes, there is a growing need for early recognition and intervention in this process.