AGE-modified proteins are believed to represent tissue damage at the molecular level. Establishing the chemical structures of these heterogeneous and sometimes labile compounds has proven difficult, but it is generally agreed that one effect of AGEs is protein crosslinking, which results when an initially glycated protein reacts with a second protein[5–7]. These products probably lie on an important route to diabetic complications. In one of the several proposed pathways, glucose-induced crosslinking of collagen increases tissue stiffness, which may lead directly or indirectly to kidney failure.

For all that it is incompletely understood, the glycation pathway nonetheless provides opportunities for tackling the damage process that occurs during normal and diabetic ageing. For example, aminoguanidine, an analogue of the side chain of arginine, can trap the initial glycation adducts, thus preventing AGE formation[8]. Aminoguanidine is an effective treatment for animal models of diabetic complication and is being evaluated in humans. But what of damage that has already occurred? This issue matters especially for non-insulin-dependent diabetic patients, who may have sustained glycation damage over a period of many years before their condition was diagnosed.

In the face of incomplete knowledge of the chemical structures of the crosslinked products of glycation, Vasan *et al.*[1] based their approach to tackling such damage on a reasonable estimation of what might be happening (see figure). The diagram depicts two plausible ways (*a* and *b*) in which an intermediate containing two adjacent carbonyl groups might complex with amino-acid side chains to form intermolecular crosslinks. In *b*, this diketone structure is still present in the final crosslink.

Working on this assumption, Vasan *et al.* went on to synthesize *N*-phenacylthiazolium bromide, a crosslink 'breaker' that can cleave the diketone bridge, which they first tested on small-molecule models. In further experiments, crosslinking of collagen in diabetic rat-tail tendon, a commonly used indicator of glucose-induced damage, could be largely eliminated by treatment *in vitro*. Finally, *in vivo* administration of the crosslink breaker to diabetic rats resulted in release of up to half of the immunoglobulin attached to the surface of circulating red blood cells; as AGE-immobilized immunoglobulins provide a convenient example of protein crosslinking that accumulates at elevated levels in diabetes, this last result provides evidence that the crosslink breaker is active under physiological conditions.

This set of experiments represents a major step forward in our chemical understanding of glucose-induced damage. To the extent that *N*-phenacylthiazolium bromide selectively cleaves diketones, one clear implication of these findings is that much of the crosslinking observed in the aged and diabetic tissue must contain these structures. If the specificity of the reagent is substantiated in further experiments, then these results can be taken as evidence favouring one (*b*) of the two crosslinking mechanisms shown in the figure.

Because *N*-phenacylthiazolium bromide appears to reverse crosslinking in live rats, we now also have evidence that AGE damage is not irreversible. This reagent therefore provides at least the conceptual basis for the design of drugs to reverse damage that has already occurred. But there are important issues that must be considered when attempting to translate these findings into benefits for patients. Long-term toxicity of possible drugs is the most obvious, but more subtle problems, such as antigenicity of the cleavage products, would also have to be considered. Nonetheless, these studies provide real prospects for reversing the effects of abnormally high glucose levels in diabetic patients. These patients are at high risk for glucose-induced damage, so some treatment, even with side-effects, may be better than nothing at all.

Glucose-induced damage is not, of course, unique to diabetic patients: even at normal levels of blood glucose there will be some degree of glycation, and the resulting damage will accumulate over time. Does the prospect of reversing glucose-mediated damage imply that a 'cure' for ageing lies around the corner? Vasan *et al.* report preliminary findings suggesting that their crosslink breaker can disaggregate the amyloid deposits that are a hallmark of Alzheimer's disease. Unfortunately, however, the association of glycation-induced crosslinking with age-related disease processes has only relatively recently come under investigation[9], and we lack a good diagnostic tool for defining patients at highest risk who could be targeted with appropriate medication. So there are high hurdles to be surmounted before reversal of glycation-induced crosslinking can be considered a potential strategy for ameliorating the effects of non-diabetic ageing. □

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DAEDALUS

The highest spin

NATURE invented the principle of the helicopter. For millions of years, her rotating winged seeds, such as those of the sycamore tree, have spun sedately to the ground each autumn. If you could somehow feed spin into a sycamore seed, it would generate lift. It could fly and soar as the simplest possible powered aircraft.

Daedalus now plans to do it. Imagine, he says, a circularly polarized beam of microwaves. Its magnetic vector rotates clockwise (say) at the beam frequency. Now mix it with a beam polarized in the opposite sense, and with a frequency just 10 Hz lower. Its magnetic vector will rotate counter-clockwise at this lower frequency. The two vectors will sum to a resultant which rotates clockwise at the difference frequency of 10 Hz. A magnetic sycamore seed exposed to the mixed beam would follow this rotating field, and would spin at 10 Hz like a little induction motor. So it would fly.

The technology could be very simple. A steerable microwave system would launch an appropriately mixed beam upwards. Its frequency difference would be slowly increased; a bladed ferrite rotor in the beam would begin to spin and would soon take off. As it rose along the beam, it would reflect or re-radiate some of it back to its source. This return would be modulated by the blade frequency, giving a feedback signal to the control system.

Steering this elegant craft will be tricky. Daedalus hopes that by offsetting the beam and polarizing it elliptically in a specific direction, it will tilt the rotor in that direction via the resulting gyroscopic precession. If (like some sycamore seeds) the rotor is almost rotationally unstable, even a small imbalance might do the job. Once the control strategy has been perfected, however, the 'sycacopter' will be free to travel anywhere its beam can reach. It will be able to climb, descend or hover, and stay up indefinitely.

Cheap and simple, sycacopters will get everywhere. Hovering at high altitude, they will replace satellites and masts as relays or reflectors for broadcasting and mobile telephony. Carrying TV cameras (whose circular scan will be provided by their spin), they will let Big Brother snoop wherever he wishes. Sycacopters with sharpened blades and explosive charges will rise into the path of cruise missiles, while versions with polishing mops will clean high windows and the inaccessible statuary of ancient cathedrals. And tiny ones, buzzing with fury, will attack flies, mosquitoes and even swarms of locusts, under manual or radar control: a splendid new way of countering mankind's small and ancient enemies. David Jones