DiabetesDIGEST
The easy way to stay up to date with developments in diabetes

Editorial

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Editor

The "tomato effect"

'Old age is the most unexpected of all the things that can happen to a man!'
Leon Trotsky

In the UK, the vast majority of diabetes specialist clinicians still contribute to looking after acute medical emergencies – the "take" (or "receiving" if you live in Scotland). One advantage of this is that it provides insights into the approaches of other non-diabetes specialists and primary care colleagues to the management of diabetes outside of the specialist arena. It also highlights the conundrums related to applying the results of published clinical trials with multiple inclusion and exclusion criteria to the general population with all of its foibles and nuances. On almost every post-take ward round, one comes across ancient individuals who have been admitted with the unwanted effects of multiple medicines to prevent diseases that they already suffer from (this is a variation of the "tomato effect", which is described below).

Most of diabetes research revolves around the use of surrogate markers, almost invariably HbA_{1c} levels. Although this approach may be useful, it is of significantly less value than hard clinical outcomes that matter to people – death, disfigurement, depression, and so on. The use of surrogate markers to assess the benefit, or otherwise, of a medicine can lead to the so-called tomato effect (Goodwin and Goodwin, 1984). The tomato effect occurs when a highly efficacious therapy for a certain condition is ignored or rejected because it does not "make sense" in the light of accepted theories of disease mechanism and drug action. Its name is derived from the history of the tomato in North America. By 1560, the tomato was a staple of the European diet. However, eating tomatoes in the US was avoided until the 1800s as the population believed them to be poisonous as they are part of the nightshade family. The fact that Europeans were eating tomatoes without harm was thought to be irrelevant (no surprises there then!). An extension of the tomato effect is the perception that because a drug improves a surrogate endpoint (such as lowering glycaemia) then it must have a clinical benefit. The diabetes literature contains many examples of the tomato effect (the UKPDS being an example: Shaughnessy and Slawson, 2003).

The results of the ACCORD (Action to Control Cardiovacular Risk in Diabetes) study have also highlighted a possible tomato effect (ACCORD Study Group, 2008). Blood glucose lowering agents lower blood glucose; lowering blood glucose is good; therefore lowering blood glucose further with more intensive therapy must be better. Unfortunately, the data demonstrated that it was not! Using the opposite reasoning of the tomato effect, we hould all keep in mind that the evidence base of the recent and upcoming advances in diabetes therapeutics is still being built.

For the jobbing diabetologist involved in the acute take, the tomato effect and its opposite are common. Within the diabetes research literature there is an almost total lack of clinical trial data involving frail and elderly people (the majority of individuals admitted nowadays as acute medical emergencies) yet many such people are prescribed complex regimens of "expensive toxic agents" – the evidence for which may be based on surrogate endpoints and by necessity on a choice population. Recently, it has been shown that in this patient group, the presence of multiple co-morbid illnesses of functional impairments is a more important predictor of limited life expectancy and fewer benefits from intensive glucose control than is age alone (Huang et al, 2008). This is actually not surprising but appears to be often forgotten when one looks at the drug list of struldbruggs admitted on the acute take (Kerr, 2003). Like it or not, it is probably in the interests of countless patients that the diabetes team continues to play an active part in acute general medicine.

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