

# Editorial

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## Diabetes: A Tale of Two Futures

**T**o paraphrase Charles Dickens, it is both the best of times and the worst of times for those of us federal practitioners who take care of patients with diabetes.

First the bad news. After decades of only gradual increases in the overall prevalence of obesity and diabetes in the United States, 1980 marked the beginning of a marked upward inflection in these prevalence curves. Why was this period such a major turning point? Amid the plethora of potential villains, two stand out in particular: the introduction of corn syrup as an almost universal sweetener in the late 1970s and the progressively widespread availability of home computers in the early 1980s.

The home computer certainly enabled our preexisting sedentary urges—which were worsened further by the introduction of cable television, with its multitude of channels, and VCRs, which greatly expanded home viewing options. At the same time, a sizable fraction of the population moved from densely populated cities to the suburbs, where a customary brisk walk to the corner grocery shop was replaced by a drive to the supermarket.

Whatever the combination of causes, the end result has been a relentlessly surging epidemic of obesity and its associated scourge, type 2 diabetes. So severe is this epidemic that some statisticians predict we may soon witness an unprecedented reduction in average life expectancy, because of the destructive vascular complications associated with poorly controlled diabetes.

The good news, however, is that we have witnessed, over the past decade, a phenomenal increase in the availability of new therapeutic options for controlling blood glucose levels. In a confluence of corporate profit and public health benefit that defies cynicism, the pharmaceutical

industry clearly has recognized a booming market in diabetes products and responded in kind.

As late as 1995, the United States had only one class of oral agent available for the treatment of elevated blood glucose levels in type 2 diabetes. That year, though, the lonely sulfonylureas, which increase the output of insulin from the failing diabetic pancreas, were joined by metformin, which suppresses the overabundant production of new glucose in the diabetic liver and kidneys. The glitazones, also known as thiazolidinediones (TZDs), came along a few years later. TZDs work through an entirely different mechanism, facilitating insulin action in muscle and adipose tissue. They were soon followed by the alpha-glucosidase inhibitors, which retard carbohydrate absorption in the gut, and by meglitinides, which produce acute, short-term stimulation of insulin release by the pancreas.

The incretin concept of facilitating nutrient-induced insulin secretion, as well as reducing appetite and the rate of gastric emptying, came to clinical fruition in 2005. That year saw the introduction of exenatide, an analogue of a human incretin derived from the Gila monster. A different approach to enhancing incretin action is represented by the concept of dipeptidyl peptidase IV (DPP-IV) inhibition, which involves chemical inhibition of the enzyme responsible for clearing the native incretins and, hence, prolonging their physiologic effects. Two DPP-IV inhibitors will be available very soon.

Also noteworthy is the introduction of “designer” insulin formulations in the past decade. These new formulations allow much greater precision in mimicking the normal physiologic secretion of insulin to modulate blood glucose levels. They include long-

acting analogues (such as glargine and detemir), as well as rapid-acting analogues taken in association with meals (such as lispro, aspart, and glulisine). There also have been great advances in insulin delivery systems, with the availability of inhaled insulin for needle-phobic patients, new insulin pumps that are far more user-friendly than the older models, and a veritable cornucopia of new glucose monitoring devices.

So which trend in the recent history of diabetes ultimately will hold sway? Will the plague of obesity and diabetes lead to a severe upswing in cardiac events, strokes, kidney failure, blindness, and amputations? Or will the teeming army of high-tech therapeutic soldiers eventually conquer the scourge of diabetes and its associated vascular complications? At this point, it is not possible to prognosticate with any real confidence. The ultimate resolution of the so-called “diabetes” epidemic may require profound societal and cultural changes—at least as much as new medication options for existing diabetes. Such changes might include a renewed emphasis on physical activity, extra taxes on the use of automobiles, smaller restaurant portions, weight-based Medicare premiums, and many other shifts in cultural paradigms. Will these changes really occur? Only time will tell. ●

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