

## Managing Type 2 Diabetes Mellitus Across the Disease Spectrum

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Financial Disclosures:

Dr Schorr discloses that he serves on the speakers' bureaus for Sanofi; Santarus, Inc; Takeda Pharmaceutical Company Ltd; and AstraZeneca (for Symlin only). He also serves on the Clinical Events Committee for Medtronic Diabetes and on the Advisory Board for Novo Nordisk, Inc.

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**T**he management of diabetes mellitus, in particular the various forms of type 2 diabetes mellitus (T2DM), has become increasingly complex over the past several decades. In the 1970s through the 1980s, options were limited. Standard treatment consisted of diet, exercise, combinations of diet, exercise, and insulin, or the use of biguanides, sulfonylureas, or both medications. Recent advances have given more choices for physicians and patients.<sup>1</sup>

The discovery and implementation of various classes of medications have made the decisions regarding treatment of individuals with T2DM more difficult. Currently, there are approximately 11 different classes of pharmaceuticals available for treatment.<sup>2</sup> These drugs include  $\alpha$ -glucosidase inhibitors, sodium-glucose cotransporter-2 inhibitors, sulfonylureas, meglitinides, dipeptidyl peptidase-4 (DPP-4) inhibitors, amylin analogs, biguanides, thiazolidinediones, dopamine agonists, insulin, and glucagon-like peptide-1 (GLP-1) receptor agonists. When and how to use these agents, whether as a single agent or in combination with other medications, places a substantial responsibility on both physicians and patients. Determining the right choice becomes more difficult with each additional drug advance or approval.

Incretins are intestinal polypeptides that enhance the secretion of insulin after meals. The term *incretin* was proposed by La Barre in 1932.<sup>3</sup> Incretin-based therapies for diabetes mellitus were developed in response to the "incretin effect," which was noted when oral glucose stimulated a larger insulin response than intravenous glucose. During the 1960s

through the early 1990s, various studies were undertaken to delineate this effect and identify medications that could be useful in treating individuals.<sup>4</sup> It was known that the half-life of GLP-1 in the human blood circulation was quite short and was a result of almost immediate inactivation by DPP-4. In 2005, the first GLP-1 receptor agonist, exenatide, was approved by the US Food and Drug Administration (FDA) for twice daily use.<sup>5</sup> A second medication, liraglutide, was then approved by the FDA for single daily use.<sup>6</sup> Today, there is a weekly version of exenatide, and several other GLP-1 receptor agonists are in clinical trials or awaiting FDA approval.<sup>3,7</sup>

The 3 articles in this supplement to *The Journal of the American Osteopathic Association* are derived from a seminar held at the 2013 Osteopathic Medical Conference and Exposition in Las Vegas, Nevada. The seminar was moderated by Jay H. Shubrook Jr, DO, who provides the first article in this supplement.

Dr Shubrook<sup>8</sup> presents an excellent overview of the role of osteopathic physicians in the diagnosis and management of recent-onset T2DM. The second article of this supplement considers middle-aged individuals who have poor glycemic control due to postprandial glucose issues. This topic is addressed comprehensively by Thomas B. Repas, DO.<sup>9</sup> In the third article, Etie S. Moghissi, MD,<sup>10</sup> discusses elegantly the difficult decisions regarding combination therapy with GLP-1 receptor agonists and the use of insulin, particularly regarding risks of hypoglycemia in patients with long-standing T2DM.

I hope the readers of this supplement find these articles to be useful in clinical practice, and I hope readers appreciate the work of the authors and their attempts to "simplify" the complexity in treating patients with T2DM. (doi:10.7556/jaoa.2014.087)



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This supplement is supported by an independent educational grant from **Novo Nordisk Inc.**