

# Pharmacotherapy of Diabetes: Past, Present, and Future

## Preface

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Many dramatic and clinically relevant changes have occurred since I was diagnosed with type 1 diabetes more than 64 years ago. I was fortunate to be referred to a new internal medicine physician who specialized in treating children and adults with diabetes. Dr. O. Charles Olson was a proponent of managing blood glucose levels as close to normal as possible *and* giving people with diabetes the education and motivation to take charge of their life with diabetes.

Within 2 weeks of being diagnosed and while taking three shots of insulin daily, I was told to attend 20 hours of education about diabetes and its treatment. On the first day, I was given a book from the Joslin Diabetes Center in Boston, Mass., and given assignments to read about the disease and its treatments. Diabetes could be managed, I read, *if* the person with it became a master charioteer of three stallions including Diet, Exercise, and Medications. I read about diabetes and the various factors that could contribute to hyperglycemia. I was educated and encouraged to test my urine glucose levels. I did so using a kit that had magic tablets and a test tube. When the tablets were added to five drops of urine and 10 drops of water, the solution would gurgle, and the color of the resultant reaction informed me of the amount of glucose that had spilled into my urine.

This was fun, fascinating, and exciting, yet also a bit scary for me and my parents. I was barely 8 years old, but I was told that I could handle it and become a master charioteer. My family owned a horse, and when I rode her, I would imagine being in control of at least one aspect of my diabetes. It did not take long to realize that mastering insulin and food intake were

challenging, yet achievable. When I exercised a lot, I would sweat, shake, and act bizarrely—sure signs that my blood glucose level was dropping too low. Dr. Olson encouraged me to have a positive attitude about managing my diabetes and, most importantly, to never give up.

I share this story to emphasize the fact that, although much has changed in the treatment of diabetes, the basic tenants remain true. Since my early years of becoming a master charioteer, we have realized major breakthroughs in treatment, including self-monitoring of blood glucose (SMBG), the A1C test, newer and cleaner insulins, and assistive devices to remind us what to do and to continuously monitor glucose levels. Remarkable advancements in educational tools and paradigms are available to help patients with carbohydrate counting and other aspects of self-management. Research driving the development of new devices, treatments, or even a cure never ceases to amaze. Work now underway holds so much potential for truly significant breakthroughs in understanding and better managing type 1 and type 2 diabetes; I personally cannot wait for the new pulmonary insulin, Afrezza, to be approved by the U.S. Food and Drug Administration. Yet, all people with diabetes still need to juggle nutrition, exercise, and medications and take charge of their diabetes.

It is not possible to do that without thorough education, the use of SMBG, and the help of a *team* of health care providers who not only educate, but also motivate and guide patients to use available tools effectively. It is also known that we need to manage not only blood glucose levels, but also blood pressure, blood lipids, blood coagulation, and inflammation. The

more we know about diabetes and its treatment, the more we realize that there is still so much to learn.

I was thrilled and honored to be asked to serve as guest editor for this *Diabetes Spectrum* From Research to Practice section focusing on the pharmacotherapy of diabetes. Although we must always remember that there is more to treating diabetes than giving drugs, medications remain a cornerstone of treatment for many of our patients. Prescribing medications seems quite simple at first glance, but when we examine the process in detail, we find that it is quite complex.

There is a need to evaluate patients and their individual characteristics and needs. There is no shortage of things to consider. What are the patient's age, weight, and height? Does he or she have insurance, and, if so, what medications are covered? What type of diabetes does the patient have, and how long has he or she been living with the disease? What other medications have been tried and at what doses? How is the patient's kidney, liver, and gastrointestinal function? What is the current A1C and fasting glucose level? Has the patient shown a history of adherence to treatment? What about his or her motivation, education level, cultural and social history, literacy level, allergies, and tolerance to medications? The list of considerations goes on and on.

After evaluating the patient, the question then becomes which one or combination of more than 13 classes of drugs is most appropriate? Does the prescriber understand the basics of pharmacotherapy? What is each medication's mechanism of action? How is it absorbed, metabolized, and excreted? Do dosing changes need to be made based on the patient's kidney or liver function or level of metabolizing enzymes? Are there potential drug interactions with medications the patient is already taking? Does the patient know how to take, where to store, and how to evaluate the effectiveness of the medications? Does he or she have the faculties and sup-

port to appropriately manage the selected regimen?

The analysis of the best medication or combination of medications to treat a given patient requires an in-depth understanding of what is available, including the pros and cons of each. For that reason, this research section should be of great value to all who read it.

As guest editor, I worked with our committee to find the best possible authors to provide a thorough and informative overview of the pharmacotherapy of diabetes. We agreed to not cover the latest developments in insulins in this issue because there are excellent summaries of insulin use available in several publications from the American Diabetes Association.<sup>1,2</sup> We then listed the top experts in the universe as we know it to cover the various topics within our theme. I pleaded with, pressured, blackmailed, and begged these very busy experts to summarize their assigned topics. I am quite confident that the panel contributing to this research section will not disappoint. I feel certain that each reader will value the information presented herein and will keep this issue of *Diabetes Spectrum* as a reference for some time.

We open this topic with an editorial by Eric P. Brass, MD, PhD (p. 75). Dr. Brass's article "The Food and Drug Administration and the Future of Drug Development for the Treatment of Diabetes" serves as a primer on the U.S. drug approval process for diabetes medications.

Next, my friend, co-worker, and co-author of many articles and a book titled *Medications for the Treatment of Diabetes*, John R. White, Jr., PA-C, PharmD, presents a highly interesting article titled "A Brief History of the Development of Diabetes Medications" (p. 82). Dr. White provides an informative account of the history of pharmacotherapeutic advancement.

In our third article, my good friend and a greatly admired diabetes specialist, Irl B. Hirsch, MD, and

his colleague Savitha Subramanian, MD, present a useful summary of a topic of great clinical importance: "Personalized Diabetes Management: Moving From Algorithmic to Individualized Therapy" (p. 87). In keeping with the latest ADA theme of individualizing therapy, this article helps us understand how to focus therapies on the needs of each patient.

The next article in our series was written by former *Diabetes Care* editor Vivian A. Fonseca, MD, FRCP, and Gandahari Rosa A. Carpio, MD (p. 92). Their article, "Update on Safety Issues Related to Antihyperglycemic Therapy," provides a timely discussion of safety considerations necessary when using currently available medications for the treatment of diabetes.

In our final article (p. 100), "Novel Agents for the Treatment of Type 2 Diabetes," highly respected diabetes physician Ralph A. DeFronzo, MD, and his colleagues Curtis L. Triplitt, PharmD, CDE, Muhammad Abdul-Ghani, MD, and Eugenio Cersosimo, MD, provide an overview of the pathophysiological defects of type 2 diabetes and describe novel therapeutic agents that directly affect these defects, thereby blunting disease progression and providing durable diabetes control.

As I read each of these articles, I was blown away by the amount of clinically useful information our authors have presented in an interesting, accurate, easy-to-read, and well-referenced manner. I sincerely hope that you find this From Research to Practice section beneficial and helpful in the important work you do with your patients and clients. It is my pleasure to present to you "Pharmacotherapy of Diabetes: Past, Present, and Future."

## References

<sup>1</sup>American Diabetes Association: *Practical Insulin: A Handbook for Prescribing Providers*. 3rd ed. Alexandria, Va., American Diabetes Association, 2011

<sup>2</sup>Kaufman FR: *Medical Management of Type 1 Diabetes*. 6th ed. Alexandria, Va., American Diabetes Association, 2012