Introduction

Classification of diabetes includes a long list of common, rare, and not-so-rare conditions characterized by hyperglycemia of variable degrees. Whereas the majority of patients with diabetes are easily classified as having type 1 or type 2 diabetes, the other forms of diabetes, in aggregate, account for approximately 10% of diabetes cases. These cases may be grouped under the umbrella of rare forms of diabetes or "atypical diabetes." Even though individually rare, these atypical types of diabetes are frequent enough that every practitioner is likely to encounter such cases in his or her practice. The challenge is in recognizing them.

Cases of atypical diabetes are not only challenging from the diagnostic perspective, but more often than not, they demand distinct therapeutic approaches, emphasizing that "one size does not fit all" in clinical medicine.

This book groups cases of atypical diabetes into three broad categories:

Part I, edited by Dr. Louis H. Philipson, illustrates the difficulties in making a diagnosis and the importance of obtaining genetic analysis in cases of monogenic diabetes, which together account for 2–3% of all cases of diabetes before ages 25–35. In some cases, the impact of proper diagnosis can be immediate and profound, such as in the use of sulfonylureas in neonatal diabetes caused by mutations in *KCNJ11* and *ABCC8*, or in diabetes caused by HNF1A mutations (MODY3) presenting in young adults that is also highly responsive to sulfonylureas. Where there might not be a change in treatment, there can

be a change in how other organs are potentially impacted, such as the great vessels in *GATA6*, thyroid abnormalities with *GLIS3*, bone abnormalities with *EIF2AK3*, or variably presenting multi-organ involvement with mitochondrial diabetes (MELAS, MIDD, etc.).

The detailed discussion of the genetic and clinical presentations of monogenic diabetes is followed by 22 cases that illustrate the most important examples of monogenic diabetes.

Part II, edited by Dr. Boris Draznin, presents important examples of diabetes arising as a consequence of insulin resistance, genetic defects in insulin action, and diseases of exocrine pancreas. The 21 cases in this part of the text clearly demonstrate challenges both in diagnosis and therapy of these conditions.

Genetic syndromes of insulin resistance are rare, but when encountered, they present challenging diagnostic and therapeutic dilemmas. Cases of lipodystrophy occur with somewhat greater frequency than genetic syndromes of severe insulin resistance, but are equally challenging, particularly in aspects of therapy. Pancreatogenic diabetes follows the destruction of exocrine and endocrine pancreas by disease processes usually initiated in the exocrine part of this important organ or after surgical removal of the pancreas due to either pancreatitis or cancer. Diabetes also develops in many patients with cystic fibrosis who have much improved life expectancy. Patients with hemochromatosis and liver diseases may develop diabetes as do those treated with certain medications that interfere with either insulin secretion or insulin action, thus promoting hyperglycemia.

Part III, edited by Dr. Janet B. McGill, highlights the clinical presentation of diabetes in patients with endocrinopathies, immune-mediated pathogenesis of diabetes, diabetes of unknown cause, and diabetes arising in patients with other genetic diseases. The discussion includes the frequent development of diabetes in patients with other endocrine diseases, such as acromegaly, Cushing's syndrome, pheochromocytoma, and glucagonoma. Successful therapy of the underlying disease in these cases usually dramatically improves or completely normalizes glycemic control.

Patients with Latent Autoimmune Diabetes of Adults (LADA)* are often initially mistakenly diagnosed as having type 2 diabetes. Once an appropriate diagnosis is made, insulin therapy is instituted and these patients are managed similarly to those with type 1 diabetes. Other examples of immune-mediated diabetes include Type B insulin resistance, polyglandular failure, and stiff person syndrome.

An unusual entity of ketosis-prone diabetes is also discussed in detail in this part of the text. This form of diabetes is not as rare as was originally thought, and many diabetologists see these atypical cases of diabetes in their practices. Finally, there are other genetic syndromes associated with diabetes and Part III of this volume offers an in-depth discussion of these conditions as well.

In summary, the growing recognition of these atypical cases underscores the importance of considering and diagnosing rare forms of diabetes accurately and expeditiously in a cost-effective manner. We hope this compilation of cases and didactic chapters will help physicians encountering similar cases in their practice understand pathophysiology of these conditions and will guide them in their effort to diagnose and treat these atypical forms of diabetes. Finally, the text offers an extensive list of references to aid practitioners to navigate the literature about atypical cases of diabetes they will certainly encounter in their offices.

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*The American Diabetes Association does not recognize Latent Autoimmune Diabetes of Adults (LADA) as a distinct form of diabetes. ADA categorizes any diabetes that is due to an autoimmune β-cell destruction as a form of type 1 diabetes. A person with LADA with evidence of autoimmune dysfunction would be said to have type 1 diabetes, otherwise the person has either type 2 diabetes or a specific type due to other causes, such as monogenic diabetes syndromes. Content about LADA provided in this book is not consistent with the information in the ADA *Standards of Medical Care in Diabetes*.