Here's to 100 Years of Insulin and Science—and More to Come!

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In the last year we've celebrated the 100th anniversary of insulin as a treatment for diabetes. Many articles were published on this topic, providing cause for gratitude and optimism in a year that has otherwise been difficult. To conclude this celebration, the January 2022 issue of *Diabetes Care* contains two fine articles. One is an historical perspective by David Harlan and colleagues (1), tracing the evolution of our understanding of insulin, the people who took part in it, and the scientific explosion stimulated by insulin-related research. The other, by Will Cefalu et al. (2), describes the proceedings of a scientific symposium staged by the Canadian Institute of Nutrition, Metabolism and Diabetes and the U.S. National Institute of Diabetes and Digestive and Kidney Diseases.

The article by Harlan and colleagues links the scientific advances leading to clinical use of insulin, and those emanating from this process, to the people—basic scientists, clinical researchers, and institutional teams—who made them. There are some wonderful stories surrounding insulin, and four Nobel Prizes. Beyond describing the human side of science, this perspective suggests how targeted research can lead to wider applications. Fredrick Sanger's chromatographic studies of the linear structure of insulin's peptide chains broke the ground for study of the sequences of nucleotides in RNA and DNA. Dorothy Hodgkin's interest in its three-dimensional structure led to studies of other molecules, including penicillin and vitamin B_{12}. Such insights culminated in the design and commercial production of insulin analogs and other biologically active peptides. Rosalyn Yalow and Solomon Berson's immunoassay for insulin opened a new chapter in the pathophysiology of diabetes and led to immunoassays for many other circulating peptides.

The article by Cefalu et al. takes a different approach. It is a cross-sectional look at diabetes-related research today, summarizing 25 presentations by active researchers. The range of their work is broad—from pancreatic islet structure and function to clinical and physiologic descriptions of various kinds of diabetes, epidemiologic studies of metabolic markers, and the potential for population-wide, personalized interventions. Beginning with the molecular basis for insulin deficiency, the article ends with tactics for preventing and treating diabetes on a country-wide scale. Bringing these scientists and their varied projects together in a symposium sponsored jointly by U.S. and Canadian research agencies is a brilliant way to celebrate both insulin and the scientific inquiry it has fostered.

What more can be said about these articles? First, they remind us that science and medicine do not always advance swiftly or in sudden breakthroughs. Many investigators laid the foundation for the first use of insulin by the Toronto group in 1921. A century later we are still trying to match normal insulin patterns with exogenous insulin, and slowly learning how the complications of hyperglycemia develop and might be prevented or mitigated by means other than insulin replacement and glycemic control. We still have much to do.

Secondly, the structure of the article by Cefalu et al. hints at where some future challenges and possibilities lie. The first group of 14 presentations focused on "Islet Biology in Health and Diabetes." A second group titled "Heterogeneity of Diabetic Phenotypes Before and After Diagnosis: Impact on Management and Treatment" included nine presentations. These sessions reveal the intensity of current efforts to find more fundamental ways to prevent or manage the underlying lesions of diabetes. The final group consisted of two presentations on "Precision Medicine in Diabetes" that addressed the possibility of a public health approach to management. They suggested how analysis of big data may identify the best therapeutic approaches for all groups and individuals in a population and apply them in the context of social determinants of health. In terms of numbers, more than half of the presentations focused on basic science, about a third dealt with broad groups of people with different clinical features, and less than a tenth took on population-based efforts. These proportions reflect the traditional emphasis on biologic and pharmaceutical research, and allocation of fewer resources to translation of scientific insights to prevention and clinical care. Basic research has served us well and continues. Clinical research is making progress, but has not yet led to routine success in glycemic control and limitation of the illness and premature mortality associated with

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diabetes. Study of the public health aspects of diabetes is still a young science.

What goals might we set for the immediate future? There are some obvious candidates. Most people with type 1 diabetes who live in wealthy countries have access to insulin therapy; in some parts of the world, this is not the case (3,4). A person with type 1 diabetes who lives in a remote, impoverished village deserves insulin and help with using it as much as anyone else. Even in the U.S., there are places where more than 20% of the low-income population lack adequate health insurance to pay for the tools of diabetes management (5). Individualized treatment based on physiologic categories of diabetes is a highly appealing goal, but we are only beginning to apply this principle (6). For example, in clinical practice the distinction between type 1 and type 2 diabetes is not always made efficiently (7). Consequently, many people with type 1 diabetes appearing in adulthood are not identified at diagnosis and given optimal insulin therapy from the start. Systematic screening and management for monogenic forms of diabetes is clearly possible but not yet a reality (8,9). Personalized treatment that also considers an individual's wishes and capabilities, and any environmental and social constraints, requires timely access to providers with deep expertise in diabetes (10). Yet referral centers with this capability are not available in many health care settings. In short, basic and clinical science have given us many insights and tools, but the infrastructure needed to put them to use is too often lacking.

The scientific community cannot regard these unmet needs as someone else's concern. They affect everyone and are, like the biology of pancreatic islets, subject to scientific inquiry. Information technologies allow tracking of health data to identify trends, pose hypotheses, propose interventions, and assess outcomes. Diabetes registries in some countries are already collecting population-based data (11,12), and regional programs for diabetes prevention and management based on such information are in development (13,14). Unified national health systems have the potential to study, refine, and deliver more effective care. Population-based research examining ways to close the loop from genetics to physiology to clinical care will be essential as this process continues.

The revolution that began with insulin continues, still driven by science. With recovery from the pandemic and avoidance of other global crises of either natural or human origin, we can expect further improvement in prevention and management of diabetes and related chronic diseases. Scientific study of pathophysiology will continue, leading to new treatments, but systematic public health research and interventions could be more important. The editorial group at *Diabetes Care* looks forward to studies in all these areas in the coming year.

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