Now at the end of my tenure as editor of *Diabetes*, I wish to offer some personal thoughts about our journal, the disease we oppose, and our Association. I am pleased, but not satisfied, with our journal. I am disappointed, but not surprised, that the disease remains recalcitrant. I am concerned, but optimistic, about our Association. The challenges are great, but so are the opportunities.

**DIABETES: PAST, PRESENT, AND FUTURE**

Established in 1952, *Diabetes* has become a leading, arguably the leading, diabetes-oriented research journal in the world. The history of the journal was summarized by my predecessor (1).

*Diabetes* will remain at Washington University in St. Louis through 1996, its second 5-year tour at this institution. However, I will step aside as editor at the end of 1995. Dr. Julio V. Santiago, the hardest working of the hard-working associate editors, will serve as editor through 1996. The rationale for this change included the perception of a potential conflict between my role as editor of *Diabetes* and my role as president-elect and then president of the American Diabetes Association, as well as the increasingly time-consuming extra-university demands of the latter. After all, I still have a rewarding day job that I hope to retain! The Association has selected Dr. Gordon C. Weir as the new editor for the term starting in 1997. I wish Dr. Weir and his colleagues well.

I am grateful to many individuals for making my term as editor both enriching and pleasurable. They include our authors. The quality of a scientific journal cannot exceed the quality of the science submitted to it for publication. They also include our reviewers, including previous and current members of the editorial board. Those invaluable volunteers provide critical expert advice to both authors and editors. It has been a particular pleasure to work with a diverse group of talented and committed associate editors, who, with their individual areas of scientific expertise, have taught me a great deal and, with their concern for science and the journal, have made my job easy. The associate editors are Drs. David D. Chaplin, Michael L. McDaniel, Mike M. Mueckler, M. Alan Permutt, Julio V. Santiago, and Joseph R. Williamson in St. Louis and Dr. George S. Eisenbarth in Denver. Special thanks are due Mary Weis, who as editorial assistant continues to lead the St. Louis editorial office so capably, Karen Muehlhauser and Lisa Chandler in that office, and the professional publications staff at the Association’s National Center, including, but not limited to, Susan Lau, Peter Banks, Matt Petersen, Stacey Wages, and Jennifer Gross. Finally, I am grateful to Dr. R. Paul Robertson, the previous editor, for his advice and support and for handling submissions to the Journal from the editors and their associates.

It is appropriate to mention some measures of journal performance. Perhaps the most informative descriptive statistic is the time between manuscript receipt and the initial editorial decision, a combined measure of the performance of the editors, the reviewers, and the editorial office (as well as the various telecommunication and mail services). For regular publication manuscripts, the mean ± SD (range) receipt to initial decision interval decreased from 56 ± 24 days (1–154 days) in 1992, our first year, to 44 ± 22 days (1–173 days) in 1993 (P < 0.001). It was unchanged at 44 ± 23 days (1–125 days) in 1994. Although it is too early to calculate the final 1995 figure, it does not appear to have changed substantially. These are similar to the 1989–1991 intervals (1). Thus, this measure seems to have been reduced to its minimum using the current editorial methods. Perhaps new methods can reduce it further.

The interval from receipt to initial (often final) decision for rapid publication manuscripts also decreased from 15 ± 10 days (1–66 days) in 1992 to 12 ± 7 days (1–33 days) in 1993 (P < 0.05), was unchanged at 12 ± 8 days (1–30 days) in 1994, and has not changed substantially in 1995. Thus, these receive substantially expedited review. The trade-off is that there is usually only one outside reviewer and written critiques are not provided routinely.

The acceptance-to-publication interval is one quantifiable measure of the activity of the National Center publications office. These intervals were 132 ± 33 days (84–270 days) in 1992, 130 ± 17 days (95–266 days) in 1993, and 120 ± 17 days (86–212 days) in 1994 for regular publication manuscripts. Surprisingly, to me at least, diskette submission has not shortened this interval substantially. It has, however, re-

---

From the Division of Endocrinology, Diabetes and Metabolism, and the General Clinical Research Center and Diabetes Research and Training Center, Washington University School of Medicine, St. Louis, Missouri.

Address correspondence to Dr. Philip E. Cryer, Division of Endocrinology, Diabetes and Metabolism, Washington University School of Medicine (Box 8127), 660 S. Euclid Ave., St. Louis, MO 63110.

Received for publication 16 June 1995 and accepted in revised form 30 June 1995.

IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; SI, Système International.

DIABETES, VOL. 44, DECEMBER 1995 1351
duced the cost of publication of the journal considerably. Parenthetically, *Diabetes* is income-neutral to the Association. Its costs are covered by revenue (including subscription fees) not public support income. The intervals for rapid publication manuscripts have been somewhat shorter. Efforts to further shorten the interval for the latter have been initiated, but I am chagrined to acknowledge a similar promissory note concerning the acceptance to publication interval for both regular and rapid publications 4 years ago (1).

Aside from understandable disagreements about negative editorial decisions, there has been rather little conflict between authors and the editors over the past 4 years. We have stayed the course with respect to Système International (SI) units in principle, although we have probably missed some violations in practice. The SI unit table was updated and modified to include suggested numbers of significant digits. Indeed, my irritation with use of excessive significant digits has been a source of amusement to some of the associate editors. Perhaps the issue that continues to raise the most discussion is our use of the figure of 6.0 to convert insulin concentrations from μU/ml (mU/l) to pmol/l. The difficulty, of course, is in converting biological activity to molar units. Veld et al. (2) found 1.0 unit to correspond to 6.0 nmol human insulin by quantitative amino acid analysis. This is very close to that of 5.95 nmol/U determined by bioassay (3). The change to the 6.0 conversion figure in the SI unit table in *Diabetes* was made in 1989 by the previous editors. We have continued to use that figure.

Changes in journal practices have included applying the Association’s duality of interest policy to authors as well as editors, accepting manuscripts on diskette, increasing page charges (to $50), and reformatting the journal. The latter made *Diabetes* more readable in my opinion. Readers seem not to have noticed; we received only one (positive) comment from a reader.

Diabetes has strict editorial page limitations, 1,680 pages per volume (year). The average was 1,686 pages published per year in 1992-1994. This necessitates rather high rejection rates: 65–71% for regular publications and 72–88% for rapid publications in 1992-1994. Nonetheless, editorial decisions have been and continue to be based on the editors’ scientific judgment. Indeed, page counts have not been made known to the associate editors, who with my concurrence have made the vast majority of the editorial decisions, until after a given volume is completed.

Particularly in view of limited editorial space, the editors believe that *Diabetes* should focus on publication of original research. Thus, the bulk of the editorial pages have been committed to regular and rapid publications. There were 203, 218, and 195 regular publications and 15, 14, and 6 rapid publications in 1992, 1993, and 1994, respectively. One, usually invited, Perspective in Diabetes has been published each month. We do not have a regular letter to the editor section, although some (five in 1992–1994) letters that clarify articles published in the journal or speak to controversial issues stimulated by a published paper have been published. We have published very few editorials.

Clearly, the journal can be improved. Overall, however, I believe *Diabetes* is not broken and does not need to be fixed in a major way. It will be interesting to learn the views of the new editors. Over its 44-year history, *Diabetes* has become a widely respected and influential subspecialty journal. Its Science Citation Index “impact factor” (basically a measure of the relationship between the number of citations of articles in a journal and the number of articles published in that journal) was 5.861 in the most recent year for which data are available (1992). That was higher than that of any other diabetes-oriented journal (range 5.261–0.111). *Diabetes* is a successful venture of the American Diabetes Association.

**DIABETES: PERFECTED INSULIN REPLACEMENT**

Were it not for hypoglycemia, diabetes would be easy to treat. One would simply give enough insulin (or, in those individuals with enough residual endogenous insulin secretion, sulfonylurea) to lower plasma glucose levels to or below the nondiabetic range. However, hypoglycemia is a reality. Glucose is a critical metabolic fuel, particularly for the brain. With current treatment methods, hyperinsulinenia, whether exogenous or endogenous, sufficient to lower plasma glucose levels carries the risk of lowering them too far. Hypoglycemia is, indeed, the limiting factor in the management of diabetes (4). Because of that reality, the management of diabetes is currently much more complex than lowering plasma glucose concentrations.

In theory, we could eliminate iatrogenic hypoglycemia if we were to learn to replace insulin in a truly physiological fashion, to prevent, correct, or compensate for compromised defenses against developing hypoglycemia, or both. The latter notion is based on the premise that it is the integrity of the glucose counterregulatory systems—in their broadest sense, including both physiological defenses against falling plasma glucose concentrations (primarily decrements in insulin and increments in glucagon and epinephrine) and symptom-initiated behavioral defenses (e.g., food ingestion) —that determines whether or not relative or absolute therapeutic insulin excess results in an episode of hypoglycemia (4). This concept likely explains the frequency and severity of iatrogenic hypoglycemia. Those people with the most compromised glucose counterregulation, e.g., most people with fully established insulin-dependent diabetes mellitus (IDDM), suffer iatrogenic hypoglycemia, including severe hypoglycemia, most frequently. However, it seems unlikely that this concept explains all iatrogenic hypoglycemia. The former notion, physiological insulin replacement, is attractive because of its conceptual simplicity despite its current impracticality.

Insufficient insulin secretion is the proximate cause of diabetes. Relative resistance to insulin action is a feature of the pathophysiology of both non-insulin-dependent diabetes mellitus (NIDDM) and IDDM. It may well play a role in the pathogenesis of NIDDM (5–8) and is relevant to the management of NIDDM to the extent that measures that reduce insulin resistance (e.g., caloric restriction and exercise) result in improved glycemic control. Nonetheless, regardless of the degree of insulin resistance, diagnosable diabetes does not develop until insulin secretion declines and becomes insufficient to meet the metabolic demand (5–8). Thus, relative or absolute insulin deficiency is a prerequisite of clinical diabetes.

Ideally, we would like to prevent a given disease. If we cannot prevent it, we would like to cure it. If we can neither prevent nor cure the disease, we would like to manage it effectively. If the disease is, like diabetes, the result of insufficient secretion of a hormone, effective management
implies physiological replacement of that hormone. Few chronic hormone deficiency diseases can as yet be prevented or cured, but several can be managed effectively. For example, in appropriate doses, thyroxine ingestion in hypothyroidism mimics normal thyroid hormone secretion and produces physiological hormone replacement. That is not the case for insulin replacement in diabetes. All current insulin replacement regimens are imperfect compared with normal insulin secretion. Insulin-treated (or sulfonylurea-treated) people with diabetes have periodic hypoinsulinemia with its resultant hyperglycemia and, not infrequently, periodic hyperinsulinemia with its risk of hypoglycemia. Parenthetically, even if drugs that enhance sensitivity to endogenous insulin (in a generic sense) are shown to be safe and effective, it is most unlikely that they would produce euglycemia that is sustained over a lifetime of NIDDM, since NIDDM is typically a progressive disease (9). Insulin replacement would ultimately be necessary in most, if not all, patients who survived to that point in the course of their diabetes.

Perfect insulin replacement would correct all of the metabolic abnormalities of diabetes that are known to be clinically relevant, perhaps with no risk of hypoglycemia. It would alleviate all symptoms and prevent acute metabolic complications, almost assuredly prevent the specific chronic complications (retinopathy, nephropathy, and neuropathy) (10), and likely reduce atherosclerotic risk. Aside from the need for therapeutic intervention, it would approximate cure of the disease just as thyroxine replacement does in hypothyroidism. Furthermore, a truly safe and effective method of perfected insulin replacement would undoubtedly be applicable to people with NIDDM as well as those with IDDM.

At a minimum, perfected insulin replacement would require minute-to-minute plasma glucose-regulated insulin delivery into the circulation. (To the extent that factors in addition to glucose are relevant to physiological regulation of insulin secretion, even that might not provide perfect insulin replacement.) Several approaches are on the horizon (some have been there for a rather long time). These include, but are not necessarily limited to, development of a closed-loop insulin delivery system (sensor, computer, pump), transplantation of normal insulin-secreting tissues (pancreas, islets), and implantation of cells converted to the task of glucose-regulated insulin secretion by gene manipulation.

Because we do not know how diabetes will be prevented and cured, we must continue to support a broad range of fundamental research potentially relevant to those goals. Diabetes will be prevented and cured, but we do not know when. Pending that time, perfected insulin replacement is a reasonable short-term goal for the diabetes research community. Pending that time, there is also a pressing need to continue to communicate the outcomes of research in peer-reviewed journals such as Diabetes and for even greater efforts by the volunteers and staff of the American Diabetes Association.

THE AMERICAN DIABETES ASSOCIATION

As the readers of Diabetes know all too well, diabetes is a common, currently incurable but treatable, potentially devastating chronic disease that is extraordinarily expensive in both human and dollar costs. An estimated 14 million Americans, more than 5% of the U.S. population, have diabetes. It is a major cause of premature death from atherosclerotic disease and the leading cause of blindness in working-age adults, of nontraumatic lower extremity amputations, and of end-stage renal disease requiring dialysis and transplantation. The cost of all health care for people with diabetes was estimated to be $105 billion, 15% of all health care expenditures, in the U.S. in 1992 (10). Notably, less than one-half of one percent of that sum was spent on diabetes research. Founded in 1940 as a professional society, the American Diabetes Association is now a remarkable amalgamation of a leading professional society and a leading voluntary health organization. Our Association has grown substantially and in many ways matured over the past few years. Our volunteers have been highly successful in fund raising, our annual expenditures, about two-thirds derived from public support and the remainder from revenue, are now about $90 million.

The mission of the American Diabetes Association is a noble one: to prevent and cure diabetes and to improve the lives of all people affected by diabetes. The Association provides organizational and fund raising support and an array of programs, organized around the themes of research, information, and advocacy, to the diabetes community. Among these programs, only research will prevent and cure diabetes. Research has improved the lives of all people affected by diabetes, and it will continue to do so.

Although our research awards and grants budget is small relative to federal research expenditures, our Nationwide Research Program is unique and makes a difference. It supports the training of the next generation of diabetes investigators through Career Development Awards, Mentor-Based Postdoctoral Fellowships, and Medical Student Fellowships. Furthermore, it supports the testing of innovative ideas through investigator-initiated Research Awards, Clinical Research Grants, and Lions SightFirst Research Awards. Finally, it supports selected areas of special research interest, including the Association's Genetics of Non-Insulin-Dependent Diabetes (GENNID) study, designed to facilitate identification of the gene abnormalities responsible for susceptibility to NIDDM, and the Diabetes Prevention Trial I, designed to determine if IDDM can be prevented. Thus, to a large extent, the Association nurtures the human and conceptual infrastructure of future diabetes research.

The American Diabetes Association's research awards and grants expenditures were $8.6 million in fiscal year 1995. These were dollars actually spent by investigators. Association overhead costs are not included in this figure, nor are other expenses conventionally allocated to research by not-for-profit charitable organizations. In fiscal year 1995, training awards (n = 73), investigator-initiated awards and grants (n = 63), and support of our areas of special research interest constituted 35, 43, and 22%, respectively, of our research awards and grants expenditures.

Over the past decade, our research awards and grants expenditures have not grown in parallel with the approximately threefold increase in our public support. Measures to increase our research expenditures are being pursued actively. Policies enacted recently will ultimately increase our research awards and grants expenditures in parallel with our public support. Among other direct inputs, affiliate voluntary contributions to research are critically important and are being solicited actively. Although it will invite the charge of parochialism, I must point out that the Missouri Affiliate continues to lead the way in this category. In fiscal year 1995, its voluntary contribution to research was $465,000. If the
other 51 affiliates were to average that sum, our research awards and grants budget would triple! Finally, the newly established American Diabetes Association Research Foundation is expected to boost the awards and grants budget in the future, hopefully the near future.

The American Diabetes Association Strategic Plan for 1995–1998 reflects widespread support for increased support of research. It envisions a near doubling of our awards and grants budget over 3 years, increased support of the training component of our research program, and increased Association-wide ownership of our Nationwide Research Program.

It seems clear to me that the research support gene is expressed, albeit at diverse rates, in all American Diabetes Association volunteers and staff and that the rate of its transcription is increasing. Nonetheless, there is a critical need for positive transcription factors. The medical and scientific community can serve as those transcription factors. I would hope that many more physicians, other health care providers, and biomedical scientists would become actively involved in their American Diabetes Association chapters and affiliates, as well as the national organization. While that involvement might be focused, ideally it would include participation in the full range of Association programmatic themes—research, information, and advocacy—and the critical area of income development. With the many already engaged and the legion of other committed Association volunteers, we can make a difference. We can accelerate the prevention and cure of diabetes and, pending that, improve the lives of all people affected by diabetes through research as well as through our other programs and services.

REFERENCES