well documented in appropriately selected hyperglycemic individuals and accounts for their widespread usage in the United States and other countries during the past 17 years. In many of the more responsive patients with maturity-onset diabetes, normal blood glucose levels are more readily attainable than with diet or insulin.

Despite numerous reports during the early years of their clinical use that these compounds would effectively lower blood glucose levels in 50 to 75 per cent of maturity-onset diabetics who were not insulin dependent or ketoacidosis-prone and whose diabetes began at age 40 or older, physicians familiar with insidious long-term problems of the diabetic have from the beginning been concerned that patients so treated might be less well controlled and more prone to premature development of these complications than individuals treated with insulin. Experience has provided ample evidence that for one reason or another oral hypoglycemic agents lose their effectiveness at varying but relatively short intervals of time after initiation of treatment. The rate of such "secondary failure" depends upon many factors, including patient selection and dietary cooperation, therapeutic objectives, and the manner in which the oral hypoglycemic agents are used. A lucid presentation of "primary" vs. "secondary failure" and the effect their definition has upon long-term "failure" has recently been published.[6] The element of convenience for middle-aged and elderly people is obvious, but always has had to be balanced against the increased cost for those who took more than minimal doses and the possibility that physicians and patients alike would rely too heavily upon their effectiveness, so that diet would be either ignored or less carefully followed.

If benefit is to be anticipated from lowering blood glucose levels as well as reversing lipid, protein, and other metabolic abnormalities associated with insulin deficit, what should be the blood glucose levels attained? From the early days of their use, many sets of criteria have been utilized by those involved in the study of diabetic patients. In general, these have fallen into two categories: (1) those who consider the oral hypoglycemic agents effective despite blood glucose levels in excess of normal, provided the symptoms of diabetes have been relieved and remain so, and (2) others, such as Marble and his associates,[7] including this author, whose objective has been normoglycemia and aglycosuria, in accordance with the criteria originally published by Camerini-Davalos et al. in 1957[8] (Table 1). In defense of the former is the fact that in many maturity-onset diabetic patients whose blood glucose levels remain elevated despite dietary adherence, the addition of oral hypoglycemic agents lowers blood glucose levels to a degree comparable to that readily obtained with insulin and relieves symptoms, so that little would be gained by insisting upon a more rigid standard of metabolic control. Recognizing that evidence for the benefits of tight metabolic control remains controversial, the adoption of such standards would seem to be reasonable. On the other hand, if it is true that protection from long-term complications is attainable only through the more rigid control of blood glucose levels, the latter criteria should be applied, and if the standards are not attained, more relentless application of diet and insulin if necessary is required. At present the fundamental controversy continues to be that related to the possible benefits of such control. Considerable new evidence is available today, unfortunately no