employed mirrors the misuse of these agents in common practice. If subsequent data provided by the UDPG group provide evidence of an unusual form of coronary artery disease in the patients treated with tolbutamide and phenformin, or of an unusual propensity to cardiac arrhythmias, to pulmonary emboli, or to shock in the patients who died of cardiovascular disease, the case may be strengthened. However, although we feel that the sulfonylureas have a limited role in the treatment of adult-onset diabetes, we would not abandon their use on the basis of the findings of the UDPG study. Nevertheless, this study has served the useful purpose of reminding physicians that the use of sulfonylureas and biguanides is not without hazard, and that as with any pharmacologic agent, the possibility of unanticipated effects must be considered.

Hypoglycemia and hypersensitivity reactions have been the major problems encountered in the use of the sulfonylureas. Hypoglycemia resulting from these drugs can be prolonged and may be fatal; this is particularly true of long acting compounds such as chlorpropamide. Many of the reported instances have resulted from the unwarranted administration of this agent to patients with impaired renal function.[24] In addition, it has been recognized that chlorpropamide can induce a syndrome characterized by hyponatremia, impaired mental function, and evidence of inappropriate antidiuretic hormone activity.[25] The pernicious aspect of this syndrome is that in elderly patients (in whom it has been most frequently observed) the impaired mental function could easily be attributed to other causes. There is little reason to believe that the effects of the sulfonylureas are restricted to the pancreatic β-cells. Specific compounds have been shown to alter thyroid function,[26] to modify adenyl cyclase activity in cardiac muscle,[27] to augment antidiuresis,[25] and to alter lipolytic activity in isolated adipose tissue.[25] However, with the exception of the UGDP study, the reported incidence of serious problems resulting from the use of the shorter acting sulfonylureas has been remarkably low. Nonetheless, the prolonged administration of sulfonylureas to adult-onset diabetics does entail an obvious risk. As with any pharmacologic agent, this risk must be justified in terms of the indications for its use, and is not acceptable unless the agent is demonstrated to be effective.

Why Do We Use the Biguanides?

As we have previously mentioned, we find it difficult to justify a role for the biguanides in the treatment of diabetics and would discourage their use. It is doubtful that these agents would be employed at all if it were not for the fact that they can be administered orally. While there are gaps in our knowledge of the manner in which insulin and the sulfonylureas lower blood glucose levels in diabetics, there is some reassurance that these effects are mediated, in part, by the correction of metabolic abnormalities resulting from an altered insulin secretory mechanism. Whether the long-term effects of the sulfonylureas result primarily from an action on the pancreatic β-cells is a point that is difficult to document, but the ability of these agents to stimulate insulin secretion in adult-