

3. A positive inotropic effect, i.e., increased force of muscular contraction, of sulfonylurea agents on the heart muscle has been demonstrated (ref. 24 and 25). The increased oxygen requirement resulting from such an effect could have a deleterious effect in patients with coronary artery disease. Limited animal studies also suggest that the sulfonylurea agents may affect the excitability of heart muscle (ref. 25), which could predispose the heart to develop abnormal rhythms, particularly in the presence of a decreased oxygen supply.

4. Results from a study on the chronic effects of tolbutamide in the rhesus monkey by R. W. Wissler et al. (FDA contract 72-114) indicate there is an increased frequency and severity of atherosclerotic lesions in the coronary arteries of the tolbutamide-fed monkeys compared to the control monkeys (ref. 26). The final report of this study is under review.

While neither of the two epidemiological studies is a prospective clinical trial such as the UGDP study, the preliminary reports indicate that further information casting doubt on the safety of the oral hypoglycemic drugs may be forthcoming. And, although the animal findings cannot be considered necessarily relevant to the issue of excess cardiovascular mortality in diabetic patients, they indicate that sulfonylureas may have potentially adverse effects on the cardiovascular system of certain animals which can be detected by appropriate pharmacological and toxicological tests.

In addition to these reports, two critiques of the Biometrics Society committee report have recently been published (ref. 27 and 28).