

and government regulations. As an example, the medical journal which published the full report of the experience of the UGDP with phenformin has continued to print advertisements for phenformin which give no warning regarding hypertension, tachycardia, and cardiovascular death as adverse reactions.

7) Teaching in medical schools and in post-graduate courses should emphasize methods of evaluation of therapeutic agents to a greater extent. At the University of Vermont during several years we have used the UGDP study and its problems as the basis for an interdepartmental teaching exercise. The excellent short book by A. L. Cochrane in England, Effectiveness and Efficiency (Nuffield Provincial Hospitals Trust 1972) should be available in this country as required reading for all health professionals.

III. AVAILABILITY OF SCIENTIFIC EVIDENCE DEMONSTRATING BENEFIT OF ORAL AGENTS

The UGDP demonstrated no increased effectiveness of tolbutamide as opposed to placebo with respect to mortality or gross evidence of vascular disease in the groups of maturity onset diabetics of the type now receiving oral agents in today's practice. As in other studies there was also evidence of secondary failure. Thus, on the issue of efficacy, were the drug up for initial review today, it doesn't seem likely that it would be approved. The UGDP study also showed that, in this group of largely overweight non-insulin dependent diabetics, lowering the blood glucose concentrations alone gave no objective benefit, although the techniques for evaluating microangiopathy were insensitive. Therefore, the one justification for continued approval of the sulfonylureas appears to be that there is a very small percent of patients who can't take or will not take insulin, do not respond to other measures, and are severely symptomatic and hyperglycemic. However, to give blanket approval for use of the drug to accommodate this relatively minute fraction of the diabetic population leaves the door wide open for continuation of widespread inappropriate use, with all the disadvantages indicated above. It is unrealistic to believe that package labeling with suitable warning and suggested priorities will alter the patterns of prescription.