surprises. A slightly more critical attitude to treatment, and an attempt to reduce insulin or the sulphonylureas whenever possible, to withdraw them even, has for several years suggested to me the frequent temporary nature of the disease. It is suggested that in suitable diabetic centres attempts might be made to systematically organize patient material in such a way that six-monthly repeated glucose-tolerance tests might give us a real clue to the nature and time limitation of the diabetic state.—I am, etc.,

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Oral Antidiabetic Agents

SIR,—Professor W. J. H. Butterfield and Dr. C. Hardwick will I hope forgive me if I challenge the view given in their letter (*Journal*, May 16, p. 1298) on the mode of action of the sulphonylureas, where they stated that "nothing found so far contraverts the suggestion that the oral antidiabetics stimulate the secretion of endogenous insulin." This statement was supported by references to the ingenious and painstaking experiments of Professor Butterfield and his associates on the glucose uptake of the forearm tissues in man. Further references (see letter) were made to the work of Williams *et al.* and Lundbaek *et al.*, which indicated a direct effect of these compounds on the uptake of glucose by muscle tissue.

However, other workers[1,2] (and these references were not cited) have failed to demonstrate any effect of these compounds on glucose uptake by the rat diaphragm technique. Further, using this same technique, no increase in the serum insulin levels has been observed following treatment with these drugs.[3,4] In addition neither the concept of a direct insulin-like effect nor of a stimulation of endogenous insulin secretion are supported by studies on the usual concomitants of an increased insulin effect such as changes in the respiratory quotient and nitrogen, lactic, and pyruvic acid metabolism.[5] In contradistinction there is evidence (also uncited) indicating an effect of the sulphonylureas on glucose release from the liver.[6,7] The current compromise in the B cytotrophic hypothesis is that insulin secreted endogenously into the portal circulation has a primary effect on hepatic glucose release rather than on the peripheral utilization of glucose. There is a certain amount of experimental support for this theory,[8,9] but even this is obviously not in agreement with the work cited by Butterfield and Hardwick which proposes a peripheral site of action.

All the clinical evidence certainly supports the view that these compounds work only in the type of diabetic patient who still has some endogenous insulin secretion, but it does not necessarily follow that an increase in this insulin secretion is involved in their hypoglycaemic effect. In terms of the classical argument about diabetes mellitus as a disease of under-utilization of glucose versus over-production of glucose, in which the blood glucose level is represented as fluid in a tank, then an effect on the level of the fluid is only clearly manifest when both the inflow and outflow from the tank is being controlled. Thus, should the sulphonylureas act mainly or entirely on the hepatic release of glucose, then this effect would be clinically appreciable only in those patients who still had adequate utilization of glucose (hence the dependence on some endogenous insulin secretion). Furthermore, from a teleological point of view I doubt whether "diseased" islet tissue is capable of increased stimulation for a prolonged period without exhaustion setting in (our own long-term studies show secondary failure to be a rare sequence).[10] In any case the islets are already under the best-known stimulus to increased insulin secretion—a raised blood glucose level.

Professor Butterfield and Dr. Hardwick have done a service in raising the problem of the mode of action of sulphonylureas in the correspondence columns of the *Journal*, since it is difficult to present adequately the more contentious aspects of this problem in an article. It is, however, unfortunate that they should add to the literature in support of the sulphonylureas as B cytotrophic agents without a discussion of the difficulties raised by some of the work cited above. For, even if some of this evidence does not contravert the suggestion that the oral antidiabetics stimulate the secretion of endogenous insulin, it certainly makes its acceptance or understanding more difficult. At present we do not know how these drugs act any more than we know how insulin acts, and it is significant that it has taken 37 years to define our ignorance in this field.—I am, etc.,

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Community Care of Mentally Ill

SIR,—Concerning the Report of the Royal Commission on the Law Relating to Mental Health, in a memorandum which has been issued by executive councils to general practitioners (E.C.N. 297) appears something which cannot but cause anxiety and suffering to many in our community.

"The Report suggests that the division of functions between the local authorities, the hospitals and other official bodies should be broadly the same in relation to mental disorders as in relation to other types of illness or disability. This implies a considerable expansion in the services provided by local health and welfare authorities for the benefit of the mentally disordered. It means too an increase in the numbers of mentally disordered persons who will remain in the community, if possible in their own home surroundings, and who will be cared for there."

In what way this cold, rather sinister official statement affects me I may best convey by relating from my personal experience one case.

When I was young and anxious for power to cast out devils I found myself in charge of mentally afflicted patients. The atmosphere of hopelessness which blanketed this branch of medicine gradually chilled my ardour. One day a young man was admitted, roughly speaking, kindly and harmless but troublesome. He soon settled down to the routine of institutional life, and later I had an interview with his nearest relative, a mature man holding very considerable national responsibility. His words altered my warped viewpoint, and I was given a glimpse of the community outside the encircling walls. "I cannot thank you too much for looking after my stepbrother. My two sisters have devoted their lives to his welfare. They were becoming prematurely old. Now they are living."—I am, etc.,

Haydon Bridge, Northumberland. RICHARD BELL.