control of hyperglycaemia at least at the end of the night instead of running the risk of severe nocturnal hypoglycaemia [10]. Of course 'pragmatic' studies [3] aimed at choosing the most practical treatment for achieving near-normalization of blood glucose levels in diabetic patients who need euglycaemia cannot readily be extrapolated since the treatments studied must be given under routine conditions. Pragmatic trials studying pump treatments are certainly needed. The 'feasibility phase' of the National Institutes of Health trial will thus probably be useful. But, as far as trials on insulin treatment are concerned, we would like to suggest that it would be more rational to spend funds not on explanatory trials but on methods designed to simplify the normalization of glycaemia and to make it safe and available for the majority of diabetic patients.

Yours sincerely
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Glucagon Induced Hyperkalaemia in Diabetes

Dear Sir,

Van Gaal and de Leeuw recently reported in a Letter to the Editor [1] their data showing a highly significant positive correlation between potassium and high blood glucose levels (> 20 mmol/l) in 22 admissions for diabetic ketoacidosis. They concluded that 'hyperglycaemia is the single most important cause of hyperkalaemia in these patients'; without evaluating any other factors.

We recently documented a hyperkalaemic role of glucagon in normal subjects [2]. Van Gaal and de Leeuw in their Letter suggest that we concluded from our work in normal volunteers that hyperglucagonaemia is a major cause of hyperkalaemia in decompensated diabetes. In fact we reported that circulating glucagon might be a contributory factor in the change in potassium homeostasis in decompensated diabetes. In further studies, we documented that in insulin-dependent diabetic patients the increase in potassium following the withdrawal of an insulin infusion, which had maintained the patients euglycaemic overnight, was not correlated with the increase in blood glucose, while it was abolished by somatostatin (which inhibits glucagon) [3]. These data do not exclude the importance of other mechanisms, but suggest again that the increase in glucagon which occurs during non-ketoacidotic decompensation could at least play a part in causing hyperkalaemia. This latter phenomenon could be due to mobilization of potassium from the liver as we have documented in normal subjects [4].

Yours sincerely,
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Virus-Induced Diabetes: Cytomegalovirus and Multiple Environmental Insults

Dear Sir,

Several viruses can cause diabetes in mice [1]. Encephalomyocarditis (EMC) virus infects pancreatic β cells and produces a severe form of diabetes in certain inbred strains of mice [2]. Under some circumstances, reovirus also infects β cells, and in addition, triggers an autoimmune response resulting in a mild form of diabetes characterized by abnormalities in glucose tolerance tests which generally disappear within several weeks [3, 4]. Diabetes may also result from cumulative β cell damage produced by sequential environmental insults. For example, in mice, a sub-diabetogenic dose of streptozotocin reduces the β cell reserve and enhances the capacity of certain viruses (e.g., Coxsackie B viruses) to produce diabetes [5, 6]. The present experiments show that murine cytomegalovirus (CMV) infection leads to mild focal β cell damage, and that multiple environmental insults can increase the severity of diabetes.

Newborn NIH Swiss male and female mice were infected with the Smith strain of CMV [7] or reovirus type 1 that had been passaged more than seven times in mouse pancreatic islet cell cultures to increase their tropism for β cells [4]. Two or four weeks later, the mice were challenged with a sub-diabetogenic dose of streptozotocin (1 mg/mouse) [5, 6], or the D variant of EMC virus [2], or CMV. Beginning one week after the challenge, each mouse was bled four times, and the glucose index and percentage of animals developing diabetes were determined as described previously [2].

Table 1 shows that when NIH Swiss male mice were infected with only CMV or reovirus, or given only streptozotocin, diabetes did not