– to: Bergman RN (2000) Non-esterified fatty acids and the liver: why is insulin secreted into the portal vein? Diabetologia 43: 946–952

To the Editor: Bergman argues in his article [1] that the reduction in hepatic glucose output does not result from insulin secreted by beta cells into the portal vein. He hypothezises that NEFA are the primary regulators of hepatic glucose output (HGO), with insulin only having an indirect effect. But this view, and the strong correlation reported between hepatic glucose output and NEFA, are not documented in this paper. His interpretation of the results on conscious fasted normal dogs does not take into account that insulin's counterregulatory action could cause the delay in the reduction of hepatic glucose output. The reduction of hepatic glucose output depends on the quantity of insulin (which is not given in the article) administered into a peripheral or into the portal vein as well as on nutritional and diabetic states. Bergman's results are irreconcilable with the direct effect of insulin, well documented in 42-year old papers on the reduction of hepatic glucose output [2–6]. These studies report the release of glucose and urea by isolated insulin-perfused liver in cases where changes in NEFA were ruled out. In addition, his findings contradict those of at least 6 important papers published between 1958–1966 (not cited by Bergman, as is the tendency of more recent studies) and my own results [7, 8, 9] on diabetic and control rats, anaesthetised with pentobarbital, which showed that the hepaportal glucose difference (H-P) was reduced 8–10 min after the injection with 0.1U/kg of insulin and later reversed from positive to negative. The effect of lower doses of insulin injected into a peripheral vein on glucose utilisation were mainly peripheral – on adipose and muscular tissue. Higher doses given intravenously could, however, suppress hepatic glucose output by reaching the liver via the hepatic artery. The application of causal logic and of the adaptive and non-adaptive teleological principle make Bergman's question "why?" a good starting point for explaining these facts. My explanation is that insulin is secreted into the portal vein and liver pulsatilly in order to restrain HGO. Insulin is secreted in larger amounts after ingestion of glucose or carbohydrates to ensure the direct deposition of glycogen from absorbed glucose and proteosynthesis from absorbed aminoacids, while triglycerides circumventing the liver are deposited in the adipose tissue. Although NEFA could have a secondary influence on insulin sensitivity, insulin is the main factor involved in reducing HGO both in diabetic animals and diabetic human beings. Finally, I am surprised to see the distorted anatomy depicted in Fig 1, 2A and 2B. The portal vein enters the liver from the caudal, concave face and the HGO and non-retained insulin flow from the hepatic veins on the cranial, convex face!

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Observations

Munchausen's syndrome manifesting as factitious hypoglycaemia

To the Editor: Factitious hypoglycaemia is a specific type of Munchausen's syndrome the diagnosis of which requires multiple expensive investigations. The incidence of this particular disorder is now equal to that of insulinoma.

Munchausen's syndrome is an unusual syndrome first reported by Asher in 1951 [1]. Sufferers describe past histories that are dramatic and believable but untrue and they present with an 'acute illness' [1]. After numerous painful and unnecessary investigations [2] or operations, the many falsehoods in a patient's history can be discovered. At this point a patient might consult a different doctor or hospital, sometimes with a different name [1].

Factitious hypoglycaemia is a specific type of Munchausen's syndrome [3] and is almost impossible to differentiate from an insulinoma at initial presentation. Reports have stated that the incidence of factitious hypoglycaemia is almost equal to that of insulinoma, [4] providing many diagnostic problems. The diagnosis of factitious hypoglycaemia is made when a patient is known to have surreptitiously self-administered insulin or oral hypoglycaemic agents to induce a hypoglycaemic attack [2].

The first diagnostic step in any patient suspected to have hypoglycaemia is to confirm by laboratory assay that the plasma glucose concentration is less than 2.2 mmol/l

(2.5 mmol/l in patients aged older than 60 years). Further investigation of samples in which true hypoglycaemia is not present could lead to incorrect diagnoses. Because insulin and C-peptide are unstable peptides, serum should be separated from the cells and frozen at –20 °C within 30 min in all cases of suspected factitious hypoglycaemia. High plasma insulin concentration (or even concentrations within the normal non-fasting reference range) in this context indicates insulin or sulphonylurea administration, or insulinoma. Insulin administration can be confirmed by showing a low plasma C-peptide concentration, whereas high C-peptide concentrations are consistent with either sulphonylureas or insulinoma. In the latter scenario, a positive plasma sulphonylurea screening test result differentiates sulphonylureas from insulinoma [5].

Factitious hypoglycaemia is a rare condition that requires many tests. In the interests of both timeliness and quality it is appropriate that they are completely carried out in a specialist reference laboratory. The key to successful diagnosis is, firstly, to consider the possible diagnosis of factitious hypoglycaemia early so that samples can be handled in the appropriate manner, and secondly, to communicate full clinical details to the reference laboratory so that the appropriate sequence of investigations can be carried out.

The first reports of factitious hypoglycaemia were made in 1946 and since then there have been several case reports published [6].

A review of the literature between 1966 and 1999 was conducted using a Medline search. Papers on the subject were found by searching under the key words: hypoglycaemia, hyperinsulinism, factitious, self-induced, drug abuse and Munchausen's. Further papers were also found from those cited in the references provided at the end of the papers.

The search identified 46 papers containing 69 case reports of factitious hypoglycaemia, with a range of 1 to 4 case reports in each paper. The majority of these articles originated from the United States (65 %), with a further 25 % from the United Kingdom. A coded theme approach was used to provide data from the 69 case reports and it was found that:

– 68 % of the case reports were of women;
– Average age was 32 years 4 months, with a range of 1 to 78 years;
– 75 % were not diabetic patients;
– 42 % had no close links with diabetic patients (family or friends);
– Occupation was detailed in 37 and 55.3 % were health professionals of which 39.5 % were nurses.
– Past medical history was detailed in 47 reports, 28 % of these involved history of depression, suicidal tendencies, psychopathy or drug abuse;
– 68 % were induced by insulin;
– Only 20.2 % of the patients admitted to self-administering hypoglycaemic agents at some point during the course of investigations;
– 32 reports detailed unnecessary surgical procedures (20 laparotomies, 10 pancreatectomies, 1 duodenectomy and ligation of the pancreas), with one patient alone undergoing 7 laparotomies, 1 pancreatectomy and ligation of the pancreas;
– 93 % of the cases survived the attack and made a full recovery, 2 patients died and 1 suffered severe impairment of short-term memory and intellectual function;
– 33 % were referred for psychiatric care and in 30.4 % of cases no further action was taken;
– In 40 case reports reasons were given for inducing hypoglycaemia which included suicide (25 %), by mistake (25 %), attention seeking (17.5 %), and to produce euphoric effects (10 %).

This information can easily be criticised, as there might be unreported cases of factitious hypoglycaemia. The use of case reports can also be criticised due to the inconsistency in the quality and quantity of data provided within them.

Factitious hypoglycaemia seems to be more common in women and more common in health care professionals, particularly nurses. The literature suggests that many patients go to extreme lengths to remain undiscovered, including allowing themselves to be subjected to multiple investigations and surgical procedures. Factitious hypoglycaemia could therefore remain undetected for many months or even years.

In patients with diabetes, hypoglycaemia is reported as an unpleasant and unwanted phenomenon encountered unintentionally in pursuit of optimum glucose tolerance. However, a group of people seem to subject themselves to this experience deliberately and in this form of self-abuse 10 % report euphoric effects. Interestingly, inducing convulsions through hypoglycaemia was used to treat depression by psychiatrists until the 1950 s [7].

Although the literature suggests the involvement of only a small number of people over a period of 43 years, many cases might not be reported and factitious hypoglycaemia could be a more common presentation of Munchausen's syndrome than is generally suspected.

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