The rise and fall of reactive hypoglycaemia

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Today's diabetes world is fast-moving and exciting; knowledge is accumulating at an astonishing rate. To help understand the present, however, it sometimes helps to examine the past.

In this instalment of *Tattersall's Tales*, Robert Tattersall tracks the history of 'reactive hypoglycaemia' from a deductive prediction of its possibility in the 1920s through to the American medical establishment's rejection of its existence in the 1970s.

It may surprise readers to know that in the 1970s research fellows in Ann Arbor, Michigan, supervised up to ten glucose tolerance tests a week in people thought (usually by themselves) to have reactive hypoglycaemia. Between 1924 and 1974 this condition, now accorded the status of a non-disease, was invoked to explain everything from tiredness to tachycardia and syncope to schizophrenia.

It was the brainchild of Seale Harris (1870–1957) of Birmingham, Alabama. In 1924 he reasoned that, by analogy with hypothyroidism and hyperthyroidism, diabetes should be called hypoinsulinism and speculated that there might be a condition in which the islets of Langerhans secreted too much insulin (Harris, 1924). When he first saw hypoglycaemic attacks, he realised that he had seen people without diabetes who had complained of the same symptoms: hunger, weakness and anxiety. His first patient was a physician who complained that every day an hour before lunch he felt weak, nervous and hungry and was cured by something sweet. His blood sugar was measured twice before lunch, when it was 3.6 and 3.9 mmol/l. He was advised to eat every 3 hours and a year later was symptom free.

The first insulinoma was diagnosed in 1927 and when Harris reviewed what he called 'hyperinsulinism' in 1936, he made much of the dramatic surgical cures reported since then. For example, he wrote about Whipple's cases (Harris, 1936):

> *'When the staff of the Neurological Institute of the Presbyterian Hospital became "hyperinsulinism conscious", they found five similar cases upon which Whipple operated with clinical cures. Thus six persons, who were doomed to institutional lives as psychotics, or to die in hypoglycaemic coma, were restored to health by the cooperation of the neuro-psychiatric and surgical staffs of one hospital. No doubt there are as many cases of hyperinsulinism passing, unrecognised and unrelieved, through the wards of every other large hospital in the country as were diagnosed and cured at the New York Presbyterian Hospital during the past twelve months.'*

He claimed that hyperinsulinism caused symptoms 'varying from drowsiness to narcolepsy, from vertigo to epilepsy, and from mental deficiency to mental degeneracy.' The more 'hyperinsulinism conscious' physicians became, the more cases they would diagnose. Diagnosis depended on a 6- or 8-hour glucose tolerance test!

Harris's critics, particularly Eddie Rynearson (1901–1987) from the Mayo Clinic, believed that hypoglycaemia was being overdiagnosed. Rynearson (1934) suggested that it:

> *'should not be made a waste-basket for vague and poorly defined conditions in which an unusual glucose-tolerance curve is a part of the picture rather than a cause of it.'*

Others, however, such as the respected Jerome Conn (1907–1994) of Ann Arbor embraced the diagnosis enthusiastically. In 1947 he described it as common and easily treated with a high-protein, low-carbohydrate diet (Conn, 1947). Remarkably 43 % of 'young business executives in their early forties or fifties who became utterly exhausted' were found to have hypoglycaemia (Portis et al, 1950). Whether they were cured by diet was not recorded.

Rynearson countered that of 77 patients referred to the Mayo Clinic with ? functional hypoglycaemia in 1953, 44 were discarded at once as suffering from hyperventilation or frankly functional complaints, such as nervous exhaustion. More than half the others did have hypoglycaemia but also had many psychosomatic complaints (Skillern and Rynearson, 1953).

Something which was frequently overlooked in the debate was the well-known, but usually ignored, lack of reproducibility of the glucose tolerance test and the fact that many normal people had at least one hypoglycaemic

value on the test without any symptoms.

Popularisation of the idea of hypoglycaemia as a disease which was common, easily treated and liable to be misdiagnosed or ignored began with the book *Body, Mind and Sugar* (Abrahamson and Pezet, 1951). Abrahamson was a physician who diagnosed hypoglycaemia in his co-author Pezet, a professional writer. 'Why,' he asks rhetorically in the introduction, had Pezet 'wandered through countless consultations and diagnoses and treatments for more than a decade without relief from his curious symptoms? Why was so little known about a disease affecting millions?'

The tone of the book is relatively sober, at least in relation to the many which followed. Like them, it is dedicated to Seale Harris, whose 'great discovery,' it was said, 'is still only vaguely known to most rank and file practitioners'. Treatment was a diet similar to that recommended by Conn except that the high protein content was modified as it was seen as being too monotonous and expensive. Sugar, candy, alcohol and caffeine were all prohibited and it was added that:

'the working girl's standard luncheonette breakfast of coffee and Danish is out! It's tough but not as bad as living in constant misery or blacking out at the wheel of your car.'

Low Blood Sugar and You by Carlton Fredericks and Herman Goodman is altogether more strident, judgemental and exaggerated (Fredericks and Goodman, 1979). The heading of Chapter 1 is:

'For one person in every ten, sugar is a deadly food, paving the way towards a hundred distressing physical symptoms, plus all the tortures of neurotic and even psychotic behavior.'

The reader is introduced to three case histories involving undiagnosed hypoglycaemia.

'In one case, [undiagnosed hypoglycaemia] made an invalid of a physician. In the second, it forced a wife to work to support her husband for a period of seven years. In the third, it made a secretive alcoholic of a beautiful actress, who then went through four futile years of psychiatric treatment she did not need.'

In the US the Hypoglycemia Foundation actively campaigned to legitimise hypoglycaemia as a real disease and ensure that it received proper attention from doctors. They believed it was caused by a combination of inherited adrenal dysfunction and unusual stress. Treatment with adrenal cortical extracts was recommended and the name changed to the Adrenal Research Society of the Hypoglycemia Foundation (Tintera, 1980).

The establishment was so worried that in 1973 the American Diabetes Association, the Endocrine Society, and the American Medical Association issued a joint statement (American Diabetes Association et al, 1973). It emphasised that there was no evidence that hypoglycaemia caused depression, chronic fatigue, allergies, nervous breakdowns, alcoholism, juvenile delinquency, childhood behaviour problems, drug addiction or inadequate sexual performance. A year later the *New England Journal of Medicine* published an article entitled 'Non-hypoglycemia is an epidemic condition' (Yager and Young, 1974). It began:

'Over the past few years people have appeared in droves with the self-diagnosis of "hypoglycemia" – a term that has become a layman's final common pathway for a variety of conditions, only a few of which are related to endocrinologic abnormalities. At [the University of California, Los Angeles] we have seen literally dozens of patients referred for the workup of a myriad of complaints that they attribute to this disorder.'

The epidemic of non-hypoglycaemia appears to have been almost exclusively an American phenomenon attributed by the medical establishment to a collusion between mischievous practitioners, gullible patients and the Hypoglycemia Foundation. My view is that if doctors had taken a proper history in the first place, they would have realised that they were dealing with unhappy people. When I told patients in Ann Arbor that they did *not* have hypoglycaemia, many burst into tears and poured out a list of their woes.

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