Brittle diabetes

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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 installment of *Tattersall's Tales*, Robert Tattersall explores the mysterious world of brittle diabetes – a condition characterised by recurrent episodes of diabetic ketoacidosis – unpicking the history behind current thinking regarding its cause.

"When I use a word," Humpty Dumpty said in a rather scornful tone, "it means just what I choose it to mean – neither more nor less" (Carroll, 1871). One of many problems with brittle diabetes is that there is no official definition so that the term is often used rather carelessly. The adjective "brittle" was apparently used in the 1930s by the Chicago physician Rollin T Woodyatt (1878–1953). He never wrote a paper on brittleness but contemporaries understood it to refer to excessive fluctuations of blood glucose levels that could not be explained by patient or doctor error (Tattersall, 1997).

As the child of two psychiatrists, it was not surprising that I was interested in the borderline between medicine and psychiatry. As a research fellow at King's College Hospital in 1972, I discussed problem patients with Helen Pond who was a clinical assistant and also the wife of the President of the Royal College of Psychiatrists. I was particularly interested in her stories of children who manipulated their diabetes (Pond, 1968).

When I delved into the literature in the early 1970s I found that estimates of the frequency of brittleness (by American doctors) varied from 10 to 90% of all young people with diabetes, which suggested that the word meant just what the author wanted it to mean. There also seemed to be a schism between those who attributed brittleness to innate metabolic eccentricity and others who pointed out that recurrent ketoacidosis in children was usually associated with a dysfunctional home life.

Some restricted the adjective "brittle" to people with diabetes whose glycaemia could not be controlled even under rigorous conditions in hospital where it was believed that interference with treatment was impossible. In fact, the history of factitious hypoglycaemia showed that deception was difficult to detect, even in hospital. For example, a patient from the Mayo Clinic had seven abdominal explorations between 1939 and 1944 in search of an insulinoma before a bottle of insulin was found hidden in her room and this person without diabetes "grudgingly admitted that sometimes she had given herself unneeded insulin" (Rynearson, 1947). When I worked in Ann Arbor, Michigan in 1973–4 "we" operated on an 18-year-old nurse with a suspected insulinoma only to discover weeks later that she had been injecting herself with insulin. I was thus primed to be sceptical of claims that manipulation was impossible in hospital.

In 1977 I reviewed the causes of brittle diabetes and tried to reconcile the biochemical and psychological camps by defining the person with brittle diabetes as one "whose life if constantly disrupted by episodes of hypo- or hyperglycaemia whatever their cause" (Tattersall, 1977). There were "obviously" organic causes such as Addison's disease, coeliac disease, gastroparesis etc., but these usually caused recurrent hypoglycaemia. By contrast, a convincing organic cause of recurrent ketoacidosis was hardly ever found. My limited experience recalled John Malins' comment that "conversation with some of these reformed characters is instructive as they reveal the extent of their deviations from the prescribed treatment" (Malins, 1968).

In the early 1980s many, or even most, diabetes specialists believed in a metabolic basis for brittle diabetes and two English groups and one American took up the challenge of uncovering the "real" basis of this mysterious condition. Thirteen patients "disabled by unpredictable metabolic swings" were studied at Guy's Hospital in 1980–3. All were tertiary referrals, females between the ages of 13 and 35 years, and none responded to continuous subcutaneous insulin infusion. Eight were treated with continuous intravenous insulin infusion but the results were unsatisfactory in seven and it was discontinued because of serious complications such as septicaemia and extensive venous thrombosis. What the authors called *relatively minor* infractions by the patients included "immobilising infusion pumps by inverting or removing the batteries, eating binges, feigning hypoglycaemia, faking insulin injections". More serious interference with treatment included cutting intravenous infusion lines and diluting intravenously infused insulin with tap water (Williams and Pickup, 1988).

Harry Keen later remarked perceptively that these patients were:

> *"Often anomalously placid in the face of apparently imminent disaster, [and] curiously plump after periods of uncontrol that should have led to cachexia. So often the doctor and medical staff finish in a state of defeat and despair, parents and friends in anxiety and disappointment but the patient placid, somehow defiant and even, dare one say it, triumphant" (Keen, 1985).*

Steel and Campbell (1996) described a defining factor of people with brittle diabetes as "remaining calm while those around them are agitated".

A similar group of young women was studied in Newcastle where it was thought that "the stereotyped clinical characteristics suggested a new diabetic syndrome possibly with a biochemical basis". A number of possibilities, including defective insulin absorption, degradation of insulin at the injection site, inappropriate secretion of glucagon, growth hormone, and catecholamines, accelerated ketogenesis etc., were investigated but eventually it became clear that many were interfering with therapy. At the same time as the

Newcastle and Guy's studies, David Schade investigated 30 patients (23 female) referred from all over the USA who, in spite of intensified insulin therapy, were unable to stay out of hospital long enough to lead anything approaching a normal life. Eighteen had been referred at least once to another major medical centre without a cause of brittleness being identified. Schade found that only six had recognised organic causes for their extreme brittleness. Of the rest, eight had factitious disease, eight were malingering and seven had what he called "communication disorders". In four the diagnosis of a non-organic cause was made by nurses on the clinical research unit, and I found that in Nottingham diabetes specialist nurses were excellent diagnosticians of the "real cause" of brittleness. Schade emphasised the fallacy of believing that screening by a psychiatrist can rule out factitious disease; one of his patients with factitious brittleness was described as a "mentally normal female with good family support". He also pointed out that one reason for missing factitious disease was that the possibility was never considered – "such a nice girl!", as Judith Steel later put it (Steel, 1994).

Research based on tertiary referral series leads to stereotyping because the referring physicians give the researchers what they think they want (or what the referrers want to get rid of). Thus it became accepted that brittle diabetes was the preserve of young women. However, in a 12-year follow-up of unselected people with brittle diabetes in Nottingham, I found that nearly half were men (Tattersall et al, 1991). When thinking about this, my mind went back to a patient who held the record for admissions with ketoacidosis at King's in the early 1970s. Everybody knew that he induced it to get away from his wicked stepfather or, if he had been thrown out of home, to get a bed and care for a few days. He was never called a brittle diabetic and nobody would have dreamed of referring him to St Elsewheres for further investigation.

A new cause of brittle diabetes that emerged in the 1980s was eating disorders (Steel et al, 1989). The main reason for the delayed recognition of what may always have been a relatively common cause of poor diabetes control or brittleness was that most remain in the diabetes clinic where they are conspicuous for their high blood glucose levels but nobody thinks to ask why with such awful control they do not lose weight. It is now clear that omission of doses of insulin, for whatever reason, is common among young people (Morris et al, 1997).

When Miss X is admitted for the umpteenth time with diabetic ketoacidosis, it is tempting to shrug one's shoulders but this is a dangerous condition, as shown by a recent follow-up of the original Guy's and Newcastle patients (Cartwright et al, 2011). Thirteen of the original 33 women could not be traced. Of the other 20, 10 had died, most of diabetes-related causes. None of the 10 still alive were brittle but all had severe microvascular complications. They also had substantial psychosocial morbidity with four having active psychiatric disease at the 20-year follow-up.

I agree with Judith Steel and Ian Campbell (1996) in their excellent article that a lot of effort should be devoted to the problem at an early stage to try to find out what is going on at home because this is almost certainly where the answer lies. One further point – life disruption does not have to include hospital admissions; severe hypoglycaemic brittleness is often concealed at home where the spouse resignedly accepts it as "one of those things".

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