

# A 45-year-old woman with an abnormal glucose tolerance test

COMMENTARY BY STEPHEN TWIGG MB BS, PhD, FRACP

Are the nonspecific symptoms in this woman likely to indicate hypoglycaemia?

## Case scenario

A 45-year-old woman who had been feeling generally tired and unwell for several months presented for a full medical check up. She was overweight (body mass index [BMI], 29 kg/m<sup>2</sup>) but appeared to have no other obvious health problems. Recently performed blood tests, including a full blood count and biochemistry, had been normal. The woman was very concerned that she could have diabetes, because she had read on the internet that sometimes people with insulin resistance have trouble with their weight. Therefore, I organised an oral glucose tolerance test (OGTT) with a 75 g glucose load, and simultaneous insulin levels.

The results were unexpected. Her normal fasting blood sugar level of 5.1 mmol/L fell to 3.6 mmol/L after the first 60 minutes and this was associated with her feeling quite unwell and tired. By the end of the second hour, the blood glucose level had risen to only 4.3 mmol/L. Her insulin levels were 7.9, 31.7 and

13.5 mU/L at baseline, one and two hours, respectively. (These levels did not indicate insulin resistance, according to the laboratory.) What is happening, and could this be related to her general feeling of fatigue and malaise?

## Commentary

This patient has one characteristic described that places her at increased risk of developing diabetes: her excessive body weight. In the absence of symptoms of hyperglycaemia, an appropriate screening test as per NHMRC guidelines is a fasting plasma glucose level. If this result is at or below 5.5 mmol/L then no further screening need be done. However, if the result is above 5.5 mmol/L, then a formal 75 gram OGTT should be performed.

The glucose results from this patient's OGTT are not in the diabetes or pre-diabetes range. In fact, the blood glucose level actually fell during the OGTT. While some patients do experience a reactive process in which their plasma glucose falls after an oral glucose load, the unusual feature in this case is that the patient's blood glucose level fell quite rapidly, within 60 minutes of taking the glucose load. (In those patients whose blood glucose falls after an OGTT, the level tends to decrease two or more hours after the glucose load.) It would be worthwhile ensuring that this patient has not had gastric surgery, which may cause rapid absorption of carbohydrate due to a gastric dumping syndrome.



## Does this woman have hypoglycaemia?

To determine whether a patient is truly experiencing hypoglycaemia there are three important features to assess:

- the lowest blood glucose level recorded by a laboratory test
- whether episodic symptoms consistent with hypoglycaemia occur during times of low blood glucose
- whether symptoms are relieved by carbohydrate intake.

These features collectively are known as the Whipple's triad of hypoglycaemia.

This patient developed a borderline low plasma glucose of 3.6 mmol/L during the OGTT. She reported feeling unwell and tired at this time. These symptoms, experienced when the blood glucose level was reduced, were not clearly characteristic of hypoglycaemia, which commonly produces hyperadrenergic symptoms (sweating, increased tremor, palpitation and hunger) and

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headache. Less commonly, neuroglycopenic symptoms (changes in mood, personality and cognitive function) occur in hypoglycaemia.

On balance and in my assessment, this patient does not appear to be experiencing reactive hypoglycaemia. This is because the lowest plasma glucose level recorded, 3.6 mmol/L, is not clearly in the abnormal range; up to 25% of relatively young women will have plasma glucose levels that decrease to as low as 2.8 mmol/L in the absence of symptoms.

In addition, it is not clear whether the tiredness the patient reported when the glucose level was 3.6 mmol/L is part of her generalised tiredness or is a true episodic symptom related to borderline low glucose levels that may indicate hypoglycaemia. If she does appear to develop such episodic symptoms following regular meals then distributing carbohydrate evenly across the day and focussing on frequent eating and low glycaemic index foods may help. An alternative option is a low dose of acarbose [Glucobay], which will inhibit the rate of carbohydrate absorption from the bowel into the blood, and thus help minimise swings in blood glucose levels.

### Measuring insulin levels

The measurement of serum insulin levels is overrated, and a practice that does not follow current clinical guidelines. Serum insulin assays are often quite unreliable and, in my experience, even accurate measures of serum insulin will not be of value in directing patient management in the setting described above. Better markers of insulin resistance or the metabolic syndrome are central adiposity and elevated serum triglycerides. There are no current data to show that treating according to a serum insulin level will lead to improved clinical outcomes for patients.

### Suggestions for this case

When a patient presents with nonspecific symptoms such as these, a broad range of differential diagnoses needs consideration, and a search for other symptoms and signs is required with a thorough systems review during history taking and physical examination.

Assuming this patient has no symptoms other than those described, it would be prudent to consider many potential underlying causes. Among the differential diagnoses that should be entertained

are hypothyroidism, anaemia due to any cause, perimenopause, Cushing's syndrome, obstructive sleep apnoea, low grade urinary tract infection, progressive fatty liver disease and chronic cholelithiasis. Investigations, such as a full blood count, urine microscopy, culture and sensitivity, C-reactive protein levels, sex hormone studies and a broad biochemical profile, will help to exclude many diagnoses. Other investigations that may be needed are an upper abdominal ultrasound and formal sleep studies. Major mood disorders such as severe depression also need to be considered.

In my experience, the most common cause of the symptoms that this woman is describing is mild chronic dysphoria (depressed mood state), associated with life stressors and a lack in cardiovascular and metabolic fitness – often found in people with a sedentary lifestyle. After excluding other conditions and reassuring the patient, a focus on lifestyle change with a reduction in caloric intake and a graduated physical exercise program may be the most important therapy to institute. MT

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DECLARATION OF INTEREST: None.