HbA1c or fructosamine

Why do we use HbA1c

The HbA1c test result reflects a person’s average blood glucose level for the previous two to three months. Specifically, HbA1c measures what proportion of haemoglobin - the protein in red blood cells that carries oxygen - is coated with glucose (glycated). The life span of red blood cells, and therefore haemoglobin in humans is 90-120 days. During this time the haemoglobin A is glycated in proportion to the amount of circulating glucose.

HbA1c is now used for the diagnosis as well as monitoring diabetes mellitus. It should be noted that HbA1c should not be used to diagnose diabetes mellitus in:
1. ALL symptomatic children and young people.
2. where symptoms suggest type 1 diabetes (any age).
3. where there is a short duration of diabetes symptoms.
4. in any patient who is acutely ill.

In these conditions, plasma glucose should be measured.

What is serum fructosamine

Serum fructosamine is formed by nonenzymatic glycosylation of serum proteins. Glycated albumin typically accounts for 80% of all fructosamine. Because the half-life of serum albumin is approximately 20 days, serum fructosamine generally reflects the state of glycaemic control for the preceding 2-3 weeks.

When do we use serum fructosamine

Serum fructosamine may be useful in situations where HbA1c cannot be reliably measured. These include:

1. In patients with haemoglobinopathies which prevent detection of HbA1c
2. In patients who have shortened red cell survival such as haemolytic anaemia or blood loss, when there is insufficient time for the haemoglobin to become glycated, causing the HbA1c test to be falsely low. Patients with some haemoglobin variants may have unpredictable shortening of red cell lifespan.
3. Rapid changes in diabetes treatment – fructosamine potentially permits the effectiveness of diet or medication adjustments to be evaluated after a few weeks rather than months.
4. Diabetic pregnancy – good control is essential during pregnancy, and the needs of the mother frequently change during gestation; fructosamine measurements may occasionally be requested but plasma glucose should be used for real time monitoring and managing insulin requirements (requests for fructosamine must be pre-arranged with the duty biochemist - see over for contact details).

Limitations of serum fructosamine test

Serum fructosamine CANNOT be used to diagnose or exclude diabetes because there are no evidence based diagnostic cut-offs. It is only of value to monitor glycaemic control in patients with diabetes where HbA1c cannot be used.

Serum fructosamine results may be invalid where plasma protein composition is abnormal e.g. nephrotic syndrome, severe liver cirrhosis, paraproteinaemia, untreated thyroid disease and malnutrition. High levels of vitamin C (ascorbic acid), lipaemia, haemolysis, and hyperthyroidism can interfere with test results. Patients should abstain from ascorbic acid supplements for a minimum of 24 hours prior to sample collection.
Prolactin

What is prolactin
Prolactin is a hormone produced by the anterior pituitary gland. Its function is to promote lactation in pregnancy.

Prolactin is secreted in men but it is unknown what function it has.

Normal ranges
The reference ranges in Leeds are < 550 mu/L in adult men and < 600 mu/L in adult women. Please note that reference ranges may be different in other laboratories.

What causes high values

Physiology
Prolactin is secreted in a pulsatile manner in response to such factors as stress, sleep, response to food, manipulation of the breasts, and after sexual activity.

Pregnancy
The commonest cause of raised prolactin is pregnancy and prolactin levels can increase to as high as 2500 mIU/L during the third trimester of a normal pregnancy. Oral oestrogen containing contraceptive pills can also cause hyperprolactinaemia.

Drugs
Prolactin secretion is regulated by hypothalamic dopamine which inhibits prolactin production and is therefore affected by medications that interfere with dopamine pathways.

Anti-psychotic medications are probably the best known cause of hyperprolactinaemia but this is probably because guidelines recommend screening. In fact, almost all psychotrophic medications will cause a degree of hyperprolactinaemia. Other drugs include oestrogens and antiandrogens, alpha-methyl DOPA and verapamil.

Other diseases
Hyperprolactinaemia is caused by primary hypothyroidism and pituitary tumours and damage to the hypothalamo-pituitary axis. Pituitary adenomas present with menstrual irregularities and galactorrhoea in adult women and impotence in men. Since men are reluctant to admit to impotence, prolactinomas can grow quite large and present as space occupying lesions.

Other causes of hyperprolactinaemia include liver failure, kidney failure, spinal cord tumours and breast cancer.

Hyperprolactinaemia
Is hyperprolactinaemia harmful? There has been for many years a suspicion that prolactin is related to some cancers and osteoporosis. However, both associations remain controversial and recent meta-analyses have concluded there is no conclusive link between hyper-prolactinaemia and cancer nor with osteoporosis, although in osteoporosis it is difficult to tease apart the effect of hyperprolactinaemia and any subsequent element of hypogonadism.

Macroprolactin
Some individuals develop antibodies to their own prolactin. When these bind a macro-molecule is formed which is biologically inactive but is detected by our prolactin assay. The reason that it is inactive is probably because the part of the prolactin molecule that binds receptors is hidden by the antibody whereas the part of the prolactin molecule that binds to the detection systems in the assay is exposed.

The macro-molecule is too big to be cleared by the kidneys. So it stays in circulation for longer and rises in concentration. This causes a diagnostic problem requiring further investigations to exclude the causes of hyperprolactinaemia above. Therefore we test for macroprolactin to avoid the need for unnecessary investigations. We do this by precipitating the macromolecule from the serum leaving the pure prolactin which we report as monomeric prolactin. All such investigations carry interpretative advice.

Contact for clinical advice
The duty biochemist is available at 9-5pm (Monday to Friday) and 9-1pm on Saturdays & bank holidays. Telephone 0113-39-26922 (option 2). Alternatively the duty biochemist can be contacted by email on: leedsth-tr.biochemist@nhs.net. At other hours contact through LTHT switchboard.