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The Thistle QA CEU No is: **MT00025**.

Each attendee should claim **THREE** CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

CHEMISTRY LEGEND

APRIL 2009

HYPOGLYCAEMIA

Hypoglycaemia is the medical term for a pathologic state produced by a lower than normal level of blood glucose. The term *hypoglycaemia* literally means "under-sweet blood". Hypoglycaemia can produce a variety of symptoms and effects but the principal problems arise from an inadequate supply of glucose as fuel to the brain, resulting in impairment of function (neuroglycopenia). Derangements of function can range from dysphoria or "feeling bad" to coma, seizures, and (rarely) permanent brain damage or death. Hypoglycaemia can arise from many causes and can occur at any age. It also sometimes occurs at what appears to be random intervals.

The most common forms of moderate and severe hypoglycaemia occur as a complication of treatment of diabetes mellitus treated with insulin or less frequently with certain oral medications. Hypoglycaemia is usually treated by the ingestion or administration of dextrose, or foods quickly digestible to glucose. The level of glucose low enough to define hypoglycaemia has been a source of controversy in several contexts. For many purposes, plasma glucose levels below 3.9mmol/L are considered hypoglycaemic.

Defining hypoglycemia

No single glucose value alone serves to define the medical condition termed hypoglycaemia for all people and purposes. Throughout the 24 hour cycles of eating, digestion, and fasting, blood plasma glucose levels are generally maintained within a range of 3.9-7.8mmol/L for healthy humans. Although 3.3 or 3.9mmol/L is commonly cited as the lower limit of normal glucose, different values have been defined as low for different populations, clinical purposes, or circumstances.

The precise level of glucose considered low enough to define hypoglycaemia is dependent on (1) the measurement method, (2) the age of the person, (3) presence or absence of effects, and (4) the purpose of the definition. While there is no disagreement as to the normal range of blood sugar, debate continues as to what degree of hypoglycemia warrants medical evaluation or treatment, or can cause harm.

Method of measurement

Blood glucose levels are venous plasma or serum levels measured by standard, automated glucose oxidase methods. For clinical purposes, plasma and serum levels are similar enough to be interchangeable. Arterial plasma or serum levels are slightly higher than venous levels, and capillary levels are typically in between. This difference between arterial and venous levels is small in the fasting state but is amplified and can be greater than 10% in the postprandial state.

On the other hand, whole blood glucose levels (e.g., by fingerprick meters) are about 10%-15% lower than venous plasma levels. Furthermore, available fingerstick glucose meters are only warranted to be accurate to within 15% of a simultaneous laboratory value under optimal conditions, and home use in the investigation of hypoglycaemia is fraught with misleading low numbers. In other words, a meter glucose reading of 2.16mmol/L could be properly obtained from a person whose laboratory serum glucose was 2.94mmol/l, even wider variations can occur with "real world" home use. Ironically, most meters sold are routinely tested for accuracy at the high-end of the scale, sometimes up to 44.4mmol/L, despite the fact that there is little immediate danger from hyperglycaemia, whereas there is very real immediate danger from hypoglycaemia, making accuracy at the low-end extremely critical.

Two other factors significantly affect glucose measurement: in newborn infants - increased hematocrit and a delay in measuring low glucose levels; or adults with polycythaemia. High neonatal hematocrits are particularly likely to confound glucose measurement by meter. Second, unless the specimen is drawn into a fluoride tube or processed immediately to separate the serum or plasma from the cells, the measurable glucose will be gradually lowered by *in vitro* metabolism of the glucose at a rate of approximately 0.39mmol/L/hr, or even more in the presence of leukocytosis.

Purpose of definition

Deciding whether blood glucose in the borderline range of 2.5-4.2 mmol/l represents clinically problematic hypoglycaemia is not always simple. This leads people to use different "cutoff levels" of glucose in different contexts and for different purposes.

Pathophysiology

Like most animal tissues, brain metabolism depends primarily on glucose for fuel in most circumstances. A limited amount of glucose can be derived from glycogen stored in astrocytes, but it is consumed within minutes. For most practical purposes, the brain is dependent on a continual supply of glucose diffusing from the blood into the interstitial tissue within the central nervous system and into the neurons themselves.

Therefore, if the amount of glucose supplied by the blood falls, the brain is one of the first organs affected. In most people, subtle reduction of mental efficiency can be observed when the glucose falls to 3.6mmol/L. Impairment of action and judgment usually becomes obvious below 2.2mmol/L. Seizures may occur as the glucose falls further. As blood glucose levels fall below 0.55 mmol/L, most neurons become electrically silent and nonfunctional, resulting in coma.

These brain effects are collectively referred to as neuroglycopenia. The importance of an adequate supply of glucose to the brain is apparent from the number of nervous, hormonal and metabolic responses to a falling glucose level. Most of these are defensive or adaptive, tending to raise the blood sugar via glycogenolysis and gluconeogenesis or provide alternative fuels. If the blood sugar level falls too low the liver converts stored glycogen into glucose and releases it into the bloodstream, to prevent the person going into a diabetic coma, for a short period of time.

Brief or mild hypoglycaemia produces no lasting effects on the brain, though it can temporarily alter brain responses to additional hypoglycemia. Prolonged, severe hypoglycaemia can produce lasting damage of a wide range. This can include impairment of cognitive function, motor control, or even consciousness. The likelihood of permanent brain damage from any given instance of severe hypoglycaemia is difficult to estimate, and depends on a multitude of factors such as age, recent blood and brain glucose experience, concurrent problems such as hypoxia, and availability of alternative fuels. The vast majority of symptomatic hypoglycaemic episodes result in no detectable permanent harm.

Signs and symptoms

Hypoglycaemic symptoms and manifestations can be divided into those produced by the counter regulatory hormones (epinephrine/adrenaline and glucagon) triggered by the falling glucose, and the neuroglycopenic effects produced by the reduced brain sugar.

<p>Adrenergic manifestations Shakiness, anxiety, nervousness, tremor Palpitations, tachycardia Sweating, feeling of warmth Pallor, coldness, clamminess Dilated pupils (mydriasis) Feeling of numbness "pins and needles" (parasthaesia) in the fingers Glucagon manifestations Hunger, vomiting, abdominal discomfort Headache</p>	<p>Neuroglycopenic manifestations Abnormal mentation, impaired judgment Nonspecific dysphoria, anxiety, moodiness, depression, crying Negativism, irritability, belligerence, combativeness, rage Personality change, emotional lability Fatigue, weakness, apathy, lethargy, daydreaming, sleep Confusion, amnesia, dizziness, delirium Staring, "glassy" look, blurred vision, double vision Automatic behavior, also known as automatism Difficulty speaking, slurred speech Ataxia, incoordination, sometimes mistaken for "drunkenness" Focal or general motor deficit, paralysis, hemiparesis Paresthesia, headache Stupor, coma, abnormal breathing Generalized or focal seizures</p>
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Treatment and prevention

Management of hypoglycaemia involves immediately raising the blood sugar to normal, determining the cause, and taking measures to hopefully prevent future episodes.

Reversing acute hypoglycemia

The blood glucose can be raised to normal within minutes by taking (or receiving) 10-20 grams of carbohydrate. It can be taken as food or drink if the person is conscious and able to swallow. This amount of carbohydrate is contained in about 100-120 ml of orange, apple, or grape juice although fruit juices contain a higher proportion of fructose which is more slowly metabolized than pure dextrose, alternatively, about 120-150 ml of regular (non-diet) soda may also work, as will about one slice of bread, about 4 crackers, or about 1 serving of most starchy foods. Starch is quickly digested to glucose (unless the person is taking acarbose), but adding fat or protein retards digestion. Symptoms should begin to improve within 5 minutes, though full recovery may take 10-20 minutes. Overfeeding does not speed recovery and if the person has diabetes will simply produce hyperglycemia afterwards.

If a person is suffering such severe effects of hypoglycaemia that they cannot (due to combativeness) or should not (due to seizures or unconsciousness) be given anything by mouth, medical personnel can establish an IV and give intravenous Dextrose, of varying concentrations depending on age. If an IV cannot be established, the patient can be given 1 to 2 milligrams of Glucagon in an intramuscular injection

References

1. Philip E. Cryer (1997). *Hypoglycemia: pathophysiology, diagnosis, and treatment*. Oxford [Oxfordshire]: Oxford University Press. ISBN 0-19-511325-X. OCLC 36188385.
2. Koh TH, Eyre JA, Aynsley-Green A (1988). "Neonatal hypoglycaemia--the controversy regarding definition". *Arch. Dis. Child.* 63 (11): 1386-8. PMID 3202648.
3. Vasudevan A Raghavan, MBBS, MD, MRCP, Assistant Professor, Department of Internal Medicine, Divisions of Endocrinology, Diabetes and Metabolism and Cardiovascular Sciences, Ohio State.

Questions

1. Define the term Hypoglycaemia.
 2. Discuss the method of measurement for glucose.
 3. Discuss the pathophysiology of hypoglycaemia including signs and symptoms.
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