Hypoglycemia

Hypoglycemia, also known as **low blood sugar**, is a fall in blood sugar to levels below normal.[1] This may result in a variety of symptoms including clumsiness, trouble talking, confusion, loss of consciousness, seizures or death.[1] A feeling of hunger, sweating, shakiness and weakness may also be present.[1] Symptoms typically come on quickly.[1]

Hypoglycemia	
Other names	Hypoglycaemia, hypoglycæmia, low blood glucose
	 Glucose meter
Specialty	Endocrinology
Symptoms	Clumsiness, difficulty talking, confusion, loss of consciousness, seizures[1]
Usual onset	Rapid[1]
Causes	Medications (insulin and sulfonylureas), sepsis, kidney failure, certain tumors, liver disease[1][2][3]
Diagnostic method	Blood sugar level < 3.9 mmol/L (70 mg/dL) in a diabetic[1]
Treatment	Eating foods high in simple sugars, dextrose, glucagon[1]

The most common cause of hypoglycemia is medications used to treat diabetes mellitus such as insulin and sulfonylureas.[2][3] Risk is greater in diabetics who have eaten less than usual, exercised more than usual or drunk alcohol.[1] Other causes of hypoglycemia include kidney failure, certain tumors (such as insulinoma), liver disease, hypothyroidism, starvation, inborn error of metabolism, severe infections, reactive hypoglycemia and a number of drugs including alcohol.[1][3] Low blood sugar may occur in otherwise healthy babies who have not eaten for a few hours.[4]

The glucose level that defines hypoglycemia is variable.[1] In people with diabetes, levels below 3.9 mmol/L (70 mg/dL) are diagnostic.[1] In adults without diabetes, symptoms related to low blood sugar, low blood sugar at the time of symptoms and improvement when blood sugar is restored to normal confirm the diagnosis.[5] Otherwise, a level below 2.8 mmol/L (50 mg/dL) after not eating or following exercise may be used.[1] In newborns, a level below 2.2 mmol/L (40 mg/dL), or less than 3.3 mmol/L (60 mg/dL) if symptoms are present, indicates hypoglycemia.[4] Other tests that may be useful in determining the cause include insulin and C peptide levels in the blood.[3]

Among people with diabetes, prevention is by matching the foods eaten with the amount of exercise and the medications used.[1] When people feel their blood sugar is low, testing with a glucose monitor is recommended.[1] Some people have few initial symptoms of low blood sugar, and frequent routine testing in this group is recommended.[1] Treatment of hypoglycemia is by eating foods high in simple sugars or taking dextrose.[1] If a person is not able to take food by mouth, glucagon by injection or in the nose may help.[1][6] The treatment of hypoglycemia unrelated to diabetes includes treating the underlying

problem as well and a healthy diet.[1] The term "hypoglycemia" is sometimes incorrectly used to refer to idiopathic postprandial syndrome, a controversial condition with similar symptoms that occur following eating but with normal blood sugar levels.[7][8]

Contents

Signs and symptoms

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

- Shakiness, anxiety, nervousness
- Palpitations, tachycardia
- Sweating, feeling of warmth (sympathetic muscarinic rather than adrenergic)
- Pallor, coldness, clamminess
- Dilated pupils (mydriasis)
- Hunger, borborygmus
- Nausea, vomiting, abdominal discomfort
- Headache

Central nervous system

- Abnormal thinking, impaired judgment
- Nonspecific dysphoria, moodiness, depression, crying, exaggerated concerns
- Feeling of numbness, pins and needles (paresthesia)
- Negativism, irritability, belligerence, combativeness, rage
- Personality change, emotional lability
- Fatigue, weakness, apathy, lethargy, daydreaming, sleep
- Confusion, memory loss, lightheadedness or dizziness, delirium
- Staring, glassy look, blurred vision, double vision
- Flashes of light in the field of vision
- Automatic behavior, also known as automatism
- Difficulty speaking, slurred speech
- Ataxia, incoordination, sometimes mistaken for drunkenness
- Focal or general motor deficit, paralysis, hemiparesis
- Headache
- Stupor, coma, abnormal breathing
- Generalized or focal seizures

Not all of the above manifestations occur in every case of hypoglycemia. There is no consistent order to the appearance of the symptoms, if symptoms even occur. Specific manifestations may also vary by age, by severity of the hypoglycemia and the speed of the decline. In young children, vomiting can sometimes accompany morning hypoglycemia with ketosis. In older children and adults, moderately severe hypoglycemia can resemble mania, mental illness, drug intoxication, or drunkenness. In the elderly, hypoglycemia can produce focal stroke-like effects or a hard-to-define malaise. The symptoms of a single person may be similar from episode to episode, but are not necessarily so and may be influenced by the speed at which glucose levels are dropping, as well as previous incidents.

In newborns, hypoglycemia can produce irritability, jitters, myoclonic jerks, cyanosis, respiratory distress, apneic episodes, sweating, hypothermia, somnolence, hypotonia, refusal to feed, and seizures or "spells." Hypoglycemia can resemble asphyxia, hypocalcemia, sepsis, or heart failure.

In both young and old people with hypoglycemia, the brain may habituate to low glucose levels, with a reduction of noticeable symptoms despite neuroglycopenic impairment. In insulin-dependent diabetic people this phenomenon is termed *hypoglycemia unawareness* and is a significant clinical problem when improved glycemic control is attempted. Another aspect of this phenomenon occurs in type I glycogenosis, when chronic hypoglycemia before diagnosis may be better tolerated than acute hypoglycemia after treatment is underway.

Hypoglycemic symptoms can also occur when one is sleeping. Examples of symptoms during sleep can include damp bed sheets or clothes from perspiration. Having nightmares or the act of crying out can be a sign of hypoglycemia. Once the individual is awake they may feel tired, irritable, or confused and these may be signs of hypoglycemia as well.[9]

In nearly all cases, hypoglycemia that is severe enough to cause seizures or unconsciousness can be reversed without obvious harm to the brain. Cases of death or permanent neurological damage occurring with a single episode have usually involved prolonged, untreated unconsciousness, interference with breathing, severe concurrent disease, or some other type of vulnerability. Nevertheless, brain damage or death has occasionally resulted from severe hypoglycemia.

Research in healthy adults shows that mental efficiency declines slightly but measurably as blood glucose falls below 3.6 mM (65 mg/dL). Hormonal defense mechanisms (adrenaline and glucagon) are normally activated as it drops below a threshold level (about 55 mg/dL (3.0 mM) for most people), producing the typical hypoglycemic symptoms of shakiness and dysphoria.[10]:1589 Obvious impairment may not occur until the glucose falls below 40 mg/dL (2.2 mM), and many healthy people may occasionally have glucose levels below 65 in the morning without apparent effects. Since the brain effects of hypoglycemia, termed neuroglycopenia, determine whether a given low glucose is a "problem" for that person, most doctors use the term *hypoglycemia* only when a moderately low glucose level is accompanied by symptoms or brain effects.

Determining the presence of both parts of this definition is not always straightforward, as hypoglycemic symptoms and effects are vague and can be produced by other conditions; people with recurrently low glucose levels can lose their threshold symptoms so that severe neuroglycopenic impairment can occur without much warning, and many measurement methods (especially glucose meters) are imprecise at low levels.

It may take longer to recover from severe hypoglycemia with unconsciousness or seizure even after restoration of normal blood glucose. When a person has not been unconscious, failure of carbohydrate to reverse the symptoms in 10–15 minutes increases the likelihood that hypoglycemia was not the cause of the symptoms. When severe hypoglycemia has persisted in a hospitalized person, the amount of glucose required to maintain satisfactory blood glucose levels becomes an important clue to the underlying cause. Glucose requirements above 10 mg/kg/minute in infants, or 6 mg/kg/minute in children and adults are strong evidence for hyperinsulinism. In this context this is referred to as the *glucose infusion rate* (GIR). Finally, the blood glucose response to glucagon given when the glucose is low can also help distinguish among various types of hypoglycemia. A rise of blood glucose by more than 30 mg/dL (1.70 mmol/l) suggests insulin excess as the probable cause of the hypoglycemia.

Long-term effects

Significant hypoglycemia appears to increase the risk of cardiovascular disease.[11]

Causes

The most common cause of hypoglycemia is medications used to treat diabetes mellitus such as insulin, sulfonylureas, and biguanides.[2][3] Risk is greater in diabetics who have eaten less than usual, exercised more than usual, or drunk alcohol.[1] Other causes of hypoglycemia include kidney failure, certain tumors, liver disease, hypothyroidism, starvation, inborn errors of metabolism, severe infections, reactive hypoglycemia, and a number of drugs including alcohol.[1][3] Low blood sugar may occur in babies who are otherwise healthy who have not eaten for a few hours.[4] Inborn errors of metabolism may include the lack of an enzyme to make glycogen (glycogen storage type 0).

Serious illness

Serious illness may result in low blood sugar.[1] Severe disease of nearly all major organ systems can cause hypoglycemia as a secondary problem. Hospitalized persons, especially in intensive care units or those prevented from eating, can develop hypoglycemia from a variety of circumstances related to the

care of their primary disease. Hypoglycemia in these circumstances is often multifactorial or caused by the healthcare. Once identified, these types of hypoglycemia are readily reversed and prevented, and the underlying disease becomes the primary problem.

Hormone deficiency

Not enough cortisol, such as in Addison's disease, not enough glucagon, or not enough epinephrine can result in low blood sugar.[1] This is a more common cause in children.[1]

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 below 65 mg/dL (3.6 mM). Impairment of action and judgment usually becomes obvious below 40 mg/dL (2.2 mM). Seizures may occur as the glucose falls further. As blood glucose levels fall below 10 mg/dL (0.55 mM), 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 by glycogenolysis and gluconeogenesis or provide alternative fuels. If the blood sugar level falls too low, the liver converts a storage of glycogen into glucose and releases it into the bloodstream, to prevent the person going into a diabetic coma, for a short time.

Brief or mild hypoglycemia produces no lasting effects on the brain, though it can temporarily alter brain responses to additional hypoglycemia. Prolonged, severe hypoglycemia 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 hypoglycemia 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. Prior hypoglycemia also blunts the counterregulatory response to future hypoglycemia [12]. While the mechanism leading to blunted counterregulation is unknown several have been proposed.[13]

It has been frequently found that those type 1 diabetics found "dead in bed" in the morning after suspected severe hypoglycemia had some underlying coronary pathology that led to an induced fatal heart attack.[14] In 2010, a case report was published demonstrating the first known case of an individual found "dead in bed" whilst wearing a continuous glucose monitor (CGM), which provided a history of glucose levels before the fatal event; the person had suffered a severe hypoglycemic incident, and while the authors described only a "minimal counter-regulatory response" they stated no "anatomic abnormalities" were observed during autopsy.[15]

The vast majority of symptomatic hypoglycemic episodes result in no detectable permanent harm.[16]

Diagnosis

The glucose level that defines hypoglycemia is variable. In diabetics a level below 3.9 mmol/L (70 mg/dL) is diagnostic.[1] In adults without diabetes, symptoms related to low blood sugar, low blood sugar at the time of symptoms, and improvement when blood sugar is restored to normal confirm the diagnosis.[5] This is known as the Whipple's triad.[5] Otherwise a level below 2.8 mmol/L (50 mg/dL) after not eating or following exercise may be used.[1] In newborns a level below 2.2 mmol/L (40 mg/dL) or less than 3.3 mmol/L (60 mg/dL) if symptoms are present indicates hypoglycemia.[4] Other tests that may be useful in determining the cause include insulin and C peptide levels in the blood.[3] Hyperglycemia, a high blood sugar, is the opposite condition.

Throughout a 24-hour period blood plasma glucose levels are generally maintained between 4–8 mmol/L (72 and 144 mg/dL).[17]:11 Although 3.3 or 3.9 mmol/L (60 or 70 mg/dL) is commonly cited as the lower limit of normal glucose, symptoms of hypoglycemia usually do not occur until 2.8 to 3.0 mmol/L (50 to 54 mg/dL).[18]

In cases of recurrent hypoglycemia with severe symptoms, the best method of excluding dangerous conditions is often a *diagnostic fast*. This is usually conducted in the hospital, and the duration depends on the age of the person and response to the fast. A healthy adult can usually maintain a glucose level above 50 mg/dL (2.8 mM) for 72 hours, a child for 36 hours, and an infant for 24 hours. The purpose of the fast is to determine whether the person can maintain his or her blood glucose as long as normal, and can respond to fasting with the appropriate metabolic changes. At the end of the fast the insulin should be nearly undetectable and ketosis should be fully established. The person's blood glucose levels are monitored and a critical specimen is obtained if the glucose falls. Despite its unpleasantness and expense, a diagnostic fast may be the only effective way to confirm or refute a number of serious forms of hypoglycemia, especially those involving excessive insulin.

The precise level of glucose considered low enough to define hypoglycemia 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.[19][20][21]

Deciding whether a blood glucose in the borderline range of 45–75 mg/dL (2.5–4.2 mM) represents clinically problematic hypoglycemia is not always simple. This leads people to use different "cutoff levels" of glucose in different contexts and for different purposes. Because of all the variations, the Endocrine Society recommends that a diagnosis of hypoglycemia as a problem for an individual be based on the combination of a low glucose level and evidence of adverse effects.[5]

Glucose concentrations are expressed as milligrams per deciliter (mg/dL or mg/100 mL) in Lebanon, the United States, Japan, Portugal, Spain, France, Belgium, Egypt, Turkey, Saudi Arabia, Colombia, India and Israel, while millimoles per liter (mmol/L or mM) are the units used in most of the rest of the world. Glucose concentrations expressed as mg/dL can be converted to mmol/L by dividing by 18.0 g/dmol (the molar mass of glucose). For example, a glucose concentration of 90 mg/dL is 5.0 mmol/L or 5.0 mM.

The circumstances of hypoglycemia provide most of the clues to diagnosis. Circumstances include the age of the person, time of day, time since last meal, previous episodes, nutritional status, physical and mental development, drugs or toxins (especially insulin or other diabetes drugs), diseases of other organ systems, family history, and response to treatment. When hypoglycemia occurs repeatedly, a record or

"diary" of the spells over several months, noting the circumstances of each spell (time of day, relation to last meal, nature of last meal, response to carbohydrate, and so forth) may be useful in recognizing the nature and cause of the hypoglycemia.

Method of measurement

Blood glucose levels discussed in this article are venous plasma or serum levels measured by standard, automated glucose oxidase methods used in medical laboratories. 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.[22] 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.[23] On the other hand, whole blood glucose levels (e.g., by fingerprick meters) are about 10–15% lower than venous plasma levels.[22] 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 hypoglycemia is fraught with misleading low numbers.[24][25] In other words, a meter glucose reading of 39 mg/dL could be properly obtained from a person whose laboratory serum glucose was 53 mg/dL; even wider variations can occur with "real world" home use.

Two other factors significantly affect glucose measurement: hematocrit and delay after blood drawing. The disparity between venous and whole blood concentrations is greater when the hematocrit is high, as in newborn infants, or adults with polycythemia.[23] 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 7 mg/dL/h, or even more in the presence of leukocytosis.[23][26][27] The delay that occurs when blood is drawn at a satellite site and transported to a central laboratory hours later for routine processing is a common cause of mildly low glucose levels in general chemistry panels.

Age

Children's blood sugar levels are often slightly lower than adults'. Overnight fasting glucose levels are below 70 mg/dL (3.9 mM) in 5% of healthy adults, but up to 5% of children can be below 60 mg/dL (3.3 mM) in the morning fasting state.[28] As the duration of fasting is extended, a higher percentage of infants and children will have mildly low plasma glucose levels, typically without symptoms. The normal range of newborn blood sugars continues to be debated.[19][20][21] It has been proposed that newborn brains are able to use alternate fuels when glucose levels are low more readily than adults. Experts continue to debate the significance and risk of such levels, though the trend has been to recommend maintenance of glucose levels above 60–70 mg/dL the first day after birth.

Diabetic hypoglycemia represents a special case with respect to the relationship of measured glucose and hypoglycemic symptoms for several reasons. First, although home glucose meter readings are often misleading, the probability that a low reading, whether accompanied by symptoms or not, represents real hypoglycemia is much higher in a person who takes insulin than in someone who does not.[29][30]

Other tests

The following is a brief list of hormones and metabolites which may be measured in a critical sample. Not all tests are checked on every person. A "basic version" would include insulin, cortisol, and electrolytes, with C-peptide and drug screen for adults and growth hormone in children. The value of additional specific tests depends on the most likely diagnoses for an individual person, based on the circumstances described above. Many of these levels change within minutes, especially if glucose is given, and there is no value in measuring them after the hypoglycemia is reversed. Others, especially those lower in the list, remain abnormal even after hypoglycemia is reversed, and can be usefully measured even if a critical specimen is missed.

Part of the value of the critical sample may simply be the proof that the symptoms are indeed due to hypoglycemia. More often, measurement of certain hormones and metabolites at the time of hypoglycemia indicates which organs and body systems are responding appropriately and which are functioning abnormally. For example, when the blood glucose is low, hormones which raise the glucose should be rising and insulin secretion should be completely suppressed.

Differential diagnosis

It can also be mistaken for alcohol intoxication.[31]

Prevention

The most effective means of preventing further episodes of hypoglycemia depends on the cause.

The risk of further episodes of diabetic hypoglycemia can often (but not always) be reduced by lowering the dose of insulin or other medications, or by more meticulous attention to blood sugar balance during unusual hours, higher levels of exercise, or decreasing alcohol intake.

Many of the inborn errors of metabolism require avoidance or shortening of fasting intervals, or extra carbohydrates. For the more severe disorders, such as type 1 glycogen storage disease, this may be supplied in the form of cornstarch every few hours or by continuous gastric infusion.

Several treatments are used for hyperinsulinemic hypoglycemia, depending on the exact form and severity. Some forms of congenital hyperinsulinism respond to diazoxide or octreotide. Surgical removal of the overactive part of the pancreas is curative with minimal risk when hyperinsulinism is focal or due to a benign insulin-producing tumor of the pancreas. When congenital hyperinsulinism is diffuse and refractory to medications, near-total pancreatectomy may be the treatment of last resort, but in this condition is less consistently effective and fraught with more complications.

Hypoglycemia due to hormone deficiencies such as hypopituitarism or adrenal insufficiency usually ceases when the appropriate hormone is replaced.

Hypoglycemia due to dumping syndrome and other post-surgical conditions is best dealt with by altering diet. Including fat and protein with carbohydrates may slow digestion and reduce early insulin secretion. Some forms of this respond to treatment with an alpha-glucosidase inhibitor, which slows starch digestion.

Reactive hypoglycemia with demonstrably low blood glucose levels is most often a predictable nuisance which can be avoided by consuming fat and protein with carbohydrates, by adding morning or afternoon snacks, and reducing alcohol intake.

Idiopathic postprandial syndrome without demonstrably low glucose levels at the time of symptoms can be more of a management challenge. Many people find improvement by changing eating patterns (smaller meals, avoiding excessive sugar, mixed meals rather than carbohydrates by themselves), reducing intake of stimulants such as caffeine, or by making lifestyle changes to reduce stress. See the following section of this article.

Treatment

Treatment of some forms of hypoglycemia, such as in diabetes, involves immediately raising the blood sugar to normal through the eating of carbohydrates such as sugars, determining the cause, and taking measures to hopefully prevent future episodes. However, this treatment is not optimal in other forms such as reactive hypoglycemia, where rapid carbohydrate ingestion may lead to a further hypoglycemic episode.

Blood glucose can be raised to normal within minutes by taking (or receiving) 10–20 grams of carbohydrate.[32] 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 3–4 ounces (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 4–5 ounces (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. A mnemonic used by the American Diabetes Association and others is the "rule of 15" – consuming 15 grams of carbohydrate followed by a 15-minute wait, repeated if glucose remains low (variable by individual, sometimes 70 mg/dL).[33]

If a person has such severe effects of hypoglycemia that they cannot (due to combativeness) or should not (due to seizures or unconsciousness) be given anything by mouth, medical personnel such as paramedics, or in-hospital personnel can establish IV access and give intravenous dextrose, concentrations varying depending on age (infants are given 2 ml/kg dextrose 10%, children are given dextrose 25%, and adults are given dextrose 50%). Care must be taken in giving these solutions because they can cause skin necrosis if the IV is infiltrated, sclerosis of veins, and many other fluid and electrolyte disturbances if administered incorrectly. If IV access cannot be established, the person can be given 1 to 2 milligrams of glucagon in an intramuscular injection. More treatment information can be found in the article diabetic hypoglycemia. If a person has less severe effects, and is conscious with the ability to swallow, medical personal may administer gelatinous oral glucose. The soft drink Lucozade has been used for hypoglycemia in the United Kingdom, however it has recently replaced much of its glucose with the artificial sugars, which do not treat hypoglycemia.[34]

One situation where starch may be less effective than glucose or sucrose is when a person is taking acarbose. Since acarbose and other alpha-glucosidase inhibitors prevents starch and other sugars from being broken down into monosaccharides that can be absorbed by the body, people taking these medications should consume monosaccharide-containing foods such as glucose tablets, honey, or juice to reverse hypoglycemia.

History

Hypoglycemia was first discovered by James Collip when he was working with Frederick Banting on purifying insulin in 1922. Collip was tasked with developing an assay to measure the activity of insulin. He first injected insulin into a rabbit, and then measured the reduction in blood glucose levels. Measuring blood glucose was a time consuming step. Collip observed that if he injected rabbits with a too large a dose of insulin, the rabbits began convulsing, went into a coma, and then died. This observation simplified his assay. He defined one unit of insulin as the amount necessary to induce this convulsing hypoglycemic reaction in a rabbit. Collip later found he could save money, and rabbits, by injecting them with glucose once they were convulsing.[35]

Etymology

The word *hypoglycemia* is also spelled *hypoglycaemia* or *hypoglycæmia*. The term means low blood sugar in Greek. *ὑπογλυκαιμία*, from *hypo-*, *glykys*, *haima*.

See also

- *Diabetic Hypoglycemia* (journal)
- Idiopathic hypoglycemia
- Neonatal hypoglycemia

References

1. "Hypoglycemia" (http://www.niddk.nih.gov/health-information/health-topics/Diabetes/hypoglycemia/Pages/index.aspx). *National Institute of Diabetes and Digestive and Kidney Diseases*. October 2008. Archived (https://web.archive.org/web/20150701034430/http://www.niddk.nih.gov/health-information/health-topics/Diabetes/hypoglycemia/Pages/index.aspx) from the original on 1 July 2015. Retrieved 28 June 2015.
2. Yanai H, Adachi H, Katsuyama H, Moriyama S, Hamasaki H, Sako A (February 2015). "Causative anti-diabetic drugs and the underlying clinical factors for hypoglycemia in patients with diabetes" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4317315). *World Journal of Diabetes*. **6** (1): 30–6. doi:10.4239/wjd.v6.i1.30 (https://doi.org/10.4239%2Fwjd.v6.i1.30). PMC 4317315 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4317315). PMID 25685276 (https://pubmed.ncbi.nlm.nih.gov/25685276).
3. Schrier RW (2007). *The internal medicine casebook real patients, real answers* (https://books.google.com/books?id=zbuKcQwh2b0C&pg=PA119) (3rd ed.). Philadelphia: Lippincott Williams & Wilkins. p. 119. ISBN 978-0-7817-6529-9.
4. Perkin RM (2008). *Pediatric hospital medicine : textbook of inpatient management* (https://books.google.com/books?id=sV6-ifUGoMYC&pg=PA105) (2nd ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins. p. 105. ISBN 978-0-7817-7032-3.
5. Cryer PE, Axelrod L, Grossman AB, Heller SR, Montori VM, Seaquist ER, Service FJ (March 2009). "Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline". *J. Clin. Endocrinol. Metab*. **94** (3): 709–28. doi:10.1210/jc.2008-1410 (https://doi.org/10.1210%2Fjc.2008-1410). PMID 19088155 (https://pubmed.ncbi.nlm.nih.gov/19088155).
6. "FDA approves first treatment for severe hypoglycemia that can be administered without an injection" (https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-severe-hypoglycemia-can-be-administered-without-injection). *FDA*. 11 September 2019. Retrieved 11 November 2019.

7. Talreja RS (2005). *The internal medicine peripheral brain* (https://books.google.com/books?id=oj-d2AgfW48C&pg=PA176). Philadelphia, Pa.: Lippincott Williams & Wilkins. p. 176. ISBN 978-0-7817-2806-5.
8. *Dorland's illustrated medical dictionary* (https://books.google.com/books?id=mNACisYwbZoC&pg=PA1834) (32nd ed.). Philadelphia: Elsevier/Saunders. 2012. p. 1834. ISBN 978-1-4557-0985-4.
9. "Hypoglycemia – National Diabetes Information Clearinghouse" (http://diabetes.niddk.nih.gov/dm/pubs/hypoglycemia). Diabetes.niddk.nih.gov. Archived (https://web.archive.org/web/20120308211445/http://diabetes.niddk.nih.gov/dm/pubs/hypoglycemia/) from the original on 8 March 2012. Retrieved 10 March 2012.
10. Cryer PE (2003). "Glucose homestasis and hypoglycemia". In Larsen PR (ed.). *Williams Textbook of Endocrinology* (10th ed.). Philadelphia: W.B. Saunders. pp. 1585–1618. ISBN 978-0-7216-9196-1.
11. Goto A, Arah OA, Goto M, Terauchi Y, Noda M (July 2013). "Severe hypoglycaemia and cardiovascular disease: systematic review and meta-analysis with bias analysis". *BMJ (Clinical Research Ed.)*. **347**: f4533. doi:10.1136/bmj.f4533 (https://doi.org/10.1136%2Fbmj.f4533). PMID 23900314 (https://pubmed.ncbi.nlm.nih.gov/23900314).
12. Davis SN, Shavers C, Mosqueda-Garcia R, Costa F (August 1997). "Effects of differing antecedent hypoglycemia on subsequent counterregulation in normal humans". *Diabetes*. **46** (8): 1328–35. doi:10.2337/diab.46.8.1328 (https://doi.org/10.2337%2Fdiab.46.8.1328). PMID 9231658 (https://pubmed.ncbi.nlm.nih.gov/9231658).
13. Martín-Timón I, Del Cañizo-Gómez FJ (July 2015). "Mechanisms of hypoglycemia unawareness and implications in diabetic patients" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4499525). *World Journal of Diabetes*. **6** (7): 912–26. doi:10.4239/wjd.v6.i7.912 (https://doi.org/10.4239%2Fwjd.v6.i7.912). PMC 4499525 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4499525). PMID 26185599 (https://pubmed.ncbi.nlm.nih.gov/26185599).
14. Secrest AM, Becker DJ, Kelsey SF, Laporte RE, Orchard TJ (March 2011). "Characterizing sudden death and dead-in-bed syndrome in Type 1 diabetes: analysis from two childhood-onset Type 1 diabetes registries" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3045678). *Diabetic Medicine*. **28** (3): 293–300. doi:10.1111/j.1464-5491.2010.03154.x (https://doi.org/10.1111%2Fj.1464-5491.2010.03154.x). PMC 3045678 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3045678). PMID 21309837 (https://pubmed.ncbi.nlm.nih.gov/21309837).
15. Tanenberg RJ, Newton CA, Drake AJ (2010). "Confirmation of hypoglycemia in the "dead-in-bed" syndrome, as captured by a retrospective continuous glucose monitoring system". *Endocrine Practice*. **16** (2): 244–8. doi:10.4158/EP09260.CR (https://doi.org/10.4158%2FEP09260.CR). PMID 19833577 (https://pubmed.ncbi.nlm.nih.gov/19833577).
16. Arieff AI, Griggs RC, eds. (1992). *Metabolic brain dysfunction in systemic disorders*. Boston: Little, Brown. ISBN 978-0-316-05067-8. OCLC 24912204 (https://www.worldcat.org/oclc/24912204).
17. Cryer PE (1997). *Hypoglycemia: Pathophysiology, Diagnosis, and Treatment*. New York: Oxford University Press. ISBN 978-0-19-511325-9. OCLC 36188385 (https://www.worldcat.org/oclc/36188385).
18. Service FJ, Cryer PE, Vella A (March 2017). "Hypoglycemia in adults: Clinical manifestations, definition, and causes" (http://www.uptodate.com/online/content/topic.do?topicKey=diabetes/14628&selectedTitle=2~150&source=search_result#H5). UpToDate Inc.
19. Koh TH, Eyre JA, Aynsley-Green A (1988). "Neonatal hypoglycaemia – the controversy regarding definition" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1779139). *Arch. Dis. Child*. **63** (11): 1386–8. doi:10.1136/adc.63.11.1386 (https://doi.org/10.1136%2Fadc.63.11.1386). PMC 1779139 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1779139). PMID 3202648 (https://pubmed.ncbi.nlm.nih.gov/3202648).

20. Cornblath M, Schwartz R, Aynsley-Green A, Lloyd JK (1990). "Hypoglycemia in infancy: the need for a rational definition. A Ciba Foundation discussion meeting". *Pediatrics*. **85** (5): 834–7. PMID 2330247 (https://pubmed.ncbi.nlm.nih.gov/2330247).
21. Cornblath M, Hawdon JM, Williams AF, Aynsley-Green A, Ward-Platt MP, Schwartz R, Kalhan SC (2000). "Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds". *Pediatrics*. **105** (5): 1141–5. doi:10.1542/peds.105.5.1141 (https://doi.org/10.1542%2Fpeds.105.5.1141). PMID 10790476 (https://pubmed.ncbi.nlm.nih.gov/10790476).
22. Tustison WA, Bowen AJ, Crampton JH (1966). "Clinical interpretation of plasma glucose values". *Diabetes*. **15** (11): 775–7. doi:10.2337/diab.15.11.775 (https://doi.org/10.2337%2Fdiab.15.11.775). PMID 5924610 (https://pubmed.ncbi.nlm.nih.gov/5924610).
23. Henry JB, ed. (1979). *Clinical diagnosis and management by laboratory methods*. Philadelphia: Saunders. ISBN 978-0-7216-4639-8. OCLC 4884633 (https://www.worldcat.org/oclc/4884633).
24. Clarke WL, Cox D, Gonder-Frederick LA, Carter W, Pohl SL (1987). "Evaluating clinical accuracy of systems for self-monitoring of blood glucose". *Diabetes Care*. **10** (5): 622–8. doi:10.2337/diacare.10.5.622 (https://doi.org/10.2337%2Fdiacare.10.5.622). PMID 3677983 (https://pubmed.ncbi.nlm.nih.gov/3677983).
25. Gama R, Anderson NR, Marks V (2000). " 'Glucose meter hypoglycaemia': often a non-disease". *Ann. Clin. Biochem*. **37** (5): 731–2. doi:10.1258/0004563001899825 (https://doi.org/10.1258%2F0004563001899825). PMID 11026531 (https://pubmed.ncbi.nlm.nih.gov/11026531).
26. de Pasqua A, Mattock MB, Phillips R, Keen H (1984). "Errors in blood glucose determination". *Lancet*. **2** (8412): 1165. doi:10.1016/s0140-6736(84)91611-8 (https://doi.org/10.1016%2Fs0140-6736%2884%2991611-8). PMID 6150231 (https://pubmed.ncbi.nlm.nih.gov/6150231).
27. Horwitz DL (1989). "Factitious and artifactual hypoglycemia". *Endocrinol. Metab. Clin. North Am*. **18** (1): 203–10. doi:10.1016/S0889-8529(18)30397-9 (https://doi.org/10.1016%2FS0889-8529%2818%2930397-9). PMID 2645127 (https://pubmed.ncbi.nlm.nih.gov/2645127).
28. Meites S, Buffone GJ (1989). *Pediatric clinical chemistry: reference (normal) values*. Washington, D.C.: AACC Press. ISBN 978-0-915274-47-5. OCLC 18497532 (https://www.worldcat.org/oclc/18497532).
29. White NH, Skor DA, Cryer PE, Levandoski LA, Bier DM, Santiago JV (March 1983). "Identification of type I diabetic patients at increased risk for hypoglycemia during intensive therapy". *The New England Journal of Medicine*. **308** (9): 485–91. doi:10.1056/nejm198303033080903 (https://doi.org/10.1056%2Fnejm198303033080903). PMID 6337335 (https://pubmed.ncbi.nlm.nih.gov/6337335).
30. Bolli GB, De Feo P, De Cosmo S, Perriello G, Ventura MM, Benedetti MM, Santeusanio F, Gerich JE, Brunetti P (August 1984). "A reliable and reproducible test for adequate glucose counterregulation in type I diabetes mellitus". *Diabetes*. **33** (8): 732–7. doi:10.2337/diabetes.33.8.732 (https://doi.org/10.2337%2Fdiabetes.33.8.732). PMID 6378698 (https://pubmed.ncbi.nlm.nih.gov/6378698).
31. Kahn CR, et al., eds. (2005). *Joslin's diabetes mellitus* (https://books.google.com/books?id=ohgjG0qAvfgC&pg=PA1154) (14th ed.). Philadelphia: Lippincott Williams & Willkins. p. 1154. ISBN 978-0-7817-2796-9.
32. "Diabetes and Hypoglycemia" (http://www.diabetes.co.uk/Diabetes-and-Hypoglycaemia.html). Diabetes.co.uk. Archived (https://web.archive.org/web/20120313090543/http://www.diabetes.co.uk/Diabetes-and-Hypoglycaemia.html) from the original on 13 March 2012. Retrieved 10 March 2012.

33. Davidson NK, Moreland P. "Living with diabetes blog" (https://web.archive.org/web/20120319034417/http://www.mayoclinic.com/health/low-blood-glucose/MY01267). Mayo Clinic. Archived from the original (http://www.mayoclinic.com/health/low-blood-glucose/MY01267) on 19 March 2012.
34. Harrold, Alice. "Diabetic patients should be warned about changes to Lucozade glucose content" (https://www.nursinginpractice.com/article/diabetic-patients-should-be-warned-about-changes-lucozade-glucose-content). *Nursing in Practice*. Retrieved 27 February 2019.
35. "Collip discovers hypoglycemia" (https://tacomed.com/chapter-7-standardization/collip-discovers-hypoglycemia/). *Treating Diabetes*. Archived (https://web.archive.org/web/20170908182717/https://tacomed.com/chapter-7-standardization/collip-discovers-hypoglycemia/) from the original on 8 September 2017. Retrieved 18 June 2017.

External links

- The National Diabetes Information Clearinghouse (http://diabetes.niddk.nih.gov/dm/pubs/hypoglycemia/)
- Hypoglycemia at the Mayo Clinic (http://www.mayoclinic.com/health/hypoglycemia/ds00198/)
- American Diabetes Association (https://web.archive.org/web/20100624105612/http://www.diabetes.org/living-with-diabetes/treatment-and-care/blood-glucose-control/hypoglycemia-low-blood.html)

Classification	**ICD-10**: E16.0 (http://apps.who.int/classifications/icd10/browse/2016/en#/E16.0)-E16.2 (http://apps.who.int/classifications/icd10/browse/2016/en#/E16.2) · **ICD-9-CM**: 250.8 (http://www.icd9data.com/getICD9Code.ashx?icd9=250.8), 251.0 (http://www.icd9data.com/getICD9Code.ashx?icd9=251.0), 251.1 (http://www.icd9data.com/getICD9Code.ashx?icd9=251.1), 251.2 (http://www.icd9data.com/getICD9Code.ashx?icd9=251.2), 270.3 (http://www.icd9data.com/getICD9Code.ashx?icd9=270.3), 775.6 (http://www.icd9data.com/getICD9Code.ashx?icd9=775.6), 962.3 (http://www.icd9data.com/getICD9Code.ashx?icd9=962.3) · **MeSH**: D007003 (ht

	tps://www.nlm.nih.gov/cgi/mesh/2015/MB_cgi?field=uid&term=D007003) · **DiseasesDB**: 6431 (http://www.diseasesdatabase.com/ddb6431.htm)
External resources	**MedlinePlus**: 000386 (https://www.nlm.nih.gov/medlineplus/ency/article/000386.htm) · **eMedicine**: emerg/272 (https://emedicine.medscape.com/emerg/272-overview) med/1123 (http://www.emedicine.com/med/topic1123.htm#) med/1939 (http://www.emedicine.com/med/topic1939.htm#) ped/1117 (http://www.emedicine.com/ped/topic1117.htm#) · **Patient UK**: Hypoglycemia (https://patient.info/doctor/hypoglycaemia)

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