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Patient Care + Research + Clinical Trials

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Hypoglycemia, hypoglycemia unawareness & brain function

Glucose, a form of sugar, is the most fundamental source of energy in the body, powering the machinery of life. Normal blood glucose in the fasting state or before meals is 3.5-6.0. Any level < 3.5 can be loosely described as low blood sugar or hypoglycemia. For individuals with diabetes treated with insulin or drugs from the sulfonylurea class any glucose value < 4.0 should be considered to be evidence of hypoglycemia.

Most body organs, the liver, kidneys, muscles & the heart function normally even when the blood glucose is <2.0. This is because the demand for glucose (and oxygen, the other essential metabolic ingredient) in those organs is relatively low and easily met by prevailing blood flow. The brain, the organ that is responsible for consciousness, personality and cognitive function (thought processes, decision making, judgment), has a high demand for glucose at all times, even during sleep, that can be met only by a steady supply of blood rich in glucose and oxygen. These ingredients are supplied to the brain by a blood flow that is high at all times and a blood flow that cannot easily be increased. Thus the supply of adequate volumes of blood rich in glucose and oxygen is absolutely essential for normal brain function. In the presence of sub-normal blood flow, even with normal prevailing levels of glucose, unconsciousness ensues within seconds – witness the effects of major blood loss. Similarly high blood flow in the presence of insufficient blood glucose results in brain dysfunction.

Brain function operates at many different levels. The most basic of brain functions is related to survival: the stimulation of breathing and the regulation of blood flow. The next level of brain function relates to the maintenance of consciousness – attention and concentration and the five senses. The final level of brain function usually referred to as “higher cortical function” includes insight, judgment, calculation, speech and memory. Not surprisingly, the higher the level of brain function, the more susceptible is that function to hypoglycemia. Hence as blood glucose levels fall from normal to slightly low (for instance 2.5 - 3.0) the only functions affected are higher cortical functions, the ones that are most difficult to test – and unless an individual’s reaction time, ability to do mental arithmetic, ability to speak a foreign language or recite a tongue twister is tested no abnormality will be detected. As blood glucose drops further (say to 2.0 - 2.4) brain dysfunction will become more obvious – akin to what one might observe in a moderately drunken individual with confusion, slurring of words, slowness of thoughts and reaction time, poor judgment and incoordination. This stage is medically described as delirium or “confusional state” or “stupor”. As blood glucose drops further (to say 1.5 - 1.9) loss of consciousness (coma

– no response to the environment: eyes closed, no speech etc) occurs. As it drops further seizures/convulsions develop. At this stage permanent brain damage begins – any further drop in glucose may lead to death.

From the perspective of safe driving, any drop in blood sugar below 3.0 would be likely to result in a measurable impairment of normal driving functions – an increase in reaction time, impaired judgment or other parameter.

Hypoglycemia unawareness

If mild to moderate hypoglycemia occurs in a diabetic individual, due to either excessive insulin or diabetes medication, blood sugar will usually return to normal even if an individual does not consume sugar or starchy food. This is because the body automatically secretes hormones that counteract insulin: adrenaline (epinephrine), glucagon, cortisol and growth hormone. In the presence of hypoglycemia adrenaline and glucagon are released within seconds while cortisol and growth hormone release follows within 20-40 minutes. Adrenaline release is accompanied by shaking, sweating, pounding heart and a sense of fear: the so-called “fight or flight” response which occurs in normal individuals when they are startled or afraid. Individuals with diabetes quickly learn to recognize these symptoms as evidence of hypoglycemia and quickly consume sugary liquids or eat starchy foods - thereby rapidly correcting the hypoglycemia. Diabetics refer to this as having a “hypo” or “reaction” or “going low” and learn to live with it.

Hypoglycemia-related glucagon release is not accompanied by any symptoms, & is usually lost at around the 5 year mark in Type 1 diabetes. Hypoglycemia-related adrenaline release in Type 1 diabetes begins to fail after 10 years of Type 1 diabetes and by the 20 year mark is almost completely gone. This is an extremely unfortunate physiological fact because it is the “fight or flight” reaction to adrenaline that alerts diabetics that they are having a hypoglycemic attack. Without the “fight or flight” symptoms a diabetic patient has no obvious warning signal of hypoglycemia and instead has to rely on detecting signals from his/her brain (symptoms of impaired higher cortical function and later of confusion) that blood sugar is falling. These symptoms of brain failure are referred to as “neuroglycopenic” symptoms and by virtue of their nature are not easily recognized by the hypoglycemic individual.

If hypoglycemia occurs in an individual who has lost the “fight or flight” symptoms of adrenaline release, the only circumstances under which hypoglycemia will be recognized and treated, and a potential driving mishap averted, are one of the following: 1) the patient is able to identify the subtle signals of brain failure/ neuroglycopenia (slowness of thought, incoordination etc) and seek food, or 2) somebody else notices abnormal behaviour and feeds the patient, or 3) the patient is in the habit of testing his/her blood sugar frequently (and before driving), identifies hypoglycemia & takes corrective action. Without one of the 3 above scenarios the spiral of decreasing brain function is likely to occur with progression from impairment of consciousness, to coma, seizure and potentially death.

Hypoglycemia unawareness is the state where an individual has hypoglycemia but is unable to appreciate that hypoglycemia is present due to a lack of both “fight or flight” symptoms and neuroglycopenic symptoms. The only condition under which somebody who has hypoglycemia unawareness can drive is if they test immediately before driving and frequently during a longer drive.

It is not clear whether hypoglycemia unawareness is a preventable complication of Type 1 diabetes. For the purposes of this report it should be assumed not only that it is not preventable, but that it is progressive – worsens with the passage of time.

Hypoglycemia unawareness increases the risk of development of severe hypoglycemia.

Severe hypoglycemia

Severe hypoglycemia is loosely defined as a state of hypoglycemia from which an individual, because of hypoglycemic impairment, is unable to rescue him/herself alone. Most individuals with a history of severe hypoglycemia have hypoglycemia unawareness. Even in the absence of hypoglycemia unawareness, if hypoglycemia is marked & progresses rapidly and if the individual has no access to sugary liquids or starchy food, severe hypoglycemia may result. The very first episode of hypoglycemia unawareness may also result in severe hypoglycemia. In general, the longer the duration of Type 1 diabetes the greater the likelihood of hypoglycemia unawareness. After 10 years of Type 1 diabetes hypoglycemia unawareness is not uncommon; after 20 years it is much more common; after 30 years it is present in a majority of individuals.

While severe hypoglycemia often occurs in the context of hypoglycemia unawareness, it also temporarily worsens any pre-existing hypoglycemia unawareness. Thus an individual who has had an episode of severe hypoglycemia, for the next week or so is more likely than otherwise to have a further episode of severe hypoglycemia.

Any episode of severe hypoglycemia while driving would be likely to result in impaired driving though the impairment per se may be difficult to identify up to the point of the accident. Individuals in a state of severe hypoglycemia may appear to an untrained observer to look, speak, behave and to act normally. Severe hypoglycemia is a cause of automatism recognized by the Canadian courts (http://www.courts.gov.bc.ca/jdb-txt/sc/03/19/2003bcsc1930.htm).

Hypoglycemia and motor vehicle accidents

True estimates of the frequency of episodes of hypoglycemia-related impaired driving are difficult to ascertain – individuals with such episodes may be reluctant to report such because of the threat of consequences with respect to driving restrictions. The best and most recent study addressing this issue is that of Cox and colleagues (2003). This study reported the results of an anonymous questionnaire given to Type 1 and Type 2 diabetic drivers and their non-diabetic partners/spouses. Over the course of the preceding 2 years, and taking North American drivers

only (excluding European drivers), 31% of Type 1 and 8% of Type 2 diabetic drivers reported an episode of “stupor” (= severe brain impairment) while 24% of Type 1 and 7% of Type 2 diabetic drivers reported having “required assistance”. With respect to motor vehicle accidents in the previous 2 years, 16% of Type 1 and 8% of Type 2 diabetic drivers and 7% of non-diabetic partner/spouses reported “crashes”. It is of interest to note that despite the fact that 8% of Type 2 diabetic drivers reported “stupor” and 7% reported “requiring assistance” due to hypoglycemia, the incidence of “crashes” in Type 2 diabetic drivers was no greater than that of non-diabetics.