

DIABETES & Hypoglycemia



8.0 Contact Hours

California Board of Registered Nursing CEP#15122

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DIABETES AND HYPOGLYCEMIA Self Study 8.0 CONTACT HOURS CEP #15122

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1. Please print or type all information.
2. Arrange payment of \$3 per contact hour to Key Medical Resources, Inc. Call for credit card payment.
3. No charge for contract personnel or Key Medical Passport holders.
4. Please complete answers and return SIGNED answer sheet with evaluation form via
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Place your answer of this sheet or the scan-type form provided.

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|----------|-----------|-----------|-----------|-----------|
| 1. _____ | 9. _____ | 17. _____ | 25. _____ | 33. _____ |
| 2. _____ | 10. _____ | 18. _____ | 26. _____ | 34. _____ |
| 3. _____ | 11. _____ | 19. _____ | 27. _____ | 35. _____ |
| 4. _____ | 12. _____ | 20. _____ | 28. _____ | 36. _____ |
| 5. _____ | 13. _____ | 21. _____ | 29. _____ | 37. _____ |
| 6. _____ | 14. _____ | 22. _____ | 30. _____ | 38. _____ |
| 7. _____ | 15. _____ | 23. _____ | 31. _____ | 39. _____ |
| 8. _____ | 16. _____ | 24. _____ | 32. _____ | 40. _____ |

My Signature Indicates that I have completed this module on my own. _____
(Signature)

EVALUATION FORM

	Poor							Excellent				
1. The content of this program was:	1	2	3	4	5	6	7	8	9	10		
2. The program was easy to understand:	1	2	3	4	5	6	7	8	9	10		
3. The objectives were clear:	1	2	3	4	5	6	7	8	9	10		
4. This program applies to my work:	1	2	3	4	5	6	7	8	9	10		
5. I learned something from this course:	1	2	3	4	5	6	7	8	9	10		
6. Would you recommend this program to others?						Yes				No		
7. The cost of this program was:				High				OK				Low

Comments:

DIABETES AND HYPOGLYCEMIA HOME STUDY

Choose the Single Best Answer for the Following Questions and Place Answers on Form:

1. Which type of diabetes is ketosis prone?
a. Type I b. Type 2 c. Gestational
2. True or False By the time IDDM appears, most of the beta cells of the pancreas have been destroyed.
3. True or False Genetics is the most significant factor for the development of diabetes.
4. The predicted percentage of persons with NIDDM is:
a. 10% b. 30% c. 75% d. 90%
5. Overt diabetes is seen during phase _____ of the pathogenesis of NIDDM.
a. 1 b. 2. c. 3 d. 4

Matching: Identify symptoms of IDDM vs NIDDM

6. Usually begins in later life. a. IDDM
7. Plasma insulin level is low or immeasurable.
8. Susceptible to hyperosmolar, nonketotic coma b. NIDDM
9. Symptoms begin gradually.
10. Based on the latest research, which fasting plasma glucose level or greater is used as the number to diagnose diabetes?
a. 110 mg/dl b. 126 mg/dl c. 140 mg/dl d. 180 mg/dl
11. All of the factors except one area considered high-risk factors for diabetes:
a. More than 20% above ideal body weight.
b. Blood pressure above 140/90 mmg Hg.
c. Northern European Caucasian.
d. Having a mother, father, brother, or sister with diabetes.
12. The type of insulin used in diabetic emergencies and in CSII and MSI programs is:
a. Rapid acting b. Intermediate acting c. Long acting
13. The best way to self-monitor glucose levels is:
a. Reagent strips b. Urine testing c. Blood glucose monitoring equipment
14. Which description best summarizes the Somogyi Effect?
a. Hypoglycemia caused by missing a meal.
b. Counter regulatory hyperglycemia after insulin administration.
c. An early morning rise in plasma glucose.

Matching: Match the drug classification to its action.

15. Sulfonylureas a. inhibits an enzyme in the GI tract resulting in delayed glucose absorption.
16. Meglitinides b. inhibits hepatic gluconeogenesis.
17. Biguanides c. Taken right before meals. Has a short half life.
18. Alpha-glucosidase Inhibitors d. reduce insulin resistance by increasing activity of insulin receptor kinase.
19. Thiazolidenediones e. stimulate release of insulin from the beta cells.

20. Glycated hemoglobin or hemoglobin A1c levels should be checked:
 a. daily b. weekly c. quarterly d. annually
21. Diabetic ketoacidosis is treated with all of the following except:
 a. 20 – 30 units of insulin each hour.
 b. Large amounts of I.V. fluids.
 c. Low dose insulin schedules.
 d. Potassium replacement.
22. True or False Blood glucose levels in DKA reach higher levels than HHNK.
23. True or False Kussmaul respirations are more common in DKA than HHNK.
24. True or False Late complications of diabetes are largely due to circulatory abnormalities.
25. True or False Neuropathy only affects the feet.
26. Insulin resistance is defined arbitrarily as the requirement of _____ or more units of insulin per day.
 a. 30 b. 50 c. 100 d. 200
27. Insulin allergy is due to _____ antibodies to insulin.
 a. IgE b. IgA c. IgF d. IgG

Hypoglycemia

28. The most common cause of hypoglycemia in the diabetic is:
 a. Not eating b. Too much insulin c. Too little exercise d. Ingestion of glucose
29. Research in health adults showed that plasma glucose levels below ____ shows mental efficiency decline: a. 65 b. 75 c. 85 d. 95
30. One of the first organs affected by hypoglycemia is the:
 a. Heart b. Lungs c. Brain d. Stomach
31. True or False Adrenergic manifestations of hypoglycemia include shakiness.
32. True or False Determining the cause is made by assessing the circumstance and ideally a critical sample of blood a the time of hypoglycemia.
33. True or False Growth hormone is the only hormone affecting hypoglycemia.
34. True or False The most common cause of hypoglycemia is overmedication with Insulin or antidiabetic pills.
35. True or False Hypoglycemia is a common problem in critically ill or newborn infants.
36. True or False In older adults, assessing drug interactions is essential.
37. True or False Treatment and prevention of hypoglycemia centers around determining the cause.
38. True or False The main treatment for hypoglycemia is insulin.
39. True or False Reversal of hypoglycemia is done by administering carbohydrates.
40. True or False Changing eating habits can help with post prandial hypoglycemia

DIABETES and HYPOGLYCEMIA HOME STUDY 8.0 CONTACT HOURS

Please note that C.N.A.s in California cannot receive continuing education hours for home study.

Outline:

- I. Diabetes Definition
- II. Types of Diabetes
- III. Pathophysiology of Diabetes
- IV. Symptoms
- V. Etiology
- VI. Treatment
- VII. Complications
- VIII. New Treatments
- IX. Hypoglycemia
 - a. Definition
 - b. Pathophysiology
 - c. Methods of Measurement
 - d. Signs and Symptoms
 - e. Causes
 - f. Age Related Considerations
 - g. Prevention
 - h. Treatment
- X. Diabetes Dictionary
- XI. Patient Education

Objectives: At the completion of this module the participant will be able to:

- 1. Differentiate different types of diabetes.
- 2. Describe the pathophysiology of diabetes.
- 3. Differentiate symptoms and etiology of IDDM and NIDDM.
- 4. Describe diagnostic criteria and procedures for diabetes.
- 5. Identify treatments for diabetes.
- 6. Describe complications of diabetes.
- 7. Discuss aspects of hypoglycemia
- 8. Complete exam components of this module at 70% competency.

Completion of this module will require linking to other internet sites for information. These sites are:

<http://www.niddk.nih.gov/health/diabetes/pubs/dmdict/dmdict.htm>

<http://www.niddk.nih.gov/health/diabetes/diabetes.htm>

DIABETES and HYPOGLYCEMIA HOME STUDY

8.0 CONTACT HOURS

An estimated 16 million people in the United States have diabetes mellitus--a serious, lifelong condition. About half of these people do not know they have diabetes and are not under care for the disorder. Each year, about 798,000 people are diagnosed with diabetes. Although diabetes occurs most often in older adults, it is one of the most common chronic disorders in children in the United States. About 123,000 children and teenagers age 19 and younger have diabetes.

What Is Diabetes?

Diabetes Mellitus is disorder of metabolism of carbohydrates, proteins and fats where there is a discrepancy between the amount of insulin the body requires versus the amount available. This is a result of an inadequate, or in some cases no production of insulin, which is produced by the pancreas. Most often, diabetes is discussed as a disorder of glucose metabolism, but the lack of insulin prevents most substances including carbohydrates, proteins and fats from entering the cell.

After digestion, the food substances pass into our bloodstream where it is available for body cells to use for growth and energy. For the glucose and food substances to get into the cells, insulin must be present. Insulin is a hormone produced by the pancreas, a large gland behind the stomach.

When we eat, the pancreas, in a ever ready state produces insulin to metabolize food. Under normal circumstances, the blood sugar remains normal whether we eat or not. For example, if I were to eat a whole box of See's candy, I would produce enough insulin to metabolize what was eaten. If I didn't eat for 2 or 3 days, the body would break down glycogen stores from the liver to produce available energy and glucose. It is only under circumstances where the pancreas cannot produce insulin or when there is extreme demands placed on the body that the blood glucose becomes abnormal.

CLASSIFICATION

The basic categories are generally are as follows:

- ◆ Type 1 – Insulin Dependent IDDM ketosis prone immune mediated

Type 1 diabetes

Type 1 diabetes (once known as insulin-dependent diabetes mellitus or juvenile diabetes) is considered an autoimmune disease. An autoimmune disease results when the body's system for fighting infection (the immune system) turns against a part of the body. In diabetes, the immune system attacks the insulin-producing beta cells in the pancreas and destroys them. The pancreas then produces little or no insulin.

Someone with type 1 diabetes needs daily injections of insulin to live. At present, scientists do not know exactly what causes the body's immune system to attack the beta cells, but they believe that both genetic factors and viruses are involved. Type 1 diabetes accounts for about 5 to 10 percent of diagnosed diabetes in the United States.

Type 1 diabetes develops most often in children and young adults, but the disorder can appear at any age. Symptoms of type 1 diabetes usually develop over a short period, although beta cell destruction can begin years earlier.

Symptoms include increased thirst and urination, constant hunger, weight loss, blurred vision, and extreme tiredness. If not diagnosed and treated with insulin, a person can lapse into a life-threatening coma.

- ◆ Type 2 – Non-insulin Dependent NIDDM ketosis resistant non-immune mediated

Type 2 diabetes

The most common form of diabetes is type 2 diabetes (once known as noninsulin-dependent diabetes mellitus or NIDDM). About 90 to 95 percent of people with diabetes have type 2 diabetes. This form of diabetes usually develops in adults over the age of 40 and is most common among adults over age 55. About 80 percent of people with type 2 diabetes are overweight.

In type 2 diabetes, the pancreas usually produces insulin, but for some reason, the body cannot use the insulin effectively. The end result is the same as for type 1 diabetes--an unhealthy buildup of glucose in the blood and an inability of the body to make efficient use of its main source of fuel.

The symptoms of type 2 diabetes develop gradually and are not as noticeable as in type 1 diabetes. Symptoms include feeling tired or ill, frequent urination (especially at night), unusual thirst, weight loss, blurred vision, frequent infections, and slow healing of sores.

◆ Gestational Diabetes

Gestational Diabetes

Gestational diabetes develops or is discovered during pregnancy. This type usually disappears when the pregnancy is over, but women who have had gestational diabetes have a greater risk of developing type 2 diabetes later in their lives.

An alternative classification system has been proposed as below:

- ◆ Type 1 IDDM
- ◆ Type 1 NIDDM
- ◆ Type 2 NIDDM

The differentiation mainly refers to the susceptibility to develop DKA or diabetic ketoacidosis. Type 2 diabetics may require insulin, but are not at risk for ketoacidosis.

There are some diabetics who are initially non-insulin dependent, then later become insulin-dependent and prone to ketoacidosis. These patients are generally nonobese and have HLA antigens associated with susceptibility to insulin-dependent diabetes. The Type 2 NIDDM is an intermediate stage of autoimmune destruction where there is just enough insulin to prevent ketoacidosis but not enough insulin to prevent hyperglycemia. Obese people with NIDDM may require insulin temporarily then revert back to NIDDM state.

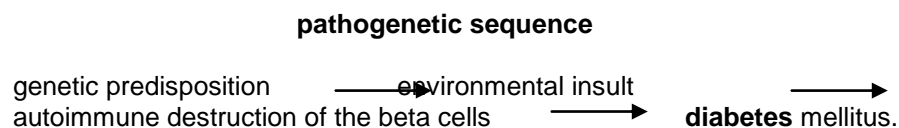
Secondary forms of diabetes may occur from:

- *Pancreatic disease*, particularly chronic pancreatitis in alcoholics
 - *Hormonal* causes include pheochromocytoma, acromegaly, Cushing's syndrome, and administration of steroid hormones.
 - "Stress hyperglycemia," associated with severe burns, acute myocardial infarctions, and other life-threatening illnesses, is due to endogenous release of glucagon and catecholamines. Hormonal hyperglycemia results from varying combinations of impairment of insulin release and induction of insulin resistance.
 - *Drugs* can lead to impaired glucose tolerance or hyperglycemia. Hyperglycemia and even ketoacidosis can be due to quantitative or qualitative defects in the *insulin receptor* or to antibodies directed against it. The mechanism is essentially pure insulin resistance.
 - *Genetic syndromes* associated with impaired glucose tolerance or hyperglycemia include the lipodystrophies, myotonic dystrophy, and ataxia-telangiectasia.
 - *Abnormal carbohydrate metabolism* in association with any of these secondary causes does not necessarily indicate the presence of underlying **diabetes**, although, in some cases, mild, asymptomatic primary **diabetes** is made overt by the secondary illness
-

PATHOGENESIS OF IDDM

By the time IDDM appears, most of the beta cells in the pancreas have been destroyed. The destructive process is most likely autoimmune in nature. Pathogenesis begins with a genetic susceptibility to the disease, and some environmental event initiates the process in such susceptible individuals. Viral infection is one triggering mechanism, but noninfectious agents also may be involved. The best evidence that an environmental insult is required comes from studies in monozygotic twins, in whom the concordance rate for **diabetes** is less than 50 percent. If **diabetes** were a purely genetic illness, concordance rates should approximate 100 percent. Autoimmune attack then follows. Although the process is clinically silent, the islets become infiltrated by monocytes/macrophages and activated cytotoxic T cells. This infiltration is usually designated *insulinitis* but is sometimes called *isletitis*. Multiple antibodies against beta cell antigens are present in blood. The patient's state while the immune attack is underway but unrecognized is termed *prediabetes*. The prediabetic state may be brief or prolonged and may be progressive and uninterrupted or intermittent. What is clear is that the insulin reserve steadily diminishes until it is insufficient to maintain blood glucose within normal bounds. At this point the diagnosis is **diabetes**.

Rarely, type 1 **diabetes** develops exclusively from an environmental insult, as from the ingestion of Vacor, a rat poison. It is also possible that autoimmune **diabetes** can develop in the absence of an environmental trigger, i.e., can be purely genetic.



Genetics The genetic link is unclear and not as strong as may have been previously thought. There is a 5 to 10 percent chance of IDDM among siblings. The presence of NIDDM in a parent increases the risk of IDDM in the offspring. A study of families showed a 16 percent chance of diabetes from parent to offspring. The risk of diabetes to offspring is five times higher when the father has Type 1 diabetes.

Genetic susceptibility to IDDM probably involves more than one gene. Candidate loci have been proposed on chromosomes 2, 6, 11, and 15. In mice, which have an autoimmune form of **diabetes** resembling human IDDM, the number of susceptibility genes may be as high as 16.

Environmental Event It is theorized that nongenetic factors are required for development of **diabetes**. Similarly, HLA identity or haploidentity does not ensure concordance.

The environmental factor in many cases is believed to be a viral infection of the beta cell. A viral etiology was originally suggested by seasonal variations in the onset of the disease and by what appeared to be more than a chance relationship between the appearance of **diabetes** and preceding episodes of mumps, hepatitis, infectious mononucleosis, congenital rubella, and coxsackievirus infections. Further support for the viral theory comes from the observation that about one-fifth of individuals with congenital rubella develop IDDM. The presence of an HLA susceptibility allele in the fetus may double the risk. Cytomegalovirus genes are present in the genome of one-fifth of patients with type 1 **diabetes**. Viral infections of the pancreas could induce **diabetes** by two mechanisms: direct inflammatory disruption of islets or induction of an immune response. Viral theories are inconclusive until further studies are done.

It has been suggested that exposure to cow's milk or milk products early in life predisposes to autoimmune **diabetes**. The proposed environmental trigger is bovine albumin, operating through the mechanism of molecular mimicry. Exposure to cow's milk is presumed to induce an immune response and the antibody would destroy certain beta cells of the pancreas. This hypothesis has not received wide support.

Insulinitis/Isletitis In animals, macrophages and activated T lymphocytes infiltrate the pancreatic islets prior to or simultaneously with development of **diabetes**. Lymphocytes are also found in the islets of

young persons dying from new-onset **diabetes**, and radioactively labeled lymphocytes localize in the pancreas in humans with IDDM. These findings are in accord with the fact that immune endocrinopathies are associated with lymphocytic infiltration of the affected tissue. It is not clear, however, that insulinitis is central to the destructive sequence in autoimmune **diabetes**; the cellular infiltration may be an epiphenomenon.

Conversion Of The Beta Cell From Self To Nonself And Activation Of The Immune System The immune system can play a role in the development of IDDM. The immune system can mediate destruction of the beta cells in the pancreas resulting in Type 1 IDDM. Some patients have antibodies directed against insulin and other beta cell antigens. The mechanism behind this autoimmune destruction is not known. The environmental agent could be a virus, a toxin, or a food and might act in one of several ways. Direct destruction of beta cells by a virus or toxin might expose cryptic antigens to the immune system, evoking an immune response. Alternatively, destructive cytokines might be released by viruses to kill beta cells, or programmed cell death (*apoptosis*) might be induced. A third possibility, currently less popular, is that viral infection, via cytokine release, induces expression of HLA D region molecules in the pancreas (where they are not normally present), converting one or more cell types into antigen-presenting cells.

Some patients may have a purely genetic form of the disease. In summary, the precise mechanisms remain a mystery, but immune attack is believed to be the fundamental cause of IDDM.

Destruction Of Beta Cells And Development Of IDDM IDDM often has abrupt onset with symptomatic hyperglycemia, polyuria, and/or ketoacidosis. Even though this onset is rapid, the loss of insulin reserve has probably occurred over a few to many years. The prediabetic phase occurs when there is decreased glucose tolerance with a normal fasting blood sugar. In the next phase fasting hyperglycemia develops but without ketosis. The clinical appearance is that of NIDDM. Continued destruction of the beta cells then leads to the IDDM stage and ketoacidosis. Once this stage is reached the patient requires lifelong insulin unless a pancreatic transplant is performed.

PATHOGENESIS OF NIDDM

NIDDM is more common than IDDM. Possibly 90% of diabetics have NIDDM. As mentioned above, a non-insulin dependent diabetic may temporarily need insulin. NIDDM has more of a family link than does IDDM.

Genetics Although NIDDM occurs in families, modes of inheritance are not known except for the variant termed *maturity-onset diabetes of the young* (MODY). MODY is usually manifested by mild hyperglycemia in young persons who are resistant to ketosis.

Pathophysiology Patients with type 2 NIDDM have two physiologic defects: abnormal insulin secretion and resistance to insulin action in target tissues. Three phases can be recognized in the usual clinical sequence.

- Phase 1 - plasma glucose remains normal despite demonstrable insulin resistance, because insulin levels are elevated.
- Phase 2 - insulin resistance tends to worsen, so that postprandial hyperglycemia develops despite elevated insulin concentrations.
- Phase 3 - insulin resistance does not change, but declining insulin secretion causes fasting hyperglycemia and overt **diabetes**. Most authorities believe that insulin resistance is primary and that hyperinsulinemia is secondary; i.e., insulin secretion increases to compensate for the resistance state.

Regardless of the mechanism, the physiologic consequences of insulin resistance are clear. There is no major abnormality in either glucose uptake by the cell or its oxidative metabolism to CO₂, water, and lactate. Rather, the major metabolic block is in glycogen synthesis ("nonoxidative metabolism"). Impaired glycogen synthesis, like hyperinsulinemia and insulin resistance, may be seen in nonobese, normoglycemic relatives of patients with NIDDM.

A rare form of type 2 NIDDM, clinically mild, is due to production of an abnormal insulin that does not bind well to insulin receptors. Persons with this variant of the disease respond normally to exogenous insulin.

CLINICAL FEATURES

The manifestations of symptomatic **diabetes** mellitus vary from patient to patient. Most often, symptoms are due to hyperglycemia (**polyuria, polydipsia, polyphagia**), but the first event may be neuropathy in the absence of a known hyperglycemia.

Insulin-Dependent Diabetes IDDM

- usually begins before age 40; in the United States, peak incidence is around age 14.
- usually not obese.
- Onset of symptoms may be abrupt, with thirst, excessive urination, increased appetite, and weight loss developing over several days.
- Type 1 patients may have normal weight or may be wasted, depending on the length of time between onset of symptoms and start of treatment.
- plasma insulin level is low or unmeasurable.
- Glucagon levels are elevated but are suppressed by insulin administration.
- Once symptoms develop, insulin therapy is required.

Non-Insulin-Dependent Diabetes NIDDM

- usually begins in middle life or later.
- typical patient is overweight.
- Symptoms begin gradually, and the diagnosis is frequently made when an asymptomatic person is found to have an elevated plasma glucose level on routine laboratory examination.
- plasma insulin levels are normal to high in absolute terms, although they are lower than predicted for the level of the plasma glucose
- Glucagon metabolism in NIDDM is complex. While the elevated fasting plasma concentrations can be lowered by large amounts of insulin, the exaggerated glucagon response to ingested nutrients cannot be suppressed; i.e., alpha cell function remains abnormal.
- do not develop ketoacidosis but are susceptible to development of hyperosmolar, nonketotic coma.

Diagnoses of Diabetes

1. A casual plasma glucose level (taken at any time of day) of 200 mg/dL or greater when the symptoms of diabetes are present.
2. A fasting plasma glucose value of 126 mg/dL or greater.
3. An OGTT value in the blood of 200 mg/dL or greater measured at the 2-hour interval.
 - *A Lower Number To Diagnose Diabetes* The expert committee also recommended a lower fasting plasma glucose (FPG) value to diagnose diabetes. The new FPG value is 126 milligrams per deciliter (mg/dL) or greater, rather than 140 mg/dL or greater. This research showed that a fasting blood glucose of 126 mg/dL or greater is associated with an increased risk of diabetes complications affecting the eyes, nerves, and kidneys.
 - Oral glucose tolerance test (OGTT). In this test, the person must come in fasting, drink a glucose syrup, and have a blood sample taken 2 hours later. This complicated procedure made detection and diagnosis of diabetes a difficult and cumbersome process, and the expert committee recommended that it be eliminated from clinical use. The change to using fasting plasma glucose for determining the presence of diabetes will make detection and diagnosis of diabetes more routine.
 - *People at High Risk for Diabetes* The experts suggest that adults age 45 years and older be tested for diabetes. If their blood glucose is normal at the first test, they should be tested at 3-year intervals. People under age 45 should be tested if they are at high risk for diabetes.

These high-risk factors include

- ✓ Being more than 20 percent above ideal body weight or having a body mass index (BMI) of greater than or equal to 27. BMI is the ratio of weight in kilograms to height in meters squared (kg/m²). (Your doctor or dietitian can provide information on your BMI.)
- ✓ Having a mother, father, brother, or sister with diabetes.
- ✓ Being African American, Alaska Native, American Indian, Asian American, Hispanic American, or Pacific Islander American.
- ✓ Giving birth to a baby weighing more than 9 pounds or having diabetes during pregnancy.
- ✓ Having blood pressure at or above 140/90 millimeters of mercury (mmHg).
- ✓ Having abnormal blood lipid levels, such as high density lipoprotein (HDL) cholesterol less than 35 mg/dL or triglycerides greater than 250 mg/dL.
- ✓ Having abnormal glucose tolerance when previously tested for diabetes.

Testing for Diabetes During Pregnancy The expert panel also suggested a change in the testing for diabetes during pregnancy, stating that women at low risk for gestational diabetes do not need to be tested. This low-risk group includes women who are

- Younger than 25 years of age.
- At normal body weight.
- Without a family history of diabetes.
- Not members of a high-risk ethnic group.

All women who are not in the low-risk category should be tested for gestational diabetes during the 24th to 28th weeks of pregnancy. The testing procedure requires drinking a glucose drink and measuring blood glucose 1 hour later. If the blood glucose value is 140 mg/dL or greater, the woman should be evaluated further.

TREATMENT

Diet

Today there is no ONE 'diabetic' or 'ADA' diet. The recommended diet can only be defined as a dietary prescription based on nutrition assessment and treatment goals. Medical nutrition therapy for people with **diabetes** should be individualized, with consideration given to eating habits and other lifestyle factors.

Insulin

Insulin is required for treatment of all patients with IDDM and many patients with NIDDM. If the physician does not use oral agents, all diet-unresponsive NIDDM subjects must be given the hormone. Even after meals, therefore, the plasma glucose level in normal subjects does not rise into the hyperglycemic or glycosuric range. As the plasma glucose level falls under the influence of insulin, release of the hormone is damped, and counterregulatory hormones enter the circulation to prevent hypoglycemia, ensuring smooth control of plasma glucose throughout the absorptive process. The patient treated with insulin by injection cannot reproduce these physiologic responses. If enough insulin is given to keep the postprandial glucose normal, too much insulin will inevitably be present during the postabsorptive phase, and hypoglycemia will result.

- *Conventional insulin therapy* involves the administration of one or two injections a day of intermediate-acting insulin such as zinc insulin (lente insulin) or isophane insulin (NPH insulin) with or without the addition of small amounts of regular insulin.
- The *multiple subcutaneous insulin injection technique* MSI most commonly involves administration of intermediate- or long-acting insulin in the evening as a single dose together with regular insulin prior to each meal. Home glucose monitoring by the patient is necessary if the goal is the return of the plasma glucose level to normal.
- *Continuous subcutaneous insulin infusion* involves the use of a small battery-driven pump that delivers insulin subcutaneously into the abdominal wall, usually through a 27-gauge butterfly needle. With CSII, insulin is delivered at a basal rate continuously throughout the day, with increases in rate programmed prior to meals. Adjustments in dosage are made in response to measured capillary glucose values in a fashion similar to that used in MSI.

Types Of Insulin

- Rapid-acting preparations are used in diabetic emergencies and in CSII and MSI programs.
- Intermediate-acting preparations are used in conventional and MSI regimens.
- Long-acting formulations are used almost exclusively in three-injection MSI schedules.

Most insulin preparations are with treated synthesized “human” insulin. Complications of insulin therapy, such as insulin allergy, fat atrophy, and fat hypertrophy, are less common than with animal insulins but still occur. Occasionally, patients may still be on beef or pork insulin. Most insulins are prepared in concentrations of 100 U/mL (U100), although higher concentrations can be obtained (e.g., U500).

Lente and NPH insulin are used in most conventional therapy and are roughly equivalent in biologic effects, although lente appears to be slightly more immunogenic and to mix less well with regular insulin than does NPH.

Self-Monitoring Of Glucose Level

The best way to self-monitor glucose levels is with blood glucose monitoring equipment. Reagent strips may also be used, but it is sometimes difficult for the patient to see the variations in color. Urine testing for glucose is rarely used. It is however extremely important to measure ketone levels in the urine.

Goals Of Therapy Intensive insulin therapy designed to keep the blood glucose level as near normal as possible has for many years been considered mandatory during pregnancy and after renal transplantation. Maintenance of a normal blood glucose level during pregnancy prevents fetal macrosomy, respiratory distress syndrome, and perinatal mortality.

The 10-year study, called the Diabetes Control and Complications Trial (DCCT), was completed in 1993 and included 1,441 people with type 1 diabetes. The study compared the effect of two treatment approaches--intensive management and standard management--on the development and progression of eye, kidney, and nerve complications of diabetes. Researchers found that study participants who maintained lower levels of blood glucose through intensive management had significantly lower rates of complications by 70%. The philosophy of accepting higher blood sugar levels in diabetics does not make sense in relation to the DCCT study.

Effects Related to Insulin

Hypoglycemia

Hypoglycemia may be caused by missing a meal or doing unexpected exercise but can occur in the absence of known precipitating events. Daytime episodes of hypoglycemia are usually recognized by autonomic symptoms, such as sweating, nervousness, tremor, and hunger. Hypoglycemia during sleep may produce no symptoms or cause night sweats, unpleasant dreams, and early-morning headache.

Hypoglycemic attacks are dangerous and, if frequent, can result in a serious or even fatal outcome. If the patient is conscious, sugar, candy, or a sugar-containing beverage can be given. If the patient is unarousable or unconscious, intravenous glucose is required. Patients should have a vial of glucagon available as well. If access to medical care is delayed, administration of 1 mg glucagon intramuscularly frequently aborts the attack.

Somogyi Effect

The *Somogyi phenomenon*, a counter regulatory response of the body, occurs when the body produces glucagons to respond to insulin administration. The body, in attempting to be homeostatic, secretes glucagons to raise the blood sugar. This results in an increasing blood sugar levels when insulin is given. If the Somogyi phenomenon is suspected, the insulin dose should be decreased as a trial, even when specific symptoms of overinsulinization are absent. The Somogyi phenomenon is probably rare in adults but may be more frequent in children.

Dawn Phenomenon

The *dawn phenomenon* refers to an early morning rise in plasma glucose requiring increased amounts of insulin to maintain blood sugar levels. The nocturnal surge of growth hormone, which increases blood

sugar may be a factor. The dawn phenomenon usually requires increased insulin to maintain glucose in the normal range.

Non-Insulin Treatments for NIDDM

Oral

- Sulfonylureas. Act primarily by stimulating release of insulin from the beta cell. These drugs can bring plasma glucose back to normal in some patients with relatively mild disease, but in patients with significant hyperglycemia, plasma glucose tends to improve but not to approach the normal range in response to these agents.
- Biguanides. The primary action of Biguanides such as metformin is thought to be inhibition of hepatic gluconeogenesis. Metformin does not cause hypoglycemia. Metformin can cause lactic acidosis. It should be stopped at once if nausea, vomiting, diarrhea, or intercurrent illness appears.
- Alpha-glucosidase Inhibitors lower blood sugar by inhibiting the enzyme alpha-glucosidase in the GI tract resulting in delayed glucose absorption.
- Thiazolidinedione derivatives such as troglitazone lower the blood levels of glucose, free fatty acids, and triglycerides and appear to reduce insulin resistance, possibly by increasing the activity of insulin receptor kinase.
- meglitinides Prandin, the first of a new class of drugs called meglitinides, is a short-acting oral antidiabetic agent with a flexible dosing schedule. Its rapid onset of action and short half-life enables **Prandin** to be taken before each meal. As a result, **Prandin** augments insulin release when it is needed, after each meal when blood glucose levels are high. Between meals and during the night, insulin levels return toward baseline, which may reduce the occurrence of severe hypoglycaemia and hyperinsulinemia (excess insulin). If a meal is missed, **Prandin** is not taken and an increased amount of insulin is not released.
- Two peptides are under evaluation as adjunct treatments for NIDDM. Both insulin-like growth factor 1 (IGF-1, somatomedin C) and glucagon-like peptide 1 (GLP-1), a peptide derived from the proglucagon molecule, lower blood glucose levels in normal subjects and in patients with **diabetes**. GLP-1 (7-36) and (7-37) amides are the lead agents under trial. Their usefulness is not established.

Commonly Prescribed Oral Diabetic Medications

<p><u>Sulfonylureas</u></p> <p>Amaryl DiaBeta Diabinese Dymelor Glucotrol Glucotrol XL Glynase PresTab Micronase Orinase Tolinase</p> <p><u>Biguanides</u></p> <p>Glucophage Metformin</p>	<p><u>Alpha-glucosidase Inhibitors</u></p> <p>Glyset Precose</p> <p><u>Thiazolidinediones</u></p> <p>Actos Avandia</p> <p><u>Meglitinides</u></p> <p>Prandin</p>
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Monitoring The Control Of Diabetes

- Hemoglobin A_{1c} or glycated hemoglobin levels quarterly in all patients. This step is particularly important in patients who do not measure glucose values frequently at home. Hemoglobin A_{1c} is present in normal persons and increases in amount in the presence of hyperglycemia. Nondiabetic subjects have hemoglobin A_{1c} values of less than 6 percent, while levels in patients with poorly controlled **diabetes** may be considerably above 10 percent. Measurement of glycated hemoglobin gives an objective assessment of metabolic control.

ACUTE METABOLIC COMPLICATIONS

- **Hypoglycemia**
- **Diabetic Ketoacidosis** Diabetic ketoacidosis occurs from a combination of insulin deficiency and glucagons excess. It is often caused by cessation of insulin intake, but it may result from physical (e.g., infection, surgery) or emotional stress despite continued insulin therapy. Epinephrine is also secreted which may block the release of the small amount of residual insulin present in some patients with IDDM which inhibits insulin-induced glucose transport in peripheral tissues.

Symptoms of Ketoacidosis

- ✓ anorexia, nausea, and vomiting, coupled with an increased rate of urine formation.
- ✓ Abdominal pain may be present.
- ✓ Altered consciousness or frank coma may occur.
- ✓ Kussmaul respiration together with signs of volume depletion.
- ✓ total-body potassium deficit of several hundred millimoles.
- ✓ serum sodium concentration tends to be low in the face of a modest osmolar concentration because the hyperglycemia draws intracellular water into the plasma space.

Diagnosis of Ketoacidosis

- ✓ ketones in the urine.
- ✓ Elevated blood glucose. Glucose can elevate to very high levels. Glucose levels may be seen as high as 500 mg/dl.

Treatment of Ketoacidosis

- ✓ Cannot be reversed without insulin.
- ✓ "low-dose" insulin schedules in which 8 to 10 units of insulin are infused intravenously each hour.
- ✓ Should acidosis persist unabated after several hours of treatment, larger amounts of insulin are clearly indicated. Ketoacidosis also can be treated adequately with intramuscular (but not subcutaneous) insulin.
- ✓ I.V. fluids. The usual fluid deficit is 3 to 5 L, Between 1 and 2 L of isotonic saline or Ringer's lactate should be given rapidly intravenously on arrival, with additional amounts determined by urine output and clinical assessment of the fluid state.
- ✓ Potassium replacement is always necessary.
- ✓ Bicarbonate therapy may be indicated in severely acidotic patients (pH 7.0 or below), especially if hypotension is present (acidosis itself can cause vascular collapse).
- ✓ The plasma glucose level invariably falls more rapidly than the plasma ketone level. Insulin administration should not be stopped because glucose concentrations approach normal; rather, as mentioned, glucose should be infused and insulin
- ✓ Plasma ketone values are not very helpful in assessing clinical response.
- ✓ All patients should be followed with a flow sheet outlining amounts and timing of insulin and fluids together with a record of vital signs, urine volume, and blood chemistries. Without such a record, therapy tends to become chaotic.
- ✓ mortality rate is around 10 percent,

Complications of Ketoacidosis

- ✓ vascular thrombosis
 - ✓ adult respiratory distress syndrome.
- **Hyperosmolar Coma or Hyperglycemic, Hyperosmolar Nonketosis (HHNK)** Hyperosmolar, nonketotic diabetic coma is usually a complication of NIDDM. This results in profound dehydration resulting from a sustained hyperglycemic diuresis under circumstances in which the patient is unable to drink enough water to keep up with urinary fluid. The absence of ketoacidosis is important in the pathophysiology of this condition. When ketoacidosis develops, nausea, vomiting, and air hunger bring the patient to the physician before extreme dehydration can occur. Such a protective mechanism is not operative in ketoacidosis-resistant, maturity-onset **diabetes**. Hyperosmolar coma can occur in insulin-dependent diabetic patients who are given enough insulin to prevent ketosis but not enough to control hyperglycemia. Although it is unusual, the same person may present on one occasion with ketoacidosis and on the next with hyperosmolar coma.

Symptoms and Syndromes with HHNK

- ✓ Hyperglycemia
- ✓ Hyperosmolality
- ✓ volume depletion
- ✓ central nervous system signs ranging from a clouded sensorium to coma
- ✓ Seizure activity
- ✓ Pneumonia is often due to gram-negative organisms.
- ✓ Bleeding, probably caused by disseminated intravascular coagulation
- ✓ acute pancreatitis may occur.
- ✓ Plasma glucose is generally around 55 mmol/L (1000 mg/dL), about twice the value seen in ketoacidosis.

Treatment of HHNK

- ✓ The mortality rate in hyperosmolar coma is high (>50 percent). As a consequence, immediate treatment is urgent.
- ✓ rapid administration of large amounts of intravenous fluids to reestablish the circulation and urine flow. The average fluid deficit is 10 to 11 L. Initial therapy should be with isotonic salt solutions, and 2 to 3 L should be given over the first 1 to 2 h.

- ✓ Insulin in small doses should be given to control the hyperglycemia more rapidly. Many authors recommend small doses of insulin, but larger amounts may be necessary, particularly in the obese patient.
- ✓ Potassium salts are usually required earlier in the treatment of hyperosmolar coma than in ketoacidosis because the intracellular shift of plasma K⁺ during therapy is accelerated in the absence of acidosis.

LATE COMPLICATIONS OF DIABETES

Diabetes can affect all blood vessels which may result in a variety of complications. The macroangiopathy (large blood vessels) and microangiopathy (small blood vessels) can create complications in every body system.

Circulatory Abnormalities

- ✓ Atherosclerosis is more extensive and occurs earlier than in the general population. In experiments, diabetes has been shown to accelerate the oxidative process. Other factors of potential importance are increased platelet adhesiveness. **Diabetes** appears to be a procoagulant state and fibrinolysis is impaired. Atherosclerosis produces symptoms in a variety of sites. Peripheral deposits may cause intermittent claudication, gangrene, and, in men, organic impotence on a vascular basis. Surgical repair of large-vessel lesions may be unsuccessful because of the simultaneous presence of widespread disease of the small vessels.
- ✓ Coronary artery disease and silent myocardial infarction occurs with increased frequency in **diabetes**.
- ✓ **Stroke**
- ✓ Cardiomyopathy, in which heart failure occurs in the face of apparently normal coronary arteries and in the absence of other identifiable causes of heart disease.
- ✓ Hypertension is a significant risk in many diabetic patients.
- ✓

Retinopathy Diabetic retinopathy is a leading cause of blindness in the United States. Retinopathic lesions are divided into two large categories, *simple* (background) and *proliferative*.

Approximately 85 percent of patients eventually develop the complication. Retinopathy appears to develop earlier in older patients. About half of patients with proliferative disease progress to blindness within 5 years. Proliferative retinopathy appears to be more common in insulin-treated patients than in those not treated with insulin.

The treatment for diabetic retinopathy is photocoagulation. Another surgical technique, pars plana vitrectomy, is used for treatment of nonresolving vitreal hemorrhage and retinal detachment. All patients with diabetic retinopathy should be followed by retinal specialists.

Diabetic Nephropathy Renal disease is a leading cause of death and disability in **diabetes**. About half of the cases of end-stage renal disease in the United States are now due to diabetic nephropathy. Approximately 35 percent of patients with IDDM develop this complication. The prevalence in NIDDM varies from 15 to 60 percent depending on ethnic background.

Diabetic nephropathy may be functionally silent for long periods (10 to 15 years).

Stages of Nephropathy

1. kidneys are usually enlarged and show "superfunction" (i.e., glomerular filtration rates may be 40 percent above normal).
2. *microproteinuria* (microalbuminuria), the excretion of albumin in the range of 30 to 300 mg/d. Normal persons excrete less than 30 mg/d. Microalbuminuria is not detected by reagent sticks for urinary protein.
3. Once the macroproteinuric phase begins, there is a steady decline in renal function, with glomerular filtration rate falling, on average, by about 1 mL/min per month.
4. Progression of renal disease is accelerated by hypertension.

There is no specific treatment for diabetic nephropathy. Meticulous control of **diabetes** can reverse microalbuminuria in some patients, and the progression of diabetic nephropathy may be slowed, as shown in the intensive treatment group of the DCCT. Chronic dialysis and renal transplantation are routine in patients with renal failure due to **diabetes**.

Diabetic Neuropathy Diabetic neuropathy may affect every part of the nervous system, with the possible exception of the brain. While rarely a direct cause of death, neuropathy is a major cause of morbidity.

Types of Neuropathy

- ✓ *peripheral polyneuropathy*. Usually bilateral, the symptoms include numbness, paresthesias, severe hyperesthesias, and pain.
- ✓ *Mononeuropathy*, though less common than polyneuropathy, also may occur. Characteristically, there is a sudden wrist drop, foot drop, or paralysis of the third, fourth, or sixth cranial nerves.
- ✓ *Radiculopathy* is a sensory syndrome in which pain occurs over the distribution of one or more spinal nerves, usually in the chest wall or abdomen. The severe pain may mimic herpes zoster or an acute surgical abdomen. Like mononeuropathy, the lesion is usually self-limited.
- ✓ *Autonomic neuropathy* may present in a variety of ways. The gastrointestinal tract is a prime target, and there may be esophageal dysfunction with difficulty in swallowing, delayed gastric emptying, constipation, or diarrhea.
- ✓ Erectile dysfunction is associated with a failure of nitric oxide generation in the penile vasculature.
- ✓ Diabetic *amyotrophy* is likely a form of neuropathy, although atrophy and weakness of the large muscles in the upper leg and pelvic girdle resemble primary muscle disease. Anorexia and depression may accompany amyotrophy. Because of the weight loss, such patients are often thought to have a paraneoplastic neuropathy.

Treatment of diabetic neuropathy is unsatisfactory in most respects.

Diabetic Foot Ulcers A special problem in the diabetic patient is the development of ulcers of the feet and lower extremities. The ulcers appear to be due primarily to abnormal pressure distribution secondary to diabetic neuropathy. All patients with ulcers should have x-rays of the feet.

All patients should be instructed about proper foot care in an attempt to prevent ulcers. Feet should be kept clean and dry at all times. Patients with neuropathy should not walk barefoot, even in the home. Properly fitted shoes are essential. The feet should be carefully inspected daily for callus, infection, abrasions, or blisters and the physician consulted about any potentially troublesome lesion.

Miscellaneous Abnormalities Of Diabetes

Diabetes affects almost every system in the body.

- ✓ *Infections* in persons with **diabetes** may not occur more frequently than in nondiabetics, but they tend to be more severe.
- ✓ *Malignant external otitis*, usually due to *Pseudomonas aeruginosa*, tends to occur in older patients and is characterized by severe pain in the ear, drainage, fever, and leukocytosis.
- ✓ *Rhinocerebral mucormycosis* is a rare fungal infection that usually develops during or following an episode of diabetic ketoacidosis.
- ✓ *Emphysematous cholecystitis* tends to affect diabetic men (in contrast to ordinary cholecystitis, a disease predominantly present in women). Gangrene of the gallbladder is 30 times more frequent than in the usual forms and accounts for high rates of perforation and higher mortality rates than in ordinary cholecystitis.
- ✓ *Hypertriglyceridemia* is common in **diabetes** and is due both to overproduction of VLDL in the liver and to a disposal defect in the periphery.
- ✓ *Necrobiosis lipoidica diabetorum* is a plaque-like lesion with a central yellowish area surrounded by a brownish border. It is usually found over the anterior surfaces of the legs.
- ✓ *Diabetic dermopathy* ("shin spots") is also usually located over the anterior tibial surface. The lesions are small, rounded plaques with a raised border; they may crust at the edges and ulcerate centrally.
- ✓ *Candida* and dermatophytes are common, and bacterial infections of a variety of types occur.

- ✓ *vaginal moniliasis* may be troublesome during hyperglycemic-glycosuric periods. While the symptoms respond to nystatin or gentian violet, recurrence is inevitable unless glycosuria is reversed.
- ✓ *Atrophy of adipose tissue* may occur at the site of insulin injections, even with recombinant human insulin.
- ✓ *Hypertrophy* of fat also may occur, producing a lipoma-like lesion visible on physical examination.
- ✓ *Hyperviscosity*
- ✓ *platelet aggregation* is enhanced
- ✓ *Wound healing* is impaired in experimental **diabetes**, but this effect probably is not a major factor clinically.
- ✓ *joint contractures* (Dupuytren's contractures) coupled with *tight, waxy skin* over the dorsum of the hands.

NONROUTINE THERAPIES

- Transplantation with whole pancreas or pancreatic segments has cured **diabetes** but is usually performed only when kidney transplantation is required.
- Transplantation of islet cells (as opposed to whole pancreas) also has been attempted, but the results are poor. The use of nonpancreatic cells that have been genetically engineered to produce human insulin under glucose control is being studied.
- Prevention of autoimmune **diabetes** by immunosuppressant agents is a desirable goal.
- Reversal of hyperglycemia without the need for insulin has been achieved in humans with new-onset **diabetes** using powerful drugs such as cyclosporine. The reversal is not permanent.
- Preventive trials are under way in which insulin is used as prophylaxis in subjects predicted to develop **diabetes** in the near future based on the presence of islet cell antibodies and diminished insulin response to an intravenous glucose load. Scattered positive results have been reported. Other trials are testing the effect of nicotinamide as a possible protective and repair agent.

INSULIN RESISTANCE

Insulin resistance is defined arbitrarily as the requirement of 200 or more units of insulin per day to control hyperglycemia and prevent ketosis. Relative insulin resistance is present in most persons with **diabetes** when carefully sought using the glucose clamp technique. It is the consequence of near-complete insulin deficiency in IDDM, whereas in NIDDM the major cause is obesity.

Insulin resistance is characterized as *prereceptor* (abnormal insulin or anti-insulin antibodies), *receptor* (decreased receptor number or diminished binding of insulin), or *postreceptor* (abnormal signal transduction, especially failure to activate the receptor tyrosine kinase). Combinations may exist. The nature of the molecular defect is known in some forms of insulin resistance but has not been identified in many.

Obesity is the most common cause of insulin resistance. There is little response to exogenous hormone. Other features include growth retardation, alopecia or premature graying of the hair, cataracts, hypogonadism, leg ulcers, atrophy of muscle, fat, and bone, soft tissue calcification, and a high frequency of sarcomas and meningiomas.

INSULIN ALLERGY

Insulin allergy is due to IgE antibodies to insulin. Manifestations include immediate reactions with local stinging or itching, delayed local reactions with brawny swelling lasting up to 30 h, and generalized urticaria or frank anaphylaxis. Systemic reactions are usually seen in patients who have stopped insulin therapy for one reason or another and have then resumed treatment. The allergic reaction may occur as early as the second injection on resumption of therapy. Mild reactions can be treated with antihistamines. If the problem is severe, desensitization procedures are required.

Hypoglycemia

From Wikipedia, the free encyclopedia <http://en.wikipedia.org/wiki/Hypoglycemia>

Hypoglycemia is the medical term for a [pathologic](#) state produced by a lower than normal level of [blood glucose](#). Hypoglycemia 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 vaguely "feeling bad" to [coma](#), [seizures](#), and (rarely) permanent brain damage or death. Hypoglycemia can arise from many causes and can occur at any age. It also sometimes occurs at random. The most common forms of moderate and severe hypoglycemia occur as a complication of treatment of [diabetes mellitus](#) treated with [insulin](#) or less frequently with certain [oral medications](#). Hypoglycemia is usually treated by the ingestion or administration of [dextrose](#), or foods quickly digestible to glucose. [Endocrinologists](#) typically consider the following criteria (referred to as [Whipple's triad](#)) as proving that individual's [symptoms](#) can be attributed to hypoglycemia:

1. Symptoms known to be caused by hypoglycemia
2. Low glucose at the time the symptoms occur
3. Reversal or improvement of symptoms or problems when the glucose is restored to normal

However, not everyone has accepted these suggested diagnostic criteria, and even the level of glucose low enough to define hypoglycemia has been a source of controversy in several contexts. For many purposes, [plasma](#) glucose levels below 70 mg/dl or 3.9 [mmol/L](#) are considered hypoglycemic; these issues are detailed below.

Defining hypoglycemia

No single glucose value alone serves to define the medical condition termed hypoglycemia 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 70-150 mg/dL (3.9-7.8 [mmol/L](#)) for healthy humans.¹¹ Although 60 or 70 mg/dL (3.3 or 3.9 [mmol/L](#)) is commonly cited as the lower limit of normal glucose, different values (typically below 40, 50, 60, or 70 mg/dL) have been defined as low for different populations, clinical purposes, or circumstances. 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. This article expresses glucose in milligrams per deciliter (mg/dL or mg/100 mL) as is customary in the United States, while millimoles per [litre](#) (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.

Alternate theory: Rate of decrease in blood sugar rather than depth of decrease affects the nervous system

An alternate view of the syndrome advanced by researchers at Johns Hopkins University Medical School is that the rate of the decrease in blood sugar rather than its absolute low mark is what triggers the reported symptoms. It is surmised that the nervous system is not given sufficient time to adjust to a rapid rather than a gradual drop in blood sugar, which then triggers the reported symptoms of anxiety, fainting, tinnitus, and so on. [Johns Hopkins Family Health Book, page 1183. \(Viewable Online\)](#) Consuming food that helps maintain a more even level of blood sugar and paying attention to the [glycemic index](#) or [glycemic load](#) of various foods are also recommended, along with eating several smaller meals a day rather than traditional three larger meals. However, the utility of the glycemic index is disputed within the medical profession, and it may be of little value in managing hypoglycemia-associated autonomic failure (HAAF).

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.^[5] 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.^[6] On the other hand, whole blood glucose levels (e.g., by [fingerprick meters](#)) are about 10%-15% lower than venous plasma levels.^[5]

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.^{[7][8]} 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. Ironically, most meters sold are routinely tested for accuracy at the high-end of the scale, sometimes up to 800 mg/dL, despite the fact that there is little immediate danger from [hyperglycemia](#), whereas there is very real immediate danger from hypoglycemia, making accuracy at the low-end extremely critical.

Two other factors significantly affect glucose measurement: hematocrit and delay after [phletocrit](#) is high,^[6] as in newborn infants, or adults with [polycythemia](#). 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/hr, or even more in the presence of [leukocytosis](#).^{[9][10][6]}

Age differences

Surveys of healthy children and adults show that plasma glucoses below 60 mg/dL (3.3 mM) or above 100 mg/dL (5.6 mM) are found in less than 5% of samples after an overnight fast.^[11] As the duration of fasting is extended, plasma glucose levels can fall further, even in healthy people. In other words, many healthy people can occasionally have glucose levels in the hypoglycemic range without symptoms or disease. The normal range of newborn blood sugars continues to be debated. 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 after the first day after birth.

Presence or absence of effects

Research in healthy adults shows that mental efficiency declines slightly but measurably as blood glucose falls below 65 mg/dL (3.6 mM) in many people. [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 symptoms of shakiness and [dysphoria](#). However, because [type 1 diabetes mellitus](#) is an autoimmune disease resulting from inflammation to the [Islets of Langerhans](#), these counterregulatory responses are severely impaired in this group. On the other hand, obvious impairment does not often occur until the glucose falls below 40 mg/dL, and up to 10% of the population may occasionally have glucose levels below 65 in the morning without apparent effects. Brain effects of hypoglycemia, termed [neuroglycopenia](#), determine whether a given low glucose is a "problem" for that person, and hence some people tend to use the term *hypoglycemia* only when a moderately low glucose is accompanied by symptoms.

Even this criterion is complicated by the facts that A) hypoglycemic symptoms are vague and can be produced by other conditions; B) people with persistently or recurrently low glucose levels can lose their threshold symptoms so that severe neuroglycopenic impairment can occur without much warning; and C) many measurement methods (especially glucose meters) are imprecise at low levels.

[Diabetic hypoglycemia](#) represents a special case with respect to the relationship of measured glucose and hypoglycemic symptoms for several reasons. First, it is almost always [iatrogenic](#). Second, although home glucose meter readings are too often misleading, the probability that a low reading which may or may not be accompanied by symptoms represents real hypoglycemia is also significantly higher in a person who takes insulin, and is 25 times higher in patients with type 1 diabetes relative to those with type 2 diabetes^{[12][13]}. Third, the hypoglycemia has a greater chance of progressing to more serious

impairment if not treated, compared to most other forms of hypoglycemia that occur in adults because insulin is dosed in a non-physiological manner. Fourth, because glucose levels are above normal more often than they are in people without diabetes, hypoglycemic symptoms may sometimes occur at higher thresholds than in people who are normoglycemic most of the time. For all of these reasons, people with diabetes are instructed to use higher meter glucose thresholds to determine hypoglycemia, although the absence of symptoms can sometimes impede patients' ability to do so.

Purpose of definition

For all of the reasons explained in the above paragraphs, 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.

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 via [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 period of 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. The vast majority of symptomatic hypoglycemic episodes result in no detectable permanent harm.^[14]

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.

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, borborygmus
- Nausea, vomiting, abdominal discomfort
- Headache

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

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 incidence.

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 patients, the brain may habituate to low glucose levels, with a reduction of noticeable symptoms despite neuroglycopenic impairment. In insulin-dependent diabetic patients 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 glycogenesis](#), when chronic hypoglycemia before diagnosis may be better tolerated than acute hypoglycemia after treatment is underway.

Nearly always, hypoglycemia 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.

Determining the cause

Hundreds of conditions can cause hypoglycemia. Common causes by age are listed below. While many aspects of the [medical history](#) and [physical examination](#) may be informative, the two best guides to the cause of unexplained hypoglycemia are usually

1. the **circumstances**
2. a **critical sample** of blood obtained at the time of hypoglycemia, before it is reversed.

The circumstances of hypoglycemia provide most of the clues to diagnosis

Circumstances include the age of the patient, 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.

An especially important aspect is whether the patient is seriously ill with another problem. Severe disease of nearly all major organ systems can cause hypoglycemia as a secondary problem. [Hospitalized](#) patients, especially in [intensive care units](#) or those prevented from eating, can suffer hypoglycemia from a variety of circumstances related to the care of their primary disease. Hypoglycemia in these circumstances is often multifactorial or even [iatrogenic](#). Once identified, these types of hypoglycemia are readily reversed and prevented, and the underlying disease becomes the primary problem.

Apart from determining nutritional status and identifying whether there is likely to be an underlying disease more serious than hypoglycemia, the physical examination of the patient is only occasionally helpful. [Macrosomia](#) in infancy usually indicates [hyperinsulinism](#). A few [syndromes](#) and [metabolic diseases](#) may be recognizable by clues such as [hepatomegaly](#) or [micropenis](#).

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 patient, the amount of glucose required to maintain satisfactory blood glucose levels becomes an important clue to the underlying etiology. 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.

In less obvious cases, a "critical sample" may provide the diagnosis

In the majority of children and adults with recurrent, unexplained hypoglycemia, the diagnosis may be determined by obtaining a sample of blood during hypoglycemia. If this **critical sample** is obtained *at the time of hypoglycemia, before it is reversed*, it can provide information that would otherwise require a [hospital](#) admission and unpleasant starvation testing. Perhaps the most common inadequacy of [emergency department](#) care in cases of unexplained hypoglycemia is the failure to obtain at least a basic sample before giving glucose to reverse it.

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.

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 patient. 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 patient, 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. Although interpretation in difficult cases is beyond the scope of this article, for most of the tests, the primary significance is briefly noted.

- [Glucose](#): needed to document actual hypoglycemia
- [Insulin](#): any detectable amount is abnormal during hypoglycemia, but physician must know assay characteristics
- [Cortisol](#): should be high during hypoglycemia if pituitary and adrenals are functioning normally
- [Growth hormone](#): should rise after hypoglycemia if pituitary is functioning normally
- [Electrolytes](#) and [total carbon dioxide](#): electrolyte abnormalities may suggest renal or adrenal disease; mild [acidosis](#) is normal with starvation hypoglycemia; usually no acidosis with hyperinsulinism
- [Liver enzymes](#): elevation suggests liver disease
- [Ketones](#): should be high during fasting and hypoglycemia; low levels suggest [hyperinsulinism](#) or [fatty acid oxidation disorder](#)
- [Beta-hydroxybutyrate](#): should be high during fasting and hypoglycemia; low levels suggest hyperinsulinism or fatty acid oxidation disorder
- [Free fatty acids](#): should be high during fasting and hypoglycemia; low levels suggest hyperinsulinism; high with low ketones suggests fatty acid oxidation disorder
- [Lactic acid](#): high levels suggest sepsis or an inborn error of gluconeogenesis such as glycogen storage disease
- [Ammonia](#): if elevated suggests hyperinsulinism due to glutamate dehydrogenase deficiency, [Reye syndrome](#), or certain types of liver failure
- [C-peptide](#): should be low or undetectable; if elevated suggests hyperinsulinism; low c-peptide with high insulin suggests exogenous (injected) insulin
- [Proinsulin](#): detectable levels suggest hyperinsulinism; levels disproportionate to a detectable insulin level suggest [insulinoma](#)
- [Ethanol](#): suggests alcohol intoxication
- [Toxicology screen](#): can detect many drugs causing hypoglycemia, especially for [sulfonylureas](#)
- [Insulin antibodies](#): if positive suggests repeated insulin injection or antibody-mediated hypoglycemia
- [Urine organic acids](#): elevated in various characteristic patterns in several types of [organic aciduria](#)

- [Carnitine](#), free and total: low in certain disorders of fatty acid metabolism and certain types of drug toxicity and pancreatic disease
- [Thyroxine](#) and [TSH](#): low T4 without elevated TSH suggests [hypopituitarism](#) or malnutrition
- [Acylglycine](#): elevation suggests a disorder of fatty acid oxidation
- [Epinephrine](#): should be elevated during hypoglycemia
- [Glucagon](#): should be elevated during hypoglycemia, except in the case of [type 1 diabetes mellitus](#) where irreparable damage is done to the cells which produce this counterregulatory hormone.
- [IGF-1](#): low levels suggest hypopituitarism or chronic malnutrition
- [IGF-2](#): low levels suggest hypopituitarism; high levels suggest non-pancreatic tumor hypoglycemia
- [ACTH](#): should be elevated during hypoglycemia; unusually high ACTH with low cortisol suggests [Addison's disease](#)
- [Alanine](#) or other plasma [amino acids](#): abnormal patterns may suggest certain inborn errors of amino acid metabolism or gluconeogenesis
- [Somatostatin](#) should be elevated during hypoglycemia as it acts to inhibit insulin production and increase blood glucose level

Further diagnostic steps

When suspected hypoglycemia recurs and a critical specimen has not been obtained, the diagnostic evaluation may take several paths. However good nutrition and prompt intake is essential.

When general health is good, the symptoms are not severe, and the person can fast normally through the night, experimentation with diet (extra snacks with fat or protein, reduced sugar) may be enough to solve the problem. If it is uncertain whether "spells" are indeed due to hypoglycemia, some physicians will recommend use of a home glucose meter to test at the time of the spells to confirm that glucoses are low. This approach may be most useful when spells are fairly frequent or the patient is confident that he or she can provoke a spell. The principal drawback of this approach is the high rate of false positive or equivocal levels due to the imprecision of the currently available meters: both physician and patient need an accurate understanding of what a meter can and cannot do to avoid frustrating and inconclusive results.

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 patient 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 patient'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.

A traditional method for investigating suspected hypoglycemia is the oral [glucose tolerance test](#), especially when prolonged to 3, 4, or 5 hours. Although quite popular in the United States in the 1960s, repeated research studies have demonstrated that many healthy people will have glucose levels below 70 or 60 during a prolonged test, and that many types of significant hypoglycemia may go undetected with it. This combination of poor [sensitivity](#) and [specificity](#) has resulted in its abandonment for this purpose by physicians experienced in disorders of glucose metabolism.

Hypoglycemia Causes

[from www.emedicinehealth.com/low_blood_sugar_hypoglycemia/page3_em.htm](http://www.emedicinehealth.com/low_blood_sugar_hypoglycemia/page3_em.htm)

There are several ways to classify hypoglycemia. The following is a list of the more common causes and factors which may contribute to hypoglycemia grouped by age, followed by some causes that are relatively age-independent.

Common causes of low blood sugar include the following:

- Overmedication with insulin or antidiabetic pills (for example, sulfonylurea drugs)
- Use of medications such as [beta blockers](#), pentamidine, and [sulfamethoxazole and trimethoprim](#) (Bactrim, Septra)
- Use of alcohol
- Missed meals
- Reactive hypoglycemia is the result of the delayed insulin release after a meal has been absorbed and occurs 4-6 hours after eating.
- Severe infection
- Cancer causing poor oral intake or cancer involving the liver
- Adrenal insufficiency
- Kidney failure
- Liver failure
- Congenital, genetic defects in the regulation of insulin release (congenital hyperinsulinism)
- Congenital conditions associated with increased insulin release (infant born to a diabetic mother, birth trauma, reduced oxygen delivery during birth, major birth stress, Beckwith-Wiedemann syndrome, and rarer genetic conditions)
- [Insulinoma](#) or insulin-producing tumor
- Other tumors like [hepatoma](#), [mesothelioma](#), and [fibrosarcoma](#), which may produce insulin-like factors

What follows are expansions on the points noted above and should be incorporated within those points (such as cancer, diabetes drugs, organ failures).

- Most cases of hypoglycemia in adults happen in people with diabetes mellitus. Diabetes has two forms, type 1 (loss of all insulin production) and type 2 (inadequate insulin production due to resistance to the actions of insulin). People with type 1 diabetes must take insulin to control their glucose level; if they skip meals or have a decreased appetite without changing their insulin dose, they may develop hypoglycemia. Insulin is also used to treat some people with type 2 diabetes.
- If a person with type 1 diabetes accidentally takes too much insulin, or a person with type 2 diabetes accidentally takes too much of their oral medications or insulin, he or she may develop hypoglycemia. Even when a diabetic patient takes medications correctly, improper meals, odd mealtimes, or excessive exercise may result in hypoglycemia.
- Often a person who has more than one medical problem may become confused about how much of a certain medication they should take, or their medications may interact to cause hypoglycemia.
- Hypoglycemia also may occur in people with cancer, which often causes loss of appetite. Many such people skip meals because they are not hungry or because [chemotherapy](#) causes foods to taste differently. To prevent this, people on chemotherapy should be encouraged by their doctors and loved ones to try to stay on special diets and take medications to keep them from feeling sick. If this does not work, special medications to help with appetite are available.
- Adrenal insufficiency results from diseases that impair the adrenal glands, which are located above the kidneys. These small structures make certain hormones and substances, mainly cortisol and epinephrine, which also help elevate glucose in addition to their other functions. If these substances are not made, [low blood pressure](#), hypoglycemia, or both can result.
- The [pituitary](#) gland makes [growth hormone](#), which also helps to maintain the balance of glucose. Deficiency of growth hormone causes hypoglycemia, especially in young infants and children.
- [Kidney failure](#) causes hypoglycemia in three separate ways. The kidneys help to generate new glucose from amino acids (called gluconeogenesis). Gluconeogenesis is impaired in kidney failure. Also, insulin circulates for a longer period of time and is cleared slowly when kidney function is poor. The third important reason is that kidney failure reduces the appetite and consequently, oral intake of food.

- The liver stores glucose in a form called glycogen. In the presence of liver failure, the abilities of the liver to generate new glucose and to release glucose are impaired.
- Insulin-producing tumors of the pancreas (called insulinomas) cause hypoglycemia by releasing inappropriately high amounts of insulin. Certain tumors of the liver called hepatomas or other tumors such as fibrosarcomas and mesotheliomas can also cause hypoglycemia by producing insulin-like factors.

Hypoglycemia in newborn infants

Hypoglycemia is a common problem in critically ill or extremely low birthweight infants. If not due to maternal hyperglycemia, in most cases it is multifactorial, transient and easily supported. In a minority of cases hypoglycemia turns out to be due to significant hyperinsulinism, hypopituitarism or an inborn error of metabolism and presents more of a management challenge.

- Transient neonatal hypoglycemia
 - [Prematurity](#), [intrauterine growth retardation](#), [perinatal asphyxia](#)
 - Maternal hyperglycemia due to [diabetes](#) or iatrogenic glucose administration
 - Sepsis
 - Prolonged fasting (e.g., due to inadequate breast milk or condition interfering with feeding)
- Congenital hypopituitarism
- [Congenital hyperinsulinism](#), several types, both transient and persistent
- [Inborn errors of carbohydrate metabolism](#) such as glycogen storage disease

Hypoglycemia in young children

Single episodes of hypoglycemia may occur due to [gastroenteritis](#) or fasting, but recurrent episodes nearly always indicate either an inborn error of metabolism, congenital hypopituitarism, or congenital hyperinsulinism. A list of common causes:

- Prolonged fasting
 - [Diarrheal](#) illness in young children, especially [rotavirus](#) gastroenteritis
- Idiopathic [ketotic hypoglycemia](#)
- Isolated [growth hormone deficiency](#), hypopituitarism
- [Insulin excess](#)
 - Hyperinsulinism due to several congenital disorders of insulin secretion
 - Insulin injected for type 1 diabetes
 - Hyperinsulin Hyperammonia syndrome (HIHA) due to [Glutamate dehydrogenase 1 gene](#). Can cause mental retardation and epilepsy in severe cases.^[15]
- [Gastric dumping syndrome](#) (after gastrointestinal surgery)
- Other congenital metabolic diseases; some of the common include
 - [Maple syrup urine disease](#) and other organic acidurias

- [Type 1 glycogen storage disease](#)
- Type III glycogen storage disease. Can cause less severe hypoglycemia than type I
- [Phosphoenolpyruvate carboxykinase deficiency](#) Causes metabolic acidosis and severe hypoglycemia.
- [Disorders of fatty acid oxidation](#)
- [Medium chain acylCoA dehydrogenase deficiency \(MCAD\)](#)
- Familial Leucine sensitive hypoglycemia ^[16]
- Accidental ingestions
 - [Sulfonylureas, propranolol](#) and others
 - Ethanol (mouthwash, "leftover morning-after-the-party drinks")

Hypoglycemia in older children and young adults

By far, the most common cause of severe hypoglycemia in this age range is insulin injected for [type 1 diabetes](#). Circumstances should provide clues fairly quickly for the new diseases causing severe hypoglycemia. All of the congenital metabolic defects, congenital forms of hyperinsulinism, and congenital hypopituitarism are likely to have already been diagnosed or are unlikely to start causing new hypoglycemia at this age. Body mass is large enough to make starvation hypoglycemia and idiopathic ketotic hypoglycemia quite uncommon. Recurrent mild hypoglycemia may fit a [reactive hypoglycemia](#) pattern, but this is also the peak age for [idiopathic postprandial syndrome](#), and recurrent "spells" in this age group can be traced to [orthostatic hypotension](#) or [hyperventilation](#) as often as demonstrable hypoglycemia.

- Insulin-induced hypoglycemia
 - Insulin injected for type 1 diabetes
 - Factitious insulin injection ([Munchausen syndrome](#))
 - Insulin-secreting pancreatic tumor
 - Reactive hypoglycemia and idiopathic postprandial syndrome
- [Addison's disease](#)
- [Sepsis](#)

Hypoglycemia in older adults

The incidence of hypoglycemia due to complex drug interactions, especially involving oral hypoglycemic agents and insulin for diabetes rises with age. Though much rarer, the incidence of insulin-producing tumors also rises with advancing age. Most tumors causing hypoglycemia by mechanisms other than insulin excess occur in adults.

- Insulin-induced hypoglycemia
 - Insulin injected for diabetes
 - Factitious insulin injection (Munchausen syndrome)
 - Excessive effects of oral diabetes drugs, beta-blockers, or drug interactions
 - Insulin-secreting pancreatic tumor

- Alcohol induced hypoglycemia often linked with ketoacidosis
- Alimentary (rapid jejunal emptying with exaggerated insulin response)
 - After gastrectomy [dumping syndrome](#) or bowel bypass surgery or resection
- Reactive hypoglycemia and idiopathic postprandial syndrome
- [Tumor hypoglycemia](#), [Doege-Potter syndrome](#)
- Acquired [adrenal insufficiency](#)
- Acquired hypopituitarism
- Immunopathologic hypoglycemia ^[17]

Treatment and prevention

Management of hypoglycemia 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 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.

If a person is suffering 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 EMTs and Paramedics, or in-hospital personnel can establish an IV and give intravenous Dextrose, concentrations varying depending on age (Infants are given 2cc/kg Dextrose 10%, Children Dextrose 25%, and Adults Dextrose 50%). Care must be taken in giving these solutions because they can be very necrotic if the IV is infiltrated. If an IV cannot be established, the patient can be given 1 to 2 milligrams of Glucagon in an [intramuscular injection](#). More treatment information can be found in the article [diabetic hypoglycemia](#).

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, patients taking these medications should consume monosaccharide-containing foods such as glucose tablets, honey, or juice to reverse hypoglycemia.

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 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 a [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.

Advances in Diabetes

In recent years, advances in diabetes research have led to better ways to manage diabetes and treat its complications. Major advances include:

- New forms of purified insulin, such as human insulin produced through genetic engineering.
- Better ways for doctors to monitor blood glucose levels and for people with diabetes to test their own blood glucose levels at home.
- Development of external and implantable insulin pumps that deliver appropriate amounts of insulin, replacing daily injections.
- Laser treatment for diabetic eye disease, reducing the risk of blindness.
- Successful transplantation of kidneys in people whose own kidneys fail because of diabetes.
- Better ways of managing diabetic pregnancies, improving chances of successful outcomes.
- New drugs to treat type 2 diabetes and better ways to manage this form of diabetes through weight control.
- Evidence that intensive management of blood glucose reduces and may prevent development of microvascular complications of diabetes.
- Demonstration that antihypertensive drugs called ACE-inhibitors prevent or delay kidney failure in people with diabetes.
- *Implantable insulin pumps* are surgically implanted, usually on the left side of the abdomen. The pump is disk shaped and weighs about 6 to 8 ounces. It delivers a basal dose of insulin continuously. Users deliver bolus insulin doses with a remote control unit that prompts the pump to give the specified amount of insulin. An advantage of this method is that, like insulin produced naturally from the pancreas, the insulin from the pump goes directly to the liver to prevent excess sugar production there.
- *The insulin patch*, placed on the skin, gives a continuous low dose of insulin. To adjust insulin doses before meals, users can pull off a tab on the patch to release insulin. The problem with the patch is that insulin does not get through the skin easily.
- *The inhaled insulin delivery system*, provides insulin as a dry powder inhaled through the mouth directly into the lungs where it passes into the bloodstream. This aerosol delivery system is about the size of a flashlight and uses rapid-acting insulin.

What Will the Future Bring?

In the future, it may be possible to administer insulin through nasal sprays or in the form of a pill or patch. Devices that can "read" blood glucose levels without having to prick a finger to get a blood sample are also being developed.

Researchers continue to search for the cause or causes of diabetes and ways to prevent and cure the disorder. Scientists are looking for genes that may be involved in type 2 diabetes and type 1 diabetes. Some genetic markers for type 1 diabetes have been identified, and it is now possible to screen relatives of people with type 1 diabetes to see if they are at risk for diabetes.

The new Diabetes Prevention Trial-- type 1 diabetes, sponsored by NIDDK, identifies relatives at risk for developing type 1 diabetes and treats them with low doses of insulin or with oral insulin-like agents in the hope of preventing type 1 diabetes. Similar research is carried out at other medical centers throughout the world.

Transplantation of the pancreas or insulin-producing beta cells offers the best hope of cure for people with type 1 diabetes. Some pancreas transplants have been successful. However, people who have transplants must take powerful drugs to prevent rejection of the transplanted organ. These drugs are costly and may eventually cause serious health problems.

Scientists are working to develop less harmful drugs and better methods of transplanting pancreatic tissue to prevent rejection by the body. Using techniques of bioengineering, researchers are also trying to create artificial islet cells that secrete insulin in response to increased sugar levels in the blood.

For type 2 diabetes, the focus is on ways to prevent diabetes. Preventive approaches include identifying people at high risk for the disorder and encouraging them to lose weight, exercise more, and follow a healthy diet. The Diabetes Prevention Program, another new NIDDK project, will focus on preventing the disorder in high-risk populations.

Diabetes Dictionary Index

Use this dictionary as tool to help your patients understand some of the terms.

<http://www.niddk.nih.gov/health/diabetes/pubs/dmdict/dmdict.htm>

Conclusion

Knowledge of diabetes pathology as well as hyperglycemia and hypoglycemia is essential to understanding this complex disease. More persons are becoming diabetics, and in the hospital setting, the healthcare worker must be in-tune to changing patient situations.

References:

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