

Diabetes Mellitus, Type 1 (or Insulin-Dependent Diabetes Mellitus)

Pronunciations: (*di''ah-BE'teez MEL-ih-tus*)

Diabetes Mellitus is a chronic condition characterized either by lack of insulin secretion (Type 1, or IDDM) or inadequate stimulation of insulin on its target cells (Type 2, or NIDDM). Diabetes results in elevated blood glucose levels, an increase in urinary glucose excretion, and abnormal fasting and postprandial glucose tolerance. IDDM is usually diagnosed before the age of 20 (juvenile-onset), although can occur at any age and accounts for 5% to 10% of all diabetes diagnoses. Following heart disease and cancer, diabetes mellitus is the third leading cause of death in the United States.

Causes

IDDM is typically an autoimmune disorder resulting in destruction of the insulin-producing beta cells of the pancreas, thereby creating an insulin deficiency. Following diagnosis, about 85% to 90% of cases show at least one circulating autoantibody (insulin, islet cell, or glutamic acid decarboxylase autoantibody) associated with beta cell destruction. The cause of the disease is still unknown however it appears to involve a genetic predisposition. Genes encoded on the major histocompatibility complex (MHC) within chromosome 6, particularly the human leukocyte antigen (HLA) class II alleles, DQ and DR, are associated with IDDM^{1,2}. The HLA-DQ locus appears to be the best single marker for susceptibility among Caucasians, however less than 10% of individuals with these genes develop IDDM, implying that environmental factors may also be responsible. For example, early exposures to cow's milk proteins, bovine albumin, beta-lactoglobulin, and beta-casein, have been associated with increased risk for IDDM³⁻⁶. Bovine serum albumin has a short amino acid sequence similar to a beta cell surface receptor ICA69 and beta casein shares a similar sequence with a glucose transporter suggesting molecular mimicry⁵. It appears that some form of "cross-reactivity" may occur with cow's milk proteins and islet-cell antigens, leading to "auto-attack" of the beta cells. In addition, Coxsackie B, an enterovirus part of a group of picornaviruses increases the expression of an enzyme glutamic acid decarboxylase (GAD) in the pancreas. GAD is a highly potent auto antigen of the autoimmune response in humans and mice models, which appears to stimulate attack of killer T cells on beta cells. Coxsackie B and GAD share a similar sequence that may also lead to cross-reactivity. Early exposure to mumps, cytomegalovirus, measles, influenza, encephalitis, polio, Epstein-Barr virus, or rubella; as well as toxin exposure, surgical removal, or trauma to the pancreas may also increase the risk of IDDM. Lower rates of the disease have been reported for the late spring and summer months and higher in the winter for populations in both the Northern and Southern hemispheres. The highest incidence rates in the world have been reported for Finland and Sardinia, Italy, while the lowest incidence rates have been observed in Japanese, Chinese, Korean, Native American, Cuban, Chilean and Mexican populations.

Diagnosis

Symptoms:

Prior to diagnosis, individuals with IDDM are usually lean and experience excessive thirst (polydipsia), frequent urination (polyuria), and unusual hunger (polyphagia) and weight loss. Ketoacidosis is also present. The pancreas is physiologically equipped to secrete more insulin than what is normally needed therefore an asymptomatic period of months to years may precede the clinical onset of the disease. Once hyperglycemia and acidotic conditions have recovered in those recently diagnosed, a “honeymoon phase” often occurs where the beta cells start to secrete insulin once again, thus decreasing the need for exogenous insulin up to one year. Diabetes is inevitable however and exogenous insulin will be increased until the disease reaches full progression in about 8 to 10 years. It is thought that IDDM ensues when 80% of the beta cells are destroyed.

Other symptoms:

Dehydration
Increased pulse rate
Ketone breath
Extreme fatigue
Irritability
Dry, flushed skin
Labored breathing
Vomiting
Stomach pains
Loss of menstrual cycle
Blurred vision
Diabetic ketoacidotic (DKA) coma

Interpretation of Laboratory Tests

The following methods are frequently used to help reach a diagnosis for IDDM. The preferred method for diagnosis is a fasting plasma glucose test however a casual plasma glucose test and an oral glucose load test can be used as well.

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LABORATORY TESTS		
Test Name	Normal values	Indicators
Fasting Plasma Glucose (FPG)	< 110 mg/dL or < 6.1 mmol/L	FPG $\geq$ 126 mg/dL or $\geq$ 7.0 mmol/L indicates diagnosis
Casual (non-fasting) Plasma Glucose (CPG)		CPG $\geq$ 200 mg/dL or $\geq$ 11.1 mmol/L plus symptoms is indicative of diabetes

Oral Glucose Tolerance Test (OGTT) with 75 grams of glucose	Plasma glucose 2 hours post glucose load (2hPG): 2hPG < 140 mg/dL or < 7.8 mmol/L	2hPG $\geq$ 200 mg/dL or $\geq$ 11.1 mmol/L can be used in diagnosis Between 140-200 mg/dL 2hPG is impaired glucose tolerance. This group is at increased risk for developing diabetes.
OTHER BLOOD TESTS		
Test Name	Normal values	Indicators
Glycosylated Hemoglobin (HbA1c)	2.2 to 4.8% of total <u>Hb</u> . Less than 4.5% is optimal.	HbA1c measures average plasma glucose levels within the past 6 to 8 weeks. Increased with poorly controlled diabetes mellitus (>12% = poor control).
Insulin Test	5-20 mcU/ml	Decrease or undetectable in blood levels.
Insulin C-peptide Test	0.5 to 3.0 ng/ml	Decrease or undetectable in blood levels.
OTHER		
Urinalysis (Glucose and Ketones)	Glucose: Random specimen is negative or 24-hour urine collection is < 0.3 g/day Ketones: Negative	Glucose: Random sample is positive or abnormally high levels Ketones: Positive

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In order to confirm diagnosis, a second test should be completed on a different day. If CPG is greater than or equal to 200 mg/dL, then either a FPG or OGTT should be used as the confirming test. A glucose tolerance test should not be conducted if it is fairly apparent that the patient has diabetes, as this will further aggravate hyperglycemia. Glycosylated hemoglobin is not recommended for diagnosis. It should also be noted that nuclear imaging, optical absorption and fluorescence spectroscopy and imaging techniques may soon be established for assessing beta cell mass, number, function, and inflammation.

Common Current Treatments

Individuals with IDDM require insulin therapy for the remainder of their lifetime. The major goal in treatment is to minimize hyperglycemia, which can lead to diabetic complications such as: angiopathy, neuropathy, nephropathy, and retinopathy. Insulin is also required to prevent ketoacidosis, a potentially dangerous situation if not handled quickly.

Medications

The following table lists some examples of insulin's prescribed for patients with IDDM. Insulin is absolutely essential for survival and must be tailored to each individual. It is important that glucose levels be monitored regularly so that proper treatment with differing forms of insulin can be provided. The order of insulin's listed in the table is not intended to represent subsequent treatments; each patient will require an individualized plan. A typical regimen contains at least one background (long-acting) and short-acting insulin, to cover meal times. Motivated patients may benefit from intensive diabetes management (3 or more injections per day or an insulin pump) which allows for added flexibility with when and what foods are consumed.

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INSULINS		
Indication	Class/Examples	Notes
Treatment of hyperglycemia and overall glucose control	Short-acting (clear): • Regular (Humulin®) • Lispro (Humalog®)	Humalog® must be followed by food consumption immediately, otherwise hypoglycemia may arise possibly leading to a seizure.
Treatment of hyperglycemia and overall glucose control	Long-Acting (cloudy): • NPH (N) • Lente (L) • Ultralente (U) Premixed (short and long-acting together): • 70/30 • 50/50	
Treatment of hyperglycemia and overall glucose control	Insulin infusion pump	
OTHER		
Indication	Class/Examples	Notes
Treatment of hypoglycemia	Glucagon Emergency Kit for Low Blood Sugar (Intravenous injection)	Glucagon "pen" should be carried at all times.

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Dietary Interventions

The nutritional goals in the treatment of IDDM are to maintain plasma glucose levels within normal range (ideal fasting glucose: ≤ 130 mg/dl and ideal postprandial glucose: ≤ 180 mg/dl) by consistent day-to-day meal times and amounts, exercise, and insulin

injections. Constant monitoring of blood glucose following diagnosis is important for patients to learn the effects that certain foods have on raising glucose levels and to understand overall metabolic control in order to develop an appropriate insulin regimen. Each time glucose is tested it should be logged in a notebook and given to the healthcare team.

Weight management must be enforced, with caloric intake based on normal growth and development (in children), activity level, and maintenance of a desirable weight. Despite the controversy over a “diabetic diet”, no such diet exists. Diabetics do have a several fold increased risk for chronic diseases therefore optimal nutrition is very important. About 50%-60% of total calories should consist of carbohydrates, with 45%-50% being complex and no more than 5% as simple sugars. The diet should be rich in fibers such as plant gums, pectins, structural fiber, and enzyme inhibitors (legumes), which delay gastric emptying and absorption of glucose although the effect is negligible. About 40 g/day or 12 g/1000 kilocalories of fiber each day can have a positive impact on blood lipids, as well as in the prevention of colon cancer. Protein requirements are the same as the RDA’s established for 97% to 98% of healthy individuals in a group (0.8 g/kg for adults), but this may increase if another illness or poorly controlled diabetes is present. At that point, albumin levels should be used to determine adequate protein intake in adults and children. Restricted protein intake should only be encouraged if an underlying nephritic disorder is present to prevent damage to the kidneys. Adequate protein intake is necessary to prevent negative nitrogen balance, which can lead to muscle atrophy, loss of lean tissue, and a drop in bodyweight.

Cardiovascular complications are common in diabetics therefore it is important to achieve optimal lipid levels. Fat intake should be no more than 30% of total kilocalories with a ratio of polyunsaturated:saturated:monounsaturated at 10%:7%:13%, respectively. Cholesterol intake should be limited to less than or equal to 300 mg per day. Although it has been shown to be “heart-healthy” in epidemiological studies, alcohol intake should be limited because of its hypoglycemic effects. If alcohol is consumed then food should be eaten throughout the drinking period.

A common phenomenon in type 1 diabetics is hyperglycemia within waking hours known as the somogyi effect (rebound effect). This usually results when too much insulin is given at bedtime, thus causing insulin to peak at about 3 a.m. and then stimulating glucose release from the liver. This problem can be avoided by decreasing the insulin dose at night, or by providing an evening snack before bedtime. Another common problem is dawn phenomenon which also results in hyperglycemia in the morning. This can be avoided by moving the longer acting insulin from supper time to the evening snack.

Each individual should understand the common protocol for sick days. Insulin must be taken whether food is being consumed or not. Ingestion of liquid carbohydrate beverages such as soups and sports drinks should be stressed to avoid electrolyte imbalances. At least 50 g of carbohydrates should be eaten every 3 to 4 hours and urinary ketone levels should be monitored throughout the day.

Overall, the end goal is to make life as normal as possible, especially in children, to ensure compliance with eating, exercise, and insulin injections and to prevent long-term complications.

Orders

Enteral jejunal feedings if possible or TPN with ketoacidosis

Ketoacidosis is treated with large doses of insulin and intravenous injection until it can be controlled. When foods can be taken by mouth, it should first start with a liquid diet, then gradually increased to soft foods, and finally regular foods.

What to Tell the Patient and Family

Family and friends must be instructed, along with the patient, on how to inject insulin (and glucagon) and how to handle a problem should one arise. Regularly scheduled meal times and consistency in food amounts help to prevent large swings in glucose levels, thus it is important that this form of eating be developed. It is also important to instruct the whole family on all aspects of the diet. This applies to spouses or partners of patients.

References:

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