

Diabetes Mellitus

A group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both

Classification of DM and other categories of glucose regulation:

- Type I
- Type II
- Other Specific Types
- Gestational

The terms insulin-dependent diabetes and non-insulin diabetes mellitus and their acronyms, IDDM, NIDDM are eliminated because some people are in a category for awhile and then switch. The terms type 1 and type 2 diabetes are retained with Arabic numerals being used rather than roman numerals

Type 1:

- Type 1 encompasses the vast majority of cases that are primarily due to pancreatic islet beta-cell destruction and that are prone to ketoacidosis
- 10% of population
- Formerly known as insulin dependent aka Juvenile onset
- Have none or little insulin secretory capacity due to lack of beta cells (lost not congenital)
- Autoimmune disease- immune system (lymphocytes) destroys beta-cells in pancreas
 - Recent coxsackie-beta virus infection in 75% with Type 1 Diabetes
 - We all have exposure but only a fraction of us have autoimmune reaction
 - Genetic component- almost all Type 1 have some gene reaction
 - Binding site of Cox virus is what antigen bind to- happens to have similar sequence of amino acids as beta-cells so destroys beta-cells
 - These people have increased IgM
- While most type 1 diabetes is characterized by the presence of islet cell, GAD, IA-2, IA-2 β , or insulin autoantibodies that identify the autoimmune process that leads to β -cell destruction, in some subjects, no evidence of autoimmunity is present; these cases are classified as type 1 idiopathic

Type 2:

- Type 2 diabetes includes the most prevalent form of diabetes, which results from insulin resistance with an insulin secretory defect
- 90% of population
 - Half of them have normal-elevated insulin but it doesn't work
 - Due mainly to obesity
- Insulin attaches to receptor on cell-activates glucose transporters to bring glucose into the cell --> hyperglycemia (builds up in blood) so you burn fat --> ketone bodies --> ketoacidosis
- When people get fat their (fat) cells expand so there is decreased density of receptors (number of receptors stays the same) and they become hypoglycemic
 - Not only does receptor density decrease but number of receptors actually decreases too
 - Person who is prone to Diabetes has the minimum number of receptors for a normal size cell- so get Diabetes when gain weight
 - Exercise helps lose weight- but also increase number of receptors (even if not lose weight)
- Quality receptor and post receptor defects- receptor doesn't work as well
 - Insulin binds but receptor doesn't fire off to signal glucose transport molecules to move to edge of cell
 - "Insulin resistance"

Other:

- Why patient has hyperglycemia? Not making insulin - many are transient
 - Genetic defects of beta-cell function
 - Disease of pancreas
 - Drug/chemical induced
 - Uncommon Immune forms
 - Other Genetic syndromes
 - Genetic defects in insulin action
 - Endocrinopathies
 - Infections

Gestational:

- Newest recognized
- Defined as any degree of glucose intolerance with onset or first recognition during pregnancy
 - Hyperglycemia while pregnant- any glucose imbalance
 - Within normal function of pancreas some are functioning very well while some function at minimal capacity- but under stress the borderline function might cross over to borderline not fx
 - After baby born- go back to normal
- Complicates about 4% of all pregnancies in the US, resulting in ~ 135,000 cases annually
- The prevalence may range from 1-14% of pregnancies, depending on the population studied
- Maternal complications related to GDM also include an increased rate of Cesarean delivery and chronic hypertension
- Although many patients with GDM will not develop diabetes later in life, others will be diagnosed many years post partum as having type 1 diabetes, type 2 diabetes, IFG or IGT

Impaired Glucose Tolerance:

The stage termed impaired glucose tolerance (IGT) has been retained

Malnutrition related diabetes mellitus:

- The class termed malnutrition related DM has been eliminated. While it appears that malnutrition may influence the expression of other types of diabetes, the evidence that diabetes can be directly caused by protein deficiency is not convincing

4/15/09

Oral glucose tolerance test is not good

- After eat glucose fasting glucose will go up
- After about 2 hours it will come back down
- Plot glucose concentration vs time
- Person with diabetes don't handle glucose well - so abnormal curve is expected
 - Their fasting glucose begins higher than non-diabetic
 - Give them glucose and their level will go way up and stay way up
 - Eventually it will come down to where it was - abnormal curve
 - ◻ Points assigned for various aspects of curve to determine if its abnormal
 - A non-diabetic after 2 hours will have glucose at 110% of normal (basically back to normal) however 30% will be abnormal despite not being diabetic (false positive)
 - ◻ Homeostatic mechanism not quite up to task
 - ◻ Is it a fair challenge to your pancreas to dump 100g of glucose on it (this is like asking a person who hasn't trained to run a marathon)
 - These people will likely be false positive:
 - ◻ Pregnant
 - ◻ Non-ambulatory
 - ◻ Over age 65
 - ◻ Inflammatory disease

★ *To make it fair the individual must have a min 3 days of a min of 2000 calorie diet and 200g of total carbs, must be ambulatory, under 65, not pregnant
This will make the test fair to the body and then if person meets these qualifications it is a much better test for diabetes.*

Diagnostic Criteria for Diabetes Mellitus

(National Diabetes Data Group, March 1998)

★ *Each test must be confirmed by repeat testing*

- Three ways to diagnose diabetes are possible

1. Symptoms with casual plasma glucose >200 mg/dl
 - Casual = Independent of eating
 - Casual is defined as any time of day without regard to time since last meal
2. FPG > 126 mg/dl *****Gold standard*****
 - i. Fasting is defined as no caloric intake for at least 8 hr
3. An OGTT with the 2-hr post load value >200 mg/dl
 - i. OGTT - oral glucose tolerance test

★ *Know 126!*

★ *Most non-diabetics can't eat their blood sugar above 200, but diabetics easily can*

★ *If someone comes in with a fasting glucose level of 300 there is no point to do an OGTT because they obviously have diabetes*

★ Grey Areas

- FPG <110 mg/dl = normal fasting glucose
- FPG >110 and <126 mg/dl = IFG (impaired fasting glucose)
 - (sometimes called pre-diabetes, however no evidence that they will get diabetes)
- FPG >126 mg/dl = provisional diagnosis of diabetes (the diagnosis must be confirmed)
- 2-h post load glucose (2-h PG) <140 = normal glucose tolerance
- 2-h PG >140 and <200 mg/dl = IGT
- 2-h PG >200 mg/dl = provisional diagnosis of diabetes (the diagnosis must be confirmed)

Each test must be confirmed by repeat testing

- Symptoms and casual glucose >200 mg/dl
- Or FBG > 126 mg/dl
- Or (OGTT) >200 mg/dl

HbA1c measurement is not currently recommended for diagnosis of diabetes

- Glycosolated hemoglobin
 - Species of hemoglobin that has glucose on it
 - 3-4% of available binding sites are occupied in normal person (3-4% glycosolated)
 - Determined by glucose environment that molecule finds itself in
 - Diabetic has higher glucose environment which jacks up glycosolation (10-12%)
 - Takes 120 days because that is the life of a RBC
- Used to monitor glucose control - Gold Standard to measure treatment effect
- Not diagnostic

Hypoglycemia would be the opposite of diabetes

★ hypoglycemia is pathophysiologic state

★ Hypoglycemia is a disease

How do you know someone has low glucose? They are symptomatic.

There are other causes of Hypoglycemia that don't relate to low glucose.

Give people saline but tell them its glucose and they will react as if you gave them glucose

Hypoglycemia is glucose under 50

Must fulfill Whipples triad to dx hypoglycemia:

- To correctly ID hypoglycemia you must have pt who is symptomatic
- When symptoms are present glucose must be 50 or less
- At this time if you give them carbs it corrects sx and normalizes glucose

Dx is not determining the cause - once you dx you must determine why/how their glucose gets so low (some of the reasons aren't that great) - don't stop at the dx

The Disease

- Several pathogenic processes are involved in the development of diabetes.
- These range from autoimmune destruction of the β -cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action
- The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues
- Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action
- Impairment of insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycemia
- Symptoms of marked hyperglycemia
 - Polyuria
 - Polydipsia
 - Weight loss
 - Polyphagia
 - Blurred vision

• Complications

- Acute Metabolic

- Hypoglycemia- the most frequent
 - 10-25% of patients
 - More common in Type I
- Ketoacidosis- most often in recognized diabetics
 - Hyperglycemia, acidosis, osmotic diuresis
 - Abdominal pain, anorexia, nausea
- Nonketotic Hyperosmolar Syndrome
 - >320 mOsm/l, >600 mg/dl, dehydration
 - Caused by lack of fluid intake

★ 285-290 mOsm = normal plasma osmolality

★ The most common chronic disabling complication of diabetes

★ Most common cause of disease is some manifestation/complication of heart disease

★ Diabetes is the most common cause of Non-traumatic amputation

- Chronic- *problems of vessels and nerves*

▪ Retinopathy

- Diabetes is the leading cause of blindness in persons aged 30 to 65 years.
- Blindness occurs 20 times more frequently in diabetic patients than others
- is most often seen after the disease has been manifest for at least 15 years. Approximately 10 to 15% of type I diabetic patients become legally blind whereas in type II diabetic patients the risk is less than half that value.
- The primary cause of visual loss is retinopathy.
- Regardless of the type of diabetes, the severity of retinopathy increases with increasing duration of the disease
- The earliest retinopathic changes are classified as nonproliferative, These lesions generally do not affect

- visual acuity
 - Proliferative retinopathy is characterized by the growth of fine tufts of new blood vessels and fibrous tissue from the inner retinal surface or optic nerve head
 - Prevalence rates of both nonproliferative and proliferative retinopathy are higher in type I than in type II diabetes
- Nephropathy
 - End-stage renal disease (ESRD) from diabetic nephropathy is a major cause of death, particularly in type I diabetes, in which it affects 30 to 35% of patients
 - Diabetes is the leading cause and accounts for one third of the ESRD cases in the United States.
 - In patients destined to develop ESRD, gross proteinuria (greater than 0.3 gram of albumin per day) begins approximately 15 years after the diagnosis of diabetes.
- Neuropathy- **the most common chronic disabling complication of diabetes**
 - Symptomatic, potentially disabling neuropathy affects nearly 50% of diabetic patients
 - It may be symmetrical or focal and often involves the autonomic nervous system as well.
 - The prevalence of symmetrical neuropathy is similar
 - in type I and II diabetes, whereas focal neuropathy is more common in older type II patients
 - *Distal Sensorimotor Neuropathy*
 - ◆ This syndrome, characterized by axonal loss, is the most common presentation of diabetic neuropathy.
 - ◆ The process involves all somatic nerves but has a distinct predilection for distal sites, i.e., the distal sensorimotor nerves of the feet and hands.
 - ◆ Patients complain of numbness and tingling in the extremities, especially the feet
 - Diabetic Foot
 - ◆ The syndrome is characterized by plantar ulcers that heal slowly and follow apparently insignificant trauma.
 - ◆ In severe cases gangrene may be a complication and amputation the outcome.
 - ◆ Diabetes accounts for about one half of non-traumatic limb amputations
- Atherosclerosis- **Most common cause of disease is some manifestation/complication of heart disease**
 - Atherosclerosis involving the arteries of the heart, lower extremities, and brain is the major cause of death from diabetes.
 - The atherosclerotic process is indistinguishable from that affecting the nondiabetic population but begins earlier and is more severe.
 - The predilection to atherosclerosis is uniformly observed over the entire spectrum of diabetes--from difficult-to-control insulin-dependent patients to patients with mild hyperglycemia not requiring insulin.
 - The risk of myocardial infarction is two- to three-fold greater in diabetes
- Hypertension
- Treatment Goals
 - Short Term
 - Restore metabolic control to as close to normal as possible
 - Improve sense of well-being
 - Long Term
 - Minimize risk of diabetic complications
 - Accelerated atherosclerosis
 - Microangiopathy (retinopathy, nephropathy)
 - Neuropathy
- Lifestyle
 - Diet
 - Weight reduction (when appropriate)
 - Carbohydrates: 45-60% (depending on severity of diabetes and triglyceride)
 - Restriction of saturated fat (to < 10% of calories)
 - Increased monounsaturated fat (depending on the need to limit carbohydrate)
 - Decreased cholesterol intake to < 300 mg per day
 - Sodium restriction in patients prone to hypertension
 - Exercise
 - Type: Aerobic strongly preferred. Avoid heavy lifting, straining, and Valsalva maneuvers that raise blood pressure.
 - Intensity: Increase pulse rate to at least 120-140, depending on the age and cardiovascular state of the patient.
 - Frequency: 3-4 days per week
 - Duration: 20-30 minutes preceded and followed by stretching and flexibility exercises for 5-10 minutes.