Etiology

Type 1 diabetes is primarily determined by genes in the HLA region of chromosome 6; HLA-DQ locus best single marker of susceptibility, particularly among Caucasians; DQA1 alleles coding for arginine at position 52 (Arg-52) associated with risk with only DQA1*0301 being shown to have significant independent effect on type 1 diabetes risk; DQA1*0501 associated with the disease in some populations; DNA sequences coding for an amino acid other than aspartic acid in position 57 (non-Asp-57) associated with type 1 diabetes in all ethnic groups, except Japanese; DQB1*0302 and DQB1*0201, which are in linkage disequilibrium with DR4 and DR3, respectively; the DQA1*0501-DQB1*0201 and DQA1*0301-DQB1*0302 haplotypes show highest type 1 diabetes risk and in combination, their effect is even stronger than that observed for individuals homozygous for DQA1*0501-DQB1*0201 or DQA1*0301-DQB1*0302 (heterodimers formed from gene products in trans (i.e., DQA1*0501 and DQB1*0302) may be diabetogenic); high risk DQ haplotypes include DQA1*0301-DQB1*0201 in African Americans, DQA1*0301-DQB1*0303 in Japanese, DQA1*0301-DQB1*0401 in Chinese; childhood chronic disorders, such as cystic fibrosis, juvenile arthritis, etc…increase risk; onset of type 1 diabetes can occur at any age, but it is usually diagnosed during childhood and adolescence, with a peak incidence around the time of puberty (10-12 years in girls and 12-14 years in boys); mostly people </ 30 years of age; lower rates reported for the late spring and summer, and higher in winter for populations in both the Northern and Southern hemispheres; highest incidence rates in the world have been reported for Finland and Sardinia, Italy, lowest incidence rates observed in the Asian countries including Japan, China and Korea, Native American, Cuban, Chilean and Mexican populations have extremely low rates; African Americans and Hispanics generally have lower incidence rates than Caucasians living in the same community; Viruses may attack and destroy the beta cells of the pancreas and directly cause diabetes, with or without autoimmunity (Coxsackie virus B (CVB), mumps, congenital rubella who carry high risk HLA alleles, cytomegalovirus, measles, influenza, encephalitis, polio or Epstein-Barr virus); exposure to enteroviruses in utero increases risk; early exposure to cow's milk triggers an immune response that may lead to beta cell autoimmunity because of molecular mimicry; autoimmune response to viral infection, toxic chemical agents, and other diseases may trigger response in genetically susceptible persons; autoantibody production leading to beta cell destruction (ICA's, IAA's, GAD's); family history (siblings with it and parents (particularly father's); injury to the pancreas from toxins, trauma, or after the surgical removal of the majority (or all) of the pancreas (rare).

Diagnosis of Type 1 Diabetes

Fasting Blood Glucose > than 126 mg/dL on two separate occasions; if blood sugar is >160 mg/dL two hours postprandial; in presence of symptoms, a confirmed nonfasting plasma glucose (casual) value or >/ 200 mg/dL indicates diabetes; GTT in adult: if at 2 hours blood sugar is 205 mg/dL and greater than 205 mg/dL at either 60 or 90 minutes; GTT in child: if >200 mg/dL at 60 or 120 minutes and if >170 mg/dL at 60 minutes, OR if >140 mg/dL at 2 hours OR if >125 mg/dL at 180 minutes; HbA1c levels >12% shows poor blood glucose control (can help with diagnosis); increased microalbumin can diagnose diabetic nephropathy; recent weightloss; polyuria, polydipsia, polyphagia, extreme fatigue, and irritability can all help in diagnosing; low or undetectable level of

the protein C-peptide, a by-product of insulin production; urinalysis showing ketone bodies or glucose; insulin test showing little or no insulin.

Physiological effects

Frequent urination; unusual thirst; extreme hunger; unusual weight loss; extreme fatigue; irritability; hyperglycemia; hypoglycemia; glucosuria; ketonemia; ketonuria; ketosis; excessive ketone bodies can lead to hyperpnea, dyspnea, and Kussmail Respiration; cold and clammy body, sweating, and weakness seen with hypoglycemia; ketoacidotic coma; lipoatrophy; somogyi effect; dawn phenomenon; chronic complications: angiopathy, neuropathy, nephropathy, retinopathy; uncontrolled diabetes can lead to negative nitrogen balance, weight loss, and decreased blood albumin levels; elevated microalbumin; increased glucagon, cortisol, growth hormone, adrenaline; ketone breath (ketosis); lack of insulin can lead to decrease in VLDL causing TG to remain in liver causing fatty liver, elevated blood TG, and increase in NEFA's; compensated metabolic acidosis; decompensated metabolic acidosis; low blood pH; increased glycosylated Hb; seizures can occur with serious hypoglycemia; electrolyte imbalances; hypertension; dehydration; low or no C-peptide present; elevated TG and total cholesterol;

Nutritional Implications in Disease State

Hyperglycemia; hypoglycemia; increased glycosylated Hb (means poor blood glucose maintenance over time); exogenous insulin needed (provides challenge with adherence, especially with kids); weight loss; seizures from hypoglycemia (prevent this); hypoglycemia as a result of taking insulin and not eating, too much insulin, illness, weight loss w/out insulin adjustment, exercise-induced; glucosuria leading to polyuria, polydipsia, and polyphagia; not eating on a consistent schedule; excessive calorie intake, along with insulin to cover can lead to weight gain by promoting TG storage, fatty acid synthesis, decreased lipolysis; DKA; negative nitrogen balance, decreased blood albumin levels in uncontrolled DM; chronic conditions that can further exacerbate nutritional implications include: angiopathy, neuropathy, nephropathy, retinopathy; lack of exercise (particularly with today's youth and adults); brittle diabetes; electrolyte imbalances; somogyi effect; dawn phenomenon; HTN; dehydration; fatigue; fever, stress, illness can all cause hyperglycemia; in children, taking control of their diet is a major step which can lead to refusal and denial; monitoring glucose levels frequently can become tiresome and embarrassing, especially for adolescents; HHNK (rare); increased TG and total cholesterol; aspiration pneumonia (ketosis);

Lab Alterations Seen in Disease State

Lab test: Urine glucose
NL Value: random specimen: negative **OR** 24-hour urine collection: < 0.5g/day
Alteration: Increase
Cause of Alteration: Lack of insulin leads to elevated blood glucose levels, causing it to spill into urine.

Lab test: Urine ketones
NL Value: Negative
Alteration: Increase or presence
Cause of Alteration: As with glucose, ketones "spill over" into the urine when the blood levels are above a certain threshold. Fatty acid release from adipose tissue is stimulated by a number of hormones including glucagon, epinephrine, and growth hormone, leading to ketone production. The levels of these hormones are increased in uncontrolled diabetes mellitus.

Lab test: Insulin test
NL Value: 5-20 mcU/ml
Alteration: Decrease or undetectable
Cause of Alteration: People with Type 1 diabetes do not produce their own insulin or produce extremely little d/t destroyed beta cells. Therefore, testing for insulin will show little or undetectable amounts.

Lab test: Insulin C-peptide
NL Value: 0.5 to 3.0 ng/ml
Alteration: Decrease
Cause of Alteration: Low values (or no Insulin C-peptide) indicates that the person's pancreas is producing little or no insulin.

Lab test: Glycosylated Hemoglobin
NL Value: 2.2 to 4.8% of total Hb
Alteration: Increase
Cause of Alteration: Uncontrolled DM. High blood glucose concentrations causes increased amounts of glucose to attach to Hb. Everyone has some glycosylated Hb, yet people with diabetes, especially uncontrolled, will show elevated levels d/t glucose being present in blood longer and in greater concentrations, giving more time and capacity for binding.

Medications Commonly Used in Disease State

Medication: Glucagon Emergency Kit for Low Blood Sugar
Action: Causes liver to release glucose into the bloodstream when hypoglycemia becomes severe.
Nutritional Concerns: HTN; diarrhea; N/V; loss of appetite.

Medication: Insulin (Humulin, Lente, NPH, Novolin, Regular, Humalog-all differ by onset, peak, and duration)
Action: Lower blood glucose
Nutritional Concerns: Weight gain; limit alcohol (increases hypoglycemia); exercise, illness, pregnancy, heavy smoking, or large weight gain increase insulin needs; hypoglycemia; transient edema; lowered blood glucose, K+, Mg++, and P; increased T4.

There are no other medical treatments that are commonly used for Type 1 diabetes. Therefore, the next 3 are for Type 2 diabetes.

Medication: Acarbose (Precose)
Action: Competitive inhibitor of alpha-glucosidases of intestinal brush-border required for the breakdown of starches, dextrins, maltose, and sucrose to absorbable monosaccharides. This delays CHO absorption and lowers postprandial glycemia.
Nutritional Concerns: Decreases Fe absorption; abdominal pain; diarrhea; gas; borborygmus; limit alcohol; lowers fasting and postpranadial glucose; slightly lowers HCT; increases SGOT and SGPT.

Medication: Glipizide (Glucotrol)
Action: 2nd generation sulfonylurea. Work by stimulating beta cells to produce more insulin.
Nutritional Concerns: High doses of nicotinic acid can increase blood glucose; increases or decreases appetite; weight gain; dyspepsia; nausea, diarrhea; constipation; limit alcohol; hypoalbuminemia may increase drug effects; increased risk of hypoglycemia in malnourished pt; decreased blood glucose and Na+; increased SGOT, LDH, alk phos, BUN, and creatinine.

Medication: Repaglinide (Prandin)
Action: Meglitinide. Stimulates insulin secretion in the presence of glucose
Nutritional Concerns: Weight gain; tooth disorder; N/V; diarrhea; constipation; limit alcohol; malnutrition increases risk of hypoglycemia; hypoglycemia; URI; increases blood insulin; decreased fasting glucose, postprandial glucose.

Back to Type 1 Diabetes

<u>Medical Treatment of the Disease</u>
Glucagon in cases of seizures d/t hypoglycemia; insulin therapies; not classified as medical, but in cases of hypoglycemia-15g of simple CHO's (honey, lifesavers, orange juice, glucose tabs) can help to alleviate the low from going further.

<u>Surgical Treatment of the Disease</u>
Whole pancreas transplants; kidney transplants for those who have renal failure; double transplants of pancreases and kidneys are also proving to have a good long-term success rate for selected type 1 patents; beta cell islets wrapped in algin have shown minimal success (those from animals showing the most).

Nutritional Treatment of the Disease

Major goal is to maintain good blood glucose control allowing us to prevent the 4 major complications of: angiopathy (leading to CHD), neuropathy (leading to removal of part of body, esp. large toe), nephropathy (leading to renal disease), or retinopathy (leading cause of blindness in US)

Weight management is key: use ht/wt measure in kids; adults should maintain lean/ideal BW.

Kcals: Based on NL growth and development (child), activity level, and maintenance of desirable wt.-BEE x 1.2-1.5 (depends on activity level)

50%-60% of total kcals should consist of CHO's. 45%-50% should be complex CHO's, with no more than 5% as simple CHO's. Glycemic index is important and its effect varies in individuals (most diabetics know what causes major swings in their blood glucose). Plant gums, pectins, structural fiber, and enzyme inhibitors (legumes) help to lower glycemic index.

40 g/day or 12 g/1000 kcals of fiber appropriate to help maintain blood glucose levels, insulin, and lipids (esp. soluble fiber). Although fiber has minimal effect on blood glucose, it is great in general for colon cancer prevention and may lower chol. Levels.

Sugar substitutes such as aspartame, acesulfame-K, saccharin can all be used freely. Other substitutes include sugar alcohol's (sorbitol, xylitol) which do not get absorbed as readily. To calculate CHO from sorbitol (if amt. of CHO from sorbitol or other sugar alc. Is 6 g or more, divide the # by 2 for actual amount of CHO's. Otherwise, it is considered a FREE on exchange. Watch it-sorbitol and fructose (also used) can cause diarrhea and cramps.

Protein: 0.8 g/kg for adults; 1.7 g/kg for children. Will be higher in adults and children if other diseases, illness, etc… then base on albumin levels. Negative N balance may occur and muscle atrophy-prevent this.

</ 30% of fat with ratio of P:S:M (10%:7%:13%). </ 300 mg cholesterol/day. These pt.s are at increased risk of heart disease.

</ 3 g Na+/day should be given

Alcohol should be avoided as well b/c can cause hypoglycemia. If drinking, food must be eaten to offset the lows that often occur.

Marijuana smoking can induce "munchies" leading to weight gain in diabetics and poorly controlled glucose.

IMPORTANT: Meals must follow a schedule and be consumed at about the same times each day and be of the same composition to avoid huge swings in blood glucose levels.

Exchange system or CHO counting extremely important.

Exercise can increase sensitivity to insulin making it more effective-know this.

Sick days: Insulin must be taken no matter if eating or not (hyperglycemia present from increase in stress hormones lead to glycogenolysis, gluconeogenesis). Push liquid CHO beverages such as soups, PowerAde and watch for electrolyte imbalances. Treating imbalances can be done by giving black tea, sports drinks, etc… At least 50 g CHO should be eaten 3-4 hours. Check for ketones throughout the day.

Treat lows with quick absorbed CHO's such as honey, lifesavers, orange juice. Teach kids and adults the importance of diet composition. Protein and fat slow glucose release and can cause hypo's in short term and hyperglycemia in long term.

Insulin pumps are now being used more frequently. Important to reinforce bolusing before or after meals (if forget).
Those who take Humalog must not inject it unless food is ready for them. Can lead to a severe low if done too soon. This poses problems especially if eating out and food not ready yet. Diabetics must know when to inject and understand the importance.
If they go out to a party, etc… they should go with someone who knows they have diabetes in case of emergencies. Also, if going to another country, should know the word for "sugar" in the native language.
Should wear wrist bracelet saying have diabetes.
Frequent testing of glucose levels very important, especially if on pumps and checking for ketones using strips also important (if glucose levels are over 250 mg/dL).
Important to know feelings of hypoglycemia. Many times they do not know they are.
Should carry a Glucagon emergency kit. Friends should know how to use it.
Lipoatrophy common problem-switch injection sites frequently.
Making life "as NL as possible", especially in kids, important for adherence and acceptance of the disease.
Injecting insulin in same site can lead to hypertrophy and when exercising, injection should not be in muscle they are using. Insulin will be used more quickly in this case and can lead to a low.
If somogyi effect occurs, can prevent this by lowering insulin at dinner or evening snack, or by increasing evening snack. Evening snack should limit fat content-can lead to high blood sugar in morning. If snack is not adequate, eating some fat and CHO's in middle of night can help regulate blood glucose through night.
If dawn phenomenon-move longer acting insulin from supper to evening snack to prevent this.
Goal: Should say "person w/ diabetes"; better to use "adherence" (gives them more control); they are patients in hospital, not "persons w/diabetes"; if cheating, should say "having difficulty with" or "having a problem with".
EVERYONE RESPONDS DIFFERENTLY TO TREATMENT-THEY ARE AN INDIVIDUAL AND SHOULD NOT BE TREATED AS A DISEASE!!!!