Diabetes

- Hormones of the Pancreas
  - Alpha Cells – glucagon
    - Secreted in response to ↓ blood glucose, ↓ protein intake, exercise, low CHO diet
  - Delta Cells – somatostatin
    - Inhibits glucagons and insulin
  - Beta Cells – insulin
    - Secreted in response to ↑ blood glucose
    - Regulates CHO
    - Promotes ↓ blood glucose by
      - Glycogenesis
      - Transporting glucose into cells
      - Inhibiting glycogenolysis
  - Insulin
    - Binds to insulin receptors in
      - Skeletal muscle
      - Liver
      - Adipose tissue
    - This allows for a cascade of events to occur that allows glucose to move from the bloodstream into the cell.
    - Insulin promotes
      - Lipogenesis but inhibits release of fatty acids from adipose tissue
      - Protein synthesis
      - Promotes movement of K+ and Mg+ into cells
      - Stimulates triglyceride synthesis

- Regulation of blood glucose
  - Insulin - ↓ blood glucose
  - Counter-regulatory hormones
    - Glucagon - ↑ blood glucose
    - Epinephrine - ↑ blood glucose
    - Growth hormone – ↑ blood glucose
    - Glucocorticoids (cortisol) - ↑ blood glucose

Diabetes
- Definition
  - Affects body’s ability to control and utilize its supply of fuel (glucose)
  - Chronic disorder of CHO, fat and protein metabolism characterized by development of vascular lesions and neuropathy
- Classification of DM
  - 11 different types
  - Not based on treatment but degree and causes of hyperglycemia
  - Diagnostic Criteria
    - Fasting blood sugar = or > 126mg/dl OR
    - Random plasma glucose = or > 200mg/dl OR
    - Plasma glucose 2 hours after a glucose challenge is = or > 200mg/dl
• Symptoms of DM,
  o 3 Ps or unexplained weight loss
• Pathophysiology
  o Insulin deficiency
    ▪ Absolute – pancreas produces no insulin or very little insulin. (Type 1 DM)
    ▪ Relative – pancreas produces normal or excessive amounts of insulin but body
      is unable to use it effectively. This is called insulin resistance. (Type 2 DM)
  o This insulin deficiency (absolute or relative) results in the abnormal metabolism of
    body fuels.
  o DM is a disease that affects how the body uses all foods (CHO, proteins and fats) not
    just sugars.
• Consequence of Insulin Deficiency
  o Liver
    ▪ Hyperglycemia
    ▪ Hypertriglyceridemia
    ▪ Ketone production
  o Skeletal Muscle
    ▪ Failure of glucose uptake
    ▪ Failure of amino acid uptake
    ▪ Consequence of Insulin Deficiency
  o Adipose tissue
    ▪ Lipolysis
    ▪ Elevated free fatty acids in the circulation
  o Kidneys
    ▪ Renal threshold is 180mg/dl –
    ▪ Excessive glucose attracts water – osmotic diuresis occurs resulting in
      polyuria.
    ▪ Polyuria also causes electrolyte loss (NA+, K+, Cl+, Phosphorus)
    ▪ Loss of water stimulates thirst center causing polydipsia.
  • Cells are starved of fuel so pt. is excessively hungry and eats a lot more – polyphagia

• Type 1 patients lose weight rapidly since they cannot use glucose for metabolism, fats and
  muscle tissues are catabolized.
• Type 2 pts. Do not have major weight loss because they produce some insulin, therefore they
  do not catabolize fat and muscle tissue. Type 2 pts are mostly obese.

Type 1
• Usually early onset
• Destruction of beta cells
• Viruses thought to stimulate an autoimmune response
• Presence of islet cell antibodies
• Genetics
• Islet showing Ab to insulin
Type 2
• Causes
  o Insulin resistance
  o Beta cell exhaustion
  o Excessive hepatic glucose
- 90% diabetics
- Usually (not always) late onset

**Etiology**
- Family history
- Prior history of impaired glucose tolerance (IGT)
- Gestational DM (GDM) especially in obese individuals
- Glucotoxicity - hyperglycemia has an effect on pancreatic islets
- Insulin resistance – inability of insulin sensitive tissues to respond normally to insulin-stimulated glucose uptake

**Type 1 S/S**
- 3 Ps more typical in type 1
- Weakness, fatigue and weight loss
- Visual blurring
- Breakdown of fat and protein for food
- ketones \(\rightarrow\) ketoacidosis

**Type 2 S/S**
- Gradual onset of symptoms
- Weight gain
- Sufficient endogenous insulin to prevent ketone formation
- Fatigue, weakness, disturbed vision
- Complications
- Peripheral neuropathy
- Recurrent infection
- Lipedemias, Obesity, HTN and CV disease
- Coma

**Diagnostic Tests**
- Fasting blood sugar 126 mg/dL
- Impaired Glucose Tolerance Test (GTT) or post prandial >200mg/dL
- Two hour postprandial blood sugar of 140mg/dl – 200mg/dl
- Glycosylated hemoglobin HbA1c
- Reflects the average blood glucose level over last three months
- Glucose in the blood attaches to HGB. Once attached, it remains for the life span of the HGB cell.
- Urine Ketone Monitoring
  - Type I
    - When ill
    - HBGM > 300 mg/dl
  - Type II
    - When ill (may be present if acutely ill)
    - Urine Ketone Monitoring
    - Positive ketones require prompt medical attention
- Ankle – Brachial Indices
  - An assessment of PVD and risk for.
  - If possible, perform this test on your patient in the clinical setting.
  - Doppler BP at radial artery bilaterally
  - Doppler BP at the dorsalis pedis and posterior tibial bilaterally
• Calculate index for each pedal site
  • Ankle pressure divided by brachial artery pressure
  • An index > 1.2 indicates calcific disease

**Interventions**

- Control of hyperglycemia
  - Diet
  - Exercise

- Type I Treatment
  - Diet, Exercise and Medication
  - Dietary CHO and exercise must be coordinated with insulin action so that
  - Insulin as available for optimal metabolism when food is eaten and absorbed
  - Food is available when insulin is acting to prevent hypoglycemic reactions
  - Exercise must be planned for and adequate amounts of CHO must be available
  - Monitoring (short term control)

- Home Based Glucose Monitoring (HBGM)
  - 4 times a day – 12 times a day

**Type I Diabetics and Insulin**

- Three properties of insulin – source, strength and type or kinetics
  - Source
    - Humulin derived from recombinant DNA technology (E Coli)
    - Novolin derived from recombinant DNA technology of bakers’ yeast
  - Why must insulin be given parenterally?
  - Strength
    - U 100
    - U 500 (not usually available)
  - Type or kinetics
    - Quick (Rapid)
    - Intermediate
    - Long Acting
    - Combination

- Insulin secreted by Pancreas
  - Basal
  - Prandial

- Quick Acting Insulin
  - Turn to table on Pg 940 in Phipps
  - Name the three quick insulins.
  - How are these insulins alike?
  - Which of these three are the most similar?
  - How are they similar? How are they different?
  - Which is the slowest of the quick insulins?
  - What time could you expect hypoglycemia after giving regular insulin?

- Intermediate Acting Insulins
  - Name the two intermediate insulins.
  - How are they alike? How are they different?
  - What is the difference between cloudy and turbid?
  - Which of these have you seen more of in the clinical setting?
  - Why are between meal snacks often given to diabetic patients?

- Long Acting Insulin
Name the two long acting insulins.
How are they alike? How are they different?
How many doses are needed per day when taking this kind of insulin?

**Combination Insulin**
Name the four combination insulins.
What is the difference between Humulin 50/50 and Humalog Mix 50/50?
What is the difference between Humalog and Lispro? (Davis Drug Guide)

**Insulin (Onset/Peak/Duration)**
- **Rapid Acting - Clear**
  - e.g. Lispro (Humalog)
  - e.g. Aspart (Novolog)
    - 15-30 min/60-90min/3-6hrs
- **Short Acting**
  - e.g. Regular (Humulin) – Clear
    - 0.5-1hr/2-4hr/5-7hr
- **Intermediate – Cloudy**
  - e.g. Humulin N, NPH (Protamine)
  - e.g. Humulin L, Lente (Zinc)
    - 1-2hr/4-12hr/18-28
- **Long Acting**
  - e.g. Humulin U, Ultralente (Zinc) - CLOUDY
    - 4-6 hr/18-20/24-36
  - e.g. Lantus – CLEAR
    - 1HR/5/24
    - 24 hour basal insulin control

**Insulin requirements**
- Increased requirements:
  - Growth
  - Pregnancy
  - Food intake
  - Stress e.g. Surgery, infection, illness
  - Some medications
- Decreased requirements:
  - food intake
  - Exercise
  - Some medications

**Complications of Insulin Use**
- Hypoglycemia – see later
- Lipodystrophies
- Lipoatrophy
- Lipohypertrophy
- Hypersensitivity (rare with DNA insulins)

**Type 2 Treatment**
Diet, Exercise and Oral Medication
- Pharmacotherapy is directed at:
Decreasing insulin resistance
Increasing insulin sensitization
Interfering with digestion and absorption of dietary CHO
Augmenting insulin secretion and action
Providing exogenous insulin

- **Biguanides E.g. Metformin (Glucophage)**
  - Decreases Hepatic Glucose Production
  - Helps endogenous insulin work better
  - Does not stimulate insulin secretion so it cannot cause hypoglycemia (monotherapy)
  - Used in obese pts with Type II
  - Average decrease in FBS is 60mg/dl
  - Average decrease in HbA1c approx 1.5 - 2%
  - Effectiveness decreases over time with beta cell failure
  - Risk of lactic acidosis
  - Take with meals to decrease n/v and diarrhea
  - Questions
    - Can a breast feeding mother take metformin?
    - Which antihypertensive drugs interact with metformin?
    - A child of 9 years is ordered Metformin is ordered 1000mg BID. Is this a safe dose?
    - After three months of metformin therapy combined with a sulfonylurea the patient’s BS is still uncontrolled. What might the physician order now?
    - What is the site of action of Glucophage?

- **Thiazolidenediones (Glitizones)**
  - Action is to increase insulin sensitivity at the tissue/cellular level. Enhances insulin action without stimulating insulin secretion
  - Monotherapy or adjunctive therapy
  - Average decrease in HbA1c approx 0.7 -2.5%
  - May cause weight gain
  - Monitor liver function
  - Questions
    - Name two thiazolidenediones.
    - Which glitizone would a young women on oral contraceptives not want to take? Why?
    - Can this drug cause hypoglycemia when used as monotherapy?
    - Which glitizone can cause increase in total cholesterol, HDL and LDL?
    - Which is the less expensive drug?

- **Alpha Glucosidase Inhibitors**
  - When taken with the first bite of food, helps decrease/slow absorption of CHO
  - Affects postprandial blood glucose
  - Lowers HbA1c by 0.5-1.5%
  - Major GI side effect is flatulence
  - Questions
    - Name two glucosidase inhibitors.
    - Why does this class of drug need to be taken with food?
    - What kind of patients can have drug/drug interactions when taking Precose?
    - What happens to the BS?
    - What is the main site of action of the glucosidase inhibitors?
    - What is a usual starting dose regime?
What is a maximum dose regime?
What is the approximate one month cost of Glyset?

- **Sulfonylureas**
  - Stimulates insulin secretion by pancreas
  - First, second and third generation sulfonylureas
  - Average decrease in FBS is 60mg/dl
  - Average decrease in HbA1c is 1.5 – 2%
  - Risk for hypoglycemia
  - Weight gain
  - Questions
    - Name three sulfonylureas.
    - What is the main site of action of the sulfonylureas
    - Name two frequent side effects of this class of drug.
    - What is a common ending of two of these drugs?
    - If you had to take one of this category of drug when pregnant, which would you want to take?
    - Why should this class of drug be administered with a meal?

- **Meglitinides**
  - Reduces post prandial glucose by stimulating burst of insulin from pancreas
  - Average decrease in FBS is 60mg/dl
  - Average decrease in HbA1c is 1.5 – 2%
  - Risk for hypoglycemia – less than with sulfonylureas
  - Questions
    - Name two drugs in this class.
    - What is the main site of action of this class of drug?
    - Name a life threatening side effect of this class of drug.
    - What lab tests should be performed to monitor the effectiveness of Repaglinide?
  - If pt is eating breakfast at 0730, what time should this Starlix be administered?
  - What strengths are available in Starlix tablets?

- **Combining Drugs**
  - A patient may be prescribed two different antidiabetic drugs. The drugs then work in two ways to promote euglycemia.
  - Glucovance is a combination of what two categories of drug?
    - What two drugs are in Glucovance?
    - What are the three strengths of Glucovance?

- **Hypoglycemia**
  - Blood glucose level < or = to 60mg/dl
  - Signs and Symptoms of Hypoglycemia
    - Adrenergic symptoms
      - Pallor, diaphoresis, tachycardia, piloerection, palpitations, nervousness, irritability, sensation of coldness, weakness, trembling, hunger
    - Neuroglycopenic symptoms
      - Headache, mental confusion, circumoral paresthesia, fatigue, incoherent speech, diplopia, emotional lability, convulsions
    - Adrenergic symptoms generally precede neuroglycopenic symptoms
Signs and Symptoms of Hypoglycemia
- Patients on beta adrenergic blockers are at special risk for hypoglycemia. These meds block early signs of hypoglycemia because they are blocking the adrenergic part of the sympathetic nervous system.
- May occur during sleep
  - Nightmares, sweating, restless sleep, morning headache, feeling exhausted when awakening

Hypoglycemia
- What are it’s causes?

Treatment of Hypoglycemia
- Eat or drink – 15gms simple CHO in any form
- IV – 25 mL D50W or Glucagon 1mg, sq or IM or if pt can’t eat or drink
- If unsure if hypo or hyper giving sugar will produce rapid recovery
- Notify MD
- After s/s passed give protein to keep BS elevated longer
- Educate patient to carry sugar supply e.g. candy, raisins, sugar cubes
- Repeat FSBS q15 mins until above 80 mg/dL

Early Morning Hyperglycemia
- Somogyi Effect
  - Undetected hypoglycemia followed by hyperglycemia (pt wakes with ↑ sugar)
  - Due to too much insulin
- Dawn phenomenon
  - High sugars on waking
  - No hypoglycemia
  - May result from secretion of counterregulatory hormones (growth hormone) which leads to insulin resistance
  - Too little insulin

Patient Education
- Diet
- Glucose monitoring
- Activity
- Medications
- PHM and foot care
- Care during infection
- Patient Eye Checks
- Patient Foot Checks
- Benefits of Self Care for Diabetes

Glucose blood levels improve
- Fewer hospitalizations
- Fewer complications
- Education vital

ADA – Check your risk for diabetes
- ADA Diabetes risk FBS
- Diabetes PHD health risk assessment http://www.diabetes.org

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