Diabetes Mellitus
Diabetes Mellitus

• Chronic metabolic disease
• One of the most common diseases in North America
  – Affects 5% of USA population (12 million people)
• Results in
  – ↓ insulin secretion by the Beta (β) cells of the islets of Langerhans in the pancreas, AND/OR
  – Defects in insulin receptors on cell membranes leading to cellular resistance to insulin
• Leads to an ↑ risk for significant cardiovascular, renal and ophthalmic disease
Regulation of Glucose

• **Dietary Intake**
  – **Components of food:**
    • Carbohydrates
    • Fats
    • Proteins
    • Vitamins
    • Minerals
Regulation of Glucose

- The other 3 major food sources for glucose are:
  - carbohydrates
  - proteins
  - fats
- Most sugars in the human diet are complex and must be broken down into simple sugars: glucose, galactose and fructose - before use.
Regulation of Glucose

• **Carbohydrates**
  – Found in sugary, starchy foods
  – Ready source of near-instant energy
  – If not “burned” immediately by body, stored in liver and skeletal muscle as glycogen (short-term energy) or as fat (long-term energy needs)
  – After normal meal, approximately 60% of the glucose is stored in liver as glycogen
Regulation of Glucose

• **Fats**
  – Broken down into fatty acids and glycerol by enzymes
  – Excess fat stored in liver or in fat cells (under the skin)
Regulation of Glucose

• Pancreatic hormones are required to regulate blood glucose level
  – glucagon released by Alpha (α) cells
  – insulin released by Beta Cells (β)
  – somatostatin released by Delta Cells (δ)
Regulation of Glucose

• Alpha (α) cells release glucagon to control blood glucose level
  – When blood glucose levels fall, α cells ↑ the amount of glucagon in the blood
  – The surge of glucagon stimulates liver to release glucose stores by the breakdown of glycogen into glucose (glycogenolysis)
  – Also, glucagon stimulates the liver to produce glucose (gluconeogenesis)
Regulation of Glucose

- Beta Cells (β) release insulin (antagonistic to glucagon) to control blood glucose level
  - Insulin \( \uparrow \) the rate at which various body cells take up glucose \( \Rightarrow \) insulin lowers the blood glucose level
  - Promotes glycogenesis - storage of glycogen in the liver
  - Insulin is rapidly broken down by the liver and must be secreted constantly
Regulation of Glucose

• Delta Cells ($\partial$) produce somatostatin, which inhibits both glucagon and insulin
  – inhibits insulin and glucagon secretion by the pancreas
  – inhibits digestion by inhibiting secretion of digestive enzymes
  – inhibits gastric motility
  – inhibits absorption of glucose in the intestine
Regulation of Glucose

• Breakdown of sugars carried out by enzymes in the GI system
  – As simple sugars, they are absorbed from the GI system into the body

• To be converted into energy, glucose must first be transmitted through the cell membrane
  – Glucose molecule is too large and does not readily diffuse
Regulation of Glucose

• Glucose must pass into the cell by binding to a special carrier protein on the cell’s surface.
  – *Facilitated diffusion* - carrier protein binds with the glucose and carries it into the cell.

• The rate at which glucose can enter the cell is dependent upon insulin levels
  – Insulin serves as the messenger - travels via blood to target tissues
  – Combines with specific insulin receptors on the surface of the cell membrane
Regulation of Glucose

• Body strives to maintain blood glucose between 60 mg/dl and 120 mg/dl.

• Glucose
  – brain is the biggest user of glucose in the body
  – sole energy source for brain
  – brain does not require insulin to utilize glucose
Regulation of Glucose

Glucagon and Insulin are opposites (antagonists) of each other.
Regulation of Glucose

• **Glucagon**
  – Released in response to:
    • Sympathetic stimulation
    • Decreasing blood glucose concentration
  – Acts primarily on liver to increase rate of glycogen breakdown
  – Increasing blood glucose levels have inhibitory effect on glucagon secretion
Regulation of Glucose

• **Insulin**
  – Released in response to:
    • Increasing blood glucose concentration
    • Parasympathetic innervation
  – Acts on cell membranes to increase glucose uptake from blood stream
  – Promotes facilitated diffusion of glucose into cells
Diabetes Mellitus

• 2 Types historically based on age of onset (NOT insulin vs. non-insulin)
  – Type I
    • juvenile onset
    • insulin dependent
  – Type II
    • historically adult onset
      – now some morbidly obese children are developing Type II diabetes
    • non-insulin dependent
      – may progress to insulin dependency
Types of Diabetes Mellitus

- Type I
- Type II
- Secondary
- Gestational
Pathophysiology of Type I Diabetes Mellitus

• Characterized by inadequate or absent production of insulin by pancreas
• Usually presents by age 25
• Strong genetic component
• Autoimmune features
  – body destroys own insulin-producing cells in pancreas
  – may follow severe viral illness or injury
• Requires lifelong treatment with insulin replacement
Pathophysiology of Type II Diabetes Mellitus

• Pancreas continues to produce some insulin however disease results from combination of:
  – **Relative** insulin deficiency
  – Decreased sensitivity of insulin receptors

• Onset usually after age 25 in overweight adults
  – Some morbidly obese children develop Type II diabetes

• Familial component

• Usually controlled with diet, weight loss, oral hypoglycemic agents
  – Insulin may be needed at some point in life
Secondary Diabetes Mellitus

- Pre-existing condition affects pancreas
  - Pancreatitis
  - Trauma
Gestational Diabetes Mellitus

- Occurs during pregnancy
  - Usually resolves after delivery
- Occurs rarely in non-pregnant women on BCPs
- Increased estrogen, progesterone antagonize insulin
Presentation of New Onset Diabetes Mellitus

• 3 Ps
  – Polyuria
  – Polydipsia
  – Polyphagia
• Blurred vision, dizziness, altered mental status
• Rapid weight loss
• Warm dry skin,
• Weakness, Tachycardia, Dehydration
Long Term Treatment of Diabetes Mellitus

• Diet regulation
  – *e.g.* 1400 calorie ADA diet

• Exercise
  – increase patient’s glucose metabolism

• Oral hypoglycemic agents
  – Sulfonylureas

• Insulin
  – Historically produced from pigs (porcine insulin)
  – Currently genetic engineering has lead to human insulin (Humulin)
Long Term Treatment of Diabetes Mellitus

• **Insulin**
  – Available in various forms distinguished on onset and duration of action
  
  • Onset
    – rapid (Regular, Semilente, Novolin 70/30)
    – intermediate (Novolin N, Lente)
    – slow (Ultralente)
  
  • Duration
    – short, 5-7 hrs (Regular)
    – intermediate, 18-24 hrs (Semilente, Novolin N, Lente, NPH)
    – long-acting, 24 - 36+ hrs (Novolin 70/30, Ultralente)
Long Term Treatment of Diabetes Mellitus

• **Insulin**
  – Must be given by injection as insulin is protein which would be digested if given orally
  • extremely compliant patients may use an insulin pump which provides a continuous dose
  • current research studying inhaled insulin form
Long Term Treatment of Diabetes Mellitus

• **Oral Hypoglycemic Agents**
  – Stimulate the release of insulin from the pancreas, thus patient must still have intact *beta* cells in the pancreas.
  – **Common agents include:**
    • Glucotrol® (glipizide)
    • Micronase® or Diabeta® (glyburide)
    • Glucophage® (metformin) [Not a sulfonylurea]
Emergencies Associated Blood Glucose Level

• **Hyperglycemia**
  – Diabetic Ketoacidosis (DKA)
  – Hyperglycemic Hyperosmolar Nonketotic Coma (HHNC)

• **Hypoglycemia**
  – “Insulin Shock”
Hyperglycemia

• Defined as blood glucose > 200 mg/dl

• Causes
  – Failure to take *medication* (insulin)
  – Increased *dietary* intake
  – *Stress* (surgery, MI, CVA, trauma)
  – Fever
  – *Infection*
  – *Pregnancy* (gestational diabetes)
Hyperglycemia

- Two hyperglycemic diabetic states may occur
  - Diabetic Ketoacidosis (DKA)
  - Hyperglycemic Hyperosmolar Non-ketotic Coma (HHNC)
Diabetic Ketoacidosis (DKA)

- Occurs in Type I diabetics (insulin dependency)
- Usually associated with blood glucose level in the range of 200 - 600 mg/dl
- No insulin availability results in ketoacidosis
Diabetic Ketoacidosis (DKA)

• Pathophysiology
  – Results from absence of insulin
    • prevents glucose from entering the cells
    • leads to glucose accumulation in the blood
  – Cells become starved for glucose and begin to use other energy sources (primarily fats)
    • Fat metabolism generates fatty acids
    • Further metabolized into ketoacids (ketone bodies)
Diabetic Ketoacidosis (DKA)

• Pathophysiology (cont)
  – Blood sugar rises above renal threshold for reabsorption (blood glucose > 180 mg/dl)
    • glucose “spills” into the urine
    • Loss of glucose in urine causes osmotic diuresis
  – Results in
    • dehydration
    • acidosis
    • electrolyte imbalances (especially K+)
Diabetic Ketoacidosis (DKA)

- **Presentation**
  - Gradual onset with progression
  - Warm, pink, dry skin
  - Dry mucous membranes (dehydrated)
  - Tachycardia, weak peripheral pulses
  - Weight loss
  - Polyuria (frequent urination)
  - Polydipsia (excessive thirst)
  - Abdominal pain with nausea/vomiting
  - Altered mental status
  - Kussmaul respirations with acetone (fruity) odor
Diabetic Ketoacidosis

- Inadequate insulin
  - Increased Blood Sugar
    - Osmotic Diuresis
      - Polyuria
        - Volume Depletion
        - Shock
      - Polydipsia
  - Cells Can’t Burn Glucose
    - Polyphagia
    - Ketone Bodies
      - Metabolic Acidosis
      - Fruity Breath
    - Cells Burn Fat
      - Kussmaul Breathing
Management of DKA

- Airway/Ventilation/Oxygen NRB mask
- Assess blood glucose level & ECG
- IV access, large bore NS
  - normal saline bolus and reassess
  - often requires several liters
- Assess for underlying cause of DKA
- Transport

How does fluid treat DKA?
Hyperosmolar Hyperglycemic Nonketotic Coma (HHNC)

- Usually occurs in type II diabetics
- Typically very high blood sugar (>600mg/dl)
- Some insulin available
- Higher mortality than DKA
Hyperosmolar Hyperglycemic Nonketotic Coma (HHNC)

• Pathophysiology
  – Some minimal insulin production
    • enough insulin available to allow glucose to enter the cells and prevent ketogenesis
    • not enough to decrease gluconeogenesis by liver
    • no ketosis
  – Extreme hyperglycemia produces hyperosmolar state causing
    • diuresis
    • severe dehydration
    • electrolyte disturbances
Hyperosmolar Hyperglycemic Nonketotic Coma (HHNC)

- Inadequate insulin
- Increased Blood Sugar
- Osmotic Diuresis
- Polyuria
- Volume Depletion Shock
- Polydipsia
Hyperosmolar Hyperglycemic Nonketotic Coma (HHNC)

• Presentation
  – Same as DKA but with greater severity
    • Higher blood glucose level
    • Non-insulin dependent diabetes
    • Greater degree of dehydration
Management of HHNC

• Secure airway and assess ventilation
  – Consider need to assist ventilation
  – Consider need to intubate
• High concentration oxygen
• Assess blood glucose level & ECG
• IV access, large bore NS
  – normal saline bolus and reassess
  – often requires several liters
• Assess for underlying cause of HHNC
• Transport
Further Management of Hyperglycemia

• Insulin (regular)
  – Correct hyperglycemia

• Correction of acid/base imbalances
  – Bicarbonate (severe cases documented by ABG)

• Normalization of electrolyte balance
  – DKA may result in hyperkalemia 2° to acidosis
    • H⁺ shifts intracellularly, K⁺ moves to extracellular space
  – Urinary K⁺ losses may lead to hypokalemia once therapy is started
Hypoglycemia

• True hypoglycemia defined as blood sugar < 60 mg/dl

• ALL hypoglycemia is NOT caused by diabetes
  – Can occur in non-diabetic patients
    • thin young females
    • alcoholics with liver disease
    • alcohol consumption on empty stomach will block glucose synthesis in liver (gluconeogenesis)

• Hypoglycemia causes impaired functioning of brain which relies on constant supply of glucose
Hypoglycemia

• **Causes** of hypoglycemia in diabetics
  – Too much insulin
  – Too much oral hypoglycemic agent
    • Long half-life requires hospitalization
  – Decreased dietary intake (took insulin and missed meal)
  – Vigorous physical activity

• **Pathophysiology**
  – Inadequate blood glucose available to brain and other cells resulting from one of the above causes
Hypoglycemia

• Presentation
  – Hunger (initially), Headache
  – Weakness, Incoordination (*mimics a stroke*)
  – Confusion, Unusual behavior
    • may appear intoxicated
  – Seizures
  – Coma
  – Weak, rapid pulse
  – Cold, clammy skin
  – Nervousness, trembling, irritability
Hypoglycemia: Pathophysiology

Blood Glucose Falls

Brain Lacks Glucose
- Altered LOC
- Seizures
- Headache
- Dizziness
- Bizarre Behavior
- Weakness

SNS Response
- Anxiety
- Pallor
- Tachycardia
- Diaphoresis
- Nausea
- Dilated Pupils
Hypoglycemia

Beta Blockers may mask symptoms by inhibiting sympathetic response
Management of Hypoglycemia

- Secure airway manually
  - suction prn
  - Ventilate prn
- High concentration oxygen
- Vascular access
  - Large bore IV catheter
  - Saline lock, D$_5$W or NS
  - Large proximal vein preferred
- Assess blood glucose level
Management of Hypoglycemia

- **Oral glucose**
  - ONLY if intact gag reflex, awake & able to sit up
  - 15gm-30gm of packaged glucose, or
  - May use sugar-containing drink or food
  - Oral route often slower

- **Intravenous glucose**
  - Adult: Dextrose 50% (D_{50}) 25gms IV in patent, free-flowing vein, may repeat
  - Children: Dextrose 25% (D_{25}) @ 2 - 4 cc/kg (0.5 - 1 gm/kg)
    [Infants - may choose Dextrose 10% @ 0.5 - 1 gm/kg or 5 - 10 cc/kg]
Management of Hypoglycemia

• Glucagon
  – Used if unable to obtain IV access
  – 1 mg IM
  – Requires glycogen stores
  – Slower onset of action than IV route

What persons are likely to have inadequate glycogen stores?
Management of Hypoglycemia

• Have patient eat high-carbohydrate meal
• Transport?
  – Patient Refusal
    • Leave only with responsible family/friend for 6 hours
    • Must educate family/friend to hypoglycemic signs/symptoms
    • Advise to contact personal physician
  – Transport
    • Hypoglycemic patients on oral agents (long half life)
    • Unknown, atypical or untreated cause of hypoglycemia
Long-term Complications of Diabetes Mellitus

- **Blindness**
  - Retinal hemorrhages

- **Renal Disease**

- **Peripheral Neuropathy**
  - Numbness in “stocking glove” distribution (hands and feet)

- **Heart Disease and Stroke**
  - Chronic state of Hyperglycemia leads to early atherosclerosis

- **Complications in Pregnancy**
Long-term Complications of Diabetes Mellitus

- Diffuse Atherosclerosis
  - AMI
  - CVA
  - PVD
    - Hypertension
      - Renal failure
      - Diabetic retinopathy/blindness
      - Gangrene
Long-term Complications of Diabetes Mellitus

Diabetics are up to 4 times more likely to have heart disease and up to 6 times more likely to have a stroke than a non-diabetic.

10% of all diabetics develop renal disease usually resulting in dialysis.
Long-term Complications of Diabetes Mellitus

- **Peripheral Neuropathy**
  - **Silent MI**
    - Vague, poorly-defined symptom complex
      - Weakness
      - Dizziness
      - Malaise
      - Confusion
    - Suspect MI in any diabetic with MI signs/symptoms with or without CP
Diabetes in Pregnancy

• Early pregnancy (<24 weeks)
  – Rapid embryo growth
  – Decrease in maternal blood glucose
  – Episodes of hypoglycemia
Diabetes in Pregnancy

• Late pregnancy (>24 weeks)
  – Increased resistance to insulin effects
  – Increased blood glucose
  – Ketoacidosis
Diabetes in Pregnancy

• Increased maternal risk for:
  – Pregnancy-induced hypertension
  – Infections
    • Vaginal
    • Urinary tract
Diabetes in Pregnancy

• Increased fetal risk for:
  – High birth weight
  – Hypoglycemia
  – Liver dysfunction-hyperbilirubinemia
  – Hypocalcemia
Assessment of the Diabetic Patient

• Maintain high-degree of suspicion
• Assess blood glucose level in all patients with
  – seizure, neurologic S/S, altered mental status
  – vague history or chief complaint
• Blood glucose assessment IS NOT necessary in all patients with diabetes mellitus!!
Assessment of the Diabetic Patient

• History and Physical Exam includes
  – Look for insulin syringes, medical alert tag, glucometer, or insulin (usually kept in refrigerator)
  – Last meal and last insulin dose
  – Missed med or missed meal?
  – Signs of infection
    • Foot cellulitis / ulcers
  – Recent illness or physiologic stressors
Blood Glucose Assessment

• Capillary vs. venous blood sample
  – Depends on glucometer model
  – Usually capillary preferred

• Dextrostick vs Glucometer
  – Dextrostick - colorimetric assessment of blood provides glucose estimate
  – Glucometer - quantitative glucose measurement

• Neonatal blood
  – Many glucometers are not accurate for neonates
This Concludes Diabetes Mellitus

Please visit the link below to take the EXAM

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