Carbohydrates

Sugars

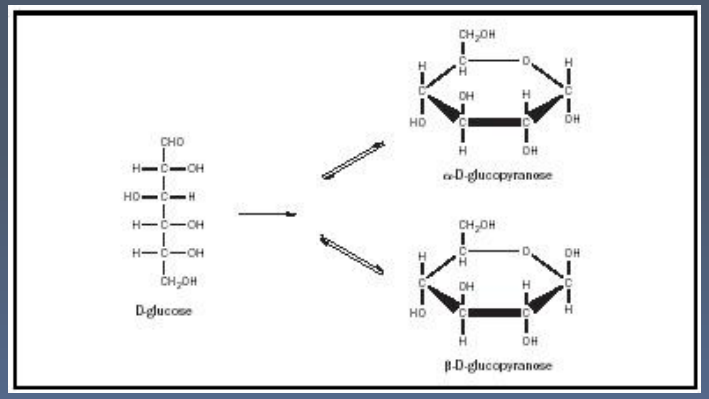
- Monosaccharides
  - Glucose – Broken down starch
  - Galactose – Dairy, sugar beets, jams, jelly
  - Fructose – Fruits, honey
  - Mannose – Plant polysaccharide, not starch
- Disaccharides
  - Maltose – Barley, beer, cereals (glu + glu)
  - Lactose – Milk sugar (glu + gal)
  - Sucrose – Table sugar, sugar cane, maples (glu + fru)

Sugars

- Polysaccharides
  - Starch: plant made
    - Amylose shorter chains
    - Amylopectin longer chain with branching
  - Glycogen: animal made
    - Similar to amylopectin, but with more branching

Sugars

- Glucose forms ring structure in solution
  - β-D Glucose 36%
    - Glucose oxidase recognizes this
  - α-D Glucose 64%



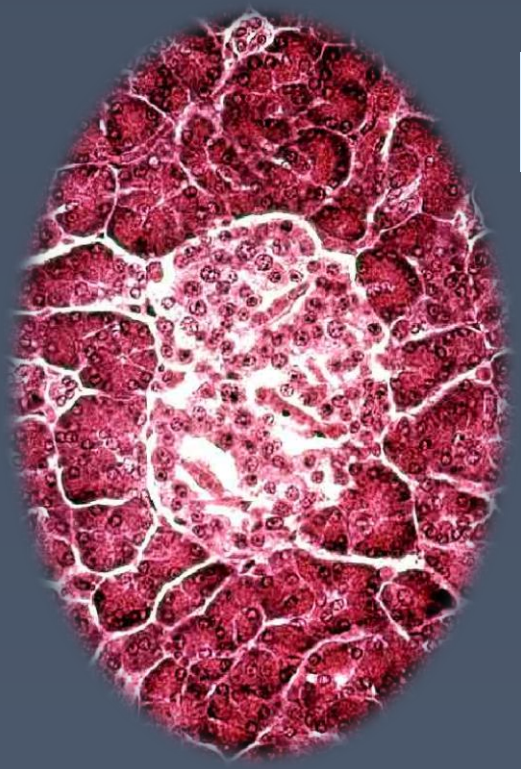
Hormone Regulation

- Lower blood glucose
  - Insulin
    - Secreted by β-islet cells of pancreas
    - Stimulates movement of glucose into cells
      - Second Messenger Duties
        - ↑Lipogenesis, protein synthesis & AA transport, glycogen synthesis
        - ↓Lipase, protein breakdown, gluconeogenesis, glycogenolysis

Hormone Regulation

- Raise Blood Glucose
  - Glucagon
    - Secreted by α-islet cell of pancreas
    - Primary hormone responsible for raising glucose
      - Stimulates glycogenolysis and gluconeogenesis
  - Epinephrine
    - Catecholamine secreted by adrenal medulla, stimulates glucagon release
  - Cortisol
    - Secreted by adrenal cortex
      - Stimulates gluconeogenesis and glucagon release

Hormone Regulation



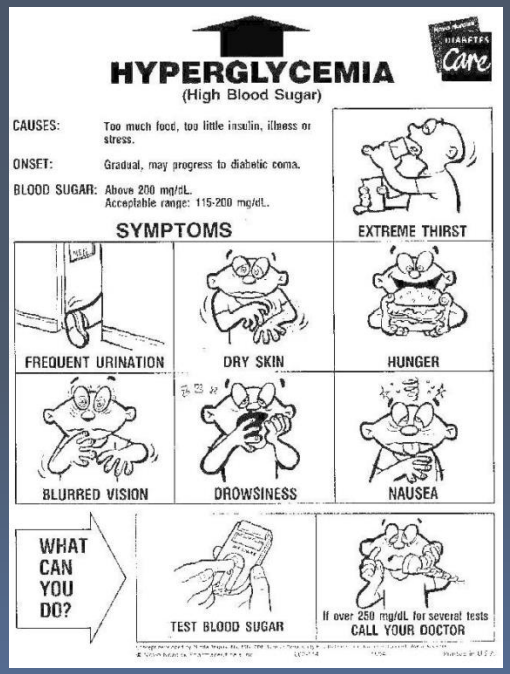
- Raise Blood Glucose
  - Growth Hormone
    - Synthesized by Anterior Pituitary
    - Inhibits glucose uptake by cells
  - Thyroxine (T4)
    - Least important, stimulates glycogenolysis
  - Somatostatin
    - Secreted by δ-islet cells of pancreas, hypothalamus, and GI tract
      - Inhibits BOTH insulin and glucagon release
  - ACTH
    - Secreted by Anterior Pituitary
      - Stimulates cortisol, Insulin antagonist

Hyperglycemia

- High glucose
  - Resolved by insulin
- Pathology: Diabetes Mellitus
  - Type 1 Absolute Deficiency
  - Type 2 Resistance with secretory defect
  - Other
    - Pancreatic disease, drug/chemical induced etc
  - Gestational
    - Metabolic and hormonal changes during pregnancy

Clinical Signs of Diabetes

- Polyuria
  - Renal threshold 160-180 mg/dL
- Polyphagia
  - “Starvation in land of plenty”
- Polydipsia
  - See: Polyuria
- Weight loss
  - “Starvation in land of plenty”
- Hyperventilation (acetone breath)
  - High ketone level



Diabetic Ketoacidosis (DKA)

- Hyperosmolar hyperketotic hyperglycemic state

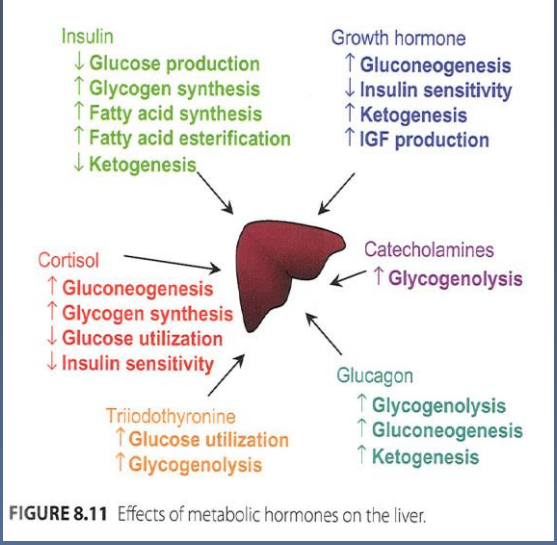


FIGURE 8.11 Effects of metabolic hormones on the liver.

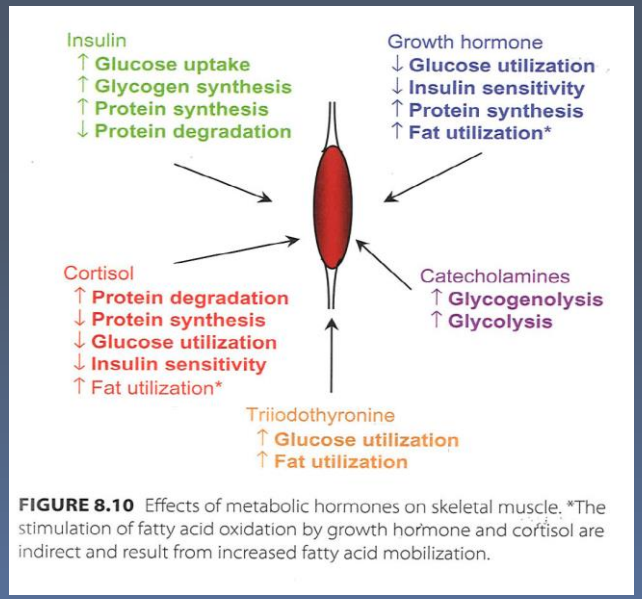


FIGURE 8.10 Effects of metabolic hormones on skeletal muscle. *The stimulation of fatty acid oxidation by growth hormone and cortisol are indirect and result from increased fatty acid mobilization.

Glucose Testing

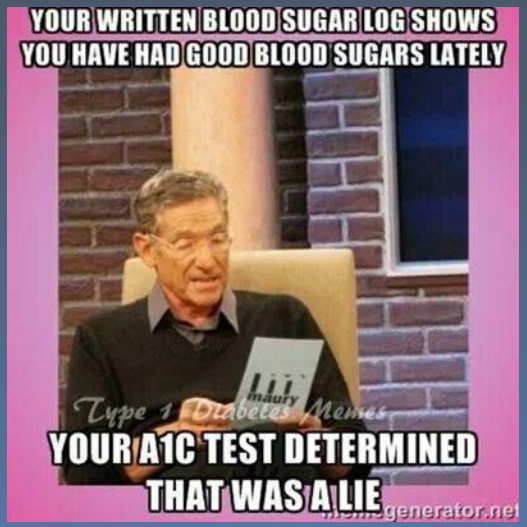
- Fasting Blood Glucose (8-10 hrs)
  - Normal 70-99 mg/dL
  - Impaired 100-125 mg/dL
  - Diabetes ≥126 mg/dL
- Random Glucose
- 2-hour Glucose Tolerance (OGTT) (8-10 hrs fast)
  - Usually time of peak after meal
  - Normal ≤140 mg/dL
  - Impaired 140-199 mg/dL
  - Diabetes ≥200 mg/dL

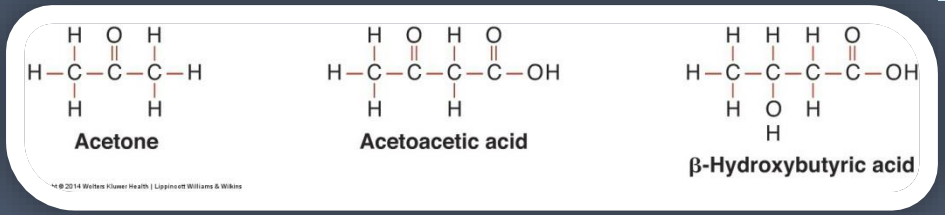
Glucose Testing

- OGTT dosages
  - 50g Gestational screen
  - 75g 2 hr OGTT
  - 100g Women who failed first gestational screen, 3 hr challenge
    - 3 hour challenge: 2 of these true for diagnosis
      - FBS ≥95 mg/dL
      - 1 hr ≥180 mg/dL
      - 2 hr ≥155 mg/dL
      - 3 hr ≥140 mg/dL

Glucose Testing

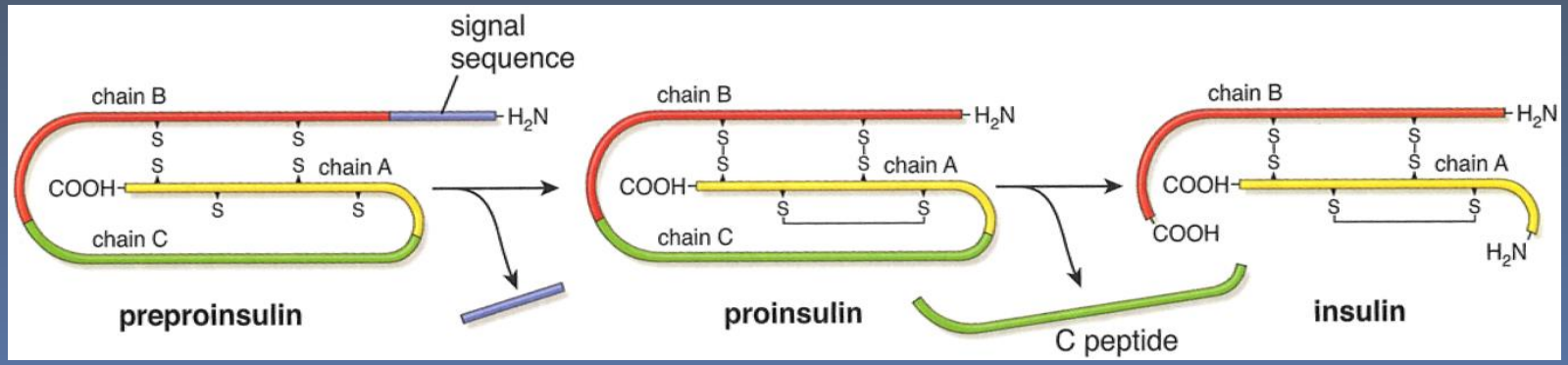
- 5 hr GTT
  - Testing for reactive (postprandial) hypoglycemia
    - Will see large drop (40 mg/dL or more)
- Hemoglobin A1c
  - Average lifespan of RBC 120 days
  - Test reflects average glucose over 2-3 months
    - Diabetes ≥6.5%
  - Hemoglobinopathies will interfere
- Fructoasmine
  - Glucose attaches to other proteins too!
    - 2-3 week period, NO FRUCTOSE INVOLVED!





Other Testing

- C-peptide
  - A product of insulin production
  - Absent in type 1 diabetes
- Ketones
  - 78% BHB, 2% acetone, 20% AAA
  - Produced more in type I diabetes (DKA)



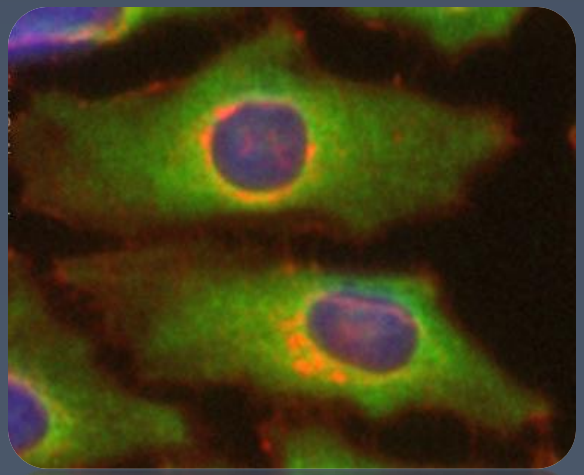
Glucose Methods

- Hexokinase (reference)
  - Glucose + ATP $\xrightarrow{HK,\ Mg^{2+}}$ Glucose−6−phosphate + ADP
  - Glucose−6−Phosphate + NADP $\xrightarrow{G-6-PDH}$ 6−phosphogluconate + NADPH
    - Increase in absorbance at 340 nm

Glucose Methods

- Glucose Oxidase
  - β−D Glucose + O_2 $\xrightarrow{GO}$ Gluconic Acid + H_2O_2
    - From here can measure with polarographic electrode
      - Measures O_2 consumption, must sequester H_2O_2
    - Trinder Reaction
      - H_2O_2+4−aninophenazone + phenol $\xrightarrow{\text{peroxidase}}$ Quinone Complex + 2 H_2O
      - Many interferences
    - Chromogenic Oxygen receptor, or dye that changes color in presence of H_2O_2

Glucose Methods



- Glucose Dehydrogenase
  - $\beta-D\ Glucose + NAD \xrightarrow{GDH} D-glucono\ \delta\ lactone + NADH + H^+$
  - Patented Rxn, only 1% of labs use
  - Increase in absorbance at 340 nm
- If glucose is in the name, it is specific for β−D Glucose
  - Mutarose coverts α to β

TABLE 14-10 METHODS OF GLUCOSE MEASUREMENT

Glucose oxidase	$Glucose + O_2 + H_2O \xrightarrow{glucose\ oxidase} gluconic\ acid + H_2O_2$
	$H_2O_2 + reduced\ chromogen \xrightarrow{peroxidase} oxidized\ chromogen + H_2O$
Hexokinase	$Glucose + ATP \xrightarrow{hexokinase} glucose\text{-}6\text{-}PO_4 + ADP$
	$Glucose\text{-}6\text{-}PO_4 + NADP^+ \xrightarrow{G\text{-}6\text{-}PD} NADPH + 6\text{-}phosphogluconate$
Clinitest	$Cu^{2+} \xrightarrow{Reducing\ substance} Cu^{1+}O$

Other methods

TABLE 14-12 METHODS OF GLYCATED HEMOGLOBIN MEASUREMENT

METHODS BASED ON STRUCTURAL DIFFERENCES		
Immunoassays	Polyclonal or monoclonal antibodies toward the glycated N-terminal group of the β-chain of hemoglobin	
Affinity chromatography	Separates based on chemical structure using borate to bind glycosylated proteins	Not temperature dependent Not affected by other hemoglobins
METHODS BASED ON CHARGE DIFFERENCES		
Ion-exchange chromatography	Positive-charge resin bed	Highly temperature dependent Affected by hemoglobinopathies
Electrophoresis	Separation is based on differences in charge	Hemoglobin F values > 7% interfere
Isoelectric focusing	Type of electrophoresis using isoelectric point to separate	Pre-HbA_1c interferes
High-pressure liquid chromatography	A form of ion-exchange chromatography	Separates of all forms of glyco-Hb: A_1a, A_1b, A_1c

- We use in Auto Chem

TABLE 14-13 METHODS OF KETONE MEASUREMENT

Nitroprusside	Acetoacetic acid + nitroprusside $\xrightarrow{\text{alkaline pH}}$ purple color
Enzymatic	3-β-Hydroxybutyrate + NAD^+ $\xrightarrow{\text{3-HBD}}$ acetoacetate + H^+ + NADH

Galactose

- Galactosemia: failure to thrive
  - Deficiency in 1 of 3 enzymes for galactose metabolism
    - Usually galactose-1-phosphate uridyltransferase
  - Diarrhea, vomiting
    - Mental retardation (DD) and catarats if untreated
- Screened for at birth
  - Why?

Seemingly unrelated?

- Microalbumin
  - Diabetes causes damage to the kidney
    - Early sign is increase in urine albumin
      - Microalbumin is not a small molecule of albumin!