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Chapter 14: Carbohydrates

By Vicki S. Freeman

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General Description of Carbohydrates

- Classification of Carbohydrates
  - Carbohydrates may be classified based on following:
    - 1. Size of base carbon chain: triose (3 carbons), tetrose (4), pentose (5), hexose (6)
    - 2. Location of CO function group
      - **Aldose:** terminal carbonyl group (aldehyde group)
      - **Ketose:** carbonyl group in middle, linked to 2 other carbon atoms (ketone group)

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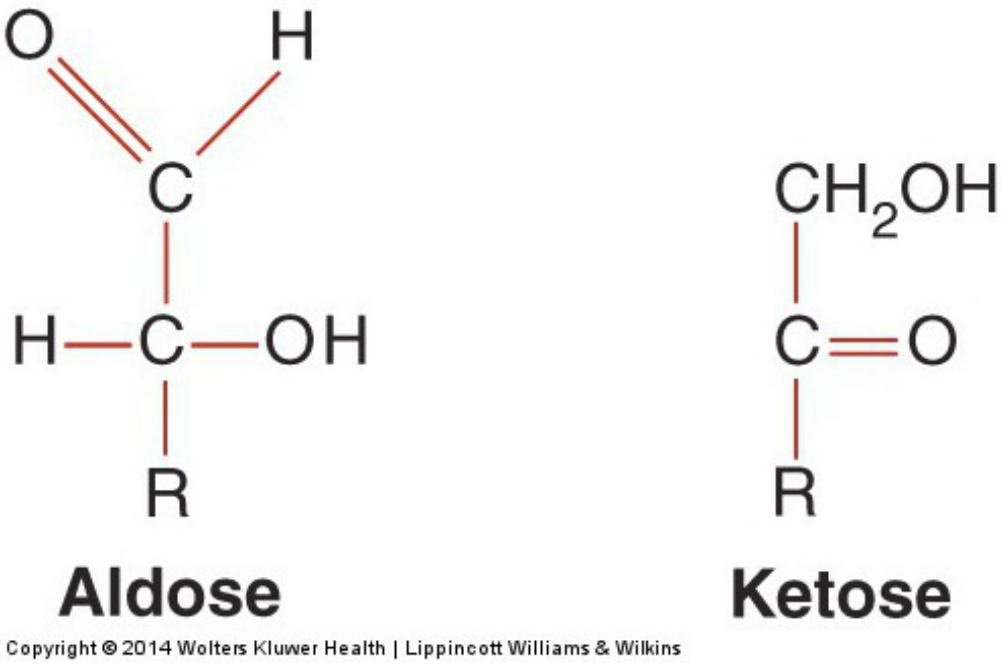
General Description of Carbohydrates (cont'd)

- Two forms of carbohydrates



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General Description of Carbohydrates (cont'd)

- Classification of Carbohydrates
  - Carbohydrates may be classified based on following:
    - 3. Stereochemistry of compound
      - Different spacial arrangements around each asymmetric carbon, forming stereoisomers
      - Two different series are possible: D and L.
    - 4. Number of sugar units in chain
      - Monosaccharides: 1 unit (glucose, fructose, galactose)
      - Disaccharides: 2 units (maltose, lactose, sucrose)
      - Polysaccharides: >10 units (starch [glucose], glycogen)

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General Description of Carbohydrates (cont'd)

- Chemical Properties of Carbohydrates
  - Reducing carbohydrates
    - To reduce, carbohydrate must have ketone or aldehyde group.
    - All monosaccharides & many disaccharides = reducing agents
    - Examples: glucose, maltose, fructose, lactose, galactose
  - Nonreducing carbohydrates
    - Do not have ketone or aldehyde group & will not reduce
- Glucose Metabolism
  - Primary source of energy for humans; nervous system totally depends on glucose from extracellular fluid

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General Description of Carbohydrates (cont'd)

- Fate of Glucose
  - Most ingested carbohydrates are polymers (starch, glycogen).
  - These are converted to disaccharides, & disaccharides are converted to monosaccharides by enzymes (amylase → dextrins and disaccharides; maltase → monosaccharides).
  - Monosaccharides are absorbed by gut & transported to liver.
  - Glucose is only carbohydrate directly used for energy or stored as glycogen; galactose & fructose must be converted to glucose.
  - Once glucose enters cell, it is shunted into 1 of 3 metabolic pathways.
  - Ultimate goal of cell is to convert glucose to carbon dioxide and water.

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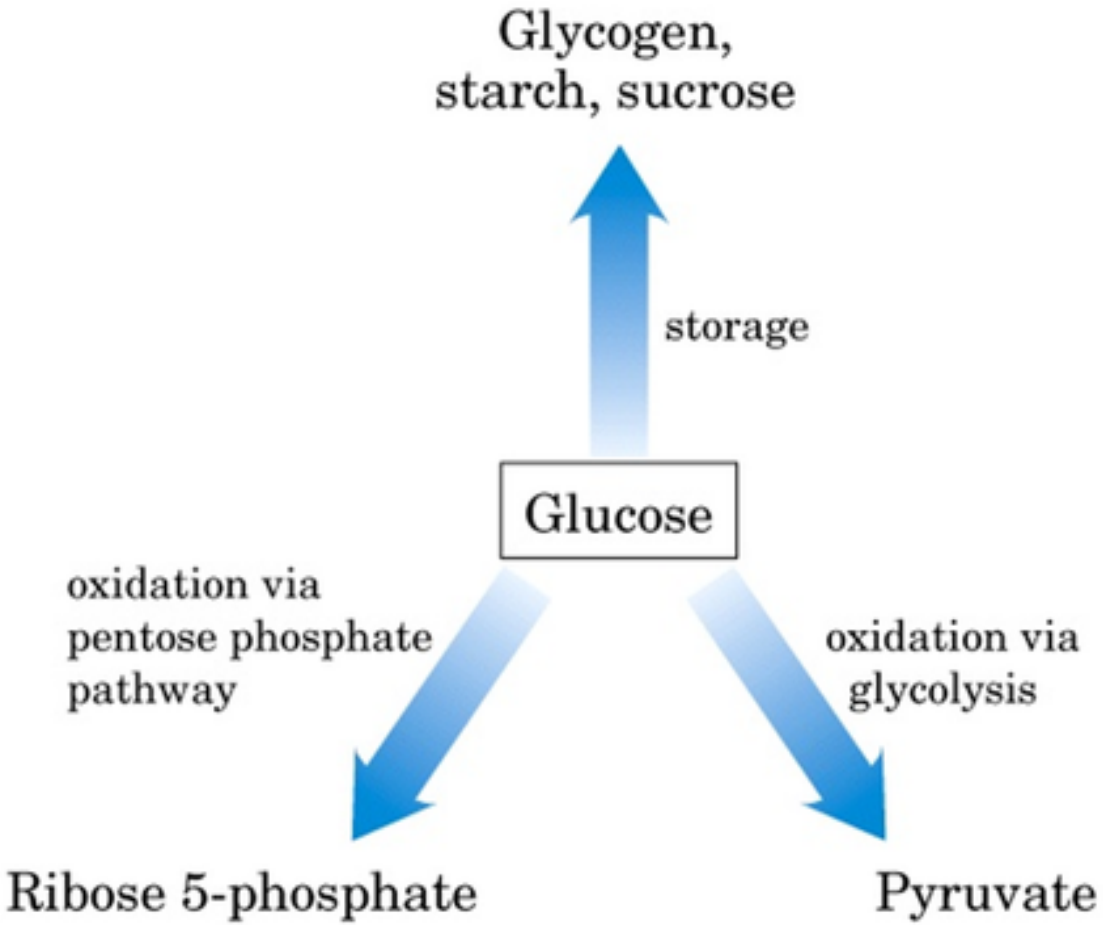

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Steps of glucose metabolism

1. Glycolysis (Embden Meyerhof pathway)
   - Glucose → glucose 6-phosphate → pyruvate + 2ATP
2. Pentose Phosphate Pathway (PPP) (Hexose Monophosphate Shunt)
   - Production of NADPH and ribose 5-phosphate
3. Glycogenesis
   - Storage of excess glucose into glycogen via glycogen synthase

- TCA cycle and Electron transport chain (ETC) complete the oxidation of glucose and provide for most ATP

- Gluconeogensis and glycogenolysis contribute to raise blood glucose

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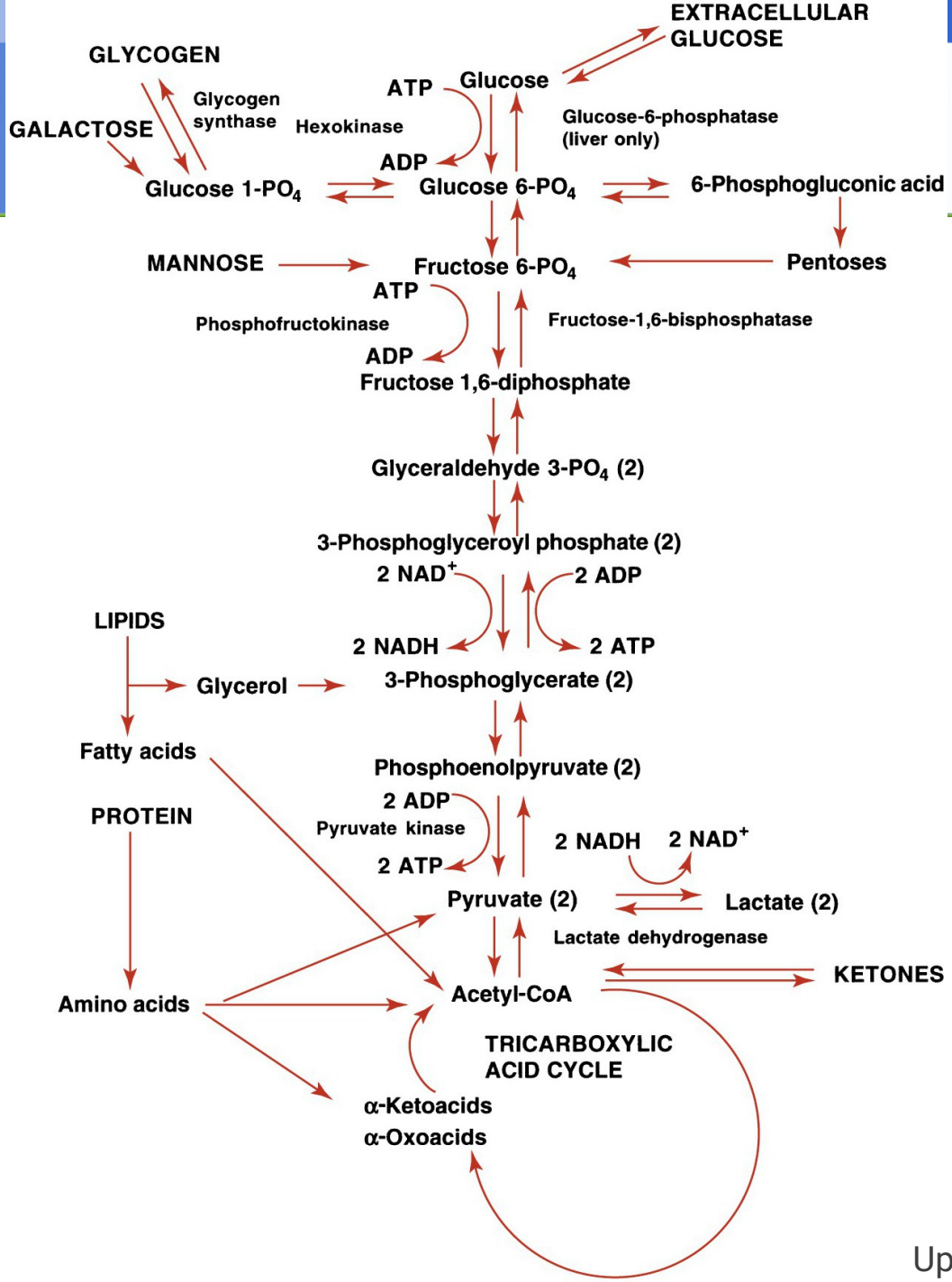

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TABLE 14-1 PATHWAYS IN GLUCOSE METABOLISM

Glycolysis	Metabolism of glucose molecule to pyruvate or lactate for production of energy
Gluconeogenesis	Formation of glucose-6-phosphate from noncarbohydrate sources
Glycogenolysis	Breakdown of glycogen to glucose for use as energy
Glycogenesis	Conversion of glucose to glycogen for storage
Lipogenesis	Conversion of carbohydrates to fatty acids
Lipolysis	Decomposition of fat

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Regulation of Carbohydrate Metabolism

- Liver, pancreas, & other endocrine glands control blood glucose concentrations within a narrow range.
- Hormones that control glucose levels (gl):
  - **Insulin:** from pancreas; ↓ gl
  - **Glucagon:** from pancreas; ↑ gl
  - **Epinephrine** & **glucocorticoids:** from adrenal gland; ↑ gl
  - **Growth hormone** & **ACTH:** from anterior pituitary; ↑ gl
  - **Thyroxine** (thyroid gland) & **somatostatin** (pancreas): ↑ gl

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Regulation of Carbohydrate Metabolism

- Liver, pancreas and other endocrine glands are involved in controlling blood glucose conc within a narrow range
- Brief fasting: glycogenolysis >> Glucose
- Fasting > 1 day: gluconeogenesis from other sources

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Insulin

- Primary hormone responsible for entry of Glucose into the cell
- Produced by β-cells of islets of Langerhans in pancreas
- Release of insulin causes an increased movement of glucose into the cells and increased glucose metabolism
- Released when glucose levels are HIGH
- Increases uptake of glucose by muscle and adipocytes

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Insulin (cont'd)

- It is anabolic hormone: stimulates uptake of glucose by muscle and fat cells, promotes conversion of glucose to glycogen or fat for storage, inhibits glucose production by liver, stimulates protein synthesis, & inhibits protein breakdown
- The only hormone that decreases glucose levels & can be referred to as **hypoglycemic agent**

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TABLE 14-2 THE ACTION OF HORMONES

ACTION OF INSULIN
Increases glycogenesis and glycolysis: glucose → glycogen → pyruvate → acetyl-CoA
Increases lipogenesis
Decreases glycogenolysis
ACTION OF GLUCAGON
Increases glycogenolysis: glycogen → glucose
Increases gluconeogenesis: fatty acids → acetyl-CoA → ketone, proteins → amino acids

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Insulin: chemistry

- Human insulin is made of 51 amino acids in two chains (A and B) joined by 2 disulfide bonds plus a 3rd disulfide bond within A-chain
- Produced as preproinsulin (100 amino acids)
- Stored in secretory granules in Golgi complex of β-cells, where proteolytic cleavage to insulin and connecting peptide (C-peptide) occurs

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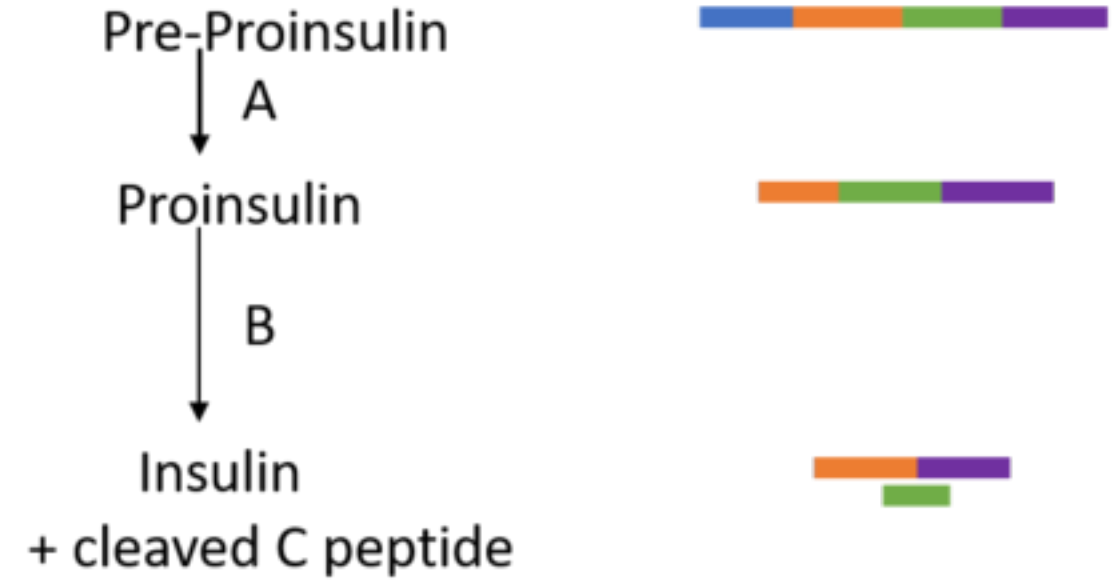

Figure 1: Progression of Insulin-like structures. A. The signal peptide of pre-proinsulin is cleaved, forming proinsulin. B) Proinsulin is folded in the ER, then transported to the Golgi apparatus where the C-peptide is cleaved using type I and type II endoproteases to form free C peptide and mature insulin.

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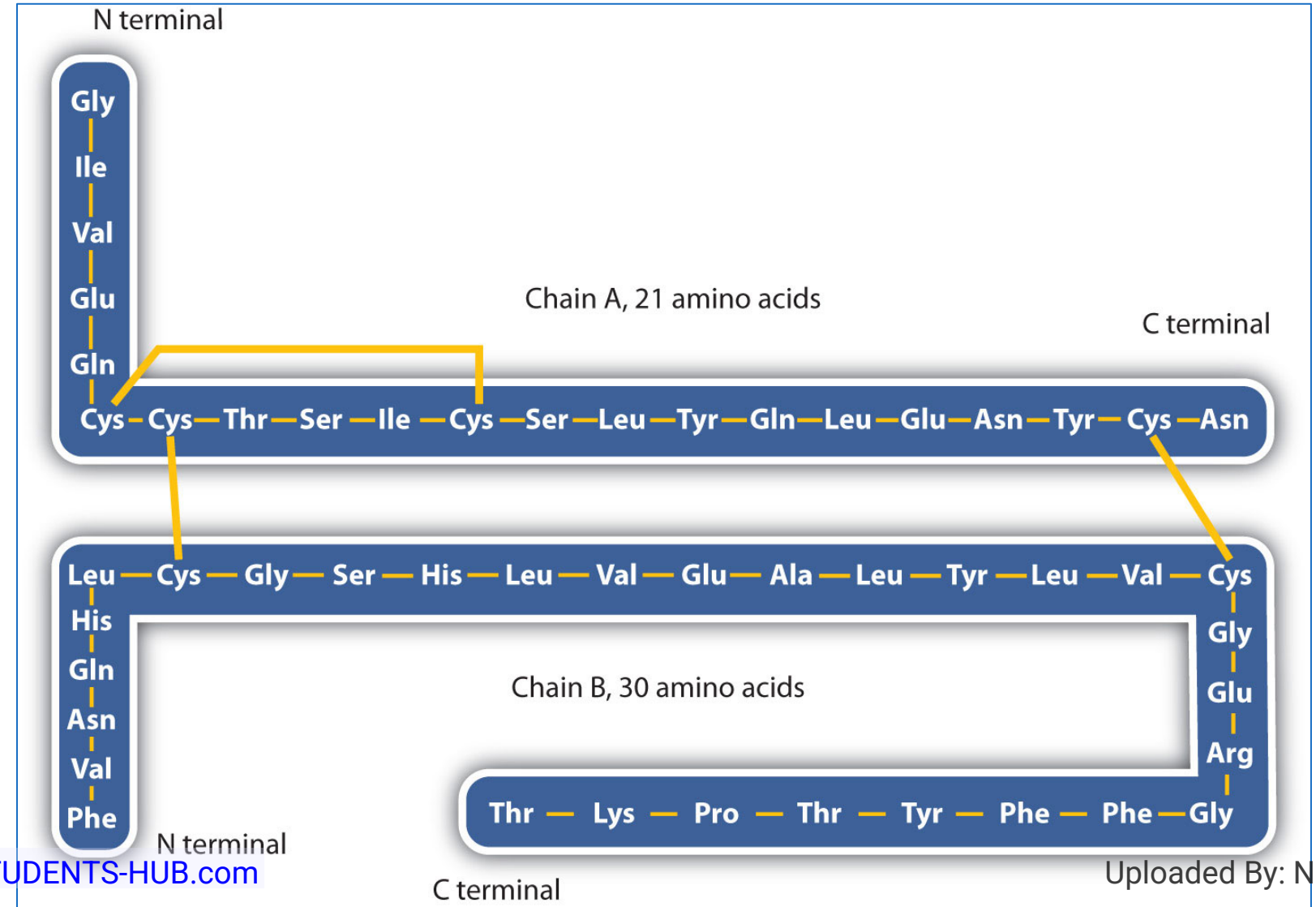
Human insulin



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Insulin release

- Release is stimulated by: Glucose, aa, pancreatic and gastric hormones & some medications (sulfonylureas, β-adrenergic agonists)
- Release inhibited by: hypoglycemia, somatostatin (produced by pancreatic δ–cells) and various drugs (α-adrenergic agonists, β-adrenergic blockers, diazoxide,…)

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Insulin degradation

- On first pass through portal circulation, approx 50% of insulin is extracted by liver, where it's degraded
- Additional degradation occurs in kidneys,
- Insulin is also filtered in glomerulus, reabsorbed and degraded in proximal tubules
- Half life in circulation is 5-4 minutes

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Proinsulin

- Has approx 10% of insulin potency
- Major storage form
- Only ~5% of insulin is proinsulin
- Its half life is ~30 minutes

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C-peptide

- Devoid of biological activity but necessary for insulin to ensure correct structure
- Its plasma levels are 5-6-fold of insulin due to its longer half life of 35 minutes

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Antibodies to insulin

- Abs to insulin develop in almost all patients who are treated with exogenous insulin
- Usually present in low titer and produce no adverse effects
- Occasionally in type 2 diabetes, high titers produce insulin resistance

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Increases glycogenolysis: glycogen → glucose
Increases gluconeogenesis: fatty acids → acetyl-CoA → ketone, proteins → amino acids

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Glucagon

- A 29-aa polypeptide
- Primary hormone responsible for increasing glucose levels
- Produced by α-cells of islets of Langerhans in pancreas
- Induced release by stress, exercise and amino acids
- Stimulates glucose synthesis in LIVER via glycogenolysis or gluconeogenesis
- It's a **hyperglycemic agent**

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Glucagon

- It enhances ketogenesis
- Has a minor effect on adipocyte >> it increases lipolysis
- Insulin inhibits Glucagon release
- Increased Glucagon levels in diabetes, secondary to insulin deficiency, contributes to hyperglycemia state

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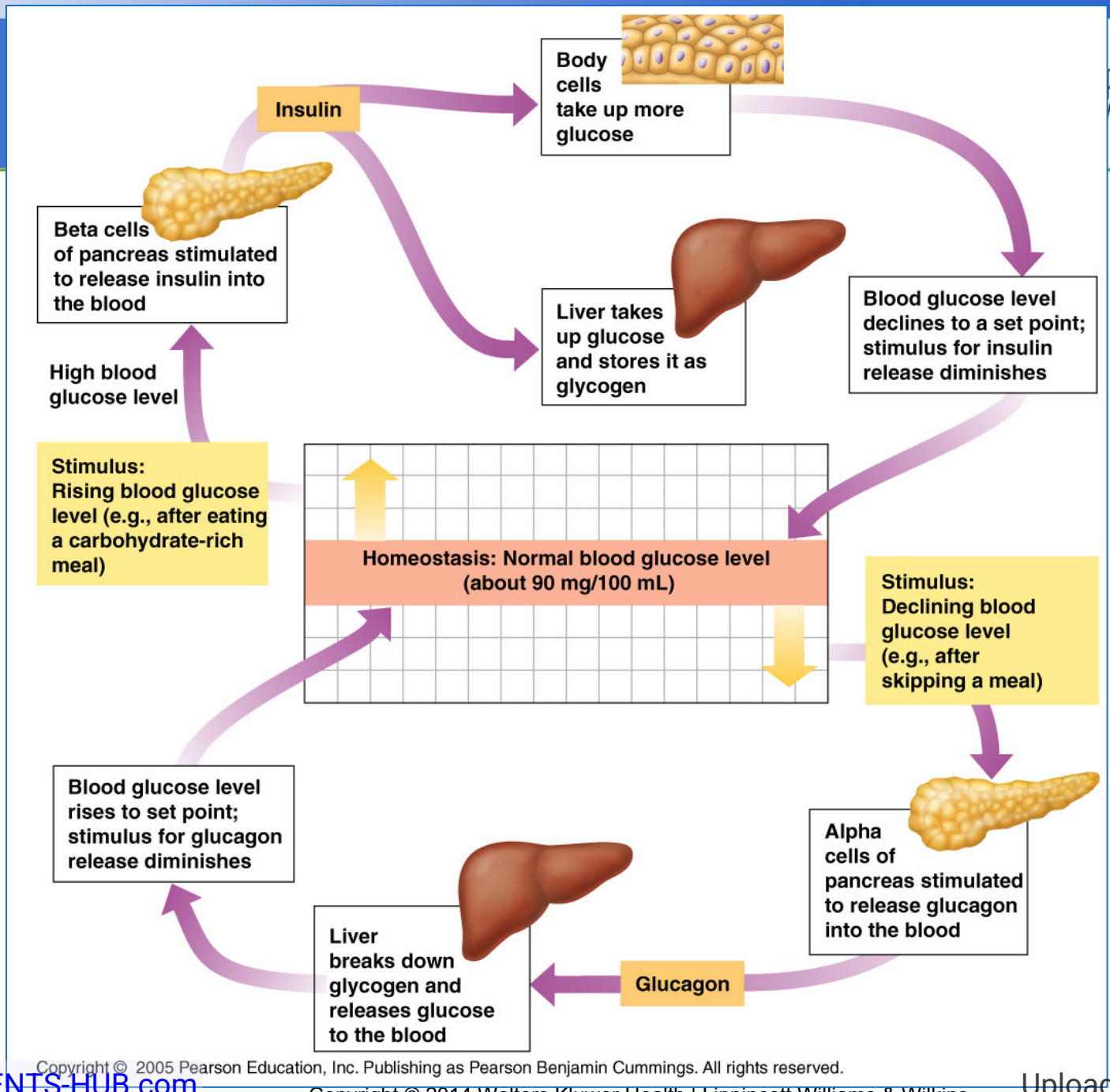

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Epinephrine (Adrenaline)

- Produced by adrenal medulla
- Increases plasma glucose by inhibiting insulin secretion, increasing glycogenolysis & promoting lipolysis
- Induced by stress

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Glucocorticoids

- Primarily cortisol
- Produced by adrenal cortex upon stimulation by ACTH
- Increases plasma glucose by decreasing intestinal entry into cells, increasing gluconeogenesis, liver glycogenolysis & lipolysis

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Other regulators of carbohydrate metabolism

- Two anterior pituitary hormones: ACTH & GH promote increased plasma glucose
- ACTH: acts via stimulation of cortisol release
- GH: decrease glucose entry into cells, increase glycolysis
- Thyroxine: increases glycogenolysis, gluconeogenesis, intestinal absorption of glucose
- Somatostatin: increases plasma glucose, via inhibition of insulin, glucagon, GH & other hormones

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Hyperglycemia

- Definition: an increase in plasma glucose levels caused by imbalance of hormones
- Diabetes Mellitus
  - A group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both
  - Type 1
    - Results from cellular-mediated autoimmune destruction of β cells of pancreas, causing *absolute* deficiency of insulin
    - Constitutes 10–20% of all diabetes cases; occurs in childhood & adolescence and is genetic
    - Initiated by environmental factors, or infection in individuals with genetic predisposition
    - Characteristics: abrupt onset, insulin dependence, ketosis tendency

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TABLE 14-4 LABORATORY FINDINGS IN HYPERGLYCEMIA

Increased glucose in plasma and urine
Increased urine-specific gravity
Increased serum and urine osmolality
Ketones in serum and urine (ketonemia and ketonuria)
Decreased blood and urine pH (acidosis)
Electrolyte imbalance

+ Increased HbA1c levels in plasma

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Markers of autoimmune reactions in type 1 DM

- One or more of the following markers are found in 85-90% of individuals with fasting hyperglycemia
  - Islet cell autoantibodies
  - Insulin autoantibodies
  - Glutamic acid decarboxylase autoantibodies
  - Tyrosine phosphatase IA-2 & IA-2B autoantibodies

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Type 1 DM: symptoms

- Polydipsia (excessive thirst),
- Polyphagia (increased food intake),
- Polyuria (excessive urine production),
- **Rapid weight loss**,
- Hyperventilation,
- Mental confusion,
- Possible loss of consciousness (due to increased glucose to brain)

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Hyperglycemia (cont'd)

- Diabetes Mellitus
  - Type 2
    - Characterized by hyperglycemia caused by an individual's resistance to insulin, resulting in a *relative* insulin deficiency
    - Constitutes majority of diabetes cases & is adult onset
    - Risk factors include age, obesity, lack of exercise, genetic predisposition.
  - Other specific types: associated with genetic defects of β-cell function or insulin action, pancreatic/endocrine diseases, etc.
  - Gestational: glucose intolerance with onset during pregnancy

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Type 2 DM Characteristics

- Adult onset of the disease
- Milder symptoms than in type 1
- Ketoacidosis seldom occurs
- Patients are more likely to go into a hyperosmolar coma and are at an increased risk of developing macrovascular and microvascular complications

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Gestational DM (GDM)

- GDM has been defined as any degree of glucose intolerance with onset or first recognition during pregnancy
- "High-risk" women are those found to have diabetes at their initial prenatal visit, using standard criteria
- Causes include metabolic & hormonal changes
- Associated with increased risk of perinatal complications and developing DM in later years
- Infants are at increased risk for respiratory distress, hypoglycemia & hyperbilirubinemia

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TABLE 14-5 DIAGNOSTIC CRITERIA FOR DIABETES MELLITUS

1. $HbA_1c \geq 6.5\%$ using a method that is NGSP certified and standardized to the DCCT assay[a]
2. Fasting plasma glucose ≥ 126 mg/dL (≥7.0 mmol/L)[a]
3. Two-hour plasma glucose ≥ 200 mg/dL (≥11.1 mmol/L) during an OGTT[a]
4. Random plasma glucose ≥ 200 mg/dL (≥11.1 mmol/L) plus symptoms of diabetes[a]

HbA_1c, hemoglobin A_1c; NGSP, National Glycohemoglobin Standardization Program; OGTT, oral glucose tolerance test.

[a]In the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeat testing on a different day. The fourth measure (OGTT) is not recommended for routine clinical use.

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- Pathophysiology of Diabetes Mellitus
  - Hyperglycemia, possibly severe
  - Glucosuria can occur after renal tubular transporter system for glucose becomes saturated (when plasma glucose >180 mg/dL).
  - Type 1
    - Absence of insulin with excess glucagon
    - Gluconeogenesis and lipolysis → Greater tendency to produce ketones
    - Lab findings in DM with ketoacidosis, reflects dehydration, electrolyte disturbances and acidosis
  - Type 2
    - Presence of insulin & hyperinsulinemia, attenuated glucagon
    - Fatty acid oxidation is inhibited; Fatty acids are incorporated into Triglycerides and released as LDL lipoprotein
    - Greater tendency to develop hyperosmolar nonketotic states

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- Diabetic hyperosmolar syndrome: glucose levels tops 600 mg/dL, blood becomes thick and syrupy → dehydration → diabetic coma
- Bicarbonate & total CO_2 are usually decreased due to deep ventilation (Kussmaul respiration), a compensation to blow off CO_2 and remove hydrogen ions.
- Serum osmolality is high as a result of hyperglycemia
- Serum Na tends to be lower due to losses (polyuria)
- The anion gap in this acidosis can exceed 16 mmol/L.
- Grossly elevated Triglycerides will displace plasma volume
- Hyperkalemia is almost always present as a result of displacement of K from cells

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Hyperglycemia (cont'd)

- Criteria for Testing for Pre-Diabetes and Diabetes
  - All adults >45 years old should have fasting blood glucose measured every 3 years, unless already diagnosed with diabetes.
  - Testing should be earlier or more frequent w/ these risk factors:
    - Overweight tendencies (BMI ≥25 kg/m^2)
    - Habitual physical inactivity
    - Family history of diabetes in a first-degree relative
    - High-risk minority population (African American, Latino)
    - History of gestational diabetes or delivering baby > 4 kg
    - Hypertension (≥140/90)

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- Risk factors continued:
  - Low high-density lipoprotein (HDL) cholesterol concentrations (<35 mg/dL [0.90 mmol/L])
  - Elevated triglyceride concentrations > 250 mg/dL (2.82 mmol/L)
  - History of impaired fasting glucose/impaired glucose tolerance
  - Women with polycystic ovarian syndrome (PCOS)
  - Other clinical conditions associated with insulin resistance (e.g., severe obesity)
  - History of cardiovascular disease

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Hyperglycemia (cont'd)

- Criteria for Testing for Pre-Diabetes and Diabetes
  - Criteria for type 2 diabetes testing in children, beginning at age 10 or at onset of puberty & with follow-up testing every 2 years
    - Overweight
    - Family history (first- or second-degree) of type 2 diabetes
    - Race/ethnicity (African American, Latino, Native American)
    - Signs of insulin resistance (e.g., acanthosis nigricans, hypertension, dyslipidemia, and PCOS)
    - Maternal history of diabetes or gestational diabetes mellitus

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Hyperglycemia (cont'd)

- Criteria for the Diagnosis of Diabetes Mellitus
  - Four methods of diagnosis (each must be confirmed by one of the first 3 methods on a subsequent day)
    1. HbA1c ≥6.5%
    2. Diabetes symptoms + random glucose level of ≥200 mg/dL
    3. A fasting plasma glucose of ≥126 mg/dL
    4. An oral glucose tolerance test (OGTT) w/ 2-hour postload (75-g glucose load) ≥200 mg/dL
  - Patients with following criteria have "pre-diabetes":
    - Fasting glucose of ≥100 mg/dL but <126 mg/dL
    - OGTT 2-hour level of ≥140 mg/dL but <200 mg/dL

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TABLE 14-6 CATEGORIES OF FASTING PLASMA GLUCOSE

Normal fasting glucose	FPG 70–99 mg/dL (3.9–5.5 mmol/L)
Impaired fasting glucose	FPG 100–125 mg/dL (5.6–6.9 mmol/L)
Provisional diabetes diagnosis	FPG ≥126 mg/dL (≥7.0 mmol/l)[a]

FPG, fasting plasma glucose.

[a]Must be confirmed.

TABLE 14-7 CATEGORIES OF ORAL GLUCOSE TOLERANCE

Normal glucose tolerance	Two-hour PG ≤140 mg/dL (≤7.8 mmol/L)
Impaired glucose tolerance	Two-hour PG 140–199 mg/dL (7.8–11.1 mmol/l)
Provisional diabetes diagnosis	Two-hour PG ≥ 200 mg/dL (≥11.1 mmol/L)[a]

PG, plasma glucose.

[a]Must be confirmed.

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Hyperglycemia (cont'd)

- Criteria for testing and diagnosis of GDM
  - All nondiabetic pregnant women should be screened for GDM at 24-28 weeks of gestation

TABLE 14-8 DIAGNOSTIC CRITERIA FOR GESTATIONAL DIABETES

Fasting plasma glucose	≥92 mg/dL (5.1 mmol/L)
One-hour plasma glucose	≥180 mg/dL (10 mmol/L)
Two-hour plasma glucose	≥153 mg/dL (8.5 mmol/L)

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Hypoglycemia

- Decreased plasma glucose levels
- Can be transient & relatively insignificant or life-threatening
- Occurs in healthy-appearing and sick patients, as a result of reaction to medication or of illness
- Symptoms appear at glucose level of about 50–55 mg/dL. (Plasma glucose level at which glucagon is released is 65-70 mg/dL)
- Symptoms: increased hunger, sweating, nausea & vomiting, dizziness, nervousness & shaking, blurred speech & sight, mental confusion

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TABLE 14-9 CAUSES OF HYPOGLYCEMIA

PATIENT APPEARS HEALTHY	
No coexisting disease	Drugs
	Insulinoma
	Islet hyperplasia/ nesidioblastosis
	Factitial hypoglycemia from insulin or sulfonylurea
	Severe exercise
	Ketotic hypoglycemia
Compensated coexistent	Drugs/disease
PATIENT APPEARS ILL	
Drugs	
Predisposing illness	
Hospitalized patient	

- Decreased plasma glucose during hypoglycemia
- Extremely elevated levels of insulin in patients with pancreatic β-cell tumors (insulinoma)

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Genetic Diseases with Hypoglycemia

- Von Gierke: glucose 6-phosphatase deficiency
  - Glycogen cannot be converted back to glucose by hepatic glycogenolysis → glycogen buildup in the liver → hepatomegaly
- Other enzyme deficiencies: glycogen synthase, fructose 1,6-bisphosphatase, phosphoenolpyruvate carboxykinase, and pyruvate carboxylase (hypoglycemia). Glycogen debranching enzyme deficiency (no hypoglycemia, only hepatomegaly)
- Galactosemia: galactose 1-phosphate uridyltransferase deficiency
- Fructose 1-phosphate aldolase deficiency, causes nausea and hypoglycemia after fructose ingestion

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Role of Laboratory in Differential Diagnosis and Management of Patients

- Methods of Glucose Measurement
  - Glucose can be measured from serum, plasma, or whole blood.
  - Serum or plasma must be refrigerated & separated from cells within 1 hour to prevent loss of glucose.
  - Fasting blood glucose should be obtained in morning after 8- to 10-hour fast (not longer than 16 h).
  - Most common methods of glucose analysis use enzymes glucose oxidase or hexokinase.
  - Nonspecific methods are used in urinalysis section of lab to detect reducing substances other than glucose.

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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	$Cu^{2+} \xrightarrow{Reducing\ substance} Cu^{1+}O$

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Role of Laboratory (cont'd)

- Self-Monitoring of Blood Glucose
  - People with diabetes should closely monitor their blood glucose levels to keep them as close to normal as possible.
  - Those with type 1 diabetes should check levels 3 or 4 times/day.
- Glucose Tolerance and 2-Hour Postprandial Tests
  - Oral glucose tolerance test (not recommended by ADA)
    - Patient drinks standardized (75 g) glucose load.
    - Glucose measurement is taken 2 hours later.
  - 2-hour postprandial test
    - A variation of OGTT because OGTT is not recommended
    - More convenient. Patient's glucose is measured after a meal.

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Normal glucose tolerance	Two-hour PG ≤140 mg/dL (≤7.8 mmol/L)
Impaired glucose tolerance	Two-hour PG 140–199 mg/dL (7.8–11.1 mmol/l)
Provisional diabetes diagnosis	Two-hour PG ≥ 200 mg/dL (≥11.1 mmol/L)[a]

PG, plasma glucose.

[a]Must be confirmed.

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- Glycated Hemoglobin/Hemoglobin A_1c
  - Long-term blood glucose regulation can be followed by measurement of glycated hemoglobin.
  - Provides clinician with time-averaged picture of patient's blood glucose concentration over past 3 months.
  - Glycated hemoglobin: formation of a hemoglobin compound produced when glucose reacts with amino group of hemoglobin
  - Glucose attaches non-enzymatically to Hb to form ketoamine
  - Affinity chromatography is preferred method of measurement.
  - Normal 4-6%
  - Estimated average Glucose (eAG, mg/dL)= 28.7 X HbA1c – 46.7
  - HbA_1c depends on the average glucose concentration and the red blood cell life span.
    - If the red blood cell life span is decreased because of another disease (hemoglobinopathies), Hb will have less time to become glycated and HbA1c will be lower.

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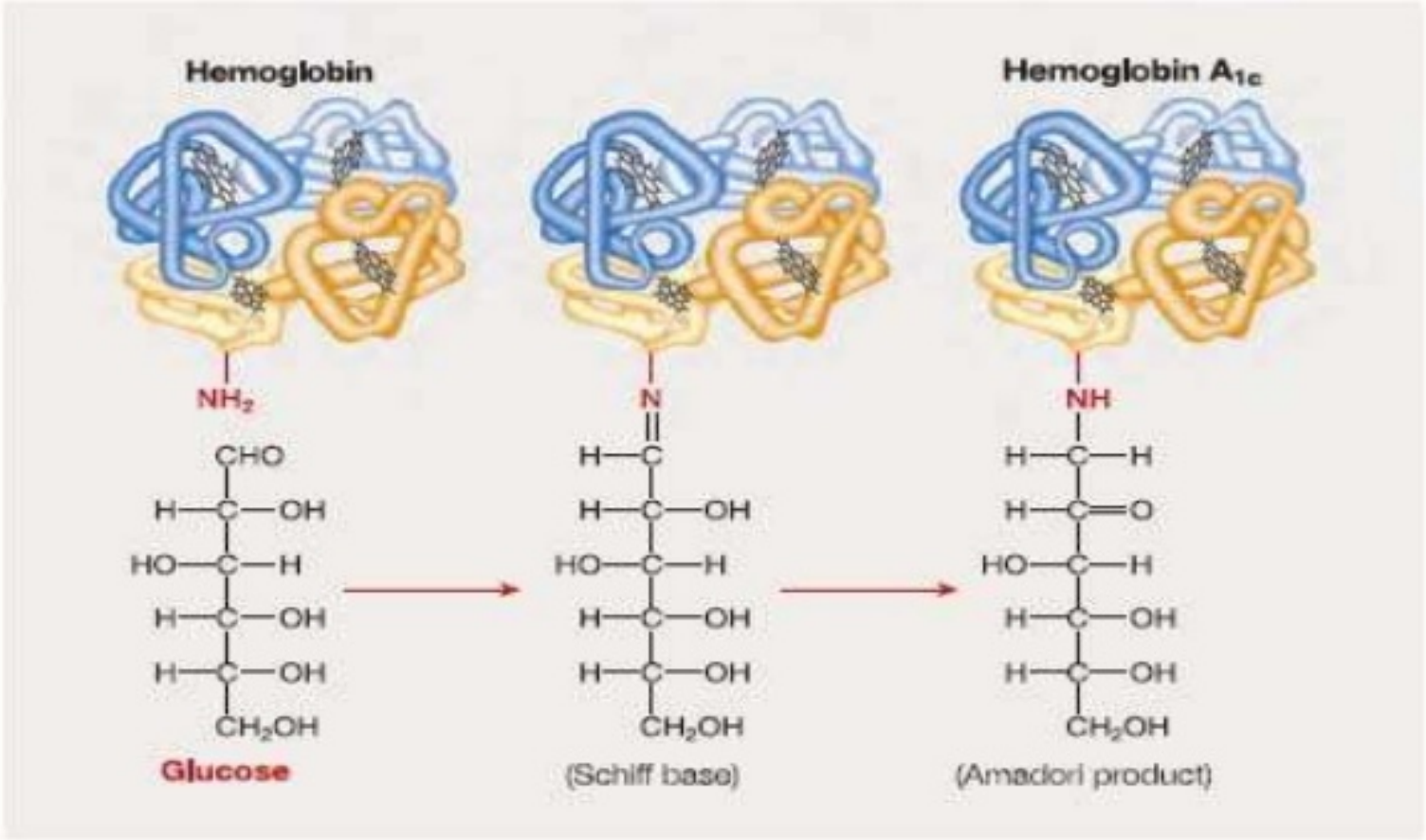
Formation of HbA1c



Formation of glycated hemoglobin A1c (HbA1c). HbA1c is an Amadori product and is formed through the intermediate Schiff base step.

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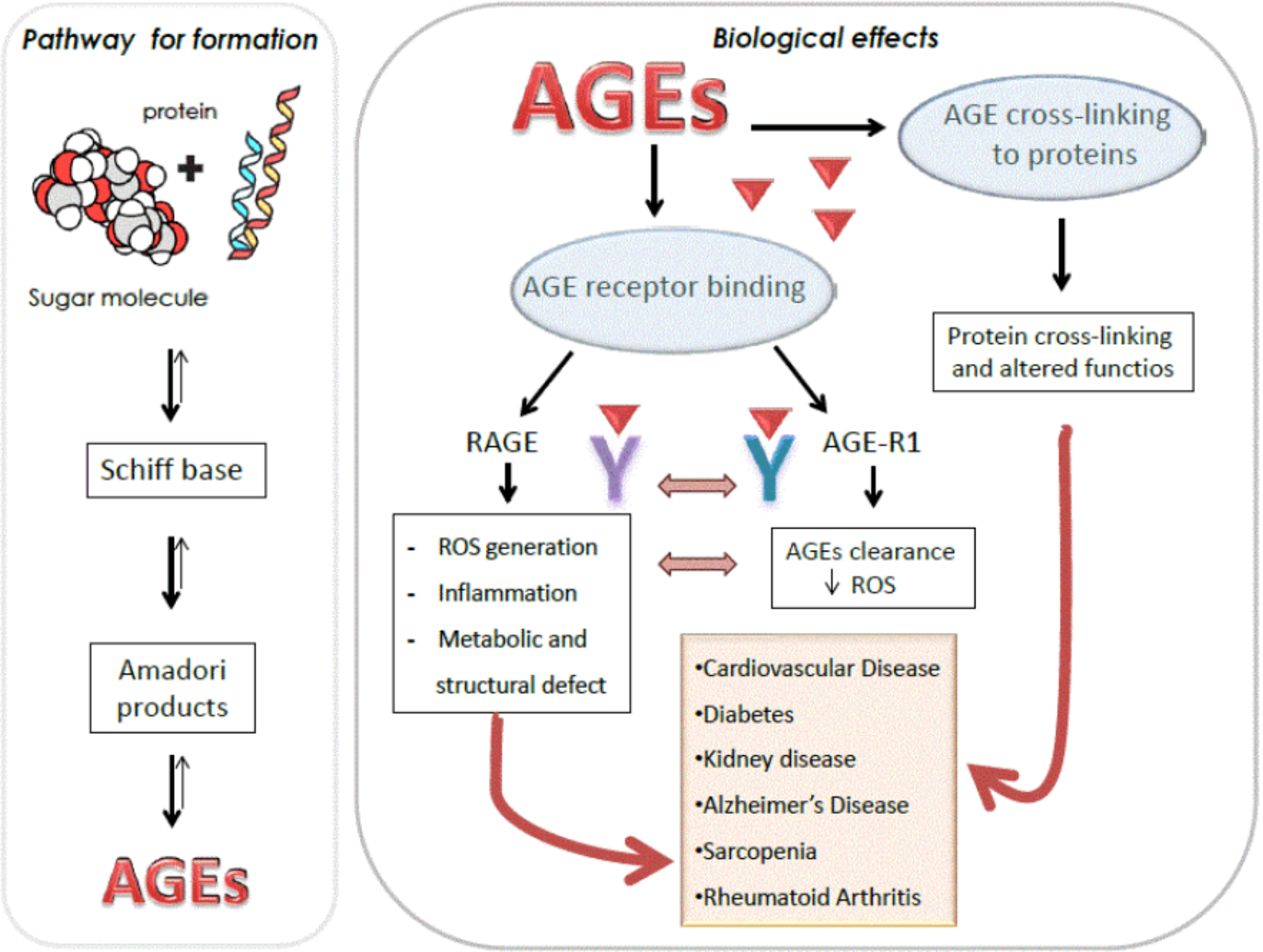

Schematic representation of AGEs formation and of their biological effects.

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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

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- Ketones
  - Produced by liver through metabolism of fatty acids
  - Provide a ready energy source from stored lipids
  - Increase with carbohydrate deprivation or decreased carbohydrate use (diabetes, starvation/fasting, high-fat diets)
  - Three ketone bodies
    - Acetone (2%)
    - Acetoacetic acid (20%)
    - 3-β-hydroxybutyric acid (78%)
  - Specimen requirement is *fresh* serum or urine.

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

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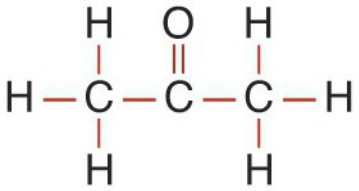
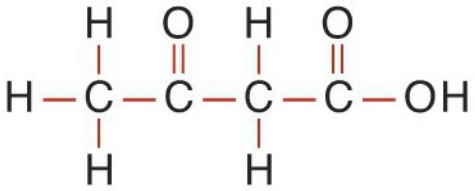
Role of Laboratory (cont'd)

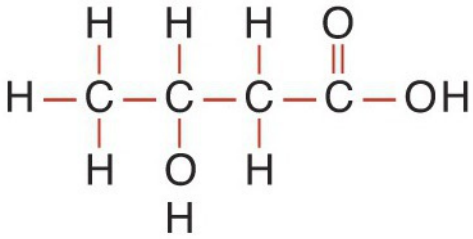
- Three ketone bodies



Acetone



Acetoacetic acid



β-Hydroxybutyric acid

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CASE STUDY 14-1

An 18-year-old male high school student who had a 4-year history of diabetes mellitus was brought to the emergency department because of excessive drowsiness, vomiting, and diarrhea. His diabetes had been well controlled with 40 units of NPH insulin daily until several days ago when he developed excessive thirst and polyuria. For the past 3 days, he has also had headaches, myalgia, and a low-grade fever. Diarrhea and vomiting began 1 day ago.

URINALYSIS RESULTS		CHEMISTRY TEST RESULTS	
Specific gravity	1.012	Sodium	126 mmol/L
pH	5.0	Potassium	6.1 mmol/L
Glucose	4+	Chloride	87 mmol/L
Ketone	Large	Bicarbonate	6 mmol/L
		Plasma glucose	600 mg/dL
		BUN	48 mg/dL
		Creatinine	2.0 mg/dL
		Serum ketones	4+

Questions

1. What is the probable diagnosis of this patient based on the data presented?
2. What laboratory test(s) should be performed to follow this patient and aid in adjusting insulin levels?
3. Why are the urine ketones positive?
4. What methods are used to quantitate urine ketones? Which ketone(s) do they detect?

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CASE STUDY 14-2

A 58-year-old obese man with frequent urination was seen by his primary care physician. The following laboratory work was performed, and the following results were obtained:

CASUAL PLASMA GLUCOSE 225 mg/dL

Urinalysis Results

Color and appearance	Pale/clear	Blood	Negative
pH	6.0	Bilirubin	Negative
Specific	1.025	Urobilinogen	Negative
Glucose	2+	Nitrites	Negative
Ketones	Negative	Leukocyte esterase	Negative

Questions

1. What is the probable diagnosis of this patient?
2. What other test(s) should be performed to confirm this? Which is the preferred test?
3. What values from #2 would confirm the diagnosis of diabetes?
3. After diagnosis, what test(s) should be performed to monitor his condition?

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CASE STUDY 14-5

A 28-year-old woman delivered a 9.5-lb infant. The infant was above the 95th percentile for weight and length. The mother's history was incomplete; she claimed to have had no medical care through her pregnancy. Shortly after birth, the infant became lethargic and flaccid. A whole blood glucose and ionized calcium were performed in the nursery with the following results:

Whole blood glucose	25 mg/dL
Ionized calcium	4.9 mg/dL

Plasma glucose was drawn and analyzed in the main laboratory to confirm the whole blood findings

Plasma glucose	33 mg/dL

An intravenous glucose solution was started and whole blood glucose was measured hourly

Questions

1. Give the possible explanation for the infant's large birth weight and size.
2. If the mother was a gestational diabetic, why was her baby hypoglycemic?
3. Why was there a discrepancy between the whole blood glucose concentration and the plasma glucose concentration?
4. If the mother had been monitored during pregnancy, what laboratory tests should have been performed and what criteria would have indicated [illegible] gestational diabetes?

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CASE STUDY 14-6

Laboratory tests were performed on a 50-year-old lean white woman during an annual physical examination. She had no family history of diabetes or any history of elevated glucose levels during pregnancy.

LABORATORY RESULTS

Fasting blood glucose	90 mg/dL
Cholesterol	140 mg/dL
HDL	40 mg/dL
Triglycerides	90 mg/dL

Questions

1. What is the probable diagnosis of this patient?
2. Describe the proper follow-up for this patient?
3. What are the appropriate screening tests for diabetes in nonpregnant adults?
4. What are the risk factors that would indicate a potential of this patient's developing diabetes?

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CASE STUDY 14-9

A nurse caring for patients with diabetes performed a fingerstick glucose test on the Accu-Chek glucose monitor and obtained a value of 200 mg/dL. A plasma sample, collected at the same time by a phlebotomist and performed by the laboratory, resulted in a glucose value of 225 mg/dL.

Questions

1. Are these two results significantly different?
2. Explain.

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Role of Laboratory (cont'd)

- Microalbuminuria
  - Increase in urinary albumin is early sign of renal nephropathy, a complication of diabetes mellitus.
  - Annual assessment of kidney function by determination of urinary albumin excretion is recommended for diabetic patients.
  - Defined as persistent albuminuria in range of 30–299 mg/24 hr or albumin-creatinine ratio of 30–300 µg/mg
- Islet Autoantibody and Insulin Testing
  - Presence of autoantibodies to β-islet cells of pancreas is characteristic of type 1 diabetes.
  - Not currently recommended for diabetes diagnosis

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