BIOCHEMISTRY TEAM
439

MED439
KING SAUD UNIVERSITY

Endocrine Block: Revision & SAQ File

Color Index

- Main Text
- Important
- Extra
- Dr.'s Notes
- Girls slides
- Boys slides

According to the Doctor:

We all know how unreliable the biochemistry department is, so please take the following notes with a grain of salt lol. #werememberFoundation #werememberNeuropsychiatry

- The 2 midterm lectures (*Actions of hormones*, and *Thyroid Hormones and Thermogenesis*) and the *Obesity: Role of hormones* lectures are most likely **not** coming as SAQs.

- We were unable to get tips regarding the *Cushing Syndome* and *Addison's Disease* lectures, but the doctor said she doesn't think any tests will come

- In the *Cushing Syndrome* and *Addison's disease* lectures, steroid hormone synthesis is important for MCQs -not SAQ (especially the enzymes).

- If there's a chain of events (basically arrows), you can draw **or** write them as sentences in your own words. Both forms are valid.

- The question will most likely tell you how many points you're expected to list, but if it doesn't, just look at how many marks it's worth (that's usually how many points you're expected to write).

- If a question asks you to list things and you're not sure of a few of your points, you can write 1-2 extra points (you won't be marked down for incorrect answers and you will be given points for the correct ones). بس عاد لا تفلونها وتكتبون ٤ مو متاكدين منهم

- Writing just the abbreviations (ex CTX1) is acceptable, but make sure to write them correctly. If you're not sure of the abbreviation, write as much as you can remember from the full form.

L3) Vitamin D, Rickets

- The Vit D Figure coming in the SAQ is unlikely
- Know the enzymes for MCQs

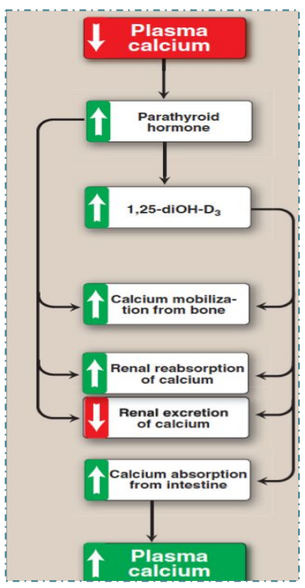
- **List the dietary sources of vitamin D**
  - Ergocalciferol (vitamin D2 in plants)
  -Cholecalciferol (vitamin D3 in meat)

★ **What is the role of the skin/liver/kidneys in Vit. D metabolism. Explain Vitamin D metabolism.**
→ It starts in the skin where 7-dehydrocholesterol is converted by UV lights to cholecalciferol.
→ in the liver cholecalciferol is converted to 25-hydroxycholecalciferol (the storage form that is measured in the plasma) by an enzyme called 25-hydroxylase .
→ in the kidney 25-hydroxycholecalciferol is converted to 1,25 dihydroxycholecalciferol by an enzyme called 1-a-hydroxylase .

- **Explain how is vitamin D regulated by plasma levels of calcium and phosphate.**
The activity of **1-a-hydroxylase** is directly increased by low plasma phosphate
And indirectly increased by parathyroid hormone (PTH) due to low calcium levels.

- **List the functions of vitamin D/What is the role of Vit D in calcium homeostasis?**
  -Regulates plasma levels of calcium and phosphate
  -Promotes intestinal absorption of calcium and phosphate
  -Stimulates the synthesis of calcium binding proteins for intestinal calcium uptake
  -Minimize calcium loss by the kidneys
  -Mobilize calcium and phosphate from the bone to maintain plasma levels

★ **What is the role of PTH in Ca++ homeostasis?**



Again, you can draw or write in your own words.

- **Enumerate the reasons behind the high prevalence of vitamin D deficiency in saudi arabia/Causes of Vit D deficiency. (Unlikely bc its too easy)**
  -Low dietary intake
  -insufficient exposure to the sun
  - lifestyles (ex: clothing)

- **Explain Rickets disease.**
It's a disease that affects children where it causes demineralization of bones with continued collagen matrix formation, the bones becomes soft and pliable leading to skeletal deformities and bowed legs.
In adults it is called - OSTEOMALACIA- and both treated by vitamin D & calcium supplements.

L3) Vitamin D, Rickets

- **List the types of rickets and how to diagnose it?**

Nutritional Rickets	Inherited Rickets
Causes - Vitamin D deficiency because of: • Poor nutrition • Insufficient exposure to sunlight • Renal osteodystrophy (causes decreased synthesis of active vitamin D in kidneys) • Hypoparathyroidism (hypocalcemia)	Vitamin D-dependent rickets (types 1 and 2) - Rare types of rickets due to genetic disorders - Causing vitamin D deficiency mainly because of genetic defects in: • Vitamin D synthesis • Vitamin D receptor (no hormone action)
Diagnosis	
Measuring serum levels of: 25-hydroxycholecalciferol (low), PTH (high), Calcium (low) , Phosphate(low) , Alkaline phosphatase (high)	

- **Explain osteoporosis.**
  It is a disease characterized by reduction in bone mass per unit volume where bone matrix composition is normal but reduced → Primary osteoporosis affect postmenopausal women more .
  There is an increase in bone fragility and susceptibility of fractures.

- **List the causes of secondary osteoporosis.**
  1- GI disease
  2-Hyperthyroidism
  3-Gonadal failure
  4-cushing syndrome
  5-smoking
  6- Alcohol
  7-immobilization

- **How can we diagnose osteoporosis?**
  According to WHO standards we can diagnose primary osteoporosis by serial measurement of bone mineral density (by DEXA) , and we can use biochemical test (calcium , phosphate and vitamin D) to diagnose secondary osteoporosis.

- **Enumerate the treatment and prevention (unlikely) options in osteoporosis.**
  Treatments: oral calcium , estrogens , fluoride therapy , bisphosphonates (inhibits bone resorption).
  Prevention : Diet , exercise and hormone replacement therapy.

★ **What are the biochemical markers of osteoporosis and list some of their features/roles. Very imp!**

1-Bone formation markers:

Osteocalcin aka Bone Gla Protein #GIT

- **Produced by osteoblasts during bone formation**
- Involved in bone remodeling process
- Released during bone formation and resorption (bone turnover)
- Short half-life of few minutes
- Blood levels are influenced by vitamin K status and renal function

Bone-specific Alkaline Phosphatase

- **Present in osteoblast plasma membranes**
- Helps osteoblasts in bone formation
- **Non-specific marker**
- Its isoenzymes are widely distributed in other tissues
- The isoenzymes also interfere with the assay

P1NP (Procollagen type-1 amino-terminal propeptide) Listed under resorption markers in M slides

- **Produced by osteoblasts**
- Involved in the process of type 1 collagen formation
- Shows good assay precision
- Stable at room temperature
- Blood levels are highly responsive to osteoporosis progression and **treatmentP** for: **P**1NP and **P**rogression

2- Bone resorption markers:

CTX-1 (Carboxy-terminal cross-linked telopeptides of type 1 collagen)

- A component of type-1 collagen
- Released from type-1 collagen during bone resorption
- Blood and urine levels are highly responsive to post-**resorptive treatment**
- Levels vary largely by circadian variation

- **What's the best marker out of them ?** **CTX-1**

L4) Cushing Syndrome

The following questions are NOT based off of the doctor's notes. All of these questions were stolen from 438's revision file (thank you queen Lina).

Steroid hormone synthesis is important for MCQs not SAQ

- **List any three functions of glucocorticoids**
  1) Increase lipolysis 2) increase proteolysis 3) inhibit glucose uptake by the cells

- **List three conditions were CBG increases**
  1) Pregnancy 2) Estrogen therapy 3) Congenital

- **List four symptoms of Cushing's Syndrome**
  1) Moon face 2) Buffalo's hump 3) Purple stria 4) Hirsutism

- **What are the 3 screening tests?**
  1) Low-dose DST 2) 24h urinary free cortisol 3) Midnight salivary cortisol

- **When can we confirm Cushing's Syndrome ?**
  When at least two of the screening test comes positive

- **50 years old male comes with symptoms of Cushing's Syndrome, ACTH: 250 ng/L, Cortisol: 1400 nmol/L, showing no suppression after DXM. What is the most likely diagnosis?**
  Ectopic ACTH secreting tumor

- **What is the test that differentiate between Cushing disease and Ectopic ACTH secreting tumor?**
  -High-dose DST - Inferior petrosal sinus sampling

- **What is the most common cause of Cushing's Syndrome (ACTH-independent)?**
  -Glucocorticoids therapy

- **What is the disadvantage of 24h urinary free cortisol test?**
  incomplete collection of urine might cause false negative result

- **How many carbon atoms in each of the following:**
  - Cholesterol: 27 **- pregnenolone:** 21 **-cortisol:** 21 **-aldosterone:** 21 **-estradiol:** 18
  - Testosteron: 19

- **List the functions of glucocorticoids in:**
  liver : - gluconeogenesis -ketogenesis -increase amino acids uptake and degradation
  Adipose tissue: increase lipolysis
  muscles : increase proteolysis
  glucose : inhibit its uptake by the muscles and fat cells

- **Enumerate four conditions cause elevation in serum cortisol**
  1) cushing's syndrome 2) alcohol abuse 3) obesity 4) increased CBG

- **List one condition cause decrease in CBG**
  Nephrotic syndrome

- **What is the value for each of the following test to exclude cushing's syndrome?**
  Low dose DST: Cortisol <50nmol/L
  24h UFC: < 250nmol/day
  Midnight salivary cortisol: <100ng/dl

L5) Addison's Disease

Again, the following questions are NOT based off of the doctor's notes. All of these questions were stolen from 438's revision file (thank you queen Lina).

Steroid hormone synthesis is important for MCQs not SAQ

- **List the Adrenal cortex zones and mentions the hormone secreted.**

Zona Glomerulosa Aldosterone → **Zona Fasciculata** glucocorticoids → **Zona Reticularis** sex hormones

- **What is the principal physiological function of Aldosterone?**
  - conserve Na+,mainly by facilitating Na+ reabsorption and reciprocal K+ or H+ secretion in the distal renal tubule.
  - major regulator of water and electrolyte balance, as well as blood pressure.

- **What is the effect of Aldosterone on the distal convoluted tubule of kidneys?**
  ↑↑ potassium excretion., ↑↑ sodium and water reabsorption.

- **What are the functions of The Renin-Angiotensin System?**
  controls aldosterone secretion, involved in blood pressure regulation.

- **What is Renin?**
  -A proteolytic enzyme produced by the juxtaglomerular cells of the afferent renal arteriole.
  - Sensitive to blood pressure changes through baroreceptors.

- **When does Renin released to the circulation?**
  In response to:
  -fall in blood volume
  -fall in renal perfusion pressure
  -loss of Na+

- **What is the difference between primary and secondary Adrenocortical Hypofunction, Fill the table:**

Adrenocortical Hypofunction (AC)	Primary	Secondary
Causes	• Autoimmune • Infection (tuberculosis) • Infiltrative lesions (amylodosis)	• Pituitary tumors • Hypothalamic diseases • Vascular lesions • Head trauma • Iatrogenic (steroid therapy, surgery or radiotherapy)
Signs and symptoms	• Lethargy, weakness, nausea & weight loss. • Hypotension especially on standing (postural) • Hyperpigmentation (buccal mucosa, skin creases, scars) • Hypoglycemia, ↓Na+, ↑K+ and raised urea. • Life threatening and need urgent care. • Deficiency of both glucocorticoids and mineralocorticoids	
Signs and symptoms of Hyperpigmentation	• occurs because melanocyte- stimulating hormone (MSH) and (ACTH) share the same precursor molecule, Pro-opiomelanocortin (POMC). • The anterior pituitary POMC is cleaved into ACTH, γ-MSH, and β-lipotropin. • The subunit ACTH undergoes further cleavage to produce α-MSH, the most important MSH for skin pigmentation.	• In secondary adrenocortical insufficiency, skin darkening does not occur.

- **How adrenocortical insufficiency in Addison disease is diagnosed?**
  The diagnosis of adrenocortical insufficiency rests on the assessment of the functional capacity of the adrenal cortex to synthesize cortisol. This is accomplished primarily by use of the rapid adrenocorticotropic hormone (ACTH) stimulation test (Cortrosyn, cosyntropin, or Synacthen).

- **What are the abnormal results in short tetracosactrin (synacthen) test (short ACTH stimulation test) in the conformational test of Addison disease?**
  emotional stress /glucocorticoid therapy /estrogen contraceptives.

- **What are the investigations for Addison's disease on either :**
  Screening: -Basal plasma ACTH and basal serum cortisol, glucose, urea and electrolytes Screening -High ACTH and Low cortisol
  Confirmation: -short stimulation test: no response
  Others: -Adrenal autoantibodies -ultrasound/CT adrenal glands

L6) Obesity

Again, the following questions are NOT based off of the doctor's notes. All of these questions were stolen from 438's revision file (thank you queen Lina).

This lecture is most likely NOT for SAQ

- **CASE: A 38-year-old woman with obesity and a 5 year history of type 2 diabetes presents with complaints of fatigue, difficulty losing weight and no motivation to exercise. She told you that she's not interested in her hobbies anymore. her BMI was 34.6 and you noticed that her body fat deposited in the central abdominal area.**

  According to her BMI result, which grade of obesity does she has? What is her mortality risk? Grade I, she has moderate mortality risk.

  What shape of obesity does she has? Android / apple-shaped / upper body obesity.

  What type of fat is strongly associated with insulin resistance? Ectopic fat,

  List 3 associated risks with obesity other than the mentioned in the case? Hypertension / coronary heart disease / dyslipidemia.

  List 3 causes of weight gain? Energy imbalance / Endocrine disorder (hormonal imbalance) / Hypothalamus (control center for hunger and satiety).

  List 3 benefits of weight-loss? Lower blood pressure / Lower blood glucose levels / Decreased serum triacylglycerols.

  List 3 metabolic changes in obesity? Dyslipidemia / Glucose intolerance / Insulin resistance.

  List 3 environmental and behavioral factors that contributed to her obesity from the case? Her gender: women / lack of physical activity / Psychogenic: emotional deprivation - depression.

  She told you that during her last visit to the doctor, 5 months ago, she was prescribed Lorcaserin along with her diet and exercise plan but there was no improvement, what other drug could you prescribe to help her lose weight? Explain briefly its action.
  Orlistat, a pancreatic and gastric lipase inhibitor that decreases the breakdown of dietary fats.

- **What are the Biochemical differences in fat deposits?**

Abdominal Fat	Gluteal Fat
Smaller cells	Larger cells
More responsive to hormones (both visceral and subcutaneous)	Less responsive (subcutaneous)
Release substance via portal vein to the liver	Release substance to circulation with no effect on the liver

- **Explain what happens to the adipocyte when there's an overnutrition?**
  Triacylglycerols (fats) are deposited in adipocytes (fat cells) which can increase in size up to a limit (hypertrophy), If overnutrition prolonged, it will stimulates pre-adipocytes in adipose tissue to proliferate & differentiate into mature fat cells which increases adipocyte number (hyperplasia).

- **Explain what happens to the adipocyte when an obese person loses weight?**
  Fat cells once gained are never lost, reduction in weight causes adipocytes to reduce in size but not in number.

- **List the factors which contribute to obesity?**
  Genetics / Environmental and behavioral / Drugs (e.g. tricyclic derivatives).

- **List 3 regulatory adipokines released by the adipocytes?**
  Leptin / adiponectin / resistin.

- **What happens to the following hormones when the body is in an undernourished state?**
  - leptin: Decreases - Adiponectin: Decreases - Insulin: Decreases - Ghrelin: Increase - CCK: Decreases

- **What is the function of Leptin hormone? In which state it decreases & increases?**
  Regulates the amount of body fat by: decreasing the appetite and increasing the energy expenditure, it helps in weight loss, it's suppressed in starvation & enhanced in well-fed state.

- **List 3 actions of the Adiponectin hormone?**
  Promotes the uptake and oxidation of FA and glucose by muscle and liver / Blocks the synthesis of FA / block gluconeogenesis.

- **What is the net effect of Adiponectin hormone?**
  increase the sensitivity to insulin, and improve glucose tolerance.

L7) Glucose homeostasis

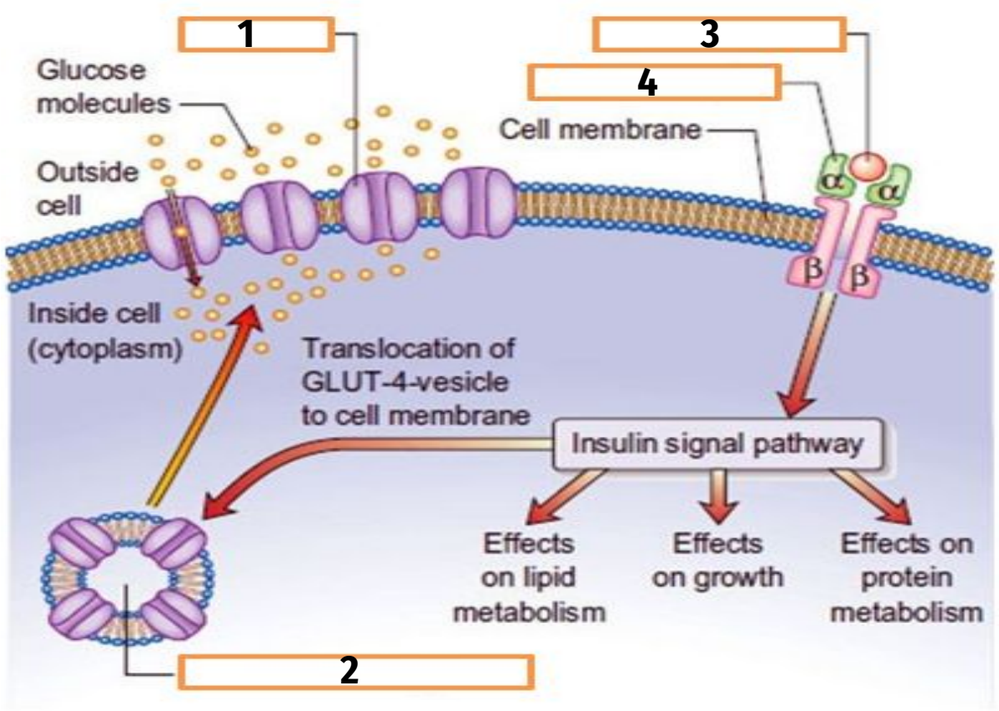
Again, the following questions are NOT based off of the doctor's notes. All of these questions were stolen from 438's revision file (thank you queen Lina).

Phases are more likely to come as MCQs

- **What are the sources of glucose?** Less likely
  1) Dietary sources 2) metabolic sources
- **List two of metabolic sources**
  1) glycerol 2) lactate 3) pyruvate 4) glucogenic amino acids
- **What are the phases of glucose homeostasis?**
  Phase I (well-fed) state, phase II (glycogenolysis), phase III (gluconeogenesis), phase IV (glucose, ketone bodies oxidation), phase V (fatty acid, ketone bodies oxidation)
- **List the phases which have hepatic gluconeogenesis as an origin of blood glucose?**
  phase II (glycogenolysis), phase III (gluconeogenesis), phase IV (glucose, ketone bodies oxidation), phase V (fatty acid, ketone bodies oxidation)
- **List the phases which have ketone bodies as major fuel of brain ?**
  phase IV (glucose, ketone bodies oxidation), phase V (fatty acid, ketone bodies oxidation)
- **List two phases with the origin of glucose, tissue using glucose and major fuel of brain.**
  Or, List two phases with 2 points regarding each phase (name of the phase is considered as a point**).**
  Phase I: exogenous, All and glucose
  Phase II: hepatic gluconeogenesis, All except liver muscle and adipose tissue and glucose
  Phase III: hepatic gluconeogenesis, All except liver muscle and adipose tissue and glucose
  Phase IV: hepatic gluconeogenesis, RBCs and ketone bodies
  Phase V:hepatic gluconeogenesis, RBCs and ketone bodies

★ **What is the effect of insulin on CHO metabolism ?** (4 points are enough)
1) stimulates glycogen synthesis 2) Increases glycolysis 3) Stimulates Protein synthesis
4) Decreases blood glucose level by increasing its uptake into cells 5) Inhibits gluconeogenesis 6) Inhibits glycogenolysis

- **What does Insulin secretion inhibits?**
  1) Lipolysis 2) Ketogenesis 3) Proteolysis 4) Glycogenolysis
- **Identify the numbers**



1. GLUT-4
2. GLUT-4 containing vesicles
3. Insulin molecules
4. Insulin receptor

★ **List the effects of cortisol .**
1) Maintain normal glucose level during fasting by :
- Mobilizes amino acids for gluconeogenesis.
- Stimulate gluconeogenesis in liver
- Inhibits glucose uptake by cells

2) Stimulates fat breakdown in adipose tissue.

★ **How does growth hormone maintain blood glucose level?**
- By inhibiting insulin action and stimulating gluconeogenesis in the liver

★ **How does epinephrine maintain blood glucose level?**
By stimulating lipolysis in adipose tissue and glycogenolysis in skeletal muscle

L8) Metabolic changes in DM

Diabetic Microvascular Complications more likely to be MCQs

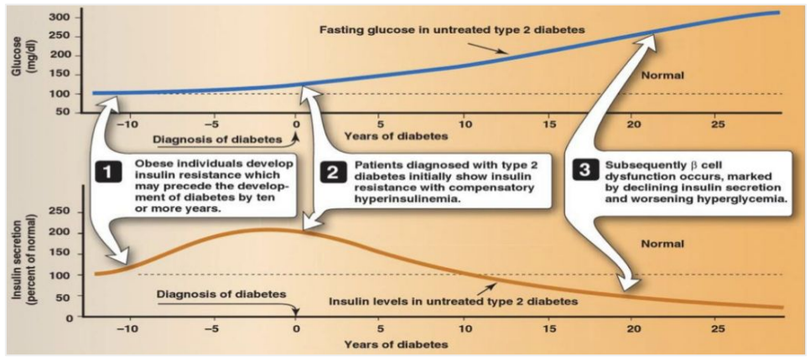
- **List any 2 differences between T1DM and T2DM?**

	Type 1 Diabetes	Type 2 Diabetes
AGE OF ONSET	Usually during childhood or puberty; symptoms develop rapidly	Frequently after age 35; symptoms develop gradually
NUTRITIONAL STATUS AT TIME OF DISEASE ONSET	Frequently undernourished	Obesity usually present
PREVALENCE	10% of diagnosed diabetics	90% of diagnosed diabetics
GENETIC PREDISPOSITION	Moderate	Very strong
DEFECT OR DEFICIENCY	β Cells are destroyed, eliminating production of insulin	Insulin resistance combined with inability of β cells to produce appropriate quantities of insulin
FREQUENCY OF KETOSIS	Common	Rare
PLASMA INSULIN	Low to absent	High early in disease; low in disease of long duration
ACUTE COMPLICATIONS	Ketoacidosis	Hyperosmolar state
RESPONSE TO ORAL HYPOGLYCEMIC DRUGS	Unresponsive	Responsive
TREATMENT	Insulin is always necessary	Diet, exercise, oral hypoglycemic drugs; insulin may or may not be necessary. Reduction of risk factors (smoking cessation, blood pressure control, treatment of dyslipidemia) is essential to therapy.

★ **In which one of the marker area in the picture you will notice a marked decrease in insulin?**

- Number **3**

- Very important pic
- They may ask you about what in the pic "empty boxes" so you HAVE to study it very well
- The question might come as (fill the empty boxes) or explain what happens in each stage



- **If you do Random blood glucose what is the number that you will be expecting in diagnosis of diabetes?**
  - **≥200 mg/dL + the classic symptoms of hyperglycemia**

- **13 y.o girl presented to emergency department complaining of increased thirst,frequent urination and weight loss, has been diagnosed with T1DM, what will you have in the circulation?**
  - hyperglycemia, ketonemia, dyslipidemia (VLDL and chylomicrons).

★ **What is the Mechanisms of Increase Hepatic Glucose Output ?**

-Decrease insulin > Decrease inhibitory effect on glucagon secretion > Increase glucagon > Increase gluconeogenesis > Increase plasma glucose

★ **What are the mechanism of action of decrease peripheral glucose uptake on....?**

adipose tissue: -Decrease insulin > decrease glucose uptake > increase plasma glucose.
Muscle : Decrease insulin >increase protein breakdown and decrease glucose uptake > increase plasma glucose and amino acid

★ **What are the General mechanisms for microvascular complications in DM?**
Or **What are metabolic changes during DM that caused by chronic hyperglycemia?**

- Chronic Hyperglycemia, leads to:

1) **Increase AGEs** of essential cellular proteins → "cellular defect".
2) **Increase Intracellular Sorbitol** → Increase cell osmolality → "cellular swelling".
3) **Increase ROS** → Oxidative stress → "cell damage".

- **What happens in Polyol Pathway?**
  - Excess Glucose is metabolized to sorbitol within the cells by **aldose reductase.**

- **How do the seminal vesicles and ovaries not be affected by sorbitol?**
  - In seminal vesicles and ovaries there is enzyme called **sorbitol dehydrogenase** that converts sorbitol to fructose.

★ **Explain the 2 pathways of AGEs, that contribute in diabetic complications.**

1) AGEs may cross link **with collagen** which leads to "microvascular complications".
2) AGEs may interact with **their receptor (RAGE)** and may generate reactive oxygen species (ROS) which leads to "Inflammation".

- **Briefly, Explain the hypotheses of sorbitol role in the pathogenesis of diabetic complications.**
  - **1st hypothesis|** During sorbitol production, consumption of **NADPH** → "oxidative stress".
  - **2nd hypothesis|** Sorbitol accumulation will:
    A) Increase the intracellular **osmotic pressure** → osmotic drag of fluid from extracellular space → "cell swelling".
    B) Alteration in the activity of **PKC** → altered **VEGF** activity → "altered vascular permeability".

- **What is the sequence of events in Diabetic Nephropathy?**
  - Glomerular hyperfiltration → Microalbuminuria → Proteinuria & ↓ GFR → End stage renal disease.

L8) Metabolic changes in DM

★ **What are metabolic effects caused by absolute or relative deficiency of insulin on carbohydrates metabolism?**

-Decrease glucose uptake by certain tissues (Adipose tissue and muscle)
- Increase glycogenolysis .
- Increase gluconeogenesis.

★ **What are metabolic effects caused by absolute or relative deficiency of insulin on lipid metabolism ?**

- Increase lipolysis.
- Increase fatty acid oxidation.
- Increase production in ketone bodies.

★ **What are metabolic effects caused by absolute or relative deficiency of insulin on protein metabolism?**

- Decrease protein synthesis.
- Increase protein degradation.

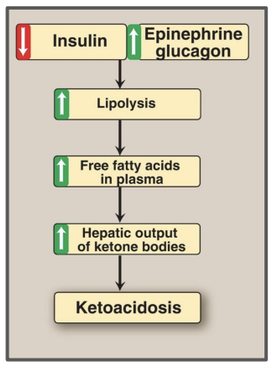
L9) Diabetic Ketoacidosis

-No brain figure
-MCQ for the enzymes
-no ketolysis picture

- **What are the ketone bodies?/list 3 ketone bodies involved in DKA.**
  Acetoacetate, acetone, β-Hydroxybutyrate

★ **Write three clinical manifestations of diabetic ketoacidosis**
1) Fruity odor on breath
2) Acidosis
3) Dehydration

★ **What is the mechanism of DKA/How do hormone changes in DM lead to DKA?**



Again, you can draw or write in your own words.

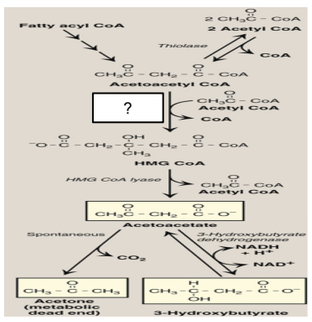
★ **What are the precipitating factors for DKA? (list 4 at least)**
Infection, Trauma, Drugs, Inadequate insulin treatment or noncompliance, severe illness

★ **Why is DKA more common in T1DM over T2DM?** (HONK pathogenesis)
In T1DM there is absolute insulin deficiency; however, in T2DM insulin levels are sufficient enough to prevent lipolysis and subsequent ketogenesis but not enough to allow appropriate glucose utilization.

- **What are the three diabetic Emergencies?**
  1) Diabetic Ketoacidosis (DKA)
  2) Hyperosmolar hyperglycaemic state (HHS)=Hyperosmolar non-ketotic acidosis (HONK)
  3) Hypoglycemia

- **What are the triad for DKA?**
  Hyperglycemia, Ketonemia, High anion gap metabolic acidosis

- **Fill in the empty box**
  HMG CoA Synthase



- **Where does Ketogenesis occur?**
  Hepatocyte mitochondria

- **What is the rate limiting Enzyme in Ketogenesis?**
  HMG CoA Synthase

- **Where does Ketolysis take place in?**
  Extrahepatic tissue

- **What is the diabetic emergency where Insulin levels are insufficient to allow appropriate glucose utilization but are adequate to prevent lipolysis and subsequent ketogenesis and the serum glucose often >50 mmol/L and Plasma osmolality may reach 380 mosmol/Kg?**
  Hyperosmolar hyperglycemic state (HHS)= Hyperosmolar non-ketotic acidosis (HONK)

- **What type of patients hypoglycemia mostly occurs?**
  Type 1 DM patients

★ **Why hypoglycemia is a medical emergency?**
The brain has absolute requirement for a continuous supply of glucose otherwise it will lose its function(cerebral dysfunction) if the hypoglycemia is transient or die(brain death) if the hypoglycemia is severe, prolonged.

L9) Diabetic Ketoacidosis

★ **Manifestations of hypoglycemia?**
CNS symptoms(confusion, aberrant behavior, or coma), low blood glucose, symptoms resolved within minutes following the administration of glucose

- **What is the impaired Protective responses in hypoglycemia?**
Insulin is supplied exogenously and its release cannot be turned off
Glucagon & adrenaline response to hypoglycemia becomes impaired later in the course of DM

★ **What is the clinical presentation of hypoglycemia** Or might specify and af for symptoms of sympathetic overactivity/neuroglycopenia. You don't need to know any numbers
Sympathetic overactivity: anxiety, tremors, sweating, and palpitation
Neuroglycopenia: headache, confusion, drowsiness, and ultimately, loss of consciousness

★ **The following table is regarding hormone involvements in the correction of hypoglycemia. Fill it in with yes or no.**

	Cortisol	Norepinephrine Epinephrine	Glucagon
Glyco-genolysis	?	?	?
Gluconeo-genesis	?	?	?

Cortisol: gluconeogenesis only
Epinephrine: glycogenolysis only
Glucagon: glycogenolysis **and** gluconeogenesis

- **what is the hormonal mechanisms to prevent or correct hypoglycemia?**
Decrease production of insulin
Increase Production of:
-Epinephrine & glucagon
-Growth hormone
-Cortisol

- **-A 14-year-old girl was admitted to a children's hospital in coma. Her mother stated that the girl had been in good health until approximately 2 weeks previously, when she developed a sore throat and moderate fever. She subsequently lost her appetite and generally did not feel well Several days before admission she began to complain of undue thirst and also started to get up several times during the night to urinate. However, on the day of admission the girl had started to vomit, had become drowsy and difficult to arouse, and accordingly had been brought to the emergency department**

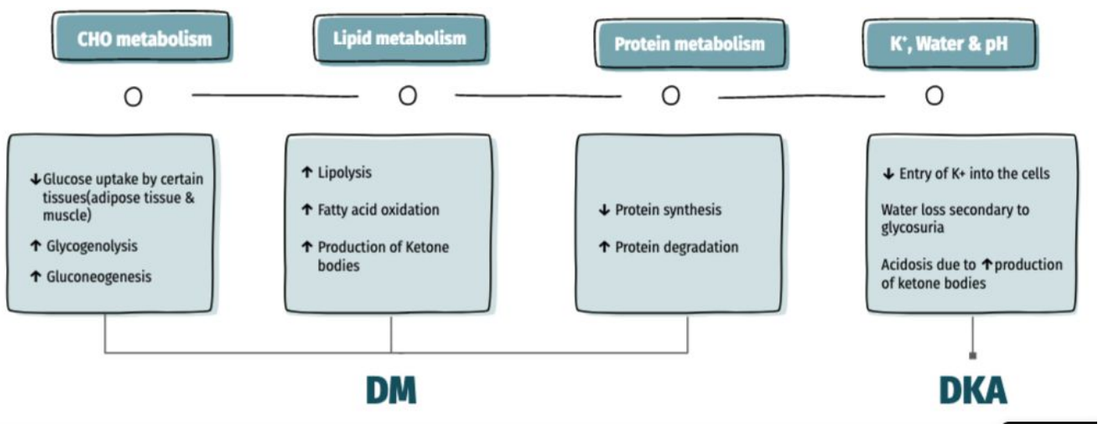
A- what do you expect to find on examination?
She will be dehydrated Her skin cold and breathing in a deep sighing manner (Kussmaul respiration) Her breath has a fruity odor. She won't be aroused

B- what is the diagnosis?
T1DM with complicating ketoacidosis and coma (DKA)

C- what do you expecting to find abnormally from urine results?
High amount of Glucose and ketoacids

D- interpret the blood results shown below.

★ **what are the metabolic changes in DM and DKA?**



L10) Metabolic Syndrome

Not imp:
-Associations, and risk factors
-Managing metabolic syndrome
-lowering blood pressure

- **Define metabolic syndrome**
  A combination of metabolic abnormalities that increase the risk of heart disease, diabetes, and other diseases.

- **List the features of metabolic syndrome?**
  Hypertension, obesity, high serum TAGs, hyperglycemia , insulin resistance , low HDL

- **Explain the pathophysiology of dyslipidemia in metabolic syndrome?** (Less likely for SAQ, more for MCQs)

Insulin resistance in adipocytes (in obese individuals) → **increased activity of hormone sensitive lipase** → **High plasma FFAs ⇒** get carried to the liver & converted to: **TG/cholesterol in the liver** → **Excess TGs/ cholesterol are released as VLDL to the blood** → **HDL levels are decreased**

★ **List the markers that are helpful in the diagnosis of metabolic syndrome?**
Lipoproteins (high LDL, low HDL)
Adipokines (high or normal Leptin, low bc is parallel with HDL levels adiponectin)
Inflammatory markers (all will be high: c-reactive protein, IL-6, IL-8, TNF-α)
Hemostatic marker (high Plasminogen activator inhibitor-1)

- **What are the components of the criteria used to diagnose metabolic syndrome based on NCEP ATP III Guideline? (Unlikely)**
- Three or more of the following:
- Weight circumference
- Triglycerides
- HDL cholesterol
- Blood pressure
- Fasting glucose

- **List the current treatments for metabolic syndrome.**
  - For hypertension → ACE inhibitors and low dose of diuretics
  - For clotting disorders → aspirin
  - For hyperglycemia (DM 2) → Metformin & thiazolidinedione
  - For dyslipidemia → statins and fibrates

- **How fibrates are helpful to a patient with metabolic syndrome ?**
- **Or, Fibrates were prescribed for a patient with metabolic syndrome, what is the MOA of these drugs?**

Reduce blood lipid levels by Activating transcription factor: Peroxisome proliferator activated receptor-α (PPAR- a). Activated PPAR- α will lead to transcription of genes of lipid degradation/uptake by the cells:

- Carnitine: palmitoyl transferase I (enhances FA uptake into mitochondria)
- Lipoprotein Lipase
- Stimulates apoAI and apoAII protein synthesis (major proteins in HDL)

This work was done by :

Leaders


Sadeem Alzayed


Ghada Alabdi


Osama Alharbi

Revised by


Shatha Aldhohair

Shout out to the 438 biochemistry team for their help. This whole file was based off of their work!

Special thanks to Fahad AlAjmi for designing our team's logo.