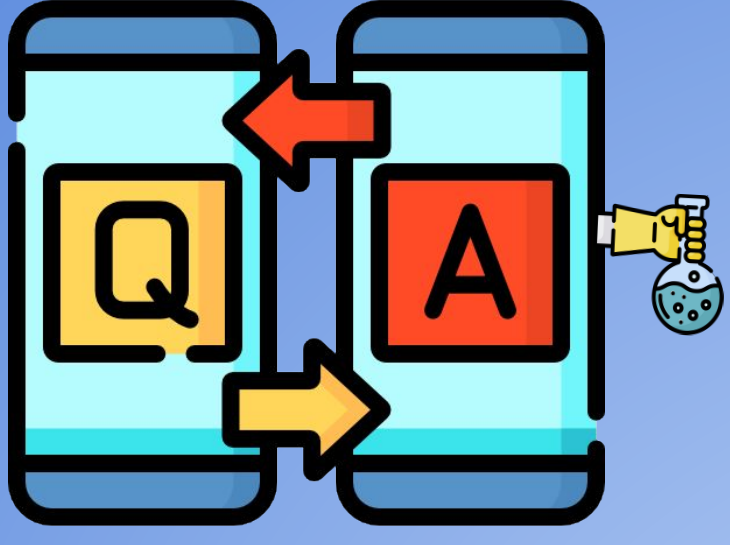
Summary



General Mechanism of Hormone Actions

Q1: Compare between lipophilic and hydrophilic hormones using the table below:

	Lipophilic	Hydrophilic
Transport proteins	Yes	No
Plasma half-life	Long (Hours-Days)	Short (Minutes)
Receptor	Intracellular	Plasma membrane
Mediator	Receptor-hormone complex	• cAMP • cGMP • Ca++, Metabolites of complex phosphoinositols • Tyrosine kinase cascade.

Q2: List the examples for each class mentioned below:

1- Steroid-Thyroid superfamily (Intracellular receptors)

- **Steroid Hormones:**
  - Glucocorticoids
  - Mineralocorticoids
  - Sex hormones:
    - **Male sex hormones:** Androgens
    - **Female sex hormones:** Estrogens & Progestins
- **Thyroid Hormones (T3 & T4)**
- **Calcitriol (1,25[OH]2-D3)**
- **Retinoic acid**

2- cAMP:

- **Catecholamines (a2- Adrenergic)**
- **Catecholamines (beta- Adrenergic)**
- **Ant. Pituitary: ACTH, FSH, LH & TSH**
- **ADH (Renal V2-receptor)**
- **Calcitonin & PTH**
- **Glucagon**

3- cGMP:

- **Atrial natriuretic peptide (ANP)**
- **Nitric oxide**

4- Ca++&PI:

- **Acetylcholine (muscarinic)**
- **Catecholamines (a1- Adrenergic)**
- **Angiotensin II**
- **ADH (vasopressin): Extra-renal V1-receptor**

5- Tyrosine kinase:

- **Insulin**
- **GH & Prolactin**
- **Erythropoietin**

Q3: Mention the biological effects of insulin:

PROMOTE: Glucose uptake, Glycogen synthesis, Fat synthesis, Protein synthesis.
INHIBIT: Gluconeogenesis, Glycogenolysis, Lipolysis.

Thyroid Hormones and Thermogenesis

- **List the types of plasma proteins transporting thyroid Hormones**
  1) Thyroxin-Binding globulin (70%)
  2) Albumin (25%)
  3) Transthyretin "pre albumin" (5%)

- **What are the key steps in thyroid hormones synthesis?**
  1. Iodination
  2. Coupling
  3. Binding to thyroglobulin

- **Give 3 examples of thyroid hormone actions**

  1. Plays an essential role in maturation of all body tissues
  2. Involved in thermogenesis and metabolic regulation
  3. Increases cellular oxygen consumption and stimulates the metabolic rate
  4. Affects the rate of protein, carbohydrate and lipid metabolism

- **Explain why hypothyroid patients have high serum cholesterol?**
  1. Down regulation of LDL receptors in liver cells
  2. Failure of sterol excretion in the gut

- **Explain the mechanism of regulation of thyroid hormone secretion**
  1. The hypothalamus senses low levels of T3/T4 and releases thyrotropin releasing hormone (TRH)
  2. TRH stimulates the pituitary to produce thyroid stimulating hormone (TSH)
  3. TSH stimulates the thyroid to produce T3/T4 until levels return to normal
  4. T3/T4 exert negative feedback control on the hypothalamus and pituitary

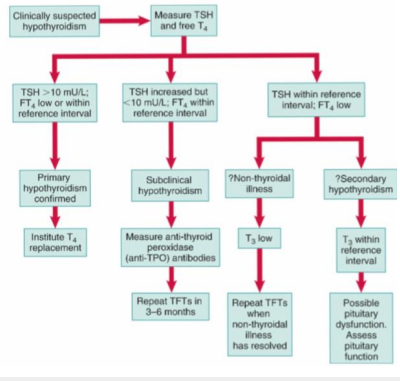
- **Give 3 types of thyroid function tests with their uses**
  1. TSH (highly sensitive)
  2. Total or free T4 (Monitors thyroid treatment)
  3. Total or free T3 (For earlier identification of thyrotoxicosis)
  4. Antibodies (diagnosis and monitoring of autoimmune thyroid disease)

- **Enumerate 4 causes of goiter**
  1. Iodine, selenium deficiency
  2. Hashimoto's thyroiditis
  3. Graves' disease (hyperthyroidism)
  4. Congenital hypothyroidism / thyroid cancer

- **Enumerate 4 causes of hypothyroidism**
  1. Hashimoto's thyroiditis
  2. Radioiodine or surgical treatment of hyperthyroidism
  3. Drug effects
  4. TSH deficiency
  5. Congenital defects in thyroid synthesis / thyroid resistance
  6. Severe iodine deficiency

- **Enumerate 4 clinical features of hypothyroidism**
  1. Tiredness
  2. Cold intolerance
  3. Weight gain
  4. Dry skin

- **Complete the following diagram**



Thyroid Hormones and Thermogenesis

- **Explain how does hyperthyroidism start?**
  it can happen by hyperstimulation of thyroid gland by pituitary gland or can be caused by hyperstimulation of the thyroid itself which will cause hypersecretion of thyroid hormones.

- **what can causes hyperthyroidism?**
  1. Graves' disease
  2. Toxic multinodular goitre
  3. thyroid adenoma

- **Enumerate 4 clinical features of hyperthyroidism**
  1. weight loss with normal appetite
  2. heat intolerance
  3. fatigue
  4. tremor

- **What is the relation between hyperthyroidism and Graves' disease?**
  1. most common cause of hyperthyroidism
  2. an autoimmune disease which causes antibodies against TSH receptors on thyroid gland these antibodies mimic the action of the pituitary hormone which causes hypersecretion of thyroid hormone.

- **How to diagnose primary hyperthyroidism?**
  1. low TSH
  2. High thyroid hormones

- **What are the problems that might affect the diagnosis in hyperthyroidism?**
  1. Total serum T4 varies due to changes in binding protein levels
  2. pregnancy due to high estrogen leading to increased TBG synthesis

- **Give 3 ways that can be used to treat hyperthyroidism?**
  1. Antithyroid drugs such as carbimazole
  2. radioiodine
  3. surgery; thyroidectomy

- **What are the two types of thermogenesis and the difference between them?**
  1. obligatory: due to basal metabolic rate
  2. facultative: on demand extra heat from brown adipose tissue and skeletal muscle

- **The thyroid hormones regulate which mitochondrial UCPs and in what cells?**
  1. UCP1 in brown adipose tissue
  2. UCP3 in muscle, other tissues

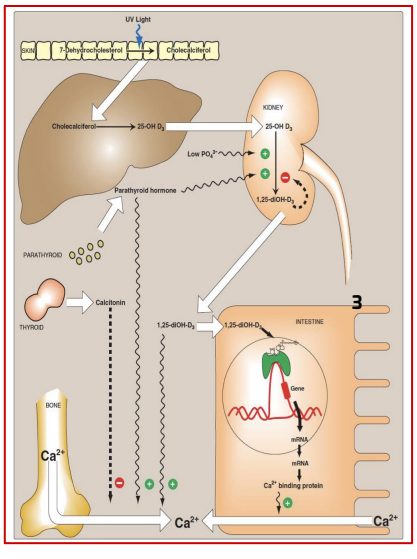
- **What is the relation between thyroid hormones and thermogenesis?**
  1. thyroid hormone play essential roles in thermogenesis
  2. it upregulates body temperature set by the brain
  3. it acts centrally on the hypothalamus that controls brown adipose tissue for thermogenesis

Vitamin D, Rickets & Osteoporosis

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

- **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 the next figure.**



1. in the skin 7- dehydrocholesterol will be converted to cholecalciferol by UV light (active)
2. first hydroxylation in the liver covert cholecalciferol to 25-hydroxycholecalciferol by the enzyme 25-hydroxylase (inactive) it's the stored and prominent form and the one measured in the lab.
3. second hydroxylation convert 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol by the enzyme 1-a-hydroxylase (active)

This reaction is tightly regulated by the level of phosphate (directly), calcium (indirectly,)and Negative feedback.

Vitamin D has a steroid like hormone activity, it diffuse through cell membrane and bind to cytosolic receptor this complex then inter into the nucleus to interact with the DNA to increase gene expression of calcium binding protein which will carry calcium from intestinal epithelium to the blood circulation.

- **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.**
  -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

- **Enumerate the reasons behind the high prevalence of vitamin D deficiency in saudi arabia.**
  -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.

- **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, Calcium (low) , Phosphate , Alkaline phosphatase	

Vitamin D, Rickets & Osteoporosis

- **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.



Fig. 2 Crush fractures of vertebral bodies in a patient with osteoporosis.
Fig. 3 Elderly woman with so-called 'Dowager's hump' from collapsed vertebrae due to osteoporosis.

- **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.

- **List the biomarkers of osteoporosis.**

Bone formation markers:

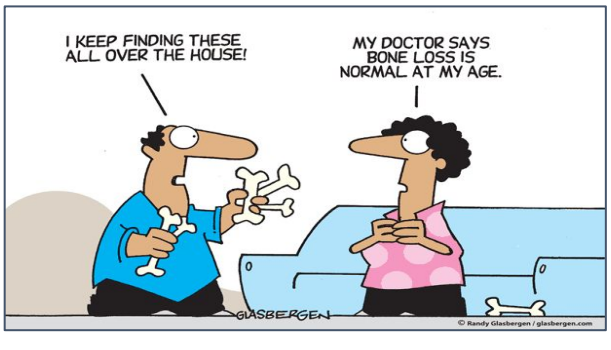
Osteocalcin
- Produced by **osteoblasts** during bone formation
- **Involved in bone remodeling process**
- Released during bone formation and resorption (bone turnover)
- Short half-life of few minutes

Bone-specific alkaline phosphatase
- Present in osteoblast plasma membranes
- Helps osteoblasts in bone formation
- A Non-specific marker
- Its isoenzymes are widely distributed in other tissues

P1NP (Procollagen type-1 amino-terminal propeptide.
- Produced by **osteoblasts**
- It has a good precision
- Involved in the process of type 1 collagen formation
- Blood levels are highly responsive to osteoporosis progression and treatment

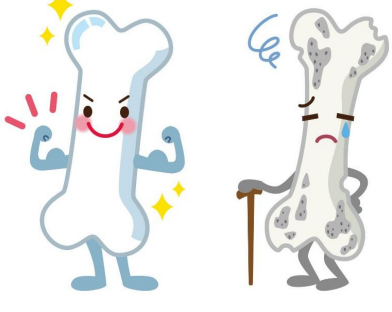
Bone resorption markers:

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



- **Enumerate the treatment and prevention options in osteoporosis.**

Treatments: oral calcium , estrogens , fluoride therapy , bisphosphonates (inhibits bone resorption).
Prevention : Diet , exercise and hormone replacement therapy.



^ See...it's up to you either you drink your milk or be prepared for the consequences
-L

Cushing Syndrome

- **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 signs 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

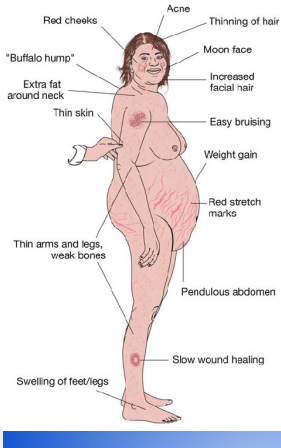
- **Enumerate four conditions cause elevation in serum cortisol**

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



Addison's Disease

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

Zona Glomerulosa	Zona Fasciculata	Zona Reticularis
Aldosterone	glucocorticoids	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 circulating 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 is adrenocortical insufficiency in Addison disease 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

Obesity

- **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.

Metabolic Syndrome

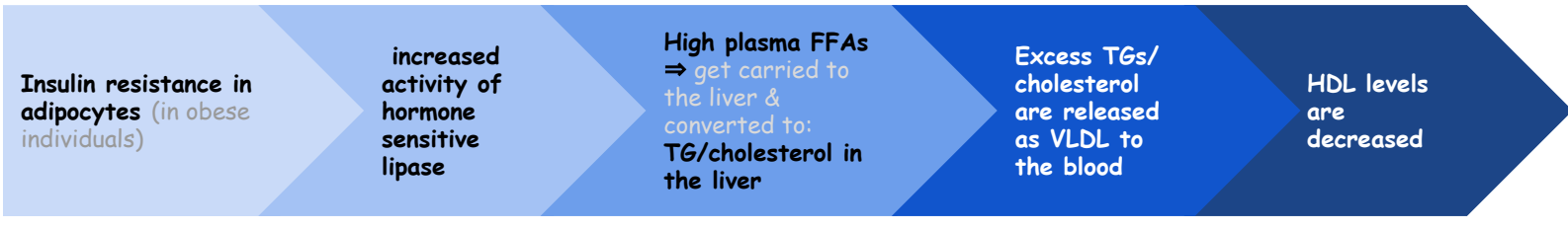
- **Define metabolic syndrome**
  A combination of metabolic abnormalities that increase the risk of heart disease, diabetes, and other diseases.

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

- **Mention 3 risk factors for metabolic syndrome?**
  Alcoholism, smoking, mutations in insulin receptor

- **What are the predominant effects of obesity?**
  Dyslipidemia, glucose intolerance, insulin resistance, hypertension

- **Explain the pathophysiology of dyslipidemia in metabolic syndrome?**



- **List 3 inflammatory markers helpful in the diagnosis of metabolic syndrome?**
  IL-6, IL-8, CRP

- **What are the components of the criteria used to diagnose metabolic syndrome based on NCEP ATP III Guideline?**

- Three or more of the following:
- Weight circumference
- Triglycerides
- HDL cholesterol
- Blood pressure
- Fasting glucose

- **What are the components of the criteria used to diagnose metabolic syndrome based on the WHO?**

- Impaired glucose tolerance, DM, or insulin resistance plus 2 of the following:
  - Hypertension > 140/90
  - Dyslipidemia
  - Central or general obesity
  - Microalbuminuria

- List everything related to metabolic syndrome.

- Heart disease - Diabetes mellitus type 2 - Kidney disease
- reproductive abnormalities in women - nonalcoholic steatohepatitis
- Cancer (esophagus , colon , rectum , liver and gallbladder)

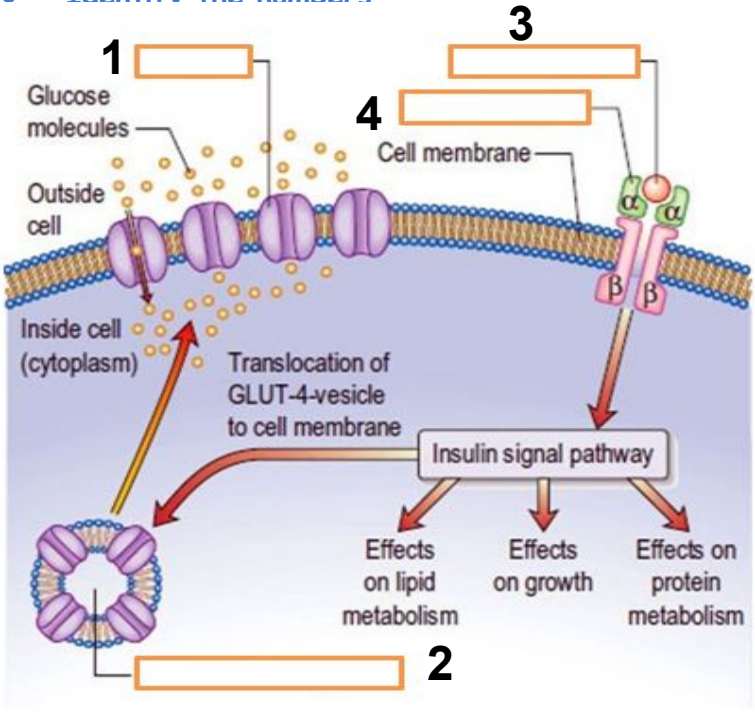
- List the current treatments for metabolic syndrome.

For hypertension → ACE inhibitors and low dose of diuretics
For clotting disorders → aspirin
For hyperglycemia (DM 2) → Metformin & thiazolidinedione
For dyslipidemia → statins and fibrates

Color me

Glucose Homeostasis

- **What are the sources of glucose?**
- 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?**
  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 does Insulin secretion stimulates?**
- 1) Glycolysis 2) Glycogen synthesis 3) Protein synthesis 4) Uptake of K+ and PO4
- **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

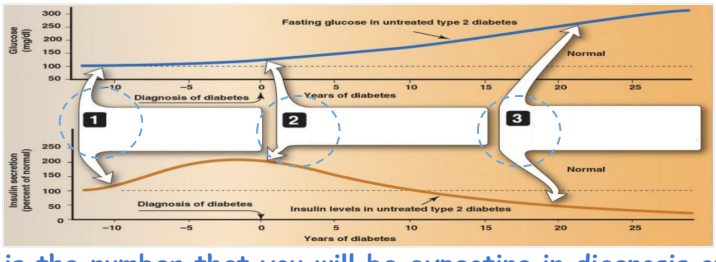
- **List three functions of cortisol**
- 1) Maintain normal glucose level during fasting 2) Stimulate gluconeogenesis in liver
  3) Mobilizes amino acids for gluconeogenesis
- **How does growth hormone maintain blood glucose level?**
- By inhibiting insulin action and stimulating gluconeogenesis in the liver

Metabolic Changes in Diabetes Mellitus

- **List any 2 different between T1DM and T2DM?**
  - See picture

	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**



- **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 are the mechanism of action of decrease peripheral glucose uptake on adipose tissue?**
  - Decrease insulin > decrease glucose uptake > increase plasma glucose.

- **What are the General mechanisms for microvascular complications in DM?**
  - 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.

Diabetic Ketoacidosis

- **Write three clinical manifestations of diabetic ketoacidosis**

- 1) Fruity odor on breath 2) Acidosis 3) Dehydration

- **What are the precipitating factors for DKA?**

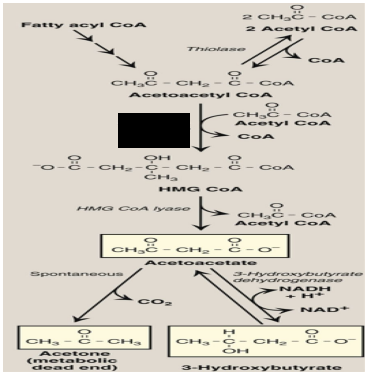
Infection, Trauma, Drugs, Inadequate insulin treatment or noncompliance, severe illness

- **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 the box on black**

- 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 he will loss his function or die

- **What is the impaired Protective responses in hypoglycemia?**

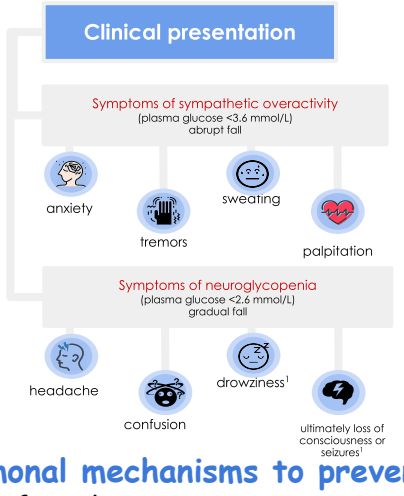
Insulin is supplied exogenously and its release cannot be turned off

impaired Protective responses

Glucagon & adrenaline response to hypoglycemia becomes impaired later in the course of DM

Diabetic Ketoacidosis

-How is the clinical presentation will be if the hypoglycemic patient has plasma glucose
A- <3.6 mmol/L
B- <2.6 mmol/L
C- <1.5 mmol/L



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

- OBJ: 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)

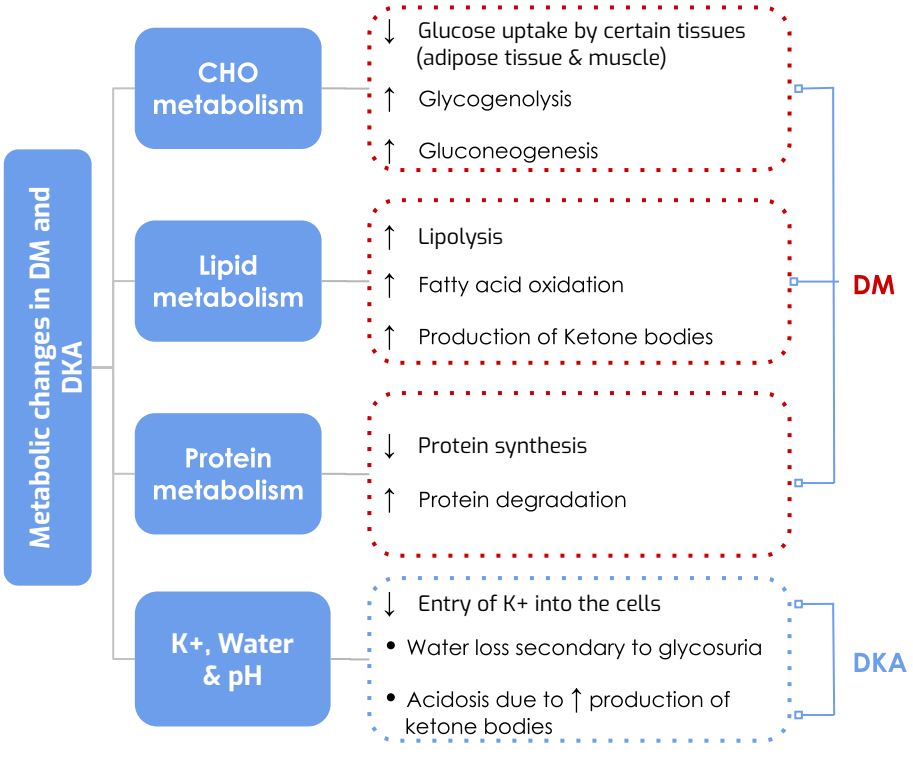
C- what do you expecting to find abnormally from urine results?
High amount of Glucose and ketoacids

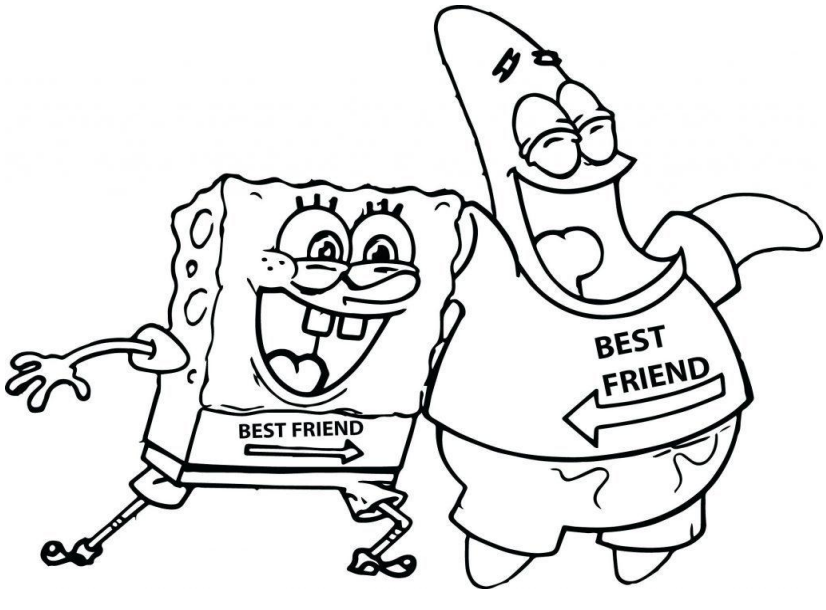
D- interpret the blood results shown below.

Result	Interpretation
Hyperglycemia	Confirm the diagnosis of DKA
Glucosuria	
Ketonemia	
Ketonuria	
↓ pH	Severe metabolic acidosis due to ↑ production of ketone bodies
↓ Bicarbonate and PCO2	Metabolic acidosis with partial respiratory compensation (the hyperventilation)
↑ Anion gap	Due to ↑ ketone bodies in the blood
↑ Urea & creatinine	1. Renal impairment (dehydration →↓ blood volume →↓ renal perfusion) 2. Dehydration 3. Degradation of protein (for urea)
↑ K+	↓ Uptake of potassium by cells in the absence of insulin
↑ Plasma osmolality	Due to hyperglycemia and fluid loss

Diabetic Ketoacidosis

- what is the metabolic changes in DM and DKA?





Color me and share it with your bestie !!

^ طلعوا مواهبكم الخفية وش ورانا غير التسدح و الاكل في الحجر المنزلي

Success is no accident. It's hard work, perseverance, learning, studying, sacrificing and most of all, love what you're doing or learning to do.

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