- why cholesteral levels may be elevated ?
  result of an individual's lifestyle

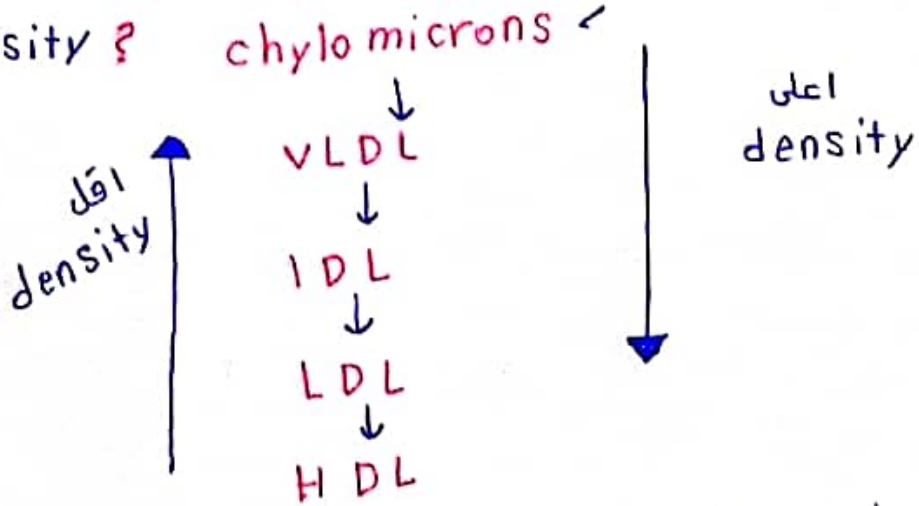
- what is cause hyperlipidemias ?
  genetic + lifestyle factors

- what is the major lipids in the body ?
  cholesterol + triglyceride + phospholipids

- what is the lipoproteins ?
  are complexes act on plasma lipids transported

- why plasma lipids are transported in the body by lipoproteins ? Because they are relatively water insolable

- Arrangement the lipoproteins according to their density ?



- what structure of lipoproteins have ?
  - hydrophobic core → cholesteryl esters.
    → triglycerides.
  - hydrophilic outer surface → unesterified cholesterol
    → phospholipids.
    → apoproteins.

Lipoproteins metabolism

① Small intestine —secretes→ chylomicron

Liver —secretes→ VLDL

→ بيحتوا على app cII وابد خلوا في الـ capillary

② تحتوي الـ capillary على lipoprotein lipase الذي يحدث له activated بواسطة app cII ويعمل على degrades الـ trigly-ceride في الـ chylomicron والـ VLDL

بيتحول جزء من الـ CM + VLDL الى fatty acid في الخلاياء → in cells: free fatty acids

VLDL بيتحول الى IDL

IDL بيتحول الى LDL

LDL → Tissue

③ LDL bind to receptor on tissue and on the liver, where they are endocytosed.

LDL → Liver

④ CM remnants bind to receptors on liver, where they are endocytosed.

chylomicron remnant → Liver

الجزء المتبقي من CM بروح الى الـ Liver وابيرتبط بـ receptors وا بحدثلة endocytosed

- what is the rate-limiting step in hepatic cholesterol Synthesis ?

HMG-(CoA) $\xrightarrow[\text{reductase}]{\text{HMG-(CoA)}}$ mevalonate

- How we can inhibit HMG-CoA reductase ?
  by Statins

- How we can reduce the cholesterol in blood ?
  by inhibit HMG-(CoA) reductase = (Statins)

- what the Rate-controlling enzyme in cholesterol Synthesis ? HMG-(CoA) reductase

- ↑ HMG-(CoA) reductase, ↑ Mevalonate , ↑ cholesterol

- what are the two mechanisms by which Statins reduce LDL levels ?
  ① ↑ LDL receptors
  ② ↓ VLDL release

- HMG-(CoA) reductase inhibitor except atorvastatin and rosuvastatin should be given in the evening if a single daily dose is used . True

- The most effective drug to reduce LDL cholesterol is?
  statins = HMG-(CoA) reductase inhibitor

- what is the adverse effects to Statins ?

① ↑ aminotransferase → upto three time normal
→ occure in some patients
→ intermittent
→ not associated with hepatic toxicity

② ↑ creatine kinase → from skeletal muscle
→ in 10% of patients
→ muscle pain
→ rhabdomyolysis
→ upto 10 time normal

③ hepatotoxicity and myopathy

④ ↑ effect of warfarin ⑥ HF

⑤ teratogenic .

- HMG-CoA reductase inhibitor Should be avoided in pregnancy. (True)

- what is the mechanism of action Bile acid-binding resins :- bile acid-binding resins bind bile acids in intestine and prevent their absorption which ↓ cholesterol in liver, thereby liver will act compensatory mechanism:
- ↑ LDL receptor
- ↑ removal of LDL from blood .

- Bile acid-binding resins → cholestyramine, colestipol, colesevelam → are taken orally

- Bile acid-binding resins
  - → insoluble
  - → very large more than 10^6
  - → nonabsorbed
  - → non metabolically altered
  - → excreted in feces

- Bile acide-binding resins should be taken in two or three doses with meals . True

- Bile acid-binding resins no metabolized in kidneys or liver . True

- what is the Adverse effects to bile acid-binding Resins ?

-GI effect → GI disturbances → (بقللالوها على GI عن طريق) 1.↑ dietary fiber. 2.↑ mixing psyllium seed .

- Impaired absorption (D, E, K, A) → At high doses → cholestyramine, colestipol

- Drug interaction :
tetracycline, phenobarbital, digoxin, warfarin, folic acid, pravastatin, fluvostatin, thiazide diuretics, aspirin, ezetimibe
\+
cholestyramine or colestipol
||
↓ absorption
الهم

- drug should be taken at least 2 hours after the bile acid-binding resins . True

- colesevelam does not bind → digoxin .
  → warfarin .
  → reductase inhibitors .

- Ezetimibe → a prodrug
  → converted in the liver to the active glucuronide form

- glucuronide → inhibits a transporter uptake of cholesterol .

- glucuronide is effective even in the absence of dietary cholesterol . True

- How ezetimibe reduces the cholesterol in the tightly regulated hepatic pool ?
  1. preventing absorption of dietary cholesterol .
  2. preventing absorption of cholesterol that is excreted in bile .

- HMG-CoA reductase inhibitors + Ezetimibe
  → ↑ risk of hepatic toxicity .

- what is the most effective agent for increasing HDL levels? Niacin (nicotinic acid, vitamin B3)

- what is the mechanism and effect niacin?

① in liver ⟶ ↓ VLDL , ↓ LDL.

② in capillary ⟶ ↑ lipoprotein lipase , ↓ Triglyceride , ↓ VLDL , ↓ LDL .

③ ↓ catabolic rate for HDL.

④ ↓ fibrinogen , ↑ tissue plasminogen activator.

- what is the adverse effects for niacin?

1. cutaneous flushing
2. nausea
3. abdominal discomfort
4. moderate elevations of liver enzymes
5. hepatotoxicity
6. Hyperuricemia
7. moderately carbohydrate tolerance

- How we can reduces the intensity of cutaneous flushing? aspirin + NSAIDs

- should be discontinued in the niacin drug if the hepatotoxicity occur. True

- اكثر ادوية فعالة في تقليل الـ LDL هي HMG-CoA reductase inhibitor

- اكثر ادوية فعالة في تقليل الـ T-G هي fibrates

- اكثر ادوية فعالة في زيادة الـ HDL : Niocin

هام جاي على سؤال

- what is the mechanism of action for fibrates? "

fibrates —binding on→ PPA-R α receptor

↓

↑ lipoprotein lipase by adipose tissue ↓ T-G

- what is the adverse effects for fibrate?

① mild GI disturbances.

② cholesterol gallstones.

③ Myopathy with HMG-(CoA) reductase inhibitors.

- Icosapent ethyl contains only EPA. unlike other fish oil, does not raise LDL-C. True

- what is the function of omega-3 fatty acids?

1. ↓ platelet aggregation.

2. antiarrhythmic → ↓ MI.
   → ↓ sudden cardiac death.

- what is the common side effect omega-3?

1. diarrhea.

2. Excess bleeding.

هديل الزعبي