

3- Biochemical aspects of digestion of lipids

<p><u>Dietary lipids</u></p> <ul style="list-style-type: none"> Dietary lipids intake is ~81 g/day , Triacylglycerol is >90% The remainder includes: <ul style="list-style-type: none"> Cholesterol Cholesterol ester Phospholipids Glycolipids Free fatty acids 	<p><u>Lipid digestion in the small intestine</u></p> <p>Emulsification:</p> <ul style="list-style-type: none"> Occurs in the duodenum Increases surface area of lipid droplets To maximize the effect of digestive enzymes Two mechanisms: <ol style="list-style-type: none"> Detergent properties of bile salts in the bile Bile salts emulsify dietary lipid particles Mechanical mixing by peristalsis 	<p><u>Pancreatic insufficiency in cystic fibrosis (CF)</u></p> <ul style="list-style-type: none"> CF is due to genetic mutations in CFTR (transmembrane conductance regulator protein) Functions as chloride channel on epithelium Defective CFTR causes: <ul style="list-style-type: none"> Decreased secretion of chloride Increased reabsorption of sodium and water Decreased hydration in pancreas thickens the pancreatic secretions Pancreatic enzymes are unable to reach the intestine Treatment: enzyme and fat-soluble vitamin supplementation
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Dietary lipids: Organs and Enzymes

<u>Stomach</u>	<u>Small intestine / Lipid degradation by pancreatic enzymes</u>			
<u>Lingual lipase , Gastric lipase</u>	<u>pancreatic Lipase / Co-lipase</u>	<u>Cholesterol esterase</u>	<u>Phospholipase A2</u>	<u>Lysophospholipase</u>
<ul style="list-style-type: none"> Triacylglycerols (TAGs) are hydrolyzed by the lipases secreted: <ul style="list-style-type: none"> Under the tongue and gastric mucosa Catalyzed by an acid-stable lipase (lingual lipase) 	TAG degradation Removes fatty acids at C1 and C3	Cholesteryl ester degradation	Phospholipids	Lysophospholipids
	Leaving 2-monoacylglycerol and free fatty acids (FFAs)	Produces cholesterol + FFAs	Lysophospholipid + fatty acid	Glycerolphosphoryl Base +fatty acid
<ul style="list-style-type: none"> Acid lipases are important for lipid (milk fat) digestion in neonates and patients with pancreatic insufficiency 	Pancreatic lipase : Found in high conc. in pancreatic secretion (2-3% of total proteins) Inhibited by Orlistat , an antiobesity drug			Glycerolphosphoryl Base excreted in the feces, degraded or absorbed

Control of lipid digestion by hormones:		Lipid absorption by enterocytes	Lipid malabsorption		
Cholecystokinin (CKK)	Secretin	<ul style="list-style-type: none"> • Products of lipid digestion (FFAs, free cholesterol, 2-monoacylglycerol) combine with bile salts and fat-soluble vitamins • They form mixed micelles (disk-shaped particles) • Mixed micelles are hydrophobic inside and hydrophilic outside • Absorbed by brush border membrane of enterocytes • Short and medium chain length fatty acids are absorbed directly 	<ul style="list-style-type: none"> • Increased excretion of lipids, fat-soluble vitamins and essential FAs in the feces • Due to defects in lipid digestion or absorption • Can be caused by CF or shortened bowel 		
<ul style="list-style-type: none"> • Acts on gallbladder to release bile • Acts on pancreas to release enzymes • Decreases gastric motility (slow release of gastric contents) 	<ul style="list-style-type: none"> • Low pH stimulates its secretion • Acts on pancreas and liver to release bicarbonate • Neutralizes the pH of the contents before entering the small intestine 				
Resynthesis of TAG / Cholesteryl esters <ul style="list-style-type: none"> • Digested lipids absorbed by enterocytes migrate to endoplasmic reticulum for complex lipid biosynthesis <ul style="list-style-type: none"> • Fatty acids → activated to acyl CoA form <ul style="list-style-type: none"> • 2-Monoacylglycerols → TAGs <p style="text-align: right; margin-right: 50px;">الخطوات التي تحتها موجودة بكلام بالاسلايد بس الدكتور شرحتها من الصورة</p>					
1. The long-chain length fatty acids are first converted into their activated form by fatty acyl-coenzyme A synthase .	2. Using the fatty acyl CoA derivatives the 2-Monoacylglycerols are converted to TAGs by Monoacylglycerol acyltransferase and Diacylglycerol acyltransferase	3. Lysophospholipids are recycled to form phospholipids by acyltransferases .	4. Cholesterol is esterified with a fatty acid by acyltransferase to form cholesteryl ester.	5. Amino acids will give Apolipoprotein B-48	
Assembly of chylomicrons by enterocytes <ul style="list-style-type: none"> • Newly synthesized TAG and cholesterol ester are packaged as lipid droplets surrounded by thin layer of: <ul style="list-style-type: none"> • Apolipoprotein B-48 (apo B-48) • Phospholipids • Free cholesterol 			Secretion of chylomicrons by enterocytes <ul style="list-style-type: none"> • By exocytosis into lymphatic vessels around villi of small intestine (lacteals) which enter into systemic circulation • Serum becomes milky after a fatty meal 		