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Lecture title: EXOGENOUS PIGMENTS

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Summary: Accumulation of these substances is occurred by three gener pathways.

1-Accumulation of normal substances, either due to increase their prod or due to failure to remove these substances by metabolism, like Fatty c in the liver.

2- anormal or abnormal endogenous substance accumulates because of or acquired defects in its metabolism, like storage diseases or alph-1 antitrypsin deficiency. (mutations cause defective folding and transport protein).

3-An abnormal exogenous substance is accumulated within the cells wit defects that are seen in previous two points. Like accumulation of carbo silica.

Fatty changes (steatosis):Abnormal accumulations of triglycerides withi hepatocytes (the main site because the liver play central role in fat metabolism) , can also involve heart, skeletal muscles, & kidney. The eti of steatosis alcoholism, starvation: increases FA mobilization from peri store., Protein malnutrition: decrease synthesis of apoprotein., Obesity, Diabetes mellitus , Hypoxia, Liver toxin like CCL4, Drugs like estrogen steroid, tetracyclinetoxins. When the fatty change is mild, it may have n effect on cellular function. More severe fatty change may impair cellula function. Recently proved, that severe form of fatty change may lead to cirrhosis & hepatocellular carcinoma

Mechanisms of Fatty changes (steatosis):

Excess accumulation of triglycerides within the liver may result from defects in any one of the events in the sequence from fatty acid entry to lipoprotein exit from hepotocytes.

Morphology of Fatty Changes:

2. In any site, Fat accumulation appears as clear vacuoles within parenchymal cells. Accumulation of glycogen & water also produce clear vacuoles. • special techniques are needed to distinguish these three types of clear vacuoles: • The identification of clear vacuoles of lipids require preparation of frozen tissue sections (avoid formalin), and then the sections are stained with Sudan IV or Oil red-O.

• The identification of glycogen clear vacuoles requires staining with periodic acid-Schiff (PAS) reaction .

3. Clear vacuoles of water are negative staining for Sudan IV or Oil red- O, & (PAS). • Gross In the liver, mild fatty change …….not affect the gross appearance. •

In progressive fatty changes the organ enlarges & more yellowish, • In extreme instances Bright yellow, soft, greasy liver.

Mic.: Early fatty change, there are minute vacuoles in the cytoplasm & around the nucleus of fat cells. As the process progresses, the vacuoles coalesce, creating cleared spaces that displace the nucleus to the periphery of the fat cells. Protein Accumulation: • Protein accumulation is less common than lipid accumulation. • Intracellular accumulations of proteins usually appear as rounded, eosinophilic droplets, vacuoles, or aggregates in the cytoplasm.

Examples of protein accumulation: • In the kidney, there is accumulation of albumin in the cytoplasm of tubular cells of proximal tubules, which occur in diseases associated with increased protein filtration through the glomeruli (like nephrotic syndrome) & increase reabsorption of albumin by the tubular

cells, accumulated protein appear as pink, hyaline cytoplasmic droplets, this is reversible process.

There is marked accumulation of newly synthesized immunoglobulins that may occur in the RER of some plasma cells, resulting in rounded, eosinophilic Russell bodies. • In alcoholic liver diseases, there is accumulation of intracellular proteins (keratin intermediate filaments) (Mallory body), which appear as an eosinophilic inclusion in the liver cells. • Neurofibrillary tangle which is aggregation of proteins that are present in the brain of Alzheimer disease. Glycogen Accumulation: Excess accumulation of glycogen can be seen in the followings: In poorly controlled Diabetes Mellitus, glycogen will accumulate in renal tubular epithelium, cardiac muscles, & beta cells of Islet cells of pancreas. 3 • In glycogen storage diseases, there is enzymatic defect that result in accumulation of glycogen in various cells of body.