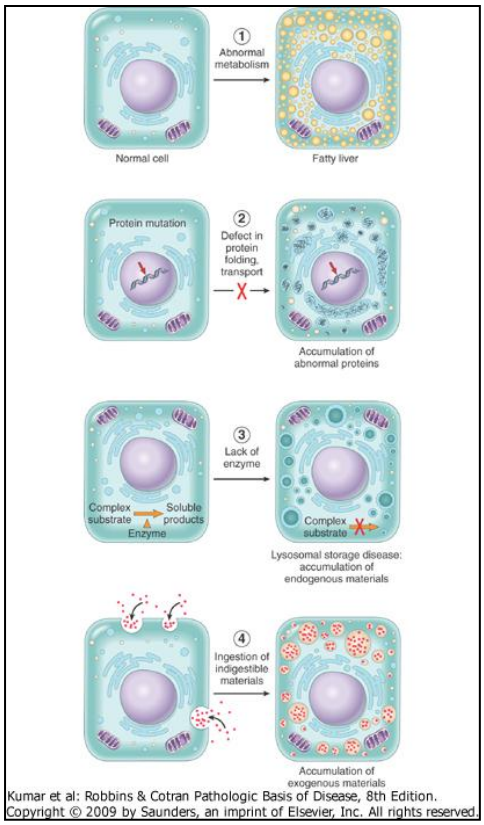
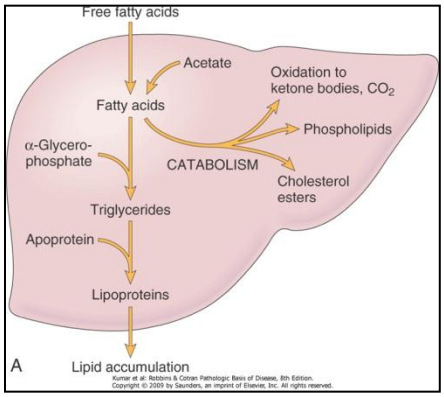
Cellular Adaptation

- Hyperplasia – increase in NUMBER (not size) of cells in an organ or tissue
    - May be seen in combination with hypertrophy
    - Physiologic hyperplasia – mechanisms include increased DNA synthesis, growth inhibitors will halt hyperplasia after sufficient growth has occurred
        - Hormonal – hyperplasia of uterine muscle during pregnancy
        - Compensatory – hyperplasia in organ after partial resection
    - Pathological – not in itself neoplastic or preneoplastic, but the trigger may place patient at risk of sequelae (dysplasia, carcinoma)
        - Excess hormones – endometrial proliferation from over increased estrogen
        - Excess growth factor stimulation – warts arising from papillomavirus
- Hypertrophy – increase in cell SIZE, leading to increase in organ size
    - Usually in terminal cells which can no longer divide, so their only recourse is enlargement
    - End result is amount of increased work that each cell must perform is limited
    - Physiologic hyperplasia – hormonal stimulation (hypertrophy of uterine wall during pregnancy)
    - Pathologic – chronic cell stressors (stenotic valves, left ventricular hypertrophy from increased afterload)
- Chronic hypertrophy – if stress that triggered hypertrophy is not resolves, likely result is organ failure
    - Hypertrophied tissue at increased risk for ischemia from metabolic demands outpacing blood supply
- Autotrophy – shrinkage in cell size (may or may not include shrinkage of organ size)
    - Cells are smaller than normal, but are still viable. They do not normally undergo apoptosis or necrosis
    - Physiologic autotrophy – tissues/structures present in embryo or childhood may undergo autotrophy as growth and development process progresses
    - Pathologic – decreased workload, loss of innervation, decreased supply, inadequate nutrition, decreased hormonal stimulation, pain, physical pressure
- Metaplasia – REVERSIBLE change in which one type of adult cell (epithelial or mesenchymal) is replaced by another type – if stress/injury abates, metaplastic tissue may revert to original cell type
        - This is a protective mechanism, not a premalignant change
        - Reprogramming of epithelial stem cells (reserve cells) from one type of epithelium to another
        - Reprogramming of mesenchymal (pluripotent) stem cells to differentiate along different mesenchymal path
    - Bronchial (pseudostratifie, ciliated columnar) to squamous epithelium – smokers
    - Endocervical (columnar) to squamous – chronic cervicitis
    - Esophageal (squamous) to gastric or intestinal – barret esophagous (acid reflux)



- Intracellular accumulations – transient or permanent, may acquire substances that arise either from cell itself or from nearby cells
    - Normal cellular constituents accumulated in excess from increased production, decreased metabolism, etc (lipid accumulation in hepatocytes)
    - Abnormal substances via decreased metabolism or excretion (storage disease)
    - Pigments via decreased metabolism or transport (carbon, silica)



- Lipid accumulation
  - Steatosis (fatty changes) – accumulation of lipids in hepatocytes
    - From ^OH, drugs, toxins
    - Can occur at any step in the pathway
- Cholesterol
  - Seen as needle-like clefts in tissue, washes out with processing so looks cleared out
  - Atherosclerotic plaque in arteries
  - Accumulation in macrophages (called "foamy" macrophages) – seen in xanthomas, areas of fat necrosis, cholesterolosis in gall bladder
- Proteins
  - May be due to cell inability to maintain proper metabolic rate
    - Increased reabsorption of proteins in renal tubules → eosinophilic, glassy droplets in cytoplasm
  - Defective protein folding
    - α-1-AT deficiency → intracellular accumulation of partially folded intermediates
    - may cause toxicity – some neurodegenerative diseases
- Glycogen
  - Intracellular accumulation can be physiologic (hepatocytes) or pathologic (glycogen storage disease)
  - Easiest seen with a PAS strain – deep pink to magenta color
- Pigments
  - Exogenous pigments – anthracotic (carbon) pigments in lungs, tattoos
  - Endogenous pigments
    - Lipofuscin ("wear and tear" pigments)
      - Results from free-radical peroxidation of membrane lipids
      - Finely granular yellow/brown pigment
      - Often seen in myocardial cells and hepatocytes
    - Melanin
      - Only endogenous brown-black pigment
      - Often (not always) seen in melanomas
    - Hemosiderin
      - Hemoglobin derived and represents aggregates of ferritin micelles
      - Granular or crystalline yellow/brown pigment
      - Often seen in macrophages in bone marrow, spleen, liver (lots of RBC and RBC breakdown); also in macrophages in areas of recent hemorrhage
      - Best seen with iron stains (Prussian blue) – makes granular pigment more visible
- Calcification
  - Dystrophic – occurs in areas of nonviable or dying tissue in the setting of NORMAL serum calcium
    - Also occurs in aging/damaged heart valves, atherosclerotic plaque
    - Tissue, not serum, is calcified
    - Gross – hard, gritty, tan-white, lumpy
    - Micro – deeply basophilic H&E stain, glassy, amorphous, may be either crystalline or non-crystalline
  - Metastatic – may occur in normal, viable tissues in the setting of hypercalcemia due to any number of causes
    - Most often seen in kidneys, cardiac muscle, soft tissue
    - Serum, not tissue, is calcified (unlike dystrophic)