Sublethal cell injury: autophagy, fatty change
Cell adaptations: hypertrophy, hyperplasia, metaplasia, atrophy

Normal SER

Responses to Cell stress

Adaptation

Hypertrophy
Hyperplasia
Atrophy
Metaplasia
Dysplasia

Reversible Lesion

Cell Death

Residual Lesions:
Lipofuscin, residual body, etc

Sublethal cell injury and subcellular changes

Autophagy—the uptake and intracellular degradation of damaged or effete organelles by lysosomes.

- Sublethal injury may result in organelle damage. “Storm cleanup” is needed.
- Occurs after cellular stresses of many types, starvation, growth factor withdrawal, and accumulation of misfolded proteins.
Sublethal cell injury and subcellular changes

- Cytoplasmic matrix and damaged organelles enveloped by cell membrane to form autophagic vacuole or autophagosome.
- Fuses with lysosome to form autophagolysosome
- Digestion of most carbs and proteins but lipids may remain. Undigested debris termed residual body which may be retained or extruded.
- Lipofuscin pigment may result from intracellular lipid peroxidation.

**Autophagy and heterophagy.** Schematic representation of heterophagy (left) and autophagy (right). The mechanisms are similar for processing cell debris, both from intrinsic sources and extrinsic sources (heterophagy). (From Kumar V, Abbas A, Fausto N: Robbins & Cotran pathologic basis of disease, 7th ed, Philadelphia, 2005, Saunders.)

> Sublethal cell injury and subcellular changes

Autophagolysosome containing degenerating mitochondrion and amorphous material. Note double membrane.

**Autophagy**

**Figure 1.28:** Autophagy. Cellular changes, such as autolysis degradative, satiate autophagy genes that encode vacuoles in which organelles are sequestered and then degraded following fusion of the vacuoles with lysosomes. The digested materials are recycled to provide nutrients for the cell.

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**Autophagy update**

- Autophagy can be selective or nonselective.
- Nonselective autophagy induced in response to availability of nutrients or trophic factors to maintain bioenergetic homeostasis.
- Selective autophagy used in processes requiring cellular remodeling. Also induced in response to toxic stimuli for sequestration of damaged components, which play a role in signaling.
  - Chaperone-mediated autophagy (CMA): a chaperone related to HSP-70 binds particular sequences in proteins and directs them to lysosomes for destruction.
  - CMA is activated as adaptive response in starvation and may be defective in aging.
- Induction of autophagy may promote cell death in some cases.
- Autophagy may play a role in a variety of disease processes, including cancer, neurodegeneration, myopathies, and infectious diseases. Complex and poorly understood.


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**Fatty change: lipidosis or fatty degeneration**

- Accumulation of triglycerides and other lipid metabolites (neutral fats and cholesterol) within parenchymal cells
- Most common and clinically relevant in liver (the main organ for lipid metabolism) but occurs also in heart muscle, skeletal muscle, and kidney
- Not used to refer to accumulation of phospholipids (e.g. in myelin figures) and lipids of lysosomal storage disease
- Not the same as fatty infiltration (increased or more apparent adipocytes between cells).

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**Fatty change: one or more of 5 mechanisms**

1) **Excessive delivery of free fatty acids** to liver results in increased triglyceride synthesis. Lipolysis and mobilization of adipose tissue is common in diseases characterized by impaired glucose availability or utilization. These diseases include starvation, inanition, diabetes mellitus, ketosis, and hyper-adrenocorticism.

2) **Blockage of fatty acid oxidation** to ketones and other substances may result from mitochondrial injury (toxins, hypoxia), impaired blood flow, and hepatocellular hypoxia.

3) **Impaired synthesis of apoprotein** ("lipid acceptor proteins"). This occurs in oxleariform and CCAO toxicoses, aflatoxicosis, or exposure to any other agent that injures the protein synthesizing apparatus.

4) **Impaired combination** of lipid and protein. This is uncommon.

5) **Impaired release** of lipoproteins. This also is an uncommon cause.
Fatty change: one or more of 5 mechanisms

1. Excessive delivery of free fatty acids
2. Blockage of fatty acid oxidation
3. Impaired synthesis of apoprotein ("lipid acceptor proteins").
4. Impaired combination
5. Impaired release.

Fatty Degeneration:
May follow acute cell swelling and be seen with less severe cases of hypoxic and cell membrane cell injury.

Sequence of events leading to fatty change and cell necrosis in carbon tetrachloride toxicity.

Hepatic Lipidosis in Domestic Animals

- Increased mobilization of fat stores most common: late pregnancy (pregnancy toxemia) and early lactation (ketosis) of dairy cows
- Nutritional disorders: obesity (increased transport), protein-calorie malnutrition (impaired apolipoprotein synthesis), starvation (increased mobilization)
- Chemicals (many, e.g. CCl₄, decreased apoprotein synthesis and decreased oxidation of free fatty acids due to mitochondrial membrane injury)
- Feline hepatic lipidosis and fat cow syndrome (mechanisms complex)
Fatty liver: gross changes

Steatosis (fatty liver, fatty change, hepatic lipidosis), liver, ox. A. Note the uniformly pale yellow surface. The liver is usually enlarged and the edges rounded. The cut surface bulges on incision and may feel greasy.

This slide demonstrates the microscopic lesion of hepatic lipidosis. The hepatocytes are clear as they contain large vacuoles filled with lipid or multiple small lipid filled vacuoles. This happens to be from a cat with FELINE FATTY LIVER SYNDROME.

Is it true?
Macrovesicular = triglycerides
Microvesicular = fatty acids

Another example of fatty liver. This time in a cat due to feline fatty liver syndrome.
This liver is also from a dog. While it is not as pale as the previous liver, it is still large, pale, and swollen. It is also friable and prone to rupture. This liver has fatty change or lipidosis.

Fatty liver: microscopic changes

Miniature horse with hepatic lipidosis. Nuclei have been displaced to the side by lipid. H&E stain.

This is a histology of liver from a dog with hepatic lipidosis or diffuse fatty change. Note the large, clear, distinct vacuoles within the hepatocytes. The nucleus is often displaced to the periphery. While several substances cause vacuolar change in liver, fat vacuoles are most distinct.
Responses to Cell stress

Injurious agent

- Normal Cell
- Reversible lesion
- Cell Death

Adaptive changes leading to changes in cell size, number, or appearance

- Adaptive changes to cell stress or injury can lead to an increase in the size of a tissue or organ (by hyperplasia and/or hypertrophy),

- A decrease in tissue and cell size (atrophy)

- A change to a different cell type (metaplasia)

- Hypertrophy is an increase in the size of cells or organs.

- Hyperplasia is an increase in the number of cells in a tissue or organ.

- The two often occur together as an adaptive change and are considered positive responses to injury or stress.

Adaptive changes leading to changes in cell size, number, or appearance
Hypertrophy: increase in the size of cells (or organ)

- No new cells (unless accompanied by hyperplasia), but cells are larger
- Increased size due to synthesis of more structural components (not acute cell swelling)
- Occurs in both dividing (usually prefer hyperplasia) and non dividing cells
- May be accompanied by polyploidy (if a cell appears much larger than normal and the nucleus is very large, suspect polyploidy)
- "Hypertrophy" often used for organ enlargement regardless of whether due to hypertrophy and/or hyperplasia.

Hypertrophy: Causes or pathways

- Increased functional demand: Physiologic
  - Skeletal muscle. Increased load results in increased size of individual fibers.
    - Endurance exercise results in increased number and size of mitochondria.
    - Heavy resistance training induces hypertrophy of contractile elements
    - Capillary network also increases
  - Heart muscle. Responds to chronic hemodynamic overload.
    - Increased pressure (hypertension) or volume (valve deficiency)
    - Synthesis of more proteins and filaments occurs
    - Increased sarcomeres can be added in series or parallel
    - Polyploidy may occur in humans

- Smooth muscle. Enlargement due to hypertrophy, hyperplasia, and polyploidy.
  - Pregnant uterus enlarges due to hormone-induced increase.
  - Estrogen acts on smooth muscle estrogen receptors to increase smooth muscle protein synthesis and cell size increase.
  - Hypertrophy occurs in stenotic tubular organs (10x increase in mass). Occurs idiopathically in horse esophagus and ileum.

Endocrine stimulation of reproductive organs.
- Prolactin and estrogen cause mammary hypertrophy during lactation
Hypertrophy: Causes or pathways

- Compensatory
  - Kidney. Increased in one kidney after loss or diminution of opposite.
  - Glomeruli enlarge with capillaries increasing but no new glomeruli or tubules.

- Over nutrition
  - Increase in adipocyte size

Hypertrophy: Mechanisms

- Cellular remodeling
  - First comes increased proteasomal degradation of selected unneeded macromolecules

- Signaling mechanisms vary by cell type. For skeletal muscle:
  - Growth factor stimulation: insulin like growth factor 1 (IGF-1) increased in load-induced muscle hypertrophy
  - Neuroendocrine stimulation: adrenergic or noradrenergic stimulation may be needed to initiate or facilitate hypertrophy
  - Ion channels: calcium channel activity may stimulate many downstream enzymes (e.g. calcineurin) to produce hypertrophy
  - Other chemical mediators: nitric oxide, angiotensin II, and bradykinin may support hypertrophy
  - Oxygen supply: angiogenesis is stimulated when tissue oxygen deficit is sensed and may be essential to adaptive hypertrophy
  - Hypertrophy antagonists: atrial and B-type natriuretic factors, high concentrations of NO and others brake or prevent hypertrophy

Hypertrophy: Mechanisms

- Effector pathways
  - Increased protein degradation. Adaptive cellular remodeling
  - Increased protein translation. Rapid with increased efficiency leading to increased protein production
  - Increased gene expression. Increased up regulation of transcription of key genes.
  - Survival. Inhibition of cell death by apoptosis
Hypertrophy: Mechanisms

- Based on cardiac muscle
  - Involve signal transduction pathways, induction of several genes, and subsequent synthesis of numerous cellular proteins.
  - These signals are the result of both mechanical and trophic triggers.

Hypertrophy: significance

- Hypertrophy is common, often protective, limited, usually reversible.
- In heart, hypertrophy may fail to compensate for increased load and result in failure.
- Degenerative changes in myofibers ensue such as lysis and loss of contractile elements.
- Myocyte death may occur by apoptosis or necrosis.
- Limiting factors for hypertrophy of heart are unclear: may be due to limited vascular supply to enlarged fibers, diminished oxidative capabilities of mitochondria, alterations of proteins synthesis and degradation, cytoskeletal alterations, or fibrosis.
Hypertrophy, heart, dog. A. Narrowing of the pulmonary outflow track caused by pulmonic valve stenosis has forced the right ventricle to contract with much more pressure. This increased workload has caused hypertrophy of the wall of the right ventricle, which is much thicker here than it would normally be. B. Note the increased size (hypertrophy) of myocytes in the overworked heart muscle.

This the heart of a calf with a hole in the proximal part of the septum between the left and right ventricles. This hole allows pressure from the left ventricle to be communicated to the typically lower pressure right ventricle. The right ventricular muscle becomes thicker than it normally is in response to this increased pressure. This is an example of compensatory hypertrophy.

Recent cases:

Muscular Pseudohypertrophy (steatosis) in a bovine fetus

*Journal of Veterinary Diagnostic Investigation, March 2007, vol. 19, 2, pp. 198-201*
Whooper swan, blood vessel (smooth muscle) hypertrophy and schistosomes. Direct irritation or immune reaction?

Hyperplasia: an increase in the number of cells in an organ or tissue

- May occur with or independently from hypertrophy
- Both can result in increase in the size of a tissue or organ
- Regeneration or renewal can be considered compensatory hyperplasia
- Hyperplasia can be physiologic (hormonal or compensatory)
- Hyperplasia can be pathologic (frequently hormonal)
- Cell numbers in a cell population in a tissue or organ depend on cell proliferation, differentiation, and death by apoptosis
- Cell type matters
- Mechanisms of regeneration and proliferation depend on cell cycle, growth factors, signaling mechanisms, transcription factors, extracellular matrix and adhesion molecules

Normal cell proliferation and growth: briefly

Physiologic stimuli or pathologic conditions stimulate proliferation
Hyperplasia: cell type matters

The traditional view: three groups of proliferative ability
- Labile tissues: continuously dividing
  - Bone marrow/hematopoietic
  - Epithelia of surfaces
    - Stratified squamous: skin, oral cavity, vagina, cervix, gland ducts
    - Columnar: GI tract, uterus
    - Transitional: bladder
- Stable cells (quiescent) – low level replication, which can accelerate on demand.
  - Parenchymal cells of liver, kidney, glands
    - E.g. liver regeneration after hepatectomy
  - Mesenchymal cells
    - Fibroblasts
    - Endothelial cells
    - Smooth muscle
    - Adult osteocytes, chondrocytes
- Permanent cells:
  - Neurons
    - Adult brain neurogenesis may occur
  - Cardiac muscle (some mitosis has been seen)
  - Skeletal muscle – regeneration from differentiation of satellite cells of endomysial sheath
  - Cells of the crystalline lens, Sertoli cells, hair cells of the cochlea, glomerular podocytes
Cell cycle landmarks:

Stem cells: even briefer (refer to renewal and repair lectures)

- Stem cells do prolonged self renewal and asymmetric replication
  one cell renews, the other differentiates and matures
- Embryonic stem cells are pluripotent, but some adult stems cells can also be pluripotent
- Stem cell locations (niches) vary by tissue (tissue stem cells)
  e.g. bulge area of human skin, colon crypts, liver stem cells (oval cells)
- Tissue stem cells (especially hematopoietic stems cells) may be very potent (developmental plasticity)

Liver stem cells: oval cells in canal of Hering. (cytokeratin 7 IHC)
Hyperplasia

- Usually induced by known stimuli and is often hormonal, but can be due to chronic irritation
- A controlled process that stops when the stimuli cease
- Can serve a useful purpose (compensatory, repair, increased function, protection
- Subject to normal growth controls
- The above are not true of neoplasia, but hyperplasia can be preneoplastic
- The significance varies and often lies in determining the cause.

Hyperplasia: morphology

A. Deficiency of maternal dietary iodine during pregnancy has resulted in hyperplasia (and hypertrophy) of thyroid follicular epithelial cells in this neonatal goat and thus results in a symmetric enlargement of the glands (goiter). Other mechanisms are possible.

B. Thyroid follicular epithelial cells from a normal thyroid gland. H&E stain.

C. Thyroid follicular epithelial cells from a case of thyroid goiter. Note the increased number (and size) of the follicular epithelial cells.

These are thyroids and parathyroids from a dog with renal failure. The parathyroids are enlarged (hard to appreciate unless you remember that normal canine thyroids are not as prominent as this) in attempts to maintain calcium levels. This response could be construed as physiologic hyperplasia due to a pathologic process elsewhere.
The uterine horns of this maned wolf are opened up to expose the endometrium, which in this case has myriads of variably sized cysts. This endometrial change is due to excess progesterone stimulation in dogs and their relatives and is an example of pathologic hyperplasia. The diagnosis for this case is cystic endometrial hyperplasia.

Histology of cystic endometrial hyperplasia demonstrates the large dilated endometrial glands that are forming grossly visible cysts. The lining of these glands contains excess numbers of cells, which is pathologic hyperplasia. The cysts form because of blockage of gland outflow because of increased numbers of cells and likely excess secretion.

In dogs (and people), the prostate often enlarges more or less diffusely and symmetrically due to relative excess of testosterone in some older individuals. This is also pathologic hyperplasia. Grossly visible enlargement of any organ is often termed hypertrophy, whether or not the enlargement is due to increased numbers (hyperplasia) or increased size (hypertrophy) of cells. See the next image for the histology of this change.
Histology of the previous case of prostatic hyperplasia shows that the prostatic alveoli are lined by increased numbers of epithelial cells, some so much so that the excess cells form papillary fronds extending into the alveolar lumens. This increase is pathologic hyperplasia. See the next image for another view of the histology of this change.

Histology of the previous case of prostatic hyperplasia shows that the prostatic alveoli are lined by increased numbers of epithelial cells, as was just stated. Note also that besides increased numbers of cells lining the alveoli, there is also an increase in the size of many of the cells. This is hypertrophy along with hyperplasia, a fairly common combination in epithelial pathologic hyperplasia due to hormonal imbalances.

Rabbit liver with hepatic coccidiosis and multifocal bile duct hyperplasia. Grossly hyperplastic lesions need to be differentiated from a variety of other general changes from neoplasia to degenerative changes.
Histology of bile duct hyperplasia due to hepatic coccidiosis (Eimeria stiedae).

The exact mechanism is not known, but generally, chronic irritation is a likely path.

The medial surface of the spleen of this sheep has a discrete nodule (cut open to show the cut surface) that is composed of tissue that closely resembles normal spleen. This is an example of nodular hyperplasia. The cause of splenic nodular hyperplasia is not known but it is common in older dogs. It must be differentiated from neoplasms.

The liver of this older dog has numerous nodules composed of normal but excess hepatocytes. This is also an example of nodular hyperplasia, the cause of which is unknown but is again common in older animals. Its importance is that it must be differentiated from neoplastic disease.
In dogs, prostatic hyperplasia is common but only occasionally causes narrowing of the prostatic urethra. When it does, as in this case, the bladder is forced to put more pressure on the urine to expel it. As a consequence, the wall of the bladder may increase in thickness as seen here. This is also an example of compensatory hypertrophy of smooth muscle, due here to pathologic hyperplasia of the prostate.

**Metaplasia**

- A (potentially) reversible change in which one adult cell type is replaced by another adult cell type of the same germ line.
- Often, but not always, an adaptive change to an adverse environment—chronic irritation.
- Most common in epithelia (especially columnar cells to squamous) but also occurs in connective tissue (not usually adaptive).
- More than a change in cell phenotype (modulation), but involves reprogramming of tissue stem cells or undifferentiated cells to differentiate along a different line.
- Metaplasia is often reversible if the cause is withdrawn, but it may be preneoplastic.

**Metaplasia**

- Depends on growth factors, cytokines, extracellular matrix (cell environment), etc.
  - For mesenchymal metaplasia the following physical conditions are known:
    - High tensile strength → fibrous tissue
    - Compression → cartilage
    - Poor vascularity → cartilage
    - Motion → cartilage
    - Low stress/strain → bone
- Tissue specific differentiation genes involved
  - E.g. TGF-beta superfamily induce chondrogenic and osteogenic
- Growth factors induce specific transcription factors and subsequent phenotypic specific genes leading to differentiation
- Vitamin A deficiency or excess: retinoic acid regulates cell growth differentiation, tissue patterning, and differentiation of stem cells.
Some examples and causes of metaplasia.

1. Chronic irritation from particles and chemicals in the lungs of smokers.
2. Vitamin A deficiency causing squamous metaplasia of the urinary tract and salivary glands.
3. Estrogen toxicity causing squamous metaplasia of the urinary tract and prostate.
5. Squamous metaplasia of salivary, biliary, and pancreatic ducts that contain stones in the lumen.
6. Metaplastic bone (osseous metaplasia) in injured soft tissue.
7. Myeloid metaplasia (extramedullary hematopoiesis) in adult spleens after bone marrow injury.
8. Metaplasia in tumors such as mixed mammary gland tumors of dogs.

Metaplasia of esophageal stratified squamous to columnar cells due to chronic gastric acid reflux (humans: Barrett Metaplasia)

Uterus of a rat that was one of many that failed to breed. Given the enlarged uterus, pyometra, mucometra, hydrometra, and endometrial hyperplasia were suspected, but...
Rat uterus microscopy of the previous gross image. Note the curious central luminal contents and the stratified squamous epithelium where endometrium should be.

The uterus is usually lined by columnar epithelium. In this rat, estrogen overdose may have led to a change to stratified squamous epithelium, therefore a metaplastic change. While squamous metaplasia can be protective in some locations, it also prevents normal bacterial clearance in the uterine and may let a bacterial infection become established as has happened in the above case. The PMNs (neutrophils) are responding to the bacterial infection.

Recall the hyperplastic canine prostate we saw a few images previously and how the acini are supposed to be lined by columnar epithelium. The tissue above is also prostate, but the acini are lined by stratified squamous epithelium and the lumens contain huge numbers of sloughed keratin squames. The squamous metaplasia seen here is due to estrogen toxicity (due to abnormal secretion from a Sertoli cell tumor of the testis.) See the next frame for a close view.
Closer view of squamous metaplasia of the canine prostate due to high estrogen levels from a Sertoli cell tumor of the testis. The keratin squames accumulate in the prostatic alveoli and cause enlargement of the prostate grossly. So, we have prostatic hypertrophy due to squamous metaplasia rather than the more typical prostatic hyperplasia.

Histology of the liver of a mouse with marrow cells (hematopoiesis.) The inset shows a higher magnification of the cells. The large multinucleate cells are megakaryocytes, a tell tale cell of bone marrow but red blood cell progenitors are also present. This is termed myeloid metaplasia or extramedullary hematopoiesis, an example of metaplasia. It happens more commonly in spleen but can also occur in liver since in the fetus both spleen and liver serve as hematopoietic tissue.

**Atrophy**

- Decrease in cell size or amount of a cell, tissue, or organ after normal growth has been reached.
- Due to decreased number and/or size of cells.
- May affect virtually any organ or part of an organ.
- A regressive change usually due to gradual and continuous injury. Cells are not dead, only smaller, but organ size can reduce due to loss of some cells (e.g., by apoptosis)
- Ischemic organs may reduce in size due to oncotic and/or apoptotic necrosis
- Organelles decrease. Fewer mitochondria, myofilaments, ER,
Atrophy

- As an adaptive response to decreased need or resources for a cell’s activities.
- A steady state may be arrived at a smaller size with less activity.
- Can lead to cell death, stay the same, or reverse.
- Can be physiologic, especially during development.
  - Atrophy of embryonic structures such as notochord, thyroglottal duct.
  - Decrease in uterine size after parturition.
  - The term involution is used in this context.
- Pathologic atrophy depends on cause and can be local or general.
- Atrophy can be an active process of cell restructuring, e.g., with decreased load or unloading of skeletal muscle.
  - Protein synthesis decreases with decreased protein elongation.
  - Protein degradation increases with ubiquitin-related specific protein pathways—contractile proteins decreased, ubiquitination of specific transcription factors.
  - Gene expression changes: increase in genes encoding ubiquitin ligase and proteasome subunit synthesis.
  - Signaling, increased NFκB activity.
  - Energy use. Decrease in free fatty acids as energy source.

Atrophy occurs by cell shrinkage and deletion

- Biochemical mechanisms are unclear, but increased protein degradation plays key role.
  - Lysosomes with acid hydrolases and other enzymes degrade intracellular as well as extracellular components.
  - Increase in autophagic vacuoles and lipofuscin.
  - Ubiquitin-proteasome pathway degrades many cytosolic and nuclear proteins.
- Atrophy can be an active process of cell restructuring, e.g., with decreased load or unloading of skeletal muscle.
  - Protein synthesis decreases with decreased protein elongation.
  - Protein degradation increases with ubiquitin-related specific protein pathways—contractile proteins decreased, ubiquitination of specific transcription factors.
  - Gene expression changes: increase in genes encoding ubiquitin ligase and proteasome subunit synthesis.
  - Signaling, increased NFκB activity.
  - Energy use. Decrease in free fatty acids as energy source.

Some causes of atrophy and Examples

- Deficient nutritive supply, especially blood supply. For example, liver atrophy due to decreased blood flow through the portal vein. Protein-calorie malnutrition leads to marked generalized cachexia.
- Decreased workload. For example, muscle fiber atrophy in sedentary people. Decreased bone density.
- Disuse. Muscles in a limb that is immobilized atrophy.
- Denervation. Muscle fibers decrease in size if a nerve is severed.
Some causes of atrophy and Examples

- **Pressure.** Atrophy, degeneration, and necrosis occur adjacent to tumors due to pressure and compromised blood supply.
- **Loss of endocrine stimulation.** Atrophy of the zona fasciculata of the adrenal follows prolonged steroid therapy.
- **Aging**

![Normal middle aged man](image1.jpg) ![82 yr man with atherosclerosis](image2.jpg)

Atrophy implies an adverse environment

Types by morphology: general

- Simple: common
- Fibrous: following chronic inflammation
- Fatty: replacement by adipocytes
- Serous atrophy of fat:
  - Found at necropsy in cases of starvation.
  - An indicator of extreme caloric deficiency for any reason (malnutrition, malabsorption, chronic infection, parasitism, neoplasia, mismothering).
  - Grossly fat deposits, especially cardiac, perirenal, and bone marrow are used up, clear to yellowish, edematous or gelatinous, sometimes with a fine vascular network.

Atrophy: Morphology:

- Gross: decreased weight and volume, may have a loose covering (wrinkled skin), tortuous blood vessels too large for volume of tissue, firmer due to fibrosis (if fibrotic type.)
- Microscopic. Cells smaller or reduced in number. May have numerous or few apoptotic cells
- EM. Fewer mitochondria, less ER, fewer myofilaments (muscle), increase in autophagic vacuoles, and maybe lipofuscin
Figure 2-54A: The two testes on the right are from a sheep that was treated with an estrogen-like compound. This causes atrophy of the testes. The testis on the left is from an untreated animal of the same age, suggesting that the two smaller testes are atrophic. The decrease in size or number of cells in these testes is termed atrophy.

Figure 2-54B: These two feline kidneys are both too small. This cat suffered from chronic renal disease that led to fibrosis and loss of renal parenchyma. This decrease in size is termed atrophy. It is possible that the left kidney was always too small, that is to say, it never reached adult size. This is a condition termed hypoplasia. Organs or tissues can be smaller than normal due to atrophy and/or hypoplasia.
Pressure atrophy of the cerebrum of a rat with an intracranial meningioma.

Histology of liver from a dog in which there is a shunt between the portal side and the systemic circulation. This shunt causes some bypassing of blood from the liver. The reduction in blood flow to the liver causes decreased nutrients to the hepatocytes and therefore decreased size of hepatocytes. The inset shows how the hepatocytes are smaller and narrower than they should be and the sinusoids are correspondingly wider. This is atrophy due to deficient nutrition.

Histology of a thymus from a mature animal. Note that only a few lymphocytes are left along with the thymic (Hassall’s) corpuscles. Thymus from a fetus and neonate will have a very cellular cortex and medulla. This reduction in thymic size is a normal physiologic process and termed involution.
This is histology of muscle to which the nerve supply has been partly lost. The decreased size of some of the muscle fibers is due to loss of nervous impulse and is called neurogenic atrophy, only one cause of muscular atrophy. Note the small size of some of the myofibers, especially the decreased amount of cytoplasm (sarcoplasm) and relative increased amount of space filled by the nucleus or even multiple nuclei.

Bovine heart and bone marrow. When animals, especially neonates, don’t receive adequate calories, they are forced to use up internal fat stores. The last fat stores to go are fat around coronary vessels, around kidneys, and in bone marrow. This change is termed serous atrophy of fat due to the watery appearance left in the areas of recently resorbed fat. These areas are often pink because of relative increase in blood flow to the fat to resorb it. Serous atrophy of fat is an important finding because there are many potential causes of decreased available calories and a cause must be sought.

Questions for Lecture 3

About the Questions.

Cell Injury Questions from Lectures 1-4 come from two sources. Those designated with this red # and ISU/Aub at the bottom of the page were created and contributed by residents and faculty of Iowa State University and Auburn University listed as a group. ⇒

Answers for these appear at the end of the question pages. Page numbers refer to Pathologic Basis of Veterinary Disease.

Other questions came from the AFIP website.
29. The mechanisms involved in cellular hypertrophy include the induction of genes for all EXCEPT:

A. Transcription factors c-fos and c-jun
B. Insulin-like growth factor-1 [IGF-1]
C. Tumor necrosis factor [TNF]
D. Endothelin-1
E. TGF-β

29. C: Robbins and Cotran, Pathological Basis of Disease, pp. 7, 9, 2005

38. The transition from respiratory epithelium to stratified squamous epithelium with vitamin A deficiency is an example of:

A. Atrophy
B. Dysplasia
C. Metaplasia
D. Hypertrophy
E. B&D

38. C: Robbins and Cotran, p. 4 2007

#2

Triglycerides can only be transported out of hepatocytes if they are converted to: (PBVD ed.4, 2006, p 49 Fig 1-44)

A. Phospholipids
B. Triglycerides
C. Lipoproteins
D. Cholesterol
E. Ketones

ISU/Aub
#16
Which of the following stains can be used to detect fat in tissue? (PBVD ed.4, p 41)
1. Periodic acid-Schiff
2. Oil-red-O
3. Sudan III
4. Scharlach R
A. 1
B. 1 and 3
C. 2 and 4
D. 1, 3 and 4
E. 2, 3 and 4

#60
Which cause-effect associations are correct regarding metaplasia? (PBVD ed.4 p. 36)
1. Chronic irritation (smoking)-squamous metaplasia of the airway epithelium
2. Vitamin E deficiency-squamous metaplasia of urinary tract and salivary glandular epithelium
3. Sialolithiasis-squamous metaplasia of salivary duct epithelium
4. Bone marrow insufficiency-osseous extramedullary hematopoiesis
5. Estrogen toxicity-osseous metaplasia of the urinary bladder smooth muscle
A. 1, 2
B. 1, 2, 3
C. 1, 2, 3, 4
D. 1, 3, 4
E. All are CORRECT

#71
All of the following are characteristic of metaplasia except (PBVD ed.4 p. 36):
A. Usually reversible if cause is withdrawn
B. Transformation of one adult cell type into another adult cell type
C. A result of estrogen toxicity
D. A result of vitamin A deficiency
E. A step in glandular healing following mastitis
Hepatic lipidosis in domestic animals is most commonly caused by (PBVD ed. 4, p. 40):

A. Impaired synthesis of apoprotein
B. Impaired release of lipoproteins from hepatocytes
C. Chronic excessive circulating corticosteroid concentrations
D. Excessive delivery of free fatty acids due to body fat mobilization
E. Decreased β-oxidation of fatty acids to ketones due to mitochondrial injury

Which are true regarding hyperplasia?
1. Prostatic hyperplasia is a form of physiological hyperplasia.
2. Permanent cells (neurons and myocytes) are intermediate in their ability to become hyperplastic.
3. Chronic irritation and excessive hormonal stimulation are often causes of pathologic hyperplasia.
4. Hyperplastic cells may also be hypertrophic.
5. Mammary gland epithelial proliferation before lactation is compensatory hyperplasia.

A. 1, 2
B. 3, 4
C. 3, 5
D. 1, 2, 3
E. 1, 3, 4

Hepatic lipidosis is associated with each of the following conditions EXCEPT (PBVD ed. 4, pp. 38-40):

A. Obesity.
B. Starvation.
C. Aflatoxicosis.
D. Vitamin E deficiency.
E. Carbon tetrachloride poisoning.
Answers to ISU/Aub questions for lecture 3.

- 2. C
- 36. E
- 60. D
- 71. B
- 75. D
- 80. B
- 122. D