The Microscopic Basis for Macroscopic Pathology
“Why We See What We See at Autopsy”

Objectives
To understand how microscopic changes produce the macroscopic attributes of gross lesions and shape the appearance of what we see during the post mortem examination (Understanding the “Rosetta stone”)

Look at a variety of gross lesions and the histopathology from the same lesion in several organs and tissues.

Liver
A dense solid organ normally **dark**, with symmetrical **lobular** microscopic **architecture** defined by peripheral portal triads and a system of bile ducts. Provides good contrast for pathologic processes causing a light or pale color.
Liver

Multifocal to miliary, well demarcated random small foci = implies a recent embolic shower. A common pattern in septicemia

Miliary – from the Latin (miliaris) for “millet seed”

Beaver liver w/ yersiniosis
Beaver Liver w/ Yersiniosis

EQ 6mo old foal; liver
Septicemia = salmonellosis

EQ Liver w/ salmonellosis
Snake Liver w/ Salmonellosis

Liver

Non random well demarcated symmetrical nodules in linear array
May indicate a pathologic process that highlights an architectural unit or subunit. i.e. bile ducts
Rabbit liver w/ hepatic coccidiosis

Multifocal poorly demarcated nodules = a process that tends to blend into the surrounding normal tissue; or the nodules are composed of altered normal tissue. Not generally abscesses, granulomas or neoplasms which tend to have an abrupt interface.
Dog w/ a porto systemic shunt
~ chronic liver disease and cirrhosis

Nodules but poorly demarcated; blend into adjacent tissue

Poorly demarcated nodules in spleen
But a different pathologic process

Cat liver w/ cholangiohepatitis
and cirrhosis

Cat liver w/ chronic cholangiohepatitis
Liver

Multifocal, well demarcated but random **red** (=hemoglobin, blood) foci can mask a process causing white (=necrosis or exudate) foci

i.e. "hemorrhage trumps necrosis"
Dog liver w/ neonatal herpesvirus infection

Red foci mask minute pale areas of necrosis

K9 liver w/ multifocal necrosis and hemorrhage ~ herpesvirus

Liver

Multifocal well demarcated but random red depressed foci

Depressed suggests necrosis; we “see” the lighter red over the darker liver color because there is loss of liver parenchyma or dilation of sinusoids with pooling of blood

i.e. telangiectasis, K9 hemangiosarcoma
Dog liver w/ metastatic HSA

Liver

Diffuse pale liver usually = lipidosis
often = systemic metabolic disorders

* Anemic animals have pale livers also but they are not yellow
Cat liver w/ hepatic lipidosis

Fel liver with diffuse Hepatic lipidosis

Cat with hepatic lipidosis and hepatic necrosis with hemorrhage
Liver

Symmetry or organization to the lesion suggests a process accentuating the normal lobular architecture. Symmetrical pale and red show high contrast but “What is the abnormal part”?
Centrilobular necrosis

Llama w/ hepatic LSA

Llama liver w/ periportal infiltration of LSA
Liver

Pan lobular pattern – "massive necrosis"

"massive" in the liver indicates the entire lobule is affected

Characteristic pattern in pigs with:
1. Vit E / Se Deficiency (hepatosis dietetica)
2. Cocklebur toxicity
3. Coal tar ("Clay Pidgeon") pitch toxicity
4. Gossypol toxicity

We “see” hemorrhage only because of the necrosis and loss of hepatic parenchyma
Pig liver w/ hepatic necrosis – Vit E/Se deficiency

“Nutmeg” patterns =
Chronic Passive Congestion.
Differential retention of blood in sinusoids; enhanced if concurrent lipidosis
Bov CPC with lipidosis ("nutmeg")

Bov liver w/ chronic Passive congestion

Spleen

A dark colored sinusoidal organ containing variable amounts of blood and multifocal lymphoid follicles ("white pulp").

Size variation can be physiologic as well as pathologic

*Immunologically stimulated spleens may have hyperplastic white pulp visible grossly
Dog spleen w/ "Raspberry Jam"
Appearance – LSA

Bison w/ anthrax and a "Blackberry Jam" spleen
Spleen

Well demarcated nodules **with** organized texture on cut surface

"Can’t spread it with a butter knife"

= viable tissue and cells attached or forming a cohesive structure
K9 spleen w/ histiocytic SA

Histiocytic sarcoma

Sharp demarcation

Spleen

Well demarcated nodules *without* organized texture on cut surface

“Spreadable with a butter knife”

= necrosis and suppurative exudate
Spleen

Poorly demarcated masses = blend into surrounding tissue; no abrupt transition from lesion to normal

Horse spleen w/ follicular lymphoid hyperplasia ~ EIA

Hyperplastic lymphoid follicles

EQ Spleen w/ lymphoid hyperplasia ~ EIA
Spleen

Diffuse pale spleen (normal size or small) with prominent stroma
May ~ loss of blood and/or lymphoid tissue; Or diffuse granulomatous inflammation, fibrosis, amyloid, hemosiderin

Prominent trabeculae because the spleen is contracted but filled with granulomatous inflammation
Lymph Nodes

Pale organs with a distinct cortex and medulla. Most significant changes cause enlargement. An “immunologically dynamic” tissue

Stromberg’s Rule
“If you can’t find them, they weren’t important!”

Lymph Nodes

Diffuse enlarged pale nodes with effacement of architecture; organized cut surface. Think viable tissue and thus a neoplasm

Always consider a “domestic” (primary) neoplasm before an “imported” (metastatic) one in any tissue or organ.
The Texture Caveat

“Sometimes granulomatous inflammation looks like neoplasia”

Noncaseating granulomatous inflammation

may infiltrate but not cause necrosis leading to an organized appearance ~ cytokine driven fibrosis, amyloidosis etc that adds organization and viable appearance
Lymph Nodes

**Diffuse enlarged pale with effacement of architecture; amorphous cut surface**

Think inflammation; suppurative or caseating

("You can spread it with a butter knife")
Diffuse enlargement with retention of corticomедullary architecture = Lymphoid hyperplasia, edema
Kidney

A complex organ with many subunits (glomeruli, tubules, lobules defined by vasculature, interstitium) and divided into cortex, medulla and pelvis. Complex patterns may highlight any combination of these.
Lesions confined to or centered on the cortex likely ~ a vascular portal of entry
Multifocal, well, poorly demarcated lesions

Raised = something added (cells)
Depressed = something taken away (necrosis, fibrosis)

Kidney

Fel w/ cryptococcosis

Feline kidney w/ Cryptococcosis
EQ kidney w/ Suppurative embolic
Nephritis – Actinobacillosis

Bov renal LSA

Bov kidney w
LSA
Kidney

Keystone, pyramidal or wedge-shaped, flat, pale or red lesions in the cortex = acute cortical infarcts

"Geometric shapes often highlight a vascular unit"

Ischemic necrosis

Thrombus

Mtn Lion Kidney w/ Septic thrombus & infarct
Kidney

Multifocal petechia in the cortex = endothelial damage, septicemia, platelet disorder, DIC

"Turkey egg kidney"

Pig kidney w/ erysipelas

Pig w/ "Turkey egg kidney" - Erysipelas
Glomerulonephritis is often difficult to see grossly.

Multifocal, symmetrical, widespread but confined to the cortex.
Kidney

Diffuse dark colored kidney hemoglobinuria myoglobinuria.
“Port wine colored urine”
Hemoglobin looks like “Ruby port”
Myoglobin looks like “Tawny port”
Check the bladder! Think hemolytic disease

Bov Hemoglobinuria ~ Leptospirosis
Box U bladder with “Port Wine” colored urine = hemolytic disease

Sheep w/ hemoglobinuria = Cu toxicity
Kidney

Diffuse cortical dark grey-brown color in goats = **Cloisonné Kidney**

Pigmented B.M ~ only PCT; mimics gold wire inlay around porcelain jewelry

Don’t Dx hemoglobinuria!

* Dark urine that is turbid = hematuria

Kidney

Diffuse soft kidney = “Pulpy kidney”

Think autolysis unless there is evidence of reaction i.e. edema, hemorrhage
Lesions confined to or centered on the medulla or pelvis likely ~ a urogenous portal of entry.

i.e. pyelonephritis

*Geometric or symmetrical lesions in the medulla may define a vascular unit and be ischemic i.e. NSAIDS

Hemorrhage ~ autolysis

Ovine Kidney w/ Pulpy Kidney Disease

Ovine enterotoxemia

Flaccid, wet kidney w/ hemorrhage

Kidney
Kidney

Lesions defining tubules – well demarcated, linear in the cortex or medulla; could be tubulointerstitial nephritis or deposits in tubules

*Tubulointerstitial nephritis can be either ascending or descending
Bov kidney w/ tubulointerstitial nephritis

Pig w/ urate deposits in medullary tubules

Pig kidney w/ urates in medullary tubules

Urates
Meuten’s Laws of Pale Kidneys

The 1st Law:
“Pale swollen, wet kidneys” = Nephrosis

Necrosis & edema ↑ P within renal capsule
When P exceeds the renal artery P, renal plasma flow stops, causing pre-renal azotemia
BUN, Cr ↑
The kidney is hypoperfused and becomes pale
Lamb w/ nephrosis - lead toxicity

Bov kidney
Oak Bud nephrosis
Bov kidney w/oak bud nephrosis

K9 Kidney w/ Ethylene glycol toxicity

Fel kidney w/ethylene glycol toxicity
Oxalate crystals – polarized light
Meuten’s Laws of Pale Kidneys

The 2nd Law:
“Pale swollen waxy kidneys” =
Amyloidosis

*Proteinuria contributes to the waxy feeling
Meuten’s Laws of Pale Kidneys

The 3rd Law:

“Pale, small, irregular (“lumpy bumpy”) firm kidneys” =
Fibrosis, Atrophy, Old infarcts.

(“End stage kidneys”)
K9 kidney w/ nephrosclerosis

Central Nervous System

Diffusely pale colored tissue due to high fat content. Some definition between grey and white matter. Hemorrhage stands out; cellular infiltrate and edema indistinct. *Symmetry very important in CNS evaluation

“The CNS is suspended in fluid within a closed space surrounded by bone. There is no room for anything else”

Central Nervous System

Lesions with hemoglobin (hemorrhage & congestion) are most visible because of the contrast.

Distribution is the key to lesion interpretation
Multifocal lesions suggest an embolic shower, w/ and w/o blood.
Septicemia, endothelial damage, platelet abnormality, DIC
Bov cerebrum w/ TEME
Thrombosis & infarction

Thrombus

Feline Cerebral Cryptococcosis

Soap Bubble
Lesion

Cat Brain w/ "Soap Bubble"
Lesion = Cryptococcus neoformans
Central Nervous System

Diffuse red may = Congestion or hemorrhage;
Distribution of lesions ~ location of the blood and may be the key to understanding the pathogenesis.
Central Nervous System

Dilated ventricles or aqueduct = Hydrocephalus
May be congenital or inflammation

K9 w/ subdural hemorrhage in brainstem ~ spinal tap

Cat w/ cerebral FIP

Hydrocephalus w/ high protein CSF
Any asymmetry in the brain is suggestive of an abnormality. Often subtle and easily overlooked.
Dog w/ Polioencephalomalacia

- Grey matter atrophy
- White matter

Asymmetrical hemispheres w/ collapse and discolored white matter = Leukoencephalomalacia

Goat w/ CAEV

Goat cerebrum w/ Leukoencephalitis – CAEV
LEW w/ leukoencephalomalacia
= mouldy corn poisoning

Horse cerebrum w/ Leukoencephalomalacia
= mouldy corn

Asymmetrical cerebrum with **swelling** = "something added"
Abscess
Neoplasia
Primary vs metastatic

Central Nervous System
EQ w/ cerebral abscess

K9 w/ oligodendroglioma

Dog w/ oligodendroglioma
Translucence in the CNS may ~ malacia and/or edema
- Can be masked by other processes and pigments i.e. hemoglobin
- Yellow may ~ malacia

Syringomyelia
Depressed and translucent

Herniation of the vermis into foramen magnum

Depressed ~ Collapsed
Spinal cord over cystic space

Cavity filled w/ clear fluid; Communicates w/ central canal

Central canal
Hollow tubular organ system separated into distinct segments all with mucous membrane and muscular tunics. Dense white color ~ musculature may mask color changes/lesions in the mucosa.

“No evaluation of the GI is complete without direct visualization of the mucosa”
Fibrinonecrotic (pseudomembranous, diphtheritic) inflammation with ulceration is a common response to necrosis on mucous membranes. Often signals lytic viral, bacterial, fungal, parasitic or ischemic disease. Focal, multifocal, segmental, diffuse may have different implications for pathogenesis.
Bov Esophagus w/ ulcers ~ BVD

- Ulcer w/ pseudomembrane
- Submucosal congestion

Boa constrictor w/ fibrinonecrotic colitis ~ salmonella

Snake w/ fibrinonecrotic colitis ~ Salmonellosis

Pseudomembrane

Colon wall
Lesions that cause thickening without mucosal ulceration and necrosis ("Morocco Leather") may be epithelial proliferation or granulomatous inflammation, ("sulci & gyri").

Granulomatous inflammation may = "space-occupying inflammation" and not cause necrosis.

Gastrointestinal System
Morocco leather

Bovine w/ chronic ostertagiosis

Morocco Leather abomasal mucosa

Ov abomasum w/ chronic ostertagiosis
K9 stomach w/ hypertrophic pyloric gastropathy

Dog pylorus w/ Hypertrophic pyloric gastropathy

Bov ileum w/ Johne's Disease
Inflammation & edema
Produce mucosal folds
= Morocco Leather

Cat w/ intestinal histoplasmosis
Morocco leather appearance of the surface of the GI

Macrophages w/ Histoplasma
EQ x-ssec of ileum w/ granulomatous enteritis

Submucosa

Lamina propria

EQ ileum w/ granulomatous enteritis

Submucosa

Lamina propria

Pig w/ proliferative enteritis ~ *Lawsonia*
Gastrointestinal System

Lesions on the serosal surface = peritonitis or serositis, not enteritis

Oesophagostomum nodules on the GI serosa

Cat Sm Int w/ FIP
A very complex organ with lobules, interstitium, many variably sized airways all of which can reflect lesions. Symmetry and organization of lesions is important in localizing disease. Physiologically dynamic size. A light pink colored, light in wt, dry tissue.

King’s Law of Pneumonia

“If its not firm, its probably not pneumonia.”

Anterior-ventral patterns suggest an aerogenous portal and often = Bronchopneumonia

If the lesions look “organized” or symmetrical, they may be defining an architectural subunit (lobule, airway etc.)
Rat lung w/ *Mycoplasma pulmonis*

Rat lung: X-sec caudal lobe
Bronchiectasis & Suppurative Inflammation – *Mycoplasma*

Bov lung w/ bronchopneumonia
Lung

Multifocal poorly demarcated pale foci may be highlighting airways without necrosis or pus;
Peribronchiolar and mucoid inflammation
Hilar to diffuse patterns suggest a vascular portal and may indicate edema or interstitial pneumonia. Interstitial pneumonia may be exudative or nonexudative.

Lungs are enlarged (rib impressions), heavy but may be wet or dry.
Sheep w/ lentiviral interstitial pneumonia
Bov lung w/ edema & emphysema
- Atypical interstitial pneumonia
- "Exudative" pneumonia

Bov lung w/ Penilla ketone toxicity
- Atypical interstitial pneumonia

Acute exudative interstitial pneumonia
- w/ edema and emphysema

Lung

Darker than normal lung often means
- atelectasis, or atelectasis with pneumonia
- Diffuse or lobular
Diffuse dark red wet heavy lung (congestion and edema) with miliary poorly demarcated white foci

“Multifocality implies an embolic shower”
Multifocal red lesions = **petecchia**
An embolic shower w/ vascular damage, sepsis, platelet defect or DIC
Swine w/ erysipelas

Pig lung w/ hemorrhage ~ Septicemia, Erysipelas

**Lung**

Multifocal white lesions = embolic shower

Septicemia ~ necrosis or abscesses, metastatic neoplasia
Antelope w/ Aspergillosis

Rat lung w/ Corynebacterium kutscheri
Rat lung w/ *Corynebacterium butcherae*
pyogranulomas

K9 lung w/ blastomycosis

Dog lung w/ pyogranulomas

~ *Blastomyces dermatitidis*
K9 lung w/ metastatic Thyroid carcinoma

Umbilication

Metastatic Thyroid Carcinoma
In the lung

Well demarcated

Central necrosis causes the collapse of the tumor producing the "umbilication" typical of some carcinomas

Bone

A dense white homogeneous hard tissue.
Marrow cavities with active marrow, vessels and hematopoietic elements provide good contrast but mostly there is poor contrast among bone, cartilage, marrow fat and cellular infiltrate
Bone

Opaque white lesions could = necrosis (infarction), cellular infiltrate (neoplastic or inflammatory) of bony proliferation;

Or...all 3!

Bov LSA

Bov rib w/ LSA
Tumor, necrotic bone, hyperostosis

Bov rib w/ LSA
Tumor, necrosis & hyperostosis
Subphyseal lesions may indicate an embolic event
~ blood supply to the growth plate. Fenestrated capillaries from the diaphysis turn back 180°
*location predisposed for septic and neoplastic emboli

K9 humerus w/ metastatic carcinoma

K9 humerus w/ Metastatic mammary CA
Goat radius w/ abscess ~ CLA
Goat humerus w/ abscess ~ CLA

EQ, foal metatarsus w/ septicemia
Hyperostosis
Subphyseal necrosis
Trabecular microfractures & fibrosis

EQ foal metatarsus w/ septicemia
Fractured trabeculae may mask or distract you from the primary problem.

Always look for the cause of the Fx."
EQ vertebral compression Fx - nutritional osteoporosis

EQ vertebral body w/ Osteoporosis & Pathologic fracture

K9 radius w/ HOD
Bone

Bony proliferation always looks the same everywhere but the location and characteristics can be instructive.

Bov mandible w/ hyperostosis and lysis – “Lumpy Jaw”

Bov humerus w/ growth retardation lattice
Pig femur, diaphysis w/ nutritional FOD
Cortical osteoporosis
Hyperostosis w/ FOD

Pig femur w/ nutritional FOD
Cortical osteoporosis
Cortical hyperostosis w/ FOD

Pig femur, epiphysis w/ nutritional FOD
Subphyseal FOD
Pig Femur w/ FOD

Subphyseal FOD

Bilaterally symmetrical maxillary FOD

EQ maxilla w/ "Big Head"

Bov humerus w/ osteopetrosis
Bov w/ congenital osteopetrosis

Fracture callus

Fractured rib

Neonatal calf w/ rib Fx
Chondroid proliferation looks a lot like bone, although somewhat translucent. But location and growth pattern are instructive.
Pig humerus w/ OCD

Horse vertebra w/ OCD lesion
On articular facet

Cartilage flap

Necrotic cartilage w/ fibrin, granulation tissue and new cartilage
Alpaca costochondral
Healed rickets

Dense disorganized trabeculae

Irregular thickening of the growth plate

Necrosis in the growth plate

Necrosis in the growth plate
Necrosis in the physis

"The Smoke that Thunders"
Victoria Falls, Zimbabwe - Zambia