Pathology of the Rat

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Pathology Of Laboratory Animals
CL Davis & SW Thompson Foundation
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Outline
• Anatomy
• Infectious Diseases
• Aging & Miscellaneous Diseases
• Neoplastic Diseases
• References

Comparative Pathology and Mouse Phenotyping

Rat Anatomy

Modified Sebaceous Glands: Preputial/Clitoral

Mammary Glands
• Rat: 6 pairs
  ❏ Absent in adult male
  ❏ Terminal duct lobular unit
    ✓ F: Many tubuloalveolar ducts, few acini around ducts
    ✓ M: Few lobuloalveolar ducts, many contiguous acini of lobules

Hematolymphoid System
• Hematopoiesis
  ❏ Bone marrow
    ✓ >90% cellular
    ✓ Myeloid: Erythroid – 1.97-1.93:1
  ❏ Spleen
    ✓ White vs. “red” pulp
    ✓ Prominent marginal zone
• Thymus completely involutes
• Mast cells everywhere!

Toxicologic Pathology 35: 199-207, 2007

Pathology of Rodents and Rabbits, 2016
**Hematolymphoid System – Lymph Nodes**

- CD Dijkstra, EWA Kampenrijk, AJP Veerman, pg 120-126, 1990
- In Hematopoietic System, TC Jones, JM Ward, U Mohr, RD Hunt (Eds)
- Monographs on Pathology of Laboratory Animals
- Sponsored by the International Life Sciences Institute

**Respiratory System**

- Right: cranial, middle, caudal, accessory lobes; Left: single lobe
- Extra-pulmonary bronchi only
- Pulmonary veins contain cardiac and smooth muscle
- BALT!

**Cardiovascular**

- Cartilage or bone at base of heart

**Salivary Glands – Sexual Dimorphism**

- Male: Submandibular gland: Granular convoluted ducts

**Liver**

- Binucleated cells
- Polyploidy: 2n (rat = 42)
- Anisocytosis/anisokaryosis
- NO GALL BLADDER!

**Kidney**

- Proximal: P1, P2, P3
- Long segment: short segment nephrons 3:1 → greater concentrating ability
- Medulla: outer (outer & inner stripes) & inner
Urine
- Urinate when handled
- >1.030 specific gravity
- Proteinuria normally!
  - Higher in males vs. females
  - Major urinary proteins = α,μ-globulins
    - Potent human allergens
    - Pheromones
    - Rat n 1

Male Reproductive
- Os penis;
- Copulatory plug;
- Spermatogenesis = 52 days

Female Reproductive

Nervous System
- Lissencephaly
- C7-T13-L6-S4-Cd27-30

Rat Pathology
- Signalement
  - Strain, age, sex
  - Husbandry
    - Caging/bedding, HVAC, diet
  - Sentinel health status
    - Know what is on institution’s exclusion list
  - Positive diagnostic pathology
  - Housing location
  - Experimental manipulation
  - Institutional/geographical variability
  - Communicate with clinical laboratory veterinarians & scientific staff
**Bacterial Diseases**

- **Mycoplasma pulmonis**
  - Murine respiratory mycoplasmosis (MRM)
    - Chronic respiratory disease (CRD)
  - Multifactorial
    - Strain, age
    - Concurrent infections, nutritional status
    - Environmental factors
    - Pet/wild rats
  - Transmission: direct contact, aerosol, intrauterine
    - Serology, PCR, culture
    - Respiratory tract, middle ear, endometrium

- **Mycoplasma pulmonis**
  - Suppurative exudate, abscessation
    - Same size, curvilinear
    - Bronchiolitis/bronchiolectasis
    - Lymphoid cuffing
  - CAR bacillus = frequent co-pathogen
  - Pathogenesis
    - Release of cytotoxic substances
    - Ciliostasis and ciliolysis
    - Neutrophils → lysozyme-rich → weakens bronchial walls
    - Intact organisms & cell membranes are mitogenic for B lymphocytes

**Mycoplasma pulmonis – Acute**

**Mycoplasma pulmonis – Chronic**

- **Veterinary Pathology**
  - 46: 952-959, 2009
- “Lymphomas” in rats in bioassays (Europe)
  - Aspartame, methyl-tertiary-butyl ether, methanol
  - Pleomorphic but immunoblastic
  - Lungs (within first 104 weeks of study)
  - Most common and often only tissue involved
    - Lymphocytes, plasma cells, neutrophils
  - Rats were not specific pathogen free (SPF)!
  - Slides not provided for review
  - 76.6% had bronchiolitis; 21.4% had otitis; seropositive for Mycoplasma
*M. pulmonis*: Eustachian tube → otitis media

**Mycoplasma pulmonis**
- Not the same as cell culture mycoplasmas!
- Lack a cell wall
- Fastidious
- Selective media for enrichment
- Keep for ~2 weeks
- Cross-reactive antigens between *M. neurolyticum* and *M. arthritidis*

**Filobacterium rodentium**
- Formerly cilia-associated respiratory (CAR) bacillus
- Transmission: direct contact, fomites
- Synergistic with other respiratory pathogens (*Mycoplasma pulmonis*)
- Gram negative bacilli among cilia
  - Warthin-starry positive
  - Bronchiolectasis
  - Lymphoid cuffing
  - Suppurative bronchopneumonia
- Serology, PCR, histology

**Corynebacterium kutscheri**
- Pseudotuberculosis
- Gram positive bacilli
- Transmission: direct contact, oronasal
- Asymptomatic carriers - persistent infection
  - Oral cavity
  - Lymph nodes
- Systemic suppurative inflammation w/ necrosis
  - Random/embolic (liver, lung, kidney)
- Prominent bacterial colonies within lesions
Streptococcus pneumoniae
- Gram positive diplococcus
- Transmission: direct contact, aerosol
  - Human/rat carriers (nose/ears)
- Systemic serofibrinopurulent inflammation
- Pathogenesis
  - Polysaccharide capsule
    - Resistant to phagocytosis
    - Activation of alternative complement pathway
  - Serotyping

Streptococcus agalactiae
- Comparative Medicine 63: 55-61, 2013
- B-hemolytic, Lancefield group B
- Munich Wistar Frömter X F344
  - Transgenic for human diptheria toxin receptor driven by podocin promoter
  - 38.5% of 21-24 day-old rats
  - Spontaneous myocardial necrosis, glomerulonephritis, abscesses, bacteria +/- inflammation
  - Resembles late-onset postnatal group B Strep infection in babies

Clostridium piliforme
- Intracellular, gram negative, spore-forming, filamentous bacilli
- Tyzzer’s disease
- “Species-specific”
- Ingest spores which remain infective for long periods in environment
- Poor husbandry, immunosuppression
- Organisms invade intestinal epithelium → dissemination

Clostridium piliforme
- Necrotizing hepatitis
- Necrotizing enterotyphlocolitis
  - Megaloileitis
- +/- Necrotizing myocarditis
- Warthin-Starry silver stain
- PCR on feces
- Cortisol provocation test for identification of subclinical carriers
Coronaviruses
- Sialodacryoadenitis virus, Parker’s rat coronavirus
- Transmission: aerosol, direct contact, fomites
  - Highly contagious!
- Hi morbidity, low mortality
- Salivary, harderian and lacrimal glands
- Rhinitis, tracheitis, bronchiolitis, alveolitis
- PCR, serology, IHC
- Prior infection protective up to 15 mo.
Rat Parvovirus

- Nonenveloped SS DNA viruses
  - Kilham’s rat virus (RV), Toolan’s H-1 virus, rat minute virus (1a-1c), rat parvovirus 1 and 2
- Transmission: oronasal, transplacental, milk, feces, fomites
- Persistence and reactivation
- Dividing cells (S) for replication → cytolysis (NS1 and NS2)
- Serology (ELISA → screen; IFA → confirmation), PCR

Rat Parvovirus

- Endothelial cells and megakaryocytes
  - Hemorrhage, thrombosis, necrosis
- Cerebellar cortex, periventriculus
  - Cerebellar hypoplasia
- Hepatocytes
  - Vacuolar degeneration
- Intranuclear inclusion bodies
- Decreased fertility, fetal resorption, small litters, runts
Fungal Diseases

http://www.biologyjunction.com/fungi_notes_b1.htm

**Pneumocystis**
- Species specific
  - Rats: *P. carinii, P. wakefieldiae*
- Ubiquitous
- Asexual: binary fission → trophic form
  - Sexual → ascus w/ 8 ascospores
- Pathogenic if immunodeficient
- Asymptomatic or 2nd bacterial/viral infections
- Dyspnea, rough hair coat, hunched, cyanosis, death

**Pneumocystis - Immunodeficiency**

- Inhalation of asci
- Ascospores released in alveoli
- Attachment to type I pneumocytes and macrophages by fibronectin-binding integrins
- Necrosis of pneumocytes w/ damage to alveolar basement membranes
- Type II pneumocyte hyperplasia
- Proposed: *Pneumocystis* binds to surfactant protein altering function

**Pneumocystis - Immunocompetency**

**“Rat Respiratory Virus”**
- Emerging disease (1997)
  - Worldwide distribution
  - 6% incidence in North America via histopath; 18% via serology/PCR
- Lymphohistiocytic interstitial pneumonia w/ perivascular lymphocytic cuffing
- Causative agent identified as *Pneumocystis carinii* in fall 2010
- Pneumocystis DNA by PCR in 87% of paraffin-embedded lung lesions attributed to RRV
- Koch’s postulate
  - PCR (1-10wks), serology (5-8wks), histopathology (4-10wks)
**Pneumocystis**

- Immunocompetent rats
  - Anesthetic complications/death
  - Inhalational toxicology studies
- Similar lesions in immunocompetent mice
  - \( P. \) *murina*
  - \( P. \) *jirovecii* in immunocompetent humans
  - SIDS
  - COPD
  - Asthma
  - Bronchiolitis

**Cysticercus fasciolaris**

- Larval stage of cat tapeworm
  - *Taenia taeniaformis*
- Ingestion of eggs in cat feces
- 1-2 cysts in liver
- Granulomatous inflammation, fibroplasia \( \rightarrow \) fibrosarcoma

**Trichosomoides crassicauda**
- Bladder threadworm (nematode)
- Urinary bladder and renal pelvis
- Embryonated, bi-operculate, brown eggs
  - Passed in urine
  - Hatch in stomach → systemic
  - Only larvae reaching urinary system survive
- White masses
  - Epithelial hyperplasia
  - Paucity of inflammation
- *“Association”* w/ calculi and neoplasia

**Aging & Miscellaneous Diseases**

**Polyarteritis Nodosa (PAN)**
- NPA: Mouse counterpart → vestibular syndrome
- PAN: Rat (Sprague Dawley, SHR, ACI) → no clinical signs - hemoabdomen
- PAN: NHP
- K9: Beagle pain syndrome / juvenile polyarteritis → neck pain
- Small- to medium-sized arteries
- Fibrinoid degeneration, neutrophilic to lymphoplasmacytic inflammation, myointimal hyperplasia and fibrosis
- Segmental, acute to chronic, multiple arteries
- Immune complexes
  - Cause?
  - NOTE: "PAN" in sheep due to ovine herpesvirus-2

Pesavento et al., *Veterinary Pathology*, 56: 87-92, 2019

Comparative Medicine 57: 370-376, 2007
Chronic Progressive Nephropathy (CPN)
• Chronic progressive nephrosis; chronic nephrosis; glomerulosclerosis; progressive glomerulosclerosis; glomerulonephritis; chronic nephritis; nephropathy; old rat nephropathy
• ≥75% incidence
• Age: ≥12 months
• Sex: M (castration = protective)
• Strain: Sprague Dawley, F344, SHR
• Diet: ad libitum, high protein
• Immune: mesangial IgM deposition
• Hormones: high prolactin
  - Chronic prolactin: no change in specific gravity, pH, volume, K; ↓ Na
  - Inhibition: ↑ volume, pH, K & Na excretion
• Microbe status: microbe-associated

CPN – Associated Clinical Findings
• Hypoproteinemia
• Proteinuria
  - Normal!!!
  - Albumin, α₂-globulin
• Azotemia
• Hypercholesterolemia
• Weight loss
• Hydrothorax, ascites
• Soft-tissue mineralization
• 2° hyperparathyroidism → fibrous osteodystrophy
• Hypertension
• Polyarteritis nodosa

CPN – Precursor Lesion (Basophilic Tubules)

Nephrocalcinosis
• F344, BD1X
• Microlithiasis
• >3% incidence
• F > M
• ↓ magnesium
• ↑ calcium
• ↑ phosphorus
• ↓ calcium:phosphorus
• Calcium phosphates at corticomedullary junction
Hydronephrosis

- Hereditary
  - Brown Norway
  - Gunn
  - Sprague Dawley
  - Zucker
- Spontaneous
- Males
- Polygenetic
- Right kidney in males
  - Passage of internal spermatic vessels across ureter

Urinary Calculi

- Renal pelvis, ureter, bladder, urethra
- Variable composition
  - magnesium ammonium phosphate (struvite)
  - carbonate, oxalate; carbonate-phosphate, magnesium, calcium
  - Alkaline urine + NH3, urease-producing bacteria: Proteus, E. coli, Klebsiella, Pseudomonas, Ureaplasma, Staph
- Genetic; retinoid supplementation, radionuclides
- Dx: copulation plug!

Hematuria / Renal Papillary Hyperplasia

- Lewis X Brown Norway
- M > F
- +/- uni- or bilateral hydronephrosis

Cardiomyopathy

- Rodent progressive cardiomyopathy, chronic progressive cardiomyopathy, myocardial degeneration and fibrosis
  - ≥25% → 100% with "enhanced sectioning"
  - Sprague Dawley
  - M > F
  - Ad libitum diet, environment, stress
- Little evidence of cardiac insufficiency
- LV, papillary muscle, IVS
- Degeneration, interstitial mononuclear cells, atrophy, fibrosis, mineralization, cartilaginous/osseous metaplasia
- Veterinary Pathology 52: 201-208, 2015
- Toxicologic Pathology 41: 1126-1136, 2013
  - Serum troponin WNL

Miscellaneous Cardiac Lesions

- Intracardiac thromboses
  - LA >> RA > LV
- Valvular endocardiosis
- Arterio-/atherosclerosis
- Hypertension
- Renal disease, polyarteritis nodosa
- Endocardial/subendocardial proliferations
  - Hyperplasia vs. schwannoma vs. sarcoma
  - Fibroblast-like, precursor to schwannoma
  - Superficial round cells; deep spindle cells whorling around chordae tendineae
  - Infiltrates into myocardium

La Perle/POLA.Rat.2019.updated
Alveolar Histiocytosis

- Subpleural histiocytes
  - FFA, cholesterol, phospholipids
- Not infectious!
- Resolved inflammation
  - Rat coronavirus/SDAV
- Localized pulmonary clearance deficit
- Pulmonary injury → type II pneumocyte hyperplasia → surfactant overproduction → accumulation in macrophages

Spontaneous Radiculoneuropathy

- Degenerative myelopathy
- Posterior paresis, loss of tail control, urinary incontinence
- Bilaterally symmetrical
- T4-L4 (lateral & ventral funiculi), cauda equina, ventral spinal nerve roots, sciatic & brachial plexus, lower brainstem
- Axonal swelling (spheroids), axonal sheath swelling, axonophagia
- Astroglialis
- Demyelination
- Lipofuscin
- Muscle atrophy

Aspiration Pneumonia

Bile Duct Hyperplasia & Portal Fibrosis

Auricular Chondropathy

- Auricular chondritis, cauliflower ear
- Uni- to bilateral misshapen ears
- +/- ear tag → trauma
- Degeneration, chondrolysis, cartilage hyperplasia, osseous metaplasia
- Granulomatous inflammation
- Humans: relapsing polychondritis
  - Multiple sites (hyaline & elastic cartilage)
  - Autoantibodies to collagen types II, IX, X
**Eosinophilic Granulomatous Pneumonia**
- Brown Norway Rats
- Asthma animal model
  - ↑ bronchiolar responsiveness
  - ↑ IgE following exposure to allergens
- Pneumonia presents without experimental manipulation
- Cause? Hypersensitivity reaction?

**Corneal Dystrophy**
- F344: 10-15%
- Wistar: 53-58%
- Punctate to linear opacities
- Ca & P w/ less Fe, Zn, Na, Al
- Calcific band keratopathy
- Anesthesia (ketamine/xylazine)
  - ↓ blink response → corneal ulceration
- Vasoconstriction → hypoxia
- Ammonia

**Retinal Degeneration**
- Age-related photoreceptor attrition
- Light intensity
  - Recommended: 325-400 lux
- Environmental & body temperature
- Exposure time
- +/- cataracts

**Malocclusion**
- Ptyalism, cellulitis, weight loss
- Powdered diet

**Ringtail**
- ↓ humidity (<25%)
- Genetic susceptibility
- ↑ environmental temperature
- Hydration status
- Nutrition
- Preweaning rats
- Annular constrictions
- Dry gangrene

**Chloral Hydrate Ileus**
- Anesthesia; euthanasia
- IP injections
- Up to 5 weeks post-administration
- Segmental atony and distention
- Peritonitis and gastric ulcers
- Abdominal wall necrotizing myositis
**Neoplastic Diseases**

<table>
<thead>
<tr>
<th>Table 1. Comparison of Incidence of Neoplasms in SD, F344 &amp; Wistar Rats, Toxicologic Pathology: 45: 64-75, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Disease</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Lymphoma</td>
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<tr>
<td>Leukemia</td>
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<td>Sarcoma</td>
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<td>Malignant Melanoma</td>
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<tr>
<td>Carcinoma</td>
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</table>

**Lymphoma & Leukemia**

- INHAND (in preparation!)
- Morphology only
  - Lymphoblastic
  - Pleomorphic, Pleomorphic/Follicular or Follicular
  - Immunoblastic
  - Plasma cells
  - Marginal Zone
  - Lymphocytic (small cell)
  - Cutaneous T cell
  - Large granular lymphocyte (LGL) leukemia

**Large Granular Lymphocyte Leukemia**

- F344 rats
- ↑ incidence with certain chemicals
- Spleen → systemic
- NK cells...maybe!

- "Mononuclear cell leukemia" (NTP to date)
  - Fundamental & Applied Toxicology 12: 252-257, 1989
  - Staged according to extent of disease

- Acute leukemia
- Concurrent IMHA, thrombocytopenia, DIC
- Similar leukemia in humans!
- No retroviruses
- Syngeneic transplantation
### Large Granular Lymphocyte Leukemia

- **Normal**
- **1 - Early**
- **2 - Intermediate**
- **3 - Advanced**

- OX-8 (CD8a)
- Granzyme

### Mammary Gland Tumors
- **Males and females!**
- Sprague Dawley
- Genetic, dietary, environmental, endocrine
- ↓ w/ food restriction, ovariectomy
- Prolactin levels
- Not associated with retroviruses!
- Fibroadenoma >>> carcinoma
- Recurrence vs. new tumor(s)?
- Rarely metastasize
- Syngeneic transplantation

### Mammary Fibroadenoma
- Recurrence vs. new tumor(s)?
- Rarely metastasize
- Syngeneic transplantation

### Pituitary Gland Tumors
- Sprague Dawley, Wistar
- Age, genetics, diet, breeding
- ↓ w/ food restriction, mating
- Adenomas > carcinomas
- Pars distalis > pars intermedia
- Chromophobe, prolactin-producing
- ↑ incidence of fibroadenomas?

### Tumors of Skin & Other Glands
- Zymbal’s gland
  - Base of external ear
  - Locally invasive
  - Not metastatic
- Preputial/cilitoral gland
  - Locally invasive
  - Metastasize to regional LNs and lungs
- Keratoacanthomas
  - Up to 8% incidence depending on strain
  - Chemically-induced!

### Mammary Fibroadenoma
- 6 pairs!

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Zymbal’s Gland Carcinoma

Preputial/Clitoral Gland Carcinoma

Keratoacanthoma

Interstitial Cell Tumor
- Leydig cells
- Aged strains
- F344
- Concurrent hypercalcemia

Mesothelioma
- F344
- 2 subtypes in humans and rats (repeated IP ferric saccharate)
  - Epithelioid/epitheliomatous
    - 1st site = tunica vaginalis of testes
    - Papillary growths
  - Mesenchymal/sarcomatous
    - Cranial abdominal organs
    - Invasiveness
    - CDKN2A/2B null and amplification of ERBB2
- Look for concurrent mesothelioma and interstitial cell tumor!
**Mesothelioma**
- **Epitheliomatous**
- **Sarcomatous**

**Rat: 3 Diagnoses?**

**Multiple Endocrine Neoplasia (MEN)**
- Frequently diagnosed concurrently in aging rats:
  - Islet cell tumor
  - Pheochromocytoma
  - Thyroid follicular adenoma
  - Thyroid parafollicular (C-cell) adenoma
  - Pituitary gland, pars distalis adenoma
- Documented in humans & veterinary species

**MEN**
- MEN1
  - Loss of function mutations in Menin
  - Parathyroid, gastroenteropancreatic, anterior pituitary
- MEN4
  - CDKN1B (p27)
  - Same tumor spectrum as MEN1
  - MENX = spontaneous rat model (autosomal recessive)
    - Parathyroid adenomas, islet hyperplasia, C-cell hyperplasia, pheochromocytomas, paragangliomas, cataracts
- MEN2
  - Gain of function mutations in RET
  - Adrenal and thyroid medullary tumors
- MEN3 (2B)
  - Adrenal/Thyroid medullary tumors
  - Mucocutaneous neuromas, intestinal ganglioneuromas, marfanoid habitus, prominent corneal nerves

**Thyroid Gland**
- Follicular
  - Hyperplasia
  - Adenoma
    - Microfollicular, macrofollicular, cystic
  - Carcinoma
    - Metastases to regional LNs, lungs
  - Thyroglobulin
- C cell
  - Focal-diffuse hyperplasia
  - Adenoma
  - Carcinoma
  - Amyloid
  - Calcitonin
Adrenal Medulla
- F344, M > F
- Environment, strain, endocrinopathies, diet, chemicals
- Lack catecholamine synthesis/release, urinary excretion or elevated BP
- Basophilic focus → hyperplasia → benign/malignant
- Pheochromocytoma
  - Chromaffin cells
  - Ganglioneuroma
- Ganglion, satellite cells, Schwann cells, nerve fibers (>80%)
- Neuroblastoma
  - Neuroblasts (>80%)
- Complex: mixture (neural component < 80%)

Pancreatic Islets
- Hyperplasia → dissecting fibrosis
- Hyperplasia
  - Duct ligation w/ destruction & atrophy of acinar parenchyma
  - Variable numbers of islets affected
- Adenoma
  - Insulin > somatostatin, glucagon, pancreatic polypeptide
- Carcinoma
  - Local/organisms invasion, anaplasia +/- lung metastases
Islet Cell Tumor

Granular Cell Tumor

- Brain/meningeal: rat, dog, ferret
- Rat: uterus
- Dogs: tongue, heart
- Horses: lung
- Granules: PAS + with diastase resistance
- Alcian blue +

Granular Cell Tumor

- Controversy: muscle or Schwann cell origin
- IHC immunoreactivity
  - Positive: vimentin, S-100, NSE, myelin-related protein → Schwann cell origin
  - Negative: GFAP, canine leukocyte antigens, epithelial markers, macrophage markers, muscle antigens
  - Uterine tumors in B6C3F1 mice: +/- desmin or SMA → smooth muscle origin (no cross striations, PTAH negative)

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Nephroblastoma

- Rare except subline of Sprague Dawley – Up: TUC/SDsprf/rb
  - Genetically predisposed
  - 14% incidence
  - Chemically-induced
  - Model for Wilms tumor in humans
- 3 components
  - Blastema
  - Stroma
  - Immature epithelium forming tubules
- Precursor lesion: intralobar nephroblastomatosis
  - Embryonal tissue in rat present until d. 7-8
**Nephroblastomatosis**

**Chordoma**
- Intraosseous remnants of notochord
- Lumbosacral/sacroccocygeal > sphenoid-occipital
- Slow growing, recur, metastasize
- Ferrets > dogs, cats, rats, mink
- Sprague Dawley, F344
- 56/115K
- M>F 3:1
- Paresis, paralysis, megacolon

**Chordoma**
- Physaliphorous cells
  - Vacuolated, eccentric nucleus
  - Cytokeratin + AND vimentin +
- Fibrous trabeculae
- Pools of mucin
- Humans
- Variant = chondroid chordoma
  - Sphenoid-occipital
  - Better prognosis

**References – 1**

**References – 2**

**References – 3**
- National Toxicology Program Nonneoplastic Lesion Atlas
- International Harmonization of Nomenclature and Diagnostic Criteria,
  - www.toxpath.org/inhand.asp
- Proliferative & non-proliferative lesions of mice & rats:
  - Cardiovascular
  - Bone, joints, teeth
  - GI tract, pancreas, salivary glands
  - Female reproductive system
  - Male reproductive system
  - Soft tissue, skeletal muscle, mesothelium
  - Integument
  - Mammary, Zymbal’s, preputial, clitoral glands
  - Urinary system
  - Central and peripheral nervous systems
  - Hepatobiliary system
  - Respiratory tract
  - Endocrine
  - Special Senses
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• Noah’s Arkive
• The Jackson Laboratory
• Dean Percy – Pathology of Laboratory Rodents and Rabbits, 4th Edition

Questions?

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