Pathology of the Rabbit

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PURPOSE

The purpose of this block of instruction is to gain knowledge and experience in the gross and histologic diagnosis of diseases of rabbits. Of course, the study of disease in this species far exceeds what can be presented in a three hour block of time, but I will attempt to cover a number of diseases of interest. In some cases, inclusion or exclusion from this collection was the result of the availability of high-quality photographs. I am a firm believer that one can learn far more from one excellent photograph of a single entity, than from many poor ones. If the only available image is of poor quality, the image won't leave a lasting impression, and the student learns nothing.

I have included a brief morphologic diagnosis for each entity. The formulation of concise, accurate morphologic diagnoses is a major pursuit of every good pathologist, especially those who seek certification in this specialty. The formulation of a good morphologic diagnosis is a learned skill; for those seeking additional experience in this endeavor, I would suggest attendance at the annual C.L. Davis Foundation Descriptive Pathology Course (given often in Europe and South America, as well as in the US).

PMID is PubMed ID. PMCID is PubMed Central ID (for free full text papers).

Slide No.	Organ	Condition	Morphologic Diagnosis	Notes
1-6	DISEASES OF LABORATORY RABBITS (*Oryctolagus cuniculus)*			
7-8	Presentation	Taxonomy	European (old world) versus American (new world) rabbits	Laboratory rabbits are nearly universally *Oryctolagus cuniculus.* Non-domesticated American rabbits (*Sylvilagus spp.)* are only rarely used. Conditions presented will be of *Oryctolagus cuniculus* rabbits except where otherwise noted. Because many reports describe conditions of pet or meat/fiber rabbits, I will attempt to be clear when incidence figures are not derived from laboratory populations.
10-36	Presentation	Normal	Normative physiologic and anatomic data for European rabbits	
14	Ear pinna	Injection-related injury	Auricular infarct, chronic, FE	The marginal ear vein is a common site for administration of intravenous medications and other substances. Thrombosis or extravasation of caustic agents may result in sloughing of the pinna distal to the site of injection. There is also a central auricular artery for blood sampling.
16	Lung	**Euthanasia solution artifact**	Barbiturate euthanasia solutions are corrosive and can obscure pulmonary histology, particularly when given in excess (PMID: 18547259)	

24	Stomach	Normal	Cecotrophs	Cecotrophs are mucus-covered feces passed in early morning and are rich in B vitamins and proteins. Cecotrophy is controlled by the adrenal glands and fusus coli, and may be altered during periods of excessive stress. Rabbits consume cecotrophs directly from their anus; ergo cecotrophy is unaffected by wire bottom cages but is prevented by Elizabethan collars.
25	Normal GI tract	Post-mortem autolysis	Because rabbits have fermentative digestion, a heavy fur coat, and often abundant visceral and subcutaneous fat, post-mortem autolysis is usually rapid, particularly within the abdomen	
27-28	Urinary bladder	Normal	Ammonium magnesium phosphate, calcium carbonate monohydrate, and anhydrous calcium carbonate	Urine crystals are found in large amounts in rabbit urine and should not be interpreted as a pathologic change. Rabbits regulate calcium metabolism primarily via renal excretion (rather than intestinal absorption); approximately 45-60% of calcium is excreted in the urine.
31	Vagina (histology)	Normal	Vaginal mucosa	Unlike rodents, the majority of the vaginal mucosa is simple columnar and mucinous, only becoming stratified squamous cornifying near the vestibule
32	Ovary (histology)	Normal	Prominent interstitial glands	Not a luteoma PMID: 4208862
35	Peripheral blood	Normal	Heterophils	Because of intense staining characteristics, the rabbit orthologue of the neutrophil is called the heterophil.

				Functionally and ultrastructurally, however, it is the equivalent of the neutrophil (unlike avian or reptilian heterophils).
36	Spleen/pancreas	Ectopic (daughter) spleen		Common incidental finding. Rabbit spleens are generally small (<2.5 g).

32	**VIRUSES**			
Slide No.	**Organ**	**Condition**	**Morphologic Diagnosis**	**Notes**
38	Presentation	Review of Current Standardized Viral Taxonomy		
39	Presentation	**Rabbit hemorrhagic disease virus (RDHV)**	Type species of *Lagovirus, Caliciviridae*	High morbidity and mortality. **<u>REPORTABLE TO USDA APHIS.</u>**
40	Whole body		Epistaxis	High mortality and hemorrhagic lesions with no premonitory signs are typical
41	Lungs		Acute pulmonary hemorrhage	
42	Liver, gross and histology		Massive acute hepatocellular necrosis	A number of hemorrhagic disease/fever viruses of concern in laboratory animal medicine target hepatocytes and monocytes/macrophages. Release of tissue factor (III (F3)) from infected MPS cells activates the extrinsic coagulation system, which combined with secondary diminished production of clotting factors (particularly the short-lived factor VII) results in bleeding tendencies. PMID: 10225271, 22325049, 30861586
43	Presentation		Coagulation cascade	

JPC (AFIP) WSC Case(s)		RDHV	**2012 conference 10 case 4** **2003 2-1** **2000 10-2** **1997 12-1** **1989 18-1**	
Noah's Archive Images			**F14536-F14546, F21969-F21977**	
44	Presentation	**Michigan rabbit calicivirus**		Single outbreak in 2001 PMID: 19961675 (PMCID: PMC3044539)
45	Conjunctiva, stomach, liver		Acute hemorrhage and necrosis	
46	Presentation	**Myxoma virus**	Type species of *Leporipoxvirus, Poxviridae*	Asymptomatic reservoir in *Sylvilagus spp,* with arthropod vectors High morbidity and mortality in *O. cuniculus* **<u>REPORTABLE TO USDA APHIS.</u>**
47	Whole body		Nodular cutaneous myxomatosis	
48	Head		Nodular cutaneous myxomatosis with acute suppurative conjunctivitis	
49	Leg		Cut nodule showing wet myxomatous appearance	
50	Skin (histology)		Nodular cutaneous myxomatosis	Atypical spindloid cells with large (pox) ICIB in a loose myxomatous matrix. Abundant necrosis. ICIB may also be found in overlying epidermis.

JPC Case(s)		**Myxoma virus**	**2016 9-1** **2012 2-2** **2006 4-3** **2002 17-4** **1983 24-4**	
Noah's Archive Images			**F00032, F04484, F04485, F04486**	
51	Presentation	**Shope fibroma virus**	*Leporipoxvirus, Poxviridae*	10% of cutaneous tumors in pet rabbits reported to be viral fibromas. PMID: 17846230
52	Whole body		Nodular cutaneous fibromatosis	Solid and less wet on cut section. More common on extremities.
53	Skin mass (histology)			Closely packed atypical spindloid cells with large eosinophilic ICIB. Dense mononuclear leukocyte infiltrates at the margins. ICIB may also be found in overlying epidermis.
JPC Case(s)			**2014 4-1** **2006 4-3** **2003 19-3** **2000 3-1** **1990 6-2** **1986 3-1** **1982 17-2**	
Noah's Archive Images			**F04577, F04578**	
54	Presentation	Rabbit pox	Tongue, glossitis, proliferative and necrotizing, multifocal	Typical pock lesions

55	Presentation	**Leporid herpesvirus-4 (LeHV4)**	*Herpesviridae, alphaherpesvirinae, simplexvirus, Leporid alphaherpesvirus-4*	Severe disease clinically and grossly resembling myxomatosis with conjunctivitis and edema *Jin L, et al.. Vet Pathol. 2008 May;45(3):369-74.* PMID: 18487496.
56	Head (gross) and skin (histology)			
57	Whole body, lungs and spleen		Pulmonary hemorrhage and splenic necrosis	*Sunohara-Neilson JR, et al.. Comp Med. 2013 Oct;63(5):422-31.* PMID: 24210019*; PMCID: PMC3796753.*
JPC Case(s)			**1992 30-3 (probably)** **2014 18-2**	
58	Presentation	Herpes simplex	*Human alphaherpesvirus-1* and *-1;* both are *Herpesviridae, Alphaherpesvirinae, Simplexvirus. HHV1* is the type species.	Reverse zoonosis. Humans are the only definitive host. PMID: 19566457, 9150545, 12056779, 25085871
JPC Case(s)			**2015 16-3**	
59	Presentation	**Sylvilagus floridanus papillomavirus -1**	AKA Cottontail rabbit papillomavirus (CRPV) or Shope papilloma virus Species *Kappapapillomavirus 2, t*ype species of *Kappapapillomavirus*	Spontaneous disease in *Sylvilagus.* Can be spread to *Oryctolagus* by mosquitoes. *O. cuniculus* can be experimentally infected as an animal model of human papillomavirus infection

60	Whole body, *Sylvilagus floridanus*	**SfPV1**	Skin, cutaneous horns	
61	Whole body		Skin, papillomas	Experimental inoculation of CRPV by scarification. ~25% will progress to squamous cell carcinoma.
62			Skin, cutaneous horn	
Noah's Archive Images			**F05296, F24705**	
63	Tongue	**Oryctolagus cuniculus papillomavirus -1 (OcPV1)**	AKA Rabbit oral papilloma virus Species *Kappapapillomavirus 1* Papillomas	*O. cuniculus* are natural host Lesions limited to oral mucous membranes, usually tongue
64	Presentation	Rotavirus Coronavirus Hepatitis E virus Adenovirus (Europe) Bornavirus (Europe)	Other pathogenic viruses of rabbits	Hepatitis E has been identified in domestic rabbits (including purpose-bred laboratory rabbits) in the US and China and represents a potential zoonosis (PMID: 24937350; 24655426; 25773737).
65	Presentation	Rabies		Rabies is of course zoonotic and reportable. This mostly occurs in pet rabbits housed outdoors. PMID: 25029313 Rabbits are also an important experimental model for rabies

66	Presentation	Leporid herpesvirus-1 Leporid herpesvirus-2 Leporid herpesvirus-3 Rabbit kidney vacuolating virus Sendai virus	Apathogenic viruses of rabbits	These agents are apathogenic in *Oryctolagus cuniculus*. May cause disease in *Sylvilagus* (e.g. Leporid herpesvirus-3 (Herpes sylvilagus*)* causes an experimental lymphoproliferative disorder). Agents may contaminate *Oryctolagus* cell cultures. PMID: 4341558; 2548035; 14077040

67	**BACTERIA**			
Slide No.	**Organ**	**Condition**	**Morphologic Diagnosis**	**Notes**
68	Presentation	***Pasteurella multocida* type A or D**	"Snuffles" is the most common presentation of pasteurellosis, with up to 70% of animals affected in some colonies. Direct contact is required for animal-to-animal transmission. This is a rare disease in modern laboratory facilities, but was historically common and may be present in commercial rabbitries.	
69	Skull		Normal anatomy	It is imperative to remove the nasal bones during rabbit necropsies to examine and culture this area.
71	Head		Purulent nasal discharge	Acute or chronic rhinitis is the most common clinical manifestation of this disease dDx: Bordetellosis

72	Head	***Pasteurella multocida* type A or D**	Atrophic rhinitis	Loss of nasal turbinates. Increased numbers of osteoblasts and osteoclasts may be seen.
73	Whole body		Torticollis	Otitis media is common. Torticollis is seen when the inflammatory process extends to the inner ear. In affected colonies, otitis media ranges up to 33%, while torticollis rarely hit 5%. Other nervous diseases (e.g. *Encephalitozoon cuniculi*) may also result in torticollis.
74	Head (radiograph)		Fluid density in tympanic bullae	Chronic otitis media
75	Brain		Acute suppurative meningitis	Meninges of ventral brainstem are cloudy with purulent exudate
76	Brain		Brain abscess	Look for concomitant rhinitis and ophthalmitis.
77	Thoracic pluck		Acute severe fibrinosuppurative pleuropneumonia	
78	Thoracic pluck		Lung abscess	Sequela to chronic lung infection. Walled-off abscesses may appear in any organ. The pus is usually viscous and difficult to drain.
79	Whole body		Empyema/pyothorax (suppurative pleuritis and pericarditis)	

80	Thoracic pluck	***Pasteurella multocida* type A or D**	Chronic fibrinosuppurative pericarditis	"Bread and butter" heart
81	Head and ventral neck		Subcutaneous abscess	Walled-off abscesses may appear in any organ. The pus is usually viscid and difficult to drain. The most common site for abscesses is the subcutaneous tissues, especially around the head, neck, and shoulders. dDx. *Staph aureus,* ranula, sialocoele
82	Abdomen		Diffuse severe fibrinosuppurative peritonitis	dDx. *Salmonella sp.*
83	Head		Chronic keratitis and hypopyon	dDx. *Staph aureus,* vitamin A deficiency
84	Testis		Chronic abscess	Male and female genital tract infections are common. This is a common site of colonization for subclinical carriers. dDx. *Staph aureus*
JPC Case(s)			**2000 7-3** **1990 6-4** **1988 19-4**	
Noah's Archive Images			**F33698, F03835, F09404, F22695, F22696**	

85	Presentation	***Bordetella bronchiseptica***		Generally indolent disease. Can cause clinical rhinitis and pneumonia, usually in kits.
86	Head		Purulent nasal discharge	
87	Whole body, thoracic pluck		Acute suppurative bronchopneumonia	
JPC Case(s)			**2010 25-2** **1995 24-1**	
88	Presentation	***Staphylococcus aureus***		Type C *Staph aureus* has occasionally been associated with "snuffles."
89	Mammary glands		Focally extensive gangrenous mastitis	Blue bag similar to dairy cattle. Can be passed to nursing kits.
90	Whole body, kits		Suppurative epidermitis	The acute septicemic form is most commonly seen in suckling kits during the first weeks of life and is associated with high mortality. Rarely, *S. aureus* may become septicemic in adult rabbits.
91	Thoracic pluck		MF lung abscesses (embolic pneumonia)	This lesion may follow septicemia in an adult animal.
JPC Case(s)			**2012 7-1** **1997 10-1** **1991 4-1**	
Noah's Archive Images			**F06519, F06520**	
92	Presentation		Differential etiologies for diarrhea in rabbits	

93	Presentation	***Clostridium spiroforme*** *Clostridioides difficile* *C. perfringens*	Clostridial typhlocolitis	Disease often follows weaning, anorexia or high energy (low roughage) diets, and is a type of dysbiosis. Administration of β-lactams, macrolides or lincosamides can precipitate disease. Diarrhea is followed by shock and death, generally with rapid disease progression barring (or in spite of) aggressive intervention. Diagnosis is not by culture, as these agents can be normal flora (PMID: 24961954, 6841578). Definitive diagnosis requires demonstration of toxin production. *C. spiroforme* can be tentatively diagnosed by clinical signs and large numbers of curved to spiral (coiled) Gram positive bacteria with spores in feces or cecal contents.
94	Whole body		Soiling of perineal hair (diarrhea)	
95	Whole body		Acute hemorrhagic typhlitis	Transmural hemorrhage with a granular appearance to the serosa due to edema and fibrin
96				
97	Cecum (Histology)		Acute ulcerative typhlitis	Ulceration and proliferation in the mucosa with submucosal edema and hemorrhage Cecum autolyzes extremely quickly. Samples from rabbits found dead are non-diagnostic.
98	Feces (Gram stain)	*Clostridium spiroforme*	Circular to spiral (coiled) filamentous Gram positive spore-forming organisms	PMID: 6841578, 6623885, PMC3318402
JPC Case(s)			**1999 19-4**	

99	Presentation	***Clostridium piliforme***		Tyzzer's disease. Trifecta of hepatitis, typhlitis and myocarditis
100	Liver		MF acute necrotizing hepatitis	
101	Liver (histology)			Intracellular filamentous bacteria (haystacks) at margins of necrosis. Wright Giemsa or silver stain (GMS, Steiner, Warthin-Starry, etc.).
JPC Case(s)			**1980 9-4**	
Noah's Archive Images			**F09412, F33755**	
102	Presentation	***Lawsonia intracellularis***	Proliferative enteropathy Ileotyphlitis	Obligate intracellular bacteria PMID: 9684975, 9001174, 18460834
103	Jejunum		Proliferative enteritis	Experimental infection PMID: 24082402
104	Cecum (histology)		Proliferative typhlitis	
105	Cecum (histology)		Argyrophilic intracellular curved bacteria in apical cytoplasm	Warthin-Starry (or Steiner)
JPC Case(s)			**2004 3-4** **2002 16-4** **1994 15-3** **1990 7-4**	

106	Presentation Whole body	***Pseudomonas aeruginosa***	Haired skin of ventral neck, moist dermatitis with discoloration of fur	Blue fur disease. Bacterial pyocyanin stains fur. Agent also causes opportunistic infections including hemorrhagic pneumonia
JPC Case(s)			**1999 12-3** **1992 21-1**	
107	Presentation Airway (histology)	***Cilia Associated Respiratory Bacillus (CARbacillus)***	BALT hyperplasia (lymphoid cuffing) and filamentous argyrophilic bacteria within and parallel to cilia	Species specific, usually subclinical. Warthin-Starry or Steiner silver stains, Wright-Giemsa, GMS.
JPC Case(s)			**1995 24-1**	
108	Presentation	***Treponema paraluiscuniculi*** *(*formerly *T. cuniculi)*	Rabbit syphilis	Benign venereal infection. No systemic infection. Serology available. **NOT ZOONOTIC.** PMID: 6895536, 6895535, 6895534
109	Whole body (male)		Chronic ulcerative balanoposthitis	
110	Whole body (female)		Chronic ulcerative vulvar dermatitis	
111	Muzzle		Chronic ulcerative nasal dermatitis/cheilitis	Smell is important in rabbit behaviour
112	Smear from lesion		Argyrophilic bacterial spirochete	Warthin-Starry or Steiner silver stains
JPC Case(s)			**1991 8-2** **1987 6-1**	

Noah's Archive Images			**F05780**	
113-114	Presentation	*Other Bacterial Infections* *Francisella tularensis* (tularemia) *Salmonella sp.* *Escherichia coli* *EPEC* *EHEC* *Klebsiella pneumoniae* *Listeria monocytogenes* *Yersinia pseudotuberculosis* *Y. enterocolitica* *Fusobacterium necrophorum* (Schmorl's disease)	Other bacteria Plague and tularemia are reportable zoonotic select agents. Endemic in the USA and spread by arthropod vectors, aerosols, and fomites.	
JPC Case(s)			**2015 14-2 (EPEC)** **2015 12-3 (Yersiniosis, European hare)** **2013 12-2 (EPEC)** **2012 15-4 (Listeriosis)** **1997 30-3 (Tularemia in *S. floridanus*)** **1995 12-2 (EPEC)** **1987 22-3 (Yersiniosis)** **1983 20-4 (Listeriosis)**	
Noah's Archive Images			**F20191**	
115	Presentation	*Mycobacterium tuberculosis* *M. avium* subspecies *paratuberculosis* Complete Freund's adjuvant	Mycobacteriosis	CFA is often used to vaccinate rabbits for antibody production
JPC Case(s)			**1998 2-2 (CFA)** **1994 3-1 (CFA)**	
Noah's Archive Images			**F24701, F24702**	

Second Presentation

2	FUNGI			
Slide No.	**Organ**	**Condition**	**Morphologic Diagnosis**	**Notes**
3	Presentation	***Encephalitozoon cuniculi*** *(*formerly *Nosema cuniculi)*	Encephalitozoonosis (Nosematosis)	Microsporidian, formerly classified as protozoan. **POTENTIAL ZOONOSIS**. (PMID: 18998169) **This agent has been eliminated from modern laboratory facilities.**
4	Whole body		Torticollis	Brain infections are common. Amputation of ear tips results from conspecific aggression (fighting).
5	Kidneys		Chronic granulomatous tubulointerstitial nephritis	Pitted kidneys are the **classic** gross appearance *<cough, BOARDS, cough>*
6	Kidneys			Organism reproduces in tubular epithelium and is shed in urine.
7	Head		Phacoclastic uveitis (cataract)	Congenital infection in dwarf rabbit breeds. Transplacental infections do occur (PMID 30853450).
8	Brain (histology)		Granulomatous encephalitis with intra-neuronal microsporidia	

9	Kidney (histology)	***Encephalitozoon cuniculi***	Granulomatous tubulointerstitial nephritis with intra-tubular microsporidia
10-12	Brain and kidney (histology)		Organisms are refractile and birefringent with Gram positive spores. Organisms stain well with Luna's stain Spores also Ziehl-Neelsen acid fast and carbol-fuchsin positive.
JPC Case(s)			**2018 10-4 (brain)** **2015 12-4 (eye)** **2013 4-3 (kidney)** **2007 7-4 (kidney)** **1997 30-2 (kidney)** **1992 14-3 (brain)** **1991 13-1 (kidney)** **1983 15-3** **1981 18-1 (kidney)** **1976 12-4** **1/29/75-4 (brain)**
Noah's Archive Images			**F34209, F34210, F34029, F19462, F19463, F22686-F22689, F28590**
13-14	Presentation	***Pneumocystis oryctolagi***	PMID: 17064284 Recently reported in CRISPR/Cas9 generated scid rabbits PMCID: PMC5854650
15	Thoracic viscera		Chronic interstitial pneumonia (pneumonitis) — Lungs fail to collapse with visible rib impressions
16	Lung (histology)		Chronic granulomatous pneumonitis, interstitial fibrosis, type II pneumocyte hyperplasia and alveolar proteinosis

17		***Pneumocystis oryctolagi***	Cyst walls visible with Gomori's methenamine silver (GMS)	
18			Ascospores and trophic forms visible with Wright-Giemsa stain	
JPC Case(s)			**2010 25-2**	
19	Head	Ringworm	Periocular scaling dermatitis and alopecia	*Trichophyton mentagrophytes* most common. *Microsporum canis* also reported. Lesions are seen primarily on the head and ears, with spread to the feet **ZOONOTIC**
20	Human arm			

21	**PARASITES**			
Slide No.	**Organ**	**Condition**	**Morphologic Diagnosis**	**Notes**
22	Fecal flotation	**Intestinal coccidiosis** <u>Highly pathogenic</u>: *Eimeria flavescens* *E. intestinalis* <u>Intermediately pathogenic</u>: *E. magna* *E. irresidua* *E. piriformis* <u>Minimally pathogenic</u>: *E. media* *E. perforans* *E. neoleporis*	Coccidian oocysts (sporulated and unsporulated)	Mixed infections are the norm
23	Presentation		Coccidian oocysts (sporulated)	Flynn's Parasites of Laboratory Animals
24	Small intestine (histology)		Intra-epithelial coccidia	
JPC Case(s)			**2007 8-4** **1983 15-3**	

25	Whole body	***Eimeria stiedae***	Chronic proliferative cholangitis (hepatic coccidiosis)	Most infections are subclinical, but severely parasitized animals may have diarrhea, cachexia, and ascites. Prominent papillary proliferations with tortuosity
26	Liver			
27	Liver (histology)			
JPC Case(s)			**2016 11-3** **2014 18-1** **2012 10-4** **2008 4-3** **1997 6-4**	
Noah's Archive Images			**F00013, F00014, F16003, F33390, F07260, F09579, F13123, F19662, F19663, F19739,-F19742, F20405-F20410, F21515-F21517, F22701, F24157, F24158, F32415**	
28	Skeletal muscle	*Sarcocystis leporum* *(Sylvilagus floridanus)*	Sarcocystosis	*Sarcocystis cuniculi in O. cuniculus.* dDx. *Toxoplasma gondii*
JPC Case(s)			**1986 6-4**	
29	Fecal flotation	***Passalurus ambiguus***	Ova	Rabbit pinworm (*Oxyurid*). Eggs are flattened on one side. Not generally clinically significant but do not belong in a well-run facility
30	Fecal flotation		Adult worms	
31	Cecum			
32	Cecum (histology)			

33	Feces in pan			
34	Abdominal viscera	*Cysticercus pisiformis*	Multiple mesenteric cysticerci	Metacestode of *Taenia pisiformis* (dog-rabbit tapeworm)
Noah's Archive Images			**F16001, F20663, F27665**	
35	Ear	***Psoroptes cuniculi***	Chronic proliferative and exudative otitis externa (earmites)	Classic
36	Adult parasite and egg			
JPC Case(s)			**1983 6-1**	
Noah's Archive Images			**F00022, F10575**	
37	Whole body	***Cheyletiella parasitovorax***	Alopecia and scaling	Chylietid fur mites result in scaliness and hyperkeratosis, but little pruritus. Infections usually occur on the neck and back, but may involve the ventral abdomen.
38	Parasite, adult and ova		Furpluck	
39	Parasite	*Leporacarus (Listrophorus) gibbus*		Other ectoparasites include: *Notoedres cati* *Sarcoptes scabiei* *Demodex cuniculi*
40	Whole body and parasite	*Cuterebra sp.*	Rabbit Bots	Larvae (maggots) of parasitic flies. Larvae breathe through a skin opening. Will crawl out when ready to pupate.

41	NON-INFECTIOUS DISEASE			
Slide No.	**Organ**	**Condition**	**Morphologic Diagnosis**	**Notes**
42	Whole body and coronal sections of head	Hydrocephalus		Congenital (OMIA ID: 840). Autosomal recessive (AR) inheritance described (*hy/hy*). Possible vitamin A deficiency (or toxicity) should be excluded
43	Head	Malocclusion and incisor overgrowth		Hypsodontic. Often due to maxillary brachygnathia (also called mandibular prognathism). AR inheritance (*mp/mp)*.
44	Stomach	Trichobezoar		"Wool block" – often associated with excessive grooming; low fiber, stress, and a sedentary may be contributing factors. Usually incidental, but may cause obstruction.
Noah's Archive Images			**F06521, F29011**	
45	Presentation	**Mucoid enteropathy** aka cecal dysbiosis		Disruption of normal cecal flora with acidosis (orthologous to rumen acidosis). Low fiber diets contributory.
46	Feces		Abundant mucus production	
47	Cecum and colon		Colon lumen filled with abundant clear mucus.	
48	Cecum and colon			

		Mucoid enteropathy	Little or no leukocytic inflammation.	
49	Colon (histology)		Marked crypt hyperplasia with goblet cell differentiation	
JPC Case(s)			**1991 4-4**	
Noah's Archive Images			**F33452, F03328, F27244**	
50	Whole body	**Injection site reaction**	Semimembranosus, gracilis, and biceps femoris, hemorrhage and necrosis, acute, severe	IM injections should be given in the epaxial muscles PMID: 1666163, 12001340, 21691294 **Xylazine and detomidine are cardiotoxic in rabbits** PMID: 10331545, 7844956 **Tiletamine is nephrotoxic in rabbits** PMID: 1320157, 8872998
51	Hindlimb dissection		Sciatic nerve, hemorrhage and necrosis, acute	
52	Sciatic nerve (histology)			
53	Hind foot		Self-trauma	Paresthesia, dysesthesia or anesthesia from sciatic nerve damage
54	Hind foot			

55	Whole body	Hip dysplasia	Abnormal position of the hindlimbs	Trauma from improper caging substrate in young kits implicated (PMID: 11926308). dDx Splayleg
56-57	Radiographs		Shallow malformed acetabula with flattened femoral heads	
Noah's Archive Images			**F19620, F19621**	
58	Whole body	Splayleg	Inability to adduct front and hindlimbs	
59	Presentation	**Trauma**	Rabbits are a flight-prone prey species with abundant skeletal muscle mass (>50% bw) and relatively light bone mass (6-7% bw). Traumatic bone fractures are not uncommon, particularly with incorrect or inadequate restraint.	
60	Whole body	Paraplegia	Vertebral fracture	
61	Radiograph	Trauma	Fracture at L7-S1	L4-L7 spinal fractures most common (23%), followed by tibial (22%). PMID: 26043132
62	Radiograph		Fracture at L6	
63	Radiograph		Simple fracture of left mid tibia	Kicked cage wall during anesthetic recovery
64	Left hindlimb		Compound fracture of distal tibia	
65	Radiograph		Comminuted fracture of left mandible	Suspect that rabbit caught tooth in caging and panicked (PMID: 23561940)

66	Whole body	Trauma	Unilateral emasculation Ear pinna laceration	Conspecific aggression (biting). Ears and gonads are preferred targets.
67	Hindlimbs	**Sorehock**	Ulcerative pododermatitis	Dirty and poor quality caging. *Staph aureus* commonly isolated.
68	Whole body	**Urine scald** or hutch burn	Moist exudative dermatitis of ventral abdomen	Poor hygiene
69	Kidney and ureter	Uroliths	Stone in ureter with hydronephrosis	Uroliths are not uncommon in rabbits due to the high levels of minerals in the urine – calcium carbonate and triple magnesium phosphate. Uroliths are usually poorly formed and soft.
70	Urolith		Very large urolith	
Noah's Archive Images			**F33397, F22690-F22962**	
71	Head	Inherited **glaucoma**	Bilateral buphthalmia	Autosomal recessive with incomplete penetrance in NZW rabbits (*bu/bu*). Absent/hypoplastic aqueous outflow channels, loss or compression of iris pillars, and incomplete cleavage of the iridocorneal angle (goniodysgenesis). Candidate genes include MYOC and PITX1 (OMIA ID: 2299). PMID: 2065722, 10459615, 22330351, 16365516

72	Eyes at iridocorneal angle (histology)	Goniodysgenesis		The right image is normal drainage angle. In the left image, there is aberrant insertion of Descemet's membrane (PAS positive) into the anterior iris surface, and the ciliary cleft and trabecular meshwork are collapsed, with no apparent pectinate ligaments. This rabbit had normal IOPs and was not clinically buphthalmic. Goniodysgenesis spectrum lesions are a common incidental background finding.
73	Head and ocular lens (histology)	Inherited **cataract**		Two types: • AR • AD with incomplete penetrance
74	Heart, aorta, kidneys Aorta (histology)	**Hypervitaminosis D** Soft tissue mineralization	Diffuse aortic medial mineralization	Rabbits are exquisitely sensitive to vitamin D toxicity. Often equated with Monckeberg's arteriosclerosis aka medial calcific sclerosis Atherosclerosis may also be mineralized.
JPC Case(s)			**2000 27-3** **1985 26-1** **1983 15-4** **1976 2-4**	
Noah's Archive Images			**F09394, F19294,**	

75	Whole body	Fatty liver	Hepatic lipidosis (steatosis)	Typical gross finding in rabbit shock disease and pregnancy toxemia (ketosis). Severe fatty liver will float in formalin.
76	Liver (histology)		Diffuse macrovesicular hepatic lipidosis	
77	Presentation	**Endometrial venous aneurysm**		May rupture and bleed into the uterine lumen. Generally nonpregnant multiparous does.
78	Female genital tract			Courtesy of: Dr. Asfaw, Duke University
JPC Case(s)			**2014 18-3** **1996 10-4**	
79	Lungs (histology)	Feed aspiration	Chronic granulomatous pneumonia in cranial lobe with foreign material	Bland foreign body type reaction with PAS and Sirius red positive acellular refractile material (consistent with plant matter). Common incidental finding in older rabbits.
JPC Case(s)			**1986 16-1**	
80	Stomach	Bleeding gastric ulcer		Rare (73/1000), stress-related. PMID: 7287950
Noah's Archive Images			**F22694**	
81	Heart	Endocardiosis	Bicuspid (mitral) valve, endocardiosis (myxomatous degeneration)	Age-related. Mitral>>tricuspid. Can lead to regurgitation and heart failure (similar to dog). PMID: 19131035
82	Mitral (bicuspid) valve (histology)			

83	Whole body	Emphysema	Right hemithorax, pneumothorax, severe [Normal rabbit on right]	Emphysema is common in older rabbits (PMID: 13835161) Rarely bullae may rupture, leading to tension pneumothorax This rabbit presented with non-dyspneic tachypnea Must be differentiated from barotrauma due to ventilator (PMID: 22645503)
84	Thoracic viscera and lung (histology)		Right lung, emphysema and diffuse atelectasis Lung, emphysema	
85	Kidney, gross and histology	Hereditary renal cortical cysts	Kidney, Bowman's space, cystic dilatation (glomerulocystic atrophy)	Tend to be glomerular, but may be tubular. AR inheritance. PMID: 5111027
Noah's Archive Images			**F19745**	
86-87	Adrenal (histology)	Hyperplastic cortical nodules	Adrenal cortex, nodular hyperplasia	These are common incidental findings in rabbits. Note ciliated epithelium lining cysts.
88	Parathyroid, gross and histology	Kursteiner's cyst	Parathyroid cyst	
89	Pituitary (histology)	Rathke's pouch cyst	Pituitary, pars intermedia, cystic remnant of Rathke's pouch	

90	Presentation	Watanabe Heritable Hyperlipidemic (WHHL) rabbit	Hypercholesterolemia	Spontaneous 12 bp deletion in the low density lipoprotein receptor (LDLR) resulting in functional inactivation Model for familial hypercholesterolemia Elevated total cholesterol (500-900 mg/dL), elevated LDLs, reduced HDLs, elevated triglycerides.
91	Aorta (opened)		Atheromatous plaques	
92	Eye		Xanthomas in the iris	
JPC Case(s)			**1988 1-2**	
93-94	Whole body and abdominal mass	Ectopic pregnancy	Syndrome, ectopic pregnancy, with detachment, fetal death and maceration	Infrequent incidental lesion in breeding does (28/550) PMID: 15226019, 24602549, 7144127
95	Whole body	Cyclosporine induced mammary hyperplasia	Diffuse severe fibroadenomatous hyperplasia of the mammary glands	Elevated plasma levels of prolactin and 17β-estradiol, and reduced progesterone levels (PMID: 11924803, 19605914). Can also see reversible gingival hyperplasia (cyclosporine-induced gingival overgrowth or CIGO, PMID: 19712576). dDx prolactin secreting adenoma of the pars distalis
JPC Case(s)			**1998 19-4**	

Neoplasia

Slide No.	Organ	Condition	Morphologic Diagnosis	Notes
97	Abdominal and pelvic viscera	**Endometrial adenocarcinoma**	Endometrial adenocarcinoma and contralateral hydrometra	**Single most common tumor of *O. cuniculus***. Age dependent incidence reported to be 4.2% @ 2-3 years, 79.1% @ 5-6 years (n=849). Overall incidence 16.2% in females. A breed effect was noted. This figure comes from Greene (1959), and did not include any NZW (PMID: 13851592). No effect of exogenous estrogens/progestins on incidence. Pulmonary metastases are frequent. Papillary type: 80% ER-/PR- Tubular/solid type: 93% positive for one or both receptors (PMID: 18424838). These were pet rabbits; none reported as NZW.
98	Abdominal and pelvic viscera		Endometrial adenocarcinoma and bilateral hydrometra	
99	Thoracic viscera		Metastasis to lungs	
JPC Case(s)			**2008 25-2** **1994 3-3** **1987 17-3** **1985 7-3**	
Noah's Archive Images			**F34281, F34282, F08009, F21440**	

700	Kidneys	**Lymphoma**		**Second most common reported malignancy of rabbits.** Kidneys and stomach most common sites with variable lymphoid organ involvement Cutaneous diffuse large B cell lymphomas reported PMID: 22308233
Noah's Archive Images			**F03811, F03820, F25477**	
101	Whole body	**Mammary and pituitary tumors**	Mammary papillary adenocarcinomas with ulceration	Rabbits are particularly susceptible to prolactin. PMID: 8028271, 18589874 Invasive mammary carcinomas (96% in pets) most common, followed by adenomas (BU). Most are ER-/PR-. PMID: 30114981 Fibroadenomas also reported.
102	Pituitary (histology)		Acidophil adenoma of the pars distalis (presumed prolactin secreting)	
JPC Case(s)			**1995 24-3** **1993 26-4**	
103	Whole body	**Wilm's tumor**	Nephroblastoma	Most common primary renal tumor of rabbits. Presenting complaint was copious frank hematuria.
104	Wilm's tumor (histology)			Renal blastema including primitive tubules and glomeruli
JPC Case(s)			**2016 14-4**	

105	Whole body	**Trichoblastoma**	Trichoblastoma	Most common spontaneous (non-viral) skin tumor in rabbits (PMID: 17846230)
106	Skin tumor (cut)			
107	Skin tumor (histology)			
JPC Case(s)			**2002 19-3**	
108	Whole body	Thymoma	Thymoma with chylous pleural effusion and diffuse pulmonary atelectasis	Uncommon tumor Paraneoplastic syndromes have been reported
109	Thymoma (pan-cytokeratin IHC)		Pan-CK positive thymic epithelium and negative lymphocytes	
110	Testes	Testicular tumor	Unilateral Leydig (interstitial) cell tumor with contralateral testicular atrophy	Most common testicular tumor.
111	Presentation	Deciduosarcoma		Unique tumor of rabbits Uterus and spleen Metastasis to lung Induced by estrogen +/- progestin (PMID: 11560246, 11560245) Rare spontaneous tumor (PMID: 16672589)

	Other JPC Rabbit Cases		**2016 2-1** **2016 11-2**	Liver lobe torsion Testicular Granular Cell Tumor
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