JVDI: Supplementary material

Rothenburger et al. Pathology of wild Norway rats in Vancouver, Canada

Supplementary Table 1. Description and prevalence of major histologic lesions in a sample of wild urban Norway rats (*Rattus norvegicus*) trapped in Vancouver, British Columbia, Canada.

Category	Histologic description	n/N*	Prevalence	95% CI
Cardiovascular				
Cardiomyopathy	Lymphoplasmacytic myocarditis, fibrosis, and/or myocardial degeneration	128/406	32	27.0–36.0
Myocardial mineralization	Granular basophilic material within interstitium and myocytes	35/406	8.6	6.1–11.7
Mineralization of pulmonary blood vessels	Granular basophilic material within the tunica intima	62/404	15	12.0–19.2
Medial hypertrophy of pulmonary arterioles	Tunica media smooth muscle thickening†	90/404	22	18.3–26.7
Right ventricular hypertrophy	Right and left ventricle free walls are of equal width	18/403	4.5	2.7-7.0
Digestive				
Non-glandular stomach lesions‡	Hyperkeratosis,§ mucosal hyperplasia, keratin pustules, and/or submucosal inflammation#	231/388	60	54.4–64.5
Endocrine				
Adrenal gland mineralization	Granular basophilic material within adrenal cortex or medulla	5/365	1.4	0.4–3.2
Thyroid gland mineralization	Granular basophilic material within interstitium and follicles	132/280	47	41.1–53.2
Thyroid gland follicular hyperplasia	Hypertrophic follicular epithelial cells surround small or absent follicular lumens that are devoid of colloid¶	142/279	51	44.9–56.9
Integumentary				
Dermatitis	Inflammation in the dermis, panniculus, and/or hair follicles not associated with a skin wound	26/355	7.3	4.8–10.5
Lymphatic				

Lymphadenitis	Severe accumulations of granulocytes and/or abscess(s)	11/342	3.2	1.6-5.7
Respiratory				
Cilia-associated respiratory bacillus	Mats of filamentous bacteria on ciliated epithelium of the trachea or nasal cavity	66/270	24	19.4–30.0
Epiglossitis/laryngitis	Lymphoplasmacytic and/or granulocytic submucosal inflammation	79/202	39	32.3-46.2
Inducible BALT**	Peribronchiolar and/or perivascular lymphoplasmacytic cuffs††	270/403	67	62.2–71.6
Perivascular mixed inflammation	Perivascular cuffs of lymphocytes, plasma cells, and granulocytes surrounding ≥3 blood vessels	80/404	20	16.0–24.0
Rhinitis	Lymphoplasmacytic and/or granulocytic inflammation in the nasal submucosa with suppurative debris in nasal cavity lumen		40	21.1–61.3
Tracheitis	Lymphoplasmacytic and/or granulocytic submucosal and/or periglandular inflammation	192/372	52	46.6–56.8
Tracheal gland ectasia	Dilation of ≥3 tracheal submucosal glands	68/364	19	14.8–23.1
Tracheal gland adenitis	Granulocytes and/or necrotic debris within ≥3 submucosal glands	25/364	6.9	4.5–10.0
Urinary				
Crystals	Birefringent crystals within ≥3 renal tubules	137/405	34	29.2–38.7
Interstitial nephritis	Interstitial lymphoplasmacytic inflammation;;	121/405	30	25.5–34.6
Mineralization	Granular basophilic material within renal tubules/interstitium	85/405	21	17.1–25.3
Pyelitis	Lymphoplasmacytic inflammation in interstitium immediately adjacent to the renal pelvis	85/255	33	27.6–39.5

CI = confidence interval.

^{*} The number of rats examined for each lesion varies because not all tissues were available for each individual rat because of sampling error, tissue artifacts, and/or autolysis.

[†] Percent medial thickness (2 [medial thickness] \times 100/external vessel diameter) = \geq 50% of the vessel diameter.

[‡] Lesions were associated with *Eucoleus* sp. infection. 85

- \$ Keratin layer >45 μ m thick in areas without artificial separation and not adjacent to the limiting ridge (junction with glandular stomach).
- | Mucosa is >4–6 cells thick, affecting mainly the basal layers and >25% of the section.
- # Granulocytes infiltrating >2 foci not adjacent to the limiting ridge.
- ¶ Follicular cells were tall cuboidal to columnar and had to affect >50% of the thyroid gland and with ≤ 10 normal follicles.
- ** Inducible bronchus-associated lymphoid tissue, which is associated with *Mycoplasma pulmonis* and cilia-associated respiratory bacillus in subsample of rats in the current study.⁸⁴
- †† Surrounds ≥3 secondary or tertiary bronchioles or 1 primary bronchiole and/or ≥3 blood vessels.
- ‡‡ Present in ≥2 locations within the renal interstitium and excluding areas immediately adjacent to the renal pelvis.

Supplementary Table 2. Neoplastic and proliferative lesions in a sample of wild urban Norway rats trapped in Vancouver, British Columbia, Canada.

Lesion	Gross description	Histologic description	No. affected*	Reference
Squamous papilloma	Proliferative mass on the dorsum of the tongue	A focal, discrete area of hyperkeratosis, moderate mucosal hyperplasia with rete pegs	1	NA
Squamous papilloma	Pedunculated mass arising from the non-glandular stomach	Severe hyperkeratosis, mucosal hyperplasia, and submucosal edema with intramucosal <i>Eucoleus</i> sp. nematodes and eggs	1	85

Cortical hyperplastic nodules	NA	Focal, discrete, expansile, encapsulated nodules comprised of cords and bundles of polygonal epithelial cells consistent with adrenal cortical cells within the adrenal gland capsule.	4†	NA
Cutaneous pox lesions	Proliferative mass spanning the nail bed to the distal interphalangeal joint on the second digit (in one rat); proliferative plaque on the left front first metacarpal (in a second rat)	A focal, discrete area of epithelial proliferation characterized by severe acanthosis, dyskeratotic hyperkeratosis, and scalloping of the epidermal–dermal junction. Keratinocytes in the stratum spinosum contained large, amorphous amphophilic intracytoplasmic inclusions that contained multiple pox-like virions (enveloped ovoid to brick-shaped viral particles, ~200 × 300 nm‡; Supplementary Figs. 7–10).	2	NA
Hibernoma	NA	A focal, expansile, pseudoencapsulated mass in the perirenal fat. Cells were round-to-polygonal and contained single or multiple variably sized lipid vacuoles.	1†	NA
Mucous cell metaplasia	Focal, circular nodule with depressed center on the surface of the right cranial lung lobe	Focal dilated, respiratory epithelium-lined alveoli containing mucin, inflammatory cell debris, mononuclear cells, and giant cells.	1	84 (Suppl. material)
Round cell tumor	Multiple neoplastic nodules arise from the cranial and middle lung lobes	Locally extensive effacement of lung parenchyma by sheets of neoplastic round cells (possibly histiocytes) with moderate anisokaryosis and copious, foamy cytoplasm and lymphocytes. Similar neoplastic cells were within multiple lymph nodes.	1	84 (Suppl. material)

NA = not applicable.

† Up to 406 individuals were examined for microscopic lesions. The exact number of tissues examined for these lesions was not systematically recorded given the rarity of these lesions.

‡ Visualized with transmission electron microscopy.

^{* 672} individuals for grossly evident lesions; lesions detected by histologic examination were assessed in up to 406 individuals and are indicated by superscript †.

Supplementary Table 3. Rare non-proliferative lesions in a sample of wild urban Norway rats trapped in Vancouver, British Columbia, Canada.

System	Lesion	Description	No. affected*
Digestive	Double esophagus	Two distinct esophageal lumens in the proximal esophagus at the level of the thyroid glands (Fig. 5).	1
	Fungal gastritis	Yeast and fungal hyphae in the superficial keratin layer of the non-glandular stomach with associated granulocytic inflammation in the keratin layer, mucosa, and submucosa. There was focal ulceration in one of these.	3
	Gastric ulceration	Focal ulceration of the glandular stomach.	1
	Meckel diverticulum	A 5-mm saccular appendage arising from the anti-mesenteric side of the jejunum.	1†
	Sialadenitis	Salivary glands were swollen and red with associated microscopic focal necrosis, granulocytic, and/or mononuclear inflammation, and/or fibrosis, and atrophy. In one affected rat, there were microscopic abscesses within the adjacent lymph node.	5†
Endocrine	Adrenalitis	Lymphoplasmacytic inflammation of the adrenal cortex and medulla; severe architectural effacement with necrosis and mineralization in one rat.	3
	Adrenal gland mineralization	Finely granular basophilic material the adrenal cortex and medulla.	4
	Thyroiditis	Bilateral, multifocal lymphoplasmacytic cellular infiltrate affecting ~50% of the thyroid gland.	1
Hemolymphatic	Lymph node abscess	Purulent material effacing lymph node architecture and surrounded by a fibrous capsule (mesenteric and retropharyngeal).	8†
	Splenic fibrosis	A band of fibrous connective tissue focally constricted the spleen.	2†
Hepatic	Lipidosis	Diffusely, hepatocytes of a gravid female in good nutritional condition contained single clear vacuoles (consistent with fat).	1
	Lymphoplasmacytic periportal hepatitis	Infiltrate of lymphocytes and plasma cells within portal regions (etiology unknown).	1
	Multifocal hepatic necrosis	Multifocal, random areas of hepatic necrosis throughout the parenchyma (etiology unknown).	

Integument	Chemical dermatosis and thermal injury	Pinnae were shrunken, deformed, hyperemic, and ulcerated along the edges of turquoise material (suspected paint) and had linear excoriations (suspected from scratching trauma). Whiskers of this rat were singed (suspected as malicious burning while rat was in the trap). Histologically, pinnae were affected by orthokeratotic hyperkeratosis, epidermal hyperplasia, congestion, granulocytes, lymphocytes, and plasma cells, and serum lakes in the dermis (suspect chronic response to paint). In multifocal areas of the pinna, the epidermis was ulcerated, and dermal collagen was pale and lacked distinct fibers. Hair follicles, adnexal structures, and blood vessels were necrotic, with colonies of coccoid bacteria throughout the dermis (suspect acute thermal injury).	1†
	Pinnal fungal dermatitis	Multifocal white crusts on the margin of the right pinna with histologic mild parakeratotic hyperkeratosis, intrakeratin pustules, moderate epidermal hyperplasia, subcutaneous lymphoplasmacytic inflammation, and septate fungal hyphae within hair follicles.	1†
	Pinnal hyperkeratosis	Grossly evident severe bilateral pinnal hyperkeratosis (Supplementary Fig. 21).	1†
Ocular	Bilateral panophthalmitis	Crusting mucopurulent discharge rimmed eyes, and corneas were opaque (Supplementary Fig. 22). Histologically, corneal melting and perforations were covered in necrotic cell debris, bacterial colonies, fibrin, and granulocytes that also extended into the anterior and posterior chambers. Free hair shafts were present deep within both globes (suggestive of trauma). The iris was prolapsed, and remnant lens capsules were coiled with no other visible lens structures. Optic nerves contained granulocytes, lymphocytes, and plasma cells. Bacterial culture results: Pasteurella dagmatis and Streptococcus gallinaceus. This rat also had multiple wounds to the left forelimb, possibly related to its lack of vision.	1†
Musculoskeletal, adipose, and connective tissue	Coxofemoral arthritis	Grossly evident left femoral head cartilage erosion and acetabulum deformation with associated thickened joint capsule, osteophytes, and synovial hyperplasia (Supplementary Fig. 23).	1†
	Generalized muscle atrophy	Grossly evident skeletal muscles were shrunken and pale with prominent bony protuberances, likely rated to concurrent malocclusion, and pulmonary neoplasia.	1†
	Limb ascending infection	A chronic footpad wound of the right hind limb was associated with an ascending infection characterized by suppurative cellulitis, subcutaneous abscesses, and edema. Bacterial culture results: <i>Staphylococcus aureus</i> , <i>Staphylococcus</i> sp., and <i>Enterobacter</i> sp.	1†
Nervous	Cerebral gliosis	Multifocal gliosis in the cerebral gray matter with no associated meningitis.	1
Respiratory‡	Laryngeal hyperkeratosis	Severe hyperkeratosis, with bacterial colonies and mucosal hyperplasia of the squamous epithelium in the larynx.	1

Female reproductive	Endometritis	Variable amounts of erythrocytes, sloughed endometrial cells, and/or granulocytes within the uterine lumen; granulocytic with or without lymphoplasmacytic inflammation in the endometrium, mesometrium, and/or broad ligament; and lymphoplasmacytic cuffing of blood vessels in the broad ligament.	4
	Endometritis with abscesses	Abscesses in the uterine horns (Supplementary Fig. 11). Lumen of affected areas contained sloughed endometrial cells, viable and degenerate granulocytes, keratinized squamous cells, necrotic cell debris, and colonies of coccobacilli. The endometrium was multifocally sloughed. Urine glands were ectatic and contained granulocytes. Granulocytes infiltrated the edematous endometrium and myometrium. Hemosiderphages were within the deep myometrium. Bacterial culture results: <i>Enterococcus faecalis, Escherichia coli, Proteus</i> sp., and <i>Bacteroides</i> sp.	1†
	Endometritis— necrotizing	Right uterine horn was focally congested and dilated by a firm coagulum that consisted of necrotic and mineralized tissues with no identifiable fetal structures microscopically (possibly necrotic placenta or mineralized necrotic cellular debris). The adjacent lumen contained granulocytes and proteinaceous fluid. The myometrium was diffusely edematous and contained a mixed population of inflammatory cells, mainly granulocytes and macrophages. Concurrently, one kidney had pyelonephritis. Bacterial culture results: <i>Salmonella</i> Enteritidis serogroup D and <i>Proteus</i> sp.	1†
	Hematometra and endometritis	Externally, there was a mucohemorrhagic vaginal discharge. Uterine horns were bilaterally dilated and contained hemorrhagic fluid. Histologically, the endometrium was infiltrated by moderate numbers of granulocytes.	1†
	Purulent clitoral adenitis	Grossly evident purulent exudate from the clitoral glands was associated histologically with multifocal granulocytic inflammation and necrosis of the clitoral gland. Bacterial culture not performed.	2†
Male reproductive	Orchitis	Lymphoplasmacytic cell infiltrate and fibrosis within the testes. In one rat, the right testicle was grossly atrophied; microscopically, a large amount of fat surrounded the few remaining seminiferous tubules, which were frequently mineralized and had no visible spermatogenesis. In another rat, granulocytic orchitis was associated with testicular necrosis, and accessory sex glands were inflamed, including one preputial gland, which was gray-green and contained purulent material. Bacterial culture results: <i>E. faecalis</i> and <i>E. coli</i> .	3†
Urinary	Chronic progressive nephropathy	Both kidneys had multifocal-to-coalescing, tan areas with microscopic evidence of depressions in the renal capsule and cortical lymphoplasmacytic interstitial nephritis and fibrosis. Tubules were occasionally dilated and contained proteinaceous fluid.	1†
	Perirenal abscess	An abscess in the retroperitoneal space adjacent to kidney. Bacterial culture results: <i>S. aureus</i> and <i>E. coli</i>	2†

Pyelonephritis	Kidney(s) were severely shrunken with an irregular surface (Supplementary Fig. 13). Histologically, tubules contained intraluminal granulocytes, protein, and necrotic debris that radiated from the renal pelvis to the cortex. In some areas, lymphoplasmacytic inflammation and severe fibrosis surrounded atrophic tubules, glomeruli, or obliterated normal renal architecture. Pyelonephritis was associated with severe metritis in one rat.	2†
Renal cyst	A single cystic structure lined by squamous epithelium within the renal cortex.	1

^{*} We examined up to 406 individuals for microscopic lesions. The exact number of tissues examined for these lesions was not systematically recorded given the rarity of these lesions. We assessed grossly evident lesions (indicated by an † following the number affected) in 672 individuals.

‡ Rare microscopic lesions of the respiratory tract are described by Rothenburger et al. 2015.⁸⁴

Supplementary Table 4. Parasites and associated lesions identified using histology in a sample of wild urban Norway rats trapped in Vancouver, British Columbia, Canada.

Location	Organism	Associated lesion	n/N*	Prevalence	95% CI	Ref.
Upper gastrointestinal tract†	Eucoleus spp.	Hyperkeratosis, mucosal hyperplasia, keratin pustules, and submucosal inflammation in the non-glandular stomach (Fig. 4).	164/399	41	36.2–46.1	85
Non-glandular stomach	Gongylonema neoplasticum	None.	Rare	NA‡	NA	NA
Small intestine	Nematode	None.	83/198	42	35.0-49.1	NA
	Cestode	None.	6/198	3.0	1.1–6.5	NA
	Coccidia	None.	13/198	6.6	3.5-11.0	

Liver	Capillaria hepatica	Multifocal, white, tortuous tracts on the liver surface and subcapsular parenchyma with microscopic viable and necrotic capillarid nematodes and/or eggs surrounded by granulocytes or mononuclear cell inflammatory infiltrates and fibrosis, sometimes with mineralization (Figs. 6, 7).	242/672	36	32.4–39.8	83
Ears, nose, distal limbs, tail	Notoedres muris	Proliferative and crusting dermatitis of the ears (primarily); poorly haired skin of the nose, distal limbs, and tail, characterized by hyperkeratosis with intracorneal pustules and adult mites and/or eggs, epidermal hyperplasia, and lymphoplasmacytic dermatitis (Supplementary Fig. 6).	2/672	0.3	0.0-1.1	1
Skin	Nosopsyllus fasciatus	Possible alopecia and exudative dermatitis.	NA§	NA	NA	NA
	Ornithonyssus bacoti	Possible alopecia and exudative dermatitis.	NA§	NA	NA	NA
	Polyplax spinulosa	Possible alopecia and exudative dermatitis.	NA§	NA	NA	NA
Urinary bladder (rarely renal pelvis)	Trichosomoides crassicauda	At least one nematode or egg cross-section in urinary bladder or renal pelvis, variably accompanied by mild submucosal lymphoplasmacytic inflammation (Fig. 19).	59/194	30	24.0–37.4	NA

CI = confidence interval; NA = not applicable; Ref. = reference to previous studies of a subsample of rats in the current study. We found no evidence of *Angiostrongylus cantonensis*, *Echinococcus multilocularis*, *Sarcocystis* spp., *Toxoplasma gondii*, or *Trichinella spiralis* infection in any of the rats.

* Rats were positive if there was at least one characteristic egg and/or adult cross-section in the sections examined. The number of rats examined for each lesion varies because not all tissues were available for each individual rat because of sampling error, tissue artifacts, and/or autolysis.

† Adults and/or eggs were present in tongue, oropharynx, esophagus, and/or non-glandular stomach.

‡ Exact numbers were not assessed given the rarity of infection.

§ Prevalence data are not available for these ectoparasites because they are being assessed by another collaborator on this research project who will present these data in a separate future study.

Supplementary Table 5. Bacteria isolated from macroscopic lesions in a sample of wild urban Norway rats trapped in Vancouver, British Columbia, Canada.

Bacterial species*	Associated lesion(s)†	No. of Isolates
Bacteroides sp.	Uterine abscess	1
Bordetella bronchiseptica	Pneumonia, pulmonary round cell neoplasia	2
Clostridium sordellii	Subcutaneous abscess	1
Corynebacterium kutscheri	Subcutaneous abscess	1
Enterobacter sp.	Ascending hind limb infection	1
Enterococcus cloacae	Cervical lymph node abscess	1
Enterococcus faecalis	Cervical lymph node abscess, mesenteric lymph node abscess, preputial gland abscess, purulent penile discharge, subcutaneous abscess, urinary bladder concretion, uterine abscess, and vaginal discharge	12
Escherichia coli	Ascending hindlimb infection, cervical lymph node abscess, perirenal abscess, lung abscess, mesenteric lymph node abscess, preputial discharge, pneumonia, subcutaneous abscess, pulmonary round cell neoplasia, seminal vesicle, uterine abscess, and vaginal discharge	15
Gemella morbillorum	Pulmonary round cell neoplasia	1
Klebsiella pneumoniae	Cervical lymph node abscess	1
Lactobacillus animalis	Vaginal discharge	1
Pasteurellaceae‡	Subcutaneous abscess	1

Pasteurella dagmatis	Panophthalmitis	1
Pasteurella pneumotropica	Submandibular abscess	1
Proteus sp.	Preputial discharge, seminal vesicle, suppurative metritis, uterine abscess, and vaginal discharge	5
Salmonella Enteritidis	Suppurative metritis	1
Staphylococcus aureus	Ascending hindlimb infection, perirenal abscess, mediastinal abscess with metal projectile pellet, purulent penile discharge, pulmonary round cell neoplasia, retropharyngeal abscess, skeletal muscle abscess, subcutaneous abscess, subscapular abscess, and vaginal discharge	13
Staphylococcus sp.	Ascending hindlimb infection, preputial gland abscess, mesenteric lymph node abscess, skeletal muscle and subcutaneous abscess	6
Streptococcus sp.	Vaginal discharge	1
Streptococcus gallinaceus	Panophthalmitis	1
Streptobacillus moniliformis	Cervical lymph node abscess and subcutaneous abscess	3

^{*} Bacteria isolated from bite wounds and associated soft tissue infections is described elsewhere⁵⁰; ancillary testing that identified *Mycoplasma pulmonis* and cilia-associated respiratory bacillus in the lungs of a subsample of rats in the current study is described elsewhere⁸⁴; this table does not include these results.

† Many infections were polymicrobial; therefore, lesions may be listed for multiple bacterial species.

‡ Isolates from a potentially novel genus that grouped most closely with *Haemophilus* sp., *Actinobacillus* sp., *Pasteurella* sp., and *Aggregatibacter* sp. using 16S DNA sequencing.⁵⁰

Supplementary Table 6. Patterns of infections by 3 parasitic nematodes among 192 Norway rats trapped in Vancouver, British Columbia, Canada.

Patterns of pathogen detection				
Capillaria hepatica	Eucoleus sp.	Trichosomoides crassicauda	Observed no. of rats with each pattern	Observed prevalence of each pattern (%)
_	_	_	57	30
_	+	_	26	14
+	+	_	26	14
+	+	+	25	13
+	_	_	24	13
+	_	+	16	8
_	+	+	11	6
_	_	+	7	6

⁻⁼ absence of pathogen; += presence of pathogen.

Supplementary Table 7. Demographic characteristics and associations with thyroid follicular hyperplasia in a group of Norway rats trapped in Vancouver, British Columbia, Canada.

	Thyroid follicu	ılar hyperplasia	r hyperplasia Univariable			N	Iultivariable	
Category/Subcategory	Present* (<i>n</i> =142)	Absent* $(n = 137)$	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Season								
Fall	58 (41)	47 (34)	ref	_	_	_	_	_
Winter	42 (30)	17 (12)	2.00	0.99-4.30	0.046†	_	_	_
Spring	29 (20)	53 (39)	0.44	0.24-0.90	0.007	_	_	_
Summer	13 (9.2)	20 (15)	0.53	0.22-1.24	0.115	_	_	_
Sex								
Female	46 (32)	71 (52)	ref	_	_	ref	_	_
Male	96 (68)	66 (48)	2.52	1.51-4.31	< 0.001	1.97	1.14-3.45	0.016
Sexual maturity								
Immature	16 (11)	34 (25)	ref			_	_	_
Mature	115 (81)	86 (63)	2.81	1.40-5.85	0.004	_	_	_
Body mass (g)‡								
<65	10 (7.0)	14 (10)	ref			ref		
65–144	27 (19)	49 (36)	0.82	0.29-2.32	0.705§	0.80	0.28-2.30	0.676
145–256	48 (35)	37 (26)	1.07	0.39-3.01	0.899	1.14	0.41-3.27	0.801
>256	68 (47)	26 (19)	4.25	1.52-12.6	0.007	3.69	1.30-11.1	0.016
Body condition score								
Poor (0)	31 (22)	45 (33)	ref	_	_	_	_	_
Moderate (1)	55 (39)	47 (34)	1.61	0.85-3.11	0.146	_	_	_
Good (2)	54 (38)	44 (32)	1.67	0.86-3.28	0.132	_	_	_

CI = confidence interval; dash (—) = no values necessary; ref = referent category.

* Frequencies and percentages (in parentheses) may not total 100% because of exclusion of rats with missing data for the variable in question.

† Overall *p* value for categorical variable: p = 0.008.

‡ Categorized by quartiles.

§ Overall p value for categorical variable: p < 0.001.

Overall p value for categorical variable was not significant (p > 0.05).

Supplementary Table 8. Demographic characteristics and associations with lymphoplasmacytic interstitial nephritis in a group of Norway rats trapped in Vancouver, British Columbia, Canada.

	Interstitial nephritis		Univariable		Multivariable			
Category/Subcategory	Present* $(n = 121)$	Absent* $(n = 284)$	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Season								
Fall	42 (35)	120 (42)	ref	_	_	_	_	_
Winter	43 (17)	45 (16)	2.46	1.03-5.71	0.026†	_	_	_
Spring	25 (21)	86 (30)	0.83	0.35-1.90	0.642	_	_	_
Summer	11 (9.1)	33 (12)	1.08	0.36-3.62	0.892	_	_	_
Sex								
Female	40 (33)	128 (45)	ref	_	_	_	_	_
Male	81 (67)	156 (55)	1.65	1.04-2.67	0.035	_	_	_
Sexual maturity‡								

Immature	1 (0.8)	77 (27)		_				
Mature	117 (97)	177 (62)	_	_	_	_	_	_
Body mass (g)§								
<65	1 (0.8)	40 (14)	ref	_	_	ref	_	_
65–144	6 (5.0)	106 (37)	2.25	0.36-43.8	0.463	2.25	0.36-43.8	0.463
145–256	35 (29)	89 (31)	21.0	4.0-390	0.004	21.0	4.02-390	0.004
>256	79 (65)	49 (17)	84.7	16.2–1,580	< 0.001	84.7	16.2–1,580	< 0.001
Body condition score								
Poor (0)	8 (6.6)	113 (40)	ref	_	_	_	_	_
Moderate (1)	34 (28)	103 (36)	4.71	2.14–11.6	< 0.001	_	_	_
Good (2)	77 (64)	66 (23)	16.3	7.58–39.6	< 0.001	_	_	_
Leptospira interrogans								
Negative	78 (65)	244 (86)	ref			_	_	_
Positive	28 (23)	26 (9.2)	4.22	2.02-9.30	< 0.001	_	_	_

CI = confidence interval; dash (—) = no values necessary; ref = referent category.

† Overall p value for categorical variable: p = 0.10.

‡ Logistic regression was not carried out because of a lack of variability in the data.

§ Categorized by quartiles.

Tested with PCR; data were previously described by Himsworth et al. 2013.⁴⁶

^{*} Frequencies and percentages (in parentheses) may not total 100% because of exclusion of rats with missing data for the variable in question.

Supplementary Table 9. Demographic characteristics and associations with lymphoplasmacytic pyelitis in a group of Norway rats trapped in Vancouver, British Columbia, Canada.

	Pye	elitis	Univariable			Multivariable		
Category/Subcategory	Present* $(n = 85)$	Absent* $(n = 170)$	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Season								
Fall	44 (52)	64 (38)	ref	_		_	_	
Winter	21 (25)	32 (19)	0.75	0.23-1.92	0.564	_	_	_
Spring	13 (15)	51 (30)	0.40	0.15-1.12	0.058	_	_	_
Summer	7 (8.2)	23 (14)	0.45	0.11-1.62	0.197	_	_	_
Sex								
Female	39 (46)	68 (40)	ref	_	_	_	_	_
Male	46 (54)	102 (60)	0.72	0.41-1.28	0.269	_	_	_
Sexual maturity†								
Immature	0 (0.0)	50 (29)	_	_	_	_	_	_
Mature	83 (98)	100 (59)	_	_	_	_	_	_
Body mass (g)‡								
<144	4 (4.7)	96 (57)	ref	_	_	ref	_	_
≥145	81 (95)	74 (44)	26.27	10.3-89.7	< 0.001	9.69	3.20-37.7	< 0.001
Body condition score								
Poor (0)	4 (4.7)	71 (42)	ref	_	_	_	_	_
Moderate (1)	30 (35)	57 (34)	9.34	3.38–32.8	< 0.001	4.92	1.40-23.1	0.021
Good (2)	50 (59)	39 (23)	22.76	8.20-79.5	< 0.001	5.24	1.41-25.4	0.020
Leptospira interrogans§								
Negative	47 (55)	147 (87)	ref	_	_	ref	_	
Positive	28 (33)	10 (5.9)	8.69	3.79–20.36	< 0.001	3.29	1.42-8.62	0.010
Trichosomoides crassicauda								

Negative	22 (26)	58 (34)	ref			_	_	_
Positive	24 (28)	17 (10)	3.72	1.70-8.55	0.001	_	_	_

CI = confidence interval; dash (—) = no values necessary; ref = referent category.

- † Logistic regression was not carried out because of a lack of variability in the data.
- ‡ Dichotomized by median weight.
- § Tested with PCR; data were previously described by Himsworth et al. 2013. 46

Supplementary Table 10. Demographic characteristics and associations with *Trichosomoides crassicauda* infection in a group of Norway rats trapped in Vancouver, British Columbia, Canada.

	Trichosomoid	osomoides crassicauda Univariable		Multivariable				
Category/Subcategory	Present* $(n = 59)$	Absent* $(n = 135)$	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Season								
Fall	36 (61)	41 (30)	ref	_	_	_	_	_
Winter	11 (19)	31 (23)	0.40	0.17-0.96	0.030	_	_	_
Spring	7 (12)	46 (34)	0.17	0.06-0.42	< 0.001	_	_	_
Summer	5 (8.5)	17 (13)	0.33	0.10-1.04	0.050	_	_	_
Sex								

^{*} Frequencies and percentages (in parentheses) may not add to 100% because of exclusion of rats with missing data for the variable in question.

Male	31 (53)	90 (67)	ref	_	_	ref	_	_
Female	28 (48)	45 (33)	1.90	0.97-3.76	0.055	2.11	1.04-4.39	0.040
Sexual maturity†								
Immature	0 (0)	29 (22)	_	_	_	_	_	_
Mature	59 (100)	94 (70)	_	_	_	_	_	_
Body mass (g)‡								
<144	2 (3.4)	62 (46)	ref	_	_	ref	_	_
≥145	57 (97)	73 (54)	23.2	6.68-146	< 0.001	24.4	6.96–154	< 0.001
Body condition score								
Poor (0)	8 (47)	46 (34)	ref	_	_	_	_	_
Moderate (1)	21 (36)	46 (34)	2.38	0.93-6.43	0.074	_	_	_
Good (2)	29 (26)	42 (31)	3.39	1.35–9.11	0.011	_	_	_

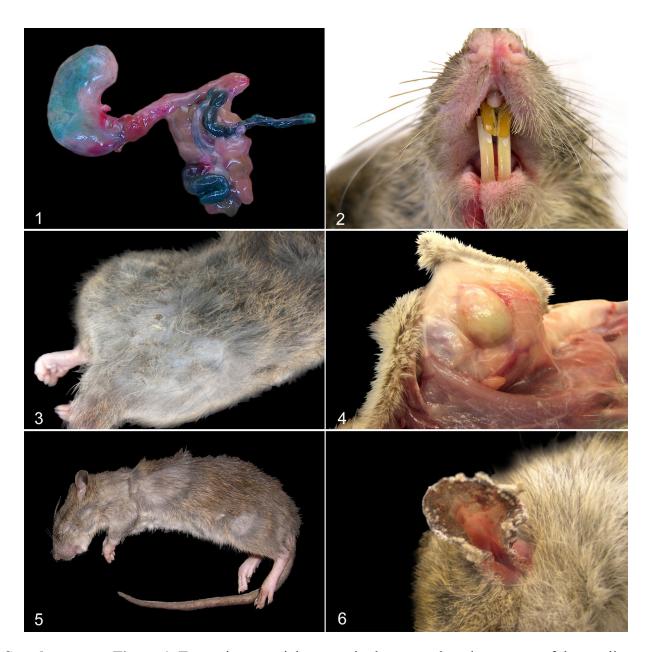
CI = confidence interval; dash (—) = no values necessary; ref = referent category.

† Logistic regression was not carried out because of a lack of variability in the data.

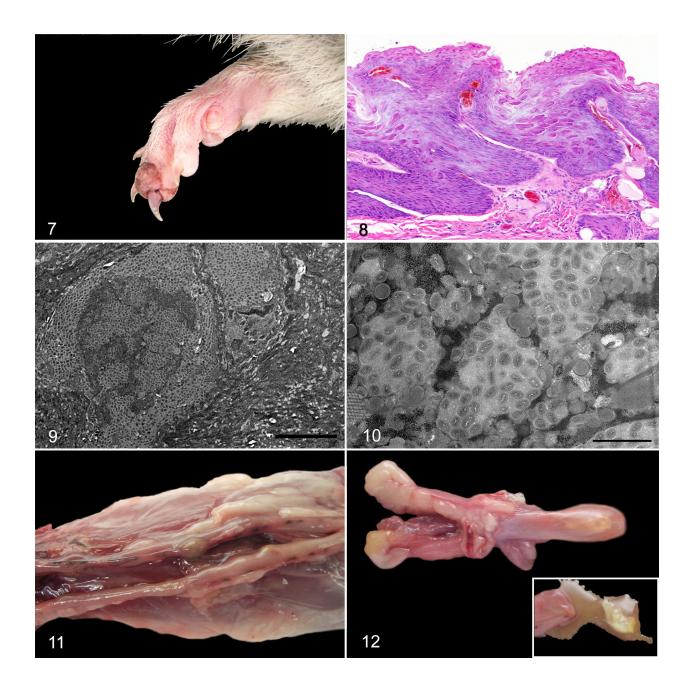
‡ Dichotomized by median weight.

 $\$ Tested with PCR; data were previously described by Himsworth et al. 2013. 46

^{*} Frequencies and percentages (in parentheses) may not add to 100% because of exclusion of rats with missing data for the variable in question.

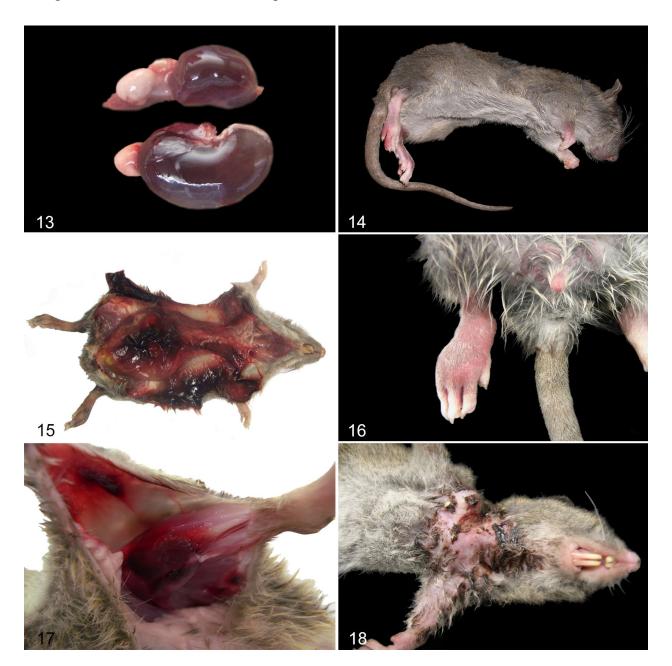


Supplementary Figure 1. Turquoise material present in the stomach and segments of the small intestine is consistent with anticoagulant rodenticide bait. Supplementary Figure 2. The lower incisors are severely overgrown, and the occlusive surface of upper incisors is slanted (malocclusion). Supplementary Figure 3. The skin over the dorsum is alopecic, and there are multiple, small bite wounds. Supplementary Figure 4. Abscess in the subcutaneous tissue overlying the lateral thorax. Abscesses were often associated with cutaneous bite wounds. Supplementary Figure 5. There are multifocal areas of alopecia over the trunk. Supplementary Figure 6. The nodular areas of proliferative dermatitis affecting the pinna are indicative of *Notoedres muris* infection.



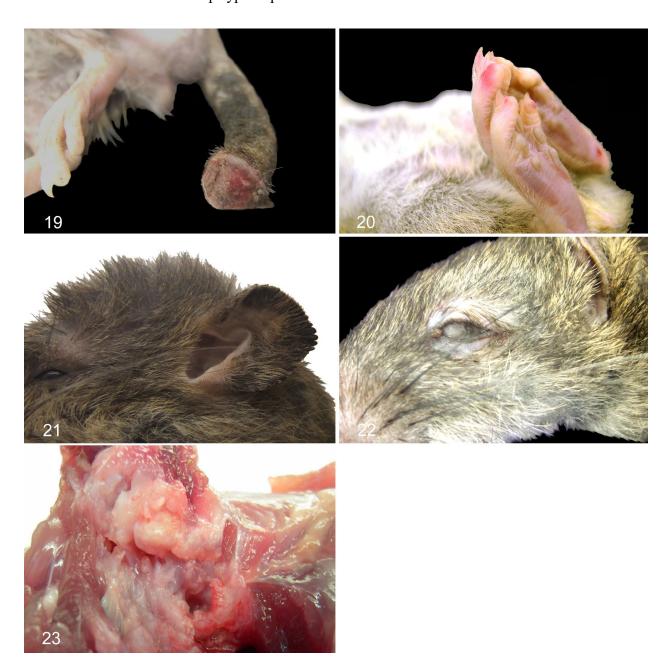
Supplementary Figures 7–12. Poxviral focal proliferative dermatitis affecting the skin of a digit in a Norway rat (*Rattus norvegicus*). Supplementary Figure 7. A focal, ulcerated, and proliferative mass spans the nail bed to the distal interphalangeal joint. Supplementary Figure 8. Epithelial proliferation is characterized by severe acanthosis, dyskeratotic hyperkeratosis, and scalloping of the epidermal-dermal junction. Keratinocytes in the stratum spinosum contain large, amorphous amphophilic intracytoplasmic inclusions. H&E. Supplementary Figure 9. There are abundant pox-like virons within the intracytoplasmic inclusions. Transmission electron micrograph. Bar = 5 μm. Supplementary Figure 10. Ovid to brick-shaped, enveloped pox-like

virons are $\sim 200 \times 300$ nm. Transmission electron micrograph. Bar = 1 μ m. Supplementary Figure 11. Focal abscess is present in the middle of the left horn. There are multiple, black placental scars (normal in parous rats). Supplementary Figure 12. Concretions of seminal fluid are within the urinary bladder. Firm, yellow concretions of seminal discharge are an agonal change in male rats. Inset shows the expelled concretion and urine.



Supplementary Figure 13. The kidney affected by pyelonephritis is shrunken with an irregular capsular surface. **Supplementary Figure 14.** Periarticular and subcutaneous hemorrhages

Supplementary Figure 15. The subcutaneous tissues have severe, locally extensive hemorrhages. Supplementary Figure 16. The right lower limb has severe subcutaneous hematoma indicative of anticoagulant rodenticide exposure. Supplementary Figure 17. The left hind limb has severe subcutaneous and periarticular hemorrhages indicative of anticoagulant rodenticide exposure. Supplementary Figure 18. A chronic, linear wound with associated crusting and alopecia surrounds the neck and cranial thorax. This lesion may have resulted from non-lethal trauma from a snap-type trap.



Supplementary Figure 19. The tail was amputated leaving an open wound overlying the stump. Supplementary Figure 20. The toes are affected by multifocal areas of hyperemia. These lesions may have been caused by acute trauma from cage-type traps. Supplementary Figure 21. The skin of the left pinna has severe hyperkeratosis. Supplementary Figure 22. The left globe is collapsed, and there is corneal opacity and mucopurulent exudate on the eyelids indicative of panophthalmitis. Supplementary Figure 23. The left coxofemoral joint is affected by arthritis that features capsule thickening and roughening of the articular cartilage.

Wild Rat Autopsy Form

Date:	Animal num	ber:
Location:		
Person completing autopsy:		
Species (based on a mammalian ic	lentification key): N	orway / Black
Weight (grams):	Nose-to-rump lengt	ch (cm):
Presence of Cutaneous Bite Wour	nds : yes / no #	of bite wounds:
Presence of <i>Notoedres muris</i> (cut	taneous nodules/defo	ormed ears): yes / no
Description:		
Body Condition Score (based on 1. Poor 2. Moderate	quantity of subcutan 3. Good	eous & visceral fat)
Reproductive		
Female: yes / no		
Open vaginal orifice:	yes / no	
Prominent nipples:	yes / no	
Visible mammary tissue:	yes / no	
Pregnant:	yes / no	# of embryos:
Placental scars:	yes / no	# of placental scars:
Male: yes / no		
Testicle position:	scrotal or inguinal	/abdominal
Prominent accessory sex g	lands: yes / no	
Visible seminiferous tubules:	yes / no	
Reproductive tract notes:		

(over)

Wild Rat Autopsy Form

Stomach contents present:	yes / no	
Stomach content description	on:	
<i>Capillaria hepatica</i> in live	er (multifocal white spots):	yes / no
Description of distribution	:	
Hemorrhage:		
□ subcutaneous	Location:	
□ periarticular	Location:	
□ other	Location:	
Additional Notes including	lesions:	

 $\hfill\Box$ pictures taken