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DEPARTAMENTO DE MEDICINA VETERINÁRIA

New insights on the age for neutering dogs

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Orientação | Prof. Doutora Catarina Lavrador

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Mestrado Integrado em Medicina Veterinária

Relatório de Estágio

Évora, 2019

Este relatório inclui as críticas e as sugestões feitas pelo júri

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To my parents, for their unconditional love and support, for your investment in my academic knowledge and for all the amazing experiences you were able to provide me. I hope you feel proud of the person you brought up and it is to you that I dedicate this thesis to.

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Abstract

The current report was carried out for the completion of the Master's degree in veterinary Medicine and is divided into two parts. The first part is formed by a description of the cases followed during the four-month traineeship completed at Priory Veterinary Surgeons. The most prevalent medical field was dermatology, with a relative frequency of 26% (n= 474), followed by gastroenterology representing 18% of total cases. The second part is composed of a review of the current literature on the proposed benefits and detriments of gonadectomy in dogs and whether performing it at a specific age causes or prevents specific health issues.

Keywords: canine, gonadectomy, pre-pubertal neutering, post-pubertal neutering, benefits, detriments

Resumo - Novas perspetivas quanto à idade de esterilização em cães

O presente relatório foi realizado no âmbito do Mestrado Integrado em Medicina Veterinária e está dividido em duas partes. A primeira parte é constituída por uma descrição da casuística observada durante o estágio curricular de quatro meses realizado no *Priory Veterinary Surgeons.* A área mais prevalente foi dermatologia, com uma frequência relativa de 27% (n=480), seguida da gastroenterologia, que representou 18% dos casos totais. Na segunda parte é realizada uma revisão da literatura atual sobre os benefícios e malefícios inerentes à gonadectomia em cães e se a sua realização em determinada idade específica causa ou impede problemas de saúde específicos.

Palavras-chave: cão, gonadectomia, esterilização pré-pubertal, esterilização pós-pubertal, benefícios, malefícios

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List of acronyms and abbreviations

ACVIM: American College of Veterinary Internal Medicine

CDMVD: Chronic degenerative mitral valve disease

CEH: Cystic endometrial hyperplasia

CKD: Chronic kidney disease

CO_2: Carbon dioxide

CVD: Central vestibular disease

CVHD: Chronic valvular heart disease

CRI: Constant rate infusion

CT: Computed tomography scan

ECG: Electrocardiogram

FeLV: Feline Leukaemia Virus

FHT: Feline hyperthyroidism

Fi: Absolute frequency

FISS: Feline injection site sarcoma

FIV: Feline Immunodeficiency Virus

FSH: Follicle-stimulating hormone

FR(%): Relative frequency in percentage

IRIS: International Renal Interest Society

kg: Kilograms

LH: Luteinizing hormone

LOV. Laparoscopic ovariectomy

NSAID's: Nonsteroidal anti-inflammatory drugs

MCT: Mast cell tumour

mg/dL: Milligrams per decilitre

mmHg: Millimetres of mercury

n: Absolute frequency

OV: Ovariectomy

OVH: Open ovariohysterectomy

PLI: Serum pancreatic lipase immunoreactivity

PVD: Peripheral vestibular disease

SDMA: Symmetric dimethylarginine

T3: Triiodothyronine

T4: Thyroxine

TTA: Tibial tuberosity Advancement

TB: Tuberculosis

UP/C: Urine protein:creatinine ratio

WSAVA: World Small Animal Veterinary Association

Part I: Report on activities performed during the traineeship

1. Introduction

The present master thesis was written following a four-month traineeship, from the beginning of September 2018 until the end of December 2018, at Priory Veterinary Surgeons, a mixed small animal and equine practice with four different branches located in Reigate, Tadworth, Redhill and Banstead, United Kingdom.

This first part includes a description of the activities developed during the traineeship, with a casuistry description accompanied by a brief bibliographical review of one of the most clinically relevant pathologies in each area.

2. Case-by-case description

In this section, the clinical cases data are processed statistically regarding preventive medicine, internal medicine, surgery and other followed diagnostic procedures.

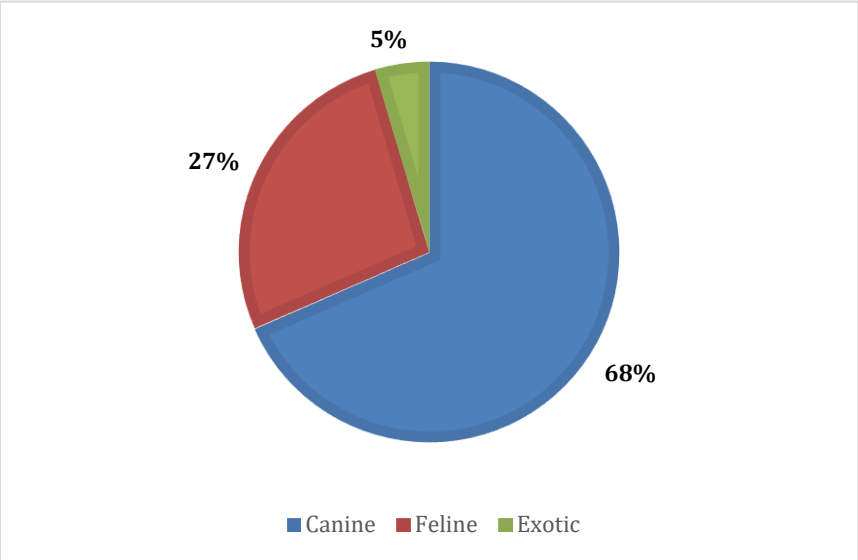
In each of the previously mentioned areas, statistical data are presented in tables by their absolute (Fi) and relative (FR) frequencies and were studied regarding each taxonomic family (for canines and felines) and group of animals (for exotic animals). The exotic animals taken into account included guinea pigs (*Cavia porcellus*) and rabbits (*Oryctolagus cuniculus*).

Regarding these data, it is important to acknowledge that the number of cases does not correspond to the total of cases of any of the practices. The total number of animals is lower than the number of cases observed, since some patients had several co-pathologies and the same animal may have been accounted in more than one clinical area.

2.1. Case distribution regarding animal species

By observing the data in table 1 and respective graphic 1, a total of 1027 different animals were observed. Canines (*Canis lupus familiaris*) were the most frequent observed species, with 703 cases, representing 68% (n= 1027), whilst feline (*Felis catus*) represented 27% (n=1027), with 277 cases witnessed. When it came to exotic animals, 47 patients were observed, representing 5% (n=1027) of cases.

Graphic 1: Case distribution regarding Animal species



Internal medicine was the most prevalent group, with 474 cases, representing 46% (n=1027) of total cases observed. It is followed by preventive medicine, with 401 cases which is 39% (n=1027) and by surgery with 152 surgeries performed, which represents 15% (n=1027) of casuistry.

Table 1: Case distribution regarding animal species and clinical area

	Canine		Feline		Exotic		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)	Fi	FR (%)		
Preventative Medicine	236	34%	149	54%	16	34%	401	39%
Internal Medicine	369	52%	90	32%	15	32%	474	46%
Surgical Medicine	98	14%	38	14%	16	34%	152	15%
Total	703	100%	277	100%	47	100%	1027	100%

2.2. Case distribution regarding clinical area

2.2.1. Preventive medicine

Preventive medicine acts such as vaccination, deworming, microchipping and issuing of passports are of utmost importance as they prevent diseases (including zoonosis) and allow an epidemiological control, contributing to public health and animal health. Besides these reasons, it constitutes an important opportunity to establish effective communication between the vet and the owner.

In the United Kingdom, all dogs are legally required to have a microchip and to wear a collar with the name and the address of the owner inscribed on the collar or on a plate or badge attached to it ("The Control of Dogs Order" 1992; "The Microchipping of Dogs" 2015).

Table 2: Case distribution regarding Preventive Medicine

Preventive Medicine	Canine		Feline		Exotic		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)	Fi	FR (%)		
Vaccination	157	67%	95	64%	11	69%	263	66%
Worming	12	5%	10	7%	0	0%	22	5%
Electronic identification	10	4%	13	9%	0	0%	23	6%
6 month health-check up	52	22%	31	21%	5	31%	88	22%
Passport Issuance	5	2%	0	0%	0	0%	5	1%
Total	236	100%	149	100%	16	100%	401	100%

In table 2 are enumerated the preventive acts carried out – the most frequent act was vaccination, representing 66% (n=401). Prevention and treatment against internal and external parasites is included in deworming. At Priory Veterinary Surgeons it is highly emphasized the importance of six-monthly health checks ups, and such are enumerated as well in table 1.

According to the WSAVA (World Small Animal Veterinary Association) guidelines for the vaccination of dogs and cats, there are different types of vaccines - infectious and non-infectious vaccines, core vaccines and non-core vaccines (Day et al. 2016).

Infectious vaccines are made of attenuated organisms or recombinant vectored vaccines, in order to reduce virulence but still be capable of inducing immunity by infection and replication in the animal, without any significant pathology or clinical signs. These vaccines are very effective when inducing mucosal immunity, hence they boost cell-mediated and humoral immunity and will usually protect with a single dose. Non-infectious vaccines incorporate an antigenically intact but inactivated pathogen, which is incapable of infecting or replicating in the animal, neither inducing pathology. These vaccines depend upon an adjuvant and multiple doses to increase efficiency (Day et al. 2016; Day 2017).

Core vaccines are defined as those which all dogs and cats must receive at recommended intervals, regardless of circumstances or geographical location, hence they provide protection from life-threatening diseases with global significance (Day et al. 2016).

For dogs, vaccines against canine adenovirus, canine distemper virus and the variants of canine parvovirus type 2 are the ones considered core. For cats, core vaccines protect from feline herpesvirus-1, feline calicivirus (two types of virus that may cause cat flu) and feline parvovirus (which causes feline panleukopenia). However, it needs to be stressed that in areas of the world where rabies is still endemic, vaccination against it must be defined as a core vaccine

for both dogs and cats and is also usually required for international pet travel (Day et al. 2016). In Portugal, immunization against rabies is legally required ("Decreto-Lei Nº 313/2003", 2003), whereas in the United Kingdom it is not.

Non-core vaccination is defined as the vaccines required only by animals whose environment, lifestyle or geographical location puts them at risk for specific infections (Day 2017). The non-core vaccination for dogs protects the species from *Leptospira* spp, *Bordetella bronchiseptica*, canine parainfluenza virus, *Borrelia* and *Leishmania canis*. The main non-core feline vaccines are against the feline leukaemia virus (FeLV), Chlamydia felis and *Bordetella* bronchiseptica (Day et al. 2016).

As the vast majority of puppies and kittens are protected by maternal antibodies in the first weeks of life, only by 8-12 weeks of age will passive immunity have waned enough to a level that enables active immunization by vaccines (Day et al. 2016; Day 2017).

In regard to the beginning of both puppy and kitten vaccination, guidelines state that initial core and non-core vaccination should start between eight and nine weeks of age, then giving them a booster three to four weeks later. Another core booster vaccine should be given at 16 weeks or older and a fourth booster at 26 weeks in order to protect those who failed to respond due to blocking maternal antibodies. Twelve months after the last primary series of core vaccination, (if not given at 26 weeks, as these may go to an adult plan), non-core vaccines can be administered (Day et al. 2016; Day 2017).

The canine revaccination should be done annually, however the components differ each year - infectious core vaccines can be given at intervals of 3 years in any adult dog, but non-infectious non-core vaccines (except rabies) or vaccines that contain bacterial antigens, should be given every year in adult dogs (Day et al. 2016; Day 2017).

At Priory Veterinary Surgeons, vaccinating against kennel cough (caused by Bordetella and Parainfluenza) is recommended. The intra-nasal kennel cough vaccination is administered every year. Leishmaniasis is not a frequent condition observed in the United Kingdom, however vaccines are available, starting with three injections, three weeks apart, followed by annual boosters (Day 2017). The global core and non-core vaccinations and timings for canines are demonstrated in Table 3.

Table 3: Core and non-core vaccinations and timings for canines

Vaccination		Weeks of age						Years of age
		3	8	12	16	26	52	
Core vaccination	Canine adenovirus		x	x	x	x	X (if not given at 26)	Triennial vaccination (at 4, 7, 10, 13 years of age)
	Canine distemper virus		x	x	x	x	X (if not given at 26)	
	Canine parvovirus type 2		x	x	x	x	X (if not given at 26)	
	Rabies virus (in endemic countries)			x			x	
Non-core vaccination	Leptospira		x	x			x	Annual vaccination
	Bordetella bronchiseptica	x					x	
	Canine parainfluenza virus	x					x	
	Borrelia						x	
	Leishmania						x	

Feline revaccination is assessed by the risk of exposure of each individual - a high-risk cat is an indoor/outdoor cat, a cat that lives in a multicat household or visits a boarding cattery regularly, whereas low risk cats are defined as lonely, indoor-only cat that never visits a boarding cattery (Day 2017).

A low risk cat is given core vaccines every three years but non-core vaccination is not required after the first year. A high-risk cat should have annual boosters for feline calicivirus, feline herpesvirus type 1, Chlamydia felis and *Bordetella* bronchiseptica before any regular annual boarding at a cattery (as most robust immunity occurs within a 3-month period) and triennial booster for feline parvovirus, FeLV and rabies. The feline vaccinations and their respective timings are demonstrated in Table 4 (Day 2017).

All types of vaccinations in cats have been considered to be linked to the pathogenesis of the feline injection site sarcoma (FISS), especially the ones containing adjuvant, as FeLV and rabies vaccines. FISS is a chronic inflammation that develops into infiltrative malignant mesenchymal cells tumour. As for these types of tumours radical surgical resection is advised, guidelines state that the riskier vaccines should be administered into anatomical sites that would facilitate the future removal. Some recommend that FeLV vaccine should be administered as distal as possible into the left hindlimb and rabies into the right hindlimb (Axiak 2012; Day et al. 2016).

Table 4: Core and non-core vaccinations and timings for felines

		Weeks of age					Years of age low-risk cat	Years of age high-risk cat
		8	12	16	26	52		
Core vaccination	Feline herpesvirus type 1	x	x	x	x	X (if not given at 26)	Triennial vaccination (at 4, 7, 10, 13 years of age)	Annual vaccination
	Feline calicivirus	x	x	x	x	X (if not given at 26)		
	Feline parvovirus	x	x	x	x	X (if not given at 26)		Triennial vaccination (at 4, 7, 10, 13 years of age)
	Rabies virus (in endemic countries)		x			x		
Non-core vaccination	Feline leukaemia virus	x	x			x	Not recommended for low-risk cats	Annual vaccination
	Chlamydia felis	x	x			x		
	Bordetella					x		

In regard to rabbit vaccination, the recommendation is to vaccinate domestic rabbits against Myxomatosis and the two strains of Rabbit Viral Haemorrhagic Disease (RHD) caused by RHDV-1 and RHDV-2. Vaccinations start at 6 weeks old with a single combined vaccine, against Myxomatosis and one strain of RHD (RHD virus type 1), two weeks after they should be given a vaccine against RHD-1 and RHD-2. An annual booster is recommended for both diseases (BSAVA 2018; NOAH 2014).

2.2.2. Internal Medicine

Internal Medicine cases are divided into 13 different areas, which are represented in table 5. The most prevalent medical field was dermatology, with a relative frequency of 26% (n= 474), followed by gastroenterology representing 18% of the total cases. In all clinical areas, the most representative group was the canine group, except for cardiology, pneumology, nephrology and urology areas, in which feline group was more represented. Exotic medicine was mostly represented in the cardiology, pneumology, dermatology and gastroenterology areas.

A brief bibliographical review of one relevant disease of each area will be developed, whether by it being the most prevalent disease in the particular clinical field or by it being author's preference.

Table 5: Case distribution regarding Internal Medicine Clinical Areas

Internal Medicine	Canine		Feline		Exotic		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)	Fi	FR (%)		
Cardiology & Pneumology	19	5%	14	16%	7	47%	40	8%
Dermatology	99	27%	19	21%	6	40%	124	26%
Endocrinology	7	2%	6	7%	0	0%	13	3%
Gastroenterology	72	20%	10	11%	2	13%	84	18%
Immunology	4	1%	0	0%	0	0%	4	1%
Infectology & Parasitology	10	3%	4	4%	0	0%	14	3%
Musculoskeletal system	55	15%	4	4%	0	0%	59	12%
Neurology	14	4%		0%	0	0%	15	3%
Nephrology & Urology	9	2%	21	23%	0	0%	30	6%
Oncology	39	11%	5	6%	0	0%	40	9%
Ophthalmology	17	5%	7	8%	0	0%	24	5%
Theriogenology & Neonatology	10	3%	0	0%	0	0%	10	2%
Toxicology	14	4%	0	0%	0	0%	14	3%
Total	369	100%	90	100%	15	100%	474	100%

2.2.2.1. Cardiology and Pneumology

Cardiology and pneumology completed 8% (n=474) of the medical practice, with 12 cases (Table 5). The most common conditions were dilated cardiopathy and chronic degenerative mitral valve disease, both with 33% (n=12), as described in table 6.

Table 6: Case distribution regarding Cardiology

Cardiology		Canine		Feline		Total	FR (%)
		Fi	FR (%)	Fi	FR (%)		
Dilated cardiopathy		2	25%	2	50%	4	33%
Hypertrophic cardiomiophaty		0	0%	2	50%	2	17%
Heart failure		1	13%	0	0%	1	8%
Pericardic effusion		1	13%	0	0%	1	8%
Chronic degenerative mitral valve disease	stage B	3	38%	0	0%	3	25%
	stage D	1	13%	0	0%	1	8%
Total		8	100%	4	100%	12	100%

Chronic valvular heart disease (CVHD), also known as degenerative valvular disease or endocardiosis (Ljungvall and Häggström 2015) is more likely to affect the left atrioventricular/mitral valve, with or without involving the right atrioventricular/tricuspid valve (Atkins et al. 2009).

Myxomatous degeneration is a pathological change in the organization of the connective tissue of the heart valves (Ljungvall and Häggström 2015), which includes collagen changes in

cellular and intercellular components as well as endothelial thickening. These deformations limit the valves coaptation, which progresses to valvular regurgitation into the atrium and leads to an increase on cardiac work and consequently to a ventricular remodelling and dysfunction (Atkins et al. 2009).

Slight to moderate regurgitation is often compensated for years by cardiac dilation, eccentric hypertrophy, increased force of contraction, increased heart rate, fluid retention and neurohormonal modulation of cardiovascular function. When valvular regurgitation can no longer be compensated, the increased venous pressure and the reduced cardiac output lead to congestive heart failure (Ljungvall and Häggström 2015).

There is still no known cause for this disease, however it looks like it has a genetic component in some breeds, being Cavalier King Charles Spaniels predisposed to develop it at a young age. CVHD is also more prevalent in males and in smaller breeds. However, whereas the disease is slow and relatively predictably progressive in dogs under 20 kilograms, with most of them being diagnosed with mitral valve regurgitation years before the clinical onset of heart failure, when it occurs in larger breeds, the progression appears to be faster (Atkins et al. 2009).

The most important clinical finding of chronic degenerative mitral valve disease (CDMVD) is the characteristic left apical systolic heart murmur. Thoracic radiographs are the first indicated diagnostic tests (as they can rule out non cardiac causes, assess the cardiac size by vertebral heart score and also indicate decompensated cardiac heart failure if there is pulmonary congestion and oedema present), however echocardiography is the test of choice for demonstrating the valve lesion, as it detects the thickened atrioventricular valve and identifies the regurgitant jet as well as changes in structure and contractile function of the heart chambers. The differential diagnosis must exclude anaemia, bacterial endocarditis, secondary mitral regurgitation due to dilated cardiomyopathy and primary respiratory disease (Ljungvall and Häggström 2015).

After the diagnosis, CDMVD should be staged according to an ACVIM system that classifies the four basic stages of heart disease and failure and helps guiding the clinical approach for each(Atkins et al. 2009; Ljungvall and Häggström 2015).

Stage A patients are at high risk for developing heart disease but presently hold no identifiable structural disorder of the heart (e.g., Cavalier King Charles Spaniel without a heart murmur). No treatment is indicated in stages A or B1, however these animals should be subjected to yearly cardiac evaluations (Atkins et al. 2009; Ljungvall and Häggström 2015).

In Stage B patients clinical signs are not present, but they do present with a systolic click (early stage) or murmur, revealing structural heart disease. Stage B1 are asymptomatic patients that have hemodynamically insignificant valve regurgitation, with no radiographic or echocardiographic evidence of cardiac remodelling in response to CVHD. Stage B2 are asymptomatic patients that have hemodynamically significant valve regurgitation, with radiographic or echocardiographic evidence of cardiac remodelling in response to CVHD (Atkins et al. 2009; Ljungvall and Häggström 2015).

Stage C patients have past or current clinical signs of heart failure associated with structural heart disease.

Stage D patients have end-stage disease with clinical signs of heart failure caused by CVHD that are refractory to standard therapy and require specialized treatment so that they remain clinically comfortable (Atkins et al. 2009; Ljungvall and Häggström 2015).

In stage B2, according to a recent study published by the Journal of Veterinary Internal Medicine in 2016, the administration of pimobendan to dogs without any other cardiovascular therapy results in the prolongation of the preclinical period, prolonging the onset of congestive heart failure by 15 months and reducing its risk by one-third. Angiotensin converting enzyme inhibitors (ACEI) and ß-blockers are other therapeutic possibilities for patients with clinically relevant left atrial enlargement on initial examination or on successive monitoring examinations. Changing to a diet with mild dietary sodium restriction and adequate protein and calories for maintaining optimal body condition, might also be an option at this stage (Atkins et al. 2009; Ljungvall and Häggström 2015).

In acute stage C, furosemide (doses related to the severity of clinical signs and response to therapy), pimobendan, oxygen supplementation, paracentesis or thoracocentesis (if effusions are causing respiratory distress), sedation (if anxiety reflects in dyspnoea) are recommended. Combining the administration of enalapril with furosemide improves pulmonary capillary wedge pressure, so it is also a possibility in these cases, as well as nitroglycerin ointment. In chronic stage C, medical therapy with furosemide, pimobendan and an ACEI (e.g. enalapril) is a indicated. Other possibilities include spironolactone (as an aldosterone antagonist), digoxin, ß-blockers (e.g. atenolol, as a protection on myocardial function and remodeling), antiarrhythmic medication, (to maintain sinus rhythm, e.g. diltiazem), cough suppressants and maintaining adequate calorie intake (Atkins et al. 2009).

In acute stage D, it is recommended to increase the dose and frequency of furosemide, spironolactone, oxygen supplementation or even mechanical ventilatory assistance, paracentesis or thoracocentesis as needed. Sodium nitroprusside, dobutamine, hydralazine, amlodipine, direct vasodilators, sildenafil, bronchodilators are also possibilities to add on. In chronic stage D, increasing the dose and frequency of furosemide, and administering spironolactone is indicated. Other possibilities include hydrochlorthiazide, pimobendan, digoxin, sildenafil, cough suppressants and bronchodilators (Atkins et al. 2009).

Although open-heart surgical repair of myxomatous mitral valve disease in dogs has been described with success, there is no treatment that reverses the myxomatous disease. Prognosis and progression of the disease depends on the age, left atrial size, heart rate, presence of other diseases and the development of complications (such as tendinous chord rupture, intracardiac thrombus) (Atkins et al. 2009; Ljungvall and Häggström 2015).

Table 7: Case distribution regarding Pneumology

Pneumology	Canine		Feline		Exotic		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)	Fi	FR (%)		
Bronchopneumonia	1	9%	0	0%	0	0%	1	4%
Bronchitis	0	0%	4	40%	0	0%	4	14%
Cat flu	0	0%	2	20%	0	0%	2	7%
Feline asthma	0	0%	2	20%	0	0%	2	7%
Kennel cough	4	36%	0	0%	0	0%	4	14%
Laryngeal saccules eversion	1	9%	0	0%	0	0%	1	4%
Pleural effusion	0	0%	1	10%	0	0%	1	4%
Pneumomediastine	1	9%	0	0%	0	0%	1	4%
Pneumonia	2	18%	1	10%	7	100%	10	36%
Elongated Soft palate	1	9%	0	0%	0	0%	1	4%
Tracheal collapse	1	9%	0	0%	0	0%	1	4%
Total	11	100%	10	100%	7	100%	28	100%

Table 7 shows the absolute frequencies and respective percentages of the cases observed in the area of pneumology, according to the species. Pneumonia was the most common condition, with 36% of cases, followed by bronchitis in cats and kennel cough in dogs, both with 14%.

Infectious tracheobronchitis, commonly denominated kennel cough or canine respiratory disease complex (CRDC), is an acute highly contagious respiratory infection/complex that affects canines. Paroxysmal cough is often the only clinical sign, although it could be accompanied by fever, anorexia and lethargy. In complicated infections, nasal and ocular discharge, respiratory distress and pneumonia (which might become life threatening) may also occur (Ford 2004).

This condition has a multifactorial aetiology, caused by one or a combination of bacterial and/or viral agents - *Bordetella bronchiseptica* and canine parainfluenza virus are the two most common, however canine adenovirus-2, canine distemper virus and canine herpesvirus, as well as environmental conditions can be involved. All are capable of colonizing the epithelium of the upper respiratory tract and causing a high-pitched cough often described as goose or seal honk. These pathogens especially threaten puppies (who are more severely affected and are at significant risk of dying if not treated) and dogs in shelters, kennels and veterinary hospitals (Ford 2004).

Diagnosis is often facilitated by the acknowledgement of recent contact with other dogs (whether or not having cough) within the previous 10 days. In addition, a positive and rapid response to cough suppressants (as an anti-inflammatory or antitussive medication) supports the diagnosis of an uncomplicated infectious tracheobronchitis with an excellent prognosis. If there is any respiratory distress or pneumonia, hospitalization and aerosol therapy is recommended.

Thoracic radiographies may be helpful to rule out pneumonia in a dog with fever or anorexia (Ford 2004).

Although vaccination stimulates immune response, it does not eliminate the risk of infection nor the development of subclinical to mild infection. Once exposed, intra-nasally vaccinated canines have significantly lower rates of coughing, nasal discharge and retching, compared to unvaccinated ones. Vaccination is recommended at least 5 days prior to a known or potential exposure (Ellis et al. 2016).

2.2.2.2. Dermatology

Table 8: Case distribution regarding Dermatology

Dermatology	Canine		Feline		Exotic		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)	Fi	FR (%)		
Acral lick dermatitis	2	2%	0	0%	0	0%	2	2%
Anal glands abscess	4	4%	0	0%	0	0%	4	3%
Anal glands furunculosis	1	1%	0	0%	0	0%	1	1%
Atopy	10	10%	0	0%	0	0%	10	8%
Burn	0	0%	1	5%	0	0%	1	1%
Contact dermatitis	1	1%	0	0%	0	0%	1	1%
Chronic Allergy	10	10%	0	0%	0	0%	10	8%
Dermatitis	7	7%	3	16%	0	0%	10	8%
Ear foreign body	1	1%	0	0%	0	0%	1	1%
Eosinophilic complex	0	0%	1	5%	0	0%	1	1%
Environmental allergy	1	1%	0	0%	0	0%	1	1%
External otitis	33	33%	2	11%	0	0%	35	28%
Facial dermatitis	1	1%	0	0%	0	0%	1	1%
Flea Allergy dermatitis	1	1%	2	11%	0	0%	3	2%
Food allergy	1	1%	0	0%	0	0%	1	1%
Harvest mites	2	2%	0	0%	0	0%	2	2%
Hotspot	1	1%	0	0%	0	0%	1	1%
Nail bed infection	1	1%	0	0%	0	0%	1	1%
Otohematoma	2	2%	0	0%	0	0%	2	2%
Pyoderma	1	1%	0	0%	0	0%	1	1%
Skin Abscess	2	2%	1	5%	4	67%	7	6%
Subcorneal pustular dermatosis	1	1%	0	0%	0	0%	1	1%
Tick granuloma	1	1%	0	0%	0	0%	1	1%
Wound	15	15%	9	47%	2	33%	26	21%
Total	99	100%	19	100%	6	100%	124	100%

Dermatology comprised 26% (n=474) of the medical practice, with 124 cases (Table 5), having been the most prevalent area. Absolute frequencies and respective percentages of the cases observed in the area of dermatology, are shown in table 8. The most common condition observed was otitis externa with 35 cases, making 28% of total dermatologic maladies.

Otitis externa is one of the most common pathologies presented by dogs regarding the dermatology area. It is characterized as an acute or chronic inflammation of the external ear canal, in which aetiology can be divided into primary (direct cause of inflammation) and secondary (perpetuating or predisposing factors that contribute to ear disease, prevent resolution and/or lead to recurrence) causes (Scott 2015; Paterson 2016).

Primary causes include allergy (food, contact, atopy), endocrine (hypothyroidism, hyperadrenocorticism), immune-mediated (pemphigus foliaceus, lupus erythema multiforme, vasculitis, drug eruption), keratisation disorders (sebaceous adenitis, primary idiopathic seborrhoea), ectoparasites (O*todectes cynotis*, *Demodex* species), foreign body and idiopathic (juvenile cellulitis particularly in young puppies, idiopathic glandular hyperplasia in spaniels). (Paterson 2016). Frequent swimming, pendulous ear pinnae, presence of hair within the canal, stenotic ear canals and excessive moisture, systemic disease (renal, pancreatic or hepatic), obstructive ear disease (neoplasia, polyps, cysts) are predisposing factors in the establishment of an otitis externa (Scott 2015; Paterson 2016).

Secondary infection with yeast (*Malassezia* and *Candida* species) or bacteria (*Staphylococcus spp., Streptococus spp., Corynebacterium spp., Enterococcus spp., Pseudomonas spp., Proteus spp., Escherichia coli*) develops after inflammation trigged by primary causes, usually combined with perpetuating and predisposing factors. Although treatment against these is essential, if it does not treat the primary cause, it will not resolve the ear disease (Scott 2015; Paterson 2016).

Owners report head rubbing, ear scratching and/or head shaking, and animals show erythema and oedema of the ear canal, auricular discharge (brown-black “coffee grounds” most of the times indicate infestation with *Otodectes cynotis*, also known as ear mites; brown or gray discharge suggest Malassezia and yellow-greenish discharge points towards bacterial infection), erosions and ulcers (which are associated with *Pseudomonas* infection), pain when opening the mouth, facial paralysis, head tilt and/or signs of generalized skin disease (Scott 2015; Paterson 2016).

Cytology, bacterial culture and sensitivity testing may be of help in establishing the diagnosis and the correct therapy. The majority of acute otitis can be treated with manual cleaning and a polyvalent topical ear product, which usually includes a glucocorticoid, an antimicrobial, and/or an antifungal. In regard to chronic cases, the underlying causes should be recognised and treated whilst managing the secondary infection (Nuttall 2016; Paterson 2016)

Pathological changes in the canal wall, glandular tissue and in the tympanum, as well as an acute or chronic otitis media, are perpetuating factors of otitis externa and should be addressed too (Nuttall 2016; Paterson 2016).

Vertical ear canal ablation, which was performed during the traineeship, is recommended in irreversible hyperplastic otitis (characterized by palpable mineralization and complete occlusion of the external ear canal by hyperplastic tissue) when the horizontal canal is healthy, which allows complete excision of vertical canal tissue with less postoperative pain and exudate than a total ear canal ablation(Bacon 2012; Scott 2015)

2.2.2.3. Endocrinology

Endocrinology comprised 3% (n = 474) of the medical practice, with 13 cases (Table 5). Table 9 displays the absolute frequencies and respective percentages of the cases observed in the area of endocrinology. *Diabetes mellitus* was the most common condition observed with 31% (n=13), followed by hyperadrenocorticism and hyperthyroidism observed both with 23% (n=13) of total cases witnessed in this medical field. A brief bibliographical review on hyperthyroidism will be made due to the author's preference on this topic.

Table 9: Case distribution regarding Endocrinology

Endocrinology	Canine		Feline		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)		
Diabetes mellitus	2	29%	2	33%	4	31%
Exocrine pancreatic insufficiency	1	14%	1	17%	2	15%
Hyperadrenocorticism	3	43%	0	0%	3	23%
Hyperthyroidism	0	0%	3	50%	3	23%
Hypothyroidism	1	14%	0	0%	1	8%
Total	7	100%	6	100%	13	100%

Hyperthyroidism, also known as thyrotoxicosis, results from an excess of active thyroid hormones (T3/triiodothyronine and T4/thyroxine) circulating in the blood stream. It usually affects cats from eight years old and beyond, with no sex predilection (Mooney and Peterson 2004; Daminet 2015)

The most common cause of this disease is a benign thyroid neoplasia (adenoma) or an adenomatous hyperplasia in one or more commonly both thyroid lobes, although a thyroid carcinoma is also a rare but possible cause. When it comes to dogs, hyperthyroidism is due to a functional thyroid carcinoma(Mooney and Peterson 2004; Daminet 2015)

Feline hyperthyroidism (FHT) is suspected when the animal presents with weight loss, polyphagia, polyuria, polydipsia, tachypnoea, tachycardia, increased vocalization and activity,

gastrointestinal disorders, palpably enlarged thyroid glands and/or unkempt hair coat. If a high total T4 serum concentration is concurrent with one or more of the previous signs, the diagnosis is confirmed. Differential diagnosis must take into account *Diabetes mellitus*, inflammatory bowel disease, gastrointestinal lymphoma, gastrointestinal malabsorption, chronic kidney disease and parasitism. As older cats are the most affected, age related comorbidities such as heart disease, hypertension, retinopathy, chronic kidney disease, gastrointestinal dysfunction and *Diabetes mellitus* may be present. A simple approach to diagnosis and management by categorizing the animal into one of six diagnostic groups, is demonstrated in table 10 (Daminet 2015; Carney et al. 2016).

Table 10: FHT diagnostic groups and management options

Group	Clinical Presentation	Options
Classical clinical disease	• Clinical signs • Elevated T4 • No identifiable concurrent disease	Treat for FHT
Clincal FHT with one or more concurrent disease	• Clinical signs • Elevated T4 • identifiable concurrent disease	Treat for FHT and manage concurrent disease
Possible FHT with probable non-thyroid disease	• Clinical signs • Normal T4	• Test for T4 and fT4ed • Test for differential diagnosis • Consider T3 suppression or thyroid scintigraphy
Enlarged thyroid without clinical signs	• No clinical signs • Normal T4	• Monitor clinical signs and T4 serum concentration
Subclinical FHT	• No clinical signs but suggestive physical findings • Elevated T4	• Confirm T4 - if elevated, treat for FHT
Clinically normal	• No clinical signs and no suggestive physical findings • Elevated T4	

There are four treatment options, which should be applied according to each patient's characteristics. Treatment with radioactive iodine or surgical thyroidectomy are the two definitive cures recommended for fairly young and healthy cats. However, for geriatric cats, cats with concurrent non-thyroidal disease and those whose owners decline definitive therapy, the long-term medical management with anti-thyroid drugs (carbimazole or methimazole) or an iodine-restricted diet are the possible therapies. Nevertheless, monitoring the patient is essential to assess efficacy and detect iatrogenic hypothyroidism (Daminet 2015; Carney et al. 2016).

Cats without concurrent chronic kidney disease have a median survival of up to 5 years, but cats with a comorbid disease have shorter survival times(Carney et al. 2016).

2.2.2.4. Gastroenterology and annexes

With a relative frequency of 27% (n=474), 84 cases of the gastroenterology medical field were seen (Table 5). Absolute frequencies and respective percentages of the cases observed this area are shown in table 11. The most common condition observed was gastroenteritis with 28 cases (33%), followed by periodontal disease with 18% (n= 84) and pancreatitis with 12% (n= 84) of gastroenterology conditions in total. A brief bibliographical review on pancreatitis will be made due to the author's preference on this topic.

Table 11: Case distribution regarding Gastroenterology and annexes

Gastroenterology and annexes	Canine		Feline		Exotic		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)	Fi	FR (%)		
Colitis	3	4%	0	0%	0	0%	3	4%
Epulis	1	1%	0	0%	0	0%	1	1%
Faecaloma	0	0%	0	0%	0	0%	0	0%
Feline odontoclastic resorptive lesion	0	0%	1	10%	0	0%	1	1%
Foreign body	1	1%	0	0%	0	0%	1	1%
Gastritis	4	6%	0	0%	0	0%	4	5%
Gastritis by food indiscretion	9	13%	0	0%	0	0%	9	11%
Gastroenteritis	28	39%	0	0%	0	0%	28	33%
Haemorrhagic Gastroenteritis	5	7%	0	0%	0	0%	5	6%
Inflammatory bowel disease	2	3%	0	0%	0	0%	2	2%
Liver failure	0	0%	1	10%	0	0%	1	1%
Megaesophagus	1	1%	0	0%	0	0%	1	1%
Pancreatitis	6	8%	4	40%	0	0%	10	12%
Periodontal disease	11	15%	3	30%	1	50%	15	18%
Stomatitis	1	1%	0	0%	0	0%	1	1%
Tooth abscess	0	0%	1	10%	1	50%	2	2%
Total	72	100%	10	100%	2	100%	84	100%

Common in both dogs and cats, pancreatitis is usually classified as acute or chronic and mild or severe. The acute inflammation of the pancreas is associated with high mortality, however it is possible to witness a complete recovery of pancreas structure and function. In the other hand, chronic pancreatitis might lead to progressive loss of the pancreas normal function, causing pain and therefore reducing quality of life (Watson 2015). However, recurrent reversible acute pancreatitis may result in progressive and irreversible chronic disease (Xenoulis 2015).

Mild pancreatitis refers to a disease where there is no multi-organ failure, whereas severe pancreatitis includes a multisystem failure and/or pancreatic or peri-pancreatic necrosis (Mansfield and Beths 2015).

The gold standard for definitive diagnosis of pancreatitis and its definition as acute or chronic disease is histological – whereas in an acute form neutrophilic inflammation, oedema and necrosis are present, in a chronic form, there are permanent, irreversible and progressive histopathological changes, such as fibrosis and acinar loss (Watson 2015; Xenoulis 2015). Although a definitive diagnostic and classification in acute or chronic pancreatitis is important for therapy management and prognosis, histology is not often performed as it is an invasive procedure and it has associated morbidity. Therefore, a presumptive diagnosis may be done on the basis of functional changes and clinical findings together with abnormal serum pancreatic lipase immunoreactivity (PLI) concentration and abdominal ultrasonography findings (enlargement of the pancreas, fluid accumulation around the pancreas, necrosis if hypoechoic, fibrosis if hyperechoic, dilated pancreatic duct). Complete blood count, serum biochemistry profile and urinalysis should always be performed in dogs and cats suspected of having pancreatitis and abdominal radiography might be performed to exclude other diseases (Steiner 2015; Xenoulis 2015).

Although many studies show environmental and genetic influences in pancreatitis pathophysiology, aetiology is often seen as idiopathic. Generally, the inflammation starts with premature and excessive activation of pancreatic digestive enzymes which may be a result of oxidative stress or hypotension. The pancreatic proteases then stimulate the migration of neutrophils to the pancreas with subsequent worsening inflammation in the pancreatic and peri-pancreatic area which leads to progression and complications(Steiner 2015)

Domestic shorthaired and Siamese cats, Miniature schnauzers, Border Collies, Cavalier King Charles and English cocker spaniels are more commonly affected. However being overweight, having hypertriglyceridaemia, being a male, having been submitted to previous surgery, having concurrent endocrine diseases, drug administration (azathioprine or potassium bromide) and dietary indiscretions increase the risks of acute fatal pancreatitis. On the other hand, in cats, risk factors include high fat diets, hypercalcaemia, blunt abdominal trauma and infections (such as *Toxoplasma gondii* and *Amphimerus pseudofelineus*). Feline pancreatitis can occur simultaneously with inflammatory bowel disease and/or cholangitis; so-called triaditis (Steiner 2015; Watson 2015).

Clinical signs vary greatly – most dogs with chronic pancreatitis present with subclinical disease or intermittent mild non-specific signs, whereas animals with acute pancreatitis may display anorexia, weakness, vomiting, diarrhoea, icterus, hypothermia or fever, bleeding diathesis and/or abdominal pain in numerous combinations (Xenoulis, 2015) and in severe cases cardiovascular shock, disseminated intravascular coagulation, multi-organ failure and even death may be observed. (Watson 2014, Xenoulis 2015). It is important to consider that additional clinical signs might also be present, in consequence of other concurrent or complicating disease, such as exocrine pancreatic insufficiency or *Diabetes mellitus*. Clinical presentation of feline pancreatitis is mostly anorexia, lethargy, dehydration, icterus, hypothermia or fever, signs of

abdominal pain and frequently a palpable abdominal mass, with less predominance of gastrointestinal signs (Steiner 2015; Xenoulis 2015; Watson 2015).

A therapeutic approach to mild acute pancreatitis, starts with intravenous fluid replacement with Ringer's solution (which by increasing pH prevents further trypsin activation) and an anti-emetic therapy with maropitant. If there is any suspicion of bacterial translocation or infected pancreatic necrosis, a course of antibiotics should be started, preferably with amoxicillin-clavulanate or ticarcillin. Reduction of gastric acidity should also be addressed, omeprazole being the first drug of choice. In unresponsive cases, hydrocortisone in a low dose can be considered. (Steiner 2015; Watson 2015).

Patients with mild disease, should be fasted until they regain appetite and eat voluntarily. However, if they reach five days of anorexia, enteral feeding is the next step. In contrast, in dogs with severe disease, a naso-oesophageal or oesophageal feeding tube should be placed as soon as possible. High fat diets should be avoided as many of the animals are hyperlipidaemic (Xenoulis et al 2008; Mansfield and Beths 2015).

In mild pancreatitis, non-steroidal anti-inflammatory agents, buprenorphine or methadone are recommended for pain management and a lidocaine and ketamine constant rate infusion (CRI) should be added in a moderate disease case. In case of severe to excruciating pain, an epidural morphine or fentanyl infusion in combination with a lidocaine/ketamine CRI is the recommended analgesia. If there is any unexpected exacerbation of the pain, assessment for pancreatic fluid collection should be made. Gabapentin may be given with any combination for any level of pain. Currently, there is no recommendation for surgical intervention in the management of pancreatitis (Xenoulis 2015)

The long-term management of chronic pancreatitis involve a fat restricted diet, resolving concurrent diseases that may trigger an acute episode and monitoring PLI concentration. Drugs associated with pancreatitis should also be avoided and there is still no evidence about pancreatic enzymes oral supplements for chronic patients (Xenoulis et al 2008).

Prognosis is directly related to the severity of the disease - animals with mild, uncomplicated disease, the prognosis is usually good. However, in severe disease outcome should be guarded, not to mention that exocrine pancreatic insufficiency and Diabetes mellitus may be long-term sequelae of chronic disease (Xenoulis et al 2008).

2.2.2.5. Immunology

Immunology comprised 1% (n = 474) of the medical practice, with three cases (Table 5). Table 12 displays the absolute frequencies and respective percentages of the four cases observed in the area of immunology.

Table 12: Case distribution regarding Immunology

Immunology	Canine	
	Fi	FR (%)
Chronic polyarthritis	1	25%
Immune-mediated hemolytic anemia	1	25%
Immune-mediated polyarthritis	1	25%
Symetric lymphoid onchodistrophy	1	25%
Total	4	100%

Polyarthritis is characterized by an inflammation of more than two joints and is classified as infectious, reactive and immune-mediated, which is in turn subcategorized into erosive (or deforming) and non-erosive(or non-deforming) form (Johnson and Mackin 2012b; Mahony 2015).

Although it may affect any dog or cat of any age or sex, classical lameness, reluctance to walk, stiffness and occasionally nonspecific signs of systemic disease (fever, inappetence, lethargy) may be more often be presented by young adults (Mahony 2015; Stone 2017).

Infectious etiologies for polyarthritis include Lyme disease, Erlichiosis, *Anaplasma phagocytum*, *Corynebacterium*, *Mycoplasma*, *Leishmania*, *Bartonella, Calicivirus* infection in cats, amongst others (Mahony 2015).

Reactive polyarthritis can develop due to vaccine or drug induced responses. Vaccine-induced polyarthritis is a possible reaction whether after a first vaccination or a booster. Recent studies suggest that canine distemper virus may be implicated, though Akitas seem to be predisposed to this adverse reaction. Treatment with doxycycline and NSAID's usually resolves the clinical signs. Drug-induced polyarthritis is widely described after sulfonamide treatment, especially in Doberman pinschers. Additionally, polyarthritis secondary to erythropoietin, penicillin, cephalosporins and phenobarbital administration has also been described (Johnson and Mackin 2012b).

A type III hypersensitivity reaction may possibly be the cause behind immune-mediated non-deforming polyarthritis - immune complexes accumulated in the joint space activate the complement which leads to neutrophilic inflammation and consequent tissue damage. Non erosive immune mediated polyarthropathy is most commonly idiopathic. However it can also be specific to the Shar-Pei and Akita breeds, or a result of polymyositis syndrome, a meningitis-arthritis or may be associated with systemic lupus erythematosus (Johnson and Mackin 2012b; Mahony 2015).

Young large breed and sporting females, such as Retrievers, Cocker Spaniels and German Shepherds, seem most frequently affected by idiopathic polyarthritis, which is classified into four subtypes, as shown in Table 13 (Johnson and Mackin 2012b).

Table 13: Subtypes of idiopathic immune mediated polyarthritis

Subtype of idiopathic immune mediated polyarthritis	
Type I	No underlying disease or aetiology diagnosed
Type II	Reaction to an infectious or inflammatory disease distant from the joint (pancreas, heart, urinary tract, spine, uterus, etc.)
Type III/Enteropathic	Presence of gastrointestinal or hepatic disease
Type IV	Caused by neoplasia outside the joints

Classical clinical signs that reveal polyarthritis/polymyositis syndrome are a muscle atrophy and fibrosis following a polyarthritis accompanied by focal or generalized muscle pain and swelling. Therapy with cyclophosphamide combined with prednisone has had some success in resolving the symptomatology. Juvenile-onset polyarthritis in Akitas is characterized by cycles of fever combined with painful and swollen joints that spontaneously resolve after 24 to 48 hours. It usually onsets between nine weeks and eight months of age. Similarly, familial Shar-Pei fever is characterized by intermittent recurring attacks of inflammation and fever due to a genetic mutation, however, in contrast to polyarthritis in Akitas, the onset of that disease can strike whether youngsters or adults (Johnson and Mackin 2012b).

Systemic lupus erythematosus is uncommon, typically starting between two and four years of age due to various and simultaneous immunologic reactions. Clinical signs consist of non-erosive polyarthritis with shifting lameness, haemolytic anaemia, glomerulonephritis, fever, skin lesions and lymphadenopathies (Johnson and Mackin 2012b).

On the other hand, erosive joint polyarthritis seems to have a type IV hypersensitivity component, combined with chronic synovitis and the presence of antibodies against distemper virus, type II collagen, immunoglobulins M, G and A. The presence of anti-IgA antibodies in the joint fluid is the primary factor to differentiate rheumatoid arthritis from osteoarthritis, thus its quantity can be used as a prognosis indicator (Johnson and Mackin 2012b) . This deforming form is very rare - rheumatoid arthritis is the most frequent, nevertheless erosive polyarthritis of greyhounds, Felty's syndrome (triad composed by rheumatoid arthritis, splenomegaly and neutropenia) and feline periosteal proliferative polyarthritis (periosteal new bone formation and erosions) have also been described. Radiographic findings that indicate subchondral bone destruction can take up to six months to become visible. Dogs primarily diagnosed with the non-deforming form in which clinical signs persist, should be periodically reassessed (Johnson and Mackin 2012b; Mahony 2015).

The diagnosis for an immune-mediated polyarthritis is only definitive after exclusion of other causes of joint disease, such as the conditions described above, and a favourable response

to immunosuppressive treatment. Further confirmatory testing by arthrocentesis and joint fluid analysis may be performed(Johnson and Mackin 2012a; Stone 2017).

Treatment must be decided according to the underlying aetiology, though NSAIDs can always be administered to treat inflammation and remove pain. In cases of idiopathic immune-mediated polyarthritis, a course of prednisolone in immunosuppressive doses is recommended until the resolution of clinical signs. Afterwards, the dosage should be slowly reduced, and the finish of the course might be between four to six months, nevertheless there are dogs who need life-long treatment to remain in remission. It is imperative to exclude bacterial infection before any glucocorticoid administration. If there is any glucocorticoid adverse reaction, azathioprine or cyclophosphamide may be options to consider. In addition, antioxidant supplementation may be a way of preventing hyaluronic acid degradation (Mahony 2015).

Long-term prognosis for erosive arthritis is poor, because it affects quality of life due to intense pain. On the other hand, non-deforming polyarthritis is associated with a fair to good prognosis. Although drug and vaccine induced polyarthritis have an excellent recovery, polyarthritis/polymyositis syndrome, meningitis-arthritis and Akitas with juvenile-onset polyarthritis have frequent relapses (Johnson and Mackin 2012b; Mahony 2015).

2.2.2.6. Infectology and parasitology

With a relative frequency of 3% (n=474), 14 cases corresponding to the infectology and parasitology medical field were seen (Table 5). Absolute frequencies and respective percentages of the cases observed this area are shown in table 14. The most common condition observed was infection by Giardia with 8 cases (57%, n= 14), followed by Coriza infection, which represented 14% (n= 14) of total cases. A brief bibliographical review on feline tuberculosis will be made due to the author's preference on this topic.

Table 14: Case distribution regarding Infectology and Parasitology

Infectology and parasitology	Canine		Feline		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)		
Campylobacter	1	10%	0	0%	1	7%
Coriza	0	0%	2	50%	2	14%
Feline tuberculosis	0	0%	1	25%	1	7%
Giardia	8	80%	0	0%	8	57%
Sarcoptic mange	1	10%	0	0%	1	7%
Toxoplasma	0	0%	1	25%	1	7%
Total	10	100%	4	100%	14	100%

Feline tuberculosis (TB) is a new fatal threat as five clinical cases due to *Mycobacterium bovis* were confirmed in 2018 in the United Kingdom. They occurred in young, mostly pedigree cats with no history of outdoor access. (O'Halloran, et al. 2018, Veterinary Times 2018)

Furthermore, all these cases were atypical, as they involve a rare gastrointestinal form of *M. bovis*, instead of the cutaneous lesions at bite and fight sites where the bacteria typically grow. Clinical signs are gastrointestinal, that might be suggestive of abdominal lymphadenopathy or feline infectious peritonitis as so is important to do a differential diagnosis. Although unclear, the only common denominator that makes sense for experts is that all five cats were fed the same commercial raw frozen food diet.(O'Halloran et al. 2018; "Investigations under Way in Wake of Feline TB Outbreak" 2018). The TB case witnessed during the traineeship correlates to all this information, and although tests were ordered to confirm it, the samples taken were not sufficient. The kitten did not survive for further sampling.

Although TB is potentially treatable with months of antibiotics, it might be fatal in humans and animals, as it is a zoonosis.

2.2.2.7. Musculoskeletal system

With a relative frequency of 12% (n=474), 59 cases involving conditions of the musculoskeletal system were witnessed during the traineeship (Table 5). Absolute frequencies and respective percentages of the cases observed in this medical field are shown in table 15. The most common condition was idiopathic lameness with 49% (n=59), followed by osteoarthritis with 17% (n=59) and cranial cruciate ligament rupture representing 10% (n=59) of total cases. A brief bibliographical review on the cranial cruciate ligament rupture will be made due to the author's preference on this topic.

Table 15: Case distribution regarding the Musculoskeletal system

Musculoskeletal system	Canine		Feline		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)		
Chronic Polyarthritis	1	2%	0	0%	1	2%
Cranial Cruciate Ligament Rupture	6	11%	0	0%	6	10%
Discospondylitis	1	2%	0	0%	1	2%
Femur head fracture	0	0%	1	25%	1	2%
Hip dysplasia	3	5%	0	0%	3	5%
Intervertebral Disk Disease (IVDD)	4	7%	0	0%	4	7%
Lameness	28	51%	1	25%	29	49%
Mandibular symphysis fracture	0	0%	1	25%	1	2%
Myositis/Tendinitis	1	2%	0	0%	1	2%

Osteoarthritis	9	16%	1	25%	10	17%
Patellar luxation	2	4%	0	0%	2	3%
Total	55	100%	4	100%	59	100%

Complete or partial rupture of the cranial cruciate ligament is widely common in dogs of all ages, mostly due to progressive degeneration or trauma. Nevertheless, female large breed dogs, Rottweilers, Newfoundlands, Staffordshire Terriers and Boxers are more prone to develop this condition. When found in small breed dogs, this condition is more likely to happen later in life, whereas large breed dogs are affected earlier. In addition, obesity, neutering and systemic diseases such as hyperadrenocorticism, cutaneous asthenia or any autoimmune disease are demonstrated to be risk factors for the onset of this ligament rupture (Kowaleski and Boudrieau 2012; Linn 2015).

Progressive degeneration that leads to a rupture of the cranial cruciate ligament is due to a weakness in the ligament properties which make it impossible to withstand the forces applied. This lack of collagen fibre maintenance and loss of fibroblasts is seen earlier and more pronounced in dogs weighing more than 15kg. Although pathophysiology is yet to be fully understood, risk factors seem to include obesity and abnormal conformation, such as a non-standard gait and an increased tibial plateau. Acute traumatic rupture of the cranial cruciate ligament may be caused by a traumatic hyperextension, excessive limb loading and/or excessive internal rotation of the tibia (Kowaleski and Boudrieau 2012)

The general signs depend on the severity - non-weight bearing lameness with dramatic pain is compatible with a complete rupture, whereas a subtle lameness only following exercise is more likely to be a partial tear (Kowaleski and Boudrieau 2012; Linn 2015).

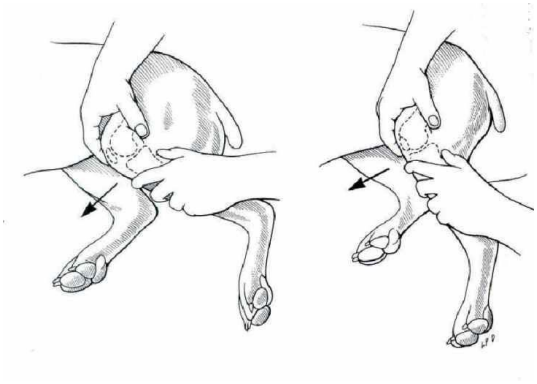
Physical examination findings include stifle pain with flexion and extension, joint effusion adjacent to the patellar tendon, crepitus whilst manipulating, stifle rotated and more flexed when walking, asymmetrical sitting position with one stifle abducted and clicking if a meniscal tear is present. In addition, chronicity might have led to a quadriceps muscle atrophy and periarticular fibrosis on the medial side of the stifle (Kowaleski and Boudrieau 2012; Linn 2015).

There are two tests to evaluate the stifle joint stability, the cranial drawer and the tibial compression tests. Though a positive test is diagnostic of a rupture, a negative test does not rule it out.

Cranial drawer test is performed with the patient in lateral recumbency, the examiner positions the thumb and forefinger of one hand on the femur to hold it stable – thumb placed behind the lateral febella and the index finger over the patella, with the remaining fingers wrapped around the thigh. The second hand is placed on the tibia, with the thumb behind the fibula and the index finger over the tibial crest. This second hand applies a force to the tibia, moving it forward and backward with the remaining fingers wrapped around the tibial shaft, as exemplified in figure 1– any significant motion in the sagittal plane is considered abnormal. Tibia must not be allowed to rotate internally as motion of soft tissues would be misinterpreted, however in puppies,

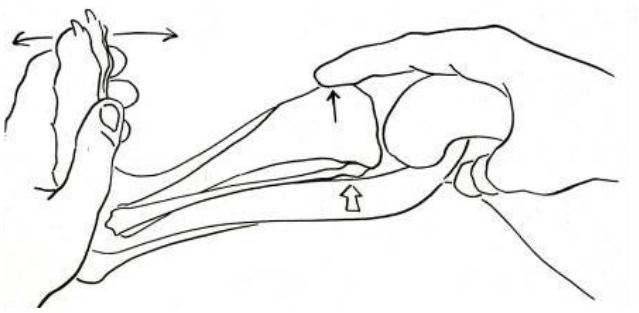
a small degree of physiologic stifle instability may exist (Kowaleski and Boudrieau 2012; Schulz 2013).

Figure 1: Cranial drawer test, adapted from Fossum, 2013



For the tibial compression test, the patient is standing or in lateral recumbency and the examiner, located caudal or caudal and lateral, places the index finger on the tibial tuberosity, the palm with the remaining fingers grasp the distal quadriceps and maintain stifle joint extension. The second hand grasps the foot at the metatarsals from the plantar surface and flexes the hock, as shown in figure 2.The index finger of the first hand will feel pressure from the patella in a healthy knee, whereas with a cruciate rupture, the tibial crest will advance forward (Kowaleski and Boudrieau 2012; Schulz 2013)

Figure 2: Tibial compression test, adapted from Fossum, 2013



When diagnosing, it is important to include patellar luxation, degenerative joint disease, meniscal injury, fractures, lumbosacral disease, hip dysplasia, neoplasia and inflammatory arthritis in the differentials. Therefore, radiographic examination is helpful when ruling out these disorders. When radiographs are performed, a typical destruction or compression of the infrapatellar fat pad and a soft tissue opacity in the lateral view, consistent with joint effusion are observed. There may also be detectable osteophyte formation. In some cases, stifle joint

arthroscopy, arthrocentesis, ultrasound and magnetic resonance imaging may be used to confirm the diagnosis (Kowaleski and Boudrieau 2012; Schulz 2013; Linn 2015).

Treatment is important because this anterior cruciate rupture causes stifle joint instability, and this can lead to meniscal injury, osteoarthritis or immune-mediated arthritis (Linn 2015).

Medical management with physical rehabilitation and NSAIDs does not have absolute success, however surgical stabilization of the stifle with different techniques such as tibial plateau levelling osteotomy (TPLO), tibial tuberosity advancement (TTA) and triple tibial osteotomy (TTO) has very high success rates and patients return to full weight bearing. Radiographic monitoring at six and ten weeks after surgery is highly recommended and rehabilitation is important for the patient to return to the previous level of performance (Linn 2015).

Prognosis is usually very good after surgical treatment, though rupture of the contralateral cranial cruciate ligament is prone to occur months after the diagnosis of the unilateral (Kowaleski and Boudrieau 2012)

2.2.2.8. Neurology

Neurology comprised 3% (n = 474) of the medical practice, with 21 cases, all of them witnessed in canines (Table 5). Table 16 displays the absolute frequencies and respective relative frequencies of the cases observed in this medical field – the most common condition was collapse, representing 40% (n=15), followed by vestibular syndrome, which completed 20% (n=15) of total cases. A brief bibliographical review on vestibular syndrome will be made due to the author's preference on this topic.

Table 16: Case distribution regarding Neurology

Neurology	Canine	
	Fi	FR (%)
Collapse	6	43%
Dementia	1	7%
Epilepsy	1	7%
Facial paralysis	1	7%
Seizures	2	14%
Vestibular syndrome	3	21%
Total	15	100%

Vestibular syndrome is a range of neurological signs that reflect disorders in the vestibular apparatus, usually in older dogs and cats at any age (Kent et al 2010; Troxel 2015). The vestibular system has two components - the peripheral (located within the temporal bone and the vestibulocochlear nerve) and the central component (located in the medulla oblongata, brainstem

and cerebellum). Therefore, vestibular disease can be divided into peripheral (PVD) or central (CVD) (Troxel 2015).

As the vestibular system is responsible for maintaining equilibrium and balance, classical signs from both PVD and CVD are the head tilt, nystagmus and/or ipsilateral loss of balance. Nausea and vomiting are also common in these patients (Kent et al 2010). The diagnostic challenge is to differentiate central from peripheral vestibular disease. Vertical nystagmus occurs only in animals with CVD, while horizontal and/or rotatory occurs in both CVD and PVD. In CVD, the mental status is often altered (depressed or stupurous), whereas a patient with PVD is alert and responsive, although disoriented (Troxel 2015). A 2005 study results suggest that non-ambulatory tetraparesis is more common in dogs with central disease when veering and leaning are considerably more common in dogs with peripheral disease (Troxel et al 2005). Horner's syndrome and concurrent facial nerve paralysis may occur in CVD and PVD, however the first is rare in animals with CVD (Troxel 2015).

The underlying disorders that can cause peripheral vestibular disease vary from otitis media/*interna*, nasopharyngeal polyps (more common in cats), hypothyroidism in dogs, neoplasia (squamous cell carcinoma, ceruminous gland adenocarcinoma), (oto) toxicosis (aminoglycosides, furosemide, chlorhexidine, fipronil), traumatic (iatrogenic, bulla fracture) and rarely congenital malformation in young animals. Idiopathic vestibular syndrome is also a common reason of peripheral vestibular disease in the dogs and cats (Kent et al 2010; Troxel 2015)..

In central vestibular disease, infectious central nervous system disease, granulomatous meningoencephalomyelitis, neoplasia, thiamine deficiency, metronidazole intoxication, cerebrovascular disease and hypothyroidism are the most common aetiology (Kent et al 2010; Troxel 2015).

Confirmatory tests include otoscopic examination, thyroid hormone analysis, radiograph or CT imaging of the bulla and cerebrospinal fluid collection for exclusion of infectious causes. Prognosis is fair to good when nutritional, toxic, vascular, infectious (depending on the agent responsible), traumatic (depending on the trauma) and idiopathic causes are present. Unfortunately, when it comes to other underlying aetiologies it is guarded to poor (Kent et al 2010; Troxel 2015).

2.2.2.9. Nephrology and Urology

With a relative frequency of 6% (n=474), 23 cases regarding nephrologic and urologic conditions were witnessed during the traineeship (Table 5). Absolute frequencies and respective percentages of the cases observed in this nephrology clinical field are shown in table 17. The most common condition was urinary tract infection, with 35% (n=23) followed by chronic kidney disease, which represents 34% (n=23) of total cases seen in this clinical area. A brief

bibliographical review on chronic kidney disease will be made due to the author's preference on this topic.

Table 17: Case distribution regarding Nephrology

Nephrology		Canine		Feline		Total	FR (%)
		Fi	FR (%)	Fi	FR (%)		
Chronic Kidney Disease	Stage 2	1	14%	6	38%	7	30%
	Stage 4	0	0%	1	6%	1	4%
Protein losing nephropathy		1	14%	0	0%	1	4%
Urinary Tract Infection		5	71%	3	19%	8	35%
Urolithiasis		0	0%	6	38%	6	26%
Total		7	100%	16	100%	23	100%

Chronic kidney disease (CKD) is defined as an abnormality in renal structure or function existing for longer than 3 months, which is a result from primary kidney disease present for an extended period of time. The specific aetiology is typically undetermined as it varies from chronic tubulointerstitial nephritis, glomerulonephritis, polycystic kidney disease and upper urinary tract obstructions to retroviruses and morbillivirus infections, amyloidosis or even renal lymphoma (Langston and Eatroff 2015; White et al. 2016) .

As the primary injury damages nephrons, the remaining ones hypertrophy, which consequently leads to glomerular hypertension and results in further nephron loss. Inflammatory infiltrates, fibrosis and sclerosis are the usual histopathological findings (Langston and Eatroff 2015; White et al. 2016) .

CKD is one of the most commonly diagnosed geriatric diseases in cats. Although occurrence in dogs is less frequent, it occurs in both geriatric and juvenile animals due to congenital causes (Langston and Eatroff 2015; White et al. 2016).

Common clinical signs in patients with CKD are polyuria/polydipsia, anorexia, weight and muscle loss, vomiting, lethargy and halitosis. However, assymptomatic chronic disease is frequently found in apparently healthy animals by routine screening. On physical exam, small and irregular kidneys, dehydration signs and oral ulceration may be present (J. White et al. 2016).

Diagnosis is often based on structural changes (renal size and shape, polycystic disease) or functional anomalies - proteinuria, azotaemia, inadequately concentrated urine (specific gravity < 1.035 in cats and <1.030 in dogs) (Polzin 2013; Langston and Eatroff 2015).

Differentials should exclude causes of prerenal azotaemia (such as dehydration, high protein diet, gastrointestinal bleeding) and postrenal azotaemia (such as a urinary obstruction or a rupture. Prerenal azotaemia is confirmed by adequate urine specific gravity, since in CKD there is inability to concentrate urine. Post renal azotaemia can be confirmed by presence of dysuria and imaging of the urinary tract (Langston and Eatroff 2015).

Staging of CKD by the guidelines developed by the International Renal Interest Society (IRIS) is fundamental in establishing the right treatment and prognosis – this system is based on

serum creatinine concentration for staging and on urine protein:creatinine ratio (UP/C) and blood pressure for substaging, as described on tables 18 and 19 (IRIS 2019).

Table 18: CKD Staging criteria, adapted from IRIS, 2019

Stage	Serum creatinine values mg/dL		Clinical signs
	Dogs	Cats	
IRIS CKD Stage 1	<1.4	<1.6	Non-azotaemic with some other renal abnormality present (inadequate urinary concentrating ability, abnormal renal palpation or imaging, renal proteinuria …).
IRIS CKD Stage 2	1..4-2.0	1.6-2.8	Mild renal azotaemia and mild/absent clinical signs
IRIS CKD Stage 3	2.1-5.0	2.9-5.0	Moderate renal azotaemia, with (early stage 3) or without (late stage 3) extrarenal signs.
IRIS CKD Stage 4	>5.0	>5.0	Risk of systemic clinical signs and uraemic crises increased

Table 19: CKD Substaging criteria, adapted from IRIS, 2019

UP/C ratio		UP/C Substage	Systolic Blood Pressure mmHg	Blood Pressure Substage	Risk of Organ Damage
Dogs	Cats		<140	Normotensive	Minimal
<0.2	<0.2	Non-proteinuric	140-159	Pre-hypertensive	Low
0.2-0.5	0.2-0.4	Borderline proteinuric	160-179	Hypertensive	Moderate
>0.5	>0.4	Proteinuric	≥ 180	Severely hypertensive	High

Symmetric dimethylarginine (SDMA) concentrations in plasma or serum might be a nore sensitive value than blood creatinine concentration. As there is still a lack of standardized methodology, the IRIS staging guidelines are not yet updated including the SDMA values. However, the guidelines make reference to some preliminary values that can be taken into account if the SDMA value is known (IRIS Staging of CKD 2017).

Treatment should be tailored for each patient and owner, but generally includes managing the organic mechanisms to slow the progression of CKD, supervise water and nutrients intake (usually with a diet adapted for renal patients) and amend clinical and biochemical consequences. Monitoring should be done at least every three to six months with biochemistry, haematology, blood pressure measurements and urine analysis (Polzin 2013).

Prognosis may vary from good to poor depending on the IRIS CKD stage (Polzin 2013).

Table 20 shows the absolute frequencies and respective percentages of the cases observed in the urology clinical area. The most common condition was cystitis, with 71% (n=7) followed by renal infection and bladder tumour, both representing each 14% (n=7) of total cases observed in this clinical field.

Table 20: Case distribution regarding Urology

Urology	Canine		Feline		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)		
Renal infection	0	0	1	20%	1	14%
Bladder tumour	0	0	1	20%	1	14%
Cystitis	2	1	3	60%	5	71%
Total	2	1	5	100%	7	100%

2.2.2.10. Oncology

Table 21: Case distribution regarding Oncology

Oncology	Canine		Feline		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)		
Lipoma	27	79%	0	0%	31	70%
Lymphoma	0	0%	3	60%	3	7%
Mammary tumours	2	5%	0	0%	2	5%
Mast cell tumour	3	8%	0	0%	3	7%
Melanoma	1	3%	0	0%	1	3%
Mesothelioma	0	0%	1	20%	1	3%
Osteossarcoma	1	3%	0	0%	1	3%
Sarcoma	1	3%	0	0%	1	3%
Squamous cell carcinoma	0	0%	1	20%	1	3%
Total	39	100%	5	100%	44	100%

Oncology comprised 8% (n=474) of the medical practice, with 41 cases (Table 5). The most common tumour was lipoma with 70% (n=44) followed by lymphoma and mast cell tumours, both with 7% (n=40) of total cases (Table 21). A brief bibliographical review on mast cell tumours will be made due to the author's preference on this topic.

Mast cell tumours (MCTs) are a neoplastic accumulation of mast cells which contain intracytoplasmic bioactive molecules, such as cytokines, heparin, leukotrienes and histamine, and are associated in many cases with a mutation in the proto-oncogene c-KIT. Whilst cutaneous tumours are common, visceral ones (splenic and gastrointestinal) are rare. When these tumours

degranulate, systemic or cutaneous deleterious effects are observed, hence they have an unpredictable biologic behaviour (Gieger 2015) .

MCTs represent the most common malignant tumours in middle age to older dogs, and brachycephalic breeds, retrievers, Beagles, Shar-Peis, Pugs, Schnauzers, Cocker spaniels, Staffordshire Terries, Rhodesian Ridgebacks and Weimaraners are at increased risk. Although brachycephalic breeds are at higher risk, they appear to be lower grade. Mastocytomas are relatively common in cats predominantly in older ones and in Siamese (Gieger 2015). Due to the differences in the clinical and pathologic features of canine and feline MCTs, only canine tumours will be discussed in this report.

In general, dogs present with a cutaneous or subcutaneous mass, which may or not be pruritic - clinical signs are often inapparent, however secondary signs to histamine-induced gastric acid secretion related to gastric ulceration can occasionally be present. The lesions are commonly solitary, generally with metastatic regional lymphadenopathy, although multifocal MCTs are also observed. Due to the bioactive molecules' presence, lesions might shrink and swell sporadically or with manipulation. In dogs with primary visceral or metastatic MCT, abdominal effusion with mast cells and organomegaly can occur (Gieger 2015; Thamn 2017).

A MCT is only definitively diagnosed when the lesion is evaluated cytologically or histopathologically, commonly on the basis of fine needle aspiration. Differential diagnosis on cytology should exclude all other round cells tumours, as they have a similar appearance, whilst on palpation differentials generally include other tumours, phlebectasia, granulomas or abscesses (Gieger 2015; Thamn 2017).

Surgery is the first treatment option – two centimetres or greater lateral and 1 fascial plane in depth margins are recommended. The procedure should be preceded by histamine blockers, corticosteroids to reduce size and/or proton pump inhibitors if gastric ulceration is suspected. After excision, the mass and respective margins should be assessed by a pathologist since grading provides prognostic information (Gieger 2015; Thamn 2017). Although the Patnaik grading system is still widely used to classify tumours into three grades (low, intermediate and high), the new system published by Kuipel eliminates the intermediate tier, as their behaviour was significantly challenging, and focuses only in low and high grade tumours, based on objective numbers of cellular features (Warland et al. 2015).

However, for tumours that are not surgically removable or were incompletely excised or have evidence of metastasis, targeted therapy (tyrosine kinase inhibitors), chemotherapy and/or radiation therapy before, after or instead of surgery may be indicated. Once treated, the patient should be re-examined at least every 6 months to detect any new skin masses, for local site evaluation and with regional lymph node and abdominal ultrasound if high risk for metastasis (Gieger 2015; Warland et al. 2015; Thamn 2017)

As canine mast cell behaviour might result in a wide range of possible outcomes, survival times depend greatly on grade, tumour recurrence, metastatic disease, location, size, completeness of surgical excision and breed (Gieger 2015; Thamn 2017).

2.2.2.11. Ophthalmology

Ophthalmology comprised 5% (n = 474) of the medical practice, with 24 different cases observed (Table 5). Table 22 displays the absolute frequencies and respective percentages of the cases witnessed, being the most common condition conjunctivitis with 38% (n =24) followed by corneal ulcers making 33% (n=24) of total cases. A brief bibliographical review on corneal ulcers will be made due to the author's preference on this topic.

Table 22: Case distribution regarding Ophthalmology

Ophthalmology	Canine		Feline		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)		
Cataract	2	12%	0	0%	2	8%
Conjunctivitis	4	24%	5	71%	9	38%
Entropion	1	6%	0	0%	1	4%
Glaucoma	1	6%	1	14%	2	8%
Corneal ulcer	8	47%	0	0%	8	33%
Uveitis	0	0%	1	14%	1	4%
Corneal oedema	1	6%	0	0%	1	4%
Total	17	100%	7	100%	24	100%

A corneal ulcer, also known as ulcerative keratitis is defined as loss of superficial corneal epithelium with or without loss of variable amounts of the underlying corneal stroma. These ulcers are classified by the depth of corneal involvement - simple, complex and indolent (Ledbetter et al 2014; Gemensky-Metzler 2015).

A simple ulcer is caused by an acute loss of epithelial layers of the cornea due to trauma and is typically not infected. On the other hand, a complex corneal ulcer may be an acute or chronic loss of both epithelial and stromal layers of the cornea, caused by trauma or infection. It can be presented as a stromal ulcer (loss of variable quantities of corneal stroma), a melting ulcer (softening and necrosis of the cornea, often related to infection), a ruptured ulcer (perforation of the cornea) or a descemetocele (loss of all stromal layers down to Descemet's membrane and endothelium). However, a simple ulcer may progress to complex as a result of bacterial infection. An indolent/refractory superficial corneal ulcer results from a failed epithelial adhesion to the corneal basement membrane and stroma (Gemensky-Metzler 2015).

Clinically, patients present with blepharospasm, ocular discharge, corneal oedema, photophobia, conjunctival hyperaemia, and occasionally miosis and aqueous flare. In complex ulcers animals may also present corneal white-yellow cellular infiltrate, corneal vascularization, dyscoria and/or hypopyon (Ledbetter et al 2014; Gemensky-Metzler 2015).

Simple and complex ulcers are common in dogs and cats of any age or sex, however there are some risk factors such as keratoconjunctivitis sicca and brachycephalic conformation.

Middle-aged to older dogs are more prone to be affected by indolent ulcers (Gemensky-Metzler 2015).

The underlying aetiology may be trauma or ocular foreign body, tear film abnormalities (quantity and quality), corneal sequestration in cats, neurologic disorders, eyelid conformational abnormalities, bacterial, fungal or viral infection (especially feline herpesvirus 1 and feline viral rhinotracheitis) (Ledbetter et al 2014; Gemensky-Metzler 2015).

Diagnosis is usually based on clinical signs, on a complete ophthalmic and neurologic examination, on a Schirmer tear test and on the retention of topically applied fluorescein staining which confirms and demarcates the ulcer. However, when dealing with a desmetocele, a fluorescein-negative clear centre of stromal ulcer might be seen, as the Descemet's membrane is hydrophobic and does not retain the fluorescein stain. When infection is suspected, it is recommended a corneal culture, antibiotic susceptibility and cytological examination to put in place the adequate antimicrobial therapy. At the time of diagnosis, it is also important to exclude neurological diseases (as Horner's syndrome, facial nerve paralysis or corneal denervation), corneal dystrophy or degeneration, anterior uveitis, glaucoma and proliferative/eosinophilic keratoconjunctivitis in cats (Ledbetter et al 2014; Gemensky-Metzler 2015).

For treatment of a corneal ulcer, first and foremost the underlying causes of ulceration must be resolved. Typically, therapy always includes a topical antimicrobial (e.g., neomycin, bacitracin, and polymixin B) every four to six hours and topical 1% atropine or tropicamide (mydriatic agents to control ciliary muscle spasm and ocular discomfort) every 12 to 48 hours. However, it should be noted that excessive topical atropine suppresses lacrimation in both eyes. A systemic nonsteroidal anti-inflammatory may be added if necessary – however, corticosteroids are contraindicated hence they delay healing. Not less important is the placement of an Elizabethan collar to avoid patients from rubbing their eyes (Ledbetter et al 2014; Gemensky-Metzler 2015).

For a melting ulcer, topical autogenous serum every three hours and intensive topical antibiotic (every one or two hours) with a spectrum that combats Gram-negative and positive bacteria should be administered while culture results are pending (Ledbetter et al 2014; Gemensky-Metzler 2015).

For an indolent/refractory ulcer, debridement of all loose corneal epithelium with a dry sterile cotton bud or a diamond burr might be enough to promote epithelialization. However, if the ulcer does not heal, a new debridement should be executed and, only in canine patients, it ought to be followed by a grid or punctate keratotomy because keratotomy in cats promotes cornea sequestration. Soft contact lens application and third eyelid flaps may be indicated to protect the cornea and minimize discomfort (Westermeyer et al 2012; Ledbetter, et al 2014; Gemensky-Metzler 2015).

Hospitalization for frequent medical treatments and monitoring might be needed for animals with deep or rapidly progressive ulcers. In addition, surgical repair by keratoplasty might be recommended if further stromal loss exists despite aggressive medical therapy, if the ulcer

exceeds 50% of stromal thickness or if it is a perforated ulcer. This full-thickness corneal transplantation uses autologous, synthetic or bioengineered grafts (Westermeyer et al 2012; Ledbetter, et al 2014; Gemensky-Metzler 2015).

Simple ulcers should heal within five to ten days with minimal corneal scar formation - any simple corneal ulcer that does not heal within this period of time, should be considered a complex or refractory ulcer, and undetected underlying causes or contributing factors must be investigated. Complex ulceration wound healing is expected to take up to eight weeks with significant scarring which may lead to impaired vision. Other possible complications besides corneal scarring and loss of vision include corneal perforation, corneal pigmentation, corneal stromal permanent defect and corneal sequestration in cats (Ledbetter et al 2014; Gemensky-Metzler 2015).

2.2.2.12. Theriogenology

With a relative frequency of 2% (n=474), 10 cases of theriogenology and neonatology were seen (Table 5). Absolute frequencies and respective percentages of the cases observed in this medical field are shown in table 23. False pregnancy, pyometra, vaginitis and post-partum checks represented each 20% (n=10), whilst abortion and cryptorchidism represented each 10% (n=10) of the conditions observed. A brief bibliographical review on cryptorchidism will be made due to the author's preference on this topic.

Table 23: Case distribution regarding Theriogenology and Neonatology

Theriogenology & Neonatology	Canine	
	Fi	FR (%)
Abortion	1	10%
Cryptorchidism	1	10%
False pregnancy	2	20%
Post-partum check	2	20%
Pyometra	2	20%
Vaginitis	2	20%
Total	10	100%

Cryptorchidism is defined as the failure of one (unilateral) or both (bilateral) testicles to descend into the scrotum, being retained within the abdomen or in the inguinal canal. It is a condition of intact male dogs and occasionally of male cats, the most common being right unilateral inguinal cryptorchidism. A genetic autosomal recessive trait and the administration of anti-androgenic drugs during gestation are believed to be factors that lead to retained testicles. Chihuahuas, Dachshunds, Pomeranians, Poodles, Boxers, English Bulldogs, Yorkshire Terriers

and Siberian Huskies are believed to be breeds at an increased risk for cryptorchidism (England 2010b; Wheeler 2015).

Descent of the testes is regulated by testosterone – whereas in dogs it may take up from 8 weeks to 6 months after birth, in cats, testicles are normally descended at the time of birth. Compared to normal males, cryptorchid animals do not have altered concentrations of testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH) nor oestrogens (England 2010b).

Although diagnosis is only definitive at six months of age, a presumptive diagnosis may be supposed at 8 weeks of age. The most relevant clinical sign is the absence of palpable freely movable testicles in the scrotum, though in cats, the presence of penile spikes without testicles within the scrotum is indicative of testosterone production and raises the suspicion of cryptorchidism. At the time of diagnosis, it is important to exclude unknown previous castration, pseudo-hermaphroditism, unilateral (monorchidism) and bilateral (anorchidism) testicular aplasia. To confirm the diagnosis, ultrasonography, human chorionic gonadotropin or luteinizing hormone stimulation test, a baseline testosterone measurement or even exploratory laparotomy may be performed (Wheeler 2015).

A wide range of disorders might be associated with testicle retention. These animals are believed to be at a greater risk of developing a testicular neoplasia, a benign prostatic hyperplasia, hyperoestrogenism and testicular torsion. In addition, if the male is bilaterally cryptorchid, infertility will be an issue (England 2010b; Wheeler 2015).

Castration is the recommended treatment, not only to prevent offspring in possession of this inheritable condition, but also to decrease risk of future testicular neoplasia and prostatic disease. Different approaches should be executed according to the location of the retained testicle(s) - inguinal cryptorchirds require a parainguinal approach, whilst abdominal cryptorchirds require an abdominal approach. A minimally invasive laparoscopic approach to remove a retained testicle in a male dog was observed during the traineeship, as described below in the case description of minimal invasive surgery. If treated, excellent prognosis is expected (England 2010b; Wheeler 2015).

There are also medical protocols for canines with variably successful rates, which suggest that various administrations of hCG or GnRH will stimulate puberty and therefore testicular descend. However, even if medical treatment results in testes descending, the risks of neoplasia and previously described disorders still remain (England 2010b; Wheeler 2015).

2.2.2.13. Toxicology

Toxicology comprised 3% (n = 474) of the medical practice, with 14 different cases observed (Table 5). Table 24 displays the absolute frequencies and respective percentages of the cases witnessed, being chocolate toxicosis the most common observed representing 71% of total cases.

Table 24: Case distribution regarding Toxicology

Toxicology	Canine	
	Fi	FR (%)
Chocolate	10	71%
Rilexine	1	7%
Rodenticide	1	7%
Sultanas	1	7%
Xylitol	1	7%
Total	14	100%

Theobromine, a methylxanthine, is the main toxic component of chocolate, which is commonly ingested by dogs, particularly during the Easter and Christmas seasons. Severity and onset of signs depend on the amount and type of chocolate ingested, as well as on the individual sensitivity to methylxanthines (Donaldson 2015).

Toxic effects in dogs occur at theobromine doses of 20 mg/kg, with severe signs at 40 mg/kg and death at 80 mg/kg (rare). Theobromine stimulates myocardium and the central nervous system, being the main toxicity signs cardiac abnormalities, respiratory hyperactivity, hypertension, tremors and hyperthermia. Gastrointestinal signs and pancreatitis are highly likely to occur due to the high sugar and fat contents present in chocolate (Donaldson 2015).

After the ingestion of a toxic dose, an emetic can be in given in the 4 subsequent hours, followed by hydration support (to support cardiovascular system and enhance secretion), repeated activated charcoal doses. In symptomatic animals, heart rate, temperature and electrocardiogram should be monitored. Diazepam should be given for convulsions, a beta-blocker if the patient presents with tachycardia and atropine if bradycardia (Bates 2015).

Fatal cases are rare and most dogs recover, however prognosis is more guarded in dogs with seizures, arrhythmias and pre-existing cardiac disease (Bates 2015).

2.2.3. Surgery

Surgery is divided into three different areas – soft tissue surgery, minimal invasive surgery and orthopaedics surgery, which are represented in table 25. Soft tissue surgery was the most prevalent with 120 cases (82%, n=147), followed by minimally invasive surgery with 19 cases (13%, n=147) and by orthopaedic surgery with 8 cases (5%, n=147).

Table 25: Case distribution regarding surgical practice

Surgery	Canine		Feline		Exotic		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)	Fi	FR (%)		
Soft tissue surgery	67	72%	37	97%	16	100%	120	82%
Minimally Invasive surgery	19	20%	0	0%	0	0%	19	13%
Orthopaedic surgery	7	8%	1	3%	0	0%	8	5%
Total	93	100%	38	100%	16	100%	147	100%

2.2.3.1. Soft tissue surgery

Soft tissue surgery represented 82% (n = 147) of the surgical practice, with 120 cases (Table 25). Table 26 displays the absolute frequencies and respective percentages of the different procedures performed and observed during the traineeship.

Table 26: Case distribution regarding Soft Tissue Surgery

Soft tissue surgery	Canine		Feline		Exotic		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)	Fi	FR (%)		
Abdominal hernia repair	1	1%	1	3%	0	0%	2	2%
Castration	13	19%	18	49%	8	50%	39	33%
Cesarean	1	1%	0	0%	0	0%	1	1%
Dew claw removal	2	3%	0	0%	0	0%	2	2%
Ear canal ablation	1	1%	0	0%	0	0%	1	1%
Exploratory laparotomy	1	1%	1	3%	0	0%	2	2%
Feeding tube placement	1	1%	1	3%	0	0%	2	2%
Feeding tube removal	1	1%	1	3%	0	0%	2	2%
Foreign body abscess	1	1%	0	0%	0	0%	1	1%
Lump/Wart Removals	14	21%	1	3%	0	0%	15	13%
Odontologic surgery	11	16%	6	16%	7	44%	24	20%
Ovariohysterectomy	12	18%	6	16%	1	6%	19	16%
Soft palate and laryngeal saccules removal	1	1%	0	0%	0	0%	1	1%
Splenectomy	1	1%	1	3%	0	0%	2	2%
Thyroidectomy	0	0%	1	3%	0	0%	1	1%
Tumour removal	4	6%	0	0%	0	0%	4	3%
Wound sutures	2	3%	0	0%	0	0%	2	2%
Total	67	100%	37	100%	16	100%	120	100%

Dystocia is the inability to expel a neonate through the birth canal resulting from either maternal or foetal incompatibilities.

Maternal incompatibilities include primary uterine *inertia* (failure of contraction due to mineral or hormonal imbalances), secondary uterine *inertia* (exhaustion of either the uterine muscle itself or depletion of pituitary oxytocin stores), birth canal obstruction and anatomy abnormalities. Foetal incompatibilities comprise foetal oversize, malposition or malformation.

Siameses, Persians, Great Danes, Boston Terriers, Chihuahuas, Irish wolf-hounds and brachycephalic breeds are most frequently affected. Risk factors include obesity, large litter size, single foetus pregnancy and previous pelvic fractures. These cases should be considered for an elective caesarean section (Fransson 2012; MacPhail 2013; Noakes 2018).

A caesarean section is recommended in high risk pregnancies, in evidence of foetal distress, primary inertia refractory to treatment and secondary uterine inertia. Pre-oxygenation and correction of electrolyte abnormalities must be performed before surgery (MacPhail 2013).

Premedication is recommended to decrease stress and anxiety and to reduce the doses of induction and maintenance agents. Opioids and benzodiazepines, which can be reversed if the neonates become bradycardic, are preferred as pre-medication agents. Acepromazine can also be used if the bitch requires more sedation than an opioid alone can provide.The anaesthetic protocol associated with a minimized maternal and puppy mortality rate and with an increased puppy vigor, is a propofol intravenous induction combined with a light isoflurane maintenance. Epidural morphine can also be administered pre- or post-operatively to provide up to 18–20 hours of analgesia, but epidural analgesia as a sole technique should not be used (Fransson 2012; MacPhail 2013; WSAVA Global Pain Council 2014).

The mother should be placed in dorsal recumbency. If vena cava pressure is present, the surgical table should be elevated, whereas if there is any diaphragm pressure it should be tilted 15 degrees to the side (Fransson 2012; MacPhail 2013).

A lidocaine or bupivacaine line block prior and/or posterior to the incision can be performed. Incision in the ventral midline should start halfway between the xiphoid process and the *umbilicus*. Incision must continue to the pubis and is then followed by a careful incision in the *linea alba*. The next step is to expose and exteriorize the uterus, in order to prevent any ruptures of the uterine wall or the broad ligaments (Fransson 2012).

The body of the uterus is incised in the ventral midline and the most caudal foetuses are the first to be “pushed” down into the incision, followed by foetuses in the horns in an alternating order. When extracting the neonates, gentle steady traction must be applied to release the placenta from its attachment zone, however if removal is impossible without haemorrhage and endometrial trauma, the umbilical cord should be clamped and the amniotic sac torn to extract the neonate. Retained placentas are left and will typically be expelled naturally. To provide postoperative analgesia in order to the bitch be able to be comfortable enough to feed the new-borns, is it important to administer a dose of NSAIDs and to continue opioids. (Fransson 2012; MacPhail 2013; WSAVA Global Pain Council 2014).

Neonatal resuscitation should begin immediately, starting by removing any fluid on the oral cavity and nostrils of fluid, a vigorous external rubbing with a dry blanket and ventilation with an oxygen mask until the puppies are breathing spontaneously. Traditional swinging should be avoided due to possibility of cerebral haemorrhage (MacPhail 2013). To encourage respiration, an acupuncture point stimulation may be performed by placing and rotating a 25-gauge needle to a depth of 3mm at the midline between the upper lip and nose of the neonate (Fransson 2012)

Before uterine closure with 3-0 or 4-0 monofilament absorbable suture, the entire uterus must be palpated for contents. A single layer continuous pattern or a two layer (inner layer with a simple appositional continuous and the outer layer with a inverting continuous, whether it would be in a Cushing or a Lembert pattern) are used. It is important to engage the endometrium but not penetrate it and to cover the uterine incision with omentum (Fransson 2012; MacPhail 2013).

A routinely three-layer closure of abdomen after a cavity lavage (to minimize contamination) and inspection of abdominal organs is recommended. If visible involution of the uterus has not started during closure or if excessive haemorrhage is observed, oxytocin should be administered. Intradermal skin closure is usually preferred as suture ends might bother the neonates. Antibiotics are indicated if there is uterine infection is suspected or if foetal death has occurred (Fransson 2012; MacPhail 2013).

Because milk production is not influenced by ovarian hormones, an ovariohysterectomy at the time of the caesarean might be requested by owners. It might be advantageous to carry out a block resection of the uterus and enclosed foetuses, besides minimizing abdominal contamination and anaesthesia time for the bitch, also permits the rapid exposure of the foetuses (Fransson 2012).

Only once the mother is recovered from the anaesthesia should she be placed together with the puppies, under close observation. As soon as possible, all of them should be discharged in order to decrease exposure to pathogens and minimize stress. Survival rates are excellent for both mother and descendants, although brachycephalic puppies have a lower survival rate (Fransson 2012; MacPhail 2013).

Possible complications of surgery include haemorrhage, post-operative infection, hypotension and laceration of any component of the urogenital and gastrointestinal tract. Risk and difficulty with vaginal delivery following a caesarean have not been correctly assessed yet (Fransson 2012).

2.2.3.2. Minimally invasive surgery

Minimally invasive surgery represented 13% (n = 147) of the surgical practice, with 19 cases (Table 25). Table 27 displays the absolute frequencies and respective percentages of the two different laparoscopic procedures, witnessed and performed in only canines during the traineeship.

Table 27: Case distribution regarding minimally invasive surgery

Minimally invasive surgery	Canine	
	Fi	FR (%)
Castration by laparoscopy	1	1%
Ovariectomy by laparoscopy	18	27%
Total	19	100%

The routine ovariohysterectomy was the procedure performed in 19 females, 12 of which were canines (table 26) and the ovariectomy by laparoscopy was the technique executed in 18 females (table 27). Looking at these statistics, it can be concluded that laparoscopy is a rather popular approach to neutering at Priory Veterinary Surgeons and well accepted by owners.

The castration performed by laparoscopy was a treatment for a unilateral cryptorchid male in order to remove the testicle retained in the abdomen.

2.2.3.3. Orthopaedic surgery

Orthopaedic surgery represented 5% (n = 147) of the surgical practice, with two cases (Table 25). Table 28 displays the absolute frequencies and respective percentages of the three different orthopaedic procedures performed and observed during the traineeship – a femoral head ostectomy, a rostral mandibulectomy and several tibial tuberosity advancements.

Table 28: Case distribution regarding Orthopaedic Surgery

Orthopaedic surgery	Canine		Feline		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)		
Femoral head ostectomy	0	0%	1	100%	1	13%
Rostral mandibulectomy	1	14%	0	0%	1	13%
TTA	6	86%	0	0%	6	75%
Total	7	100%	1	100%	8	100%

A tibial tuberosity advancement (TTA) is the preferred procedure used in Priory Veterinary Surgeons to treat a cranial cruciate ligament rupture. This surgical technique stabilizes the stifle joint during weight bearing by neutralizing the cranial tibial thrust force. This is achieved by the

osteotomy of the tibial crest, moving it sufficiently to maintain a patellar tendon angle 90 degrees or less from the point of maximal stifle joint extension (Kowaleski et al 2012).

2.2.4. Other procedures

This last part of the report on activities performed during the traineeship, describes a miscellaneous group of the medical procedures. Imaging procedures included endoscopy, radiographies and ultra-sound scans. Abdominal ultrasound scans were the most prevalent with 15 cases, representing 38% (n=70) of total cases, as shown in table 29.

Table 29: Case distribution regarding imaging procedures

Imaging procedures		Canine		Feline		Total	FR (%)
		Fi	Fr	Fi	Fr		
Endoscopy		1	2%		0%	1	1%
Ultra-sound	Abdominal	9	17%	1	7%	10	15%
	Heart	7	13%	2	13%	9	13%
Radiography	Abdomen	10	19%	2	13%	12	18%
	Appendicular skeleton	17	33%	2	13%	19	28%
	Dental x-rays	2	4%	4	27%	6	9%
	Thorax	4	8%	3	20%	7	10%
	Spine	2	4%	1	7%	3	4%
Total		52	100%	15	100%	67	100%

Other medical diagnostic or treatment procedures witnessed, are shown in table 30, with a total of 144 cases. Blood sample collections were the most frequent act, representing 38% (n=147) of total cases.

Table 30: Case distribution regarding other medical procedures

Other procedures	Canine		Feline		Total	FR (%)
	Fi	FR (%)	Fi	FR (%)		
Bile stimulation profile	1	1%	0	0%	1	1%
Biopsies gut	1	1%	0	0%	1	1%
Biopsies skin	2	2%	0	0%	2	1%
Blood pressure measurement	10	11%	5	9%	15	10%
Blood sample collection	32	34%	24	45%	56	38%
Blood transfusion	0	0%	1	2%	1	1%
Chemotherapy with vincristine	1	1%	0	0%	1	1%
Cystocentesis	1	1%	4	8%	5	3%
ECG	2	2%	1	2%	3	2%
Emesis induction	12	13%	0	0%	12	8%
Enema	0	0%	1	2%	1	1%
Euthanasia	13	14%	11	21%	24	16%
FNA	9	10%	2	4%	11	7%
Foreign body removal	1	1%	0	0%	1	1%
Glucose curve	3	3%	0	0%	3	2%
Paracentesis	2	3%	1	3%	3	2%
Pericardiocentesis	1	1%	0	0%	1	1%
Suture removal	3	3%	1	2%	4	3%
Urinary catheterisation	0	0%	2	4%	2	1%
Total	94	100%	53	100%	147	100%

Part II: Monograph

1. Introduction

Elective gonadectomy, defined as the removal of the gonads, is the most common surgical procedure performed in small animal practice. Castration in males and either ovariectomy (OV) or ovariohysterectomy (OHE) in females, are the most widely used surgeries (Fransson 2012; Kustritz 2012).

Recently, this routine practice has become a very controversial topic, because these procedures may have some unintentional consequences that are only now being recognised.

The purpose of this monograph is to review the current scientific literature on the proposed benefits and detriments of gonadectomy in dogs and whether performing it at a certain age causes or prevents specific health issues. A simple description of the most common surgical techniques used nowadays and recommendations on the optimal age to perform them in dogs, will also be reviewed. Because disadvantages and advantages of gonadectomy have been studied more thoroughly in dogs than in cats, this report will be limited to the canine species.

The primary benefit of gonadectomy it to control pet overpopulation, however, it has been observed that certain conditions are more frequent in gonadectomised animals than in intact dogs. Studies' results suggest that hormones may have an influence (both positively and negatively), on the susceptibility to some type of disorders, ranging from neoplasia and certain orthopaedic disorders to hormone-associated conditions and urinary incontinence (Howe 2015; Waters et al. 2017)

Knowledge of the benefits and disadvantages associated with elective gonadectomy and with the age it is performed, will allow veterinary professionals to promote animal health by providing the best advice to clients.

2. Defining pre-pubertal neutering

First and foremost, for the purpose of this review it is important to specify what pre-pubertal neutering in dogs is – a gonadectomy performed before the onset of puberty. Puberty is defined as the time when animals reach sexual maturity and become capable of reproduction.

In female dogs, the first/pubertal oestrus onset marks the reach of puberty. Normally it occurs between six and ten months of age in small and middle size breeds, whilst in large and giant breeds begins between 18 or 24 months (two years) old. Nevertheless, it can occur as late as two and a half years old. It is believed that the onset of puberty is connected to the stage when the bitches reach about 80% of adult bodyweight and height. As so, hence larger breeds take longer to reach adult bodyweight than smaller breeds, they also take longer to reach sexual maturity (A. Davidson 2004a; England 2010a)

In male canines, they reach puberty around ten to twelve months of age. At this time, dogs are generally able to ejaculate normal sperm. Nevertheless, over the next months, the

number of sperm (Torres de la Riva et al. 2013; Hart et al. 2014) in the ejaculate increases until it reaches a *plateau* around two years of age (England 2010b).

Whenever late neutering is referred in this monograph, it is relative to canines neutered after 12 months old.

3. Surgical Techniques

3.1. Closed versus open orchiectomy

Orchiectomy, also known as castration, is defined as the surgical removal of the testes. It can be performed using a pre-scrotal approach with a closed or an open technique. Though the pre-scrotal approach is more commonly performed, a scrotal approach can be performed in pre-pubertal puppies or a perineal approach when performing a perineal hernia repair at the same time (MacPhail 2013).

Usually, a concurrent scrotal ablation is not necessary, hence the scrotum will normally regress on his own. However, a prophylactic ablation should be considered in older intact dogs to minimize the risk of oedema, haematoma formation and poor cosmetic outcome (Towle 2012; Hamilton et al. 2014).

In both open and closed castrations, the initial approach is performed in the same manner. With the patient is positioned in dorsal recumbency, pressure is applied to the scrotum to advance one of the testicles cranially into the pre-scrotal area. The incision is done directly over the testicle into the skin, subcutaneous tissue and the spermatic fascia, exposing the testicle involved by the parietal vaginal tunic. Scrotal fat and fascia are detached from the tunic with a gauze to permit maximal testicle exteriorisation (Towle 2012; Hamilton et al. 2014).

At this point, in the closed technique, the parietal vaginal tunic that covers the spermatic cord is left intact. A three-clamp technique is applied to the spermatic cord. A circumferential ligature is applied bellow the proximal clamp, followed by the removal of the middle clamp and a second circumferential or transfixion ligature placed where the clamp “crushed” the spermatic cord. When using a transfixion ligature, the needle should be inserted in an avascular area of the spermatic fascia. After these two ligatures are in place, the spermatic cord is severed between the two remaining clamps, and before removing the proximal clamp, the stump should be inspected for haemorrhage before releasing it gently. The remaining testicle is then removed performing the same technique and through the same pre-scrotal skin incision (Towle 2012; MacPhail 2013).

On the other hand, in an open technique, the parietal vaginal tunic is incised without incising the tunica albuginea or the visceral vaginal tunic, and that opening is extended towards the spermatic cord. The three-clamp technique can then be used on the entire spermatic cord or on each group of structures, if the surgeons opts by separating the vascular cord from and the cremaster muscle, the *ductus deferens* and the parietal tunic. After removing both testes, the

parietal vaginal tunic is closed with an interrupted or continuous suture pattern, the subcutaneous tissue with a continuous pattern and skin with intradermal, subcuticular, or simple interrupted pattern (Towle 2012; MacPhail 2013).

The major mentioned advantage when performing an open orchiectomy is the minimal risk of ligature slippage and loosening. However, this approach is associated with additional tissue trauma and handling, not to mention it breaches the peritoneal space below, increasing the risk of peritoneal contamination and the herniation potential of the intestine *via* the space between the abdomen and the parietal vaginal tunic. Therefore, it is associated with a higher complication rate in the first ten days after surgery, when compared to closed orchiectomy. In addition, frequency of scrotal complications (scrotal haematoma, swelling, bruising and pain) are interestingly more often present than in closed castration. For these reasons, it is concluded that closed orchiectomy is a preferred method in dogs (Towle 2012; Hamilton et al. 2014).

Regardless of the technique performed, analgesics and restriction of physical activity are recommended. Also, since the majority of complications are identified by 24 hours post-surgery, monitoring incisions for any discharge, abnormal swelling or discomfort are of extreme importance at this time following surgery (Hamilton et al. 2014).

3.2. Laparoscopic ovariectomy (LOV) versus open ovariohysterectomy (OVH)

In females, the removal of the gonads (also known as spay) can be performed by ovariectomy or by ovariohysterectomy. Both these techniques can be performed either by an open surgical approach or by laparoscopy. However, during the traineeship, only ovariectomies via laparoscopy (LOV) and open ovariohysterectomies (OVH) were observed.

In open surgical ovariohysterectomy, an incision is made in the ventral midline, immediately caudal to the umbilicus extending it caudally. One of the ovaries can be located caudal to the kidneys or by identifying and following a uterine horn. A pair of haemostatic forceps is placed on the proper ligament of the ovary and caudo-medial traction is applied to retract it from the abdominal cavity. The suspensory ligament may or may not be digitally broken to allow further exposition (Fransson 2012; MacPhail 2013)

With haemostatic forceps, a window in the mesovarium caudal to the ovarian pedicle is created, in an area with no or little fat. This pedicle is clamped with a three-clamp technique and an encircling absorbable ligature is placed dorsal to the most dorsal forceps, which is removed as the ligature is tightened (allowing the ligature to lie in the groove crushed by the forceps). A transfixing-encircling ligature is then placed between the first ligature and the second forceps. When these two ligatures are in place, the second clamp is removed and the pedicle is transacted between the second ligature and the third clamp (closest to the ovary), as shown in figure 3. The pedicle is held in forceps during transection, and after inspection for bleeding, it is released into the abdomen. Afterwards, the ovarian bursa should be opened and examined to be sure that the entire ovary was totally removed. The contralateral uterine horn is then identified *via* the uterine

bifurcation and the remaining ovary is removed in a similar manner (Fransson 2012; MacPhail 2013).

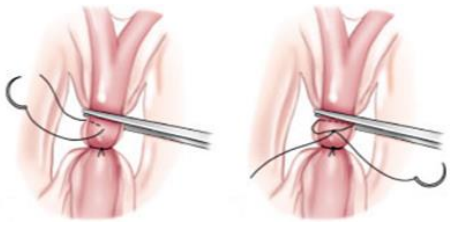
Figure 3: Ovaries' surgical approach in an open ovariohysterectomy, adapted from Tobias and Johnston, 2012

Bilateral defects in the mesometrium are created laterally to the uterine vessels at the level of the caudal uterine body. If the bitch is in oestrus or pregnant, the mesometrium may have to be ligated with one or two encircling ligatures (Fransson 2012).

In bitches, a forceps is applied cranial to the planned transection place and the uterine body is double ligated just cranial to the cervix, with the suture pattern based on the uterine body size. In multiparous bitches, one encircling and one transfixing-encircling or two encircling ligatures are placed within three millimetres distance. The uterine body is then transacted cranial to the most cranial ligature, as demonstrated in figure 4. In bitches that are pregnant or with pyometra, bilateral transfixing-encircling ligatures to guarantee attenuation of each uterine artery and vein and the enlarged uterine body might be required (Fransson 2012; MacPhail 2013).

After the uterus and ovaries have been removed from the abdominal cavity, inspection for haemorrhage before closure is essential. The *linea alba*, subcutaneous tissue and skin are closed in separate layers, the first two in a simple continuous or simple interrupted pattern and the skin in an interrupted cruciate or an intradermal suture pattern (MacPhail 2013).

Figure 4: Uterus' surgical approach in an open ovariohysterectomy, adapted from Tobias and Johnston, 2012



There are multiple variations of minimally invasive techniques for neutering - the two-port median laparoscopic ovariectomy was the one performed at Priory Veterinary Surgeons and therefore it is the technique being described below. By using two cannulas instead of three, veterinarians are diminishing the postoperative pain. Though an ovariohysterectomy can also be performed by laparoscopy, surgical time and complication rates are greater, despite postoperative

pain scores being lower. It is important to mention that patients with a diaphragmatic hernia are not suitable for this procedure, because abdominal insufflation is more hazardous to breathing (Case et al. 2011; Fransson 2012).

The animal is placed in dorsal recumbency in a table that allows lateral rotation of the patient, in order to facilitate identification and manipulation of the ovaries. A skin incision is made the same length as the diameter of each cannula prior to its placement. A *Veress* needle is used to enter the peritoneal cavity and insufflate the abdomen with carbon dioxide (CO_2) to a pressure of ten to twelve mmHg, which is maintained throughout the rest of the surgical procedure. A five millimetre cannula (visualization port) is placed two to four centimetres caudal to the umbilicus and another five (in dogs less than 15kg) or a ten millimetre cannula (instrument port) two to four centimetres cranial to the umbilicus (Case et al. 2011).

The laparoscope is inserted in the caudal cannula and a closed grasping forceps in the cranial cannula. The animal is slightly tilted to one side – it is rotated into right lateral oblique recumbency for removal of the left ovary and then into left lateral oblique recumbency for removal of the right ovary.

The closed forceps retracts the intestines medially, locates the ovary and then opens to grasp the proper ligament of the ovary against the body wall. A one metric nylon with a large curved needle is introduced through the body wall (transabdominally) to temporarily secure the ovary to the body wall. The needle is directed through the proper ligament under direct visualization, and then back through the body wall. The suture is anchored with a haemostat to keep the ovary away from the abdominal viscera. The laparoscopic forceps is removed from the proper ligament and is replaced with a vessel sealing device (laparoscopic haemoclips, harmonic scalpel, extracorporeal sutures, laser or electrocoagulation), which is then used to transect the suspensory ligament, the ovarian vascular pedicle and the proper ligament. The ovary is then removed from the abdominal cavity through the instrument port. The animal is tilted to the opposite side and the procedure is performed in the same way on the remaining ovary. After removal of both ovaries, the pneumoperitoneum should be evacuated, the *linea alba* and the subcutaneous tissue at each cannula site should be closed with an absorbable cruciate suture, and the skin incisions with a cruciate, an interrupted suture pattern or tissue glue (Davidson et al. 2004; MacPhail 2013; Case et al. 2011).

Laparoscopic ovariectomy has numerous advantages when compared with the traditional open procedures, including superior visualization, less traction on the genital tract, less surgical time and smaller abdominal incisions. Portal incisions in dogs submitted for LOV therefore have minimal wound inflammation, erythema, irritation and infections when compared with dogs subjected to OVH. All these factors combined result in less postoperative pain and a faster recovery time for the patient (Davidson et al. 2004; Case et al. 2011).

However, inadvertent puncture or laceration of the spleen during initial blind trocarisation, pedicle haemorrhage and subcutaneous emphysema are minor but possible risks when performing a LOV. In addition, the creation of a pneumoperitoneum with CO_2 may induce chemical

pain (due to formation of carbonic acids) and/or mechanical pain as a consequence of the stretching of the abdominal cavity and dehydration of the serosal surfaces. Uterine concerns (endometritis, pyometra and tumours) also represent a minimal risk, hence the endogenous source of progesterone is removed (Davidson et al. 2004; Case et al. 2011).

Performing an OVH is appropriate when neutering in animals with an unhealthy uterus, with abdominal hernias that need repairing or in other health conditions that need abdominal exploration in the same surgery. However, besides being more time consuming and having a longer surgical incision, complications such as persistent ovarian pedicle haemorrhage, seroma formation, inflammation and irritation of the incision site (which often result in dehiscence by self-trauma) are fairly common. Ureteral damage, granuloma formation and intestinal obstruction are less common but possible complications of an open ovariohysterectomy. Postoperative pain and recovery time are greater when compared to animals submitted to LOV. (Davidson et al. 2004; Case et al. 2011; Fransson 2012)

Long term complications such as urinary incontinence and obesity are not significantly different for LOV and OVH (Fransson 2012). In conclusion, performing a laparoscopic ovariectomy offers a better alternative to the traditional OVH because of reduced postoperative pain and because of less severe and less frequent complications.

4. Elective gonadectomy indications

4.1. Societal benefits

The primary societal benefit of surgical sterilization of dogs and cats is pet population control and in consequence, fewer animals relinquished to humane organizations (M. V. Kustritz 2007, M. V. Kustritz 2012).

Annually, millions of dogs and cats undergo euthanasia in animal welfare premises. Therefore, in order to prevent overpopulation, many of these premises are performing gonadectomy of all unowned animals prior to adoption. Despite the possible detriments, until correct education of owners and availability of other safer and affordable options, surgical gonadectomy will remain the most reliable measure to control pet overpopulation.

4.2. Medical indications in males

Performing an orchiectomy provides prevention against benign prostatic hyperplasia, prostatitis, prostatic cavitary lesions and testicular neoplasms. It may also serve as a treatment, or an adjunct treatment for these same conditions.

Besides the medical indications developed below, there are obviously other indications for surgical castration, such as testicular or epididymal congenital abnormalities, inguinal-scrotal herniorrhaphy or scrotal urethrostomy (Hamilton et al. 2014; Yates and Leedham 2019).

4.2.1. Benign prostatic hyperplasia

Benign prostatic hyperplasia is the most common non-neoplastic prostatic disease in dogs. Although it can happen as early as three years of age, it affects 80% of sexually intact dogs by 6 years of age and 95% by 9 years of age (Smith 2008; Howe 2015).

As a part of ageing, the androgen:oestrogen *ratio* changes. In consequence, dihydrotestosterone stimulates the prostatic parenchyma and causes symmetric, eccentric prostatic parenchymal hyperplasia and hypertrophy. Though almost all intact dogs develop BPH, not all will develop clinical signs. Only after disease has progressed to the point where it causes colonic compression, will constipation and tenesmus be observed. Sanguineous preputial discharge, haematuria and rarely a stilted gait due to prostatic pain may also occur (Smith 2008). To confirm the diagnosis, ultrasonography, cytology and biopsy may be used (Gobello and Corrada 2002).

Castration is an effective treatment for uncomplicated BPH, as most cases resolve after it – prostatic size is reduced by 70% within two weeks after surgery and complete involution is accomplished in three months (Freitag et al. 2007; Howe 2015).

In valuable breeding dogs with uncomplicated BPH, therapy with anti-androgenic drugs is also a reasonable option. These treatments inhibit conversion of testosterone into dihydrotestosterone, that results in prostatic involution and does not produce adverse effects or changes in semen quality (Gobello and Corrada 2002; Freitag et al. 2007).

In more complicated cases, BPH predisposes dogs to the development of prostatitis, life-threatening prostatic cysts and life-threatening abscesses. (Freitag et al. 2007; Howe 2015)

Surgical gonadectomy is the most effective preventative for development of benign prostatic hyperplasia. Hence androgens and oestrogens are secreted by the testes, by removing them, the primary source of stimulation is removed (Smith 2008).

Though most dogs with BPH do not show any clinical signs and, therefore, do not require immediate treatment, as this hyperplasia can develop as early as three years of age, castration before this time has been advocated for preventative treatment (Howe 2015).

4.2.2. Prostatitis

Prostatitis is the inflammation of the prostatic gland, which usually affects intact male dogs with more than five years old. Although it is uncommon in dogs, dogs with benign prostatic hyperplasia are predisposed to its development (Freitag et al. 2007; Christensen 2018).

Prostatitis often results of an infection by *Escherichia coli* (although any opportunistic bacteria ascending from the urethra may cause the infection) as a result of a compromise of the prostatic defence mechanisms, which may occur due to BPH or cysts. It can also result from a cystitis that extends to the prostate (Smith 2008; Christensen 2018).

Besides the history and physical examination (including trans-rectal examination), the diagnosis is established based on abdominal ultra-sound (heterogenous echogenic appearance to the prostatic parenchyma can be observed), haematology (shows a mature neutrophilia with a left shift), urinalysis (pyuria), semen and prostatic fluid analysis (with several neutrophils with evidence of engulfed bacteria), and bacterial cultures (Smith 2008; Christensen 2018).

Prostatitis is classified into acute and chronic, both of them susceptible to abscessation, with clinical signs depending on the type – dogs with an acute prostatitis present painful signs, whereas chronic cases present subclinical signs (Smith 2008).

The clinical presentation of acute prostatitis includes signs of systemic illness as lethargy, anorexia and fever, as well as vomiting, caudal abdominal pain, stiff or stilted gait and sanguineous preputial discharge. On the other hand, dogs with chronic prostatitis commonly present to consultation with recurrent urinary tract infections or urethral discharge. As these patients may not demonstrate any specific signs or findings of prostatic disease, it is difficult to establish the right diagnosis (Smith 2008; Christensen 2018).

Usually, treatment requires prolonged antibiotic therapy (based on culture and sensitivity) for between four to six weeks in acute cases and six to eight weeks in chronic cases or cases with abscessation. When prescribing antibiotic therapy for any prostatic condition, it is important to consider the unique physiology of the prostate – the initial inflammation makes the blood-prostate barrier less functional, allowing adequate diffusion of antibiotics. However, once the barrier heals after initial progress, diffusion across the barrier is limited to drugs containing specific pharmacokinetic properties. Antibiotics recommended should be lipophilic, not highly bound to proteins and be a weak base (as it will be more concentrated in the acidic canine prostatic fluid). Drugs such as trimethoprim, fluoroquinolones, erythromycin, tylosin and chloramphenicol match this description and must be chosen according to the sensitivity test. (Smith 2008; Christensen 2018)

Adjunct castration or any other medical option discussed for resolving BPH is warranted, because the hyperplasia predisposes dogs to prostatic infections. Re-examination after the end of the treatment to confirm resolution of the infection is recommended (Smith 2008; Christensen 2018).

Prognosis is good in general – acute prostatitis is more amenable to cure than chronic prostatitis. Nevertheless, the acuteness makes it a more urgent and potentially life-threatening condition (Brownlee 2015).

Elective castration is the most effective way to decrease the incidence of prostatitis, since it decreases the incidence of BPH, which is a recognized risk factor.

4.2.3. Prostatic cavitary lesions - abscesses and cysts

Prostatic cavitary lesions include abscesses and cysts, which are not common conditions in dogs. Benign prostatic hyperplasia is a predisposing factor to the development of these because the glandular hyperplasia may transition into cystic hyperplasia, which in its turn might lead to the formation of abscesses (Freitag et al. 2007; Smith 2008).

Cysts are often found in dogs with concurrent BPH or other prostatic pathology. Prostatic retention cysts are located in the prostatic parenchyma and they develop secondary to increased production or decreased drainage of prostatic secretions. Paraprostatic cysts are fluid-filled vesicles adjacent to the prostate which do not communicate directly with the prostatic parenchyma. Both kinds of cysts predispose dogs to abscessation and therefore require an intervention, whether or not clinical signs are present. Though both types are uncommon, when developed, they cause perineal swelling, abnormal urination and defecation, with a pelvic or abdominal mass palpable on physical examination. Definitive diagnosis is typically based on abdominal ultrasonography, where the structures appear as anechoic or hypoechoic with smooth margins (Freitag et al. 2007; Christensen 2018).

Prostatic abscesses may develop following a suppurative prostatitis or a secondary infection of prostatic cysts, being *Escherichia coli* the most common agent isolated. Clinical signs of systemic illness, such as pyrexia, anorexia, lethargy, associated or not with an urinary tract infection, painful defecation, urination and abdominal palpation. On clinical examination, a doughy, asymmetric enlargement of the prostate may be felt and on an abdominal ultrasonography, a hypoechoic or anechoic lesion surrounded by a defined capsule is present (Freitag et al. 2007).

Both conditions require castration (to decrease prostatic fluid secretion and accelerate bacterial infection resolution) and drainage, which may be surgical or percutaneous. (Freitag et al. 2007).

When it comes to the removal of retention cysts, surgical drainage by omentalization (omentum provides an alternate vascular and lymphatic supply) is the recommended technique. On the other hand, when dealing with paraprostatic cysts, though omentalization is also a good option, local resection is often the preferable treatment (Christensen 2018).

Prostatic abscesses should be treated with appropriate antibiotic therapy for the infection combined with active drainage of the abscess. This drainage can be done via omentalization, marsupialization, Penrose drainage, or percutaneous ultrasound-guided drainage if the cavitary lesions are well circumscribed and neither concurrent systemic illness nor prostatic neoplasia is suspected (Freitag et al. 2007; Christensen 2018).

Although these therapies are often effective, prognosis is guarded to poor. If percutaneous drainage is performed, owners should be aware that postoperative urinary incontinence and iatrogenic peritonitis due to seeding of the needle tract with bacteria are risks. Furthermore, multiple drainage procedures may be needed to fully resolve the clinical signs and

even so more than 50% of aspirated abscesses or cysts recur. (Freitag et al. 2007; Christensen 2018).

Since the prevalence of prostatic cysts in adult large-breed dogs is approximately 14% and of those, 42% have evidence of bacterial infection, it is of utmost importance to prevent both these maladies by castration (Smith 2008).

4.2.4. Cryptorchidism

As previously stated, cryptorchidism is associated with a greater risk of developing testicular neoplasia, testicular torsion, benign prostatic hyperplasia and hyperoestrogenism.

Despite castration being the optimum treatment, it should be delayed until after at least six months of age – the time at which the definitive diagnosis can be made because the inguinal rings are closed (Yates and Leedham 2019).

4.2.5. Testicular tumours

Testicular tumours are the second most common tumour in intact male dogs over seven years old, with three different histologic types – Sertoli cell tumour, Leydig cell tumour and Seminoma. Intra-abdominal testes (in cryptochird animals) have a great risk for neoplasia development. Metastasis are very rare, with the clinical signs including decreased libido, signs of prostatomegaly and inappetence. On physical examination, asymmetric testicles and prostatomegaly (secondary to oestrogen) may be observed. Also, dogs with Sertoli cell tumours may have signs of hyperoestrogenism, such as alopecia, pendulous prepuce and gynecomastica (Borrego 2017).

To establish a diagnosis and to stage these tumours, haematology, testicular ultrasound and thoracic radiographies should be performed, plus a cytology on a fine need aspirate.

A high rate cure can be achieved by a bilateral orchiectomy with scrotal ablation, however, if metastasis in regional lymph nodes is detected, an excisional biopsy of these should be performed as well. Nevertheless, it is important to remember that bone-marrow suppression is a rare but well documented complication of hyperoestrogenism, leading to a guarded to poor prognosis, as it requires months of haematological support and antibiotic therapy (Borrego 2017).

In conclusion, though castration prevents testicular neoplasia, generally only older sexually intact male dogs are at risk of developing this condition. Therefore, there is no need to perform a pre-pubertal gonadectomy to prevent this condition (Howe 2015).

4.2.6. Perianal adenomas

Perianal adenomas arise from the circumanal or hepatoid glands. They are androgen driven, being the most common perianal neoplasia. Older sexually intact males are at a high risk,

ten years old being the average age of diagnosis. Therefore, castrated males are at a reduced risk of developing adenomas (Hamilton et al. 2014; Unterer 2017).

Diagnosis can be established by a fine needle aspiration of the perianal mass for cytologic evaluation, though it might not differentiate benign from malignant perianal tumours. Since adenomas are benign, they have a high rate cure and a favourable prognosis with castration and mass removal. Nevertheless, curative surgery in an older dog always presents a higher risk than performing a preventive castration in a younger dog (Unterer 2017).

4.3. Medical indications in females

Performing a surgery to remove the ovaries and/or the uterus is indicated as prevention and/or treatment for ovarian and uterine tumours, pyometra and mammary gland neoplasms. Gonadectomy can also be performed to prevent hormonal changes that can interfere with medical therapy in patients with endocrine diseases and to prevent recurrence of vaginal hyperplasia (Van Goethem et al. 2006; Fransson 2012).

4.3.1. Pregnancy and parturition-related disorders

Neutering both males and females is a permanent solution to avoid breeding and unplanned pregnancies. In addition, by preventing pregnancy, neutering also prevents dystocia, as mentioned before, and other pregnancy-associated complications, as metritis, uterine prolapses, uterine ruptures, eclampsia and mastitis (A. Davidson 2010; Yates and Leedham 2019).

Metritis is an acute infection of the postpartum endometrium. Suspicion should arise when a foetid vaginal discharge coupled with lethargy, anorexia and fever occur. It may lead to systemic inflammatory reaction, endotoxaemia and septicaemia. Dystocia, contaminated obstetrical manipulations and retained foetuses and/or placentas are risk factors for the development of this condition. Treatment consists of antibiotic therapy confirmed by bacterial culture and sensitivity (oral if patient is stable; intravenous if patient is in shock), intravenous fluid and electrolyte support and pharmacological uterine evacuation, usually with prostaglandin F2α. Prognosis for recovery after medical management is dependent on early diagnosis If the response to medical management is weak, an ovariohysterectomy is be indicated (A. Davidson 2010).

Uterine prolapse is defined as a complete or partial prolapse of the uterus. Although it is an uncommon postpartum condition in the bitch, prolapsed uterine tissues are at risk of desiccation and infection from exposure and contamination. Any condition that causes excessive straining may predispose to prolapse (dystocia, necrotic vaginitis, constipation, diarrhoea or even severe cystitis). Manual replacement and ovariohysterectomy are the recommended therapies for the treatment of this condition. Prognosis is generally good (Davidson 2010; Lopate 2015).

Uterine rupture may occur with big litters that cause vast stretching and thinning of the uterine wall. Immediate caesarean with and repair or removal of the uterus, as well as culture and lavage of the abdominal cavity, is recommended. Prognosis is fair to good with timely intervention and appropriate monitoring (Davidson 2010, 2017).

Eclampsia, also known as puerperal tetany is a life-threatening condition that may occur in the last weeks of gestation or during the first four weeks postpartum. A depletion of ionized calcium is the cause, which may be predisposed by inappropriate perinatal nutrition and by large litters. Signs before tonic-clonic muscle contractions include ataxia, stiffness, hyperthermia and tachycardia. A slow intravenous infusion of 10% calcium gluconate should be administered right away and once the bitch is stable, oral supplementation, an adequate nutritional plan and a decrease on lactational demands are recommended. Prognosis is fair to good with timely intervention and appropriate monitoring (Davidson 2010, 2017).

Mastitis is an inflammation with or without infection of one or more mammary glands, which normally occurs during the *postpartum* or in pseudopregnancy due to haematogenous or ascending colonisation from the nipple, due to suction trauma and poor hygiene. Mastitis is classified into acute or chronic and it can also be associated with metritis. Signs such as mammary discomfort and heat, galactostasis, palpable intramammary mass, red or brownish milk increase suspicion of mastitis. Severe cases can progress to septic shock with abscessation or necrosis of the gland. Treatment must include protection of the affected gland from trauma, an adequate antibiotic therapy (safe for neonates and according to antibiogram), gentle physical therapy, analgesics and if needed, antiprolactin therapy. If severe necrosis occurs mastectomy might be needed (Davidson 2010, 2017).

4.3.2. Mammary gland neoplasms

Mammary gland neoplasia is the most common tumour in bitches - 50% of them are malignant and frequently metastasise to the lungs (Kustritz 2007).

Boxers, Spaniels, Beagles, Dachshunds, English Setters, German Shepherd Dogs, Pointers, Poodles, and Yorkshire Terriers are at increased risk of developing mammary gland tumours. Nevertheless, there are variations in the risk of malignancy amongst breed sizes - in small breed dogs, the risk of histologically malignant mammary tumours is 25%, whilst large breeds have a considerable 58% risk (Kustritz 2007; Howe 2015). Diet and previous hormone therapy with progesterone or oestrogen are also other risk factors for the development of this condition (Malone 2015).

Mammary tumours are classified into epithelial (adenocarcinomas, cystadenocarcinomas, carcinomas), mesenchymal (fibrosarcoma, osteosarcoma), and mixed tumours (epithelial, myoepithelial, and mesenchymal tissue, like fibroepithelial and carcinosarcoma) (Malone 2015).

A precise cause-effect connexion between mammary gland neoplasia and neuter status has not been yet defined. A wide number of factors may have a combined association. For instance, oestrogens and progesterone have stimulatory effects on mammary gland tissue and oestrogen receptors in the mammary gland tissues decrease as tissue becomes more anaplastic. Moreover COX-2 is overexpressed in most mammary carcinomas and prostaglandin E2, the product of COX-2, might promote tumour development and angiogenesis/metastasis (Kustritz 2012; Malone 2015). The fact is that neutered females are at a lower risk of developing mammary gland neoplasia, when compared to their counterparts (Priester 1979; Schneider et al 1968; Misdorp 1988; Sonnenschein et al 1991; Beauvais 2012; Malone 2015; Kustritz et al. 2017).

Preventing a mammary gland neoplasia remains one of the main reasons why owners and veterinarians submit pets to gonadectomy, because studies indicate that dogs spayed before their first oestrus have a 0.5% risk, bitches spayed after one oestrus have an 8.0% risk and dogs spayed after two oestrous cycles or after reaching two and a half years of age have a 26.0% risk of developing mammary gland neoplasms at an older age (Schneider et al 1968; Beauvais 2012).

However, one recent systematic review of the literature based on Cochrane guidelines by Beauvais et al in 2012 found that this association between the age at spaying and the risk of mammary neoplasia may not be as marked as previously suggested, since there are flaws in the design of the studies. Therefore, Beauvais et al 2012 suggested that the greatest benefit seems to be associated with spaying bitches before two and a half years old (Beauvais et al 2012; Howe 2015; Waters et al. 2017).

When presented with a mammary neoplasia, surgical excision of the mass(es). An OVH as an adjuvant therapy (in detriment of laparoscopic ovariectomy purely because a concurrent mastectomy may be needed), specially if peri-surgical serum estradiol concentration is increased, is advised because of a reduced but still evident decrease in recurrent mammary gland neoplasms in the future (Kustritz 2007, Malone 2015; Kristiansen et al. 2016).

Though bitches with benign mammary tumours are likely to have a surgical cure, the prognosis for those with malignant tumours is tremendously variable going from a cure with surgery to rapid recurrence and metastasis within the first year after surgical excision. Prognostic factors include tumour histological characteristics, tumour size and clinical stage (lymph node involvement and metastasis presence) (Malone 2015).

In conclusion, until further research is done, the high potential for metastasis and the grave prognosis if mammary tumours are developed, remain a substantial risk for sexually intact females (Beauvais et al 2012; Howe 2015; Kustritz et al. 2017; Waters et al. 2017).

4.3.3. Other reproductive neoplasia

By removing the reproductive organs susceptible to develop neoplasia, neutering prevents and treats uterine and ovarian neoplasia. As vaginal and vulvar tumours appear to be hormone dependent, neutering also offers a protective effect.

Uterine neoplasia is very uncommon in dogs accounting for 0.3% to 0.4% of all neoplastic conditions in bitches over 10 years old. Benign mesenchymal tumours and leiomyomas are the most common, which generally are slow-growing, non-invasive and non-metastatic. Therefore, clinical signs are infrequent, though abdominal distension, vaginal discharge and urinary symptoms may be observed. Since most uterine tumours are benign, ovariohysterectomy is curative for dogs. It must be taken into account that in German Sheperd dogs, there is a syndrome characterized by uterine leiomyomas accompanied by cystoadenocarcinomas and nodular dermatofibrosis (Borrego 2017; Houlihan 2017).

Ovarian tumours are very rare, most being of epithelial or sex cord-stromal origin. Asymptomatic ovarian neoplasia is frequent in older intact bitches, but it should be considered as a differential diagnosis when signs of an abdominal mass or ascites are observed in older sexually intact females. Metastasis into the peritoneum, lymph nodes, liver and lungs may occur in malignant forms. Ovariectomy or OHE is preventive and the effective treatment for benign or localized malignant tumours. Unfortunately, metastatic dissemination carries a poorer prognosis (Borrego 2017; Houlihan 2017).

Vaginal and vulvar tumours develop in sexually intact and generally multiparous bitches, accounting for 2.4% to 3% of all tumours of dogs. The vast majority are benign smooth muscle tumours, such as leiomyoma, though other benign tumours (as lipomas and haemangiomas), malignant leiomyosarcomas and adenocarcinomas a have been described. Depending on the localization of the tumour, different clinical signs may be observed. In the presence of an intraluminal tumour, stranguria, protrusion of the mass during micturition or defecation and vaginal discharge may observed; on the other hand, when dealing with an extraluminal tumour, it appears as a slow growing perineal mass. For benign cases, OHE performed as an adjunct treatment to surgical excision of the primary vaginal or vulvar tumour is almost always curative and reduces the recurrence risk. For invasive and malignant neoplasia, episiotomies and vaginectomies may be performed (Borrego 2017; Houlihan 2017).

Transmissible venereal tumours are generally localized to the external genitalia, being locally invasive, whether in males or females. As the primary transmission is by coitus, it normally occurs mostly in young sexually active animals., Since neutering prevents sexual behaviours, it decreases the risk of the occurrence of this specific type of tumour (Houlihan 2017). Regardless of the location or pattern of metastasis, the prognosis is excellent with recommended surgical excision, chemotherapy or radiotherapy (Páramo-Ramírez 2015).

4.3.4. Pyometra

Pyometra, also known as pyometritis, is defined as an accumulation of purulent material in the uterine lumen, which commonly affects middle-aged to older sexually intact bitches, being the mean age at diagnosis of seven years old. Incidence of pyometritis is believed to be higher in

some breeds as Great Danes, Collies, Golden and Labrador retrievers, Rottweilers, and German Shepherds(Howe 2015; Onclin-Verstegen 2015).

Though bacterial factors are involved, progesterone is considered to be a significant aspect in the establishment of infection with ascending opportunistic bacteria (most predominantly *Escherichia coli*). Cystic endometrial hyperplasia (CEH) is also a predisposing factor, hence it increases the uterine susceptibility for infection. Nevertheless pyometra and CEH may develop independently (Onclin-Verstegen 2015; Hagman 2018).

Two subtypes of this condition may occur – an open pyometra (which has mucoid, purulent or muco-purulent vulvar discharge with or without with systemic signs of illness); and a closed pyometra (with no or minimal vulvar discharge, but with systemic signs of illness). Generally, the disease develops during the luteal phase and animals present two to four months after oestrus with a history of various systemic and reproductive tract signs. Classic systemic signs of this condition include anorexia, lethargy, polydipsia, polyuria, tachycardia and tachypnoea. Physical findings on examination may include purulent vulvar discharge, signs of abdominal pain, abdominal distension, dehydration, fever (or hypothermia if already in septic shock), tachycardia and tachypnoea (Onclin-Verstegen 2015; Hagman 2018).

Though it can be challenging, early diagnosis is of utmost importance because pyometra leads to endotoxemia and sepsis, a life-threatening condition. Leucocytosis, with neutrophilia and left shift, and monocytosis are typical findings along with normocytic normochromic regenerative anaemia. Diagnostic imaging to identify intra-uterine fluid and other additional pathological changes that may affect the outcome of the treatment should also be done. A bacteriologic culture is not advantageous as the same microorganisms are natural inhabitants of the vaginal flora of healthy animals. Differential diagnosis should exclude mucometra, hydrometra and haemometra (Hagman 2018).

Surgical ovariohysterectomy is the treatment of choice, as it is the most secure and effective treatment as well as being preventative, because the source of infection is removed. Although laparoscopic techniques have been performed, they are not commonly executed unless it is a very mild case (Hagman 2018).

Though medical treatment is not recommended in the majority of cases, it can be an alternative choice in young and otherwise healthy breeding dogs without other reproductive tract pathologies and with an open pyometra, or in a patient for which anaesthesia and surgery is dangerous (Hagman 2018).

Pyometra is a life-threatening condition and although ovariohysterectomy is curative, the mortality with surgical management is up to 17% (Yates and Leedham 2019).Therefore, prevention by performing an elective gonadectomy is preferable. However, as the onset of pyometra is more commonly after seen seven years of age it does not need to be performed before puberty when it comes to preventing the occurrence of this specific disease.

4.3.5. Pseudo-pregnancy

Pseudo-pregnancy, commonly known as false pregnancy, is a normal physiologic phenomenon experienced by any non-pregnant bitch completing the luteal phase of an oestrous cycle. There is a decline of progesterone and an increase of prolactin concentrations.

The clinical expression of this luteal phase varies from indiscernible to serious. Yet, the concentrations are similar in bitches with and without symptoms, which suggests an individual sensitivity to prolactin or influence of environmental factors such as the level of physical activity and nutrition.

Mammary gland development, lactation, mucoid vulvar discharge, restlessness, nesting and mothering of inanimate objects are the classical signs exhibited (Davidson 2004b; Martin and Fernandez 2010).

The most important differential diagnosis to exclude is, obviously, a real pregnancy. Usually, this condition is self-limiting in one to three weeks and medical therapy is only recommended if the signs are unusually prolonged or pronounced, such as causing mastitis. Discouraging maternal behaviour and sometimes fitting Elizabethan collars to prevent licking of the mammary glands may be sufficient in mild cases. In severe cases, cabergoline treatment is aimed at decreasing or eliminating lactation to reduce the risk of developing a mastitis. Other adjuvant therapies such as decrease of food intake, increase of exercise and the application of local cold compresses may be of help (Davidson 2004b; Martin and Fernandez 2010).

If the bitch is predisposed to false pregnancies in every oestrous cycle, the best method for permanent resolution is gonadectomy, after the signs of pseudopregnancy have ceased. In addition, there is evidence that repetitive pseudopregnancy increases the risk of developing mammary gland neoplasia (Davidson 2004b; Martin and Fernandez 2010).

Unusual persistent cases should be evaluated for hypothyroidism, because excess thyrotropin-releasing hormone may cause increases in prolactin (A. Davidson 2004b).

4.4. Behavioural Benefits

Positive behavioural effects of neutering are seen in both genders, because hormones produced by the gonads act as behaviour influencers - the decrease of gonadal hormones correlates with a decrease in sexually dimorphic behaviours.

When it comes to males, behaviours as mounting, territorial marking and vagrancy associated with testosterone will be reduced and even eliminated (Kustritz et al. 2017; Yates and Leedham 2019).

In females, reproductive behaviours related to oestrus will not occur, as increased aggression (specially towards other females), roaming and urine marking (Kustritz et al. 2017; Yates and Leedham 2019).

It is known that there is an increased sensitivity to fear in puppies between seven and nine weeks of age, followed by a second increase between six and eight months of age. Therefore, neutering should not be performed before this age, at the expense of increasing fear and anxiety responses to loud noises, unfamiliar objects and people (Spain et al 2005; Clark 2012; Warnes 2018)

In regard to neutering to reduce the incidence of non-sexually driven behaviours such as aggressiveness, it will not be approached in this review. The evidence is variable as to its influence.

5. Risks according to the age of neutering

Negative risks and consequences may arise when neutering is performed at an pre-pubertal or at an age that does not suit the individual and breed characteristics. Important increased risks to have in consideration are urinary incontinence, tumours of non-reproductive organs, immune disorders and diseases of the locomotor system, which will be discussed below.

5.1. Early-age Gonadectomy Surgical and Anaesthetic Risk

Safety of anaesthesia and surgery on paediatric animals is different when compared with adult patients. Therefore, the decision to perform elective surgeries at an early-age, must have into account several peculiar features and situations that may arise whilst carrying out a surgery in puppies.

5.1.1. Intraoperative considerations

First and foremost, deep anaesthesia in pre-pubertal animals must be avoided hence they have an immature hepatic and renal function and therefore greater reliance on heart rate for cardiac output. Consequently, drugs must be used with care and at lower doses, especially when the drugs undergo hepatic or renal metabolism or excretion (Fransson 2012).

Greater risk of hypoglycaemia in paediatric animals submitted to surgery is important to be considered, as they have small reserves of glycogen in liver and skeletal muscle, along with slower glycogenolysis and gluconeogenesis (Fransson 2012; Towle 2012).

Paediatric animals have an increased risk of perioperative hypothermia (due to a lower body weight, a greater body surface area/volume ratio, reduced ability to thermoregulate and less subcutaneous fat). As known, hypothermia may induce bradycardia, which is an undesirable situation during surgery (Fransson 2012).

Intra-abdominal haemorrhage can be a life-threatening complication, whether in males, females, adults or puppies, resulting from inadequate suture placement or knot tying. Because

pediatric tissues are more fragile and friable than adult tissues, they must be handled gently to prevent any inadvertent haemorrhage, because even the minimal blood loss can become worrisome. (Fransson 2012; Towle 2012; Case et al. 2011; MacPhail 2013).

A compromise between the anaesthetic risks and the medical benefits of such an early sterilization in should be made.

5.1.2. Postoperative complications

Incidence of postoperative complications is associated with increases in the surgery time, which is in turn positively correlated with increasing body weight of the animal. Most are considered minor problems, which include self-resolving haemorrhage, inflammation at the incision site and gastrointestinal tract upsets (Kustritz 2007).

When comparing complications of elective gonadectomy performed at various ages, an increased incidence of postoperative infectious disease in dogs undergoing elective gonadectomy when they are under 12 weeks old is detectable (Kustritz 2007).

Immature animals are more vulnerable to infectious diseases than immunized adults, so gonadectomy should be delayed until vaccination is completed (Kustritz 2007).

5.2. Effects on metabolism/Obesity

Obesity is defined as an excessive body fat sufficient to cause or contribute to disease – animals with an accumulation of more than 20% of their ideal body weight are considered obese (Holloway 2015).

Neuter status is found to be a risk factor in the development of obesity (Edney and Smith 1986; Lefebvre et al. 2013; Mao et al. 2013), with a higher incidence in female-neutered dogs (which are twice as likely to be obese when compared with intact bitches) and in certain breeds such as Labrador retrievers, Cairn terriers, Cocker spaniels, Dachshunds, Basset Hounds and Cavalier King Charles spaniels (Van Goethem et al 2006; Courcier et al. 2010; Kustritz et al. 2017).

Other factors reported to be associated with obesity include increasing age and factors specific to the owner - such as age, income and ownership by an overweight person. It is important to keep in mind that these can be are more influential on the development of obesity than factors regarding the dog. (Courcier et al. 2010; Kustritz et al. 2017).

The cause-effect relationship for an increased risk of obesity after neutering is not yet well defined. Theories include a decrease in metabolic rate, a decrease in physical activity, an increase in food intake and other alterations in feeding behaviour (Courcier et al. 2010). In certain studies, spayed female dogs have been demonstrated to have an increase in food intake and increase in indiscriminate appetite after spaying (Kustritz et al. 2017).

Although there is proof that gonadectomised dogs have a greater risk of becoming overweight than sexually intact dogs, this risk is not influenced by age at gonadectomy (Spain, et

al 2005; Kustritz et al. 2017; Yates and Leedham 2019). In addition, no significant difference in weight gain is observed between dogs that had OVE versus OVH (Van Goethem et al 2006).

Prevention of obesity is important because of its association with increased risk of other medical problems such as musculoskeletal disorders, heart disease and reduced life expectancy. It is of utmost importance that clinicians brief the owners about appropriate diet and exercise in order to ensure the maintenance of an appropriate body condition after neutering (Spain et al 2005; Holloway 2015).

5.3. Diabetes mellitus

Canine diabetes mellitus is a complex endocrinopathy caused by a decreased production of insulin by the pancreatic beta cells and/or a decreased insulin use by peripheral tissues. Independently of the underlying aetiology, it results in a syndrome associated with protracted hyperglycaemia (Mattin et al. 2014; Stojanovic 2015; Behrend et al. 2018). The reported incidence of diabetes mellitus in canines is 0.5-0.6% (Hess et al 2000 and Guptill 2003 referred by Kustriz et al 2017)

Diagnosis is generally made between five and twelve years old, although rare cases in juvenile dogs have been reported. It is usually established based on persistent hyperglycaemia, persistent glycosuria and presence of clinical signs. Common clinical signs observed are polyuria, polydipsia, polyphagia and weight loss. Some may present with lethargy, cataracts, weakness or systemic signs due to diabetic ketosis/ketoacidosis, such as anorexia, vomiting and dehydration (Mattin et al. 2014; Stojanovic 2015; Behrend et al. 2018).

Canine diabetes mellitus develops as a result of environmental and genetic factors. Other than neutering, risk factors associated with greater incidence are increasing age, obesity, diabetogenic medication and previous diagnosis of pancreatitis, hyperadrenocorticism, hypothyroidism or urinary tract infection. Specific breeds as Yorkshire terriers, Australian terriers, Beagles and Samoyeds are more susceptible (Mattin et al. 2014; Stojanovic 2015; Kustritz et al. 2017; Behrend et al. 2018).

The associations between gonadectomy and a greater risk of diabetes mellitus are the increased probability of neutered canines being obese and the effect of progestogens in insulin resistance.

In entire females, the dioestrus phase involves high concentrations of progesterone, which may lead to transient or permanent diabetes due to its insulin-resistant effects. This is probably why the incidence of diabetes in neutered females is not significantly higher than in sexually intact females (Guptill et al 2003; Mattin et al. 2014; de Rooster and Porters 2017; Kustritz et al. 2017; Behrend et al. 2018)

Entire males may benefit from a protective effect of sex hormones as they have reduced incidence of diabetes mellitus, when compared to neutered males (Mattin et al. 2014; Kustritz et al. 2017).

The pillar treatment for clinical diabetes is insulin administration (in dogs, common exogenous insulin therapy includes porcine insulin zinc suspension as first-choice, although neutral protamine Hagedorn is another acceptable option). This should be paired up with a dietary modification (equal sized meals of a high protein and low carbohydrate diet be offered twice daily at the time of each insulin injection), in order to control blood glucose. Performing an ovariohysterectomy in intact diabetic bitches will support the treatment, as the effect of progestogens in insulin resistance will be eliminated. (Behrend et al. 2018)

If left untreated or inadequately controlled, life-threatening ketonemia, ketonuria, and ketoacidosis will develop. The prognosis depends mainly on the owner's commitment and the presence and reversibility of concurrent disorders and chronic complications associated with diabetes. Older dogs or those with pancreatitis at the time of diagnosis usually have a less favourable prognosis (Mattin et al. 2014; Stojanovic 2015; Behrend et al. 2018).

5.4. Acquired urethral sphincter mechanism incompetence in neutered bitches

Urinary incontinence is defined as an involuntary leakage of urine during the storage phase of the urinary cycle. One of the most common causes of incontinence arises from an incompetence of the urethral sphincter mechanism - a weakness of the muscles that control urine outflow from the bladder (Cohn 2015; Labato 2017).

Whilst less than one percent of sexually intact female dogs develop acquired urinary incontinence, in neutered bitches the prevalence varies from four to twenty percent, developing most frequently 2–4 years after ovariohysterectomy. Middle-aged or older and medium and large-sized dogs are the most often affected. The most common clinical presentation is an intermittent or continuous dribbling of urine combined with episodes of normal voiding (Brodbelt et al. 2017; Byron et al. 2017; Kustritz et al. 2017).

It has been demonstrated that the pathophysiology of acquired urinary incontinence involves changes in tissue structure and vasculature, such as an increase in collagen ratio in the urethra, which leads to a reduced urethral smooth and striated muscle which in its turn causes a decrease of maximum urethral closure pressure. After removing the ovaries, serum concentration of follicle stimulating hormone and luteinizing hormone are persistently elevated and oestrogen levels are low. This is thought to have an effect on the development of these structural changes. However, a cause-effect relationship between urethral sphincter mechanism incompetence and gonadectomy has not been yet defined (Brodbelt et al. 2017; Byron et al. 2017; Kustritz et al. 2017)

Besides neuter status and age at neutering, the incidence of acquired urinary incontinence is also increased in certain breeds such as German Sheperd Dog, Irish Setter and Dobermann Pinscher; in bitches with weight at or above the mean adult bodyweight for the breed, and with individual conformational characteristics such as tail docking or the presence of recessed vulva (Byron et al. 2017; Yates and Leedham 2019)

Studies have demonstrated increased incidence when bitches were spayed at fewer than three to five months, greater than six months, or before their first oestrus (Thrusfield et al 1998, Holt el al 1993, Hart et al 2016, Spain et al 2004, Reichler et al 2005, Forsee et al 2013, Byron et al 2017, referred by Kustritz et al. 2017). In 2012, a systematic review of journal articles was conducted by Beauvais et al, based on Cochrane guidelines. The authors reached the conclusion that, although weak, there was some evidence of an association between neutering and urinary incontinence - as the age at spaying increases, the risk of urinary incontinence decreases. However, after 12 months of age there was no evidence of an effect of age at spaying. Also, there was no evidence found that the occurrence or absence of oestrous before neutering is involved in the aetiology of urinary incontinence (Beauvais et al 2012). After a dog reaches sexual maturity, it can be assumed that the impact of oestrogen cessation on adult tissues and risk of urinary incontinence has a different physiology than during the developmental stages (Byron et al. 2017).

A 2017 study by Byron et al established a significant association between the weight of the dog and the age at spaying - to neuter bitches expected to be over 25 kg in adult weight later in their first year of life decreases the risk of developing urinary incontinence. On the other hand, age at neuter of bitches that will be under 25 kg as adults may not impact incontinence development, hence heavier dogs have an increased risk.

Fortunately, this disorder is commonly hormone responsive (supporting the fact that in some individuals, the lack of hormones eventually results in weakness of the urethral sphincter).

Diagnosis is always presumptive and therefore it is important to exclude other reasons for incontinence such as neurological diseases, urethral obstruction, vaginal stricture/stenosis, urethrovaginal fistula, congenital and acquired urinary tract structural defects (Cohn 2015).

Replacement with hormones such as diethylstilbestrol (that increases sensitivity of internal urethral sphincter to catecholamines) is the recommended treatment. If clinical signs are difficult to stabilise, the alpha-agonist phenylpropanolamine may be used, which increases internal urethral sphincter tone. (Cohn 2015).

The evidence suggests that it is beneficial to delay to beyond one year of age the neutering of bitches of predisposed breeds, as well as of breeds that reach over 25kg in adult body weight.

5.5. Musculoskeletal disorders

Hip dysplasia and cranial cruciate ligament rupture are two of the most common orthopaedic problems in dogs. Although neither represent a life-threatening condition, they do cause pain, affect physical performance and quality of life. Gonadectomy is a risk factor for the development of both musculoskeletal disorders in male and female dogs (Duval et al 1999; Slauterbeck et al. 2004; Spain et al 2004; van Hagen et al. 2005; Duerr et al. 2007; Witsberger et al. 2008; Torres de la Riva et al. 2013; Hart et al. 2014; Taylor-Brown et al. 2015; Hart et al. 2016).

It is known that most bone physes only close after puberty - by neutering at an early age, the lack of gonadal hormones results in a delayed closure of growth plates by 8 to 9 weeks, which is associated with an increased bone length and an asymmetric closure. Besides bones being more susceptible to injury and fracture, this asymmetric closure also causes misalignment of joints, which can lead to deformity and laxity of hip and stifle joints. It is thought that the combination of the influence of pre-pubertal neutering on the growth plate closure and on increased body weight, leads to a higher risk of developing cranial cruciate ligament disease and hip dysplasia (MacPhail 2013; Houlihan 2017; M. V. R. Kustritz et al. 2017; Yates and Leedham 2019).

In studies of Golden and Labrador Retrievers, by performing a gonadectomy before six months old, there is an increased incidence of joint disorders (cranial cruciate ligament rupture, hip and elbow dysplasia) - twice as high in Labradors and four to five times higher in Goldens, than sexually intact dogs (Torres de la Riva et al. 2013; Hart et al. 2014; Houlihan 2017).

Surgical correction and/or medical management of these maladies can be unaffordable for owners, therefore in conditions where chronic orthopaedic pain cannot be effectively controlled, euthanasia may be considered (Houlihan 2017).

The validity of extrapolation of the findings of studies in specific breeds to other breeds is not known in many instances.

5.5.1. Canine hip dysplasia

Canine hip dysplasia an inherited condition caused by an abnormal development of the coxo-femoral joint. This lack of adequate fitting between the femoral head and acetabulum, results in joint laxity in young patients and leads degenerative joint disease (osteoarthritis) of variable severity.

When present, hip dysplasia is most often bilateral. Large and giant breeds such as German Sheperd dogs, Boxers, Rottweilers, Newfoundlands, Labrador and Golden retrievers are more susceptible to the development of this disorder (Glassman and Spencer 2015; Marcellin-Little 2017).

Although heritability is the primary factor for the development of hip dysplasia, it has a multifactorial aetiology – environment, neutering, obesity, exercise and housing also play an important role in the development and in clinical manifestations of the disorder (Howe 2015; Houlihan 2017; Kustritz et al. 2017; de Rooster and Porters 2017; Marcellin-Little 2017).

Non-breed specific studies are contradictory – though Spain et al 2004 established that the risk for hip dysplasia is higher in gonadectomised animals (especially the ones neutered before five and a half months of age), Witsberg et al 2008 states that gonadectomy only increases hip dysplasia risks in males, with no reference to the age it is performed (Spain, Scarlett, and Houpt 2004; Witsberger et al. 2008).

Pre-pubertal neutering of male Golden Retrievers doubled the risk of hip dysplasia compared with unneutered males. There is also a significant difference in the age of onset of clinical signs between early and late neutered males – whilst the mean age for the onset of hip dysplasia in intact dogs is 4.4 years, in early neutered is 3.6 and late-neutered male dogs is 4.7 years. However, females are not commonly affected, independently of their neuter status and of the age at gonadectomy (Torres de la Riva et al. 2013; Hart et al. 2014; Yates and Leedham 2019).

When it comes to Labrador Retrievers, the incidence is three times higher in spayed females when compared to intact females. In contrast, castrated male Labradors do not appear to be any more vulnerable that unneutered males.(Hart et al. 2014)

In Boxers, gonadectomised females and males are one and a half times higher more likely to develop hip dysplasia then intact dogs (van Hagen et al. 2005).

5.5.2. Elbow dysplasia

Elbow dysplasia is a consequence of abnormal growth of the radius relative to the ulna, which be represented by conditions such as fragmented medial coronoid process, ununited anconeal process, elbow incongruity and/or *osteochondritis dissecans* that then result in a degenerative disease in the elbow joint. It is the most common source of pain in growing dogs, causing a forelimb lameness and osteoarthritis, especially in Retriever breeds, Bernese Mountain dogs, Australian shepherds, Rottweilers, Newfoundlands and Mastiffs (Balfour 2015; Marcellin-Little 2017).

In male Labrador retrievers, elbow dysplasia is seen more frequently in neutered dogs. Dogs neutered at before six months of age present an incidence of 4.2% and males castrated between two and eight years old have an incidence of 2.2%, when intact males have a low incidence of 0.57% (Hart et al. 2014; Houlihan 2017; Yates and Leedham 2019).

No differences were seen in female Labradors at any spaying age interval compared to intact dogs. In Golden Retrievers, the occurrence of elbow dysplasia was also not significantly above the one of intact dogs (Hart et al. 2014).

5.5.3. Cranial cruciate ligament rupture

As stated in part one, a complete or partial tear of the cranial cruciate ligament is common in large breed dogs due to progressive degeneration or trauma. Other than neutering, obesity, systemic or autoimmune disease are risk factors for the onset of this rupture (Kowaleski and Boudrieau 2012; Linn 2015).

By neutering before puberty, large-breed dogs are at increased risk for development of excessive tibial plateau angle, which is a known risk factor for development of this particular

disorder (Duerr et al. 2007; MacPhail 2013). Studies have found that gonadectomised dogs have a significantly higher prevalence for cruciate ligament disease than their sexually intact counterparts, with neutered females having the highest prevalence (Whitehair, Vasseur, and Willits 1993; Duval, Budsberg, and Flo 1999; Slauterbeck et al. 2004; Witsberger et al. 2008; Torres de la Riva et al. 2013; Taylor-Brown et al. 2015; Houlihan 2017).

A study regarding Golden Retrievers revealed that when neutered before one year of age, the risk a of cranial cruciate ligament rupture was 5.1% in males and 7.7% in females, compared to a risk of 1.4% in late-castrated males and 0% in late-spayed females and intact males and females (Torres de la Riva et al. 2013; Howe 2015).

In Labrador Retrievers it was found that males castrated before 6 months of age had a higher risk (with an incidence of 7.6%) of developing cranial cruciate ligament rupture compared to intact males (with an incidence of 2.3%). However, no alterations were seen amongst the risk on gonadectomised females compared with sexually intact ones (Hart et al. 2014; Howe 2015).

When it comes German Sheperd dogs, cranial cruciate rupture occurs in less than 1% both in intact males and females. However, when castration is performed prior to six months of age it occurs in 12.5% and if performed between six and eleven months it happens in 8.3% of males. In females, cruciate disease occurred in 4.6% of females neutered prior to six months and in 8.3% between six and eleven months (Hart et al. 2016; Yates and Leedham 2019).

5.6. Oncologic considerations

The incidence of more than one type of cancer in dogs is greatly influenced by neutering. Neutered animals are at higher risk of developing specific tumours outside the genital organs than intact animals. Gonadectomised females appear to be more severely affected than castrated males, which have relatively minor increases in the occurrence of tumours (Grüntzig et al. 2016; Kustritz et al. 2017).

Besides theories of decreased immunity against cancerous cells due to lack of endogenous steroids, a causal nexus between gonadectomy and neoplasia has not yet been established (Kustritz et al. 2017).

5.6.1. Prostatic neoplasia in neutered males

Prostatic neoplasia is very rare and includes prostatic adenocarcinoma (which arises directly from glandular tissue) and an invasion of transitional cell carcinoma from the prostatic urethra into the prostatic parenchyma (which is the most common type diagnosed). The average age at diagnosis is of ten years old and it affects both intact and neutered males (Smith 2008; M. V. R. Kustritz et al. 2017).

Contrary to common belief, castration does not prevent canine prostatic neoplasia and has actually been identified as a risk factor on the development of prostatic neoplasia. Prostatic neoplasia is not androgen dependent, hence they arise from ductal or urothelial tissues. Neutered males are therefore predisposed to develop prostatic transitional cell carcinoma, having four times greater incidence in neutered males that in entire males (Teske et al. 2002; Sorenmo et al. 2003; Bryan et al. 2007; Smith 2008; Kustritz et al. 2017; Christensen 2018).

Nevertheless, besides castrated dogs being at an increased risk of developing prostatic neoplasia, the age at neutering does not appear have an effect on the incidence or the onset of prostate neoplasia (Teske et al. 2002; Houlihan 2017).

The reasons for the increased incidence of prostatic neoplasia in castrated dogs are unidentified, but theories include the loss of protective effects of androgens and an alteration in the prostatic stroma which may favour tumour development (Christensen 2018).

Although reported incidence of prostatic carcinoma is between 0.2% and 0.6%, prognosis for prostatic neoplasia is very poor, hence prostatic tumours tend to be highly aggressive and metastatic, animals are usually diagnosed late in the course of the disease, plus treatment options are only palliative. Though prostatic neoplasia without evidence of metastasis may be managed with total or subtotal prostatectomy, in conjunction with intraoperative radiotherapy or postoperative chemotherapy, chances of recurrence are very high (Freitag et al. 2007; Smith 2008; Christensen 2018).

5.6.2. Transitional cell carcinoma non-prostatic

Transitional cell carcinoma is defined as a neoplasia of epithelial cells with their origin in the bladder parenchyma. It relatively common in older dogs and females appear to be at a higher risk than males. Scottish Terries are very predisposed, as well as West Highland white and Wirehaired fox terriers, Airedales, Shetland sheepdogs, Collies and Beagles. Exposure to herbicides and insecticides is also associated with an increased risk (Bryan 2015).

A 1990s research paper established that gonadectomy at a non-specified age increases the risk up to three times in both male and female dogs (Norris et al. 1992).

The other only study existing in relating non-prostatic transitional cell carcinoma to neutering was done regarding only Scottish Terriers, a breed that has a hereditary predisposition to transitional cell carcinoma. Therefore, extrapolation to the entire dog population is problematic (Glickman et al. 2004).

Although the incidence of transitional cell carcinoma is at best 1%, this disease is locally aggressive with a significant metastatic potential. Owners of predisposed breeds should be informed about this condition when planning neutering (Bryan 2015; Kustritz et al. 2017).

5.6.3. Osteosarcoma

Osteosarcoma is a malignant tumour of mesenchymal tissue due to bone production by malignant osteoblasts. Large- and giant-breed dogs are predisposed, with the average age at diagnosis being between seven and nine years old (Bailey 2015, Diessner et al. 2019).

Body size (height and weight) is an important fact of prognosis - compared to dogs weighing less than 10 kg, the risk is eight times higher in dogs weighing between 20 and 30 kg, and 60 times higher in dogs weighing more than 30 kg.

There are three subtypes of osteosarcoma. In the appendicular form (which arises from the appendicular skeleton) the distal radius, the proximal humerus, the distal femur, the proximal and distal tibia are most commonly affected. The axial form (which arises from the remainder of the skeleton), generally affects vertebrae, ribs, the mandible and the maxilla. Extraskeletal osteosarcoma arises in soft tissues and is very rare.

The most common site for metastasis are the lungs, followed by other bones and by different soft tissues. Treatment options may involve amputation, chemotherapy, radiotherapy, pain management but survival times are usually short, due to the primary tumour and/or the metastatic disease (Bailey 2015).

The risk of bone sarcoma is increased by performing an elective gonadectomy (Cooley et al. 2002; Grüntzig et al. 2016). Exposure to endogenous sex hormones appears have a protective effect, with a strong inverse association between lifetime exposure to gonadal hormones and risk of spontaneous bone sarcoma. Investigation shows that gonadal hormone exposure is a significant risk factor of bone sarcoma independent of adult body size, which is a recognized key risk factor for bone sarcoma. (Torres de la Riva et al. 2013).

Nevertheless, evidence for exactly how gonadal hormones interfere in sarcoma genesis remains undiscovered. It is known that endogenous steroids as oestrogen and testosterone are essential for skeletal homeostasis, and an hypothesis states that they might be pro-differentiation agents that inhibit the malignant transformation of osteoblasts. The indirect effects of sex steroids on body conformation and on physical activity may also be an influence (Torres de la Riva et al. 2013).

In Golden Retrievers, the odds for the development of osteosarcoma increased by double by performing an elective gonadectomy in the first year of life. In the Rottweiler breed, which normally has a high incidence of spontaneous bone sarcoma, neutering before the first year of life increased the occurrence of osteosarcoma by four times (Cooley et al. 2002; Torres de la Riva et al. 2013).

5.6.4. Haemangiosarcoma

Haemangiosarcoma is a malignant, highly metastatic tumour which arises from vascular endothelium or endothelial precursor cells. The spleen, the right auricle or atrium and the skin or

subcutaneous tissues are the common sites where this neoplasm can be found. The cutaneous form is common in adult dogs with no breed or sex predisposition, whilst the non-cutaneous form common is overrepresented in Golden Retrievers, German Shepherd dogs and other large or giant breeds. (Chun 2015; Clifford and De Lorimier 2017).

Regardless of the different presentations, the overall prognosis for dogs with haemangiosarcoma is extremely poor, even after surgical tumour removal and adjunctive chemotherapy (Chun 2015; Clifford and De Lorimier 2017).

Splenic haemangiosarcoma and hematoma more likely to be found in gonadectomised animals, especially in neutered females (in which odds are twice as high compared to sexually intact ones). However, in contrary to other cancers, the risk for developing haemangiosarcoma seems increased with post pubertal neutering (Prymak et al. 1988; Ware and Hopper 1999; Torres de la Riva et al. 2013; Grüntzig et al. 2016; Zink et al. 2014).

The risk for developing cardiac haemangiosarcomas in Golden Retriever females spayed after 12 months of age is four times greater than in either intact or prepubertally neutered females. In contrast, no differences were identified between the risk of neutered and entire male dogs in this study (Torres de la Riva et al. 2013).

In another paper regarding Vizlas, females neutered at any age and males neutered after the first year of age were at a significantly greater risk of developing this type of tumour when compared with their intact counterparts (Zink et al. 2014).

In contrast, research on German Shepherd Dogs established that neutering at any age was not a risk factor in the development of haemangiosarcoma in either gender (Hart et al. 2016). Other non- breed-specific studies in the 1990's have shown similar findings for splenic and cardiac haemangiosarcoma (Prymak et al. 1988; Ware and Hopper 1999; Goh 2016).

The cause-and-effect relationship between gonadectomy and haemangiosarcoma and the fact that in specific dog breeds, the ones neutered before one year old and entire dogs have a similarly reduced risk for haemangiosarcoma has not been yet established. (Houlihan 2017; Kustritz et al. 2017).

5.6.5. Lymphoma

Lymphoma, defined as a proliferation of malignant lymphoid cells, is the most common hematopoietic malignant neoplasm diagnosed in dogs, with an incidence of 1.1%. The lymph nodes, the liver and the spleen are the ones primarily affected. Though several types of lymphoma exist (multicentric peripheral nodal, alimentary, cutaneous, mediastinal, extranodal) this condition's aetiology is multifactorial and poorly understood (Williams 2015; Houlihan 2017; Vail 2017).

Besides environmental, infectious and immunological factors, genetics play a great influence, as Boxers, Golden Retrievers, Scottish terriers, Rottweilers, Basset hounds, German

Shepherds, Airedales, Bulldogs are at an increased risk (Williams 2015; Houlihan 2017; Vail 2017).

Lymphoma presents a rapid onset and disease progression, however prognosis for individual dogs differs widely. Prognostic factors may include histological grade, immunophenotype (B-cell better than T-cell), clinical stage, gender (females better) and weight (small dogs better). Despite being rarely curable, complete remission can be achieved with chemotherapy administration which results in good quality of life during extended remissions of six to thirteen months (Williams 2015; Houlihan 2017; Vail 2017).

A study regarding lymphoma epidemiology, established that intact females have a significantly lower risk of developing this type of cancer than neutered females, neutered males or intact males (Villamil et al. 2009; Kustritz et al. 2017; Goh 2016).

In Golden Retrievers, though analysis revealed that pre-pubertal neutering was associated with an increased occurrence of lymphoma in both genders, the difference was only statistically significant in early-neutered males, which had three times the risk compared to their entire counterparts. No cases of lymphoma were found in the group of male dogs neutered at after the first 1 year of life (Torres de la Riva et al. 2013; Houlihan 2017).

Similar findings regarding German Shepherd Dogs, show that there is a non-significant increase in incidence of lymphoma in pre-pubertal neutered males, whilst in females, neutering is not associated with any evident increase in cancer development (Hart et al. 2016).

For Vizslas, analysis suggested that odds of neutered males and females developing lymphoma were 4.3 times higher than their sexually intact counterparts to have lymphoma. Interestingly, the ones gonadectomised after six months of age had significantly higher odds of having lymphoma than intact dogs (Zink et al. 2014).

5.6.6. Mast cell tumours

As stated in the monograph, mast cell tumours are defined as a neoplastic accumulation of mast cells, either cutaneous or visceral. These malignant tumours affect mostly brachycephalic dogs, retrievers, Beagles, Shar-Peis, Pugs, Schnauzers, Cocker spaniels, Staffordshire Terries, Rhodesian Ridgebacks and Weimaraners. Surgical excision, targeted therapy, chemotherapy and/or radiation therapy are the common treatments, however the diverse behaviours of canine mast cells leads to a variety of prognosis, dependent on multiple factors, including grade, recurrence, metastasis presence, location, size, completeness of surgical excision and breed (Gieger 2015; Warland et al. 2015; Thamn 2017)

Neuter status was associated with an increased risk of developing mast cell tumours. However, whilst spayed females had more than four times the odds of developing a mast cell neoplasm, when it came to castrated males, they were found to be only slightly more likely to

develop it than entire ones. In contrast, in this same study it was also proved that intact males were more prone to develop this neoplasia than entire females (White et al. 2011).

Similar findings were reported in female Golden Retrievers - no cases of MCT in intact Golden Retriever females where found, but the occurrence doubled in early-neutered females and quadrupled in late-neutered females, revealing an effect of late neutering on the onset of mast cell tumours in this specific breed. No differences were found in the occurrence of MCT in male Golden Retrievers (Torres de la Riva et al. 2013; Hart et al. 2014).

In the same way, the odds of gonadectomised Vizslas of either sex developing mast cell tumours were 3.5 times the odds of sexually intact Vizslas developing mast cell tumours, regardless of the age at which the dog was gonadectomised (Zink et al. 2014).

In contrast, regarding the incidence in German Sheperd dogs and Labrador Retrievers, MCT incidence was not higher in the neutered than in the intact dogs (Hart et al. 2014, 2016; Yates and Leedham 2019).

5.7. Auto-immune disorders

Auto-immune-mediated disorders are a consequence of a dysregulation of the immune system, which is activated inappropriately. This results in humoral or cell-mediated immune response against the body's own constituents and generally causes a clinical disease(Scott-Moncrieff 2004).

Research has proven the importance of sexual steroids on immune function emphasizing the role of these hormones on tissue self-recognition. In auto-immune diseases in which the onset mechanism involves inflammation, endogenous steroids may have an anti-inflammatory protective effect. Therefore gonadectomy is an important aspect to consider when dealing with breeds predisposed to immunity deficiencies (Sundburg et al. 2016; M. V. R. Kustritz et al. 2017).

Neutered males and females appear to have a significantly greater risk of atopic dermatitis, autoimmune haemolytic anaemia, hypoadrenocorticism, hypothyroidism, immune-mediated thrombocytopenia and inflammatory bowel disease than intact dogs. Also, gonadectomised females appear to be at greater risk than castrated males for all of the above stated conditions except for autoimmune hypoadrenocorticism (in which neutered males where at a higher risk) and haemolytic anaemia (which had similar risk in both neutered genders).

In regard to lupus erythematosus, neutered females, but not males, have significantly higher odds of developing it than their entire counterparts (Sundburg et al. 2016).

In addition, hypersensitivity reactions following vaccinations were more common in neutered animals, probably due to the lack of negative feedback by gonadal hormones, which may increase pituitary hormone secretion, influencing immune response to vaccination (de Rooster and Porters 2017).

Nevertheless, timing of gonadectomy was not associated with the onset of auto-immune disorders (Sundburg et al. 2016).

6. Validity of study results & Potential future research

First and foremost, it is important to state that detecting an association does not indicate causation.

Most studies analysed were retrospective, without any control over why decisions to neuter or not at a certain age were made, resulting an inherent selection bias. Also, when dealing with records of referral hospitals, it can be problematic to assess the validity of the researches hence these hospitals deal with non-standard disorders. Individual characteristics may have influenced choices and even where there are strong correlations between neuter status and disease it is not possible to prove causality from a retrospective study.

In addition, the aetiology of many disorders is unknown or multifactorial, and so, a profounder understanding of how and when sex hormones affect each disease process is needed before concrete assumptions can be concluded (Houlihan 2017; Kustritz et al. 2017).

Moreover, when analysing papers evaluating different breeds, significant variations in the effects of neutering on incidences of health conditions can be found. Therefore, results of breed specific studies cannot be extrapolated and applied the entire canine population.

An adequate sample size in longitudinal randomized clinical trials provide the strongest link between potential cause and potential effect, selecting unbiased subjects (hence dogs at referral hospitals or at breed clubs are not representative of the dog population). Whilst it is important to measure accurately the characteristics of interest, control and discussion of the confounding factors is of utmost importance as well for the validity of study results (Houlihan 2017; Kustritz et al. 2017).

Dogs Trust in association with the Royal Veterinary College, as well as the VetCompass are already setting up a large-scale prospective cohort study to deliver more precise information on the risk for developing health problems, including effects of neutering and age of neutering. These projects, by following random dog's lives from puppyhood to old age will probably provide a more generalizable information (Warnes 2018).

Since there has been established an association in ferrets, a potential area of research is the relation between adrenal gland tumours and neutering. Similarly, new studies on the relationship between neutering and cognitive dysfunction, hypothyroidism, epilepsy and life expectancy would also be valuable, since the existing ones show conflicting results, probably due to faulty study design. Nevertheless, further studies on the association of oncologic and orthopaedic disease with gonadectomy should be considered, as they are particularly relevant conditions.

7. Discussion

First and foremost, it is important to keep in mind that recommendations may be different for owned companion animals and those living in a shelter or a rescue centre, hence gonadectomy is clearly the most cost-effective method recommended to control pet over-population.

Nevertheless, when considering owned companion dogs, their health is the priority. Therefore, a veterinary surgeon is the responsible to, based on each animal's individuality, prevalence of breed-specific conditions, gender, ownership and lifestyle, use its best medical judgment to weigh the potential benefits and detriments when deciding whether gonadectomy is appropriate and, if so, tailor the timing of the procedure to each patient.

Recommendations regarding the pros, the cons and the optimal age for neutering a dog are complex and dependent upon several factors. However, general recommendations from the author, based on the recent research reviewed in this monograph, would be as follows.

In females, there is no doubt that the risk of mammary carcinoma and pyometra increases with longer ovary exposure and that gonadectomy is beneficial in preventing these life-threating conditions. Nevertheless, gonadectomised bitches appear to be at an increased risk of developing acquired urethral sphincter mechanism incompetence, cranial cruciate ligament rupture and osteosarcoma if neutered before one year of age. Regardless of the time of gonadectomy, odds for being obese and for developing lymphoma, transitional cell carcinoma, haemangiosarcoma, mast cell tumours, hip dysplasia, and immune disorders are also higher for neutered females.

Therefore, by standardizing the optimal time age for neutering a female between the first and the second heat, a considerable reduction of the risk of mammary neoplasia (risk of 8%) can be achieved with only a moderate potential for undesired urinary, neoplastic and orthopaedic side effects.

When it comes to male dogs, after taking a closer look at the literature, it has become clear that the health benefits of pre-pubertal elective gonadectomy are less obvious and do not outweigh the potential detriments.

Diseases of the prostate and testicular neoplasms are the two main reasons for orchiectomy at an early age provides. However, the onset of BPH and associated diseases is common in older male dogs. Therefore, these are still prevented by neutering males after only after sexual maturity, which in turn will avoid the increased rates of occurrence of hip dysplasia, cranial cruciate ligament rupture and osteosarcoma. Similarly, to females, regardless of the time of gonadectomy, risk for being obese and for developing lymphoma, transitional cell carcinoma, haemangiosarcoma, mast cell tumours and immune disorders are also higher for castrated dogs.

Table 31: Benefits of gonadectomy in females

	Condition	Incidence	Prognosis	Effect of Spaying	Age at gonadectomy consideration
Benefits in females	**Mammary neoplasia**	Very Common	Life-threatening without treatment	Decreases	Decreases risk of tumour development in: - 0.5% if spayed before first oestrus - 8% if before second oestrus - 26% if spayed after second oestrus
	Pyometra	Very Common (higher in some breeds and older intact bitches)	Life-threatening even with treatment	Prevents	Non-existent
	Pseudo-pregnancy	Very Common	Excellent, easily medically treatable	Prevents	Non-existent
	Pregnancy and parturition-related disorders	Uncommon but very high in certain breeds	Variable	Prevents	Non-existent
	Other reproductive organs neoplasia	Uncommon	Variable, but the majority is surgically treatable	Prevents	Non-existent

Breed-specific disease vulnerabilities should also be thoughtfully considered. Although timing of gonadectomy may play a role in the development of certain diseases, genetics and environment are likely to be equally, if not more, important. Special considerations for German Sheperd Dogs, Golden and Labrador Retrievers which are more prone to develop orthopaedic conditions; Scottish Terriers for transitional cell carcinomas and Rottweillers for osteosarcomas.

Table 32: Benefits of gonadectomy in males

	Condition	Incidence	Prognosis	Effect of Castration	Age at gonadectomy consideration
Benefits in Males	**Benign Prostatic Hyperplasia**	Very Common	Good	Decreases	BPH can develop as early as three years of age, so castration is advocated before this
	Testicular neoplasia	Common	Good, most benign and surgically removable	Prevents	In cryptorchid dogs, should be delayed until 6 months of age
	Perianal adenomas	Common	Good, most benign and surgically removable	Decreases	Non-existent
	Prostatitis	Uncommon	Variable	Decreases	Prostatitis can develop as early as five years of age, so castration is advocated before this
	Prostatic cavitary lesions	Uncommon (higher in large breed dogs)	Guarded to poor	Decreases	Prostatic cavitary lesions can develop as early as three years of age, so castration is advocated before this

When weighing the risks and benefits of gonadectomy and the age that it should be performed at, it is important to consider the prevalence of the disease, the severity of the disease, the availability of effective treatments and the effect of neuter age. A simple approach of all these can be found in tables 31, 32 and 33, using the research available to this date. Nevertheless, further updated investigation will be important for making recommendations about individual patients and may confirm or refute these conclusions.

Table 33: Detriments of gonadectomy in females and males

	Condition	Incidence	Prognosis	Effect of Gonadectomy	Age at gonadectomy consideration
Detriments	**Urinary incontinence**	Common in neutered females, uncommon in intact females	Medically manageable in most of cases	Increases	Neutering after 12 months of age decreases risk of this detriment
	Obesity	Very Common in both genders	Variable, but prevented with calorie restriction	Increases in double	Not discovered
	Cruciate ligament disease	Common in both genders	Variable, can be surgically treated	Increases	Neutering after 12 months of age decreases risk of this detriment
	Hip dysplasia	Common in both genders (higher in certain breeds)	Moderate, decreases quality of life	Increases	Neutering after 12 months of age decreases risk of this detriment
	Osteosarcoma	Common in both genders (higher in certain breeds)	Very Poor	Increases	Risk increases in double if neutering is performed before 12 months of age
	Mast cell tumours	Common	Variable	Increases	Not discovered to date
	Diabetes mellitus	Common	Variable	Increases	Not discovered to date

	Haemangiosarcoma	Uncommon	Very Poor	Increases	Risk increases with post pubertal neutering
	Transitional cell carcinoma	Uncommon	Very Poor	Increases	Not discovered to date
	Lymphoma	Uncommon	Poor	Increases	Contradictory
	Elbow dysplasia	Common in large breeds	Moderate, decreases quality of life	Possibly increases	Not discovered to date
	Prostatic neoplasia	Uncommon	Very Poor	Increases	Non-existent
	Immune disorders	Uncommon	Variable	Increases	Non-existent

8. Conclusion

The traineeship at Priory Veterinary Surgeons and the following report was the conclusive element of the Veterinary Medicine degree initiated at Universidade de Évora in 2013.

Since it was possible to acquire new skills as a veterinary surgeon by the high-quality standards at Priory Veterinary Surgeons, the traineeship allowed immeasurable growth not only at a professional level, but also at a personal level.

The writing of this report was also important for the consolidation of the knowledge acquired throughout the years at university. Not only did it allowed to review and deepen knowledge of those that have often been the most commonly observed affections, but it also allowed to conclude that neutering benefits may be less marked than was once believed and that the optimal age of gonadectomy depends on each individual dog.

In conclusion, both experiences proved to be of great importance, since they allowed a closer contact with the professional reality of a near future and provided acquisition of further knowledge.

Bibliography

Atkins, C., J. Bonagura, S. Ettinger, P. Fox, S. Gordon, J. Haggstrom, R. Hamlin, B. Keene, V. Luis-Fuentes, and R. Stepien. 2009. “Guidelines for the Diagnosis and Treatment of Canine Chronic Valvular Heart Disease.” *Journal of Veterinary Internal Medicine* 23 (6): 1142–50. https://doi.org/10.1111/j.1939-1676.2009.0392.x.

Axiak, S. 2012. “Feline Injection-Site Sarcoma.” *NAVC Clinician’s Brief*, 71–73.

Bacon, Nicholas J. 2012. “Chapter 122: Pinna and External Ear Canal.” In *Veterinary Surgery: Small Animal*, edited by Spencer A. Tobias, Karen M.; Johnston, 2059–77. St. Louis, Missouri: Elsevier Saunders.

Bailey, Dennis. 2015. “Osteosarcoma.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 740–43. St. Louis, Missouri.

Balfour, Raviv. 2015. “Elbow Dysplasia.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 308–10. St. Louis, Missouri: Elsevier.

Bates, Nicola. 2015. “Chocolate Toxicity.” *Companion Animal*. https://doi.org/ISSN: 2053-0889.

Beauvais, W., J. M. Cardwell, and D. C. Brodbelt. 2012. “The Effect of Neutering on the Risk of Urinary Incontinence in Bitches - a Systematic Review.” *Journal of Small Animal Practice* 53 (4): 198–204. https://doi.org/10.1111/j.1748-5827.2011.01176.x.

Behrend, Ellen, Amy Holford, Patty Lathan, Renee Rucinsky, and Rhonda Schulman. 2018. “2018 AAHA Diabetes Management Guidelines for Dogs and Cats.” *Journal of the American Animal Hospital Association* 54 (1): 1–21. https://doi.org/10.5326/jaaha-ms-6822.

Bell, F.W., J.S. Klausner, D. W. Hayden, D.A. Feeney, and S.D. Johnston. 1991. “Clinical and Pathologic Features of Prostatic Adenocarcinoma in Sexually Intact and Castrated Dogs: 31 Cases (1970-1987) 1991;199:” *Journal of the American Veterinary Medical Association*, no. 199: 1623–30.

Borrego, Juan. 2017. “Chapter 351: Urogenital and Mammary Gland Tumours.” In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 5147–48. St. Louis, Missouri: Elsevier.

Brodbelt, D. C., D. B. Church, J. L. Hall, L. Owen, D. G. O’Neill, and A. Riddell. 2017. “Urinary Incontinence in Bitches under Primary Veterinary Care in England: Prevalence and Risk Factors.” *Journal of Small Animal Practice* 58 (12): 685–93. https://doi.org/10.1111/jsap.12731.

Brownlee, Lisa. 2015. “Prostatic Infections.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 849–51. St. Louis, Missouri: Elsevier Mosby.

Bryan, Jeffrey N. 2015. “Transitional Cell Carcinoma.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 1015–16. St. Louis, Missouri: Elsevier Mosby.

Bryan, Jeffrey N., Matthew R. Keeler, Carolyn J. Henry, Margaret E. Bryan, Allen W. Hahn, and Charles W. Caldwell. 2007. “A Population Study of Neutering Status as a Risk Factor for Canine Prostate Cancer.” *The Prostate*, no. 67: 1174–81. https://doi.org/10.1002/pros.

BSAVA. 2018. “BSAVA Position Statements -Vaccination.” BSAVA Position Statements - Vaccination. 2018. https://www.bsava.com/Resources/Veterinary-resources/Position-statements/Vaccination.

Byron, J. K., K. H. Taylor, G. S. Phillips, and M. S. Stahl. 2017. “Urethral Sphincter Mechanism Incompetence in 163 Neutered Female Dogs: Diagnosis, Treatment, and Relationship of Weight and Age at Neuter to Development of Disease.” *Journal of Veterinary Internal Medicine* 31 (2): 442–48. https://doi.org/10.1111/jvim.14678.

Carney, Hazel C, Steven J Bailey, David Bruyette, A Renee Rucinsky, Duncan Ferguson, Cynthia R Ward, Sonnya Dennis, and Amy Hinc. 2016. “2016 AAFP Guidelines for the Management of Feline Hyperthyroidism.” *Journal of Feline Medicine and Surgery* 18 (5): 400–416. https://doi.org/10.1177/1098612x16643252.

Case, J Brad, Sarah J Marvel, Pedro Boscan, and Eric L Monnet. 2011. “Surgical Time and Severity of Postoperative Pain with One , Two , or Three Instrument Cannulas.” *JAVMA, Journal of American Veterinary Medical Association* 239: 203–8.

Christensen, Bruce W. 2018. “Canine Prostate Disease.” *Veterinary Clinics of North America - Small Animal Practice* 48 (4): 701–19. https://doi.org/10.1016/j.cvsm.2018.02.012.

Chun, Ruthanne. 2015. “Hemangiosarcoma.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 441–43. St. Louis, Missouri: Elsevier.

Clark, Kathryn. 2012. “Neutering: How Early Is Too Early?” *The Veterinary Record*. https://doi.org/10.1136/vr.e2953.

Clifford, Craig, and Louis-Philippe De Lorimier. 2017. “Chapter 347: Hemangiosarcoma.” In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 5062–85. St. Louis, Missouri: Elsevier.

Cohn, Leah. 2015. “Urethral Sphincter Mechanism Incompetence.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 1036–37. St. Louis, Missouri: Elsevier.

Cooley, Dawn M., Benjamin C. Beranek, Deborah L. Schlittler, Nita W. Glickman, Lawrence T. Glickman, and David J. Waters. 2002. “Endogenous Gonadal Hormone Exposure and Bone Sarcoma Risk.” *Cancer Epidemiology Biomarkers and Prevention* 11 (11): 1434–40. https://doi.org/10.1361/arpe2007p033.

Courcier, E. A., R. M. Thomson, D. J. Mellor, and P. S. Yam. 2010. “An Epidemiological Study of Environmental Factors Associated with Canine Obesity.” *Journal of Small Animal Practice* 51 (7): 362–67. https://doi.org/10.1111/j.1748-5827.2010.00933.x.

Daminet, Sylvie. 2015. “Hyperthyroidism.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 515–17. St. Louis, Missouri: Elsevier Mosby.

Davidson, Autumn. 2004a. “Chapter 56: The Practice of Theriogenology.” In *Small Animal Internal Medicine*, edited by Guillermo Nelson, Richard; Couto, Fifth, 897–914. St. Louis, Missouri: Elsevier.

Davidson, Autumn. 2004b. “Chapter 57: Clinical Conditions of the Bitch and Queen.” In *Small Animal Internal Medicine*, edited by Guillermo Nelson, Richard; Couto, Fifth, 915–43. St. Louis, Missouri: Elsevier.

Davidson, Autumn. 2010. “Chapter 14: Problems during and after Parturition.” In *BSAVA Manual of Canine and Feline Reproduction and Neonatology*, edited by Angelika von; England, Gary; Heimendahl, Second, 128–42. British Small Animal Veterinary Association.

Davidson, Autumn. 2017. “Chapter 315: Pregnancy, Parturition and Periparturient Problems in Dogs and Cats.” In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 4516–39. St. Louis, Missouri: Elsevier.

Davidson, Ellen B., H. David Moll, and Mark E. Payton. 2004. “Comparison of Laparoscopic Ovariohysterectomy and Ovariohysterectomy in Dogs.” *Veterinary Surgery* 33 (1): 62–69. https://doi.org/10.1111/j.1532-950X.2004.04003.x.

Day, M. J., M. C. Horzinek, R. D. Schultz, and R. A. Squires. 2016. “WSAVA Guidelines for the Vaccination of Dogs and Cats.” *Journal of Small Animal Practice* 57 (1): 4–8. https://doi.org/10.1111/jsap.12431.

Day, Michael J. 2017. “Small Animal Vaccination: A Practical Guide for Vets in the UK.” *In Practice* 39 (3): 110–18. https://doi.org/10.1136/inp.j615.

"Decreto-Lei Nº 313/2003." 2003. *De 17 de Dezembro, Diário Da República Nº 290/03 - I Série A. Ministério Da Agricultura, Desenvolvimento Rural e Pescas. Lisboa.*

Donaldson, Caroline. 2015. "Chocolate Toxicosis." In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 178–79. St. Louis, Missouri: Elsevier Mosby.

Duerr, Felix M., Colleen G. Duncan, Roman S. Savicky, Richard D. Park, Erick L. Egger, and Ross H. Palmer. 2007. "Risk Factors for Excessive Tibial Plateau Angle in Large-Breed Dogs with Cranial Cruciate Ligament Disease." *Journal of the American Veterinary Medical Association* 231 (11): 1688–91. https://doi.org/10.2460/javma.231.11.1688.

Duval, J.M., S.C. Budsberg, and G.L. Flo. 1999. "Breed, Sex, and Body Weight as Risk Factors for Rupture of the Cranial Cruciate Ligament in Young Dogs." *Journal of the American Veterinary Medical Association*, no. 215: 811–14.

Edney, A. T. B., and P.M. Smith. 1986. "Study of Obesity in Dogs Visiting Veterinary Practices in the United Kingdom." *Veterinary Record*, no. 118: 391–96.

Ellis, J. A., S. P. Gow, C. L. Waldner, S. Shields, S. Wappel, A. Bowers, S. Lacoste, Z. Xu, and E. Ball. 2016. "Comparative Efficacy of Intranasal and Oral Vaccines against Bordetella Bronchiseptica in Dogs." *Veterinary Journal*. https://doi.org/10.1016/j.tvjl.2016.04.004.

England, Gary. 2010a. "Chapter 1: Physiology and Endocrinology of the Female." In *BSAVA Manual of Canine and Feline Reproduction and Neonatology*, edited by Angelika von; England, Gary; Heimendahl, Second, 1–12. British Small Animal Veterinary Association.

England, Gary. 2010b. "Chapter 2: Physiology and Endocrinology of the Male." In *BSAVA Manual of Canine and Feline Reproduction and Neonatology*, edited by Angelika von England, Gary; Heimendahl, Second, 13–22. British Small Animal Veterinary Association.

"Feline Hyperthyroidism." 2004. In *BSAVA Manual of Canine and Feline Endocrinology*, Third, 95–111. Dorset, United Kingdom.

Ford, Richard. 2004. "Chapter 49: Infectious Tracheobronchitis." In *Textbook of Respiratory Disease in Dogs and Cats*, edited by Lesley King. Elsevier Saunders.

Fransson, Boel A. 2012. "Chapter 109: Ovaries and Uterus System." In *Veterinary Surgery: Small Animal*, edited by Spencer A. Tobias, Karen M.; Johnston, First, 1871–90. St. Louis, Missouri: Elsevier Saunders.

Freitag, Thurid, Richard M Jerram, Alex M Walker, and Chris G A Warman. 2007. "Surgical Management of Common Canine Prostatic Conditions." *Compendium (Yardley, PA)* 29 (11): 656–8, 660, 662–3 passim; quiz 673. http://www.ncbi.nlm.nih.gov/pubmed/18210976.

Gemensky-Metzler, Anne. 2015. "Corneal Ulceration." In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 229–32. St. Louis, Missouri: Elsevier Mosby.

Gieger, Tracy. 2015. "Mast Cell Tumors." In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 643–48. St. Louis, Missouri: Elsevier Mosby.

Glassman, Mathieu;, and Johnston Spencer. 2015. "Hip Dysplasia." In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Êtienne Côté, Third, 487–89. St. Louis, Missouri: Elsevier Mosby.

Glickman, L. T., M. Raghavan, D. W. Knapp, P. L. Bonney, and M. H. Dawson. 2004. "Herbicide Exposure and the Risk of Transitional Cell Carcinoma of the Urinary Bladder in Scottish Terriers." *Journal of the American Veterinary Medical Association* 224 (8): 1290–1297.

Gobello, Cristina, and Yanina Corrada. 2002. "Noninfectious Prostatic Diseases in Dogs." *Compendium* 24 (2): 99–108.

Goethem, Bart Van, Auke Schaefers-Okkens, and Jolle Kirpensteijn. 2006. "Making a Rational Choice between Ovariectomy and Ovariohysterectomy in the Dog: A Discussion of the Benefits of Either Technique." *Veterinary Surgery* 35 (2): 136–43.

https://doi.org/10.1111/j.1532-950X.2006.00124.x.

Goh, Clara S. S. 2016. “A Mater of Opinion - Age of Neutering in Large- and Giant-Breed Dogs.” *Clinician’s Brief*, 20–23. https://www.cliniciansbrief.com/sites/default/files/attachments/AMO_Age of Neutering in Large- %26 Giant-Breed Dogs.pdf.

Grüntzig, K., R. Graf, G. Boo, F. Guscetti, M. Hässig, K. W. Axhausen, S. Fabrikant, et al. 2016. “Swiss Canine Cancer Registry 1955–2008: Occurrence of the Most Common Tumour Diagnoses and Influence of Age, Breed, Body Size, Sex and Neutering Status on Tumour Development.” *Journal of Comparative Pathology* 155 (2–3): 156–70. https://doi.org/10.1016/j.jcpa.2016.05.011.

Guptill, L., L. Glickman, and N. Glickmanc. 2003. “Time Trends and Risk Factors for Diabetes Mellitus in Dogs: Analysis of Veterinary Medical Data Base Records (1970–1999).” *The Veterinary Journal* 163 (3): 240–47.

Hagen, M.A. van, B.J. Ducro, J. van den Broek, and B. W. Knol. 2005. “Incidence, Risk Factors, and Heritability Estimates of Hind Limb Lameness Caused by Hip Dysplasia in a Birth Cohort of Boxers.” *American Journal of Veterinary Research*, no. 66: 307–12.

Hagman, Ragnvi. 2018. “Pyometra in Small Animals.” *Veterinary Clinics of North America - Small Animal Practice* 48 (4): 639–61. https://doi.org/10.1016/j.cvsm.2018.03.001.

Hamilton, K. H., E. R. Henderson, M. Toscano, and G. P. Chanoit. 2014. “Comparison of Postoperative Complications in Healthy Dogs Undergoing Open and Closed Orchidectomy.” *Journal of Small Animal Practice* 55 (10): 521–26. https://doi.org/10.1111/jsap.12266.

Hart, Benjamin L., Lynette A. Hart, Abigail P. Thigpen, and Neil H. Willits. 2014. “Long-Term Health Effects of Neutering Dogs: Comparison of Labrador Retrievers with Golden Retrievers.” *PLoS ONE* 9 (7). https://doi.org/10.1371/journal.pone.0102241.

Hart, Benjamin L, Lynette A Hart, Abigail P Thigpen, and Neil H Willits. 2016. “Original Article Neutering of German Shepherd Dogs : Associated Joint Disorders , Cancers and Urinary Incontinence,” 191–99. https://doi.org/10.1002/vms3.34.

Holloway, Cheryl. 2015. “Obesity.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 711–12. St. Louis, Missouri: Elsevier Ltd.

Houlihan, Kendall. 2017. “A Literature Review on the Welfare Implications of Gonadectomy of Dogs.” *Journal of the American Veterinary Medical Association* 250 (10): 1155–66. https://doi.org/10.1007/BF00726005.

Howe, Lisa. 2015. “Current Perspectives on the Optimal Age to Spay/Castrate Dogs and Cats.” *Veterinary Medicine: Research and Reports*, 171. https://doi.org/10.2147/vmrr.s53264.

“Investigations under Way in Wake of Feline TB Outbreak.” 2018. Veterinary Ttimes. 2018. https://www.vettimes.co.uk/news/investigations-under-way-in-wake-of-feline-tb-outbreak/.

IRIS Staging of CKD. 2017. “IRIS Staging of CKD (Modified 2017).” *Elanco Animal Health*, no. 10213173: 1–8.

Johnson, Kirstin C., and Andrew Mackin. 2012a. “Canine Immune-Mediated Polyarthritis: PART 2: Diagnosis and Treatment.” *Journal of the American Animal Hospital Association* 48 (2): 71–82. https://doi.org/10.5326/JAAHA-MS-5756.

Johnson, Kirstin C., and Andrew Mackin. 2012b. “Canine Immune-Mediated Polyarthritis.” *Journal of the American Animal Hospital Association* 48 (1): 12–17. https://doi.org/10.5326/JAAHA-MS-5744.

Kent, Marc, Simon R. Platt, and Scott J. Schatzberg. 2010. “The Neurology of Balance: Function and Dysfunction of the Vestibular System in Dogs and Cats.” *Veterinary Journal* 185 (3): 247–58. https://doi.org/10.1016/j.tvjl.2009.10.029.

Kowaleski, Michael P.; Boudrieau, Randy J. 2012. “Stifle Joint.” In *Veterinary Surgery: Small Animal*, edited by Spencer Tobias, Karen; Johnston, 906–98. Elsevier Mosby.

Kristiansen, V. M., Pena, L., Diez Cordova, L., Illera, J. C., Skjerve, E., Breen, A. M., ... & Sørenmo, K. U. 2016. Effect of ovariohysterectomy at the time of tumor removal in dogs with mammary carcinomas: a randomized controlled trial. *Journal of veterinary internal medicine*, *30*(1), 230-241.

Kustritz, Margaret Root. 2007. “Determining the Optimal Age for Gonadectomy of Dogs and Cats.” *Journal of the American Veterinary Medical Association* 231 (11): 1665–75. https://doi.org/10.2460/javma.231.11.1665.

Kustritz, Margaret V. Root, Margaret R. Slater, G. Robert Weedon, and Philip A. Busby. 2017. “Determining Optimal Age for Gonadectomy in the Dog: A Critical Review of the Literature to Guide Decision Making.” *Clinical Theriogenology* 9 (2): 167–211. https://pdfs.semanticscholar.org/261b/4fbcaedb2d1ece83d05442c76e620920cc91.pdf.

Labato, Mary Anna. 2017. “Chapter 46: Pollakiuria, Stranguria, and Urinary Incontinence.” In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 666–72. St. Louis, Missouri: Elsevier.

Langston, Cathy; Eatroff, Adam. 2015. “Chronic Kidney Disease.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 186–90. St. Louis, Missouri: Elsevier Mosby.

Ledbetter, Eric, Brian C Gilger, and N Gelatt. 2014. “Diseases and Surgery of the Canine Cornea and Sclera.” *Veterinary Ophthalmology* Fifth Edit (Chapter 11): 216–48.

Lefebvre, Sandra L., Mingyin Yang, Mansen Wang, Denise A. Elliott, Preston R. Buff, and Elizabeth M. Lund. 2013. “Effect of Age at Gonadectomy on the Probability of Dogs Becoming Overweight.” *Journal of the American Veterinary Medical Association* 243 (2): 236–43. https://doi.org/10.2460/javma.243.2.236.

Linn, Kathleen. 2015. “Cranial Cruciate Ligament Injury and Associated Disorders.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 237–39. St. Louis, Missouri: Elsevier Mosby.

Ljungvall, Ingrid; Häggström, Jens. 2015. “Mitral/Tricuspid Regurgitation Due to Myxomatous Valve Degeneration.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 668–70. St. Louis, Missouri: Elsevier Mosby.

Lopate, Cheryl. 2015. “Uterine Disorders, Non-Neoplastic.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third. St. Louis, Missouri: Elsevier Mosby.

MacPhail, Catriona. 2013. “Chapter 27: Surgery of the Reproductive and Genital Systems.” In *Small Animal Surgery*, edited by Theresa Welch Fossum, Fourth, 714–29. St. Louis, Missouri: Elsevier Mosby.

Mahony, Orla. 2015. “Polyarthritis.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 821–23. St. Louis, Missouri: Elsevier Mosby.

Malone, Erik. 2015. “Mammary Gland Neoplasia, Dog.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 635–37. St. Louis, Missouri: Elsevier Mosby.

Mansfield, C., and T. Beths. 2015. “Management of Acute Pancreatitis in Dogs: A Critical Appraisal with Focus on Feeding and Analgesia.” *Journal of Small Animal Practice* 56 (1): 27–39. https://doi.org/10.1111/jsap.12296.

Mao, J., Z. Xia, J. Chen, and J. Yu. 2013. “Prevalence and Risk Factors for Canine Obesity Surveyed in Veterinary Practices in Beijing,China.” *Prev Vet Med*, no. 112: 438–42.

Marcellin-Little, Denis. 2017. “Chapter 353: Skeletal Disorders in Companion Animals.” In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 5179. St. Louis, Missouri: Elsevier.

Martin, Josep; Fernandez, Sonia. 2010. “Chapter 17: ‘Clinical Approach to Mammary Gland Disease.’” In *BSAVA Manual of Canine and Feline Reproduction and Neonatology*, edited by Angelika von; England, Gary; Heimendahl, Second, 162–73. British Small Animal Veterinary Association.

Mattin, M, D O Neill, D Church, P D Mcgreevy, P C Thomson, D Brodbelt, and Hawkshead Lane. 2014. “An Epidemiological Study of Diabetes Mellitus in Dogs Attending First Opinion Practice in the UK.” *Veterinary Record*, no. 2003. https://doi.org/10.1136/vr.101950.

Misdorp, W. 1988. “Canine Mammary Tumours: Protective Effect of Late Ovariectomy and Stimulating Effect of Progestins.” *Vet Q*, no. 10: 26–31.

NOAH. 2014. “National Office of Animal Health: Veterinary Medicine Classifications.” National Office of Animal Health. 2014. http://www.noahcompendium.co.uk/Compendium/Overview/-42802.html.

Noakes, David E. 2018. “Chapter 10: Caesarean Hysterotomy in Dogs and Cats.” In *Arthur’s Veterinary Reproduction and Obstetrics*, edited by David E. Noakes, Timothy J. Parkinson, and Gary C. W. England, Tenth, 330. Elsevier Health Sciences.

Norris, Alan M., Elizabeth J. Laing, Victor E. Vallii, Stephen J. Withrow, Dennis W. Macy, Gregory K. Ogilivie, Jim Tomlinson, Dudley McCaw, Guy Pidgeon, and Robert M. Jacobs. 1992. “Canine Bladder and Urethral Tumors: A Retrospective Study of 11 5 Cases.” *Journal of Veterinary Internal Medicine* 6: 145–53.

Nuttall, Tim. 2016. “Successful Management of Otitis Externa MANAGING THE DISEASE.” *In Practice FOCUS*, no. May: 17–21.

O’Halloran, Conor, Danièlle Gunn-Moore, Nicki Reed, Julie Vickers, Eili Dettmering, Olympia Ioannidi, and Kevin Murtagh. 2018. “Mycobacterium Bovis in Pet Cats.” *Veterinary Record* 183 (16): 510. https://doi.org/10.1136/vr.k4452.

Onclin-Verstegen, Karine J.; Kutzler Michelle A. 2015. “Pyometra.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 877–79. St. Louis, Missouri: Elsevier Mosby.

Páramo-Ramírez, Rosa María. 2015. “Transmissible Venereal Tumor.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 1016–18. St. Louis, Missouri: Elsevier Mosby.

Paterson, Sue. 2016. “Discovering the Causes of Otitis Externa.” *In Practice*, no. 38: 7–11.

Polzin, David J. 2013. “Evidence-Based Step-Wise Approach to Managing Chronic Kidney Disease in Dogs and Cats.” *Journal of Veterinary Emergency and Critical Care* 23 (2): 205–15. https://doi.org/10.1111/vec.12034.

Priester, W. A. 1979. “Occurrence of Mammary Neoplasms in Bitches in Relation to Breed, Age, Tumour Type, and Geographical Region from Which Reported.” *Journal of Small Animal Practice*, no. 20: 1–11.

Prymak, C., L. J. McKee, M. H. Goldschmidt, and L.T. Glickman. 1988. “Epidemiologic, Clinical, Pathologic, and Prognostic Characteristics of Splenic Hemangiosarcoma and Splenic Hematoma in Dogs: 217 Cases (1985).” *Journal of the American Veterinary Medical Association*, no. 193: 706–12.

Rooster, Hilde de, and Nathalie Porters. 2017. “Effect of Spay or Castration on Long-Term Health of Dogs and Cats.” In *Textbook of Veterinary Internal Medicine: Diseae of the Dog and the Cat*, 4493–4501.

Root Kustritz, M. V. 2012. “Effects of Surgical Sterilization on Canine and Feline Health and on Society.” *Reproduction in Domestic Animals* 47 (SUPPL.4): 214–22. https://doi.org/10.1111/j.1439-0531.2012.02078.x.

Schneider, Robert, C. Richard Dorn, and D. O. N. Taylor. 1968. “Factors Influencing Canine

Mammary Cancer Development and Postsurgical Survival." *National Cancer Institute*, no. 43: 1249–61. http://jnci.oxfordjournals.org/.

Schulz, Kurt S. 2013. "Chapter 34: Diseases of the Joints." In *Small Animal Surgery*, edited by Theresa Welch Fossum, Fourth. St. Louis, Missouri: Elsevier Mosby.

Scott-Moncrieff, J. C. R. 2004. "Chapter 98: Pathogenesis of Immune- Mediated Disorders." In *Small Animal Internal Medicine*, edited by Guillermo Nelson, Richard; Couto, Fifth, 1398–1441. St. Louis, Missouri: Elsevier.

Scott, Danny W. 2015. "Otitis Externa." In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 742–44. St. Louis, Missouri: Elsevier Mosby.

Slauterbeck, J. R., K. Pankratz, K.T. Xu, S.C. Bozeman, and D.M. Hardy. 2004. "Canine Ovariohysterectomy and Orchiectomy Increases the Prevalence of ACL Injury." *Clinical Orthopaedics and Related Research*, no. 429: 301–5.

Smith, J. 2008. "Canine Prostatic Disease: A Review of Anatomy, Pathology, Diagnosis, and Treatment." *Theriogenology* 70 (3): 375–83. https://doi.org/10.1016/j.theriogenology.2008.04.039.

Sonnenschein, E. G., L.T. Glickman, and M.H. Goldschmidt. 1991. "Body Conformation, Diet, and Risk of Breast Cancer in Pet Dogs: A Case-Control Study." *American Journal of Epidemiology*, no. 133: 694–703.

Sorenmo, K. U., M. Goldschmidt, F. Shofer, C. Goldkamp, and J. Ferracone. 2003. "Immunohistochemical Characterization of Canine Prostatic Carcinoma and Correlation with Castration Status and Castration Time." *Veterinary and Comparative Oncology* 1 (1): 48–56. https://doi.org/10.1046/j.1476-5829.2003.00007.x.

Spain, C. Victor, Janet M. Scarlett, and Katherine A. Houpt. 2004. "Long-Term Risks and Benefits of Early-Age Gonadectomy in Dogs." *Journal of the American Veterinary Medical Association*. https://doi.org/10.2460/javma.2004.224.380.

Steiner, Jorg M. 2015. "Pancreatitis in Dogs and Cats." In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 755–59. St. Louis, Missouri: Elsevier Mosby.

Stojanovic, Vladimir. 2015. "Diabetes Mellitus." In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third. St. Louis, Missouri: Elsevier Mosby.

Stone, Michael. 2017. "Chapter 203: Immune-Mediated Polyarthritis and Other Polyarthritides." In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 2151–60. St. Louis, Missouri: Elsevier.

Sundburg, Crystal R., Janelle M. Belanger, Danika L. Bannasch, Thomas R. Famula, and Anita M. Oberbauer. 2016. "Gonadectomy Effects on the Risk of Immune Disorders in the Dog: A Retrospective Study." *BMC Veterinary Research* 12 (1): 1–10. https://doi.org/10.1186/s12917-016-0911-5.

Taylor-Brown, F.E., R.L. Meeson, D.C. Brodbelt, D. B. Church, P. D. McGreevy, P.C. Thomson, and D.G. O'Neill. 2015. "Epidemiology of Cranial Cruciate Ligament Disease Diagnosis in Dogs Attending Primary-Care Veterinary Practices in England." *Veterinary Surgery*, no. 44: 777–83.

Teske, E., E. Naana, E.M. van Dijk, E- Van Garderen, and J.A. Schalken. 2002. "Canine Prostate Carcinoma: Epidemiological Evidence of an Increased Risk in Castrated Dogs." *Molecular and Cellular Endocrinology* 197 (1–2): 251–55.

Thamn, Douglas. 2017. "Chapter 349: Mast Cell Disease." In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 5118–1530. St. Louis, Missouri.

"The Control of Dogs Order." 1992. *Statutory Instruments No.901*.

"The Microchipping of Dogs." 2015. *England Regulations*.

Torres de la Riva, Gretel, Benjamin L. Hart, Thomas B. Farver, Anita M. Oberbauer, Locksley L.Mc V. Messam, Neil Willits, and Lynette A. Hart. 2013. "Neutering Dogs: Effects on Joint Disorders and Cancers in Golden Retrievers." *PLoS ONE* 8 (2). https://doi.org/10.1371/journal.pone.0055937.

Towle, Heather A. 2012. "Chapter 111: Testes and Scrotum." In *Veterinary Surgery: Small Animal*, 1903–16.

Troxel, M.; Drobatz, K.; Charles, V. 2005. "Signs of Neurologic Dysfunction in Dogs with Central versus Peripheral Vestibular Disease." *Journal of the American Veterinary Medical Association*, no. 227 (4): 570–74. https://doi.org/10.2460/javma.2005.227.570.

Troxel, Mark. 2015. "Vestibular Disease." In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 1069–70. St. Louis, Missouri: Elsevier Mosby.

Unterer, Stefan. 2017. "Chapter 278: Rectoanal Disease." In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 3893–3923. St. Louis, Missouri: Elsevier.

Vail, David M. 2017. "Chapter 344: Hematopoietic Tumors." In *Textbook of Veterinary Internal Medicine*, edited by Etienne Ettinger, Stephen; Feldman, Edward; Côté, Eighth, 5000–5015. St. Louis, Missouri: Elsevier.

Villamil, J. Armando, Carolyn J. Henry, Allen W. Hahn, Jeffrey N. Bryan, Jeff W. Tyler, and Charles W. Caldwell. 2009. "Hormonal and Sex Impact on the Epidemiology of Canine Lymphoma." *Journal of Cancer Epidemiology* 2009: 1–7. https://doi.org/10.1155/2009/591753.

W. Beauvais, J. M. Cardwell and D. C. Brodbelt. 2012. "The Effect of Neutering on the Risk of Mammary Tumours in Dogs – a Systematic Review." *Journal of Small Animal Practice* 53 (June): 1–9. https://doi.org/10.1111/j.1748-5827.2012.01220.x.

Ware, W. A., and D. L. Hopper. 1999. "Cardiac Tumors in Dogs:1982-1995." *Journal of Veterinary Internal Medicine*, no. 13: 95–103.

Warland, James, Valentina Brioschi, Laura Owen, and Jane Dobson. 2015. "Canine Mast Cell Tumours: Decision-Making and Treatment." *In Practice* 37 (7): 315–32. https://doi.org/10.1136/inp.h3440.

Warnes, Caroline. 2018. "An Update on the Risks and Benefits of Neutering in Dogs." *The Veterinary Nurse* 9 (3): 150–55. https://doi.org/10.12968/vetn.2018.9.3.150.

Waters, D. J., S. S. Kengeri, A. H. Maras, C. L. Suckow, and E. C. Chiang. 2017. "Life Course Analysis of the Impact of Mammary Cancer and Pyometra on Age-Anchored Life Expectancy in Female Rottweilers: Implications for Envisioning Ovary Conservation as a Strategy to Promote Healthy Longevity in Pet Dogs." *Veterinary Journal* 224: 25–37. https://doi.org/10.1016/j.tvjl.2017.05.006.

Watson, P. 2015. "Pancreatitis in Dogs and Cats: Definitions and Pathophysiology." *Journal of Small Animal Practice* 56 (1): 3–12. https://doi.org/10.1111/jsap.12293.

Watson, Penny. 2015. "Canine and Feline Pancreatitis." *Journal of Small Animal Practice* 56 (January): 1–2. https://secure.vlsstore.com/ME2/Audiences/dirmod.asp?nm=CE+Programs&type=Publishing&mod=Publications::Article&mid=8F3A7027421841978F18BE895F87F791&tier=4&id=462D7CFE2AAF4872AE16AAE8C9E0CC7D&AudID=BE924B06C44442DE9033CA13B621B284.

Westermeyer, Hans; Hendrix, Diane. 2012. "Chapter 124: Basic Ophtalmic Surgical Procedures." In *Veterinary Surgery: Small Animal*, edited by Spencer Tobias, Karen; Johnston, 2091–2119. Elsevier Saunders.

Wheeler, Richard. 2015. “Cryptorchidism.” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Third, 244. St. Louis, Missouri: Elsevier Mosby.

White, Carrie R, Ann E Hohenhaus, Jennifer Kelsey, and Elizabeth Procter-gray. 2011. “Cutaneous MCTs : Associations with Spay / Neuter Status , Breed , Body Size , and Phylogenetic Cluster,” 210–16. https://doi.org/10.5326/JAAHA-MS-5621.

White, Joanna, Natalie Finch, Jessica Quimby, Isuru Gajanayake, Catherine Langston, Jonathan Elliott, Serge Chalhoub, Andrew H Sparkes, Hervé P Lefebvre, and Sarah Caney. 2016. “ISFM Consensus Guidelines on the Diagnosis and Management of Feline Chronic Kidney Disease.” *Journal of Feline Medicine and Surgery* 18 (3): 219–39. https://doi.org/10.1177/1098612x16631234.

Whitehair, J. G., P.B. Vasseur, and N.H. Willits. 1993. “Epidemiology of Cranial Cruciate Ligament Rupture in Dogs.” *Journal of the American Veterinary Medical Association*, no. 203: 1016–19.

Williams, Laurel E. 2015. “Lymphoma, Dog (Multicentric).” In *Clinical Veterinary Advisor: Dogs and Cats*, edited by Etienne Côté, Fiftth, 618–20. St. Louis, Missouri: Elsevier Mosby.

Witsberger, Tige H., J. Armando Villamil, Loren G. Schultz, Allen W. Hahn, and James L. Cook. 2008. “Prevalence of and Risk Factors for Hip Dysplasia and Cranial Cruciate Ligament Deficiency in Dogs.” *Journal of the American Veterinary Medical Association* 232 (12): 1818–24. https://doi.org/10.2460/javma.232.12.1818.

WSAVA Global Pain Council. 2014. “Caesarean Section.” *Journal of Feline Medicine and Surgery*.

Xenoulis, P. G. 2015. “Diagnosis of Pancreatitis in Dogs and Cats.” *Journal of Small Animal Practice* 56 (1): 13–26. https://doi.org/10.1111/jsap.12274.

Xenoulis, Panagiotis G, Jan S Suchodolski, and Jorg M Steiner. 2008. “Chronic Pancreatitis in Dogs and Cats.” *Compendium (Yardley, PA)* 30 (3): 166-80; quiz 180-1. http://www.ncbi.nlm.nih.gov/pubmed/18409143.

Yates, David, and Rosa Leedham. 2019. “Prepubertal Neutering of Dogs — Some Risks and Benefits.” *Companion Animal* 24 (1): 38–42. https://doi.org/10.12968/coan.2019.24.1.38.

Zink, ChristineM., Parvene Farhoody, Samra E. Elser, Lynda D. Ruffini, Tom A. Gibbons, and Randall H. Rieger. 2014. “Evaluation of the Risk and Age of Onset of Cancer and Behavioral Disorders in Gonadectomized Vizslas.” *Journal of the American Veterinary Medical Association* 244 (3): 309–19. https://doi.org/https://doi.org/10.2460/javma.244.3.309.