



UNIVERSITI PUTRA MALAYSIA

***CANCER CHEMOTHERAPY PRACTICE IN DOGS AND CATS IN
UNIVERSITY VETERINARY HOSPITAL, UPM: A RETROSPECTIVE
STUDY FROM 2013 TO 2017***

EVELYN TIE YII YII

FPV 2018 22

**CANCER CHEMOTHERAPY PRACTICE IN DOGS AND CATS IN
UNIVERSITY VETERINARY HOSPITAL, UPM: A RETROSPECTIVE STUDY
FROM 2013 TO 2017**

EVELYN TIE YII YII

A project paper submitted to the
Faculty of Veterinary Medicine, Universiti Putra Malaysia

In partial fulfilment of the requirement for the
DEGREE OF DOCTOR OF VETERINARY MEDICINE

Universiti Putra Malaysia
Serdang, Selangor Darul Ehsan.

MARCH 2018

It is hereby certified that we have read this project paper entitled “**CANCER CHEMOTHERAPY PRACTICE IN DOGS AND CATS IN UNIVERSITY VETERINARY HOSPITAL, UPM: A RETROSPECTIVE STUDY FROM 2013 TO 2017**” by Evelyn Tie Yii Yii and in our opinion, it is satisfactory in terms of scope, quality and presentation as partial fulfilment of the requirement for the course VPD 4999 – Final Year Project.

ASSOC. PROF. DR. GAYATHRI THEVI SELVARAJAH
D.V.M (UPM), PhD (Netherlands)
Senior Lecturer
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Supervisor)

DR. THONG HOE FOONG
D.V.M. (UPM)
Veterinary Officer
University Veterinary Hospital
Universiti Putra Malaysia
(Co-Supervisor)

This project is special dedicated to:

All veterinarians

My family and friends who always beside me

Dogs and cats we so value.



COPYRIGHT

UPM

ACKNOWLEDGEMENTS

First and foremost, I would like to thank my project supervisor, Assoc. Prof. Dr. Gayathri Thevi Selvarajah for the time, wisdom, expertise, and guidance that she had granted me throughout the duration of this project, and my studies at the faculty.

I also would like to thank my project co-supervisor, Dr. Thong Hoe Foong for his assistance, unwavering support and encouragement to improve this project.

Besides, I would like to thank assistant veterinary officer, Ms. Aisas and staff of University Veterinary Hospital (UVH), UPM: Mr. Didi and Ms. Mageswari for always lending me a helping hand when retrieving case files and collecting data.

A special thank you to my final year project gang including Xhirryne Yong, Lee Jie Min, Set Thing, Joy Xine, Samuel and Ikhwan who collecting data together with me throughout the duration of final year project. I also would like to thank all my classmates of DVM 2018 who assisted my directly or indirectly.

Last but not least, my most heartfelt gratitude to my family, especially my parents for their support throughout my studies.

TABLE OF CONTENTS

TITLE	i
CERTIFICATION	ii
DEDICATION	iii
ACKNOWLEDGEMENTS	iv
TABLE OF CONTENTS	v
LIST OF TABLES	vii
LIST OF FIGURES	viii
ABSTRAK	ix
ABSTRACT	xi
1.0 INTRODUCTION	1
2.0 LITERATURE REVIEW	
2.1 Demographic of tumour in dogs and cats	4
2.2 Common types of tumour in dogs	5
2.3 Common types of tumour in cats	6
2.4 Current treatments for tumour in dogs and cats	7
2.5 Basic cancer chemotherapy principle	
2.5.1 Use of chemotherapy	9
2.5.2 Mechanism of action	10
2.6 Use of cancer chemotherapeutic agents	
2.6.1 Common classes of chemotherapeutic agents	10
2.6.2 Combination of chemotherapeutic agents	15

2.6.3 Routes of administration of chemotherapeutic agents	16
2.7 Side effects of chemotherapeutic agents	
2.7.1 Hematologic toxicity	18
2.7.2 Gastrointestinal toxicity	19
2.7.3 Skin reaction	20
2.7.4 Specific drugs associated toxicities	21
2.8 Cost of chemotherapy	22
3.0 MATERIALS AND METHODS	
3.1 Study population	23
3.2 Retrospective data acquisition	23
3.3 Data analysis	24
4.0 RESULTS	26
5.0 DISCUSSION	45
6.0 CONCLUSION	53
REFERENCES	54
APPENDIX	61

LIST OF TABLES

	Page
Table 1: Types of breed in dogs receiving chemotherapy	27
Table 2: Types of tumour in dogs receiving cancer chemotherapy	31
Table 3: Types of tumour in cats receiving cancer chemotherapy	31
Table 4: Side effects of cancer chemotherapy in dogs	38
Table 5: Side effects of cancer chemotherapy in cats	39
Table 6: Risk factors of receiving cancer chemotherapy between types of breed in dogs and cats	44

LIST OF FIGURES

	Page
Figure 1: Number of animals treated with cytotoxic cancer chemotherapy.	26
Figure 2: Age distribution in dogs receiving chemotherapy.	28
Figure 3: Age distribution in cats receiving chemotherapy.	29
Figure 4: Tumour locations in dogs receiving chemotherapy.	30
Figure 5: Tumour location in cats receiving chemotherapy.	30
Figure 6: Number of injectable cytotoxic chemotherapy drugs.	32
Figure 7: Types of injectable cytotoxic drugs.	33
Figure 8: Types of injectable cytotoxic drugs used in dogs.	34
Figure 9: Types of injectable cytotoxic drugs used in cats.	34
Figure 10: Vincristine used in dogs and cats.	35
Figure 11: Carboplatin used in dogs and cats.	35
Figure 12: Cyclophosphamide used in dogs and cats.	36
Figure 13: Doxorubicin used in dogs and cats.	36
Figure 14: Injection sites of cytotoxic chemotherapy drugs in dogs and cats.	37
Figure 15: Total income generated by UVH through cancer chemotherapy service.	40
Figure 16: Total income generated through cancer chemotherapy in dogs and cats.	41
Figure 17: Kaplan-Meier survival curve in dogs between types of pedigree.	42
Figure 18: Kaplan-Meier survival curve in dogs between lymphoma and TVT.	42
Figure 19: Kaplan-Meier survival curve in cats between DSH and other breeds.	43

ABSTRAK

Abstrak daripada kertas projek yang dikemukkakan kepada Fakulti Perubatan Veterinar untuk memenuhi sebahagian daripada keperluan kursus VPD 4999 – Projek Ilmiah Tahun Akhir.

EVELYN TIE YII YII**Penyelia: Prof. Madya Dr. Gayathri Thevi Selvarajah****Penyelia bersama: Dr. Thong Hoe Foong****AMALAN KEMOTERAPI KANSER PADA ANJING DAN KUCING DI
HOSPITAL VETERINAR UNIVERSITI (UVH), UPM: SATU KAJIAN
RETROSPEKTIF DARI TAHUN 2013–2017**

Kebanyakan amalan veterinar haiwan kecil yang menyediakan amalan kemoterapi berada di kawasan Selangor, dan Hospital Veterinar Universiti (UVH) adalah salah satu daripadanya (Loh *et al.*, 2014). Maklumat mengenai amalan kemoterapi di UVH, UPM belum dinilai secara retrospektif. Objektif kajian ini adalah (1) menentukan bilangan dan jenis kanser pada anjing dan kucing yang dirawat dengan kemoterapi sitotoksik, (2) menentukan jenis ubat, kekerapan penghantaran dan kesan sampingan yang dilaporkan berdasarkan pelbagai ubat sitotoksik yang dihantar dan (3) untuk menentukan kos yang dikenakan dalam protokol kemoterapi pelbagai kanser dalam anjing dan kucing yang dirawat di UVH antara tahun 2013 dan 2017. Kajian ini dijalankan secara retrospektif

dengan mengkaji buku log kes yang terdapat dalam Bilik Kemoterapi dan rekod dalam UVH. Data yang dikumpulkan tertakluk kepada analisis deskriptif menggunakan SPSS versi 20.0. Ujian sebenar Fisher dan analisis Kaplan-Meier telah dilakukan di mana perlu. Nilai $P < 0.05$ dianggapkan tererti statistik pada selang keyakinan 95%. Sebanyak 113 haiwan menerima kemoterapi sitotoksik untuk kanser dalam UVH (83 anjing dan 30 kucing). Sebanyak 429 dos (78%) ubat sitotoksik suntikan diberikan kepada anjing dan 123 dos (22%) kepada kucing. Kanser yang paling biasa dirawat pada anjing adalah tumor venereal boleh pindah manakala limfoma pada kucing. Vinkristin adalah ubat kemoterapi anti-kanser sitotoksik suntikan yang paling kerap digunakan dengan jumlah 474 dos selama lima tahun. Kesan sampingan kemoterapi dalam kedua-dua anjing dan kucing adalah anemia dan thrombocytopenia, dengan satu tindak balas tisu ubat extravasation. Kos purata untuk setiap rawatan kemoterapi tanpa mengira spesies adalah RM 247. Kajian ini menunjukkan bilangan ubat sitotoksik yang diberikan kepada anjing adalah paling tinggi berbanding dengan kucing dan bagaimanapun langkah keselamatan diperlukan oleh semua pengendalian kakitangan yang bekerja dengan kemoterapi sitotoksik.

Kata Kunci: Kemoterapi kanser, UVH, tumor venereal boleh pindah, limfoma, vinkristin, anaemia, thrombocytopenia

ABSTRACT

An abstract of the project paper presented to Faculty of Veterinary Medicine in partial fulfilment of the course VPD 4999 – Final Year Project.

EVELYN TIE YII YII

Supervisor: Assoc. Prof. Dr. Gayathri Thevi Selvarajah

Co-Supervisor: Dr. Thong Hoe Foong

CANCER CHEMOTHERAPY PRACTICE IN DOGS AND CATS IN UNIVERSITY VETERINARY HOSPITAL, UPM: A RETROSPECTIVE STUDY FROM 2013 TO 2017

Most of small animal veterinary practices which provide chemotherapy are in Selangor area, and University Veterinary Hospital (UVH) is one of them. Information on chemotherapy practice in UVH, UPM has not been evaluated retrospectively. The objectives of this study were (1) to determine the number and types of cancer in dogs and cats treated with cytotoxic chemotherapy, (2) to determine the drug types, frequency of delivery and reported side effects based on the various cytotoxic drugs delivered and (3) to determine the costs incurred in chemotherapy protocols of various cancers in dogs and cats presented to UVH between 2013 and 2017. The study was conducted retrospectively by reviewing case log books available in the Chemotherapy Room and records in UVH. The data collected was subjected to descriptive analysis using SPSS version 20.0. Fisher's

exact test and Kaplan-Meier analysis were performed where necessary. P-value <0.05 was considered statistically significant at 95% confidence interval. A total of 113 animals received cytotoxic chemotherapy for cancer in UVH (83 dogs and 30 cats). A total of 429 doses (78%) of injectable cytotoxic drugs were delivered to dogs and 123 doses (22%) to cats. The most common cancer treated in dogs was transmissible venereal tumour while lymphoma in cats. Vincristine is the most frequently used injectable cytotoxic anti-cancer chemotherapy drug with a total of 474 doses delivered over the five years. Common side effects of chemotherapy in both dogs and cats were anaemia and thrombocytopenia, with a single case of drug extravasation tissue reaction. The average cost for chemotherapy delivery per visit regardless of species was RM 247. This study revealed that high number of cytotoxic drugs are delivered to dogs compared to cats and nevertheless the safety precautions are necessary for all staff handling and working with cytotoxic chemotherapy.

Keywords: Cancer chemotherapy, UVH, transmissible venereal tumour, lymphoma, vincristine, anaemia, thrombocytopenia

1.0 INTRODUCTION

Cancer chemotherapy is defined as the use of anti-neoplastic agents in the treatment of malignant growth (Studdert *et al.*, 2012). Cancer chemotherapy is indicated for being most effective single therapy for lymphoproliferative and myeloproliferative disorders such as lymphoma, myeloma and leukaemia; as adjuvant treatment after surgical resection for highly metastatic neoplasia such as osteosarcoma; shrinking large tumour prior to surgery and relieve pain; improving cell kill with combination of radiotherapy (Morris & Dobson, 2001; North & Banks, 2009).

Mechanism of action of cancer chemotherapy to cure and treat tumours is through killing rapid dividing cells generally via targeting DNA in the cell nucleus or affect a cell's ability to synthesize protein (Shields, 2016). Cancer chemotherapeutic agents are classified into several groups based on their mode of action, anti-neoplastic activity and toxicity (Dobson, 1998). The drug classes include alkylating agents, antimetabolites, anti-tumour antibiotics, vinca alkaloids, hormones, anthracycline analogues and miscellaneous agents (Chun *et al.*, 2007; Dobson, 1998; Lana & Dobson, 2010). Examples of alkylating agents are cyclophosphamide, chlorambucil, melphalan, thiotepa, lomustine and busulphan (Chun *et al.*, 2007; Dobson, 1998). Antimetabolite agents include cytarabine, gemcitabine, methotrexate, and 5-Fluorouracil (Barber & Burgess, 2016; Chun *et al.*, 2007; Dobson, 1998). Anti-tumour antibiotics consist of doxorubicin, mitoxantrone, and actinomycin D (Biller *et al.*, 2016) whereas hormone includes prednisolone. Examples of vinca alkaloids include vincristine and vinblastine while miscellaneous agents contain cisplatin, carboplatin, paclitaxel, piroxicam, hydroxycarbamide and L-Asparaginase (Lana & Dobson, 2010).

Chemotherapeutic agents can be used as a single agent or multi-agent therapy in dogs and cats. Combination drug protocol reported more advantaged than single drug protocol, which is maximizing cell kill and maintaining acceptable toxicities, having greater efficacy against a heterogeneous tumour population, and slower development of drug resistance (Lana & Dobson, 2010; Chun *et al.*, 2007). For example, combination chemotherapy protocol (vincristine, L-asparaginase, cyclophosphamide, doxorubicin, prednisolone) had increased remission rate for dogs with stage I-III lymphoma, particularly in young and small animal (Zemann *et al.*, 1998).

The most common route of administration of chemotherapeutic agent in small animals is intravenous. The route of administration depends on chemotherapy drugs used, type of tumour being treated and patient receiving medication (Steffy-Morgan, 2009).

Chemotherapeutic agent cannot differentiate normal and tumour cells because both normal and tumour cells are active dividing cells (Chun *et al.*, 2007). Toxicity is the major concern of side effect caused by cytotoxic chemotherapy drugs. The most common toxicity of cancer chemotherapy is hematopoietic toxicities (MacDonald, 2009). Other common toxicities include gastrointestinal toxicities and cutaneous reaction such as alopecia, hypersensitivity and extravasation. Several toxicities including hepatotoxicity, pancreatitis, cardiotoxicity, uroepithelial toxicity, pulmonary toxicity, neurotoxicity, and nephrotoxicity are caused by selected cytotoxic chemotherapy agents (Dhaliwal, 2009).

Cancer chemotherapy is one of the expensive aspects of health care in human medicine (Vanderpuye & Yarney, 2014). Veterinary cancer therapy is more likely similar to human cancer chemotherapy. Cost of chemotherapy of each patient varies depending, chemotherapy protocol for specific types of tumour, treatment duration, hospitalization if

necessary, and diagnostic tests such as blood test, radiography and ultrasonography (Chauhan *et al.*, 2018).

Most of the small animal veterinary practices which provide chemotherapy are in Selangor area and University Veterinary Hospital (UVH) is one of them (Loh *et al.*, 2014). However, the information of chemotherapy practice in University Veterinary Hospital (UVH) has not been evaluated retrospectively. Therefore, the objectives of this study are (1) to determine the number and types of cancer in dogs and cats treated with cytotoxic chemotherapy, (2) to determine the drug types, frequency of delivery and reported side effects based on the various cytotoxic drugs delivered and (3) to determine the costs incurred in chemotherapy protocols of various cancers in dogs and cats presented to UVH between 2013 and 2017.

REFERENCES

- Adams, V. J., Evans, K. M., Sampson, J., & Wood, J. L. N. (2010). Methods and mortality results of a health survey of purebred dogs in the UK. *Journal of Small Animal Practice*, 51(10), 512–524.
- Allen R, Crump K. (2011). Chemotherapy handling, safety, and disposal. In Crump, K., & Thamm, D., *Cancer chemotherapy for the veterinary health team*. West-Sussex, UK: Wiley-Blackwell, 57-69.
- Amorim, R. L., Grandi, F., & Ferreira, M. (2018). Brazilian Consensus For The Diagnosis, Treatment and Prognosis of Cutaneous Mast Cell Tumours in Dogs. *Ivestigação*, 17(1), 01–15.
- Arjona, A., Escolar, E., Soto, I., Barquero, N., Martin, D., & Gomez-Lucia, E. (2000). Seroepidemiological survey of infection by feline leukemia virus and immunodeficiency virus in Madrid and correlation with some clinical aspects. *Journal of Clinical Microbiology*, 38(9), 3448–3449.
- Baba, A. I., & Câtoi, C. (2007). Chapter 19: Principles of anticancer therapy. In Baba, A.I., & Câtoi, C., *Comparative Oncology* (pp. 671-787). Bucharest: The Publishing House of the Romanian Academy.
- Baioni, E., Scanziani, E., Vincenti, M. C., Leschiera, M., Bozzetta, E., Pezzolato, M., Desiato, R., Bertolini, S., Maurella, C., Ru, G. (2017). Estimating canine cancer incidence: Findings from a population-based tumour registry in northwestern Italy. *BMC Veterinary Research*, 13(1), 1–9.
- Bande, F., Arshad, S. S., Hassan, L., Zakaria, Z., Sopian, N. A., Rahman, N. A., & Alazawy, A. (2012). Prevalence and risk factors of feline leukaemia virus and feline immunodeficiency virus in peninsular Malaysia. *BMC Veterinary Research*, 8(1), 33.
- Barber, L., & Burgess, K. (2016). Overview of Antineoplastic Agents. In *The Merck Veterinary Manual 11th Edition: 1603-1615*.
- Bhaiyat, M. I., Chikweto, A., Tiwari, K. P., Deallie, C., Pawaiya, R. S., Inga, A., Younger, C. H., Sharma, R. N. (2013). Research Article: A retrospective Study of Canine Tumours in Grenada , West Indies. *Advances in Animal and Veterinary Sciences*, 1(5), 134–139.
- Biller, B., Berg, J., Garrett, L., Ruslander, D., Wearing, R., Abbott, B., Patel, M., Smith, D., Bryan, C. (2016). 2016 AAHA Oncology Guidelines for Dogs and Cats. *Journal of the American Animal Hospital Association*, 52(4), 181–204.
- Boscós, C. M., & Ververidis, H. N. (2004). Canine TVT--Clinical Findings, Diagnosis and Treatment. *Sci. Proc WSVA-FECAVA-HVMS World Congress*, 2, 758–761.

- Brønden, L. B., Lindstrand, S., Nielsen, S. S., Toft, N., & Kristensen, A. T. (2009). Validation of data collected in the Danish Veterinary Cancer Registry. *Veterinary and Comparative Oncology*, 7(3), 207–211.
- Calvet, C. A., Leifer, C. E., & McEwen, E. G. (1982). Vincristine for the treatment of Transmissible Venereal Tumour in the dog. *Journal of American Veterinary Medicine Association*, 181(2), 163–164.
- Cave, T. A., Norman, P., & Mellor, D. (2007). Cytotoxic drug use in treatment of dogs and cats with cancer by UK veterinary practices (2003 to 2004). *Journal of Small Animal Practice*, 48, 371–377.
- Charney, S. C., Bergman, P. J., McKnight, J. A., Farrelly, J., Novosad, C. A., Leibman, N. F., & Camps-Palau, M. A. (2005). Evaluation of intracavitary mitoxantrone and carboplatin for treatment of carcinomatosis, sarcomatosis and mesothelioma, with or without malignant effusions: A retrospective analysis of 12 cases (1997-2002). *Veterinary and Comparative Oncology*, 3(4), 171–181.
- Chauhan, A. S., Prinja, S., Ghoshal, S., Verma, R., & Oinam, A. S. (2018). Cost of treatment for head and neck cancer in India. *PLoS ONE*, 13(1), 1–13.
- Chu, C., & Rubin, S. (2018). Basic Principles of Chemotherapy. In P. DiSaia, W. Creasman, R. Mannell, S. McMeekin, & D. Mutch, *Clinical Gynecologic Oncology* (9th Edt, pp. 449–469). Canada: Elsevier.
- Chun, R., Garrett, L., & Vail, D. M. (2007). Cancer Chemotherapy. In S. J. Withrow & D. M. Vail (Eds.), *Withrow and MacEwen's Small Animal Clinical Oncology* (4th Edt, pp. 163–188). United States: Saunders Elsevier.
- Couto, C. G. (2014). Complications of Cancer Chemotherapy. In R. Nelson, & C. G. Couto, *Small Animal Internal Medicine* (5th Edt, pp. 1144-1153). Mosby.
- Davis, H. (2009). Chapter 61 – Peripheral Venous Catheterization. In D. C. Silverstein & K. Hopper (Eds.), *Small Animal Critical Care Medicine* (pp. 260–263). Canada: Saunders Elsevier.
- Dhaliwal, R. S. (2009). Tumour-and Treatment-Related Complications. In C. Henry & M. L. Higginbotham (Eds.), *Cancer Management in Small Animal Practice* (pp. 122–128). Canada: Saunders Elsevier.
- Dobson, J. (1998). Options for the use of chemotherapy in small animals Part 1. Anticancer drugs. *In Practice*, 20, 403–413.
- Dobson, J. M. (2010). Introduction: Cancer in Cats and Dogs. In J. Dobson & B. Lascelles (Eds.), *BSAVA Manual of Canine and Feline Oncology* (3rd ed., pp. 1–5). BSAVA.
- Dobson, J. M. (2013). Breed-Predispositions to Cancer in Pedigree Dogs. *ISRN Veterinary*

Science, 1–23.

- Dobson, J. M., Samuel, S., Milstein, H., Rogers, K., & Wood, J. L. N. (2002). Canine neoplasia in the UK: Estimates of incidence rates from a population of insured dogs. *Journal of Small Animal Practice*, 43(6), 240–246.
- Elliott, J. (2014). Paraneoplastic syndromes in dogs and cats. *In Practice*, 36(9), 443–452.
- Falk, E. F., Lam, A. T. H., Barber, L. G., & Ferrer, L. (2016). Clinical characteristics of doxorubicin-associated alopecia in 28 dogs. *Veterinary Dermatology*, 26, 142–150.
- Farese, J. P., & Withrow, S. J. (2013). Surgical Oncology. In S. J. Withrow, D. M. Vail, & R. L. Page (Eds.), *Withrow and MacEwen's Small Animal Clinical Oncology* (5th ed., pp. 149–156). Elsevier Inc.
- Freres, P., Jerusalem, G., & Moonen, M. (2017). *Categories of Anticancer Treatments*. In P. Lancellotti, J. Zamorano, & M. Galderisi (Eds.), *Anticancer Treatments and Cardiotoxicity: Mechanisms, Diagnostic and Therapeutic Interventions* (pp. 7-11). Elsevier Inc.
- Gandotra, V., Chauhan, F., & Sharma, R. (1993). Occurrence of Canine Transmissible Venereal Tumour and Evaluation of Two Treatments. *Indian Vet. J.*, 70:854-857.
- Ganguly, B., Das, U., & Das, A. (2013). Canine Transmissible Venereal Tumour: A Review. *Vet Comp Oncol*, 14(1), 1-12.
- Graf, R., Grüntzig, K., Hässig, M., Axhausen, K. W., Fabrikant, S., Welle, M., Meier, D., Guscetti, F., Folkers, G., Otto, V., Pospischil, A. (2015). Swiss Feline Cancer Registry: A Retrospective Study of the Occurrence of Tumours in Cats in Switzerland from 1965 to 2008. *Journal of Comparative Pathology*, 153(4), 266–277.
- Grüntzig, K., Graf, R., Boo, G., Guscetti, F., Hässig, M., Axhausen, K. W., Fabrikant, S., Welle, M., Meier, D., Folkers, G., Pospischil, A. (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), 156–170.
- Grüntzig, K., Graf, R., Hässig, M., Welle, M., Meier, D., Lott, G., Erni, D., Schenker, N. S., Guscetti, F., Boo, G., Axhausen, K., Fabrikant, S., Folkers, G., Pospischil, A. (2015). The Swiss canine cancer registry: A retrospective study on the occurrence of tumours in dogs in Switzerland from 1955 to 2008. *Journal of Comparative Pathology*, 152(2–3), 161–171.
- Gustafson, D. L., & Page, R. L. (2013). Cancer Chemotherapy. In S. J. Withrow, D. M. Vail, & R. L. Page (Eds.), *Withrow and MacEwen's Small Animal Clinical Oncology* (5th Edt, pp. 157–179). Saunders Elsevier.

- Hantrakul, S., Klangkaew, N., Kunakornsawat, S., Tansatit, T., Poapolathep, A., Kumagai, S., & Poapolathep, S. (2014). Clinical Pharmacokinetics and Effects of Vincristine Sulfate in Dogs with Transmissible Venereal Tumour (TVT). *J Vet Met Sci*, 76(2): 1549-1553.
- Henry, C. (2010). Hormonal Impact on Carcinogenesis. In C. Henry & M. L. Higginbotham (Eds.), *Cancer Management in Small Animal Practice* (pp. 25–27). Canada: Saunders Elsevier.
- Hong, S.-H. & Khanna, C. (2003). Chapter 165 Chemotherapy of neoplasia. In Slatter, D. (ed.) *Textbook of Small Animal Surgery (Third Edition)*. United States: Saunders, pp. 2345–2355.
- Kimura, K. C., Gárate, A. P., & Dagli, M. L. Z. (2012). Retrospective study of neoplasms in domestic animals: A survey between 1993 and 2002 of the Service of Animal Pathology, Department of Pathology, School of Veterinary Medicine and Animal Science, University of Sao Paulo, Southeast Brazil. *Brazilian Journal of Veterinary Pathology*, 5(2), 60–69
- Kirby, J. S., & Miller, C. J. (2010). Intralesional chemotherapy for nonmelanoma skin cancer: a practical review. *J Am Acad Dermatol*, 63:689-702.
- Kitchell, B., & Dervisis, N. (2010). Pathophysiology and Tumour Cell Growth. In C. Henry, & M. Higginbotham, *Cancer Management in Small Animal Practice* (pp. 1-9). Canada: Saunders Elsevier.
- Kitchell, B. E., Brown, D. M., Luck, E. E., Woods, L. L., Orenberg, E. K. & Bloch, D. A. (1994). Intralesional implant for treatment of primary oral malignant melanoma in dogs. *J Am Vet Med Assoc*, 204:229-236.
- Kitchell, B. K., Orenberg, E. K., Brown, D.M., Hutson, C., Ray, K., Woods, L., & Luck, E. (1995). Intralesional sustained-release chemotherapy with therapeutic implants for treatment of canine sun-induced squamous cell carcinoma. *Eur J Cancer*, 31(12):2093-2098.
- Komazawa, S., Sakai, H., Itoh, Y., Kawabe, M., Murakami, M., Mori, T., & Maruo, K. (2016). Canine tumour development and crude incidence of tumours by breed based on domestic dogs in Gifu prefecture. *Journal of Veterinary Medical Science*, 78(8), 1269–1275.
- Lana, S., & Dobson, J. (2010). Principles of Chemotherapy. In J. Dobson, & B. Lascelles, *BSAVA Manual of Canine and Feline Oncology 3rd Edition* (pp. 60-79). BSAVA.
- Larue, S. M., & Gordon, I. K. (2013). Radiation Therapy. In S. J. Withrow, D. M. Vail, & R. L. Page (Eds.), *Withrow and MacEwen's Small Animal Clinical Oncology (5th Edt)*, pp. 180–197). Saunders Elsevier.

- Loh, C. Y., Abdullah, R., & Selvarajah, G. T. (2014). Cancer Chemotherapy In Dogs and Cats In Malaysian Small Animal Veterinary Practices. *Final Year Project Presented to University Putra Malaysia*, pp. 1-56.
- MacDonald, V. (2009). Chemotherapy: Managing side effects and safe handling. *Canadian Veterinary Journal*, 50(6), 665–668.
- Macy, D., & Reeds, K. (2010). Viral Carcinogenesis. In C. Henry, & M. L. Higginbotham, *Cancer Management in Small Animal Practice* (pp. 20-25). Canada: Saunders Elsevier.
- Markman, M. (1999). Intraperitoneal Chemotherapy. *Critical Reviews in Oncology/Hematology* 31, 239–246.
- Merlo, D. F., Rossi, L., Pellegrino, C., Ceppi, M., Cardellino, U., Capurro, C., Ratto, A., Sambucco, P. L., Sestito, V., Tanara, G., Bocchini, V. (2008). Cancer Incidence in Pet Dogs: Finding of the Animal Tumour Registry of Genoa, Italy. *J Vet Intern Med*, 22, 976–984
- Moore, A. (2010). Commonly Used Chemotherapy Drugs. *NAVCA Clinician's Brief*, 61-66; 101-106.
- Morris, J. (2001). Haematopoietic System. In J. Morris & J. Dobson (Eds.), *Small Animal Oncology* (pp. 228–251). Blackwell Science.
- Morrison, W. (2002). Cancer In Dogs and Cats: Medical and Surgical Management (2nd Edition, pp. 332-358). Lippincott, Williams & Wilkins
- Nak, D., Nak, Y., Cangul, I. T., & Tuna, B. (2005). A clinico-pathological study on the effect of vincristine on Transmissible Venereal Tumour in the dog. *J. Vet. Med. A. Physiol. Pathol. Clin. Med.*, 52(7), 366–370.
- Norris, A. M., & Withrow, S. J. (1984). A Review of Cancer Chemotherapy for Pet Animals. *The Canadian Veterinary Journal*, 25(4), 153–157.
- North, S., & Banks, T. (2009). *Small Animal Oncology: An Introduction*. Saunders Elsevier, pp. 31–60.
- Overley, B., Shofer, F. S., Goldschmidt, M. H., Sherer, D., & Sorenmo, K. U. (2005). Association between ovariectomy and feline mammary carcinoma. *Journal of Veterinary Internal Medicine*, 19(4), 560–563.
- Papich, M. (2016). *Saunders Handbook of Veterinary Drugs (Fourth Edition)*. United State: Elsevier, pp. 643–645.
- Pope, E. R. (2009). Surgical Interventions in Cancer. In C. Henry & M. L. Higginbotham (Eds.), *Cancer Management in Small Animal Practice* (pp. 136–145). Canada:

Saunders Elsevier.

- Purohit, G. (2008). Canine transmissible venereal tumor (TVT): a review. *The Internet Journal of Veterinary Medicine*, 6(1), 1–7.
- Rodriguez, C. O. (2009). Basic Chemotherapy Principles. In C. Henry & M. L. Higginbotham (Eds.), *Cancer Management in Small Animal Practice* (pp. 101–104). Canada: Saunders Elsevier.
- Sahabi, K., Selvarajah, G. T., Noordin, M. M., & Dhaliwal, G. K. (2015). Retrospective histopathological study of canine mammary gland tumours diagnosed from 2006 - 2012 in University Putra Malaysia. *J. Vet. Malaysia*, 27(1), 1–6.
- Santiago-flores, M. L., Jaro, M. C., Recuenco, F. C., Reyes, M. F., & Amparo, M. R. G. (2012). Clinical Profile of Canine Transmissible Venereal Tumour Cases. *Philipp. J. Vet. Anim. Sci.*, 38(1), 63–72.
- Schneider, R., Dorn, C., & Taylor, D. (1969). Factors Influencing Canine Mammary Cancer Development and Postsurgical Survival. *J Natl Cancer Inst*, 43, 1249–1261.
- Shelton, G., Grant, C., Cotter, S., Gardner, M., Hardy, W., & DiGiacomo, R. (1990). Feline immunodeficiency virus and feline leukemia virus infections and their relationships to lymphoid malignancies in cats: a retrospective study (1968-1988). *J Acquir Immune Defic Syndr*, 3(6), 632-630.
- Shields, M. (2017). Chapter 14: Chemotherapeutics. In S. McCreath, & R. Delgoda, *Pharmacognosy* (pp. 295-307). Mica Haley.
- Smith, A. (2014). The Role of Neutering in Cancer Development. *Vet Clin Small Anim*, 965-975.
- Steffy-Morgan, J. D. (2009). Chemotherapy Administration. In C. Henry & M. L. Higginbotham (Eds.), *Cancer Management in Small Animal Practice* (pp. 114–118). Canada: Saunders Elsevier.
- Studdert, V. P., Gay, C. C., & Blood, D. C. (2012). *Saunders Comprehensive Veterinary Dictionary* (Fourth Edt, pp. 211). United States: Saunders Elsevier
- Taylor, K. (2010). Female Reproductive Tumours. In C. Henry, & M. L. Higginbotham, *Cancer Management in Small Animal Practice* (pp. 268-274). Canada: Saunders Elsevier.
- Teske, E., Van Straten, G., Van Noort, R., & Rutteman, G. R. (2002). Chemotherapy with cyclophosphamide, vincristine, and prednisolone (COP) in cats with malignant lymphoma: New results with an old protocol. *Journal of Veterinary Internal Medicine*, 16(2), 179–186.
- Theilen, G., & Madewell, B. (1979). Tumours of the Skin and Subcutaneous Tissues. In

- G. Theilen, & B. Madewell (Eds.), *Veterinary Cancer Medicine* (pp. 123-191). Philadelphia: Lea and Febiger.
- Todorova, I. (2006). Prevalence and Etiology of the Most Common Malignant Tumours in Dogs and Cats. *Bulgarian Journal of Veterinary Medicine*, 9(2), 85–98.
- Tvedten, H. (2012). Hemostatic Abnormalities. In M. Willard, & H. Tvedten (Eds.), *Small Animal Clinical Diagnosis by Laboratory Methods (Fifth edition)* (pp. 102-105). United State: Saunders Elsevier.
- Vail, D. M. (2009). Lymphoma in Dogs : Diagnosis & Treatment. *NAVCClinician's Brief*, 15–19.
- Vail, D. M. (2009). Supporting the Veterinary Cancer Patient on Chemotherapy: Neutropenia and Gastrointestinal Toxicity. *Topics in Companion Animal Medicine*, 24(3), 122–129.
- Vanderpuye, V. D., & Yarney, J. (2014). Cost Effectiveness of Cancer Therapies in Africa. *J Med Diagn Meth*, Vol 3:1-3.
- Vascellari, M., Baioni, E., Ru, G., Carminato, A., & Mutinelli, F. (2009). Animal tumour registry of two provinces in northern Italy: incidence of spontaneous tumours in dogs and cats. *BMC Veterinary Research*, 5:39.
- Williams, J., Phillips, C., & Byrd, H. M. (2017). Factors which influence owners when deciding to use chemotherapy in terminally ill pets. *Animals*, 7(3), 1–12.
- Zambelli, A. B. (2015). Feline Cancer Prevalence in South Africa (1998 – 2005): Contrasts with the Rest of the World. *Journal of Basic and Applied Sciences*, 11(31), 370–380.
- Zemann, B. I., Moore, A. S., Rand, W. M., Mason, G., Ruslander, D. M., Frimberger, A. E., Wood, C. A., L'Heureux, D. A., Gliatto, J., & Cotter, S. M. (1998). A Combination Chemotherapy Protocol (VELCAP-L) for Dogs with Lymphoma. *J Vet Intern Med*, 12:465-470.
- Withrow, S. J., Liptak, J. M., Straw, R.C., Dernell, W. S., Jameson, V. J., Powers, B. E., Johnson, J. L., Brekke, J. H. & Double, E. B. (2004). Biodegradable cisplatin polymer in limb-sparing surgery for canine osteosarcoma. *Ann Surg Oncol*, 11(7):705-713.