From Dogs: Domestication History, Genetics,
Behavior and Implications for Health,
K. M. Cohen, L.R. Diaz, Eds.
NOVA SCIENCE PUBLISHERS, INC. 2013
PAGE 115-120

Commentary

CAUGHT IN AN ACT OF CONVENIENCE: DISENTANGLING OUR THINKING ABOUT THE INFLUENCE OF OVARIOHYSTERECTOMY (SPAYING) ON HEALTHY LONGEVITY IN DOGS

David J. Waters[1,2, 3*] and Emily C. Chiang[3]

[1]Department of Veterinary Clinical Sciences, and [2]Center on Aging and the Life Course, Purdue University; [3]Center for Exceptional Longevity Studies, Gerald P. Murphy Cancer Foundation, W. Lafayette, Indiana,USA

INTRODUCTION

In our pets, we see the upside of domestication – an impressive quality of life and average lifespan that is the prized product of protection from infectious diseases, starvation, and predators. But the downside of domestication is that, like humans, highly protected canine populations experience the deleterious

* Corresponding author: David J. Waters DVM, PhD. Center for Exceptional Longevity Studies, Gerald P. Murphy Cancer Foundation, 3000 Kent Avenue Suite E2-100. West Lafayette, Indiana 47906. Phone: 765-775-1005; Fax: 765-775-1006; E-mail: waters@purdue.edu.

consequences of aging, including development of cancer and other age-related degenerative diseases [1]. When it comes to aging and cancer, pets and people are in the same boat. Now scientists and health professionals are beginning to place a high priority on gaining a better understanding of the aging process, finding the factors that can promote "healthspan" – living longer, healthier lives not just tacking on more years [2]. Increasing healthy longevity is becoming the goal for which humanity aspires.

To this end, in 2005, our research group at the Center for Exceptional Longevity Studies established The Exceptional Longevity Data Base, the first systematic study of the factors that favor highly successful aging in dogs. Instead of probing for interventions that might benefit geriatric pets, we committed ourselves to a novel approach to studying canine longevity: We focused on a *life course perspective on aging* – embracing the idea that early life events can profoundly influence adult health outcomes, including disease resistance and longevity. Our research sought to identify critical "windows" during the life course where superior early lifestyle choices and interventions could be applied to enable highly successful aging trajectories [3].

In 2008, this deeper sense of life course perspective led us to an important discovery: *No peer-reviewed manuscript in the veterinary literature had ever evaluated the association between canine longevity and the actual number of years of lifetime ovary exposure.* Instead, previous reports [4,5] exposed veterinarians to data on how long two groups of female dogs lived – "spayed" vs. "intact". "Intact" was the name given to bitches that were still sexually intact at the time of death. "Spayed" was the name given to bitches that lost their ovaries at some undetermined time during their lives. What became apparent to us was that ovariohysterectomy – the ovary-removing spaying procedure and elective act of endocrine organ excision widely advocated by DVMs in North America – had never been rigorously evaluated in terms of its impact on longevity.

In 2009, after carefully studying the association between the number of years of lifetime ovary exposure and highly successful aging in Rottweilers, we discovered that *keeping ovaries longer is associated with living longer* [6]. This link between ovaries and longevity was independent of lifetime investment in reproduction [7], as well as cause of death or familial longevity [6]. Our work pointed to a new line of thinking: *Ovaries are part of a system that promotes longevity*. This transformational way of thinking – seeing ovaries not just as reproductive units but as healthspan-promoting endocrine organs – is now supported by newer research on the longevity-extending effects of ovaries in women and mice [8-12].

Should the Rottweilers we studied be viewed as unreliable informants of the real relationship between ovaries and healthy longevity? Or could our non-conforming view derived from Rottweilers simply reflect that the method we used – analyzing the number of years of ovary exposure – is a more precise, health-relevant measure of interindividual differences in lifetime gonad exposure? It seemed prudent that we should probe this possibility. And in a follow-up study [13], we found that by using the common method of categorizing females as spayed or intact at the time of death (so-called dichotomous binning) – *ignoring the timing of spaying in each bitch* – a statistically significant relationship between number of years of ovary exposure and longevity could be distorted [13]. Our conclusion: The habit of veterinarians categorizing bitches as spayed or intact based upon gonadal status at the time of death is inadequate for representing important biological differences in lifetime ovary exposure, which can lead to misleading assumptions regarding the overall health consequences of ovariohysterectomy [13].

So how can we disentangle our thinking about ovaries and health amidst the new data supporting the potential longevity benefits of keeping ovaries? First, we need to broaden our thinking. It is time to expand our thinking of ovaries beyond reproduction, *seeing spaying as a physiological disturbance* capable of exerting system-wide effects [14]. Yet, early elective endocrinological disruption continues to be a widely recommended, "health-promoting" procedure for bitches in North America. If we can agree that the removal of endocrine organs (i.e., ovaries) can disturb normal physiology and physiological resilience in unforeseen ways, we encounter a fresh opportunity: *We might transform elective spaying from an act of convenience to a strategic disturbance – an intervention whose timing should be individualized to optimize each dog's chance of achieving healthy longevity.*

Second, by broadening our thinking, we can begin to change the dialogue. Instead of perpetuating the tiresome debate of whether spaying is "good" or "bad", finding the optimal window of ovary exposure for disease resistance and successful aging will become the prescient issue. Progress in science is measured not so much by the "facts" we generate, but by the new questions we ask [15]. And so it is that we must build the quality of our questions about spaying. When we ask "Is spaying good or bad?" or "Do spayed females live longer than intact females?", we pose the wrong questions. When we ask "What is the relationship between the *timing* of spaying and longevity?" or "What is the window of ovary exposure that will optimize healthy longevity?", we ask better ones. Categorizing bitches as spayed or intact without regard for

the timing of spaying muddles thinking. We oversimplify biology and muddle information whenever we fall into the trap of either-or-ness [16]. Continued use of careless vocabulary can only hinder us as we seek to define the life-long, system-wide influences of ovaries on key cellular processes, health outcomes, and physiologic trade-offs.

It is difficult to predict just how well prepared the veterinary profession is to engage in this conversation, to skillfully weigh and consider new information on the biology of aging and healthy longevity. Veterinarians are not trained in the biology of aging as part of their DVM curriculum. So it might be expected that veterinarians would feel ill-prepared, reluctant to participate in any biogerontological debate. But if we have learned anything from the general semanticists – those experts who study how language shapes and limits perception – it is that *we see the world through our categories* [17]. And if we can express to veterinary students the idea that ovaries are more than just reproductive units, we arm them with a new and powerful categorizing scheme: Ovaries joining the ranks of thyroid glands, adrenal glands, and the insulin-producing pancreas as organs for which we generally advocate a retaining, a refraining from elective removal. We see this re-categorizing of ovaries as endocrine organs as a foundational step toward any serious re-evaluation of the lifelong health consequences of the act of elective ovary removal.

Finally, as our thinking and our conversations lead to new angles of vision, we will come to see that the ovary-longevity connection is an idea ripe for further inquiry. No longer will we be satisfied with review articles showcasing their bloated list of references, giving a false sense that "what we know" is extensive [18,19]. These offerings to practitioners and veterinary scientists have fallen far short of critically analyzing the relationship between lifetime gonad exposure and health outcomes, instead relying upon studies that categorize dogs as spayed or intact to "cover" the subject. Today, the subject calls for no more covering. *We need more uncovering, more discovering*. We must take action to advance the kinds of original investigative efforts that can provide a progressive framework for ongoing debate, future inquiry, and the pursuit of possibilities.

More than a quarter century ago, the Nobel Prize-winning immunologist Sir Peter Medawar wrote that all experimentation is criticism – the criticism that naturally arises from a dissatisfaction with prevailing beliefs [20]. Dissatisfaction beckons for disentangling. And as we grow to see the need for disentangling our thoughts about spaying, we prepare the ground for hastening a healthy reconsidering – not by imprisoning minds in an act of convenience,

but rather by freeing them from past wanderings. This creative freedom can best be achieved through constraint: by staking the attention of veterinary scientists and practitioners in close proximity to the new ideas about ovaries. Here, we submit that continued investigation is sorely needed to more deeply understand the ovarian ecology that sustains healthier aging trajectories. Such inquiry is at the root of disentangling our thinking about how to effectively offset the downside of domestication – enhancing resilience and delaying the onset of age-related disease and disability by making more informed choices about the elective removal of endocrine organs.

REFERENCES

[1] Waters, D. J. and Wildasin, K. (2006). Cancer clues from pet dogs. *Sci. Am.*, 295, 94-101.

[2] Waters, D. J. (2011). Aging research 2011: exploring the pet dog paradigm. *ILAR J.*, 52, 97-105.

[3] Waters, D. J. and Kariuki N. N. The biology of successful aging: watchful progress at biogerontology's known-unknown interface. In: Wilmoth, J. M. and Ferraro, K. F., editors. *Gerontology: Perspectives and Issues*. New York: Springer Publishing Company; 2013; 19-48.

[4] Bronson, R. T. (1982). Variation in age at death of dogs of different sexes and breeds. *Am. J. Vet. Res.*, 43, 2057-2059.

[5] Mitchell, A. R. (1999). Longevity of British breeds of dog and its relationships with sex, size, cardiovascular variables and disease. *Vet. Rec.*, 145, 625-629.

[6] Waters, D. J., Kengeri, S. S., Clever, B., Booth, J. A., Maras, A. H., Schlittler, D. L., and Hayek, M. G. (2009). Exploring mechanisms of sex differences in longevity: lifetime ovary exposure and exceptional longevity in dogs. *Aging Cell*, 8, 752-755.

[7] Kengeri, S. S., Maras, A. H., Suckow, C. L., Chiang, E. C., and Waters, D. J. (2013) Exceptional longevity in female Rottweiler dogs is not encumbered by investment in reproduction. *Age*, DOI: 10.1007/s11357-013-9529-8.

[8] Parker, W. H., Broder, M. S., Chang, E., Feskanich, D., Farqhar, C., Liu, Z., Shoupe, D., Berek, J. S., Hankinson, S., and Manson, J. E. (2009). Ovarian conservation at the time of hysterectomy and long-term health outcomes in the Nurses' Health Study. *Obstet. Gynecol.*, 113, 1027-1037.

[9] Rocca, W. A., Gorssardt, B. R., de Andrade, M., Malkasian, G. D., and Melton, L. J. (2006). Survival patterns after oophorectomy in premenopausal women: a population-based cohort study. *Lancet Oncol.*, 7, 821-828.

[10] Rocca, W. A., Shuster, L. T., Gorssardt, B. R., Maraganore, D. M., Gostout, B. S., Geda, Y. E., and Melton, L. J. (2009). Long-term effects of bilateral oophorectomy on brain aging: unanswered questions from the Mayo Clinic Cohort Study of oophorectomy and aging. *Women's Health*, 5, 39-48.

[11] Cargill, S. L., Carey, J. R., Müller, H. G., and Anderson, G. (2003). Age of ovary determines remaining life expectancy in old ovariectomized mice. *Aging Cell*, 2, 185-190.

[12] Mason, J. B., Cargill, S. L., Anderson, G. B., and Carey, J. R. (2009). Transplantation of young ovaries to old mice increased life span in transplant recipients. *J. Gerontol. A Biol. Sci. Med. Sci.*, 64, 1207-1211.

[13] Waters, D. J., Kengeri, S. S., Maras, A. H., and Chiang, E. C. (2011). Probing the perils of dichotomous binning: how categorizing female dogs as spayed or intact can misinform our assumptions about the lifelong health consequences of ovariohysterectomy. *Theriogenology*, 76, 1496-1500.

[14] Waters, D. J. (2011). In search of a strategic disturbance: some thoughts on the timing of spaying. *Clin. Theriogenol.*, 3, 433-437.

[15] Pirie, N. W. Selecting facts and avoiding assumptions. In: Berthoff, A. E., editor. *Reclaiming the imagination*. New Jersey: Boynton/Cook Publishers Inc.; 1984; 203-211.

[16] Waters, D. J. (2012). The paradox of tethering: key to unleashing creative excellence in the research-education space. *Informing Sci.*, 15, 229-245.

[17] Johnson, W. *People in Quandaries*. New York: Harper and Brothers; 1946.

[18] Root Kustritz, M. V. (2007). Determining the optimal age for gonadectomy of dogs and cats. *J. Am. Vet. Med. Assoc.*, 231, 1665-1675.

[19] Root Kustritz, M. V. (2012). Effects of surgical sterilization on canine and feline health and on society. *Reprod. Domest. Anim.*, Suppl. 4, 214-222.

[20] Medawar, P. B. *Advice to a Young Scientist*. New York: Basic Books; 1979.