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## Foundation Update ..... Winter 2009

### Message to Women and Dogs: Keeping Ovaries is Linked to Longevity

"During the last 6 months, we've witnessed a compelling convergence. Results from three independent investigators, from three different species are pointing us toward a new line of thinking — that keeping ovaries longer is associated with living longer. Taken together, it suggests that physiological processes that regulate aging are under ovarian control."

David J. Waters PhD, DVM  
Director, Murphy Cancer Foundation

This summer, a research study of 29,000 women showed that women who keep their ovaries at the time of hysterectomy live longer than women who have their ovaries removed. **Do ovaries regulate longevity?** One way to test this hypothesis is to see if ovary removal early in life can re-set the aging clock. This idea has never been tested in humans, because too few women undergo early ovary removal. In contrast, a large percentage of pet dogs undergo elective ovary removal at different ages throughout the life course, creating a **research opportunity to study whether females who keep their ovaries longer, live longer.**

And that's precisely what we found. Our research results are the first to document that lifetime ovary exposure (i.e., how long a female keeps her ovaries) is associated with exceptional longevity. These findings were published this month in *Aging Cell*, the world's top impact biology of aging journal. To learn more about turning to pet dogs for aging clues, read the **Press Release (insert in this newsletter)**, or go to our website <http://www.gpmcf.org/ovarianhome.html> for a free download of the scientific article.

### Ovaries & Longevity

exploring sex differences in healthspan



#### Explore More

To explore with us the serious role that ovaries may play in regulating longevity, click on a topic below.

★ Press Release

★ Questions About the New Research

- Our Article Published in *Aging Cell* (free PDF download)
- Sex Differences in Healthy Longevity
- Upcoming Symposium on Sex Specific Differences in Health
- A Healthier Respect for Ovaries – An Essay by Dr. David Waters

## Inside this Issue

Research is a dynamic process. In this issue of **Foundation Update**, we share with you stories that capture the essence of our intellectual encounters – how we are thinking, who we are training, and what’s next. As you peruse the newsletter, we hope you will find thought-provoking details that move you to reconsider what we really know about health. **Mark Twain** wrote: “Whenever you find yourself on the side of the majority, it is time to pause and reflect.” Good research is really good at challenging conventional wisdom and blazing new paths of understanding. We invite you to experience our stories, pause, and reflect.

## Updates

**Murphy Scientists Exploring New Terrain: Media Ecology** — In June 2009, Dr. Waters attended the 10<sup>th</sup> Annual Convention of the Media Ecology Association in St. Louis, Missouri. **Media ecology** is the field of study that looks at how the way we get our information advances or hinders



the public well-being. Dr. Waters’ speech to 200 attendees cut right to the chase: “But They Say More is Better: How the Media Makes it Difficult to Promote Health and Prevent Cancer in a U-Shaped World”. The Media Ecology Association was founded in 1998 by trainees of **Neil Postman**, a scholar whose book *Teaching as a Conserving Activity* has strongly influenced Dr. Waters’ teaching methods. **Message from Murphy scientists:** To promote public health, we must do better at communicating health-related news to the public. The public hears much of its health news

out of context, i.e. news that no one should use. Clearly, health promotion is a media ecology concern and Murphy scientists intend to play an increasingly active role in better communicating health-related research. The Murphy Foundation will sponsor a symposium at the 2010 Media Ecology Association Convention held at the University of Maine. Stay tuned for details about the symposium, which will feature talks about how scientists, science writers, and media ecologists can help to create health news you can use.

**From Radiation to Selenium, Dose Matters** — In April 2009, Dr. Waters delivered a research talk at the University of Massachusetts in Amherst at the **8th International Conference on Dose Response**. The conference serves as the annual meeting of the International Dose Response Society, a multi-disciplinary group of scientists interested in understanding the response of cells and organisms to nutrients, drugs, and environmental exposures. Dr. Waters’ talk entitled, “Selenium, Apoptosis, and DNA Damage: Defining the Optimal Dose for Human Prostate Cancer Prevention” stimulated much discussion. The Murphy Foundation’s provocative data from dogs showing a U-shaped dose response between the level of the cancer-fighting nutrient selenium and genetic damage has provided key insights into interpreting the results from men in the SELECT prostate cancer prevention trial (**see insert in this newsletter: Making Sense of the Disappointing Results of SELECT**). At the conference, **Dr. Edward Calabrese**, founder of the International Dose Response Society, was awarded the Marie Curie Prize from the World Council of Nuclear Workers in honor of his important discoveries on the potentially *beneficial* effects of low dose irradiation. That’s right, a little bit of “bad things” like radiation might just be good for you! Murphy scientists are joining Calabrese and colleagues in transforming how we think about the importance of dose, not only in environmental risk assessment, but also in designing human clinical trials. **The take home message:** Dose matters. More of a good thing is not necessarily better. Dr. Waters’ talk will be published in 2010 in *Dose-Response*, the official scientific journal of the international society.

## **A View From the Mountaintop: Murphy Scientists Poised at the Gateway to Future Medicine**

— In June 2009, Murphy scientists traveled to Beijing, China to present research data at BIT's 2nd Annual World Cancer Congress. The theme of the conference, Gateway to Future Medicine, emphasized the importance of scientific exchange between investigators from all corners of the world. "What a great opportunity for us to share ideas and advance our thinking," said **Emily Chiang, Research Associate at the Murphy Foundation**. Her presentation, "Finding the Optimal Selenium Status for Cancer Reduction", was part of a symposium on Cancer Prevention, Epidemiology, and Cancer Surveillance that featured 9 speakers from 6 different countries. A great opportunity indeed to ignite international interest in our research at the intersection of cancer and aging.



## **Shorts**

### **Outrumbling Mt. Redoubt: Aging Research in Pet Dogs Ready to Blow** —

The radio announcer in Anchorage, Alaska said the surgical masks sold out in less than an hour. The city was bracing for the eruption of a not so sleeping volcano, Mt. Redoubt. But just when Redoubt's awakening was capturing peoples imagination, there was another activity that was taking place in Anchorage. On that day, Dr. Waters arrived in Anchorage after traveling more than 2500 miles to perform an autopsy on an exceptional dog. **The dog named "Hummer", one of the oldest-living Rottweilers in the United States, had been tracked by Murphy scientists at the Center for Exceptional Longevity Studies.** "From Tampa to Anchorage — that's how wide we've cast our net to gather this critical information", said **Seema Kengeri, MPH, coordinator of the Exceptional Longevity Database**. Three years ago, Dr. Waters flew to Florida to conduct an autopsy on "Champ", another of these exceptional "centenarian" Rottweilers. Murphy scientists know that the careful examination of tissues that can only be achieved by autopsy provides a one-of-a-kind look at what it takes to age successfully. It's clear that Murphy Foundation scientists are leaders in this eruptive new research on aging — transforming the pet dog population into a national resource to better understand aging and cancer. "The payoff for such work is big — a win-win situation for both pets and people", Kengeri said.

### **What are the Odds of Getting Health Messages Right?** — In November 2009,

Dr. Waters led a group of science writers in a discussion about overcoming some of the obstacles to successfully communicating the "good things" that promote health. Each year, a dozen internationally-recognized science writers are invited to **Purdue University** to conduct a town hall style meeting open to faculty, students, and the public. This year's **Science Journalism Laureates Program**, entitled "Science Journalism in the Age of Twitter", centered on the drastic changes in the way information is exchanged. If the public is getting its stories in 140 character snippets, does this affect the accuracy of information exchange or the amount of reflective thinking? After the town hall meeting, Dr. Waters engaged in a closed-door, 2-hour discussion with the laureates about: the challenges of putting health news in the proper context; how scientists and media often co-conspire to muddle information; and how the deep-rooted metaphor "more is better" misinforms folks about the benefits of dietary supplements. Among the notables who participated were **Moira Gunn, host of National Public Radio's "Tech Nation"**, and **Kevin Maney**, author of the recent book *Trade-Off: Why Some Things Catch On and Others Don't*. By shedding light on the challenges confronting science writers, the Murphy Foundation seeks to increase the odds that scientists, science writers, and the public will get health messages right.

## **Murphy Foundation and the Renaissance of Environmental Mutagenesis —**

In August 2009, scientists from around the world who study how agents in the environment influence cancer risk flocked to Florence, Italy, the heart of the 16th century Renaissance. What they encountered



was a rebirth of sorts — a flood of new ideas bursting forth from the more than 250 scientific talks and 800 scientific posters, presented by 900 scientists from 63 countries. Dr. Waters' paper titled "**Pet Dogs as Sentinels of Environmental Cancer Risk**" introduced a new idea to scientists working in the field of toxicology: utilizing the naturally-occurring cancers that develop in pet dogs as an early warning system of cancer hazards in the environment that are relevant to humans. In Florence, the Foundation was proud to

organize and sponsor a scientific symposium on U-Shaped Dose Responses and Cancer Risk. Dr. Waters chaired the symposium, featuring talks by **Dr. Pentti Tuohimaa** of Finland and **Dr. Andrew Reynolds** of Great Britain on the topics of vitamin D and anti-angiogenic agents. The resounding success of the U-shaped symposium, co-sponsored by **Bostwick Laboratories**, garnered the Murphy Foundation an invitation to further its international stature by creating a scientific symposium at a cancer conference that will convene in Sao Paulo, Brazil in September 2010.

## **The Murphy – da Vinci Connection: Scientists in Search of Visual Literacy —**

Gerald Murphy and Leonardo da Vinci were forward-looking guys, who could see clearly things that others could not. Today, the Murphy Foundation continues to place a very high priority on this art of seeing. That is why the Foundation was proud to financially support PhD students to attend a statistical graphics course taught by **Edward Tufte** in August 2009. Tufte, an emeritus professor at Yale University, is the godfather of **statistical graphics** — the art of visual display that makes information jump off the page. His book, *The Visual Display of Quantitative Information*, was selected by Amazon.com as one of the best 100 non-fiction books of the 20<sup>th</sup> century. About Tufte's book *Envisioning Information*, Whole Earth Review remarks: "Tufte is promoting a new standard of visual literacy. No other book has been so highly recommended to us by so many varieties of professionals — architects, teachers, hackers, artists." Add cancer researchers to that list. It's easy to see why Tufte has earned the title of "**The Leonardo da Vinci of Data**". What a great privilege for the Murphy Foundation to make it possible for 5 young trainees to learn to creatively and effectively present their research data at the foot of the master.

## **Kudos**

**Recognition for Our Trailblazing Research Efforts** — For the last decade, we have rolled up our sleeves to seriously evaluate how pet dogs living in the same environment as people might play an important role in better understanding the complex association between aging and cancer. In recognition of these trailblazing efforts, the Glenn Foundation for Medical Research has selected Dr. Waters as the recipient of a **2009 Glenn Award for Research in Biological Mechanisms of Aging**. The award provides financial support to augment the research conducted in the Murphy Foundation's Center for Exceptional Longevity Studies. But the good news doesn't stop there. In November 2009, the **National Institute on Aging (NIA)** of NIH formally issued to the scientific community a request for information soliciting input on the feasibility of employing pet dogs in the study of aging. It is anticipated that the information gathered will be used to develop research opportunities advancing the application of aging studies in pet dogs as a win-win situation to promote healthy aging in pets and people. Never before have pet dogs been considered by the NIA as serious workhorses for aging research. It's clear that **our work has illuminated a new research path** — the notion that studying healthy aging in pet dogs can really add something to the work other aging researchers are doing using "conventional" species ... worms, flies, and mice in cages. Taken together, the Glenn Award and the call-out by NIA are turning the spotlight on Murphy scientists as innovators ready to take a leadership role in the field of aging research.



The idea economy is here®

December 1, 2009

## **Message for women and dogs: keeping ovaries is linked to longevity**

WEST LAFAYETTE, Ind. - This year, hundreds of thousands of women and pet dogs will undergo a hysterectomy and have their ovaries removed along with their uterus. Now, two independent research studies looking at longevity may challenge almost four decades of standard operating procedures used in women and in pets.

Research published Tuesday (Dec. 1) shows female dogs that keep their ovaries longer also live longer. The study, exploring the factors that favor successful aging in pet dogs, was conducted by a research team led by David J. Waters, Ph.D., D.V.M.

Waters' work is the first investigation to look for a link between retaining ovaries and reaching exceptional longevity in mammals. Waters is executive director of the [Gerald P. Murphy Cancer Foundation](#), based at the Purdue Research Park of West Lafayette. The Murphy Foundation is home to the Center for Exceptional Longevity Studies, which tracks the oldest living pet dogs in the United States.

The researchers collected and analyzed lifetime medical histories, ages and causes of death for 119 canine "centenarians" - exceptionally long-lived Rottweiler dogs living in the United States and Canada that survived to 13 years, which is 30 percent longer than average Rottweilers. These exceptionally long-lived dogs were compared to a group of 186 Rottweilers that had usual longevity, approximately nine years.

"A female survival advantage in humans is well-documented - women outnumber men by 4:1 among those who reach 100," said Waters, who is associate director of Purdue University's Center on Aging and the Life Course and a professor in the Department of Veterinary Clinical Sciences. "Like women, female dogs in our study had a distinct survival advantage over males. But taking away ovaries during the first four years of life completely erased the female survival advantage. We found that female Rottweilers that kept their ovaries for at least six years were four times more likely to reach exceptional longevity compared to females who had the shortest lifetime ovary exposure.

"Clearly, we have tapped into a unique resource with our Exceptional Longevity Database. We like to think of it as the pet dog equivalent of the New England Centenarian Study. We want to better understand the biology of aging.

Our quest to validate pet dogs as a model for the study of healthy human aging is at the core of this research."

Murphy Foundation scientists think it is time to tackle a new set of research questions relevant to the biology behind aging. At the top of the list are identifying ovary-sensitive processes that may influence the rate of aging and defining the critical window of ovary exposure that optimizes longevity.

The pet dog research published in *Aging Cell* mirrors the findings of the Nurses' Health Study published this summer by Dr. William Parker and colleagues from the John Wayne Cancer Institute in Santa Monica, Calif.

Parker's group studied more than 29,000 women who underwent a hysterectomy for benign uterine disease. The findings showed that the upside of ovary removal - protection against ovarian, uterine and breast cancer - was outweighed by increased mortality from other causes. As a result, longevity was cut short in women who lost their ovaries before the age of 50 compared with those who kept their ovaries for at least 50 years.

"For the last 35 years, most doctors have been routinely advising women undergoing hysterectomy to have their ovaries removed to prevent ovarian cancer," Parker said. "We believe that such an automatic recommendation is no longer warranted."

Waters believes it boils down to systems thinking.

"Nobody would argue that taking the caterpillars out of an environment does not change that environment in unforeseen ways," he said. "You're not simply left with the old environment minus caterpillars. Likewise, we are dealing with an ovarian ecology that urges us to pause and consider the long-term health consequences of taking out ovaries."

Taken together, the emerging message for dogs and women seems to be that when it comes to longevity, it pays to keep your ovaries.

"What we have here is a compelling convergence," Waters said. "The data from women and dogs, together with reported longevity benefits from ovary transplants in mice, are pointing in the same direction - the notion that a network of processes regulating longevity is under ovarian control."

Parker believes the results point to a need for a new conversation between patient and doctor, framed by the patient's specific risk factors and personal concerns. Waters concurs.

"In this era of personalized medicine, it seems only fitting that we should be directing the conversation about elective ovary removal in women and dogs toward a more forward-looking, individualized script," Waters said.

UPDATE



## Making Sense of the Disappointing Results of SELECT: Were the Results Expected or Unexpected?

by David J. Waters

In late 2008, the field of cancer prevention was turned upside down by the announcement that SELECT, the largest-ever prostate cancer prevention trial, was being halted. Interim analysis of data from more than 32,000 men indicated that selenium supplements were not protecting men against prostate cancer. Moreover, selenium supplementation was associated with an alarming trend toward increased risk of developing type 2 diabetes. As a result, the Murphy Foundation, along with more than 400 other centers across North America, instructed all study participants that they must discontinue their study supplements.

But upon careful examination of the study results, published in the prestigious **Journal of the American Medical Association (JAMA)** in December 2008, an intriguing fact surfaced: the average selenium status in men before starting the SELECT study was *already in the optimal selenium range predicted by Murphy researchers*. In our eyes, failing to show benefit by further supplementing a group of men already replete with the cancer-fighting nutrient was **more of an expected result than an unexpected one**.

For this reason, **Dr. Waters**, along with two other experts on selenium — **Dr. Margaret Rayman** of Great Britain and **Dr. Gerald F. Combs, Jr.** from the USDA Human Nutrition Research Center in North Dakota — submitted a **letter to the editor of JAMA** requesting that the SELECT study results be put into proper context. Further, they urged scientists to abandon the belief that any particular agent administered at the same dose should benefit everybody and instead move toward a strategy of **personalized cancer prevention**.

So, what should men do about taking selenium supplements? Today, muddled messages about the health-promoting vs. health-detrimental effects of selenium abound. **Our advice, unchanged by the results of SELECT, is this : Each man should get his selenium level right.** It's still sound advice, just like getting your blood pressure right. Men (and women!) can get their selenium in the optimal range — not too low, not too high — by using the Murphy Foundation's personalized cancer prevention product, the **SeleniumHealth™ toenail test**.

This selenium story so clearly illustrates one of the big problems that the Murphy Foundation is tackling head on: helping the public get information on health research that is in context and relevant. You can count on us to continue working hard to accomplish just that — personalizing your cancer prevention.