

GERONTO-McGILL

BULLETIN OF THE MCGILL CENTRE FOR STUDIES IN AGING



May - June 2006

ISSN 0838-2263

Volume 22, No. 3

DO MICE THAT EAT LESS HAVE SOMETHING TO TELL US ABOUT LONGEVITY?

by Daniel Auld

What determines our longevity? Despite the complexity of this question, over the years, scientists have unearthed a few telling clues. In species ranging from fruit flies to mice, caloric restriction (defined as a 30% decrease) increases lifespan. Exactly how eating less can do this has been a topic of considerable debate.

A group of researchers from Illinois has shed light on this question. They recently showed that animals that eat a normal diet, but are genetically incapable of producing a protein called the Growth Hormone Receptor (i.e. 'knockout' animals), live longer than mice that have the receptor. But why is this interesting with respect to caloric restriction and longevity?

The authors also found that giving the Growth Hormone Receptor knockout

(Continued on page 4)

THE REALITIES OF LOW VISION: AN EYE-OPENER

An interview with Olga Overbury, Ph.D., Department of Ophthalmology, McGill University

by Tania Elaine Schramek

Many, if not most of us take for granted that we are sighted individuals and we presume that this will always be the case. The reality is however, that if we were to live long enough we would likely all become visually impaired to a certain degree. Dr. Olga Overbury of the Ophthalmology Department of McGill University has in fact devoted her career to understanding conditions that lead to low vision and how to



(Continued on page 2)

POLICY AND POLITICS

COST VERSUS LIVES: DRAWING THE LINE WITH EXPENSIVE NEW DRUGS

by Daniel Auld

A disturbing scenario is playing out across the country: new and improved drugs that could help patients, but are too expensive for provincial health plans and hospitals to afford. With pharmaceutical and biotechnology companies endeavoring every day to improve upon existing therapies, this dilemma will only grow deeper as more new drugs appear, clouding the already murky waters associated with life-threatening illnesses.

The anti-colorectal cancer drug Avastin has highlighted this predicament, and is useful to illustrate a few key questions in the debate: Do the new drugs really need to be so expensive? Is the benefit to patients worth the cost? Given the limited resources of government, can they afford to pay?

Avastin was approved by Health Canada last September. This drug is effective for the treatment of metastatic colorectal cancer, and has been shown to increase patient survival. Naturally, many cancer sufferers are anxious to be treated with it. Unfortunately, Avastin is remarkably expensive. It has a price tag of several thousand dollars for one treatment, with a full treatment course running over \$30,000.

Although this price may sound exorbitant, from the pharmaceutical/biotechnology industry's perspective, certain realities have contributed to it. First, antibodies (Avastin is an antibody) are expensive to

(Continued on page 4)

IN THIS ISSUE

Caloric restriction and lifespan	1
Interview with Olga Overbury	1
Cost versus lives: expensive new drugs	1
Of mice and Alzheimer's	3
NSAIDs in the fight against breast cancer	5
Aging and homosexuality	5



An interview with Olga Overbury, Ph.D., Department of Ophthalmology, McGill University

(Continued from page 1)

better detect their presence.

As was the case for many professionals in the field of vision today, Dr. Overbury was inspired by the famous work of Hubel and Wiesel on visual processing in anesthetized cats. But unlike many others, what particularly fascinated her was the fact “that animals rendered functionally blind could recover through behavioural means and use their eye again”. She wondered if adult human recovery of visual functioning had been studied before. Much to her surprise, it had not, and as such her Master’s and Doctoral research projects were born.

One would be hard pressed to find an academic who had not at one point questioned whether they had made the right choice of career path. Being no exception to this, Dr. Overbury got her answer while she was a teacher’s assistant for a statistics class. One of her students was visually impaired and came to class with assistive devices. Dr. Overbury was naturally drawn to the student and they developed an acquaintance over the course of the term. In one conversation, Dr. Overbury explained that her attempt to gain access to the clientele served in agencies for the visually impaired for her research had been unsuccessful. Her student, who happened to be the director of funding for the Quebec Association for Partially Sighted, suggested that she directly approach ophthalmologists and conduct her research that way. As Dr. Overbury put it, “and the rest is history”.

This began a very fruitful collaboration with Dr. W. Bruce Jackson, M.D., who was then at McGill University and readily gave her access to his patients. Quite impressively, while still a doctoral student, Dr. Overbury, along with Dr. Jackson, became a founding director of the McGill Low Vision Centre, now based at the Sir Mortimer B. Davis Jewish General Hospital of Montreal.

Over the years Dr. Overbury had developed expertise in both basic vision research in the lab and applied research

through her work in the ophthalmology clinic and the Low Vision Centre. The one thing she felt was missing was a good understanding of rehabilitation practices. She headed off to Palo Alto, California, and completed post-doctoral studies at the Western Blind Rehabilitation Center under the Veterans Affairs Department.

Today, Dr. Overbury’s work centers on “developing methods to best assess how much vision one truly has left”. She explains that the eye charts that are typically used in an eye-care professional’s office cannot provide a true map of visual functioning. More sophisticated techniques are required when vision loss has occurred or when one is at risk for developing a condition resulting in low vision. Dr. Overbury and her research team strive to develop the most precise sensory assessment tools available to specialists. For individuals with partial vision this can mean the difference between being eligible or not for government-funded assistive devices and rehabilitation programs, thus the implications of her work are far-reaching indeed.

Dr. Overbury explains that the most common causes of low vision in older adults are cataracts, age-related macular degeneration (ARMD), glaucoma, and diabetic retinopathy. Cataract is a clouding of the crystalline lens of the eye or its surrounding transparent membrane that obstructs the passage of light and causes a reduction in vision. Symptoms of cataracts include blurred vision, glare, halos around lights, and colours that are less bright. Happily, cataract surgery is a relatively easy and highly successful procedure that restores vision in the vast majority of people who have this problem.

Second in importance is ARMD. Here the light-sensing cells in the macula (an oval yellow spot near the center of the retina) malfunction, resulting in a loss of central vision. Symptoms usually include blurred vision, shadows or missing areas of vision, distorted vision, trouble discerning colours (especially dark on dark or light colours

from other light colours), and slow recovery of visual function after exposure to a bright light. Again, age puts one at the greatest risk but smoking, a family history of ARMD, high blood pressure, high cholesterol, obesity, and race (more prevalent in Caucasians) have been associated with the disease. Next, glaucoma is a group of eye diseases characterized by fluid pressure build-up in the eye to a point that the optic nerve cannot withstand. This results in peripheral vision loss (tunnel vision) and if left untreated, blindness. The danger in glaucoma is that there are few detectable initial symptoms. This silent thief – as Dr. Overbury puts it – primarily affects older adults with a family history of the disease, those with diabetes or extreme nearsightedness, and four times more African Americans than Caucasians. Finally, diabetic retinopathy is a complication of diabetes that damages the tiny blood vessels that supply blood to the back part of the eye (retina). The vessels swell and leak liquid into the retina, resulting in blurred vision and sometimes blindness.

The greatest risk factor for low vision however, is FEAR. “Vision loss is among the top 3 fears of the general public coming in third after cancer and Alzheimer’s”. Dr. Overbury explains that their fears, although unfortunate, are well-founded. “Historically, society has treated blind or visually impaired individuals rather negatively, like outcasts; one could even consider it a form of modern-day leprosy. Even scripture portrays the blind as impoverished beggars who have somehow caused or are deserving of their blindness – he was struck blind –”, she quotes. This, coupled with the lack of exposure in the media (or stereotypical portrayal), renders at risk older adults who are less likely to consult the eye care specialist they should.

“Contrary to popular belief, visual impairment is not a death sentence, especially today when there are numerous services and devices available for almost any

(Continued on page 3)

An interview with Olga Overbury, Ph.D., Department of Ophthalmology, McGill University

(Continued from page 2)

degree of vision loss". Despite this, for many older adults visual impairment means a loss of independence, isolation, possible institutionalization, or becoming a burden for their families. "Also of importance is a fear that being visually impaired renders older adults more vulnerable to crime, many thinking that a white cane essentially paints a bull's eye on their back, even though the statistics do not support this".

Dr. Overbury stresses that individuals with the risk factors outlined above, or those experiencing current symptoms should definitely talk to their family physicians about their concerns. Ideally, they should be seen by an ophthalmologist; there are several hospital-based clinics that can proceed with the initial evaluation of vision loss or risk thereof. These clinics are good at managing the early stages of vision loss and providing

access to high-tech assistive devices. After that, agencies such as the Montreal Association for the Blind or the Institut Nazareth et Louis Braille help individuals adapt their homes to their given forms of vision loss (e.g. specialized knobs for the stove, tips on products with large labels, ways to place the furniture), provide them with mobility training and psychological help. The primary objective of these agencies is helping each person to maintain autonomy and quality of life, a welcome goal for older adults to be sure.

Lastly, Dr. Overbury reminds us that our family physicians do not always give us the required referral to see an ophthalmologist let alone a service agency; "if someone falls, a referral to a physiotherapist is a reflex, but this is often not the case when it comes to vision, so

individuals should not be afraid to ask for these services". Dr. Overbury is soon to begin research as a new faculty member at the Université de Montreal; Geronto-McGill wishes her continued success and sincere thanks for her dedicated work at the McGill Low Vision Centre.

OF MICE AND ALZHEIMER'S

by Daniel Auld

Alzheimer's disease (AD) is a devastating neurodegenerative disorder that has no known cure. Although treatments are currently available, they are not a panacea. However, if there is one disease for which research is expected to make a real difference, it is AD. In fact, the last 15 years have been witness to an explosion in our understanding of AD. Some of that research, like that of Dr. Frank LaFerla, has important implications for the development of new treatments.

In AD, a type of brain cell, called a cholinergic neuron, is selectively vulnerable. Normally, these cells set up important communication links with other cells by secreting the neurotransmitter acetylcholine. Impairments in this communication network occur in AD, and this contributes to some of the learning and memory deficits. Moreover, acetylcholine

activates cells – through what are called receptors – and reduces the production of beta-amyloid, which is thought to cause much of the damage in AD.

With this knowledge in mind, this research team from California treated mice that develop the mouse equivalent of AD – because they were given certain genes that cause AD in humans – with a chemical that imitates acetylcholine. Specifically, they used a muscarinic M1 agonist, a drug that activates specific brain cells through acetylcholine receptors. Their exciting findings show that the drug improved learning and memory in these mice, probably by artificially activating some of the communication networks that are impaired in AD. Very interestingly, the treatment also reversed some of the physical signs of AD, notably the accumulation of beta-amyloid. This makes

sense considering that acetylcholine normally reduces the production of beta-amyloid, and that the drug imitates and artificially increases acetylcholine-related communication.

This research gives excellent clues for those that develop drugs for human use. It is expected that this and other basic research will fuel the development of new and improved treatments for human AD.

Source : Caccamo A, Oddo S, Billings LM, Green KN, Martinez-Coria H, Fisher A, and LaFerla FM (2006) M1 Receptors Play a Central Role in Modulating AD-like Pathology in Transgenic Mice Neuron 49, 671–682

COST VERSUS LIVES: DRAWING THE LINE WITH EXPENSIVE NEW DRUGS

(Continued from page 1)

manufacture. Second, drug development in general is very expensive. For instance, an upstart biotechnology company might expect to spend more than 20 million dollars before their compound even has a clinical trial, and clinical trials cost many millions of dollars more. Moreover, from a company's perspective, drug development is fraught with risk. For every drug that is approved, many others end up as expensive failures. Thus, companies use profits from the successes (like Avastin) to fund the development of future treatments. The reality is that if there is no profit, the system breaks down and there is no new research.

From the governments' side, they are faced with ethical and economic challenges when confronted with the high cost of new drugs. So far in Canada, with respect to Avastin, the provinces have weighed in differently. For example, British Columbia has decided to pay for it. Quebec is still waiting to make a decision, but in the meantime is offering it to a limited number of patients for free. Saskatchewan and Ontario, on the other hand, have decided that the cost of the drug is not worth the benefit derived from it, and have chosen not to offer it. In both of these provinces, however, patients who can afford the price tag – or who have private insurance – can pay for it themselves and receive the course of treatment in a public hospital. Without a doubt, decisions like this have served as lightning rods for patient advocates and for those opposed to a two-tiered medical system. Indeed, that Avastin is offered to patients who can afford it is a fairly stark reminder that our public system is under pressure.

Leaving the tenuous debate concerning public healthcare aside, as the system currently stands, there are certain realities that must be faced. If too much money is spent on new drugs that offer marginally improved outcomes for patients, will governments be able to

continue to offer the other drugs that we currently benefit from? As is clear, this is a very complex issue that must be addressed by governments and society as a whole.

Adding to the debate is that some physicians question whether the cost of Avastin is worth the benefit. Avastin can prolong life, but it is likely not a cure. With this in mind, the high cost forces people to make gut-wrenching decisions: should the house be re-mortgaged or the retirement savings cashed in to buy one spouse a few extra months of life? Clearly, this is a horrible position to be in.

All told, an ethical and economic dilemma pitting cost versus lives has emerged. Government and industry must find a solution that is fair and will enable those who would benefit from expensive new drugs to receive them. Without a doubt, there will be no simple solution. Moreover, whatever decisions are made with respect to our much loved public medical system will likely have important implications for the availability of new and expensive new drugs.

Further reading:

CBC News, Cancer drug debate: What's 6 more months of life worth? 31 March 2006 (<http://www.cbc.ca/story/news/national/2006/03/31/cancer-060331.html>)

Fidelman, C., Cancer drug has OK - it just isn't available: Quebec may pay for it; other provinces are withholding funds. *The Gazette*, 27 March 2006 (<http://www.canada.com/components/print.aspx?id=c5d9271c-d0be-42cd-8e0a-4c326514ec77>)

Priest, L., Ontario changes tack on cancer drugs. *The Globe and Mail*, 5 May 2006
Shimo, A., Better screening, newest drugs. *MacLeans*, 25 April 2006 (http://www.macleans.ca/topstories/health/article.jsp?content=20060501_125978_125978)

DO MICE THAT EAT LESS HAVE SOMETHING TO TELL US ABOUT LONGEVITY?

(Continued from page 1)

animals a calorie-restricted diet did not result in extra longevity compared to the increase in longevity that they already have. This is in stark contrast to the increase in lifespan observed upon caloric restriction in normal mice. The authors hypothesize that the longevity increase seen upon caloric restriction and that associated with Growth Hormone Receptor knockout may actually work through the same mechanism. Accordingly, the authors conclude that the Growth Hormone Receptor and the larger hormone system that it is a part of (the somatotropic system) could be important contributors to determining lifespan, and may play a role in increased longevity observed upon caloric restriction.

While this research is interesting, there is still much to learn before caloric restriction will be recommended for humans. We have to keep in mind that these animals have been under this restricted regimen their entire lives. However, it is likely safe to say that not overeating is good for all of us on multiple levels!

Source:

Bonkowski MS, Rocha JS, Masternak MM, Al Regaiey KA, Bartke A. (2006) Targeted disruption of growth hormone receptor interferes with the beneficial actions of calorie restriction. Proc Natl Acad Sci U S A. 103(20):7901-5

A STEP FORWARD IN THE FIGHT AGAINST BREAST CANCER

by Tania Elaine Schramek

Stop for a moment and bring to mind nine women you know. In Canada, one out of those nine women will be diagnosed with breast cancer in her lifetime¹. In the United States, the numbers are one in seven, which translates to a breast cancer diagnosis every 2 minutes². There can be no doubt as to why so much effort is put into finding a cure.

The most common form of breast cancer in postmenopausal women is estrogen-dependent. Estrogen is a natural mitogen – a substance that causes cells to divide – and in this form of breast cancer, cells are dividing too quickly. Now, to get estrogen, hormones known as androgens must be converted by the enzyme aromatase. A lot of aromatase means more estrogen, which in turn means more cells dividing quickly.

Treatment for this form of cancer typically involves drugs that prevent the production of aromatase. Although aromatase inhibitors effectively decrease

the amount of estrogen available, they do so in the entire body. This means that other tissues (e.g. the brain and bones) that rely on aromatase for their normal functioning tend to suffer.

A new study from Ohio State University has shown that derivatives of a pain killer called nimesulide stopped the production of aromatase in breast cancer cells but did not affect aromatase levels in a control tissue sample (placental tissue). Nimesulide is a non-steroidal anti-inflammatory drug (NSAID) normally used in the treatment of pain and inflammation. The researchers altered the chemical structure of the drug creating an analog. The analog prevented the first step (transcription) in the aromatase production process in breast cancer cells. This was critical because compared to other tissues breast cancer cells use a slightly different signal to indicate when it is time to make more aromatase.

The researchers are now in the process of making sure that the analog's actions are

isolated to breast tissue and will start testing it in animals to get an idea of what side effects might be associated with its use. The hopeful results from this and other studies are telling us that continued investment in research and public fundraising efforts like 'Walking for the Cure' are truly making a difference.

Source:

http://www.hc-sc.gc.ca/hl-vs/alt_formats/hpb-dgps/pdf/facts_cancer.pdf

http://www.breastcancer.org/press_cancer_facts.html

Bin Su, Edgar S. Diaz-Cruz, Serena Landini, and Robert W. Brueggemeier* (2006). *Novel Sulfonanilide Analogues Suppress Aromatase Expression and Activity in Breast Cancer Cells Independent of COX-2 Inhibition*. *J. Med. Chem.* 49, 1413-1419

SCIENCE HERE AND NOW

SHARI BROTMAN, PH.D.: ON THE REALITIES OF AGING AND HOMOSEXUALITY

by Tania Elaine Schramek

McGill University and its School of Social Work have cause indeed to be proud of the efforts of Associate Professor Shari Brotman, Ph.D. The month of March was abuzz with media activity as Dr. Brotman and her research team revealed results from the first multi-city study investigating the health and social service needs of gay and lesbian older adults in Canada.

Over a series of 90 interviews with older adults, caregivers, and health care and social service providers in Montreal,

Vancouver, and Halifax, the study evaluated how past experiences of discrimination, current homophobia, oppressing secrecy, and experiences in long-term care contribute to the current experiences of homosexual older adults within the health and social service systems of Canada.

Much to the dismay of the research team, the 4-year study revealed that gay and lesbian older adults face discrimination in the form of homophobia (extreme fear or hatred of homosexuals) or heterosexism (the assumption that all forms of sexuality other

than heterosexual are deviant). In real terms, this translates to experiences such as doctors showing disgust upon finding out that their patient is homosexual or a caregiver trying to 'rid' her patient of his homosexuality through imposed religion. One man felt the need to hide all the pictures of his dead partner before his caregiver arrived at his home, while another man wanting to hug his ailing partner carried him to the washroom of his long-term care facility to do so. Further still, one woman legally changed her

(Continued on page 6)

SHARI BROTMAN, PH.D.: ON THE REALITIES OF AGING AND HOMOSEXUALITY

by Tania Elaine Schramek

last name to that of her partner's so that they could live in the same room as 'sisters'.

According to the work of Dr. Brotman and other experts in this field, current attitudes can be in part understood, but by no means excused, by taking a closer look at the history of homosexuality within the health care context. Up until 1973, homosexuality was considered a mental illness from which people needed to be 'cured' usually through electroshock or aversion therapy. Although we have progressed since those days, the findings of this study clearly show that there is still considerable work to be done where people's attitudes and treatment practices are concerned.

In fact, in a recent scientific article, Dr. Brotman reports that "gay and lesbian

patients of all ages still report negative reactions from service providers. These include embarrassment, anxiety, inappropriate reactions, direct rejection of the patient or exhibition of hostility, harassment, excessive curiosity, pity, condescension, ostracism, refusal of treatment, detachment, avoidance of physical contact, or breach of confidentiality. Many older adults who were openly gay or lesbian (i.e. had 'come out') have gone back into hiding when they began to require healthcare services". Dr. Brotman adds that "in the absence of formalized training or a set of standards in caregiver organizations, it leaves it wide open for the caregivers' ignorance and prejudices to come shining through".

Dr. Brotman reminds us that the gay and lesbian older adults of today are those that lived through the discrimination of yesterday and were thus not afforded the greater tolerance that came about as a result of the gay liberation movement of the 1960's in Canada and the United States. Their experiences continue to shape their lives today. For this 'preliberation' cohort as Dr. Brotman puts it, keeping their sexual orientation hidden was the survival strategy of choice.

For many of this generation, living openly as gay or lesbian adults has resulted in being shunned by their families. But it is often the very same individuals who were disapproving of their orientation that are called upon to make important decisions regarding their welfare. In the current system, the partner's of the patient or their surrogate family are unrecognized and as such do not have a say.

To be sure, gay and lesbian rights are at the heart of these issues and until standards of care are developed and put into practice Dr. Brotman fears that many older adults will unfortunately not get the care their

lifelong work and struggles should afford them. Not is all bleak however. The study did reveal that Montreal fared rather well compared to the other cities in that health and social services employees here had more education and awareness about gay and lesbian issues. Moreover, many gay and lesbian older adults wished to move to Montreal for precisely these reasons.

Sources

Sue Montgomery: Tough to be Gay and Aging The Gazette March 15th 2006

Brotman, S. Ryan, B.& Cormier, R (2003) The Health and Social Service Needs of Gay and Lesbian Elders and Their Families in Canada. The Gerontologist, Vol. 43, No. 2, 192-202.

McGILL CENTRE FOR STUDIES IN AGING

6825 Lasalle Blvd.
Verdun, Québec H4H 1R3
Tel.: (514) 766-2010 / Fax: (514) 888-4050
E-mail: mcsainfo@po-box.mcgill.ca
Website: <http://www.aging.mcgill.ca>

EDITORIAL TEAM

EDITOR-IN-CHIEF

Sonia Lupien (Douglas Hospital, MCSA)

EDITOR

Ginette Lacoste

ADMINISTRATOR

Silvana Aguzzi (MCSA)

JOURNALISTS

*Daniel Auld
(Freelance Medical Writer)*

*Tania Schramek
(Douglas Hospital Research Centre)*

TRANSLATION

Lacoste Royal

LAYOUT AND PRINTING

Imprimerie Miro inc.

**WE THANK NOVARTIS
FOR THEIR GENEROUS SUPPORT TO
THE GERONTO-McGILL.**