THE TENSION BETWEEN MEDICAL PROMISE AND ETHICAL CONTROVERSY: STEM CELL AND GENE THERAPY
An Interview with Dr. Kathleen Cranley Glass, Associate Professor, Departments of Human Genetics and Pediatrics, and Director, Biomedical Ethics Unit, McGill University

Medical breakthroughs splash their promises of cures for debilitating disease on headlines at an ever increasing rate. But in the midst of the euphoric furor that follows these announcements, there are those who say “Yes, now we can do this. But should we?” This is often the role of bioethicists, such as Dr. Kathleen Glass.

Dr. Glass achieved a doctorate in health law and bioethics at McGill in 1992. Her doctoral work concerned the ethical and legal issues surrounding elderly persons in the medical system. Dr. Glass did post-doctoral work with Benjamin Freedman and Abraham Fuks in the Biomedical Ethics Unit’s Clinical Trials Research Group (CTRG). Now the CTRG’s primary investigator, she explains that “the primary proposition of the CTRG is that there is no aspect of research that is devoid of ethical content, whether it be the choice of what research to fund, the design of the research, the implications of the research, or the follow up.” She is also the clinical ethicist at The Montreal Children’s Hospital, and is a member of that hospital’s Clinical Ethics Committee and Institutional Review Board, and is the chair of the Bioethics Master’s program at McGill offered by the interdisciplinary Biomedical Ethics Unit.

Dr. Glass and her CTRG colleagues now have four main projects on the go. Some of these projects involve the ethical analysis of stem cell therapy and gene therapy. Theoretically, these two therapies could have a huge impact on some of the

AGGRESSIVE HYPERTENSION TREATMENT CAN BENEFIT OLDER ADULTS

by Alison McTavish

High blood pressure is one of the commonest and least adequately treated cardiovascular conditions in older adults. A new study has shown that older adults with multiple risk factors for cardiovascular disease may benefit the most from antihypertensive treatment.

Among Canadians over the age of 65 years, 28% of men and 36% of women have hypertension. Less than a third of these patients have their blood pressure under control with antihypertensive medication.
FIGHTING AGEISM: INFORMATION AND REINFORCEMENT MAY BE KEY

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contained in the tape. The third group viewed the tape and participated in a discussion in which the moderator verbally reinforced any comments that conveyed non-ageist beliefs. Immediately after viewing the tape, all three groups of students showed positive changes in their beliefs about aging, as measured by changes on a test questionnaire which had also been administered before the viewing. Discussion groups were repeated a week later under the same conditions. When one month later all subjects were assessed on the ageism questionnaire, only those who had expected and received reinforcement, as conditioned through the discussion group, showed maintenance of this positive attitudes change towards the elderly.

The authors suggest that the mechanism for the maintenance of attitudinal change may be in the additional thought given to the information when reinforcement is known to be forthcoming. Since subjects in the reinforcement group knew before the second session that they would be talking about how the information had changed their views towards aging and the elderly, they may have continued to reflect on this information over the intervening week.

While these findings may point towards useful strategies in incorporating both positive information and reinforcement into educational programs which combat ageism, Ragan and Brown suggest that it is still more important to demonstrate that such attitude changes translate directly into alterations in discriminatory behaviours or practices against the aged.


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most debilitating diseases that strike seniors, such as Parkinson’s and Alzheimer’s. However, the enthusiasm for the potential healing promised by this research is tempered by the controversy it provokes.

Stem Cell Research

Unlike most human cells, such as skin or kidney cells and neurons, which are specialized to carry out specific tasks, stem cells are unspecialized. And herein lies their great promise: under the right conditions, stem cells could be coaxed into becoming any type of cell. The hope is that if disease or injury were to damage an organ, such as the brain through a stroke or Parkinson’s, then the cells that were destroyed (neurons, for example) could be replaced with new cells generated from stem cells. The main ethical concern with stem cells is their source. There are five possible sources of human stem cells: adults, human germ cells removed from electively aborted fetuses, “left over” in vitro fertilization (IVF) embryos, embryos created by IVF solely for use in research, and human (or hybrid) embryos created through cloning techniques for research. The use of adult stem cells is relatively non-controversial, although some issues need to be resolved, such as stem cell donation. We already have guidance in this area since we have been doing stem cell transplants for years, either using a patient’s own cells or a donor’s: bone marrow transplants. The haemopoetic stem cells, which replenish our blood cells, are found in the bone marrow.

Where the ethics get sticky and emotions run high is when the stem cells come from embryos or aborted fetuses. These are embryonic stem (ES) cells and embryonic germ (EG) cells, respectively. The position of the proponents for doing ES and EG cell research is that these cells are more plastic and easier to work with than adult stem cells, and so to rely solely on adult stem cell research may delay bringing a cure to horrible and debilitating diseases. These researchers argue that the potential good – cures for disease and relief of suffering – that will result from ES and EG cell research far outweigh the perceived harm of destroying some human embryos. To this, Dr. Glass responds that we must step back and consider the nature of the human embryo, and what value we place upon it. For some, whether due to religious beliefs or not, the answer is unequivocal: at conception, a human embryo is a person, enjoying the full human rights that all persons are entitled to. To kill one person, even if it may benefit many others, is wrong.

Therefore, these people believe abortion and all research that may harm or destroy human embryos is wrong. On the other hand, some people believe the human embryo is merely a bunch of cells, no more valuable than skin and intestinal cells people shed every day.

Clearly, these two views are not easily reconciled. This was a problem the USA faced in September 2001 when Bush came up with the compromise that federal funding would only go to researchers using the 60-65 embryonic stem cell lines already extant, but not to researchers who made new lines. Dr. Glass thinks this was a political compromise that made little moral sense. “If it is OK to use existing cell lines originally derived from ‘leftover’ IVF embryos, then why would it be wrong to make new cell lines from ‘leftover’ IVF embryos?” She points out that in contrast to Bush’s compromise, the Canadian report from the CIHR Working Group on stem cell research recommended that research with ‘leftover’ IVF embryos be permitted upon the parents’ consent, the logic being that these embryos were already scheduled to be destroyed. However, no funding would go to researchers who wished to produce embryos solely with the intent of using them for research. The Canadian compromise reflects the view that though a human embryo should not be viewed as a person, it still merits respect.

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Exercise in Your Later Years: A Little Goes a Long Way
by Jeff Boyczuk

No pain, no gain? Maybe the old adage is true if you're a 20-year-old bodybuilder craving bigger biceps. But if you're an older adult, a daily after-dinner walk might be exertion enough to give you a healthier heart, and protect you from certain age-related chronic diseases.

This news comes from Loretta DiPietro of the Yale School of Medicine. DiPietro waded through the large number of studies examining the health benefits of exercise for elderly individuals, and found that even moderate amounts of activity can make a difference. While most research has focused on the protective effects of vigorous activities (e.g., swimming, jogging, playing tennis), there is also considerable evidence that less strenuous forms of exercise can have equal health benefits, if sustained over longer periods of time. For instance, one study that looked at the relationship between heart health and physical activity found that seniors who engaged in low-intensity exercise, equivalent to 1 1/2 hours of brisk walking every week, derived the same cardiovascular benefits as those who engaged in 45 minutes of more vigorous exercising. Other research has shown that regular moderate activity decreases the chances of developing type 2 diabetes, or improves the glucose response for those suffering from this disease.

Small lifestyle changes, such as choosing the stairs over the elevator, or walking to the store rather than driving, may be important for seniors who are more sedentary, says DiPietro. Physiological changes in flexibility, strength and balance may prevent many older adults from engaging in sports and fitness activities that are more physically taxing. Furthermore, the high cost of fitness and sport equipment, or memberships at gymnasiums, may make organized fitness activities less accessible to seniors in their retirement years.


Walking Improves Brain Health
by Hannah Hoag

Older women who walk regularly may reduce their risk of developing cognitive impairment. Kristine Yaffe of the University of California, San Francisco, and her colleagues studied the effects of moderate exercise on cognitive decline in 5925 women aged 65 years or older.

The researchers used the Mini-Mental State Examination to determine the cognitive function of each woman at the beginning of the study. The women were also interviewed about the amount, duration, and intensity of physical activity performed each week.

Six to eight years later, the MMSE was repeated. Yaffe and her colleagues found that 24% of the women in the lowest exercise quartile lost three or more points in the follow-up MMSEs, indicating cognitive decline. When compared to the lowest quartile, women in the highest quartile were 37% less likely to develop cognitive decline.

When women were stratified into subgroups according to age, co-morbid medical conditions, and educational level, the women who participated in physical activity were always less likely to have suffered cognitive decline during the interim period.

While other studies have suggested that intense physical activity may reduce cognitive decline, this study revealed that moderate forms of exercise such as walking 1.6 km per day, playing 18 holes of golf once a week, or playing tennis twice a week can reduce cognitive decline in elderly women.

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Interview with Dr. Kathleen Cranley Glass.

What are the ethical concerns about gene therapy? First, it is important to distinguish between somatic gene therapy and germ line gene therapy. In humans and all other multicellular organisms, most of our cells are somatic—they form our body, and many of them can replicate themselves, but their genetic material is not passed on to offspring. In contrast, our germ cells—ovum and sperm—pass on parents’ genes to their children. Mutations in specific genes can cause disease. Somatic gene therapy seeks to restore a functional copy of the affected gene to the patient in hope of curing his or her disease. On the other hand, germ line gene therapy alters the genes in the germ cells. All of the resultant offspring’s cells—somatic and germ—are permanently altered genetically, and all of the descendents of this offspring are altered as well. Those advocating germ line gene therapy see it as the ultimate way to eradicate terrible genetic diseases—why “fix” people one by one if you could do all of a person’s descendents in one fell swoop? At first blush this does seem appealing. However, as Dr. Glass puts it, “with somatic gene therapy we are dealing with one person who can choose to consent to the procedure. By contrast, with germ line gene therapy we face what one commentator called an ‘infinite cohort of research subjects’— the future generations who can not give consent to their genetic makeup being altered.” This is especially a concern given that there could be unforeseen side effects of gene therapy. Unlike a drug that can be discontinued if side effects are severe, a genetic change is permanent. While a competent patient may decide to have the procedure despite the risks, do they, or anyone else, have the right to impose these risks on future generations? Furthermore, Dr. Glass says “deliberately manipulating the genome of

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The other two thirds are either inadequately treated or are not treated at all.

Hypertension is a blood pressure persistently higher than 140/90 mmHg. However, in many older adults only the systolic blood pressure is high, a condition known as isolated systolic hypertension (ISH). For these patients, the systolic pressure is at or above 140 mmHg but the diastolic pressure appears normal at under 90 mmHg. Typically diastolic blood pressure rises until about age 55 and then begins to fall, while systolic blood pressure increases steadily with age.

Although hypertension usually causes no symptoms, it can have serious consequences if left untreated. Patients with hypertension are at increased risk for heart disease, stroke and kidney failure. Heart disease and stroke alone account for 37% of all deaths in Canada each year. Patients who are at the highest risk for developing these conditions are often not treated for hypertension either because of problems with medications or because of the belief that lowering blood pressure may be risky for the elderly.

A recent study published in the journal Circulation studied the risk of future heart attacks, stroke and heart failure in 4,453 adults over age 60 who participated in the Systolic Hypertension in the Elderly Program (SHEP). The participants in the study had systolic blood pressure readings of at least 160 mmHg.

Previous results from SHEP have shown that treating ISH in people over age of 60 lowered the risk of future strokes, heart attacks and congestive heart failure. The purpose of the new study was to establish the benefits of treatment for patients at different risk levels. Researchers divided the participants into four groups based on their risk of developing future heart attacks, stroke and heart failure. Patients who were smokers and had high cholesterol, for example, were considered to be at higher risk. The researchers found that treating patients with the highest risk was four times more effective than treating the low-risk group. The authors conclude that older adults with several risk factors should therefore be prime candidates for antihypertensive therapy.


SETBACK FOR ALZHEIMER’S VACCINE

by Alison McTavish

A clinical trial of a new vaccine for Alzheimer’s disease was recently halted when four patients became ill. The drug, called AN-1792, has so far been given to about 360 patients worldwide. The four ill patients were part of a group of 97 patients in France, and they all developed an inflammation of the central nervous system. Researchers from Elan, the pharmaceutical company that helped develop the drug, hope that the trial can resume once they establish the cause of the patients’ illness.

Youth Project

The NDG Community Committee on Elder Abuse, the Alzheimer Society of Montreal and the McGill Centre for Studies in Aging are working together as partners in developing a new project that is going to be held in selected schools during the year 2002. The project’s main objective is to develop intergenerational links between seniors and teenagers. A series of 5 workshops that will involve interactive discussions between seniors and teenagers have been planned. Each workshop will present a different subject and one of the sessions will be dedicated to Alzheimer’s disease. Teenagers and seniors will receive information about the disease and will be invited to discuss about its impact on families affected.

The Education Committee, McGill Centre for Studies in Aging

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future generations is an enormous responsibility that I don’t think anyone ought to take on.”

Even if one agrees that somatic gene therapy is acceptable, there is the risk that genetic manipulation of the somatic cells could inadvertently result in alteration of the person’s germ cells as well. Researchers may choose to simply disclose this risk in the informed consent process, or they may design protocols that only include those who do not intend to have children, or those who have already had their children. This could mean that seniors may have a better chance of participating in gene therapy trials. Whether or not this would truly be an advantage to seniors remains to be seen! In any event, Dr. Glass believes these issues should be addressed now, and further cautions “there have been gene therapy protocols since 1989, and we still are a long way from proven treatment that works.”

Like most compassionate people, Dr. Glass sees the value in trying to alleviate human suffering. However, she does not believe this goal should be pursued at all cost, for then we may risk eroding the very foundations of what makes us human.

For more information on the work of Dr. Glass, see:

More Good News for Moderate Drinkers?

by Julie Comber

It has been shown that a drink or two a day may be good for the heart, but could it also be good for the brain? It is known that too much alcohol is detrimental - studies of alcoholics have shown brain atrophy with magnetic resonance imaging (MRI), and heavy drinking is associated with an increased risk of stroke. However, moderate alcohol consumption is associated with a lower risk of stroke and better cognitive performance.

Mukamal et al. published a study this past September that sought to determine the relationship between alcohol consumption and subclinical MRI findings in persons 65 years and older drawn from the Cardiovascular Health Study (CHS). Subclinical findings on MRI of the brain, such as white matter changes, infarcts and enlarged ventricles are associated with poorer neurological and cognitive function, and infarcts and larger ventricular volume are associated with greater decline in cognitive function over time. A total of 3376 participants free of any past cerebrovascular disease were subjected to MRI. Alcohol consumption was evaluated by self reporting and subjects were classified according to their weekly intake in the following categories: none (abstainers), former (drank in the past but currently abstaining), less than 1 drink weekly, 1 to 7 drinks weekly, 7 to 15 drinks weekly, and more than 15 drinks a week.

Mukamal et al. found that moderate alcohol consumption (7 to 15 drinks weekly) was associated with a lower prevalence of white matter abnormalities and infarcts, which are thought to be of a vascular origin. This may help explain why moderate alcohol consumption appears to be protective against strokes. However, the association of ventricular and sulcal size (these are measures of atrophy, with larger spaces meaning the brain’s volume is smaller) with alcohol consumption was linear, with the prevalence of atrophy increasing in a dose-dependant manner.

These results were consistent in women and men, Caucasians and African Americans and across socioeconomic classes. The beverage type (wine, beer and liquor) did not appear to have any significant effect on the results.

Based on these findings alone, it is difficult to weigh the benefits and risks in order to make recommendations to seniors regarding alcohol consumption, and the authors stress the need for more research to assess the overall effects of alcohol consumption on cognitive function and quality of life. However, if one factors in the benefits of moderate alcohol consumption on the heart, it just might tip the scale over to enjoying a drink or two a day. Cheers!

Physical changes inevitably accompany aging. The following websites offer information about the impact of these changes on activity patterns, and offer suggestions for older adults who wish to maximize health benefits through exercise.

**EXERCISE FOR LIFE**
http://www.aoa.gov/aoa/pages/agepages/exercise.html
Fact sheet from the National Institute of Aging. Offers practical tips before starting a fitness program.

**EXERCISE TIPS FOR SENIORS- AMERICAN PHYSICAL THERAPY ASSOCIATION**
http://www.geriatricspt.org/consumer/Young.html
Exercise suggestions with diagrams.

**EXERCISE AND YOUR HEART**
A pamphlet from the National Institutes of Health offering information on cardiovascular health and its relation to exercise.

**SURGEON GENERAL'S REPORT ON PHYSICAL ACTIVITY & HEALTH**
http://www.cdc.gov/nccdphp/sgr/olderad.htm
Fact sheets on fitness and older adults, including tips on how to encourage fitness among seniors through community-based efforts.

**AGING MUSCLE: CHARACTERISTICS & STRENGTH TRAINING**
From the American Physical Therapy Association. Directed at health professionals.

**ENCYCLOPEDIA OF SPORTS MEDICINE & SCIENCE**
http://www.sportsci.org/encyc/
Click on "Aging and Exercise" on the left. Information about energy consumption, aerobic performance, and exercise risks for elderly individuals. Directed towards health professionals.

**PHYSICAL ACTIVITY AND PUBLIC HEALTH -- A RECOMMENDATION FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION AND THE AMERICAN COLLEGE OF SPORTS MEDICINE**
http://wonder.cdc.gov/wonder/prevguid/p0000391/p0000391.asp
A 1995 report.

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