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Adult Stem Cells

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The use of stem cells in treatment of disease continues to develop in many areas and there have been some successful applications of treatments derived from them. It is important to be aware that responsible researchers are careful to explain that some of these treatments are not yet universally applicable, but are still classified as experimental. More evidence is needed, but there is general optimism about their expanded use in the immediate future as well as in the long term.

The Catholic Church continues to endorse the use of adult stem cells. It is well known that its stance is that embryonic stem cell research is not morally permissible, since such research results in their death. Embryonic stem cell research is, however, legal in Canada as long as the women who have had the embryos created through in vitro fertilization agree to release them for experimentation purposes. The results of embryonic stem cell experimentation continue to be mostly problematic. When they have been used in animal experiments to create tissue, the tissue does develop, but cancerous tumours accompany it. Clearly, such results would cause more harm than they purport to solve, were they to be applied to human subjects. Further, in those experiments, the regenerated tissue tends to be rejected by the recipient.

These two factors have delayed what had been expected to be a relatively straightforward path to finding cures based on the use of embryonic stem cells, since, as pluripotent, they have a great capacity to form new tissue, etc. The accompanying problems have marred their predicted success, and, twenty years later, all the successes in treatments for humans have come from the use of adult stem cells.

VATICAN INVOLVEMENT

The Vatican is keenly aware of developments in these areas, and has hosted two major conferences to bring together senior scientists and theologians to discuss these new treatments. The more recent gathering took place on April 11-14, 2013, led by a group called *Stem for Life*, and hosted by the Pontifical Council for Culture. The conference included *NeoStem Inc.,* (a stem cell research company) and *STOQ International*, (*Science, Theology and the Ontological Quest*, a collaboration of Catholic Universities coordinated by the same Council).

The Vatican has gone so far as to invest in a multi-million dollar partnership with *NeoStem, Inc.*, to promote research with adult stem cells. Most people have no idea that the Vatican is involved in such a venture, and it gives the lie to those who think that the Church is not interested in, or worse, is ignorant of science.

This recent conference served to highlight progress in adult stem cell research, relaying several examples of successful applications in people with serious illnesses. It is important to remember, however, that while there have been successes, the scientific world must look at long term as well as immediate results. *Stem for Life* and *NeoStem Inc.,* are based in the US, and they are both careful to point out the need for FDA approval for these new procedures, as well as the need for similar approval from regulatory bodies in other countries. Overall, though, the potential of these successful developments gives cause for optimism.

At the same time, although there is clearly need for caution for the foreseeable future about the application of treatments in humans until possible long term effects may become apparent, the outlook is so promising in some areas that the Pontifical Council for Culture announced this second conference in order to let people know about recent progress. It expressed a desire to make the knowledge of scientific progress in these areas more accessible to lay people, who often do not understand scientific and research terminology, let alone the possible implications of such research and its regulation.

A "readable" book for these purposes had been requested after the proceedings of the first conference, and this was presented to the Council by *Stem for Life* before the second meeting in April 2013. The head of the Council's Science and Faith Foundation said the Council hoped "…to have a cultural influence on society, pointing to research models that are in tune with the highest moral values of protecting life and dignity of the human being from the moment of conception." [1] To further this end, it is recognized that others must be involved: e.g., religious, social and political leaders. Scientists do not reside in neutral silos, but are influenced by religious, social and political values in the same way as everyone else.

The Council added that it desired to promote "...the positive, encouraging and optimistic message of the church's support of high quality ethical research to both scholars –so that they have no doubt of our commitment – as well as to those who are struggling with the pain of degenerative disease and who are awaiting hopeful signs from the research."[2]

THE HEALING CELL

Stem for Life's book is called *The Healing Cell: How the Greatest Revolution in Medical History is Changing Your Life.*[3] While this may sound somewhat exuberant for a scientific text, it carries a message from (then) Pope Benedict XVI, as well as a foreword by Gianfranco Cardinal Ravasi, the President of the Pontifical Council for Culture.

Pope Benedict wrote in his address: "It follows that dialogue between culture and ethics is of the greatest importance in order to ensure that medical advances are never made at unacceptable human cost," and there is no doubt that he is referring to the use of human embryos.[4] Cardinal Ravasi noted in the foreword that: "Today, studies on adult stem cells are a sign of hope that needs to be brought to public attention."[5] He noted the long history of collaboration between church and science and stated: "The current

contentious issue of stem cell technologies need be no different."[6]

NEW BLADDERS AND URETHRAS

The book relates the circumstances of several successful adult stem cell applications, some regarded as fairly straightforward, others of a more experimental nature. It discusses the possibility of organ regeneration, illustrating it through examples of people whose bladders have been regenerated through the use of their own bladder stem cells.

In one case a young woman with spina bifida faced the prospect of renal failure due to an overly stressed bladder. Stem cells from her bladder were seeded onto a 3D model of a bladder made of collagen, which was then implanted with her stem cells.[7] Ten thousand of those were developed into more than 1.5 billion stem cells; the collagen structure biodegraded, and the replacement grew and blended into her urinary system within a few weeks.[8] Six other children with spina bifida have had the same successful treatment, and that surely gives hope to the 73,510 cases of bladder cancer estimated in the US alone in 2012, of whom an estimated 14,880 will die from the disease.[9]

Urethras have been grown in the same way, using a model structure and seeding it with the patient's own stem cells. Five boys with damaged urethras have all been successfully treated using this method.[10] An important point about the use of a patient's own stem cells is that it greatly reduces the possibility of the person's body rejecting the new tissue or organ.[11] Over the very long haul, a further possibility is that the long waiting period for a tissue or organ donation will be reduced, once tissues and organs can be 'grown' from patients' own stem cells.

REGENERATION OF HEART TISSUE

Another successful area of treatment is in patients who have experienced several heart attacks, living subsequently with the knowledge that the next one could be fatal. The book relates the case of one such patient who was able to enrol in a clinical trial for end-stage heart disease. Stem cells were harvested from bone marrow extracted from her hip bone and concentrated for specific stem cells that were marked with the protein CD34+.[12] Experiments on mice had shown that these particular cells promote the growth of the blood vessels needed to bring nutrients to damaged heart tissue, and clinical trials were started to see if the same results would occur in humans. The patient's heart did begin to heal after injection of these stem cells, but it was observed that although the damaged tissue began to grow back, the stem cells used did not become heart stem cells themselves, as researchers had thought they might, but seemed to promote the growth of new blood vessels and perhaps encouraging growth factors in almost dead tissue.[13]

An earlier Harvard study in *Molecular Therapy* had reported a similar conclusion: "…CD34+ stem cells… restored early cardiac function…" and noted that they repaired hearts without themselves becoming stem cells.[14] This result adds to the growing list of capacities of adult stem cells, which were once thought to have limited functions, compared to embryonic stem cells.

Further, CD34+ stem cells are not the only stem-like cells that mobilize in the blood stream after a heart attack. [15]There is also a

five-fold increase in the number of circulating VSELs (very small embryonic-like cells) that live in the adult body but retain their pluripotency, that is, they have some of the capacities of embryonic stem cells. It is important to stress that these VSELs are not themselves embryonic stem cells, yet, according to some studies, they may even have the potential to become new heart tissue.[16]

REPLACEMENT TRACHEAS

A recent article in Canada's *National Post* described how a baby born without a trachea has had a new one "grown" from her own stem cells.[17] It looks as if further surgery will be needed eventually, and the child still needs to use a ventilator, but she no longer needs a feeding tube. Bone marrow stem cells were extracted from her hip bone and seeded onto a plastic model of a trachea. It took less than a week for her stem cells to multiply into the number needed to fashion a new wind pipe, which has grown into place in her body. At two years old, she is the youngest person in the world to have had this treatment and fourteen others have already been so treated using their own stem cells.

CRITICAL LIMB ISCHEMIA

In another development reported in November, 2011, a biotechnology company named *Aastrom Biosciences* did a twelve month follow-up study of its phase II clinical trial for patients who have critical limb ischemia (CLI), which means that patients have an inadequate blood supply to their limbs.[18]

Some of them had a mixture of their own stem cells injected into twenty points in their diseased lower thighs, calves and feet. [19]Those so treated showed a 62% reduction in complications compared to those treated in the study with a placebo.[20]

A study done with similar patients was published in *Vascular and Endovascular Surgery* in 2011, where ten patients with CLI who had not responded to treatment faced the prospect of amputation. They were first treated with a drug that encourages bone marrow to release stem cells into the blood stream and the muscles surrounding the critical zones of the ischemia were then injected with their own, concentrated mesenchymal stem cells (cells that can differentiate into a variety of cell types).[21] Seven avoided amputation and three required amputation of tissues far below the injected area that had already decayed beyond repair. In the seven successfully treated, their legs grew new blood vessels.

NEED FOR PROPER REGULATION

While these results are positive and encouraging, they must be balanced by other results such as those referred to in an article in *Forbes*, indicating different results from those included in *The Healing Cell.* [22] One such study of CLI, for example, found that half of the patients experienced severe complications from treatments using adult stem cells, and that study was terminated. Complications were serious, including heart attack and thrombosis. The study was very small (only 9 patients), and the mean age was 77, yet the results would indicate that use of patients' own stem cells is still not completely safe, highlighting the need for proceeding through the proper channels of animal testing, achieving FDA (or equivalent) approval, conducting proper clinical trials, and so on.

The authors of *The Healing* Cell are clear about which treatments have been approved and which treatments are still at the clinical trial stage. The latter are still experimental, with no solid approval yet as to efficacy or safety. The former include treatments based on adult stem cells already approved and in use for burns, brain trauma, stroke, psychiatric disorders, Alzheimer's and neurodegenerative diseases, arthritis, and many others. The last chapter of their book gives helpful information on which stem cell therapies are safe, available, and approved, at least in the US.

The Vatican also emphasizes that any treatments intended for curing or treating human beings must be thoroughly tested and subjected to regulatory scrutiny and approval. These precautions are clearly necessary to protect vulnerable patients, and the authors acknowledge this as primary, even as the book relates one type of successful treatment after the other.

They do point out that, however, that when a patient's prospect of dying from an illness is imminent and no other treatment is available, he or she could consider being enrolled in an appropriate clinical trial.[23] The outcome *could* be successful, and in a sense, there is nothing to lose at this stage by taking part. The authors point out numerous successes in people who have done so.

They also note that, while approved clinical trials do exist, patients must be their own agents in pursuing enrollment in one of them. Although it is possible to enroll in trials in several countries, the authors strongly advise caution, since some countries do not have the same level of monitoring as, for example, Canada or the US. Non-FDA approved treatments may be offered in the US itself, but the authors warn people to enroll only in trials that combine scientific enquiry with monitored testing and high ethical values. [24]

This book is certainly quite different from other books written with a papal foreword. Its real point is to convey the reality of the successes of treatments derived from adult stem cells and applied in human subjects. The authors recognize a slight conundrum in the fact that some scientists and even the media seem to have difficulty in acknowledging these successes, perhaps because they hope that the embryonic stem cell research they initially espoused will yet yield even better results. This may eventually be the case, but the current lack of endorsement from these sources is puzzling.

One final point: while the Vatican clearly endorses only those treatments that are properly and responsibly tested, their endorsement of *NeoStem Inc.* raises a slight ethical concern. There is, naturally, a commercial aspect to this company, and while that is certainly legitimate, it seems strange, not that the Vatican would encourage its work but that it took the step of investing in it. That does not seem necessary, when sheer observation and advice from many other sources have been pointing to the successes of adult stem cells over the years. There are many individuals and companies involved in this field, and supporting one group seems arbitrary.

To be sure, that gripe does not detract from the admirable work being done by *NeoStem* and other responsible companies, and it is truly gratifying that breakthrough treatments

are occurring through the use of stem cells that do not raise the ethical dilemmas associated with embryonic stem cells. We can thank God and excellent scientists for that! ■

(A following article will look at developments in the creation and uses of embryonic and induced pluripotent stem cells.)

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[1] Vatican Information Service, Vatican City, 5 April 2013. Msgr. Tomasz Trafny made these remarks at the Second International Vatican Adult Stem Cell Conference, April 11-13. 2013.
[2] *Ibid.*
[3] Smith, Robin L., Trafny, Msgr. Tomasz, Gomez, Max, PhD. *The Healing Cell: How the Greatest Revolution in Medical history is Changing Your Life.* (Center Street: New York) 2013.
[4] Pope Benedict XVI. *The Healing Cell,* Pp. x-xi.
[5] Cardinal Gianfranco Ravasi. *The Healing Cell,* P. xv.
[6] *Ibid.*
[7] *The Healing Cell,* P.4.
[8] *Ibid.*
[9] *Ibid.* P.5.
[10] *Ibid.* P.6.
[11] *Ibid.* Pp. 6-7.
[12] *Ibid.* P.14.
[13] *Ibid.* P.19.
[14] *Ibid.*
[15] *Ibid.* P.25. Referencing an article in *The American Journal of Cardiology,* 2009.
[16] *Ibid.* Referencing an article in *The Lancet,* 2011.
[17] Lindsay Tanner. "Windpipe grown with Stem Cells." National Post, May 1, 2013. P. A3.
[18] *Ibid.* P.27.
[19] *Ibid.*
[20] *Ibid.* P.28.
[21] *Ibid.*
[22] John Farrell, "Researchers Highlight Warning Signs on Adult Stem Cell Treatments." http://www.forbes.com/sites/johnfarrell/2013/02/12/researchers-highlight-warning-signs-on-adult-stem-cell-treatments/Accessed May 18, 2013
[23] *The Healing Cell.* Chapter 18. http://www.clinicaltrials.gov/ is the most comprehensive data base for clinical trials in the US. In Canada, see: http://www.clinicaltrialscanada.com
[24] *Ibid.* Pp. 208-11.