Stem Cell Treatments

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Committee on Health and Human Services, the Kansas House
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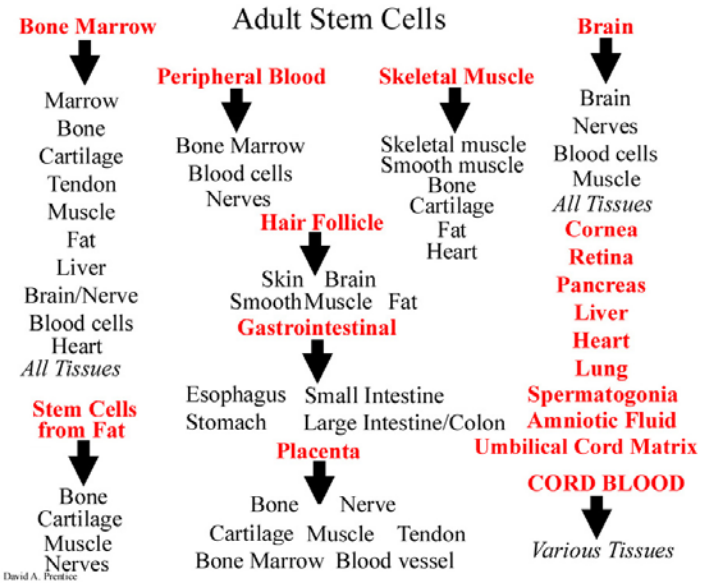
Madam Chair, the Distinguished Ranking Member, and Honored Members of the Committee.

Thank you for the opportunity to testify on this important topic.

I am a cell biologist, currently working for a policy think tank in Washington, D.C. For the previous 20 years I was Professor of Life Sciences at Indiana State University and Adjunct Professor of Medical & Molecular Genetics at Indiana University School of Medicine, and I have done federally-funded laboratory research, lectured, and advised on these subjects extensively, in the U.S. and internationally. I was selected by the Bush President's Council on Bioethics to write the comprehensive review of adult stem cell research for the Council's 2004 publication "Monitoring Stem Cell Research".

A 2008 paper in the journal *Biology of Blood and Marrow Transplantation* calculated that there was a 1 in 200 chance that you or I, or anyone living in the U.S., would undergo an adult stem cell transplant during our lifetime.[1] You've heard from the other panelists about some of the amazing stem cell treatments that are ongoing, some that are on the way, and the need for much more in the way of patient treatments, as well as accessibility and education for both physicians and patients about current and potential stem cell treatments. I'd like briefly to discuss a few more examples.

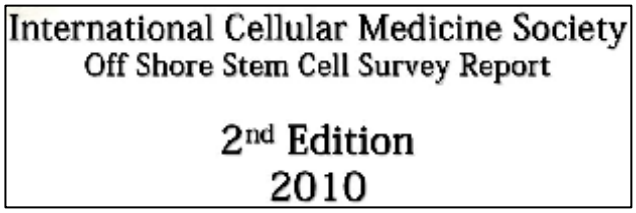
The chart shows examples (not all-inclusive) of tissues from which adult stem cells have been isolated, as well as some of the derivatives from those stem cells. Many references also show that adult stem cells can multiply in culture, retaining their ability to differentiate, and providing sufficient numbers of cells for clinical treatments. Adult stem cells have already shown great promise in treating various diseases in animal studies.



[1] Nietfeld JJ *et al.*, Lifetime Probabilities of Hematopoietic Stem Cell Transplantation in the U.S., *Biology of Blood and Marrow Transplantation* 14, 316-322, 2008

But of even greater significance, **adult stem cells are already being used clinically to treat many diseases in human patients**. This is a fact that many Kansans, the public and physicians alike, do not know. The lack of knowledge affects health as well as life. There have been a few attempts to educate people about the possibilities and availabilities of stem cell treatments. For example, the Cell Therapy Foundation has used famous actor Dick Van Dyke to make people aware of stem cell therapies.

But patients also need to be aware of the risks involved, and learn the difference between legitimate treatments and clinical trials, backed by published scientific evidence and good technique, versus possible scams, especially via the internet, that would likely only take their money. While there have been some attempts to educate as well as categorize stem cell treatments, there is still little information available to doctors as well as to the public.

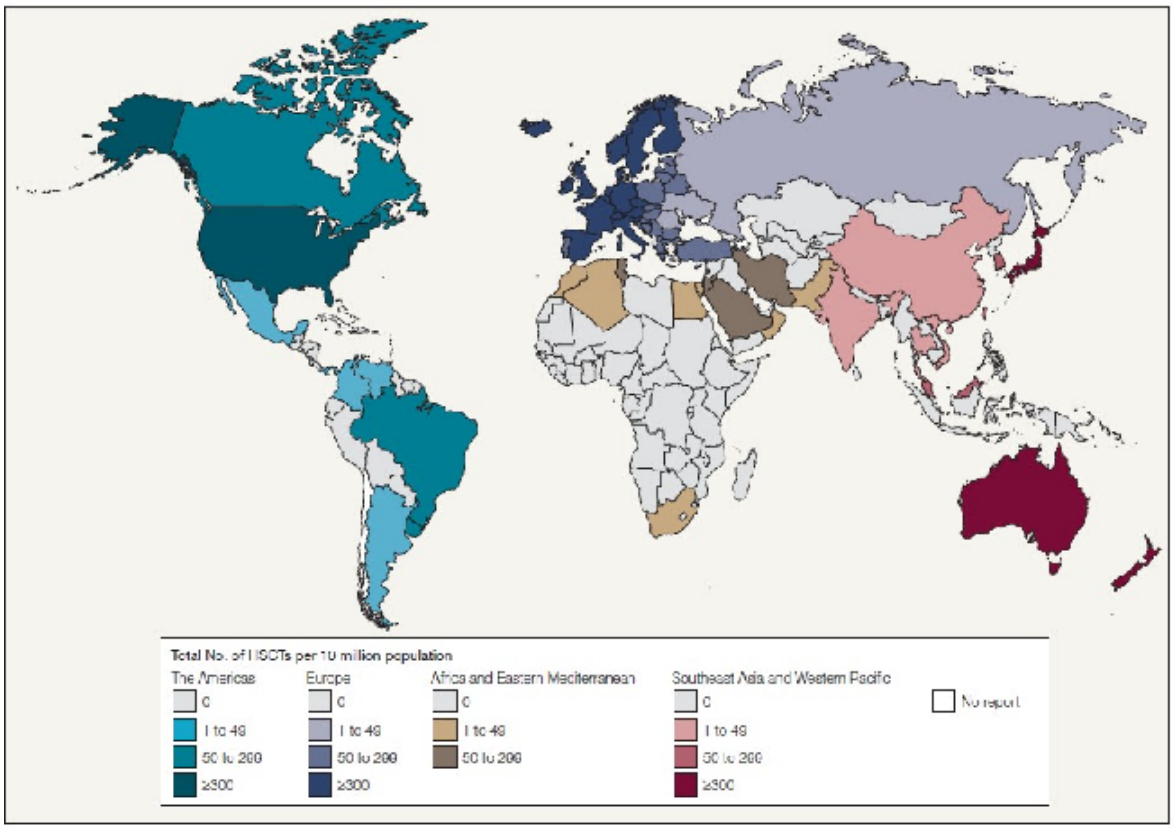


At this point there are few sources for patients or physicians. One that is often used is the website **clinicaltrials.gov**, run by the FDA and NIH. This site lists over 2,300 stem cell clinical trials, but still does not capture all of those available globally.

A 2010 article in the *Journal of the American Medical Association* provides a global perspective on adult stem cell transplants.[2] Researchers looked at how many adult stem cell transplants were taking place in various parts of the world. This particular study looked only at hematopoietic stem cell transplants, *i.e.*, transplants of blood-forming cells, obtained from bone marrow, peripheral blood, and umbilical cord blood; and did not survey uses of other adult stem cell types, such as mesenchymal, adipose-derived, or nasal adult stem cells. The published report found that in 2006, a total of 50,417 transplants were performed worldwide using these adult stem cells. Of that total, 57% used the patient's own adult stem cells, and 43% used donor adult stem cells. Almost half (48%) took place in Europe, followed by the Americas (36%), Asia (14%), and the Eastern Mediterranean and Africa (2%). They note that adult stem cell transplants have become "**the standard of care for many patients**" with blood disorders and malignancies, though they are starting to be used for other conditions including autoimmune disorders and heart disease. They also note that their study "**demonstrates that it is an accepted therapy worldwide**".

[2] Gratwohl A *et al.*, Hematopoietic stem cell transplantation, *JAMA* 303, 1617-1624, 2010

Figure 1. Global Distribution of Hematopoietic Stem Cell Transplantations (HSCTs) in 2006



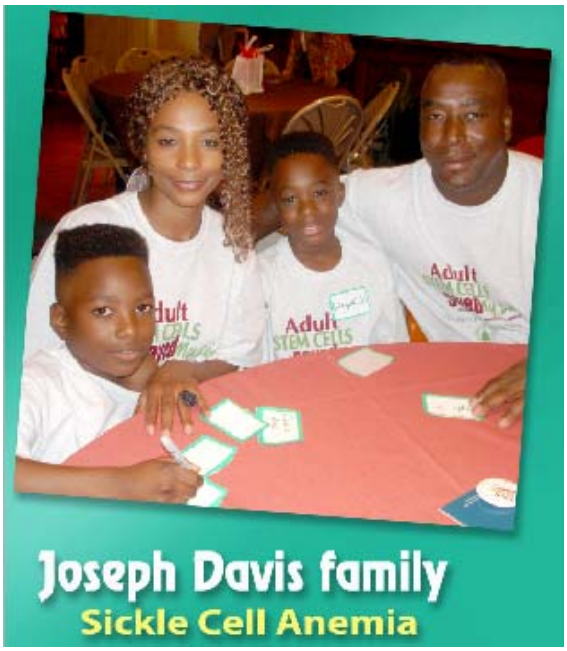
Regions are colored by World Health Organization regional office code (see text) (http://www.who.int/about/regions/en/). Transplant rates indicate the number of first HSCTs per 10 million inhabitants in 2006 and are allogeneic and autologous by continental region.

You've already heard some of the successes of stem cell treatments for patients, for numerous types of autoimmune diseases such as multiple sclerosis,[3], as well as type I (juvenile) diabetes.[4] And stem cell transplants have a solid record in treatment of various cancers such as multiple myeloma and leukemia.

[3] Fassas A *et al.*, Long-term results of stem cell transplantation for MS, *Neurology* 76, 1066-1070, 2011; Rice CM *et al.*, Safety and Feasibility of Autologous Bone Marrow Cellular Therapy in Relapsing-Progressive Multiple Sclerosis, *Clinical Pharmacology & Therapeutics* 87, 679-685, June 2010, published online 5 May 2010, doi:10.1038/clpt.2010.44; Burt RK *et al.*, Autologous non-myeloablative haemopoietic stem cell transplantation in relapsing-remitting multiple sclerosis: a phase I/II study, *Lancet Neurology* 8, 244, March 2009

[4] Voltarelli JC and Couri CEB, Stem cell transplantation for type 1 diabetes mellitus, *Diabetology & Metabolic Syndrome* 1, 4, 2009; doi:10.1186/1758-5996-1-4; Couri CEB *et al.*, C-Peptide Levels and Insulin Independence Following Autologous Nonmyeloablative Hematopoietic Stem Cell Transplantation in Newly Diagnosed Type 1 Diabetes Mellitus, *JAMA* 301, 1573-1579, 2009; Voltarelli JC *et al.*, Autologous Nonmyeloablative Hematopoietic Stem Cell Transplantation in Newly Diagnosed Type 1 Diabetes Mellitus, JAMA 297, 1568-1576, 2007

But there are other success stories with published evidence. According to several published medical authors, "Hematopoietic stem cell transplantation (HSCT) is the only curative therapy for sickle cell disease."[5] Young Joe Davis, Jr. is alive and well because his younger brother Isaac was a match with his umbilical cord blood stem cells for transplant.



Even more exciting are some of the experimental applications of adult stem cells, including the "skin gun" developed by Dr. Gerlach at Pittsburgh.[6] Dr. Gerlach and colleagues have developed a way to isolate adult stem cells from burn patients and spray them back onto wounds, speeding healing.

<video>

[5] Bernaudin F *et al.*, Long-term results of related myeloablative stem cell transplantation to cure sickle cell disease, *Blood* 110, 2749-2756, 2007

[6] Gerlach JC *et al.*, Method for autologous single skin cell isolation for regenerative cell spray transplantation with non-cultured cells, *Int. J. Artif. Organs* 34, 2011; Gerlach JC *et al.*, Autologous skin cell spray-transplantation for a deep dermal burn patient in an ambulant treatment room setting, *Burns* 2011

Growth of new tissue and organs has been accomplished as well, with first reports of growth new functional bladders for patients,[7] as well as construction of functional urethras.[8] Kaitlyn McNamara had her new functional bladder constructed from her own tissue stem cells.

Other scientists have used the patients cells to regrow bone and cartilage and to repair joint damage.

An early clinical trial has shown initial success in treating a patient for Parkinson's disease[9] Dennis Turner was the first patient treated with his own adult neural stem cells from his brain, in an attempt to help his Parkinson's symptoms. Though treated in only one-half of his brain, Turner went almost 5 years with few symptoms.

Another recent example in the neurological area is the initiation of clinical trials to treat stroke and traumatic brain injuries. Initial results of the stroke trials have been very encouraging.[10] Roland Henrich was the first patient enrolled in the trial. He was treated within 24 hours after his stroke with his own bone marrow adult stem cells. Within 11 days after treatment he showed no signs of paralysis and said his first word since the stroke.

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[7] Atala A *et al.*, Tissue-engineered autologous bladders for patients needing cystoplasty, *The Lancet* 367, 1241-1246, 2006

[8] Raya-Rivera A *et al.*, Tissue-engineered autologous urethras for patients who need reconstruction: an observational study, *The Lancet* 377, 1175-1182, 2011

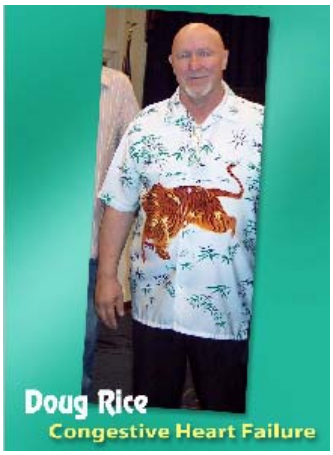
[9] Levesque MF *et al.*, Therapeutic Microinjection of Autologous Adult Human Neural Stem Cells and Differentiated Neurons for Parkinson`s Disease: Five-Year Post-Operative Outcome, *Bentham Open Stem Cell Journal* 1, 20-29, 2009; doi: 10.2174/1876893800901010020

[10] Savitz SI *et al.*, Intravenous autologous bone marrow mononuclear cells for ischemic stroke, *Ann. Neurol* 70, 59-69 2011

Other recent peer-reviewed publications document patient improvement with adult stem cells in treatment of spinal cord injury.[11] Silvio Folegnani is one of the patients who has participated in the trials. Two years after an accident left him quadriplegic, he was treated with adult stem cells from his own nasal tissue, and has shown significant improvement.

Peripheral artery disease has now been treated successfully in a number of patients, restoring circulation to limbs and preventing amputation.[12] Helen Thomas at right is one example of such success.

Adult stem cells have also shown documented success at treating chronic heart failure in 191 patients.[13] Doug Rice had been told that he had only a short time to live, but after treatment with his own adult stem cells he has thrived for years.



Stem cell treatments for heart damage are being studied in numerous clinical trials now, both in the U.S. and internationally. Germany in particular has been a leader in such studies.

Numerous peer-reviewed papers document improvement in patient health after adult stem cell treatment, including a paper published in 2008 in the *Journal of the American Medical Association* reviewing 10 years of studies and 69 published patient trials that documented the benefit to patient health of adult

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[11] Lima C *et al.*, Olfactory Mucosal Autografts and Rehabilitation for Chronic Traumatic Spinal Cord Injury, *Neurorehabilitation and Neural Repair* 24, 10-22, 2010, published on 30 September; Mackay-Sim A *et al.*, Autologous olfactory ensheathing cell transplantation in human paraplegia: a 3-year clinical trial, *Brain* 131, 2376, September 2008; Lima C *et al.*, Olfactory Mucosa Autografts in Human Spinal Cord Injury: A Pilot Clinical Study, *Spinal Cord Medicine* 29, 191, July 2006

[12] See, *e.g.,* Burt RK *et al.*, Autologous peripheral blood CD133þ cell implantation for limb salvage in patients with critical limb ischemia, *Bone Marrow Transplantation* 45, 111-116, 2010, published online 18 May 2009; Amann B *et al.*, Autologous Bone Marrow Cell Transplantation Increases Leg Perfusion and Reduces Amputations in Patients With Advanced Critical Limb Ischemia Due to Peripheral Artery Disease, *Cell Transplantation* 18, 371-380, 2009

[13] Strauer B-E, *et al.*, The acute and long-term effects of intracoronary Stem cell Transplantation in 191 patients with chronic heARt .failure: the STAR-heart study; *Eur. J. Heart Failure* 12, 721-729, 2010

stem cells for autoimmune conditions such as multiple sclerosis, juvenile diabetes, systemic lupus, and Crohn's disease, as well as acute and chronic heart damage and peripheral vascular disease.[14]

Another recent example involves restoring sight to blind patients with corneal blindness, even after 50 years of blindness.[15]

In another first, adult stem cells have been used successfully to treat children with a deadly skin disease known as recessive dystrophic epidermolysis bullosa (RDEB; one of the most severe forms of epidermolysis bullosa, a set of genetic skin diseases.) EB affects the skin and lining of the mouth and esophagus, causing skin to blister and scrape off with the slightest friction. The blistering, peeling skin also leads to recurrent infections, and an aggressive form of skin cancer. Most children with EB do not live past their 20′s. Previously, there was no treatment and it was considered incurable. Wagner and colleagues published results in the *New England Journal of Medicine* showing effective treatment of EB using donor adult stem cells.[16] One of the interesting aspects of this treatment is that it documents that bone marrow adult stem cells can travel to sites of injured skin, increasing production of collagen for these patients.

Tissue engineering using the patient's own adult stem cells has been used successfully in the production of a new trachea or windpipe;[17] the group reports unpublished results that within the past year they have improved the technique using *in vivo* regeneration of tissue, successfully treating three more patients, including two patients with tracheal cancer.[18]

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[14] Burt RK *et al.*, Clinical applications of blood-derived and marrow-derived stem cells for nonmalignant diseases, *Journal of the American Medical Association* 299, 925-936, 27 February 2008

[15] Rama P *et al.*, Limbal Stem-Cell Therapy and Long-Term Corneal Regeneration, *New England Journal of Medicine* 363, 147-155, 2010

[16] Researchers Use Stem Cells to Treat Children with Life-Threatening, Blistering Skin Disease, August 12, 2010, http://www.ahc.umn.edu/media/releases/ebtreatment/index.htm; Wagner JE *et al.*, Bone Marrow Transplantation for Recessive Dystrophic Epidermolysis Bullosa, *New England Journal of Medicine* 363, 629-639, August 12, 2010

[17] Macchiarini P *et al.*, Clinical transplantation of a tissue-engineered airway, *Lancet* 372, 2023, December 2008

[18] UCL surgeons perform revolutionary transplant operation, 19 March 2010, http://www.ucl.ac.uk/news/news-articles/1003/10031903; Transplant advance in windpipe cancer, http://www.physorg.com/news199887055.html; Bader A and Macchiarini P, Moving towards in situ tracheal regeneration: the bionic tissue engineered transplantation approach, *Journal of Cellular and Molecular Medicine* 14, 1877–1889, July 2010

This is just a brief overview of some of the exciting potentials for patient treatments. While many of these stem cell therapies are in clinical trials and experimental, there is significant hope as well as opportunity to move forward with stem cell treatments for patients. Educating the public as well as physicians will be key (e.g., please see one strategy at http://www.stemcellresearch.org/facts/treatments.htm), and opportunities abound for Kansas to become a leader in several key areas of stem cell treatment. The benefits for patients are incalculable.

Thank you for the opportunity to contribute speak to you on this very important issue.