**Considering the Impact of Age-Related Conditions on the Effectiveness of Regenerative Medicine**

Most people would like to focus on the impact of [regenerative medicine](https://www.fightaging.org/archives/2003/11/stem-cells-regenerative-medicine-and-tissue-engineering.php) on age-related conditions, but there is every reason to suspect the existence of a negative impact in the other direction. These conditions may well have varied detrimental effects on the class of cell transplant therapies that are presently fairly widely available via medical tourism. Aging is [a matter of cellular and molecular damage](https://www.fightaging.org/archives/2006/11/the-engineers-viewpoint-treat-change-as-damage.php), but damage spirals out to cause systematic dysfunction that in turn leads to more and different forms of damage: it is an accelerating curve downwards towards frailty and death once it gets going in earnest. These later types of damage and system failure can certainly turn around and influence the progression of earlier root cause damage, and can also potentially interfere in efforts to fix that root cause. It is the same in every complex machine, and things can break in ways that actively hinder repair. It all depends on the details of course, but even though researchers can now very partially treat the attenuation of a few of the various important cell populations and loss of tissue maintenance via cell transplants, that doesn't mean there is a direct and unhindered path to the goal of ending this contribution to aging.

So far the data somewhat mixed on the degree to which cell transplant treatments work less well in the old than in the young. A number of studies suggest that old stem cells can work just as well as young ones, if given the same cues. Other studies suggest the opposite, and it may well be that outcomes can vary widely by cell type and by the methodologies used in the clinic. Many types of stem cell transplant are producing clear and measurable benefits, and are somewhat better than any of the other available treatment options, but others are struggling in the labs or trials to bring reliable benefits to older patients.

A while back I suggested that [we should feel fairly good about the long term development of regenerative medicine and tissue engineering](https://www.fightaging.org/archives/2012/02/the-goals-for-stem-cell-medicine-ultimately-include-repair-of-aging.php) as it pertains to aging because near all of the potential profits in this industry involve treating age-related diseases. Therefore the research and development community is highly motivated to identify and fix all of the potential problems inherent in treating older people. At the core that essentially boils down to understanding why [stem cell activity fails with age](https://www.fightaging.org/archives/2012/03/an-introduction-to-the-stem-cell-niche-what-is-it-really.php), and in enough detail to be able to safely reverse that process at least for the duration of a cell therapy, but there will be much more to than that. Cell therapies themselves are going to become far more broad than simply a matter of stem cells and transplants. Ultimately the goal is a sophisticated control over cellular behavior wherever those cells might be. Currently the tools and outcomes are very crude, but they will become much sharper in the years ahead.

Here is a consideration of some of the hurdles that might be presented by the existence of specific age-related diseases in a patient, considered distinctly from the underlying aging process. What to do when one part of the machinery is very much more broken in this particular machine? That line of thought seems useful, I think, all part of the nuts and bolts of making the next generation of therapies work reliably and well:

[Is stem cell therapy less effective in older patients with chronic diseases?](http://www.eurekalert.org/pub_releases/2015-01/mali-isc011215.php)

Quote:

A promising new therapeutic approach to treat a variety of diseases involves taking a patient's own cells, turning them into stem cells, and then deriving targeted cell types such as muscle or nerve cells to return to the patient to repair damaged tissues and organs. But the clinical effectiveness of these stem cells has only been modest, which may be due to the advanced age of the patients or the effects of chronic diseases such as diabetes and [cardiovascular disease](https://en.wikipedia.org/wiki/Cardiovascular_disease).

[Autologous Stem Cell Therapy: How Aging and Chronic Diseases Affect Stem and Progenitor Cells](http://online.liebertpub.com/doi/full/10.1089/biores.2014.0042)

Quote:

Cardiovascular diseases (CVD), particularly [coronary artery disease (CAD)](https://en.wikipedia.org/wiki/Coronary_artery_disease), are the most frequent causes of mortality worldwide, and along with metabolic pathologies, especially [diabetes mellitus type 2 (T2DM)](https://en.wikipedia.org/wiki/Type_2_diabetes), they approach an epidemic status. An ongoing high frequency of CVD is caused both by the progressive aging of the population and an unhealthy lifestyle associated with risk factors such as obesity, [hyperglycemia](https://en.wikipedia.org/wiki/Hyperglycemia), [hyperlipidemia](https://en.wikipedia.org/wiki/Hyperlipidemia), and arterial [hypertension](https://en.wikipedia.org/wiki/Hypertension), which promote early development of [atherosclerosis](https://en.wikipedia.org/wiki/Atherosclerosis) and progression of cardiovascular pathologies.

Aging is characterized by numerous morphological and functional changes within different tissues and organs. The elasticity of blood vessels declines with age along with an [increase in their stiffness](https://en.wikipedia.org/wiki/Arterial_stiffness), which predetermines the progression of arterial hypertension. As people age, their [adipose tissue](https://en.wikipedia.org/wiki/Adipose_tissue) mass increases, while their [muscle volume decreases](https://en.wikipedia.org/wiki/Sarcopenia), leading to the development of [insulin resistance](https://en.wikipedia.org/wiki/Insulin_resistance), the most important pathogenic factor of T2DM. Aging is also associated with [comorbidities](https://en.wikipedia.org/wiki/Comorbidity), the simultaneous presence of two or more different diseases, often with chronic long-lasting progression. The most frequent age-associated comorbidities confounding each other are CAD and T2DM and obesity, arterial hypertension, and T2DM.

The target affected by the most CVD risk factors is the blood vessel wall. [Endothelial](https://en.wikipedia.org/wiki/Endothelium) dysfunction is considered to be the key pathogenic mechanism of [angiopathies](https://en.wikipedia.org/wiki/Angiopathy) associated with CAD and T2DM. It should be noted that endothelial dysfunction develops as a result of the interaction of different risk factors, such as insulin resistance, hyperglycemia, and dyslipidemia. The long-term presence of these factors affects endothelial cells and promotes their [apoptosis](https://en.wikipedia.org/wiki/Apoptosis), which leads to the [nitric oxide (NO) production failure](https://www.fightaging.org/archives/2012/07/nitric-oxide-and-aging-blood-vessels-1.php). As a consequence, the [vasodilatation](https://en.wikipedia.org/wiki/Vasodilation) and anti-aggregation functions of the endothelium are dysregulated along with its ability to inhibit [smooth muscle](https://en.wikipedia.org/wiki/Smooth_muscle) cell proliferation. These factors potentiate [atherosclerosis](https://en.wikipedia.org/wiki/Atherosclerosis) progression, forming the morphological basis of CAD.

Many types of [stem](https://en.wikipedia.org/wiki/Stem_cell)/[progenitor cells](https://en.wikipedia.org/wiki/Progenitor_cell), including [mesenchymal stem cells (MSCs)](https://en.wikipedia.org/wiki/Mesenchymal_stem_cell), have already been used in clinical trials of cell therapy for [ischemic pathologies](https://en.wikipedia.org/wiki/Ischemia), and their safety and feasibility have been demonstrated, but the clinical effectiveness of these protocols was relatively modest and could not corroborate the promising results of preclinical studies. One reason for the insufficient effectiveness of[autologous cell therapy](https://en.wikipedia.org/wiki/Autologous_stem_cell_transplantation) may be a lack of understanding about stem/progenitor cells properties in patients with CVD. Most data regarding the regenerative potential of these cells were obtained from cells derived from relatively healthy young donors. However, aging and disease itself may negatively affect stem/progenitor cells and their microenvironment, and impaired stem/progenitor cell functional properties may diminish the effectiveness of autologous cell therapy in aged patients with CAD and metabolic disorders. In this review, we analyze how aging and chronic diseases such as CAD and T2DM affect the properties of stem/progenitor cells.