**REGENERATIVE MEDICINE 2.0**

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The field of regenerative medicine has moved well beyond the results reported from the first decade of clinical trials of both stem cells and genes for CV disease. The early trials used almost exclusively autologous stem cells harvested from the bone marrow. There are now many new sources and types of stem cells including new international Phase III trials of allogeneic stem cells that allow use of ideal very young donors rather than older and chronically ill subjects, to genetic engineering of cardiomyocytes, and identification of resident progenitor cells in the heart that may be an important end pathway for effecting native cell regeneration from several cell types. Most of the trials in regenerative Medicine in CV Disease have targeted either chronic refractory angina or congestive heart failure, but newer trials are being conducted for peripheral vascular disease and stroke. Several of the trials are moving from Phase II to pivotal Phase III trials that is the final step for commercialization.

There has been significant progress in the use of specific genes shown to be important in the genesis and progression of cardiovascular disease, which have now moved to Phase IIB trials. The premise of using targeted genes rather than stem cells is that cells only remain in the tissues in which they are delivered for several days, and seem to exert their benefit by activating specific genes that then drive native repair. This would suggest that genes would be potentially as potent as cells alone. There are trials upcoming that will transfect a target gene into the cells to be transplanted, taking advantage of both strategies.

All data reported to date on stem cell and gene therapy have used only a single delivery of that agent. Given the proven safety of current stem cells and genes that provoke no immune response, new trials using multiple deliveries are starting. This may be one of the most important new strategies to enhance the benefit of this therapy.

The other area of significant progress in this field is in tissue engineering which is developing new ways to significantly increase cell retention when transplanted. This includes scaffolds and stents that are coated with cells or trophic agents, as well as novel agents that stimulate native repair in patients with heart failure. One other very promising application of tissue engineering is referred to as organogenesis which is the decelluarization of the heart with repopulation of stem cells, including cells obtained from the patient who would be a candidate of for that organ transplant.