Position Statement: Autologous Stem Cell Therapy Is Not Recommended for the Treatment of COPD.

Background: Several effective medical therapies have been developed over the past few decades for the management of COPD. Most can help relieve the symptoms associated with COPD, increase functional ability and improve quality of life. Some interventions have been shown to reduce the chance of acute exacerbations of COPD. This is important because exacerbations are primary drivers for morbidity and decline in health that affect individuals with COPD. Some interventions, such as oxygen supplementation when appropriate, quitting smoking and Lung Volume Reduction Surgery in selected cases, have been shown to extend life. The scientific proof of the efficacy of these interventions has come from painstaking research, particularly in the form of well-designed clinical trials. Unfortunately, no curative therapy has been developed for COPD and none offer significant improvement for most individuals who have severely advanced COPD.

Stem cells are relatively immature or undifferentiated cells that have been found to take up residence within a variety of organs, including the lungs or arise in more distant sites (particularly the bone marrow) in even more undifferentiated forms. Their role is not yet fully understood, but there is some evidence that these cells can participate in the reparative process following an injury. The observation that stem cells derived from one’s own body – autologous stem cells – might possess the ability to repair injured tissues has given hope that stem cells may be used to restore normal function to severely damaged organs, including the lungs. What is not yet understood is which cells are most appropriate for this purpose, or how to direct those cells to repair and restore normal function, particularly in an organ as complex as the lung.

Autologous stem cells can be harvested from the bone marrow or circulating blood. These in turn can develop into mature blood cells if present in the right environment within the body. Many of these cells are quite immature (multipotent), and they have the ability to develop or differentiate into a variety of more developed cell types. This includes the use of these multipotent cells to reconstitute bone marrow after high dose chemotherapy to treat various forms of cancer. Reconstitution of a more structurally complex organ than bone marrow poses a much greater challenge than simply administering stem cells into the circulating blood. Because of immaturity, these cells would need to be “programmed” to differentiate along one particular pathway to help accomplish this assigned task. Their immaturity also poses the risk that cells could develop along an unwanted pathway, including the development of disregulated cell growth, which leads to cancer.
Several clinics have begun operation both within and outside of United States based on the promise for potential use of autologous stem cells to treat a variety of incurable diseases. These clinics have borrowed on the success of autologous bone marrow transplant and recent basic research on the use of induced pluripotential stem cells that are derived from connective tissue. Common for these clinics is the use of autologous stem cells that are derived from one body tissue, usually adipose or fat tissue (mesenchymal stem cells) and processing these cells to enrich their number. Reinjection of these cells into the blood stream or via inhalation provides hope that they will stick to the target organ, such as the lung. Claims of improvement and cure are implied, but are not stated explicitly, at least by clinics operating within the United States. Rather, these clinics rely on personal testimonials from patients who have undergone this type of therapy. None claim direct scientific proof of the efficacy of autologous stem cell therapy, a fact acknowledged by their noting that the Food and Drug Administration has not approved this type of therapy to treat lung diseases such as COPD.

**Position:** Autologous stem cell therapy is not currently recommended for the treatment of COPD. Instead, participation in clinical trials that test the development and potential benefit of this technique is strongly encouraged.

**Rationale:** Embryonic, pluripotent stem cells have the potential to differentiate into almost any cell in the body. In contrast, stem cells that are derived from adults tend to have the ability to develop into other cells that are derived from the same tissue (multipotent), or into only specific cell types (unipotent). Examples of these are blood stem cells and germ cells, respectively. A technique can be used to alter adult stem cells to become less mature or differentiated (induced pluripotent stem cells), providing greater promise to their use to treat degenerative conditions in organs that are unrelated to the site of origin of the stem cells. A related discovery is that some stem cells can alter reparative or inflammatory pathways in a tissue or organ without necessarily becoming incorporated or engrafted into its structure. These observations have led to the hope that stem cell therapy can be an important adjunct in the management of a condition such as COPD that is marked by both chronic inflammation and the loss of structural and functional integrity of the lung.

Stem cells can alternatively be derived from an unrelated donor (allogeneic) and administered to a recipient to treat a variety of diseases. This strategy is used to treat certain forms of leukemia, for example. While potentially efficacious, using allogeneic stem cells presents greater complexity than the use of autologous stem cells because there is a risk of rejection, tumor growth or other unwanted sides effects including graft versus host disease. The use of allogeneic mesenchymal stem cell therapy was tested in a well-designed randomized clinical trial for subjects who had moderate or severe COPD. Comprehensive studies using autologous mesenchymal stem cells to treat COPD are not yet available. The therapy was judged to be safe and well tolerated, an observation that has been made regarding the use of autologous stem cell therapy in other studies. However, there was no measureable difference after two years of follow-up in a variety of measures that characterize COPD, including an improvement in lung function (lung volume, spirometry, oxygenation and diffusion capacity), exercise capacity (6-minute walk distance), shortness of breath or quality of life in those who did or did not receive stem cells. There was a difference in the level of one marker of inflammation (C-reactive protein) in a subset of these patients, but no difference was observed in several other inflammatory markers when comparing the two groups.
There are many clinical trials ongoing worldwide that are addressing the use of stem cell therapy in the treatment of a wide variety of diseases. Over 4,000 such trials are listed within the United States, summarized in the website www.clinicaltrials.gov. At least ten studies are actively recruiting subjects to test this therapy in the management of COPD. None of these COPD trials are at the phase-3 level of attempting to definitively prove their effectiveness. Rather, their focus is to address safety and test some aspects of effectiveness. This underscores the type of incremental and careful research that can contribute to our knowledge of how to best treat COPD and how to incorporate stem cell therapy with existing proven strategies to manage this disease.

It is understandable that people who are desperate might seek any means of improvement or hope of a cure for their condition, even if unproven. This appears to be the promise of autologous stem cell therapy available now. Relying on patient testimonials does not satisfy the statutory requirements for providing proof of efficacy and safety that falls under the purview of the Food and Drug Administration. These testimonials based on patient experience can be misleading to those who are seeking treatment of their COPD. Autologous stem cell therapy may someday fulfill this promise, but there is scant evidence that this therapy will be helpful within the foreseeable future. The COPD Foundation strongly recommends against the use of autologous stem cell therapy in the treatment of COPD or other lung disease until there is more rigorous scientific and medical proof of its effectiveness. In contrast, the COPD Foundation strongly encourages support for further research and well-designed clinical trials to further develop this therapeutic approach.

References:

National Institute of Health Stem Cell Information: http://stemcells.nih.gov/info/basics/Pages/Default.asp

Daniel J. Weiss, MD, PhD; Richard Casaburi, PhD, MD, FCCP; Robin Flannery; Michelle LeRoux-Williams, PhD; Donald P. Tashkin, MD, FCCP Chest. 2013;143(6):1590-1598. doi:10.1378/chest.12-2094.