CHEST

Ethics and Policy Issues for Stem Cell Research and Pulmonary Medicine

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Stem cell research and related initiatives in regenerative medicine, cell-based therapy, and tissue engineering have generated considerable scientific and public interest. Researchers are applying stem cell technologies to chest medicine in a variety of ways: using stem cells as models for drug discovery, testing stem cell-based therapies for conditions as diverse as COPD and cystic fibrosis, and producing functional lung and tracheal tissue for physiologic modeling and potential transplantation. Although significant scientific obstacles remain, it is likely that stem cell-based regenerative medicine will have a significant clinical impact in chest medicine. However, stem cell research has also generated substantial controversy, posing a variety of ethical and regulatory challenges for research and clinical practice. Some of the most prominent ethical questions related to the use of stem cell technologies in chest medicine include (1) implications for donors, (2) scientific prerequisites for clinical testing and use, (3) stem cell tourism, (4) innovation and clinical use of emerging stem cell-based interventions, (5) responsible translation of stem cell-based therapies to clinical use, and (6) appropriate and equitable access to emerging therapies. Having a sense of these issues should help to put emerging scientific advances into appropriate context and to ensure the responsible clinical translation of promising therapeutics. CHEST 2015; 147(3):824-834

ABBREVIATIONS: FDA = US Food and Drug Administration; iPS = induced pluripotent stem; SCNT = somatic cell nuclear transfer

Stem cell research and regenerative medicine have stimulated considerable scientific and popular excitement.[1] Since 1998, when embryonic stem cells were first derived from human embryos, efforts have focused on unlocking the potential of stem cells in a variety of different applications, from disease modeling and drug discovery to tissue regeneration and stem cell-based therapies.[2] By combining stem cells with novel tissue engineering strategies and biomaterials, scientists are exploring the possibility that whole tissues and organs can be engineered for replacement of damaged or diseased ones.

Stem cells and related technologies can be used to screen new drugs for efficacy and toxicity in cells from affected patients and for transplantation using patient-matched sources of cells to minimize rejection. As

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such, stem cells offer hope for those affected by an array of intractable diseases and conditions. However, stem cell research has also been surrounded by public controversy. Most prominent have been concerns about human cloning and debates about the moral status of embryos that must be destroyed to derive embryonic stem cells, including questions concerning potential moral distinctions of using donated surplus embryos from in vitro fertilization compared with embryos created specifically for stem cell research.

As research involving stem cells and regenerative medicine has progressed, new ethical and policy questions have emerged. In this article, after reviewing some of the major potential applications of stem cell science and tissue engineering in pulmonary medicine, we describe some of these ethical and policy issues that will need to be addressed as stem cell research advances further toward the possibility of translation into clinical use, both in general and specifically in chest medicine. Although the primary intent of this article is to describe the ethical issues involved, where there is consensus concerning particular issues, we offer prescriptive recommendations.

Regenerative Medicine in Chest Medicine

The term "stem cells" refers broadly to cells that have the capability of differentiating into diverse cell types. These include pluripotent stem cells (eg, embryonic stem cells, induced pluripotent stem [iPS] cells, and those derived by somatic cell nuclear transfer [SCNT]), which are capable of self-renewal and can become any cell type, as well as "adult" stem cells (eg, hematopoietic stem cells, mesenchymal stem cells, adipose-derived stem cells, and umbilical cord blood stem cells) that have a more limited ability in terms of cell types that they can become.[3]

Of special interest to regenerative medicine are pluripotent stem cells that can be a "match" for a patient with a disease, which include SCNT-derived cells and iPS cells. SCNT-derived cells are created when the nucleus from an adult cell is transferred into a donor egg whose nucleus has been removed, creating an embryo through a process known as "therapeutic cloning." Of note, this process is distinct from "reproductive" cloning, which many find to be ethically problematic; however, SCNT involves the creation and subsequent destruction of an embryonic blastocyst.

iPS cells are derived from virtually any human cell that is reprogrammed to a naive state where it can become any other cell type. A variation is the direct conversion of one cell type to another without reverting to a stem cell state as an intermediate (but using similar laboratory techniques), known as direct reprogramming or "transdifferentiation."[4] Deriving these cells does not require the destruction of human embryos, thus obviating some religious, moral, and political concerns. Table 1 describes different types of stem cells and some of the ethical issues related to them.

Although regenerative medicine has focused considerable attention on the spinal cord, the eye, and the heart, remarkable progress has been made regarding the respiratory tract.[5-10] For example, stem cells and regenerative medicine may offer solutions for disorders as diverse as acute lung injury, ARDS, idiopathic pulmonary fibrosis, COPD, genetic disorders (eg, cystic fibrosis and sickle cell disease), and reactive airway disease.[11-14] Translating stem cell-based therapies for the respiratory tract faces a number of hurdles, including ensuring safety and optimizing routes of delivery and dosage, but excitement abounds.[15]

The clinical use of stem cell-based therapies is not just theoretical.[16] In fact, clinical trials involving both embryonic stem cells and iPS cells aimed at retinal diseases have started, and trials for cardiovascular disease are planned in the near future. Applications especially relevant for chest medicine include Prochymal (Osiris), a mesenchymal stem cell-based intervention that is currently in phase II trials for COPD[17]; and AdipoCell (Bioheart, Inc), a stem cell-based intervention derived from autologous adult stem cells from adipose tissue that is slated for clinical testing in patients with ischemic cardiomyopathy.[18] Selected recent and current trials of stem cell therapies in chest medicine are listed in Table 2. Of note, at present these are early-stage trials using adult stem cell sources.

Although a comprehensive review of the scientific bases for stem cell and regenerative medicine-based therapies in chest medicine is beyond the scope of this article, it is helpful to understand that related research is currently progressing along several distinct paths:

1. Exploring endogenous "adult" stem and progenitor cell populations in the lung, with the hope of activating regeneration pathways that are otherwise overwhelmed in disease.[19-21]
2. Harvesting adult stem/progenitor cells that can be expanded and manipulated to promote regeneration.[11,22]
3. Producing pluripotent stem cells from skin, blood, and/or lung tissue harvested from patients with lung disease to model these diseases and test drug candidates in vitro.

TABLE 1] Stem Cell Sources and Selected Ethical Distinctions

Stem Cell	Description	Domains		
		Risks to Donor	Embryo	Risks to Recipients
Adult stem cells	Multipotent stem or progenitor cells derived from adult or fetal tissue	Harvesting may require invasive procedures or mobilization procedures	Not applicable	Cells have been tested as therapy/transplant while in a multipotent state without a clear rationale, mechanism, or evidence base; potential for risks to recipient
	Cells generally can only form multiple cell types within a single germ layer, although some (mesenchymal stromal cells) have been shown to cross germ layers			
Embryonic stem cell from donated embryos	Cells derived from embryos created for clinical (assisted reproduction/in vitro fertilization) purposes and donated by couples who no longer need them	No incremental risk	Current methods necessitate destruction of embryos; questions about the adequacy of prior clinical consent for the use of surplus embryos for the derivation of stem cells	Teratoma formation from residual pluripotent cells in transplant; genomic instability; unpredictable migration of cells in vivo
	Cells are pluripotent and can form cells from all three germ layers			
Embryonic stem cell from embryos produced from donated gametes	Cells derived from embryos created for research purposes from gametes (sperm and oocyte) donated for research by individuals who consent to research use	Medical risks of donation of oocytes; ethics of compensating donors (undue inducement); vulnerable populations; body commodification	Embryos created de novo will likely be destroyed as opposed to using surplus embryos originally created for assisted reproduction that will otherwise be discarded; concerns about the adequacy of consent may be addressed directly	Teratoma formation from residual pluripotent cells in transplant; genomic instability; unpredictable migration of cells in vivo
	Cells are pluripotent and can form cells from all three germ layers			

(Continued)

TABLE 1] *(continued)*

Stem Cell	Description	Domains		
		Risks to Donor	Embryo	Risks to Recipients
Embryonic stem cell from somatic cell nuclear transfer	Nucleus from a partially or fully differentiated adult cell is removed and transferred to a donated oocyte whose haploid nucleus has been removed; embryonic stem cell line is produced from resulting blastocyst	Oocyte: medical risks of donation of oocytes; ethics of compensating donors (undue inducement); vulnerable populations; body commodification	Embryos created de novo will likely be destroyed as opposed to using surplus embryos originally created for assisted reproduction that will otherwise be discarded; concerns about the adequacy of consent may be addressed directly	Teratoma formation from residual pluripotent cells in transplant; genomic instability; unpredictable migration of cells in vivo
	Stem cell product is matched to donor of original nucleus, and mitochondrial DNA transferred via oocyte	Somatic cell: harvesting may require invasive procedures		
	Cells are pluripotent and can form cells from all three germ layers			
Induced pluripotent stem cells	Adult somatic cells are "reprogrammed" back to a state of pluripotency	Harvesting may require invasive procedures	Not applicable	Teratoma formation from residual pluripotent cells in transplant; mutagenesis from using viral vectors to reprogram cells; genomic instability; unpredictable migration of cells in vivo
	Cell lines can theoretically be produced from any cell in the body; cells are, thus, matched to the original donor			
	Methods of reprogramming include viral vectors as well as nonviral methods; efficiency varies			
	Cells are pluripotent and can form cells from all three germ layers			

TABLE 2] Selected Clinical Trials of Stem Cell-Based Therapies for Pulmonary Disease

Chest Application	Cell Type	Stem Cell Source	Sponsor	Notes
ARDS[a,b,c]	Blood progenitor cells	Menstrual blood	S-Evans Biosciences, Inc	Phase I
	Mesenchymal stem cells	Autologous bone marrow	Asan Medical Center	Phase II
				Trial known as "STELLAR"
	Mesenchymal stem cells	Allogeneic bone marrow	UCSF/NHLBI (Michael Matthay)	Phase II
				Trial known as "START"
Bronchiolitis obliterans[d]	Mesenchymal stem cells	Allogeneic bone marrow	Mayo Clinic	Phase I
Bronchopulmonary dysplasia[e]	Mesenchymal stem cells	Allogeneic human umbilical cord blood (adult stem cells)	MEDIPOST	Phase I/II
				Therapy known as "PNEUMOSTEM"
COPD[f,g,h,i,j]	Mesenchymal stem cells	Allogeneic (haploidentical) bone marrow	Osiris	Phase II
				Therapy known as "PROCHYMAL"
	Adipose-derived stem cells	Autologous adipose tissue	Kimera Society	Phase I/II
	Adipose-derived stem cells	Autologous adipose tissue	Arkansas Heart Hospital	Phase I
COPD/emphysema[k,l]	Adipose-derived stem cells	Autologous adipose tissue	Ageless Regenerative Institute	Phase I/II
	Adipose-derived stem cells	Autologous adipose tissue	Bioheart, Inc	Phase I/II
				Therapy known as "AdipoCell"
				Also being tested in chronic ischemic cardiomyopathy
	Bone marrow mononuclear cells	Autologous bone marrow	UPECLIN	Phase II
	Mesenchymal stem cells	Allogeneic bone marrow	Federal Medical and Biologic Agency, Russia	Phase I/II
Pulmonary arterial hypertension (familial/drug-induced)	Endothelial progenitor cells (transfected with eNOS)	Autologous peripheral blood	Northern Therapeutics, Inc	Phase I

(Continued)

TABLE 2] *(continued)*

Chest Application	Cell Type	Stem Cell Source	Sponsor	Notes
				Trial known as "PHACeT"
Pulmonary arterial hypertension (idiopathic)[m]	Endothelial progenitor cells	Autologous peripheral blood	Zhejiang University	Phase I

eNOS = endothelial nitric oxide synthase; NHLBI = National Heart, Lung, and Blood Institute; PHACeT = Pulmonary Hypertension: Assessment of Cell Therapy; START = Stem Cells for ARDS Therapy; UCSF = University of California, San Francisco; UNESP = Universidade Estadual Paulista "Julio de Mesquita Filho"; UPECLIN = Unidade de Pesquisa Clinica da FMB.
[a]http://www.europeanlung.org/en/news-and-events/media-centre/press-releases/study-sheds-light-on-how-stem-cells-can-be-used-to-treat-lung-disease.
[b]http://clinicaltrials.gov/ct2/show/NCT02095444.
[c]http://clinicaltrials.gov/ct2/show/NCT02112500.
[d]http://clinicaltrials.gov/ct2/show/NCT02181712.
[e]http://www.digitaljournal.com/pr/2185440.
[f]http://clinicaltrials.gov/ct2/show/NCT00683722.
[g]http://clinicaltrials.gov/ct2/show/NCT02216630.
[h]http://clinicaltrials.gov/ct2/show/NCT02161744.
[i]http://clinicaltrials.gov/ct2/show/NCT01559051.
[j]http://clinicaltrials.gov/ct2/show/NCT02041000.
[k]http://clinicaltrials.gov/ct2/show/NCT01110252.
[l]http://clinicaltrials.gov/ct2/show/NCT01849159.
[m]http://clinicaltrials.gov/ct2/show/NCT00641836.

4. Differentiating pluripotent stem cells into cell populations found in the lung and trachea and transdifferentiating cells from other tissues and germ layers directly to lung phenotypes.
5. Using genome editing to correct genetic defects in stem cell lines derived from patients with hereditary diseases affecting the lung, including cystic fibrosis and sickle cell disease.

The ultimate goal is stem cell-based therapy, that is, directly transplanting or transfusing healthy or engineered cells to replace, repair, or otherwise treat damaged, diseased, or mutant tissues in the lung.

A related approach involves the engineering of macroscopic, functional lung tissue for transplantation.[23,24] These efforts aim to relieve the shortage of suitable lungs for transplant.[25] Researchers are exploring the possibility of using a variety of stem cell sources, in combination with natural and synthetically-derived scaffolds, to bioengineer lung tissue for transplantation.[26,27] Strategies include harvesting intact lungs from cadaveric donors, removing cells from the tissue to leave a scaffold, and reseeding those scaffolds with patient-matched stem cells or other mixtures of appropriate cell types.[25,28,29]

A much publicized example involves the transplantation of engineered tracheal tissue in patients with congenital tracheal stenosis, TB-damaged tracheas, tracheobronchomalacia, and tracheal cancer.[30-33] The transplanted materials have been produced through a variety of means, but most often they have used cadaveric tracheas, from which endogenous cells were removed and then reseeded with a patient's own stem cells.

Ethics and Regulatory Issues

The push toward developing stem cell-based therapies reflects a deep hope that stem cells can be used not only for ameliorative treatments but also for cures. However, excitement about such possibilities has been accompanied by important ethical debates. Aside from moral concerns regarding embryo destruction and human cloning, there are a variety of other ethics and regulatory issues related to stem cell research and treatment. These issues include (1) implications for donors, (2) scientific prerequisites for clinical testing and use, (3) stem cell tourism, (4) innovation and clinical use of new stem cell-based interventions, (5) responsible translation of stem cell-based therapies to clinical use, and (6) appropriate and equitable access to emerging therapies. We discuss each of these in turn.

Donors

As evidenced by the recent controversies surrounding HeLa cells that followed the publication of the best-selling book, *The Immortal Life of Henrietta Lacks*,[34] human cell lines can be ethically complex and attract considerable public attention. Although consistent with practices at the time, the cervical cancer tissue used to create HeLa cells was taken without consent, which contributes to part of the controversy about these cells. Although HeLa cells are not stem cells, there are clear implications for the current collection of biologic materials for stem cell research, especially regarding consent. Currently, stem cell researchers can obtain or purchase stem cell lines or tissue samples from other researchers, institutions, or commercial vendors and use this biologic material to derive new stem cells lines. Human stem cell lines have been derived from a variety of sources, including living donors, embryonic or fetal tissue, and cadaveric specimens. Each of these has its own associated ethical concerns related to provenance and consent.

Given expectations for consent in most research settings as well as concerns about immortalization of cell lines, their distribution and commercialization, and uncertainty regarding their potential future uses, the general consensus is that explicit consent should be obtained for the collection of biologic materials.[35,36] For example, such concerns must be taken into account when researchers obtain consent for blood draws, lung biopsies, lavages, or bronchoscopies to collect samples, as may be necessary for stem cell-based research on cardiopulmonary disorders.

Related to the issue of consent are concerns about confidentiality. Biologic materials are often collected from patients with particular conditions, stem cell lines are frequently banked and shared with researchers all over the world, and these lines are also increasingly undergoing genome sequencing. Confidentiality can be particularly important when conducting stem cell research on genetic and/or rare conditions. In research on hereditary conditions, or where the genetic or familial basis of a disorder is suspected but not confirmed, potential donors may have concerns about genetic discrimination, the possibility of genetic results being returned (and the related biopsychosocial implications of these results for donors as well as family members), and the implications for carrier screening.[37-40] Given scientific interest in using stem cells to model pathogenesis for many types of lung diseases (such as ARDS, newborns with hereditary lung conditions, and interstitial lung disease), there is a desire to obtain, store, and share biospecimens from affected individuals. Consequently, these issues are particularly relevant to those involved in chest medicine.

Scientific Prerequisites for Clinical Testing and Use

For clinical testing and use of stem cell-based interventions to proceed responsibly, the cell types needed for treating the disease in question must be able to be reliably produced and manufactured in a clinical-grade manner. Once this is possible, the biologic products must be tested for safety and potential benefit prior to use in humans. However, the complex nature of such biologic products complicates the assessments that are typically used prior to human testing.[41]

Clinical testing and use of stem cell-based therapies will involve determining whether the transplanted cells engraft or generate an immunologic reaction; this needs to be modeled in systems that recapitulate human physiology as closely as possible, usually large animal models. Thus, key considerations relate to the reliability of these animal models in helping make such determinations.[42] Although not unique to stem cell research, these efforts abut fundamental ethical questions related to using animals in research and the potential availability of alternative methods to minimize or otherwise replace animal testing.

Aside from direct use of stem cell-derived cell transplants, some have suggested that disease modeling and drug toxicity screening using patient-derived stem cell lines can be considered sufficient for satisfying many preclinical requirements without the use of animal models.[43] Three-dimensional lung models have been constructed using a combination of stem cells, tissue engineering, biomaterials (to mimic the lung extracellular environment), and bioreactors (to mimic physiologic lung conditions and generate shear stress, pulsatile airflow, and an air-liquid interface). Of particular interest in this regard are microfluidic devices and microscale "organ-on-chip" technologies, which can incorporate stem cell-derived lung tissue to reconstitute organ-level lung functions on microchips.[44] This technology has been shown, for example, to reproduce IL-2-induced pulmonary edema at a biomimetic alveolar-capillary interface.[45,46] Models such as these are scalable and have the potential to perform patient-specific drug assays with sugar cube-sized artificial lungs.[47] If proven to be reliable models and predictors of therapeutic efficacy, the benefits of these technologies go beyond

the particular scientific question at hand. That is, they also have the potential to reduce the use of animals in research and make the path of clinical translation more efficient.

Stem Cell Tourism

Although conventional stem cell research is proceeding, the normal pace of science has been understandably too slow for patients suffering from diseases and conditions that cannot be currently cured. In hope for cures, many patients have sought treatment with untested stem cell-based therapies for intractable conditions internationally—a practice known as "stem cell tourism."[48] Stem cell "tourists," who may be in a state of advanced disease, may travel long distances, often at considerable personal expense, usually to jurisdictions with weak regulations governing such activities. The treatments themselves may be based on a weak scientific rationale and lack poor quality assurance, leading to tragic medical complications (as illustrated by high-profile cases involving brain and spinal tumors following stem cell treatments) as well as psychosocial consequences.[49-51] There is also evidence of widespread hype in Internet advertising of stem cell treatments,[52] and media exposés have revealed unapproved therapies being proffered at clinics of questionable repute run by individuals whose methods were exposed as fraudulent.[48,53,54] Thus, there are huge health and financial risks to patients and families, with scientific responsibility and medical professionalism at stake.[51,55-59]

Despite these hazards, valid arguments support the view that patients (and their physicians) should be able to seek out nonstandard therapeutic options. In fact, some jurisdictions in the United States have passed "right-to-try" legislation to expand access to experimental therapies for patients without other viable options, and this legislation is already having an effect on the stem cell field.[60] However, these experimental and unapproved therapies may be delivered outside of a research setting, precluding careful oversight and the opportunity to learn from the experiences, and may expose vulnerable patients to risks they do not fully appreciate. This issue is relevant for those in chest medicine, because some patients are seeking unapproved stem cell treatments for lung diseases (eg, interstitial fibrosis), and patients with an array of medical conditions may suffer pulmonary complications after receiving unapproved stem cell therapies.

There are many proposals for addressing this issue: universal regulations; oversight and punishment mechanisms; loosened requirements for testing experimental therapies (including flexible frameworks for defining and testing these therapies); patient education and information dissemination; and efforts to enhance the public's understanding of and trust in mainstream science and medicine—particularly relevant in the stem cell field, where the science is often shrouded in controversy.[61-64] What may also be needed are new approaches to understanding and communicating with patients who may be experiencing "spiritual distress" and "therapeutic hope" in this context.[57]

Given this tension between the need to safeguard public safety and the desire of patients for access to experimental therapies, it is challenging to outline appropriate policies for stem cell research that strike the right balance.[65] In the near term, the US Food and Drug Administration (FDA) plans to regulate most experimental stem cell-based interventions (treating them akin to drugs and other biologic products), because most of these interventions, including iPS cells, meet the criteria of being "more than minimally manipulated."[66]

Innovation and Clinical Use

Although some assert that, for both scientific and ethical reasons, close FDA scrutiny is warranted,[67] other options have been proposed. In fact, some advocate that certain unproven medically innovative stem cell interventions should be available outside of normal clinical trials to seriously ill patients or those with limited alternatives.[64,68] Hyun[68] describes three specific circumstances in which stem cell-based innovative therapies should be allowed outside a clinical trial setting: (1) stem cell interventions that are not initially amenable to normal clinical trials (eg, treatments analogous to surgical innovations), (2) innovative therapy available under the FDA's expanded access regulations ("compassionate use" under 21 CFR 312.300 and 312.305), and (3) off-label use of FDA-approved products. In these circumstances, Hyun[68] recommends implementing an oversight mechanism modeled off a framework proposed by the Society of University Surgeons.[69] Other proposals include systems whereby physicians would have the freedom, either through FDA mechanisms or otherwise, to test autologous cell-based therapies in individual patients, provided that the patients meet certain eligibility criteria and that outcomes data and any adverse events be published in a centralized registry for oversight and analysis.

Addressing these issues in practice requires determining when a particular intervention should be considered to be research, medical treatment, or "innovative therapy"

to determine what would properly fall under an "innovation pathway."[65,70] Although there is no clear line defining these distinctions, intent is an important consideration (ie, treatment is provided to benefit a patient, whereas research is aimed at gaining new knowledge).[71] Nonetheless, it is difficult to determine the appropriate framework for the regulation of "innovative treatments" involving stem cells and engineered tissues.[72] Despite the appeal of considering stem cell-based interventions as "innovations," the transplantation of engineered tracheas highlights the great deal of uncertainty involved.[32,73] The International Society for Stem Cell Research and the Production Assistance for Cellular Therapies initiative of the National Heart, Lung, and Blood Institute have provided guidance for the appropriate translation of promising cell-based interventions to clinical practice.[74-76]

Clinical Testing

Regardless of these discussions of testing stem cell-based therapies under an innovation framework, the gold standard remains staged testing in controlled trials. When there appear to be adequate preclinical data, carefully designed first-in-human phase I trials may be conducted. In designing these trials, it will be important to determine the appropriate study population, balance potential risks and benefits, and ensure adequate protections are in place for those in the trials.[77,78]

Particularly difficult decisions for first-in-human trials include choices of participant groups. For example, should these trials be conducted with healthy or irreversibly ill patients? Acutely or chronically ill patients? Those who have been systematically excluded from research in the past, such as pregnant women, the elderly, some minority groups, those with rare conditions? Should there be restrictions placed on enrolling those who are not able to provide consent because of age (ie, children) or limited cognitive capacity?[78-80]

Obtaining informed consent may also be complicated by the need to convey complex information, such as the stem cell-based sources of the interventions being tested and the uncertainties of the related risks. Further, potential participants may be particularly vulnerable to hype, desperation, and the therapeutic misconception (not appreciating the difference between usual clinical care and research).[81-83]

Appropriate and Equitable Access

Should stem cell-based interventions prove to be successful, many health policy decisions related to the integration of stem cell-based therapies into clinical practice will need attention. For instance, the cost of integrating stem cell therapies into clinical practice raises significant issues about resource allocation and just distribution of benefits from translational stem cell research. Cell therapies are a particularly cost-intensive and labor-intensive form of treatment, which is important to consider given recent discussions about health-care costs and insurance affordability.[84] Unlike many small-molecule therapies, the costs of stem cell-based therapies include the costs of treating long-term complications and follow-up, as these therapies and their effects may vary unpredictably (intensity of immunosuppression or ablation of the immune system, allogeneic vs autologous, potential for migration or transformation of delivered cells, organ systems involved, and so forth). For example, the first-year cost of an allogeneic hematopoietic stem cell transplant is in the range of $96,000 to $204,000.[84]

Fundamentally, it is important to consider whether such an expensive therapy is also likely to be effective enough to reduce or eliminate the long-term cost of otherwise treating a disease to justify its use. On the other hand, engineering stem cells to cure genetic disorders such as cystic fibrosis or sickle cell anemia has the theoretical potential to dramatically reduce long-term health-care costs associated with those disorders.

Very much intertwined with costs are disparities in access to care, which continue to be a problem in health care in general and in cardiopulmonary medicine in particular. Consider, for example, the racial, sex, and socioeconomic disparities in diagnosis and timely access to treatment of asthma,[85,86] COPD,[87,88] and lung cancer.[89,90] The equitable distribution of the benefits of a new technology in the population is thus a significant consideration for the clinical use of stem cell-based therapies.

Conclusions

The translation of stem cell, regenerative medicine, and tissue engineering research to clinical use raises a number of important ethical and policy issues that those involved in chest medicine are likely to encounter. Having a sense of these issues should help to put emerging scientific advances into appropriate context and to ensure the responsible clinical translation of promising therapeutics.

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