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Commentary

The Role of Gene and Cell Therapy in the Era of Health Care Reform

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After nearly thirty years of biological discovery underpinning gene therapy vectors and more than twenty years of clinical gene therapy trials, cases with clear evidence of clinical efficacy have now been demonstrated. Examples include restoration of immune function in children with X-linked severe combined immune deficiency (X-SCID) and chronic granulomatous disease (CGD), restoration of vision in Leber Congenital Amaurosis (LCA), and marked improvement in motor function of Parkinson disease (PD). Likewise, cell-based therapies beyond the well-established bone marrow transplant techniques are emerging, including the use of mesenchymal (MSC) and hematopoietic (HSC) bone marrow stem cells, umbilical cord cells, human embryonic stem (hES) cells and induced pluripotent stem (IPS) cells. Applications for these new forms of cell-based therapies include a variety of neurodegenerative disorders (such as amyotrophic lateral sclerosis [ALS]) and ophthalmologic disorders, such as age-related macular degeneration.

At the same time U.S. spending for health care has been on an unyielding upward path—reaching $2.5 trillion in the aggregate, $8,100 per person, and 17.6 percent of gross domestic product (GDP) in 2009 (Schoenman and Chockley, 2011). The ever-rising cost of health care has serious consequences for individuals and the country. For example, from 1999–2009 health care costs cancelled out real income gains for an average U.S. family (Auerbach and Kellerman, 2011), and the 2011 Medicare Trustees report projects that Medicare has an unfunded liability of over $38 trillion (www.cms.gov/ReportsTrustFunds/downloads/tr2011.pdf). The unfunded liability is the difference between the benefits that have been promised to current and future retirees and what will be collected in dedicated taxes and Medicare premiums. These facts have led to proposals that radically redesign the funding of health care in the United States, with the goals of providing access to care for all Americans, improving quality, and reducing costs. Ironically, the emergence of all the potential promise of these innovative molecular therapies is coinciding with a future in which the costs of new therapies may be the major determinate of whether they will be available to patients.

Is there a future state that will embrace the equally noble goals of using cutting-edge science to devise advanced biological therapeutics for previously untreatable illnesses and of using systems engineering to provide all Americans with the lowest cost care possible? The answer is far from certain. What is clear is that if cost-effectiveness is to be addressed in the context of gene and cell therapy, it will have to include a long time-horizon in which the therapy may avoid or ameliorate complications of the disease and accurate monetization of the gains in quality of life and function for the individuals who are treated. Incorporating these elements into an economic model of the value of gene and cell therapy is challenging but not unprecedented. What is even more problematic is the uncertainty about what the new payment models will include, and whether such models are truly suited to look at global lifelong benefits to patients.

Possible New Payment Models in the Reform Era

On-average health care spending per person has grown over two percentage points faster than per capita GDP for the last 40 years. The reasons for the continuous increase in costs are aging of the population, personal income growth, supply induced demand, defensive medicine, and administrative costs (Congressional Budget Office, 2008). In addition, a third party fee-for-service payment system that encourages the use of new technology in medical practice (Congressional Budget Office, 2008; Roehrig and Rousseau, 2011). The spread of new and often expensive diagnostic and therapeutic modalities is the leading factor, accounting for fifty percent of the growth in real per capita health care spending care providers and suppliers to raise prices and increase the volume and complexity of services, has fueled the rise in costs. ◀AU2

On March 23, 2010, President Barack Obama signed into law the Patient Protection and Affordable Care Act (PPACA), whose overriding goals were to make health insurance accessible to all Americans and to decrease the rate of rise in health care costs. Moreover, private insurance companies are beginning to explore new payment methodologies that focus on the Total Cost of Care (TCOC). The TCOC experiments

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Table 1. Examples of New Risk-based Payment Mechanisms

Payment Model	*Brief Description*
Capitation	Insurer pays fixed annual "per-head" payment to provider, providing an incentive to utilize less resources.
Bundled Payment	Insurer pays fixed amount for a single episode of illness, to be divided among providers by mutual agreement.
Shared Savings	Insurer predicts annual cost of health care (based on severity of illness and historic medical inflation) and shares any savings from this predicted cost with the providers.

aim to change the payment mechanisms for care from purely fee-for-service payments based on volume to a fee-for-value payment system that links payments to the rate of growth in total cost of care provided to a patient annually (Morris and Eggbeer, 2011). The "fee-for-value" may be accomplished through a number of payment mechanisms, examples of which are provided in Table 1. Each of these mechanisms has the advantage for the insurer of sharing with the providers some aspect of the "risk" of care being more expensive than predicted.

One may note that in each of these cases the term "provider" is not precisely defined. This is because the total cost of care for an individual (under capitation or shared savings), or for an episode of illness (under a bundled payment), may actually be split between primary care physicians, specialist physicians, hospitals, clinics, providers of ancillary diagnostic services (radiology and laboratory), and providers of rehabilitation services (either in rehabilitation facilities or in the home). In previous systems, each of these individual providers would bill and collect from the insurer for any covered services they provided. Because of the insurers' interest in containing the entire cost of providing care to an individual or population, there has been a movement to aggregate these costs together and hold a single entity accountable for the total cost of care. These so-called "Accountable Care Organizations" (ACOs) do not yet exist, but could take the form of fully integrated corporate structures employing all of the providers and resources mentioned above, or could take the form of consortia of organizations agreement to jointly enter contractual arrangements with the provider.

The Center for Medicare and Medicaid Services (CMS) has recently published draft guidelines (for public comment) on how Medicare might recognize an ACO as being eligible to enter into a gain-sharing style arrangement for the coverage of Medicare beneficiaries. These proposed guidelines view savings in health care cost over a year-to-year basis. Thus, a high-cost, high-impact therapy, such as a stem cell transplant or a gene therapy administration, might not fare so well initially under such a plan, particularly if the cost of the therapy was accrued in a single year.

Cost Justification for High-Cost, High-Impact Interventions

There are three fundamental arguments in favor of high-cost, high-impact interventions, such as a hypothetical sight-restoring gene therapy for LCA or a life-sustaining stem cell therapy for ALS. First, these therapies could decrease the utilization of other resources in later years, particularly if patients become healthier and utilize emergency room visits, hospital stays, long term care, and other therapies less frequently. This would be a fairly conventional rationale for any "primary prevention," although the time-horizon for the payback of the high-cost, high-impact therapy could stretch over a number of years.

Second, high-cost, high-impact therapies could improve the patient's quality of life in a manner that might result in generating a greater economic impact on the society, assuming they might be able to return to work, pay taxes, and utilize less disability services. These costs could also be quantified utilizing fairly standard techniques in economics.

Finally, the value of a life saved or of vision restored has long been recognized and acknowledged by our society, even above and beyond the decrease in utilization of other health care resources and the restoration of the individuals economic productivity. Nevertheless, new therapies will receive much more scrutiny than in the past, and a strong case will need to be made to justify their costs by provider organizations (Fuchs, 2011).

Gene and Cell Therapies as Platform Technologies

One additional aspect of gene and cell therapeutics is the promise of a "second wave" of therapeutics. While this first wave of agents proving to be clinically efficacious are targeted to rare (often single gene disorders), there is hope that these successes will lay the groundwork (i.e., become a technology platform), for future gene and cell-based therapies for disorders with much higher incidence rates, such as diabetes, coronary artery disease, stroke, and Alzheimer's disease. In these latter cases, the total societal costs of the diseases are better characterized, and even partial reductions of these costs could be more readily assessed. Nonetheless, taking care to measure the cost benefit of such therapies will be important in assuring acceptance by payers, providers, and patients. The quicker gene and cell therapy move from the first phase to the second, the more readily demonstrable the societal benefits may be.

Summary

The full realization of the impact of gene and cell therapies on human diseases will take place in a health-care payment environment that is not particularly well designed to weigh the advantages and disadvantages of such interventions. In fact, noted scholars are calling for a retrenchment from high technology therapies and using scarce societal resources on primary care and public health (Callahan and Nuland, 2011). However, history would suggest that other high-cost, high-impact interventions, such as bone marrow and solid organ transplantation, open heart surgery, and advanced radiation

therapies (such as proton beam therapy), can and will be introduced if they provide better outcomes for patients in the long run. If our scientific community is able to demonstrate these long-term benefits in quality or quantity of life, these advanced therapies seem likely to move forward to general use despite their unconventional cost structures.

References

Auerbach, D.I., and Kellerman, A.L. (2011). A decade of health care cost growth has wiped out real income gains for an average US family. Health Affairs 30, 1630–1636.

Callahan, D., and Nuland, S.B. (2011) The quagmire: how American medicine is destroying itself. The New Republic. Available at www.tnr.com/article/economy/magazine/88631/american-medicine-health-care-costs

Congressional Budget Office. (2008). Technological change and the growth of health care spending. (CBO, Washington, DC) Publication No. 2764.

Fuchs, V.R. (2011). The doctor's dilemma—what is "appropriate" care? N. Engl. J. Med. 2011;365: 585–587.

Morris, D., and Eggbeer, B. (2011). Total cost of care contracts: early lessons. BDC Advisors, LLC, Miami, FL.

Roehrig, C.S., and Rousseau, D.M. (2011). The growth in cost per case explains far more of U.S. health spending increases than rising disease prevalence. Health Affairs 30:1657–1663.

Schoenman, J.A., and Chockley, N. (2011). Understanding US Health Care Spending. National Institute for Health Care Management Foundation Data Brief July 2011. NIHCM Foundation, Washington, DC.

2011 Annual Report of the Board of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Funds. (May 13, 2011). Available at www.cms.gov/ReportsTrustFunds/downloads/tr2011.pdf

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AU1: Please provide location and postal code of affiliations.
AU2: The last part of this sentence, starting with "care providers and suppliers to raise prices …" does not seem to make sense. Please rewrite or remove?