CENTRAL NERVOUS SYSTEM (CNS) repair in mammals represents one of the major scientific and therapeutic challenges of the day. Given the permanent and functionally devastating results of CNS damage, the potential clinical benefits of effective repair are enormous. Unfortunately, conceptual and technical barriers to repair are equally impressive.

Each new advance in biomedical science brings hope for progress in CNS repair. The identification of pathological neurotransmitter loss, beginning with dopamine in Parkinson disease, suggested a strategy for pharmacological treatment of degenerative brain disease. Unfortunately, little evidence has emerged to indicate that transmitter replacement therapy counteracts underlying neurodegenerative processes.

The isolation of trophic factors within the CNS, beginning with nerve growth factor, pointed to a possible solution to this problem by attempting to preserve existing neurons and regrow damaged neuronal processes. In general, however, growth factors have failed to benefit patients with neurodegenerative diseases or CNS injury.

More recently, genetic therapy has been touted as a potential tool for CNS repair. In the case of inherited CNS disorders, one strategy has been to replace erroneous genetic information by using viral vectors. For other diseases, attempts have been made to boost intrinsic restorative CNS function by enhancing or suppressing the expression of specific genes. However, it is difficult to deliver enough virus particles to efficiently transfect neurons over the large expanse of the human CNS. Furthermore, a novel engineered virus must be developed and tested to treat each CNS disorder. Finally, therapy targeted to a single gene is unlikely to result in the restoration of anatomically sophisticated and developmentally specific neuronal networks.

The latest “revolution” in biomedical science involves the identification, characterization, and purification of pluripotent stem cells. Cynics may predict that this scientific advance will fail to yield meaningful clinical progress; however, stem cells display a number of characteristics ideally suited to CNS repair. First, they may have the ability to migrate significant distances within the CNS. Second, they may adapt to the host environment, providing transmitter, enzymatic, or other secretory products appropriate to the disease process. Third, and perhaps most important, stem cells may be able to recapitulate appropriate developmental and anatomical fates, restoring complex neuronal circuitry.

Although the stem cell “revolution” is early in its course, extensive public attention creates the risk of overstating progress in the field and unrealistically accelerating expectations. Investigators are just beginning to apply problems and solutions identified in preclinical studies to the challenge of CNS cellular transplantation in humans. Many areas of this work are described in this issue of Neurorsurgical Focus, emphasizing the current status of basic research, feasibility of clinical applications, and regulatory and ethical limitations. The issue is organized into 6 sections.

The first section addresses the biology of embryonic and lineage-specific stem cells. The second section reviews cellular therapy for neurodegenerative and metabolic disorders of the brain and retina, including Parkinson, Huntington, motor neuron, and lysosomal storage diseases. This section is accompanied by a podcast interview with Dr. Ole Isacson in which he covers the current status and promise of cellular therapy for Parkinson disease. The third section addresses stem cell therapy for stroke and epilepsy. The fourth section covers attempts to treat brain and spinal injuries using stem cell transplantation. The fifth section addresses clinical trial design as well as policy and ethical considerations raised by stem cell therapy. The final section concentrates on brain tumor stem cells.

In addition to scientific complexity, stem cell research faces another significant challenge arising from conflict over ethical norms. Both opponents and proponents of stem cell research cite concern for human life as a motivating factor. Opponents, in general, are concerned with stem cell harvest and the possibility that human life may be created or arbitrarily destroyed for the sole purpose of obtaining cells. Proponents are largely concerned with the preservation of health and life among people suffering from serious illnesses with no known effective treatment.

Scientific developments that have come to light during the preparation of this issue of Neurorsurgical Focus pro-
vide new hope that stem cells effective for human therapy can be created without the destruction of embryonic or fetal tissue. The scientific nature and implications of these advances are discussed in a number of the articles that follow.

In the meantime, it appears that both proponents and opponents of stem cell research are motivated by sincerely and deeply held convictions that merit the attention and respect of the scientific and medical communities.

We must also ensure that the debate about the origin of stem cells, which often dominates media coverage, does not obscure other important ethical issues related to stem cell research. For example, what are the boundaries for the appropriate use of stem cell therapy? Who should own the intellectual property and biological materials needed for medical treatment? How can we best design scientific controls in trials that involve neurosurgical intervention? Most importantly, how can we guard the interests of patients, including children and cognitively disabled adults, enrolling in experimental trials of stem cell therapeutics? Progress in stem cell research should occur within the bounds of careful regulatory oversight and ethical guidelines.

Patients participating in Phase I experimental trials may hope to benefit personally from the treatment they receive. If history is any indication, however, the greatest benefit of their generous sacrifice may accrue to those who fall ill in the future. Therefore, we will owe them a great burden of gratitude. Through my own involvement in the first Food and Drug Administration–approved trial of neural stem cells (http://clinicaltrials.gov, key word “NCL”), I have gained appreciation for the contributions made by these patients and their families to stem cell research and to the field of neurosurgery. I offer them my respect and sincere personal thanks.

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