What once was dogma—that the central nervous system cannot regenerate—has been dismissed. This newly discovered potential for central nervous system (CNS) regeneration and repair has opened up numerous therapeutic targets and opportunities.

Recognizing this wealth of new opportunity, the New York Spinal Cord Injury Research Board asked the Institute of Medicine (IOM) to examine future research directions in spinal cord injury. The IOM was asked to advise not just New York State on its research program, but to look more broadly at research priorities for funders of spinal cord research—federal and state agencies, academic organizations, pharmaceutical and device companies, and nonprofit organizations.

This report by the IOM Committee on Spinal Cord Injury provides a broad overview of the current status of spinal cord injury research, examines the research and infrastructure needs, and provides recommendations for advancing and accelerating progress in the treatment of spinal cord injuries with particular attention to issues regarding translational research. The committee also addresses the contributions that the New York program can make to complement the scientific efforts of other state, federal, and private supporters of research in this area.

DEFINING A CURE

After carefully considering input from the community of individuals with spinal cord injuries, researchers, and clinicians, the committee decided to take a broad approach to “defining a cure” and to frame its definition around alleviating the multiple disabilities that result from spinal cord injury.

Spinal cord injury research should focus on preventing the loss of function and on restoring lost functions—including sensory, motor, bowel, bladder, autonomic, and sexual functions—with the elimina-
tion of complications, particularly pain, spasticity, pressure sores (decubitus ulcers), and depression, with the ultimate goal of fully restoring to the individual the levels of activity and function that he or she had before injury.

IDENTIFYING RESEARCH DIRECTIONS

A number of therapeutic interventions for spinal cord injuries have been explored over the past several decades. Advances have been made in emergency medical treatment and in rehabilitation efforts, and there is an increased understanding of the specific mechanisms and pathways that are targets for therapeutic interventions. Additionally, recent advances in neuroscience research are opening up new opportunities for the development of therapeutic approaches. Research toward addressing the consequences of spinal cord injuries focuses on a natural progression of strategies: preventing further tissue loss, maintaining the health of living cells, replacing cells that have died through apoptosis or necrosis, growing axons and ensuring functional connections, and strengthening and reestablishing synapses that restore the neural circuits required for functional recovery. These strategies lead to a range of therapeutic targets and priorities for spinal cord injury research (Table 1), each of which could theoretically be pursued together with others. For example, cell therapies that replace myelin could be combined with agents such as neurotrophic factors that promote axon regrowth.

TABLE 1. Priorities for Spinal Cord Injury Research

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<th>Develop neuroprotection therapies:</th>
<th>identify interventions that promote neuroprotective mechanisms that preserve the spinal cord.</th>
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<td>Promote axonal sprouting and growth:</td>
<td>enhance understanding of the molecular mechanisms that promote and inhibit axonal regeneration—including the roles of glia (astrocytes and oligodendrocytes), scar formation, and inflammation and inhibitory molecules—and develop therapeutic approaches to promote growth.</td>
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<tr>
<td>Steer axonal growth:</td>
<td>determine the molecular mechanisms that direct axons to their appropriate targets and regulate the formation and maintenance of appropriate synaptic connections.</td>
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<tr>
<td>Reestablish essential neuronal and glial circuitry:</td>
<td>advance the understanding of the molecular mechanisms that regulate the formation and maintenance of the intricate neuronal and glial circuitry, which controls the complex multimodal function of the spinal cord, including autonomic, sensory, and motor functions. Increase knowledge of the mechanisms that control locomotion, including the differences in the central pattern generator between bipeds and quadrupeds.</td>
</tr>
<tr>
<td>Prevent acute and chronic complications:</td>
<td>develop interventions that prevent and reverse the evolution of events that lead to the wide range of outcomes that result from chronic injury and disability after a spinal cord injury.</td>
</tr>
<tr>
<td>Maintain maximal potential for recovery:</td>
<td>expand the understanding of the requirements for proper postinjury care and rehabilitation that are needed to maintain the maximal potential for full recovery.</td>
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ACCELERATING PROGRESS

Progress in spinal cord injury research offers the potential to make significant improvements in the lives of individuals with spinal cord injuries. The challenges are to move research efforts forward in such a way as to accelerate the translation of the findings from research in the laboratory to clinical trials and then into practice while
ensuring patient safety and effectiveness. The committee believes that accelerating progress in spinal cord injury research involves the following three key efforts that, in addition to the recommendations for the New York State program, are the focus of the committee’s recommendations and highlight the need for a concerted national priority effort to find the best treatments for spinal cord injuries.

**Focus on increasing knowledge of basic neurobiology and therapeutic approaches.** Many research avenues remain to be examined in understanding the biochemical mechanisms responsible for spinal cord injuries and thus the targets of therapeutic interventions (Table 1). As no one solution for spinal cord injuries likely exists, strategies need to be developed to provide an organized approach to testing and evaluating therapies in combination. To conduct this research, new and refined technologies are needed. In addition, assessment measures need to be standardized to provide insights into potential therapeutic interventions.

**Emphasize and coordinate translational multidisciplinary research and clinical trials.** Research on spinal cord injuries is now at the point at which the biological targets and pathways that can be the focus of interventions can be identified. It is important for the pharmaceutical industry to be involved in these efforts and for collaborative approaches to be developed among industry, university, nonprofit, state, and federal resources. Furthermore, it is critically important that ongoing efforts in patient care and rehabilitation be coordinated with efforts directed toward the development of therapeutic interventions for spinal cord injuries.

**Strengthen the research infrastructure and enhance training.** Progress in spinal cord injury research depends on adequate research funding and an adequate physical infrastructure for research; well-trained and innovative investigators with career development opportunities; translational efforts that move the findings of preclinical studies to clinical trials with humans, as safe and appropriate; and an environment that promotes and encourages interdisciplinary collaboration. Key to accelerating progress in the treatment of spinal cord injuries is the development of a coordinated, focused, and centralized National Spinal Cord Injury Research Network that connects individual investigators, research programs, and research centers; and facilitates collaborative and replicative research projects. Further, Spinal Cord Injury Research Centers of Excellence need to be established to foster collaborations between basic and clinical researchers and promote the interdisciplinary research that is needed to explore the translation of effective laboratory therapies into the clinical setting.

**STRENGTHENING NEW YORK’S RESEARCH PROGRAM**

Currently, 14 states have enacted legislation to fund spinal cord injury research at an annual total level of funding of about $27 million. Many of the states that fund spinal cord injury research do so through surcharges on fines for traffic violations. There is much that the states can learn from one another in developing and strengthening their spinal cord injury research programs.

In 1998, New York State passed legislation to establish a new program whose ambitious mission is to support research “towards a cure for [spinal cord] injuries and their effects.” Funding for the program comes from a surcharge on fines for traffic violations, which is directed to the newly created Spinal Cord Injury Research Trust Fund. The estimated annual funding of $8.5 million is the largest amount of state-designated funding for spinal cord injury research. Its size and scope place the program in the position to become a leader in spinal cord injury research. Furthermore, New York has a strong biomedical and neuroscience research infrastructure that could be drawn upon to build a strong research program in spinal cord injuries.
Opportunities to strengthen New York’s program, to reduce the administrative bureaucracy, and to bolster its impact also exist. The committee’s recommendations focus on the following four areas:

- building and strengthening New York State’s research infrastructure;
- developing a regional clinical trials center;
- restructuring the research funding and oversight processes; and
- ensuring independent evaluation of the progress that has been made toward the stated mission of the New York Spinal Cord Injury Research Board.

FOR MORE INFORMATION...


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