NEUROBIOLOGY

STEPS TO RECOVERY

Researchers find ways of coaxing spinal nerves to regrow

Nerves throughout most of the body regenerate when they are damaged, just like any other tissue. Damage to the central nervous system, however—the brain and spinal cord—is different. Something goes tragically wrong. Nerve bundles start feebly to repair themselves but then degenerate around the site of the injury. For many patients, that means life confined to a wheelchair.

Experiments in two laboratories now seem to bear out earlier indications that the degeneration is not because of an intrinsic inability of spinal nerves to regrow. Rather it seems to be a consequence of a separate effect that may be controllable.

Nurit Kalderon and Zvi Fuks of the Memorial Sloan-Kettering Cancer Center in New York City did most of their experiments on rats that had just one side of their spinal cord cut. The investigators found that treating the injury with high doses of x-rays during the third week after injury allowed nerve cells to grow across the site and prevented the usual degeneration. Subsequent experiments confirmed that nerve impulses could be transmitted across injury sites following x-ray treatment during the critical time window. The treatment even allowed some rats that had suffered a complete cut across their spinal cord to regain partial use of their hind limbs. Kalderon, who described the work in the *Proceedings of the National Academy of Sciences,* believes the effect works because the x-rays kill specialized nervous system cells that slowly migrate to the site of an injury and cause incidental damage.

Michal Schwartz and her colleagues at the Weizmann Institute of Science in Israel used a different system to encourage regeneration in severed rat optic nerves. Schwartz found evidence that she could promote regrowth of nerve cells by injecting the injury with immune system cells—macrophages—that she had previously incubated with nerves that

FIELD NOTES

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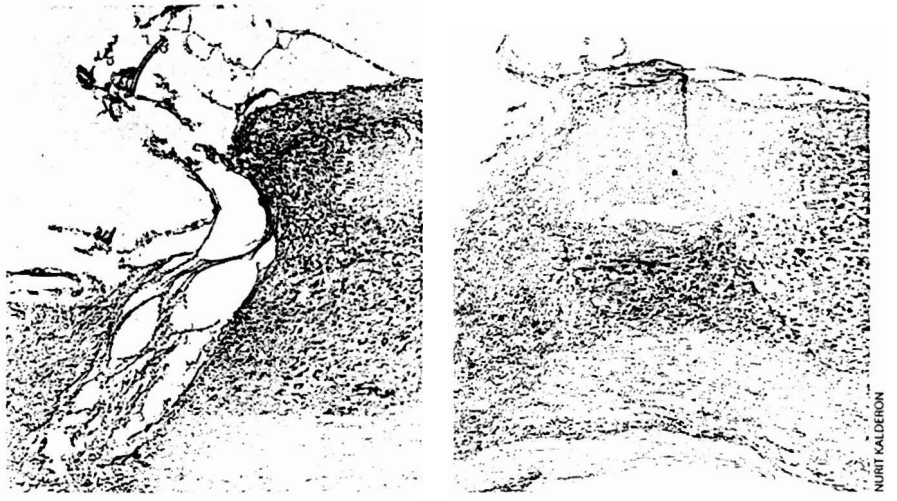

TREATMENT OF HALF-SEVERED RAT SPINAL CORDS
with x-rays 18 days after injury prevents degeneration usually observed weeks later. Cord on the left was untreated; that on the right was irradiated.

can regenerate, such as the sciatic nerve in the leg. Macrophages allowed to sit for 24 hours with sciatic nerve caused optic nerve cells to regrow across the cut. Schwartz, who described the results last fall in the *FASEB Journal*, has conducted similar experiments on spinal cord and achieved the same kind of results.

Schwartz believes, in contrast to Kalderon's theory, the central nervous system of mammals prevents immune cells from carrying out a function that is essential to recovery. Perhaps, she suggests, mammals have evolved a way of suppressing immune system activity in the central nervous system in order to avoid damaging inflammation that could disrupt mental functioning. The suppression might have a net benefit except in serious injuries. Schwartz maintains that she has identified a previously unknown molecule in the central nervous system that causes immune suppression, and an affiliate of the Weizmann Institute has licensed her system for spinal cord regrowth to a start-up firm in New York City, Proneuron Biotechnologies.

Wise Young of the New York University Medical Center, a prominent researcher in the field, says he has no doubt that Kalderon "has a very interesting phenomenon on her hands" with x-ray-induced healing. But he emphasizes that her experiments must be repeated, because untreated rats often exhibit a surprising degree of recovery from incomplete damage, sometimes learning to walk again. Young wonders whether an infection or other extraneous effect might have hurt Kalderon's untreated animals, thus making the x-ray-treated groups appear better off by comparison. Schwartz's results, which employed only a few animals, also have alternative explanations, Young thinks. The central nervous system might, for example, simply lack an important element rather than have some active means to suppress immune function.

Young asserts that the value of Kalderon's and Schwartz's theories should become clearer when current studies with standardized experimental systems are complete. But some success with a different approach to spinal cord repair had been reported earlier by Henrich Cheng, Yihai Cao and Lars Olson of the Karolinska Institute in Stockholm. The team, which described its results last July in *Science*, removed a section of rats' spinal cords, bridged the gap with nerves transplanted from another part of the body and finally added a protein glue containing a nerve growth factor. The rats regained some use of their hind limbs, a demonstration that Young terms a "milestone."

The Swedish technique is not directly applicable to humans, unless a way is found to achieve regeneration without removing a section of cord that may still perform some function (most injuries leave tissue intact). Experiments are continuing, although Young says progress is still slower than he would like. Fewer than 30 laboratories in the U.S. are engaged in spinal cord injury research. And the $40 million the U.S. spends on the field will need to be doubled, he says, to pursue all promising avenues.

—Tim Beardsley in Washington, D.C.