The symposium on spinal cord transplantation has been shadowed, this year, by the loss of Dr. Michael Goldberger (Medical College of Pennsylvania, Philadelphia, USA) who passed away in January 1992. Michael Goldberger’s contribution to the field of spinal cord plasticity and restoration, including transplantation, has been enormous. His impact on the field is best exemplified by the fact that all speakers in this symposium had, at one point or another, collaborated with him. It was therefore decided that this symposium would be dedicated to his memory.

Five speakers presented their latest data in the symposium. Four of them dealt with various aspects of transplantation after mechanical lesions of spinal cord neuronal populations and pathways while the last speaker considered the potential for therapeutic transplantation in motoneuronal diseases.

Dr. Barbara Bregman (Georgetown University, Washington, D.C., USA) presented a summary of her work devoted to the comparative analysis of plastic phenomena in the developing and adult spinal cord /1/. After spinal cord lesions at birth, fetal CNS transplants are able to support the regeneration of all spinal projections. In the long term, specific connections between regrowing afferents and appropriate grafted targets are required for maintenance of projections when fibers originate from supraspinal structures, whereas a similar specificity is not required when fibers originate from the dorsal root ganglia. Projections from the dorsal root ganglia can be maintained even by non-target tissue transplants. Behavioral experiments indicate that the regrowth of severed afferents from supraspinal structures allows some recovery of motor function at this stage. Some plasticity of afferent systems in the adult is observed, but to a much lesser extent as concerns supraspinal fibers. Altogether, these data point to the fact that different sets of afferents display varying degrees of plasticity, and that responses are largely, but not entirely, dependent upon the stage of maturation.

Dr. Alan Tessler and colleagues (Medical College of Pennsylvania, Philadelphia, USA) analyzed another aspect of the same model by looking at the prevention of retrograde cell death after axotomy that can be provided by transplants /8/. They showed two different phenomena. The first is a regeneration of severed fibers comparable to that described by Dr. Bregman. This phenomenon, studied using both anatomical and electrophysiological techniques, can be best observed after rhizotomy, when transplants can allow calcitonin gene-related peptide (CGRP) fibers to regrow. The second phenomenon is a rescue of axotomized neurons that do not send axons to their appropriate targets, but survive due to the presence of the transplant. This was shown by comparing the effect of an axotomy at the T8 level, with or without a concurrent transplant, on the survival of Clarke’s nucleus neurons at L1. Normally, 30 to 40% of these neurons die after axotomy, while different types of transplants (spinal, cerebellar or cortical) provide the neurons with enough survival factors for them to survive for several months after the lesion. By examining the relevant literature, the authors concluded that the neuronal survival, the authors used another tissue, the kidney, which contains high levels of NT3 but is not of neural origin. They thus demonstrated that...
rescue of Clarke's neurons from retrograde neuronal death depends upon NT3.

Last in this series, Dr. Dena Howland (from Michael Goldberger's group at the Medical College of Pennsylvania, Philadelphia, USA) presented her results concerning behavioural recovery produced by spinal transplants in newborn kittens with spinal cord transection /4/. After transection, quadrupedal locomotion is normally lost in kittens and never recovers. When the transected area is filled with fetal spinal cord tissue, allowing anatomical connectivity to be reformed across the lesion site using the transplant as a bridge, the development of quadrupedal locomotor function, although not normal, recovers significantly as compared to the lesioned-only animals. In particular, animals with transplants demonstrate weight-supported over-ground locomotion and coordination between forelimbs and hindlimbs.

Altogether, these three talks indicate that spinal cord transection does not obligatorily lead to a complete loss of function, and that the use of fetal transplanted tissue to fill in the gap provides a suitable substrate for the rescue of neurons, axonal growth, and functional improvement. Grafts are most effective when the lesions and grafts are carried out during development.

Dr. Paul Reier (University of Florida, Gainesville, USA) presented data on a different model (contusion/compression damage) that closely resembles spinal cord trauma encountered clinically /6/. In this model, it should be noted that not all long pathways are severed, and preservation/recovery of function may depend upon protection of these fibers from secondary injury. Transplants of fetal spinal tissue, as a cell suspension, into contusion injuries may provide such a protective effect. Indeed, transplanted cells colonized the contusion lesion and provided an anatomical substrate for better preservation of primary afferent and descending fiber systems. Electrophysiological analysis of reflexes elicited at levels below the lesion showed that, indeed, transplants allowed a more normalized pattern of reflex attenuation. Some locomotor improvement was also recorded. This approach, based upon a search for experimental models more closely related to human injuries, provided some results which, if extended to a longer period post-lesion and replicated in larger animals, may eventually be of clinical relevance.

The last talk was given by Dr. Marc Peschanski (INSERM, Creteil, France) who presented a summary of the work carried out by his group on models of motoneuronal diseases in rats /5/. By transplanting fetal spinal neurons as a cell suspension, it is possible to obtain some anatomical reconstruction of the spinal circuitry. Afferent fibers respond differently to the loss of postsynaptic target neurons and to the introduction of transplanted cells, but maintenance of afferent systems can still be observed — at least in the most peripheral portions of the transplants — several months after the lesion/transplant procedure. Transplanted neurons are, however, unable to send an axon out into the ventral root. Long axonal extension out of the spinal cord can be obtained, nevertheless, if a peripheral nerve guide is provided. In a follow-up study, this group used a “panning” technique that allows fractionation of cell suspensions specifically enriched in motoneurons. Using the low affinity nerve growth factor receptor as a ligand, it is possible to enrich the motoneuronal pool in transplants. These motoneurons develop well after transplantation and receive innervation from the host. Although the use of transplants to replace motoneurons at all levels of the spinal cord in motoneuronal diseases is not foreseeable, the potential may exist eventually for local replacement of a subset of motoneurons, allowing for functional recovery of a specific neuromuscular connection.

During the discussion, Drs. Sieradzan (London, U.K.), Horvat (Paris, France) and Bunge (Miami, FL, USA) presented their results concerning various types of transplants into the spinal cord /2,3,7/, exemplifying further the breadth of interest in this topic. The entire session concerned experimental work, and it is clear to everyone that spinal cord transplantation has not reached the point for clinical attempts. Clinical indications and even potentials cannot yet be clearly defined. The talks and discussion demonstrated, however, that this far-fetched goal is not entirely out of reach, and that both anatomical and functional recovery
can be observed in specific experimental conditions.

REFERENCES
