The proper time to repair a severed peripheral nerve continues to be debated. The response to traumatic nerve sectioning and the recovery after a neurorrhaphy varies greatly from nerve to nerve and with different levels of the same nerve. Earlier guidelines have now become clouded. Some recent textbooks and articles avoid any explicit instructions concerning the timing of a repair; others advocate immediate repair; still others hold out for a short 2 to 3 week delay; and, finally, some state it makes no difference. The policy within the medical service of the Army has been that nerve suture should be done as soon as possible after a short waiting period of 2 to 3 weeks. This conclusion is based on articles written after World War II, which were concerned mostly with allowing peripheral demarcation of a war wound, and which were clinically supported by evaluation of motor return of function. Delays beyond the initial 19 to 21 day waiting period were accompanied by a 1% reduction in motor recovery for every 6 days of postponement of the definitive neurorrhaphy. For the moderate size nerves such as the median, ulnar, radial, peroneal, and tibial, these guidelines hold true. For large nerve trunks, such as the sciotic nerve or brachial plexus, regardless of the timing of a repair, the outlook remains poor. For the smaller digital nerves, any delay appears unnecessary, and the prognosis after repair is generally very good. Thus, previously defined rules concerned with timing of a nerve repair possessed both usefulness and shortcomings.

Method of Study

The metabolic background or base for these observations has never been defined. Accordingly, we thought it important to: 1) review the literature; 2) review our past experimental data; 3) examine the neurorrhaphies and spinal cord from animals in our present experiments which were sacrificed at different time intervals after peripheral nerve lesions; and 4) study current clinical cases from casualties of the war in Vietnam. From this background, we have drawn several conclusions concerning the metabolic changes in response to trauma and during regeneration of the peripheral nerve after injury.

The metabolic response to trauma and regeneration concerns three different cellular levels:
1. The spinal cord, particularly the anterior horn cell body
2. The proximal nerve stump
3. The distal severed and separated part of the peripheral nerve and its associated end organs.

Metabolic Response in the Anterior Horn Cell

Within the spinal cord, the cell body whose axon has been severed progressively enlarges for approximately 10 to 20 days, remains enlarged while there is active regeneration, and thereafter with maturation returns slowly to normal size. For many years it was thought that the enlargement of the cell body represented retrograde degeneration. The basis of such thinking centered on the post-injury histologic appearance of the cell,
for the staining properties of the cell become less concentrated. Ribonucleic acids (RNA) in the cytoplasm and in the Nissl substances migrate peripherally and break up into smaller particles. The actual total amount of RNA begins increasing from the fourth day onward, and the changes of RNA aggregations from large particles to submicroscopic particles give the picture of "chromatolysis" but represent in reality a transformation of RNA into a more active form. Increases in enzymatic activity and in the incorporation of aminoacids point to increased metabolism and are confirmed by the finding of an increased total amount of nucleic acids in these hypertrophic cells. The anabolic proteosynthesis evidently is required for maintenance of neuronal survival and cellular function after trauma and for regeneration of a new distal axon (Fig. 1).

The chromatolytic hypertrophic changes are more pronounced the closer the cut is made to the nerve cell (Fig. 2). There are two reasons for this phenomenon. First, the amount of the total neuron cut away and separated is larger, and thus the amount of cellular disruption is greater. When a nerve lesion is close to the cell body, a large percentage of cell mass is lost. The cellular insult will exceed the tolerance of the neuron. In such cases, the cell hypertrophies in an abortive effort to maintain itself. However, in time it becomes atrophic. Such changes of the cell body in the cord may take up to 2 years in rats and many years in man. Second, even if the cells were to survive the more proximal injury, the amount of distal axon to be replaced may exceed the metabolic capability of the cell. The nerve cell during successful regeneration replaces 50 to 100 times the organic material contained in the cell body. The exact upper limit of the cell's metabolism is not known. In unsuccessful nerve repairs, regeneration into the peripheral endoneural tubes does begin; the central cell, however, does not maintain its hypertrophic anabolic state for the extended period of months required to complete the resynthesizing process. This observation is especially true in animals high on the phylogenetic scale and old in chronological age. Also, during this period of time, degenerative changes occur in the distal endoneural tubes and the distal muscle, which further downgrade the prognosis; these will be discussed later.

The changes in the central body of the anterior horn cell are less marked in more peripheral lesions where the neuronal disruption is minimal (Fig. 2). The phase of neuronal survival is shortened to less than 2 weeks and the phase of repair to 2 to 3 months (Fig. 2). If the extent of destruction of the peripheral stump at the time of original trauma is minimal, the definitive operative repair may be safely carried out earlier than usual. This has been clearly shown by Grabb for nerve lesions caused by sharp objects at the wrist in young monkeys. In turn, the prognosis is very good as the regeneration requirements are small.

The metabolic changes of the severed neuron follow a definite pattern in time and substance even with surgical intervention at 3 weeks. The clinical experience of World War II provides statistically significant proof that in general a delay in definitive neurorrhaphy up to 19 days had no harmful effect. In fact, over one-half the cases of suture repair performed earlier than 2 weeks required resuture because of excessive mesenchymal tissue buildup within the anastomosis. These facts coincide with the metabolic changes observed, in that the cell body had to markedly increase its proteosynthesis first to survive and, second, to provide the metabolic environment necessary to regenerate and synthesize a new distal axon. Only after the neuron has shown the chromatolytic hypertrophic alterations, which take from several days to 2 weeks to develop fully, is the cell capable of regenerating peripherally. Operative intervention at this time alters the appearance of the cell within the spinal cord minimally and the neuron continues a pattern of changes nearly identical to that of a crush lesion where surgical repair was not required. The hypertrophic cell with its increased proteosynthesis acts as if it were metabolically primed for a delayed repair.

Only the central cell body is capable of large scale conversion of amino acids to the proteins which are required at the periphery in regeneration. Migration of these proteins down the axon has been shown by autoradiographic techniques to occur at a rate of 0.8 mm per day in the adult rat and 1.5 mm in