Degeneration and Regeneration of Nerve Fibers

■ INTRODUCTION

When a nerve fiber is injured, various changes occur in the nerve fiber and nerve cell body. All these changes are together called the **degenerative changes.**

Causes for Injury

Injury to nerve fiber occurs due to following causes:

1. Obstruction of blood flow
2. Local injection of toxic substances
3. Crushing of nerve fiber
4. Transection of nerve fiber.

■ DEGREES OF INJURY

Sunderland had classified the injury to nerve fibers into five categories depending upon the order of severity.

■ FIRST DEGREE

First degree injury is the most common type of injury to the nerves. It is caused by **applying pressure** over a nerve for a short period leading to occlusion of blood flow and hypoxia.

By first degree of injury, axon is not destroyed but mild demyelination occurs. It is not a true degeneration. Axon looses the function temporarily for a short time, which is called conduction block. The function returns within few hours to few weeks. First degree of injury is called **Seddon neuropraxia.**

■ SECOND DEGREE

Second degree is due to the **prolonged severe pressure,** which causes **Wallerian degeneration** (see below). However, the endoneurium is intact. Repair and restoration of function take about 18 months. Second degree of injury is called **axonotmesis.**

■ THIRD DEGREE

In this case, the **endoneurium** is interrupted. Epineurium and perineurium are intact. After degeneration, the recovery is slow and poor or incomplete. Third, fourth and fifth degrees of injury are called **neurotmesis.**

■ FOURTH DEGREE

This type of injury is more severe. Epineurium and perineurium are also interrupted. Fasciculi of nerve fibers are disturbed and disorganized. Regeneration is poor or incomplete.

■ FIFTH DEGREE

Fifth degree of injury involves **complete transaction** of the nerve trunk with loss of continuity. Useful regeneration is not possible unless the cut ends are rearranged and approximated quickly by surgery.

■ DEGENERATIVE CHANGES IN THE NEURON

Degeneration refers to deterioration or impairment or pathological changes of an injured tissue. When a peripheral nerve fiber is injured, the degenerative changes occur in the nerve cell body and the nerve fiber of same neuron and the adjoining neuron.

Accordingly, degenerative changes are classified into three types:

1. Wallerian degeneration
2. Retrograde degeneration
3. Transneuronal degeneration.

■ WALLERIAN DEGENERATION OR ORTHOGRADE DEGENERATION

Wallerian degeneration is the pathological change that occurs in the distal cut end of nerve fiber (axon). It is named after the discoverer **Waller.** It is also called orthograde degeneration. Wallerian degeneration starts within 24 hours of injury. Change occurs throughout the length of distal part of nerve fiber simultaneously.

Changes in Nerve

i. Axis cylinder swells and breaks up into small pieces. After few days, the broken pieces appear as debris in the space occupied by axis cylinder (Fig. 137.1).
ii. Myelin sheath is slowly disintegrated into fat droplets. The changes in myelin sheath occur from 8th to 35th day.
iii. Neurilemmal sheath is unaffected, but the Schwann cells multiply rapidly. Macrophages invade from outside and remove the debris of axis cylinder and fat droplets of disintegrated myelin sheath. So, the neurilemmal tube becomes empty. Later it is filled by the cytoplasm of Schwann cell. All these changes take place for about 2 months from the day of injury.

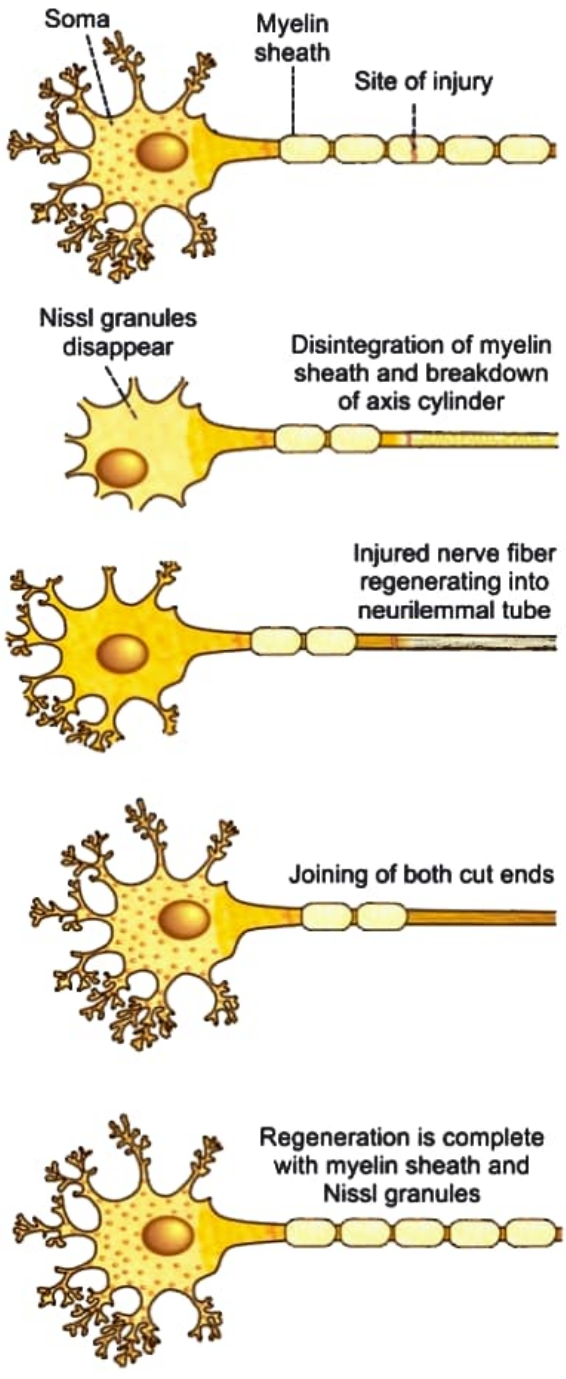

FIGURE 137.1: Degeneration and regeneration of nerve fiber

■ RETROGRADE DEGENERATION

Retrograde degeneration is the pathological changes, which occur in the nerve cell body and axon proximal to the cut end.

Changes in Nerve Cell Body

Changes in the nerve cell body commence within 48 hours after the section of nerve. The changes are:

i. First, the Nissl granules disintegrate into fragments by chromatolysis
ii. Golgi apparatus is disintegrated
iii. Nerve cell body swells due to accumulation of fluid and becomes round
iv. Neurofibrils disappear followed by displacement of the nucleus towards the periphery
v. Sometimes, the nucleus is extruded out of the cell. In this case, death of the neuron occurs and regeneration of the injured nerve is not possible.

Changes in Axon Proximal to Cut End

In the axon, changes occur only up to first node of Ranvier from the site of injury. Degenerative changes that occur in proximal cut end of axon are similar to those changes occurring in distal cut end of the nerve fiber.

■ TRANSNEURONAL DEGENERATION

If an afferent nerve fiber is cut, the degenerative changes occur in the neuron with which the afferent nerve fiber synapses. It is called transneuronal degeneration.

Examples:

i. Chromatolysis in the cells of lateral geniculate body occurs due to sectioning of optic nerve
ii. Degeneration of cells in dorsal horn of spinal cord occurs when the posterior nerve root is cut
iii. Degeneration of cells in ventral horn of spinal cord occurs when there is tumor in cerebral cortex.

■ REGENERATION OF NERVE FIBER

The term regeneration refers to **regrowth** of lost or destroyed part of a tissue. The injured and degenerated nerve fiber can regenerate. It starts as early as 4th day after injury, but becomes more effective only after 30 days and is completed in about 80 days.

■ CRITERIA FOR REGENERATION

Regeneration is possible only if certain criteria are fulfilled by the degenerated nerve fiber:

1. Gap between the cut ends of the nerve should not exceed 3 mm
2. Neurilemma should be present; as neurilemma is absent in CNS, the regeneration of nerve does not occur in CNS
3. Nucleus must be intact; if it is extruded from nerve cell body, the nerve is atrophied and the regeneration does not occur
4. Two cut ends should remain in the same line. Regeneration does not occur if any one end is moved away.

■ STAGES OF REGENERATION

1. First, some pseudopodia like extensions grow from the proximal cut end of the nerve. These extensions are called **fibrils** or **regenerative sprouts**. The number of fibrils is up to 100.
2. Fibrils move towards the distal cut end of the nerve fiber
3. Some of the fibrils enter the **neurilemmal tube** of distal end and form axis cylinder
4. Schwann cells line up in the neurilemmal tube and actually guide the fibrils into the tube. Schwann cells also synthesize nerve growth factors, which attract the fibrils form proximal segment.
5. Axis cylinder is fully established inside the neurilemmal tube. These processes are completed in about 3 months after injury.
6. Myelin sheath is formed by Schwann cells slowly. Myelination is completed in 1 year.
7. Diameter of the nerve fiber gradually increases. However, the degenerated nerve fiber obtains only 80% of original diameter. Newly formed internodes are also shorter than the original ones.
8. In the nerve cell body, first the Nissl granules appear followed by Golgi apparatus
9. Cell looses the excess fluid; nucleus occupies the central portion
10. Though anatomical regeneration occurs in the nerve, functional recovery occurs after a long period.