

Degeneration and Regeneration of Neurons

PHYA-Sem-II-CC3TH

Compiled and Prepared
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Causes of Degeneration

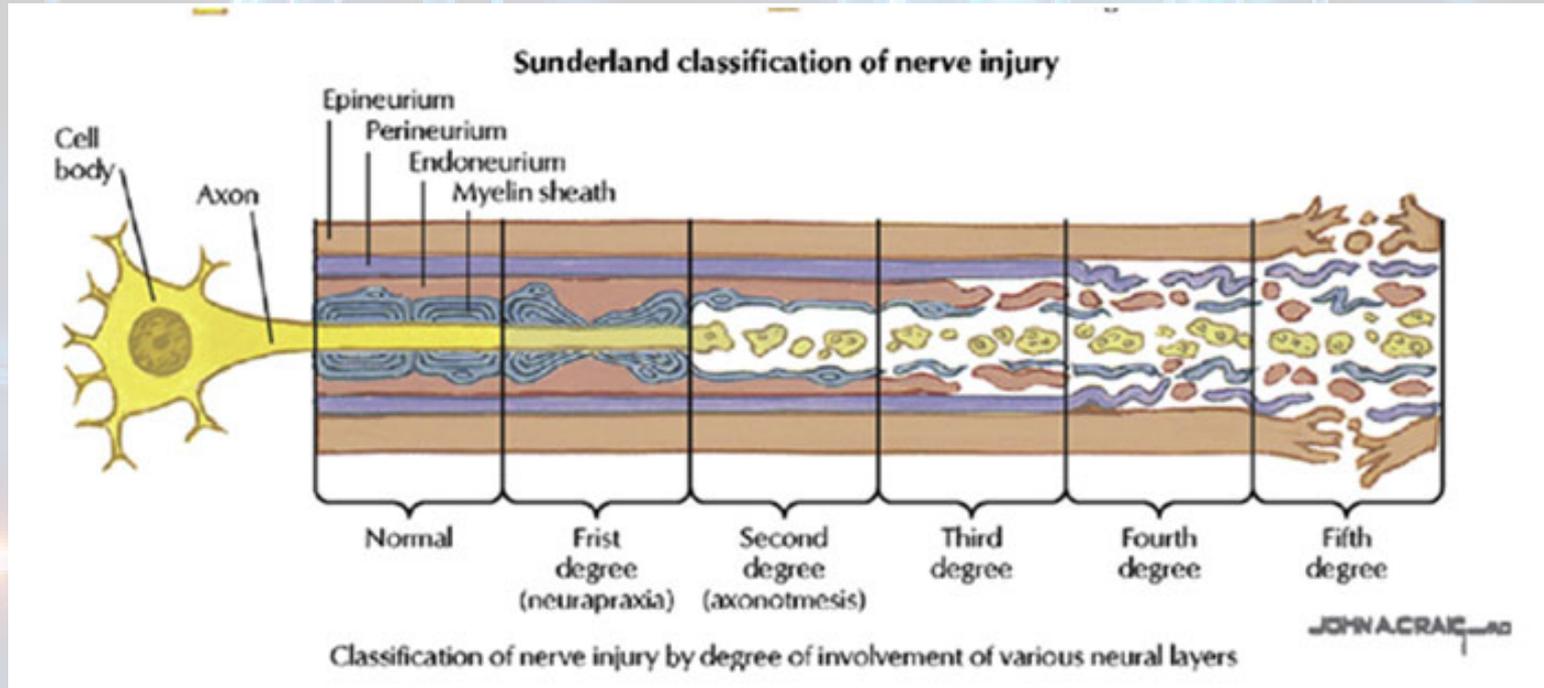
Peripheral nerves can be damaged in several ways:

- Injury from an accident, a fall or sports can stretch, compress, crush or cut nerves.
- Medical conditions, such as diabetes, Guillain-Barre syndrome and carpal tunnel syndrome.
- Autoimmune diseases including lupus, rheumatoid arthritis and Sjogren's syndrome.
- Other causes include narrowing of the arteries, hormonal imbalances and tumours.

Classification

	<i>Sunderland</i>	<i>Seddon</i>	<i>Description of Injury</i>	<i>Recovery Period</i>
Mildest	I	Neurapraxia	Conduction block, nerve is in-continuity, Wallerian degeneration does not take place	≤ 3 months
	II	Axonotmesis	Axon not continuous, nerve itself remains intact, axonal sprouting, Wallerian degeneration	1 inch per month
	III		During healing, excessive scarring of the endoneurium occurs that hinders axon regeneration	< 1 inch per month where it is slowed by the scar tissue; determined by degree of scarring and involved fascicles
	IV		Nerve is still in-continuity, scar build up blocks nerve regeneration	Surgical intervention required to re-establish nerve transduction by removing scar tissue and reconnecting nerve segments
Most Severe	V	Neurotmesis	Rupture of the nerve, it is no longer a continuous fiber	Recovery requires surgical intervention

Sunderland Classification of Degeneration



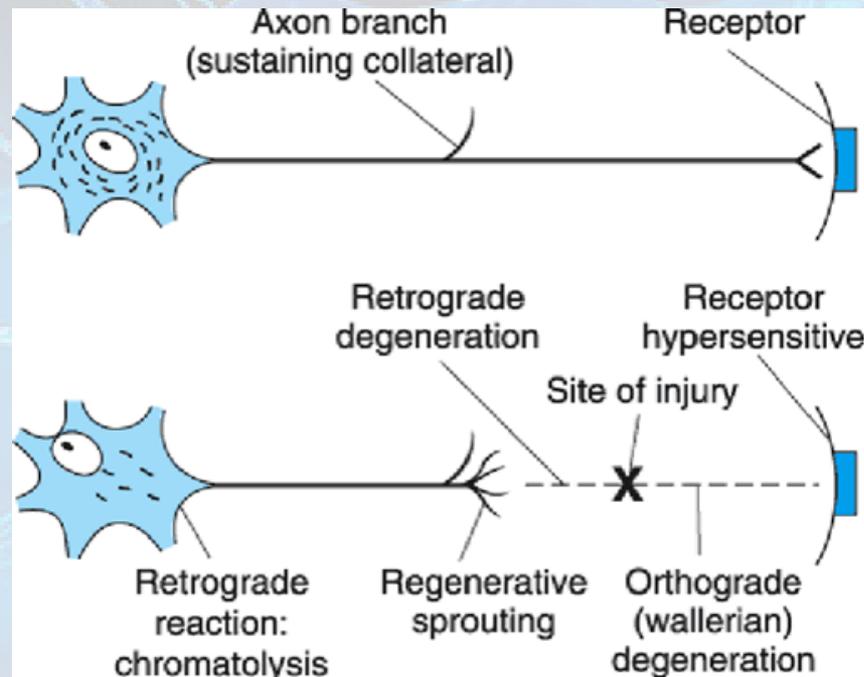
Stage of Degeneration

Orthograde/ Anterograde/Wallerian

Changes in the part of axon distal to the site of injury

Retrograde

Changes in the part of axon proximal to the site of injury



Source: Ganong WF: *Review of Medical Physiology*, 22nd Edition:
<http://www.accessmedicine.com>

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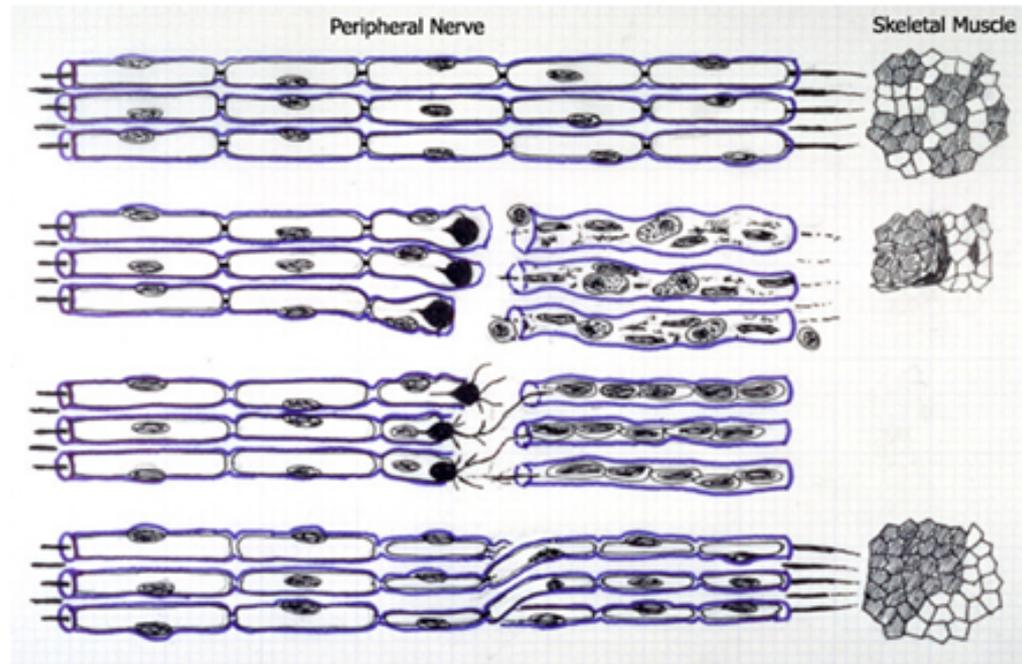
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Normal nerve innervating skeletal muscle. The blue lines indicate the basement membrane.

The nerve has been transected and Wallerian degeneration has begun. There is corresponding atrophy in the muscle

Proximal nerve terminals send sprouts toward the Schwann cell tubes.

Some of the sprouts make it into tubes and reinnervate the muscle, which has undergone neurogenic rearrangement



Degeneration

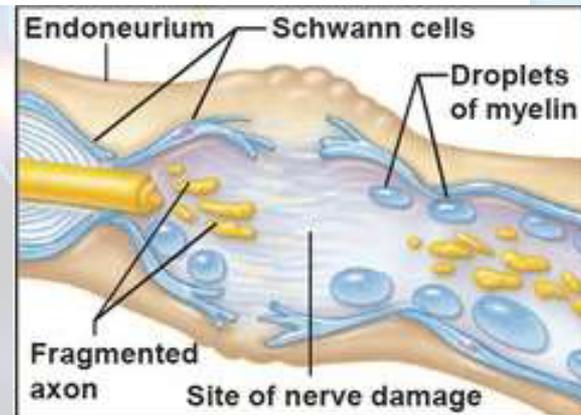
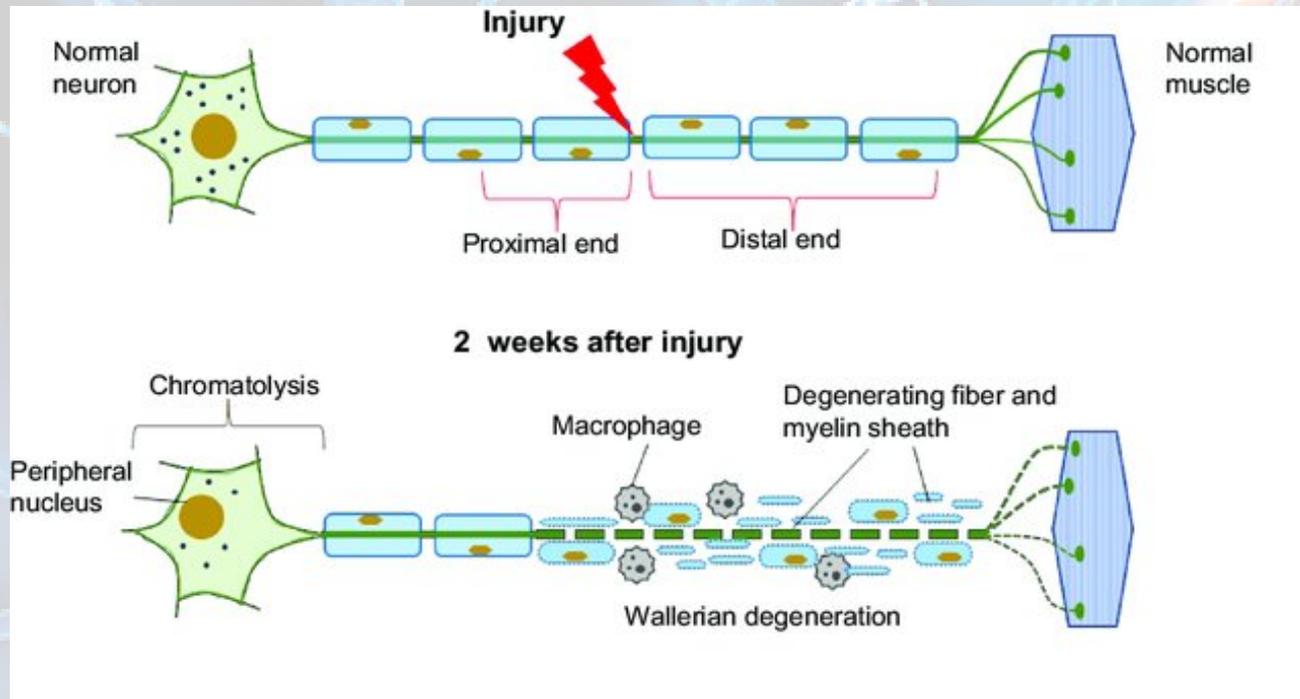
- **Wallerian degeneration** is the pathological change that occurs in the distal cut end of nerve fibre (axon).
 - It is named after the discoverer **A. Waller (1862)**.
 - It is also called **Orthograde / Anterograde** degeneration.
 - Wallerian degeneration starts within 24 hours of injury.
 - Change occurs throughout the length of distal part of nerve fibre simultaneously
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- **Retrograde degeneration** is the pathological changes, which occur in the nerve cell body and axon proximal to the 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 fibre.

Degenerative changes

A. Changes in Axis cylinder

1. **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.
2. **Myelin sheath** is slowly disintegrated into fat droplets. The changes in myelin sheath occur from 8th to 35th day.
3. **Neurilemmal sheath** is unaffected, but the Schwann cells multiply rapidly.
4. **Macrophages** invade from outside and remove the debris of axis cylinder and fat droplets of disintegrated myelin sheath.

Degenerative changes



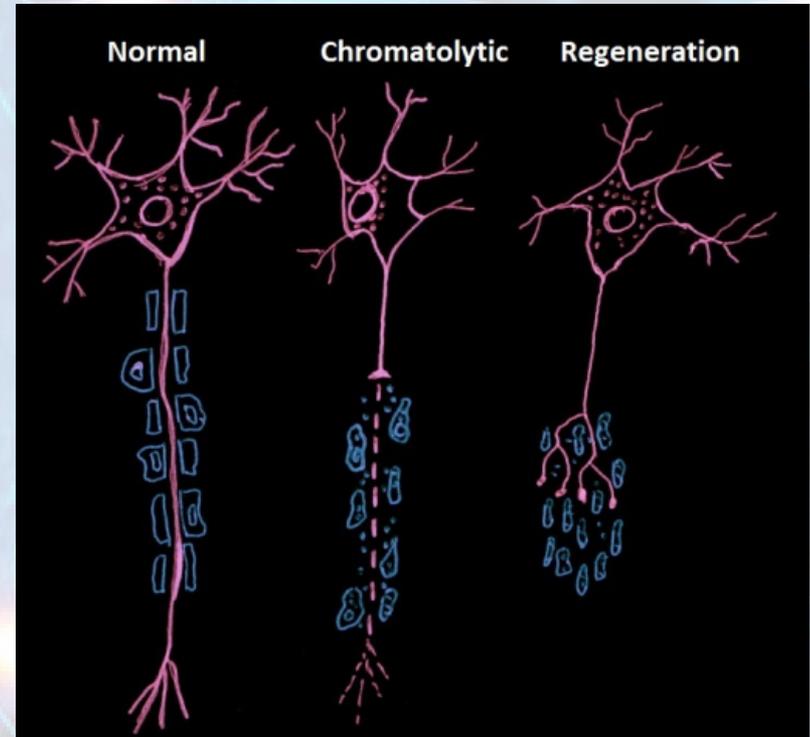
Degenerative changes

B. Changes in Cell body of neuron

Changes in the nerve cell body commence within 48 hours after the section of nerve.

The changes are:

- First, the Nissl granules disintegrate into fragments by **chromatolysis**
- Golgi apparatus is disintegrated
- Nerve cell body swells due to accumulation of fluid and becomes round
- Neurofibrils disappear followed by displacement of the nucleus towards the periphery
- 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.



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**.

Example:

- 1. Degeneration of cells in dorsal horn of spinal cord occurs when the posterior nerve root is cut.
- 2. Degeneration of cells in ventral horn of spinal cord occurs when there is tumor in cerebral cortex.

Regeneration

- 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:

- Gap between the cut ends of the nerve should not exceed 3 mm.
- Neurilemma should be present.
- Nucleus must be intact; if it is extruded from nerve cell body, the nerve is atrophied and the re generation does not occur.
- Two cut ends should remain in the same line.
- Regeneration does not occur if any one end is move away.

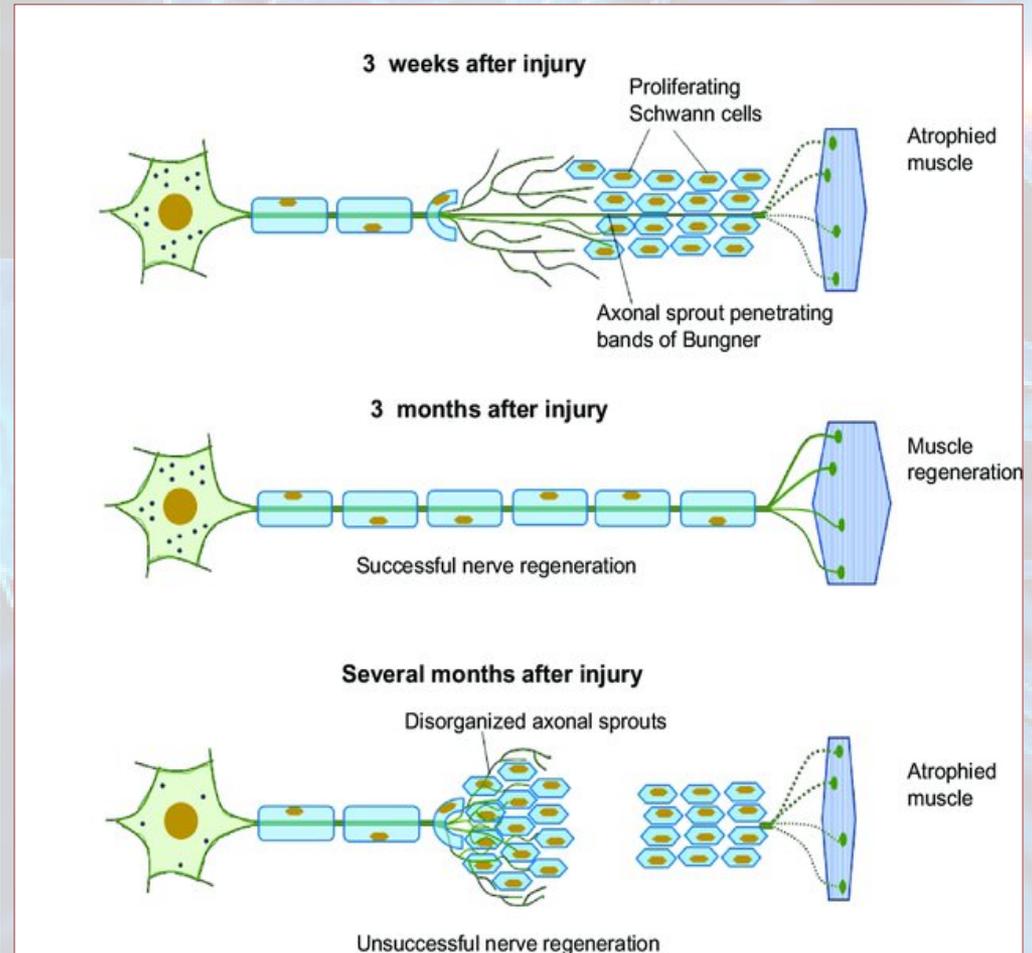
Stages of Regeneration

- First, some pseudopodia like extensions grow from the proximal cut end of the nerve. These extensions are called **fibrils or regenerative sprouts**.
- Fibrils move towards the distal cut end of the nerve fiber
- Some of the fibrils enter the **neurilemmal tube** of distal end and form axis cylinder
- 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 from proximal segment.
- Axis cylinder is fully established inside the neurilemmal tube. These processes are completed in about 3 months after injury.
- Myelin sheath is formed by Schwann cells slowly.
- Myelination is completed in 1 year.

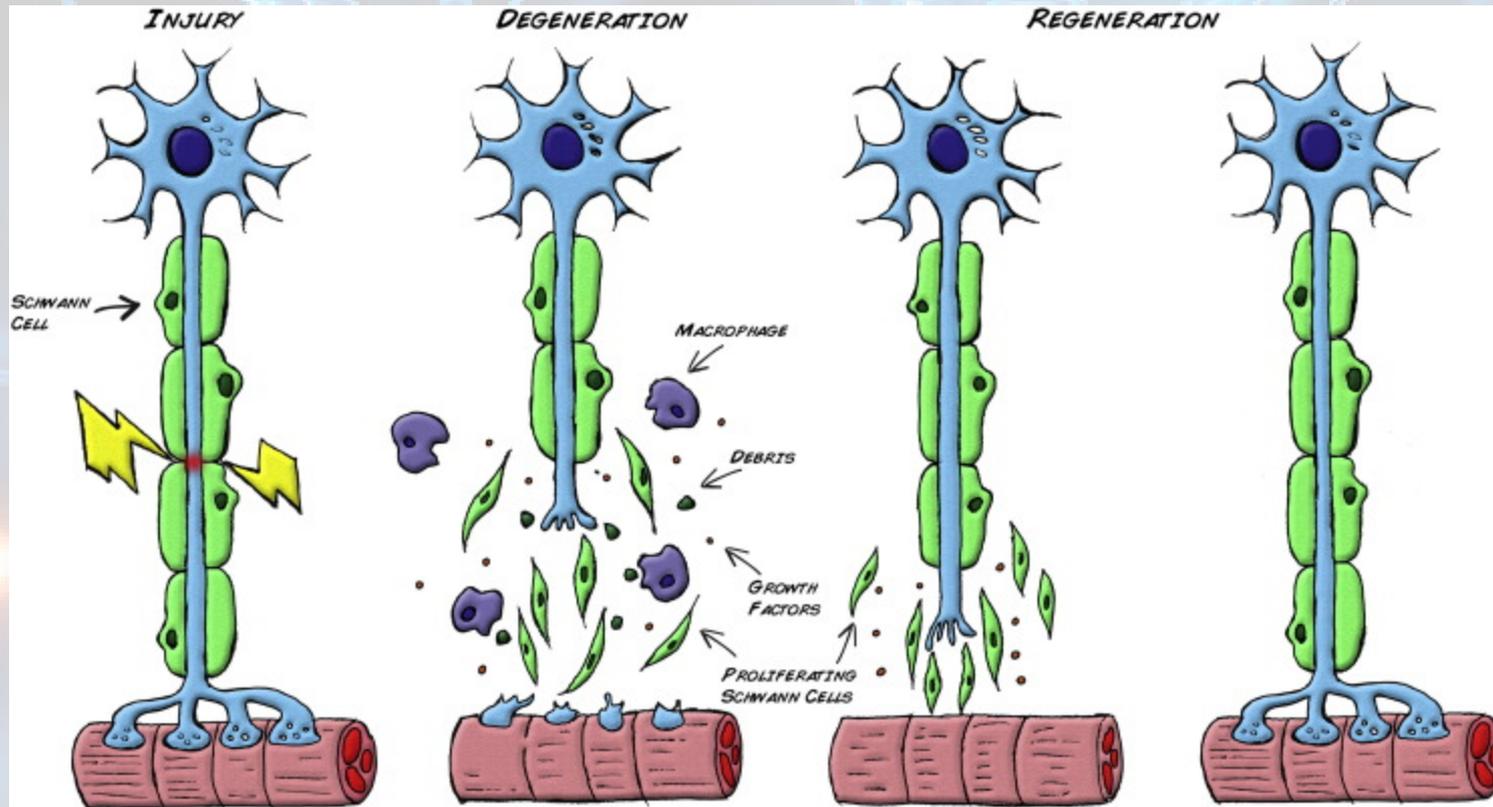
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Stages of Regeneration contd..

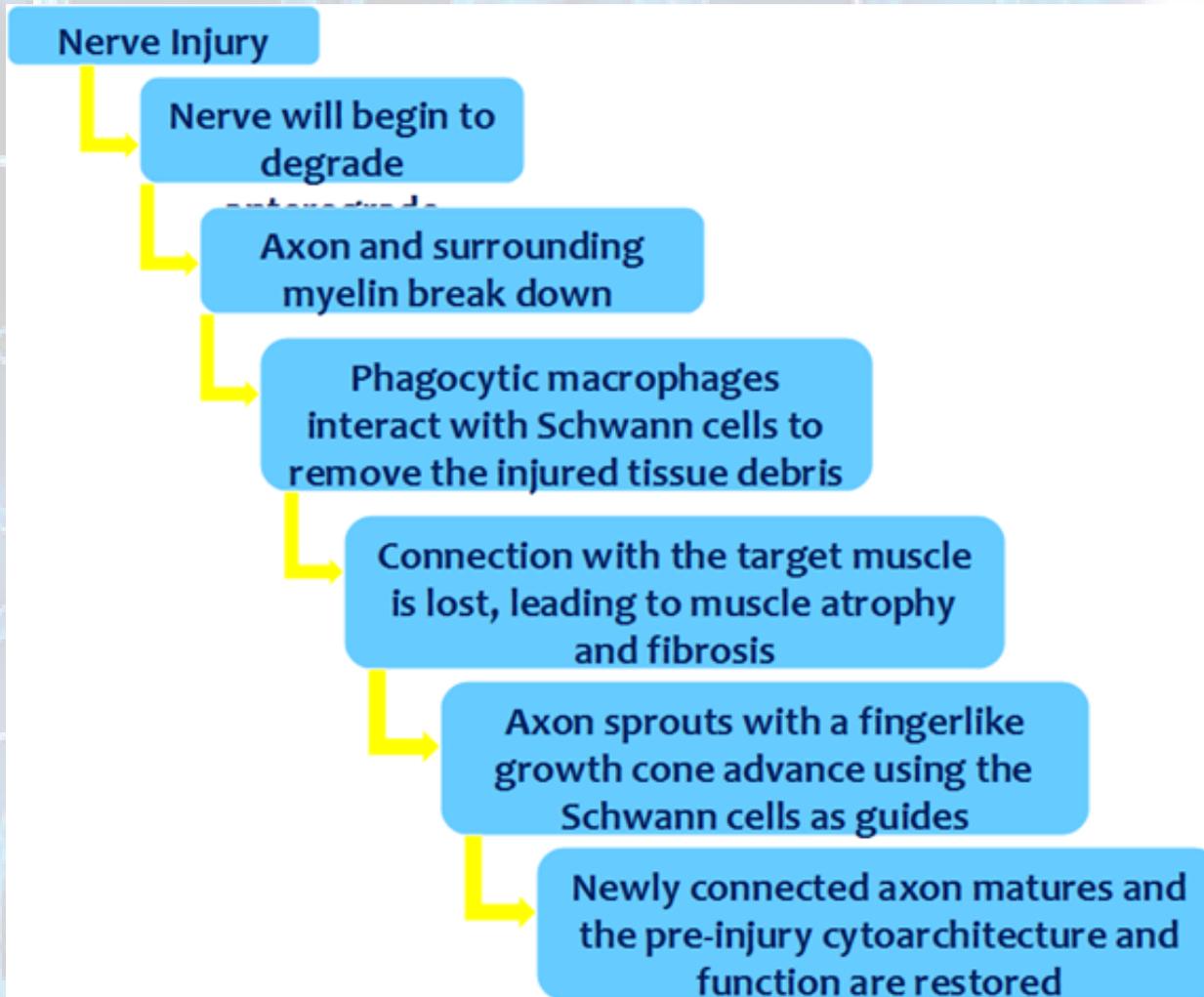
- Diameter of the nerve fiber gradually increases.
- In the nerve cell body, first the Nissl granules appear followed by Golgi apparatus.
- Cell loses the excess fluid; nucleus occupies the central portion.
- Though anatomical regeneration occurs in the nerve, functional recovery occurs after a long period.



Degeneration and Regeneration



Summary



References:

- Guyton and Hall Textbook of Medical Physiology
- Concise Textbook of Human Physiology by Indu Khurana
- <https://www.youtube.com/watch?v=KruZ4FCNlaM>
- <https://www.youtube.com/watch?v=P02ea4jf50g>