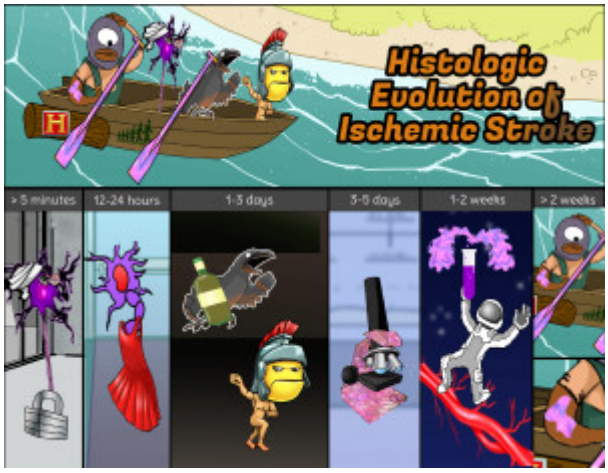
Histologic Evolution of Ischemic Stroke

Immediately following an ischemic stroke, the histological appearance of neuronal tissue begins to change. The progression is as follows: irreversible neuronal injury after 5 minutes, then red neurons in 12-24 hours. Liquefactive necrosis is evident in 1-3 days after injury while microglia begin to appear 3-5 days after injury. At the 1-2 week point, astrocytes form glial scars via reactive gliosis and blood vessels proliferate. After 2 weeks, the glial scar is virtually complete.



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> 5 Minutes

Irreversible Neuronal Injury
Lock on Neuron Injured
Hypoxia that occurs for more than 5 minutes can result in irreversible neuronal injury. The hippocampus is the most vulnerable part of the brain to this type of neuronal injury, specifically its CA1 (cornu ammonis) region. This region has a prominent Ca²⁺ mobilization potential that results in a long-standing calpain (proteolytic enzyme) activation during hypoxia. Other vulnerable parts of the brain include the neocortex, cerebellum (Purkinje cells), and watershed areas.

12-24 hours

Red Neurons
Red-dress Neuron
Red neurons are the first pathological microscopic finding, appearing 12-24 hours after ischemic stroke. Their red color comes from acidophilic cytoplasmic granules of eosinophilic neurons. Red neurons can persist in the ischemic penumbra for 2-6 months. They are readily identified due to their deep red eosinophilic cytoplasm, darkly stained pyknotic nuclei, loss of Nissl substance, and cell body shrinkage.

1-3 days

Liquefactive Necrosis (Neutrophils)
Liquor Necrosis-crow with Nude-trojan
Liquefactive tissue necrosis and neutrophilic infiltration are seen within 1-3 days after an ischemic stroke. The brain is one of the few tissues of the body that exhibits liquefactive necrosis. The brain's necrotic tissue becomes liquefied because of proteolytic enzymes released by microglial cells.

3–5 Days

Microglia
Microscope-glitter
Microglial activation occurs 3-5 days after an ischemic stroke. Microglia are a type of macrophage specific to the central nervous system. Microglia are activated around the dying neuron cells to clean cell debris and release mediators of inflammation.

1-2 Weeks

Reactive Gliosis (Astrocytes)
Reaction Glitter Astronaut
Reactive gliosis from astrocytes occurs 1-2 weeks after ischemic stroke. It is a response to brain tissue damage. This process limits damage and restores homeostasis in the brain. It is triggered by cytokines and growth factors such as IL-6, TNF-alpha, CNTF, and LIF. Hypertrophy of astrocytes and up-regulation of GFAP is the process' hallmark.

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Vascular Proliferation

Vascular-growths

Vascular proliferation is also seen 1-2 weeks after an ischemic stroke. Reactive astrocytes stimulate angiogenesis, which induce vascular proliferation by secreting vascular endothelial growth factor (VEGF).

> 2 weeks

Glial Scar

Glitter Scar

Glial scars are seen > 2 weeks after an ischemic stroke. It is a healing process of the brain's damaged tissue formed to separate and sanction off damaged tissue. Glial scar formation can be seen as the result of continued gliosis. Pericytes also seem to contribute to glial scar formation.

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