Recent studies have suggested that the brain preconditioning could induce tolerance to ischemia in humans. It has been believed that newly synthesized proteins are required for the acquisition of delayed tolerance in the brain and spinal cord. However, the mechanism other than the synthesis of neuroprotective proteins may also play a pivotal role. Preconditioning may reprogram the response to ischemic injury as seen during hibernation. Preconditioning with hyperbaric oxygen, volatile anesthetics, and xenon seems to be the focus of the attention from the standpoint of the clinical setting. Strong neuroprotection by the preconditioning with isoflurane and xenon is reported in animal experiments and may change the traditional idea of neuroprotection by anesthetics. The discovery that erythropoietin exerts neuroprotective properties has opened new therapeutic avenues. Erythropoietin is induced in the brain by hypoxic preconditioning and by the pharmacological preconditioning. In addition, the intravenous administration of erythropoietin has been shown to be safe and beneficial for acute stroke in humans. Therefore, erythropoietin is now one of the most promising neuroprotective agents. The research in the brain and spinal cord preconditioning will contribute to the elucidation of the mechanism of ischemic injury and to the establishment of new therapies for neuroprotection.