GLOSSARY

MODIFIED RANKIN SCALE
A scale that is used to measure disability in stroke victims; ranges from 0 (no residual symptoms) to 5 (severe disability—bedridden and requiring constant care)

achieved remission (defined as at least 1 year free from seizures with or without auras) while taking one or two AEDs, and the effects of subsequent attempts to reduce and eventually discontinue AEDs.

Of 301 patients who achieved remission after discharge, 291 were on at least one AED at the time of remission. Of these, 129 patients attempted to reduce their AEDs from two to one or from one to zero after achieving remission; 162 patients did not attempt any AED reduction. Relapse was experienced by 41/129 patients (32%) who reduced their AEDs, compared with 73/162 patients (45%) who did not reduce AEDs ($P = 0.02$).

The authors conclude that the risk of relapse after surgery for intractable seizures appears to be no greater for those who reduce AEDs than for those who maintain them. They caution, however, that because of potential differences between patients who maintain and those who reduce AEDs, randomized prospective trials are needed to clarify the impact of AED reduction in postsurgical patients who achieve remission.

Christine Kyme

Original article Berg AT *et al.* (2005) Reduction of AEDs in postsurgical patients who attain remission. *Epilepsia* **47:** 64–71

Inhibition of a downstream effector of COX2 can attenuate excitotoxic brain injury

Cyclo-oxygenase 2 (COX2) inhibitors can be used to protect against neurotoxicity in conditions such as cerebral ischemia and neurodegeneration; however, their long-term use is associated with cardiovascular complications thought to result from blockade of the vasoprotective effects of COX2-derived prostacyclin. Data from a recent study reported in *Nature Medicine* indicate that inhibition of a downstream effector of COX2—the prostaglandin E_2 EP1 receptor—can selectively attenuate hypoxic–ischemic brain lesions without any loss of vasoprotection.

Kawano and colleagues carried out a series of experiments using an animal model of hypoxic–ischemic *N*-methyl-D-aspartate (NMDA)-induced brain injury. They showed that, following neocortical microinjection of NMDA to mice, administration of an EP1-receptor inhibitor reduced the lesion volume by 31%. Similarly, mice without the gene encoding the EP1 receptor showed a 35% reduction in NMDA lesion volume. In a model of focal cerebral ischemia, administration of an EP1-receptor inhibitor 6 h after transient occlusion of the middle cerebral artery resulted in a 43 ± 10% reduction in infarct volume ($P < 0.05$). Importantly, this protective effect occurred within a therapeutic window similar to that of a COX2 inhibitor. The researchers went on to show that inhibition or inactivation of the EP1 receptor was associated with a preservation of the activity of the Na^+–Ca^{2+} exchanger responsible for enabling neurons to cope with excitotoxicity-associated Ca^{2+} accumulation.

The authors suggest that pharmacological inhibition of the EP1 receptor might be a viable method of attenuating the detrimental effects of COX2 without impinging on the beneficial activities of this enzyme.

Christine Kyme

Original article Kawano T *et al.* (2006) Prostaglandin E_2 EP1 receptors: downstream effectors of COX-2 neurotoxicity. *Nat Med* **12:** 225–229

Is NXY-059 beneficial in ischemic stroke?

Acute ischemic stroke is a major cause of death in industrialized countries and is usually treated with thrombolysis using alteplase. This treatment, however, must be started within 3 h of stroke onset, and can cause bleeding. A recent randomized, placebo-controlled trial investigated clinical use of NXY-059, an agent that has been shown to reduce infarct size and preserve brain function in animal models of stroke.

Patients with acute ischemic stroke were enrolled from May 2003 to November 2004 in hospitals in 24 countries. In total, 1,705 patients received a 72 h infusion of either NXY-059 ($n = 853$) or placebo ($n = 852$) within 6 h of stroke onset and were included in the safety analysis; 1,699 patients were included in the efficacy analysis. Mean time from stroke onset to treatment was 3 h 46 min; 28.7% of all patients also received alteplase.

The primary endpoint—disability at 90 days as measured by the MODIFIED RANKIN SCALE—was improved in patients who received NXY-059 compared with those who received placebo ($P = 0.038$). NXY-059 did not alter neurological improvement as measured by change in the

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