Yesterday

- Epilepsy refers to a large group of neurological disorders characterized by chronic, spontaneous seizures. By the 1960s, scientists had made great strides in detecting patterns of abnormal electrical activity in the brain that cause epileptic seizures. A technology to measure brain activity, called electroencephalography (EEG), became a widespread tool to diagnose epilepsy.

- New methods for screening potential anticonvulsant medications were setting the stage for epilepsy drug development, but treatment options were limited. Only a handful of drugs were available to treat epilepsy, and each had problematic side effects. In some people, EEG could be used to locate and surgically remove the epileptic focus, the source of seizure activity in the brain.

- Although scientists recognized that genetic factors are important contributors to many types of epilepsy, causative gene variants remained largely unknown. Similarly, while various insults to the brain – including traumatic brain injury (TBI), stroke, and infections – were known risk factors for acquired epilepsy, the mechanisms involved were poorly understood.

- Comorbid conditions that frequently accompany epilepsy, including depression and other cognitive and behavioral impairments, were largely viewed as consequences of seizures that would disappear with adequate seizure control.

Today

- Collectively, epilepsy disorders are estimated to affect approximately 3 million Americans of all ages and ethnic groups, with a lifetime risk to age 80 of 3%. The incidence of epilepsy is highest in early childhood and is growing fastest in the elderly population.

- Over twenty antiepileptic drugs are now commonly used to treat epilepsy, and most people with epilepsy can successfully control their seizures with medication, surgery, vagal nerve stimulation, or some combination of these therapies. NIH-supported researchers and special programs have contributed significantly to these advances in treatment options. Unfortunately, adverse treatment effects remain a challenge, and about one third of people with epilepsy fail to achieve adequate seizure control, which sometimes leads to devastating consequences.

- Brain imaging technologies now help surgeons map critical areas of the brain prior to surgery. These sophisticated tools allow precise localization and removal of the seizure focus while sparing normal tissue. NIH-funded researchers studying functional MRI (fMRI), magnetic resonance spectroscopy (MRS), and single photon emission computed tomography (SPECT), along with traditional MRI and PET have helped to make these technical improvements possible.

- In 1995, researchers identified the first gene linked to a type of idiopathic epilepsy (or epilepsy without a symptomatic cause such as injury, infection or brain malformation). The discovery of dozens of other genes associated with different types of epilepsy has followed, including many by NIH-supported scientists. Animal models of genetic and acquired forms of epilepsy are enabling researchers to better understand the mechanisms leading to the development of chronic seizures.

- Beyond seizures, cognitive and behavioral impairments and other comorbid conditions, as well as sudden unexpected death in epilepsy (SUDEP), are increasingly recognized within a broad spectrum of health impacts associated with epilepsy. NIH-funded research to understand SUDEP has identified biological links between epilepsy and cardiac dysfunction, suggesting potential risk factors and targets for intervention.

Tomorrow

- New and better treatments will enable more people with epilepsy to control their seizures with fewer undesirable side effects. NIH is working toward such
advances by supporting a targeted initiative focused on therapy development for intractable forms of epilepsy and for the prevention of epilepsy in those at risk.

- Researchers will identify more genes linked to epilepsy through studies like the Epilepsy Phenome/Genome Project (http://clinicaltrials.gov/ct2/show/NCT00552045), a multi-institutional effort to uncover the genetic basis of some of the most common epilepsies. Such genetic research will further advance the development of rational treatments based on disease mechanisms and may also help determine which people are most likely to benefit or suffer side effects from different treatments. For example, an NIH-funded clinical trial comparing drugs for childhood absence epilepsy includes a search for genetic markers associated with treatment responses (http://clinicaltrials.gov/ct2/show/NCT00088452).

- Implantable devices will be capable of recording electrical brain activity, predicting the onset of a seizure, and administering electrical current or antiepileptic medications that can stop the abnormal activity even before a seizure starts. An international team of NIH researchers are working closely with industry partners to develop pattern-recognition algorithms and safe, effective implantable devices.

- Preventive therapy will halt the development of epilepsy in those at risk of the disease, preventing epilepsy before the onset of chronic seizures. NIH funds a large portfolio of basic, translational, and clinical research on the processes by which epilepsy develops, including mechanisms associated with brain malformations, genetic defects, and precipitating insults like TBI, stroke, brain tumor, childhood febrile seizures, or infection. These studies are identifying changes in brain circuits and signaling pathways that may be targeted to prevent escalation into chronic epilepsy.

- Strategies will be available to treat and prevent comorbid conditions associated with epilepsy. Contrary to previous views, recent findings suggest such comorbidities may be present at or before the onset of epilepsy and may fail to improve with seizure control. NIH-funded researchers are working to understand what causes comorbidities, which could include shared mechanisms leading to both seizures and other conditions, neurobiological effects of recurrent seizures, treatment effects, and psychological responses to living with epilepsy.

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