Benchmarks for Epilepsy Research: A Guide for the General Public

Introduction

The 1990s' Decade of the Brain led to many advances in understanding how the brain works and what causes neurological disorders such as epilepsy. Epilepsy is a serious disorder. It consists of recurring seizures that affect awareness, sensation, or movement. More than 2.3 million Americans and 50 million people worldwide have epilepsy. While successful treatment enables many to live productive lives, large numbers of people continue to have seizures despite all efforts to control them. For them, epilepsy remains a devastating condition, affecting education, employment, and personal fulfillment. A 1995 study sponsored by the Epilepsy Foundation estimated the annual cost of epilepsy at nearly $12.5 billion, including indirect costs such as loss of employment.

In March 2000, leading scientists, health care providers, and leaders of voluntary health organizations came together to discuss what it would take to find a cure for epilepsy, defined as preventing epilepsy in people who we know are at a higher risk of developing it, and "no seizures, no side effects" in those who are already being treated for the disorder. This landmark White House initiated conference, "Curing Epilepsy: Focus on the Future," was sponsored by the National Institute of Neurological Disorders and Stroke in collaboration with the American Epilepsy Society, Citizens United for Research in Epilepsy, Epilepsy Foundation, and the National Association of Epilepsy Centers. The conference encouraged scientists nationwide to take a new look at methods of understanding and treating seizures. It resulted in an agenda for epilepsy research that will guide the community towards a cure. Key benchmarks to evaluate that progress include:

1) Understanding how epilepsy develops
2) Finding ways to prevent seizures from developing in at-risk individuals
3) Finding better ways to stop seizures without side effects in those who have epilepsy

This document is a summary of critical areas that need to be explored in the search for a cure. These ***Benchmarks for Epilepsy Research*** are just one part of epilepsy research efforts considered necessary to better understand and treat the disorder. They correspond directly to the more formal Benchmarks developed for the research community. Each research goal listed below is followed by a number of steps that scientists believe are needed to help them reach that goal.

Benchmarks for Epilepsy Research

I. Basic Disease Mechanisms

Understand the biological factors that might contribute to the development of epilepsy.

A. Discover what happens in the brain to create seizures, including changes in individual brain cells and the molecules they contain; identify other signs in the brain that predict who is at risk of developing epilepsy.

Background for A. *Epilepsy is a disorder produced by malfunctions in the chemical and electrical systems that control the normal activity of the brain. Understanding the precise chain of events that contribute to these disruptions will help scientists develop better treatments for epilepsy and ways to prevent the development of the disorder.*

A1. Specific Benchmark
For at least one form of epilepsy, develop a way of observing brain chemistry and function in real time (i.e., as a seizure is occurring), so that it is possible to identify areas likely to produce seizures.

A2. Specific Benchmark
Improve the technology that allows scientists to obtain detailed images of the brain by:

1) Creating a large collection of detailed MRI images of the brains of people with epilepsy. The collection would be designed so that it could be analyzed in many different ways and its images could be compared with images and information developed by researchers worldwide.

2) Use part of this collection of brain images, together with information from a variety of other tests that record how the brain works, to understand the link between brain structure and brain function.

A3. Specific Benchmark
Establish a network of scientists who will work together to compare the results of gene-chip studies from several animal models that are used to help understand how epilepsy develops. Gene chips are research tools that allow scientists to easily measure the activity of large numbers of genes at the same time.

B. Find more of the genes that make people likely to develop epilepsy.

Background for B. *In about 70 percent of all cases of epilepsy, the cause is unknown. It is likely that genes are involved in at least some of them. In fact, some genes that can lead to epilepsy have already been found. Identifying more of these genes should help scientists create new methods of treatment and prevention.*

B1. Specific Benchmark
Increase communication and cooperation among physicians, experts in human genetics, and families with epilepsy to make it easier to study genes involved in epilepsy.

B2. Specific Benchmark
Organize a national group of scientists to work together in search of genes that might contribute to epilepsy by doing a large screening project that links people with epilepsy to particular gene patterns. This process should begin with a conference of leading experts to agree on which types of epilepsy should be looked at first, how the screening project will take place, and what the end results should be.

C. Determine how closely the various animal models for epilepsy resemble human disease and use the appropriate models to discover and test new kinds of treatment.

Background for C. *In the search for new treatments for epilepsy, scientists usually must first conduct research on animals whose epilepsy closely resembles the disorder in humans. Several different models are needed to study the different types of epilepsy in people already affected as well as those at high risk for developing it.*

C1. Specific Benchmark
Develop a plan to determine how well existing animal models for epilepsy resemble what happens in human epilepsy and use the appropriate models to search for new treatments for human patients.

C2. Specific Benchmark
Describe and develop new animal models to study how seizures and epilepsy begin early in life and test therapies for types of epilepsy that currently cannot be successfully treated.

C3. Specific Benchmark
Discover and describe biological markers for epilepsy — changes in cells, tissues or organs that occur when epilepsy is developing or has developed in the brain. Use these markers in animal models to test substances with the potential to prevent epilepsy.

II. Prevention

Create new treatments for preventing epilepsy in people who are thought to be at high risk of developing the disorder.

Background. *Epilepsy has many causes. Sometimes it occurs as a result of developmental problems before birth. Other cases are caused by infection, tumors, stroke, or injury that damages the brain. Months, even years, can pass between the time of an injury and the development of epilepsy. With more knowledge of how epilepsy develops before birth or following injury, it may be possible to develop treatments that will stop the process and prevent epilepsy.*

A. Specific Benchmark
Using the methods developed in Benchmark IA1, identify an area of the brain where seizures may begin and that has the potential to respond to preventive treatment.

B. Specific Benchmark
Design clinical trials to test preventive therapies in people at highest risk for developing epilepsy. Begin planning now, so that trials can begin as soon as scientists identify potential interventions. Complete at least two major, multi-center trials.

III. Treatment

Create new medications or other treatments that will stop seizures in people with epilepsy without causing any side effects.

Background: *Current treatment for most people with epilepsy consists of long-term use of antiepileptic drugs. If drug therapy is not successful in controlling seizures, surgery, dietary changes, or use of an electronic implant may be tried. At least one million Americans of all ages continue to have seizures despite treatment or are affected by unpleasant side effects of current therapies.*

A. Specific Benchmark
Assess how well preventive treatments work in individual patients by looking for biological markers (i.e., changes in cells, tissues or organs that occur when epilepsy is developing or has developed in the brain) that become apparent as epilepsy develops and that can be monitored during drug treatment. Develop new treatments that are tailor-made for individuals based on their age (infants, children, adults), and on the presence of other factors that influence seizures, such as stress or hormonal cycles (in women).

B. Specific Benchmark
Develop genetic tests that will help physicians identify people who may respond to a specific treatment, people who might not respond, and risk factors that may cause treatment side effects.

C. Specific Benchmark
When certain natural processes in the human brain that prevent seizures don't function properly, seizures might develop. Identify and understand these processes, and use them to stop seizures or make them less severe.

D. Specific Benchmark
Cure a genetic type of epilepsy by developing a therapy based on understanding the effects of a flawed or damaged gene.

E. Specific Benchmark
Successfully use a device (e.g., a very small detector and/or drug pump that can be placed in the brain) that, in at least one type of epilepsy, will detect an oncoming seizure and apply treatment to stop the seizure before it begins.

F. Specific Benchmark
Expand the use of surgery for epilepsy, including trying it earlier in the course of treatment. Develop new surgical treatments for epilepsy and improve existing techniques.

G. Specific Benchmark
Significantly reduce seizures in at least one form of epilepsy by using a completely new type of treatment, such as cell transplantation or vaccination.

Conclusion

The 2000 Curing Epilepsy conference resulted in benchmarks for critical research areas that need to be explored in the search for a cure. However, they do not address all aspects of epilepsy. For example, the consequences of living with epilepsy, particularly the impact of seizures and epilepsy on a person's thinking, emotions, behavior, and daily life activities were not addressed directly. However, the groups involved recognize that seizures have physical and social consequences – brain damage and increased mortality, reduced marriage and fertility rates, and a lingering stigma that fuels discrimination and isolation. These are consequences that add immeasurably to the burden of epilepsy on individuals and families. It is hoped that efforts to better understand, prevent, and treat epilepsy will also lead to increased efforts and further research to address the real-life problems that people with epilepsy face.

The 2000 Curing Epilepsy conference was a landmark event for the epilepsy field because, for the first time, scientists, clinicians, and patients began to focus on curing epilepsy, rather than on just treating its symptoms. Out of the conference emerged the Benchmarks for Epilepsy Research that serve as milestones to measure progress towards a cure. All of those involved in this effort, including NINDS, epilepsy scientists, and the patient and advocacy communities, are committed to working together to achieve the Benchmarks and move closer to the ultimate goal of curing epilepsy.