



Proceed With Caution

When it comes to new treatments for neurologic disease, haste makes waste.

Neuroscience research is our hope for new treatments and cures for neurologic diseases, which is why the American Brain Foundation—formerly the American Academy of Neurology (AAN) Foundation—has raised more than \$16 million dollars for research into brain disease and is now intensifying its efforts.

The timeline for new drug development, however, can be painfully slow. While we all want better treatments faster, there is reason to proceed with caution.

Work often begins using test tubes or animal models in a laboratory. If promising results are seen, small studies begin in humans, first to test the safety of a new therapy by looking for any harm that it might cause. If that bar is passed, larger studies are done to help establish the correct dose, provide evidence that the therapy might be effective in treating the disease, and collect more information about possible negative side effects.

If those larger studies are successful, the most expensive and reliable study will be performed: the randomized controlled trial. Such a trial usually enrolls large numbers of people who are randomly assigned (as by flip of a coin) to receive the new therapy or a placebo (a treatment that looks just like the new therapy but has no active ingredients). All study subjects go through the same process, and no one involved in the study—researchers or study subjects—knows who is in the active therapy or placebo group. The results of this kind of study are considered the highest level of evidence.

While this research process takes time, it is necessary to make sure a new treatment really works as we think it does and to uncover side effects, which all drugs have. The decision to take a drug is based on the benefit of the drug outweighing the potential harm.

Medical journals and the lay press publish stories about promising new treatments at all stages of the drug development process. Many therapies have made it through that process and are in use today. The clot-busting medication tPA, for example, has proven very successful in restoring blood flow in blocked arteries, improving chances of re-

covery when given within 4.5 hours after a stroke.

But research on other drugs to further protect the brain from damage after stroke has not fared so well. Some of these drugs worked dramatically well in animal studies of stroke but not when given to human patients with stroke. Some even caused unexpected harm in humans not seen in animals.

An exciting new animal study of a drug to treat Alzheimer's disease (AD) was recently published in the *Journal of Neuroscience*. Researchers used a drug that had been stud-

ied to treat skin cancer. The drug, called epothilone D, was predicted to stabilize microtubules in the brain, which are vital to nerve cell function. After three months of treatment, mice that are prone to develop AD showed improved memory and less AD-related brain damage than mice that didn't get the treatment. Similar results, published in the journal *Science*, were found in mice with AD who were given the skin-cancer drug bexarotene (see page 16).

Several patients have asked me about prescribing epothilone D. I hope that as this research progresses, the results will be upheld and no serious harmful effects will be found. But I explain to my patients and their families that until we have the results of a randomized controlled trial—or at the very least, studies that have evaluated the safety and benefit of the drug in humans—it is simply not safe to prescribe this medication.

I urge all of you to stay informed about research into the neurologic diseases that affect you. And if your neurologist tells you that a new treatment is not ready for prime time, the highest level of evidence is probably not available—at least not yet.

Take good care,

Robin L. Brey, M.D.
Editor-in-Chief



While we all want better treatments faster, there is reason to proceed with caution.