EWAITING ROOM

THIS WAY IN

Making Newer Antiepileptic Drugs Available to Children

BY OLGA RUKOVETS

ost medications are tested in adults. Years later—after safety and effectiveness have been proven in adults—a medication may be tested in children. In the meantime, doctors who treat children have one of two options: Not prescribing newer and potentially more effective drugs to children, or prescribing these drugs "off label," which means differently than indicated by a regulatory agency such as the U.S. Food & Drug Administration (FDA). However, prescribing a drug off label can involve greater risk than prescribing it as indicated—and can cost more, because it might not be covered by insurance.

This is exactly what has happened with many of the newer antiepileptic drugs (AEDs), according to John M. Pellock, M.D., chairman of the Division of Child Neurology at the Medical College of Virginia at Virginia Commonwealth University in Richmond and a Fellow of the American Academy of Neurology (AAN). When prescribing a drug off label to children, Dr. Pellock tells their families the restrictions and risks involved. "I tell them that we'll have to fight with the insurance companies and monitor the children much more closely than we would if we had more information about the effect of the drug on chil-

dren," Dr. Pellock says. Still, parents are "desperate to have these medications for children," he says.

But can these newer AEDs be made available to children safely and efficiently?

REVIEWING THE DATA

In order to help answer these questions, Dr. Pellock and his colleagues examined the results of clinical trials of AEDs in adults to see if these results could predict treatment response in children.

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-JEFFREY BUCHHALTER, M.D., PH.D.



The authors reviewed 30 clinical trials for partial onset seizures, which start in one area of the brain (as opposed to generalized seizures, which begin in both sides of the brain at the same time). Six of the studies were in children ages 2 to 18, and 24 studies were in adults. The review included five trials for gabapentin (Neurontin), six for lamotrigine (Lamictal), 10 for levetiracetam (Keppra), two for oxcarbazepine (Trileptal), and seven for topiramate (Topamax).

The treatment response to the AEDs studied was similar for children (ages 2 to 18) and adults, the investigators found. Their review, funded by UCB Pharma, was published in *Neurology*, the official medical journal of the AAN, in 2012.

ONE STEP FORWARD

The review is a "major advance," Dr. Pellock says, since the drugs studied were shown to be as effective in children as they were in adults. But it should not be interpreted to mean that "we don't have to study drugs more in kids. We need to bring both international and national experts together—including academics, industry representatives, and regulatory authorities—to decide what other kinds of studies need to be done," he says.

Future studies will likely focus on two factors that make the treatment response of adults different from that of children: pharmacokinetics and pharmacodynamics. Pharmacokinetics is the process by which a drug is absorbed, metabolized, and eliminated by the body. It depends on the age and weight of the individual taking the drug. Pharmacodynamics refers to the biochemical and physiological effects of a drug on the body—in other words, what the drug does to the body.

"This review confirms our clinical impression that AEDs which work in adults have equal efficacy in children," says pediatric neurologist and epileptologist Jeffrey Buchhalter, M.D., Ph.D., director of the epilepsy program at Alberta Children's Hospital in Calgary, Alberta in Canada and a Fellow of the AAN, who was not involved with the study. However, the adverse effects of AEDs in children, particularly with regard to cognition, may be different from those in adults. For example, some AEDs have been associated with lower IQ in children. As a result, he says, it is important to study and compare these in the two groups.

More research on AEDs for pediatric epilepsy is critical, according to Raj D. Sheth, M.D., chief of neurology at Nemours and professor of neurology at Mayo Clinic College of Medicine in Jacksonville, FL. "The lack of information makes it difficult for neurologists, who have to prescribe off label; difficult for the insurance companies, who often restrict medications if they're not clearly FDA approved; and very difficult for pediatric patients, because they are denied use of medications that older people are able to take."

WHAT'S NEXT?

What Dr. Pellock and colleagues have done with their comprehensive review is hopefully removed one of the blocks—"we no longer need a double-blind placebo-controlled study for efficacy, and the ethical problem of doing those kinds of studies is removed, we hope," he says.

"If regulatory authorities—both in the United States (the FDA) and in Europe (the European Medicines Agency)—were to accept our approach of extrapolating the treatment response of adults to the treatment response of children, then we could move on to safety and pharmacologic studies," Dr. Pellock says. The goal would be to establish an FDA indication for the already approved drugs in children.

The speed at which new drugs could become available to children would then improve, as would the comfort level of the physician prescribers and insurance providers. In addition, Dr. Pellock says, caregivers would have the ability to read about the medications and their data specifically in children. Most importantly, he says, "kids could get the good medicines that they need."

WHAT CAN YOU DO?

If your child has epilepsy that is not controlled on typical medications, you should first seek out a center that treats pediatric epilepsy. Many times, Dr. Pellock notes, those centers will have a study looking at new AEDs in which your child can be enrolled and very carefully followed. "Enrolling in studies is one way to help change our policies surrounding pediatric prescription and study practices, among other things," he says.

NEUROLOGY NEWS

The American Brain **Foundation Wants You**

ne in 6 people — more than 50 million Americans — is affected by a brain disease, and that number is growing. Autism and epilepsy are affecting more young people than ever. Multiple sclerosis and migraine are disabling increasing numbers of people in the prime of life. And stroke, Alzheimer's disease, and Parkinson's disease are robbing people of their retirement dreams at an unprecedented rate.

New treatments are within reach, but research does not have enough funding. That's why the goal of the American Brain Foundation—the foundation of the American Academy of Neurology (AAN)—is to become the world's leader in raising money to cure brain disease.

"Research is poised to deliver new opportunities for treatments in all neurologic diseases," says John Mazziotta, M.D., Ph.D., Chair of the American Brain Foundation's Board of Trustees, and Fellow of the AAN. Take Alzheimer's disease: Approximately

5.4 million Americans have it, and millions more family members are affected. Even modest improvements in treatment would make an enormous difference in people's lives, according to Dr. Mazziotta. "Treatment that would delay the



onset of Alzheimer's disease by only five years would drop the number of people with the disease by 50 percent. A ten year delay would reduce the prevalence by 75 percent," he says.

Public outreach is a vital component in the Foundation's efforts. The Foundation's Public Leadership in Neurology Award has recognized remarkable people who have advanced public understanding and awareness of brain disease, including actors Michael J. Fox, Dame Judy Andrews, and Jerry Lewis; television and radio journalist Leeza Gibbons; pianist Leon Fleischer; astronaut Rich Clifford; football player Tedy Bruschi; former U.S. Attorney General Janet Reno; and Microsoft co-founder Paul G. Allen.

In addition, the Foundation holds an annual Brain Health Fair and Neuro Film Festival. The Brain Health Fair attracts thousands of people who seek more information on brain disease and want to connect with local neurologists and support groups. The Neuro Film Festival invites the public to submit, view, and vote on short videos that address the need to support research into the prevention, treatment, and cure of brain diseases.

In 2012, the American Academy of Neurology Foundation was rebranded the American Brain Foundation, reasserting its vision to cure brain disease. The AAN continues to be the Foundation's largest supporter, contributing more than \$1 million annually to support the quest for cures.

Please see page 9 of this issue to learn more about how you can make an impact, or visit CureBrainDisease.org.