



presents a Professional Roundtable

**Cognition Across the Lifespan:  
Antiepileptic Drugs, Epilepsy or Both?**

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Bruce Hermann, PhD

Kimford Meador, MD

William Gaillard, MD

Joyce Cramer

**JUST MY OPINION: THOUGHTS FROM  
EPILEPSY.COM EDITORIAL BOARD MEMBERS**



**The (Potential) Problems with Generics in Epilepsy**

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In the past year or so, new generic equivalents have been approved for lamotrigine, topiramate, oxcarbazepine, and levetiracetam. While this is good news in that cost consciousness is always an issue in medicine, and generic equivalents usually offer substantial savings, there is still concern that epilepsy is a condition where more caution should be exercised.

The American Food and Drug Administration sets strict standards for the approval of generic equivalents. Each must be compared to the approved brand-name drug in normal volunteers to ensure that two measures, Area Under the Curve (AUC, a measure of total drug absorbed) and Cmax (the peak concentration) are comparable. To do this, single doses of the proposed generic are tested against the brand name drug. The 95% confidence interval for each of these measures must fall between 80 and 125% of the branded drug. Usually, that translates into an average variability of 3-5%. For most conditions, this would be an insignificant amount. Think of a headache: if a 600 mg generic ibuprofen actually delivers only 570 mg, that probably doesn't translate into a major problem for the patient. At worst, the headache may last a bit longer, or another dose would be needed.

In epilepsy, there is a relatively narrow therapeutic window that must be maintained for extended periods of time. Too much, and the patient experiences toxicity. Too little, and a seizure may occur. So the consequences of a slight fall in delivered dose may be severe: a patient who was seizure free may have a sudden seizure, potentially resulting in injury, loss of driver's license, or even death. Under most circumstances we wouldn't expect a 5% change to cause this. However, there are other, at least theoretical reasons that that variability could be greater. First, generic equivalents are tested in normal

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DISCUSSION ON:**

**Cognition Across the Lifespan:  
Antiepileptic Drugs, Epilepsy, or  
Both?** with guests Dr. Bruce  
Hermann, Dr. Kimford Meador, and  
Dr. William Gaillard.



Webcast hosted by Joyce Cramer, President, Epilepsy Therapy Project.

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Upcoming epilepsy-related Hallway Conversations, conferences, symposia, and events include:

**August 5, 2009  
Hallway Conversations:  
Interview with Dr. Lawrence J.**

volunteers. Epilepsy patients may have greater differences in absorption or metabolism due to their condition or to concurrently administered drugs. Second, generic agents are not tested against each other (only to the brand). As there are multiple, sometimes dozens, of approved generic manufacturers for each epilepsy drug, this results in increased potential for variability; each time the patient returns to the pharmacy, a generic equivalent from a different manufacturer may be dispensed. The roughly 5% variability compared to the brand could then become a 10% swing from one generic to another. A handful of states (including Hawaii and North Carolina) have limited changes in generic manufacturers dispensed to a given epilepsy patient. Several others (Florida, Kentucky, Maine, Maryland, Minnesota, Missouri, and Rhode Island) limit substitution for drugs, however the practice of substitution is still the norm.

How often do problems occur? We really don't know. While most neurologists have anecdotes of a problem resulting from a generic switch – a sudden seizure in a previously controlled patient being most common – it is often difficult to prove it is due to the generic substitution. We all certainly see patients with unexplained seizures without a change in brand. There are a few cases where the time course and documented changes in levels make generic change the likely culprit but these are rare.

Generic equivalents in epilepsy are not unreasonable, however should be used more cautiously than in other conditions. How can we best protect our patients? First is with education: when a generic is available, alert the patient that a change in the appearance of the drug likely means generic substitution. Possible changes should be discussed with a patient, whether from brand to generic, generic to brand, or between different generics though the latter may be the most difficult to control. Get baseline levels on all anticonvulsant drugs when the patient is stable; this way if a problem arises it will be easier to know if a result of a brand change. And when generic equivalents are used, ask the patient to work with a pharmacist to stay with a single manufacturer. Some will be willing to do this, further reducing the potential for variability. Finally, when a suspected problem arises physicians should report to the F.D.A. MedWatch: [www.fda.gov/medwatch/](http://www.fda.gov/medwatch/). Going forward, this will help the FDA – and us – to better understand the scope of the problem.

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## **Epilepsy.com/Professionals Announcements from Joseph I. Sirven, MD, Editor-in-Chief**

Don't forget to peruse other *epilepsy.com* offerings during the month of August. We have 2 Hallway Conversations scheduled this month. August 5, 2009, Dr. Larry Hirsch from Columbia University joins us to discuss the latest in **ICU management of Status Epilepticus**. On August 13, Dr. Scott Mintzer from Jefferson Medical College sits down with us to discuss the **metabolic consequences of anti-seizure medications particularly on cholesterol**. Please search through our announcements, updates and other offerings. We hope that you find the content useful for you and your patients.

**Check out this month's featured online roundtable: Cognition Across the Lifespan: Antiepileptic Drugs, Epilepsy, or Both?** with guests Dr. Bruce Hermann, Dr. Kimford

**Hirsch**

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**August 13, 2009**

**Hallway Conversations:  
Interview with Dr. Scott Mintzer**

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Meador and Dr. William Gaillard, and hosted by Joyce Cramer, President, Epilepsy Therapy Project.



### REMINDER: New Grant Opportunities – Letters of Intent Due August 3

New grant opportunities are being made available through the Epilepsy Research Foundation's New Therapy Grants Program. These will be awarded to scientific and clinical investigators pursuing innovative projects that demonstrate a clear path to commercialization. To view the request for proposals and to apply, please visit [www.epilepsy.com/etp/grant\\_application](http://www.epilepsy.com/etp/grant_application).

**Please join us this month.**

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[epilepsy.com/Professionals](http://www.epilepsy.com/Professionals) is building a resource section of useful practice tools for the professional community. If you have a form, patient information sheet, or other useful handout for patients with epilepsy, and you'd like to share it with thousands of your colleagues by adding it to the **resource section of [epilepsy.com/professionals](http://www.epilepsy.com/professionals)**, please email it to [info@epilepsytherapyproject.org](mailto:info@epilepsytherapyproject.org) or fax it to (540) 687-8066, and we'll take it from there. Thanks!!

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**Epilepsy Therapy Project**, the sponsor of [epilepsy.com](http://www.epilepsy.com), is a non-profit organization whose mission is to advance new treatments for people living with epilepsy. ETP helps scientists develop new drugs and brain stimulators to treat epilepsy. The goal is to fast-track great ideas into treatments to reach people as fast as possible. Your donations go directly toward development of new treatments as well as maintain [epilepsy.com](http://www.epilepsy.com). Read more about the **Epilepsy Therapy Project**.

The Epilepsy Therapy Project is also the sponsor of [epilepsy.com](http://www.epilepsy.com) and [epilepsy.com/professionals](http://www.epilepsy.com/professionals). We are working to build [epilepsy.com/professionals](http://www.epilepsy.com/professionals) into the most comprehensive source of information, tools, and interchange available online for patients, practicing neurologists, and for the research and therapy development community.

To learn more about our programs, please visit us at: [www.epilepsy.com/epilepsy\\_therapy\\_project](http://www.epilepsy.com/epilepsy_therapy_project).

