

# What's New in the Patient Safety World

April 2016

## Can Antibiotics Lead to Delirium?

When confronted with patients having delirium our first approach is to look for and remove any precipitating or contributing factors. One such factor we tend to forget about is the use of antibiotics. Given the high prevalence of delirium in the ICU and post-operative settings, it would not be surprising to find antibiotic use frequent in such patients.

A recent review of antibiotic-associated encephalopathy ([Bhattacharyya 2016](#)) is very timely and identifies 3 unique clinical phenotypes: encephalopathy commonly accompanied by seizures or myoclonus arising within days after antibiotic administration (caused by cephalosporins and penicillin); encephalopathy characterized by psychosis arising within days of antibiotic administration (caused by quinolones, macrolides, and procaine penicillin); and encephalopathy accompanied by cerebellar signs and MRI abnormalities emerging weeks after initiation of antibiotics (caused by metronidazole). Those clinical features of each phenotype can and should lead to recognition of the pathogenetic role being played by the antibiotic and lead to its discontinuation.

The phenotype characterized by myoclonus and/or seizures (Type 1 AAE) is often due to penicillin or cephalosporins and often occurs in the setting of renal insufficiency. It usually appears within days of antibiotic administration. Seizures associated with cephalosporin-associated encephalopathy were frequently nonconvulsive. EEG may show generalized slowing but often shows periodic discharges with triphasic morphology or epileptiform discharges. MRI is normal in these cases. The encephalopathy usually resolves within days of discontinuation of the offending antibiotic.

Type 2 AAE also typically begins within days of antibiotic initiation and is characterized by frequent occurrence of psychosis and resolution within days of discontinuation of the offending antibiotic. Seizures are rare in this type and the EEG is more likely to be normal (or show nonspecific findings). MRI is usually normal. This phenotype may occur with procaine penicillin, sulfonamides, fluoroquinolones, and macrolides.

The third type (Type 3 AAE) occurs with metronidazole begins weeks after initiation and is characterized by frequent occurrence of cerebellar dysfunction. Seizures are rare and EEG usually shows only nonspecific abnormalities but the MRI is typically abnormal, showing a typical pattern of T2 hyperintensities in the dentate nuclei of the cerebellum with variable involvement of the brainstem, corpus callosum, or other regions.

The authors also note that isoniazid (INH) may cause an encephalopathy that does not fit nicely into one of the 3 above phenotypes. Onset is weeks to months after INH initiation. Psychosis is common but seizures are rare and EEG may just show nonspecific abnormalities.

The Bhattacharyya paper acknowledges the issue of strength of association with antibiotic use in each phenotype and also has a nice discussion on the possible pathophysiologies of each phenotype and the pharmacokinetic and patient-related factors that are important.

Overall this is an important contribution to the clinical management of the patient with delirium and a key reminder to evaluate all aspects of care.

**Some of our prior columns on delirium assessment and management:**

- October 21, 2008 “[Preventing Delirium](#)”
- October 14, 2008 “[Managing Delirium](#)”
- February 10, 2009 “[Sedation in the ICU: The Dexmedetomidine Study](#)”
- March 31, 2009 “[Screening Patients for Risk of Delirium](#)”
- June 23, 2009 “[More on Delirium in the ICU](#)”
- January 26, 2010 “[Preventing Postoperative Delirium](#)”
- August 31, 2010 “[Postoperative Delirium](#)”
- September 2011 “[Modified HELP Helps Outcomes in Elderly Undergoing Abdominal Surgery](#)”
- December 2010 “[The ABCDE Bundle](#)”
- February 28, 2012 “[AACN Practice Alert on Delirium in Critical Care](#)”
- April 3, 2012 “[New Risk for Postoperative Delirium: Obstructive Sleep Apnea](#)”
- August 7, 2012 “[Cognition, Post-Op Delirium, and Post-Op Outcomes](#)”
- September 2013 “[Disappointing Results in Delirium](#)”
- October 29, 2013 “[PAD: The Pain, Agitation, and Delirium Care Bundle](#)”
- February 2014 “[New Studies on Delirium](#)”
- March 25, 2014 “[Melatonin and Delirium](#)”
- May 2014 “[New Delirium Severity Score](#)”
- August 2014 “[A New Rapid Screen for Delirium in the Elderly](#)”
- August 2014 “[Delirium in Pediatrics](#)”
- November 2014 “[The 3D-CAM for Delirium](#)”
- December 2014 “[American Geriatrics Society Guideline on Postoperative Delirium in Older Adults](#)”
- June 16, 2015 “[Updates on Delirium](#)”
- October 2015 “[Predicting Delirium](#)”
- April 2016 “[Dexmedetomidine and Delirium](#)”

## References:

Bhattacharyya S, Darby RR, Raibagkar P, et al. Antibiotic-associated encephalopathy. *Neurology* 2016; published online before print February 17, 2016  
<http://www.neurology.org/content/early/2016/02/17/WNL.0000000000002455>

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