

Brief summaries of recent drug approvals, interactions, and adverse events

Predicting MRSA Risk

A negative nares screening may not be the best predictor of which patient is at risk for methicillinresistant Staphylococcus aureus infection (MRSA). But combining that screen with certain risk factors can help pinpoint with nearly 100% accuracy, say researchers from University Hospitals Case Medical Center, Case Western Reserve University, and Cleveland Veterans Affairs Medical Center (VAMC), all in Cleveland, Ohio. Their prediction rule, tested in patients at the Cleveland VAMC, could potentially reduce overuse of empirical vancomycin without missing any patients with MRSA infection, they say.

Over the 6-month study period, the researchers collected 3,495 clinical microbiology cultures from 1,246 patients who had concomitant nares screening. Of those patients, 199 (16%) had a positive nares screen result; 25 (2%) had MRSA infection. Only 13 patients with MRSA infection had a positive nares screen.

The remaining 12 patients who had negative nares screens and MRSA infection were compared with 15 patients without MRSA infection. The researchers developed a prediction rule, narrowing to 8 clinical risk factors: homelessness, long-term care facility residence, incarceration, immunosuppressive medications, skin or soft tissue infection, spinal cord injury, previous MRSA colonization or infection, and both end-stage renal disease and diabetes. That rule was able to predict 24 of 25 patients with MRSA infection (sensitivity 96%). Skin and soft tissue infections were

the only factors significantly associated with MRSA infection in patients with negative nares results: 8 of 12 infected patients had it, compared with 1 of 15 control patients.

Only 43 (10%) of 451 patients treated with empiric vancomycin had MRSA infection. Using the prediction rule could help reduce the use of anti-MRSA drugs by as much as 29% at their institution, the researchers say. However, they add that their study patients were mostly elderly men from a single hospital, and the results may not be generalizable to other patient populations.

Source: Jinno S, Chang S, Donskey CJ. *Am J Infect Control*. 2012;40(9):782-786. doi: 10.1016/j.ajic.2011.10.010.

Are Mood Stabilizers Safe for Pregnant Women?

Treating bipolar disorder in a woman of childbearing age requires particularly delicate decision making: Mood-stabilizing drugs have been associated with adverse outcomes in pregnancy. But the risk may not lie with the drugs alone, according to researchers, from Karolinska Institutet and Uppsala University, both in Uppsala Sweden, who conducted a population-based study analyzing data on 332,137 women who gave birth between 2005 and 2009.

Antipsychotics taken during pregnancy have been associated with congenital malformations, preterm birth, and abnormal fetal growth, the researchers say, as well as with a higher risk of gestational diabetes. Similarly, lithium, valproate, and carbamazepine have been linked to congenital malformations, although the data are conflicting for

lithium, which is sometimes suggested as a first-line treatment of choice for pregnant women with bipolar disorder.

The researchers, who had previously studied antipsychotics and pregnancy, decided to pursue the influences—or confluences—of the illness, drugs, lifestyle, and comorbidity. They grouped women with at least 2 recorded bipolar diagnoses as treated (n = 320) or untreated (n = 554). Those women were compared with all other women giving birth (331,263). Of the treated mothers, roughly equal numbers had used lamotrigine, lithium, or antipsychotic drugs during pregnancy. The researchers also looked at potentially confounding factors, such as smoking, body mass index, and alcohol and substance misuse.

Bipolar disorder on its own has been linked to slightly increased risks of pregnancy complications, preterm birth, and giving birth to small-for-gestational-age infants, the researchers note, although those studies did not consider lifestyle and other drugs the women might have been taking. In this study, women had a higher risk of adverse pregnancy outcomes simply by virtue of having bipolar disorder, whether they were taking mood stabilizers or not.

Of the treated women, 3.4% had an infant with a congenital malformation, compared with 1.9% of the untreated women and 2.0% of women without bipolar disorder. Both untreated and treated women had higher risks of cesarean delivery, instrumental delivery, a nonspontaneous start to delivery, and preterm delivery, although the risk of preterm delivery was higher in

treated women.

Untreated women had a higher risk of having infants with microcephaly (part of a general fetal growth restriction, the researchers believe) and neonatal hypoglycemia. One possible explanation, the researchers say, is that untreated bipolar disorder could lead to higher psychosocial stress and higher serum cortisol levels, which have been connected to low birth weight and short birth length. Lifestyle could also be a powerful contributor, as both treated and untreated women more often were overweight, smoked, and misused alcohol and drugs, compared with women without bipolar disorder. The researchers add that infants who are small for gestational age are known to be at risk for neonatal hypoglycemia.

Treated women were more likely to have infants large for gestational age, although the risk estimates were "imprecise." The researchers suggest that the treatment drugs may have masked the growth restriction associated with the illness and with related lifestyle factors by enhancing fetal growth. Atypical antipsychotics have been associated with having large-for-gestationalage babies, and valproate has been linked to weight gain in adults.

Source: Bodén R, Lundgren M, Brandt L, Reutfors J, Andersen M, Kieler H. *BMJ*. 2012;345:e7085. doi: 10.1136/bmj.e7085.

Lung Disease? Watch for Treatable Heart Disease, Too

Coronary artery disease (CAD) is a common but life-threatening companion to chronic obstructive pulmonary disease (COPD) and interstitial lung disease. It's treatable—but it may not be obvious. Diagnosis is difficult because its symptoms may be masked or mimicked by those of lung disease, say

researchers from the University of Maryland in Baltimore, Maryland; the University of Iowa in Iowa City, Iowa; and Johns Hopkins University in Baltimore, Maryland. One result is that many patients with advanced lung disease aren't getting the benefits of guideline-recommended therapies for prevention of cardiovascular disease. The omission, the researchers say, could represent a "frequently overlooked opportunity to offer medical treatments with potential to improve survival"

In their study of 473 patients with advanced lung disease, 60% had angiographically proven CAD; 16% had severe CAD. More than half of the patients had occult CAD.

Medical regimens included a statin in 78% of cases, antiplatelet therapy in 62% of the cases, angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) in 42% of the cases, and a beta-blocker in 37% of the cases.

Overall, the researchers found. use of cardiovascular medications with clinically apparent or proven CAD was low-rates were only moderately higher than those of the cohort as a whole. Only half the patients with clinically apparent CAD were on 2 or fewer cardioprotective drugs, and 10% were not receiving any. Most were on antihypertensive medicines. In patients with severe occult CAD, the researchers say, cardioprotective drugs were "severely underutilized," with 88% of patients taking 2 or fewer and 31% of patients taking none.

The low rates of beta-blocker use is probably due to a misperception that beta-blockers aren't safe in patients with COPD, the researchers say. However, they note that data show that cardioselective beta-blockers are well tolerated

in COPD and are associated with lower rates of exacerbations, as well as mortality. They point, as well, to guidelines that specifically advise not withholding beta-blockers from these patients.

The low rates of statin use in COPD patients may reflect physicians' avoidance of the drugs because those patients typically have higher high-density lipoprotein cholesterol levels. The higher levels may affect physicians' assessment of cardiac event risk, the researchers suggest. However, the physicians say the underuse of statins is also conceivably due to the general underdiagnosis of CAD in these patients.

As a caveat, the researchers note that at the time of the study, the 2006 guidelines recommended 4 classes of medication: statins, betablockers. ACE inhibitors or ARBs. and aspirin or clopidogrel. The updated 2011 guidelines give class I indications (recommended) to antiplatelet agents as well as statins, and class II indications (evidence in favor of usefulness/efficacy) for both ACE-inhibitor and beta-blocker therapy in uncomplicated CAD. Reevaluation of their data based on the current guidelines with attention only to the class I indications, they say, "continues to demonstrate room for improvement in cardiovascular care."

Source: Reed RM, Eberlein M, Girgis RE, et al. *Am J Med*. 2012;125(12):1228.e13-1228.e22. doi: 10.1016/j.amjmed.2012.05.018.

