Pharmacology Watch

Evidence-based updates in clinical pharmacology

By William T. Elliott, MD, FACP

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New Research Supports Safety of Receiving Vital Vaccination During Pregnancy

Combined tetanus, diphtheria, and acellular pertussis (Tdap) vaccinations are safe during pregnancy, according to a new study. The CDC recommends Tdap vaccinations during each pregnancy, preferably during the third trimester when antibodies can be passed to the fetus, providing protection against pertussis during the first months of life. In 2014, Brazil began a prenatal Tdap vaccination program, which overlapped with the Zika outbreak. The subsequent increase in cases of infant microcephaly raised concerns that Tdap may be contributing to birth defects. Authors of this new study examined associations between maternal Tdap vaccinations and structural birth defects, including microcephaly in offspring. Researchers reviewed vaccination records of nearly 325,000 singleton births from six states from 2007 to 2013. About 13% of babies were exposed to Tdap. These infants were no more likely to develop structural birth defects, including microcephaly, than offspring of unvaccinated mothers. The findings were the same regardless of when the mother was vaccinated during pregnancy (*JAMA* 2016;316;1823-1825. DOI:10.1001/jama.2016.14432).

CDC Calls for Two-shot HPV Regimen

Good news for young adults: The CDC recommends only two doses of the human papillomavirus (HPV) vaccine instead of the previously recommended three-shot regimen. Recent studies have shown if the first shot is administered before age 15, two shots confer immunity. If the series begins after age 15, the CDC still recommends three shots over a six-month period. For the two-shot regimen, the second shot should be administered six to 12 months after the first dose. The HPV vaccine prevents cervical, vaginal, anal, and head and neck cancers, as well as precancerous lesions and genital warts.

Growing Evidence of Link Between Cognitive Dysfunction, Androgen Deprivation Therapy

Is there a link between androgen deprivation therapy (ADT) for prostate cancer and dementia? That is what a cohort study of men treated with ADT sought to determine. Researchers reviewed the records of nearly 9,300 men with prostate cancer, of whom about 20% received ADT. After a mean follow-up of 3.4 years, there was a statistically significant association between use of ADT and risk of dementia (hazard ratio, 2.17; 95% confidence interval, 1.58-2.99; $P < 0.001$). The absolute risk of dementia was 7.9% for those who received ADT vs. 3.5% for those who did not. Men treated for at least 12 months demonstrated the greatest absolute risk of dementia. The authors suggested ADT in the treatment of prostate cancer may be associated with an increased risk of dementia. This finding should be further evaluated in prospective studies (*JAMA Oncol*. Published online Oct. 13, 2016. DOI:10.1001/jamaoncol.2016.3662). This study confirms a growing body of evidence that ADT is associated with cognitive dysfunction, including Alzheimer's disease.

Study: No Connection Between Cranberry Products, Fewer Urinary Tract Infections

Cranberry products do not prevent urinary tract infections (UTI) in older women, according to new research. In a randomized clinical trial of 185 older female nursing home residents, subjects were randomized to two oral cranberry capsules daily, each containing 72 mg of proanthocyanidin (equivalent to 20 ounces of cranberry juice) or matching placebo. The women were assessed for bacteriuria plus pyuria every two months over the 12-month study period. Symptomatic UTI also was assessed as well as all-cause death, hospitalization, presence of multidrug antibiotic-resistant organisms, and antibiotic administration. Adherence was 80%, and 147 women completed the study. There was no difference in the rate of bacteruria or pyuria between the treatment and control groups. There also was no significant difference in the number of symptomatic UTIs, rate of death, hospitalization, multidrug-resistant bacteria, antibiotics administered for suspected UTIs, or total antibiotics used. The authors concluded that among older women who are nursing home residents, administration of cranberry capsules vs. placebo was of no benefit in preventing bacteriuria plus pyuria over one year (*JAMA*. Published online Oct. 27, 2016. DOI:10.1001/jama.2016.16141).

FDA Actions

The FDA has added a warning to the labeling for testosterone products regarding abuse and dependence. Abuse is a problem particularly for adults and adolescents, including athletes and body builders. Abuse of testosterone, usually at higher doses than those prescribed for androgen deficiency and often in association with other androgenic steroids, affects the heart, brain, liver, mental health, and endocrine system. Serious outcomes included myocardial infarction, heart failure, stroke, depression, hostility, liver injury, and male infertility. Those on high doses of testosterone also experienced withdrawal symptoms when high doses were discontinued. The FDA suggests checking serum testosterone levels if a clinician suspects abuse.

The FDA has approved the first immunotherapy for first-line therapy in non-small cell lung cancer (NSCLC). Pembrolizumab is a checkpoint inhibitor, a class of cancer drugs that overcome cancer cells' ability to fend off attack by T cells. The drug is approved for treatment of tumors that express high PD-L1 levels as determined by an FDA-approved test. The approval also expands the indication in second-line treatment of lung cancer to include all patients with PD-L1-expressing NSCLC. The approval was based on the results of two randomized, controlled trials that showed statistically significant improvements in progression-free survival and overall survival for patients randomized to pembrolizumab compared with chemotherapy. Pembrolizumab is marketed by Merck as Keytruda. It is significant that Merck tested pembrolizumab in patients with tumors expressing high PD-L1 levels. The drug's main competition, Bristol-Myers Squibb's checkpoint inhibitor nivolumab (Opdivo) was the subject of headlines in August when a highly anticipated trial of the drug in lung cancer failed to show benefit, although the study was conducted with patients presenting with all lung cancers, regardless of PD-1 levels.

The FDA has approved the first new drug for treatment of soft tissue sarcoma in more than 40 years with the accelerated approval of olaratumab, a platelet-derived growth factor receptor alpha-blocking antibody. The drug is approved in combination with doxorubicin to treat adults with certain types of soft tissue sarcomas who cannot be cured with radiation or surgery. Approval was based on a randomized, clinical trial of 133 patients presenting with different subtypes of metastatic sarcoma, which show a 12-month improvement in overall survival with the combination compared to doxorubicin alone. Olaratumab received fast-track designation as well as breakthrough therapy designation and priority review status. It also received orphan drug designation, which gives financial incentives for the development of drugs for rare conditions. Olaratumab is marketed as Lartruvo.

The FDA has approved the first insulin delivery system that monitors blood glucose and provides appropriate basal insulin doses for type 1 diabetics ≥ 14 years of age. Medtronic's new MiniMed 670G hybrid closed looped system is the first of the so-called "artificial pancreas" devices. Manufacturers tested the MiniMed on 123 patients with type 1 diabetes over a three-month period. No serious adverse events, diabetic ketoacidosis, or severe hypoglycemia (low glucose levels) were reported during the study. The device is not approved for children or those who require < 8 units of insulin per day. ■

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Author: **William T. Elliott, MD, FACP,** Medical Director, Pharmacy, Northern California Kaiser Permanente Assistant Clinical Professor of Medicine, University of California, San Francisco

Executive Editor: Leslie Coplin

Assistant Editor: Jonathan Springston

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Customer Service: (800) 688-2421

Email Address: Jonathan.Springston@AHCMedia.com

Website: AHCMedia.com

Address Correspondence to: AHC Media, One Atlanta Plaza, 950 East Paces Ferry Road NE, Suite 2850, Atlanta, GA 30326.