Pharmacology Watch

Evidence-based updates in clinical pharmacology

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Analysis Shows U.S. Drug Spending Far Exceeds All Other Nations

Drug costs have been increasing more rapidly than inflation for years. Several recent high-profile cases, including the dramatic price increases in pyrimethamine and EpiPen, as well as the introduction of several new high-cost drugs, have increased scrutiny on the genesis of exploding drug costs. A new article in *JAMA* analyzes such price increases. The authors found that per capita, prescription drug spending in the United States exceeds that of all other countries, driven largely by brand-name drug prices. Although the pharmaceutical companies claim that research and development drives high costs, the most important factor is the ability for manufacturers to set high prices based on market exclusivity protected by monopoly rights awarded by the FDA and patents. Generic drug availability after patents expire is the primary counter to high drug prices, but access to generics may be delayed for years by numerous business and legal strategies. Government policies also undermine the ability of institutions to contract for better prices. The authors concluded that there is "no evidence of an association between research and development costs and prices; rather, prescription drugs are priced in the United States primarily on the basis of what the market will bear." The authors suggested creating better policies on extending patents, enhancing timely generic availability, improving opportunities for price negotiations by government payers, mining better cost effectiveness data, and providing better education for prescribers, patients, payers, and policymakers. (*JAMA* 2016;316:858-871)

Report: Certain Cholesterol-lowering Drugs Too Expensive

The PCSK9 inhibitors used to lower LDL cholesterol are far too expensive and are not cost effective, according to a new analysis. Using an annual cost of just over $14,000 per year (based on mean wholesale acquisition costs of evolocumab and alirocumab in 2015), the drugs were found to cost more than $500,000 per quality-adjusted life-year (QALY) for patients with familial hypercholesterolemia compared to standard care (statin + ezetimibe). For patients suffering from atherosclerotic cardiovascular disease, the cost was $414,000 per QALY. If PCSK9 inhibitors were used in all eligible U.S. patients, they would reduce cardiovascular care costs by $29 billion while increasing drug costs by $592 billion. The authors estimated that the manufacturers of these drugs would need to reduce the annual cost by nearly $10,000 per year, from $14,000 to about $4,500, to make them cost effective. (*JAMA* 2016;316:743-753)

Connecting Calcium Supplementation to Dementia in Elderly Women

Calcium supplementation for postmenopausal women has fallen out of favor in recent years in the wake of reports of increased risk for vascular events. A new study raises fresh concerns about calcium supplementation and dementia in women suffering from cerebrovascular disease. Swedish and British researchers examined a cohort of women in Gothenburg, Sweden, including 700 dementia-free women

70-92 years of age. About 100 women were treated with calcium supplements. Of those, calcium supplementation was associated with the development of dementia in women with a history of stroke (odds ratio [OR], 6.77; 95% confidence interval [CI], 1.36-33.75; *P* = 0.020) or presence of white matter lesions on CT scan (OR, 2.99; 95% CI, 1.28-6.96; *P* = 0.011), but not in groups without these conditions. The authors acknowledged that this is a small observational study, but their data suggest that calcium supplementation may increase the risk of developing dementia in elderly women with cerebrovascular disease. (Published online Aug. 17, 2016. doi: http://dx.doi.org/10.1212/WNL.0000000000003111 *Neurology* 10.1212/WNL.000000000000311)

Two Flu Vaccines Show Comparable Efficacy

Does the nasal flu vaccine work after all? The CDC has recommended against using the live attenuated influenza vaccine (LAIV) this year due to low efficacy rates. Previously, LAIV was considered superior to the inactivated influenza vaccine (IIV). The Canadian Institutes of Health Research studied children in Hutterite colonies in northern Canada, where members live in close-knit, small, rural communities in which influenza virus infection regularly occurs. The goal was to compare LAIV to IIV to assess real-world protection of the two vaccines against flu from October 2012 to May 2015 during the course of three flu seasons. The primary outcome was laboratory-confirmed influenza A or B. The rate of influenza was the same in both groups (5.3% LAIV group vs. 5.2% IIV group) (hazard ratio, 1.03; 95% confidence interval, 0.85-1.24). (*Ann Intern Med*. Published online Aug. 16, 2016. doi: 10.7326/M16-0513) While this study was designed to establish if LAIV was superior to IIV, it showed that the vaccines were of equal efficacy, at least in preventing influenza.

FDA Actions

The FDA has strengthened its warning regarding the combination of opioids and benzodiazepines. The FDA has conducted and reviewed studies showing serious side effects with the combination, which can cause extreme sleepiness, respiratory depression, coma, and death. The warning includes all opioids to treat pain and opioid-based cough medication, along with benzodiazepines and other central nervous system depressants. A boxed warning, the FDA's strongest warning, will be added to the labels of prescription opioid pain and prescription opioid cough medicines, as well as benzodiazepines. The agency recommends that healthcare professionals limit opioid pain medicines with benzodiazepines or other central nervous system depressants to patients for whom alternative treatment options are inadequate. (http://bit.ly/2bVW0NU)

The FDA has approved the first biosimilar to etanercept for multiple inflammatory diseases. Based on the FDA's new naming convention for biosimilars, the drug is called etanercept-szzs. The drug is approved for the same indications as the reference drug, including rheumatoid arthritis, severe polyarticular juvenile arthritis, psoriatic arthritis (including use in combination with methotrexate), active ankylosing spondylitis, and chronic to severe plaque psoriasis. Approval was based on evidence that included structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamics data, clinical immunogenicity data, and other clinical safety and effectiveness data that demonstrate etanercept-szzs is biosimilar to etanercept. Although considered biosimilar, it is not an interchangeable product. Etanercept-szzs carries the same boxed warning as etanercept, including risk of serious infections such as tuberculosis, invasive fungal infections, and others. The warning also notes that lymphoma and other malignancies have been reported in children and adolescents treated with tumor necrosis factors blockers, including etanercept. Etanercept-szzs will be marketed as Erelzi. The drug represents the third biosimilar approved in the United States after infliximab-dyyb and filgrastim-sndz.

The FDA has banned 19 specific active ingredients of over-the-counter antiseptic wash products because manufacturers "did not demonstrate that the ingredients are both safe for long-term daily use and more effective than plain soap and water in preventing illness and the spread of certain infections." The ban included triclosan, mostly used in liquid soaps, and triclocarban, mostly used in bar soaps, including popular brands. The FDA first proposed the rule in 2013, and many companies began removing triclosan, triclocarban, and other listed agents at that time. There has been concern that these agents are no more effective than washing with plain soap and water and potentially led to negative outcomes, including affecting hormones in unborn children and infants and potentially promoting drug-resistant bacteria. The ruling did not affect hand sanitizers and wipes, although the agency is studying the active ingredients ethanol, ethyl alcohol, isopropyl alcohol, and benzalkonium chloride. (http://bit.ly/2cvEP93) ■

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