مركز معلومات الدوية والسموم
Drug & Poison Information Center

# Drug & Poison Information Center BULLETIN

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**Older adults with arthritis need just 45 minutes of activity per week**

Federal guidelines suggest achieving 150 minutes of moderate activity per week to prevent premature death and serious illness, however only one in 10 older American adults with arthritis in their knees meet these guidelines. Approximately one third of participants improved or had high function after two years. But those participants who achieved this minimum of 45 minutes of moderate activity, such as brisk walking, per week were 80 percent more likely to improve or sustain high future function over two years compared with those doing less. This finding was true for both men and women. ***Source: Arthritis Care & Research,*** **2016; DOI: 10.1002/acr.23181**

**In this issue .. ..**





# Medical News

## A result from observational study states Heartburn Medication Linked to Increased risk of Stroke

Proton pump inhibitors (PPIs) used widely to reduce stomach acid and treat heartburn have been linked to an increased risk for ischemic stroke in a new study. A nationwide observational study, presented at the recent American Heart Association (AHA) 2016 Scientific Sessions, showed a dose-related increased risk for ischemic stroke with all four PPIs investigated, but no increased risk with histamine-2 ($H_2$) blockers, which are used for similar indications.

The reports of the preclinical studies have shown PPIs reduce the production of nitric oxide leading to endothelial dysfunction, and several observational clinical studies have linked their use to cardiovascular disease. This is the first study to look at the effect of PPI drugs on ischemic stroke. The results of the study should be regarded as preliminary as they come from an observational study which has not yet been published.

However, the study recommend that people should not take these drugs unless there is a clear indication for them. Many people are taking them unnecessarily or they are continuing to take them long-term when they don't need to. I would urge doctors to review their patients on PPIs and look at why they are taking these drugs and consider whether they really need them or if they could take a lower dose. Although PPIs are available over the counter in many countries and many patients take them off label, which "is a concern." For the current study, the researchers used nationwide Danish registries to identify all individuals older than age 30 years who had elective gastroscopy between 1997 and 2012. Patients with prior cardiovascular disease at baseline were excluded. This database was linked to the Danish registry for medicinal products to identify patients taking various medications, including PPIs and $H_2$ blockers.

Association between PPI exposure and risk of first-time ischemic stroke was analyzed in a time-dependent multivariable-adjusted Poisson regression model. A total of 244,679 individuals were included in the study (mean age, 57 years). Approximately 44% had filed a prescription for a PPI. During follow-up, there were 9489 (3.9%) events of first-time stroke. Results showed that the crude stroke incidence rates per 10,000 person-years were 88.9 for PPI use vs 55.7 for no PPI use. After adjustment for age, sex, atrial fibrillation, hypertension, diabetes, heart failure, peptic ulcer, cancer, chronic kidney disease, and use of nonsteroidal anti-inflammatory drugs, current use of a PPI was associated with a 20% increased risk for stroke, with an incidence rate ratio (IRR) of 1.19 (95% confidence interval [CI], 1.14 - 1.24; $P < .0001$). $H_2$ receptor antagonists showed no association with stroke risk, with an IRR of 1.05 (95% CI, 0.88 - 1.23; $P = .60$). On further investigation, a clear dose-response relationship between PPI use and risk for stroke was seen for all 4 PPIs. At the highest dose for these 4 PPIs, stroke risk increased from 33% for lansoprazole to 79% for pantoprazole.

In this nationwide cohort of patients undergoing gastroscopy, we found an association between use of PPIs and increased risk of first-time ischemic stroke and a positive dose-response relationship between PPI dose and stroke risk. Considering the wide use of proton pump inhibitors worldwide, our study further questions the cardiovascular safety of these drugs and further studies are warranted.

*Source: Circulation. 2016;134:A18462*

## *Common Vaccine Misconceptions and Fears*

Considerable discussion about the effectiveness and safety of vaccines has led to debate about the usefulness of vaccination in general, and especially in defined populations.

Myth 1: Vaccination Is No Longer Necessary

The belief that vaccination is no longer necessary stems from the misunderstanding that most of the illnesses for which we are vaccinated have disappeared. It is true that diseases that used to be common in the past some of which, such as diphtheria and poliomyelitis, have been associated with considerable morbidity have become rare in developed countries, to the point that people and perhaps even some healthcare professionals believe that these diseases have now disappeared. This, however, is not true. In fact, the only infectious disease that has officially been eradicated globally is smallpox, with the last naturally occurring case in 1977 in Somalia. Of course, vaccines have achieved substantial reductions in the incidence of several infectious diseases, including tetanus, diphtheria, pertussis (whooping cough), congenital rubella, measles, mumps, and poliomyelitis. The case of measles demonstrates the importance of mass vaccination for the prevention of severe diseases. Measles is a highly contagious viral illness with potentially severe complications. It was very common in the United States before vaccination was introduced in 1963, with an estimated 4 million cases and 450 deaths related to measles annually. In 2000, endemic measles was declared eradicated from the United States, but cases have still been imported from other countries. In 2015, a total of 159 cases of measles were reported in the United States. The vast majority of these patients had not received the vaccine (45%) or had an unknown vaccination status (38%).

Myth 2: Vaccines Cause Autism; an association between measles, mumps, and rubella (MMR) vaccination and autism, based on eight cases, prompting significant concern about the safety of vaccines. However, after extensive investigation, several important issues related to this research were identified, including severe methodological inconsistencies and conflicts of interest. This controversy resulted in a partial retraction of the article by the Lancet in 2004, followed by a full retraction in 2010.The main author of the study also had his license to practice medicine in England revoked by the General Medical Council owing to serious professional misconduct.

A 2011 meta-analysis evaluated the data collected from five cohort studies (involving 1,256,407 children) and five case/control studies (involving 9920 children) on the association between vaccines and the development of autism or autism spectrum disorders. No association was found between the MMR vaccine and autism (odds ratio [OR], 0.84; 95% confidence interval [CI], 0.70-1.01). In addition, two vaccine components (thimerosal and mercury) that have also been accused of causing autism have been further studied. No association was found between thimerosal (OR,1.00; 95% CI, 0.77-1.31) or mercury (OR,1.00; 95% CI, 0.93-1.07) and autism. Although the association between MMR vaccination and autism has been disproven, it should be emphasized that the considerable burden of morbidity and mortality of potentially preventable infectious diseases is certain, including deaths due to diphtheria in developed countries; for example, the death of a 6-year-old boy in Spain in 2015 and a 3-year-old girl in Belgium in 2016, both of whom had not been vaccinated.

*Myth 3: Vaccines Cause Autoimmune Disease*

The role of vaccination in the pathogenesis of autoimmune diseases has long been a matter of debate. Although the cause of these diseases is still unclear, several factors, including genetic predisposition, environmental factors, and infectious diseases, may play a role. The relationship between vaccines and autoimmunity is still under study; however, no definitive evidence supporting a causative association exists to date. Most of the data linking vaccines with autoimmunity comes from case studies, which are considered to offer a low level of evidence. So far, no large epidemiologic studies have been conducted to provide us with relevant compelling clinical evidence. Given the nature and heterogeneity of autoimmune disorders, such studies are very difficult to be performed. Studies have examined the incidence of autoimmune diseases in vaccinated vs unvaccinated groups. None have shown that vaccines cause an increase in any autoimmune disease. Our opinion is that this theoretical risk should not prevent us from supporting vaccinations, in view of their undeniable benefits.

*Myth 4: Influenza Is a Harmless Illness, so Vaccination Is Unnecessary*

Although influenza is commonly considered to be a mild illness, this is certainly not always the case. Influenza is a large threat to public health, with three pandemics and millions of deaths from influenza in the 20th century. During the last pandemic period of the H1N1 virus, 18,449 deaths were attributed to influenza, although the global death rate was certainly higher.

*Myth 5: Vaccines Should Not Be Administered to Pregnant Women*

Most vaccines are not only safe during pregnancy, but they are recommended. Two vaccines are especially important for pregnant women: Tdap (tetanus, diphtheria, acellular pertussis) vaccine (preferably given between 27 and 36 weeks of pregnancy) and influenza vaccine. Tetanus, pertussis, and influenza are diseases with potentially severe consequences for the child and/or the mother that can be prevented through vaccination. The vaccination of a pregnant woman against pertussis offers substantial protection of the newborn against this infection. The safety of influenza vaccination has been evaluated in various studies. In a meta-analysis, no association was found between influenza vaccination and congenital malformations, in any trimester (OR, 0.96; 95% CI, 0.86-1.07). Hepatitis B, pneumococcal polysaccharide, and meningococcal polysaccharide vaccines have also been evaluated and were found to be safe for administration during pregnancy.

Live-virus vaccines, such as the vaccine against varicella-zoster virus and MMR, are not recommended 1 month before or during pregnancy, owing to the potential risk for transmission of the virus to the fetus. Although retrospective studies of women who received live-virus vaccinations while pregnant did not demonstrate higher risk for congenital infection, the administration of live-virus vaccines continues to be contraindicated in pregnancy.

***Source: http://www.medscape.com/viewarticle/873530#vp_2***

# Omega-3 supplements can prevent childhood asthma

Taking certain omega-3 fatty acid supplements during pregnancy can reduce the risk of childhood asthma by almost one third, according to a new study from the Copenhagen Prospective Studies on Asthma in Childhood (COPSAC) and the University of Waterloo.

The study, published in the *New England Journal of Medicine*, found that women who were prescribed 2.4 grams of long-chain omega-3 supplements during the third trimester of pregnancy reduced their children's risk of asthma by 31 per cent. Long-chain omega-3 fatty acids, which include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are found in cold water fish, and key to regulating human immune response. There was a link between the anti-inflammatory properties of long-chain omega-3 fats, the low intakes of omega-3 in Western diets and the rising rates of childhood asthma," said Professor Hans Bisgaard of COPSAC at the Copenhagen University Hospital. "This study proves that they are definitively and significantly related.

The study used rapid analytical techniques developed and performed at the University of Waterloo to measure levels of EPA and DHA in pregnant women's blood. The University of Waterloo is one of a few laboratories in the world equipped to run such tests. Measuring the levels of omega-3 fatty acids in blood provides an accurate and precise assessment of nutrient status," The testing also revealed that women with low blood levels of EPA and DHA at the beginning of the study benefitted the most from the supplements. For these women, it reduced their children's relative risk of developing asthma by 54 per cent.

A total of 695 children were included in the trial, and 95.5% completed the 3-year, double-blind follow-up period. The risk of persistent wheeze or asthma in the treatment group was 16.9%, versus 23.7% in the control group (hazard ratio, 0.69; 95% confidence interval [CI], 0.49 to 0.97; P=0.035), corresponding to a relative reduction of 30.7%. Prespecified subgroup analyses suggested that the effect was strongest in the children of women whose blood levels of eicosapentaenoic acid and docosahexaenoic acid were in the lowest third of the trial population at randomization: 17.5% versus 34.1% (hazard ratio, 0.46; 95% CI, 0.25 to 0.83; P=0.011).

Analyses of secondary end points showed that supplementation with n−3 LCPUFA was associated with a reduced risk of infections of the lower respiratory tract (31.7% vs. 39.1%; hazard ratio, 0.75; 95% CI, 0.58 to 0.98; P=0.033), but there was no statistically significant association between supplementation and asthma exacerbations, eczema, or allergic sensitization.

Supplementation with n−3 LCPUFA in the third trimester of pregnancy reduced the absolute risk of persistent wheeze or asthma and infections of the lower respiratory tract in offspring by approximately 7 percentage points, or one third.

**Source :*New England Journal of Medicine*, 2016; 375 (26): 2530 DOI: 10.1056/NEJMoa1503734**

## FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women

The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains. Consistent with animal studies, recent human studies suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure affects children's brain development.

To better inform the public about this potential risk, we are requiring warnings to be added to the labels of general anesthetic and sedation drugs (see List of General Anesthetic and Sedation Drugs Affected by this Label Change). We will continue to monitor the use of these drugs in children and pregnant women and will update the public if additional information becomes available. Anesthetic and sedation drugs are necessary for infants, children, and pregnant women who require surgery or other painful and stressful procedures, especially when they face life-threatening conditions requiring surgery that should not be delayed. In addition, untreated pain can be harmful to children and their developing nervous systems.

**Health care professionals** should balance the benefits of appropriate anesthesia in young children and pregnant women against the potential risks, especially for procedures that may last longer than 3 hours or if multiple procedures are required in children under 3 years. Discuss with parents, caregivers, and pregnant women the benefits, risks, and appropriate timing of surgery or procedures requiring anesthetic and sedation drugs.

**Parents and caregivers** should discuss with their child's health care professional the potential adverse effects of anesthesia on brain development, as well as the appropriate timing of procedures that can be delayed without jeopardizing their child's health. **Pregnant women** should have similar conversations with their health care professionals. Also talk with them about any questions or concerns

Published studies in pregnant animals and young animals have shown the use of general anesthetic and sedation drugs for more than 3 hours caused widespread loss of nerve cells in the brain. Studies in young animals suggest these changes result in long-term effects on the animals' behavior or learning (see Data Summary). Studies have also been conducted in children, some of which support findings from previous animal studies, particularly after repeated or prolonged exposure to these drugs early in life. All the studies in children had limitations, and it is unclear whether any negative effects seen in children's learning or behavior were due to the drugs or to other factors, such as the underlying medical condition that led to the need for the surgery or procedure. Fda has been investigating the potential adverse effects of general anesthetic and sedation drugs on children brain development since the first animal study on this topic was published. More research is still needed to provide additional information about the safe use of these drugs in young children and pregnant women.

We urge health care professionals, patients, parents, and caregivers to report side effects involving anesthetic and sedation drugs or other medicines to the FDA Med Watch program.

***SOURCE : http://www.fda.gov/***

# Medication Safety Updates

## FDA Approves Crisaborole (*Eucrisa*) for Atopic Dermatitis

The US Food and Drug Administration (FDA) has approved crisaborole (Eucrisa, Anacor Pharmaceuticals, Inc) for the treatment of mild to moderate atopic dermatitis (eczema) in patients aged 2 years and older. Atopic dermatitis, a chronic inflammatory skin disease, is often referred to as "eczema," which is a general term for the several types of inflammation of the skin. The cause of atopic dermatitis is a combination of genetic, immune and environmental factors. In atopic dermatitis, the skin develops red, scaly and crusted bumps, which are extremely itchy. Scratching leads to swelling, cracking, "weeping" clear fluid, and finally, coarsening and thickening of the skin.

Eucrisa, applied topically twice daily, is a phosphodiesterase 4 (PDE-4) inhibitor, although its specific mechanism of action in atopic dermatitis is not known.

The safety and efficacy of Eucrisa were established in two placebo-controlled trials with a total of 1,522 participants ranging in age from two years of age to 79 years of age, with mild to moderate atopic dermatitis. Overall, participants receiving Eucrisa achieved greater response with clear or almost clear skin after 28 days of treatment.

Serious side effects of Eucrisa include hypersensitivity reactions. Eucrisa should not be used in patients who have had a hypersensitivity reaction to Eucrisa's active ingredient, crisaborole. The most common side effect of Eucrisa is application site pain, including burning or stinging.

**Source : http://www.fda.gov/**

## FDA Approves for Xultophy 100/3.6 (insulin degludec and liraglutide injection) for Type 2 Diabetes.

U.S. Food and Drug Administration (FDA) approved the New Drug **Xultophy** 100/3.6 (insulin degludec 100 units/mL and liraglutide 3.6 mg/mL injection). Xultophy 100/3.6 is a once-daily, combination of Tresiba and Victoza (liraglutide) injection indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes inadequately controlled on less than 50 units of basal insulin daily or less than or equal to 1.8 mg of liraglutide daily.[1]Xultophy 100/3.6 enters into a new class of diabetes treatments that combine a basal insulin and a glucagon-like peptide-1 receptor agonist (GLP-1 RA) in a single, once-daily injection.

The approval of Xultophy 100/3.6 is based on efficacy and safety data from the DUAL™ (Dual Action of Liraglutide and Insulin Degludec in Type 2 Diabetes) clinical development program. In three DUAL™ trials involving 1,393 adults with type 2 diabetes, patients who were inadequately controlled on liraglutide or basal insulin therapy and switched to Xultophy 100/3.6 achieved reductions in A1C. For adults uncontrolled on basal insulin, Xultophy 100/3.6 demonstrated significant reductions in A1C from baseline of 1.67% and 1.94%. The starting dose of Xultophy 100/3.6 is 16 units (16 units insulin degludec and 0.58 mg liraglutide).The maximum dose of 50 units of Xultophy 100/3.6 corresponds to 50 units of insulin degludec and 1.8 mg of liraglutide

The most common adverse events seen during the DUAL™ clinical development program included nasopharyngitis, headache, nausea, diarrhea, increased lipase, and upper respiratory tract infection.

***Source: Xultophy 100/3.6 [package insert]. Plainsboro, NJ: Novo Nordisk Inc; November 2016.***

## "الغذاء و الدواء" تحذر من مستحضر (Correction Plus) بسبب احتوائه على إدعاءات طبية مخالفة لعلاج مرض السكري

1438/01/30


حذرت الهيئة العامة للغذاء والدواء من مستحضر (Correction Plus) الذي يسوق عبر أحد المواقع الالكترونية على أنه يعالج مرض السكري، في حين أنه يحتوي على إدعاءات طبية مخالفة.

وأوضحت في بيان على موقعها الالكتروني www.sfda.gov.sa ،أنها وضمن دورها الرقابي المتمثل في ضمان مأمونية وجودة وفعالية الدواء وسلامة المستحضرات الصيدلانية المسوقة داخل المملكة، رصدت أحد المواقع الإلكترونية يسوق لمستحضر يحمل اسم (Correction Plus) ، يدعي مسوقوه قدرته على علاج داء السكري، وأنه مكمل غذائي لا يلزم الحصول على ترخيص من الهيئة لتسويقه.

وحذرت "الهيئة" المستهلكين من خطر استخدام هذا المستحضر، لأنه لا تعرف الظروف التصنيعية التي مر بها، وطرق تخزينه، أو محتوى المواد الصيدلانية فيه، إضافة إلى غياب وسائل تأكيد الجودة والفاعلية للدواء، وتسويقه بناء على ادعاءات غير مثبتة علمياً.

ونصحت بعدم الانسياق وراء الإعلانات المضللة في وسائل التسويق المختلفة غير المرخصة، والتي تبيع الأدوية مجهولة المصدر وغير المسجلة بالهيئة، وأوصت المستهلكين بتجنب استخدام هذا المستحضر والتخلص مما لديهم من عينات، مشددة على ضرورة عدم استهلاك المستحضرات الصيدلانية غير المسجلة لديها أو التي لم يتم الإذن بفسحها عن طريقها. مشيرة إلى أنها تنسق مع الجهات ذات العلاقة لتعقب هؤلاء المسوقين وتطبيق الأنظمة بحقهم. ويمكن معرفة المستحضرات المسجلة عن طريق موقع الهيئة الالكتروني والتحقق من وجود رقم التسجيل الخاص بالهيئة على عبوة المستحضر.

***المصدر:*** *الهيئة العامة للغذاء والدواء .*

## نصائِح صحيَّة حول الوقاية من مُقاومة المضادَّات الحيويَّة!

09-Nov-2016

تحدُث مُقاوَمة المُضادَّات الحيويَّة antibiotic resistance عندما يُصبِح الدواء غيرَ قادرٍ على القضاء على البكتيريا مثلما هُو مُفترَض، ويرى الخبراء أنَّ السبب في هذا يعود إلى الاستخدام الفوضوي للمضادَّات الحيويَّة.

تنصح مُنظَّمة الصحَّة العالميَّة باتخاذ الخطوات التالية للمساعدة على تعزيز دور المضادات الحيوية في القضاء على البكتيريا:

- تناوُل المضادَّات الحيويَّة التي يصفها الطبيب فقط.
- تناوُل الشوط الدوائيّ للمضادَّات الحيويَّة كاملاً، فالتوقُّف عن استخدامها بعد فترةٍ وجيزةٍ جداً قد يسمح للبكتيريا بالاستمرار في الحياة وتطوير سلالات مُقاومة للمضاد الحيوي.
- عدم الاحتفاظ بالفائض من المضادات الحيويَّة لاستخدامها لاحقاً، وعدم مشاركة شخص آخر في استخدامها.
- غسل اليدين لعدَّة مرات وأخذ اللقاحات وتجنُّب ملامسة المرضى، وذلك للتقليلِ من خطر العدوى في المقام الأوَّل.

***المصدر:*** *موسوعة الملك عبد الله بن عبد العزيز العربية للمحتوى الصحي .*

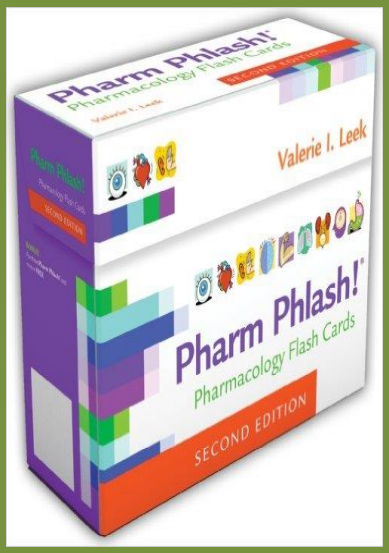
# Scientific Books: New Release

**Pharm Phlash Cards!: Pharmacology Flash Cards 2nd Edition**
**By Valerie I. Leek MSN RN CMSRN**

**Pharmacology Flash Cards** that increases pharmacology test scores. Decreases and prevents medication errors in the clinical setting. Improves NCLEX pharmacology scores…and expands understanding of pharmacological agents!

The 2nd Edition of these test-yourself review cards cover critical clinical information for nearly 400 of the top generic medications. And, you can count on them for accuracy, because each card is based on content from *Davis's Drug Guide for Nurses®*

*"These cards not only give you the most important aspects of each med, but also provide you with nursing tips. These cards are great for new nursing students!"*




**If you want to receive the DPIC bulletin in your E-mail please contact us via: *malarifi@ksu.edu.sa***

# Upcoming Conferences

- 18th - 19th January 2017 6th annual Pharmaceutical Microbiology, at the Holiday Inn Kensington Forum in London, United Kingdom.
- 30th January - 1st February 2017 Global Summit on Pharmaceutical Sciences and Clinical Trials 2K17 at the Holiday Inn in Copenhagen, Denmark
- 1st - 2nd February 2017, Pharma Market Research Conference USA at the Hilton Parsippany Hotel in Parsippany, United States.
- 21st - 22nd February 2017eyeforpharma Data and Technology in Clinical Trials 2017. at the Sonesta Hotel, 1800 Market Street, 19103 in Philadelphia, PA, United States

# Editorial Board



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