SOP Newsletter

Drug Information News From the School of Pharmacy Faculty Members

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In this edition:

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FDA NEWS & UPDATES IN THERAPY

Razan Mehanna, PharmD.

NEWS # 1: FDA APPROVES THE FIRST MOLECULAR (GENE-BASED) TEST TO DETERMINE RED BLOOD CELL TYPES IN TRANSFUSION MEDICINE

Key point: The Immucor Precise Type Human Erythrocyte Antigen (HEA) Molecular Bead Chip Test, manufactured by BioArray Solutions Ltd. of Warren, New Jersey, is the first FDA-approved molecular assay used in transfusion medicine to assist in determining blood compatibility.

Finer points: The surfaces of red blood cells display minor blood group antigens in addition to the major ABO blood group antigens. Some people develop antibodies to non-ABO antigens following repeated transfusions or pregnancy. The development of such antibodies can cause red blood cell destruction. This test works by detecting genes that govern the expression of 36 antigens that can appear on the surface of red blood cells. The test uses thousands of coded beads that bind with the genes coding for non-ABO red blood cell antigens that are present in a blood sample. A light signal is generated from each bead that has captured a specific gene. Accompanying computer software decodes the light signals and reports which antigens are predicted to be present on the red cells based on the genes that are detected.

NEWS# 2: FDA APPROVES THE FIRST ANTI-HEMOPHILIC FACTOR, FC FUSION PROTEIN FOR PATIENTS WITH HEMOPHILIA A

Key point: Eloctate, Fc fusion protein, is the first Hemophilia A treatment approved for adults and children and designed to require less frequent injections when used to prevent or reduce the frequency of bleeding.

Finer points: Eloctate, manufactured by Biogen Idec, Inc., is approved to help control and prevent bleeding episodes, manage bleeding during surgical procedures, and prevent or reduce the frequency of bleeding episodes (prophylaxis). It consists of the Coagulation Factor VIII molecule (known as Anti-hemophilic Factor) linked to a protein fragment, Fc, which is found in antibodies. This makes the product last longer in the patient's blood. The safety and efficacy of Eloctate were evaluated in a clinical trial of 164 patients that compared the prophylactic treatment regimen to on-demand therapy. Eloctate received orphan-drug designation for this use by the FDA because it is intended for treatment of a rare disease or condition.

FDA NEWS & UPDATES IN THERAPY

NEWS # 3: FDA AND EPA ISSUE A DRAFT OF THE UPDATED ADVICE FOR FISH CONSUMPTION

Key point: The U.S. Food and Drug Administration and the U.S. Environmental Protection Agency have concluded that pregnant and breastfeeding women, those who might become pregnant, and young children should eat more fish that is lower in mercury in order to gain important developmental and health benefits.

Finer points: An FDA analysis of seafood consumption data from over 1,000 pregnant women in the United States found that 21 % of them haven't eaten any fish in the previous month, and those who did, ate far less than the recommendation of the Dietary Guidelines for Americans. The draft of the updated advice recommends that pregnant women should eat at least 8 ounces and up to 12 ounces (2-3 servings) per week of a variety of fish that is lower in mercury to support fetal growth and development. Pregnant or breastfeeding women should avoid four types of fish that are associated with high mercury levels: tilefish from the Gulf of Mexico, shark, swordfish, and king mackerel. In addition, the draft also recommends limiting consumption of white (albacore) tuna to 6 ounces a week. Choices that are lower in mercury include some of the most commonly eaten fish, such as shrimp, pollock, salmon, canned light tuna, tilapia, catfish and cod.

"...young children should eat more fish that is lower in mercury in order to gain important developmental and health benefits."

NEWS # 4: FDA APPROVES FIRST HUMAN PAPILLOMAVIRUS TEST FOR PRIMARY CERVICAL CANCER SCREENING

Key point: The cobas HPV Test, manufactured by Roche Molecular Systems, is the first FDA-approved HPV DNA test for women 25 and older that can be used alone to assess the need to undergo additional diagnostic testing for cervical cancer and assess the patient's future risk for developing cervical cancer.

Finer points: Using a sample of cervical cells, the cobas HPV Test detects DNA from 14 high-risk HPV types. Based on results of the cobas HPV Test, women who test positive for HPV 16 or HPV 18 should have a colposcopy. Women testing positive for one or more of the 12 other high-risk HPV types should have a Pap test to determine the need for a colposcopy. Data from a three years follow up study of more than 40,000 women who were 25 years and older undergoing routine cervical exams, showed that the cobas HPV Test was safe and effective for the new indication of use.

"...the cobas HPV Test detects DNA from 14 high-risk HPV types..."

Source: 1. U.S. Food and Drug Administration: www.fda.gov. 2. Federal Register: The Daily Journal of the United States Government. Environmental Protection Agency and Food and Drug Administration Advice About Eating Fish: Availability of Draft Update. 2014.

NEW DRUG OF THE MONTH

Dalal Hammoudi, RPh, MSc

VORAPAXAR

Key point: On May 8th, 2014, the US Food and Drug Administration (FDA) approved vorapaxar (Zontivity®), to prevent thrombotic cardiovascular events in patients with a history of myocardial infarction (MI) or with peripheral arterial disease. The tablets, manufactured by Merck Sharp & Dohme, supply a dose of 2.08 mg of vorapaxar to be taken once daily, with or without food, in combination with either aspirin and/or clopidogrel.

Finer points: Vorapaxar is the first in a new class of anti-platelet agents acting as a reversible antagonist of protease-activated receptor-1 (PAR-1). Expressed on platelets, PAR-1 has the principal role of mediating platelet activation at low concentrations of thrombin. Varopaxar is a small non-protein molecule having high affinity to PAR-1, and can competitively inhibit thrombin-mediated platelet activation. In in-vitro studies, vorapaxar also inhibits thrombin-induced and thrombin receptor agonist peptide (TRAP)-induced platelet aggregation.

Thrombin-mediated platelet activation via PAR has been subject to extensive clinical research, and several PAR-1 antagonists have been developed. However, vorapaxar is the only one that has completed large-scale clinical investigation. The full results of phase III trial (TRA 2ºP-TIMI 50) on varopaxar were reported in early 2012. They showed that the drug significantly reduced the risk of cardiovascular death or ischemic events in patients with stable atherosclerosis who were receiving standard therapy, but increased the rate of moderate or severe bleeding and intracranial hemorrhage. The FDA has slapped a black-box warning on the drug to advise physicians of the potential for fatal episodes. Vorapaxar is contraindicated in patients with a history of stroke, transient ischemic attack, or intracranial hemorrhage, or patients with active pathological bleeding.

"FDA-approved as an add-on to aggressive secondary preventive measures…"

What you need to know: Vorapaxar is a novel anti-platelet agent that selectively inhibits the cellular actions of thrombin through antagonism of PAR-1. Ischemic recurrences in selected patients with a history of MI are reduced through that mechanism.

Source: 1. Cho JR, Rollini F, Franchi F, Ferrante E, Angiolillo DJ. Unmet needs in the management of acute myocardial infarction: role of novel protease-activated receptor-1 antagonist vorapaxar. Vasc Heal Risk Manag. 2014;10:177–88. 2. Rosser G, Tricoci P, Morrow D, Christopoulos C, Niespialowska-Steuden MN, Kozarski R, et al. PAR-1 antagonist vorapaxar favorably improves global thrombotic status in patients with coronary disease. J Thromb Thrombolysis. March 2014; ahead of print. 3. Morrow DA, Braunwald E, Bonaca MP, Ameriso SF, Dalby AJ, Fish MP, et al. Vorapaxar in the secondary prevention of atherothrombotic events. N Engl J Med. 2012 Apr 12;366(15):1404–13.

CARDIOVASCULAR DISORDERS

Samar Younes, PharmD.

EDOXABAN VERSUS WARFARIN IN PATIENTS WITH ATRIAL FIBRILLATION

Key point: Edoxaban is an oral, once-daily, direct factor Xa inhibitor under investigation for stroke prevention in patients with atrial fibrillation (AF) and for the treatment and secondary prevention of venous thromboembolism (VTE). It was approved in July 2011 in Japan for the prevention of VTE following lower-limb orthopedic surgery.

Finer points: Accordingly, the "Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48" (ENGAGE AF-TIMI 48) trial was designed to compare two dose regimens of once-daily edoxaban (30 mg or 60 mg) with warfarin in patients with atrial fibrillation who were at moderate-to-high risk for stroke.

The trial was a three-group, randomized, double- blind, double-dummy trial conducted at 1393 centers in 46 countries. Eligible patients were 21 years of age or older and had atrial fibrillation documented by means of an electrical tracing within the 12 months preceding randomization, a score of 2 or higher on the CHADS2 risk assessment, and anticoagulation therapy planned for the duration of the trial.

Patients were randomly assigned, in a 1:1:1 ratio, to receive warfarin, dose-adjusted to achieve an international normalized ratio (INR) of 2.0 to 3.0, or to receive high-dose or low-dose edoxaban. The primary efficacy end point was the time to the first adjudicated stroke (ischemic or hemorrhagic) or systemic embolic event. Results obtained showed that the annualized rate of the primary end point during treatment was 1.50% with warfarin, as compared with 1.18% with high-dose edoxaban ($P<0.001$ for noninferiority) and 1.61% with low-dose edoxaban ($P = 0.005$ for noninferiority). In the intention-to-treat analysis, there was a trend favoring high-dose edoxaban versus warfarin ($P = 0.08$) and an unfavorable trend with low-dose edoxaban versus warfarin ($P = 0.10$). The annualized rate of major bleeding was 3.43% with warfarin versus 2.75% with high-dose edoxaban ($P<0.001$) and 1.61% with low-dose edoxaban ($P<0.001$). The corresponding annualized rates of death from cardiovascular causes were 3.17% versus 2.74% ($P = 0.01$), and 2.71% ($P = 0.008$), and the corresponding rates of the key secondary end point (a composite of stroke, systemic embolism, or death from cardiovascular causes) were 4.43% versus 3.85% ($P = 0.005$), and 4.23% ($P = 0.32$).

What you need to know: It was concluded that both once-daily regimens of edoxaban were

non-inferior to warfarin with respect to the prevention of stroke or systemic embolism, and were associated with significantly lower rates of bleeding and death from cardiovascular causes. Subsequently, edoxaban may be a viable alternative to warfarin for stroke prevention in AF patients.

Source: 1. Giugliano, R et al. Edoxaban versus Warfarin in Patients with Atrial Fibrillation. N Engl J Med 2013;369:2093-2104. 2. Büller, H et al. Edoxaban versus Warfarin for the Treatment of Symptomatic Venous Thromboembolism. N Engl J Med 2013;369:1406-1415.

ENDOCRINOLOGIC DISORDERS

Nisreen Mourad, PharmD.

ALBIGLUTIDE: A NOVEL GLUCAGON-LIKE PEPTIDE-1 (GLP-1) RECEPTOR AGONIST FOR THE TREATMENT OF ADULTS WITH TYPE 2 DIABETES

Key point: Diabetes is a global epidemic disease, affecting 382 million individuals worldwide. The more prevalent form is type 2-diabetes, which affects up to 95 percent of all diabetics. In Lebanon, it is estimated that 1 in every 6 persons suffers from diabetes. Diabetes mellitus type 2 is a life-long, progressive condition characterized by hyperglycemia; if left untreated it could lead to serious complications and even death. Current treatment options include lifestyle modifications. As the condition progresses, patients may require the addition of oral and injectable medications to further control blood glucose levels and, ultimately, they may require the use of insulin. On April 15, 2014 the U.S. Food and Drug Administration (FDA) approved albiglutide (Tanzeum™, GlaxoSmithKline), a once-weekly subcutaneously injectable glucagon-like peptide-1 (GLP-1) receptor agonist to treat adults with type 2-diabetes.this novel agent has already been approved by the European Union on March 26, 2014 under the trade name (Eperzan®, GlaxoSmithKline).

Finer points: Albiglutide comes to join other approved GLP-1 receptor agonists which are liraglutide and exenatide. The safety and effectiveness of albiglutide were evaluated in eight clinical trials involving over 5,000 patients during which albiglutide was assessed against commonly-used classes of antidiabetic agents, in patients at different stages of the disease, as well as those with renal impairment where it showed an improvement in the patients' HbA1c levels. As a result, it was approved as monotherapy or in combination with other antidiabetic agents such as metformin, glimepiride, pioglitazone, or insulin to improve glycemic control in adults with type 2 diabetes mellitus. However it shouldn't be considered as first-line therapy for patients who can't be managed with diet and exercise.

"Albiglutide offers an effective new weekly GLP-1 treatment option…for the management of…type 2 diabetes mellitus."

The recommended starting dosage of albiglutide is 30 mg once weekly injected subcutaneously in the abdomen, thigh, or upper arm and can be increased up to 50 mg once weekly. In clinical trials, the most common adverse effects reported with its use were diarrhea, nausea, upper respiratory tract infection, and injection-site reactions. However, it carries a boxed warning stating that thyroid C-cell tumors have been observed in rodent studies with some GLP-1 receptor agonists, but it is still unknown whether this drug causes these types of tumors in humans. Thus, albiglutide is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Despite its approval, the FDA is requiring postmarketing studies, including a trial to evaluate dosing, efficacy, and safety in pediatric patients, an MTC case registry of at least 15 years, and a cardiovascular-outcomes trial in patients with high baseline risk of cardiovascular disease.

What you need to know: Albiglutide offers an effective new weekly GLP-1 treatment option for adult patients requiring such drugs for the management of their type 2 diabetes mellitus.

Source:1.http://www.dailystar.com.lb/News/Lebanon-News/2013/Dec-20/241732-diabetes-on-the-rise-thanks-to-modern-lifestyle.ashx#axzz33tIjk85j. 2. http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm393289.htm. 3. Pratley R, Barnett A, Feinglos M et al. Efficacy and safety of once-weekly (qw) albiglutide vs. once-daily (qd) liraglutide in Type 2 diabetes (t2d) inadequately controlled on oral agents: Harmony 7 Trial. Presented at: ADA 72nd Scientific Sessions. Philadelphia, PA, USA, 8–12 June 2012.

GASTROENTEROLOGICAL DISORDERS

Zainulabedeen Al Jammaly, PharmD.

LARAZOTIDE FOR THE INSENSITIVE HYPERSENSITIVE GLUTEN ENTEROPATHY (CELIAC DISEASE)

Key point: "Celiac disease" is an autoimmune disease with antibodies against the water-insoluble gliadin traction of gluten, a protein found in wheat, barley, rye, and oats. Age at presentation varies, but it classically occurs in infants during the time of cereal introduction. Patients with celiac disease may present with classic symptoms related to mal-absorption, including diarrhea, steatorrhea, and weight loss, and nutrient or vitamin deficiencies. However, the majority of patients with celiac disease exhibit only minor gastrointestinal (GI) complaints, have non-gastrointestinal manifestations, or are asymptomatic.

Finer points: For long periods of time, the treatment of celiac disease was achieved by simply avoiding the triggering food substances, including wheat, barley, rye, and to a minor degree oats. However they often recur as a result of inadvertent exposure to gluten or non-adherence to the diet, and thus increasing the demand for new therapeutic agents to improve the GI symptoms.

Larazotide acetate is a first-in-class oral peptide that prevents tight junction opening, and may reduce gluten uptake and associated sequela. The drug was compared to placebo in a double-blind, randomized, placebo-controlled study that included 184 patients maintaining a gluten free diet (GFD) before and during the study. After a GFD run-in, patients were randomized to larazotide acetate (1, 4, or 8 mg three times daily) or placebo and received 2.7 grams of gluten daily for 6 weeks.

Outcomes included an experimental biomarker of intestinal permeability, the lactulose-to-mannitol (LAMA) ratio and clinical symptoms assessed by the Gastrointestinal Symptom Rating Scale (GSRS) and anti-transglutaminase antibody levels.

No significant differences in LAMA ratios were observed between larazotide acetate and placebo groups. Larazotide acetate 1-mg limited gluten-induced symptoms as measured by GSRS ($P = 0.002$ vs. placebo). Mean ratio of anti-tissue transglutaminase IgA levels over baseline was 19.0 in the placebo group, as compared with 5.78 ($P = 0.010$), 3.88 ($P = 0.005$) and 7.72 ($P = 0.025$) in the larazotide acetate 1-, 4-, and 8-mg groups, respectively. The rate of adverse events was the same in both groups.

What you need to know: Larazotide acetate reduced gluten-induced immune reactivity and symptoms in patients with celiac disease undergoing gluten challenge and was generally well tolerated. However, there wasn't a significant difference in the LAMA ratios between larazotide acetate and the placebo group.

Source: 1. DICKE WK, WEIJERS HA, VAN DE KAMER JH. Coeliac disease. II. The presence in wheat of a factor having a deleterious effect in cases of coeliac disease. Acta Paediatr 1953; 42:34. 2. Rostom A, Dube C, Cranney A, et al. Celiac disease. Summary, evidence report/technology assessment No 104 (Prepared by the University of Ottawa Evidence-based Practice Center, under Contract, No. 290-02-0021), AHRQ publication No 04-E)29-1, Agency for Healthcare Research and Quality, Rockville, MD 2004. 3. National Institutes of Health Consensus Development Conference Statement. Celiac Disease 2004. Available at: http://consensus.nih.gov/ (Accessed on October 25, 2004). 4. C. P. Kelly, et al. Larazotide Acetate in Patients With Coeliac Disease Undergoing a Gluten Challenge. Aliment Pharmacol Ther. 2013;37(2):252-262.

OBSTETRICS & GYNECOLOGIC DISORDERS

Rima Abdul Khalek, PharmD.

AN UPDATE ON VANCOMYCIN DOSING FOR INTRAPARTUM PROPHYLAXIS TO PREVENT GBS DISEASE IN THE NEONATE

Key point: Group B streptococcus (GBS) remains one of the leading causes of early-onset neonatal sepsis in the United States, despite the dramatic declines in disease incidence that followed screening and prevention strategies. In fact, incidence has decreased from 1.7 cases per 1,000 live births in the early 1990s to 0.34–0.37 cases per 1,000 live births in recent years. .

Finer Points: Pregnant females colonized with GBS are at high risk for transmitting the bacterium to the newborn. Administering intravenous (IV) antibiotics during labor (intrapartum) to colonized females has been shown to prevent early-onset invasive diseases, i.e. diseases which occur during the first week of life.

Antibiotic	Dose
Penicillin	5 million units IV as initial dose, then 2.5-3 million units every 4hrs until delivery
Ampicillin	2 g IV initial dose, then 1g IV every 4 hrs until delivery
Cefazolin	2 g IV initial dose, then 1 g IV every 8 hrs until delivery
Clindamycin	900 mg IV every 8 hrs until delivery
Vancomycin	1 g IV every 12 hrs until delivery

The dose used for prophylaxis should achieve adequate levels in the fetal circulation and amniotic fluid.

The antibiotics which have demonstrated efficacy through clinical trials include only ampicillin and penicillin. Cafazolin is the alternative medication that can be used in penicillin allergic mothers with no anaphylaxis, angioedema, respiratory distress or urticaria history. Furthermore, for a history of severe allergic reactions at high risk for anaphylaxis, clindamycin and erythromycin have been recommended. However, where resistant GBS isolates to clindamycin and erythromycin are encountered or where susceptibility tests lacking, the recommendation is to administer vancomycin 1g every 12 hrs until delivery.

"In the case where vancomycin is indicated, a study has shown that the dose recommended by the Centers for Disease Control and Prevention (CDC) 2010 revised guideline is sub-therapeutic."

The results of the following study were presented in the 34th annual meeting of the Society for Maternal-Fetal Medicine, New Orleans, LA in February 2014. For the 55 patients that participated in the study, different vancomycin doses were used and maternal and neonatal cord blood levels were evaluated at the time of delivery. The study participants received the medications in 3 phases.

- **Phase 1** participants received the traditional dose of 1g every 12 hrs
- **Phase 2** participants received a dose of 15mg/kg every 12 hrs
- **Phase 3** participants received a dose of 20mg/kg every 8 hrs

Therapeutic vancomycin levels were obtained in only 9% of neonates of phase 1, increased to reach 33% in phase 2, and 83% in phase 3. Therefore, a dose of 20 mg/kg every 8 hrs is rather recommended for prophylaxis in this study.

Given the high prevalence of GBS colonization in Lebanon and the studies that are showing resistant strains, screening all pregnant females and performing antibiotic susceptibility tests should be recommended. Correct dosing should be implemented in cases of penicillin allergic patients with isolates resistant to clindamycin and erythromycin, where vancomycin is thus recommended.

Finally, although vaccines are still not marketed, a GBS vaccine phase 1 and 2 studies have shown the vaccine to be well tolerated. If it becomes available, it will reduce maternal colonization and newborn morbidity and mortality, and thus infections due to GBS in neonates will hopefully become uncommon.

What you need to know: The current dosing of vancomycin for prevention of GBS infection has been shown to be subtherapeutic, and therefore the 2010 CDC recommendations may need to be changed. The new proposed dosing takes into consideration the mother's weight and does not generalize the dose for all patients.

Source: 1. Onwuchuruba CN, Towers CV, Howard BC, Hennessy MD, Wolfe L, Brown MS. Transplacental passage of vancomycin from mother to neonate. Am J Obstet Gynecol. 2014 Apr;210(4):352.e1-4. 2. 2. American Academy of Pediatrics. Recommendations for the Prevention of Perinatal Group B Streptococcal (GBS) Disease. American Academy of Pediatrics Committee on Infectious Diseases and Committee on Fetus and Newborn. Pediatrics. 2011 Sep;128(3):611-6. 3.Centers for Disease Control and Prevention. Prevention of Perinatal Group B Streptococcal Disease: revised guidelines from CDC. MMWR 2010;59(No. RR-10):1-36. 4. Hannoun A, Shehab M, Khairallah MT, Sabra A, Abi-Rached R, Bazi T, Yunis KA, Araj GF, Matar GM. Correlation between Group B Streptococcal Genotypes, Their Antimicrobial Resistance Profiles, and Virulence Genes among Pregnant Women in Lebanon. Int J Microbiol. 2009;2009:796512.

CARDIOVASCULAR DISEASES

Michelle Cherfan, PharmD.

EFFECT OF ACEIS AND ARBS ON CARDIOVASCULAR OUTCOMES IN PATIENTS WITH DIABETES MELLITUS

Key points: Individuals with diabetes are at an increased risk for cardiovascular (CV) events, with death from CV disease increasing twofold to fourfold in this patient population as compared with patients without diabetes. Current guidelines recommend the use of ACE inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) in patients with diabetes to reduce the risk of adverse CV and renal outcomes. However, recent evidence suggests that there may be differences in the CV effects of these two classes of drugs.

Finer points: Cheng et al. conducted a meta-analysis of 35 randomized controlled trials (i.e., 23 with ACEIs and 13 with ARBs; 1 trial assessed both) involving 56,444 patients with type 1 or type 2 diabetes to assess drug class effects on selected CV outcomes. All trials had a median or mean follow-up period of at least 12 months and assessed the effects of ACEIs or ARBs against active drugs or placebo/no treatment.

"…there are clinical differences for CV protection between ACEIs and ARBs in patients with diabetes…"

Use of ACEIs was associated with a 13% reduction in all-cause mortality (relative risk [RR] 0.87; 95% confidence interval [CI] 0.78–0.98), a 17% reduction in CV deaths (RR 0.83; 95% CI 0.70–0.99), and a 14% reduction in major CV events (RR 0.86; 95% CI 0.77–0.95). These findings included a 21% reduction in myocardial infarction (RR 0.79; 95% CI 0.65–0.95) and a 19% decrease in heart failure (RR 0.81; 95% CI 0.71–0.93). Meta-regression analysis showed that the ACEI treatment effect on all-cause mortality and CV death did not vary significantly with the starting baseline blood pressure and proteinuria of the trial participants and the type of ACEI and DM.

Conversely, ARBs use was associated with a 30% reduction in heart failure (RR 0.70; 95% CI 0.59–0.82), with no significant effects on all-cause mortality, CV death, or overall major CV events. Neither agent had a significant effect on risk of stroke.

This analysis suggested that there are clinical differences for CV protection between ACEIs and ARBs in patients with diabetes, with ACEIs having significantly better effects on CV outcomes. However, key limitations need to be taken into consideration when determining the clinical validity of the results. This analysis was essentially an indirect comparison between ACEIs and ARBs, with only one trial directly comparing an ACEI with an ARB (enalapril versus telmisartan). In addition, variability among the studies included medications and doses, blood pressure and glycosylated hemoglobin (A1C) targets, and baseline demographics of study participants. Study authors highlighted these limitations and concluded that "this meta-analysis cannot confirm that ACEIs are superior to ARBs on survival in patients with diabetes."

What you need to know: Results of a large meta-analysis involving more than 56,000 patients showed that ACEIs had greater benefits on CV outcomes as compared with ARBs in patients with diabetes. The authors concluded that ACEIs should be used as a first line to limit excess mortality and morbidity in this population.

Source: Cheng J et al. Effect of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers on all-cause mortality, cardiovascular deaths, and cardiovascular events in patients with diabetes mellitus: a meta-analysis. JAMA Intern Med. 2014: 1;174(5):773-85.

ONCOLOGIC DISEASES

Mariam Dabbous, PharmD.

LENALIDOMIDE PLUS R-CHOP: EFFECTIVE IN ELDERLY DLBCL PATIENTS

Key Point: The addition of lenalidomide to a standard rituximab/chemotherapy combination is impressively effective in elderly patients with newly diagnosed diffuse large B-cell lymphoma (DLBCL), and does not add to toxicity, according to a phase 2 trial.

Finer Points: In the trial, 49 elderly patients were treated with R-CHOP (rituximab, cyclophosphamide, doxorubicin, and vincristine), and half were randomly assigned to also receive lenalidomide.

Adding the immunomodulatory agent increased the overall response rate to 92%, as well, 86% of the patients achieved a complete response (CR) and 6% achieved a partial response. Only 3 patients did not respond to the combination strategy. One patient died for reasons unrelated to the treatment or disease.

"The results seem "provocative," but still need to be validated in a randomized trial."

If young patients with DLBCL fail or relapse after R-CHOP chemotherapy, they have a chance to be salvaged with high-dose chemotherapy and autologous stem cell transplantation, but in the elderly, this type of treatment cannot be given because of age and co-morbidities.

In the elderly, second-line treatment options are very limited and not that effective, which is why it's most important to have better first-line treatments and avoid relapse or failure in the beginning.

REAL07 Study

The REAL07 study was an open-label multicenter trial that was carried out in 13 centers in Italy and 1 in Germany. Of the 49 patients, 45 had newly diagnosed, untreated, CD-20-positive stage II to IV DLBCL and 4 had grade 3b follicular lymphoma.

Patients were stratified according to the International Prognostic Index score; 19 (39%) were low to intermediate risk and 30 (61%) were intermediate to high risk or high risk. All patients received standard doses of R-CHOP21, and those in the lenalidomide group received oral lenalidomide 15 mg on days 1 to 14 of the 21-days cycle. Patients were scheduled to undergo 6 cycles of R-CHOP rather than the 8 used in other trials because other studies found no difference in efficacy between 6 and 8 cycles.

The median dose of lenalidomide per patient was 1185 mg, and patients received 94% of the planned dose during the study. Patients also received at least 90% of the R-CHOP doses in approximately 90% of cycles. All patients received granulocyte colony-stimulating factor (G-CSF) to prevent neutropenia and low-molecular-weight heparin to prevent deep vein thrombosis.

One month after the completion of the 6 cycles, 18F-fluorodeoxyglucose PET was used to assess the overall treatment response.

Toxicity Profile

The addition of another agent to an existing combination is not without risk because of concerns about increased toxicity.

Grade 3/4 neutropenia was documented in almost one-third of the cycles, despite the use of G-CSF. However, this did not translate into an excess of infections. Most adverse events were of mild to moderate intensity, and were similar to those recorded with standard R-CHOP alone. There were no grade 4 non-hematologic adverse events and no deaths related to toxicity.

What you need to know: More than a decade has passed since the first reports of survival benefit with the addition of rituximab to standard CHOP. However, efforts to improve R-CHOP by increasing dose intensity have not been successful and the regimen is still delivered every 21 days (R-CHOP21) in 6 cycles as the worldwide standard. Unfortunately, 30% to 40% of DLBCL patients do not do well on R-CHOP21 alone and die of their disease. Thus, novel agents have been added to the existing R-CHOP21 schedule in an effort to improve overall efficacy. The results seem "provocative," but still need to be validated in a randomized trial. Currently, other agents, including bortezomib, ibrutinib, and everolimus, are being tested in large randomized studies of DLBCL.

Source: Witzig TE. Origins research in large cell lymphoma-time for action? Lancet Oncol 2014;15(7):674-5

DERMATOLOGIC DISORDERS

Nermine Chouman, PharmD.

THE REAL SMURFS: PEOPLE WHO TURNED BLUE!

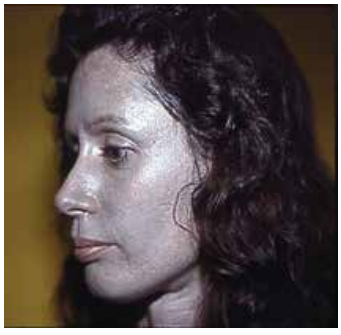
Key point: Everyone has heard of the smurfs, the little blue creatures that have captured so many children's imagination. But a rare condition called "Argyria" actually causes a sufferer's skin to turn blue.

Finer points: Argyria from the greek "arguros" (meaning silver), is a rare disorder characterized by a permanent grayish blue discoloration of the skin and mucous membranes from prolonged contact with or ingestion of silver salts. It is often the result of occupational exposure or self-administration of silver-containing products for unproven medicinal purposes (Table 1).

Table 1: Sources of silver salts

Source	Example
Occupational exposure (Most common)	Workers involved in silver mining, silver refining, silverware and metal alloy manufacturing
Medication containing silver salts	Prolonged use of silver salts for the irrigation of urethral or nasal mucous membranes, in eye drops, wound dressing
Colloidal silver dietary supplements	Marketed widely as a treatment for arthritis, diabetes, cancer, herpetic infections and AIDS
Surgical and dental procedures	Silver sutures used in abdominal surgery and silver dental fillings

For many years, claims have been made that the oral administration of the elemental compound silver can serve as a cure for all. In the late 19th century and early 20th century, colloidal silver proteins (CSPs) were used as oral medications to treat a variety of diseases, including syphilis, epilepsy, and nasal allergies. However, due to health concerns and the emergence of more effective therapies, the use of CSP preparations eventually fell out of favor. In 1999, the US Food and Drug Administration (FDA) issued a final rule that all over-the-counter (OTC) drug products containing colloidal silver ingredients or silver salts were not generally recognized as safe and effective, and were misbranded. Regardless, the topical use of silver sulfadiazine, a silver salt, remained among the initial treatments in patients with burn injuries.



Generally, argyria does not develop until middle age because time is required for the silver to build up in the body. Argyria can be localized (e.g., oral cavity, nasal mucosa, trachea, urinary tract, vagina) or generalized (e.g, eyes, nails, mucous membranes, skin). What is apparent is that the degree of discoloration, mainly in the sun-exposed areas of the skin, is directly correlated with the amount of silver absorbed or ingested and the production of melanin. In fact, with the presence of light, silver further stimulates melanogenesis, increasing melanin in light-exposed areas, which could explain the mechanism behind increased pigmentation on sun-exposed areas.

Skin biopsy is generally unnecessary to establish the diagnosis of argyria. However, when obtained, histopathology shows deposition of fine brown-black, extracellular granules within the dermis, both singly and in clusters. Urine and serum concentrations of silver can be measured also as indices of silver exposure. In patients without a history of medicinal silver ingestion or occupational exposure, the serum silver concentration reference range is < 2.3 mcg/L and

the urinary silver concentration reference range is < 2 mcg/day (24-hour urine collection). The oral reference dose for argyria published by the US Environmental Protection Agency is 5 mg/kg/d, with the critical dose estimated at approximately a total accumulation of 8 g.

Treatment of argyria remains limited, and the overall cessation of silver ingestion remains essential. Chelators have proven ineffective in treating both silver toxicity and argyria. The use of hydroquinone cream 5% may slightly reduce the number of silver granules in the upper dermis and around the sweat glands as well as diminish the number of melanocytes. Decreased sun exposure and use of sun protection and opaque cosmetics have shown limited reduction in pigmented appearance on sun-exposed areas. However, breakthrough in laser therapies may prove beneficial effects. A study using a Q-switched 1064 - nm neodymium-doped yttrium aluminium (Nd:YAG) laser successfully improved the appearance of argyria both clinically and microscopically. Yet, the study was limited to localized argyria and the effectiveness in larger, more generalized disease must still be evaluated.

What you need to know: As modern society continues to evolve, the perception of alternative medicine continues to gain popularity. Despite providing some probable symptomatic relief, these remedies must be carefully monitored and used with extreme caution, as their long-term consequences remain in question.

Source: 1. Rhee DY, Chang SE, Lee MW, et al. Treatment of argyria after colloidal silver ingestion using Q-switched 1,064-nm Nd:YAG laser. Dermatol Surg. 2008;34:1427-1430. 2. Padlewska KK, Schwartz RA. Argyria. Emedicine [serial online]. http://emedicine.medscape.com/article/1069121-overview. Updated August 15, 2011. Accessed April 16, 2012. 3. Over-the-counter drug products containing colloidal sil¬ver ingredients or silver salts. Department of Health and Human Services (HHS), Public Health Service (PHS), Food and Drug Administration (FDA). final rule. Fed Regist. 1999;64:44653-44658.

INFECTIOUS DISORDERS

Fouad Sakr, PharmD.

LEVOFLOXACIN SHOWS NO EVIDENCE OF CARTILAGE TOXICITY IN KIDS

Key point: Joint injuries resulting from fluoroquinolone use have been observed in animal studies, leading to caution about using these drugs in children. Levofloxacin, a fluoroquinolone antibiotic, was not linked to joint cartilage injuries in a non-blinded study that followed-up children for 5 years after they took the drug. As the first long-term follow-up (LTFU) study on levofloxacin's effects on the joints of growing children, it provides reassurance for pediatricians to use the drug, especially with regard to multidrug-resistant infections for which there are few treatment options.

Finer Points: The study included 124 children who had taken levofloxacin and 83 children who had taken a non-fluoroquinolone drug. All of those patients had been identified during a 12-month surveillance phase follow-up study as having more than 1 of the following: growth impairment or possible growth impairment 12 months post-treatment, abnormal bone or joint symptoms during the 12 months after treatment, musculoskeletal adverse events that persisted at the end of the 12-month study, or concerns about joint toxicity. Participants were not randomized at the time of entry into the LTFU study, and parents were not blinded.

"This study provides additional reassurance to pediatricians who must weigh the benefits and risks of the drug on a case-by-case basis."

The researchers asked patients to return for annual examinations, during which they gave them a questionnaire about musculoskeletal injuries and measured their height to assess growth. However, many children did not return for all of the follow-up visits or visited outside the requested window for each visit.

The investigators considered a wide range of musculoskeletal injuries, including arthritis, arthralgia, gait abnormality, tendinopathy, and growth impairment caused by damage to an epiphyseal plate.

At the beginning of the LTFU study, 1 year after taking the drug, 29 children in the levofloxacin group (2% of those exposed) and 10

children in the comparator group (1%) were judged to have a "possible" drug-related injury. After 5 years, 1 child in each group had ongoing concerns about possible joint toxicity, even though the Data Safety and Monitoring Committee did not consider these "likely" to be drug-related.

What you need to know: This study provides additional reassurance to pediatricians who must weigh the benefits and risks of the drug on a case-by-case basis. Moreover, this is consistent with the American Academy of Pediatrics' guidelines on fluoroquinolones, which recommend the drugs when there is no safe and effective alternative, as in the case of multidrug-resistant infections.

Source: Bradley JS, Kauffman RE, Balis DA, Duffy CM, Gerbino PG, Maldonado SD, Noel GJ6. Assessment of Musculoskeletal Toxicity 5 Years After Therapy With Levofloxacin. Pediatrics. 2014 Jun 2. pii: peds.2013-3636. [Epub ahead of print]

WOMEN'S HEALTH

Diana Malaeb, PharmD.

EXTENDED OR CONTINUOUS USE OF COMBINED HORMONAL CONTRACEPTIVE PILLS

Key Points: Extended hormonal contraception delays menstruation, whereby the continuous use eliminates menstruation.

Finer Points: Many hormonal contraceptive products have been approved for extended or continuous contraception, including Seasonale®, Seasonique®, and Lybrel®.

- Seasonale® contains 84 days of active pills and 7 days of inactive pills
- Seasonique® contains 84 days of active pills and 7 days of low-dose estrogen pills
- Lybrel® contains a full year of active pills with no inactive pills

Extended-regimen contraception is used to relieve menstrual-related complaints and to treat women with menorrhagia, dysmenorrhea, endometriosis, chronic pelvic pain, and anemia. Menstrual suppression through continuous combined oral contraceptives use is associated with reduction in menstrual migraines, endometriosis, acne, and an improved sense of well-being. Pregnancy risk is highest when a woman misses more than 7 days of the pills. There is an increase in breakthrough bleeding during the first few cycles of use as the body adjusts to the new hormonal balance. The main advantages are the delay or elimination of menstruation, and the ability to adjust the cycle at particular times, for life events, or based on preference. As for the disadvantages, they are the same as those of the conventional combined hormonal contraception.

While using this type of contraception, it is very important to counsel the female patients about the following tips:

- It is not necessary to bleed every month when using hormonal contraceptives
- Having a monthly menses is not a proof of lack of pregnancy
- Unscheduled bleeding will lessen over time
- This method does not protect against sexually transmitted diseases.

What you need to know: The avoidance of menstruation through extended or continuous administration of COCs has gained legitimacy through its use in treating multiple female disorders. This has lead to their use for additional advantages to women. But it is very important to always counsel our patients about the use of such pills in order not to fall in the trap of their misuse.

Source: 1.Wright KP and Johnson JV. Evaluation of extended and continuous use oral contraceptives. Ther Clin Risk Manag. 2008 Oct;4(5):905-11. 2. Godfrey EM, Whiteman MK, and Curtis KM. Treatment of unscheduled bleeding in women using extended- or continuous-use combined hormonal contraception: a systematic review. Contraception. 2013 May;87(5):567-75.

NUTRITION NEWS

Sawsan El Hussein, RPh, PhD

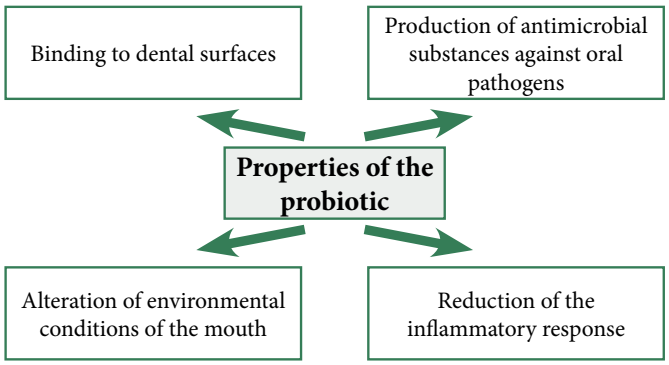
PROBIOTICS: BENEFITS BEYOND GUT HEALTH

Key Point: Probiotics are live microorganisms which, when administered in adequate amounts, confer a health benefit on the host. Specific probiotic strains have been shown to be effective in the prevention and treatment of atopic eczema, alleviating allergic inflammation both locally and systemically. Dental caries, periodontal disease and halitosis are among the oral disorders that have been targeted too. In this review, we will focus on two uncommon uses of probiotics: Nasal and buccal.

Finer Points: An alternative to the use of ingested probiotics is to administer airway commensal bacteria by means of nasal or oral spray. Recolonisation can reduce the levels of real pathogens and consequently limit the number of new respiratory infections. Other research indicates that probiotics could be helpful in reducing the congestion and other symptoms associated with seasonal allergies.

Oral Health

Probiotics can also play a role in maintaining the oral health by secreting anti microbial substances such as organic acids, hydrogen peroxide and bacteriocins. In addition, they compete with pathogenic agents for adhesion sites on the mucosa. Probiotics can also modify the surrounding environment by modulating the pH and/or the oxidation–reduction potential, which may compromise the ability of pathogens to become established.



Dental Care

Dental caries is a multifactorial disease of bacterial origin that is characterized by acid demineralization of the tooth enamel. It appears to be caused by changes in the homeostasis of the oral ecosystem that leads to the proliferation of the bacterial biofilm, composed notably of streptococci from the mutans group. To have a beneficial effect in limiting or preventing dental caries, a probiotic must be able to adhere to the dental surfaces and integrate into the bacterial communities making up the dental biofilm. It must also compete with and antagonize the cariogenic bacteria and thus prevent their proliferation. Finally, metabolism of food-grade sugars by the probiotic should result in low acid production. The advantage of incorporating probiotics into dairy products lies in their capacity to neutralize acidic conditions.

What you need to know: The benefits of probiotics go way beyond GUT health. With their growing popularity, there is a huge variety of supplements from which we can choose. The most important thing is to determine what type of probiotic microorganism we need for our condition. A better understanding of the effects of different probiotic strains and a deeper insight into their mechanisms of action are needed for the validation of specific strains. Thus, this carries a potential to modify the frequency and severity of different health issues.

Source: 1. Esposito et al., Do children's upper respiratory tract infections benefit from probiotics? BMC Infectious Diseases 2014 April 14: 194. 2. Ivory et al., Oral delivery of a probiotic induced changes at the nasal mucosa of seasonal allergic rhinitis subjects after local allergen challenge: a randomised clinical trial. PLoS One. 2013 Nov 15;8 (11). 3. Wassenberg at al., Effect of Lactobacillus paracasei ST11 on a nasal provocation test with grass pollen in allergic rhinitis. Clin Exp Allergy. 2011 Apr;41(4):565-73.

ALTERNATIVE MEDICINE CORNER **Marwan Akel, PharmD.**

EFFICACY AND SAFETY OF MEDICAL MARIJUANA

Key Point: The endocannabinoid system is widely distributed in the brain, spinal cord and peripheral nerves. Stimulating this system may help in relieving the symptoms of multiple painful syndromes.

Finer Points: The activation of the endocannabinoid system through G-coupled membrane proteins causes physiologic responses including:

- A feeling of well-being or psychosis
- Impaired memory and cognitive processing
- Slowed locomotor function
- Antinociceptive, antiemetic, antispasticity, and sleep-promoting effects

Receptor activation inhibits the release of multiple neurotransmitters, including acetylcholine, dopamine, and glutamate. Indirect effects on opiate, serotonin, NMDA, and gamma-aminobutyric acid receptors, allow endocannabinoids to modulate other networks.

Twenty states and the District of Columbia have legalized the medical use of marijuana, and 2 have decriminalized all its usage. Thus researchers are seeking answers to the benefits of marijuana use in patients with a neurologic illness. (Table 2)

The adverse effects include nausea, fatigue, increased weakness, behavior or mood changes, suicidal thoughts or hallucinations, dizziness or vasovagal symptoms, fainting, feelings of intoxication and seizures.

What you need to know: Regardless of all the beneficial effects of marijuana, still "medical marijuana" should only be prescribed when the standard treatment is not helpful in controlling the patients' symptoms.

Source: Report of the Guideline Development Subcommittee of the American Academy of Neurology, 2014.

Table 2: Medical Marijuana Use

Condition	Findings
Spasticity in Multiple Sclerosis (MS)	• Oral Cannabis Extract (OCE) is effective • Nabiximols and Tetrahydrocannabinol (THC) are probably effective
Central pain and painful spasms in MS (excluding neuropathic pain)	• OCE is effective • Nabiximols and THC are probably effective
Urinary dysfunction in MS	• Nabiximols are probably effective for the reduction of the number of bladder voids per day • THC and OCE are probably ineffective
MS related tremors	Probably ineffective
Levodopa-induced dyskinesia in Parkinson's disease	Probably ineffective
Huntington's disease **Tourette syndrome** **Cervical Dystonia** **Seizure frequency in epilepsy**	Unknown efficacy

PHARMACY MANAGEMENT

Farah Chehimi, RPh, MBA, MSc

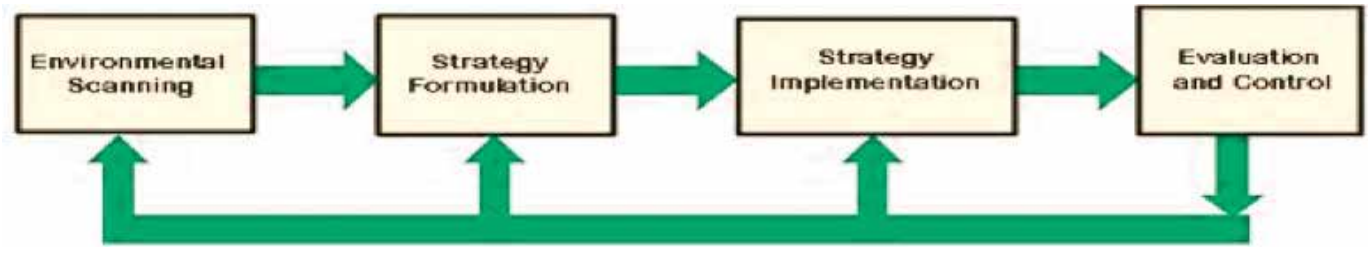
STRATEGIC MANAGEMENT IS THE ANSWER TO WHY A PHARMACY OUT-PERFORMS ANOTHER

Strategy comes from Greek origins and means the "art of troop leader, command, and generalship." A strategy is a comprehensive plan to achieve one or more goals under conditions of uncertainty. It identifies long-term directions and guides resource utilization to accomplish organizational goals with a sustainable competitive advantage.

Strategic Management is the process of formulating, implementing and evaluating to accomplish long-term goals and sustain a competitive advantage. It involves the formulation and implementation of the major goals and initiatives taken by a company's top management on behalf of the owners, based on the consideration of resources and an assessment of the internal and external environments in which the organization competes. Strategic management provides overall direction to the enterprise and involves specifying the organization's objectives, developing its policies and plans designed to achieve these objectives, and then allocating resources to implement the plans. Strategic management is not static in nature; the models often include a feedback loop to monitor execution and inform the next round of planning.

The Basic Model of Strategic Management

1. **Environmental Scanning** includes external analysis of opportunities and threats in the social, cultural, political, technological and task environments, as well as an analysis on internal strengths and weakness of resources and the business's function areas such as management, marketing, finance and accounting. It involves a SWOT analysis; Strenghts, Weaknesses, Opportunities and Threats.
2. **Strategy Formulation** includes formulation of a vision, mission, objectives, strategies, and policies.
   a. Vision means what you want to become.
   b. Mission is defining your business, the purpose of the business, allocating resources, structuring the work, and choosing the organizational climate, e.g. products, services, customers, employees, market, philosophy, and public image.
   c. Objectives are the planned end-results that should be accomplished. Objectives should be SMART, i.e. Specific, Measurable, Achievable, Realistic and within a Time-frame.
   d. Strategies undertaken, may be on a corporate, business or functional-level.
   e. Policies are broad guidelines for decision-making that link the strategy formulation with its implementation.
3. **Strategy Implementation** deals with programs, budgets and procedures.
   a. A program is a statement of activities or steps needed to accomplish a plan.
   b. A budget is a statement of the business's program in terms of money.
   c. Procedures are a system of techniques that describe in details how a task should be done.
4. **Strategy Evaluation and Control** includes internal/external review, measuring performance and strategic audit.
5. **Feedback/Learning Process** includes internal/external review, revision of decisions, corrective actions.



Benefits of strategic management for a pharmacist:

1. Allows the pharmacist to be more proactive than reactive in shaping his business's future
2. Allows the pharmacist to initiate and influence business activities
3. Allows the pharmacist to take control over the work-cash flow, and destiny of his pharmacy
4. Provides a clear sense of strategic vision of the pharmacy
5. Sharpens the pharmacists' focus on what is strategically important
6. Improves the pharmacists' understanding of rapidly changing environment and demands
7. Enables the pharmacist to have better communication with the employees and patients
8. It increases the commitment of the pharmacist and employees, and thus enhances performance and profitability

Source: 1. Nag, R.; Hambrick, D. C.; Chen, M.-J (2007). "What is strategic management, really? Inductive derivation of a consensus definition of the field" (PDF). Strategic Management Journal 28 (9): 935–955. doi:10.1002/smj.615. Retrieved October 22, 2012. 2. Hill, Charles W.L., Gareth R. Jones, Strategic Management Theory: An Integrated Approach, Cengage Learning, 10th edition 2012. 3. Porter, Michael E. (1996). "What is Strategy?". Harvard Business Review (November–December 1996).

CASE REPORT OF THE MONTH

Jihan Safwan, PharmD.

DERMATOLOGIC INFECTION OF LOWER LIMBS CAUSED BY PSEUDOMONAS AEROGINOSA

Key Point: Faculty members at the SoP including Drs. Faraj Saadeh, Jihan Safwan and Marwan Akel investigated the following case report that illustrated the risk of the dermatologic manifestation of pseudomonas aeroginosa in an outpatient setting.

Finer Points: The patient is a 21 years old female, who presented with typical pustules on her lower legs that have the prototype of a staphylococcus aureus infection. The patient was living in the Kingdom of Saudi Arabia (KSA) for 19 years, who then moved to Lebanon for college and work. She stated visiting her parents twice during the past year in KSA. After returning back to Lebanon from both trips, her lower limbs showed a typical presentation of a gram positive dermatologic infection that was accompanied by a stinging feeling, pruritis, fatigue, and inability to walk. After the first manifestation, she was prescribed a first generation cephalosporin: cefadroxil 500 mg orally twice daily, to treat the suspected causative staphylococcus aureus infection, and a first generation antihistamine: hydroxyzine 10 mg orally twice daily, to alleviate the symptoms of itching. After adhering to the treatment for ten days, the patient reported a slight improvement, and confirmed absence of symptoms at day fourteen. The second episode occurred after her second visit, where she re-experienced the same symptoms, and she self medicated herself by repeating the same regimen for 10 days, but no improvement was noted this time. So for this reason, she sought the help of a clinical community pharmacist, who asked for a culture and an antibiogram after taking a full history from the patient. The culture was positive for pseudomonas aeroginosa which was sensitive to the following antibiotics: amikacin, gentamycin, tobramycin, carbenicillin, piperacillin, piperacillin plus tazobactam, imipenem plus cilastatin, cefepime, ceftazidime, ciprofloxacin, levofloxacin, norfloxacin, and aztreonam. Thus, the patient was prescribed ciprofloxacin 500 mg orally twice daily for fourteen days along with desloratadine 5 mg orally once daily for pruritus. After having finished the antibiotic course, the patient reported full healing, absence of symptoms, and ability to walk normally again. After extensive questioning about her past medical, social, and family history, the young lady reported that both of her parents work at a medical center, and she used to share her mothers' clothes. Upon further analysis, it has been hypothesized that the source of the infection might be the colonization of pseudomonas aeroginosa from the mothers work environment, which lead to the transmission of the pathogen through the clothes from the mother to the daughter.

What you need to know: The risk of having a pseudomonas aeroginosa infection in the community setting is quite uncommon. Regardless of this fact, colonization by such a microorganism may occur if the patient is exposed to the right risk factors which may be overlooked in an outpatient. For this reason, such exposures should be carefully assessed in order to give the appropriate treatment and prevent the emergence of resistance.

Faraj Saade, Pharm D., BCPS

HIGHER VITAMIN D LEVELS LINKED WITH BETTER COLORECTAL CANCER OUTCOMES

Key point: In 2014 about 136,830 people are predicted to be diagnosed with colorectal cancer in the US, and about 50,310 people are predicted to die of the disease. In both men and women, colorectal cancer is the third most commonly diagnosed cancer and the third leading cause of cancer death. Researchers from the United Kingdom and Ireland performed a prospective study of 1,598 patients with stage I to III colorectal cancer (CRC) who underwent surgical resection in order to investigate the association between 25-hydroxyvitamin D (25-[OH]D) and survival.

Finer points: They analyzed patient factors with established links to CRC mortality or etiology, and postoperatively tested for interactions with

".. higher plasma 25-(OH)D level is associated with lower cancer-specific and all-cause mortality"

total 25-(OH)D plasma levels (reflecting both dietary and skin-synthesized vitamin D) and polymorphic variation at the vitamin D receptor (VDR) gene locus. Median time to sampling was 105 days after surgery.

Higher 25-(OH)D levels were associated with lower CRC-specific mortality (P=.008) and overall mortality (P=.003). Comparing highest vs. lowest 25-(OH)D tertiles, adjusted HRs were 0.68 (95% CI, 0.5-0.9) for CRC-specific mortality and 0.7 (95% CI, 0.55-0.89) for overall mortality. The adjusted HR for stage II CRC-specific mortality was 0.44 (95% CI, 0.25-0.76). Higher 25-(OH) D levels were more protective for stage II and III patients not undergoing chemotherapy compared with those who did (lowest vs. highest tertiles; HR=0.42; 95% CI, 0.22-0.8), with the most prominent effect in stage II patients (HR=0.34; 95% CI, 0.14-0.81). Gene-environment interactions were detected between 25-(OH)D levels and rs11568820 genotype (P=.008) and number of protective alleles (P=.004) for CRC-specific mortality, and GAGC haplotype at the VDR locus for overall mortality (P=.008).

What you need to know: It has been concluded that higher plasma 25-(OH)D level is associated with lower cancer-specific and all-cause mortality. The interaction between 25-(OH)D and genetic VDR locus in relation to survival provides additional evidence implicating the vitamin D pathway and provides support for a causal relationship.

Source:1. Zgaga L. J Clin Oncol. 2014;doi:10.1200/JCO.2013.54.5947.

Faraj Saade, Pharm D., BCPS

ANTIDEPRESSANTS, PSYCHOLOGICAL THERAPIES EFFECTIVELY TREATED IBS

Key point: Irritable bowel syndrome (IBS) affects as many as one in ten people, and is difficult to treat. Antidepressants and various psychological therapies effectively treated symptoms of IBS in a recent study.

Finer points: An updated systematic review and meta-analysis was performed. It reviewed randomized controlled trials (RCTs) from several databases up to December 2013. Studies that compared antidepressants or psychological therapies with placebo or controls in patients with IBS aged 16 years or older were included. Of the 46 studies analyzed, 10 psychological therapy trials and four antidepressant RCTs were published after the researchers' previous meta-analysis.

Among the 17 included antidepressant RCTs evaluating 1,084 patients, 10 studied tricyclic antidepressants, six studied selective serotonin reuptake inhibitors and one studied both. A combined 43.9% of the antidepressant groups reported unimproved symptoms compared with 65% of the placebo groups. The relative risk for unimproved IBS symptoms after using antidepressants vs. placebo was 0.67 (95% CI, 0.58-0.77), with heterogeneity observed between studies (P=.06).

"Antidepressants and various psychological therapies effectively treated symptoms of IBS.."

Cognitive behavioral therapy, relaxation therapy, hypnotherapy, multicomponent psychological therapy, dynamic psychotherapy, meditation therapy and stress management were among the 30 articles comparing psychological therapies with controls (n=2,189). Controls received symptom monitoring, "usual management" or supportive therapy. A pooled 51.9% of therapy groups reported unimproved symptoms compared with 76.1% of controls.

The RR of symptoms that failed to improve with psychological therapy vs. controls was 0.68 (95% CI, 0.61-0.76); heterogeneity was observed between studies (P<.001).

What you need to know: Antidepressants and many of the psychological therapies studied have shown to be beneficial in IBS. The use of antidepressants by gastroenterologists should be encouraged and efforts to improve access for both patients and physicians to psychological therapies should be promoted.

Source: 1. Ford AC. Am J Gastroenterol. 2014;doi:10.1038/ajg.2014.148.

Jihan Safwan, PharmD.

I CAN'T SMELL!! I MIGHT HAVE ALZHEIMER'S DISEASE

Major point: Two new studies link impaired olfactory function to elevated brain amyloid and greater neurodegeneration in cognitively normal adults, as well as progression to Alzheimer's disease (AD), among patients with mild cognitive impairment (MCI).

Finer points: The findings suggest testing olfactory function may be a useful screening biomarker in the diagnostic work-up for AD in patients at risk for dementia. Previous research has shown that regions of the brain that process odor input, including the olfactory bulb and entorhinal cortex, are particularly susceptible to AD pathology, and are affected at early stages of the disease. Building on this, there has been interest in the field to develop clinical tests of odor identification.

Most notably, the one we're talking about today is the University of Pennsylvania Smell Identification Test, or UPSIT [Sensonics Inc], which is a very low-cost, easy-to-administer, 40-item scratch-and-sniff test that can be used easily in the clinic. In 1 study, the researchers looked at whether there was an association between olfaction, memory performance, and biomarkers of neurodegeneration and amyloid deposition in clinically normal individuals participating in the Harvard Aging Brain Study. The sample includes 215 community-dwelling individuals aged 64 to 88 years, who undergo annual testing, including comprehensive neuropsychological testing, hippocampal volume and entorhinal cortex thickness — both structures important for memory and both measured using MRI — and amyloid burden using Pittsburgh Compound B positron emission tomography (PET).

Among all the individuals in their study, smaller entorhinal cortex and hippocampal size were associated with worse odor identification using the UPSIT tool, and worse memory. These were statistically significant and modest effects.

What you need to know: In the face of the growing world-wide Alzheimer's disease epidemic, there is a pressing need for simple, less invasive diagnostic tests that will identify the risk of Alzheimer's much earlier in the disease process. It's not yet "ready for prime time," and more longitudinal follow-up is required to confirm that poor olfactory performance does translate to higher AD risk.

Source: Jeffrey, S. Loss of Smell linked to brain abnormality, transition to AD. www.medscape.com/viewarticle/828189

Jihan Safwan, PharmD.

HOW MUCH ALCOHOL IS TOO MUCH?

Major point: Drinking alcohol, even light to moderate consumption, appears to be associated with an increased risk of developing atrial fibrillation (AF), according to a new analysis.

Finer points: Among individuals who drank between 15 and 21 drinks per week and those who drank more than 21 drinks in a week, the risk of AF was increased 14% and 39%, respectively, when compared with nondrinkers. Binge drinking, defined as having five or more drinks on any one occasion, was associated with a 13% higher risk of developing AF regardless of how many drinks were consumed in the week.

The risk of AF was also increased among those who consumed just one to two drinks per day, or seven to 14 drinks per week. Among those who drank lightly and who had no coronary heart disease or heart failure at baseline, the risk of atrial fibrillation was increased 12% compared with nondrinkers. However, in the entire cohort, which included those with baseline heart disease, the risk of atrial fibrillation was not elevated among the light drinkers.

Prospective Study plus Meta-Analysis

After 12 years of follow-up, there were 7245 incident cases of atrial fibrillation.

In addition to light and moderate alcohol consumption, the risk of AF was also observed among those who drank heavily. The relationship between alcohol consumption and AF remained even after excluding patients who were identified as binge drinkers. When stratified by the type of alcohol consumed, the relationship with AF was strongest for those who drank liquor, weaker for those who drank wine, and weakest for those who drank beer.

It has been pointed out that hypertension and obesity are two important risk factors that explain about 40% of the population-attributable risk for AF, but there is no explanation for the remaining 50% or 60%.

What you need to know: The present study supports the widely held contention that significantly elevated alcohol consumption, particularly binge drinking, is related to AF and should be avoided. The study also agrees with other prospective data suggesting that chronic levels of alcohol intake above two drinks per day may modestly elevate atrial fibrillation in men and women. Although there is a weak association with even less amounts of alcohol, this study does definitively answer how much alcohol is too much.

Source: O'Riodan, M. More bad booze news: even moderate drinking linked to AF. www.medscape.com/viewarticle/828211

Alcohol Drinking Status and Risk of Atrial Fibrillation

Drinks per week	Multivariable relative risk (95% CI)	Multivariable relative risk (95% CI)*
<1	Reference	Reference
1–6	1.01 (0.94–1.09)	1.06 (0.98–1.15)
7–14	1.07 (0.98–1.17)	1.12 (1.02–1.23)
15–21	1.14 (1.01–1.28)	1.18 (1.03–1.35)
>21	1.39 (1.22–1.58)	1.43 (1.25–1.65)

*Excludes patients with baseline coronary heart disease or heart failure

FACTS ABOUT PHARMACY

In the United States, pharmacists are an important part of the health care team. It's important to have someone face-to-face who can answer questions and tell you what to expect for the drug prescribed.

Check out these capsules:

$307 billion — Amount spent on medicines by Americans in 2010 — up to $60 billion since 2005.
54 % — Percentage of all prescriptions that are filled at retail pharmacies.
5,859 — Number of pharmacies that offer online services.
5 top-selling medications:

1. Lipitor - to reduce the risk of heart attack and stroke
2. Nexium - for gastroesophageal reflux disease
3. Plavix - to prevent stroke and heart attack
4. Advair Diskus - to treat asthma
5. Abilify - for mental disorders

$10.73 — Cost of an average patient prescription copay.
3.6% — Amount of average annual increase in retail prescription prices.
1852 — The year that the American Pharmacists Association, the first national professional society of pharmacists, was established.
78% — Percentage of all prescriptions that are filled in the generic form.
70% — Average savings on cost of generic medications purchased online versus a 30 percent savings on name brand prescriptions purchased online.
269,900 — Number of pharmacists in the U.S.

FUN FACTS ABOUT PHARMACY

1. According to Chinese legend, the benefits of acupuncture were discovered when a soldier who had suffered from a stiff shoulder for many years was cured when an enemy arrow hit him in the leg!
2. Mithridates the Great of Pontus (a region of Persia) was in constant battle with Rome. Because he feared being poisoned, he would concoct different poisons and swallow them himself to build up a resistance. When the day came that he actually wanted to kill himself, he tried to poison himself, but it wouldn't work.
3. Paracelsus was actually born Philippus Theophrastus Aureolus Bombastus von Hohenheim. He was a very high-spirited, independent and even rebellious individual, though he saw his father – a doctor/chemist – as a role model. Around 1516, when he graduated with his doctorate degree, he changed his name to Paracelsus because it translated to beyond/more than Celsus (a famous Roman physician).
4. Ever wonder where the name Listerine© came from? It's named after Joseph Lister who spread the word about using antiseptics in hospitals.
5. Here's some irony for you: Ignaz Semmelweis figured out that doctors need to wash their hands after performing an autopsy on another doctor who got sick from cutting his finger during surgery.
6. During the Black Plague, doctors wore amulets (charms) made of dried blood and ground up toads!
7. During World War II, Britain feared that the Germans would invade their country and consequently, get a hold of their penicillin. As a preventative measure, researchers smeared pocket linings with the penicillin mold to transport to the U.S.

ANNOUNCEMENTS

EVENTS

- The department of pharmaceutical sciences has organized two field visits to two industrial companies:

  May 16th 2014: Reviva Laboratory (Third year pharmacy students, Beirut campus)
  May 23rd 2014: Beesline (Third year pharmacy students, Bekaa campus)

- The faculty members at the school of pharmacy attended the 20th Pharmacy Day which was organized by the Order of Pharmacist in Lebanon. It took place in Le Royal Hotel in Dbayye on May 18th, 2014 under the title "The Profession of Pharmacy: Vision 2020." The SOP at LIU was represented by Dr. Marwan Akel as a member of the "Academia" committee, while Dr. Katia Iskandar as a member of the "Hopsital Pharmacy" committee.

- As part of the mission of the SOP, the extracurricular activities committee held a fundraising campaign for the Children Cancer Center of Lebanon (CCCL) on May 22nd, 2014. The event consisted of selling 500 golden ribbons for the CCCL. The mission was fulfilled through this event by raising awareness among the students and faculty members, getting involved in community work, and emphasizing on patient centered care.

- Under the patronage of the president of the order of pharmacists in Lebanon, Dr. Rabih Hassouneh, the school of pharmacy (SOP) at the Lebanese International University (LIU) organized its "9th Pharmacy Day" in Bekaa campus on May 31st, 2014. This Pharmacy Day was entitled: "Women and Children: Your Health… Our Mission", and it aimed at building a healthier society. The pharmacy day included multiple speeches from the attendees, a scientific exhibition of 35 student posters, and a fundraising campaign (bake sale) for "Dar al Hanan" for Orphans in Bekaa. Eventually, the mission of this annual traditional day was accomplished: "Together towards a healthier community."

- The organizing team of the "Pharmacy Day" arranged a gathering on June 3rd, 2014 for the distribution of certificates of participation to the students. Dr. Mohamad Rahal, the dean of the SOP, delivered a speech of gratitude to the students and the faculty members, and wished them prosperity and continuity in all their efforts.

- The extracurricular activities committee at the SOP is preparing for its "Annual Iftar" during the holy month of Ramadan, which will take place on July 16th, 2014.

Useful Links

Pharmacy-related

- LIU e-library: www.liu-elibrary.com
- Order of Pharmacists of Lebanon: www.opl.org.lb
- Ministry of Health: www.moph.gov.lb
- Scientific Association of Colleges of Pharmacy in the Arab World: www.asscph-aw.net
- U.S Food and Drug Administration: www.fda.gov
- Center for Disease Control and Prevention: www.cdc.gov

LIU Social Media

- Facebook: www.facebook.com/liu.edu.lb
- Youtube: www.youtube.com/lebintuni
- Twitter: @lebintuni
- Instagram: @lebintuni
- BBM: 25b43b71

The Scope

- Facebook: www.facebook.com/thescopeliu
- Youtube: www.youtube.com/thescopeliu
- Twitter: @thescopeliu