TOPIC IN THE NEWS

POLIOVIRUS OUTBREAK IN THE MIDDLE EAST
Nermine Chouman, PharmD.

Key point: Poliomyelitis (Polio) is a highly infectious disease that mainly affects children under five years of age. While endemic transmission is limited to three main countries (Nigeria, Pakistan and Afghanistan), an outbreak of polio has been detected in the Syrian Arab Republic in October 2013 after a 15 year absence (Table1).

Finer points: Polio is caused by poliovirus, a human enterovirus and member of the family of Picornaviridae. There are three serotypes of wild poliovirus, PV1, most commonly encountered, PV2, and PV3. By entering the body through the mouth, the virus multiplies in the throat and gastrointestinal tract, then invades the nervous system, and can cause total paralysis in few hours. Initial symptoms are fever, fatigue, headache, vomiting, stiffness in the neck, and pain in the limbs. Among those infected, some may develop a condition known as “Acute Flaccid Paralysis” (AFP) where breathing muscles become weak, poorly controlled and completely paralyzed.

On October, 17th, 2013, a cluster of 22 AFP cases was detected in Deir Al Zour province in the north-east of the Syrian Arab Republic. Following case investigations, stool samples were collected where 16 cases were confirmed positive for Wild Poliovirus 1 (WPV1) in predominately under-immunized young children aged less than 2 years. Genetic sequencing indicates that the isolated viruses are most closely linked to the virus detected in environmental samples in Egypt in December 2012 as well as Israel and the occupied Palestinian territory since February 2013. The occurrence of this outbreak reflects declining immunization rates due to the severe interruption of public health services and to the conditions in which the people are living. Moreover given the frequent population movements into neighboring countries, the variable immunization level in key areas and the prolonged period of undetected virus circulation in the region, a multi-country response is needed to contain and eliminate the outbreak.

Thus within 24 hours of confirmation that polio had returned to the Middle East, the ministers of health from across the Eastern Mediterranean declared this reinfection a public health emergency. The World Health Organization (WHO) and United Nations International Children’s Emergency Fund (UNICEF) have worked with each country in cooperation with ministries of health, Non-governmental Organization (NGOs), United Nations (UN) agencies and other partners to produce
national plans for this response. A large-scale awareness and vaccination campaigns across the Syrian Arab Republic and surrounding countries began in November and will last for at least six to eight months, depending on the area and based on the evolving epidemiology. According to the particular national immunization schedule, oral polio virus (OPV) and inactivated polio virus (IPV) are being administered. Bivalent and trivalent oral polio vaccines (bOPV, tOPV) are currently used to target all children aged fewer than 10 and 5 years respectively. Some campaigns also included measles and rubella vaccination along with polio. Additionally, WHO’s International Travel and Health recommends that all travelers to and from polio-infected areas be fully vaccinated against polio. Furthermore, to strengthen the national AFP surveillance system, detect epidemic threats early, monitor, respond and control outbreaks, an early warning and response system (EWARN) was established since 2012.

What you need to know: Lebanon has been polio free since 1994 although one case was reported in January 2003 and was found to be caused by a virus closely related to the strains circulating in India. However, given the high risk of virus expansion to regional countries and potentially beyond, global efforts are needed to tackle polio widespread by building and maintaining effective surveillance and immunization systems.

Table 1: Wild Poliovirus (WPV) cases worldwide (2013 – Present)

<table>
<thead>
<tr>
<th>Country</th>
<th>WPV cases</th>
<th>Country</th>
<th>WPV Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somalia</td>
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**NEW DRUG OF THE MONTH**

RIOCIGUAT IN PULMONARY ARTERIAL HYPERTENSION

Diana Malaeb, PharmD.

**Key point:** The US Food and Drug Administration (FDA) approved Riociguat (Adempas®) in October 2013 for the treatment of pulmonary arterial hypertension (PAH) and the treatment of chronic thromboembolic pulmonary hypertension (CTEPH).

**Finer points:** Specifically, Riociguat is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension after surgical treatment or inoperable CTEPH to improve exercise capacity. Riociguat is a vasodilator that restores the nitric-oxide–soluble guanylate cyclase-cyclic guanosine monophosphate (NO-sGC-cGMP) pathway by directly stimulating sGC independent of NO and sensitizing sGC to low levels of NO. Concomitant administration of Riociguat and nitrates, nitric oxide donors, or phosphodiesterase inhibitors is contraindicated. The recommended starting dosage of Riociguat is 1 mg taken three times daily, but therapy may be initiated at 0.5 mg three times daily if the patient is unlikely to tolerate the drug's hypotensive effects. Doses may be increased in 0.5-mg increments up to a maximum of 2.5 mg taken three times daily, if tolerated. At least two weeks should lapse between dose increases. The adverse events reported with this drug included headache, dizziness, gastrointestinal symptoms, and anemia. Rare but serious bleeding episodes, including a fatal incident of hemoptysis, also occurred during the clinical studies.

“Riociguat has the potential to overcome a number of limitations of currently approved PAH therapies”
**What you need to know:** With its novel mechanism of action, Riociguat has the potential to overcome a number of limitations of currently approved PAH therapies, including nitric oxide (NO) dependence, and is the first drug which has shown clinical benefits in CTEPH, where until the approval of Riociguat no pharmacological treatment was available.

**DRUG APPROVAL**

**SUCROFERRIC OXYHYDROXIDE APPROVAL DECREASES PILL BURDEN**

**Key point:** Hyperphosphatemia in chronic kidney disease (CKD) is associated with increased cardiovascular events and mortality. Thus, phosphate binders have been used as a treatment option to prevent or reduce hyperphosphatemia. Sucroferric oxyhydroxide (Velphoro®), also known as PA21, is a novel calcium-free polynuclear iron (III)-oxyhydroxide phosphate binder that has been approved by the FDA (November 2013) and is now available in the United States.

**Finer points:** Sucroferric oxyhydride when taken with meals adsorbs dietary phosphate, resulting in its elimination with feces and preventing its absorption into the circulation. The flavored tablets of 500mg should be chewed and taken 3 times daily with meals. Titration of sucroferric oxyhydroxide can start 1 week after treatment initiation. Serum phosphorus levels should be monitored regularly to keep it between 3.5 and 5.5mg/dL, with weekly decrements or increments of 500 mg (1 tablet) per day as needed.

The approval was based on a phase III study (that followed a phase I and a phase II study). Sucroferric oxyhydroxide was non-inferior to sevelamer in reducing serum phosphate levels, also a non-calcium containing phosphate binder.

Patients received PA21 1-3g/day (2-6 chewable tablets/day) or sevelamer 4.8-14.4g/day (6-18 tablets/day) for 24 weeks, that included titration and maintenance periods. Following week 24, the patients were re-randomized into a 3-week superiority analysis, which showed superiority of the maintenance dose (reached at week 24) over a low dose of 250 mg/day in maintaining serum phosphorus control.

Non-adherence was higher with sevelamer (21.3%) compared to PA21 (15.1%). Patients receiving dialysis face a high pill burden, with a median of 19 tablets/day, in which phosphate binders represent a median daily pill burden of nine. This promotes non-adherence and is therefore associated with hyperphosphatemia. In this study the pill burden remained higher with sevelamer than PA 21 over the whole trial period (mean of 8.1 vs. 3.1).

PA21 was however associated with higher treatment-emergent adverse events (TEAE) leading to withdrawal (15.7% vs. 6.6% for PA21 and SEV respectively). These were mostly gastrointestinal (GI) TEAEs, in particular diarrhea (20.1%), discolored feces (15.4%) and hyperphosphatemia (11.2%) for PA21. Also noted was a higher incidence of few severe (1%) or serious (0.3%) but not fatal TEAEs with PA21. There was an increase in iron parameters that plateaued on continuing treatment and therefore indicated no iron accumulation. This was explained by the use of IV iron by study participants.

“Sucroferric oxyhydroxide offers similar efficacy to sevelamer, with a lower pill burden and better adherence”

**What you need to know:** For patients with CKD on dialysis, the novel phosphate binder sucroferric oxyhydroxide offers similar efficacy to sevelamer, with a lower pill burden and better adherence. GI adverse effects are more likely to occur.

**Key point**: Diabetic foot ulcer is a principal cause of hospital admission for people with diabetes in the developed world and presents a high morbidity, often leading to pain, suffering, poor quality of life, and lower-leg amputations. In fact, diabetic foot ulcers readily become chronic, and chronic ulcers have biological properties that differ substantially from acute ones. Currently, diabetic foot ulcers are managed with bandages, therapeutic footwear, and hyperbaric chamber treatment. Novel therapeutic approaches are much needed in the treatment of diabetic foot ulcers, which still represent a major issue in people with diabetes.

**Finer points**: A novel treatment with polydeoxyribonucleotide (PDRN), an adenosine A2A-receptor agonist, nearly doubled the rate of complete healing of difficult-to-treat Wagner 1 or 2 diabetic foot ulcers compared with placebo, achieved earlier ulcer closure, and resulted in an “impressive” reduction in ulcer area as early as 8 weeks after the start of therapy, a new study indicates.

“In polydeoxyribonucleotide doubled the rate of complete healing of difficult-to-treat Wagner 1 or 2 diabetic foot ulcers...”

In a prospective, randomized, double-blind, placebo-controlled clinical trial, patients with chronic, hard-to-heal diabetic foot ulcers were recruited; half of them received placebo (n = 106) and the remainder PDRN (n = 110). The researchers ensured that all patients had adequate blood supply to the foot, to avoid the scenario whereby healing differences could be due to poor circulation. Participants were treated by daily intramuscular injection of PDRN (5.625 mg in a 3-mL vial), or placebo, for 5 days of the week and by the perilesional route (5.625 mg in a 3-mL vial), or placebo, for 2 days over a period of 8 weeks. The first perilesional administration was performed by an experienced physician in the hospital setting, and thereafter the subjects (or their caregivers) were carefully instructed to perform the perilesional and intramuscular treatment at home between each visit.

Among patients who completed the 8 weeks of treatment (101 PDRN and 91 placebo), complete ulcer healing was observed in 37.3% of those treated with PDRN compared with 18.9% of those who received placebo (P = .0027).

Closure of foot ulcers was twice as likely in patients on PDRN compared with placebo (hazard ratio, 2.20; P = .004), and the median time to complete wound healing was 30 days for patients on PDRN and 49 days for those on placebo (P = .0027). The median epithelialized area of the ulcers was also significantly greater in the treatment group, at 82.2%, vs 49.3% in patients on placebo (P = .001). No difference was observed between patient groups in the incidence of serious adverse events, indicating that PDRN is safe, at least in the treatment of diabetic ulcers.

**What you need to know**: Diabetic foot ulceration is a significant health issue and a challenge to manage. It appears, at first evaluation, that delivery of A2A-receptor agonists may result in a higher proportion of healing than placebo. This improvement suggests that this treatment deserves further investigation. Indeed, low oxygen levels at the wound site explain why hyperbaric oxygen therapy is effective, and hypoxia is also responsible for the up-regulation of adenosine A2A receptors, which make PDRN so effective because it activates adenosine A2A receptors, enhancing, in turn, new blood vessel formation.

**DALI STUDY: DEFINING ANTIBIOTIC LEVELS IN INTENSIVE CARE UNIT PATIENTS**

**Key point:** Morbidity and mortality for critically ill patients with infections remains a global healthcare problem. DALI study aimed to determine whether β-lactam antibiotic dosing in critically ill patients achieves concentrations associated with maximal activity and whether antibiotic concentrations affect patient outcome.

**Finer points:** This was a prospective, multinational pharmacokinetic point-prevalence study including 8 β-lactam antibiotics. Two blood samples were taken from each patient during a single dosing interval. The primary pharmacokinetic/pharmacodynamic targets were free antibiotic concentrations above the minimum inhibitory concentration (MIC) of the pathogen at both 50% (50% fT>MIC) and 100% (100% fT>MIC) of the dosing interval. Researchers used skewed logistic regression to describe the effect of antibiotic exposure on patient outcome. This study included 384 patients (361 evaluable patients) across 68 hospitals. The median age was 61 (inter-quartile range [IQR], 48–73) years, the median Acute Physiology and Chronic Health Evaluation II score was 18 (IQR, 14–24), and 65% of patients were male. Of the 248 patients treated for infection, 16% did not achieve 50% fT>MIC and these patients were 32% less likely to have a positive clinical outcome (odds ratio [OR], 0.68; P= .009). Positive clinical outcome was associated with increasing 50% fT>MIC and 100% fT>MIC ratios (OR, 1.02 and 1.56, respectively; P< .03), with significant interaction with sickness severity status.

**What you need to know:** According to this study, infected critically ill patients may have adverse outcomes as a result of inadequate antibiotic exposure; a paradigm change to more personalized antibiotic dosing may be necessary to improve outcomes for these most seriously ill patients.


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**CLINICAL PRACTICE**

**HYPONATREMIC MANAGEMENT: AN UPDATE**

**Key point:** Hyponatremia, defined as a serum sodium concentration of less than 135 mmol/L, is the most common disorder of body fluid and electrolyte balance encountered in clinical practice. A wide range of conditions can cause hyponatremia, including heart failure, nausea and vomiting, adrenal failure, and ectopic vasopressin secretion as part of a malignancy. As a result, it is managed by clinicians from a broad spectrum of backgrounds. This has resulted in a variety of approaches to its diagnosis and treatment.

**Finer points:** New guidelines on the diagnosis, classification, and treatment of true hypotonic hyponatremia have been published online in the European Journal of Endocrinology.

**Treat Serious Hyponatremia First. Avoid Overcorrection**

- Mild hyponatremia → Na+ levels between 130 and 135 mmol/L
- Moderate hyponatremia → Na+ levels between 125 and 129 mmol/L
- Profound hyponatremia → Na+ levels less than 125 mmol/L

If hyponatremia is serious and symptomatic:

- It is life-threatening because it can cause brain edema
- The first line of treatment will be prompt intravenous infusion of hypertonic saline, with a target increase of 6 mmol/L over 24 hours (and not exceeding 12 mmol/L) and an additional 8 mmol/L during every 24 hours.
thereafter until the serum sodium concentration reaches 130 mmol/L

• Watch out for overcorrection, because it represents a real danger too because it can result in osmotic demyelination syndrome (ODS), which has disastrous consequences for the brain that may persist for the rest of life.

Guidelines Stress Measures of Urine Osmolarity and Urine Sodium

Once symptomatic hyponatremia is under control, the next issue is to investigate the underlying cause of hyponatremia. People see hyponatremia as a lack of sodium, whereas instead it is an excess of water. Patients can have low, normal, or high sodium for the body, but relative to that there is too much water on board.

To figure out the underlying cause of hyponatremia, clinicians must perform 2 simple measurements including osmolality and urine sodium.

- If urine osmolality is low (<100 mOsm/kg), this is usually caused by the body taking on too much water (either by overdrinking or low electrolyte infusions)
- If urine osmolality is too high, however, (defined as being higher than normal serum osmolality, at around 275 mOsm/kg), the cause of hyponatremia is another reason, such as too much vasopressin
- If urine osmolality is higher than 100 mOsm/kg and urine sodium concentration is 30 mmol/L or less, low effective arterial volume may be a cause of the hyponatremia
- If urine sodium concentration is greater than 30 mmol/L, extracellular fluid status and diuretic use should be assessed

First-line Treatment is Water Restriction; then Urea. No “Vaptans”

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) constitutes about 40% of hyponatremia cases.

For patients with SIADH and moderate or profound hyponatremia:

- First-line treatment should be fluid restriction
- Equal second-line treatments are increasing solute intake with 0.25–0.50 g/kg per day of urea or a combination of low-dose loop diuretics and oral sodium chloride
- For those with reduced circulating volume, extracellular volume should be restored with intravenous infusion of 0.9% saline or a balanced crystalloid solution at 0.5 to 1.0 mL/kg per hour
- In case of hemodynamic instability, the need for rapid fluid resuscitation outweighs the risk of an overly rapid increase in serum sodium concentration (overcorrection)
- Avoid lithium or demeclocycline
- Do not recommend the use of vasopressin receptor antagonists, known as the “vaptans”. They include tolvaptan, conivaptan, lixivaptan, and satavaptan. Some of these are approved for use in SIADH, while others have hit hurdles. The guidelines have reviewed all the clinical-trial evidence with the vaptans and have found that overcorrection can occur with their use. This overcorrection can have dire clinical consequences in the form of osmotic demyelination syndrome. In addition, the guidelines determined that there are no good outcomes data with vaptans.

What you need to know:

- Treat serious hyponatremia first and avoid overcorrection
- Guidelines stress on the measurement of urine osmolality and urine sodium
- In SIADH, the first-line treatment is water restriction; then urea. Guidelines do not recommend the use of “Vaptans”

Macitentan in the Treatment of Pulmonary Arterial Hypertension

**Key point:** Pulmonary arterial hypertension (PAH), a severe disease characterized by a sustained elevation of pulmonary vascular resistance, ultimately leads to right heart failure and death. Disease progression occurs despite the availability of drugs that are specific for the disorder.

**Finer points:** Initial therapy should be directed at the underlying cause of the PAH, along with the assessment for the need for diuretics, oxygen, and anticoagulant therapy. Patients should undergo a vasoreactivity test with either inhaled nitric oxide or systemic epoprostenol (prostacycline analogue). Patients, who have a positive vasoreactivity test, should be started on calcium channel blocker (CCB) therapy with a dihydropyridine agent.

Other treatment options include: endothelin-receptor antagonists, phosphodiesterase type 5 inhibitors, and prostacyclin analogues. All of the above mentioned treatments have been approved for the treatment of PAH and adopted clinically on the basis of short-term trials (12 to 16 weeks) that have shown improvements in exercise capacity as measured by the distance walked in 6 minutes.

The dual endothelin-receptor antagonist Macitentan was developed by modifying the structure of Bosentan to increase efficacy and safety. In the Study with an Endothelin Receptor Antagonist in Pulmonary Arterial Hypertension to Improve Clinical Outcome (SERAPHIN), oral Macitentan was compared to placebo in 250 patients with moderate to severe PAH (WHO functional class II-IV). Over a two-year period, fewer patients treated with Macitentan (3 mg or 10 mg daily) progressed or died on therapy (38 and 31 percent versus 46 percent). This benefit was observed independent of whether patients were receiving additional advanced oral therapy for PAH. Exercise capacity and WHO functional class also improved with Macitentan treatment. The degree of liver dysfunction was the same between treatment and placebo groups and adverse events associated with Macitentan compared to placebo were headache, nasopharyngitis, and anemia.

**What you need to know:** PAH is a life-threatening disease with very fast progression and limited therapeutic options. Treatment includes agents that are not only associated with severe side effects, but also none of the previous agents have proven to decrease mortality in patients with PAH. Macitentan, a new endothelin receptor antagonist, was compared with placebo in patients with moderate to severe PAH, and has showed to decrease mortality and morbidity with minimal side effects profile.

FOCUS ON

PEDIATRIC DISORDERS

LOW BIRTH WEIGHT: AN EFFECT FOR LIFE

Key point: The World Health Organization (WHO) defines low birth weight as weight at birth of less than 2,500 grams. This definition was based on epidemiological observations that showed that infants weighing less than 2,500 g are approximately 20 times more likely to die than heavier babies. Worldwide, there is a significant variation in the incidence of low birth weight across regions. In fact, it is more common in developing than developed countries, where it accounts for 17% of all births in the developing world versus only 7% in industrialized countries; this reflects that most likely these babies are born in poor socio-economic conditions. Regionally speaking, 15% of infants are born with low weight in the Middle East, where in Lebanon it accounts for 12%. The most important question is: How can it matter many years later that a person was born small?

Finer points: In the beginning of the 80’s, the English epidemiologist David Barker formulated a hypothesis proposing that many events such as under-nutrition and other insults that occur during the intrauterine life and early postnatal life can permanently change the body’s structure, physiology and metabolism and thus influence the occurrence of many diseases during adulthood. Later on in the 90’s, Lucas suggested the term “Fetal Programming” to describe the process by which an adverse event happening at a critical period of development, can have a lifelong significance. Therefore, a low birth weight can contribute to a wide range of poor health outcomes. During the newborn period, these babies present increased risk of hypoglycemia, hypothermia, hypotension, respiratory distress syndrome… and are at a higher risk of dying during their early months and years. Later in life, many epidemiological studies have confirmed the link between low birth weight and the development of adult diseases such as metabolic syndrome, insulin resistance, type 2 diabetes, mortality by ischemic heart diseases, hypertension, dyslipidemia, obesity…

Recently, researchers from Oregon State University and Oregon Health & Science University published in the European Journal of Pharmacology a research indicating another concern related to low birth weight, where they showed that it may not only cause increased risk of diseases, but rather extend to lessen the effectiveness of the drugs used to treat those diseases and thus complicating disease management. This places low birth weight as a permanent factor that affects a person’s lifetime response to drugs. They state that low birth weight affects the development of organs, such as the kidney and thus impairs its ability to filter and excrete drugs. As a result, one might think that low birth weight individuals always have an increased drug response but what sometimes happens is the contrary due to the fact that the biologic impact of a medication is not only affected by its excretion but also by its absorption and metabolism.

What you need to know: In conclusion, certainly additional studies are needed, however if they came to confirm these results, we might see drug dosages modified according to birth weight status in the future.

FOCUS ON

BARIATRIC SURGERY

Marwan Akel, PharmD.

DRUG CONSIDERATION IN BARIATRIC SURGERY PATIENTS (II)

Key point: In the previous issue of the SOP Newsletter (January 2014; Vol 1, issue 4), we have tackled the resultant pharmacokinetic and pharmacodynamic changes due to bariatric surgeries. As has been discussed, those changes may warrant a manipulation in the route or dose of many drugs, in order to ensure adequate delivery. In this issue, we will be discussing the use of a number of those drugs having special considerations post bariatric surgeries.

Finer points: There is a long list of drugs that can be discussed in this notion. Yet we managed to select a number of drugs that have been discussed in much of the literature. Those medications include: drugs with long absorptive phases, non steroidal anti inflammatory drugs, oral bisphosphonates, sulfonylureas and meglitinides, and oral contraceptives.

• Drugs with long absorptive phases that remain in the intestine for extended periods are likely to exhibit decreased bioavailability in patients who have undergone mal-absorptive procedure (Roux-en-Y and Duodenal switch). Therefore, products with prolonged dissolution times, such as extended-release formulations, should be avoided in this population. These same principles can also apply to delayed-release and enteric- or film-coated dosage forms. So it is preferred to give immediate release formulations for this category of patients.

• The reduced size of the stomach after surgery can place patients at risk for adverse events with some medications. To note is the scenario of gastric ulceration with the use of a non steroidal anti inflammatory drugs. Most bariatric surgery centers recommend that patients avoid the use of these agents. But given the lack of primary literature on this topic, the risks and benefits of daily aspirin therapy should be considered on an individual basis. If oral pain medications are required, other options may include acetaminophen, opioids, and tramadol.

• The oral bisphosphonates are another class of medications that could present problems due to a reduced pouch size, which may increase the risk of gastrointestinal ulceration. Since these patients can be at risk for osteoporosis along with the decrease in calcium absorption, other treatment options, such as calcitonin, synthetic parathyroid hormone (teriparatide), raloxifene and HRT, should be considered.

• Post-op hypoglycemia and decreased insulin needs is very common after bariatric surgeries. Oral sulfonylureas and meglitinides should be discontinued postoperatively as these medications may lead to hypoglycemia. Metformin is the safest oral drug in the postoperative period, since it is not associated with fluctuations in blood glucose.

• Although data on the effect of bariatric surgery on fertility is limited, it is well established that weight loss can improve fertility. Since oral contraceptives (OCs) may be subject to extensive first-pass metabolism and enterohepatic circulation, absorption and efficacy may be reduced in bariatric surgery patients. Given the potential for increased fertility and decreased OC efficacy and the paucity of clinical data, it is preferred to use an alternative method of contraception other than COCs.

What you need to know: Pharmacists are important members of the bariatric surgery healthcare team. They may provide care and expertise pre-, peri-, and post-surgery. Some medications may need to be changed after surgery as shown in the above cases.

FOCUS ON

ONCOLOGIC DISEASES

Etwal Bou Raad, PharmD.

UPDATES IN IMMUNIZATIONS IN HEMATOPOIETIC CELL TRANSPLANT CANDIDATES AND RECIPIENTS

Key point: Prevention of infection is of paramount importance to the ever-increasing population of patients who have impaired immunity, such as those who have undergone hematopoietic cell transplantation (HCT).

Finer points: Infection in these patients often results in excessive morbidity and mortality, and antimicrobial therapy is typically less effective than in the immunocompetent host. Although immunization appears to be an obvious way to prevent infection, many patients with impaired immunity are unable to mount a protective immune response to active vaccination. Furthermore, immunization with live virus vaccines may result in unchecked proliferation of attenuated strains. Although the 2009 guidelines make recommendations regarding the optimal time to initiate each of the vaccine series following HCT, no recommendations were made regarding dosing intervals when more than one dose is required, given the lack of data regarding this issue. However, European guidelines from the year 2005 made recommendations regarding dosing intervals. In 2013, the IDSA published guidelines for vaccination of immunocompromised hosts, including HCT recipients.

What you need to know: The table below summarizes the different vaccines required pre- and post- HCT.

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<thead>
<tr>
<th>Vaccine</th>
<th>Pre-HCT</th>
<th>Post-HCT</th>
<th>Vaccine</th>
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<td>Haemophilus influenzae b conjugate</td>
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<td>R; 3 months; 3</td>
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<td>XΔ</td>
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<td>Hepatitis A</td>
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<td>R•¥: age 50 to 59 years*</td>
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*What you need to know: The table below summarizes the different vaccines required pre- and post- HCT.
**FOCUS ON**

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<tr>
<th>Vaccine</th>
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<th>R; 3 months; 3 doses</th>
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<td>DTaP, DT, Td, Tdap</td>
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<td>R◊</td>
<td>R; ≥12 months post if no GVHD</td>
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</tbody>
</table>

**DT**: diphtheria toxoid, tetanus toxoid; **DTaP**: diphtheria toxoid, tetanus toxoid, acellular pertussis; **GVHD**: graft-versus-host disease; **HCT**: hematopoietic cell transplant; **R**: recommended - administer if not previously administered or current; such patients may be at increased risk for this vaccine-preventable infection; **Td**: tetanus toxoid, reduced diphtheria toxoid; **Tdap**: tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis; **U**: usual - administer if patient not current with recommendations for dose(s) of vaccine for immunocompetent persons in risk and age categories; **X**: contraindicated.  

* Indicates recommendation for a course of action that deviates from recommendations of the Advisory Committee on Immunization Practices, United States Centers for Disease Control and Prevention (CDC).

- These live vaccines should not be administered unless the vaccine is otherwise indicated based on the annually updated CDC recommendations AND the patient is not immunosuppressed AND there will be an interval of ≥4 weeks prior to transplant.
- Δ Administer to adolescents and adults (strong, low) and to children (strong, moderate) if measles seronegative, the timing is ≥24 months after transplant, no GVHD is present, and the patient is not receiving immunosuppressive medication. Two doses should be administered.
- ⊹ If not previously administered.
- § Administer if varicella seronegative, the timing is ≥24 months after transplant, no GVHD is present, and the patient is not receiving immunosuppressive medication. Two doses should be administered (strong, low).
- ¥ Consider if the patient is not severely immunosuppressed AND the patient is varicella immune as defined by documentation of age-appropriate varicella vaccination, serologic evidence of immunity, documentation of varicella or zoster infection, or birth in the United States before 1980[1] AND there will be an interval of ≥4 weeks prior to transplant.


### ALTERNATIVE MEDICINE

**TIANQI, A CHINESE MEDICINE FOR THE PREVENTION OF DIABETES TYPE 2**

**Key point:** Tianqi is a Chinese medicine composed of 10 different herbs that is used for the treatment of diabetes mellitus type 2 (DMII). In these patients, it has been shown to reduce hemoglobin A1C and blood glucose levels. However, the effect of Tianqi in preventing the progression of impaired glucose tolerance (IGT) to DMII has not been evaluated in a well-designed trial.

**Finer points:** Researchers conducted a double-blind, randomized, placebo-controlled, parallel-group, multicenter trial that included 420 patients in China with IGT to determine if use of Tianqi capsules would prevent progression to type 2 diabetes or restore normal glucose tolerance. IGT was defined as having a 2-hour plasma glucose concentration of 7.8 mmol/L to 11.1 mmol/L (i.e., 140.4 mg/dL to 199.8 mg/dL) after a 75-g oral glucose tolerance test and fasting plasma glucose...
greater than 7.0 mmol/L (i.e., 126 mg/dL). Patients with IGT were randomized to take five Tianqi or five placebo capsules three times daily before each meal for 12 months (n = 210 in each group). All patients were given lifestyle guidance at baseline and every 3 months for the duration of the study.

“...reduced the risk of diabetes”

Of the 389 patients who completed the study, 18.2% of those in the Tianqi group (n = 36/198) and 29.3% of those in the placebo group (n = 56/191) developed diabetes (emP/em = 0.01). In addition, more patients in the Tianqi group developed normal glucose tolerance compared with the placebo group (63.1% vs. 46.6%, emP/em = 0.001). After adjusting for age and sex, the analysis showed that the use of Tianqi capsules reduced the risk of diabetes by 32.1% compared with placebo (hazard ratio, 0.679; 95% CI, 0.471–0.979). No significant differences were observed between groups with respect to adverse events or changes in body weight or body mass index. Six patients in the Tianqi group and nine individuals in the placebo group reported gastrointestinal events such as nausea, flatulence, constipation, and/or diarrhea.

The overall risk reduction for diabetes observed in this trial with the use of Tianqi capsules was similar to that achieved by acarbose (25%) and metformin (31%). Long-term use of antidiabetic medication is often avoided in the preventive setting because of the potential for adverse events, these researchers noted. Tianqi capsules may be a potentially safe alternative for prevention of type 2 diabetes in patients with IGT.

What you need to know: The use of a traditional Chinese medicine, Tianqi, reduced the risk of diabetes by almost one-third compared with placebo in Chinese patients with over a 12-month period. While these study results are promising, pharmacists should caution patients that, more data are needed on efficacy and long-term safety of Tianqi. Additional studies with more diverse demographics and longer follow-up times would also be helpful to confirm findings from this trial.

Source: Lian F et al. Chinese herbal medicine Tianqi reduces progression from impaired glucose tolerance to diabetes: a double-blind, randomized, placebo-controlled, multicenter trial. J Clin Endocrinol Metab. 2014;99:[Epub ahead of print]

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**FOCUS ON**

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**NUTRITION NEWS**

**MEDITERRANEAN DIET PROTECTS AGAINST DIABETES REGARDLESS OF WEIGHT LOSS**

**FOCUS ON**

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study concluded that long-term adherence to a Mediterranean diet supplemented with olive oil without energy restriction resulted in a substantial reduction in the risk for type 2 diabetes among older people with high cardiovascular risk.

**What you need to know:** In short, a Mediterranean diet enriched with extra-virgin olive oil but without energy restriction reduces diabetes among persons with high cardiovascular risk, and provides a useful insight into the nutraceutical/dietary prevention of type 2 diabetes mellitus.

This represents an added value to its well-known effects on lipid profile and protecting against cardiovascular disease.


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### WHY PHARMACISTS SHOULD HAVE A BUSINESS PERSPECTIVE

**Key point:** Recognizing the functional areas of business and making them fit into their proper places is a way of running a business both efficiently and effectively. While the functions of business can be categorized in many ways, the most important ones to pharmacy can be grouped as: accounting, finance, human resource management, operations management and marketing.

**Finer points:** Thus a pharmacist, as a manager, must understand these functions and how they interact.

- Accounting function involves monitoring and reporting on the pharmacy’s financial resources. It is used to keep track of the inflow-outflow process in monitory terms. It allows the manager to maintain an updated record of the current status of resources and what is available for use. In particular, it monitors and controls the cash position, expenses, the collections of receivables and the payment of liabilities and taxes to achieve its profits goals.

- Financial function includes determining financial needs of the pharmacy, identifying sources of funds and equity capital, obtaining needed capital, managing cash and receivables, and investing in the inventory.

- Human Resource function is essential in providing a high quality patient care and controlling costs of operations. Employees are the most direct contact between the pharmacy and the patients, thus they constitute the most valuable asset in the pharmacy. The pharmacist’s role is to find, hire, train, develop, motivate and retain the right personnel who will work in the pharmacy’s best interest over the long term.

- Operations Management function includes determining the pharmacy’s layout, identifying the jobs to be performed, in addition to defining and completing the workflow at the pharmacy. It develops an efficient method for purchasing products, and converting the inputs into outputs in the benefit of the patients.

- Marketing Management function is not about advertising and personal selling. It includes the assessment of the strengths and weaknesses of the pharmacy and the market, identifying competitors and target markets, developing an appropriate products/services mix, ensuring the availability of convenient products, pricing, and promoting the pharmacy in the best way to satisfy patients’ needs. Marketing also plays a role in building physician relations for referrals to improve patient care through drug therapy.

**What you need to know:** Accordingly, professional pharmacists are not the ones who only focus on the clinical aspects of their career; they must as well understand the business and economic environment within which they work to maximize patients’ satisfaction and personal success in the business.

ELECTRONIC CIGARETTE

WHY E-CIG? AND WHY NOT?

What is the E-Cig?
Electronic cigarette (e-cig or e-cigarette) / electronic vaping device / personal vaporizer (PV) / digital vapor device or electronic nicotine delivery system (ENDS)
Those are battery-powered devices, which simulate tobacco smoking, and have been patented in 1963 by Herbert A. Gilbert. They generally use a heating element known as an atomizer that vaporizes a liquid solution.

How does the E-Cig work?
The electronic cigarette (e-cig) was introduced to the U.S. market in 2007, and offers the nicotine-addict an alternative to smoking tobacco. Most “e-cigs” are similar enough in appearance to be mistaken for regular cigarettes, but one look inside and you’ll see the main difference: E-cigarettes don’t contain tobacco. Instead, those battery-operated products work by a mechanism that heats up liquid nicotine, flavors, and other chemicals, which turn into a vapor that smokers inhale and exhale. Currently unregulated, these products are aggressively marketed as a “safe” alternative to conventional tobacco products and as smoking cessation aids.

Is the E-Cig safe?
Far from claims that electronic cigarettes (e-cigarettes) may help curb conventional cigarette use in youth, new research suggests that these increasingly popular products may actually contribute to nicotine addiction, whereby it has been realized that there are high rates of dual use of e-cigarettes and conventional ones. This brings into question the products’ efficacy as cigarette substitutes and/or smoking cessation aids.

A large, cross-sectional study of US middle school and high school students showed that the use of e-cigarettes was associated with higher odds of ever or current cigarette smoking, higher odds of established smoking, higher odds of planning to quit smoking among current smokers, and, among experimenters, lower odds of abstinence from conventional cigarettes. Use of e-cigarettes does not discourage, and may encourage, conventional cigarette use among US adolescents.

While much remains to be learned about the public health benefits and/or consequences of ENDS use, their exponential growth in recent years, including their rapid uptake among youths, makes it clear that policymakers need to act quickly. Adopting the right mix of policies will be critical to minimizing potential risks to public health while maximizing the potential benefits.

Key Point: Major cancer organizations in English-speaking countries have collectively received millions of dollars and pounds in donations over the past 2 weeks as young women triggered an avalanche of donations through social media.

Finer Points: Women took smartphone pictures of themselves with no makeup, posted the “selfies” on Twitter and Facebook, and provided links to cancer research donation Web sites. The tweets were also done in the name of promoting cancer awareness.

Celebrities such as actress Gwyneth Paltrow and pop singer Beyoncé have participated with shots of themselves looking less glamorous than usual. Use of the hashtag #nomakeupselfie, which apparently involved no centralized organizing effort by charities, took on a life of its own. Hashtags provide a digital hub for Twitter users to follow whoever is involved in sending out photos or messages, known as tweets, under a particular rubric.

As of March 26, the campaign had raised £8 million ($13 million) for Cancer Research UK in London, according to that organization. The greatest charitable activity has been in the United Kingdom, but other national cancer organizations are also involved. Cancer Council Australia, the Canadian Cancer Society, and the Irish Cancer Society have all reportedly received donations through the #nomakeupselfie phenomena. The cancer organizations have been tickled pink by the flood of money.

The selfies started with American mystery author Laura Lippman. To show support for Kim Novak after the actress was criticized in social media for her looks on the televised Academy Awards in March, Lippman took a picture of herself with no makeup.

Other celebrities then took similar pictures, which somehow morphed into #nomakeupselfie. The campaign has been decried as narcissistic and shallow in some corners of the Internet. However, a number of commentators have observed that cosmetics might pose a health concern to cancer patients undergoing treatment, whereby, developing dry or sensitive skin during chemotherapy and radiation is common. Such skin changes can render wearing makeup challenging. Some cosmetics can irritate skin, and might pose a risk for infection, which is a concern for immunocompromised cancer patients. Thus the no-makeup selfies and cancer could actually have quite a deep connection.

What you need to know: The selfie campaign does not clearly articulate information about cosmetics, nor does it directly explain the relationship between selfies and cancer awareness. Maybe the photos are meant to express that beauty comes in all forms; maybe by taking off their makeup, by momentarily washing away an aspect of their own sense of self, these women are showing their solidarity for others who are experiencing so much more. Or, maybe it doesn’t matter — whether it’s running, walking, taking pictures, or growing facial hair, if the funds raised by these campaigns help make 187,600 annual cancer diagnoses a part of the past, then there’s a lot to be said for the madness in the method.

EVENTS

The faculty members of the school of pharmacy:

- Dr. Etwal Bou Raad participated in the “Arab Health Congress 2014 & Exhibition” that was held from the 27th till 30th of January, 2014 at the Dubai International Conventions and Exhibition Center.
- The dean, Dr. Mohamad Rahal, accompanied by the chair of the biomedical sciences department Dr. Fadi Hdaib, and the clinical coordinator Dr. Marwan Akel, travelled to LIU Yemen, Sana’a Campus to attend the clinical pharmacy week from the 9th till 13th of February, 2014.
- The dean, Dr. Mohamad Rahal, attended the meeting of the Executive Committee of the Scientific Society of the Colleges of Pharmacy in the Arab World, which took place on the 6th and 7th of March, 2014 in Umm Dorman University in Khartoum, Sudan.
- The SOP hosted a blood donation campaign entitled “Blood Drive” that took place on Thursday, April 3rd, 2014 from 9:00 AM to 3:00 PM in auditorium B1. This event was organized by the help of “Donner Sang Compter (DSC)” in partnership with Rafic Hariri University Hospital.
- The SOP organized 2 seminars:
  - “Capsugel: France”; presented by Dr. H. Nicolas Madit on Tuesday, February 25th, 2014 at Beirut campus
  - “Teaching Innovation And Learning Excellence”; presented by Dr. Shihadeh Nayfeh on Friday, March 14th, 2014 at Beirut Campus
- The dean, Dr. Mohamad Rahal, distributed certificates for students listed on the “Dean’s Honor List.”
- The SOP is preparing for the 9th Annual Pharmacy Day, which will take place in Bekaa Campus on Saturday May 24th 2014. This pharmacy day will be entitled “Women and Children: Your Health.. Our Mission.”

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