
Current and emerging therapies for type 2 diabetes mellitus, managing postoperative complications of anesthesia, reducing cardiovascular risk through the management of dyslipidemia, and optimizing immunization strategies for adult patients across the health system were the focus of four CE in the Mornings programs presented at the 47th ASHP Midyear Clinical Meeting and Exhibition in Las Vegas, Nevada, in December 2012. Archived versions of these programs are available on demand at the CE in the Mornings web portal (www.cemornings.com). One hour of continuing pharmacy education credit is available at no charge for each of the four programs. Membership in ASHP is not required. Recent developments in the four CE in the Mornings topics are described in an eNewsletter released in late January 2013 and this eNewsletter.

## DISPELLING OBESITY MYTHS AND PRESUMPTIONS

Weight loss through the use of a low-carbohydrate, low-fat calorie-restricted or Mediterranean diet, physical activity, and behavior modification is recommended by the American Diabetes Association for overweight or obese persons with or at risk for type 2 diabetes. These patients are bombarded by sometimes erroneous messages in the popular media and advice from well-intentioned but often misinformed friends and family members about how to lose weight through diet and exercise. Guidance from health care providers, including dietitians, may be based on beliefs that are unproved but widely accepted. Hearing the same message repeatedly or from multiple sources can reinforce false or unsubstantiated beliefs by clinicians as well as patients.

A special article identifying myths (beliefs with contradictory evidence), presumptions (beliefs without supporting scientific evidence), and facts about obesity based on a review of the popular media and scientific literature was published in the *New England Journal of Medicine* on January 31, 2013. Some of these facts pertain to the role of drug therapy and bariatric surgery in managing obesity. Health-system pharmacists should be aware of common myths and presumptions about obesity and endeavor to dispel patient misconceptions about the role of diet, exercise, behavior modification, and other interventions in losing weight. Patient education plays a vital role in the success of self-management efforts by patients with type 2 diabetes. Providing facts about dietary, exercise, pharmacotherapeutic, and behavior-modification strategies based on scientific evidence can help patients with diabetes who are overweight or obese achieve their weight loss goals.

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### Selected Myths about Obesity

- Small, sustained changes in energy intake or expenditure produce large, cumulative long-term weight changes
- Setting realistic goals in obesity treatment is important to avoid frustration, which can impede weight loss
- Large, rapid weight loss is associated with poor long-term weight outcomes compared with slow, gradual weight loss
- Assessing the stage of behavioral readiness for dietary change is important for success in losing weight
- A bout of sexual activity burns 100 to 300 kcal per person

### Selected Presumptions about Obesity

- Regularly eating breakfast instead of skipping it protects against obesity
- Increasing consumption of fruits and vegetables can result in weight loss or minimize weight gain, regardless of other behavioral or environmental changes
- Weight cycling (i.e., yo-yo dieting) increases mortality
- Snacking contributes to weight gain and obesity
- The built environment (e.g., availability of sidewalks for walking, parks for recreation) affects obesity

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### Selected Facts About Obesity

- Although genetic factors play a large role, obesity is not inevitable because environment also contributes to the problem
- Moderate environmental changes can promote as much weight loss as the most efficacious drug therapy currently available
- Dieting (i.e., reducing energy intake) is very effective for reducing weight, but it generally is not effective on a long-term basis
- Increasing the amount of exercise improves health, regardless of body weight or weight loss

### Additional Facts About Obesity

- Physical activity or exercise in a sufficient amount promotes long-term weight maintenance
- Continuation of conditions that promote weight loss facilitates maintenance of weight loss
- Provision of meals and use of meal-replacement products promote weight loss
- Some drug therapies facilitate clinically-meaningful weight loss and maintenance of the loss
- In certain patients, bariatric surgery results in long-term weight loss and reduces the rate of incident diabetes and mortality

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# PREVENTING OPIOID-INDUCED RESPIRATORY DEPRESSION

Opioid analgesics play a vital role in managing postoperative pain. However, these drugs are a common cause of adverse effects in hospitalized patients, and opioid-induced respiratory depression is among the most serious adverse effects. Opioid-induced respiratory depression is a decrease in the effectiveness of the ventilatory function after opioid administration. In severe cases, a breathing rate of 8-10 breaths per minute or even slower may be observed. Opioid-induced respiratory depression usually is preceded by advancing sedation and can lead to loss of consciousness and respiratory arrest.

Opioid-induced respiratory depression increases the length and cost of hospital stays. The incidence of opioid-induced respiratory depression in postoperative patients is approximately 0.5%, but it may be underreported. The opioid drug class, dosage, formulation, route of administration, duration of therapy, concomitant medication administration, and patient-specific characteristics are among the factors that affect the incidence of opioid-induced respiratory depression. The incidence of opioid-induced adverse effects may be increasing because of clinician efforts to improve the management of pain to meet The Joint Commission pain management standards. These standards were implemented in 2001 to address reports of inadequate pain control in postoperative patients and other patients with acute or chronic pain. In August 2012, The Joint Commission published a Sentinel Event Alert on the safe use of opioids in hospitals because of a large number of opioid-related adverse drug events in hospitals, including deaths, reported to the Joint Commission's Sentinel Event database between 2004 and 2011. In this Sentinel Event Alert, screening of patients for risk factors for opioid-induced respiratory depression is recommended:

- Older age (>60 years)
- Obesity
- Smoker
- Untreated obstructive sleep apnea or snoring
- Preexisting pulmonary or cardiac disease or dysfunction (e.g., chronic obstructive pulmonary disease, congestive heart failure) or major organ failure (e.g., kidneys)
- Upper abdominal or thoracic surgery or other surgical incision that impairs breathing
- Prolonged surgery or general anesthesia
- Concomitant administration of sedating agents (e.g., benzodiazepines, antihistamines, central nervous system depressants)
- No recent opioid use
- Increased opioid dosing requirement

The risk for opioid-induced respiratory depression is particularly high during the first 24 hours after surgery. Preoperative assessment of the patient's history of analgesic use or abuse, duration, and adverse effects is recommended by The Joint Commission to identify opioid tolerance or intolerance. An individualized multimodal treatment plan with nonpharmacologic interventions (e.g., ice) and nonopioid analgesics

 

(e.g., nonsteroidal anti-inflammatory drugs) should be used for postoperative pain management. The Joint Commission also recommends that clinicians consult a pharmacist (or pain management expert if available) when switching from one opioid analgesic to another or one route of opioid administration to another. Extra precautions when using opioid analgesics in opioid-naïve patients and at transitions of care also are recommended.

The following are suggested by The Joint Commission in its Sentinel Event Alert to avoid adverse events from opioids, including respiratory depression:

- Safe technology for opioid prescribing (e.g., computerized physician order entry systems to avoid error) and administration (e.g., patient-controlled analgesia to prevent overdose)
- Clinician education about the potential for sedation and respiratory depression from opioid analgesics, role of multimodal therapy in pain management, and recognition of advancing sedation during opioid therapy
- Patient and family member or caregiver education about proper use of opioid analgesics
- Effective standardized tools for screening patients for risk factors for excessive sedation and respiratory depression
- Policies and procedures for monitoring opioid analgesic therapy using serial assessment of the quality and adequacy of respiration and depth of sedation
- Use of pulse oximetry to monitor oxygenation (oxygen saturation) and capnography (end-tidal carbon dioxide) to monitor ventilation

*Collaboration among nursing and pharmacy staff may improve the success of efforts to avoid opioid-induced respiratory depression, which is a potentially serious postoperative complication.*

The American Society for Pain Management Nursing (ASPMN) has published guidelines on monitoring for opioid-induced sedation and respiratory depression. The frequency, intensity, duration, and type of monitoring should be individualized based on the patient's risk factors for opioid-induced respiratory depression and the analgesic drug regimen. Patients with signs of respiratory depression (e.g., slow breathing rate), poor respiratory effort or quality, evidence of advancing sedation, snoring or other noisy respiration, or oxygen desaturation should be aroused immediately and instructed to take deep breaths.

The ASPMN guidelines on monitoring for opioid-induced sedation and respiratory depression and the suggestions from The Joint Commission should help guide clinicians in developing strategies to prevent opioid-induced respiratory depression. Collaboration among nursing and pharmacy staff may improve the success of efforts to avoid this potentially serious postoperative complication.

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## STATINS

# POTENTIAL ANCILLARY BENEFITS

Statins are widely used to treat dyslipidemia because of their demonstrated benefits in reducing low-density lipoprotein cholesterol concentrations and cardiovascular events. Reports of benefits from statin therapy for a variety of other conditions were recently published. Some of these ancillary benefits have been attributed to pleiotropic effects that are independent of the lipid-lowering effects of the drugs, including anti-inflammatory, immunomodulatory, antioxidant, antiangiogenic, and antithrombotic effects.

In November 2012, the results of an analysis of statin use and mortality in patients 40 years of age or older with cancer identified in the Danish Cancer Registry were reported in the *New England Journal of Medicine*. Statin use at the time of cancer diagnosis was associated with a 15% reduction in death from cancer compared with patients who never used statins. A dose-response relationship was not observed. The effect of statins on cancer-related mortality was attributed largely to a reduction in cancer cell proliferation and migration due to reduced cholesterol availability.

In a matched case-control study of statin use by men who died of prostate cancer in New Jersey published in *Cancer* in August 2012, statin use was associated with a 51% reduction in the odds of dying of prostate cancer compared with matched control cases. The protective effect of statins was even greater (a 63% reduction) after controlling for education, waist size, body mass index, comorbid conditions, and antihypertensive medication use. There was little difference in the reduction in odds of prostate cancer death between hydrophilic statins (i.e., atorvastatin, fluvastatin, pravastatin) and lipophilic statins (i.e., cerivastatin, lovastatin, simvastatin), but a significantly greater reduction was associated with the high-potency statins atorvastatin, cerivastatin, and simvastatin (73%) than the low-potency statins fluvastatin, lovastatin, and pravastatin (31%).

A reduction in the risk for venous thromboembolism (VTE) from statin therapy has been suggested based on observations from clinical trials with primary endpoints other than VTE (i.e., studies in which VTE was reported as an adverse event). A meta-analysis of these studies

*The potential for ancillary benefits from statins may resonate with and promote adherence in patients who are appropriate candidates for statin therapy to manage dyslipidemia.*

 

published in *Public Library of Science Medicine* in September 2012 suggests that the effect of statins on VTE (if any) probably is small and it is no different when high-dose statin therapy is used instead of low-dose statin therapy. An accompanying editorial suggests that the effect of the statin with the highest potency, rosuvastatin, on risk for VTE may be greater than that of other statins, which would be consistent with other data suggesting that ancillary benefits from statins may depend on potency. Clinical trials in which VTE is an endpoint are needed to clarify whether there are differences among statins in their effect on risk for VTE.

The results of a prospective study of the effect of statin use on the development of Parkinson's disease in two large cohorts of American men and women who were followed for 12 years were reported in March 2012. Regular statin use was associated with a modest but significant 26% reduction in the risk for Parkinson's disease compared with statin nonuse. When the patients were stratified by age at the beginning of the follow-up period, the protective effect of statin use was significant only in participants less than 60 years of age (a 69% reduction in risk in this subgroup). The reduction in risk for Parkinson's disease in older participants (17%) was not significant. The protective effect of statins was attributed to anti-inflammatory and antioxidant effects.

Because influenza infection induces an immune response and immunomodulatory activity has been associated with statins, data from a Centers for Disease Control and Prevention population-based surveillance system were analyzed to determine whether statin use is related to influenza-related mortality in hospitalized patients. An analysis of 151 influenza-related deaths in 3071 adults hospitalized with laboratory-confirmed influenza during the 2007-2008 influenza season was published in January 2012. One-third of the patients were statin users. More than half of the patients (57%) had been immunized against influenza. Approximately one in four patients received antiviral therapy within the first 48 hours of hospitalization. Compared with statin nonuse, statin use was associated with a significant 41% reduction in the risk for influenza-related death after adjusting for age, race, comorbid conditions (cardiovascular, lung, and renal disease), influenza immunization, and use of antiviral therapy.

The findings from these and previous studies suggest a variety of potential ancillary benefits from statin use beyond reduction in risk for cardiovascular disease due to the pleiotropic and lipid-lowering effects of these drugs. Many of these potential benefits are attributed to anti-inflammatory activity. Clinical research is needed to clarify these benefits and determine whether there are clinically-relevant differences among the statins and between high- and low-dose statin therapy. The potential for ancillary benefits from statins may resonate with and promote adherence in patients who are appropriate candidates for statin therapy to manage dyslipidemia. Health-system pharmacists should clearly explain the uncertainty behind these possible ancillary benefits when answering questions from patients.

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UPDATED AND CLARIFIED

# ADULT PNEUMOCOCCAL IMMUNIZATION RECOMMENDATIONS

Pneumococcal pneumonia and invasive pneumococcal disease (IPD) are common causes of morbidity and mortality in the United States. Rates of adult immunization against these illnesses improved between 2010 and 2011 (the most recent year for which data are available), but the increases were small. In adults 19-64 years of age at high risk for these illnesses, the pneumococcal immunization rate increased by 1.6% to 20.1% in 2011. In elderly patients (age 65 years or older), a particularly vulnerable age group, the immunization rate was 62.3% in 2011, reflecting an increase from 2010 by 2.6%. The 2011 immunization rates are far below the goals established in Healthy People 2020 (60% for non-institutionalized high-risk adults 19-64 years of age, and 90% for the elderly). Further improvement is needed in immunization rates to stem the morbidity and mortality associated with pneumococcal pneumonia and IPD.

The Centers for Disease Control and Prevention Advisory Committee on Immunization Practices (ACIP) revised its recommendations for pneumococcal immunization of adults in June 2012. The 2013 recommended immunization schedule for adults released by ACIP in late January reflects these changes. Two pneumococcal vaccines are available. A 23-valent pneumococcal polysaccharide vaccine (PPSV23) traditionally has been used and continues to be recommended by ACIP for elderly persons, residents of nursing homes or long-term-care facilities, adults who smoke cigarettes, and adults 19-64 years of age with certain chronic diseases or conditions that increase the risk for IPD:

- Chronic lung disease (including chronic obstructive pulmonary disease, emphysema, and asthma)
- Chronic cardiovascular diseases
- Diabetes mellitus
- Chronic liver disease (including cirrhosis) and alcoholism
- Cochlear implants
- Cerebrospinal fluid leaks
- Immunocompromising conditions (e.g., chronic renal failure, nephrotic syndrome, malignancy, HIV infection, solid organ transplant)
- Functional and anatomic asplenia (e.g., sickle cell disease and other hemoglobinopathies, congenital or acquired asplenia, or splenectomy)

Revaccination with PPSV23 is recommended 5 years after the first dose (i.e., patients should receive two doses before the age of 65) in immunocompromised patients and patients with functional or anatomic asplenia, but not immunocompetent patients with chronic lung, heart, or liver disease; cirrhosis; alcoholism; diabetes mellitus; cigarette smoking; cerebrospinal fluid leaks; or cochlear implants. All adults should receive another PPSV23 dose at or after the age of 65 (if at least 5 years have elapsed since the most recent dose) regardless of underlying medical conditions or previous administration of the vaccine. Thus, some patients will receive three PPSV23 doses in their lifetime.

A 7-valent pneumococcal conjugate vaccine (PCV7) was used for primary immunization of infants and children until 2010 when the Food and Drug Administration (FDA) approved a new 13-valent pneumococcal conjugate vaccine (PCV13) that protects

 

against pneumococcal disease caused by a larger number of serotypes than PCV7. In late 2011, FDA approved PCV13 for prevention of pneumococcal pneumonia and IPD in adults 50 years of age or older based on immunogenicity studies, not pneumococcal pneumonia or IPD incidence data from clinical studies. The availability of PCV13 for use in adults has led to confusion among health-system pharmacists and other clinicians about the roles of PPSV23 and PCV13 in pneumococcal immunization of adults and questions about the number and timing of doses of the two vaccines. Clarification of the approach to pneumococcal immunization in adults is provided in the 2012 ACIP recommendations and the 2013 recommended adult immunization schedule.

ACIP now recommends routine one-time administration of PCV13 in addition to PPSV23 for adults 19 years of age or older with immunocompromising conditions (including chronic renal failure and nephrotic syndrome), functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants, although the recommendation does not extend to immunocompetent patients with chronic lung, heart, or liver disease; cirrhosis; alcoholism; diabetes mellitus; or cigarette smoking. This recommendation was made despite the lack of an FDA-approved indication for PCV13 use in adults 19-49 years of age, and it was based on immunogenicity studies in older patients.

The updated ACIP recommendations for adult pneumococcal immunization and the 2013 adult immunization schedule present several possible scenarios involving patients with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants and provides the recommended timing of PCV13 administration:

*Some patients will receive three PPSV23 doses for pneumococcal immunization in their lifetime*

- Patient has not received either the PCV13 or PPSV23 vaccine: give PCV13 followed by PPSV23 at least 8 weeks later (followed by another PPSV23 dose 5 years after the first PPSV23 dose in an immunocompromised patient or patient with functional or anatomic asplenia)
- Patient has received one or more PPSV23 doses: give PCV13 one or more years after the most recent PPSV23 dose. If an additional PPSV23 dose is required for an immunocompromised patient or patient with functional or anatomic asplenia, it should be given no sooner than 8 weeks after PCV13 and at least 5 years after the most recent PPSV23 dose.
- Patient has unknown or uncertain vaccine status: give PCV13 followed by PPSV23 at least 8 weeks later (followed by another PPSV23 dose 5 years after the first PPSV23 dose in an immunocompromised patient or patient with functional or anatomic asplenia)

Health-system pharmacists should routinely assess patient immunization histories and advise patients to obtain the immunizations recommended by ACIP. Immunizations should be documented in the patient medical record, and patients should be given a copy of the record.

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