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In This Issue…

- Obstructive Sleep Apnea
- FDA Approves Merck's Zinplava to Reduce Recurrence of Clostridium difficile Infection

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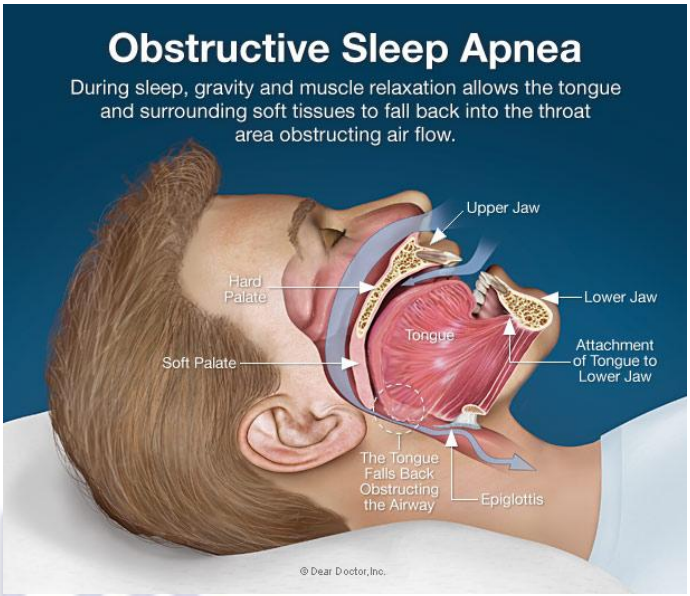
Obstructive Sleep Apnea



Obstructive sleep apnea (OSA) consists of episodes of partial or complete closure of the upper airway that occur during sleep and lead to breathing cessation (defined as a period of apnea > 10 sec). Most cases remain undiagnosed and untreated.
In at-risk patients, sleep destabilizes patency of the upper airway, leading to partial or complete obstruction of the nasopharynx, oropharynx, or both.

Obstructive sleep hypopnea occurs when breathing is diminished, even if it is not absent.
The prevalence of OSA is 2 to 9% in adults; the condition is under-recognized and often undiagnosed even in symptomatic patients. OSA is up to 4 times more common among men and 7 times more common among people who are obese (i.e., body mass index [BMI] > 30). Severe OSA increases the risk of death in middle-aged men.
OSA can cause excessive daytime sleepiness, increasing risks of automobile crashes, loss of employment, and sexual dysfunction. Long-term cardiovascular sequelae of untreated OSA include poorly controlled hypertension, heart failure, and atrial fibrillation (even after catheter ablation) and other arrhythmias.

Etiology

Anatomic risk factors which are common among obese people include:

- An oropharynx “crowded” by a short or retracted mandible
- A prominent tongue base or tonsils
- A neck circumference > 43 cm (> 17 in)
- Thick lateral pharyngeal walls
- A rounded head shape and a short neck
- Lateral parapharyngeal fat pads

Other identified risk factors include postmenopausal status, aging, and alcohol or sedative use. A family history of OSA is present in 25 to 40% of cases, perhaps reflective of heritable factors affecting ventilatory drive or craniofacial structure. The risk of OSA in a family member is proportional to the number of affected family members.
Acromegaly, hypothyroidism, and sometimes stroke can cause or contribute to OSA.

Because obesity is a common risk factor for both OSA and obesity-hypoventilation syndrome, the conditions frequently coexist.

Symptoms and Signs

Although loud disruptive snoring is reported by 85% of OSA patients, most people who snore do not have OSA. Other symptoms of OSA may include

- Choking, gasping , or snorting during sleep
- Restless and unrefreshing sleep
- Difficulty staying asleep

Most patients are unaware of these symptoms (because they occur during sleep) but are informed of them by bed partners, roommates, or housemates. Some patients may awake with a sore throat or a dry mouth.

When awake, patients may experience hypersomnolence, fatigue, and impaired concentration. The frequency of sleep complaints and the degree of daytime sleepiness do not correlate well with number of nocturnal arousals.

Diagnosis

- Symptom criteria
- Sleep studies

The diagnosis is suspected in patients with identifiable risk factors, symptoms, or both. Criteria for diagnosis consist of daytime symptoms, nighttime symptoms, and sleep monitoring that documents > 5 episodes of hypopnea and/or apnea per hour. Specifically, in regard to symptoms, there should be ≥ 1 of the following:

- Daytime sleepiness, unintentional sleep episodes, unrefreshing sleep, fatigue, or difficulty staying asleep
- Awakening with breath holding, gasping, or choking
- Reports by a bed partner of loud snoring, breathing interruptions, or both in the patient's sleep

The patient and any partners, roommates, or housemates should be interviewed. The differential diagnosis of excessive daytime sleepiness is broad and includes:

- Reduced quantity or quality of sleep due to poor sleep hygiene
- Sedation or mental status changes due to drugs, chronic diseases (including cardiovascular or respiratory diseases), or metabolic disturbances and accompanying therapies
- Depression
- Alcohol or drug abuse
- Narcolepsy
- Other primary sleep disorders (eg, periodic limb movement disorder, restless legs syndrome)
- An extended sleep history should be taken in all patients who
- Are age ≈ 65 or older
- Are overweight
- Report daytime fatigue, sleepiness, or difficulty staying asleep
- Have poorly controlled hypertension (which may be caused or exacerbated by OSA), atrial fibrillation or other arrhythmias, heart failure (which may cause OSA), stroke, or diabetes
- Most patients who report only snoring, without other symptoms or cardiovascular risks, do not need an extensive evaluation for OSA.

The physical examination should include evaluation for nasal obstruction, tonsillar hypertrophy, and pharyngeal structure and identification of clinical features of hypothyroidism and acromegaly.

Polysomnography is best for confirming the diagnosis and quantifying the severity of OSA. It records brain waves, the oxygen level in blood, heart rate and breathing, as well as eye and leg movements during the study.

The **apnea-hypopnea index** (AHI), which is the total number of episodes of apnea and hypopnea occurring during sleep divided by the hours of sleep time, is the common summary measure used to describe respiratory disturbances during sleep.

The **respiratory disturbance index** (RDI), a similar measure, describes the number of episodes of certain arousals related to respiratory effort plus the number of apnea and hypopnea episodes per hour of sleep.

An **arousal index** (AI), which is the number of arousals per hour of sleep, can be computed if EEG monitoring is used.

Prognosis

Prognosis is excellent if effective treatment is instituted.

Untreated or unrecognized OSA can lead to cognitive impairment as a result of sleeplessness, which, in turn, can lead to serious injury or death caused by accidents, especially motor vehicle crashes. Sleepy patients should be warned of the risks of driving,

operating heavy machinery, or engaging in other activities during which unintentional sleep episodes would be hazardous.
In addition, perioperative complications, including cardiac arrest, have been attributed to OSA, probably because anesthesia can cause airway obstruction after a mechanical airway is removed. Patients should therefore inform their anesthesiologist of the diagnosis before undergoing any surgery and should expect to receive continuous positive airway pressure (CPAP) when they receive preoperative drugs and during recovery.

How is Sleep Apnea Treated?

The treatment of choice for obstructive sleep apnea is **continuous positive airway pressure device (CPAP)**. CPAP is a mask that fits over the nose and/or mouth, and gently blows air into the airway to help keep it open during sleep. This method of treatment is highly effective. Using the CPAP as recommended by the doctor is very important.

Other methods of treating sleep apnea include: dental appliances which reposition the lower jaw and tongue; upper airway surgery to remove tissue in the airway; nasal expiratory positive airway pressure where a disposable valve covers the nostrils; and treatment using hypoglossal nerve stimulation where a stimulator is implanted in the patient's chest with leads connected to the hypoglossal nerve that controls tongue movement as well as to a breathing sensor. The sensor monitors breathing patterns during sleep and stimulates the hypoglossal nerve to move the tongue to maintain an open airway.

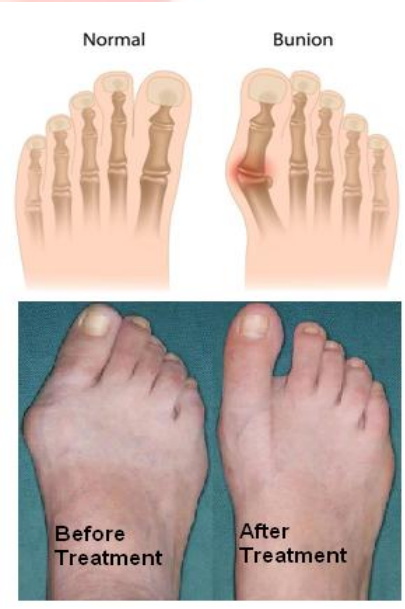
Lifestyle changes are effective ways of mitigating symptoms of sleep apnea. These include weight loss and smoking cessation. Some patients with mild sleep apnea or heavy snoring have fewer breathing problems when they are lying on their sides instead of their backs.

References:

1) www.merckmanuals.com/professional/pulmonary-disorders/sleep-apnea/obstructive-sleep-apnea
2) www.mayoclinic.org/diseases-conditions/sleep-apnea/basics/definition/con-20020286
3) emedicine.medscape.com/article/295807-workup#showall
4) sleepfoundation.org/sleep-disorders-problems/sleep-apnea-treatment
5) www.webmd.com/sleep-disorders/sleep-apnea/default.htm

Terminology

Hallux Valgus



Outward displacement of the great toe, which is always associated with a bunion. It is due to the pressure of footwear on an unduly broad foot. In adolescents, this broad foot is inherited; in adults it is due to splaying of the foot as a result of loss of muscle tone. The bunion is produced by pressure of the footwear on the protruding base of the toe. In mild cases the wearing of comfortable shoes may be all that is needed. In more severe cases the bunion may need to be removed, while in the most severe the operation of arthroplasty may be needed.

Source: Marcovitch H. *Black's Medical Dictionary.* 41th ed. London: A&C Black Publishers Limited. 2005.

Complementary Medicine
Pulsatilla (شقار الصفح)

Species (Family):
Pulsatilla vulgaris Mill. (Ranunculaceae)
Pulsatilla pratensis (L.) Mill.
Pulsatilla patens (L.) Mill.

Part(s) Used: Herb

Constituents
Flavonoids Delphinidin and pelargonidin glycosides.
Saponins Hederagenin (as the aglycone).
Volatile oils Ranunculin (a glycoside); enzymatic hydrolysis yields the unstable lactone protoanemonin which readily dimerises to anemonin.
Other constituents Carbohydrates (e.g. arabinose, fructose, galactose, glucose, rhamnose), triterpenes (e.g. β-amyrin) and β-sitosterol.

Herbal Use
Pulsatilla is stated to possess sedative, analgesic, antispasmodic and bactericidal properties. Traditionally, it has been used for dysmenorrhoea, orchitis, ovaralgia, epididymitis, tension headache, hyperactive states, insomnia, boils, skin eruptions associated with bacterial infection, asthma and pulmonary disease, earache, and specifically for painful conditions of the male or female reproductive system. Pulsatilla is widely used in homeopathic preparations as well as in herbal medicine.

Dosage: Dried herb 0.12–0.3 g as an infusion or decoction three times daily.

Pharmacological Actions
In vitro and animal studies
Utero-activity as an emmenagogue and antispasmodic has been documented for pulsatilla. In vivo sedative and antipyretic properties in rodents have been documented for anemonin and protoanemonin. Cytotoxicity has been reported for anemonin.

Side-effects, Toxicity
There is a lack of clinical safety and toxicity data for pulsatilla and further investigation of these aspects is required. Fresh pulsatilla is poisonous because of the toxic volatile oil component, protoanemonin. Protoanemonin rapidly degrades to the non-toxic anemonin. Inhalation of vapour from the volatile oil may cause irritation of the nasal mucosa and conjunctiva. Allergic reactions to pulsatilla have been documented and patch tests have produced vesicular reactions with hyperpigmentation.

Drug interactions
None documented. However, the potential for preparations of pulsatilla to interact with other medicines administered concurrently, particularly those with similar or opposing effects, should be considered.

Pregnancy and lactation
Pulsatilla is reputed to affect the menstrual cycle. Utero-activity has been documented for pulsatilla. In view of this, the use of pulsatilla during pregnancy and lactation should be avoided.

References: *1)* Barnes J, Anderson L A, and Phillipson J D. *Herbal Medicines,* 3rd ed. London: Pharmaceutical Press; 2007. 2) Hoffmann D. *MEDICAL HERBALISM: The Science and Practice of Herbal Medicine*. Vermont: Healing Arts Press; 2003.

1. The refrigerator in the pharmacy that is used for storage of pharmaceutical products should be kept at a temperature of:
   A. 0–3˚C B. 2–8˚C C. C. 5–10˚C
   D. 6–12˚C E. -3–8˚C

2. Which one of the following is suitable for the management of lower urinary tract infection in a pregnant woman?
   A. co-trimoxazole B. ciprofloxacin C. aztreonam
   D. co-amoxiclav E. doxycycline

3. The product that may be recommended safely for use by an infant with nasal congestion is:
   A. topical pseudoephedrine B. normal saline
   C. systemic pseudoephedrine D. cetirizine
   E. mefenamic acid

4. All of the following drugs affect the renin—angiotensin system EXCEPT:
   A. hydralazine B. valsartan C. losartan
   D. perindopril E. lisinopril

Clinical Nutrition

What are the main nutritional supplements & diet changes that can help patients with Parkinson's disease?

A low-protein diet helps the body use levodopa and carbidopa most efficiently, so limited protein in diet, eaten mostly during the evening hours rather than morning and afternoon might be suggested by the doctor. A fiber supplement may help prevent constipation, which is a common symptom of Parkinson disease.
Many supplements may interact with medications taken for Parkinson's, or may work only at particular doses. Therefore, any diet changes or supplements, even vitamins, should be done only by prescription and with the knowledge of all prescribing doctors.

- **Coenzyme (CoQ10).** Some studies suggest that taking high doses of CoQ10, a substance made by the body that helps cells get energy from oxygen, may slow the progression of Parkinson's in the early stages. However, not all studies agree. CoQ10 can promote blood clotting, and can interact with blood thinners such as warfarin, clopidogrel, or aspirin. CoQ10 may lower blood pressure, so in hypertensive patients, it could increase the risk of hypotension. It may also interact with some chemotherapy drugs.
- **Creatine.** Some studies suggest that taking creatine, an amino acid that helps supply energy to muscles, may help slow progression of Parkinson's among people who are in the early stages, and who do not need medication to control symptoms. In another study, creatine did not work as well for people with advanced disease. Creatine may also help people with Parkinson's get more benefit from resistance training. The doctor should know of any kidney problems before taking creatine.

- **Vitamin C and vitamin E.** In one study, high doses of these antioxidant vitamins helped delay the need for medication. But taking vitamin E alone did not seem to have the same effect. More studies are needed to know whether there is any real benefit. Vitamin E supplements can increase the risk of bleeding, especially with blood thinners.
- **Cytidinediphosphocholine, or CDP-choline.** Another substance made in the body that seems to increase dopamine levels. In one study, people who took 400 mg, 3 times per day were able to lower their levodopa dose.
- **Phosphatidylserine (PS).** A substance made by the body that is important to brain function. People with Parkinson's often have low levels of PS. One study showed that taking 100 mg of PS, 3 times per day improved mood and brain function in people with Parkinson's and Alzheimer-type dementia.
- **NADH.** NADH is the active form of vitamin B3, and helps raise levels of dopamine in the brain. Studies in Parkinson's have shown mixed results, and some have used injections rather than oral doses.
- **Vitamin D.** People with Parkinson disease often have low levels of vitamin D. Taking a supplement can help prevent osteoporosis.
- **Vitamin B6.** Has been used to treat Parkinson disease, but it is controversial. Vitamin B6 can make some Parkinson's medications less effective. Naturally-oriented physicians may use vitamin B6, to reduce the side effects of these medications.
- **Coffee** and **caffeine** may lower the risk and progression of Parkinson disease.
- **Fava beans.** Can have both good and bad effects in people with Parkinson's. Fava beans contain levodopa. For some people, getting more levodopa in their diet may help with symptoms. For others, it could cause an overdose.
- **Epigallocatechin-3 Gallate.** A of tea that has powerful neuroprotective effects.

Source: umm.edu/health/medical/altmed/condition/parkinsons-disease

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional healthteam as well as from others. Here's one of the enquiries received at the center:
Enquiry received from: Pharmacist A.A.- *Cardiac Hospital – Assiut Univ*ersity.
Enquiry: Can I store the remaining part of Adrenaline ampoule BP 1/1000 (1mg/1ml) after opening for future use?
Summary of the answer: **If only a part is** used, the remaining solution should be discarded. Epinephrine, epinephrine salts, and preparations containing the drug gradually darken on exposure to light and air and must be stored in tight, light-resistant containers.
Withdrawal of doses even from multi-dose vials intended for multidosing, introduces air, which results in oxidation. Discard solutions with a color that is pinkish or darker than slightly yellow or those contain a precipitate.

Commercially available preparations vary in stability, depending on the form in which epinephrine is present and on the preservatives used. Follow the manufacturer's directions with respect to storage requirements for each product. Visual inspection for colour changes may be inadequate to assess compatibility of epinephrine admixtures.

References:

1) Trissel L. *Injectable Drugs*. 17th ed. Bethesda: American Society of Health –System Pharmacists; 2013.
2) McEvoy G K. *AHFS Drug Information Essentials*. Bethesda: American Society of Health-System Pharmacists; 2011.
3) SPC (Adrenaline). Accessed via www.medicines.org.uk/emc/

FDA News

FDA Approves Merck's Zinplava (bezlotoxumab) to Reduce Recurrence of Clostridium difficile Infection

Company: Merck
Approval Status: Approved October 2016 and was based on two phase III trials.
Specific Treatments: recurrent Clostridium difficile infection in patients receiving antibacterial treatment

General Information
Zinplava (bezlotoxumab) is a human monoclonal antibody that binds to C. difficile toxin B and neutralizes its effect.
Zinplava is specifically indicated to reduce recurrence of Clostridium difficile infection (CDI) in patients 18 years of age or older who are receiving antibacterial drug treatment of CDI and are at a high risk for CDI recurrence.
Zinplava is supplied as an injection for intravenous infusion. The recommended dose is a single dose of 10 mg/kg administered as an intravenous infusion over 60 minutes. ***Zinplava*** must be diluted prior to intravenous infusion.

Side Effects
Adverse effects associated with the use of Zinplava may include, but are not limited to: nausea, pyrexia, and headache.
In addition, heart failure was reported more commonly in Zinplava-treated patients with a history of congestive heart failure (CHF) in the two Phase III clinical trials. In patients with a history of CHF, Zinplava should be reserved for use when the benefit outweighs the risk.

Mechanism of Action
Zinplava is a human monoclonal antibody that binds C. difficile toxin B with an equilibrium dissociation constant (Kd) of <1×10-9M. Bezlotoxumab inhibits the binding of toxin B and prevents its effects on mammalian cells. Bezlotoxumab does not bind to C. difficile toxin A.

Source: www.centerwatch.com

Answers:

1. B) The refrigerator in the pharmacy intended for the storage of pharmaceutical items should be kept at a temperature of between 2˚ and 8˚C.
2. D) Co-amoxiclav containing the β-lactam amoxicillin (penicillin) and the β-lactamase inhibitor clavulanic acid can be safely administered during pregnancy. Co-trimoxazole is contraindicated in pregnancy because of a teratogenic effect. The use of ciprofloxacin (quinolone) in pregnancy is contraindicated because of possible arthropathy in weight-bearing joints of the fetus. Aztreonam (monocyclic β-lactam antibiotic) is avoided in pregnancy. Doxycyline (tetracycline) is contraindicated because of deposition in the bones and teeth of the fetus.
3. B) Normal saline (0.9%) relieves nasal congestion by liquifying mucous secretions thereby acting as a nasal decongestant. It is safely recommended for use in infants. Topical administration of sympathomimetic nasal decongestants such as pseudoephedrine in infants may lead to irritation with narrowing of the nasal passages. Systemic use of the sympathomimetics increases the risk of side-effects, such as tachycardia, making systemic use of nasal decongestants all the more contraindicated in infants. Cetirizine is a non-sedating antihistamine. Antihistamines tend to be more effective in reducing rhinorrhoea and sneezing rather than nasal congestion. Mefenamic acid is a non-steroidal anti-inflammatory.
4. C) In response to the presence of antigenic stimuli, in seasonal allergic rhinitis (hay fever), mast cells and basophils are sensitised and inflammatory mediators, such as leukotrienes and prostaglandins, are released. Osteocytes are bone cells involved in bone formation.