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Feb 2006 "*New Drugs for ED*" 707-000-06-002-H01

THIS MONTH
"New Drugs
For ED"

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It's a new year. When you send in quizzes, always keep a copy. You may email or fax them. Fax # is 847-945-5037. Or send a conventional email with your answers. (info@wfprofessional.com).

Erectile dysfunction is a real problem, and now there are new drugs that are effective in its treatment. Our goal in this lesson is to discuss these therapeutic options. This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings.

The program ID # for this lesson is 707-000-06-002-H01.

Pharmacists completing this lesson by February 28, 2009 may receive full credit.

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

The objectives of this lesson are such that upon completion the participant will be able to:

1. Define ED & state its incidence.
2. List the possible causes of ED.
3. Describe the diagnosis for ED.
4. Comment upon newer drugs that are being used for treating ED.
5. Explain the mechanism of action of the PDE-5 inhibitors.
6. List the adverse effects & contraindications that are associated with the PDE-5 inhibitors.

To better understand the use of drugs in the management of erectile dysfunction (ED), we will begin with a review of physiology.

Physiology

The penis is the male organ that contains the urethra through which semen and urine are delivered. It consists mostly of sponge-like tissue that enlarges with blood following stimulation. Blood circulation is under pressure, and a number of valves keep the blood within the tissue in order to maintain erection. The increase in blood flow and prevention of blood from leaving are essential. The shaft ends in an enlarged cone-shaped tip known as the glans. It is composed of erectile tissue organized in three columns covered with loose skin. Corpus spongiosum surrounds the urethra and extends to the glans, while the corpora cavernosa are two lateral columns that surround the corpus spongiosum. Blood is supplied through the branches of the internal pudendal artery which opens into the corpora cavernosa. The penis contains both autonomic and somatic nerves. The sympathetic and parasympathetic nerves meet in the pelvis forming the cavernous nerves located in the corpus cavernosum, corpus spongiosum and glans in order to control blood flow during erection and flaccidity. The somatic nerve contributes to sensation and contraction as well as relaxation of the penile striated muscles.

Physiology of Erection and Detumescence

Erection is a neurovascular process that occurs as a result of a delicate interrelationship between psychological, vascular and hormonal factors. Neural input from the brain is important. Erection can be carried by psychogenic stimulation, which originates in the mind, and by reflex as seen in paraplegics, or by physical contact. Following stimulation, the nerve impulses trigger the release of neurotransmitters from the nerve endings and of arterial muscular relaxant factors from penile endothelium that line blood vessels. The released chemicals include nitric oxide (a powerful vasodilator), vasoactive polypeptide and prostaglandin E1. Relaxation of the smooth muscles of the arteries and arterioles increases blood flow into the penis; thereby causing erection. It has been estimated that the blood volume in the erect penis is about 11 times greater. Relaxation of the smooth muscles also results in entrapment of venous outflow. This further increases rigidity and duration. Detumescence usually occurs as a result of discontinuation of neurotransmitter release, degradation of the second messenger (camp) by phosphodiesterases (PDE-5), or sympathetic discharge during ejaculation. This is followed by contraction of the smooth muscles and reopening of venous outflow, resulting in flaccidity.

The major neurotransmitter that triggers erection is nitric oxide. This chemical activates guanylyl cyclase, which elevates the intracellular concentration of cylic guanosine monophosphate (cGMP). The cylic (cGMP) initiates a series of events that eventually lead to relaxation of the smooth muscles and to erection. The concentration of cGMP is controlled by the rate of synthesis and degradation by the enzyme PDE-5. In the flaccid phase, cGMP is broken down to GMP by phosphodiesterase, followed by reopening of venous channels, escape of trapped blood, and return of flaccidity. Inhibition of PDE-5 enhances erection by increasing the concentration cGMP in the corpus cavernosum.

CE PRN® (ISSN 0199-5006) is owned and published by W-F Professional Associates, Inc.
400 Lake Cook Road, Suite 207, Deerfield, Illinois 60015.
William J. Feinberg, President
CE PRN® is published eleven times per year, monthly, January through November.
Subscription rate is $99.00 per year. Second-Class Postage paid at Deerfield, Illinois 60015
and at additional mailing offices.

POSTMASTER: Send all address changes to
W-F Professional Associates, Inc., 400 Lake Cook Road, Suite 207, Deerfield, IL 60015.
February 2006

Erectile Dysfunction (ED)

ED is a significant men's health issues. ED is defined as the failure of a man to achieve and maintain erection. The terms impotence and ED were often used interchangeably to denote this disorder. However, the term ED is the most currently used name. It is estimated that there are over 30 million men who experience ED in the USA, and over 150 million worldwide. The incidence increases with age. The disorder affects about 2.5%, 25%, 55% and 65% of men 40, 56, 75 and 80 years old, respectively. ED is more prevelent in men who suffer from a concomitant illness. Introduction of sildenafil (Viagra®) into the market in 1998, and the media publicity surrounding its use, has propelled ED into a prominent position among men's health concerns, and prompted men to discuss the disorder more candidly with both their physician and partner. One indicator of this disorder to the well-being of patients is the fact that six million prescriptions for sildenafil were dispensed in the USA within the first 8 months following its introduction into the market.

Etiology

In the past ED was believed to be due solely to psychological problems. While psychological and emotional situations are important contributing factors, it is now recognized that ED is primarily a disorder of organic causes (neurogenic, hormonal, arterial, or drug-induced). Parkinson's disease, stroke, hypotension, multiple sclerosis, chronic alcoholism, spinal injury, diabetes which may lead to diabetic neuropathy, renal failure, pelvic or perineal surgery, hormonal abnormalities, smoking and the intake of certain medications can often lead to ED. In many cases, men may have a combination of psychological and organic causes. Organic factors account for about 70% of the cases, and about 30% are due to psychogenic causes. Antihypertensives, antidepressants, antipsychotics, anticonvulsants, antiandrogens, histamine H_2 receptor antagonists, narcotics, or nonsteroidal anti-inflammatory drugs, may contribute to ED. Although aging may contribute to ED, it is not inevitable. Some men in their 70's and 80's never experience ED. However, a decrease in the production of male hormones, which is age-related, is a risk factor. What increases the likelihood of this disorder in older men is the increased intake of medications as well as the presence of medical conditions that often accompany the aging process. Smoking and alcoholism appear to increase occurrence. It has been reported that smoking as few as 2 cigarettes can decrease blood flow to the tissues. Persons with poor arterial blood circulation to the erectile tissue, cardiovascular disease, testicular damage or patients who underwent surgery for the prostate, bladder, colon and urinary tract are at risk of developing ED.

Diagnosis

Even though there is no specific test to diagnose ED, physical examination and laboratory tests should be conducted to determine the adequacy of the vascular, neurological and endocrine systems. Tests such as PSA, blood flow in the penis, serum chemistry profile and hormonal screening, such as thyroid-stimulating hormone and testosterone level, may reveal a disease process that could lead to ED. Nocturnal and morning tumescence studies that involve measurement of erection episodes occurring during sleep and upon awakening in the morning are helpful diagnostic measures. A healthy man at any age should experience such erections that occur without stimulation. The presence of an organic disease process may interfere with these.

Treatment

Treatment of ED is determined by the cause(s) responsible for the disorder as well as age of the patient, mental and physical condition, and tolerance to therapy. In the scope of this lesson oral therapy using the PDE-5 (phosphodiesterase) inhibitors will be discussed.

Sildenafil (Viagra®)

Introduction of Sildenafil in 1998 opened a new era in the management of ED. The public demand for a specific, conveniently administered and relatively effective medication was realized with the discovery of this drug.

Efficacy

Even though the extensive media coverage of the efficacy of sildenafil was positive and the initial patients' satisfaction ranged from 15% to 90%, current clinical reports indicate that the success rate of this drug is approximately 50%. Results of these studies were based on a variety of measures that include:

1. Patient/partner diaries.
2. The International Index Erectile Function (IIEF) self-administered questionnaire, that includes questions related to erection, sexual desire, satisfaction with intercourse, and overall sexual satisfaction.
3. Percentage of successful attempts of intercourse or erections in a 4-week period.

Sildenafil has low efficacy in men who undergo radical prostatectomy, and no efficacy if the procedure did not preserve the nerves in the prostate. Men with spinal injury reported improvement in erection following sildenafil intake compared to placebo. Studies have shown that sildenafil has improved the quality of erection to a degree sufficient for intercourse in men with ED regardless of the cause. It has been shown that 88% of men who use sildenafil are still taking the drug one year after the initial use. There is evidence to suggest that sildenafil and other PDE-5 inhibitors are the current treatment of choice for ED regardless of the cause, and their use is warranted in the absence of contraindications. It must be kept in mind that sildenafil has no effect on libido. Stimulation is necessary for the drug to exert its activity.

Safety and Adverse Effects

Results of studies conducted to determine the safety of sildenafil are favorable. Since the smooth muscle of the vasculature, bronchi, esophagus, anal sphincter, urethra and prostate contain type-5 phosphodiesterase, adverse effects may occur in these body parts following the intake of sildenafil due to inhibition of the aforementioned enzyme by the drug. Thus, incidence of nasal congestion (4%), dyspepsia (7%), diarrhea (3%), headaches (16%), and facial flushing (10%) have occurred when taking in doses ranging from 25 mg to 100 mg. The rates of these adverse effects were twice as high when 100 mg of the drug is taken. Headache development is due to dilation of cerebral vessels. About 3% of men have developed mild to transient color 'ting' in their vision. These visual adverse effects are due to inhibition of type-6 phosphodiesterase found in the retina. The use of the drug is contraindicated in the presence of retinitis pigmentosa. Men with a history of retinal disorders should consult an ophthalmologist prior to use of the drug. Adverse vascular effects such as nasal congestion, headache and facial flushing, usually are mild and transient. The rate of myocardial infarction events following the use of sildenafil and following placebo administration were practically identical. However, because men taking nitrates or having medical conditions were excluded from those studies, it is assumed that serious cardiovascular side effects may be higher in the general population. From March to November 1998, the FDA received reports of 130 deaths associated with sildenafil treatment. Even though the number of prescriptions dispensed during this period was over 6 million, the deaths caused public concern and were widely reported in the media. Some of the deaths were caused by the concurrent use of sildenafil with nitrates, and some occurred within 4-5 hours of sexual activity, while others occurred during or immediately after. Considering the fact that sexual intercourse is associated with sudden deaths in 0.6% to 3.3% of men, that the risk of developing MI within two hours of intercourse is 2.5 times higher than at any other time, and that sildenafil did not affect the heart rate, blood pressure, or EKG of a study group of more than 2,000, indicates that the drug probably has no significant cardiovascular toxicity. However, the American College of Cardiology and the American Heart Association issued guidelines recommending that caution be exercised in using sildenafil in men with congestive heart failure, unstable angina, borderline low-blood pressure and in patients who are taking multiple antihypertensives and drugs that prolong the half-life of sildenafil. Again, the concurrent use of sildenafil with nitrates is absolutely contraindicated, since this combination could cause a severe drop in blood pressure. It is essential that the pharmacist should convey to his patrons that sildenafil is to be used only for the management of ED and not as an aphrodisiac or to improve sexual desire. The recreational use of the drug by men who are not experiencing ED should be discouraged. In July 2005, the FDA announced new labeling for the PDE-5 inhibitors. The new cautionary statement in the package inserts states that in rare instances, men taking PDE-5 inhibitors reported a sudden decrease or loss of vision in one or both eyes. This type of vision loss may be attributed to non-arteritic ischemic optic neuropathy (NAION). This condition results in blockade of blood flow in the optic nerve. It is encountered mostly in men who suffer from heart disease, diabetes, hypertension, cigarette smokers and in persons

over 50 years of age. Even though some men lost vision in one eye after using these drugs, it is not clear whether NAION occurred as a result of the use of PDE-5 inhibitors or due to other related factors. NAION may occur in men who are not using these drugs. These drugs should be discontinued if the user experiences vision loss and a health provider should be consulted.

Sildenafil is well absorbed from an empty stomach, reaching a maximum blood concentration in 30 to 120 minutes. The recommended starting dose is 50 mg taken one hour prior to sexual activity, with maximum frequency of once daily. Depending on its effectiveness and patient tolerance to side effects, the dose may be increased to 100 mg or reduced to 25mg, which is the lowest effective dose. This dose may be initially used if the patient is 65 years of age or older, has severe liver or kidney problems, or is taking protease inhibitors for treating HIV. If the patient is taking an alpha adrenergic blocker for high blood pressure or is being treated for prostate problems, then this individual should not take more than 25 mg sildenafil and an alpha blocker within 4 hours of each other.

Mechanism of Action

Sildenafil acts by inhibiting type-5 phosphodiesterase (PDE-5 Inhibitor). PDE-5 is the enzyme responsible for inactivation of cGMP. Several types of PDE exist in the body. The most abundantly found enzyme in the penile muscle is PDE-5. Other enzymes include PDE 1,2,3,4,6,7,8,9,10 and 11. Erection is a hemodynamic process triggered by relaxation of the smooth muscle in the glans penis, corpus cavernosum, and corpus spongiosum and their arterioles. Following sexual stimulation, nitric oxide is released from the nerve endings and endothelial cells of penile smooth muscles. A function of nitric oxide is to activate the enzyme, guanylate cyclase, which causes an increase in the level of cGMP within the penile smooth muscle. A function of cGMP is to cause relaxation of the smooth muscle allowing increased blood flow into the penis, and this in turn results in erection. The enzyme PDE-5 regulates the synthesis of cGMP. Consequently, inhibition of PDE-5 enhances erection by increasing the concentration of cGMP in penile muscle. It is important to note that sexual stimulation is necessary to trigger the release of nitric oxide.

Vardenafil (Levitra®)

Vardenafil was approved in 2003 as an oral therapy for the management of ED. It is a highly selective inhibitor of cGMP-specific phosphodiesterase type -5 (PDE-5).

Pharmacokinetics

Vardenafil is well absorbed from the GI tract resulting in bioavailability of approximately 15%. Peak blood concentration following the intake of a 20 mg dose on an empty stomach is reached between 30 minutes and 2 hours, with a median of one hour. Intake of the drug following a meal rich in fat resulted in a reduction in blood concentration by 18% to 50%. Following an oral dose, vardenafil is well distributed in body tissue. The drug, and its metabolite, bind strongly to plasma proteins. It has been estimated that 95% of the dose binds to the protein. This process, however, is reversible. Metabolism of vardenafil occurs mainly in the liver. The hepatic enzymes responsible for this process are CYP3A4 and CYP3A5 and CYP2C isoforms. Concurrent administration of CYP3A4 inhibitors such as indinavir and ketoconazole and itraconazole may result in elevation of blood concentration of vardenafil. Once the drug is metabolized, the concentration of the metabolite M1 is about 26% of vardenafil. The drug metabolites exhibit PDE-5 inhibitory effect similar to that of the parent drug. The terminal half-life of vardenafil, and its metabolites, is about 4-5 hours. The vast majority of the drug dose is excreted in the feces, and only about 2-6% is excreted in the urine.

Efficacy

In a double-blind, randomized, placebo controlled study of 2,431 men aged 20 to 83 (mean age 57), doses of 5 mg, 10 mg, and 20 mg of vardenafil were administered. The separate studies were conducted on the general population, patients with diabetes and patients who underwent prostatectomy. No consideration was given to meals. Data was collected using (International Index Erectile Function) IIEF. The studies revealed that the intake of vardenafil has significantly enhanced achieving penetration and the ability to maintain erection for completion of intercourse, compared to placebo. Similar results were obtained when trials in a general ED population were conducted. The rate of achieving an erection suitable for penetration at doses of 5 mg, 10 mg, and 20mg compared to placebo. A

placebo effect rate of 52% was achieved while rates of 65%, 75% and 80% were obtained as a result of the intake of vardenafil in doses of 5 mg, 10 mg and 20 mg, respectively.

Studies in individuals with ED and diabetes mellitus showed that vardenafil significantly improved erection with doses of 10 mg and 20 mg. The mean age was 57 years, and the range was 33-81. Likewise, significant improvement in both penetration and maintenance of erection to successful intercourse has occurred in patients with ED after radical prostatectomy.

Contraindications

Vardenafil is contraindicated with nitrates due to the potential for severe hypotensive effects, myocardial infarction and possibly death. The PDE-5 inhibitors can cause slight reduction in blood pressure without significant change in heart rate. A study was conducted to determine the blood pressure and heart rate response to 0.4 mg of nitroglycerin administered sublingually 1 to 4 hours prior to the intake of 20 mg vardenafil. Data indicates that the drug caused an additional drop in blood pressure and an increase in heart rate.

Adverse Effects

In placebo-controlled clinical trials the following adverse effects were reported: 15% of the patients reported headache; 11% reported flushing; 9% rhinitis; 4% dyspepsia; 3% sinusitis; 3% flu syndrome; 2% dizziness and 2% nausea. Only 3.4% of the users discontinued taking vardenafil as a result of the adverse effects. Some adverse effects such as headache, flushing, nausea, dyspepsia, and rhinitis appear to be dose related. Infrequent adverse effects such as anaphylactic reactions, chest pain, palpitation, postural hypotension, tachycardia, abdominal pain, abnormal liver function tests, diarrhea, dry mouth, backache, vertigo, insomnia, abnormal vision, blurred vision, chromatopsia (a visual defect in which colored objects appear unnaturally colored and colorless objects appear tinged with color), change in color vision, dim vision, abnormal ejaculation, and priapism were experienced. Like other PDE-5 inhibitors, vardenafil may cause NAION (non-arteritic ischemic optic neuropathy). However, as indicated earlier, it is not clear if vardenafil is the culprit, since most patients who developed this disorder have underlying anatomic or vascular risk factors to trigger NAION. Vardenafil may interact with erythromycin, ketoconazole, and HIV protease inhibitors.

The patient should make the physician aware of all prescriptions, OTC, drugs or herbal products being taken. The medication maybe taken on an empty stomach, however, high-fat meals and concurrent intake of grapefruit juice should be avoided. Patients with moderate hepatic problems should start with a dose of 5 mg and a maximum dose of 10 mg. There is no data on patients with severe hepatic impairment. Patients, who are taking antiarrhythmic drugs, such as amiodarone (Cordarone®) and sotalol (Betapace®), should refrain from using vardenafil. Caution should be exercised when vardenafil is used by patients with anatomical penile deformity such as angulation and Peyronie's disease. Patients should inform their healthcare provider of any health problems such as angina, heart failure, arrhythmia, hypotension, history of strokes, hepatic or renal impairment, retinitis pigmentosa, history of vision loss, peptic ulcers, deformed penis shape, and prolonged erection that lasted more than four hours. Erections that may last for hours, if not treated, may cause damage to the penis and may result in inability to have erection. In healthy persons, the starting dose is 10 mg, and should not be taken more than once a day.

Tadalafil (Cialis®)

Tadalafil is a PDE-5 inhibitor and, thus, is used in the management of ED. To be effective, sexual stimulation is required.

Pharmacokinetics

Tadalafil is well absorbed from the GI tract. Maximum plasma concentration is reached between 30 minutes and 6 hours with a median time of 2 hours. Food appears to have no influence on the absorption rate. Tadalafil is well distributed in body tissue after oral administration. About 94% of the drug is bound to plasma when taken at the required dose. Tadalafil is predominately metabolized in the liver by CYP3A4. The main metabolite that circulates in the blood stream is methylcatechol glucuronide. However, at the concentrations in which they are present, the metabolite does not exert any significant pharmacological activity. The drug is mainly eliminated as the metabolite in the feces, and secondarily in the urine.

Efficacy

Clinical studies have shown that tadalafil is effective in the management of ED. The recommended starting dose for a healthy individual is 10 mg, but can be increased to 20 mg or decreased to 5 mg depending on the patient's tolerance to side effects as well as the efficacy of the dose. The drug should not be taken more than once daily. Studies have shown that tadalafil may still be effective 36 hours after dosing. The manufacturers of tadalafil emphasize this characteristic in their advertisements. Tadalafil can exert therapeutic effect on an empty or full stomach, and it is not adversely affected by meals rich in fat. However, excessive alcohol consumption (5 glasses of wine or 5 shots of whiskey) may cause dizziness or hypotension.

Mechanism of Action

Tadalafil has a similar mechanism of action to the other PDE-5 inhibitors. The drug does not cure ED or increase libido.

Clinical studies have shown that the discontinuation rate of the use of the drug because of adverse effects was 3.1% compared to 1.4% in placebo. The main side effects reported after the intake of 10 or 20 mg include: headache, dyspepsia, back pain, myalgia, nasal congestion, and facial flushing. Caution must be exercised when taking tadalafil with ketoconazole, HIV protease inhibitors, erythromycin and grape fruits, as these drugs may result in an increase in blood concentration of tadalafil due to inhibition of cytochrome P450. However, CYP3A4 inducers such as rifampin, H2 antagonists, phenytoin, and phenobarbital may decrease tadalafil exposure. As with other PDE-5 inhibitors, tadalafil should not be administered concomitantly with nitrates. The FDA warning concerning the emergence of NAION following the administration of PDE-5 inhibitors applies to tadalafil. The drug is not recommended in men for whom sexual activity is inadvisable due to cardiovascular disease. Patients should be advised to consult with a healthcare provider if priapism occurs, or if erection for longer than 4 hours takes place.

Summary

ED is the inability of a man to achieve and maintain erection of sufficient rigidity. The disorder may be encountered after the age of 40. Complaints may range from chronic complete lack of erection, to partial or brief erection. ED can be a source of emotional and relationship difficulties and may lead to diminished self-esteem. ED is treatable, and it is not an inevitable result of the aging process.

Erection is a physiological process that involves the nervous, vascular and hormonal systems. Following sexual stimulation, neurotransmitters released from the nerve endings trigger this process. Nitric oxide is the transmitter that plays an essential role in achieving erection. The physical or psychological stimulation results in impulses that cause an increase in blood flow to the penis, resulting in an increase in size and its rigidity. Following ejaculations, release of transmitters is discontinued; blood leaves the penis, and within a short period of time resumes its normal flaccid state. The enzyme phosphodiesterase is responsible for degradation of cGMP. Inhibition of this enzyme results in improving erection by increasing the concentration of cGMP.

Sildenafil, vardenafil, and tadalafil act by inhibition of the enzyme phosphodiesterase type 5. Clinical studies have shown that these medications cause an improvement in erection and its duration. Tadalafil possesses a duration of action of up to 36 hours and may have an onset of action after 30 minutes of its intake. Adverse effects of these medications include headache, nausea, back ache, facial flushing, dyspepsia, transient color 'ting' in vision. These drugs should not be given concurrently with nitrates, as this may result in a drop in blood pressure. In July 2005, the FDA announced new labeling for the PDE-5 inhibitors sildenafil, vardenafil, and tadalafil. The new cautionary statement in the package inserts states that in rare instances, men taking PDE-5 inhibitors reported a sudden decrease or loss of vision in one or both eyes. This type of vision loss may be attributed to non-arteritic ischemic optic neuropathy (NAION). This condition results in blockade of blood flow in the optic nerve. However, NAION may occur in men who are not using these medications.

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LESSON EVALUATION

Please fill-out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

Define ED & state its incidence	Yes	No
List the possible causes of ED	Yes	No
Describe the diagnosis of ED	Yes	No
Comment upon newer drugs that treat ED	Yes	No
Explain the mechanism of action of the PDE-5 inhibitors	Yes	No
List the adverse effects & contraindications of the PDE-5 inhibitors	Yes	No

2. Was the program independent & non-commercial? Yes No

	Poor			Average			Excellent
3. Relevance of topic to your practice	1	2	3	4	5	6	7

4. What did you like most about this lesson?_____

5. What did you like least about this lesson?_____

(WATCH OUR WEBSITE FOR RESULTS OF PARTICIPANT EVALUATIONS)

Quiz—Please Select the Most Correct Answer

1. The main neurotransmitter that triggers erection is:
   A. Serotonin
   B. Dopamine
   C. Nitric oxide
   D. Adrenaline
2. Which statement is false?
   A. Urination occurs while the penis is erect
   B. The glans consists of erectile tissue
   C. The penis contains autonomic & somatic nerves
   D. Corpus spongiosum surrounds the urethra & extends to the glans
3. The mechanism of action of sildenafil, vardenafil & tadalafil is:
   A. Enhancement of reflexes
   B. Inhibition of PDE-5
   C. Decrease blood flow
   D. Increase sensitivity of nerve endings
4. Which statement is true about tadalafil?
   A. Recreational use is encouraged
   B. Tadalafil is an aphrodisiac
   C. Taken immediately before sexual activity
   D. Tadalafil is not an aphrodisiac
5. Which of these is not an adverse effect of PDE-5 inhibitors?
   A. Headache
   B. Backache
   C. Color 'ting' in vision
   D. Excessive salivation
6. Which of these is contraindicated with sildenafil, vardenafil & tadalafil?
   A. Aspirin
   B. Nitrates
   C. Antilipidemics
   D. Insulin
7. Which of these may remain effective 36 hours?
   A. Sildenafil
   B. Tadalafil
   C. Vardenafil
   D. None of these
8. Inhibition of PDE-5 causes an increase in concentration of **THIS** chemical in corpus cavernosum.
   A. cGMP
   B. Prostaglandin
   C. Norepinephrine
   D. Corticosteroids
9. Vardenafil does not interfere with:
   A. Erythromycin
   B. Ketoconazole
   C. Aspirin
   D. HIV protease inhibitors
10. Which state is correct?
    A. PDE-5 inhibitors may cause NAION
    B. ED can be diagnosed with lab tests
    C. PDE type 6 is found only in the liver
    D. Intercourse is associated with sudden deaths in 10% of men

Contributing Author
Farid Sadik, PhD, Dean
University of South Carolina
College of Pharmacy
Columbia, SC

Executive Editor
William J. Feinberg,
BS Pharm, MBA

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Pharmacists completing this course by February 28, 2009 may receive full credit. This program has been approved by the State Boards of Pharmacy in Alabama and Oklahoma.

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Program ID #707-000-06-002-H01.

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