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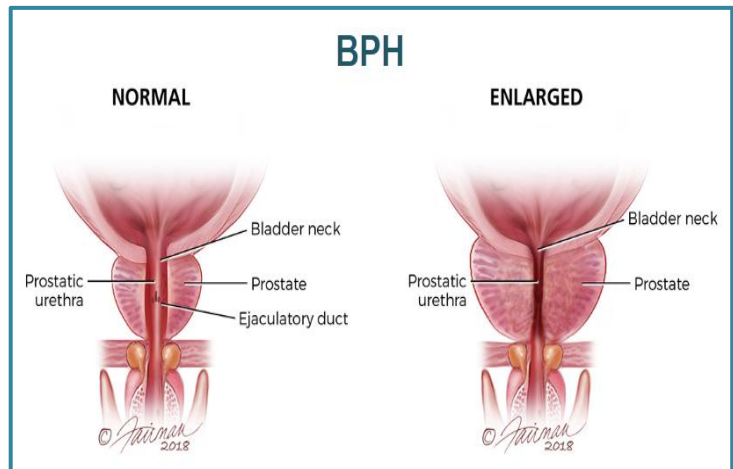
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Benign Prostatic Hyperplasia (BPH)

BPH is an enlarged prostate. The prostate goes through two main growth cycles during a man's life. The first occurs early in puberty, when the prostate doubles in size. The second phase of growth starts around age 25 and goes on for most of the rest of a man's life. BPH most often occurs during this second growth phase.

As the prostate enlarges, it presses against the urethra. The bladder wall becomes thicker. One day, the bladder may weaken and lose the ability to empty fully, leaving some urine in the bladder.



Narrowing of the urethra and urinary retention— being unable to empty the bladder fully – cause many of the problems of BPH.

BPH is not cancer. It does not cause or lead to cancer. However, BPH and cancer can happen at the same time. BPH is common. Based on autopsy studies, the prevalence of BPH increases from 8% in men aged 31 to 40 yr. to 40 to 50% in men aged 51 to 60 yr. and to > 80% in men > 80 yr. The etiology is unknown but probably involves hormonal changes associated with aging.

Symptoms and Signs

Lower urinary tract symptoms

Symptoms of BPH include a constellation of symptoms that are often progressive, known collectively as lower urinary tract symptoms (LUTS): urinary frequency, urgency, nocturia, hesitancy, intermittency.

Frequency, urgency, and nocturia are due to incomplete emptying and rapid refilling of the bladder. Decreased size and force of the urinary stream cause hesitancy and intermittency.

Pain and dysuria are usually not present. Sensations of incomplete emptying, terminal dribbling, overflow incontinence, or complete urinary retention may ensue. Straining to void can cause congestion of superficial veins of the prostatic urethra and trigone, which may rupture and cause hematuria. Straining also may acutely cause vasovagal syncope and, over the long term, may cause dilation of hemorrhoidal veins or inguinal hernias.

Urinary retention

Some patients present with sudden, complete urinary retention, with marked abdominal discomfort and bladder distention. Retention may be precipitated by any of the following:

- Prolonged attempts to postpone voiding
- Immobilization, exposure to cold
- Use of anesthetics, anticholinergics, sympathomimetics, opioids, or alcohol

Symptom scores

Symptoms can be quantitated by scores, such as the 7-question American Urological Association Symptom Score. This score also allows doctors to monitor symptom progression:

- Mild symptoms: Scores 1 to 7
- Moderate symptoms: Scores 8 to 19
- Severe symptoms: Scores 20 to 35

Diagnosis

The lower urinary tract symptoms of BPH can be caused by other disorders, including infection and prostate cancer. Furthermore, BPH and prostate cancer may coexist. Although palpable prostate tenderness suggests infection, digital rectal examination findings in BPH and cancer often overlap. Although cancer may cause a stony, hard, nodular, irregularly enlarged prostate, most patients with cancer, BPH, or both have a benign-feeling, enlarged prostate. Thus, testing should be considered for patients with symptoms or palpable prostatic abnormalities.

Digital rectal examination

On digital rectal examination, the prostate usually is enlarged and nontender, has a rubbery consistency, and in many cases has lost the median furrow. However, prostate size as detected with digital rectal examination may be misleading; an apparently small prostate may cause obstruction. If distended, the urinary bladder may be palpable or percussible during abdominal examination. Firm or hard areas may indicate prostate cancer.

Urinalysis, urine culture and uroflowmetry

Typically, urinalysis and urine culture are done. Men with moderate or severe symptoms of obstruction may also have uroflowmetry (an objective test of urine volume and flow rate) with measurement of postvoid residual volume by bladder ultrasonography. Flow rate < 15 mL/sec suggests obstruction, and postvoid residual volume > 100 mL suggests retention.

Prostate-specific antigen (PSA) level

Interpreting PSA levels can be complex. The PSA level is moderately elevated in 30 to 50% of patients with BPH, depending on prostate size and degree of obstruction, and is elevated in 25 to 92% of patients with prostate cancer, depending on the tumor volume.

In patients without cancer, serum PSA levels > 1.5 ng/mL usually indicate a prostate volume \geq 30 mL. If the PSA is elevated (level is >4 ng/mL), further discussion/shared decision making regarding other tests or biopsy is recommended.

For men < 50 or those at high risk of prostate cancer, a lower cutoff (PSA > 2.5 ng/mL) may be used. Other measures, including rate of PSA increase, free-to-bound PSA ratio, and other markers, may be useful.

Other testing

Transrectal biopsy is usually done with ultrasound guidance and is usually only indicated if there is suspicion of prostate cancer. Transrectal ultrasonography can also measure prostate volume.

Treatment

Urinary retention

Urinary retention requires immediate decompression. Passage of a standard urinary catheter is first attempted; if a standard catheter cannot be passed, a catheter with a coude tip may be effective. If this catheter cannot be passed, flexible cystoscopy or insertion of filiforms and followers may be necessary (this procedure should usually be done by a urologist). Suprapubic percutaneous decompression of the bladder may be used if transurethral approaches are unsuccessful.

Drug therapy

For partial obstruction with troublesome symptoms, all anticholinergics and sympathomimetics (many available in OTC preparations), and opioids should be stopped, and any infection should be treated with antibiotics.

For patients with mild to moderate obstructive symptoms, alpha-adrenergic blockers (eg, terazosin, doxazosin, tamsulosin, alfuzosin) may decrease voiding problems. The 5 alpha-reductase inhibitors (finasteride, dutasteride) may reduce prostate size, decreasing voiding problems over months, especially in patients with larger (> 30 mL) glands. A

combination of both classes of drugs is superior to monotherapy. For men with concomitant erectile dysfunction, daily tadalafil may help relieve both conditions. Many OTC complementary and alternative agents are promoted for treatment of BPH, but none, including the thoroughly studied saw palmetto, has been shown to be more efficacious than placebo.

Surgery

Surgery is done when patients do not respond to drug therapy or develop complications such as recurrent UTI, urinary calculi, severe bladder dysfunction, or upper tract dilation. Transurethral resection of the prostate (TURP) is the standard. Erectile function and continence are usually retained, although about 5 to 10% of patients experience some postsurgical problems, most commonly retrograde ejaculation. The incidence of erectile dysfunction after TURP is between 1 and 35%, and the incidence of incontinence is about 1 to 3%. However, technical advances such as the use of bipolar resectoscopes, which allow use of saline irrigation, have greatly improved the safety of TURP by averting hemolysis and hyponatremia.

About 10% of men undergoing TURP need the procedure repeated within 10 yr because the prostate continues to grow. Various laser ablation techniques are being used as alternatives to TURP. All surgical methods require postoperative catheter drainage for 1 to 7 days.

Other procedures

Alternatives to TURP include microwave thermotherapy, electrovaporization, various laser techniques, high-intensity focused ultrasonography, transurethral needle ablation, radiofrequency vaporization, pressurized heated water injection therapy, urethral lift, steam injection therapy, and intraurethral stents. The circumstances under which these procedures should be used have not been firmly established, but those done in the physician's office (microwave thermotherapy and radiofrequency procedures) are being more commonly used and do not require use of general or regional anesthesia. Their long-term ability to alter the natural history of BPH is under study.

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OTC Medicines Corner

Herbal Management of Benign Prostatic Hyperplasia



Saw palmetto berries (*Serenoa repens*) are a well-known natural remedy that may help to treat BPH. According to a 2016 review, some studies have suggested that berry extracts from saw palmetto can help to reduce the symptoms of BPH. The authors state that they may even be as effective as α -blockers and finasteride.

Bark extract from *Prunus africana*, the African cherry, may also be effective for relieving symptoms of BPH.

Source: Nyamai DW, Arika WM, Rachuonyo HO, Wambani JR, Ngugi MP (2016) Herbal Management of Benign Prostatic Hyperplasia. *J Cancer Sci Ther*.8:130-134.

FDA New Molecular Entity Approvals

Turalio™ (pexidartinib)

FDA approved Daiichi Sankyo's **Turalio™ (pexidartinib)** for the treatment of select patients with tenosynovial giant cell tumor (TGCT), a rare, locally aggressive and debilitating tumor.

Turalio is the only approved therapy for adult patients with symptomatic TGCT associated with severe morbidity or functional limitations and not amenable to improvement with surgery. The FDA advises health care professionals to tell females of reproductive age and males with a female partner of reproductive potential to use effective contraception during treatment with **Turalio**. Women who are pregnant or breastfeeding should not take **Turalio** because it may cause harm to a developing fetus or newborn baby. **Turalio** must be dispensed with a patient Medication Guide that describes important information about the drug's uses and risks.

Accrufer (ferric maltol)

The FDA has approved **Accrufer** for the treatment of iron deficiency in adults with chronic kidney disease. **Accrufer**, manufactured by U.K.-based Shield Therapeutics plc, is an oral treatment that provides an alternative to salt-based oral iron therapies, according to a company press release. The drug is absorbed from the ferric maltol molecule and generally does not cause gastrointestinal adverse events (ie, nausea, bloating and constipation) typically observed with salt-based therapies.

Under the name Feraccru, the drug is already approved in both the European Union and Switzerland.

XPOVIO (selinexor)

The FDA granted accelerated approval to **selinexor (XPOVIO, Karyopharm Therapeutics)** in combination with dexamethasone for adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.

As a condition of accelerated approval, further clinical trials may be required to verify and describe **selinexor's** benefit.

NUBEQA (darolutamide)

The FDA approved **darolutamide (NUBEQA, Bayer HealthCare Pharmaceuticals Inc.)** for non-metastatic castration-resistant prostate cancer.

The most common adverse reactions ($\geq 2\%$) in patients who received **darolutamide** were fatigue, pain in extremity, and rash. Ischemic heart disease (4.3%) and heart failure (2.1%) were more common on the darolutamide arm.

The recommended **darolutamide** dose is 600 mg administered orally twice daily with food. Patients should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

Sources:

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- 2) Healio. *FDA approves new oral iron drug for CKD* [Internet]; Aug 02, 2019 [cited Aug 05, 2019]. Available from: <https://www.healio.com/nephrology/chronic-kidney-disease/news/online/%7B74e9721b-62ee-4dec-b2c3-5087a2db0f75%7D/fda-approves-new-oral-iron-drug-for-ckd>
- 3) US Food and Drug Administration. *FDA grants accelerated approval to selinexor for multiple myeloma* [Internet]; July 03, 2019 [cited Aug 05, 2019]. Available from: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-selinexor-multiple-myeloma>
- 4) US Food and Drug Administration. *FDA approves darolutamide for non-metastatic castration-resistant prostate cancer*. [Internet]; July 03, 2019 [cited Aug 05, 2019]. Available from: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-darolutamide-non-metastatic-castration-resistant-prostate-cancer>

Test Your Knowledge

- 1) Opioids are used for all the following conditions *except*:
 - a) cough
 - b) severe chronic pain
 - c) arthritis
 - d) severe diarrhea
 - e) pre-anesthetic.
- 2) Which of the following compounded sterile products should NOT be prepared in a horizontal laminar flow hood?
 - a) Total parenteral nutrition (TPN)
 - b) Dopamine
 - c) Cisplatin (Platinol)
 - d) Nitroglycerin
 - e) Bretylium tosylate
- 3) A 12-year-old boy is treated for otitis media with cefaclor. On the seventh day of therapy, he spikes a fever and develops an urticarial rash on his trunk. Which of the following laboratory tests could best confirm the physician's suspicion of an allergic reaction?
 - a) Complete blood count (CBC) and differential
 - b) Serum hemoglobin (Hb) and reticulocyte count
 - c) Liver function test profile
 - d) Lactate dehydrogenase (LDH) isoenzyme profile
 - e) Red blood cell (RBC) count and serum bilirubin

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional healthteam as well as from the community. Here's one of the enquiries received at the center:

Enquiry received from: G.S.-Pharmacy Student, Faculty of Pharmacy-Assiut University

Enquiry: Is it safe for a 5 yr old child to take medications for weight loss? The specialist prescribed her orlistat capsules t.i.d. and a once daily dose of metformin 850 mg.

Summary of the answer:

Staying active and consuming healthy foods and beverages are important for a child's well-being and maintaining a healthy weight. Encourage the child to increase her level of physical activity, even if she does not lose weight as a result. Exercise can bring the other health benefits (for example, reduced risk of type 2 diabetes and cardiovascular disease).

According to The National Institute for Health and Care Excellence (NICE) Guidelines, obesity drug treatment is not generally recommended for children younger than 12 years. In children younger than 12 years, drug treatment may be used only in exceptional circumstances, if severe comorbidities are present. Prescribing should be started and monitored only in specialist pediatric settings.

Currently there is only one medication, orlistat, that is approved for childhood obesity, but its effect on weight is modest and its acceptability is limited by side effects related to decreased fat absorption. In children aged 12 years and older, treatment with orlistat is recommended only if physical comorbidities (such as orthopaedic problems or sleep apnea) or severe psychological comorbidities are present. Treatment should be started by multidisciplinary teams with experience of prescribing in this age group. If orlistat is prescribed for children, a 6–12 month trial is recommended, with regular review to assess effectiveness, adverse effects and adherence.

The Endocrine Society clinical practice guideline (2017) on pediatric obesity discourages the use of any obesity medication unless the patient has failed a formal program of intensive lifestyle modification. It specifically states that "given its limited weight-loss efficacy, metformin is not considered a weight-loss treatment."

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Overweight. [Online]; Sept 2018 [cited Nov 2018]. Available from: <https://www.niddk.nih.gov/health-information/weight-management/helping-your-child-who-is-overweight>

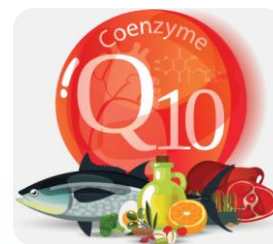
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Coenzyme Q10

Coenzyme Q10 (CoQ10) is used for cardiovascular diseases and to reduce statin-associated muscle symptoms (SAMS). The supplement has also been used for migraine prevention, Parkinson's disease, and breast cancer, and to reduce chemotherapy-associated adverse effects.



Physiologic activity

CoQ10, also known as ubiquinone, is converted to ubiquinol, which is found in every cell, primarily in mitochondria. Its concentrations are greatest in cells in the heart, kidney, liver, and muscle. CoQ10 is involved in the production of cellular energy and the regeneration of antioxidants such as vitamin E.

Dosage and product considerations

For heart failure, the dosage has been 100 mg taken two to three times daily with meals to aid absorption, while 50 mg to 100 mg once daily has been used for statin-associated muscle symptoms. Products meeting USP standards should be recommended.

Summary of clinical evidence

Heart failure is a common disease for which multiple effective drugs are available even though long-term outcomes remain poor. Over the past decades, studies have evaluated the potential effects of CoQ10, but the findings have been limited by small numbers of participants and frequently suboptimal concurrent drug therapy. As a result, the evidence for CoQ10 to treat heart failure has been contradictory.

A 2014 study of 420 patients with either New York Heart Association (NYHA) functional class III or IV disease and reduced ejection fraction heart failure compared use of CoQ10 100 mg three times daily with placebo, with assessments at 16 weeks and 106 weeks. At 2 years, CoQ10 reduced the risk of cardiovascular death and hospitalization for heart failure, among other important outcomes. These findings were unexpected, and multiple study limitations have since been raised about the outcomes.

SAMS are the most common adverse effects reported by patients taking statins, even though they were rare in clinical trials. SAMS include a broad range of symptoms from myalgias to more serious conditions, with significant increases in serum creatine kinase (CK). Multiple strategies are available to manage SAMS, and key clinical pearls about SAMS have been summarized. Use of CoQ10 has been suggested as one of these strategies.

The evidence for efficacy of CoQ10 for SAMS has been conflicting in published clinical trials and meta-analyses, in part because of different definitions of the syndromes, as well as varying CoQ10 dosages and products.

A 2018 meta-analysis evaluated 12 English language randomized controlled studies of 575 patients taking either CoQ10 or placebo for periods ranging from 30 days to 3 months. Ten of the studies evaluated CK levels. The meta-analysis reported significant improvements in muscle pain, muscle weakness, muscle cramp, and muscle tiredness with CoQ10 compared with placebo. CK levels did not change. The authors reported that the benefits did not depend on the CoQ10 dosage or duration of treatment.

Safety considerations

CoQ10 is a generally safe supplement that may have some value as an adjunct to standard therapy in heart failure but should never replace prescription drug therapy. Many patients discontinue statins because of SAMS, but statin adherence is essential, so CoQ10 can be considered for reducing muscle symptoms.

Adverse effects are mild. Mild liver enzyme increases have been reported. Because of a lack of information on its effects in pregnancy and lactation, CoQ10 should not be used by women who are pregnant or breastfeeding.

There are concerns that CoQ10 can reduce the effectiveness of warfarin because it is structurally similar to vitamin K, but the evidence is mixed and contradictory. Since the potential interaction between CoQ10 and warfarin remains unclear, other health care providers should be aware of patients' CoQ10 use.

Source:Hume A L. Coenzyme Q10. *PharmacyToday*.2019;25(2):16.



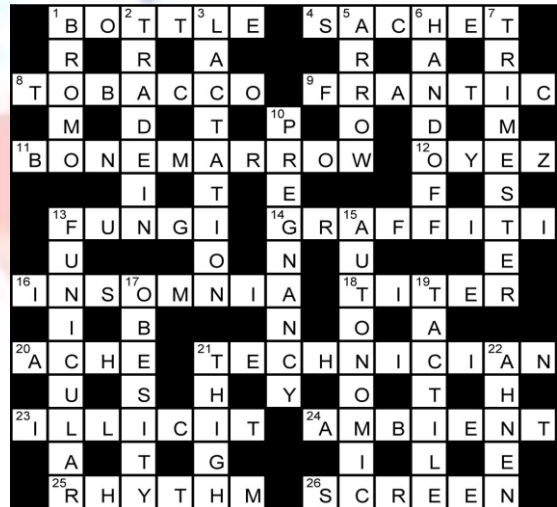
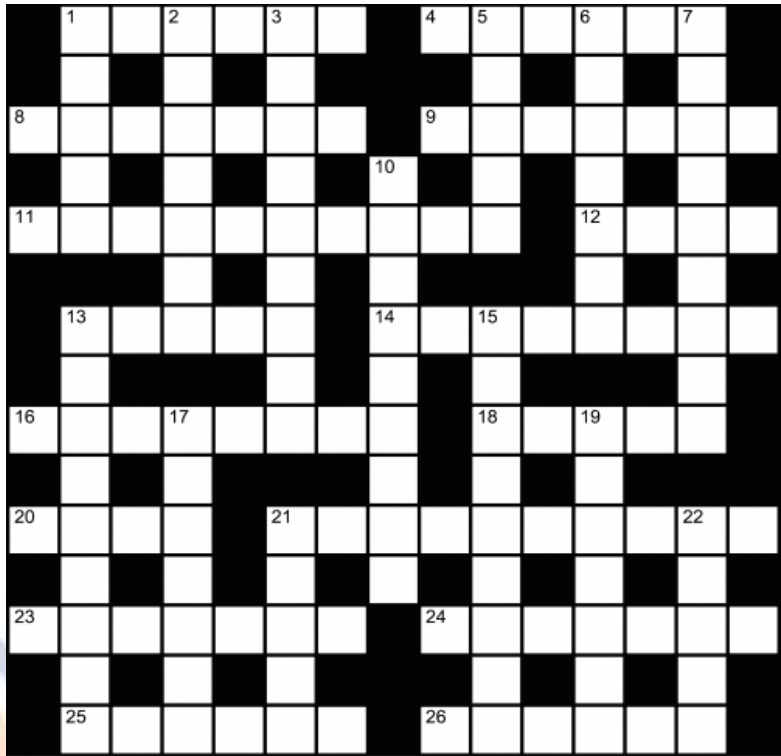
Crossword Challenge

Across

- 1-Medication is often supplied in this container
- 4-Some medications can be packaged or supplied in this form (e.g., fosfomycin)
- 8-Pharmacists can help with _____ cessation
- 9-Stressed patients may be _____ when they can't access their medications
- 11-Where new blood cells originate from in the body
- 12- "Hear Ye!"
- 13-Mushrooms and yeasts are members of this kingdom
- 14-Drawings made on a wall, often without permission
- 16-Some medications for this condition can cause sleepwalking
- 18-A test that measures the concentration of antibodies in the blood
- 20-A dull pain
- 21-Essential member of the pharmacy staff
- 23-Illegal, as in _____ drugs
- 24-Relating to the immediate surroundings, such as temperature
- 25-Tempo or beat
- 26-E.g., a blood pressure check for hypertension

Down

- 1-_____seltzer, antacid containing sodium bromide
- 2-Patients often wish they could do this with an outdated medication
- 3-Some medications are restricted while new mothers are in this phase
- 5-Symbol that can be used on a prescription label to alert patients to a possible adverse effect
- 6-A pharmacist may do this with a filled prescription (to a technician)
- 7-Morning sickness often occurs in the first _____ of 10 down.
- 10-See 7 down
- 13-Type of railway often used on steep slopes
- 15-A body system that regulates its function without conscious thought is this
- 17-Condition that can increase the risk of heart disease and diabetes
- 19-Related to the sense of touch
- 21-Common location for an I.M. injection
- 22-To foresee, in Munich



Test Your Knowledge Answers:

1. **c)** Opioids are used to treat all the following conditions except arthritis, which is often treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and immunosuppressants, depending on the type of disease and severity.
2. **c)** Cisplatin is an antineoplastic agent and, consequently, should be prepared only in a vertical laminar flow hood because of the potential hazard of these toxic agents to the operator.
3. **a)** An allergic drug reaction will usually produce an increase in the eosinophil count (eosinophilia). This could be determined by ordering a WBC (white blood cell) differential.