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DRUG INFORMATION BULLETIN

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كليـة الصيدلـة

Ebola Virus Disease (EVD)

Ebola virus disease (EVD), formerly known as Ebola haemorrhagic fever (Ebola HF) is one of numerous Viral Hemorrhagic Fevers. It is a severe, often fatal disease in humans and primates. Ebola viruses are found in several African countries.

Ebola first appeared in 1976 in 2 simultaneous outbreaks, in Nzara, Sudan, and in Yambuku, Democratic Republic of Congo. The latter was in a village situated near the Ebola River, from which the disease takes its name.. Since then, outbreaks of Ebola among humans have appeared sporadically in Africa. The death toll for the deadly Ebola virus continues to climb higher, exceeding 600 deaths in West Africa. This current outbreak is the deadliest of its kind on record. The current (2014) Ebola outbreak is occurring in the West African countries: Guinea, Liberia, Sierra Leone and Nigeria.

Symptoms of Ebola typically include

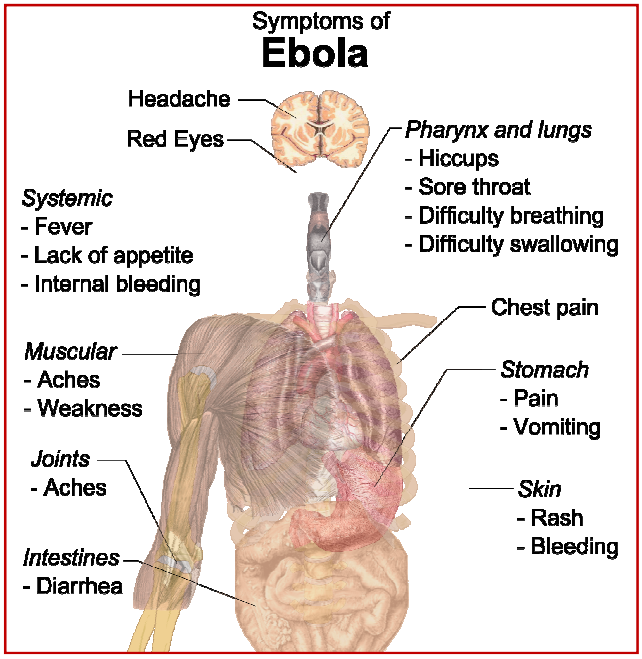
- Fever (greater than 38.6℃ or 101.5℉)
- Severe headache
- Muscle pain
- Weakness
- Diarrhea
- Vomiting
- Abdominal (stomach) pain
- Lack of appetite

Symptoms may appear anywhere from 2 to 21 days after exposure to ebolavirus, although 8-10 days is most common.

Some who become sick with Ebola are able to recover. However, patients who die usually have not developed a significant immune response to the virus at the time of death.

In This Issue

Transmission



Because the natural reservoir of ebolaviruses has not yet been proven, the manner in which the virus first appears in a human at the start of an outbreak is unknown. However, researchers have hypothesized that the first patient becomes infected through contact with an infected animal.

When an infection does occur in humans, the virus can be spread in several ways to others. The virus is spread through direct contact (through broken skin or mucous membranes) with

- a sick person's blood or body fluids (urine, saliva, feces, vomit, and semen)
- objects (such as needles) that have been contaminated with infected body fluids
- infected animals

Healthcare workers and the family and friends in close contact with Ebola patients are at the highest risk of getting sick because they may come in contact with infected blood or body fluids.

Diagnosis

Diagnosing Ebola haemorrhagic fever in an individual who has been infected for only a few days is difficult, because the early symptoms, such as red eyes and a skin rash, are nonspecific to ebolavirus infection and are seen often in patients with more commonly occurring diseases.

However, if a person has the early symptoms of Ebola HF and there is reason to believe that Ebola HF should be considered, the patient should be isolated and public health professionals notified. Samples from the patient can then be collected and tested to confirm infection.

Laboratory tests used in diagnosis include:

Timeline of Infection	Diagnostic tests available
Within a few days after symptoms begin	• Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing • IgM ELISA • Polymerase chain reaction (PCR) • Virus isolation
Later in disease course or after recovery	• IgM and IgG antibodies
Retrospectively in deceased patients	• Immunohistochemistry testing • PCR • Virus isolation

Treatment

No specific vaccine or medicine (e.g. antiviral drug) has been proven to be effective against Ebola.

Symptoms of Ebola are treated as they appear. The following basic interventions, when used early, can increase the chances of survival.

- Providing intravenous fluids and balancing electrolytes (body salts)
- Maintaining oxygen status and blood pressure
- Treating other infections if they occur

Timely treatment of Ebola HF is important but challenging because the disease is difficult to diagnose clinically in the early stages of infection. Because early symptoms, such as headache and fever, are nonspecific to ebolaviruses, cases of Ebola HF may be initially misdiagnosed.

However, if a person has the early symptoms of Ebola HF and there is reason to believe that Ebola HF should be considered, the patient should be isolated and public health professionals notified. Supportive therapy can continue with proper protective clothing until samples from the patient are tested to confirm infection.
Experimental treatments have been tested and proven effective in animal models but have not yet been used in humans.

Prevention & Control

Because it is still not known exactly how people are infected with Ebola, few primary prevention measures have been established.
When cases of the disease do appear, risk of transmission is increased within healthcare settings. Therefore, healthcare workers must be able to recognize a case of Ebola and be ready to use practical viral hemorrhagic fever isolation precautions or barrier nursing techniques. They should also have the capability to request diagnostic tests or prepare samples for shipping and testing elsewhere.

Barrier nursing techniques include:

- Wearing of protective clothing (such as masks, gloves, gowns, and goggles)
- Using infection-control measures (such as complete equipment sterilization and routine use of disinfectant)
- Isolating patients with Ebola from contact with unprotected persons.

The aim of all of these techniques is to avoid contact with the blood or secretions of an infected patient. If a patient with Ebola dies, direct contact with the body of the deceased patient should be avoided.
If you must travel to an area with known Ebola cases, make sure to do the following:

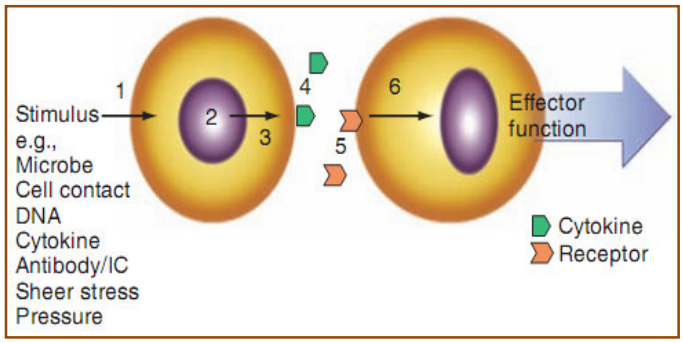
- Practice careful hygiene. Avoid contact with blood and body fluids.
- Do not handle items that may have come in contact with an infected person's blood or body fluids.
- Avoid funeral or burial rituals that require handling the body of someone who has died from Ebola.
- Avoid contact with bats and nonhuman primates or blood, fluids, and raw meat prepared from these animals.
- Avoid hospitals where Ebola patients are being treated. The U.S. embassy or consulate is often able to provide advice on facilities.

- After you return, monitor your health for 21 days and seek medical care immediately if you develop symptoms of Ebola.

References: 1) www.cdc.gov/vhf/ebola/about.html
2) www.who.int/mediacentre/factsheets/fs103/en/

Terminology
Cytokines

A family of PROTEIN molecules that carry signals locally between cells. Cytokines are released by cells when activated by antigens, behaving as enhancing mediators for immune response. These proteins include interleukins (produced by leucocytes), lymphokines (produced by lymphocytes), interferon and tumour necrosis factor, one of whose many functions is killing tumour cells.



Source: *Marcovitch H. 2005. Black's Medical Dictionary. 41th ed. London: A&C Black Publishers Limited. p 178*
Picture from: www.us.elsevierhealth.com/media/us/samplechapters/9781416048428/Ch023.pdf

10 Drug Interactions Every Pharmacist Should Know

1) Fluoxetine (SSRIs) and Phenelzine (MAOI)

This interaction can result in a central serotonin syndrome. The symptoms of serotonin syndrome can develop quickly with only 1 or 2 doses of fluoxetine when combined with phenelzine.
It is recommended that fluoxetine be stopped for at least 5 weeks before a MAOI is prescribed because of the long half-life of fluoxetine and its primary metabolite, norfluoxetine. Also, 2 weeks should be allowed after discontinuation of a MAOI before starting SSRI treatment.

2) Digoxin and Quinidine

This interaction can lead to a marked increase in plasma concentration levels of digoxin in more than 90% of patients .Significant changes in serum digoxin are noticed within 24 hours. The average increase is roughly 2-fold .The effects from this interaction range from nausea and vomiting to death. The primary mechanism for this interaction is a decreased volume of distribution of digoxin, secondary to its displacement from binding sites in body tissues. Quinidine also decreases renal and non renal excretion rates of digoxin, which leads to increased steady-state concentrations of the cardiac glycoside.Ideally, patients taking digoxin should avoid the use of quinidine; however, if the combination is necessary, the patient should be closely watched. Pharmacists should anticipate the need to reduce the digoxin dose by one half.

3) Sildenafil and Isosorbide Mononitrate

Sildenafil may markedly increase the hypotensive effects of isosorbide mononitrate.

When sildenafil was made available in the United States, most deaths were among patients with 1 or more risk factors, including obesity, hypertension, and cigarette smoking. Sildenafil was developed as a phosphodiesterase-5 (PDE5) inhibitor. In the presence of PDE5 inhibitors, nitrates can cause intense increases in cyclic guanosine monophosphate and dramatic drops in blood pressure Patients taking isosorbide mono-nitrate or any nitrate, including nitroglycerin, should be advised not to take sildenafil.

4) Potassium Chloride and Spironolactone

The combination may result in hyperkalemia.The resulting hyperkalemia can be serious and may lead to cardiac failure and death. Patients with renal impairment are especially prone to this effect. Spironolactone is a competitive antagonist of mineral corticoids, of which aldosterone is a potent example.This mechanism occurs in the kidney at the distal portion of the nephron and leads to the excretion of sodium ions while saving potassium ions. Patients receiving other potassium-sparing diuretics, such as amiloride or triamterene, may also experience this interaction. These diuretics can interact with all absorbable forms of potassium bicarbonate, citrate, acetate, gluconate, and iodide salts.

5) Clonidine and Propranolol

The combination may produce a mysterious hypertension that is unrelated to the pharmacology of either agent when administered independently. A sudden withdrawal of clonidine from adjunctive therapy with propranolol may cause fatal rebound hypertension.
Clonidine is a central alpha-2 adrenergic agonist that suppresses the sympathetic nervous system from the brain. This activity leads to a decrease in the norepinephrine amounts available in the synaptic cleft of the adrenergic neuron. Alpha-1 receptors then become sensitized because of less norepinephrine available in the cleft. When clonidine is suddenly withdrawn, the result is a large increase in norepinephrine in the synaptic cleft of the adrenergic neuron. The sensitized alpha-1 receptors are stimulated, leading to an exaggerated vasoconstriction. The body cannot compensate for this response because the beta-2 receptors are blocked when a patient is concurrently taking propranolol. Within 24 to 72 hours, a dramatic rebound hypertension is noticed.

6) Warfarin and Diflunisal

Nonsteroidal anti-inflammatory drugs (NSAIDs), such as diflunisal, have been shown to increase the risk for gastrointestinal (GI) bleeding and the anticoagulant response of warfarin.Other NSAIDs such as ketoprofen, piroxicam, sulindac, diclofenac, and ketorolac have been shown to have similar interactions with warfarin. In most patients, however, indomethacin has little effect on hypothrombinemic response.Because the interaction between warfarin and diflunisal can lead to GI bleeding or even fatal hemorrhaging, an alternative to diflunisal is suggested. Acetaminophen is the alternative of choice. Yet, if a NSAID is needed, nonacetylated salicylates such as magnesium salicylate or salsalate are safer because of minimal effects on platelets and gastric mucosa.

7) Theophylline and Ciprofloxacin

Concurrent administration may lead to toxic increases in theophylline.This problem occurs because the hepatic metabolism of theophylline is inhibited by ciprofloxacin via the cytochrome P-450 enzyme system. Theophylline is metabolized by CYP1A2 and to a lesser extent by CYP3A4. Ciprofloxacin and other drugs, including clarithromycin, erythromycin, fluvoxamine, and cimetidine, are all potent inhibitors of CYP1A2. Because they have little effect on CYP1A2, levofloxacin or ofloxacin should be considered as an

alternative to ciprofloxacin. Signs of theophylline toxicity include headache, dizziness, hypotension, hallucinations, tachycardia, and seizures.

8) Pimozide and Ketoconazole

Pimozide alone can prolong the QT interval, and it has been linked with ventricular arrhythmias (torsades de pointes).When pimozide is combined with ketoconazole, the combination can be deadly. Pimozide is a CYP3A4 enzyme substrate, and ketoconazole is a potent inhibitor of CYP3A4. This leads to marked increases in pimozide serum levels.Other drugs such as itraconazole, clarithromycin, erythromycin, diltiazem, and nefazodone are also potent inhibitors of CYP3A4 and should not be administered with pimozide. Fluconazole is weaker, but in larger doses it also inhibits CYP3A4. Terbinafine is a safer choice because it does not affect CYP3A4.

9) Methotrexate and Probenecid

When probenecid is administered with antineoplastic doses of methotrexate, the result can be a 2- to 3-fold increase in methotrexate levels. Probenecid acts as an active tubular secretion inhibitor and prevents methotrexate from being excreted, thus potentially causing toxicity. The symptoms of severe methotrexate toxicity include diarrhea, vomiting, diaphoresis, and renal failure, and it may result in death.This interaction with methotrexate also occurs with penicillins (eg, amoxicillin, carbenicillin) and salicylates.The risk with low-dose methotrexate (commonly used for rheumatic arthritis) is lower; in fact, NSAIDs in combination with low-dose methotrexate are often prescribed purposely.Possible alternatives include acetaminophen, as opposed to salicylates or NSAIDs. Celecoxib does not affect methotrexate pharmacokinetics and could be an alternative. However, rofecoxib produces some increases in methotrexate serum concentrations and therefore should be avoided.

10) Bromocriptine and Pseudoephedrine

The interaction can lead to severe peripheral vasoconstriction, ventricular tachycardia, seizures, and possibly death.Bromocriptine is an ergot-derived dopamine agonist with several uses, including antiparkinsonian therapy. New treatment guidelines for Parkinsons disease recommend a first-line therapy change from levodopa to bromocriptine or other dopamine agonists, such as ropinirole, pramipexole, or pergolide. Notable side effects of bromocriptine include thickening of bronchial secretions and nasal congestion.This is significant because it increases the likelihood of a patient taking bromocriptine to self-medicate with an OTC decongestant such as pseudoephedrine. Patients receiving bromocriptine should be advised to avoid all sympathomimetics.

Source: www.pharmacytimes.com

Test Your Knowledge

XY is a 49-year-old patient who is allergic to penicillin. She was prescribed erythromycin for cellulitis. She developed a rash and erythromycin was withdrawn.

Q1: Which of the following antibacterial agents is the most appropriate for XY:

A- flucloxacillin
B- cefuroxime
C- nalidixic acid
D- fluconazole
E- isoniazid

Q2: When XY is started on the new treatment:

1- Development of a rash should be monitored.
2- Signs of anaphylaxis should be detected.
3- An allergic reaction could develop after a month after last drug administration.

A- 1, 2, 3
B- 1, 2 only
C- 2, 3 only
D- 1 only
E- 3 only

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional health team as well as from others. Here's one of the enquiries received at the center!

Enquiry received from Ph. Huda El-sayed - Assiut Univ. Hospital- Cardiology dept.
Enquiry: Is Midazolam compatible with Dobutamine in Y- site injection?

***Summary of* Answer:** Both drugs are variably compatible, depending on concentrations:

Midazolam (Roche) 1mg/ml + 4mg/ml Dobutamine (LI): Compatible for 24 hrs at 23º C

Midazolam (Roche) 2mg/m + 4mg/ml Dobutamine (LI): Compatible for 4 hrs at 27º C

Midazolam (Roche) 1mg/ml + 2mg/ml Dobutamine (GNS): Incompatible; particles form in 8 hrs.

References: 1) Trissel L.A.(2013). Handbook On Injectable Drugs. 17th ed. Bethesda: American Society of Health- System Pharmacists. 1254p.
2) McEvoy G.K. (2011). Drug Information Essentials. Bethesda: American Society of Health- System Pharmacists. 2060p.

Ask the expert

Are there any particular foods that should be included or excluded from the diet of an individual suffering from arthritis?

First, there are many forms of arthritis, each of which differs in the do's and don'ts of diet. So, the answer is that it depends to some degree on the form of arthritis.

- People with **gouty arthritis** should tend to avoid red meats, shellfish, alcohol, fructose (such as from corn syrup in soft drinks, etc.), and dehydration. At the same time, dairy products such as low fat milk and yogurt, as well as adequate hydration, and cherries are encouraged in people with gout.
- People with **inflammatory arthritis**, such as rheumatoid arthritis, may benefit by taking the omega-3 fatty acids that are in the oils of fish, particularly salmon. Sometimes minimizing salt intake can reduce swelling in the tissues of the hands and feet that can aggravate inflammatory arthritis.
- Both people with **psoriatic arthritis** and **osteoarthritis** can benefit from vitamin D supplementation. Those with osteoarthritis also might benefit from the food supplement glucosamine.

It is worth noting that none of the dietary recommendations or supplementations have been proven to stop the progression of any of the forms of arthritis.

Answers:

A1(B) In penicillin-allergic patients, macrolides are usually the preferred drugs.Alternatively, a cephalosporin such as cefuroxime may be used with care.Some patients who are sensitive to penicillins may be also cephalosporin hypersensitive. Cephalosporins have a similar spectrum of activity to penicillins and macrolides and are usually effective against Gram-positive cocci. Cefur-oxime is a second generation cephalosporin that is less susceptible to inactivation by beta-lactamases compared with first-generation cephalosporins.

A2 (B) Hypersensitivity reactions may occur with any antibacterial agent. They are more commonly recognised with penicillins. Hypersensitivity reactions vary in presentation and may include development of a rash, an urticarial rash, fever or an acute anaphylactic reaction. Onset of allergic reaction may occur up to 14 days from first dose administration.

Did you know?!

"How long have you had the light headedness?"

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