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The Crux

BIMONTHLY FORUM FOR THE LABORATORIANS

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Editorial

Ebola, *also known as* ***Ebola virus disease (EVD) and Ebola hemorrhagic fever (EHF)****, is a zoonotic viral hemorrhagic fever in humans and other primates, caused by four of the six known ebolaviruses. Symptoms typically start anywhere between two days and three weeks after infection. The first symptoms are usually fever, sore throat, muscle pain, and headaches. These are usually followed by vomiting, diarrhoea, rash, hepatic and renal dysfunction, at which point some people begin to bleed both internally and externally. Outbreaks of the disease have had a mortality rate of between 25 and 90%, averaging out at approximately 50%. The viral species involved and timing of treatment play a critical role in its prognosis. Death is often due to shock from fluid loss, and typically occurs between 6 and 16 days after the first symptoms appear.*

The viruses have caused intermittent outbreaks in sub-Saharan Africa since 1976 when the disease was first reported, with the largest one being the 2013–16 Western African epidemic. They spread through direct contact with body fluids, such as blood from infected humans or other animals, or from contact with items that have recently been contaminated with infected body fluids. There have been no documented cases, either in nature or under laboratory conditions, of spread through the air between humans or other primates. After recovering from Ebola, semen or breast milk may continue to carry the virus for anywhere from several weeks to several months. Fruit bats are believed to be the natural host of the viruses; they are able to spread the viruses without being affected by it. The symptoms of Ebola may resemble those of several other diseases, including malaria, cholera, typhoid fever, meningitis and other viral hemorrhagic fevers. Diagnosis is confirmed by testing blood samples for the presence of viral RNA, viral antibodies or the virus itself. ***DISEASE DIAGNOSIS*** *talks about ebola virus in ample detail.* ***UNDERSTANDING*** *highlights Melena,* ***TROUBLESHOOTING*** *discusses* ***STOOL ANALYSIS.*** *Well.* ***BOUQUET*** *is not omitted.*

DISEASE DIAGNOSIS

THE EBOLA VIRUS INFECTION

Background

Ebola virus is one of at least 30 known viruses capable of causing viral hemorrhagic fever syndrome. Although agents that cause viral hemorrhagic fever syndrome constitute a geographically diverse group of viruses, all of those identified to date are RNA viruses with a lipid envelope, all are considered zoonoses, all damage the microvasculature (resulting in increased vascular permeability), and all are members of 1 of the following 4 families:

- Arenaviridae
- Bunyaviridae
- Flaviviridae
- Filoviridae

Although some of the hemorrhagic fever viruses are normally spread by ticks or mosquitoes, all but one (ie, dengue hemorrhagic fever) are capable of being spread by aerosols, and this capability makes these viruses potential bioterrorism agents. The family Filoviridae resides in the order Mononegavirales and contains the largest genome within the order. This family contains 2 genera: *Ebolavirus* (containing 5 species) and the antigenically distinct *Marburgvirus* (containing a single species). In patients who have Ebola virus infection, exposure to the virus may be either primary (involving presence in an *Ebolavirus* -endemic area) or secondary (involving human-to-human or primate-to-human transmission). Physical findings depend on the stage of disease at the time of presentation. Studies have demonstrated that patients who die of Ebola viral infection do not develop a humoral immune response. However, in survivors neutralizing antibody can be detected. It is likely that a broad humoral immune response can increase the likelihood of an infected patient surviving Ebola. No specific therapy is available that has demonstrated efficacy in the treatment of Ebola hemorrhagic fever, and there are no commercially available Ebola virus vaccines. General medical support is critical. Care must be administered with strict attention to barrier isolation. Because the source of Ebola virus is unknown, education and prevention of primary cases is problematic. Education of communities at risk, especially healthcare workers, can greatly reduce the number of secondary person-to-person transmissions.

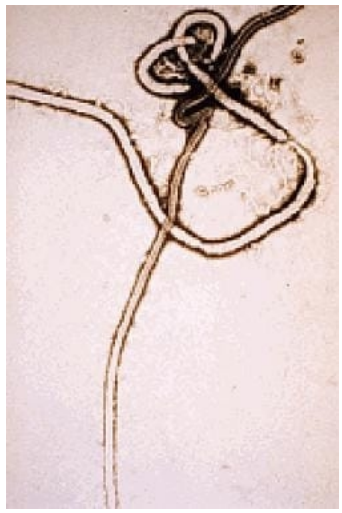
Pathophysiology and Etiology

Ultrastructure and pathogenesis

The known members of the family Filoviridae are the genera *Ebolavirus* (Ebola virus) and *Marburgvirus* (Marburg virus). According to the 2012 virus taxonomy of the International Committee on Taxonomy of Viruses, *Ebolavirus* is classified into the following 5 separate species:

1. *Sudan ebolavirus*
2. *Zaire ebolavirus*
3. *Tai Forest ebolavirus* (formerly and perhaps still more commonly *Ivory Coast ebolavirus* or *Côte d'Ivoire ebolavirus*)
4. *Reston ebolavirus*
5. *Bundibugyo ebolavirus*

Filoviruses such as Ebola virus share a characteristic filamentous form, with a uniform diameter of approximately 80 nm but a highly variable length. Filaments may be straight, but they are often folded on themselves.



Ebola virus.

RNA genome containing 7 structural and regulatory genes. The Ebola genome codes for 4 virion structural proteins (VP30, VP35, nucleoprotein, and a polymerase protein [L]) and 3 membrane-associated proteins (VP40, glycoprotein [GP], and VP24). The GP gene is positioned fourth from the 3' end of the 7 linearly arranged genes.

After infection, human and nonhuman primates experience an early period of rapid viral multiplication that, in lethal cases, is associated with an ineffective immunologic response. Although a full understanding of Ebola virus disease must await further investigations, part of the pathogenesis has been elucidated. Most filovirus proteins are encoded in single reading frames; the surface GP is encoded in 2 frames (open reading frame [ORF] I and ORF II). The ORF I (amino-terminal) of the gene encodes for a small (50-70 kd), soluble, nonstructural secretory glycoprotein (sGP) that is produced in large quantities early in Ebola virus infection. The sGP binds to neutrophil CD16b, a neutrophil-specific Fc g receptor III, and inhibits early neutrophil activation. The sGP also may be responsible for the profound lymphopenia that characterizes Ebola infection. Thus, sGP is believed to play pivotal roles in the ability of Ebola to prevent an early and effective host immune response. One hypothesis is that the lack of sGP production by Marburg virus may explain why this agent is less virulent than African-derived Ebola virus. Leroy and colleagues reported their observations of 24 close contacts of symptomatic patients actively infected with Ebola. Eleven of the 24 contacts developed evidence of asymptomatic infection associated with viral replication. Viral replication was proven by the authors' ability to amplify positive-stranded Ebola virus RNA from the blood of the asymptomatic contacts. A detailed study of these infected but asymptomatic individuals revealed that they had an early (4-6 days after infection) and vigorous immunologic response with production of interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF), resulting in enhanced cell-mediated and humoral-mediated immunity. In patients who eventually died, proinflammatory cytokines were not detected even after 2 to 3 days of symptomatic infection. A second, somewhat larger (120-150 kd) GP, transmembrane glycoprotein, is incorporated into the Ebola virion and binds to endothelial cells but not to neutrophils. Ebola virus is known to invade, replicate in, and destroy endothelial cells. Destruction of endothelial surfaces is associated with disseminated intravascular coagulation, and this may contribute to the hemorrhagic manifestations that characterize many, but not all, Ebola infections.

Clinical infection in human and nonhuman primates is associated with rapid and extensive viral replication in all tissues. Viral replication is accompanied by widespread and severe focal necrosis. The most severe necrosis occurs in the liver, and this is associated with the formation of Councilman-like bodies similar to those seen in yellow fever. In fatal infections, the host's tissues and blood contain large numbers of Ebola virions, and the tissues and body fluids are highly infectious. The 5 *Ebolavirus* species were named for the locations where they caused documented human or animal disease. Two African species, *Sudan ebolavirus* and *Zaire ebolavirus*, have been responsible for most of the reported deaths. Clinical disease due to African-derived Ebola virus is severe and, with the exception of a patient who survived infection with a third African species, *Ivory Coast ebolavirus*, is associated with a mortality ranging from 65% (Sudan, 1979) to 89% (Democratic Republic of the Congo [DRC], December 2002-April 2003). A fourth *Ebolavirus* species, *Reston ebolavirus,* was first isolated in 1989 in monkeys imported from a single Philippine exporter. A virtually identical isolate imported from the same Philippine exporter was detected in 1992 in Siena, Italy. To date, this species has not been documented to cause human disease. The fifth *Ebolavirus* species, also of African lineage, is *Bundibugyo ebolavirus*, which caused an outbreak in Uganda in 2007 to 2008, with a mortality of 25%. Between 1994 and 1997, a stable strain of Ebola virus caused 3 successive outbreaks of hemorrhagic fever in Gabon (mortality, 60%-74%). Because the Gabon strain shares a greater than 99% homology of the nucleoprotein and GP gene regions with *Zaire ebolavirus*, it has not been considered a distinct species. A likely reservoir for filoviruses has been identified. In 1996, members of the National Institute for Virology of South Africa went to Kikwit, DRC, and evaluated the infectivity of Ebola virus for 24 species of plants and 19 species of vertebrates and invertebrates. Insectivorous bats and fruit bats were found to support Ebola virus replication without dying. Furthermore, serum Ebola titers in infected fruit bats reached as high as 10 fluorescent focus-forming units/mL, and feces contained viable Ebola virus.

Mechanisms of dispersion

African-derived filovirus infections are characterized by transmission from an unknown host (possibly bats) to humans or nonhuman primates, presumably via direct contact with body fluids such as saliva or blood or other infected tissues. Evidence in nonhuman primates indicates that *Sudan ebolavirus* and *Zaire ebolavirus* may be transmitted by contact with mucous membranes, conjunctiva, pharyngeal and gastrointestinal surfaces; through small breaks in the skin; and, at least experimentally, by aerosol. Dogs have been shown to acquire asymptomatic Ebola virus infections, possibly by contact with virus-laden droplets of urine, feces, or blood of unknown hosts. Of epidemiologic significance was the observation that seroprevalence rates in dogs rose in a linear fashion as sampling approached areas of human cases, reaching as high as 31.8%. Thus, an increase in canine seroprevalence may serve as an indicator of increasing Ebola virus circulation in primary vectors within specific geographical areas. Human infection with African-derived strains has often occurred in caregivers (either family or medical) and in family members who have prepared dead relatives for burial. Late stages of Ebola virus disease are associated with the presence of large numbers of virions in body fluids, tissues, and, especially, skin. Individuals who are exposed to patients infected with Ebola without proper barrier protection are at high risk of becoming infected. A report from the DRC identified Ebola virus RNA in 100% of oral secretions from patients who had the viral RNA in their serum. Both serum and oral secretions were tested with reverse-transcriptase polymerase chain reaction (RT-PCR) assay. Thus, oral secretions may be capable of transmitting Ebola virus. Among infection survivors, only males had been shown to transmit the virus, via semen, in which the virus can persist for up to 2 years. However, a 2018 study found that previously infected women may also harbor a reservoir of dormant virus, which is theorized to have reactivated upon immunosuppression (suspected to result from pregnancy in the study case). The first recorded outbreak occurred in 1976, in Yambuku, DRC, where 316 patients were infected. In the largest recorded urban outbreak to date (DRC, 1995; 318 cases), admission to a hospital greatly amplified the frequency of transmission. The lack of proper barrier protection and the use and reuse of contaminated medical equipment, especially needles and syringes, resulted in rapid nosocomial spread of infection. Only after adequate barrier protection and alteration in burial rituals were implemented was the outbreak contained. Unlike Asian-derived Ebola virus (ie, *Reston ebolavirus,* traced to a Philippine supplier of primates), African-derived species appear to be spread more often by direct contact than via the respiratory route. However, the Reston species has repeatedly been demonstrated to spread among nonhuman primates and possibly from primates to humans via the respiratory route. Fortunately, although the Reston species has been documented to be capable of infecting humans, it does not appear to be pathogenic to humans.

Epidemiology

Ebola virus is not endemic in the United States, although, during the 2014-2016 Ebola outbreak, several US healthcare personnel were in Africa and were transported to the United States for treatment, in addition to a traveller from Liberia who became ill and sought treatment while visiting Texas. The patient later died of the infection. One of his treating nurses then presented with a low-grade fever and tested positive for Ebola virus infection. In addition, individuals in several US states who travelled to West Africa developed fever and other symptoms, prompting evaluation for Ebola virus infection at US hospitals. Before the 2014 - 2016 outbreak, several human infections with the Reston strain of Ebola had been acquired by animal care workers at primate holding facilities within the United States. Fortunately, the Reston strain has not demonstrated pathogenic effects in humans. Others at potential risk are laboratory workers who work with inf ected animals or with the virus in tissue culture.

International statistics

On May 8, 2018, a new outbreak of Ebola virus disease was declared in the Democratic Republic of the Congo (DRC) following laboratory confirmation of 2 cases of EVD. Before confirmation of the outbreak, 21 patients with signs of hemorrhagic fever had recently been reported in the country, 17 of whom died. As of September 17, 2019, 3,034 confirmed cases had been reported and 111 probable cases, including 2,103 attributable deaths. Ebola and Marburg viruses are responsible for well-documented outbreaks of severe human hemorrhagic fever, with resultant case mortalities ranging from 23% for Marburg virus to 89% for Ebola virus in which more than one case occurred. The 2014-2016 Ebola virus outbreak was significant and primarily involved 3 African countries—Guinea, Liberia, and Sierra Leone. Localized transmission was been reported in Nigeria. Based on genetic analysis, the virus was 97% identical to the Zaire ebolavirus identified in cases in Gabon and the Democratic Republic of the Congo earlier in 2014. At least 3 Americans in Africa were infected with Ebola in the 2014-2016 outbreak, 1 of whom died of the disease.

Table 1. History of Sudan Ebola Virus Outbreaks

Year	Country	Cases	Deaths	Case Fatality Rate
2012	Uganda	7	4	57%
2012	Uganda	24	17	71%
2011	Uganda	1	1	100%
2004	Sudan	17	7	41%
2000	Uganda	425	224	53%
1979	Sudan	34	22	65%
1976	Sudan	284	151	53%
Data from World Health Organization				

Table 2. History of Zaire Ebola Virus Outbreaks

Year	Country	Cases	Deaths	Case Fatality Rate
2018-2019	Democratic Republic of the Congo (DRC)	Ongoing		
2018	DRC	54	33	61%
2017	DRC	8	4	50%
2015	Italy	1	0	0%
2014	Spain	1	0	0%
2014	UK	1	0	0%
2014	USA	4	1	25%
2014	Senegal	1	0	0%
2014	Mali	8	6	75%
2014	Nigeria	20	8	40%
2014-2016	Sierra Leone	14,124*	3,956*	28%
2014-2016	Liberia	10,675*	4,809*	45%
2014-2016	Guinea	3,811*	2,543*	67%
2008	DRC	32	14	44%
2007	DRC	264	187	71%
2005	Republic of the Congo	12	10	83%
2003 (Nov-Dec)	Republic of the Congo	35	29	83%
2003 (Jan-Apr)	Republic of the Congo	143	128	90%
2001-2002	Republic of the Congo	59	44	75%
2001-2002	Gabon	65	53	82%
1996	South Africa (ex-Gabon)	1	1	100%
1996 (Jul-Dec)	Gabon	60	45	75%
1996 (Jan-Apr)	Gabon	31	21	68%
1995	DRC	315	254	81%
1994	Gabon	52	31	60%
1977	DRC	1	1	100%
1976	DRC	318	280	88%
*Includes suspected, probable, and confirmed EVD cases. Data from World Health Organization.				

Table 3. History of Tai Forest (Ivory Coast, Côte-d'Ivoire) Ebola Virus Outbreaks (No Deaths Reported)

Year	Location	Reported Cases, No.
1994	Côte-d'Ivoire	1
Total		**1**
Data from Centers for Disease Control and Prevention and World Health Organization.		

Table 4. History of Reston Ebola Virus Outbreaks (No Deaths Reported)

Year	Location	Proven Cases Reported, No.
1989	Virginia, Texas, Pennsylvania	0
1990	Virginia and Texas	4
1989-1990	Philippines	3
1992	Italy	0
1990	Alice, TX	0
1996	Philippines	0
Nov 2008	Philippines	6
Total		**13**
Data from Centers for Disease Control and Prevention and World Health Organization. Humans with serologic evidence of infection but without clinical disease. Associated with pig farming.		

Table 5. History of Bundibugyo Ebola Virus Outbreak

Year	Location	Reported Cases, No.	Deaths, No. (%)
Dec 2007 to Jan 2008	Uganda	149	37 (25)
Jun to Nov 2012	Democratic Republic of the Congo	57	29 (50.1)
Total		**206**	**66 (32)**
Data from Centers for Disease Control and Prevention and World Health Organization.			

Individuals considered at risk for Ebola hemorrhagic fever include persons with a travel history to sub-Saharan Africa, persons who have recently cared for infected patients, and animal workers who have worked with primates infected with African-derived Ebola subtypes. In 2011, Uganda experienced a reemergence of the disease.

Age-related demographics

In the 1995 outbreak in Kikwit, DRC, infection rates were significantly lower in children than in adults. During this outbreak, only 27 (8.6%) of the 315 patients diagnosed with Ebola virus infection were 17 years of age or younger. This apparent sparing of children occurs even though 50% of the population of the DRC is younger than 16 years. Although definitive evidence is lacking, epidemiologic evidence suggests that children are less likely to come into direct contact with ill patients than adults are. Other viral hemorrhagic syndromes, such as Crimean-Congo hemorrhagic fever and hantavirus infections, also show a predominance of adult patients and a relative sparing of young children.

Sex-related demographics

Ebola virus infection has no sexual predilection, but men and women differ with respect to the manner in which direct exposure occurs. Men, by the nature of their work exposure in forest and savanna regions, may be at increased risk of acquiring a primary infection from gathering "bush meat" (primate carcasses) for food, as well as an unknown vector or vectors. Evidence from Africa and the Philippines is compatible with bats being a principal vector of Ebola virus. Because women provide much of the direct care for ill family members and are involved in the preparation of the bodies of the deceased, they may be at increased risk of acquiring Ebola virus infection through their participation in these activities; however, men and women who are medical healthcare providers seem to share a high and equal risk for infection.

Race-related demographics

Because most cases of Ebola virus infection have occurred in sub-Saharan Africa, most patients have been black. However, no evidence exists for a specific racial predilection.

Prognosis

The overall prognosis for patients with Ebola virus infection is poor. However, those who survive for 2 weeks often make a slow recovery. With the exception of the Reston strain, Ebola virus is associated with very high morbidity and mortality among patients who present with clinical illness, though these vary according to the causative species. The most highly lethal *Ebolavirus* species is *Zaire ebolavirus*, which has been reported to have a mortality rate as high as 89%. *Sudan ebolavirus* also has high reported mortality, ranging from 41% to 65%.

Physical Examination

Physical findings depend on the stage of disease at the time of presentation. Early in the disease, patients may present with fever, pharyngitis, and severe constitutional signs and symptoms. A maculopapular rash, more easily seen on white skin than on dark skin, may be present around day 5 of infection and is most evident on the trunk. Bilateral conjunctival injection is also common. Late in the disease, patients often develop an expressionless facies. At this point, bleeding from intravenous (IV) puncture sites and mucous membranes is common. It is worth noting that in the 1976 Ebola outbreak, bleeding was seen in most cases, whereas in the 1995 Ebola outbreak, bleeding occurred in only half of the patients. Myocarditis and pulmonary edema also are seen in the later stages of the disease. Terminally ill patients often die tachypneic, hypotensive, anuric, and in a coma.

Clinical course

Human infections with African-derived *Ebolavirus* species are characterized by an incubation period that is typically 3 to 8 days in primary cases and slightly longer in secondary cases. However, cases with incubation periods of 19 and 21 days have been observed. The onset of clinical symptoms is sudden. Severe headache (50-74%), arthralgias or myalgias (50-79%), fever with or without chills (95%), anorexia (45%), and asthenia (85-95%) occur early in the disease. Gastrointestinal symptoms, including abdominal pain (65%), nausea and vomiting (68-73%), and diarrhea (85%), soon follow. Evidence of mucous membrane involvement includes conjunctivitis (45%), odynophagia or dysphagia (57%), and bleeding from multiple sites in the gastrointestinal tract. Bleeding from mucous membranes and puncture sites is reported in 40-50% of patients. A rash, which in survivors desquamates during convalescence, is seen in approximately 15% of patients. Terminally ill patients often are obtunded, anuric, tachypneic, normothermic, and in shock. Although the mechanism is unclear, hiccups were noted in fatal cases of Ebola virus disease in both the 1976 and the 1995 outbreaks in the Democratic Republic of the Congo (DRC). In the 1995 Ebola virus outbreak in Kikwit, DRC, tachypnea was the single most discriminating sign that separated survivors (none of whom had tachypnea) from patients who died (37% of whom had tachypnea).

Complications

Ocular complications were reported in 3 (15%) of 20 survivors of the 1995 Ebola outbreak in the Democratic Republic of the Congo (DRC). Patients reported ocular pain, photophobia, increased lacrimation, and decreased visual acuity. All had documented uveitis, and all improved with topical application of 1% atropine and steroids.

Survivors of Ebola virus disease have developed the following late manifestations:

- Myalgias
- Asymmetric and migratory arthralgias
- Headache
- Fatigue
- Bulimia
- Amenorrhea
- Hearing loss
- Tinnitus
- Unilateral orchitis
- Suppurative parotitis

Diagnostic Considerations

Ebola hemorrhagic fever should be considered in patients who have recently traveled to areas where Ebola has been reported or in patients who have been exposed to known cases and who exhibit signs and symptoms consistent with Ebola virus infection. A main concern in dealing with Ebola virus infections is the potential for human-to-human spread of virus before the correct diagnosis is made. This risk includes all medical personnel in direct contact with the patient, the patient's blood, or other body fluids or tissues. Family members who care for patients or who are involved in burial ceremonies and come into contact with the body, blood, or other body fluids are also at high risk for Ebola virus infection.

In addition to the conditions listed in the differential diagnosis, other problems to be considered include the following:

- Acute surgical abdomen (as distinct from abdominal signs of Ebola hemorrhagic fever)
- Crimean-Congo hemorrhagic fever
- Marburg hemorrhagic fever
- Other hemorrhagic fevers

Differential Diagnoses

- Malaria
- Enteric fever

RELATED LAB WORK

Authorization for 2 new tests for detecting Ebola in humans. The tests, which can detect Ebola in blood or urine samples in 1 hour, can be performed on-site in hospitals with the proper lab equipment from the tests' manufacturer, BioFire Defense. In other tests, samples must be sent from hospitals to be run in specialized labs and require 24 to 48 hours to produce results. Emergency use authorizations by the FDA permit the use of unapproved medical products in dealing with life-threatening illnesses when no approved or available alternatives exist.

Laboratory Studies

Basic blood tests

The early phase of infection is characterized by thrombocytopenia, leukopenia, and a pronounced lymphopenia. Neutrophilia develops after several days, as do elevations in aspartate aminotransferase and alanine aminotransferase. Bilirubin may be normal or slightly elevated. With the onset of anuria, blood urea nitrogen and serum creatinine increase. Terminally ill patients may develop a metabolic acidosis that may contribute to the observation that these patients often have tachypnea, which may be an attempt at compensatory hyperventilation.

Studies for isolating virus

Definitive diagnosis rests on isolation of the virus by means of tissue culture or reverse-transcription polymerase chain reaction (RT-PCR) assay. However, isolation of Ebola virus in tissue culture is a high-risk procedure that can be performed safely only in a few high-containment laboratories throughout the world.

Serologic testing for antibody and antigen

The indirect fluorescence antibody test (IFAT) is associated with false-positive results. Concerns over the sensitivity and utility of this test have resulted in the development of confirmatory serologic tests. In infected patients who survive long enough to develop an immune response, the immunoglobulin M (IgM) and immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) tests may be useful in the diagnosis of Ebola virus infection. Both ELISA tests have been demonstrated to be sensitive and specific. IgM-capture ELISA uses *Zaire ebolavirus* antigens grown in Vero E6 cells to detect IgM antibodies to this strain. Results become positive in experimental primates within 6 days of infection but do not remain positive for extended periods. These qualities indicate that the IgM test may be used to document acute Ebola infection. IgG-capture ELISA uses detergent-extracted viral antigens to detect IgG anti-Ebola antibodies. It is more specific than the IFAT, and it remains positive for long periods. Accordingly, this test appears to be superior for seroprevalence investigations. An antigen detection ELISA test is available that identifies Ebola virus antigens.

Other studies

The risks in viral isolation have led to the development of various modalities that better lend themselves to laboratories with limited containment systems. Tests used to confirm the diagnosis of Ebola virus infection include an immunohistochemical test performed on formalin-fixed postmortem skin taken from patients who have died of Ebola hemorrhagic fever. This test is safe, sensitive, and specific, and it can be used for diagnosis and surveillance. Electron microscopy has been used to identify filoviruses in tissue but has obvious limitations as a diagnostic modality in the areas where human outbreaks have occurred. It is not readily available in areas where Ebola virus is endemic.

Histologic Findings

Although capable of involving many tissues, Ebola virus has a predilection for endothelial cells, hepatocytes, and mononuclear phagocytes. Viral replication is associated with extensive focal necrosis and is most severe in the liver, spleen, lymph nodes, kidney, lung, and gonads. In the liver, eosinophilic globules derived from focal necrosis of hepatic cells (Councilman-like bodies), similar to those seen in yellow fever, are prevalent. However, the focal necrosis associated with Ebola virus replication results in a minimal effective inflammatory response. Late in the disease, the intestinal mucosa may separate from the lamina propria and slough.

TREATMENT

A safe and effective vaccine is an important tool to protect and prevent the introduction and spread of Ebola. Ebola Zaire vaccine (rVSV-ZEBOV; V920; Merck) has been approved in the United States and Europe. This vaccine is genetically engineered to express a glycoprotein from *Zaire ebolavirus* to provoke a neutralizing immune response. It has shown an efficacy of 97.5% in preventing infection among 90,000 individuals in an active Ebola virus outbreak in the Democratic Republic of the Congo. In the Ring vaccination study, in which patients were vaccinated during the 2014 outbreak in the Republic of Guinea, results among the people who received the vaccine showed no Ebola cases were recorded 10 days or more after vaccination. In comparison, there were 23 cases 10 days or more after vaccination among those who did not receive the vaccine. General medical support is critical and should include replacement of coagulation factors and heparin if disseminated intravascular coagulation develops. Such care must be administered with strict attention to barrier isolation. All body fluids (blood, saliva, urine, and stool) contain infectious virions and should be handled with great care. The recombinant monoclonal antibody combination, atoltivimab/ maftivimab/ odesivimab (Inmazeb), was approved by the FDA in October 2020 and is the first approved treatment for Zaire ebolavirus. It is indicated for treatment of Zaire ebolavirus in adults and children, including neonates born to a mother who is reverse-transcriptase polymerase chain reaction (RT-PCR) positive for Zaire ebolavirus infection.

UNDERSTANDING

Melena is a form of blood in stool which refers to the dark black, tarry feces that are commonly associated with upper gastrointestinal bleeding. The black color and characteristic strong odor are caused by hemoglobin in the blood being altered by digestive enzymes and intestinal bacteria.

Iron supplements may cause a grayish-black stool that should be distinguished from melena,[3] as should black coloration caused by a number of medications, such as bismuth subsalicylate (the active ingredient in Pepto-Bismol), or by foods such as beetroot, black liquorice, or blueberries.

Causes

The most common cause of melena is peptic ulcer disease. However, any bleeding within the upper gastrointestinal tract or the ascending colon can lead to melena.Melena may also be a complication of anticoagulant medications, such as warfarin. Causes of upper gastrointestinal bleeding that may result in melena include malignant tumors affecting the esophagus, stomach or small intestine, hemorrhagic blood diseases, such as thrombocytopenia and hemophilia, gastritis, stomach cancer, esophageal varices, Meckel's diverticulum and Mallory-Weiss syndrome. Causes of "false" melena include iron supplements, Pepto-Bismol, Maalox, and lead, blood swallowed as a result of a nosebleed (epistaxis), and blood ingested as part of the diet, as with consumption of black pudding (blood sausage), or with the traditional African Maasai diet, which includes much blood drained from cattle. Melena is considered a medical emergency as it arises from a significant amount of bleeding. Urgent care is required to rule out serious causes and prevent potentially life-threatening emergencies. A less serious, self-limiting case of melena can occur in newborns two to three days after delivery, due to swallowed maternal blood.

Diagnosis

In acute cases, with a large amount of blood loss, patients may present with anemia or low blood pressure. However, aside from the melena itself, many patients may present with few symptoms. Often, the first approach is to use endoscopy to look for obvious signs of a bleed. In cases where the source of the bleed is unclear, but melena is present, an upper endoscopy is recommended, to try to ascertain the source of the bleed. Lower gastrointestinal bleeding sources usually present with hematochezia or frank blood. A test with poor sensitivity/specificity that may detect the source of bleeding is the tagged red blood cell scan. This is especially used for slow bleeding (<0.5 ml/min). However, for rapid bleeding (>0.5 ml/min), mesenteric angiogram ± embolization is the gold standard. Colonoscopy is often first line, however.

Melena versus hematochezia

Bleeds that originate from the lower gastrointestinal tract (such as the sigmoid colon and rectum) are generally associated with the passage of bright red blood, or hematochezia, particularly when brisk. Only blood that originates from a more proximal source (such as the small intestine), or bleeding from a lower source that occurs slowly enough to allow for enzymatic breakdown, is associated with melena. For this reason, melena is often associated with blood in the stomach or duodenum (upper gastrointestinal bleeding), for example by a peptic ulcer. A rough estimate is that it takes about 14 hours for blood to be broken down within the intestinal lumen; therefore if transit time is less than 14 hours the patient will have hematochezia, and if greater than 14 hours the patient will exhibit melena.] One often-stated rule of thumb is that melena only occurs if the source of bleeding is above the ligament of Treitz although, as noted below, exceptions occur with enough frequency to render it unreliable.

TROUBLESHOOTING

Stool Analysis

A stool analysis is a series of tests done on a stool (feces) sample to help diagnose certain conditions affecting the digestive tract. These conditions can include infection (such as from parasites, viruses, or bacteria), poor nutrient absorption, or cancer.

For a stool analysis, a stool sample is collected in a clean container and then sent to the laboratory. Laboratory analysis includes microscopic examination, chemical tests, and microbiologic tests. The stool will be checked for color, consistency, amount, shape, odor, and the presence of mucus. The stool may be examined for hidden (occult) blood, fat, meat fibers, bile, white blood cells, and sugars called reducing substances. The pH of the stool also may be measured. A stool culture is done to find out if bacteria may be causing an infection.

Why It Is Done

Stool analysis is done to:

- Help identify diseases of the digestive tract, liver, and pancreas. Certain enzymes (such as trypsin or elastase) may be evaluated in the stool to help determine how well the pancreas is functioning.
- Help find the cause of symptoms affecting the digestive tract, including prolonged diarrhea, bloody diarrhea, an increased amount of gas, nausea, vomiting, loss of appetite, bloating, abdominal pain and cramping, and fever.
- Screen for colon cancer by checking for hidden (occult) blood.
- Look for parasites, such as pinworms or Giardia.
- Look for the cause of an infection, such as bacteria, a fungus, or a virus.
- Check for poor absorption of nutrients by the digestive tract (malabsorption syndrome). For this test, all stool is collected over a 72-hour period and then checked for fat (and sometimes for meat fibers). This test is called a 72-hour stool collection or quantitative fecal fat test.

How To Prepare

Many medicines can change the results of this test. You will need to avoid certain medicines depending on which kind of stool analysis you have. You may need to stop taking medicines such as antacids, antidiarrheal medicines, antiparasite medicines, antibiotics, laxatives, or nonsteroidal anti-inflammatory drugs (NSAIDs) for 1 to 2 weeks before you have the test. Be sure to tell your doctor about all the nonprescription and prescription medicines you take.

Be sure to tell your doctor if you have:

- Recently had an X-ray test using barium contrast material, such as a barium enema or upper gastrointestinal series (barium swallow). Barium can interfere with test results.
- Traveled in recent weeks or months, especially if you have traveled outside the country. This helps your doctor look for the parasites, fungi, viruses, or bacteria that may be causing a problem.

If your stool is being tested for blood, you may need to avoid certain foods for 2 to 3 days before the test. This depends on what kind of stool test you use. And do not do the test during your menstrual period or if you have active bleeding from hemorrhoids. If you aren't sure about how to prepare, ask your doctor.

Do not use a stool sample for testing that has been in contact with toilet bowl cleaning products that turn the water blue.

How It Is Done

Stool samples can be collected at home, in your doctor's office, at a medical clinic, or at the hospital. If you collect the samples at home, you will be given stool collection kits to use each day. Each kit contains applicator sticks and two sterile containers.

You may need to collect more than one sample over 1 to 3 days. Follow the same procedure for each day.

Collect the samples as follows:

- Urinate before collecting the stool so that you do not get any urine in the stool sample.
- Put on gloves before handling your stool. Stool can contain germs that spread infection. Wash your hands after you remove your gloves.
- Pass stool (but no urine) into a dry container. You may be given a plastic basin that can be placed under the toilet seat to catch the stool.
  - Either solid or liquid stool can be collected.
  - If you have diarrhea, a large plastic bag taped to the toilet seat may make the collection process easier; the bag is then placed in a plastic container.
  - If you are constipated, you may be given a small enema.
  - Do not collect the sample from the toilet bowl.
  - Do not mix toilet paper, water, or soap with the sample.
- Place the lid on the container and label it with your name, your doctor's name, and the date the stool was collected. Use one container for each day's collection, and collect a sample only once a day unless your doctor gives you other directions.

Take the sealed container to your doctor's office or the laboratory as soon as possible. You may need to deliver your sample to the lab within a certain time. Tell your doctor if you think you may have trouble getting the sample to the lab on time.

If the stool is collected in your doctor's office or the hospital, you will pass the stool in a plastic container that is inserted under the toilet seat or in a bedpan. A health professional will package the sample for laboratory analysis.

You will need to collect stool for 3 days in a row if the sample is being tested for quantitative fats. You will begin collecting stool on the morning of the first day. The samples are placed in a large container and then refrigerated.

You may need to collect several stool samples over 7 to 10 days if you have digestive symptoms after traveling outside the country.

Samples from babies and young children may be collected from diapers (if the stool is not contaminated with urine) or from a small-diameter glass tube inserted into the baby's rectum while the baby is held on an adult's lap.

Sometimes a stool sample is collected using a rectal swab that contains a preservative. The swab is inserted into the rectum, rotated gently, and then withdrawn. It is placed in a clean, dry container and sent to the lab right away.

How It Feels

There is no pain while collecting a stool sample. If you are constipated, straining to pass stool may be painful.

If your health professional uses a rectal swab to collect the sample, you may feel some pressure or discomfort as the swab is inserted into your rectum.

Risks

Any stool sample may contain germs that can spread disease. It is important to carefully wash your hands and use careful handling techniques to avoid spreading infection.

Results

A stool analysis is a series of tests done on a stool (feces) sample to help diagnose certain conditions affecting the digestive tract.

The normal values listed here-called a reference range-are just a guide. These ranges vary from lab to lab, and your lab may have a different range for what's normal. Your lab report should contain the range your lab uses. Also, your doctor will evaluate your results based on your health and other factors. This means that a value that falls outside the normal values listed here may still be normal for you or your lab.

Stool analysis test results usually take at least 1 to 3 days.

Stool analysis

Normal:	The stool appears brown, soft, and well-formed in consistency.
	The stool does not contain blood, mucus, pus, undigested meat fibers, harmful bacteria, viruses, fungi, or parasites.
	The stool is shaped like a tube.
	The pH of the stool is 7.0–7.5.
	The stool contains less than 0.25 grams per deciliter (g/dL)[less than 13.9 millimoles per liter (mmol/L)] of sugars called reducing factors. The stool contains 2–7 grams of fat per 24 hours (g/24h).
Abnormal:	The stool is black, red, white, yellow, or green.
	The stool is liquid or very hard.
	There is too much stool.
	The stool contains blood, mucus, pus, undigested meat fibers, harmful bacteria, viruses, fungi, or parasites.
	The stool contains low levels of enzymes, such as trypsin or elastase.
	The pH of the stool is less than 7.0 or greater than 7.5.
	The stool contains 0.25 g/dL (13.9 mmol/L) or more of sugars called reducing factors.
	The stool contains more than 7 g/24h of fat (if your fat intake is about 100 g a day).

Many conditions can change the results of a stool analysis. Your doctor will talk with you about any abnormal results that may be related to your symptoms and past health.

Abnormal values

- High levels of fat in the stool may be caused by diseases such as pancreatitis, sprue (celiac disease), cystic fibrosis, or other disorders that affect the absorption of fats.
- The presence of undigested meat fibers in the stool may be caused by pancreatitis.
- A low pH may be caused by poor absorption of carbohydrate or fat. Stool with a high pH may mean inflammation in the intestine (colitis), cancer, or antibiotic use.
- Blood in the stool may be caused by bleeding in the digestive tract.
- White blood cells in the stool may be caused by inflammation of the intestines, such as ulcerative colitis, or a bacterial infection.
- Rotaviruses are a common cause of diarrhea in young children. If diarrhea is present, testing may be done to look for rotaviruses in the stool.
- High levels of reducing factors in the stool may mean a problem digesting some sugars.
- Low levels of reducing factors may be caused by sprue (celiac disease), cystic fibrosis, or malnutrition. Medicine such as colchicine (for gout) or birth control pills may also cause low levels.

What Affects the Test

- Reasons you may not be able to have the test or why the results may not be helpful include:
- Taking medicines such as antibiotics, antidiarrheal medicines, barium, bismuth, iron, ascorbic acid, nonsteroidal anti-inflammatory drugs (NSAIDs), and magnesium.
- Contaminating a stool sample with urine, blood from a menstrual period or a bleeding hemorrhoid, or chemicals found in toilet paper and paper towels.
- Exposing the stool sample to air or room temperature or failing to send the sample to a laboratory within 1 hour of collection.

What To Think About

- Stool may be checked for hidden (occult) blood. Testing for faecal Occult Blood confirms.
- A stool culture is done to find the cause of an infection, such as bacteria, a virus, a fungus, or a parasite.
- A bowel transit time test is done to help find the cause of abnormal movement of food through the digestive tract.
- The D-xylose absorption test is done to help diagnose problems that prevent the small intestine from absorbing nutrients in food. This test may be done when symptoms of malabsorption syndrome (such as chronic diarrhea, weight loss, and weakness) are present.
- A stool analysis to measure trypsin or elastase is not as reliable as the sweat test to detect cystic fibrosis.

BOUQUET

In Lighter Vein

If salary *is cut if you come to office 15 mins late, why can't extra be added if you leave office 15 mins late?*

Doctors *are confused because corporate employees takes so many sick leaves but never come to their Clinic.*

On my last working day, *my Manager asked me to return everything the Company has given me...*

So, I asked him what is the procedure to return "DEPRESSION"?

Wisdom Whispers

"Success is the sum of small efforts repeated daily."

"Perseverance is the hard work you do after you get tired of doing the hard work you already did."

"Results happen over time, not overnight—work hard and be patient."

“No one can whistle a symphony. It takes a whole orchestra to play it."

Brain Teasers

1. **What family does the Ebola virus belong to?**
   A) Picornavirus
   B) Filovirus
   C) Poxvirus
   D) Influenza virus

2. **What type of genetic material does the Ebola virus contain?**
   A) Double-stranded DNA
   B) Single-stranded RNA
   C) Double-stranded RNA
   D) Single-stranded DNA

3. **What is the typical incubation period for the Ebola virus?**
   A) 1 to 2 days
   B) 2 to 21 days
   C) 30 to 40 days
   D) 45 to 60 days

4. **How is the Ebola virus primarily transmitted between humans?**
   A) Through the air via coughing
   B) Through mosquito bites
   C) Through direct contact with body fluids of a sick person
   D) By drinking contaminated water

ANSWER: 1-B, 2-B, 3-B, 4-C

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