Emerging infectious diseases with cutaneous manifestations

Viral and bacterial infections

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Learning objectives
After completing this learning activity, the participant should be able to describe the cutaneous manifestations of emerging viral and bacterial infections and identify appropriate therapy for case studies of emerging viral and bacterial infections with cutaneous manifestations.

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Given increased international travel, immigration, and climate change, bacterial and viral infections that were once unrecognized or uncommon are being seen more frequently in the Western Hemisphere. A delay in diagnosis and treatment of these diseases can lead to significant patient morbidity and mortality. However, the diagnosis and management of these infections is fraught with a lack of consistency because there is a dearth of dermatology literature on the cutaneous manifestations of these infections. We review the epidemiology, cutaneous manifestations, diagnosis, and management of these emerging bacterial and viral diseases. (J Am Acad Dermatol 2016;75:1-16.)

Key words: *Acinetobacter baumannii*; Chikungunya; dengue; Ebola; emerging infections; HFMD; Lyme; measles; melioidosis; rickettsia; trichodysplasia spinulosa; Zika.

EMERGING VIRAL DISEASES

The endemic areas of viral diseases, their clinical manifestations, and their diagnosis and treatment are summarized in Table I.

Ebola

Key points

- **Ebola is highly virulent and contagious, and the 2014 epidemic was declared a "public health emergency of international concern"**
- **Clinical manifestations include bleeding and nonspecific macules and papules**
- **Diagnosis is by reverse transcription polymerase chain reaction**
- **Treatment is mainly supportive**

Ebola is a hemorrhagic fever disease caused by the viruses of the *Ebolavirus* genus, a member of the Filoviridae family. Ebola was first discovered in 1976 near the Ebola River in the Democratic Republic of

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Abbreviations used:

ACA:	acrodermatitis chronica atrophicans
CDC:	Centers for Disease Control and Prevention
CVA6:	coxsackievirus A6
DHF:	dengue hemorrhagic fever
E71:	enterovirus 71
ELISA:	enzyme-linked immunosorbent assay
EM:	erythema migrans
HFMD:	hand foot and mouth disease
HGA:	human granulocytotropic anaplasmosis
HME:	human monocytotropic ehrlichiosis
MDR:	multidrug resistant
MRSA:	methicillin-resistant *Staphylococcus aureus*
PCR:	polymerase chain reaction
PRNT:	plaque reduction neutralization test
RMSF:	Rocky Mountain spotted fever
RNA:	ribonucleic acid
RT-PCR:	reverse transcriptase-polymerase chain reaction
STI:	soft tissue infections
TB:	tuberculosis
TIBOLA:	tick-borne lymphadenopathy
TSPyV:	trichodysplasia spinulosa–associated polyomavirus
WHO:	World Health Organization

Congo. Since then, outbreaks have appeared sporadically in Central Africa. The largest epidemic in history occurred in 2014, affecting multiple countries in West Africa.[11] Five different ebolaviruses are known, with *Zaire ebolavirus* being the most virulent and causative agent in the most recent epidemic.[12] With a fatality rate of ≤90%, the World Health Organization (WHO) declared Ebola a "public health emergency of international concern."[13] In January 2016, the WHO declared the end of Ebola transmission in all West African countries.[10] In the US, 2 imported cases, including 1 death, and 2 locally acquired cases in health care workers were reported. Ebola can be transmitted via direct contact with body fluids. Dermatologists should be cautious of the high risk of contamination through skin biopsy specimens and dermatologic examination because of the virus' high virulence.

Skin findings begin 4 to 5 days after fever, starting with nonspecific macules and papules.[12] Pinpoint papules are first observed around hair roots[14] and are seen on the proximal extremities and can extend centrally. The rash progresses to a diffuse erythroderma. In darker skin, fine scaling has been described. Ebola causes a high rate of cell death, leading to heavy internal hemorrhage. Bleeding is frequently observed, causing petechiae, purpura, ecchymoses (Figs 1 and 2), and hematomas, particularly around needle or puncture sites.[15]

Infection initially presents with sudden nonspecific flu-like symptoms.[15] Ebola is often deadly and runs its course in 14 to 21 days. Acute phase detection of viral RNA by reverse transcriptase-polymerase chain reaction (RT-PCR) is the standard method of diagnosis and is vital for prognosis.[16]

Management is centered on supportive care with hydration, transfusion (when available), and critical care.[17] Strict isolation of suspected cases, aseptic burials of known victims, and quarantine of potential contacts is necessary to decrease the risk of epidemics. No definitive treatment exists, although experimental drugs and vaccines are undergoing testing. Two vaccine candidates, chimpanzee adenovirus serotype 3 (ChAD3-ZEBOV) and recombinant vesicular stomatitis virus (VSV-EBOV), are currently in phase III clinical trials. Several other vaccine candidates are currently in earlier phases of human testing.[18] The experimental drug ZMapp has been administered to a limited number of victims with promising results.[19]

Dengue fever

Key points

- **Dengue fever is a leading cause of morbidity and mortality in the tropics and subtropics**
- **Clinical manifestations vary widely, from asymptomatic infection to dengue hemorrhagic fever**
- **Diagnosis is made clinically followed by viral detection or antibody testing**
- **Treatment is mainly supportive**

Dengue viruses are members of the family Flaviviridae. With an estimated 390 million infections worldwide each year, dengue is the most prevalent mosquito-borne viral disease and a leading cause of illness and death in the tropics and subtropics.[20,21] Dengue virus complex has 5 serotypes transmitted by the *Aedes* mosquitos, primarily *Aedes aegypti*.[22] The fifth serotype was first isolated in October 2013.[23] In the US, sporadic outbreaks with local transmission have occurred in Florida, Hawaii, and along the Texas–Mexico border.[24]

Clinical manifestations of the disease vary and include asymptomatic infection, mild dengue, classic dengue, and dengue hemorrhagic fever (DHF).[23,25] About 75% of dengue infections are asymptomatic.[24] Mild dengue can mimic any acute febrile illness.[26] Classic dengue fever is a febrile viral syndrome of sudden onset, characterized by fever for 2 to 5 days, severe headache, intense myalgia, arthralgia, retro-orbital pain and, sometimes, a diffuse morbilliform rash that may be pruritic and heals with desquamation.[27] DHF (Fig 3) is more likely to develop if an individual previously infected with 1 serotype is later infected with a different viral strain. It is seen primarily in children <15 years of age and is characterized