Emerging Infectious Diseases

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SYNOPSIS

Emerging and reemerging infectious diseases (EID) are increasing globally. Zoonotic diseases are transmitted from animals to humans through direct contact or through food, water, and the environment. Vector-borne diseases are major sources of mortality and morbidity globally. Three mosquitoborne viruses are yellow fever, Chikungunya virus, and dengue virus. Recent EIDs include *Candida auris, Elizabethkingia anopheles,* The Lone Star Tick, and avian influenza H7N2. In addition, *mcr*-1 may contribute to the dissemination of drug resistance to Gram-negative bacteria. Nurses play a major role in the identification and prevention of EID within health care settings.

KEYWORDS: Emerging infections, zoonotic diseases, vector-borne diseases, *Candida auris, Elizabethkingia anopheles,* avian influenza, *mcr*-1.

KEY POINTS

- Most emerging infectious diseases (EID) are caused by zoonotic pathogens.
- Vector-borne diseases are a major public health problem in the US.
- Factors contributing to EID include population growth, spread in healthcare facilities, ageing population, global travel, and changing vector habitats related to climate change.

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INTRODUCTION

Emerging infectious diseases (EID) are defined as infectious diseases that are newly recognized in a population or have existed but are rapidly increasing in incidence or geographic range. Simply put, they may be new infections resulting from changes or evolution of existing organisms, known infections spreading to new geographic areas or populations, previously unrecognized infections appearing in areas undergoing ecologic transformation, or old infections remerging because of antimicrobial resistance in known agents or breakdowns in public health measures.[1,2] Emerging infections account for at least 15% of all human pathogens according to the 10th International Conference on EID.[3] A major concern is the synergistic communication between emerging diseases and other infectious and non-infectious conditions. Many emerging diseases are zoonotic or synoptic – an animal receptacle incubates the organism with random transmission into human populations. Likewise, EID may be foodborne, vector-borne, airborne. Regardless, for an EID to become established, the infectious agent must be introduced into a vulnerable population and the agent must have the ability to spread from human-to-human and cause disease.[4]

In contrast to other human diseases, infectious diseases may be unpredictable with the potential for global outbreaks. While they are transmissible, there is the potential for immunity against reinfection. Many are preventable through vaccines with the potential for eradication. There is interdependence on nature and human behavior.[5] The challenge of EID relates to their impact on humans -pandemics, epidemics a well as the threats to human health and global stability.[5,6] We know that the appearance of new infections is inevitable. That said, despite the advances in the development of countermeasures diagnostics, therapeutics, and vaccines, world travel and increased global interdependence have added to problems in diagnosing and

containing these diseases. Most of us can relate to the HIV/AIDS, severe respiratory syndrome (SARS) and pandemics such as the 2009 H1N1 influenza as emerging infections in modern day. The societal and economic impact of these diseases was phenomenal, not to mention the quality of life among infected individuals and their families. Understanding the categories of infectious diseases is important (Table 1). These include those that are new emerging, those that have become established and may periodically reemerge, and those that have become stably endemic.[5,6]

Insert Table 1

ZOONOTIC DISEASES

Zoonotic diseases are those diseases transmitted from animals to humans through direct contact or through food, water, and the environment contributing to 61% of infectious organisms affecting humans.[7,8] Zoonotic diseases may be categorized by their ability to spread among humans through five stages ranging from only spread among animals (stage 1) to fully human pathogens (stage 5). Figure 1 illustrates the stages through which pathogens of animals evolve to cause human diseases.[9]

Insert Figure 1

The National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) aims to protect people from domestic and global health threats. Their scope is broad to include foodborne and waterborne illnesses, infections that spread in hospitals, infections that are resistant to antibiotics, deadly diseases like Ebola and anthrax, illnesses that affect immigrants, migrants, refugees, and travelers, diseases caused by contact with animals, and diseases spread by mosquitos, ticks, and fleas.[10] Clearly, the interface among humans, animals, and the

environment invite diseases impacting public health and social/economic wellbeing of the global population. Consider the driving factors previously noted. The incidence of zoonoses increases when humans live in close contact with animals and when humans encounter animals in new geographical regions. Some examples include Lyme disease (spread by ticks) and salmonella (spread by poultry). You may recall recent outbreaks of Salmonella in shell eggs, chicken products, raw turkey products and pet guinea pigs.

ONE HEALTH STRATEGY

The One Health concept began as an initiative among multiple disciplines in 2006. One Health is a collaborative local and global effort to achieve the best health for people, animals, and the environment.[11]

The Centers for Disease Control & Prevention (CDC) uses the One Health approach by working with health care providers, veterinarians, ecologists, and others to monitor and control public health threats and to learn how diseases spread among people, animals and the environment.[12] The opportunity for nurses to embrace the One Health approach in community and patient education is exponential. For example, working as part of an interprofessional team to educate youth residing in rural agricultural areas about preventing the spread of diseases shared between people and animals. There are One Health teams working with 4-H and Future Farmers of America groups. Likewise, educate Americans about diseases they may get from their pets such as *Salmonella* infections.

VECTOR-BORNE EID

As alluded to previously, vectors are blood-feeding insects & ticks capable of transmitting pathogens between hosts.[13] These diseases are major causes of mortality and morbidity globally.

In the US the most common pathogens are transmitted by ticks and mosquitoes, including Lyme disease, Rocky Mountain spotted fever, West Nile, dengue, and Zika virus diseases. These diseases represent a growing public health problem for the US and globally. Data are tracked by local and state health departments, however, national improvement in surveillance, diagnostics, reporting, and vector control as well as new vaccines have been identified.[13] Mosquito transmitted EID can spread locally in the US due to the presence of the specific vector. Likewise, global travel and immigration can bring these infections to the US with potential transmission.[14] Four mosquito borne viruses of concern are Zika virus, yellow fever, Chikungunya virus, and dengue virus [8,14-17] (**Table 2)**. I refer the reader to the discussion of the Zika virus in this journal.

Insert Table 2

FACTORS CONTRIBUTIONG TO EMERGENCE OF OUTBREAKS

Three hundred thirty-five EID events were identified between 1940-2004. The majority (60.3%) originated from wild animal reservoirs with approximately one in five transmitted from animal reservoirs hosts to humans by disease vectors, e.g., ticks, mosquitos).[18] Fast forward to 2008 and beyond with the discovery of severe fever with thrombocytopenia virus and Middle East respiratory syndrome coronavirus (MERS-CoV) as well as unusual outbreaks of Zika virus, yellow fever, and Ebola. These EID bring to the forefront the significance of demographic change, global travel and trade, and possible climate change as drivers.[2,19] (Petersen et al., 2018; van Doom, 2014). Biological, social, and environmental drivers, which are interrelated include:

- Microbial adaptation and change (e.g., genetic drift and shift in Influenza A)
- Susceptibility to infection
- Increased density of human population

- Poverty and social inequality (e.g., tuberculosis)
- Stress from farmland expansion on the environment
- Globalization of food market & manufacturing
- Environmental contamination
- Climate change
- Additional opportunities for emerging infections
    - Population growth
    - Spread in health care facilities
    - Ageing population
    - International travel
    - Changing and expanding vector habitats (warmer temperatures may allow mosquitos -and diseases they transmit-to expand to new regions.
    - Drug resistance (contributes to re-emergence of bacteria, viruses and other microorganisms that change over time)
    - Breakdown in public health
    - Intentional biological attacks

A timely example of how these drivers influence emerging diseases is influenza, a causative virus that changes its genetic information. When these changes are marked the human immune system is challenged and pandemics may occur. The risks of genetic changes and human infection are increased when humans reside near agricultural animals such as chickens, ducks, and pigs, which are natural hosts of the virus. Avian H5N1 influenza (bird flu) is limited to infection due to direct contact with diseased birds. While this virus is deadly, it does not have the ability to pass between humans unlike the H1N1 influenza, which passed into humans from

swine. In 2009 this virus reached had a global impact because of human activity, especially air travel.[4]

Another example of an infectious disease attributed to human behaviors is HIV. A leading hypothesis is that humans were first infected with HIV through close contact with chimpanzees, perhaps through bushmeat hunting, in isolated regions of Africa. The spread from rural regions to internationally occurred through air travel. Human behaviors, e.g., intravenous drug use, sexual transmission, and transfer of blood products occurred before the new disease was identified resulting in rapid spread.[4]

Considering changes in climate, consider the tropical disease of chikungunya (discussed previously). This virus is transmitted by a mosquito originally confined to tropical regions around the Indian Ocean. In 2007 over 200 residents of a town in Italy suffered from an outbreak of this disease. Subsequently, outbreaks have occurred on all continents.[4]

As health care providers within healthcare systems, the changing demography of the population merits further discussion. With ageing comes the increased risk factors for infection and subsequent hospitalization adding to the patient's vulnerability. I will be discussing the emerging fungal species *Candida auris* causing outbreaks in healthcare facilities, which is associated with high mortality in patients with underlying comorbidities.[2,20]

NAID EID CATEGORIES

Not to confuse the reader but recognizing a resource in the prioritization of emerging pathogen threats to the US, I refer to the National Institute of Allergy and Infectious Diseases (NIAID) categorization.[21] **Table 3** highlights the categories with selected examples. NIAID reviews the

list in conjunction with federal partners, e.g., U.S. Department of Homeland Security and the Centers for Disease Control and Prevention.

NIAID continues to identify additional emerging and reemerging diseases and pathogens. Within the past five years alone, over 12 diseases and pathogens have ben recognized to include *Bordella pertussis,* Enterovirus 68, Hepatitis C and E, Poliovirus, and Rubeola.

Insert Table 3

EMERGING INFECTIONS FROM FUNGUS TO ZOONOTIC FLU VIRUSES

What do Candida *auris*, *Elizabethkingia anopheles,* The Lone Star Tick, and avian influenza H7N2 have in common? They have been identified among the newest emerging infections within the US. In addition, the plasmid-borne coliston resistance mediated by *mcr-1* (mobilized colistin resistance) may contribute to the dissemination of pan-resistant Gram-negative bacteria.[20,22]

Candida auris

An emerging fungal species that is multidrug resistant was identified in 2009 from ear drainage from a Japanese patient. The fungus spread through international travel most notably in New York and New Jersey causing outbreaks in health care facilities.[20,23,24]

Clinical manifestations of *C.auris* include invasive infections with a high mortality rate from bloodstream infections in patients with serious underlying comorbidities and indwelling devices. Of the 51 persons with the infection in New York from 2013-2017[23], the major concurrent condition (65%) was respiratory insufficiency. The medical intervention noted for most persons was being administered antibiotics within 14 days before the first culture for *C. auris.*

The diagnosis can be difficult because of misidentification as another yeast. Because of the misidentification, CDC recommends specific testing methods when select yeast organisms have been reported, e.g., *C. haemulonii,* another emerging drug-resistant strain. [24] Adults should be suspect if they had overnight admissions to health care facilities in affected areas (e.g., India, Pakistan, South Africa, Kenya). Clinicians must work with local health departments if infection with this fungus is a possibility.

Management recommendations are outlined by CDC[25]. Most cases in the US are resistant to azoles and are susceptible to echinocandin antifungals, which target the fungal cell wall. Cases must be reported immediately to the local public health department.

Prevention begins with being proactive. A response plan for healthcare staff and environmental services staff should be in place for infection prevention and control of *C. auris*. Patients at high risk should be identified within your healthcare setting, especially if they previously received care in a post-acute care setting. Nurses have expertise in assessing patients through comprehensive histories and appropriate physical examinations. Attention should be afforded patients with recent history of healthcare outside of the US with known *C. auris*.[25]

Elizabethkingia anopheles

This common gram-negative bacillus was discovered in 1959 by Elizabeth King, an American bacteriologist while working on a bacterium attributed to meningitis in infants. There are four species found in soil, river water, and reservoirs worldwide rarely making people sick. Since 2004 there has been an increased incidence among hospitalized patients – an emerging pathogen.[26,27] The species of concern for this discussion is *E. anopheles,* which is known to cause respiratory tract illness in humans.[27] While the bacteria have been isolated from Anopheles

mosquitoes, their role in transmission is unclear (Malviya). Outbreaks have occurred in Wisconsin[28,29], Michigan, and Illinois. Over 63 patients have been confirmed with 20 deaths.

Clinical manifestations are more common in immunocompromised patients, those over 65 years and with co-morbidities. Symptoms include fever, shortness of breath, chills, or cellulitis. The symptoms may mimic an acute viral syndrome, however, if the patient has multiple comorbid conditions (e.g., cancer, diabetes mellitus, chronic kidney disease), they should be assessed for *E. anopheles.*[27]

Diagnostic criteria include blood cultures. Clinical labs may be unable to differentiate between *E, anopheles* and *E. meningoseptica.* Results should be reported to the state health department as recommended by CDC treating presumptively as *E. anopheles.*[27]

Management of outbreaks merit immediate antibiotic therapy, especially because septicemia is prevalent. While Elizabethkingia in general is resistant to most antibiotics used to treat gram-negative infections, the patients in multistate outbreaks have been managed with several antibiotics (combination treatment preferred to include fluoroquinolones, minocycline, rifampin, and trimethoprim/sulfamethoxazole. [20,27,28]

Prevention measures include contact precautions to avoid disease transmission from affected patients to others. The transmission mode is unclear; therefore, conservative precautions should be used for the duration of admission in acute care facilities.[20,27,28]

Lone Star Tick

This aggressive tick *Amblyomma* americanum, is found in the southeastern, South central, and eastern US.[20] The distribution and numbers have increased over the past three decades. The Lone

Star Tick does not cause Lyme disease despite the occasional rash in the early stages that may mimic that of Lyme disease.[30]

Disease hosts include deer, e.g., wild white-tailed deer, and ground dwelling birds.[20,31]. Likewise, the tick will feed on humans and the blood of various domestic and wild animals throughout its life cycle and can be brought home on pets. A cause of vector-borne diseases it is associated with the transmission of Ehrlichia, which can cause human ehrlichiosis, Heartland virus, tularemia, and southern tick-associated rash illness.[32] In addition, the Lone Star Tick may be a vector of the Bourbon virus to humans.[20]

Clinical manifestations usually occur within seven days after a tick bite with the erythematous rash. The skin lesions are smaller in size than those with Lyme disease (~6-10 cm), circular in shape with central clearing.[30] Symptoms may include fatigue, fever, headache, joint and muscle pain, but resolve with antibiotic therapy. Heartland virus infections are more common than the Bourbon virus and should be suspected in affected areas when adults present with fever, fatigue, nausea, diarrhea, and anorexia. These individuals do not respond to doxycycline. The Bourbon virus can be fatal in immunocompromised adults and should be. Included in a differential diagnosis if the patient has thrombocytopenia, and leukopenia after a recent tick exposure.

Management is symptomatic with topical corticosteroids for mild local reactions. Doxycycline is the antibiotic of choice.[30]

Prevention includes avoidance measures, e.g., tick habitats -dense woods, brushy areas. Use insect repellent containing DEET or permethrin. Wear long pants, socks, and perform tick checks with prompt removal.[30] Environmentally, remove leaf debris, which is a source of hydration for

the ticks. An interesting recommendation is the importation of fire ants, which serve as a natural means of tick control by eating tick eggs.[31]

Zoonotic Flu Viruses (Not your seasonal Flu)

There are four types of influenza virus: A,B, C, & D. Type A infects humans as well as many animals. The emergence of new influenza A viruses with the ability to infect people and human to human transmission can cause a pandemic.[20,33,34] Persistent influenza threats include the highly pathogenic strains of avian H7N9, H5N1, and H5N6 plus the swine viruses H1N1, H1N2, and H3N2. [20]

Humans can be affected with avian, swine, and other zoonotic influenza viruses. Direct contact with infected animals or contaminated environments are modes of transmission. Most human cases of influenza A (H5N1) and A (H7N9) are associated with direct or indirect contact with infected live or dead poultry. Seasonal influenza viruses normally circulate in humans in lieu of birds, e.g., H1N1, H3N2.[20, 35] The avian influenza A (H7N2) is unique in its ability to infect humans in contact with domestic animals.[35] A veterinarian in New York had close unprotects contact with an infected cat from an animal shelter. While the pathogenicity is low and the risk of human transmission is unlikely, the possibility of a widespread problem has to be considered. Influenza in cats spreads the same way as human flu spreads, through direct contact, air droplets, contaminated surfaces, Germs in cat saliva may be transferred onto the cat's coat during grooming. The virus may manifest through persistent coughing, lip smacking, runny nose, and fever in cats. The overarching concern is animal viruses changing to pose a potential threat to otherwise non-immune humans. Without existing immunity outbreaks can occur.[35]

Clinical manifestations following an incubation of two to five days range from mild upper respiratory tract infection to severe pneumonia, sepsis with shock, acute respiratory syndrome, and death. Individuals at high risk for influenza are the same as those of seasonal flu, e.g., children younger than 5, adults 65 and older, pregnant women, and people with chronic health conditions, immunocompromised.[33,34]

Diagnosis is confirmed with laboratory tests using molecular, e.g., RT-PCR. Rapid influenza diagnostic tests (RIDTs) have lower sensitivity.

Management includes some antiviral drugs (neuraminidase inhibitors), which can reduce duration if prescribed within 48 hours of onset and continued for at least five days. Symptomatic treatment is key.[33-35]

Prevention includes controlling the animal source. Surveillance in animal and human populations is critical (see One Health discussion). Personal protective measures include regular handwashing and proper drying of hands, respiratory hygiene, early self-isolation, avoid touching your eyes, nose or mouth. All health care providers must use airborne precautions.[33,34]

Travelers to countries with outbreaks of avian influenza should avoid poultry farms, contact with animals in live poultry markets; and practice food safety. Travelers returning from affected regions should report to local health authorities if respiratory symptoms occur.

MCR genes

While there is no immediate public threat, *mcr*-1 brings to the forefront the global challenges in addressing antibiotic resistance and best practices for antibiotic use.[20] The *mcr*-1 gene causes resistance to colistin, which is considered by CDC to be a "last resort "antibiotic.[36] Consider the overuse and misuse of antibiotics in humans and animals. The common bacterial infections once

treatable have become resistant to other antibiotics or require the last line of antibiotics, which can have serious side effects.[37,38]

The *mcr* gene is found on small pieces of DNA (plasmids) that carry genetic instructions from one bacterium to another enabling resistance to be shared. This includes carbapenem-resistant Enterobacteriaceae (CRE).[36,37] This gene was first identified in November 2015 in China. What is unique about *mcr*-1 is its potential to spread to other bacteria, some of which may have resistance to major antibiotics and could become resistant to colistin, a last resort option. CDC and its federal partners continue to track *mcr*-1 in the US. In May 2016, *E. coli* bacteria carrying the gene was found in a urine sample from a patient in Pennsylvania and from intestinal samples of two pigs from South Carolina and Illinois. Fortunately, the patient from Pennsylvania was not resistant to all antibiotics. This discovery emphasized the importance of coordinated efforts among the CDC, state and local health departments, CDC has developed a rapid laboratory test to help clinical labs find bacteria with *mcr*-1.

NURSES' ROLES IN EID IDENTIFICATION AND PREVENTION

As clinicians we recognize that emerging infectious diseases are inevitable and unpredictable. Partnering with interprofessional teams, patients, and communities we must become vigilant in acknowledging unusual presentations and seeking appropriate diagnostics. According to the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) emerging Infections Task Force Expert Panel, mathematical modeling has not been able to predict outbreaks. Being knowledgeable about emerging infections increases our ability to include these in our differential diagnoses in clinical practice as well as recognizing best practices in care

through evidence-based resources. In addition, best practices for self-care should be implemented to include adherence to vaccination recommendations.

Targeted screening for migrants arriving from highly endemic countries can be a front-line defense and can be cost-effective. Recommending preventative vaccinations programs concentrating resources on those who need it most. Successful integration of migrants into the local health care system and partnering with public health facilities will ensure better diagnosis and management of diseases.[39]

Nurses 'unique skill sets brought to healthcare settings enhances the ability to assess patients for EID as well as promoting health of the community.[28] Each patient history must include a detailed travel history. It is the astute clinician who makes the connection among patient histories and recognizes the first signs of an EID.[19]

Nurses must be current on EID in their geographical areas as well as globally and know where to locate resources in a timely manner, e.g., WHO, CDC, subscribing to medical reference apps.

Selected resources

http://www.niaid.nih.gov/research/emerging-infectious-diseases-pathogens

http://wwwnc.cdc.gov/eid

EID on Twitter (http://twitter.com/CDC_EIDjournal)

Morbidity and Mortality Weekly Report (MMWR) (https://www.cdc.gov/mmwr/)

NCEZID Follow @CDC NCEZID on Twitter (http://twitter.com?#!/CDC NCEZID)

CDC Vital Signs (https://www.cdPc.gov/vitalsigns/)

http://www.cdc.gov/vaccines/index.html.

http://wwwnc.cdc.gov/travel/destinations/list

SUMMARY

Emerging and re-emerging infectious diseases are difficult to predict let alone manage. Emerging pathogens include vector-borne diseases such as the Lone Star virus as well as numerous mosquito-borne diseases. New candida and Elisabethkinga infections threaten patients in hospital settings. Recognizing drivers contributing to outbreaks helps shape strategies for health care providers to work together embracing One Health. Integrating emerging infections into differential diagnoses within our practice settings is one way to impact patient and community health outcomes.

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Table 1
Categories of Infectious Diseases

Type of Disease	Description
Established diseases	Widespread diseases with a relatively stable and predictable level of morbidity and mortality (e.g., viral and bacterial respiratory and diarrheal diseases, drug-susceptible malaria and tuberculosis; nosocomial infections)
Newly emerging diseases	Diseases identified first in humans (e. g., HIV/AIDS, severe acute respiratory syndrome)
Reemerging diseases	Diseases infecting humans that reappear in new locations (e. g., West Nile Virus in the US) or in resistant forms (e.g., influenza, methicillin-resistant Staphylococcus aureus) or reappear after apparent control (e. g., polio in parts of Africa, cholera in Haiti, dengue in Florida) or under atypical circumstances (e. g., deliberately released agents, including the anthrax release in 2001)

Adapted from Fauci AS, Morens DM. The perpetual challenge of infectious diseases. N Engl J Med 2012; 366 (5): 456; with permission.

Table 2
Mosquito-borne Viral EID

Name	Epidemiology	Transmission	Clinical Manifestations	Diagnosis	Management	Prevention
Yellow Fever	Endemic in sub-Saharan Africa, Central & South America & Caribbean. Endemic in 47 different countries. In US all cases imported & in unimmunized travelers to risk areas. True incidence unknown due to lack of surveillance.	Zoonotic infection spread by mosquitoes In Americas *A. aegypti.* Potential for rapid spread by international travelers. Mosquitoes acquire the virus by feeding on infected primates (human or non-human) transmitting virus to other primates. People infected with yellow fever virus are viremic shortly before the onset of fever and up to 5 days after onset.	Incubation 3-6 days. Wide spectrum including asymptomatic. Early flu like symptoms -fever, malaise, myalgia, headache, vomiting, Majority will have bimodal disease. Fever returns within 24 hours-hepatitis, jaundice, renal failure, In severe cases hemorrhage & shock. Among those who develop severe disease, 30-60% die. Most people with the initial symptoms improve within one week.	Yellow fever infection is diagnosed based on laboratory testing, symptoms, and travel history. Difficult in early phase - confused with malaria and other Flavi-viruses.	Supportive & symptomatic care. Avoid certain medications, such as aspirin or other nonsteroidal anti-inflammatory drugs, which increase the risk of bleeding. No specific antiviral treatment IV gammaglobulin in early infection WHO considers confirmed case as seminal event indicating transmission - mass vaccination is required. Issue is not enough vaccine. Vaccine	Control of vector & prevention of mosquito bites. Use Environmental Protection Agency (EPA)-registered insect repellents, e.g., DEET, Picaridin) One vaccine Yellow Fever-Vax (Sanofi Pasteur, Swiftwater, PA) approved by FDA in US (www.cdc.gov/vaccines) CDC & WHO recommend those traveling and living in endemic areas receive 1 dose

		Yellow fever virus has three transmission cycles: jungle (sylvatic), inter-mediate (savannah), and urban. The urban cycle involves transmission of the virus between humans and mosquitoes, primarily. Virus brought to the urban setting by a viremic human who was infected in the jungle or savannah.	Residual weakness and fatigue might last several months.		sparing strategies to immunize enough people for herd immunity & population protection.	
Chikungunya Virus Ramachandran et al. 2016) Rathore et al. 2017	Endemic to Africa & Asia	Arbovirus like Zika, Yellow Fever, and dengue transmitted by mosquito (*A aegypti)*. (See previous	Can cause infections in adults & children. Up to 28% asymptomatic. Incubation 3-7 days. Abrupt	Differentail diagnosis dengue fever, malaria, leptospirosis, group A streptococcus, rubella,	No specific antiviral treatment Supportive management. Only acetaminophen for joint pain &	Focus on vector control and avoiding further bites to humans to disrupt mode of transmission of infection (See previous discussion on Yellow Fever).

		discussion on Yellow Fever) Recent outbreaks in Europe and Americas (including US)	onset high fever for up to 2 weeks, severe polyarthralgia, transient skin rash maculopapular on trunk and extremities. Relapse may occur 2-3 months after onset. At risk are older adults (>65), persons with comorbidities, neonates exposed intrapartum, Infants & children high risk of atypical or severe disease, e.g., vesiculobullous lesions, neurological complications	measles, parvo virus. Lab tests combined with history. In US lab test at CDC. Rely on detection of the virus.	fever until determined is not dengue fever	No licensed vaccine for virus although WHO is evaluating several.
Dengue Virus	Global arboviral. Endemic in more than 120 countries,e.g., SE Asia &	Transmitted by *Aedes* genus of mosquito (primarily *A.aegypti*)	WHO defines in terms of complexity: without warning signs (fever with nausea/vomiting;	Confirmatory tests: viral antigen or nucleic acid detection & serology.	No specific antiviral agent. Fluid therapy.	Tetravalent vaccine approved in some countries, e.g., Mexico. WHO recommends: Remove all sources of stagnant water to

	Western Pacific areas, Caribbean, Latin America, some regions of the US, Africa, Middle East 3.9 billion at risk worldwide. In 2016 large outbreaks worldwide affecting children and adults. Epidemics in the US in 18th and early 20th centuries. Reemerged in 2016 (Texas & Hawaii) -764 confirmed cases.	Four antigenically distinct virus serotypes, all RNA viruses belonging to Flavivirus (also includes yellow fever, West Nile, Zika, among others.	rash, myalgias); with warning signs (in addition to above, abdominal pain, clinical fluid accumulation, lethargy); severe dengue (all of the above with severe plasma leakage, severe bleeding)	Difficult to distinguish clinically from ZIKA & chikungunya virus infections.		prevent mosquito breeding Prevent mosquito bites -wear appropriate clothing, use of insecticides (see Yellow Fever) Use of mosquito nets and coils around people sick with dengue fever to prevent mosquitoes biting and transmitting Vector surveillance and control is important.

Data from: Centers for Disease Control and Prevention (CDC) Dengue. Available at: http://www.cdc.gov/dengue/index.html. Accessed October 9, 2018. CDC Yellow fever. 2018 Available at: https://www.cdc.gov/yellowfever/index.html. Accessed October 3, 2018. Ramachandran VG, Das S, Roy P, Hada V, Mogha, NS. Chikungunya: A reemerging infection spreading during 2010 dengue fever outbreak in National Capital Region of India. VirDis; April-June 2016; 27(2): 183-1286 and Rathore MH, Runyon J, & Haque TU. Emerging infectious diseases. Advances in Pediatrics, 2017: 64:27-71. World Health Organization (WHO).Zoonoses. Available at: http://www.who.int/zoonoses Accessed October 3, 2018;

Table 3
NIAID Emerging Infectious Diseases/Pathogens

Definition	Pathogens
Category A Organisms/biological agents that pose the highest risk to national security and public health • Can be easily disseminated or transmitted from person to person • Result in high mortality rates; potential for major public health impact • Might cause public panic and social disruption • Require special action for public health preparedness	Category A Priority Pathogens • *Bacillus anthracis* (anthrax) • *Clostridium botulinum* toxin (botulism) • *Yersinia pestis* (plague) • Variola Major (smallpox) and other related pox viruses • *Francisella tularensis* (tularemia) • Viral hemorrhagic fevers: Arenaviruses, Bunyaviruses, Flaviviruses, Filoviruses
Category B Second highest priority organisms/biological agents • Moderately easy to disseminate • Result in moderate morbidity rates and low mortality rates • Require specific enhancements for diagnostic capacity and enhanced disease surveillance	Category B Select Priority Pathogens • *Burkholderia pseudomallei* (melioidosis) • *Coxiella burnetii* (Q fever) • *Brucella* species (brucellosis) • Ricin toxin (Clostridium perfringens) • Staphylococcus enterotoxin B (SEB) • Typhus fever (*Rickettsia prowazekii*) • Food and water-borne pathogens: bacteria (e.g., *E.coli, shigella;* salmonella, *campylobacter*); viruses (e.g., hepatitis A); protozoa (e.g., C*ryptosporidium parvum, Giardia lamblia)*, Fungi. • Mosquito-borne viruses (e.g., West Nile, Yellow Fever, Chikungunya, Zika)
Category C Third highest priority. Includes emerging pathogens that could be engineered for mass dissemination in the future because of • Availability • Ease of production and dissemination • Potential for high morbidity and mortality rates and major health impact	Category C Select Priority Pathogens • Nipah and Hendra viruses • Additional Hantaviruses • Tickborne hemorrhagic fever viruses (Bunyaviruses, Flaviviruses) • Tickborne encephalitis complex flaviviruses • Tuberculosis, including drug-resistant TB • Influenza virus

	• Other Rickettsias • Rabies virus • Severe acute respiratory syndrome associated coronavirus

Data from NIH National Institute of Allergy and Infectious Diseases. NIAID emerging infectious diseases/pathogens. Available at:

https://www.niaid.nih.gov/research/emerging-infectious-diseases-pathogens. Accessed at July 26, 2018.