

DOI: 10.14744/etd.2019.57805

Manuscript Type: Invited Review

Title: Emerging infections and future threats

Running Title: Emerging infection threats

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Cite this article as: Petrosillo N. Emerging infection threats. Erciyes Med J 2019; DOI: 10.14744/etd.2019.57805

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Abstract

Emerging infections represent a concern especially when their increase is rapid and their mortality high. They can be caused by previously undetected or unknown pathogens, or by known agents affecting new geographic sites or new populations, or by re-emerging agents whose incidence of disease had significantly declined in the past. Main causes of emerging infectious disease spread include crowding, mobility (tourism, migration, asylum seekers, refugees), centralization of food production and supply and new food vehicles, war, famine and displacement, and change in vector distribution and susceptibility. Another important issue regarding emerging infectious diseases is the source of pathogens, that in 60.3% of cases is a non-human animal origin (zoonotic pathogens). If viral emerging infections represent a concern mainly in underdeveloped area of the world, the emergence of antimicrobial resistance is a growing concern worldwide but especially in developed and high income countries, where misuse and overuse of antibiotics among humans and in the veterinary setting, including animal feeding, artificially created the selection of resistant strains. Future threats include not only diseases caused by viral agents, such is the case of Ebola virus disease periodical re-emergence, but also infections with antibiotic resistant bacteria: it is estimated that in 2050 deaths due antimicrobial resistant infections will overcome those by cancer.

Keywords: Emerging infections, Ebola virus disease, antimicrobial resistance, zoonosis.

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Introduction

The history of Humankind has been greatly determined by infectious diseases. In the past, epidemics of plagues and undetermined infections have changed the face of the world. The Black Plague, in [human history](#) one of the most ravaging [pandemics](#), resulted in an estimate of 75 to 200 million people in Europe and Asia, peaking in [Europe](#) from 1347 to 1351, finally killing around 30% of the population (1).

In the past century a decline of infectious diseases, including cholera, tuberculosis and smallpox was reached thanks to vaccination, clean drinking water, improved sewage system and a wider improvement in living conditions and social infrastructure. Indeed, decrease in infectious diseases was strongly related to decrease in host susceptibility and in disease transmission. Host susceptibility was in turn decreased by better housing, better nutrition and use of antibiotics, as occurred in developed countries in the past century (2).

On the beginning of the second half of the past century, in developed countries there was an optimistic wave about the defeat of infectious diseases; this optimistic attitude was mainly determined by the introduction of antibiotics, immunization and by a better quality of life. As occurred many times in the history, things went differently. A series of outbreaks and epidemics, emerging infections and the appearance of the resistance to antibiotics evidenced that the war was far from being won.

The Ebola virus infection epidemic in 1976 in central Africa, the Legionnaire disease epidemic in 1977 at Philadelphia, the HIV pandemic in 1981 firstly identified in S. Francisco were the alarm bell that infectious diseases were far from being canceled. Moreover, another challenge was represented by the fact that these diseases occurred both in the developing and developed countries, thus indicating that much was still unknown about infectious diseases. A new world became familiar to scientist and media, i.e. “emerging infectious diseases”, largely occurring because of changing in demographics and behaviors, changes in industry and technology, change of the environment and of land use, international commerce

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and travel, collapse of public health measures and microbial adaptation and changes, all conditions linked to industrialization, urbanization, globalization and political/economical changes seen in the last decades (2). The 2013 Ebola virus outbreak in West Africa was indeed sustained by a change in travel, urbanization and economical conditions; previous Ebola virus outbreaks were bounded in to rural villages and ran out quickly. During the 2013 Ebola epidemic, because of scarce health infrastructure in their villages, and a wider attitude to travel, sick people were more prone to migrate from rural villages to big cities, thus determining a wider spread of the infection. In that conditions, poor, crowded city provided an “ideal incubator for outbreaks” (3).

Emerging Infectious Diseases (EID)

The definition of EID is complex, because includes

- events caused by newly evolved organisms, such as multidrug-resistant tuberculosis, plasmid mediated colistin resistance in gram negatives, etc...;
- organisms that entered human population for the first time recently, such as HIV-1 infection in 1981, severe acute respiratory syndrome (SARS) coronavirus in 2003, Middle East respiratory syndrome caused by a novel coronavirus (Middle East respiratory syndrome coronavirus, or MERS-CoV) that was first identified in 2012 in Saudi Arabia;
- pathogens present in humans historically, but with a recent dramatic increase, such as Ebola virus disease in Western Africa in 2014.

Main causes of EID spread include

- crowding: this is valid both for community (SARS, MERS-CoV) and healthcare associated infection;
- mobility that includes tourism, migration, asylum seekers, refugees. Travel can model infectious disease dynamics by introducing potential pathogens into susceptible

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populations or by modifying the rate of contacts and exposures between infected and susceptible individuals: HIV, tuberculosis, multidrug-resistant organisms, etc..

- Centralization of food production and supply and new food vehicles: *Cyclospora cayetanensis* outbreaks linked to fresh express salad mix sold at a chain of restaurants in US in 2018 (<https://www.cdc.gov/parasites/cyclosporiasis/outbreaks/2018/b-071318/index.html>), haemolytic uraemic syndrome (HUS) clusters of cases caused by Shiga toxin-producing *Escherichia coli* (STEC) O157 in Germany in 2016-2017 likely associated with packaged minced meat consumption (4).
- War, famine, displacement: infectious diseases ruthlessly exploit the conditions created by these conditions. War determines often a deterioration or a stop to ongoing prevention and control programmes, and as a consequence an increase of infectious diseases highly dependant from these programmes occurs. (5). This is the case of the case of re-emergence of malaria by *Plasmodium falciparum* in Afghanistan, trypanosomiasis in Democratic Republic of Congo, AIDS, vaccine-preventable diseases such as measles, etc... (5).
- Change in vector distribution and susceptibility: the emergence of Zika, the spread of Dengue, Chikungunya, West Nile fever in countries where was not present in the past, clearly document an ecological change involving especially vectors.

Between 1940 and 2004, Jones et al. (6) reported the emergence of 335 infectious diseases in the human population. Even though viral agents, especially RNA virus such as Ebola, pose a major threat due to high rates of nucleotide substitution, poor ability of mutation error-correction, and as a consequence better capacity to adapt to humans (7) emerging infectious diseases events in the last decades were due mostly to bacteria, i.e. vancomycin resistant *Staphylococcus aureus*, or rickettsiae (54.3% of cases) (6). Indeed, viral and prion pathogens constitute only 25.4% of emerging infectious diseases events. It is likely that in the recent years this proportion has been stable due to the spread of high multidrug-resistant Gram negative bacteria.

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Sources and mode of transmission of EID

Another important issue regarding emerging infectious diseases is the source of pathogens, that in 60.3% of cases is non-human animal origin (zoonotic pathogens). In many cases these pathogens have a wildlife origin, such as Nipah virus in Perak, Malaysia and SARS in Guangdong Province, China. More recently, Anthony SJ et al presented a new framework for the discovery of wildlife novel viruses for estimating the number of viruses that exist in a mammalian host. They estimated the existence of at least 320,000 mammalian viruses to be discovered within nine families. According to an economical analysis, the cost for discovering these viruses would represent a minimal part of the total expenses due to many pandemic zoonoses (8). This supports the suggestion that zoonotic EIDs represent a major and increasing threat to global health (9-11).

More than 10,000 years ago, in the neolithic age, the human-domestic animal sphere was 0.1% of the total mammalian mass, while currently it is 90% (12). The transformation of the earth's biomass has greatly conditioned the modes of transmission of pathogens, from showing only animal to animal transmission gradually evolving to being only human to human transmission (13). This transformation is hypothesized to be caused by repeated short introductions of these agents in humans, initially without ability to sustain human to human transmission; for HIV this "viral chatter" has been estimated to be consistent in at least ten entries (14).

Another interesting chatter occurred in the 2002 Severe Acute Respiratory Syndrome (SARS) epidemic. In this outbreak the viral agent was introduced into humans from civet cats that represent a "bushmeat" sold for human consumption around 4.5 million tons of bushmeat are sold from the West and Central Africa every year (15). However, the original reservoir was not the civet cat, but the Horseshoe bat (16). Bats harbor many viruses that can sometimes infect people, including Ebola and Marburg; genetic studies of viruses from horseshoe bats in one cave in China suggested the animals are reservoirs of SARS coronaviruses (17).

Another interesting model of "viral chatter" is represented by Henipaviruses, a genus of the family Paramixoviridae including two members: Hendra virus and Nipah virus. Hendra virus was identified in Australia, in 1994, as cause of an outbreak of acute and highly lethal

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respiratory disease among horses in a racing stable, causing also a lethal disease in humans in contact with the stable (18). In the following 17 years Hendra spilled from its natural host (fruit-bat) on 14 known episodes, infecting at least 45 horses and seven people in close contact with horses (19).

Nipah virus was first described in Malaysia in 1999 as the cause of a respiratory/neurological syndrome in farm pigs with a fatal infection in attendant pig farm workers (20). Also for this virus, the natural host was identified in the fruit bats; the difference was that the virus spilled from bats to pigs to people. Another peculiar characteristic of this virus is the possibility of the transmission bat-to-human and human-to-human. Both Hendra and Nipah have a high fatality rate, sometimes exceeding 70% (19).

Viral spillover was the cause of the spread in the human population of another virus, the Rift Valley fever virus (RVFV), a member of the genus *Phlebovirus* in the family *Bunyaviridae*, causing the Rift Valley Fever (RVF). This virus is transmitted by mosquitoes and blood feeding flies affecting mostly cattle and sheeps; however also humans can become infected. In 1987, during the construction of the Senegal River Project in west Africa, due to flooding in the lower Senegal River area, ecological conditions and interactions between animals and humans were altered; as a result, a large RVF outbreak occurred in humans and animals (21). If viral emerging infections represent a concern mainly in underdeveloped area of the world, the emergence of antimicrobial resistance is a growing concern worldwide but especially in developed and high income countries, where misuse and overuse of antibiotics among humans and in the veterinary setting, including animal feeding, artificially created the selection of resistant strains. Over the past decades, bacteria with specific clones expressing resistant to several antimicrobials spread worldwide. This is the case of Enterobacteriaceae, mainly *Klebsiella pneumoniae* resistant to carbapenems with different resistance enzymes including KPC (*Klebsiella pneumoniae* carbapenemase), NDM-1 (New Delhi Metalloprotease), and other metallo-beta-lactamases. More recent pan-resistant strains, expressing also resistance to polymyxins, have been identified as cause of severe diseases; some colistin resistant strains had a chromosomal resistance, likely induced by antibiotic pressure, but in other cases colistin resistance was linked to mobile elements, plasmids, like

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MCR-1 and others. This emerging resistance represents an important concern due to its potential for spreading among bacteria of different species; as evidenced recently in China, environment is one of the main sources of these mobile elements, likely due to the wide use of colistin in agriculture (22).

Surveillance of EID: a room for epidemiology, diagnostics and clinics.

The first and essential step in facing an emerging infectious disease is prompt recognition and identification. Before any response can be implemented, the event must be detected, recognized and then identified as needing special doing. Detection requires indeed surveillance. Traditional surveillance systems often operate with considerable delay; syndromic surveillance systems may overcome these problems providing the necessary lead time. Syndromic surveillance uses clinical characteristics that are detectable before the confirmation of diagnosis or activities suggested by the onset of symptoms as a signaling of modification of the activity of diseases. Information may be obtained from various existing sources, such as emergency department records, counter medication sales, etc... These systems can play as an early warning by furnishing data in close to real time, thus allowing detection of sporadic emerging infectious diseases or naturally occurring outbreaks. Indeed, the list of potential EID is disconcerting, and laboratory panels do not cover every potential infectious agent. Syndrome surveillance coupled with targeted diagnostic assessment is the best way for detecting EIDs. Recently, Petersen E et al. described the “diagnostic pyramid” with the tip of the iceberg represented by what we know (Theranostics), i.e. diagnosis of treatable etiologies, routine, commercial applications, and the submerged part of the iceberg represented by what we should know, i.e. differential diagnosis of known etiologies, diagnostics less common that may not inform the treatment, and much deeper, what we may never know, i.e. unknown pathogens, emerging infectious diseases, novel platforms for discovery (14). This is the challenge of syndromic surveillance associated with extensive diagnostic assessment. It seems not realistic that diagnostic assessment based on syndromic surveillance should be expanded on routine basis. However, increased surveillance

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and assaying for unusual infectious diseases should be developed and available, hopefully inside novel platforms that allow for broad range of diagnostics.

Future Threats

The 2014 Ebola virus outbreak in West Africa was the widest since the virus was first discovered in 1976, with a total number of cases and deaths higher than from all others combined. Indeed a total of 28,616 confirmed, probable, and suspected Ebola virus disease (EVD) cases were reported with 11,310 deaths up to the end of the epidemic in April 2016, with a case fatality rate of 39.5%. The countries involved in the epidemic were principally Guinea, Liberia, and Sierra Leone; however, also Nigeria (20 cases and 8 deaths), Mali (8 cases and 6 deaths), and Senegal (one case, no deaths) were involved as well (<https://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/index.html>). This epidemic was also characterized by some EVD cases evacuation from West Africa to Western countries. A total of 26 cases, of which 4 were fatal [Center for Infectious Diseases Research and Policy (CIDRAP)], were treated in Europe (23-25) and North America (26,27) during the outbreak. A without equal number of health-careworkers, including physicians, nurses, housekeepers, epidemiologists, psychologists, sociologists, statisticians, expert in ethics, and especially personnel dedicated to logistics and administrative problems, from different countries and settings were involved in caring for EVD patients. Well renowned organizations with EVD experience provided with guidelines, recommendations and guidances on infection prevention and control and clinical management of suspected or confirmed EVD patients (28,29). The EVD epidemic reminded the people of the hazards of pathogen transfer from animal reservoirs, and highlighted the importance of drivers for emergence of new infectious diseases or for re-emergence of well known ones, such as global travel and trade, demographic and climate changes. Another lesson from this outbreak was the fact that its beginning was sustained by lack of infection control measures in the healthcare facilities where patients were admitted. EVD outbreak pointed out also the weaknesses of health care systems across the

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three countries involved (Liberia, Sierra Leone and Guinea) and other neighboring areas, including the lack of reliable public health surveillance systems (30).

The recent EVD outbreak in Democratic Republic of Congo further highlighted the same problems seen in the 2014 outbreak, with the addition of the challenges the government and health organizations face in tackling Ebola in an area where years of instability and war has undermined locals' confidence in the authorities.

Strengthening the healthcare systems, including laboratory facilities and clinical centers, surveillance and awareness in countries where emerging infections are more common represent some barriers for minimizing the spread of these agents.

However, the struggle is inconsistent if we do not overview the global health animal situation (One Health approach), with particular consideration to those zoonoses of particular relevance for human health (table 2), as reported in the 86th General Session of the World Organisation for Animal Health in 2018

(<http://www.oie.int/en/for-the-media/press-releases/detail/article/state-of-play-of-the-global-animal-health-situation/>).

Moreover, there is a need to limit the use of antimicrobials in the veterinary/animal setting. Indeed, the drivers of antimicrobial resistance include antimicrobial use and abuse in human, animal, and environmental sectors. Of note, most of the classes of antimicrobials used to treat bacterial infections (cephalosporins, fluoroquinolones, polymyxins, tetracyclines and macrolides) in humans are also used in animals as mass medication or for growth promotion (31).

The burden of infections with antimicrobial resistant bacteria is a current and future concern. It is estimated that in 2050 deaths due antimicrobial resistant infections will overcome those by cancer (32). Recently, the European Center for Disease Control published in *Lancet Infectious Diseases* a study in which the authors estimated more than 670,000 infections with antibiotic-resistant bacteria between Jan 1, 2015, and Dec 31, 2015 (33). The infections caused an estimated number of deaths more than 33,000. In addition, for the first time, the health burden of five types of infection with antibiotic-resistant bacteria was expressed in disability-adjusted life-years (DALYs) that was estimated to be over 870,000. The burden for

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the EU and European Economic Area (EEA) appeared to be highest in infants under the age of one year and people aged 65 years or older. The authors further stated that “the contribution of various antibiotic-resistant bacteria to the overall burden varies greatly between countries, thus highlighting the need for prevention and control strategies tailored to the need of each EU/EEA country”. As more than 63% of the infections were associated with healthcare, it was stressed once more the importance of proper infection prevention and control measures, as well as antibiotic stewardship in order to reduce the number of healthcare-associated infections. This is even more important when considering that 39% of the burden is caused by infections due to bacteria resistant to antibiotics such as carbapenems and colistin, that represent the last-line treatment options.

It is possible to up-to-date information on emerging infectious diseases on the sites of the main international (WHO, CDC, ECDC, etc...) and national organizations, and on those of scientific societies (PROMED for the International Society of Infectious Diseases).

The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in March 2017 established an Emerging Infections Task Force (EITaF) to evaluate the possible role of clinical virology and microbiology at the forefront of disease detection; moreover, EID preparedness, at the light of the challenges posed by the budgetary restraints to laboratory medicine was among the scope of this taskforce, together with the creation of a network of infectious disease and clinical microbiology experts. Indeed, EITaF aims to establish a network of experts who can raise awareness on EID within the society and beyond, collaborate with other networks targeted on emerging diseases, develop knowledge on EID early detection and diagnosis, and stimulate research on EIDs in the field of surveillance, diagnostics, prevention and clinical management. One of the activities of EITaF was to update the outbreak occurrence worldwide; in 2018 38 news were posted, ranging from Yellow Fever in Sao Paulo, to Extensively Drug-Resistant *Salmonella enterica* Serovar Typhi outbreak in Pakistan, to colistin resistance in bacteria from humans and animals, to EVD in DRC, monkeypox in Nigeria and Marburg in Sierra Leone (https://www.escmid.org/research_projects/emerging_infections_task_force/).

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Conclusions

Mobility, people traveling much more frequently and far greater distances than in the past, living in more densely populated areas, centralization of food production and supply and new food vehicles, war, famine and displacement, change in vector distribution and susceptibility, and more opportunities to come into closer contact with wild animals, all represent a potential for emerging infectious diseases, either caused by new or well known viral agents or by antimicrobial resistant bacteria, to spread rapidly and cause outbreaks locally or globally.

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References

1. Raoult D, Mouffok N, Bitam I, Piarroux R, Drancourt M. Plague: history and contemporary analysis. *J Infect* 2013;66(1):18-26.
2. Cohen ML. Changing patterns of infectious disease. *Nature* 2000; 406: 762-7.
3. Stirrups R. Farewell to the god of plague. *Lancet Infect Dis* 2019; 19: 34.
4. Vygen-Bonnet S, Rosner B, Wilking H, Fruth A, Prager R, Kossow A, et al. Ongoing haemolytic uraemic syndrome (HUS) outbreak caused by sorbitol-fermenting (SF) Shiga toxin-producing *Escherichia coli* (STEC) O157, Germany, December 2016 to May 2017. *Euro Surveill* 2017;22(21).
5. Conolly MA, Heymann DL. Deadly comrades: was and infectious diseases. *Lancet* 2002; 360 Suppl: S23-24.
6. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. *Nature* 2008;451(7181):990-3.
7. Woolhouse M E J, Gowtage-Sequeria S. Host range and emerging and reemerging pathogens. *Emerging Infect Dis* 2005; 11; 1842–1847.
8. Anthony SJ, Epstein JH, Murray KA, Navarrete-Macias I, Zambrana-Torrel CM, Solovyov A, et al. A strategy to estimate unknown viral diversity in mammals. *MBio* 2013;4(5):e00598-13.
9. Morens D M, Folkers G K, Fauci A S. The challenge of emerging and reemerging infectious diseases. *Nature* 2004; 430: 242–249.
10. Weiss R A, McMichael A J. Social and environmental risk factors in the emergence of infectious diseases. *Nature Med* 2004;10: S70–S76.
11. King D A, Peckham C, Waage J K, Brownlie J, Woolhouse M E J. Infectious diseases: Preparing for the future. *Science* 2006; 313: 1392–1393.
12. Vince G. A Epoch Debate. *Science* 2011;334:32-7.
13. Wolfe ND, Dunavan CP, Diamond J. Origins of major human infectious diseases. **Nature** 2007; 447:279-83.
14. Petersen E, Petrosillo N, Koopmans M; ESCMID Emerging Infections Task Force Expert Panel. Emerging infections-an increasingly important topic: review by the Emerging Infections Task Force. *Clin Microbiol Infect* 2018;24:369-37.
15. Smith KM, Anthony SJ, Switzer WM, Epstein JH, Seimon T, Jia H, et al. Zoonotic viruses associated with illegally imported wildlife products. *PLoS One* 2012;7:e29505.
16. Lau SK, Woo PC, Li KS, Huang Y, Tsoi HW, Wong BH, et al. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoebats. *Proc Natl Acad Sci U S A* 2005;102(39):14040-5.
17. Hu B, Zeng L-P, Yang X-L, Ge X-Y, Zhang W, Li B, et al. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. *PLoS Pathog* 2017; 13: e1006698.

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18. Murray K, Selleck P, Hooper P, Hyatt A, Gould A, Gleeson L, et al. A Morbillivirus that caused fatal disease in horses and humans. *Science* 1995;268:94-97.
19. Field HE. Hendra virus ecology and transmission. *Curr Opin Virology* 2016; 16:120-125.
20. Chua KB, Bellini WJ, Rota PA, Harcourt BH, Tamin A, Lam SK, et al. Nipah virus: A recently emergent deadly paramyxovirus. *Science* 2000;288:1432-1435.
21. Thonnon J, Picquet M, Thiongane Y, Lo M, Sylla R, Vercruysse J. Rift valley fever surveillance in the lower Senegal river basin: update 10 years after the epidemic. *Trop Med Int Health* 1999;4:580-5.
22. Zhou HW, Zhang T, Ma JH, Fang Y, Wang HY, Huang ZX, et al. Occurrence of Plasmid- and Chromosome-encoded mcr-1 in Water-borne Enterobacteriaceae in China. *Antimicrob Agents Chemother* 2017; 61:8.
23. Kreuels B, Wichmann D, Emmerich P, Schmidt-Chanasit J, de Heer G, Kluge S, et al. A case of severe Ebola virus infection complicated by gram-negative septicemia. *N Engl J Med* 2014; 371; 2394-2401.
24. Mora-Rillo M, Arsuaga M, Ramírez-Olivencia G, de la Calle F, Borobia A M, Sanchez-Seco P, et al. Acute respiratory distress syndrome after convalescent plasma use: treatment of a patient with Ebola virus disease contracted in Madrid. Spain. *Lancet Respir Med* 2015; 3:554-562.
25. Wolf T, Kann G, Becker S, Stephan C, Brodt H R, de Leuw P, et al. Severe Ebola virus disease with vascular leakage and multiorgan failure: treatment of a patient in intensive care. *Lancet* 2015; 385, 1428_1435.
26. Liddell A M, Davey R T Jr, Mehta A K, Varkey J B, Kraft C S, Tsegay G K, et al. Characteristics and Clinical Management of a Cluster of 3 Patients With Ebola Virus Disease, Including the First Domestically Acquired Cases in the United States. *Ann Intern Med* 2015; 163: 81-90.
27. Lyon G M, Mehta A K, Varkey J B, Brantly K, Plyler L, McElroy A K, et al. Clinical Care of Two patients with Ebola Virus Disease in the United States. *N Eng J Med* 2014; 371: 2402-2409.
28. World Health Organization (WHO). (2014). Ebola Virus Disease (EVD). Retrieved from <http://www.who.int/csr/disease/ebola/en>
29. Médecins Sans Frontières (MSF). (2014). MSF Reference Books. Retrieved from http://refbooks.msf.org/msf_docs/en/MSFdocMenu_en.htm
30. Camara A, Diallo L, Camara M, Kouyaté M, Keita S, et al. A comparative study of Ebola hemorrhagic fever epidemic trends in three West African countries (Guinea, Liberia and Sierra Leone). *Int J Community Med Public Health* 2016;3:559–65.
31. McEwen SA, Collignon PJ. Antimicrobial Resistance: a One Health Perspective. *Microbiol Spectr* 2018;6(2).
32. O'Neill J. The Review on Antimicrobial Resistance. May 2016.
33. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis. *Lancet Infect Dis* 2019;19:56-66.

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Table 1. Main causes of Emerging Infectious Disease spread

1. Crowding in the community and healthcare setting
2. Mobility: tourism, migration, asylum seekers, refugees
3. Centralization of food production and supply and new food vehicles
4. War, famine, displacement
5. Change in vector distribution and susceptibility

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Table 2. Zoonoses of particular relevance for human health, as reported in the 86th General Session of the **World Organisation for Animal Health in 2018**

1. **Highly pathogenic avian influenza (HPAI) in birds:** the data collected since 2017 shows that the world is experiencing a massive spread of avian influenza in animals. Accurate and real time information is crucial to continuously monitor virus behaviour.
2. **Rabies** was reported as present in 57% of the 183 countries and territories which notified information to the OIE and continues to cost the lives of thousands of people every year mainly in Africa and Asia. A global business plan for the elimination of dog-mediated human rabies was launched in 2017, under the initiative of the “United against rabies”.
3. **Bovine tuberculosis:** in 2017 and early 2018, the disease was reported present by 43% of the reporting countries and territories and is distributed in every region of the world. A Roadmap for Zoonotic Tuberculosis was launched in 2017 to support the worldwide effort needed to end the global tuberculosis epidemic.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as: Petrosillo N. Emerging infection threats. *Erciyes Med J* 2019; DOI: 10.14744/etd.2019.57805