



## Narrative review

## Emerging infections—an increasingly important topic: review by the Emerging Infections Task Force

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## ABSTRACT

**Objectives:** This paper review trends in emerging infections and the need for increased clinical and laboratory surveillance.**Methods:** Factors that contributed to the emergence of recent outbreaks have been reviewed. Known, major outbreaks over the past two decades were reviewed.**Results:** We identified at least four major drivers of emergent infections: (i) increasing density of the human population; (ii) stress from farmland expansion on the environment; (iii) globalization of the food market and manufacturing; (iv) environmental contamination. The factors creating new opportunities for emerging infections include: (i) population growth; (ii) spread in health care facilities; (iii) an ageing population; (iv) international travel; (v) changing and expanding vector habitats.**Conclusions:** Emerging infections are unpredictable. In this review we argue that to discover new trends in infectious diseases, the clinicians have to look for the unusual and unexpected and ensure proper diagnostics and that syndromic surveillance must be supported by highly specialized laboratory services. Mathematical modeling has not been able to predict outbreaks More emphasis on the biology of evolution is needed. EID rarely stands out as unusual, and the continuous pressure on health care budgets forces clinicians and laboratories to prioritize their diagnostic work-up to common and treatable conditions. The European Society for Infectious Diseases and Clinical Microbiology, ESCMID, has established an Emerging Infections Task Force, EITaF, to strengthen the activities of the society on emerging infections and ensure that emerging infections is included in differential diagnostic considerations in everyday clinical practice. **E. Petersen, Clin Microbiol Infect 2018;24:369**

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## Introduction

A seminal paper published in 2008 listed 335 new human pathogens discovered between 1940 and 2004 [1]. The majority (60.3%) of these emerging infectious diseases (EID) originated from (wild) animal reservoirs, and approximately one in five was transmitted from animal reservoir hosts to humans by disease vectors (ticks, mosquitos, midges) [1]. Pathogen discovery

programs sampling wildlife hosts that are considered major reservoirs for EID (rodents, bats) have identified tremendous enzootic virus diversity, confirming their potential as sources of novel human pathogens [2]. Since 2008, 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 highlight the importance of demographic change, global travel and trade, and possibly climate change as drivers for emergence [3–7] (<http://www.promedmail.org/>, archive no. 20140322.2349696 2014-03-22). While the field is dominated by viruses from wildlife reservoirs, the Q fever outbreak in the Netherlands, the enterohemorrhagic *Escherichia coli* outbreak in Germany and the ongoing vast cholera outbreak in Yemen are examples of bacterial pathogens that have expanded

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massively—which is included in the definition of an EID (Box 1) [8–10]. There is broad consensus that we need to prepare for more EID in the future.

What makes EID so special? An important aspect is our inability to predict the emergence of new or changing health threats, and thereby to diagnose them when they occur. Even the much researched influenza virus field is struggling to predict the public health impact of the global spread of avian viruses with zoonotic potential through wild birds [11]. Therefore, the burden of disease detection shifts to clinicians and diagnostic laboratories.

Clinical presentation of EID, however, rarely stands out as unusual, and the continuous pressure on healthcare budgets forces clinicians and laboratories to prioritize their diagnostic assessment to common and treatable conditions.

While this is entirely understandable given the low likelihood of coming across an EID in routine clinical practice, it creates a catch-22 situation—that is, unexplained disease does not often get evaluated, and therefore new diseases will be detected late. Of concern is that the recent Ebola and MERS-CoV outbreaks have had a significant toll in healthcare personnel, who became infected while unknowingly being exposed to these highly lethal infections.

The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in March 2017 established an Emerging Infections Task Force to start discussing the possible role of clinical microbiology and virology at the front line of disease detection, the challenges posed by the budgetary restraints to laboratory medicine and the need for collaboration in order to improve on these aspects of EID preparedness. This scoping review signals the start of this task force.

## Drivers of EID

A primary driver of EID comprises anthropogenic changes at the human–animal–ecosystem interface and the One Health paradigm. We live in a world with an increasing density of humans and a consequential increase in the demand for animal protein. This is supplied either by livestock farming or through natural resources (bushmeat and fish). Animal farming plays a crucial role in providing nutrition to the planet, and by itself it does not constitute a human infection risk. However, the environmental impact and the massive increase in the demand for animal protein do, and it has become clear that there are challenges in balancing the advantages of economic growth in a free market with public and ecosystem health. It is believed that today humans and livestock comprise 90% of the world's biomass, compared to 10% from wildlife, and also compared to 0.1% of the world's biomass in the Neolithic age [12]. This in part explains why so many EID have a zoonotic origin. A study by Wolfe et al. [13] categorized zoonotic diseases by their ability to spread among humans after a species jump into five stages, ranging from dead-end primary infections (stage 2) to human-transmissible zoonotic threats (stage 4) and ultimately to new fully human pathogens (stage 5) (Fig. 1).

### Box 1

Definition of emerging infectious diseases.

Emerging infectious diseases are diseases that are newly recognized, newly introduced or newly evolved, or they are diseases that have recently and rapidly changed in incidence or expansion in geographical, host or vector range. Adapted from: World Health Organization (WHO), 'Diseases' (<http://www.who.int/zoonoses/diseases/en/>), and WHO, 'Emerging zoonoses' ([http://www.who.int/zoonoses/emerging\\_zoonoses/en/](http://www.who.int/zoonoses/emerging_zoonoses/en/)).

Wolfe coined the term 'viral chatter' (reflecting the fact that most attention in this field is focused on viruses) for stages 2 and 3 to reflect repeated zoonotic infections, initially without the ability to sustain transmission among humans [13,14] ([http://www.who.int/influenza/human\\_animal\\_interface/Influenza\\_Summary\\_IRA\\_HA\\_interface\\_06\\_15\\_2017.pdf?ua=1](http://www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_06_15_2017.pdf?ua=1)). HIV is thought to have made at least ten entries into humans before stage 5 was reached [14]. The >2000 cases of MERS-CoV reflect multiple stage 2 infections, with occasional human-to-human transmission in healthcare settings (stage 3), whereas avian influenza H5N1 and H7N9 infections are rarely transmitted among humans (stage 2) [15] (<http://www.who.int/emergencies/mers-cov/risk-assessment-july-2017.pdf>). As an example of emerging parasites, *Plasmodium knowlesi*, a malaria parasite usually infecting macaque monkeys, has emerged during the past decade as a cause of human malaria in Southeast Asia, especially in Malaysian Borneo [16]. While the parasite causes a mild or asymptomatic infection in its natural host, in humans the disease can be fatal. Humans—both locals and tourists—entering the natural habitats of infected macaque monkeys are at risk [17]. The recognition of the importance of the human environment in the emergence of new diseases lies at the root of the One Health approach (Box 2).

A specific risk is the consumption of semiwild or wild animals (bushmeat) combined with animal trading. The severe acute respiratory syndrome (SARS) coronavirus (CoV) outbreak is believed to have been introduced into humans from civet cats sold for consumption at markets, which had acquired infection from the original reservoir, horseshoe bats [18]. Similarly, many of the Ebola outbreaks have been linked to the consumption of bushmeat, of which an estimated 4.5 million tons are sold from West and Central Africa alone every year (<http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2014.3884/epdf>). A risk assessment conducted by the European Food Safety Agency identified the sizeable illegal market in Europe as a risk factor for exposure to zoonotic pathogens [19]. The risk associated with this practice can change over time: the increase in monkeypox infections in the Democratic Republic of Congo has been linked to bushmeat consumption coupled with decreasing population immunity since the cessation of smallpox vaccination [20,21].

A third factor for disease emergence from animal production is related to the pressures from farmland expansion on the environment. It was proposed that deforestation through forest fires in Sumatra triggered migration of virus-carrying fruit bats, leading to outbreaks of pneumonia and encephalitis in farmers and abattoir workers in Malaysia and Singapore, who in turn had been infected when contaminated fruit fed to pigs caused infection [22,23]. Since then, it has become clear that Nipah viruses can be transmitted among humans, and the continued occurrence of outbreaks linked to consumption of foods contaminated by fruit bat secretions is a cause for concern, as there is increasing evidence that Nipah virus may be transmitted via the respiratory route [23–25].

An indirect route of transmission of zoonotic pathogens through the food chain is through contamination of food with animal and human waste. Most of the organisms associated with zoonotic food-borne outbreaks are not new pathogens, but every EID outbreak should trigger the question whether food (and water) could be a vehicle for transmission [26]. The rapidly expanding scale and globalization of the food market—while controlled through food safety systems—is vulnerable, as a breach in the processes can lead to dispersed outbreaks that are difficult to chart. Bovine spongiform encephalitis emerged in the United Kingdom in 1986 after a change in the processing of animal feed including animal meal introduced the disease from sheep into cattle and subsequently humans [27]. In 2011, an outbreak of haemolytic uraemic syndrome due to a Shiga toxin-producing *E. coli*,

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