Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Microbiology and Infection 24 (2018) 369–375

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative review

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

E. Petersen [1, *], N. Petrosillo [2], M. Koopmans [3], the ESCMID Emerging Infections Task Force Expert Panel[†]

[1] Institute for Clinical Medicine, University of Aarhus, Denmark and Department of Infectious Diseases, The Royal Hospital, Muscat, Oman
[2] Clinical and Research Department, National Institute for Infectious Diseases 'Lazzaro Spallanzani', IRCCS, Rome, Italy
[3] Viroscience Department, Erasmus University of Rotterdam, The Netherlands

ARTICLE INFO

Article history:
Received 5 September 2017
Received in revised form
20 October 2017
Accepted 30 October 2017
Available online 15 November 2017

Editor: L. Leibovici

Keywords:
Emerging infections
Food borne
New virus
Outbreaks
Prediction
Surveillance

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**

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

* Corresponding author. E. Petersen, Institute for Clinical Medicine, Faculty of Health Sciences, Aarhus University, Aarhus, Denmark.
E-mail address: eskild.petersen@gmail.com (E. Petersen).
† Members of the ESCMID Emerging Infections Task Force Expert Panel are listed in the Acknowledgements.

https://doi.org/10.1016/j.cmi.2017.10.035
1198-743X/

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/).

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). 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 secreta 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*,

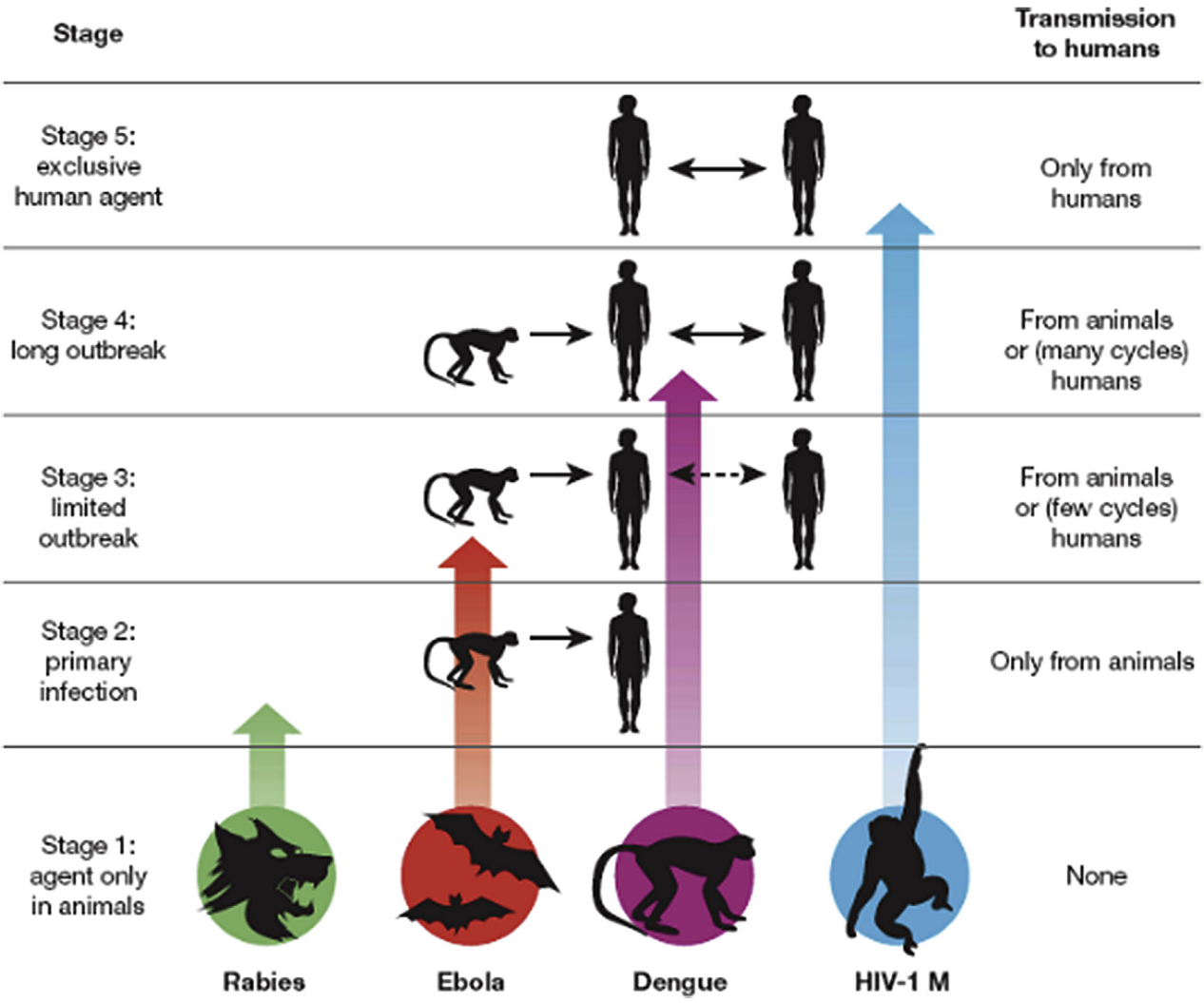

Fig. 1. Illustration of five stages through which pathogens of animals evolve to cause diseases confined to humans. From Wolfe et al. [13].

Box 2
Definition of One Health concept.

> One Health recognizes that the health of people is connected to the health of animals and the environment. The goal of One Health is to encourage the collaborative efforts of multiple disciplines—working locally, nationally, and globally—to achieve the best health for people, animals, and our environment.
> From: US Centers for Disease Control and Prevention, One Health (https://www.cdc.gov/onehealth/index.html).

enterohemorrhagic *E. coli*/enteroaggregative *E. coli* O104:H4, was detected in Hamburg, Germany, and cases were soon identified in several European countries [8,28,29]. The source was traced to a single producer of sprouts in Germany who used seeds produced and contaminated in Egypt [8]. A similar outbreak was reported from the United Kingdom, presumably from handling raw leeks and potatoes [30]. Multistate outbreaks in the United States of *Cyclospora cayetanensis* were linked to imported lettuce from a single manufacturer [31].

Finally, a possible concern related to increasing density animal production systems is the environmental contamination, interchange with wildlife and their excreta, and subsequent human exposure. Examples include the unprecedented outbreak of Q fever in the Netherlands, related to a massive but unnoticed increase in goat farming density, and exposure of humans through contaminated dust [7]. Avian influenza viruses are transmitted from wild birds to commercial poultry and *vice versa*, and wind- or rodent-mediated spread is thought to play a role in these exchanges as well [32,33].

Opportunity for rapid spread of pathogens

After World War II, the increasing awareness of the importance of infection prevention, sanitation, pest control and food safety, coupled with the development of vaccine programs and antibiotics, reduced the mortality gap between industrialized and poor societies, but these gains appear to be levelling off [34]. Population growth and crowding provides increased opportunity for pathogen transmission. Amoy Gardens in Hong Kong, with 50 000 people per square kilometer [35], had most cases of SARS-CoV. Despite the fact that the R_0 of SARS-CoV remained well below 1, dispersal of virus-containing droplets and aerosols through a faulty sewage and

plumbing system in the tightly spaced high-rise buildings led to a cluster of 330 cases [36]. The MERS-CoV outbreak in South Korea is another example of the potential for human-to-human spread of an emerging coronavirus, in this case in the healthcare system, where close contacts in crowded hospital waiting rooms and the cultural practice of 'doctor shopping' facilitated spread [37]. Overcrowded healthcare facilities with long waiting times in hospital emergency rooms can be important hot spots for transmission of organisms, thus favouring the spread of emerging infections at the early stage of their appearance.

A factor related to increased risk of introduction and transmission of EID through healthcare systems is the changing demography of the population. The world's population over 65 years of age is expected to increase from 460 million in 1990 to 1.4 billion in 2013, with more than half in developing countries [38]. With ageing comes increased prevalence of risk factors for infection and the outcomes thereof. The prevalence of diabetes is rapidly increasing globally, leading to increased risk of complications to infections including tuberculosis [39], SARS [40], influenza [41], pneumococcal infections [42] and MERS-CoV. Age-related diseases like cancers are followed by immunosuppressive therapy and will result in individuals susceptible to infections including emerging and reemerging infections. Diabetes is a main driver of chronic kidney failure in developing countries, followed by an increasing number of renal transplants, leaving patients immunosuppressed [43].

An ageing population will also present with an increasing prevalence of autoimmune diseases, many of which will be treated with antibodies directed to specific parts of the immune system, such as anti–tumor necrosis factor compounds. These patients will be immunosuppressed, with a consequent increased risk of acquiring infections. One example is patients receiving eculizumab, who are at much greater risk of developing meningococcal disease (https://www.cdc.gov/mmwr/volumes/66/wr/mm6627e1.htm).

Elderly persons and persons with comorbidities are more often hospitalized, with the attendant risk of acquiring infections in hospitals. Overall, these trends increase the vulnerability of the healthcare setting as amplification point for EID outbreaks. This includes healthcare workers, who—sadly—are common among fatalities in healthcare-associated EID outbreaks.

While amplification in healthcare settings has been highlighted in recent EID threats, the greatest potential impact of EID is when infections can transmit in the community, thus becoming true pandemic threats.

International travel and migration increase every year, and the number of forcibly displaced people is at the highest since World War II, at almost 65 million people (http://www.unhcr.org/figures-at-a-glance.html). Tourism is reaching new records every year [44]. Diseases move with people, and the geographical background of a person must be taken into account when discussing differential diagnosis like HIV, tuberculosis, hepatitis B virus and leishmaniasis, which have incubation periods that can last 10 years or more [45].

Global travel is not restricted to humans: a particular concern is the successful spread of disease vectors through global trade. One spectacular example is the global dispersal of *Aedes albopictus* mosquitos through the trade in reused tires and ornamental plants [46]. A recent mathematical model of risk of Zika virus transmission, assuming that not only *Aedes aegypti* but also *Ae. albopictus* could act as a vector, found risk in the southern United States and in major cities in Europe like Rome, Madrid, Paris, London and Amsterdam, but also in major cities in Southeast Asia [47–49]. Autochthonous dengue fever cases have been observed in Croatia, but a bigger outbreak of dengue in Madeira was related to transmission through the more competent dengue vector *Ae. aegypti* that had been established there [50]. The outbreak of chikungunya virus infections in the Italian province of Emilia-Romagna in 2007 underlines the risk of introducing vector-borne infections once a new vector, in this case *Ae. albopictus,* has been established [51]. The index case is believed to be a traveller from India to Italy [51].

The most recent example of a surprising spread of a known virus is the Zika virus epidemic, which expanded rapidly since 2007, causing a series of outbreaks in Micronesia and the South Pacific before spreading to South and Central America and the United States [52].

What should we do?

Surveillance must become part of routine diagnostic procedures

Infectious disease clinicians and laboratory experts play a crucial role in the early detection of EID events. A challenge, however, is how to keep primary care providers on alert when needed. The list of potential EID is daunting, routine diagnostic platforms mostly target specific known common diseases and a substantial proportion of disease episodes with possible infectious aetiology remains undiagnosed (Fig. 2). Syndromic surveillance coupled with extensive diagnostic assessment would be the way forwards. Novel platforms allowing for broad range of diagnostics are actively researched but are not yet widely accessible for routine clinical care, although this is likely to change in the coming years. An important question, therefore, is how enhanced surveillance and testing for unusual infectious diseases could be developed (Fig. 2). It is not realistic and not necessary to expand the diagnostic assessment on a routine basis. A more targeted approach may be the way forwards.

A recent study modelled the likely hot spots for zoonotic infections crossing from different animal species to humans [2]. The study concluded that it remains challenging to predict specific diseases, but it found increased likelihood of cross-species transmissions in specific regions [2]. For vector-borne diseases, prediction of regions at risk for outbreaks is done routinely in certain tropical regions. Clinicians in regions with high-density animal farming should include exposure to such farms in their history taking. The global threat alert systems operated by the World Health Organization, European Centre for Disease Prevention and Control (ECDC) and other organizations do provide a valuable source of information for preparedness for clinicians and diagnostic laboratories, but this system is only as good as the input it receives. A key challenge is represented by the fact that outbreaks outside industrialized countries are less likely to be rapidly identified, and easy access to advanced laboratory capability on every continent is urgently needed. The establishment of an African centre for disease control is most welcome, but it must be followed by investment in advanced laboratory capabilities [53]. Closer to home, surveillance should include veterinary partners, as is done, for instance, for avian influenza. Again, however, this is not necessarily fully developed: even though the most recent influenza pandemic originated from swine, pigs are susceptible to both animal and human influenza viruses and pandemic influenza viruses have evolved both in humans and in pigs with occasional reverse jumps, there is no routine surveillance of influenza in pigs to complement the pandemic preparedness system.

In view of the above, enhanced surveillance of infections in travellers, migrants, persons working with animals and persons living in regions with a high risk of vector-borne disease outbreaks is crucial to identify outbreaks at an early stage. A valuable source of information regarding EID are the weekly communicable disease threat reports and risk assessments provided the ECDC (https://ecdc.europa.eu/en/publications-data) that can be used when triaging patients. Samples from severely ill individuals belonging to

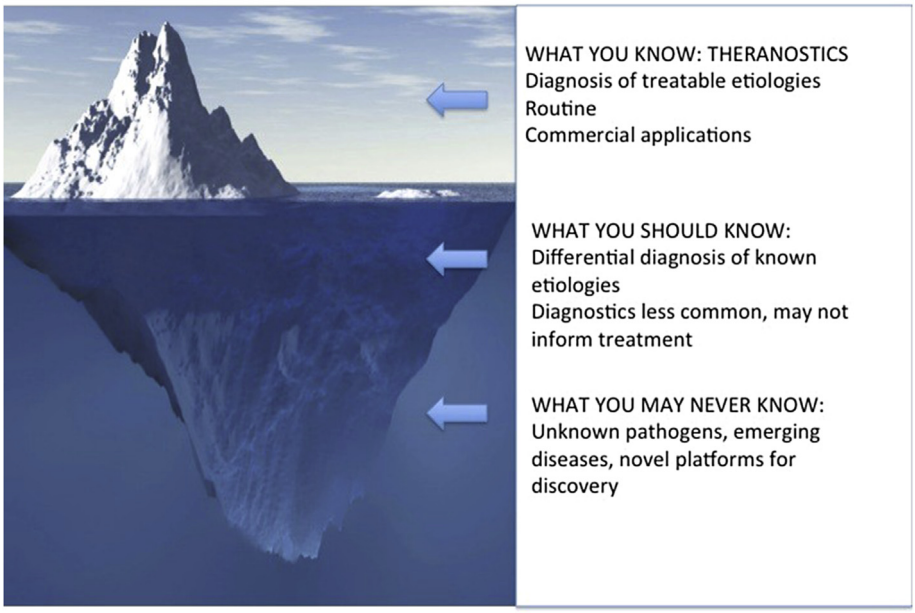

Fig. 2. Diagnostic pyramid.

Table 1
List of EU-funded networks focusing on EID

Acronym	Focus	Link
EVDlabnet	(Development of) diagnostic support and expert advise for zoonotic and vector-borne viruses	https://www.evd-labnet.eu/
EMERGE	(Development of) diagnostic support and expert advice for high-threat pathogens (class III bacteria, class IV viruses)	http://www.emerge.rki.eu/Emerge/EN/Home/Homepage_node.html
PREPARE	Clinical and laboratory preparedness for research during EID outbreaks	https://www.prepare-europe.eu/
COMPARE	Development of analytical tools and dat- sharing infrastructure for detection of EID and food-borne outbreaks based on genomic data	http://www.compare-europe.eu/about
GEOSENTINEL	Network of infectious disease clinics specializing in travel-associated diseases	http://www.istm.org/geosentinel

EID, emerging infectious diseases.

these sentinel groups without a clear diagnosis should rapidly (within days) be referred to reference laboratories. Europe has networks of diagnostic and research laboratories capable of diagnosing a broad range of rare zoonotic and vector-borne diseases, and of rapid deployment of assays for detection of EID, but there is room for improvement in linking these laboratories to primary clinical practice and in the sharing of essential information (Table 1).

Further support can be provided with advanced diagnostics, including methods capable of detecting a broad range of (potential) pathogens such as metagenomics. Such methods do not come without challenges, as they detect not only pathogens but also the resident microbiome and virome, and a rapidly approaching new bottleneck will be the capacity for storage and analysis of the rich data produced by the new sequencing platforms [54,55]. Therefore, active collaborations between clinicians and laboratory experts are needed to take this field forwards.

These are some of the challenges that will be discussed by the ESCMID Emerging Infections Task Force.

How can EID preparedness be increased without massive increase in workload and costs, and a high number of false scares?

How can international shipment of samples to reference laboratories be organized with the challenges of the Nagoya protocol, biosafety and biosecurity regulation, and the huge costs involved with this? Looking for solutions starts with an active multidisciplinary network with the ambition to take this discussion forwards and to improve on our current practice.

This includes the outbreak scenario. Once an outbreak occurs, there is a massive influx of public health, clinical and research activities from different sources, including public, private and nongovernmental organizations, occasionally with conflicting interests. Predefined rules of engagement will help speed up the essential diagnostics and research need for swift outbreak response.

ESCMID Emerging Infections Task Force: aims and actions

The task force aims to establish a network of experts within clinical microbiology and infectious diseases who can raise awareness on EID within the society and beyond, liaise with other networks focusing on emerging diseases, develop a knowledge base on early detection and diagnosis of EID and stimulate research on emerging infections including surveillance and diagnostics.

An important aim of the task force is to ensure that awareness of emerging infections becomes part of the workup of every patient with a suspected infection. Just as a travel history is mandatory for all patients, the thought that an illness may be important when it defies standard diagnostic investigations should be in the mind of every specialist in infectious diseases and microbiology.

Acknowledgements

Members of the ESCMID Emerging Infections Task Force Expert Panel are as follows: N. Beeching, Clinical Infectious Diseases, Liverpool School of Tropical Medicine and Tropical and Infectious Disease Unit, Royal Liverpool University Hospital, Liverpool, United Kingdom; A. Di Caro, Microbiology Laboratory and Infectious Diseases Biorepository, National Institute for Infectious Diseases 'L. Spallanzani,' Rome, Italy; E. Gkrania-Klotsas, Addenbrooke's Hospital, Wellcome Trust Sanger Institute, Cambridge, United Kingdom; A. Kantele, University of Helsinki; Infectious Diseases, Inflammation Center, Helsinki University Hospital, Helsinki, Finland; Karolinska Institutet, Stockholm, Sweden; R. Kohlmann, Department for Medical Microbiology, Ruhr-Universität Bochum, Bochum, Germany; P.-L. Lim, Department of Infectious Diseases, IIDE, Tan Tock Seng Hospital and Communicable Disease Division, Ministry of Health, Singapore; A. Markotic, University Hospital for Infectious Diseases, Zagreb, Croatia; R. López-Vélez, Unidad de Referencia Nacional para Enfermedades Tropicales, Servicio de Enfermedades Infecciosas, Hospital Universitario Ramón y Cajal, IRYCIS, Madrid, Spain; L. Poirel, Emerging Antibiotic Resistance Unit, Medical and Molecular Microbiology, Department of Medicine, Faculty of Science, University of Fribourg and National Reference Center for Emerging Antibiotic Resistance (Switzerland), Fribourg, Switzerland; J. W. A. Rossen, Molecular and Sequencing Unit of Clinical Bacteriology, University Medical Center, Groningen University, The Netherlands; Y. Stienstra, Department of Infectious Diseases, University Medical Center Groningen, The Netherlands; M. Storgaard, Department of Infectious Diseases, Aarhus University Hospital, Denmark.

Transparency declaration

All authors report no conflicts of interest relevant to this article.

References

[1] Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. Nature 2008;451:990–3.
[2] Olival KJ, Hosseini PR, Zambrana-Torrelio C, Ross N, Bogich TL, Daszak P. Host and viral traits predict zoonotic spillover from mammals. Nature 2017;546:646–50.
[3] Yu XJ, Liang MF, Zhang SY, Liu Y, Li JD, Sun YL, et al. Fever with thrombocytopenia associated with a novel bunyavirus in China. N Engl J Med 2011;364:1523–32.
[4] Zanluca C, Melo VC, Mosimann AL, Santos GI, Santos CN, Luz K. First report of autochthonous transmission of Zika virus in Brazil. Mem Inst Oswaldo Cruz 2015;110:569–72.
[5] Grobbelaar AA, Weyer J, Moolla N, Jansen van Vuren P, Moises F, Paweska JT. Resurgence of yellow fever in Angola, 2015–2016. Emerg Infect Dis 2016;22:1854–5.
[6] van der Hoek W, Morroy G, Renders NH, Wever PC, Hermans MH, Leenders AC, et al. Epidemic Q fever in humans in The Netherlands. Adv Exp Med Biol 2012;984:329–64.
[7] Buchholz U, Bernard H, Werber D, Böhmer MM, Remschmidt C, Wilking H, et al. German outbreak of *Escherichia coli* O104:H4 associated with sprouts. N Engl J Med 2011;365:1763–70.
[8] Nishiura H, Tsuzuki S, Yuan B, Yamaguchi T, Asai Y. Transmission dynamics of cholera in Yemen, 2017: a real time forecasting. Theor Biol Med Model 2017;14:14.
[9] Lipsitch M, Barclay W, Raman R, Russell CJ, Belser JA, Cobey S, et al. Viral factors in influenza pandemic risk assessment. Elife 2016;5, e18491.
[10] Vince GA. Epoch debate. Science 2011;334:32–7.
[11] Wolfe ND, Dunavan CP, Diamond J. Origins of major human infectious diseases. Nature 2007;447:279–83.
[12] Ward MP, Maftei D, Apostu C, Suru A. Estimation of the basic reproductive number (R0) for epidemic, highly pathogenic avian influenza subtype H5N1 spread. Epidemiol Infect 2009 Feb;137(2):219–26. https://doi.org/10.1017/S0950268808000885. Epub 2008 Jun 18.
[13] Wolf N. The viral storm. New York: Times Books; Holt; 2011.
[14] Majumder MS, Rivers C, Lofgren E, Fisman D. Estimation of MERS–coronavirus reproductive number and case fatality rate for the spring 2014 Saudi Arabia outbreak: insights from publicly available data. PLoS Curr 2014;6. ecurrents.outbreaks.98d2f8f3382d84f390736cd5f5fe133.
[15] Kantele A, Jokiranta TS. Review of cases with the emerging fifth human malaria parasite. Plasmodium Knowlesi Clin Infect Dis 2011;52:1356–62.
[16] Singh B, Kim Sung L, Matusop A, Radhakrishnan A, Shamsul SS, Cox-Singh J, et al. A large focus of naturally acquired *Plasmodium knowlesi* infections in human beings. Lancet 2004;363:1017–24.
[17] Lau SK, Woo PC, Li KS, Huang Y, Tsoi HW, Wong BH, et al. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. Proc Natl Acad Sci U S A 2005;102:14040–5.
[18] 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.
[19] Rimoin AW, Mulembakani PM, Johnston SC, Lloyd Smith JO, Kisalu NK, Kinkela TL, et al. Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo. Proc Natl Acad Sci U S A 2010;107:16262–7.
[20] Kantele A, Chickering K, Vapalahti O, Rimoin AW. Emerging diseases—the monkeypox epidemic in the Democratic Republic of the Congo. Clin Microbiol Infect 2016;22:658–9.
[21] Outbreak of Hendra-like virus—Malaysia and Singapore, 1998–1999. Centers for disease control and prevention (CDC). MMWR Morb Mortal Wkly Rep 1999;48:265–9.
[22] Daszak P, Zambrana-Torrelio C, Bogich TL, Fernandez M, Epstein JH, Murray KA, et al. Interdisciplinary approaches to understanding disease emergence: the past, present, and future drivers of Nipah virus emergence. Proc Natl Acad Sci U S A 2013;110(Suppl. 1):3681–8.
[23] Lo MK, Rota PA. The emergence of Nipah virus, a highly pathogenic paramyxovirus. J Clin Virol 2008;43:396–400.
[24] Rockx B. Recent developments in experimental animal models of *Henipavirus* infection. Pathog Dis 2014;71:199–206.
[25] Newell DG, Koopmans M, Verhoef L, Duizer E, Aidara-Kane A, Sprong H, et al. Food-borne diseases—the challenges of 20 years ago still persist while new ones continue to emerge. Int J Food Microbiol 2010;139(Suppl. 1):S3–15.
[26] Hope J. Bovine spongiform encephalopathy: a tipping point in one health and food safety. Curr Top Microbiol Immunol 2013;366:37–47.
[27] Fruth A, Prager R, Tietze E, Rabsch W, Flieger A. Molecular epidemiological view on Shiga toxin–producing *Escherichia coli* causing human disease in Germany: diversity, prevalence, and outbreaks. Int J Med Microbiol 2015;305:697–704.
[28] Tahden M, Manitz J, Baumgardt K, Fell G, Kneib T, Hegasy G. Epidemiological and ecological characterization of the EHEC O104:H4 outbreak in Hamburg, Germany, 2011. PLoS One 2016;11, e0164508.
[29] Launders N, Locking ME, Hanson M, Willshaw G, Charlett A, Salmon R, et al. A large Great Britain–wide outbreak of STEC O157 phage type 8 linked to handling of raw leeks and potatoes. Epidemiol Infect 2016;144:171–81.
[30] Buss BF, Joshi MV, Dement JL, Cantu V, Safranek TJ. Multistate product traceforward investigation to link imported romaine lettuce to a US cyclosporiasis outbreak—Nebraska, Texas, and Florida, June–August 2013. Epidemiol Infect 2016;144:2709–18.
[31] Velkers FC, Blokhuis SJ, Veldhuis Kroeze EJB, Burt SA. The role of rodents in avian influenza outbreaks in poultry farms: a review. Vet Q 2017;37:182–94.
[32] Ypma RJ, Jonges M, Bataille A, Stegeman A, Koch G, van Boven M, et al. Genetic data provide evidence for wind-mediated transmission of highly pathogenic avian influenza. J Infect Dis 2013;207:730–5.
[33] Soares RR. On the determinants of mortality reductions in the developing world. Pop Dev Rew 2007;33:247–87.
[34] Lee S, Chan LY, Chau AM, Kwok KP, Kleinman A. The experience of SARS-related stigma at Amoy Gardens. Soc Sci Med 2005;61:2038–46.
[35] McKinney KR, Gong YY, Lewis TG. Environmental transmission of SARS at amoy gardens. J Environ Health 2006;68:26–30.
[36] Nam HS, Park JW, Ki M, Yeon MY, Kim J, Kim SW. High fatality rates and associated factors in two hospital outbreaks of MERS in Daejeon, the Republic of Korea. Int J Infect Dis 2017;58:37–42.
[37] Kinsella K, Velkoff VA. In an ageing world. Washington DC: US Census Bureau; 2001.
[38] Girardi E, Sañé Schepisi M, Goletti D, Bates M, Mwaba P, Yeboah-Manu D, et al. The global dynamics of diabetes and tuberculosis: the impact of migration and policy implications. Int J Infect Dis 2017;56:45–53.
[39] Chan JW, Ng CK, Chan YH, Mok TY, Lee S, Chu SY, et al. Short term outcome and risk factors for adverse clinical outcomes in adults with severe acute respiratory syndrome (SARS). Thorax 2003;58:686–9.
[40] Breitling LP. Evidence of non-linearity in the association of glycemic control with influenza/pneumonia mortality: a study of 19 000 adults from the US general population. Diabetes Metab Res Rev 2016;32:111–20.
[41] Torres A, Blasi F, Dartois N, Akova M. Which individuals are at increased risk of pneumococcal disease and why? Impact of COPD, asthma, smoking, diabetes, and/or chronic heart disease on community-acquired pneumonia and invasive pneumococcal disease. Thorax 2015;70:984–9.
[42] Schieppati A, Perico N, Remuzzi G. Eliminating treatable deaths due to acute kidney injury in resource-poor settings. Semin Dial 2015;28:193–7.
[43] McNamara LA, Topaz N, Wang X, Hariri S, Fox L, MacNeil JR. High risk for invasive meningococcal disease among patients receiving eculizumab (Soliris) despite receipt of meningococcal vaccine. MMWR Morb Mortal Wkly Rep 2017 Jul 14;66(27):734–7.

[44] Schlagenhauf P, Weld L, Goorhuis A, Gautret P, Weber R, von Sonnenburg F, et al., for EuroTravNet. Travel-associated infection presenting in Europe (2008–12): an analysis of EuroTravNet longitudinal, surveillance data, and evaluation of the effect of the pre-travel consultation. Lancet Infect Dis 2015;15:55–64.
[45] Khyatti M, Trimbitas RD, Zouheir Y, Benani A, El Messaoudi MD, Hemminki K. Infectious diseases in North Africa and North African immigrants to Europe. Eur J Publ Hlth 2014;24(Suppl. 1):47–56.
[46] Medlock JM, Hansford KM, Schaffner F, Versteirt V, Hendrickx G, Zeller H, et al. A review of the invasive mosquitoes in Europe: ecology, public health risks, and control options. Vec Bor Zoon Dis 2012;12:435–47.
[47] Gardner L, Chen N, Sarkar S. Vector status of *Aedes* species determines geographical risk of autochthonous Zika virus establishment. PLoS Negl Trop Dis 2017;11, e0005487.
[48] Sigfrid L, Reusken C, Eckerle I, Nussenblatt V, Lipworth S, Messina J, et al. Preparing clinicians for (re-)emerging arbovirus infectious diseases in Europe. Clin Microbiol Infect 2018;24:229–39.
[49] Liu-Helmersson J, Quam M, Wilder-Smith A, Stenlund H, Ebi K, Massad E, et al. Climate change and *Aedes* vectors: 21st century projections for dengue transmission in Europe. EBioMedicine 2016;7:267–77.
[50] Gjenero-Margan I, Aleraj B, Krajcar D, Lesnikar V, Klobučar A, Pem-Novosel I, et al. Autochthonous dengue fever in Croatia, August–September 2010. Euro Surveill 2011;16:19805.
[51] Rezza G, Nicoletti L, Angelini R, Romi R, Finarelli AC, Panning M, et al., CHIKV Study Group. Infection with chikungunya virus in Italy: an outbreak in a temperate region. Lancet 2007;370:1840–6.
[52] Weaver SC, Costa F, Garcia-Blanco MA, Ko AI, Ribeiro GS, Saade G, et al. Zika virus: history, emergence, biology, and prospects for control. Antivir Res 2016;130:69–80.
[53] Zumla A, Dar O, Kock R, Muturi M, Ntoumi F, Kaleebu P, et al. Taking forward a 'One Health' approach for turning the tide against the Middle East respiratory syndrome coronavirus and other zoonotic pathogens with epidemic potential. Int J Infect Dis 2016;47:5–9.
[54] Aarestrup FM, Brown EW, Detter C, Gerner-Smidt P, Gilmour MW, Harmsen D, et al. Integrating genome-based informatics to modernize global disease monitoring, information sharing, and response. Emerg Infect Dis 2012;18, e1.
[55] Aarestrup FM, Koopmans MG. Sharing data for global infectious disease surveillance and outbreak detection. Trends Microbiol 2016;24:241–5.