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EMERGING INFECTIOUS DISEASES - A PERSPECTIVE Jayakumar K¹, Aneen Suresh^{2,*}, Sony Peter³

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Abstract

Infectious diseases continue to impose unpredictable burdens on global health and economies. Therefore, this has become a concern, even in terms of national security. In this sense, the objective of the present article was to review the role of wild animals as reservoirs and/or dispersers of etiological agents of human infectious diseases in order to compile data on the main wild animals and etiological agents involved in zoonotic outbreaks. The zoonotic threat of these etiological agents and the impact on public health can be enormous as shown by the ongoing epidemic of 2019 novel coronavirus (2019-nCoV) infections.

Keywords: Infection, Emerging, Virus, Epedimiology, Pandemic, COVID

Introduction:

In 2008 saw the publishing of a landmark paper which 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, rodents, flies) (1). Since 2008, the discovery of Nipah, Zika, Ebola, Middle East respiratory syndrome coronavirus (MERS-CoV), and the recent Coronavirus outbreak, highlight the importance of demographic change, global travel and trade, and possibly climate change as drivers for emergence. While the field is dominated by viruses from wildlife reservoirs, we must mention the bacterial scourges, such as the Q fever outbreak in the Netherlands, the enterohemorrhagic Escherichia coli outbreak in Germany Globally, there exists several ecosystems with rich biodiversity, which are gradually deteriorating due to an increase in anthropogenic (2). The activities economic and technological advancement in agriculture & industrialization, population growth, changes in food habits, migration and tourism are a few determinant factors linked to the degradation of such environments. Correspondingly, these conditions encourage and establish new potentially harmful relationships, revamping the existent ecological niches, potentiating disease transmission. A major concern is our inability to predict the emergence of new or changing health threats, and thereby to diagnose them when they occur. 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.

Catalysts of emerging infectious diseases

Ebola, SARS, Nipah Virus Encephalitis (NiVE), and 2019nCoV are some of the more prominent Emerging Infectious Diseases originating from wildlife, presenting global epidemic risks, and generating, today, vast economic and social burdens to humanity (3). Moreover, the transmission of these diseases to humans casts a significant burden on global health systems (4,5). These infectious diseases continue to impose huge and unforeseeable burdens to the global health and economy. Thus, adequate surveillance of these diseases and preparation for potential epidemics and pandemics is fundamental to mitigate the impact of future outbreaks (6). One of the challenges of con trolling the dissemination of etiological agents is precisely the copious diversity of the animal reservoirs, making it easier for these agents to perpetuate in several habitats (2). A primary catalyst comprises anthropogenic changes at the human animal ecosystem interface. 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 ravaging natural resources like the sea. 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 (7). This in part explains why so many EID have a zoonotic origin.

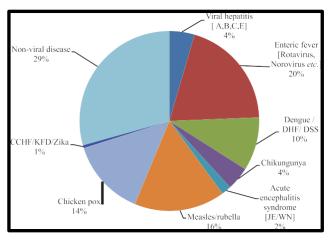


Figure 1: Distribution of viral diseases across the Indian Subcontinent

A study by Wolfe et al. (8) 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) 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. HIV is thought to have made at least ten entries into humans before stage 5 was reached (9).

A specific risk is the consumption of semi wild or wild animals, combined with animal trading, acute respiratory syndrome (SARS) coronavirus (CoV) outbreak is believed to have been introduced into humans from civette cats sold for consumption at markets, which had acquired infection from the original reservoir, horseshoe bats (10). Another 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 (11,12). 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 (13)

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 (14). 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 (15). In 2011, an outbreak of HUS (Hemolytic Uremic Syndrome) due to a Shiga toxin producing E. coli, E. coli O104:H4, was detected in Hamburg, Germany, and cases were soon identified in several European countries (16,17). The source was traced to a single producer of sprouts in Germany who used seeds produced and contaminated in Egypt (18). A similar outbreak was reported from the United Kingdom, presumably from handling raw leeks and potatoes (19). Multistate outbreaks in the United States of Cyclospora cayetanensis were linked to imported lettuce from a single manufacturer (20).

Opportunity for rapid spread of pathogens

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 (21). With ageing come 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 (22), SARS (23), influenza (24), pneumococcal infections (25) 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 (26). International travel and migration increase every year, and the number of forcibly displaced people is at the highest since World War II. Tourism is reaching new records every year (27). 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 (28). Global travel is not restricted to humans: a particular concern is the successful spread of disease vectors through global trade. Dengue fever cases have been observed in Croatia, but a bigger outbreak of dengue in Madeira was related to trans- mission through the more competent dengue vector Ae. aegypti that had been established there (29).

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. The index case is believed to be a traveler from India to Italy (30). 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. The infectious diseases whose microbial transmission benefits from diverse environmental factors, through adapting & building resistance, usually attack humans after they have established themselves in these ecosystems (31,32). The origins of this kind of transmission are influenced by ecological components, such as climatic variations, fauna and flora. Thus, one has to confront the capricious efficacy of prophylactic strategies, since they are required to complement the dynamic pace of the mechanisms involved in the human-health-environment equilibrium. When considering the prevention of epidemics constant surveillance of viral, bacterial, fungal and parasitic loads from migrant birds and wild animals

In 2018, Ebola, HIV, West Nile, Avian Influenzas Coronavirus, Hantavirus, Borrelia burgdorferi spread via Bats, Wild Birds, Amphibians like salamanders and via mammals like Chimpanzees 3 In a study conducted in 2017, Ebola spread in Africa due to a lack of policy interventions in wildlife trade regulation and the need to conduct investment assessments of developmental projects (33). In 2015, in Colombia, the Anger virus was spread via bats. The proposed reason for spread was linked to deforestation and the modification of ecological niches due to urban habitation (34). HTLV4 spread in 2014 due to the evolution of retroviruses via gorillas (35). West Nile fever spread in Africa in 2001, was attributed to Chimpanzees, bats dogs and monkeys due to the threat posed by human environmental changes (36). Wild boar domestication was considered responsible for the spread of the Hepatitis E virus in Italy (37). Arbovirus was considered to be spread by wild birds due to habitat reconstruction (38). With these facts, one can lead to the conclusion that human interference in natural ecological niches, can lead to far reaching devastating effects.

What should we do?

We must (1) find potentially relevant data analysis about zoonosis, (2) must encompass in its study some relation between an infectious disease and wild animals in the transmission cycle of the etiological agent.

The majority of zoonoses cited in studies, had links to mammals. The types of mammals, more expressively, were bats and primates (Non-Human Primates) (36,39,40), Cercocebus atys (41,42), Pan troglodytes (41,42), and Gorilla gorilla (35), and, less expressively, wild rodents, buffalos, wild boars (42,43). Among the etiological agents found included: Influenza Virus, Coronavirus, Nipah Virus, Ebola Virus, Paramyxovirus, Rhabdovirus, Hendra Virus, Menangle Virus, West Nile Virus, Bird Influenza, Filovirus, Human **Immunodeficiency** Virus (HIV), Orthohantavirus/Hantavirus, Human Type-4 Cells Lymphotropic Virus, Hepatitis E Virus, Leptospirosis, Borrelia burgdorferi, Marburg Virus, Rift Valley Fever Virus, Parvovirus, Arbovirus, and gastrointestinal parasites in general. 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. 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.

A recent study modelled the likely hot spots for zoonotic infections crossing from different animal species to humans. The study concluded that it remains challenging to predict specific diseases, but it found increased likelihood of cross-species trans- missions in specific regions (44). 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. 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 disease control centers must be followed by investment in advanced laboratory capabilities (45). Closer to home, surveillance should include veterinary partners. In view of the above, enhanced surveillance of infections in travelers, 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. Samples from severely ill individuals belonging to these sentinel groups without a clear diagnosis should rapidly (within days) be referred to reference laboratories.

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 platform (46,47).Therefore, sequencing collaborations between clinicians and laboratory experts are needed to take this field forwards. 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.

Conclusion

There is a huge gap in the scientific knowledge on the actual role of wild animals in human infectious diseases outbreaks. There are many challenges to identifying which wild animals are reservoirs to specific etiological agents. Another challenge is determining the possible biotic interactions that trigger the emergence of new efficient subtypes and/or strains. It was identified that viruses are the main etiological agents involved in this process and the principal wild animals are birds and mammals, due to their genetic proximity to humans, although these agents do not trigger symptomatology in these animals, nonetheless, there is insignificant research and diagnostic data. Surveys need to be constant and perennial. Only then, will the predictability of complex biotic relationships between these distinct pathogens and their wild animal reservoirs be more analogous. This lack of adequate research leads to failure in Eco-epidemiological control strategies of the diseases, allowing for greater occurrence throughout major geographical zones, and the development of new diseases with a detrimental impact to public health.

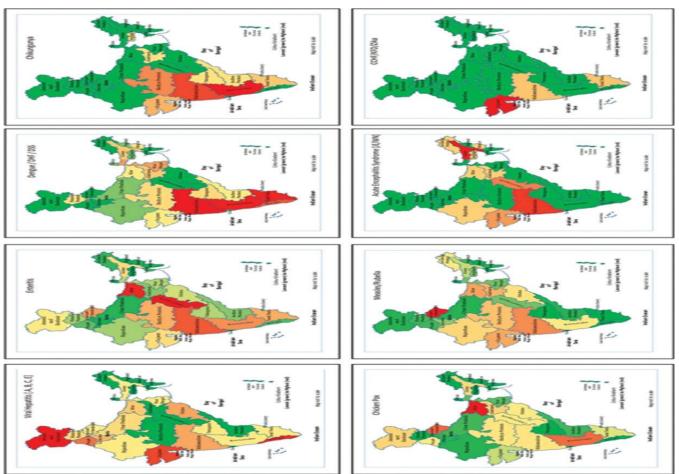


Figure 2: Viral load of diseases across India

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