



WE ARE NOT PREPARED : AN AGE OF EMERGING AND RE-EMERGING PANDEMIC THREATS IS HERE

Healthcare

Prof. S.A Tabish

FRCP, FACP, FAMS, MHA (AIIMS), Doctorate in Educational Leadership (USA), Sher I Kashmir Institute of Medical Sciences, Srinagar

Nabil Syed

MA (King's College London)

ABSTRACT

Infectious diseases remain among the leading causes of death and disability worldwide. Epidemics of new and old infectious diseases periodically emerge, greatly magnifying the global burden of infections. Humans are constantly exposed to a huge diversity of viruses, though those of others mammals are of greatest importance. Moreover, these viruses are very genetically diverse and new genotypes, strains and species evolve rapidly. The emergence of new human viruses is a long-standing and ongoing biological process. We must anticipate the emergence and/or discovery of more new human viruses in the coming years and decades. The first line of defence against emerging viruses is effective surveillance. Rapid detection and identification of emerging pathogen leading to the rapid introduction of preventive measures can prove highly effective in combating outbreaks of novel diseases. A coordinated, global surveillance network is essential if we are to ensure rapid detection of novel viruses. Improving the situation will require both political will and considerable investment in infrastructure, human capacity and new tools. To ensure global preparedness, newer vaccines, diagnostics and antiviral agents are being developed. Infectious diseases can be prevented at a variety of points, depending on the infectious cycle for the particular disease. Disease prevention, health promotion, strengthening public health systems, translational research, focus on drug discovery, tailored therapies by personalized precision medicine, developing newer effective and affordable vaccines are crucial to prevent and control emerging pandemics. Countries have to be in a state of Emergency preparedness.

KEYWORDS

EID, Pandemic, coronaviruses, monkeypox, new Langya virus, Henipaviruses

Humans are constantly exposed to a huge diversity of viruses. Emerging infectious diseases result from either natural processes such as the evolution of pathogens over time or as a result of human behavior and practices. Factors that have contributed to these changes are population growth, migration from rural areas to cities, international air travel, poverty, wars, and destructive ecological changes due to economic development and land use.

For an emerging disease to become established at least two events have to occur – the infectious agent has to be introduced into a vulnerable population and the agent has to have the ability to spread readily from person-to-person and cause disease. The infection also has to be able to sustain itself within the population, that is more and more people continue to become infected.

Many emerging diseases arise when infectious agents in animals are passed to humans. As the human population expands in number and into new geographical regions, the possibility that humans will come into close contact with animal species that are potential hosts of an infectious agent increases. When that factor is combined with increases in human density and mobility, it is easy to see that this combination poses a serious threat to human health.

Climate change is increasingly becoming a concern as a factor in the emergence of infectious diseases. As Earth's climate warms and habitats are altered, diseases can spread into new geographic areas.

Bacteria, viruses, and other microorganisms can change over time and develop a resistance to the drugs used to treat diseases caused by the pathogens. Therefore, drugs that were effective in the past are no longer useful in controlling disease.

Decline in vaccine coverage can cause a disease to re-emerge, so that even when a safe and effective vaccine exists, a growing number of people choose not to become vaccinated. This has been a particular problem with the measles vaccine.

Emergence of new pathogens

The case of the coronaviruses SARS-CoV, MERS-CoV, and SARS-CoV-2, represents instances of how viruses can move from animals into humans, acquire the ability to spread from person to person and then, with great speed, reach around the globe as a result of air travel.

Several high impact zoonotic disease outbreaks have been linked to bat-borne viruses during the last two decades. These include SARS coronavirus, Hendra virus and Nipah virus. In addition, it has been suspected that ebola viruses and MERS coronavirus are also linked to bats. It is being increasingly accepted that bats are potential reservoirs

of a large number of known and unknown viruses, many of which could spillover into animal and human populations.¹ Emerging diseases with their disastrous consequences might be surprising and unpredictable, but they could be foreseen.

Zoonotic Disease Outbreaks

In spite of significant advances in diagnostics and therapeutic countermeasures during the past century, the risk of cross-species transmission of known and unknown pathogens has emerged as a threat to human and animal populations due to a variety of factors, including industrialization, intensive farming, urbanization, rapid transportation and climate change. It is generally accepted that approximately 75% of emerging infectious diseases for humans are zoonoses. The rate of emergence of novel viruses appears to be increasing as a result of both increased spillover from their natural reservoirs and our improved ability in detection.

Among the newly emerged and most deadly zoonotic viruses discovered in the past few decades, bat-borne viruses occupy a greater proportion than viruses from any other mammalian order. Several studies have now concluded that bats are exceptional in their ability to act as natural reservoir of viruses and they are able to harbour more diverse viruses per animal species. Nearly 75% of emerging infectious diseases for humans are zoonoses.² The rate of emergence of novel viruses appears to be increasing as a result of both increased spillover from their natural reservoirs and our improved ability in detection.³ During the last two decades, several high impact zoonotic disease outbreaks have been linked to bat-borne viruses. These include SARS coronavirus, Hendra virus and Nipah virus. It is being increasingly accepted that bats are potential reservoirs of a large number of known and unknown viruses, many of which could spillover into animal and human populations. Bat coronaviruses may be a more likely cause of future spillover into both human and livestock populations due to their greater genetic diversity already known in bats around the world, their large positive strand RNA genome size with a high rate of recombination, and proven spillover events in both human and animals.⁴

Infectious diseases will undoubtedly persist as permanent and main threats to humanity in the future, especially due to increased longevity that almost always comes at cost due to impaired immunity. One reason among many others is certainly the continuous co-evolution of pathogens with the host immunity, especially in the case of opportunistic and zoonotic pathogens, which is enabling pathogen transmission between different mammalian or animal hosts.⁵

The world witnessed how COVID-19 has become a leading global cause of death within just 9 months after its discovery, and all that

despite intense health warnings.⁶ Establishing proper “preparedness,” is essential for both swift and appropriate actions to deal with emerging infectious disease threats.

Anti-infective drugs and vaccines, along with tailored therapies by personalized precision medicine for many cancers and circulatory diseases, as well as access to high-end medical technologies, have been saving uncounted millions of human lives and increased longevity. Despite all, and this is deeply concerning, infectious diseases stand out by far as the single major causes of childhood mortality until the age of 14 all over the world. Across all age groups, infectious disease deaths are similar to cardiovascular diseases.⁷

Stages in the emergence of infectious diseases

There are two distinct stages in the emergence of infectious diseases: the introduction of a new infection to a host population, and the establishment within and dissemination from this population.

Nearly 1,400 pathogens capable of infecting humans, of which 500 are capable of human-to-human transmission, and among which fewer than 150 have the potential to cause epidemic or endemic disease; evolution drives pathogens up the pyramid. .

We are aware of the importance of infectious diseases throughout history, including the Plague of Justinian (541–542), the first known pandemic on record and the Black Death in the fourteenth century. Another devastating disease that was once much feared is smallpox, which is said to have killed more people than all the wars in history. The eradication of smallpox was therefore a triumph of public health. The 1918 influenza pandemic is one of our paradigms of a nightmare emerging infectious disease event. It caused about 50 million or more deaths.

There has been complacency about infectious diseases, partly for reasons—the antibiotic era, immunizations, improved public health measures—all of which have led to the fact that we now live longer and tend to die later of chronic diseases.

Disease Burden

Emerging infectious diseases (EIDs) are a significant burden on global economies and public health. Their emergence is thought to be driven largely by socio-economic, environmental and ecological factors. A study analysed a database of 335 EID 'events' (origins of EIDs) between 1940 and 2004, and demonstrate non-random global patterns. EID events are dominated by zoonoses (60.3% of EIDs): the majority of these (71.8%) originate in wildlife (for example, severe acute respiratory virus, Ebola virus), and are increasing significantly over time. Study reveals that 54.3% of EID events are caused by bacteria or rickettsia, reflecting a large number of drug-resistant microbes in our database. Global resources to counter disease emergence are poorly allocated, with the majority of the scientific and surveillance effort focused on countries from where the next important EID is least likely to originate.⁸

EIDs of recent origin

Here we will discuss most recent Emerging Infectious Diseases of public health importance.

1. Monkeypox

More than 80 countries where monkeypox is not endemic have reported outbreaks of the viral disease, which the World Health Organization has declared a global health emergency, as confirmed cases crossed 27,800 and non-endemic countries reported their first deaths. An emerging outbreak of monkeypox infection is quickly spreading worldwide.⁹

Monkeypox is a disease of global public health importance as it not only affects countries in west and central Africa, but the rest of the world. Human monkeypox was first identified in humans in 1970 in the Democratic Republic of the Congo in a 9-month-old boy in a region where smallpox had been eliminated in 1968. Since then, most cases have been reported from rural, rainforest regions of the Congo Basin, particularly in the Democratic Republic of the Congo and human cases have increasingly been reported from across central and west Africa.

The case fatality ratio of monkeypox has historically ranged from 0 to 11 % in the general population and has been higher among young children. In recent times, the case fatality ratio has been around 3–6%.⁹

From 1 January through 7 August 2022, 27 814 laboratory confirmed cases of monkeypox and 11 deaths have been reported to WHO from 89 countries/territories/areas in all six WHO Regions. The virus has hit parts of the population where people have been in close contact with each other and also travel internationally.⁹

The current outbreak in non-endemic countries suggests that sustained human-to-human transmission is quite feasible, so it suggests that ongoing human transmission could also be happening in Africa on a larger scale than generally thought.

Routine immunization against smallpox stopped in the early 1970s in places like the US and UK. As smallpox vaccines can be 85% effective at preventing its related virus, monkeypox, many people born after that time are not immune anymore.⁹

Monkeypox virus, a zoonotic orthopox DNA virus related to the virus that causes smallpox, was first described in humans in 1970 in the Democratic Republic of Congo. Sporadic outbreaks of infection have been reported in Africa, typically originating from contact with wildlife reservoirs. Such outbreaks and travel-associated cases outside Africa have had limited secondary spread, and therefore human-to-human transmission has been deemed inefficient.

The current global outbreak of monkeypox virus infection in humans suggests changes in biologic aspects of the virus, changes in human behavior, or both; such changes might be driven by waning smallpox immunity, relaxation of Covid-19 prevention measures, resumption of international travel, and sexual interactions associated with large gatherings. The current spread has disproportionately affected men who are gay or bisexual and other men who have sex with men, which suggests amplification of transmission through sexual networks. Monkeypox can affect anyone including heterosexual men.

In a study, monkeypox manifested with a variety of dermatologic and systemic clinical findings. The simultaneous identification of cases outside areas where monkeypox has traditionally been endemic highlights the need for rapid identification and diagnosis of cases to contain further community spread.¹⁰

The world needs to move cohesively and quickly to close knowledge gaps and to contain the outbreak. Without widely available treatment or prophylaxis, rapid case identification is vital to containment.

The WHO declared on 23 July 2022 that the multi-country outbreak of monkeypox is a public health emergency of international concern (PHEIC). A coordinated response can stop transmission and protect vulnerable groups. Monkeypox is a rare disease that is rarely fatal. With the tools we have right now, we can stop transmission and bring this outbreak under control. Now, we just need to scale up our collective response.¹¹

In India, the outbreak was first reported on 14 July 2022 in Kerala State - suspected imported case which was confirmed hours later by the NIV. India was the tenth country to report a monkeypox case in Asia and the first in South Asia. An analysis conducted by the Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV) revealed that the first two Monkeypox cases diagnosed in India which was a duo that had returned from the UAE- were infected with the virus strain A.2. Notably the strain A.2, is different from the strain causing the worrying outbreak of Monkeypox cases in Europe. The clinical specimens of both the cases were tested with real-time PCR for Orthopoxvirus, monkeypox virus (MPXV). The complete genome sequences obtained from skin lesions of cases 1 and 2 showed similarity of 99.91 and 99.96 per cent respectively with MPXV_USA_2022_FL001 West African clade. Phylogenetic analysis revealed that the two cases were infected with monkeypox virus strain A.2 which belong to hMPXV-1A lineage of clade 3 (West African clade), the study by the NIV under the ICMR found.¹²

The West African clade is found to be circulating in the current ongoing outbreaks of 2022 in non-endemic countries. It is less severe than Congo lineage reported earlier, The A.2 strain, which was detected in the US last year, has not been linked to major clusters. The current outbreak is being driven by the B.1 strain of monkeypox virus. The West African and Central African (Congo Basin) are the two known clades of the monkeypox virus, of which Congo basin strain causes more severe illness, 0–11% mortality and increased transmissibility.

The study found that the two cases were infected with monkeypox virus strain A.2 which belong to hMPXV-1A lineage of clade 3 (West African clade). Of the two known clades- West African and Central African--the West African clade is found to be less severe than Central African lineage. According to the study, people with no history of sexual contact can also contract the virus. In the first case, the person had a history of similar lesions amongst his friends and contact with a suspected Monkeypox case.¹²

Since the start of the monkeypox outbreak and as of 22 August 2022, 16750 confirmed cases of monkeypox (MPX) have been reported from 29 EU/EEA countries. Two deaths have been reported by Spain in July 2022.¹³ According to WHO, cases in the Americas accounted for 60% of cases in the past month, while cases in Europe comprised about 38%. The number of monkeypox cases reported globally dropped by 21% in the mid August, 2022, reversing a month-long trend of rising infections and a possible signal the outbreak in Europe may be starting to decline.¹⁴

Since 1 January and as of 22 June 2022, 3413 laboratory confirmed cases and one death have been reported to WHO from 50 countries/territories in five WHO Regions. The majority of laboratory confirmed cases (2933/3413; 86%) were reported from the WHO European Region. Other regions reporting cases include: the African Region (73/3413, 2%), Region of the Americas (381/3413, 11%), Eastern Mediterranean Region (15/3413, <1%) and Western Pacific Region (11/3413, <1%). One death was reported in Nigeria in the second quarter of 2022. Since June, there have been over 10,000 confirmed cases in the U.S.¹⁵

The ongoing epidemic differs from previous outbreaks in terms of age (54.29% of individuals in their thirties), sex/gender (most cases being males), risk factors, and transmission route, with sexual transmission being highly likely. The clinical presentation is atypical and unusual, being characterized by anogenital lesions and rashes that relatively spare the face and extremities. The most prevalent sign/symptom reported was fever (in 54.29% of cases) followed by inguinal lymphadenopathy (45.71%) and exanthema (40.00%).¹⁶

The virus may be exploiting a change in population behaviour and increased global travel but it can still be stopped from spreading further, say scientists. What started as one unusual case of monkeypox has now spread to several countries, with many cases having no link to Central or Western Africa where the disease is endemic.

The current outbreak in non-endemic countries suggests that sustained human-to-human transmission is quite feasible, so it suggests that ongoing human transmission could also be happening in Africa on a larger scale than generally thought. Human-to-human transmission can result from close contact with respiratory secretions, skin lesions of an infected person or recently contaminated objects. Transmission via droplet respiratory particles usually requires prolonged face-to-face contact, which puts health workers, household members and other close contacts of active cases at greater risk.¹⁷

Monkeypox was disease containment on easy mode, and yet it is looking very likely that we're going to fail to contain it. Some of the most glaring errors have been in communication, where people are getting sick because of reluctance to tell them they are at higher risk. Relentlessly tracking down the people whom the sick person has been in close contact with and encouraging them to get tested as well, is crucial.

According to a study in the *New England Journal of Medicine*, 98 percent of documented cases were found in gay or bisexual men. While the disease isn't a sexually transmitted infection like syphilis, which spreads nearly exclusively through sex, monkeypox transmission requires close physical contact, and sex appears to be a major opportunity for the virus — 95 percent of the transmissions documented in the study occurred during sexual relations. While it might seem obvious that the best way to serve the population of men who have sex with men is by getting them truthful information, high-quality health care, and priority vaccine access, public health agencies are too often failing to communicate clearly about this.¹⁸

Endemic monkeypox is generally self-limited, with clade-dependent case fatality rates of 1 to 10%. Before April 2022, monkeypox virus infection in humans was seldom reported outside African regions

where it is endemic. Currently, cases are occurring worldwide. Transmission, risk factors, clinical presentation, and outcomes of infection are poorly defined.¹⁹

The draft sequence of the virus responsible for the rapidly growing monkeypox outbreak shows it is most closely related to strains detected in the UK, Singapore and Israel in 2018 and 2019. The monkeypox virus is much larger – around 200,000 DNA letters long compared with 30,000 RNA letters for the coronavirus – and for now at least not nearly as intensively studied.²⁰

Mass vaccination is not yet needed, and targeted vaccination strategies with vaccines from the smallpox stockpile, as well as other public health measures such as quarantine and isolation, can contain the outbreaks. As the spread of the virus indicates we will need rapid and strong containment measures including targeted vaccination with the smallpox vaccine, to contain the clusters.²¹

Post-exposure prophylaxis (PEP) is recommended for close contacts of cases, ideally within four days of first exposure, to prevent onset of the disease. Primary preventive vaccination before exposure (PPV) is recommended for high-risk groups including individuals at high risk of exposure.

Vaccination programmes should be accompanied by information campaigns conveying that it takes approximately two weeks from completion of a vaccination series for immunity to fully develop and that the level of protection conferred by these vaccines under different circumstances has not yet been determined for this outbreak.

The risk is considered to be high in the European Region due to its report of a geographically widespread outbreak involving several newly-affected countries, as well as a somewhat atypical clinical presentation of cases. The unexpected appearance of monkeypox and the wide geographic spread of cases indicate that the monkeypox virus might have been circulating below levels detectable by the surveillance systems and sustained human-to-human transmission might have been undetected for a period of time.

There appears to have been a recent change in the epidemiologic characteristics of monkeypox in Africa, where cases are now occurring in new geographic areas, perhaps facilitated by climate change and deforestation leading to changes in the environmental interface between humans and the animal reservoir (or reservoirs).²²

Lessons learned during the responses to AIDS and Covid-19 should help us to marshal a more efficient and effective response to monkeypox, and the response to monkeypox should, in turn, help to inform our response to the inevitable next emerging or reemerging infectious disease of pandemic potential.²³

Appropriate measures should be taken: physical distancing between people infected with monkeypox and domestic pets; proper waste management to prevent the disease from being transmitted from infected humans to susceptible animals at home.²⁴

Caring for patients with suspected or confirmed monkeypox requires early recognition through screening protocols adapted to local settings, prompt, isolation and rapid implementation of standard and transmission-based precautions.

To enable reliable evaluations of interventions, further research (randomized trials) is crucial. Tecovirimat is an antiviral drug with recent regulatory approval from the

2. Coronaviruses

The SARS outbreak in 2002–2003 remains as one the most impactful pandemic outbreaks of the 21st century mainly due to the fact that the aetiology was totally unknown during the outbreak, which made accurate diagnosis and effective control impossible. The outbreak lasted more than six months with rapid spread of the virus from southern China to more than 30 countries on all major continents, and resulted in more than 8000 human infections and 774 deaths.

Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-CoV) are two highly transmissible and pathogenic viruses that emerged in humans at the beginning of the 21st century. Both viruses likely originated in bats,

and genetically diverse coronaviruses that are related to SARS-CoV and MERS-CoV were discovered in bats worldwide. Researchers highlighted the diversity and potential of spillover of bat-borne coronaviruses, as evidenced by the recent spillover of swine acute diarrhoea syndrome coronavirus (SADS-CoV) to pigs.²⁵

SARS-CoV most likely originated in bats through sequential recombination of bat SARSr-CoVs. Recombination likely occurred in bats before SARS-CoV was introduced into Guangdong province through infected civets or other infected mammals from Yunnan. The introduced SARS-CoV underwent rapid mutations in *S* and *orf8* and successfully spread in market civets. After several independent spillovers to humans, some of the strains underwent further mutations in *S* and became epidemic during the SARS outbreak in 2002–2003. However, a recent serological investigation revealed the presence of antibodies against the SARSr-CoV nucleocapsid in humans living around a bat cave but who had not shown clinical signs of disease, suggesting that the virus can infect humans through frequent contact.²⁶ Coronavirus disease 2019 (caused by SARS-CoV-2), has had a catastrophic effect on the world's demographics resulting in over 6 million deaths worldwide as of March 2022, emerging as the most consequential global health crisis since the era of the influenza pandemic of 1918. After the first cases of this predominantly respiratory viral illness were first reported in Wuhan, Hubei Province, China, in late December 2019, SARS-CoV-2 rapidly disseminated across the world in a short span of time, compelling the World Health Organization (WHO) to declare it as a global pandemic on March 11, 2020. Since being declared a global pandemic, COVID-19 has ravaged many countries worldwide and has overwhelmed many healthcare systems. The pandemic has also resulted in the loss of livelihoods due to prolonged shutdowns, which have had a rippling effect on the global economy.

SARS-CoV-2, while adapting to their new human hosts, is prone to genetic evolution with the development of mutations over time, resulting in mutant variants that may have different characteristics than its ancestral strains. Several variants of SARS-CoV-2 have been described during the course of this pandemic, among which only a few are considered variants of concern (VOCs) by the WHO, given their impact on global public health. Based on the recent epidemiological update by the WHO, as of December 11, 2021, five SARS-CoV-2 VOCs have been identified since the beginning of the pandemic:

Alpha (B.1.1.7): first variant of concern described in the United Kingdom (UK) in late December 2020

Beta (B.1.351): first reported in South Africa in December 2020

Gamma(P.1): first reported in Brazil in early January 2021

Delta (B.1.617.2): first reported in India in December 2020

Omicron (B.1.1.529): first reported in South Africa in November 2021. Despite robust global mass vaccination efforts including vaccine boosters, the emergence of these new SARS-CoV-2 variants threatens to overturn the significant progress made so far in limiting the spread of this viral illness.²⁷

SARS-CoV-2 causing COVID-19, despite its early discovery and alerts about its pandemic potential has shown that even healthcare systems in developed countries are ill-prepared to cope with rapidly emerging pandemics, especially when treatments are unavailable and disease phenotypes are pleiotropic. The world should have been better prepared after HIV/AIDS or the Spanish Flu, the latter killing an estimated 50–100 million people at the onset of the 20th century. This explains why the COVID-19 pandemics has been receiving unprecedented global attention.

Infectious diseases will undoubtedly persist as permanent and main threats to humanity in the future, especially due to increased longevity that almost always comes at cost due to impaired immunity. One reason among many others is certainly the continuous co-evolution of pathogens with the host immunity, especially in the case of opportunistic and zoonotic pathogens, which is enabling pathogen transmission between different mammalian or animal hosts.²⁸

3. Henipaviruses

Henipaviruses - of which Nipah and Hendra are the most infamous - belong to the Paramyxoviridae family of viruses, and have sparked a number of deadly spillovers into humans - and epidemics - across South East and Central Asia - and to a lesser extent Australia - over the past 25 years. Characteristics of Nipah virus that increase its risk of becoming a global pandemic include: humans are already susceptible;

many strains are capable of limited person-to-person transmission; as an RNA virus, it has an exceptionally high rate of mutation; and that if a human-adapted strain were to infect communities in South Asia, high population densities and global interconnectedness would rapidly spread the infection. Normally carried by Fruit bats, these viruses can carry a high mortality rate in humans, and human-to-human transmission of Nipah has been demonstrated.²⁹

The deadlier of the two - Nipah - was only first discovered 25 years ago after an outbreak in Malaysia, which spread from bat to pigs - and then from pigs to humans - eventually infecting at least 265 people, killing 105 - often with a case fatality rate of between 70% and 90%.²⁹

Characteristics of Nipah virus that increase its risk of becoming a global pandemic include: humans are already susceptible; many strains are capable of limited person-to-person transmission; as an RNA virus, it has an exceptionally high rate of mutation; and that if a human-adapted strain were to infect communities in South Asia, high population densities and global interconnectedness would rapidly spread the infection.³⁰

Last year, researchers announced the discovery of a Novel Variant Of the Hendra Virus in Australia, and it is a fair assumption there are other as yet undiscovered variants in the wild. And while bats are presumed to be the primary reservoir host for Henipaviruses, they may not be the only ones. Researchers described a phylogenetically distinct henipavirus - dubbed Langya henipavirus (LayV) - which they isolated from the throats of 35 fever patients who reported recent animal exposure.³¹

Starting with Ebola in 1976, and followed by HIV in the early 1980s, we've seen a procession of emerging zoonotic disease threats which now includes avian flu, Nipah, and COVID. Instead of a 'golden age', we've entered an age of emerging and reemerging pandemic threats, one where an obscure virus from a far off land can spark a global crisis with little or no warning. Fifty years ago, it seemed as if we had entered the golden age of medicine, and were on the verge of conquering infectious diseases.³⁰

The genus Henipavirus (family Paramyxoviridae) currently comprises seven viruses, four of which have demonstrated prior evidence of zoonotic capacity. These include the biosafety level 4 agents Hendra (HeV) and Nipah (NiV) viruses, which circulate naturally in pteropodid fruit bats. Henipaviruses include highly pathogenic emerging zoonotic viruses, derived from bat, rodent, and shrew reservoirs. Bat-borne Hendra (HeV) and Nipah (NiV) are the most well-known henipaviruses, for which no effective antivirals or vaccines for humans have been described. Angavokely virus (AngV), isolated from wild fruit bats in Madagascar. Genomic characterization of AngV reveals all major features associated with pathogenicity in other henipaviruses, suggesting that AngV could be pathogenic following spillover to human hosts. Our work suggests that AngV is an ancestral bat henipavirus that likely uses viral entry pathways distinct from those previously described for HeV and NiV. In Madagascar, bats are consumed as a source of human food, presenting opportunities for cross-species transmission. Characterization of novel henipaviruses and documentation of their pathogenic and zoonotic potential are essential to predicting and preventing the emergence of future zoonoses that cause pandemics.³¹ Henipavirus infections are characterized by their systemic nature, with evidence of infection in multiple organ systems.

4. New Langya virus

An international team of scientists identified a new virus that was likely to have been transmitted to humans after it first infected animals, in another potential zoonotic spillover less than three years into the coronavirus pandemic. Genetic sequencing of the Langya virus subsequently showed that the pathogen is part of the henipavirus family, which has five other known viruses. Two are considered highly virulent and are associated with high case-fatality ratios, according to the U.S. Centers for Disease Control and Prevention. The Hendra virus and the Nipah virus, which belong to the genus henipavirus in the family Paramyxoviridae, are known to infect humans and cause fatal disease; however, other related henipaviruses have been detected in bats, rodents, and shrews. During sentinel surveillance of febrile patients with a recent history of animal exposure in eastern China, a phylogenetically distinct henipavirus, named Langya henipavirus (LayV), was identified in a throat swab sample from one patient by

means of metagenomic analysis and subsequent virus isolation. The genome of LayV is composed of 18,402 nucleotides with a genome organization that is identical to that of other henipaviruses. LayV is most phylogenetically related to Mojiang henipavirus, which was discovered in southern China. In a study, a newly identified henipavirus of probable animal origin was associated with febrile illness, a finding that warrants further investigation to better understand associated human illness.³²

Future Pandemics

The looming threat caused by the many pathogens circulating in populations of wild and domestic animals that have the potential to infect humans serve as a reminder. Viruses that spill over from animals to humans are not uncommon. Some 70 percent of emerging infectious diseases in humans are of zoonotic origin and nearly 1.7 million undiscovered viruses may exist in mammals and birds. The Hendra and Nipah viruses, two henipaviruses with high mortality rates, can be contracted through close contact with sick horses, pigs and bats. Scientists who study zoonotic diseases had warned even before the coronavirus pandemic that practices such as unregulated wildlife trade, deforestation and urbanization have brought people closer to animals, thereby increasing the odds of viral spillovers.³³

It is advisable to think of animals as partners whose health and habitats should be protected to stave off the next global outbreak.

Pandemics as a whole are increasing in frequency. It is caused by what we do to the environment. We need to start connecting that chain and say we need to do these things in a less risky way.

Some 70 percent of emerging infectious diseases in humans are of zoonotic origin and nearly 1.7 million undiscovered viruses may exist in wildlife. Many researchers are searching for the ones that could cause the next animal-to-human spillover. The likeliest hot spots have three things in common: lots of people, diverse plants and animals, and rapid environmental changes.

About half of mammal species are rodents, and about a quarter are bats. But bats make up about 50 percent of mammals in the most biodiverse tropical regions, and while they are valuable pollinators and pest eaters, they are also astounding virus vessels. Bats have a superhero-like immune system that allows them to become “reservoirs to many pathogens that do not impact them but can have a tremendous impact on us if they're able to make the jump.

Scientists point to the 1998 emergence in Malaysia of Nipah virus as a vivid example of spillover fueled by environmental change and agricultural intensification.

As Earth's human population hurtles toward 8 billion, no one thinks human-animal interaction is going to decrease. The key is reducing the risk of a devastating spillover, scientists say — and not by killing bats. But they acknowledge that cultural and economic pressures make change difficult.

Many researchers say the coronavirus pandemic underscores the need for a more holistic “one health” approach, which views human, animal and environmental health as interconnected. There needs to be a cultural shift from a community level up about how we treat animals, our understanding of the dangers and biosecurity risks that we're exposing ourselves to. Leaving ecosystems intact, not destroying them.³⁴

Ecological Changes

Out of several documented pandemics, the 1918 pandemic was by far the worst. The Asian flu of 1957 was not much fun, to put it mildly, but nothing was ever like 1918.²⁹ The 1918 influenza pandemic was the deadliest pandemic of the Twentieth Century. The number of deaths was estimated to be at least 50 million worldwide with about 675,000 occurring in the United States. Mortality was high in people younger than 5 years old, 20-40 years old, and 65 years and older. The high mortality in healthy people, including those in the 20-40 year age group, was a unique feature of this pandemic.³⁵

In pandemic influenza viruses, the novel or new genes tend to come from avian influenza. There are some recognizable factors responsible for precipitating or enabling emergence, such as ecological factors or globalized travel and trade.

Since 1980 new human pathogen species have been discovered at an average rate of over 3 per year. Almost 75% of these have been virus species even though viruses still represent a small fraction (less than 14%) of all recognized human pathogen species. Overall, no more than 50 to 100 species are specialist human pathogens. The 87 new species of human pathogen are associated with public health problems of hugely variable magnitudes.³⁰

Pathogen Pyramid

Level 1: Exposure - The first stage of the emergence of a new pathogen is the exposure of humans to that pathogen.

Level 2: Infection - The second stage of pathogen emergence is reached if the pathogen proves capable of infecting humans, possibly causing disease.

Level 3: Transmission The third stage of pathogen emergence is reached if a pathogen that can infect humans also proves capable of transmission from one human to another.

Level 4: Epidemic Spread - The fourth and, in our version, final level of the pathogen pyramid is reached if a pathogen is sufficiently transmissible within the human population to cause major epidemics or pandemics and/or to become endemic, without the involvement of the original reservoir.³⁰

A more efficient strategy to address future emerging diseases is to combine rigorous analyses of the fine-scale ecological and demographic changes within hotspot regions (the risk factors) with state-of-the-art molecular approaches to viral discovery. Techniques such as pyrosequencing and mass tag polymerase chain reaction will rapidly decrease the expense and logistical challenges involved in identifying new viral groups, and if applied to key groups of wildlife species within hotspot regions, will provide the most cost-effective way to proactively address the EID challenge.³⁰ Disease surveillance is a crucial. We need better early-warning systems and more effective disease control, implemented without delay. Outbreaks of new diseases, and the public reaction to them, can cause economic and political shocks far greater than might be anticipated.

Future Trends

For the kinds of pathogens that are most likely to emerge in the future, four characteristics are expected to be particularly important: RNA virus (most new pathogens are RNA viruses); Nonhuman animal reservoir (most new human pathogens are associated with or originate from other kinds of host, usually other species of mammal); Broad host range (pathogens that are already capable of exploiting a range of different hosts species are more likely to have the potential to infect us).

The first line of defense against any emerging pathogen is its rapid detection and identification. Surveillance needs to be global, especially considering the unprecedented rates of international travel and trade that can allow new infectious diseases, to spread around the world over time scales of days or weeks. Pathogen emergence is an international problem. Estimating the transmission potential of a new pathogen within the human population can only be achieved by closely monitoring initial outbreaks.

It is extremely likely that we will encounter new species of human pathogen in the near future. The scientific and logistic capacity to rapidly detect and evaluate the threat that new pathogens present and to intervene quickly and effectively wherever necessary, is urgently needed.

Efficient Strategy

The constant spillover of viruses from natural hosts to humans and other animals is largely due to human activities, including modern agricultural practices and urbanization. Therefore, the most effective way to prevent viral zoonosis is to maintain the barriers between natural reservoirs and human society, in mind of the 'one health' concept.³⁶

There are 219 virus species that are known to be able to infect humans. The first of these to be discovered was yellow fever virus in 1901, and three to four new species are still being found every year. There is still a substantial pool of undiscovered human virus species, although an apparent slow-down in the rate of discovery of species from different

families may indicate bounds to the potential range of diversity. More than two-thirds of human viruses can also infect non-human hosts, mainly mammals, and sometimes birds. Many specialist human viruses also have mammalian or avian origins. A substantial proportion of mammalian viruses may be capable of crossing the species barrier into humans, although only around half of these are capable of being transmitted by humans and around half again of transmitting well enough to cause major outbreaks. A few possible predictors of species jumps can be identified, including the use of phylogenetically conserved cell receptors. It seems almost inevitable that new human viruses will continue to emerge, mainly from other mammals and birds, for the foreseeable future. For this reason, an effective global surveillance system for novel viruses is needed.³⁷

Globally, about one billion cases of illness and millions of death occur every year from zoonoses. Some 60% of emerging infectious diseases that are reported globally are zoonoses. Over 30 new human pathogens have been detected in the last three decades, 75% of which have originated in animals.^{38,39}

Humans are constantly exposed to a huge diversity of viruses, though those of others mammals (and perhaps birds) are of greatest importance. Moreover, these viruses are very genetically diverse and new genotypes, strains and species evolve rapidly.

The emergence of new human viruses is a long-standing and ongoing biological process. We must anticipate the emergence and/or discovery of more new human viruses in the coming years and decades.

The first line of defence against emerging viruses is effective surveillance. A coordinated, global surveillance network is essential if we are to ensure rapid detection of novel viruses.

Improving the situation will require both political will and considerable investment in infrastructure, human capacity and new tools.

Rapid detection and identification of emerging pathogen leading to the rapid introduction of preventive measures can prove highly effective in combating outbreaks of novel diseases. Only if a new strain is detected in the very earliest stages and interventions are put in place extremely promptly is their any realistic prospect of curtailing an epidemic. Surveillance for novel pathogens, however, does present some particular challenges. It will initially depend on clinical observation, such as the reporting of clusters of cases of disease with unusual symptoms. Internet surveillance for reports of unusual disease outbreaks is also possible and, in the longer term, generic diagnostic tools—for example, lab-on-a-chip tests for all known human viruses—should become available.²⁹

CONCLUSION

Infectious diseases remain among the leading causes of death and disability worldwide. Epidemics of new and old infectious diseases periodically emerge, greatly magnifying the global burden of infections. Raising awareness of risk factors and educating people about the measures they can take to reduce exposure to the virus is the main prevention strategy for emerging pathogens. Surveillance and rapid identification of new cases is critical for outbreak containment. To ensure global preparedness, newer vaccines, diagnostics and antiviral agents are being developed. Infectious diseases can be prevented at a variety of points, depending on the infectious cycle for the particular disease. Integrated surveillance coupled with evidence-based epidemiologic data can help formulate better public health policies and increase preparedness to meet the future challenges presented by emerging/re-emerging infectious diseases. We should aim at translating scientific discoveries into affordable, globally accessible. public health solutions to face the challenges of Emergent Infection on a priority basis.

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