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The disease X: waiting for the next pandemic

Abstract

In 2008 the WHO published a report on infectious diseases against which there is no effective treatment or vaccines and therefore – diseases able to cause pandemic. In addition, so called disease X was mentioned – potentially deadly, with no herd immunity against it, holding pandemic potential, unknown in medicine yet. In 2019 such disease X was COVID-19. There is a plausibility, that next pandemic will be induced by zoonotic RNA virus (alike SARS-CoV-2) infecting people in place of intensified human-animal contacts (like high-density animal farming) without proper legal regulations in terms of animal husbandry and high population density. Also in the past major pandemics in XX and XXI centuries were result of zoonotic transmissions (HIV/AIDS, SARS, MERS, Spanish flu, avian flu, swine flu, Ebola). The key in risk recognising is governments and international healthcare agencies' reaction – proper countermeasures to control pandemic range should be taken. Animal trade should be legally regulated and deforestation limited. There is also an urgent need for funding R&D studies on diseases listed by the WHO.

Keywords: zoonosis, emergency infectious disease, pandemic, pathogen.

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INTRODUCTION

Rate of emergence of new infectious diseases is exponentially increasing [1] and this pace is high enough to seriously disturb epidemiologists and national healthcare systems specialists. The World Health Organisation regularly releases report [2] that "focuses on severe emerging diseases with potential to generate a public health emergency, and for which insufficient or no preventative and curative solutions exist". In 2018 the WHO added to the list so called 'disease X', which is a placeholder for unknown but potentially world threatening disease. In 2019 the disease X was COVID-19 and the 'pathogen X' – SARS-CoV-2 (some voices say that Zika virus should also be counted as one). The world is still facing up the current pandemic but there is a possibility that a new unnamed disease X is lurking for suitable moment to spread.

The WHO list of diseases with an urgent need for accelerated research and development [8]:

- COVID-19;
- Crimean-Congo hemorrhagic fever;
- Ebola virus disease and Marburg virus disease;
- Lassa fever;
- Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS);
- Nipah and henipaviral diseases;
- Rift Valley fever;
- Zika;
- Disease X.

Viruses on the rise

Disease X might be caused by any factor – virus, bacteria, fungus, parasite or prion. The majority of contagious diseases that have appeared since year 1980, were caused by bacteria (37%). Viruses were responsible for 33%, protozoa – 7%, fungi –7%, parasites – 15% (Figure 1)[3]. Studies based on data from previous years generally confirm these observations [4].

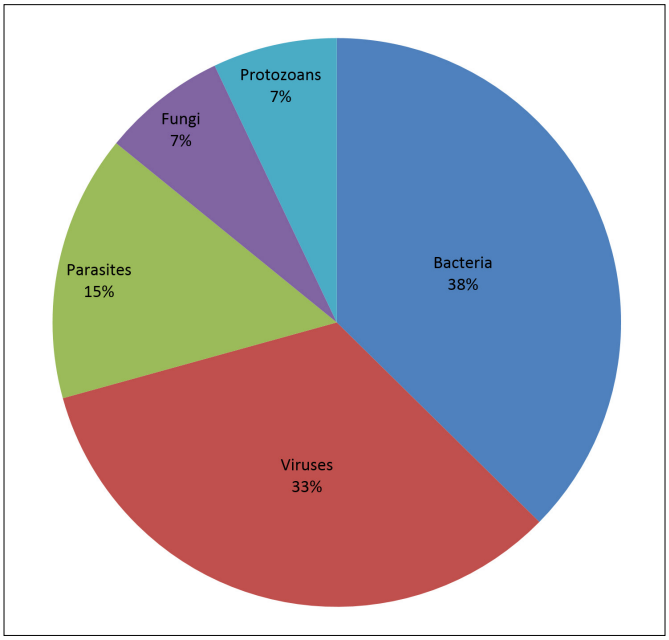

FIGURE 1. Factors responsible for contagious diseases.

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An overall picture points that viral diseases are serious threat, what is more, most recent epidemics were caused due to viruses, to mention HIV/AIDS, H1N1 influenza, SARS, MERS, Ebola, H5N1. Moreover, all of them are RNA viruses [1,5].

Data from studies of EID (emerging infectious diseases) 'events' shows that 60.3% of them is caused by zoonotic pathogens. On top of that 71.8% of these zoonotic EID were caused by pathogens with a wildlife origin – for example, Nipah virus or SARS in China [4]. It is worth noticing that 94% of zoonotic viruses affecting humans are also RNA viruses, which is no surprise because RNA viruses might infect broad range of hosts due to error-prone replication system that allows rapid reaction and adaptation to changing conditions [4,5].

TABLE 1. Major selected pandemics and epidemics since 1918 worldwide. [1].

Pandemic/epidemic	Date	Pathogen	Reservoir
Spanish flu	1918-1919	H1N1	Birds
Ebola	1976-1977, 1995, 2000, 2003, 2007, 2014 and other smaller outbreaks	EBOV	Bats
HIV/AIDS	1980 first cases and ongoing	HIV	Chimpanzees
SARS	2002-2003	SARS-CoV-1	Bats, Asian palm civet
Avian influenza	2003 – first cases and ongoing	H5N1	Birds
Swine influenza	2009-2010	H1N1	Pigs
MERS	2012-2020	MERS-CoV	Camels, bats
Zika	2015-2016	ZIKV	Mosquitos
COVID-19	2019 first cases and ongoing	SARS-CoV-2	Bats, pangolins

Source: Elaborated by the authors based on epidemiological data from the WHO, FAO and CDC.

TABLE 2. Endemic diseases listed in the WHO blueprint.

Disease (pathogen)	Date and place of occurrence	Fatality ratio	Reservoir
Crimean-Congo hemorrhagic fever (CCHFV)	1944 – first cases in Crimea, in 1969 recognised in Congo. Since then endemic outbreaks in Africa, Middle East, Asia and Balkans	10-40%	*Hyalomma* sp. ticks
Marburg virus disease (MVD)	1967 first cases in laboratories in Marburg and Frankfurt, Germany, and Belgrade, Serbia (initially - laboratory workers exposed to infected monkey tissues). Sporadic cases in Angola, the Democratic Republic of the Congo, Kenya, South Africa and Uganda	24-88%	Fruit bat -Rousettus aegyptiacus
Lassa fever (LASV)	1969 in Nigeria, endemic in parts of West Africa including Sierra Leone, Liberia, Guinea and Nigeria	1-15%	African rat
Nipah and henipaviral diseases (NiV)	Discovered in 1999 in Singapore and Malaysia, since then regular outbreaks	40-70%	Pigs, bats
Rift Valley fever (RVFV)	1931 first cases in Kenya, major outbreaks: 1977 in Egypt, 1997-1998 in Kenya, Somalia and Tanzania, 2000 in Saudi Arabia and Yemen	1%	Mosquito, infected cattle

Source: Elaborated by the authors based on epidemiological data from the WHO and CDC.

Zoonosis as possible scenario

Analysis of main pandemic and endemic events since year 1918 shows, that all of them were of zoonotic origin (Table 1, 2). For example bats constitute a reservoir for Ebola, MERS, SARS, COVID-19, birds for avian flu, Spanish flu, chimpanzee – HIV/AIDS, mosquitoes – Zika virus, pigs – swine flu. Three of them – Spanish flu, HIV/AIDS and COVID-19 were global and influenced economic growth. Also national healthcare systems did not manage to recognise risk quickly enough and governments implemented restrictions too late [1].

Efforts taken to provide food for a growing population like high-density farming systems and deforestation for agriculture force more frequent interactions between humans and animals and hence – contact with new pathogens. On the other side, globalisation and rising mobility favor spreading germs around the world, also in populations without immunity against them. Taken all of this into consideration, next pandemic will be possibly result of human/animal interface, the absence of robust protective immunity, extreme population density and constrained laboratory capacity. Future pathogen X is probably an RNA virus, that will appear in hotspot where a mix of risk factors listed above and population dynamics make effective person-to-person transmission possible [1,2].

Future challenges

We know of around 250 viruses that 'jumped' from animals to humans and caused pandemics. It is estimated that another 1.7 million animal viruses exist and about half of them might be able to infect people; each one is potentially pathogen X [1]. Crucial action for preventing zoonotic transmissions is contact reduction between people and animals by, e.g. mitigating deforestation and putting regulations on and limiting animal trade. That kind of preventative measures is worth taking – first, they help mitigate damage from outbreaks and minimalize morbidity, second – it is cheaper to prevent than to manage with results of zoonotic spillover [1,6].

After the SARS outbreak, the WHO developed guidelines needed to control a pandemic, vital steps about preparedness, managing and communication with governments and society during the pandemic. Unfortunately, these steps were ignored at the dawn of COVID-19 pandemic. In recent years the WHO was criticised from many sides – on the one hand during swine flu in 2009 for causing panic and on the other hand – during COVID-19 for lack of coordination and underreacting. The problem is, the WHO is underfunded and faces bureaucracy and is overloaded with data collected from 194 countries. Centers for Disease Control and Prevention (CDC) also struggles with funding and has no political impact. Academic voices have even smaller influence in public discussion [7].

Universal steps needed to control the pandemic [7]:

1. More pandemics will appear so be prepared;
2. Report cases early;
3. Alert the world;
4. Promote international scientific collaboration;
5. Provide leadership and consistency;
6. Avoid speculation;
7. Provide safety guidelines;
8. Institute travel limitations and screening;
9. Early testing and contact tracking;
10. Stockpile medications and equipment;
11. Bolster healthcare systems;
12. Protect healthcare workers;
13. Professional education;
14. Prepare the public.

Ongoing COVID-19 pandemic has lasted over 2 years already but have we learnt our lesson? Is there political understanding for necessity of R&D funding? Do we have authorities able to monitor and to react in case of another infectious disease emergence? All those questions will be answered in the future, when a placeholder for 'disease X' will get its proper name. Hope we will be ready. And such a future challenge might be already there – the WHO 2018 R&D Blueprint mentions monkeypox as a potential threat and "stresses the risk it poses" [2]. First human monkeypox was identified in 1970 in Africa and since then cases have been reported in 11 African countries. A large outbreak took place in Nigeria in 2017, over 200 people were infected there, cases have been reported until today. In 2003 the USA confirmed first cases of monkeypox outside Africa. They were connected with imported from Ghana pouched rats and dormice. The outbreak led to over 70 cases in USA. Since May 2022, multiple cases of monkeypox have been identified in several non-endemic countries in Europe. Situation here is under control (in June 2022) [9].

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