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# What's new in infectious diseases: Nipah virus, MERS-CoV and the Blueprint List of the World Health Organization

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Sometimes, late in the '60s, an authoritative American politician declared *'It's time to close the books on infectious diseases, declare the war against pestilence won, and shift national resources to such chronic problems as cancer and heart disease'* (Figure 1).

How wrong it was!
As shown in Figure 2, in 2010 of the estimated 52.8 million deaths that occur throughout the world yearly, almost 10 million are directly caused by infectious diseases. Millions more deaths are a secondary effects of infections [1]. Infectious diseases cause 63% of all childhood deaths and 48% of premature deaths [2].
Moreover, today, on one hand, we observe the so-called antibiotic paradox (*How the Misuse of Antibiotics Destroys Their Curative Powers*), with the increase in multidrug resistant bacteria and the epidemics of preventable infections favored by the no vax campaigns, on the other the emergence and re-emergence of new and old infectious diseases; some of them, reported, in the Table 1 below represent examples of emerging infectious diseases.
The 2014-2016 West Africa Ebola epidemic (the largest since the virus was first discovered in Zaire in 1976, with a total of 28,616 confirmed, probable and suspected cases and 11,310 deaths) saw a large mobilization to find new technologies to address the disease and save lives.
The Blueprint was a successor project to the work


**Figure 1** - William H. Stewart, the Surgeon General.

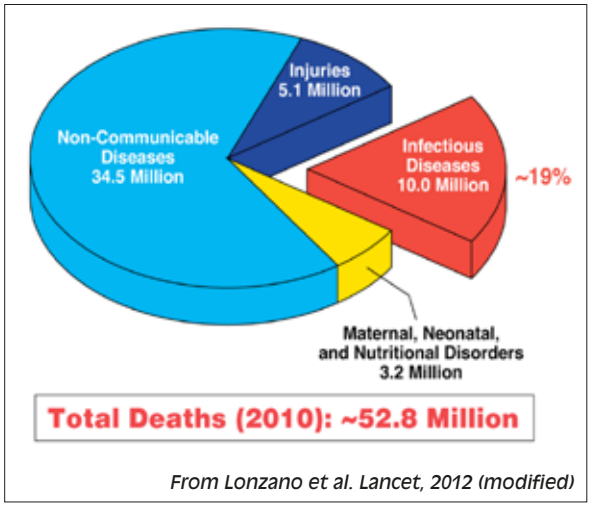


**Figure 2** - Infectious diseases cause ~19% of all deaths worldwide.

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**Table 1** - Examples of emerging infectious diseases.

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| *Legionella pneumophila* (first outbreak in 1976 as Legionnaire disease and since associated with similar outbreaks linked to poorly maintained air conditioning systems) |
| *Ebola virus* (first outbreaks in 1976 and the discovery of the virus in 1977) |
| *E. coli 0157:H7* (first detected in 1982, often transmitted through contaminated food, has caused outbreaks of hemolytic uremic syndrome) |
| *Borrelia burgdorferi* (first detected in 1982 and identified as the cause of Lyme disease) |
| *HIV/AIDS* (virus first isolated in 1983) |
| *Hepatitis C* (first identified in 1989, now known to be the most common cause of post-transfusion hepatitis worldwide) |
| *Influenza A(HSN1) virus* (well known pathogen in birds but first isolated from humans in 1997) |
| *Severe Acute Respiratory Syndrome (SARS)* (first detected in 2003 in Asia; the first emerging infectious disease of the 21st century) |
| *Swine Flu Influenza A (H1N1)* |

that World Health Organization (WHO) did during this recent Ebola outbreak in West Africa and was initiated at the WHO Ebola Research and Development (R&D) Summit held in May 2015. The Ebola epidemic demonstrated the inadequacy of current approaches to vaccine, drug, and diagnostics development. Learning from mistakes, for the purposes of the R&D Blueprint, WHO has developed a special tool for determining which diseases and pathogens pose a public health risk because of their epidemic potential and for which countermeasures are insufficient. The R&D Blueprint works on the basis of a list of identified priority diseases. The blueprint outlines global strategies to reduce the time lag between the identification of an outbreak and the approval of diagnostics, vaccines, and drugs needed to save lives and thwart disease spread. For each disease an R&D roadmap is created, followed by target product profiles [3].

The first list of prioritized diseases was released in December 2015 (4). The second list was published this year (see Table 2) [5].

Several other diseases that could have major public health risks, (arenaviral hemorrhagic fevers other than Lassa fever, and emergent nonpolio enteroviruses - including EV71, D68-, chikungunya), were also discussed, but not included in the priority list. Monkeypox and leptospirosis were also recognized and discussed at the meeting as public health risks to watch.

In this article we would shortly emphasizes some of the diseases included in 2018 list.

**Table 2** - Diseases posing significant risk of an international public health emergency for which there is no, or insufficient, countermeasures. Source: WHO, 2018.

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| Crimean-Congo haemorrhagic fever (CCHF) |
| 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 (RVF) |
| Zika |
| Disease X |

## NIPAH AND HENIPAVIRAL DISEASES

Nipah virus (NiV) is an emerging zoonotic virus [6]. NiV is an RNA virus, part of the Paramyxovidae family that was first identified as a zoonotic pathogen after an outbreak involving severe respiratory illness in pigs and encephalitic disease in humans in Malaysia and Singapore in 1998 and 1999. Limited human to human transmission of NiV has also been reported among family and care givers of infected NiV patients. During the later outbreaks in Bangladesh and India, Nipah virus spread directly from human-to-human through close contact with people's secretions and excretions. In Siliguri, India, transmission of the virus was also reported within a health-care setting: 75% of cases occurred among hospital staff or visitors. From 2001 to 2008, around half of reported cases in Bangladesh were due to human-to-human transmission through providing care to infected patients. Other regions may be at risk for NiV infection, as serologic evidence for NiV has been found in the known natural reservoir (Pteropus fruit bat species): the evidence of Henipavirus infection in *Pteropus* bats from Australia, Bangladesh, Cambodia, China, India, Indonesia, Madagascar, Malaysia, Papua New Guinea, Thailand and Timor-Leste. Nipah virus can be transmitted to humans from animals (bats, pigs), and can also be transmitted directly from

human-to-human [7]. The incubation period is between 4 and 14 days. However an incubation period as long as 45 days has been reported. Human infections range from asymptomatic infection, acute respiratory infection (mild, severe), and fatal encephalitis. Infected people initially develop influenza-like symptoms as fever, headaches, myalgia, vomiting and sore throat. This can be followed by dizziness, drowsiness, altered consciousness, and neurological signs. Some people can also experience atypical pneumonia and severe respiratory problems, including acute respiratory distress. Encephalitis and seizures occur in severe cases, progressing to coma within 24 to 48 hours. Most people who survive acute encephalitis make a full recovery, but long term neurologic conditions have been reported in survivors. Approximately 20% of patients are left with residual neurological consequences such as seizure disorder and personality changes. The case fatality rate is estimated at 40% to 75%; however, this rate can vary by outbreak depending on local capabilities for epidemiological surveillance and clinical management. NiV infection can be diagnosed together with clinical history during the acute and convalescent phase of the disease. Different tests include: enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR) assay, virus isolation by cell culture [8]. There is no treatment or vaccine available for either people or animals. Intensive supportive care is recommended to treat severe respiratory and neurologic complications.

## MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS (MERS-COV)

Middle East respiratory syndrome is a viral respiratory disease caused by a novel coronavirus (MERS-CoV) that was first identified in Saudi Arabia in 2012 [9]. Since then, as of 31 May 2018, the World Health Organization (WHO) has been notified of 2,220 laboratory-confirmed cases of MERS-CoV infection, including at least 790 deaths, from 27 countries [10].
Several studies have shown that humans are infected through direct or indirect contact with infected dromedary camels. MERS-CoV has been identified in dromedaries in several countries, including Egypt, Qatar, Oman, and Saudi Arabia, and MERS-CoV specific antibodies have been identified in dromedaries in the Middle East, Africa and South Asia. However, the exact role of dromedaries in transmission of the virus and the exact route of transmission are unknown. The majority of human cases of MERS have been attributed to human-to-human infections in health care settings. The incubation time is 2-14 days and the infectious period 1-11 day from illness onset. The clinical manifestations range from no symptoms or mild respiratory symptoms to severe acute respiratory disease and death. A typical presentation of MERS-CoV disease is fever, cough and shortness of breath. Pneumonia is a common finding, but not always present. Gastrointestinal symptoms, including diarrhoea, have also been reported. Severe illness can cause respiratory failure that requires mechanical ventilation and support in an intensive care unit. The virus appears to cause more severe disease in older people, people with weakened immune systems, and those with chronic diseases (*i.e.*, diabetes, cancer, chronic renal impairment, BPCO) [11]. Fatality rate of the disease is approximately 35%; this percentage may be an overestimate as mild cases of MERS may be missed by existing surveillance systems (until more is known about the disease, the case fatality rates are counted only amongst the laboratory-confirmed cases).
Real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) of respiratory secretions is the mainstay for diagnosis, and samples from the lower respiratory tract have the greatest yield among seriously ill patients.
To date, there is no antiviral therapy of proven efficacy and, even in this case, treatment remains largely supportive. Potential vaccines are at an early development phases.

## DISEASE X

The WHO included "Disease X" in its 2018 global plan for accelerating research and development during health emergencies. So, what exactly is the "Disease X"? According to the WHO' experts "X" stands for unexpected (a serious international epidemic could be caused by a pathogen currently unknown to cause human disease!). Disease X is just an idea to remind us that we should be prepared. Experts on the WHO 2018 panel say Disease X could emerge from a variety of sources and strike at any time.

## CONCLUSIONS

The advent of vaccines and antibiotics in the mid-twentieth century gave false hope to medical professionals and politicians that infectious diseases would be a relic of the past. On the contrary, new emerging infectious diseases as well as the re-emergence of older, known microbes has occurred in the last decades.
The WHO' Blueprint list aims to address new challenging infections that humankind will likely be facing in the 21st Century.

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