

Ingredients of Potential Pandemics

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Approximately 60% of emerging infectious diseases of humans are zoonotic, and since the 1940s approximately 70% originate from wildlife. Recently, zoonotic pathogens (primarily viruses) and diseases such as HIV/AIDS, Henipah viruses, SARS, *Streptococcus suis*, Rift Valley Fever, and pandemic influenza A (H1N1) have invaded human populations. Concurrently, livestock-wildlife interface diseases (foot-and-mouth disease, African and classical swine fever, bovine tuberculosis, *peste des petits ruminants*) can affect production, food security, and livelihoods, while having negative wildlife conservation implications. Most recently, public and animal health emergencies have focused around the emergence of Middle East Respiratory Syndrome (MERS)-CoV and influenza viruses, including highly pathogenic avian influenza HPAI (H5N1) and avian influenza A (H7N9).

Whether a zoonotic pathogen comes from livestock or wildlife, global factors drive pathogen evolution to take place in two major systems: 1) human-modified natural ecosystems where natural resources are being consumed, biodiversity is being lost, and ecological services are not being sustained; and 2) agro-ecological systems where the need to meet increasing global demands for livestock-based protein leads to expansion or intensification of farming systems.

In developing countries, a combination of poverty and food insecurity often leads to people sharing their living quarters with livestock without proper bio-security or hygiene, and subsistence-associated wildlife consumption. In developed countries, cultural preferences and wealth enable consumers to purchase exotic pets and food items from anywhere in the world creating an opportunity for pathogens (and the animals they travel within) to travel across the globe in less than 24 hours through globalized value chains and market trade. Ultimately, the characteristics of developed and developing countries lead to higher contact rates between people, livestock and wildlife, creating opportunities for pathogens

to jump the 'host bridge' from the original hosts, where many pathogens do not cause sickness, into new human hosts, where they can be deadly.

On 31st March 2013, China notified the World Health Organization of the first human cases of avian influenza A (H7N9), an influenza virus that had never been detected in humans before. More than three-quarters of the initial 77 human cases had recent exposure to animals. Of these, 76% either had direct contact with chickens or had visited live bird markets, with poultry exposure considered as the most likely source of infection as there was no sustained person-to-person transmission at the time.

Influenza viruses are sub-typed on the basis of haemagglutinin (HA) and neuraminidase (NA) glycoproteins present on the outer surface of the virus. Ordinary strains of virus routinely circulate in wild birds (mostly waterfowl) and poultry. What makes H7N9 unique is that over time it has undergone a series of genetic re-assortments and mutations, leading to increased replication and pathogenicity in people. As with pandemic influenza A (H1N1) which emerged in 2009, H7N9 is a combination of progenitor viruses: H1N1 consisted of viruses derived from pigs, birds and people; H7N9 results from at least three different domestic and wild bird viruses. It is important to recognize that intensification, replication and co-circulation of multiple progenitor viruses in the same geographical area increases the risk of generating next stage viruses closer to pandemic strains. If mutations happened in viruses located in separate geographic places, it is unlikely that re-combinations would ever take place and become a public health threat.

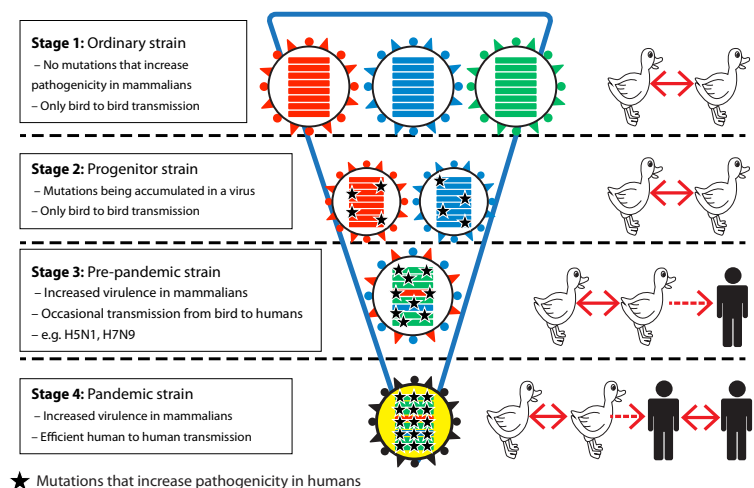
It is impossible to determine the extent to which human-modified natural and agricultural systems contribute to changes in influenza viruses that make them of greater risk to human health, but we can be confident that wild migratory waterfowl, farmed domestic ducks, and farmed wild waterfowl have no choice but

to utilize human-modified wetland systems, especially in Southeast Asia where millions of domestic waterfowl are farmed. Furthermore, with the recent growth in poultry production in this region and elsewhere, farming system expansion and intensification is a dominant trend that will persist into the foreseeable future to meet food security demands of a growing population. Finally, poverty remains a major global issue and results in high-risk behaviours that enable transmission of pathogens across species.

Unravelling the complexity of these pathogen-host relationships, defining the epidemiology of transmission among livestock, wildlife and people within an ecological context, and identifying the drivers of disease emergence, are the foundations of the 'One Health' approach needed. If we are only able to detect emerging viruses when they cross the 'host bridge', we can only react to these emergency events, and this often requires significant financial commitment and results in loss of lives and impacts to livelihoods and food security. If we are able to move further upstream, to determine which progenitor viruses are present in the modified natural and agro-ecological systems, we can move towards predicting and preventing new threats to global health security. Not only is this a much more cost-effective approach, it will prevent loss of human life, safeguard livelihoods, and protect food security.

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Stages of virus evolution depicting how pandemic influenza strains can emerge.