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THE EVOLUTIONARY DRIVERS OF INFECTIOUS DISEASES

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Introduction

This study addresses what has led pathogens to evolve and the selection pressure upon the infectious agents. These changes are inferred through phylogenetic studies, complex life cycles, host switches, shifts, and modes switches. The evolution of pathogens is complex and diverse. Moreover, they vary among pathogen strains and host populations.

When pathogens compete for a common resource and natural selection often favors aggressive strategies, which results in the selection of pathogens with evolved ways of transmission as a response. As transmission mode is the key to diseases, it is necessary to ascertain when and how rapidly new transmission modes arise to meet urgency concerning disease threats.

Aim

To interpret the evolution trend in infectious diseases, to meet the disease emergencies, and for effective disease control measures.

Material and methods

This study is based on the resources obtained from the articles and lectures released from the year 2015 to 2020.

In epidemiology, there is a triad model called the chain of infection, which encompasses a host, a pathogen, and their environment. Transmission modes are the line that connects these dots.

The term way/mode of transmission relates to how an infectious agent can be transferred from one person to another, object, or an animal. Ways by which an infectious agent is passed from an infected host, involve multiple levels from single host pathogens to multi-host pathogens, simple life cycle pathogens to complex. Also, infectious agents can use simultaneously or sequentially multiple modes of transmission.

EXAMPLE:

Single host + single mode: Measles, Rubella

Multi-host + single mode: Rabies

Single host + multiple modes: HIV, Bovine viral diarrheas

Multi-host + multiple modes: Influenza A, Ebola.

Transmission Modes between infected and susceptible hosts can be Direct or Indirect.

Direct means: by direct contact, sexual, blood-borne transmission, or vertical (i.e. transplacental, vaginal birth or breastfeeding), Indirect: aerosol/airborne, vector, fomites, water, and foodborne.

Many infectious agents have the potential to transmit the disease to targeted groups by more than one way of transmission, and pathogens may use all possible transmission modes simultaneously or even switch according to conditions.

Ex: Rift valley fever virus is usually transmitted among cattle, sheep goats. Also to humans by the fecal-oral way.

Toxoplasma gondii is usually transmitted from undercooked meat and cats but also can be transferred as water-borne infections.

The law of nature reinforces the pathogen for better means of transmission, thus paving the way to host switches and host shifts, and mode switches.

This is an evolutionary process whereby a pathogen successfully jumps from one host species to another. It is an unpredictable consequence due to adaptations by the pathogen to the changing evolutionary pressures, including those exerted by disease control interventions. Example: the shift of HIV to the human host population.

Pathogens, particularly those with high mutation rates, antigenic diversity, and short generation times, may rapidly adapt to new host species. Moreover, evidence suggests that RNA viruses are the most likely group of infectious agents to switch hosts and establish in humans. This is illustrated by influenza A viruses, for which avian and swine hosts are the main reservoirs.

A pathogen to get adapted to a novel host it has to undergo several mutations. Rarely single mutation is sufficient like in the Venezuelan equine encephalitis virus when the virus shifted from rodents to horses. Nevertheless, for better adaptations within novel hosts, pathogens undergo several mutations and multiple replications to increase the aggressiveness for survival. Such mutations lead to a dramatic increase in the virulence of the pathogens thus, dormant infections in one host can be fatal to others due to the increased severity of the disease. Example: Ebola, SARS virus, Henipa virus, and HIV.

Besides, if we consider the pros of the host switch, by inoculating wild-type virus to a foreign host we can manufacture live attenuated vaccines for the original host. Example; live attenuated *Salmonella* vaccine.

Mode switches

It is whereby a pathogen successfully switches to a new mode of transmission or mode shift, whereby a pathogen successfully alters the predomination of one mode to another. Shreds of evidence pointed that in the 1991 cholera epidemic in South America, *Vibrio cholera* can shift towards predominantly foodborne transmission modes in countries with high sanitation, while it's more virulent waterborne mode predominates under conditions of poor sanitation.

It is suggested that endemic syphilis may have switched mode from the direct skin contact mode, usually transmitted in tropical developing countries during childhood as endemic syphilis to the sexually transmitted mode of venereal syphilis (*T. pallidum* subsp. *pallidum)* in temperate developed countries.

There are current fears and gathering evidence that the Zika virus may also be transmitted at a high rate, despite increased vector control, through a mode switch (or shift) towards the sexual transmission.

Vertical transmission and horizontal transmission.

The concept of horizontal transmission is the transmission between the individuals of a generation that are not related by parent-offspring relationships, whereas vertical transmission is between parent and progeny. It is stated that evolutionary transitions within symbiotic organisms, focuses mostly on mutualistic relationships. They concluded that free-living forms preceded host-associated ones and that horizontal transmission was the most basal type and occurred when bacteria were acquired from the outside environment. Exclusive vertical transmission was rare.

They also suggested vertical transmission is often an evolutionary endpoint that is irreversible because of the negative genetic effects such as accumulation of mutations and gene loss that strict vertical transmission may have on the symbiotics.

Sexual transmission and asexual transmission.

There are arguments that sexual transmission is the ancestral transmission way. Sexually transmitted diseases are often persistent in the host. Because sexual reproduction is a regular feature of the life cycle, sexual transmission may be considered relatively reliable. On the other hand, sexual transmission severely limits opportunities for cross-species transmission. Sexually transmitted pathogens have lower host ranges, which might be a critical factor in determining long-term persistence on alternative hosts.

Evolution of complex life cycles.

Complex life cycles, where several life stages of a parasite are found in different hosts, are a remarkable feature of both animal and plant parasites. The hosts in such life cycles can be extremely unrelated phylogenetically, making it hard to envisage how such host shifts could ever have occurred. Moreover, the occurrence of a complex life cycle makes pathogen to evolve into different transmission modes for subsequent spread

Transmission by vectors

Blood-feeding arthropods such as mosquitoes and ticks transmit a broad range of microorganisms that cause disease in humans. Some vector-borne pathogens can also be transmitted via other modes such as direct contact, vertical transmission, or aerosol transmission, in many cases at a low rate (for example, dengue virus). For such a system to evolve, possible precursors to vector-borne parasites could have been exclusively arthropod pathogens that infected a dead-end vertebrate host and acquired the ability to cause transmissible infections.

Phylogenetic analyses show that ancestral arthropod-borne viruses (arboviruses) initially infected the arthropods itself but later acquired vertebrate hosts. Subsequently, these have evolved transmissible by yet other blood-feeding arthropod groups to humans.

Transmission modes and human diseases

Changes in transmission mode are often involved in disease emergence, and it remains a matter of urgency to determine with confidence whether new transmission modes may evolve in extant disease threats or if currently, minor transmission modes could become major routes given new circumstances and opportunities. Thus, in the recent Ebola epidemic, there were fears that the Ebola virus might evolve aerial transmission given greater opportunities for this mode of transmission in crowded human situations, especially as the aerosol transmission of filoviruses has been shown in laboratory experiments. Furthermore, it also concerns that vaccination policies may change pathogen replication rates and virulence. There is substantial circumstantial evidence that historical changes towards reduced virulence of syphilis were associated with a shift from non-sexual to sexual transmission.

Severe acute respiratory syndrome-associated coronavirus (SARS-CoV) can be the best example for host shifts, according to recent studies it was found that ancestral strains of this virus are present in bats, and close relative species is found in pangolins too. It is said that SARS CoV-2 is evolved for aerial transmission to spread successfully for better spread among individuals. On the other hand, if we consider the past 20 years there are 3 outbreaks of coronaviruses (SARS, MERS, SARS CoV-2) via expansion of host range, which implies the future possibilities of new disease outbreaks.

Combating the evolutionary changes.

The evolution trend in infectious agents is a result of human interventions either by disease control or by genetic engineering. As control measures becoming stronger parallelly infectious agents are evolving too; multidrug-resistant bacteria, vaccine escape in influenza.

As pathogens evolve, we humans to co-evolve to combat the diseases, which explains why the world didn't perish during the Bubonic plague.

Evolutionary biology predicts that an insecticide that kills later, once most reproduction has occurred, will minimize selection for resistance, as the strength of natural selection, decreases with age. In parasites where transmission generally occurs from older vectors, for example, *Plasmodium*, there may be an age window that could be targeted when selection for insecticide resistance is weak and before transmission.

The necessity for the advancement of strategies to manage and alleviate pathogen evolution is an emerging concern of the future. In that sense, interventions that have strong ecological and evolutionary dimensions, such as microbiota transplantation, new ways of administrating drugs (varying doses, alternating or combining molecules), or even advances in phage therapy, could be the future

Conclusions

The successful evolution of pathogens into new transmission modes gives them a higher probability of the emergence of new diseases to the human population. Pathogens undergone host switches will try to act aggressively in the naïve host resulting in disease severity. This signifies the necessity to know when and how new diseases evolve, dynamicity, and the complexity of diseases for successful disease control. Concerning the future combats of new diseases, this understanding paves for better countermeasures. Thus, it also highlights the need for a sufficient understanding of new trends in and broader development in studies of evolutionary biology and infectious disease.

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