Disinfection as a Selection Pressure on RNA Virus Evolution

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Emerging infectious diseases, including severe acute respiratory syndrome, filovirus disease, and Middle East respiratory syndrome, have led researchers during the last two decades to focus on RNA virus evolution studies. Changes in land use and increased urbanization are also raising alerts about the emergence of viral pathogens jumping into a new host, mainly from animals to humans. An understanding of virus evolution mechanisms is thus pivotal to obtain knowledge about how to predict and control viral infectious diseases.

The evolution of RNA viruses is characterized by multiple features, including a small genome size, an explosive replication rate, and a high mutation rate caused by the lack of a proofreading function of the RNA-dependent RNA polymerase, which results in the formation of quasispecies in a viral population composed of mutant spectra.[1] The formation of quasispecies is key in the population dynamics theory of RNA viruses, in which mutation, natural selection, genetic drift, and recombination are mainly working.[1] A mutation is caused by the error-prone replication of a viral genome in a host cell, thereby increasing the genetic diversity of an RNA virus population. Meanwhile, natural selection, which is mainly caused primarily by immune pressure in a host, decreases genetic diversity. For example, the evolution of norovirus GII.4 strains, which are an icosahedral single-stranded RNA virus with 69—97% nucleotide similarity observed among strains, is explained by the emergence of mutants that have escaped immune pressure.[2] Genetic drift is caused by the bottleneck effect in the life cycle of the RNA virus and is exerted by the random attainment to the next host after release to outside the host body. Recombination of RNA viruses has also been reported. Such recombination decreases genetic diversity by eliminating detrimental genetic sequences for efficient replication.[3]

Among these driving forces in RNA virus evolution, the natural selection process also may be exerted by another factor that has not been fully discussed so far: social infrastructure, including water and wastewater treatment practices. Water and wastewater treatment processes, one of the important infrastructure for public health, usually include a disinfection step. For example, the United States Environmental Protection Agency demands 99.99% enteric virus removal with appropriate disinfection technologies such as ultraviolet (UV) light or using chemical oxidants such as free chlorine, chloramines, ozone, and chlorine dioxide for drinking water resources.[4] However, the genogroup/genotype/serotype-dependent inactivation efficiency of RNA viruses has been reported. For example, the log reduction values of norovirus GI, GII, and GIV with free chlorine are different, with GI strains having higher resistance compared to the other genogroups.[5] Coxsackievirus B4 isolated from drinking water treated by free chlorine has shown higher resistance to free chlorine compared to a laboratory isolate.[6] After repetitious chlorine dioxide exposure, each mutant in a bacteriophage MS2 population exhibited different sensitivity to chlorine dioxide and tended to obtain lower susceptibility to chlorine compared to an initial population.[7] A similar phenomena was observed for echovirus 11 (EV11), where an initial population exhibited higher susceptibility compared to a population that was exposed to chlorine dioxide repeatedly.[8] At the quasispecies level, natural selection caused by chlorine dioxide decreased the number of higher susceptibility haplotypes among MS2 and EV11 populations, resulting in the survival of a less susceptible population, which can be proliferated in a subsequent replication. At the phenotypic level, lower susceptibility was caused by nonsynonymous mutations to more stable amino acids against chlorine dioxide treatment, and these mutation led to more stable host binding of mutants compared to the wild type.[8] These responses of RNA viruses to disinfection may result in the release of the surviving less susceptible strains to the environment, which means that the

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disinfection processes may work as a natural selection pressure in the life cycle of RNA viruses (Figure 1).
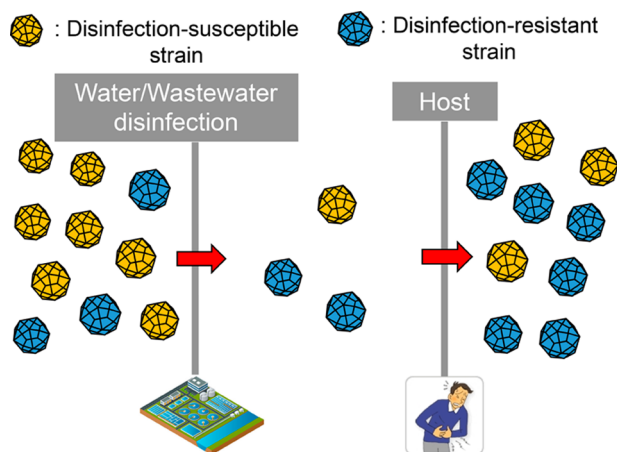
Figure 1. Natural selection process caused by water/wastewater disinfection.

The finding of genogroup/genotype/serotype/strain-dependent inactivation efficiency of RNA viruses calls attention to the impact of the social infrastructure-driven pressure on RNA virus evolution. To the best of our knowledge, no publications have discussed the impact of disinfection on RNA virus evolution. The viral strain-dependent susceptibility to the disinfectant highlights the importance of employing less susceptible strains in the disinfection tests, because the disinfection rate values obtained from more susceptible strains would be less useful in predicting the virus inactivation efficiency of circulating strains under practical disinfection conditions. It is critical we quantitatively investigate the contribution of disinfection practices to the RNA virus evolution.

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Notes
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