MedCrave
Step into the World of Research

Gastroenterology & Hepatology: Open access

Mini Review

Open Access

# Will a re-emergence of ancient infectious diseases pose a new risk to humanity in the coming millennia?

## Abstract

Infectious diseases including smallpox, the black plague, cholera, and others have been responsible for the loss of millions of lives over the past millennia, prior to the development of effective treatment strategies during the recent century. Throughout history, epidemics and pandemics are known to have occurred intermittently throughout the world for over 2,500 years. During the 20th century, many of the causative infectious agents were identified, the evolution of vaccines and antimicrobials were developed, resulting in treatment strategies and public health measures that brought about the resolution and presumed virtual eradication of some of the infectious agents. Cholera is transmitted via the fecal-oral route, and outbreaks continue to occur, with the most recent epidemic in Haiti following the massive earthquake of 2010 despite the development of effective vaccines and supporting public health measures. While smallpox was deemed to have been eradicated by the WHO, the recent discovery of Alaskapox, a novel strain of orthopoxvirus that is genetically similar to 'old-world' smallpox claimed its first fatality in January 2024. The bubonic plague also continues to reappear in clusters, most recently in rural Oregon in the USA in early 2024. Thus, the emergence of variants of these and other devastating ancient diseases continues to require diligence in establishing and delivery of public health measures and therapeutic options to ensure the plagues of former millennia remain in the history books and not in the community during the present and future generations.

Volume 15 Issue 1 - 2024

**Orien L Tulp, PhD, MD, FACN, CNS**
Professor, Colleges of Medicine and Graduate Studies, University of Science Arts and Technology, Montserrat, British West Indies MSR1110 and the Einstein Medical Institute, USA

**Correspondence:** Orien L Tulp, Professor, Colleges of Medicine and Graduate Studies, University of Science Arts and Technology, Montserrat, British West Indies MSR1110 and the Einstein Medical Institute, North Palm Beach FL, USA,
Email o.tul@usat.edu

**Received:** February 20, 2024 | **Published:** February 28, 2024

## Introduction

From the first known occurrence, epidemics and pandemics have changed the course of history, as the infectious agents are typically immune from any specific population group, and can infect individuals of all social, political, religious, economic or cultural identity.[1] As early civilizations expanded into empires, their leaders conquered different and more distant parts of the world, which enabled prevalent infectious diseases then of unknown origin to gain more opportunities to spread.[2] The middle ages were marked with multiple epidemics and pandemics that were responsible for the deaths of upwards of 50 million people worldwide, decimating much of the global populations as the move to transition from small rural communities to larger more populous urban communities that were more conducive to disease transmission evolved over the past 10,000 years.[1,2] Despite remarkable advances in modern diagnostics, therapeutics and public health measures, the prevalence of infectious diseases continues to take a staggering toll on humankind as evidenced by the recent COVID-19 pandemic.[3-5] Global transmission is easily facilitated by the ease international travel undertaken by unsuspecting carriers in the present day. The continued prevalence of cholera outbreaks across the globe is but one notable example of an ancient illness that continues to persist as an opportunistic infectious organism to the present day, in part due to asymptomatic carriers who may inadvertently introduce the organism to new and naive environments as occurred in Haiti in 2010.[6,7]

Cholera infection commonly follows environmental disasters and once introduced, may continue to persist for many years following an outbreak.[6,7] Cholera outbreaks can occur wherever contaminated water can infiltrate the domestic water and food supply including typical home or commercial usage of unclean, unchlorinated water. Cholera is caused by two infectious strains of Vibrio cholerae, a motile, morphologically-curved gram negative organism. The 0.1 And O:139 are the most common strains associated with cholera infection.[7] Because an active infection usually requires a substantial infectious dose of 100,000 or more organisms to be consumed, as stomach acidity can inactivate the organism; of the organisms that survive the gastric environment, they readily multiply in the intestinal tract, where they produce a potent endotoxin capable of causing an extraordinary and profound loss of water and electrolytes via vomiting and profuse diarrhea, which can cause a severe loss of potassium along with sodium within a few hours after infection. The extraordinary loss of water and electrolytes may result in the development of hypovolemic shock and become fatal in up to 50% of previously healthy individuals. Treatment via early intervention with both oral and intravenous rehydration can prevent most deaths. Because of the sodium loss, oral rehydration should contain 5% glucose in order to support sodium-glucose cotransport across the luminal epithelium. The recent epidemic of Cholera in Haiti was caused by fecal contamination of a community water supply and persisted for nearly a decade (2010-2019) and resulted in 819,000 infections approximately10,000 deaths during the 8 years following the earthquake.[6,7] Extensive public health measures were introduced, and Haiti had been considered cholera free in early 2022. Unfortunately, the illness returned in September 2022, resulting in an additional 20,000 inhabitants becoming ill, and in an additional 285 cholera deaths by years end. The likelihood is that cholera may remain endemic in Haiti for an indefinite duration and continue to pose a risk to surrounding communities and other nations in the near and distant future.[8,9]

Genomic analysis of ancient bone fragments have traced the origins of the bubonic and pulmonic plague and revealed their ancient origin, and confirmed their genetic similarity to present day strains of the infectious agent.[10] The infamous Black plague pandemic that ultimately lasted for several centuries, is believed to have first become introduced to Europe from Crimea, where it may have originated many years previous.[1] Once established in Crimea, it was most likely carried by flea-infested rats that typically travelled with the trading ships, thereby enabling the plague virus to spread throughout the Mediterranean Basin, North Africa, Western Asia, and Europe over the next five centuries.[1] The bubonic plague made another grand entrance of major proportions in 14th century Europe, where it is generally believed to have resulted in the deaths of over half of the European population. The Great Plague of London re-emerged as the bubonic plague again in 1665 where it resulted in the deaths of 20% of the city's population during its deadly reign. Over the centuries, the bubonic plague has resulted in the deaths of over 100 million people. Each year, the World health Organization still reports between one thousand and two thousand cases of the bubonic plague, occurring mostly in Madagascar and Sub-Saharan Africa, where it continues to spread via flea infested rodents and person to person contact.[11,12] Recent genomic analysis of specimens obtained from ancient skeletal remains have now linked the various strains of Y. pestis that were causative of the numerous epidemics *throughout* the world and provided confirmation of the origins and continuity of the bacterium over the many centuries.[11] It is a popular misconception that the Bubonic Plague an 'old' medieval disease, but in 2023 and 2024, the bubonic plague emerged in the Northwestern United States, where, a rare case of human plague was confirmed in rural Oregon.[13] According to Deschutes County Health Services. The unnamed individual is likely to have been infected by a pet cat, which had symptoms. The case was identified and treated early posing little risk to the community, and no additional cases have emerged. In recent decades, an average of seven human plague cases are reported each year, according to the Centers for Disease Control and Prevention.

The bubonic plague is the most common form of the plague[11] and is characterized by painful, swollen lymph nodes known as "buboes." While not totally eradicated, the plague is most commonly transmitted via flea-infested rodents and cats; the World Health Organization reports that human to human transmission of bubonic plague is deemed rare. Because there is no commonly available vaccine for the plague, development of antibiotic resistance remains a future concern as it has for other infectious organisms.[21] Although improved sanitation, better living conditions and health care have helped temper the disease, the present day disease itself is the same as the one that swept through Europe during the Black Death outbreak and could pose significant challenges were it to continue to be transmitted through unsuspecting present day populations.[13]

Smallpox is believed to be an extinct disease since 1980, when the WHO determined it to have been eradicated.[14,15] Smallpox was an infectious disease of great concern caused by one of two strains of variola virus (v. major and v. minor) which belong to the genus Orthopoxvirus. Orthopoxviruses consist of several strains of the virus with varying magnitudes of human pathogenicity.[15] Historically Smallpox disease has been estimated to have killed up to 300 million people in the 20th century and as many as 500 million people during the last century of its existence. The last naturally occurring confirmed case of smallpox is believed to have occurred in October 1977. Because effective smallpox vaccines have now been available globally for over half a century their widespread administration has dramatically decreased the prevalence of the disease and have enabled the World Health Organization to declare smallpox as having been eradicated by 1980, the first such infectious disease to earn that distinction to date.[14]

In addition to the smallpox viruses, several other members of the orthopoxviruses species have also recently been recognized, including the Akhmeta virus, the Abatino virus, and the Monkeypox virus, that highlight the possibility of additional unknown members of this genus with zoonotic and human contact potential unceremoniously lurking in the environment and with an unpredictable outcome. Alaskapox is the most recent of those viruses to be identified, which to date has been limited to a total of 7 infections since 2015 including one fatality by January 2024, all having occurred in a rural area of Alaska in the United States.[16-19] Alaskapox is believed to become spread via zoonotic exposure, from small rodents infected with the virus and passed on to their predators and to humans via animal exposure. The diagnostic characteristics of Alaskapox are similar but less virulent than those of smallpox and appear to be genetically linked to ancient strains of the virus. Mpox (monkeypox) is an infectious disease caused by the monkeypox virus, another variant of the orthopoxvirus that can cause a painful rash, enlarged lymph nodes and fever.[20] Most people fully recover from mpox, but some may become very ill. Since May 2022, when the multinational mpox (formerly known as monkeypox) clade IIb virus outbreak was first reported, more than 30,000 cases have been identified in the United States, with a high prevalence of about 35% in patients who also had immunocompromised states including human immunodeficiency virus (HIV) infection. To date one human fatality has been reported due to disseminated Clade IIb mpox infection that was determined to have become resistant to antiviral treatment. Whole-genome sequencing of specimens obtained during autopsy identified six known mutations linked with high-level resistance to tecovirimat in vaccinia virus encoding the VP37 protein, and increasing concern for the development of treatment resistant variants of the virus that may lead to future more severe outbreaks of the illness.[21,22]

## Discussion and conclusion

The recent emergence of genetic descendants of ancient infectious organisms and viruses has led to speculation that their potentially devastating impact on global populations remains a concern for public health as they continue to evolve into variants of the original disease. In addition, therapeutic and preventive options previously developed may prove to be ineffective as treatment resistant variants continue to evolve.[22] Many infectious agents tend to develop survival strategies following exposure to antimicrobials and chemical agents, as demonstrated by the ongoing evolution of the COVID-19 virus, where subsequent variants of the spike protein are able to continue to thrive by evading immunity evoked by previous immunization or exposure to earlier variants of the virus, often with dire consequences.[2] The examples summarized for cholera, bubonic plague and orthopoxviruses are additional examples of such survival despite the passage of time and distance from their origins and previously effective therapeutic options. Heightened emphasis on available public health measures, renewed vigilance, combined with continuing development of novel treatment strategies may hopefully hold the key to prevention and further evolution of both ancient and evolving infectious agents and the ultimate survival of humanity.

## Acknowledgments

None.

## Conflicts of interest

None.

## References

1. Sakai T, Morimoto Y. The history of infectious diseases and medicine. *Pathogens.* 2022;11(1):1147.
2. Tulp O L, Einstein GP. Efficacy of biophotonics as a therapeutic option in resolving microbial and viral infectious diseases. Enliven: Immunology and Immunotechniques 2024.
3. Noh JY, Jeong HW, Shin EC. SARS-CoV-2 mutations, vaccines, and immunity. Implication of variants of concern. 2021.

**Citation:** Tulp OL. Will a re-emergence of ancient infectious diseases pose a new risk to humanity in the coming millennia? *Gastroenterol Hepatol Open Access.* 2024;15(1):17–19. DOI: 10.15406/ghoa.2024.15.00572

4. CDC Centers for disease prevention and control. Omicron Variant: What You Need to Know. 2021.
5. Elflein J. Coronavirus (COVID-19) in the U.S. - Health, Pharma & Medtech Statistics & Facts, Statistica, 2023.
6. Sanon V, Sainvil F, Awan AR, et al. Haiti's cholera epidemic: will it return in 2021? *Gastroenterol Hepatol Open Access.* 2021;12(4):124–126.
7. Finkelstein RA. Cholera, Vibrio cholerae O1 and O139, and Other Pathogenic Vibrios. Ch 24, In: Medical Microbiology. 4th edition. UTMB Galveston. 1996.
8. Orien L Tulp, Valentine Sanon, Frantz Sainvil, et al. Haiti's Cholera Epidemic: Did it return as an Endemic in 2022 ? Running Title: Haiti's Cholera Epidemic returned as an Endemic in 2022 in press. MOJ Public Health. March 2024.
9. Achtman M, Zurth K, Morelli G, et al. Yersinia pestis, the cause of plague, is a recently emerged clone of Yersinia pseudotuberculosis. *Proc Natl Acad Sci U S A.* 1999;96(24):14043–14048.
10. Spyrou MA, Tukhbatova RI, Wang CC, et al. Analysis of 3800-year-old Yersinia pestis genomes suggests Bronze Age origin for bubonic plague. *Nature Communications.* 2018;9(1):2234.
11. World Health Organization (November 2014). "Plague Fact sheet N°267". 2015.
12. Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Vector-Borne Diseases (DVBD), Symptoms, November 15, 2021.
13. The Guardian, 2024. A case of bubonic plague was reported in Oregon. Here's what to know. The Guardian, 2024.
14. WHO. Smallpox announcement. 2016.
15. International Committee on taxonomy of viruses. 2017.012.0155 9xlsx), UK: International Committee on taxonomy of viruses (ICTV):2019.
16. Alaska man is first reported person to die of Alaskapox virus; exposure may be linked to stray cat. CBS News. 2024.
17. Springer Yuri P, Hsu Christopher H, Werle Zachary R, et al. Novel Orthopoxvirus Infection in an Alaska Resident. *Clin Infect Dis.* 2017;64(12):1737–1741.
18. Elderly Alaska man is first reported person to die of recently discovered Alaskapox virus. AP News. 2024.
19. Hollander Zaz. State reports first known fatal case of Alaskapox. Anchorage Daily News. 2024.
20. Gigante CM, Gao J, Tang S, et al. Genome of Alaskapox virus, a novel osrthopoxvirus isolated from Alaska. *Viruses.* 2019;11(8):708.
21. Alarcón J, Kim M, Terashita D, et al. An Mpox-Related Death in the United States. *N Engl J Med.* 2023;388:1246–1247.
22. Reygaert WC. An overview of the antimicrobial resistance mechanisms of bacteria. *AIMS Microbiol.* 2018;4(3):482–501.

**Citation:** Tulp OL. Will a re-emergence of ancient infectious diseases pose a new risk to humanity in the coming millennia? *Gastroenterol Hepatol Open Access.* 2024;15(1):17–19. DOI: 10.15406/ghoa.2024.15.00572