ECRONICON OPEN ACCESS

EC PULMONOLOGY AND RESPIRATORY MEDICINE

Perspective

From Endogenous Viral Elements to COVID-19: It's Complicated

Zeena Nackerdien*

Rockefeller University, New York, New York, USA

***Corresponding Author:** Zeena Nackerdien, (Formerly) Rockefeller University, New York, New York, USA.

Received: September 14, 2020; **Published:** September 28, 2020

Abstract

COVID-19 is a reminder that viruses are effective in causing pandemics. Because of their dramatic effects on vulnerable individuals and precontact populations, zoonotic viruses highlight human vulnerability to large-scale infections. While the world remains focused on fighting pandemics caused by sporadically emerging pathogens, it is worth remembering the continued evolutionary process that exists between viruses and humans. In this 'personal view' article, I discuss this phenomenon in greater detail, within the context of the 1918 flu and current COVID-19 pandemics.

Keywords: *Endogenous Viral Elements; Retroviruses; COVID-19; Influenza*

Abbreviations

ACE2: Angiotensin-Converting Enzyme 2; CRISPR/CAS: Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-Associated; COVID-19: Coronavirus Disease 2019; MERS: Middle East Respiratory Syndrome; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2

Virus-human relationships

Literature forecasted a contagion that would wipe out millions, leaving behind wretched survivors. Scientists steered away from such evocative prose and couched the 'arms race' between viruses and mankind in evolutionary terms. After all, dramatic viral outbreaks have shaped the evolution of animals for millennia. Indeed, about eight percent of the human genome is composed of retroviral fossils [1,2].

Co-evolution of different mobile genetic elements, including transposable elements, retroelements, and viruses are a matter of record. Up to 30% of bacterial genomes, roughly half of mammalian genomes, and more than 70% of plant genomes are comprised of mobile genetic elements [3].

Of these elements, viruses are the most abundant genetic entities, capable of infecting all three domains of life, as well as other viruses. Many viruses can integrate into the genetic material of host species, enabling vertical transmission and fixation in hosts [4].

Simply put, one outcome of the virus-host arms race is that genetic material is transferred from the virus to the host. Examples of immune systems fully or partially derived from mobile genetic elements include the CRISPR-Cas system of prokaryotes and the RAG1/2 system of vertebrates. These systems provide immunologic memory of foreign genetic elements and help to give rise to antibody and T cell diversity, respectively [3].

While retroviruses are the only known eukaryotic viruses requiring chromosomal integration for successful lifecycle completion [4], Katzourakis and Gifford identified non-retroviral endogenous viral elements representative of ten families of viruses, including hepatitis B, Ebola, rabies, dengue and yellow fevers, integrated into animal genomes [5].

Echoes of the virus-host arms race unearthed from animal genomes, enabled the inference that host genomes will continue to adapt to counteract either new viruses or variants of viruses previously vanquished by the host [1].

According to the Global Virome Project (http://www.globalviromeproject.org), there are an estimated 1.7 million yet-to-be-discovered viral species from important viral families in mammalian and avian hosts and up to 827,000 of these unknown viruses have zoonotic potential [6]. Others found vertebrate-specific families known to infect mammals and birds (e.g. influenza viruses) were also present in amphibians, reptiles and fish [7].

When European colonists first settled in the Americas, they brought with them diseases so devastating that about 90 percent of pre-contact populations were killed [8]. However, nowadays the Centers for Disease Control and Prevention (CDC) estimates that about three-quarters of emerging infectious diseases originate in animals [9]. Bacteria, parasites, prions and viruses are known to have caused zoonoses [10].

The current outbreak of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) which causes coronavirus disease-2019 (COVID-19) has highlighted the global disruptiveness of zoonotic infectious diseases. COVID-19 is the latest in a long line of modern pandemics. Other examples include the Ebola virus disease outbreak in West Africa (2013 - 2016), the Zika virus in the Americas and southeast Asia (2016 - 2018), Lassa fever in Nigeria (2018), Yellow fever in Latin America and Africa (2016 - 2018) and Nipah virus in India and South Asia (2017 - 2018) [11].

However, pandemic influenza remains the most feared because it has infected and affected humans for centuries. Ten percent of the global population is infected by an influenza virus every year, totaling $87 billion in costs. Infants (< 1 year), the elderly (> 65 years), and people with preexisting comorbidities, including chronic respiratory abnormalities, heart disease, immunodeficiency and pregnant females are particularly vulnerable to influenza infections [12].

Influenza pandemics sporadically appear due to the spread of an antigenically distinct influenza A virus in populations. There have been four influenza pandemics over the course of the past century: the 1918 - 1919 Spanish flu pandemic, subtype H1N1; the 1957 - 1958 Asian flu pandemic, subtype H2N2; the 1968 - 1970 Hong Kong flu pandemic, subtype H3N2; and the 2009 - 2010 swine flu pandemic, subtype H1N1 [12].

While the clockwork frequency of influenza has led to acceptance and familiarity with the disease, the consequences of the emergence of influenza subtype H1N1 in 1918 have been etched in human history. Over the course of 12 months, 500 million people were infected and at least 50 million succumbed to the flu; roughly half of these occurred within the fall of 1918. The case fatality rate among young adults at the time was so severe that the average life expectancy in the U.S. dropped by about a dozen years [12].

One century later, the world has moved on from World War I, poor health, and sanitation that prevailed at the time. Scientific advances have also led to a growing understanding that the balancing act between microbe and Man trends over the long term towards coadaptation i.e. "the host acquires factors for resistance and the virus acquires factors for mitigation and longer survival of (and thereby in) the host," according to Nobel laureate, Joshua Lederberg [13].

Descendants of the 1918 flu virus have been responsible for nearly every seasonal influenza A infection globally over the last century [14]. However, if improved public health measures, vaccinations and evolutionary coadaptation mean that the flu no longer kills or debilitates us all, something else might.

Prior to COVID-19's global spread, researchers focused mainly on four "benign" coronaviruses responsible for 20 to 30 percent of common colds, SARS-CoV (which initiated an outbreak in 2002 and killed more than 700 people worldwide) and a different strain that caused a Middle East Respiratory Syndrome (MERS) outbreak that began in 2012 (and took more than 800 lives).

Far from burning out like SARS, or lingering like MERS, SARS-CoV-2 - which is genetically similar to SARS-CoV and uses the same cell entry receptor, angiotensin-converting enzyme 2 (ACE2) [15] - has proven to be a stealthier and deadlier adversary. People infected with SARS-CoV did not transmit the virus until up to 36 hours after displaying symptoms, enabling effective quarantining of affected individuals before they made others sick. By contrast, people with COVID-19 could transmit SARS-CoV-2 before they are clearly sick [16].

As the global COVID-19 death toll ticks upward towards the one-million mark, the world eagerly awaits the development of effective therapeutics and vaccines. While effective and safe vaccines may "train" the immune system to fight future infections, drugs could stop a virus from attaching to cellular receptors, impede viral reproduction if the microbe does enter the cell, or dampen an overreaction by the immune system of infected individuals.

There are also other COVID-19-related lessons to be learned from 2020. Leadership and public trust can aid the maintenance of resilient health systems with surge capacity in case of emergencies and in the context of healthcare disparities. Robust investment will be necessary to generate robust, consistently disseminated scientific evidence that, in turn, may lead to the medical tools necessary to combat human health threats such as COVID-19.

Conflict of Interest

None.

Bibliography

1. Patel MR., *et al.* "Paleovirology - ghosts and gifts of viruses past". *Current Opinion in Virology* 1 (2011): 304-309.
2. Blanco-Melo D., *et al.* "Co-option of an endogenous retrovirus envelope for host defense in hominid ancestors". *ELife* 6 (2017): e22519.
3. Broecker F., *et al.* "Evolution of Immune Systems from Viruses and Transposable Elements". *Frontiers in Microbiology* 10 (2019).
4. Feschotte C., *et al.* "Endogenous viruses: insights into viral evolution and impact on host biology". *Nature Reviews Genetics* 13 (2012): 283-296.
5. Katzourakis A., *et al.* "Endogenous viral elements in animal genomes". *PLoS Genetics* 6 (2010): e1001191.
6. Carroll D., *et al.* "The Global Virome Project". *Science* 359 (2018): 872.
7. Shi M et al. "The evolutionary history of vertebrate RNA viruses". *Nature* 556 (2018): 197-202.
8. McKenna M. "In the Fight against Infectious Disease, Social Changes Are the New Medicine". In: Scientific American (2020).
9. Belay ED., *et al.* "Zoonotic Disease Programs for Enhancing Global Health Security". *Emerging Infectious Diseases* 23 (2017): S65-S70.
10. Konda M., *et al.* "Potential Zoonotic Origins of SARS-CoV-2 and Insights for Preventing Future Pandemics Through One Health Approach". *Cureus* 12 (2020): e8932.
11. Zumla A., *et al.* "Emerging and Reemerging Infectious Diseases: Global Overview". *Infectious Disease Clinics of North America* 33 (2019): xiii-xix.

12. Nickol ME., *et al.* "A year of terror and a century of reflection: perspectives on the great influenza pandemic of 1918-1919". *BMC Infectious Diseases* 19 (2019): 117.

13. Lederberg J. "Emerging infections: an evolutionary perspective". *Emerging Infectious Diseases* 4 (1998): 366-371.

14. Taubenberger JK., *et al.* "1918 Influenza: the mother of all pandemics". *Emerging Infectious Diseases* (2006): 15-22.

15. Wang H., *et al.* "The genetic sequence, origin, and diagnosis of SARS-CoV-2". *European Journal of Clinical Microbiology* 39 (2020): 1629-1635.

16. Fischetti M., *et al.* "What scientists know about the inner workings of the pathogen that has infected the world". In: Scientific American (2020).

Volume 9 Issue 10 October 2020