The science and sociology of SARS

Part 1: Viruses and the nature of present outbreak

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The outbreak of a new virus responsible for what is known as severe acute respiratory syndrome (SARS) raises a number of scientific, medical and social problems. Thanks in part to the quick response and collaborative effort of a team of international scientists, the virus has remained fairly well contained. However, it has infected 7,000 people worldwide and has killed over 500. It poses an enormous health risk in China, and there is still the possibility of an international epidemic that would have devastating consequences.

This is the first of two articles exploring the science and sociology of SARS. In it we explain some of the scientific and historical background necessary to understand the present outbreak. The second article will consider the social significance of the effort to contain SARS and achieve an understanding of its cause.

Viruses and virology

SARS is now known to be a viral infection, caused by a new type of virus, probably of animal origin. In order to understand the specific nature of SARS, it is necessary first to understand how viruses propagate and what efforts have been made in the past to halt their spread.

Viruses are simple in structure, consisting of a piece of genetic material—DNA or RNA—covered by a protein coat and sometimes an additional membrane. It is still an open question as to whether viruses should be categorized as living material or not. In contrast to bacteria—such as *E. coli* and the different bacteria that cause typhoid, tuberculosis, and a host of other diseases—viruses are not cells and do not possess the chemical components necessary to sustain life. They therefore cannot propagate independently of their host.[1]

Thus, viruses are fundamentally parasitic in nature. They reproduce by invading a cell of a host plant or animal. The internal mechanisms of the cell are used to replicate the genetic material and produce more viruses, which can in turn invade more cells. This process generally kills the host cells, or at least injures them, and this can have mild to serious consequences for the host organism. A common cold is generally a viral infection, and the symptoms associated with the infection—such as sore throat or muscle aches—arise when the virus invades cells in different areas of the body.

In order for a virus to infect a cell, it must first pass through the cell's protective membrane, which is unique for each type of cell. In essence, the virus accomplishes this task by disguising itself outwardly as a protein that is accepted by the cell and the molecular receptors on the cell's membrane. Thus, different viruses attack different cells by mimicking different proteins. The Ebola virus, for example, attacks in particular the cells lining blood vessels, causing catastrophic bleeding and often death.

Because viruses cannot subsist independently of a host, they are generally transmitted through direct contact or through the exchange of bodily fluids containing the virus. For example, droplets released by coughing can spread viruses that cause measles, chicken pox or SARS; water contaminated with feces can spread rotaviruses, which plague poor and unsanitary regions; and sexual contact or blood transfusions can spread the human immunodeficiency virus, or HIV.

The human body protects against viruses through the immune system. In order to attack an invading virus, however, the immune system must first be able to recognize the virus as a foreign substance. This recognition can be achieved only for a certain group of viruses, including those that have previously infected the host. Thus, vaccines generally work by introducing a small amount or a less potent strain of the virus in order to build immunity within the host and prevent future infection.

Their specialized character means that viruses generally remain loyal to specific host species; however, it occasionally happens that a virus will cross from one species to another. HIV is believed to have originated in non-human primates, and an outbreak of a form of Hanta virus in the United States in 1993 had its origins in deer mice. As humans increase their interaction with nature, the risk of such exchanges is increased, especially in unsanitary or overcrowded conditions.

Modern virology—and indeed the scientific understanding of viruses as distinct from bacteria and other pathogens—developed in the early decades of the twentieth century. Because they are so small, it became possible to observe viruses directly only with the invention of the electron microscope in 1938, which was itself made possible with the development of quantum physics in the 1920s. After the structure of DNA was determined in the 1950s, scientists came to understand the physical structure of viruses and how they propagate.

These scientific advances have greatly strengthened the ability of humans to contain viral epidemics. This can be seen, for example, in the ongoing battle against influenza, which is one of the most common viral infections. Flu outbreaks occur every year, with epidemics recurring approximately every decade. Flu epidemics can cause hundreds of thousands of deaths, while pandemics, which occur more infrequently, can be absolutely devastating.

These flu outbreaks occur repeatedly because the influenza virus is constantly mutating, thus bypassing immunities that would otherwise develop after one infection. The so-called Spanish flu pandemic erupted after World War I in 1918. It infected half the world's population and killed one in 20 of those infected, or over 25 million people. The "Asian flu" of 1956 and the "Hong Kong" flu of 1968 combined killed 4.5 million.

Flu vaccinations are available, but must be constantly updated to keep up with the mutations. The World Health Organization (WHO) coordinates an international effort to track the development of the virus and manufacture new vaccines, which are made available before each flu season. These efforts have helped contain the influenza virus, and experience with flu has made scientists alert to the specific danger posed by SARS.

Another great achievement in viral science and international coordination over the past half century was the eradication of the smallpox virus, one of the greatest health threats in modern human history. During the twentieth century alone, smallpox killed some 300 million people. Smallpox vaccinations, first developed in the late eighteenth century, were implemented on an international scale by the WHO beginning in 1966. Over the course of 15 years, the intensive effort led to the complete eradication of the virus by 1980.

The character of the SARS virus

The history of viruses indicates the danger posed by new strains for which no immunities or vaccines exist. Several such threats have emerged over the past decade, the most deadly of which has been HIV. Over 13 million have died from AIDS, and many more are currently affected by HIV. The virus has wreaked havoc especially in underdeveloped countries in Africa and Asia, but has spread to every country in the world.

As the case of AIDS demonstrates, the growing international integration of human society increases the ability of viruses to spread great distances. So it is with SARS, which is believed to have originated in rural China and remained confined there for several months. However, after making its way to the major business hub of Hong Kong, the virus quickly posed a global threat, prompting the WHO to issue a global health alert.

Every viral disease has a certain incubation period, the period between exposure to the virus and the development of symptoms. The incubation period for SARS is two to ten days. This relatively long incubation period allows infected persons to travel and infect without knowing that they are themselves infected, thus aiding the global spread. A virus such as Ebola is much more deadly; however, infected patients tend to progress in their disease so rapidly that it is difficult to transmit the virus to others.

The illness produces a fever, headache and tiredness, which is generally followed by a dry cough and difficulty breathing. For a certain percentage of patients, self-sustained breathing becomes impossible and artificial ventilation must be used. Perhaps 15 percent of patients who contract SARS die of the disease, though this number has been sharply rising in recent weeks as more early terminal cases end in death.

It is now known that SARS is a viral infection caused by a new strain of coronavirus, a membrane-enclosed RNA virus. Coronaviruses are the largest of any of the RNA viruses, with approximately 30,000 nucleotides (the building blocks of DNA and RNA) making up the gene sequence.

Coronaviruses are one type of virus that is generally associated in humans with mild upper-respiratory infections (common colds) that may cause pneumonia in patients with poor immune systems. SARS is a much more virulent strain, leading scientists to believe that the virus had its origins in a non-human animal, where the coronavirus can have more severe effects.

The genome sequence of the virus has been completed by researchers based in Vancouver, Canada, and separately by the US Centers for Disease Control and Prevention (CDC). The two sequences are essentially identical [for the published results, see www.sciencemag.org/feature/data/sars/].

The genetic makeup of the virus is different from known viruses. “The whole genome is essentially new,” noted University of Hong Kong microbiologist Malik Peiris. “The virus did not originally exist in humans, it definitely comes from animals,” said Yuen Kwok-yung, another microbiologist at the university. However, from the genome sequence, there are no clear indications as to what animal it came from, as it does not display any clear similarities to coronaviruses that are known to infect animals.

Like most cold viruses, the coronavirus that causes SARS can be spread from person to person by coughs and sneezing or through close personal contact. Each cough sends tiny droplets of saliva or mucous into the air, which can transmit the virus.

Researchers in Hong Kong have suggested that the virus may be mutating rapidly, perhaps into more virulent strains or strains that can be transmitted more easily. They point in particular to an incident in late March in which the virus infected a cluster of 268 people in a single apartment complex, though they had not come into direct contact with each other. The cause of the spread is still unclear, but may have been the result of contaminated water or some other means.

“The virus is mutating fast. Such a quick mutation meant that even if there is a cure, it may become ineffective. Even a diagnostic test may not be able to detect it if it has undergone change,” said Dennis Lo, a member of the University of Hong Kong team that has been studying the virus.

Julie Gerberding, director of the CDC, felt this was probably not the case. However, she noted, “This is a single-stranded RNA virus, and that kind of virus, as it reproduces itself ... makes mistakes. The HIV virus is an RNA virus that does that too. And so it is not surprising that we see new strains emerge over time.” One of the great difficulties in developing a vaccine for HIV is precisely that it is constantly mutating.

There are still numerous questions concerning how the virus spreads. Certain patients seem to act as “superspreaders.” Over 100 patients in Singapore can be traced to a single flight attendant who brought the disease from Hong Kong. What makes for a superspreader is still unclear, but could be a mix of biological/genetic and environmental causes. “From a clinical point of view, there are no clear indicators for us to recognize who will be the ones who spread SARS more effectively than others,” says Dr. Ling Ai Ee, a virologist and chief of Singapore’s SARS investigation team.

Notes:

1. For a good introduction to virology, see *The Invisible Enemy: A Natural History of Viruses*, Dorothy H. Crawford, Oxford University Press, 2000.