# 7. Emerging Infectious Diseases



Infectious diseases that have either appeared within the past two decades or become more prevalent in that time are considered "emerging" diseases. They can be caused by newly identified infectious agents, such as the viruses in severe acute respiratory syndrome (SARS) and acquired immune deficiency syndrome (AIDS); by reemerging infections, such as drug-resistant tuberculosis; or by nosocomial infections, such as methicillin-resistant *Staphylococcus aureus*, which often develop antibiotic resistance in hospitals. It is interesting to note that many emerging diseases are zoonotic, meaning the organism incubates inside of an animal, with only occasional transmission into human population: notable examples are avian influenza and swine influenza.

Several factors contribute to outbreaks of emerging infectious diseases: genetic drift of microbial adaption, such as in influenza A; changing human susceptibility as seen in immunocompromised conditions; varying weather and climate as seen in diseases with zoonotic vectors; the use of antibiotics to increase meat yield; war and famine; the breakdown of public health; or poverty.

In southern China, the dense population and close proximity of people to animals enable viruses to jump the species barrier and become pathogenic in humans. Globalization and rapid air travel allow microbes to propagate rapidly around the globe. SARS is a vivid case in point.

Hong Kong has experienced several emerging or reemerging infections in recent decades. AIDS, avian influenza, and SARS are the most prominent. These deadly epidemics, especially SARS, severely tested Hong Kong's ability to tackle a medical crisis.

## Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) Epidemic

The US Centers for Disease Control and Prevention (CDC) reported that in the spring of 1981 in Los Angeles, California, five previously healthy young men between 29 and 36 years of age had contracted pneumocystis pneumonia (PCP), a rare form of fungal pneumonia. PCP typically only occurs in people who are severely immunocompromised—for example, patients who have been taking powerful immunosuppressive drugs for medical problems. The only feature the patients had in common in this puzzling outbreak was that they were all young gay men.

In July of the same year, 26 men developed Kaposi's sarcoma, a rare form of cancer caused by a virus that typically produces flat purple tumors of the blood vessels, visible on the skin and invisible elsewhere. All the men lost weight, developed swollen lymph glands, and soon died. Again, the disease seemed to affect only homosexual men.[1] The two outbreaks marked the beginning of the AIDS epidemic in the West.

These two clusters of patients died from multiple infections, due to a depletion of infection-fighting CD4 lymphocytes. Soon other groups, such as drug users who shared needles, and hemophiliacs who required frequent blood transfusions, developed the same symptoms of marked weight loss and unusual infections. The disease was no longer limited to homosexual men.

The new disease swept through the United States and, in November 1982, the CDC reported 788 cases in 33 states. By then it was formally named acquired immune deficiency syndrome (AIDS), and the race was on to isolate the causal agent. In May 1983, a French group, led by Luc Montagnier and Francoise Barré-Sinoussi, discovered a new retrovirus that they suspected of causing AIDS. They called it lymphadenopathy-associated virus. At around the same time an American group led by Peter Gallo found a virus that they believed to be the culprit. The two groups of scientists were, in fact, looking at the same organism. Since the French group discovered the virus first, they were honored with the Nobel Prize in Physiology/Medicine in 2008.[2]

In 2011, there were roughly one million cases of HIV infection in the United States, and 56,000 or so new cases continue to be recorded each year—a remarkably high number given the enormous effort spent on sexual education. HIV affects nearly every country. In 2015, 36.7 million people worldwide were living with HIV, of whom 17.8 million

were women and 1.8 million were children, while 2.1 million were newly infected cases. In some southern African countries, as high as 70% of hospitalized patients were HIV-infected, and in certain populations the prevalence of infection exceeded 45%. HIV infection created the greatest orphan crisis in the world—in 2006, more than 13 million children were orphaned by HIV, most of them in the poverty stricken sub-Sahara Africa where most AID-related deaths occurred.[3]

## *Origin of HIV Infection*

The early cases reported in the United States in 1981 were not the first cases of AIDS. Missionary doctors had described similar symptom profiles in Central African patients almost a decade earlier. Research suggests that the most common form of HIV probably originated when simian immunodeficiency virus passed from chimpanzees to humans in Central Africa between 1902 and 1921. There are two strains of HIV: HIV-1 and HIV-2. The former, generally more virulent and dangerous, is found mostly in the United States and the rest of the world; the latter is less aggressive and found mostly in West Africa. HIV-1 reached Haiti in 1966 and arrived in the United States about four years later. There it quietly spread for a decade before fully manifesting in the early 1980s.[4]

As a retrovirus, HIV is remarkably delicate. It needs a human host and does not survive well outside the body. It is usually transmitted through exposure to infected blood or bodily fluids such as semen, genital secretions or breast milk. Transfusions of contaminated blood or blood products carried the highest risk of infection until a screening method for detecting HIV in blood became available in 1985. Other high risks of HIV transmission include pricks from contaminated needles, needle-sharing among intravenous drug addicts, and anal sex. HIV may be transmitted from mother to child during pregnancy, delivery, and breast feeding. The risk is highest during labor and delivery, and can be drastically reduced by the use of antiviral drugs and delivery by Caesarean section.[5]

## *How Does the Virus Cause Disease?*

The virus's sole mission is to replicate itself by multiplying. HIV does so by attaching itself to a specific receptor (CD4) on the cell membrane of a host lymphocyte, which is a white blood cell of the lymphatic system

that plays a pivotal role in the body's defense system. Once attached, it destabilizes the surface of the CD4 lymphocyte cell and enables it to pass into the cytoplasm of the infected cell.

Inside the cell, the virus moves to the nucleus where its two viral enzymes, reverse transcriptase and integrase, begin their work. The former starts copying the HIV RNA into HIV DNA, and the latter integrates the HIV DNA into the host cell's DNA. The HIV virus remains in the cell, and the infection can stay dormant until the infected cell is activated when a favorable environment presents itself. The infected cell then begins to produce not only its own proteins, but many HIV proteins. To carry on their single mission, the newly formed HIV viruses break off from the surface of the cell to infect other lymphocytes.

When the CD4 cell dies and ruptures, millions of viruses are released to infect other cells.[6] If the disease is untreated, over the course of several years, the number of CD4 cells will decline, and dwindle to 200 cells per microliter (μL).

## *Clinical Course of HIV Infection*

Once the HIV particles are ingested by the CD4 lymphocytes and macrophages, the immune system is activated. The patient in this early stage may have fever, diffuse pain, and fatigue as the immune system fights the infection. Usually these symptoms are self-limiting.

The diagnosis of HIV infection is made by demonstrating the presence of HIV antibodies in the blood using one of two blood tests: the enzyme immunoassay (EIA) or enzyme-linked immunosorbent assay (ELISA). As both techniques can give rise to a false-positive result, a highly specific western blot assay is performed to confirm a positive test. Routine testing for HIV antibodies in donors' blood has led to effective identification of contaminated blood and increasing confidence in the safety of blood supplied for transfusions.[7]

A normal, immunocompetent person has anywhere from 500 to 1500 CD4 cells per μL of blood. It is only when the number of CD4 cells drops to 200 per μL that an infected person is considered to have the disease AIDS, which represents the last stage of the HIV infection.[8] By destroying the CD4 lymphocytes, the virus markedly weakens the immune system and the body loses its ability to fight off opportunist infections. At that point, the patient frequently presents with opportunistic viral, fungal,

**Figure 7.1 Chest X-ray of a patient with pneumocystis pneumonia showing bilateral diffuse ground glass shadows**

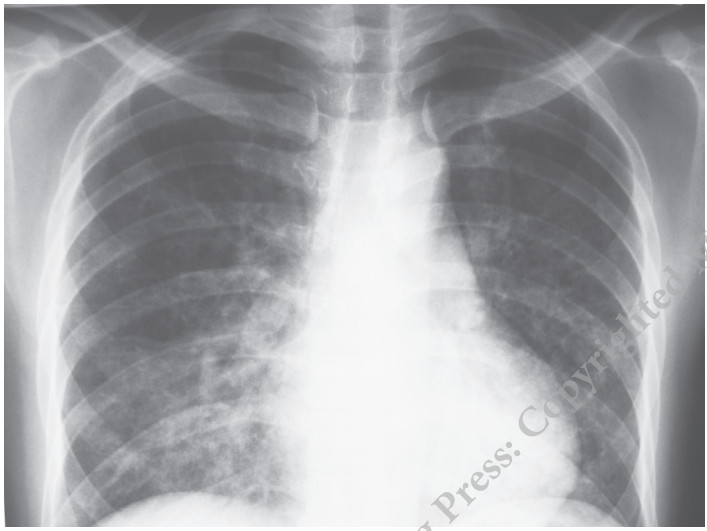

Photo courtesy of Drs. Julie Wang and C. L. Lam



or bacterial infection, alone or in any combination. Examples are PCP, cryptococcosis, mycobacteria *avium intracellulare*, and reactivation of toxoplasmosis or cytomegalovirus infections.

HIV infection can coexist with other non-opportunistic infections such as hepatitis B or C, tuberculosis, or syphilis, and may worsen these infections. Tuberculosis, in the presence HIV coinfection, can be difficult to diagnose. The presence of syphilis increases the risk of HIV infection.[9]

Immunocompromised AIDS patients are also prone to developing various types of unusual tumors, most notably Kaposi's sarcoma, a malignant form of vascular tumor, and lymphoma. These lymphomas frequently appear in unconventional extra-nodal sites, such as the central nervous system and the body cavity.

Anti-HIV medications have developed and evolved at an amazingly rapid pace. In the quarter-century since the discovery of nucleoside reverse transcriptase inhibitors (NRTIs), and azidothymidine (AZT) in 1990, more than 30 drugs in five different classes have been developed, tested and approved for use. The enzyme reverse transcriptase of the HIV virus is often capable of causing mutation by making changes in the viral genome, allowing it to evade the immune system or to develop