
Preface

The idea for this book came from a class that I taught at Indiana University in the years 2005–2008. The class, “Viruses and human history: the effect of viruses on human society,” was intended for freshman non-biology majors, and fulfilled a science requirement. Michael Oldstone’s *Viruses, Plagues and History* was the assigned text. Although I considered this an excellent text, some students (specifically those with no science background) found it difficult and too detailed. I initially introduced material on molecular biology, including nucleic acid structure and protein structure as simply as I could in class, but since a proportion of the students were from the business or music school, this, too, proved too difficult. In addition, many students had no chemistry background. I therefore taught the course with minimal references to Molecular biology and chemistry—a difficult task for someone who had taught both graduate and undergraduate courses to virology majors for many years. I have used the same approach in this book—a minimal amount of chemistry—but I do describe viral structure and viral cell interaction.

I had originally thought of dividing the book into three segments: past, present and future. The “future” would not be predictions of new epidemics, rather the use of viruses as tools to cure disease, viral vectors carrying genes to cure genetic diseases, viral treatment of tumors (viral oncolysis), and phage therapy against antibiotic-resistant bacteria. However the “past” and “present” are difficult to separate. What is past in the USA and the Western World is unfortunately present in the Third World. The development of vaccines has eliminated most common childhood diseases in “our world,” but there are still millions dying from these diseases in Africa and parts of Asia. We have conquered smallpox, and almost wiped out polio, but millions are still dying from diseases such as measles, hepatitis A, hepatitis B and other viruses in the rest of the world.

In the course of my research for this book, I was struck by the effect of infectious disease on armies and military campaigns. This should not have come as a surprise, since in the military, the conditions are such that hundreds of thousands of men live together, in crowded barracks with little sanitation. Not only did smallpox interfere with military campaigns during the American War of

Independence and the American Civil War, but other diseases—measles, yellow fever, and hepatitis A (jaundice)—affected the military during World War II. One historian claims that jaundice forced the U.S. to alter its plans for D-Day. The great influenza epidemic of 1918 spread due to the proximity of soldiers to each other in the trenches, and, as pointed out by Sir Martin Gilbert, by the celebrations that accompanied the victory at the end of the war see <http://virus.stanford.edu/uda/> and Martin Gilbert.

The introductory chapter covers the development of the germ theory and history of infectious disease until the early 1900s. Viruses were elusive, unseen and “imaginary” entities. Chapters on the history of virology follow it in more detail, as do the development of cell culture (without which modern virology would not exist), the discovery of bacteriophage, and the immense contribution such organisms made to molecular biology. There is also a brief history of immunology.

This last chapter was one of the hardest to write, since modern immunology is unbelievably complex, and in order to understand it one needs knowledge of cell biology, signaling mechanism, the functions of various types of cells, biochemistry, etc. I have concentrated on the early history of the events leading to clonal selection of antibodies by going back to the original literature. Discussed, albeit briefly, are the roles of each of the immune cell types, as they are known today. It is possible that within 2 or 3 years additional immune cells and cytokines will be discovered by immunologists. Although interferon is now considered to be one of many cytokines produced by the body as a component of the immune system, it has played a prominent role in the history of virology and the direction that viral research has taken. Interferon biology was an area of research that I have been active in for some 25 years; once predicted as a “cure” for virus infections, this expectation unfortunately has not been realized.

Likewise, viruses, for a considerable time during my own career, were thought to be the causative agent of most cancers. Extensive research was done connecting cancer and viruses, and many Nobel Prizes were awarded for this work. However, although most viruses are not directly connected, the oncogene theory and mutational basis of cancer arose from this research. For this reason, I have included a chapter on viruses and cancer, and of course there are viruses that *do* cause cancer, such as Epstein-Barr, hepatitis B and C, retroviruses and papilloma—all of which are discussed in separate chapters.

Continuing sequentially, I have described in some detail the history of smallpox epidemics and its impact on society; the story of yellow fever and its profound effect on American history; polio—a disease of the affluent as well as the poor; herpes viruses and hepatitis viruses, both of which are modern-day scourges; and the great influenza epidemic with the amazing story of how this virus was reconstructed after 75 years.

I have attempted to bring the HIV and AIDS story up to date and present the current situation. Much of it is troubling, with society biases, problems with blood supplies, and denial by scientists as well as government bodies of the connection between HIV and AIDS—and the personal arguments over the discovery of HIV.

However, there is a bright side to the AIDS story, in that thanks to modern-day medications, although expensive, AIDS is no longer a fatal disease.

Under emerging viruses, I discuss those viruses that are relatively new to man. They are not “new” viruses appearing out of nowhere; rather, they are viruses of other animals—usually bats—that accidentally infect man. They are only new in the sense that man has become an accidental victim and host by encroaching on new territory and, in some cases, altering the environment.

It is impossible in a text of this kind to cover all the classes of viruses. I have selected those viruses where there is an interesting story attached to their discovery or vaccine development, with all of them having caused immense suffering at one time. I have also confined myself to viruses that attack man, and not other vertebrates, fish, or plants. I have included bacterial viruses, since their discovery led to the molecular biology revolution.

One of the most successful chapters in human history has been the development of vaccines against most childhood illnesses. New vaccines are being introduced and licensed in the U.S. and subsequently in the rest of the world at a surprisingly high pace. In my own lifetime, vaccines have been introduced for all the childhood illnesses I was aware of while growing up: measles, chickenpox, mumps, whooping cough, and diphtheria, to list just a few. Within the last few years, vaccines have been developed against hepatitis A, hepatitis B, and papilloma viruses. With the advent of commercially available, cheap nucleic acid synthesis and sequencing and the technological know-how of synthesizing a virus in vitro, it should be possible to develop vaccines, either killed or attenuated against most viral infections.

As to the future, viruses are now being clinically tested in the U.S., U.K., and China as tools against deadly cancers. Brain tumors are among the most untreatable cancers, and a positive diagnosis of such is a death sentence. Today, adenovirus and herpesvirus vectors are being used as a mode of treatment in China and are being tested elsewhere. Viral treatment does not have the side effects found with radiation therapy or chemotherapy, and initial results look promising. I have delved into the background of viral oncolysis, an old idea that is now at the forefront of research. Another old idea being revisited is that of phage therapy, selecting bacteriophage to target specific antibiotic-resistant strains of bacteria, or using bacteriophage in the food industry to destroy salmonella contaminants. The history of d’Herelle and phage therapy is a fascinating one, and has been told in detail in two publications; Summers WC: *Felix d’Herelle and the Origins of Molecular Biology*, Yale University Press, 1999, and Hausler T: *Viruses versus Superbugs*, Macmillan, 2006. I cover this history only briefly here, and I recommend these texts for more details.

In the future we will see more and more viruses being constructed outside the cell, either being made in cell-free solutions or by adding DNA to cells in culture. A dangerous aspect of this research is the alteration of a wide range of viruses, which is a daring experiment and will lead to publication, but may be hazardous to the public.

Finally, I close with a chapter on biological weapons. Again, this is not a new topic, since man has always looked for the most efficient way to kill other humans. In the twentieth century this was developed to perfection with the atom bomb, gas chambers, and the development of tons of smallpox ready to be used in a global war. Luckily, this last never happened.

In most cases, I have gone to the available primary literature. This book would have been much more difficult to write had it not been for the Internet and access to information on Wikipedia, the Centers for Disease Control (CDC), and the World Health Organization (WHO). All three of these Internet sites have astonishing amounts of information; wherever possible, I checked their facts against primary sources.

This book is being written in a new era of information technology. In earlier days, I would have spent my time in the library looking for material among the stacks. In other times, I would have traveled to museums and repositories to search for archival material. With the availability of various search engines and access to downloading from the Indiana University Library, I have been able to write this book from home. The Indiana University Library has to be commended for easy access to most journals, and to the ease of obtaining books through interlibrary loans; even the rarest material is available.

I wish to thank those who spent time reading and reviewing a few chapters; they include Dr. Maurizio Mirolli, Professor Emeritus of the IU Medical Sciences program, and my colleague Dr. Pranav Danthi, friends Phyllis Guskin, Laura Kao, and Luca Peragallo. I would also like to thank all those who gave permission to use their illustrations, many of which are on the Internet. I also thank my wife, Mimi, for her patience in spending time at home while I was writing, for putting up with my occasional frustrations, and for her encouragement to complete the book.

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