Influenza
Influenza

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This book is dedicated to the memory of Frank L. Horsfall, Jr., mentor and friend, in whose laboratory at the Rockefeller Institute for Medical Research I first met the virus of influenza and learned the methods of quantitative biology.
Preface

My lifetime encompasses the postwar subsidence in the early 1920s of the greatest influenza pandemic in history, direct encounters with FM1 virus at Fort Monmouth in 1947, the care of influenza patients in the 1950s, the pursuit of the influenza virus through the modern pandemics of 1957 and 1968, and a present in which the genes of the virus have dissembled in the DNA of vaccinia virus and Escherichia coli through the wand of "high tech."

If my corpus could be fossilized for archival and archaeological purposes, it would be found to contain immune cells branded with the imprint of the "swine" influenza virus of post-1918 and brain cells no less imprinted with memories of the abortive return of its descendant during America's bicentennial. But before that unlikely event, I wanted to try to make some sense out of this baffling disease and its viruses—expecting no definitive revelations but hoping for a sharper definition of problems. Hence this book.

It is an audacious act in these days of specialization to essay a book such as this singlehandedly, but I have done so for selfish reasons. I wanted to reexamine old questions about the nature of influenza and its epidemics in the light of the dazzling advances in molecular biology of the past few years. No virus has been better studied, but few diseases are less well understood. The influenza virus glycoproteins have become models for biologists interested in membrane assembly and function; knowledge of their tertiary (and even quaternary) structure surpasses that available for most other proteins. The rapidly mutating RNAs of influenza virus have captured the interest and fired the imagination of evolutionary geneticists. Cellular immunologists have discovered this enveloped virus and, in collaboration with molecular geneticists, have studied the recognition of single viral proteins introduced by cloning vectors.

I marvel, properly, at all this activity and applaud it, but the physician in me asks, what about influenza? What about the disease? At this time, after a professional lifetime of laboratory investigations and 2 years of intensive scholarship, I cannot tell you why people get sick with influenza or how they do. How this elegantly characterized virus causes aches and pains and fever is simply not understood. Nor do we fully comprehend viral virulence or the genesis of pandemics. But we shall. The only prophecy that I dare to make is that we are on the threshold of deep insights into pathogenesis that will come from the convergence of presently parallel studies of the molecules of both virus and host. I hope
That this book can expedite this convergence by illuminating gray areas and drawing attention to studies outside the mainstream of virology.

One day we shall "see influenza plain."

Edwin D. Kilbourne

New York
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I take pleasure in acknowledging the unfailing generosity of colleagues throughout the world who have shared their research findings with me in advance of publication. They include the following, none of whom should be held responsible for my interpretation of their work:


I am deeply indebted to Marilyn Tartaglia for her dedicated and tireless efforts in the preparation of the major portion of this manuscript and to Valerie M. Josephson, whose editorial skills facilitated its completion.

E.D.K.
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INTRODUCTION

Because influenza is defined as much by its epidemiology as by its symptomatology, and because its causative virus rapidly and progressively changes, historical considerations are uniquely important in defining and evaluating this disease. The continual antigenic evolution of the virus is soon followed by specific and reciprocal changes in the immune status of infected human populations so that the pattern of influenza each year or decade reflects the experience of the community during the preceding one.

THE CREDIBILITY OF HISTORICAL EVIDENCE

As we probe, still, at the terminus of the 20th century, for the origin of pandemics, we seek answers to many of the same questions raised in earlier centuries about meteorological conditions, disease outbreaks in animals, and other associated natural phenomenon. But the credibility of historical records is, in general, inversely proportional to their antiquity. With influenza, remote observations are clouded not only by temporal distance but by a background of poxes, murrains, plagues, agues, pestilence, and famine that often obscured the perception of influenza as a distinct and specific entity. To make matters worse, reliable chroniclers of disease seem to have been few, so that one is often left at the mercy of inept or imaginative observers. Then, too, influenza lacks the patho-