THE ETIOLOGY AND EPIDEMIOLOGY OF INFLUENZA

HANS ZINSSER

New York

TABLE OF CONTENTS

Introduction.....	213
Historical résumé.....	215
Clinical course of influenza.....	217
Etiology of influenza.....	223
Former epidemics.....	223
Carriers.....	230
Recent epidemic of 1918.....	232
The bearing of serological evidence on etiology.....	247
Vaccination.....	251
Inoculation experiments.....	253
Filtrable virus.....	258
Summary.....	264
Epidemiology of influenza.....	268
Former epidemics.....	268
Manner of transmission of influenza.....	271
Onset of epidemics of influenza.....	277
Secondary outbreaks.....	280
The origin of epidemics of influenza, with particular reference to the origin and course of the last pandemic outbreak.....	285
Course of the pandemic of 1918.....	291
The problem of immunity in influenza.....	296
Fluctuations of virulence, and epidemiology.....	299
Summary.....	303
References.....	304

INTRODUCTION

The etiological and epidemiological problems of no disease can be intelligently discussed until we can precede discussion with a clear cut definition of the disease itself. In infectious diseases like smallpox, scarlet fever, measles, diphtheria, and pneumonia, investigation is sure to deal with a material which is amenable to reliable selection on clinical grounds. In the case of influenza it is the difficulty of sharply defining the disease, which has been, and still is, at the bottom of the confusion prevailing in research. Whenever widespread epidemics

of so-called "catarrhal fever" have swept over large sections of the world, the epidemic characteristics in themselves, as well as a certain regularity of onset, sequence and similarity of course, have sufficiently indicated the basic identity of the cases. It has been clearly recognized, however, that except at the very beginnings of every epidemic, clinical manifestations have been dominated by the complications, rather than by the original infection. And these complications, in their localizations, pathology and bacteriology have been subject to wide variations. For these reasons the diagnosis of influenza made upon isolated cases of respiratory infection at times when no epidemic prevailed, has been admittedly more a clinical surmise than a scientifically formulated conclusion. This has been clear to well trained physicians for many years, and the term "influenza" has been used by them during interepidemic periods as a term of clinical convenience, to characterize conditions ranging in seriousness from severe coryza, with systemic symptoms, to fatal lobular pneumonia. It may well be that many of these cases have had a specific influenzal basis, and represent the smouldering embers from which the flames of new epidemics are lighted, but there is no way at the present time of being sure of this in individual cases.

It would be a relatively simple matter if we could base the diagnosis of true influenza upon the isolation of Pfeiffer bacilli, just as we determine the diagnosis of diphtheria by the isolation of the Klebbs-Loeffler bacillus. But for reasons which will become clear presently, this cannot be done. For, even through the Pfeiffer bacillus should eventually prove to be the specific etiological factor in influenza, it is still so frequent as a complicating agent in other respiratory infections, or perhaps as a symbiant in the upper air passages of normal individuals, that its mere presence in the secretions of a catarrhally inflamed mucosa, does not characterize the infection etiologically.

The relationship of this bacillus to the disease presents a problem of great complexity and of many uncertainties which will be discussed more extensively below. Before we can proceed to this, however, it will be necessary to specify more precisely just what we believe should be the proper characterization of uncomplicated influenza in a clinical sense. For unless this is clear it will be impossible to determine

whether bacteriological or other etiological investigations have dealt with the disease itself or with one or another of the manifold complications.

HISTORICAL RÉSUMÉ

In the older works many accurate descriptions of uncomplicated influenza are available. Huxham writing of the epidemic which occurred in Plymouth in the first half of the eighteenth century, describes the disease as one of very sudden onset, chilliness and fever, usually lasting about four days, and rarely ending fatally. He mentions catarrhal inflammations of the nose and throat, and the frequent occurrence later in the disease, of a cough, but lays stress not upon these catarrhal symptoms, but rather upon the suddenness of onset, the fever, the short duration and the low mortality. Arbuthnot in 1732 speaks of a remarkable uniformity of symptoms, "a small rigor or chilliness, succeeded with fever of a duration seldom above three days." He says, "this disease was not in itself mortal, but it swept away a great many of poor, old and consumptive people." Thompson in his *Annals of Influenza* (London, 1852) summarizes the clinical manifestations by laying stress upon the sudden feverish onset, chilliness, and pains in the neck, back and loins, suffusion of the eyes; coryza and bronchitis are mentioned as later developments. Most of these writers, more especially Thompson, recognized the inflammations of the bronchi, pleura, and lungs as probable complications frequently present, but not as uniformly characteristic as the fever, pains, and the prostration which was often extreme without sufficient apparent reason in any discoverable lesions. It is interesting to note that these early writers described an intestinal form. Thompson speaks of it as follows: "When the lungs are not materially affected, the force of the morbid influence is in some instances directed to the bowels, producing pain and tenderness of the abdomen, and diarrhea, with mucous or dysenteric evacuations."

Leichtenstern described "typical influenza" as follows (we translate literally):

Typical influenza consists in a sudden fever which is initiated by a chill or frequent chilly sensations, and lasts from one to several days, is associated with severe headache, especially in the frontal regions, vertigo, pain in the