JAMA Revisited

November 4, 1922

Experimental Epidemiology

Sydenham defined disease as “an effort of Nature, striving with all her might to restore the patient by the elimination of morbibic matter,” an implication of the modern idea of disease as a struggle for existence between invading microorganisms and those factors residing in the body which make for immunity. The development of bacteriology emphasized the desirability of keeping the harmful germs away from the individual—of preventing disease by eliminating or restrain- ing its causative agents. The accomplishments of public hygiene in this direction have undoubtedly been most significant; yet the hopes of many health officials have been somewhat disappointed because infectious ailments have not been eliminated in civilized communities. They have failed, however, to reckon with the innumerable unknown modes of invasion. Thus, the menace of the healthy carrier of infectious micro-organisms was scarcely recognized a generation ago; and, year by year, new sources of bacterial danger are being brought to notice. The great epidemics of meningitis or cerebrospinal fever, poliomyelitis, influenza and epidemic encephalitis, ravaging even the countries in which the medical sciences and protective arts have been most assiduously cultivated, have brought discouragement to many.

One outcome of the modern development of epidemiology has been to direct greater attention to the individual himself. It has become clearer that if his microbial enemies cannot be kept away successfully, he himself must be better prepared to cope with them. Thus, the study of artificial, acquired immunity is being fostered in increasing measure. Garrison1 has remarked that opinion is divided between those who maintain that the prevention of disease and mortality rests mainly with the individual, and those who believe that cau- sation and prevention are multiplex and largely external to the individual; so, in the infantile science of epidemiology, just emerging from the descriptive stage, he adds, there are already two schools, one relying on the bacterial theory of in- fection for its data, and one, headed by Crookshank, harking back to the Sydenham doctrine of epidemic constitutions, family relationships between diseases, and external (cosmic and telluric) phenomena as contributory causes of epidemics.

Flexner2 likewise has discovered a reaction in certain quarters against the teachings of modern bacteriologic epidemiology. That this return to older, and as it must seem, more mys- tical doctrines is widespread cannot be affirmed, he concludes, but it has even happened that in the effort to elucidate the epidemic prevalences of the last two decades already enumerated and eventuating in the colossal outbreak of influenza, the notions of epidemic constitutions as defined by Hippocrates, and especially by Sydenham, have been more or less sported with, if not actually invoked. Flexner contends that the way to the understanding of the enormous complexity of interre- lation between microbe and host and their reaction on each other is not through a return to the “indefinite concepts of epi- demic constitutions” but through further investigation of the phenomena out of which a real science of epidemiology can finally be built.

Accordingly, he has fostered an elaborate experimental study of epidemic outbursts of disease among colonies of animals under conditions of control not attainable with man. The earliest of these novel researches relate to a gastro- intestinal infection in mice. They have already shown that not only do specific differences exist among so-called mouse typhoid bacilli, but all the pathogenic varieties appear ex- tremely labile. Strains of the bacilli artificially enhanced as they pass from mice to mice quickly fall to an average of infectiv- ity and are, as it seems, at low pathogenic ebbs at the time of the death of the infected animals. But this ability of the bacilli is determined, in part, by the hosts; that is, the mice through which they pass. In this respect, mice may be viewed as consisting of different biologic classes according as they re- spond to ingestion of the bacilli with infection and death, with mere carriage of the bacilli, or with nonreactability. The dis- tinctions of classes are not, however, absolute, but are deter- mined, partly at least, by the quantity of dosage of the bacilli. It is the latter factor which plays so conspicuous a part in the phenomenon of recurrent epidemic waves superinduced by the introduction of new mice in the replacement experi- ments described. While it is the “carrier” among the old mice which provides the “seed” for the next following epidemic outbursts, it is the highly susceptible individuals among the new which furnish the living “culture” medium enabling rapid increase and wide dissemination of the bacilli to be effected, just as it is the succumbing and nonreactable mice which check the growth and multiplication that tend to arrest the epi- demic spread. The outcome of these studies, in which Amoss3 has collaborated, will be awaited with interest. The demon- stration, already accomplished, of the rôle of the influx of new uninfected population in maintaining epidemic waves is it- self of the foremost significance.
