EPIDEMIOLOGY BIBIORICAL AND EXPERIMENTAL

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EPIDEMIOLOGY:

HISTORICAL AND EXPERIMENTAL

The Herter Lectures for 1931

BY

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To Maud and Raymond Pearl

In grateful memory of December 2nd–10th, 1931

PREFACE

In 1931 the Herter Lectureship Committee of Johns Hopkins University did me the great honour of choosing me to give the 20th course of lectures on the Herter Foundation. Some of my kind hosts expressed a wish that the lectures might be made into a small book and, since this would provide me with a tangible souvenir of one of the pleasantest experiences of my life, I have done as they advised.

The only substantial changes from the spoken word occur in the first lecture, which has been expanded by, perhaps, a quarter. I have long been convinced not only that the history of ideas is an essential part of the education of both public health officers and laboratory workers, but that we must try to study the ideas of our predecessors sympathetically. Because some remote predecessor held opinions very different from ours, it does not follow that his work was unimportant, while to have anticipated some doctrine now held to be true is not a proof of greatness. Hence I have devoted almost as much space to what is, formally, an introduction to my subject as to the subject itself. The kindness of the audience makes me hope that this does not need an apology.

Major Greenwood.

January 1932.

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may be more effective than selection although the evidence is not conclusive. The limitations of artificial pre-immunisation as a means of controlling a herd sickness. Proof that pre-immunised animals suffer a lower mortality than non-immunes, but that in a herd recruited wholly from pre-immunised animals the disease does not die out. Pre-immunisation an invaluable means of reducing the mortality of persons exposed for a short time to great risks, but not a substitute for environmental betterment. Reasons for thinking that in virus as distinct from bacterial diseases active immunisation may be an effective prophylaxis.

FIRST LECTURE

I

It is, I know, deemed a mere formula of good manners when one on whom a great honour has been conferred acknowledges his unworthiness. I can hardly expect you to believe that, making the confession, I mean more than others similarly placed, more than the really distinguished men who have preceded me here, meant. Yet I do ask you to believe that I mean something more than politeness. Partly from peculiarities of temperament, partly from other circumstances beyond my control, my scientific work has been concerned with problems on the borderland of different wellsettled scientific territories; I have never been able to feel, not even when I was much younger than I am, that I was a master of any one scientific technique, that I was anything but a more or less intelligent amateur. This confession may move you to judge me with a forbearance of which my predecessors had no need.

For nearly a quarter of a century I have given particular attention to the measurement of biological events, to biometry, more particularly to that subdivision of biometry which is concerned with disease. Although I have no special aptitude for mathematical investigation and no claim to the title of mathematician I was, like Raymond Pearl, trained by the greatest teacher of mathematical statistics of our generation and thus acquired a technique which, among clinicians or laboratory workers, passes for mathematical. Hence, it has long been part of my business to consider those problems of collective morbidity and mortality which

the medical profession thought suitable for arithmetical treatment, epidemics and pandemics. During the last ten years it has been my privilege to be associated with a bacteriological friend and colleague; together we have sought to create a microcosm, the happenings within which we could study in more detail than those of the macrocosm to which we belong because the working of this microcosm was to some extent under our control.

The purpose of these lectures is to confess to my colleagues how far the experiences of these later years have modified the opinions I had formed from such study of human experience as I had lived long enough to undertake. But, while much that I have to say will have reference to these studies of the past few years I desire to take as my motto, as the text of these sermons, the motto which Haeser chose from Hippocrates for the title page of that history which has not yet been superseded—"But medicine has long had all its means to hand and has acquired both a principle and a method through which the discoveries made during a long period are many and excellent while full discoveries will be made if the enquirer be competent, conduct his researches with knowledge of the discoveries already made and make them his starting point. But anyone who, casting aside and rejecting all these means, attempts to conduct research in any other way or after another fashion, and asserts that he has found out anything, both deceives and is deceived. The thing is impossible."

Epidemiology, the mass aspects of disease, where not the sick individual but the group, the herd, is the unit of observation, is a very old subject of inquiry; it has interested most of the great physicians from the dawn of knowledge to now. He who neglects the teaching of

their experience, who despises even the errors of the past is in truth deceiving and deceived; not less than he who, sneering at the technique of his contemporaries and affecting the rôle of scholarly philosopher, supposes that the writings of a past age, the work of men whose intellectual background is unfamiliar to him, whose very language he has never mastered, render modern laboratory investigations superfluous. No one here is likely to make the latter mistake, and, lecturing in one of the few great Universities where the history of medicine is seriously studied. it is perhaps superfluous to caution you against the former one. I think, however, it is necessary, in order to determine what can and what cannot be expected of experimental epidemiology, to emphasise facts which human experience has revealed, facts which, if irreconciliable with apparent deductions from experimental study show that those deductions must be erroneous: in other words, to outline the history of epidemiological teaching.

Scientific epidemiology, the observation of the phenomena of mass disease by men who believed that these were ordered phenomena, not capricious workings of some arbitrary supernatural power, began, like almost everything which makes life worth living, in Ancient Greece.

Hippocrates (1)* in the first and third books of *Epidemics* and in the notebook called *Airs, Waters and Places*, gave us examples of the inductive method of studying herd sickness which, had they been sedulously copied, might have brought us to a knowledge of some truths hundreds of years sooner. It may be, as Celsus (2) implies, that the method was followed, but only

^{*}Throughout this book numbers in brackets refer to the notes placed at the end of each of the chapters.

by a school of physicians whose works have perished and whose doctrines are chiefly known to us through the writings of their bitterest enemy, a sect whose very name, empiric, has become a by-word. The explanation of this tragedy, for it was a tragedy, is simple, it was due to a defect of the quality to which we owe the existence of science. The Greeks of the great age had that intellectual courage which persuaded them, in an age when hardly any exact data of observation existed, when man was a prey of irrational fears, that the world-order could be grasped by the intellect of man. That courage enabled them to make a beginning; it is not strange that they who achieved so much by sheer force of intelligence, should have over-rated the potentialities of mere intellect and come to believe that the laborious compilation of particulars, the addition of one to one of Browning's low man, was unnecessary. Already, in the Hippocratic corpus, even in the particular "genuine" works I have mentioned, there is a good deal of pure speculation. and, as time passed, the ratio of theoretical explanation to objective observation grew, until in the Hellenistic age it dominated the whole field. Five hundred years after Hippocrates, another man of Greek culture. a man with far greater opportunities of carrying out the inductive scheme of the *Epidemics* than Hippocrates had had, declined the task. Instead, he put together the fragments of theory, building an edifice which commanded the admiration of all educated men for more than a thousand years. It is in ruins now, but even the ruins are imposing and a great many modern builders who speak of Galen with an ignorant contempt have used unwittingly many of his bricks, often some of the worst.

One of these days, Galen's writings will be made as accessible as the Hippocratic collection. At present most of them, and all which are of primary epidemiological interest, are only available in a-as I am told. by those competent to judge-poor text, and bad-as I can certify—Latin translation. Yet, even through this linguistic fog, they can be recognized as the production of a powerful intelligence, of a mind ranking very high among those of the second order. As mere belles lettres, the works of Galen are not to be despised. It has been said that the Hellenistic writers were mere logic choppers, cock-sure folk with no sense of that reverence before the unknown which characterised the great Hippocrates. Yet Galen can reprove a too confident author in these terms: "But they are both mistaken. In one way, both equally, because they have presumed to draw a general conclusion from a particular example. Secondly because they do not remember the creative power of nature which shapes parts according to the traits of the mind. Aristotle. dealing with this very subject, wondered whether there were not a beginning more divine, something greater than just heat and cold and moist and dry. Wherefore I think it wrong of men to draw such rash conclusions in matters so great and assign to the qualities alone the power of shaping the parts. It is possible that these are nothing more than the instruments and something else the master-hand." (De Temperamentis II, 6.) Hardly the language of a mere logic-chopper! Of wit, or at least sarcasm, there is enough to make the fortune of a modern controversialist-"Such are the opinions of Sabinus and his school, persons who invent improbable explanations of events which do not happen"! How many reviewers of modern medical papers would like to express their judgments as succinctly.

Fundamentally Galen's epidemiological doctrine is logical and self consistent (3). He held that the generation of a herd sickness depended upon the interplay of three sets of factors. (a) An atmospheric factor, the katastasis; (b) An internal factor, the crasis; (c) A predisposing or procatarctic factor. By the katastasis he understands what we should call the specific factor, by the crasis what we should call the natural susceptibility of the herd and its members, by the predisposing factors what we still call predisposing factors, viz. eating and drinking, manner of life, and he is of opinion that the crasis and procatarctic factors determine the severity of a herd illness. Given a particular katastasis an epidemic must arise but whether it shall be great or small depends upon the condition of the exposed to risk, their innate character (the crasis) (4) their habits of life (the procatarctic factor). But if we include in the first group the biological materies morbi, which was not recognised as a separate factor before the time of Fracastorius, then Galen's doctrine does not differ from that of the leading American experimental epidemiologist. Dr. Webster. Indeed it is really only the unanalysed conception of the atmospheric katastasis, leading to the miasmatic doctrine of herd sickness, which we are justified in rejecting as wholly obsolete.

II

To the Semites who took over the torch of science from the feeble grasp of the Byzantine Greeks, we owe valuable observations of herd sickness, particularly to those Persian writers who used the Arabic language and are known to us as Rhazes and Avicenna, but they

adopted without essential modification Galen's theoretical schema. From the time of Galen to that of Fracastorius (4) hardly any progress was made in the study of general epidemiology. Fracastorius first clearly stated the principle of contagium vivum, a conception wholly different from that of the contagion of the Greek and Arabist writers since it involved the notion of something living and reproducing itself. Yet although we should pay honour to the genius of Fracastorius, we should not over-rate his historical importance. He himself did not push his idea to its logical conclusion or maintain that an infective principle was an essential link in the chain of epidemiological causation. His immediate influence on epidemiological thought was small and the modern history of epidemiology really began with an attempt to follow in the footsteps of Hippocrates. Two names are associated with this attempt in our memories, Baillou, or Ballonius, and Sydenham.

Ballonius conscientiously tried to do in Paris what Hippocrates did on the island of Thasos and a reader of his book (5) sees the difficulties of the undertaking much more clearly than in Hippocrates' essay. Some readers of Hippocrates have been repelled by a certain inhumanity—as it seems—a cold bloodedness in the method of description of the lives and deaths of named men and women whom the author knew, perhaps treated. As a criticism of Hippocrates the physician this is, as Littré remarked, incomplete and unjust: still any reader will recognise its basis. Ballonius at least could not forget that his patients were men and women and in reading his much fuller chronicle we do often lose sight of, and interest in, the wood for the sake of its trees.

The fame of Sydenham has overshadowed that of Ballonius, his reputation as a pioneer of epidemiology is far the greater, unreasonably so, I believe; a confession I make the more freely because I am one of the many minor authors who have exaggerated his epidemiological merits (6). Of course I am speaking of Sydenham as an epidemiologist, his claims to reverence as a physician have been acknowledged by those who are competent judges, both contemporaries and successors; his merits as a clinician not as an epidemiologist justify the honourable title of English Hippocrates. Sydenham was bitterly opposed to what he conceived to be the Galenical doctrine; he attached hardly any importance to two of Galen's factors, that of the innate crasis and that of procatarctic causes, and exalted the other factor, the katastasis, into omnipotence while divesting it of any merely meteorological significance. For him some mysterious terrestrial or cosmic determinants of an epidemic constitution were all in all. To these was due the alleged fact that all acute illnesses prevalent in a particular cycle bore a common stamp, so that "the aforesaid species of disease, in particular the continued fevers, may vary so enormously that you may kill your patient at the end of the year by the method which cured sufferers at the beginning of it". "This", he says, "is the state of the case. There are different constitutions of years due to some hidden inexplicable change in the bowels of the earth when the air is contaminated by such effluvia as predispose and determine the bodies of men towards some disease or other; heat or cold, dryness or moisture, are not the causes; this state of affairs endures so long as the particular constitution is dominant and then yields its place to another. Each of these constitutions is characterised by a particular kind of fever,

not seen under other circumstances, and fevers of this class I term Stationaries." Med. Obs. I ii 5.) Sydenham's able young contemporary Freind (7) pointed out that this doctrine that the continued fevers of different epidemic constitutions needed wholly different treatment, had no apparent influence on Sydenham's clinical practice, that Sydenham seems always to have treated continued fevers in the same way, whatever the prevalent epidemic constitution. In the controversy between those two able epidemiologists Sir William Hamer (8) and Dr. E. W. Goodall (9), the one maintaining the other denying that modern experience confirms Sydenham's assertion that the epidemic "constitution" impresses a common character upon the illness of an epoch, my own judgment inclines very decidedly to the negative side. Even the ingenious simile I have heard Dr. Crookshank use, that the admitted differences between the vintages of the same wine in different years illustrate the notion, does not satisfy me. Sydenham would lead us to require not only that the port of 1887 should be different from the port of 1889 but that all the wines of 1887 should be more like one another than the port of 1887 is like the port of 1889.

Hence, as I think, Sydenham's general theory is of little value. But that does not mean he had nothing to teach us. What was fruitful and just was his conception of an epidemic succession, which if present in the minds of his predecessors, was never so forcibly and even magnificently expressed as by him.

We all remember with admiration his comparison of the rise, decline and fall of epidemics to that of empires. His prediction that such diseases as plague and smallpox, which were of primary epidemiological interest in his generation might lose all interest and be succeeded by illnesses which he never knew. We may be unable to accept the very wide generalisations of Hamer, that learned and loving disciple of Sydenham, and yet agree that he and Crookshank (10) have established their case that between unusual outbreaks of illnesses where the clinical feature is involvement of the nervous system and pandemic influenza, there exists not a pathological bond in the narrow sense but an epidemiological affinity as, perhaps, Sydenham surmised. Still, one cannot say that Sydenham or his disciples really brought us nearer to an understanding of the general principles of epidemiology than Galen had done.

Indeed, as I think, such increase of knowledge of epidemiology as was effected in the century and a half which separate Sydenham from the epoch to which we belong—our age began in the third decade of the 19th century—was gained by methods which he ignored or disdained.

Contemporary with Sydenham was a London tradesman, one John Graunt (11). Graunt was not a physician, he was not, in the conventional sense of the phrase, an educated man at all. Haeser who devotes twenty pages to Sydenham does not even mention Graunt. Yet Graunt, who would have been perplexed if anybody had suggested to him that his work was of epidemiological importance, has, in my opinion, a much more substantial claim to the title of father of modern epidemiology than ever Sydenham had. Of course I know I shall be reminded of Falstaff's tailor's unwillingness to accept Bardolph as a surety, and told that, since everybody-except, perhaps, the Marquis of Lansdowne, who suspects that his famous ancestor wrote Graunt's book (12)—acknowledges that Graunt was the father of vital statistics, a professor of vital statistics has a trade bias. It may be so. I am firmly con-