

EXPERIMENTAL EPIDEMIOLOGY.

By

M. Greenwood etc.

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# MEDICAL RESEARCH COUNCIL

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LONDON

HIS MAJESTY'S STATIONERY OFFICE

1936

Universal Decimal Classification

616—036.22

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## PREFACE

It would be difficult to imagine a subject of study more important for human welfare than the spread of epidemic diseases among mankind. To this a noteworthy contribution has been made by Professor W. W. C. Topley and Professor M. Greenwood, with the assistance of colleagues, in experimental researches at the London School of Hygiene and Tropical Medicine. The cost of these necessarily prolonged investigations has been provided during a period of eighteen years by the Medical Research Council, who are now glad to issue this report dealing comprehensively with the whole scheme of work; many of the results on particular points have of course already been made known by preliminary publications in scientific journals.

The experimental method which the report describes was devised to solve a particular type of problem that has proved refractory to other forms of study. On the one hand, laboratory experiments, performed under strictly controlled conditions, have yielded a mass of information with regard to the response of the individual host to artificial infection, and as to methods by which that response may be modified. On the other hand, the data collected by the epidemiologist have taught much in regard to the behaviour of naturally infected herds, and something of the effect of interfering in the natural course of events, as for instance by prophylactic immunisation against small-pox, diphtheria or typhoid fever. The collection of statistical evidence under field conditions, however, is so beset with difficulties that the assessment of the relative importance of the interrelated factors, determining the course of events in infected communities or herds, has so far proved impossible.

It is to problems of this kind that the method of the experimental epidemic can be applied. Given that continued exposure to risk of infection raises the average resistance of the surviving members of a herd, whether by active immunisation or by selection of the innately more resistant animals, or by both mechanisms together, various questions arise. Is this increase so great that the infection will eventually die out, if none but uninfected immigrants are admitted to the herd? Is it possible by the active immunisation of all entrants to reduce mortality to zero, or eventually to eliminate the infecting organism by depriving it of access to susceptible hosts? If dietetic factors play a significant part in resistance to infection, is their influence so important that on an optimal diet animals will be indifferent, or relatively indifferent, to prolonged exposure to the risk of natural infection? If no single factor is found to exert a decisive effect, will it be possible to attain the desired level by combining several different methods of raising the average resistance of a herd?

To some of these questions the evidence set out in this report offers limited and tentative answers. The work should be regarded

however, as a preliminary survey of the field, rather than as an application of the technique to a well-defined series of problems. Experimental epidemiology has its own technical difficulties and limitations: these are discussed in some detail in Section I. Before one can assess the effect of any method of interference with the natural course of events, it is necessary to obtain an adequate picture of the behaviour of herds that are exposed, over prolonged periods, to the full risks of natural infection. Such a picture is outlined, for mouse typhoid and mouse pasteurellosis, in Sections II and III, and for a virus disease of mice—ectromelia—in Section IV.

The remaining sections are devoted to the influence on herd infection and herd resistance of variations in the virulence and infectivity of the infecting organism, of artificial immunisation of the animal hosts at risk, of changes in diet, of the presence of a bacteriophage, or of dispersal of an infected herd at different phases of the epidemic process. It is of some interest to note that the existence of "epidemic strains" of bacteria, which have been postulated by many epidemiological workers to explain happenings observed in the field, has been confirmed by these experimental studies, and that it has been possible to define certain of their properties.

None of the methods of interference so far attempted has sufficed to eliminate the risks of disease and death under the conditions of severe and continuous exposure to which the herds were subjected in most of the experiments under review. The most promising results were obtained in active immunisation against ectromelia. The negative findings must, of course, be regarded as applying only to the actual infective agents used and to the experimental conditions obtaining: this part of the inquiry is as yet in its infancy.

There can be little doubt that the experimental epidemic affords a more natural, and more severe, method of testing the value of any prophylactic procedure than assays carried out by more artificial tests on individual animals. It can never, of course, replace field observations made under completely natural conditions; but it may well indicate possible solutions to many of the more important practical problems, and so direct the field epidemiologist along the most fruitful lines of inquiry.

MEDICAL RESEARCH COUNCIL,  
38 Old Queen Street,  
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19th March, 1936.

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