A FURTHER CONTRIBUTION TO THE EXPERIMENTAL STUDY OF EPIDEMIOLOGY.

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(With Graphs I—X.)

CONTENTS.

I. Introduction.

In the Goulstonian Lectures, delivered in 1919, one of us (W. W. C. T.) discussed the possibility of attacking epidemiological problems by the method of direct experiment, and reported a few preliminary observations on the spread of enteric infection among mice. Since then a series of reports have been published dealing with the investigation of particular problems along these lines (Topley, 1921 *a* and *b*, 1922 *a* and *b*, 1923, Topley and Wilson, 1923 *a* and *b*, Topley and Ayrton, 1924 *a*, *b* and *c*, Topley, Ayrton and Lewis, 1924 *a* and *b*, Topley, Wilson and Lewis, 1925).

In 1922 appeared the first series of reports on an independent investigation, along similar lines, carried out at the Rockefeller Institute, New York, and this investigation has since been steadily pursued, by Webster and others, and is still continuing (Flexner, 1922, Lynch, 1924, Amoss, 1922 *a* and *b*, Webster, 1922 *a* and *b*, 1923 *a*, *b*, *c*, *d*, *e*, *f* and *g*, 1924 *a*, *b*, *c*, *d*, *e*, *f*, *g*, *h*, *i*, Pritchett, 1924). More recently Bloomfield and Felty have attempted to employ the experimental method in the study of the spread of infection, along somewhat different lines (Bloomfield and Felty, 1923, 1924, Felty and Bloomfield, 1924).

Neufeld (1924 *a*) has recently published a critical summary of the results so far obtained in this field, and his collaborators at the Robert Koch Institute in Berlin have dealt with closely related problems in a number of recent reports (Neufeld, 1924 *a*, *b* and *c*, Lange, 1921 and 1924, Lange and Yoshioka, 1924, Lange and Keschischian, 1924).

In the course of the investigations already reported in this *Journal*, and referred to above, it became obvious that many of the data collected would

be of a kind that would necessitate, for adequate treatment, the application of statistical methods. It was equally clear that, if any generalisation could be formulated on the basis of the experimental results obtained with a mouse-population, the applicability of such generalisations to epidemic disease in man could best be tested by the statistical analysis of the available data in human disease. The relations between statistical and experimental methods as instruments of research have recently been discussed by one of us elsewhere (Greenwood, 1924).

Co-operation along these lines has been rendered possible by the approval and assistance of the Section of Medical Statistics of the Ministry of Health, and of the Committee on Industrial Health Statistics of the Medical Research Council. This paper is therefore the product of a co-operative study; the authors named at the head are responsible for the form in which it is presented, but they fully recognise, and desire the readers to recognise, that a great part of the labour involved has been borne by their collaborators; on the experimental side by Dr G. S. Wilson, Mrs Joyce Wilson and Miss E. R. Lewis, and on the statistical side by Miss E. M. Newbold, Miss Thomas and Messrs Faning and Martin.

Although Neufeld's general summary mentioned above is an excellent account of the experimental studies published down to the middle of 1924, the reader who desires to preserve a just sense of proportion, to see these particular investigations in proper perspective, must have a knowledge of earlier epidemiological theory and practice which Neufeld assumes his reader to possess, but which can hardly be postulated of all whom an account of experimental, or even statistical, researches may be supposed to interest. On these grounds we have thought it desirable to write a somewhat longer introduction to this memoir than is usual in reporting current investigations. We cannot flatter ourselves that we have justly appraised the opinions and results of the earlier writers; many of their ideas are intrinsically difficult to grasp, and when it is a question of ascertaining the purport of a few pages or even sentences written hundreds or even thousands of years ago, it is obvious that only a width of culture and depth of historical scholarship far beyond our compass can ensure one against the risk of very serious misunderstanding. The risk must, however, be faced, because these older writers have powerfully influenced epidemiological opinion, and only when the gulf which divides the epidemiologist and the experimenter has been closed (it can only be closed by mutual comprehension) is a rational science of epidemiology attainable.

One of us (Greenwood, 1919) has pointed out that the business of an epidemiologist is to study disease as a mass phenomenon, the inter-relations of the external exciting, external predisposing and intrinsic causes of disease when not the individual but the herd is the unit of observation. If this contention be just, there is an epidemiology of all forms of sickness; but in practice, from the very earliest times, epidemiology has concerned itself with the phenomena of diseases not always ravaging or not always ravaging to the

same extent; the idea of *discontinuous* prevalence is at once called up in everyone's mind by the very word epidemic. To adapt a famous witticism, the contrast of a disease which affects all the people some of the time with a disease which affects some of the people all the time, is the contrast of an epidemic with an endemic. This antithesis is presented in the first collection of scientific writings on medicine, the Hippocratic corpus; Hippocrates sought to discover the factors which determined epidemicity, why such a disease broke out when it did and why cases of it had such and such clinical characters. He conceived that a principal factor was the katastasis or *constitution* of the atmosphere and endeavoured to correlate the clinical types of disease prevalent through a series of years with the conditions of the atmosphere; this was the origin of the theory of *Epidemic Constitutions*. Flexner (1922) has referred to the doctrine of *Epidemic*, or Medical, *Constitutions* as mystical. If by this adjective we are to understand "unintelligible" or "metaphysical," it is not applicable to the original use of the concept in the first and third books of *Epidemics* (Sticker, 1923), although it may justly be applied to scattered remarks in other books of the Hippocratic collection and to more recent lucubrations. Actually the design and to some extent the achievement of Hippocrates was to ascertain whether particular types of disease did become prevalent at particular seasons of the year and under particular meteorological conditions; his two slender volumes of records remained as an example of method, an example which for centuries found none to profit by it. What he began nobody has completed, perhaps, as we shall shortly suggest, because the task is impossible of achievement. Galen, whose direct influence has been far greater than that of Hippocrates, recorded no epidemiological observations but elaborated a theory of the way in which changes of the atmosphere generated epidemics, a theory the details of which, although intellectually interesting, are no longer of serious importance. He made, however, valuable contributions to the stock of ideas (Greenwood, 1921)—at least they would have been valuable if anybody had attended to them. He clearly apprehended that resistance to what we should call infection is innately variable, like any other biological character, and he distinguished accurately exciting from predisposing factors. No further contributions to our knowledge of epidemiology by the use of the Hippocratic method were made down to the sixteenth century; with some honourable exceptions, especially among physicians writing in Arabic—even faithful descriptions of particular epidemics are scanty. How the lack of a good *notation*, or method of description, cripples even an able man may be judged from such a book as that of the famous Dr Caius on the *English Sweat*. In the seventeenth century a really great clinician, Bailou, or Ballonius, resumed the Hippocratic task and attempted to do in Paris what Hippocrates attempted to do in Thasos. Although Ballonius has been described by a famous historian as a slavish adherent of the Galenical tradition, a reader of his book is likely to conclude that Ballonius was really less tendencious and more objective than Sydenham whose undoubted independence

of thought has been so widely praised. Ballonius quite obviously did attempt to record impartially and to collate clinical happenings and meteorological conditions, to define *real* epidemic constitutions. But he did not, we think, succeed. The modern cynic will say that was because epidemic constitutions are mythical, an explanation we hesitate to accept; a much simpler explanation is possible. Ballonius, like Hippocrates and Sydenham, was primarily a physician not an epidemiologist; the unit of the physician, as we have suggested, is a sick man, the unit of an epidemiologist is a herd, a group of men. It is very hard to see a group of people each of whom one knows intimately *as* a herd; just as, to quote William James, it is hard to judge what a language sounds like if one understands the words of that language. Some method, pre-eminently the statistical method, is required to cloak the humanity of the individuals of a herd before one can satisfactorily visualise the herd as distinct from the individuals composing it. The exposition of Ballonius is frequently interrupted by the discussion of individual cases; we do not think that the reader of his book will be able to flatter himself that he knows what the epidemic constitutions of Paris between 1565 and 1588 were, still less how they were engendered; but he will certainly have a vivid picture of the thoughts and feelings of a man of ability consciously grappling with intellectual difficulties.

The next great writer on the subject was Sydenham, and it is to Sydenham that the doctrine of epidemic constitutions as now accepted by those epidemiologists who do not consider the doctrine to be mythological, is usually attributed.

Sydenham's objective contribution is his study of epidemic happenings in London over 25 years. The general plan is that of Hippocrates, but much less stress is put upon records of what we should call meteorology and far more directly clinical and therapeutic material is woven into or—if one prefers the phrase—interpolated in the epidemiological record.

To this record the criticism we have passed upon that of Ballonius is equally applicable. In Ballonius' time there were no statistics of disease; in Sydenham's time there were statistics of a sort, statistics which a contemporary of Sydenham's, a man of quite as great powers of mind, John Graunt, used to very good purpose. Sydenham, however, never used this material and, on that account, as the statistician will think, his record of epidemics is quite as difficult to follow as that of Ballonius. We think that Sydenham's true claim to reverence depends upon what from the epidemiological point of view, as defined by us, were interpolations, his *clinical* observations and reflections; had he not been a great physician, nobody would have paid much attention to his epidemiology.

Sydenham's contribution to the theory of epidemiology was this. He abandoned definitely and specifically the attempt to account for epidemics by meteorological happenings; his *constitution* is not of the atmosphere in the simple connotation of the word but a mysterious, unexplained and, as he thought, inexplicable influence perhaps arising in the bowels of the earth

which imprinted a characteristic stamp upon all illnesses prevalent at one time, so that small-pox and measles of one constitution might be, clinically and epidemiologically, more alike than the small-pox of two different constitutions. Almost within Sydenham's life-time, at least one acute critic noticed an inconsistency between Sydenham's theory and Sydenham's practice. Thus Sydenham says decisively (Latham's translation): "This, at least, on the strength of a multiplicity of accurate observations, I am convinced of; viz. that diseases of the character alluded to, and more especially continued fevers, differ from one another like north and south, and that the remedy which would cure a patient at the beginning of a year, will kill him perhaps at the close" (Vol. I. p. 33). The acute Freind, who had perhaps as real an appreciation of Sydenham's essential greatness as any man, commented: "But if we consider the method which this writer has adopted in curing these fevers, of, as he says, utterly different type (generis dissimillimi), a method in which he was eminently successful, we shall find no trace of this distinction (nullum hujus rei reperiemus vestigium)" (Freind, 1733, p. 238).

Such an inconsistency, however, not to speak of difficulties as to what Sydenham really *did* mean by a "Stationary Fever" (Greenwood, 1919), did not deter epidemiologists from the quest of the Epidemic Constitution which ultimately became, in the apprehension of many not illiterate persons quite as mysterious as that of the Holy Grail. Its later developments are described sympathetically in Sarda's *Cours de Pathologie générale*, an excellent and succinct description of the teaching of Montpellier 30 years ago. Sarda accepts in a general way the doctrine of Sydenham.

"Usually," he says, "the epidemic constitution aggravates diseases or renders a group of symptoms more intense, or gives to a disease a contagious quality which it did not possess before. It effaces reigning diseases to a point that all pathologically distinct cases seem either to belong to it or to have disappeared. This is what happens during epidemics of cholera, this is what happened in the last epidemic of influenza. One may say that all diseases are *absorbed* [italics in the original] by the disease proper to the medical constitution of the moment. The fact without being universal is frequent.

"These constitutions are announced to experienced practitioners by pathological conditions of abnormal or indeterminate character which should arouse suspicion; febrile gastric disturbances precede the onset of an epidemic of typhoid fever; painful diarrhoeas precede epidemics of cholera; bronchitis with obstinate cough and painful symptoms is a forerunner of an epidemic of influenza, which may also be announced by numerous cases of pains in the loins or chest, etc." (*op. cit.* p. 270).

Sarda, who of course accepted the results of modern bacteriological research, suggested that in the factors which exalt and depress the rate of growth and other biological properties of bacteria might be found the key to the mystery of epidemic constitutions, and quoted with approval the following words of Charrin:

Everywhere we encounter causes proper to lower or enhance the growth and functioning of bacteria. Must we not seek amongst these data a part at least of the epidemic genius? For what is then this epidemic genius if it is not a manner of existing, a modality of virulence

attributable to the environment? Thus one sees that the ancients were not far from the truth, or rather part of the truth, when they referred the epidemic genius to cosmic, climatic, meteorological factors, upon which Assmann insisted at the Berlin Congress (*op. cit.* p. 271).

It will be observed that Sarda, a representative of the Montpellier school, leaves to bacteriological research the elucidation of the factors which generate an "Epidemic Constitution"; he tacitly recognises that the successors of Sydenham have had no more success than their master in identifying them. It may be asked whether epidemiologists of Sydenham's school have achieved *any* result at all, whether, putting it plainly, the whole concept may not belong, like the greater part of the Galenical pathology and some part of modern clinical "Endocrinology," to the extensive realms of medical mythology.

We think such studies of epidemic successions as, to name two living epidemiologists, Hamer and Crookshank, have furnished of influenza (Crookshank, 1922) must satisfy any reader that even our imperfect historical record can be made to tell a story perfectly concordant with the doctrine of Epidemic Constitutions and that, particularly in their scrutiny of the multiform "nervous" clinical forerunners and trails of pandemic influenza, they have indicated a method of prognosis of one important change of type in epidemic disease which Sydenham had not discovered.

This is a considerable achievement, and to demonstrate the existence of a phenomenon is surely a step towards explaining it; but it is not easy to see how to advance another step. Crookshank has indeed (*op. cit.* 497 *et seq.*) sketched a plan of epidemiological research, but it will perhaps seem to most readers rather apocalyptic than feasible.

The conclusion we draw is that until more concrete suggestions have been furnished by the study of some working model, such as is provided by the researches with which we are concerned, it is not likely that the doctrine of Epidemic Constitutions will prove a generally valuable organon in the investigation of human epidemic disease.

It is especially in those diseases which have been investigated from a broad biological view-point that the most striking successes of preventive medicine have been obtained. It happens that this method is indicated with especial clearness in those diseases in which an insect vector of infection is involved, and it happens that such diseases are, at the present time, peculiarly prevalent in tropical or subtropical countries; so that it is to the investigators of diseases peculiar to the Tropics that the earliest and most striking victories have fallen, as the result of this method of attack. There seems, however, little reason to doubt that the same method will produce equally satisfactory results in other fields. We believe that the great lesson to be learned is that preventive medicine is nothing other than applied biology, and that all those methods which have proved fruitful in the hands of the biological investigator have their proper place in research in the field of hygiene. We would suggest that direct experiment and biometry are likely to justify themselves here as elsewhere.

There are still to be mentioned lines of investigation specifically epidemiological but not inspired by the teaching of Sydenham. A few authors, notably again Hamer (1906), have applied precise quantitative methods to evaluate the effect of *changes in the constitution of the population exposed to risk* in generating epidemic disease. The special characters of an epidemic disease appearing in "virgin soil" have long been almost a commonplace in connection with the zymotics; in recent years many authors have emphasised the importance of this factor in the particular case of tuberculosis. Those who have dealt with the subject quantitatively have not been numerous. Hamer, however, in his Milroy Lectures of 1906 showed how the growth of a susceptible population by natural generation might go far to account for the periodicity of epidemic measles.

This leads us to speak of the important epidemiological researches of Brownlee directed to discover and measure the periodicity of measles, scarlet fever and other diseases. The importance of these investigations is certainly great, but their interpretation obscure. Brownlee's discovery that the periodicity of measles is different in different parts of London (Brownlee, 1919), is, as Hamer and Yule remarked, perplexing. If periodicity is referred to a property of the life-cycle of the specific parasite, as Brownlee holds, the adaptability of the parasites to a change of human host is strangely small, yet its varietal survival power is remarkably great; a strain able to maintain itself for generations in hosts on one side of Waterloo Bridge cannot survive transfer to hosts on the other side. For our part we do not feel that we have sufficiently mastered the intricacies of the technique or are sufficiently secure from entanglement in the very numerous pitfalls that lie in wait for the student of periodogram analysis in its application to the data of human disease to be able to read aright the indications.

There remains the question—what light has been thrown upon the problem of epidemiocity by the researches from which, in their infancy of 25 years ago, Sarda, quoting Charrin's words, hoped so much? In this quarter of a century the volume of published work has been vast; some of the contributors have been men of great genius. Immunology is now a special discipline. In a considerable number of instances the sequence and mechanism of events in the process of *individual* attack and defence, when the tissues of a host are confronted with a parasite, are known with considerable exactitude. The triumphs won have been notable. There are several instances, in which the application on a large scale of prophylactic measures, based on immunological data, have yielded results which are significant from the epidemiological standpoint. The success of prophylactic inoculation against typhoid and paratyphoid fevers in large bodies of men exposed to conditions peculiarly suitable for the spread of enteric infection, and among whom isolated cases of such infection were actually occurring, has afforded definite evidence that an increased average resistance among a population exposed to risk is effectual in preventing the epidemic spread of infection. Recent results, obtained in attempts to

reduce the incidence of diphtheria among a given population, by detecting susceptibles by means of the Schick test, and immunising them with toxin-antitoxin mixtures, has added further evidence in the same direction. But a perusal of any competent treatise, such as Bordet's, will reveal limitations. There we may read many curious facts of racial immunity and of local immunity, but systematic attempts to explain them have not been made and one is often reminded of the words of Darwin in the first chapter of the *Origin of Species*: "Some instances of correlation are quite whimsical: thus cats which are entirely white and have blue eyes are generally deaf; but it has been lately stated by Mr Tait that this is confined to males. Colour and constitutional peculiarities go together, of which many remarkable cases could be given amongst animals and plants." To the reader of a modern treatise on immunology, variations in susceptibility of laboratory animals must still appear "quite whimsical," for they have not been made the object of serious investigation; we do not even know of any adequate study of the range of natural variation of resistance, save incidental records of "controls," before Webster's observations on the natural resistance of mice to enteric infection. In immunological, as in clinical studies, the great majority of investigators have been so occupied with the individual that they have neglected the herd.

II. The Experimental Method employed.

The method employed in these experiments has consisted essentially in the addition of normal mice, at different rates, to cages in which a bacterial infection was known to be spreading, and the observation of the subsequent course of events. The disease chosen for study, mouse pasteurellosis, arose spontaneously some five years ago among a batch of mice purchased from a dealer. It may be emphasised at this point that we have never, since that date, encountered this particular infection among our normal stock.

This disease is particularly suitable for such studies as those here reported, because it spreads readily among a susceptible population, gives rise to a high mortality, and produces lesions which are readily recognisable at post-mortem examination. In a typical case one finds a double pleural effusion, often slight in amount, but always purulent in character, a pericardial effusion of the same type, and a variable degree of purulent peritonitis. The lungs usually show areas of consolidation of a haemorrhagic type, while the remaining organs usually show no gross changes. In particular, the spleen is seldom noticeably enlarged. The macroscopical picture is, indeed, always dominated by the presence of purulent effusions into the serous cavities. In such effusions *Pasteurella muris* is always present in large numbers, and it is usually demonstrable in films from the heart's blood. Its morphological characteristics are sufficiently distinctive to ensure its easy recognition in film preparations, and its ready growth on meat-infusion agar, combined with the absence of growth on bile-containing media, renders the cultural confirmation of the microscopical findings peculiarly simple.

In these experiments every mouse which has died, and has not been devoured by its companions, has been submitted to a post-mortem examination, including the microscopical examination of film preparations, and the cultivation of the heart's blood, and of a portion of spleen tissue, on ordinary agar and on McConkey's bile-salt-lactose medium.

In the very great majority of cases the mice so examined during the course of these experiments have died from a pure pasteurellosis. In certain cases, however, as will be recorded later, a superadded infection with an organism of the enteric group has been present. In such cases the pasteurellosis has always dominated the picture found at post-mortem, although the splenic enlargement and necrotic foci in the liver, characteristic of mouse typhoid, have very occasionally been present. In the great majority of those deaths which have been recorded as due to mixed infection, the post-mortem picture has been that of a pure pasteurellosis, but *B. aertrycke* (mutton), and in one experiment *B. gaertner*, have been isolated in culture in addition to *Pasteurella muris*.

The main technical difficulty in such experiments is concerned with the actual housing and handling of the mice, and especially with the collection and maintenance of an adequate normal stock. The various points in technique, which must be scrupulously adhered to, have been dealt with in many previous reports. The cages employed, and the method of dealing with them, have been fully described (Topley, 1923). It will suffice to recapitulate very briefly the more important points.

The experimental mice are housed in special zinc cages, of uniform design, which can be connected in series so that the cage-room expands with increase in size of the population at risk.

The cages are treated as though they were culture vessels, that is to say, they are never cleaned by an attendant without previous sterilisation. Each day, except Sunday, the mice from any given cage are transferred to a clean cage, already containing the requisite grain and litter, and the dirty cages are at once transferred to a large steam steriliser, and steamed for two hours. They are then cleaned, dried, and prepared for use on the following day. The experimental mice, dead or alive, are removed from the cages with forceps, which are immediately thrown into a steriliser which is kept in the animal house devoted to this work. Metal pots, containing bread and milk, are placed in the cages with forceps, and are sterilised in the cages on the following day. All members of the staff handling the experimental cages wear rubber gloves, which are afterwards sterilised by boiling. In this way it has proved possible to conduct concurrently many experiments, involving the study of different infecting organisms, without any accidental spread from one experimental cage to another.

The really formidable difficulty is met with in maintaining an adequate supply of normal mice. The term "normal" is, in reality, so vague as to be almost meaningless. It is clear that, quite apart from intrinsic differences of an inheritable kind, a stock of mice kept at a total level varying between one and

two thousand will be harbouring a very complex flora and fauna of parasitic organisms. By a "normal" mouse we really mean one which is not already infected with the organism the activity of which we desire to study, nor with any other parasite which will spread readily among the population at risk, and so interfere with the course of the experiment. Fortunately, it would appear that the pathogenic microbial parasites, which spread rapidly among a mouse population, are either relatively few in number or are not widely distributed under natural conditions, or that these few have such a power of dominance over other infective organisms that, when present, they run their course as though they were in complete possession of the field. In our experience, lasting over seven years, we have only encountered four bacterial organisms which have been able to compete, between themselves, on anything like equal terms. These include two organisms of the enteric group, *B. aertrycke* and *B. gaertner*, an organism of the haemorrhagic septicaemia group, *P. muris* and *B. murisepticus*, which is closely allied to, if not identical with, the organism of swine erysipelas. We have evidence that several other bacterial parasites, including for instance *B. morgani*, *B. proteus*, the *Enterococcus* and *C. pseudo-tuberculosis murium*, may spread to some extent among a mouse population, but, from the present point of view, they appear to be of minor importance.

Pasteurella muris and *B. murisepticus* have never, since their first appearance several years ago, given rise to any trouble; but the case with *B. aertrycke*, and to a less extent with *B. gaertner*, is very different. Although it is, in our experience, quite exceptional to find carriers of these organisms among our normal stock it is not an uncommon event to receive from dealers, especially during the summer months, batches of mice which are suffering from enteric infection. Such infection usually declares itself within a relatively short time, and the period of quarantine employed usually ensures that no mice infected with these bacteria shall be added to the experimental cages. Occasionally, however, these precautions fail; and the present report includes four experiments which were brought to an untimely end by a mischance of this kind. It is quite clear that, for such investigations as these, the ideal procedure is to employ mice coming from a single inbred stock, kept under constant observation from birth onwards, and to exclude all mice from outside sources. We hope eventually to be in a position to adopt this plan, but it is not possible to accumulate rapidly a stock that will meet the needs of many experiments of this type, running concurrently.

The plan which has been adopted throughout these experiments is as follows. Mice are obtained from a few large breeders, and once an infected batch has been received from a given breeder no more are taken from that source. All normal mice are housed in cages similar to those used in the experimental work, five to eight mice being placed in each cage. All mice are quarantined for three weeks or more after being received from a dealer. All normal mice which die are examined post-mortem. If any death occurs in a cage of normal mice, and this death is found to be due to any infection

known to cause epidemic disease, all the mice which belonged to the same batch, as received from the dealer, are immediately killed. This may mean sacrificing several hundred mice, but experience has taught us that it is the only safe method to pursue. If a death occurs for which, after post-mortem examination, no known cause can be assigned, or if it is due to some cause other than those referred to above, then that cage is regarded as suspect for the succeeding 14 days. If no further death occurs during that interval, the remaining mice are regarded as normal. If a second death occurs in that cage, the survivors are killed.

Using these precautions, it appears that the risk of introducing infected mice into the experimental cages is slight. Except in the case of enteric infection it seems to be negligible. But, in experiments which must be carried on without intermission for months or years, it is a risk which it seems impossible to eliminate. It is doubtful whether the exclusive use of mice bred in the laboratory will eliminate it entirely.

The Existence of Different Serological Types of Pasteurella muris, *and their relation to the Epidemic Spread of the Disease.*

It will be convenient to deal at this point with one question, which was studied during the course of one of the experiments to be considered in this report. The spontaneous outbreak of pasteurellosis among our normal stock arose at the end of 1920. Within a comparatively short period two batches of mice obtained from different sources became infected with this disease, and there had been no obvious opportunity for cross infection. Agglutination tests, carried out on strains isolated from mice dying in these two outbreaks, showed that they were caused by serologically distinct races of *Pasteurella*. When it became clear that a definite characteristic of long-continued epidemics of pasteurellosis was the occurrence of successive waves of mortality, the character of which will later be discussed in detail, it was natural to enquire whether or not the existence of these different serological races had any significance in this respect, whether, that is, several serological races were involved in the epidemic, and were unequally represented in the successive waves.

The results of this part of the enquiry may be dealt with quite briefly. Agglutinating sera were prepared against strains of *Pasteurella* isolated from mice dying during the two outbreaks referred to above. Between January, 1921, and the end of April, 1924, 1256 strains of *Pasteurella*, isolated from mice dying during the course of a single prolonged epidemic, referred to in this report as Exp. 2, were tested against sera corresponding to each of the two serological types. Considerable difficulty was met with in carrying out these agglutination tests, since many of the strains proved to be inagglutinable when first isolated, and it was often necessary to prepare three or more suspensions from a single strain, before obtaining satisfactory results. In a few cases, in which the results of direct agglutination tests were unsatisfactory,

owing to cross agglutination, we employed the absorption test for confirmation. The results were as follows. Of the 1256 strains examined, 949 were shown to belong to a single serological type, referred to in our records as Type 116. The antigenic structure of the remaining 307 strains was not satisfactorily determined. They proved inagglutinable when first tested, and it was not considered necessary to re-examine them, in view of the fact that in every case in which repeated tests had been carried out, the strains so examined had eventually been proved to belong to the one serological type. Moreover, during the early months of the experiment, to June, 1921, six sera were prepared against inagglutinable strains, or against strains which gave cross agglutination with the two type sera employed; and in every case these sera reacted in the same way as the serum prepared against the original strain No. 116. During the whole period of the experiment no evidence was obtained that more than one serological race of *Pasteurella* was concerned in the epidemic, and it seems quite clear that the successive waves of mortality were not associated with successive phases of prevalence of different serological races.

III. General Character of the Experiments.

Before detailing the peculiarities of our results, we can usefully notice features common to all the experiments, save one, and discuss how far the experimental method, in our hands, has attained its true end, viz. isolation of the phenomena which we desire to study.

We have seen that the multiplicity of factors, certainly or probably modifying the evolution of epidemic disease in man, is so great that nobody has yet succeeded in unravelling the tangled skein. We have also seen that, in the hands of modern experimenters in the laboratory, simplifying experiments have elucidated many particular problems of immunity and susceptibility but have not furnished any connected account, have not given a bird's-eye view of the course of events in an epidemiological unit, a herd. The experimenter, on the other hand, has usually taken the individual, not the group, as his unit. How far have we succeeded in filling the gap, in producing a result less complex than that of epidemics naturally occurring, less artificially simple than the particular experiments? The principle of the study has been this. Starting with a community within which the seed of an infectious malady was known to have been planted, we have added to the community a number, constant for the same experiment but different in different experiments, of healthy individuals, and we have recorded what happened. Our unit has been a herd of mice, and this herd has been subjected in each case to conditions one of which was invariable. In an ordinary herd the number of additions in each unit of time is essentially variable, neither immigration, emigration nor fertility have such relations that, wholly irrespective of mortality, the same number of newcomers enter always in each unit of time. A human analogy would be that of a strict monastery, receiving each year

the same number of novices, losing no members save by death. But the statement of this analogy at once suggests that it is false.

Our population is essentially artificial in that the complete omission from our records of any increase of population by births, what young were born were devoured or, when found alive, were removed from the cage, separates our herd from any natural population of mice. Not only is it artificial, but the specification of the members of the herd is incomplete. We do not know the ages or the sexes of the immigrants. The analogy of a monastery is false. It would be more correct to liken the experimental herd to a collection of savages, men and women, practising infanticide and cannibalism and receiving in each unit of time a constant number of other savages of both sexes and between the ages of puberty and early middle life. This, perhaps, *over-states* the case against the cleanness of our experimental method, in that variations of ages and sex may be, and probably are, less influential upon mortality rates in the mouse herd than in the human herd. But even were the analogy perfectly fair, it would be admitted that a series of compounds of savages, so composed and so recruited, the number of additions being widely varied from experiment to experiment, and *the period of observation being prolonged over more than an average human generation*, would certainly throw light upon one fundamental problem, viz. what is the effect of varying the immigration rate upon the general death-rate and growth of the population?

Suppose then that at any moment the population consists of P mice, then, since in every unit of time a fixed number of mice is added to the cage, the change in the population effected in a very small interval of time, *i.e.* dP, will be made up of an addition Adt and a subtraction $Pmdt$, where m is the rate of mortality per unit of time, so that the differential equation of the system is

$$dP/dt - A + mP = 0.$$

The solution of which is

$$P = Ae^{-\int m \cdot dt}\left(\int e^{\int m \cdot dt}\, dt\right) + ce^{-\int m \cdot dt},$$

where c is constant.

When m is, like A, a constant we get

$$P = \frac{A}{m} + \left(p_0 - \frac{A}{m}\right)e^{-mt}$$

where p_0 is the initial population.

The population increases or decreases to the asymptotal value A/m, as is indeed obvious without algebra.

But if m is not a constant but a function of t and P, *i.e.* if the death-rate changes with time and changes with the increase or decrease of the population, whether we can solve our equation or not depends upon whether we can give symbolical expression to the functional relation connecting P, t and m and whether, having done so, we can integrate the equation.

Supposing the death-rate to be a function of the time merely, for instance of the form $a - b/(c+t)$, it is easy to see, without any algebraical assistance, that the population will tend to stabilise itself at the value A/a when t becomes infinite. If, on the other hand, m is a function of P of the form $a - b/(c+P)$, the population will still tend to stability, we shall reach an expression of the form

$$(P - \lambda_1)^{w_1}(P - \lambda_2)^{w_2} = e^{k-t},$$

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where λ_1, λ_2, w_1, w_2 and k are all constants, so that when t is infinite, P will be a root of the equation

$$(P-\lambda_1)^{w_1}(P-\lambda_2)^{w_2}=0.$$

These are, indeed, only roundabout ways of saying that a population *must* tend to the limit A/m, and that, if m tends to any finite limit, the population must also tend to a finite limit. If now we *vary* A from experiment to experiment, whether the limit of population will be raised, remain constant or be diminished, depends on the relation between A and m; it will remain constant if, and only if, kA is equal to m, where k is a constant.

The statistics of human populations on the whole concord with the view that m does not increase so fast as A; our experiments give the same result. As A increases, m increases, not uniformly, but it tends on the whole to increase. In the experiment in which one mouse was added every third day, the mean daily death-rate was 0·0155; in the experiment in which six were added daily it was 0·0303, and the mean populations in the later phases of the experiments were 15 and 214 respectively. Had the respective death-rates been constant, the ratios of additions to death-rates would give the limiting populations; the ratios are 21 and 198 respectively, fair approximations to the truth (in other experiments, the accord is still closer, *e.g.* in the experiment where three mice were added daily the observed final average population was 63, the expected on the hypothesis taken 65).

In other words, populations subject to the conditions of such experiments as these (one of which is, of course, that the *food* supply is always adequate) are regulated as to size mainly by the births. It is not possible, or at least, it has not been observed in these experiments, so to increase the mortality by introducing more and more susceptible persons that the level of population will be lower with a higher rate of addition[1].

This memoir is not concerned with the general problem of population, so that these remarks will be sufficient to deal with that particular aspect.

Let us now briefly review the vital-statistical history of the various populations. In each case we have a community within which a specific infection, a pasteurellosis, existed; in all for some time, and in some during the whole effective period of observation, this specific infection was the principal cause of mortality. In this memoir we mean by the terms *Specific Deaths* (or, in relative terms, *Specific Death-rate*), deaths either caused by a *Pasteurella* infection, or by a mixed infection of which *Pasteurella* was part, in both cases proof being afforded by post-mortem examination, together with some deaths not verified owing to the destruction of the corpse (by cannibals). The inclusion of the last category under Specific Deaths may seem arbitrary, but we were moved by these considerations: (1) mice devoured by their fellows were probably ill and, in epidemic phases, the larger proportion of verifiable deaths were specific in the stricter sense; (2) the course of the

[1] We cannot, of course, ensure that there is a perfect mixture of the herd; effective density *may* not increase as the additions.

death-rate amongst mice not examined showed roughly the same features as that determined from truly specific deaths alone. The proportion of such deaths is not, in any case, sufficient to affect the deductions we make from the results[1].

The experiments studied were six in number, one being, however, divisible into two parts. Exp. 2[2] falls into two periods. In the first, three mice were added daily for a long time and thereafter only one mouse was added daily. In Exp. 3, six mice were added daily; in Exp. 4, two were added daily; in Exps. 5 and 6 a mouse was added every second and every third day respectively. In Exp. 7, large batches of mice were added at different times.

The general course of events in each experiment is best followed on a diagram upon which the daily death-rates are plotted[3]. To reduce casual irregularities we have plotted a smoothed rate of mortality; each entry is the representation of the ratio formed by dividing the sum of the deaths for the five days of which the day entered on the base is central by the sum of the populations for the same five days. Throughout our work, we use not the death-rate of most medical publications, *i.e.* not the central death-rate (m_x)[4], but the probability of dying within the unit of time, *i.e.* the actuarial rate of mortality (q_x). The difference is not important for the present comparison; actually $q_x = \frac{2m_x}{2+m_x}$ so that, as m_x is small compared with 2, there is little difference, but we shall subsequently need life-table constants, and it is simpler to work with the same rate of mortality throughout. The graphs also show the numbers living on each day in each experiment.

Although such a diagram is much the most convenient instrument to use, in using it one must not forget that the real significance of what is graphically a striking rise or fall of the curve may be small, because at various points the numbers exposed to risk are very small. Hardly any attention should be paid to isolated movements based upon small numbers, not because they cannot be due to important changes but because we cannot be sure that they are not mere casual happenings (see Graph VII and footnote, p. 63).

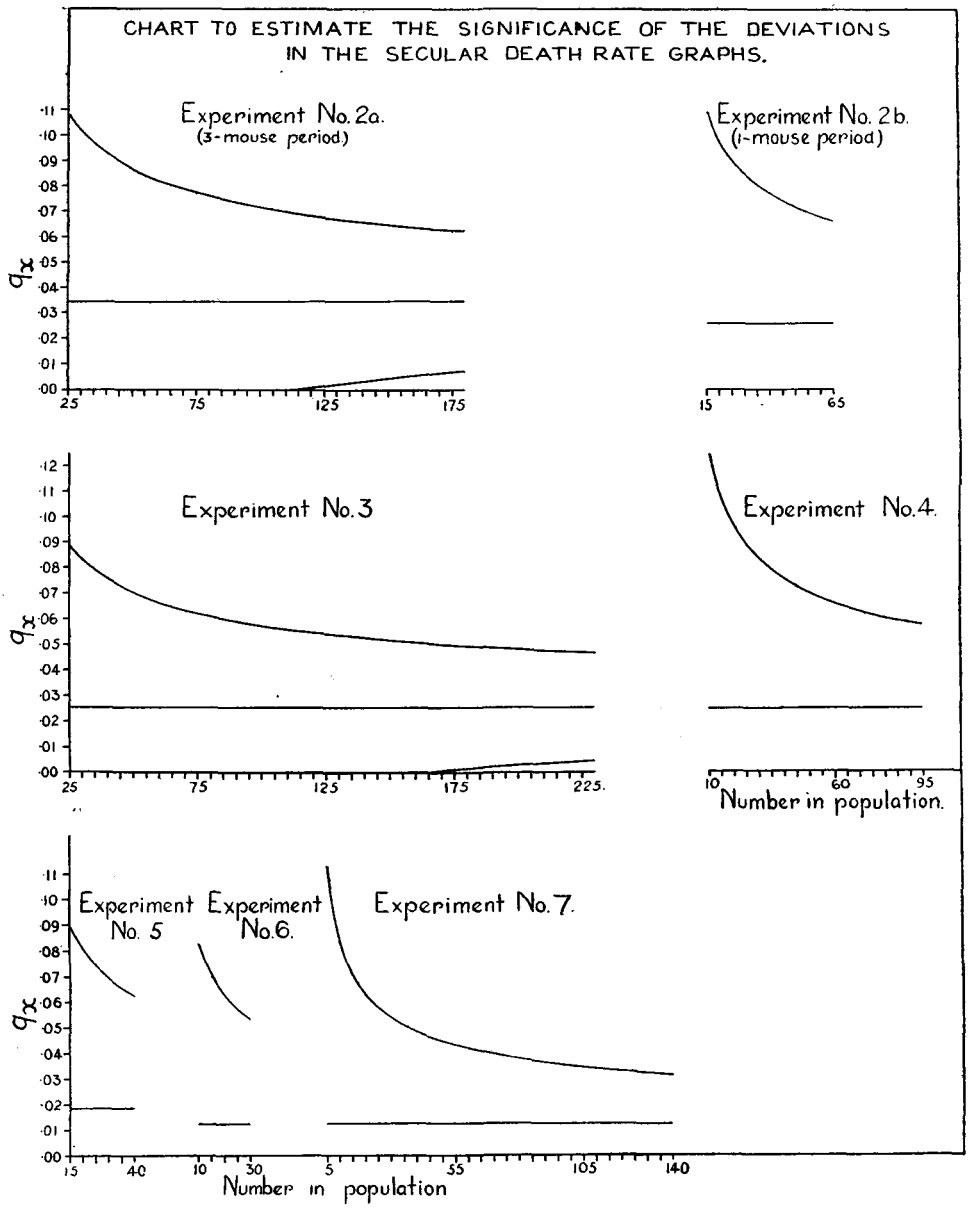
Paying no attention to differences of age composition in the herds, we shall first consider the death-rates at all ages together.

[1] In times of *very low* death-rate these unexamined mice form a larger proportion of the deaths, and when no epidemic of pasteurellosis is running, as for example in the latter part of Exp. 6, the chart of our 'specific deaths' may be misleading.

[2] There is *no* Exp. 1 in this series; the numeration is a survival from a previous plan which, to avoid confusion in our records, we have retained.

[3] We have traced the death-rates rather than the actual deaths, as the populations vary from day to day, so that the deaths might give a misleading picture of the mortality.

[4] The central death-rate, m_x, of a group observed during any age period is the ratio of the number of deaths in the period to the average number living during the period. The probability of dying, q_x, in the same period is the ratio of the deaths to the numbers alive at the beginning of the period, thus, if 1000 people are alive at age x and 20 die before age $x+1$, $q_x = \frac{20}{1000}$, $m_x = \frac{20}{990}$, since $990 = \frac{1}{2}(1000+980)$.



Graph VII. Chart of three times the Probable Error for the secular graphs.

Note. The horizontal lines represent the mean daily death-rates for the whole period of each experiment. The lines on either side represent ± 3 times the probable error of this mean for the different numbers in the population given in the abscissae. To test the significance of any deviation in the secular graphs, note the population on the day required and see if the deviation lies within 3 times the probable error for that population.

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Exp. 2. (See footnote 2 of p. 59.) *From* 6. iii. 21 *to* 30. iv. 23*: period of three daily additions.* (See Graph I *a*.)

This herd consisted at first of 26 survivors of a previous experiment. Within ten days a movement began and four waves lasting from about 16. iii. 21 to 20. vii. 21 appear, each wave measured (which can only be done roughly) from the initial rise to the resumption of the general trend lasted 25, 19, 17 and 60 days respectively. The first, which is two-peaked, reached the highest maximum (0·124) of any; the fourth is long and irregular. There followed a quiet interval with low death-rate and increasing population, until, at the end of about two months, the rate of mortality began to rise slowly (at first the non-specific deaths increased faster than the specific deaths, for which no obvious cause could be assigned), reached a comparatively low maximum of 0·076 on 26. xi. 21, and fell away to 14. i. 22, a period of 121 days. Over the period of low mortality the population was of course increasing and attained a maximum of 182 on 8. x. 21. The low death-rate equally implied an increase in the proportion of mice more than 30 days old[1], and when the mortality began to rise the numbers under and over 30 days of age were about equal; during the slow rise those older than 30 days were in a majority. Their number began to decline before that of mice in other age groups, until, when the death-rate began to fall again, there was approximate equality between the numbers in the two groups.

The population fell below 50 on 4. iii. 22 and thereafter until the end of this phase of the experiment fluctuated between 55 and 30, tending to maintain a higher level in the last three months of the experiment.

During the last 16 months of the period, from the middle of January, 1922, to the beginning of May, 1923, the chart of death-rates is an almost continuous succession of waves without steady intervals of constant rates. Very approximately—measuring the intervals between successive minima on the smoothed graph—a process obviously affected by personal equation—one has 21, 21, 22, 19, 13, 18, 21*, 14*, 12*, 35*, 49*, 42 (19, 14, 9)[2], 31 (23, 8), 33 (18, 15), 117 (19, 17, 20, ... 21, 17). In the waves starred the difference between specific and non-specific mortality was greater than at any other time and the second wave of the group was hardly affected by mortality from *Pasteurella*. Most of the deaths were due to infection with *B. aertrycke* (mutton), which subsequently died down.

Exp. 2. *Second phase from* 1. v. 23 *to* 30. ix. 24. *One mouse added daily.* (See Graph I *b*.)

On 1 May, 1923, the condition of the herd was changed. Its absolute increase was reduced to one-third of the previous number. When this was done, the herd was passing through a wave of mortality, the last sub-wave

[1] Here, and throughout the memoir, by age we mean cage-age. A mouse *n* days old is a mouse which has been *n* days in the herd.

[2] Numbers in brackets are attempts to subdivide irregular waves into their constituents.

of which, 17 days in length, was almost wholly due to non-specific deaths. When it ceased there was a quiet period, from 22. v. 23 to 8. vii. 23, and, in spite of the reduced immigration, the population increased, rising to between 60 and 70. This process was brought to an end by a wave lasting 31 days, due almost entirely to *Pasteurella*, and reducing the population to 22. There followed a quiet period of some 26 days, then a wave covering 38 days, then 50 days included three irregular waves or wavelets, then an interval of 22 days, followed by a wave of 35 days' duration, next a long steady period of 102 days, followed by a short wave of 22 days' duration. In the following 90 days, there was very little *Pasteurella* infection, but towards the end of June *B. aertrycke* again made its appearance[1] and the slowly rising death-rate in August, 1924, the last month of observation, was wholly due to this cause and other non-specific deaths. No proven case of pasteurellosis later than June exists, although, of course, some of the devoured mice may have died from this cause.

The contrast between the general course of this phase and that of the first part of the experiment is striking; the waves are longer and the quiescent periods much longer than before. The average rate of mortality is lower, towards the end much lower, than in the first phase.

This description, necessarily very tedious and only to be followed with the aid of the graphs, covers a period of $3\frac{1}{4}$ years of observation (down to the end of June, when the last certain death from pasteurellosis was recorded) of an initially infected population recruited by immigrants known to be uncontaminated. Until we have exact information respecting the vital statistics of caged herds of mice not deliberately exposed to a particular infection, the translation of human time intervals into time intervals in terms of the life of a mouse is conjectural. If, however, the *average* life of a mouse is not more than two or three years, our observation period is equivalent to from 50 to 70 human years. During this long period a fatal infectious disease has been maintained, it has been nearly all the time the chief and in part of the time almost the whole cause of mortality, yet in that time not a single infected immigrant has been admitted to the herd[2]. This long experiment, therefore, confirming similar results (*e.g.* Topley (1921 *a*) or Amoss (1922 *a*)), fully established the proposition that with populations living under such

[1] This reappearance of *B. aertrycke* infection was not due to the survival of this organism among the animals at risk, from the earlier infection mentioned above, but to importation into the cage with the added mice, owing to a failure in our method of quarantine. After the appearance of the infection, it was found that considerable stock of supposedly normal mice, recently obtained from a dealer, were carrying both *B. aertrycke* and *B. gaertner*. Additions made from this stock to other cages brought other experiments to an untimely end, a fact to be referred to later.

[2] The system of quarantine established for mice of the normal stock before admission to the experimental cages has been described and, as has been pointed out, cannot, in the nature of things, always succeed. Pasteurellosis, however, seems to be an uncommon disease of mice in this country, and we have met with no spontaneous infection amongst our normal stock during the past five years. Since many thousands of mice have passed under observation during that period, we may feel reasonably confident that this infection has not been reintroduced into our experimental cages with the normal mice.

conditions as described and, in the matter of infectious diseases, *in pari materia* with the one here used, the disease as a herd phenomenon will continue certainly for generations on the sole condition of adding regularly to that herd adequate numbers of immigrants with a clean bill of health. It is not possible to bring such a disease to an end by the most sedulous selection of immigrants, unless that selection extends to the determination of the natural or acquired immunity of the immigrants. Whether, in that case, immigration would be innocuous, this experiment does not determine; we have an opinion on the subject but it is not relevant to the present discussion. A further deduction from this long experiment is that only by maintaining observations over a long period can an adequate knowledge of the general course of events be gained. It will have been noticed on the graphs, or even in our verbal description, that had there been available for discussion only sections of the graph, even sections covering what most people would regard as a long period of experimental observation (such experiments as these, however simple they may appear to the reader, involve a great expenditure of time and money), very definite and altogether incorrect conclusions might have been drawn. This consideration must be had in mind in reading the accounts of our other experiments which had to be closed after much shorter periods of observation.

Finally, we must warn the student of the mortality curves that, in assessing the significance of wave-movements, the smallness of the experience, numerically, cannot be ignored. We provide a chart (see Graph VII), enabling an easy assessment of the "probable error[1]" of the death-rates to be made. This measure, based upon the numbers exposed to risk and, by its nature, ignoring the *quality* of the individuals all of whom are counted as each a unit of equal value with any other unit, is far from being an ideal criterion; it is, however, some criterion. We are satisfied that the variation of the rates of mortality with time around the average of the whole period cannot be dismissed as mere random fluctuation, and that some, at least, of the waves register significant movements of the disease, but we should deprecate the putting of much emphasis upon the precise shapes or position in series of all the many waves shown in the charts.

Exp. 3. *Six mice added daily* (14. ii. 24 *to* 29. ix. 24). (See Graph II.)

The course of events in this herd contrasted with the record of the previous experiment in its presenting a continuous succession of waves without any real intervals of quietness. This is the story down to 21 August, 1924,

[1] The probable error gives a rough criterion of the likelihood of variations of given size arising by chance. The odds are even for the occurrence in pure random sampling of differences as great or greater than the probable error either above or below the mean. The odds against the occurrences of differences in excess or defect as great as or greater than twice, two and a half times, three times or four times the probable error are respectively 4·6 to 1, 9·9 to 1, 22·2 to 1 and 142 to 1. Chart VII gives the value of $\pm$ three times the probable error for the various sizes of population marked on the horizontal axis, *i.e.* the odds are 22 to 1 against a variation from the mean coming outside these limits by pure chance.

i.e. down to a period about a month after the immigrations ceased. Measuring the waves from minimum to minimum their lengths were approximately 22, 17, 17, 19, 20, 16, 10, 13, 7, 10, 10 and 29 days. Although, down to the last wave, the crests never reached the height of some waves in the previous experiment, their frequency more than compensated this so far as the average rate of mortality was concerned, the latter was higher than in the previous experiment. But the higher rate of mortality was not sufficient to keep pace with the higher quota of immigrants and the population tended to increase until, by the end of June, it seemed tending to a constant level. Unfortunately, the experiment was spoiled at this interesting point by the appearance of *B. aertrycke* infection; this increased in July and the experiment was discontinued. We decided to leave the herd to die out or become stable and no mice were added after 27. vii. 24. At that date the population was 214, which had dwindled to 14 by the end of September. In some previous work (Topley, 1921 *a*) it had been found that a herd isolated in this way decreased more slowly than when additions were made. This did not happen in the present case, but there is no clean comparison, for two infections were present.

In this herd, the herd receiving the largest number of immigrants, the rate of mortality fluctuated less than in any other experiment and seemed to be tending to a value between 0·025 and 0·030, with small deviations on either side of an average. Actually, according to the "probable error" test, no deviations from the mean rate of mortality between 1 June and the date on which immigration ceased are significant. The population increased more or less steadily until the end of June and then fluctuated between the narrow limits of 226 to 212 until immigration ceased. It is extremely unfortunate that this experiment broke down when it did break down, because the *prima facie* inference is that with larger immigrations the fluctuations around a fairly stable mean became smaller, that in fact one does approach the elementary case discussed in the opening paragraphs of this section, that of a population subject to a constant death-rate and receiving constant numbers of immigrants. There is in fact some resemblance between the vital statistics of the herd of mice under notice and those of still more specialised herds of *Homo sapiens* such as the Royal Society of London, or the Royal College of Physicians, which recruit their numbers by the annual admission of a fixed number of individuals, and rely on death to set a limit to their total quota of Fellows. Since 1848 the Royal Society of London has admitted annually 15 ordinary Fellows. The Fellowship (ordinary Fellows only, persons elected under special conditions or before 1848 are excluded) gradually rose until 1903 and for the past 23 years has fluctuated about an average of 443. The widest range of fluctuation in that period has been 21 or 4·7 per cent. of the mean. The society of mice admitting six new Fellows a day has shown an extreme range of about 6 per cent. through the period of approximate stability.

Having regard to the warning given in our remarks on the much longer Exp. 2, we do not dwell upon this. There is, however, a suggestion that

increasing the absolute number of immigrants will stabilise the death-rate and obliterate the waves. Further, it appears that although by adding healthy immigrants to a herd we can ensure that an infectious disease present will not die out for (certainly) more than a generation, we cannot ensure the destruction of a herd by increasing the number of regular additions. When we were medical students it was usual (probably it still is) to describe any pathological phenomenon by some similitude: tumours were the size and consistence of cherries, grapes or oranges, infections "flared up" and so on. If, following this time-honoured practice, we compare an infection to a fire and the herd in which it exists to a city and the healthy immigrants to fuel, we *can* keep the fire burning by adding fuel; but if we add more and more fuel, we shall neither smother the fire nor cause it to spread so that the whole city is destroyed.

Exp. 4. *Two mice added daily* (14. ii. 24 *to* 30. ix. 24). (See Graph III.)

This herd experienced four small waves at the beginning (the third of which hardly affected the specific rate of mortality), then passed through a period of low death-rate, followed by two small waves and then a somewhat more distinct increase of mortality. Thereafter we have a quiescent period of 33 days and then four more waves of increasing amplitude. In the middle of June, 1924, a *B. gaertner* infection appeared and was still effective at the end of September, although pasteurellosis was more effective until the end of August, from which date the Gaertner infection began to develop rapidly and did not wane until towards the end of September. Measuring the length of the waves from minimum to minimum we have 11, 12, 11, 13 (or ? 24), (? 23), (? 16), 29, 18, 20, 18 and 15 (unfinished). The crests of the last two waves are high, but by this time the population is small.

Exp. 5. *One mouse added every other day* (14. ii. 24 *to* 30. ix. 24). (See Graph IV.)

The experiment followed almost exactly the same course as No. 4 down to the end of June. Like No. 4 it began with four small waves followed by a quiet interval of some 59 days; then there were two well-defined waves and thereafter an irregular course to the end of September. The waves, measured from minimum to minimum, were of 11, 10, 10, 18, 22 and 19 days. In the quiet period the population reached 40, but for the rest it usually fluctuated between 20 and 30 and sometimes fell below 20. No statistical importance attaches, therefore, to the irregularities.

This herd did not suffer from an extraneous infection.

Exp. 6. *One mouse added every third day* (14. ii. 24 *to* 30. ix. 24). (See Graph V.)

This herd experienced the lowest rate of mortality of any. Its history began with three moderate elevations on the curve of mortality, there followed

a quiet period of 70–80 days, having a small elevation in the middle, there was a sharp rise at the beginning of July, then quiescence[1]. The first three waves measured some 15, 23 and 18 days. Nearly all deaths were due to *Pasteurella*. The experimental population was of course small throughout; it never rose much above 20.

Exp. 7. *Irregular Immigration.* (See Graph VI.)

In this experiment, with 20 original settlers, immigrants were admitted in two batches of 80 and three of 50. Eighty were admitted on 14. ii. 24, 80 more on 19. iii. 24, 50 on 3. v. 24, 50 on 11. vi. 24 and 50 on 1. vii. 24.

At the beginning of the experiment, the death-rate was rather high. The first and, until the middle of August, only large wave lasted about 32 days and showed two crests. After this subsided the rate of mortality was very low until towards the end of August, when another well-defined wave emerged. In September (two months after immigration ceased) the population was becoming so small that the irregularities of the rate of mortality deserve little attention; by the end of the month only two survivors remained. The admission of each batch of immigrants (except the last, the entrance of which is followed by a hardly noticeable increase of mortality) was attended within a few days by an increase, a slight increase, of the rate of mortality; the sharpest of these minor increases attended the entrance of the June batch, which arrived during the decline of a wave. The March immigrants also entered during a phase of decreasing mortality, but the subsequent increase was small. Just before the arrival of the last batch of immigrants, an infection of *B. aertrycke* developed, running with *Pasteurella*—the two tending to alternate—down to the end of the experiment. The mean population of this herd was the second largest of all, but the death-rate from pasteurellosis was low. It appears that average population alone is not a predominant factor of mortality in an infected herd, and suggests that the essential reason of the low rate of mortality when the immigrants are few is not a mere function of population-size. One notices also that although the minor waves following immigration usually affect the whole population, they specially affect the immigrants. This experiment is not sufficient to justify any general comparison between the effects of continuous and discontinuous immigration.

The Course of Rates of Mortality at Ages.

Smoothed rates of mortality in the age groups (the reader is again reminded that by age we mean cage-age) have been prepared for the age groups 0–4, 5–9, 10–29 and 30 or over days for the effects of pasteurellosis and doubtful[2]

[1] See footnote 1 on p. 59.

[2] Owing to a mistake which arose in connection with the transmission of records, in part of the analysis deaths due to *Pasteurella* and deaths in which no evidence of pasteurellosis was found post-mortem were grouped together, instead of *Pasteurella* and deaths not verified post-mortem. For reasons stated above, we think this was wrong, but in fact the effect of the method of grouping was usually so small that when the results were negative, as in the periodic analysis and in the

deaths. Such curves naturally fluctuated more than the curves for general mortality, but, on the whole, one must hesitate to draw any confident deductions from the discrepancies, hence we have not added to the already long series of graphs by reproducing these curves here. There is only one striking and uniform distinction; in all experiments the rate of mortality in the 30 group is least and that of the groups 5–9, 10–29, greatest. Sometimes there is a tendency for the curve of mortality at 30 to lag behind the others, but this is neither an invariable nor a striking phenomenon. With this partial exception, there is no evidence of any tendency for a wave to begin in one age group rather than another, indeed most commonly a simultaneous movement affects all four. It is also noticeable that the secular differences within an age group are much greater than any simultaneous differences between age groups. The inference is that age constitution alone is not an important factor in determining the rise or fall of a wave of mortality. We shall return to this point again.

IV. PERIODICITY OF DEATH-RATES.

The most obvious feature of the graphs described in the last sections is the wave-like course of the rate of mortality. Such a phenomenon is obvious enough in any chart showing the incidence or mortality of a human infectious disease which covers as long a period in the life of man as our chief experiment covers in the life of a mouse.

We do not have in our experiments, any more than in the record of human disease, an uninterrupted series of waves, excepting perhaps Exp. 3, that covering the largest mean population and almost the highest mean rate of mortality. In all the others practically steady rates are intercalated between the waves; the length of these intervals tends to increase from experiment to experiment as the rate of immigration decreases[1]. In the most regular succession, of Exp. 3, the interval between corresponding phases of the waves is about 18–19 days. In the three mouse epoch of Exp. 2, where the succession is interrupted by a long latent period and there are also long compound waves not observed in Exp. 3, the average wave interval is 19–22 days; in the one mouse period it is 22 days. The precise forms of the waves are variable, but on the whole they do not depart widely from symmetry, and what asymmetry there is, is not constant in sign; waves of steeper ascent than descent are not appreciably more frequent than waves of steeper descent than ascent.

Before discussing the possible significance of these waves, we must inquire whether there exists any regular periodicity apt to be demonstrated by the method of the periodogram.

correlation work, the laborious re-calculation has not been made. In all cases where the results of the old grouping are used reference is made to this note. All the graphs and life tables and any positive conclusions relating to specific deaths are based upon what we consider to be a correct grouping of the data.

[1] Cf. Topley (1921 *a*), adducing evidence that the period of fluctuation might depend on the rate of addition of susceptibles.

To bring this to trial, we have used the 786 days of the three mouse stage of Exp. 2 and the 457 days (down to the end of July, 1924) of the one mouse stage. For this trial age standardised[1] death-rates were computed, the standard population chosen consisting of nine mice of cage-age under 5 days, seven of cage-age 5–9, 15 of cage-age 10–19 and 19 of cage-age 30 days and over. This standard population has approximately the mean composition in age groups of the whole period. In the death rates *Pasteurella* and ? deaths were taken together (see note 2, p. 66), but owing to the dominance of the former this does not affect any conclusions.

Whittaker's form of computation (Whittaker and Robinson, 1924, p. 345) was adopted and all possible periods from 1 to 75 days were studied.

No significant period was disclosed in the three mouse epoch. In the one mouse stage, a probably significant period of 59 days[2] was discovered, its amplitude 0·0165 being 57 per cent. of the mean standardised death-rate. There is a suggestion of another period slightly short of 75 days, but the experiment has not lasted long enough to justify any decided inference; a period of 75 days would only occur six times in the available 457 days. This examination proves that in the three mouse stage there was no period of *constant length* and in the one mouse stage only one (of 59 days) sufficiently important to deserve notice. Does this mean that there is no periodic phenomenon involved at all? The answer is, we think, "certainly not." Although (as specifically stated in our Introduction) we express any opinion on the methods of studying periodic phenomena with the utmost diffidence and fully

[1] The object of a standardised death-rate is to eliminate differences in the death-rate due to varying age-composition of the population. For instance, on a day when the population consisted largely of mice at the more vulnerable early ages, the death-rate would naturally be higher than on a day when it consisted mainly of the more immune older mice, quite apart from any other circumstance of the epidemic. The method followed is to choose a standard population with constant numbers at each age group, and apply to these the observed age group death-rates for the day in question. The ratio of the sum of the deaths thus obtained to the number in the standard population gives the standardised death-rate.

A numerical example may make this clearer:

	Observed			Standardised	
Age group	Population	Deaths	Death-rates	Population	Deaths
Under 5 days	12	2	·1667	9	$9 \times ·1667 = 1·5$
5–9 days	5	3	·6000	7	$7 \times ·6 = 4·2$
10–29 days	10	0	0·0	15	$15 \times 0 = 0·0$
30 days and over	40	7	·175	19	$19 \times ·175 = 3·325$
Total	67	12		50	9·025

Crude (unstandardised) death-rate $= \frac{12}{67} = ·1791.$ Standardised death-rate $= \frac{9·025}{50} = ·1805.$

The crude death-rate shows what *is* happening, the standardised death-rate shows what *would* happen if the age composition of the population never altered but was always that of the standard population, when the age group death-rates were as observed. The standardised death-rate can of course only be used for comparative purposes and never absolutely.

[2] By Schuster's test for significance, the amplitude expected on the hypothesis of chance is only 0·00405 and the probability of an amplitude so great as 0·0165 arising by chance is less than one in a million, *i.e.* it is negligibly small.

recognise that our command of this most difficult branch of mathematical research is far too limited to entitle us to express anything but the most diffident opinion, we do not see how periodogram analysis can be brought to bear upon a periodic phenomenon subject to variation of period, while even a period of rigidly constant length, the course of which was interrupted by irregular intervals of latency, might wholly elude the scrutiny of the periodogram.

But it seems to us that such disturbing factors, change of period, intercalation of masking factors, etc. are almost certainly involved in such experiments as ours.

This at once brings us face to face with the really important problem, why is there periodicity at all? The most obvious explanation in our case as in that of human measles epidemics is that, given the ubiquitous presence of an infective agent, epidemic disease breaks out when those apt to take it are at or about a critical proportion, when in fact the frequency distribution of susceptibility (*i.e.* the proportions in the population exposed for each grade of susceptibility assumed to be a continuous variable) approximates to a particular form. In a later section we shall show that it is not proved that at the starting-point of a wave the percentage composition of the population grouped by cage-age differs significantly from its composition at another phase, in fact we cannot from a scrutiny of the age composition predict with success the date of the next epidemic; we cannot even show that numbers alone constitute a criterion, *i.e.* that when the total population has reached such or such a value, an epidemic occurs. But it is also a fact that the apparent periodicity is most regular, though of smaller amplitude, in the experiment with most immigration and greatest population.

In other words, the waves are more regular but lower where the population, in virtue both of its absolute magnitude and its rate of change, contains the most representative sample of the mice used in our experiments. For these reasons, we do not think that a failure to establish, by the method of the periodogram, a regular succession entitles us to ignore the wave-like features of the mortality charts and to evade the discussion of their aetiology. Epidemiologists have invoked four different explanations of epidemic periodicity, a meteorological—using that term in its broadest sense, see our general introduction; changes of human receptivity (the explanation especially favoured in the case of measles); re-importation; a special life-cycle of the parasite. We have dealt in other sections with the two former doctrines, of which the first does not seem to be relevant to our observations. The doctrine of re-importation is, we think, that commanding the largest amount of support and in the form advocated by, for instance, Kisskalt, which differs from the popular form (the latter assumes the introduction of a *materies morbi* into a virgin soil) in postulating an increased epidemicity by the grafting upon an endemic form of a new infection, we cannot say that our facts are irreconcilable with it; we can only say that we do not see how, with our technique,

reimportation could occur, and it is hard for us to conceive how and why there should be even so much regularity in the wave form and intervals between waves as we have actually found. Brownlee's views are set out in the following passage which we quote from his latest (1919) memoir on epidemic measles.

Having spoken of the appearance and the temporary disappearance of a 97 weeks' cycle in measles he continues:

It must therefore be taken that the phenomena have some permanence and that the recurrence is not due to chance alone. The irregularity observed in this case is similar to that which has brought the analyses of some disease statistics into disrepute. In the absence of a long series of statistics permanence is difficult to demonstrate. What has held for a considerable time has seemed, in a number of cases, apparently to hold no longer. Change in the nature of a phenomenon leads much more readily to doubt, than permanence of a limited duration to belief. In the case of London, however, a series of statistics of sufficient length exists to demonstrate that the disappearance of a phenomenon may be apparent only and not permanent. What then is the explanation of this permanence? I think it comparatively simple. It is that an epidemic is due chiefly to the properties of the organism causing it, and that the periodicity of epidemics which occur at regular intervals depends for the most part on the life-history of the organism. Many biologists and statisticians doubt this at present, but a step in the proof of the accuracy of this opinion is, I think, given by the phenomena under consideration. In a large city like London, the organisms which produce epidemics of measles belong not to one strain but to several, each of these strains possessing different properties. The property alone at present considered is that which determines the periodicity of the epidemic. Grant that one strain of an organism is capable of producing an attack of the disease which confers a certain degree of immunity against another strain, and grant that its life-history on the average is the same, then the phenomena which follow will be of the nature of those observed. To illustrate this the fifth line of the graph in the diagram has been constructed. It shows what would happen if two epidemics occasioning an equal number of deaths occurred periodically, the one epidemic having a periodicity of 97 weeks, as is the case with the chief London epidemic, and the second a periodicity of 87 weeks. These epidemics are supposed to be at their maxima simultaneously at the point marked × in the diagram. With the first recurrence, the maxima of these epidemics will be separated by an interval of ten weeks, while by the time the fifth or sixth recurrences are reached the maximum of one period will coincide with the minimum of the other. A dead level of epidemicity at this period is the phenomenon requiring explanation. As, however, time goes on the epidemics will again have their maxima simultaneously and epidemic outbursts will be associated with intervals free from the disease. Comparing the last graph with the combined graph of the 24½ years' periods for the city of London the similarity is obvious.

Having then described the data of other cities, Brownlee continues:

The meaning of the phenomena found now falls to be considered. The common explanation of the periodicity of epidemics of children's diseases is that the susceptible children take the disease in sufficient numbers to limit the further spread. The epidemic thus dies out to recur when a sufficient number of susceptible children have accumulated. This is quite a feasible theory and certainly explains periodicity of epidemics. The forms of epidemic curves which arise on this hypothesis are not unlike those actually found, the differences being no more than might be expected between a mathematical formula based on an hypothesis and the natural conditions to which the hypothesis is only an approximation. This explanation, however, must fail if epidemics of different periods can be shown to exist in the same town at the same time, and I think this has been shown. In London, which

on account of its size might be assumed deserving of special treatment, the existence of periods of different length has been demonstrated. In Edinburgh, Glasgow and Birmingham also it has been shown that epidemics with periods in the neighbourhood of 98 weeks and 110 weeks intermix. The same epidemicity even applies to districts of London. In the west end of London we have almost a replica of what occurs in Glasgow, Birmingham and Edinburgh. The main period there is 97 weeks, the secondary period 109½ weeks. In the south of London one period is that of 97 weeks, but almost equally prominent is that of 87 weeks. The whole evidence, therefore, seems to point to some condition in the organism which produces the disease as the potent cause of the difference rather than the number of susceptible children. Compare the *Paramecium* which in natural conditions divides asexually for several hundred times and then dies out unless conjugation takes place. The resting stage following conjugation persists for some time.

There is, however, one point of great importance which must be considered. If an epidemic begin in a definite locality and spread from that locality, and if there is no loss of infectivity on the part of the organism, it is demonstrable that a similar proportion of the population should be attacked in each zone as the epidemic spreads outward. On the other hand, if the organism lose the power of infecting with the lapse of time, in each additional zone invaded the proportion of susceptible persons infected should become smaller and smaller. Of course this might not be true for any one epidemic, as in many parts of the area invaded the population might be more or less insusceptible because of recent attack of the disease, but when an average of twenty epidemics has been taken this effect should be eliminated, the number of times the invading organism comes into contact with an insusceptible population being balanced by the number of times which it meets one more susceptible than the average. The method of spread of epidemic on the average should thus give some indication regarding the laws which determine the course of the phenomenon. Now with regard to London, the clearest facts refer to the 87 weeks', the 97 weeks', and the 109½ weeks' periods. The 97 weeks' period starts at the same time all over the city and there is no evidence of any special centre. The infection seems generalised. With regard to the 87 weeks' epidemic, however, the case is different. This seems to start in St Saviour's parish and to spread thence to Camberwell, Lambeth, etc. In this epidemic the rate of spread can be definitely measured. The maximum occurs later and later as the difference distance from the centre is increased and the percentage of children infected is also observed to fall as the time increases. With regard to the 109½ weeks' period epidemic the facts are similar though not quite so definite. This seems to show that for at least two strains of organism the epidemic ceases because the organism has lost its power of infecting. It may be inferred then that an epidemic ceases because the organism varies in its potency to cause infection. A cycle of epidemics now coinciding and now differing in their maxima can thus be explained. Some kind of life-cycle exists in the infecting organism. In this life-cycle high powers of infecting are attained probably after a resting stage: a period of activity follows and gives place to a period of rest; the average length of the cycle is determined by the strain of the organism.

The value of any hypothesis is in its power of resuming and relating phenomena and enabling man to forecast what will happen; one element, then, of value is subjective and thus the criticism of an hypothesis which is valid for one person is not for another. To Brownlee it is easier to hold the facts together by an hypothesis of changing parasites than to admit the special modifications of the common doctrine of varying human susceptibility and casual importation of *materies morbi*, which must be made in order to co-ordinate the epidemic varieties which he has described. To him, the hypothesis of a parasitic life-cycle is simpler and therefore, on Occam's principle, he is

logically justified in adopting it. To us, the hypothesis of a life-cycle is no simplification. Such analogies as those Brownlee has sometimes invoked, plagues of voles, locusts, etc. remain mere analogies. We are to suppose that at some past epoch there emerged varieties of an organism which, unmodified in their essential properties by passages through generations of host, in spite of transfer, in spite of admixture, pass through a cycle of change, regularly recurrent and productive of essentially the same effects upon the human herd. We do not say there is anything inherently impossible in this doctrine, but merely that it is not, to us, any simplification of the difficulties; it is only another way of saying that there *is* a secular periodicity of epidemics. The phenomenon under study in our experiment is much less complex than those with which Brownlee has dealt, yet even here we cannot see how the postulation of a life-cycle of the organism really helps us. We see that the rate of mortality in a population wherein infective material is present is not constant, that when a wave has spent itself, time elapses before another makes head; we have seen that the length of the latent period is probably a function of the rate of immigration. Beyond this we cannot go; perhaps further experiment will enlighten us, perhaps others in the light of Brownlee's reasoning, which we have given, we hope, fairly, may be able to explain our present results.

V. Comparison of Average Death-Rates in the Different Experiments.

Since, in the general introduction, we have dealt with this matter, it will be sufficient here to give a tabular statement (Table I).

Table I. *Average death-rates in the different experiments.*

Exp.	Rate of addition	No. of mouse-days exposure to risk	Av. daily death-rates q_x (all deaths)	Av. daily death-rates q_x (specific deaths)	Av. daily ratio of Nos. under 30 to Nos. over 30 days	Av. daily population
3	Six mice per day (14. ii. 24 to 27. vii. 24)*	25,697	·0303	·0264	2·1	155·7
2 *a*	Three mice per day (6. iii. 21 to 30. iv. 23)	49,880	·0460	·0366	2·3	63·5
4	Two mice per day (14. ii. 24 to 30. viii. 24)	12,059	·0304	·0244	1·6	60·6
2 *b*	One mouse per day (1. v. 23 to 30. viii. 24)	19,900	·0258	·0184	0·97	40·8
5	One mouse per 2 days (14. ii. 24 to 29. ix. 24)	4,636	·0211	·0190	1·2	20·2
6	One mouse per 3 days (14. ii. 24 to 29. ix. 24)	3,477	·0155	·0124	1·0	15·2
7	Mice in batches at intervals (14. ii. 24 to 29. ix. 24)	16,968	·0182	·0126	Varies abruptly	74·1

* Entries were stopped on 27. vii. 24.

The most reliable comparison is between the two parts of Exp. 2, having regard to the scale of the experience. Here the higher death-rate is associated with a larger average population and a greater proportion of young mice. This

is the general tendency; it is true that the death-rate of the experiment with six daily immigrants is not so high as that with three, but the period of exposure was shorter and we see in the longer experiments such variations from time to time that conclusions drawn from a less extended trial must be held suspect.

The contrast between Exp. 7, in which immigrants arrived in batches, and the others is worth emphasising. Excepting No. 6 its death-rate is the least, although its average population is the second largest. Evidently continuity of immigration as well as average population must be important. It seems that a continuous supply is required to maintain a high death-rate, although, as observed before, the increase of mortality does not outstrip or equal the increase of population.

VI. DEATH-RATES AT AGES. LIFE TABLES.

In these populations, as in human populations, the rates of mortality upon those of the same age change, exhibit secular variation, while the rates of mortality sustained by groups of mice of different ages at the same phase of the experiment are not identical. In this section we shall examine facts belonging to the second category and study the influence of *average* environmental forces applied at different times of the individual's life. The life tables[1] about to be described picture the average force of mortality operating upon mice, after different lengths of exposure to infection. Very unfortunately we have no standard of comparison such as a life table based upon the experience of captive mice not deliberately exposed to an epidemic disease would provide. Nobody has published any suitable data and our inquiries amongst breeders have done no more than elicit the opinion that mice usually live about two years, but some survive four or five[2].

[1] A life table gives a picture of the conditions of an imaginary population of, say, 10,000 persons, supposed all born on the same day and observed to the end of their lives, who suffer at each age the same rates of mortality as those found among the population considered. The constants usually given in a life table are (1) the number l_x who survive to a given age x; (2) the number d_x who die between ages x and $x+1$; (3) the probability q_x at age x of dying between ages x and $x+1$, $\left(q_x = \frac{d_x}{l_x}\right)$; (4) the expectation of life e_x, at age x, which is the average lifetime *after* age x of all those who survive to age x. For example, take the entry for age 10 in Table III: $l_x = 5802{\cdot}74$, $d_x = 279{\cdot}6$, $q_x = {\cdot}048184$, $e_x = 23{\cdot}20$; this means that out of 10,000 mice entering the cage on day 0, 5803 may be expected to be still alive on day 10, 280 of these will probably die on that day, so that the probability of dying on day 10 is ·048184, and that the average after lifetime of these 5803 mice is 23·20 days. We have used two other constants ${}_5q_x$, which means the probability at age x of dying in the next 5 days and ${}_{60}e_x$, the expectation of life limited to 60 days ahead, *i.e.* the average after-life time of survivors to age x, ignoring any part of such after-time that exceeded 60 days.

Thus, in Table X, for age 20 ${}_5q_x = {\cdot}2071$ and ${}_{60}e_x = 29{\cdot}62$, which means that ·2071 of the survivors to age 20 will die before age 25, and that the average number of days these survivors live after 20 is 29·62, counting as 60 any number of days exceeding 60.

[2] From the particulars of the normal mice contained in Murray's paper (1913) we should infer that at the age of six months the expectation of life of a mouse was less than a year and that mice which do survive to the age of two years will, on the average, live about another year,

We are under the further disadvantage that the exact ages of the mice at entry are also unknown; almost certainly they were all more than six weeks and less than six months old. As none survived into old age, this defect may not be very serious[1]. Lastly, no distinction of sex has been drawn.

Complete unsmoothed life tables of both phases of Exp. 2 have been made and also for Exps. 3 and 4. For Exp. 2 separate tables for all deaths and for specific *Pasteurella* deaths were preferred[2]; in Exps. 3 and 4 the tables are for specific mortality (see Table II).

Exps. 5, 6 and 7 were not suitable for complete calculations and the death-rates at five day intervals have been used.

Table II. *Data used in the Life Tables.*

	Exp. 2		Exp. 3	Exp. 4
	Three mice added per day	One mouse added per day	Six mice added per day	Two mice added per day
Period covered	6. iii. 21 to 30. iv. 23	1. v. 23 to 30. viii. 24	14. ii. 24 to 27. vii. 24‡	14. ii. 24 to 30. viii. 24
No. of calendar days	786	488	165	199
No. of mice concerned*	2354	549	990	396
No. who die	2292	514	778	367
No. who die of specific deaths†	1827	366	678	294
No. existing at beginning of period	—	62	—	—
No. surviving at end of period	62	35	212	29
No. of mouse days exposed to risk	49880	19900	25697	12059
Expectation of life at entry in days:				
(*a*) From specific deaths only ...	28·45	55·47	39·03	39·53
(*b*) From all deaths	21·48	37·92	—	—
Life table death-rate (daily):				
(*a*) From specific deaths only ...	·0352	·0180	·0256	·0253
(*b*) From all deaths	·0466	·0264	—	—

* The 26 original mice in Exp. 2, and the 20 original mice in Exps. 3 and 4, some of whom were directly infected, have not been included.

† Specific deaths = mice in whom *Pasteurella* (either alone or with another infection) was found on post-mortem examination, and all mice who could not be examined post-mortem.

‡ 27. vii. 24 was the date on which entries were stopped.

In point of length of exposure, the first part of Exp. 2 is the most reliable; it covered more than two years. The second part, one daily immigrant, covered one year and four months but concerns only 549 mice. Exp. 3 only lasted five and a half months but concerned 990 mice; the life table for this experiment does not include the time after additions ceased to be made.

A general study of the secular graphs had suggested that the mice which had been exposed long were more resistant, an impression confirmed by sampling (*vide infra*), which also suggested that such immunity was not permanent but waxed and waned. The number of deaths at any age is,

but the data are not suitable for exact statistical measurements. Lynch (1924) says: "at two years old a female mouse has passed the reproductive period and is considered old." Kirkham (1919) put the expectation of life at about two years.

[1] Webster (1923 *c*) thinks that for mouse typhoid (infection *per os*) while the young, adult and old mice showed no striking differences of susceptibility, there is a distinct racial variation.

[2] We have included under *Pasteurella* deaths those of animals not examined post-mortem, as well as mixed infections (*vide supra*).

however, a function not only of the general conditions of exposure at that age, but of the conditions of exposure at earlier ages; hence the importance of some averaging process (*vide infra*) such as that here used.

Table III.

Exp. 2. Life table (unsmoothed) for the whole of the period during which three mice per day were added (6. iii. 21 *to* 30. iv. 23 *inclusive*).

All deaths. 2354 mice.

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
0	10000·00	216·65	·021665	21·48	54	1012·19	46·01	·045455	36·35
1	9783·35	327·53	·033478	20·95	55	966·18	23·00	·023810	37·06
2	9455·82	349·27	·036937	20·66	56	943·17	27·61	·029268	36·95
3	9106·55	563·03	·061827	20·43	57	915·57	23·00	·025126	37·05
4	8543·52	512·61	·060000	20·74	58	892·56	23·00	·025773	36·99
5	8030·91	513·16	·063898	21·04	59	869·56	23·00	·026455	36·96
6	7517·75	501·18	·066667	21·44	60	846·56	32·38	·038251	36·95
7	7016·57	377·19	·053757	21·93	61	814·17	13·88	·017045	37·40
8	6639·38	428·90	·064599	22·15	62	800·30	32·38	·040462	37·04
9	6210·48	407·74	·065653	22·65	63	767·91	27·92	·036364	37·58
10	5802·74	279·60	·048184	23·20	64	739·99	4·65	·006289	37·98
11	5523·14	296·80	·053738	23·35	65	735·34	18·62	·025316	37·22
12	5226·34	275·52	·052718	23·65	66	716·72	4·65	·006494	37·17
13	4950·82	331·49	·066957	23·94	67	712·07	18·62	·026144	36·41
14	4619·33	306·23	·066293	24·62	68	693·45	13·96	·020134	36·38
15	4313·10	375·24	·087000	25·33	69	679·49	51·19	·075342	36·11
16	3937·86	280·66	·071272	26·70	70	628·29	13·96	·022222	38·01
17	3657·20	246·70	·067456	27·71	71	614·33	13·96	·022727	37·87
18	3410·50	264·68	·077608	28·68	72	600·37	4·65	·007752	37·74
19	3145·82	212·91	·067680	30·05	73	595·72	9·31	·015625	37·03
20	2932·91	200·76	·068452	31·19	74	586·41	23·27	·039683	36·61
21	2732·15	174·58	·063898	32·45	75	563·14	4·65	·008264	37·10
22	2557·57	174·88	·068376	33·63	76	558·48	37·55	·067227	36·40
23	2382·69	122·41	·051376	35·06	77	520·94	23·68	·045455	37·99
24	2260·28	91·99	·040698	35·93	78	497·26	9·47	·019048	38·78
25	2168·29	70·23	·032389	36·44	79	487·79	23·68	·048544	38·52
26	2098·06	74·62	·035565	36·64	80	464·11	23·68	·051020	39·46
27	2023·44	87·79	·043384	36·97	81	440·43	18·94	·043011	40·55
28	1935·66	88·18	·045558	37·63	82	421·49	—	—	41·35
29	1847·47	66·14	·035800	38·40	83	421·49	4·74	·011236	40·35
30	1781·34	57·46	·032258	38·80	84	416·75	—	—	39·81
31	1723·87	39·78	·023077	39·08	85	416·75	14·37	·034483	38·81
32	1684·09	48·75	·028947	38·99	86	402·38	—	—	39·18
33	1635·34	31·19	·019074	39·14	87	402·38	14·37	·035714	38·18
34	1604·15	53·47	·033333	38·89	88	388·01	9·58	·024691	38·57
35	1550·68	53·63	·034582	39·22	89	378·43	—	—	38·54
36	1497·05	26·89	·017964	39·60	90	378·43	9·58	·025316	37·54
37	1470·16	26·98	·018349	39·32	91	368·85	9·58	·025974	37·50
38	1443·18	26·98	·018692	39·04	92	359·27	—	—	37·48
39	1416·21	31·47	·022222	38·78	93	359·27	28·74	·080000	36·48
40	1384·74	31·57	·022801	38·65	94	330·53	4·79	·014493	38·61
41	1353·16	27·15	·020067	38·54	95	325·74	9·58	·029412	38·17
42	1326·01	31·68	·023891	38·32	96	316·16	—	—	38·31
43	1294·33	22·63	·017483	38·24	97	316·16	4·79	·015152	37·31
44	1271·70	18·10	·014235	37·91	98	311·37	14·60	·046875	36·88
45	1253·60	31·68	·025271	37·45	99	296·77	14·84	·050000	37·67
46	1221·92	40·73	·033333	37·41	100	281·93	—	—	38·63
47	1181·19	18·10	·015326	37·68	101	281·93	9·89	·035088	37·63
48	1163·09	13·63	·011719	37·26	102	272·04	10·08	·037037	37·98
49	1149·46	31·93	·027778	36·70	103	261·96	—	—	38·42
50	1117·53	22·90	·020492	36·73	104	261·96	5·04	·019231	37·42
51	1094·63	27·48	·025105	36·49	105	256·93	—	—	37·14
52	1067·15	41·22	·038627	36·42	106	256·93	—	—	36·14
53	1025·93	13·74	·013393	36·86	107	256·93	—	—	35·14

Table III (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x
108	256·93	5·04	·019608	34·14
109	251·89	5·04	·020000	33·81
110	246·85	—	—	33·49
111	246·85	10·08	·040816	32·49
112	236·77	5·04	·021277	32·86
113	231·74	5·04	·021739	32·56
114	226·70	5·04	·022222	32·27
115	221·66	15·11	·068182	31·99
116	206·55	15·11	·073171	33·30
117	191·43	—	—	34·89
118	191·43	—	—	33·89
119	191·43	5·04	·026316	32·89
120	186·40	10·08	·054054	32·76
121	176·32	—	—	33·61
122	176·32	5·04	·028571	32·61
123	171·28	10·08	·058824	32·55
124	161·21	10·08	·062500	33·55
125	151·13	5·04	·033333	34·76
126	146·10	10·08	·068966	34·94
127	136·02	5·04	·037037	36·49
128	130·98	—	—	36·87
129	130·98	—	—	35·87
130	130·98	5·04	·038462	34·87
131	125·94	—	—	35·25
132	125·94	5·25	·041667	34·25
133	120·70	—	—	34·72
134	120·70	10·50	·086957	33·72
135	110·20	—	—	35·88
136	110·20	—	—	34·88
137	110·20	5·25	·047619	33·88
138	104·95	—	—	34·55
139	104·95	5·25	·050000	33·55
140	99·71	—	—	
141	99·71	5·25	·052632	
142	94·46	5·25	·055556	
143	89·21	5·25	·058824	
144	83·96	5·25	·062500	
145	78·71	—	—	
146	78·71	10·50	·133333	
147	68·22	5·25	·076923	
148	62·97	—	—	
149	62·97	—	—	
150	62·97	—	—	
151	62·97	5·25	·083333	
152	57·72	10·50	·181818	
153	47·23	5·25	·111111	
154	41·98	—	—	
155	41·98	—	—	
156	41·98	—	—	
157	41·98	—	—	
158	41·98	—	—	
159	41·98	—	—	
160	41·98	—	—	
161	41·98	—	—	
162	41·98	—	—	
163	41·98	—	—	
164	41·98	—	—	
165	41·98	—	—	
166	41·98	—	—	
167	41·98	—	—	
168	41·98	—	—	
169	41·98	—	—	

Cage-age in days	l_x	d_x	q_x	e_x
170	41·98	—	—	
171	41·98	—	—	
172	41·98	—	—	
173	41·98	—	—	
174	41·98	5·25	·125000	
175	36·73	5·25	·142857	
176	31·49	—	—	
177	31·49	—	—	
178	31·49	—	—	
179	31·49	5·25	·166667	
180	26·24	—	—	
181	26·24	—	—	
182	26·24	5·25	·200000	
183	20·99	—	—	
184	20·99	—	—	
185	20·99	—	—	
186	20·99	—	—	
187	20·99	—	—	
188	20·99	—	—	
189	20·99	—	—	
190	20·99	—	—	
191	20·99	—	—	
192	20·99	—	—	
193	20·99	—	—	
194	20·99	—	—	
195	20·99	—	—	
196	20·99	—	—	
197	20·99	—	—	
198	20·99	5·25	·250000	
199	15·74	—	—	
200	15·74	—	—	
201	15·74	—	—	
202	15·74	—	—	
203	15·74	—	—	
204	15·74	—	—	
205	15·74	—	—	
206	15·74	—	—	
207	15·74	—	—	
208	15·74	—	—	
209	15·74	—	—	
210	15·74	—	—	
211	15·74	—	—	
212	15·74	5·25	·333333	
213	10·50	—	—	
214	10·50	—	—	
215	10·50	—	—	
216	10·50	—	—	
217	10·50	—	—	
218	10·50	—	—	
219	10·50	—	—	
220	10·50	—	—	
221	10·50	—	—	
222	10·50	—	—	
223	10·50	—	—	
224	10·50	5·25	·500000	
225	5·25	—	—	
⋮				
340	5·25	—	—	
341	5·25	5·25	1·000000	
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Table IV.

Exp. 2*a*. *Life table for three mouse period* (6. iii. 21 *to* 30. iv. 23 *inclusive*).

Specific deaths. 2354 mice.

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
0	10000·00	89·21	·008921	28·45	61	1375·53	23·45	·017045	42·33
1	9910·79	155·12	·015652	27·70	62	1352·08	54·71	·040462	42·05
2	9755·67	276·85	·028378	27·14	63	1297·37	31·45	·024242	42·81
3	9478·82	475·05	·050117	26·91	64	1265·92	7·96	·006289	42·86
4	9003·77	436·68	·048500	27·31	65	1257·96	23·88	·018987	42·13
5	8567·09	469·87	·054846	27·67	66	1234·08	8·01	·006494	41·93
6	8097·22	466·00	·057550	28·25	67	1226·07	24·04	·019608	41·20
7	7631·22	358·95	·047037	28·94	68	1202·03	24·20	·020134	41·02
8	7272·27	394·62	·054264	29·35	69	1177·83	80·67	·068493	40·85
9	6877·65	375·49	·054596	30·00	70	1097·16	24·38	·022222	42·82
10	6502·16	245·82	·037806	30·71	71	1072·78	24·38	·022727	42·78
11	6256·34	267·99	·042835	30·89	72	1048·40	8·13	·007752	42·76
12	5988·35	266·37	·044481	31·25	73	1040·27	16·25	·015625	42·09
13	5721·98	303·51	·053043	31·69	74	1024·02	40·64	·039683	41·75
14	5418·47	263·08	·048553	32·43	75	983·38	8·13	·008264	42·46
15	5155·39	381·50	·074000	33·06	76	975·25	57·37	·058824	41·81
16	4773·89	287·90	·060307	34·66	77	917·88	33·08	·036036	43·39
17	4485·99	233·59	·052071	35·86	78	884·80	25·04	·028302	43·99
18	4252·40	275·92	·064886	36·80	79	859·76	41·74	·048544	44·26
19	3976·48	219·70	·055249	38·32	80	818·02	41·74	·051020	45·49
20	3756·78	195·66	·052083	39·53	81	776·28	25·04	·032258	46·91
21	3561·12	170·66	·047923	40·67	82	751·24	—	—	47·46
22	3390·46	179·66	·052991	41·70	83	751·24	8·44	·011236	46·46
23	3210·80	135·50	·042202	43·00	84	742·80	—	—	45·98
24	3075·30	101·32	·032946	43·87	85	742·80	25·61	·034483	44·98
25	2973·98	84·28	·028340	44·35	86	717·19	—	—	45·57
26	2889·70	90·68	·031381	44·63	87	717·19	8·54	·011905	44·57
27	2799·02	78·93	·028200	45·06	88	708·65	17·50	·024691	44·10
28	2720·09	86·75	·031891	45·35	89	691·15	—	—	44·20
29	2633·34	69·13	·026253	45·83	90	691·15	—	—	43·20
30	2564·21	76·35	·029777	46·05	91	691·15	8·98	·012987	42·20
31	2487·86	51·03	·020513	46·45	92	682·17	—	—	41·75
32	2436·83	51·30	·021053	46·41	93	682·17	54·57	·080000	40·75
33	2385·53	45·50	·019074	46·40	94	627·60	9·10	·014493	43·25
34	2340·03	52·00	·022222	46·29	95	618·50	18·19	·029412	42·88
35	2288·03	46·16	·020173	46·33	96	600·31	—	—	43·16
36	2241·87	33·56	·014970	46·28	97	600·31	9·10	·015152	42·16
37	2208·31	33·77	·015291	45·97	98	591·21	27·71	·046875	41·80
38	2174·54	33·87	·015576	45·68	99	563·50	9·39	·016667	42·84
39	2140·67	27·18	·012698	45·39	100	554·11	—	—	42·55
40	2113·49	34·42	·016287	44·97	101	554·11	19·44	·035088	41·55
41	2079·07	34·77	·016722	44·71	102	534·67	19·80	·037037	42·05
42	2044·30	34·89	·017065	44·46	103	514·87	—	—	42·64
43	2009·41	28·10	·013986	44·22	104	514·87	9·90	·019231	41·64
44	1981·31	21·15	·010676	43·84	105	504·97	—	—	41·45
45	1960·16	42·46	·021661	43·31	106	504·97	—	—	40·45
46	1917·70	63·92	·033333	43·26	107	504·97	—	—	39·45
47	1853·78	28·41	·015326	43·73	108	504·97	—	—	38·45
48	1825·37	14·26	·007813	43·41	109	504·97	10·10	·020000	37·45
49	1811·11	35·93	·019841	42·74	110	494·87	—	—	37·20
50	1775·18	36·38	·020492	42·60	111	494·87	20·20	·040816	36·20
51	1738·80	36·38	·020921	42·48	112	474·67	10·10	·021277	36·72
52	1702·42	29·23	·017167	42·38	113	464·57	10·10	·021739	36·51
53	1673·19	22·41	·013393	42·11	114	454·47	10·10	·022222	36·31
54	1650·78	52·52	·031818	41·67	115	444·37	20·20	·045455	37·14
55	1598·26	38·05	·023810	42·03	116	424·17	31·04	·073171	36·82
56	1560·21	38·05	·024390	42·04	117	393·13	—	—	38·69
57	1522·16	30·60	·020101	42·08	118	393·13	—	—	37·69
58	1491·56	30·75	·020619	41·93	119	393·13	10·35	·026316	36·69
59	1460·81	38·65	·026455	41·80	120	382·78	20·69	·054054	36·67
60	1422·16	46·63	·032787	41·93	121	362·09	—	—	37·74

Table IV (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x
122	362·09	10·35	·028571	36·74
123	351·74	20·69	·058824	36·80
124	331·05	10·35	·031250	38·07
125	320·70	10·69	·033333	38·28
126	310·01	21·38	·068966	38·58
127	288·63	10·69	·037037	40·41
128	277·94	—	—	40·94
129	277·94	—	—	39·94
130	277·94	10·69	·038462	38·94
131	267·25	—	—	39·48
132	267·25	11·14	·041667	38·48
133	256·11	—	—	39·13
134	256·11	22·27	·086957	38·13
135	233·84	—	—	40·72
136	233·84	—	—	39·72
137	233·84	11·14	·047619	38·72
138	222·70	—	—	39·63
139	222·70	11·14	·050000	38·63
140	211·56	—	—	39·63
141	211·56	11·13	·052632	38·63
142	200·43	11·14	·055556	39·75
143	189·29	—	—	41·06
144	189·29	11·83	·062500	40·06
145	177·46	—	—	41·70
146	177·46	23·66	·133333	40·70
147	153·80	11·83	·076923	45·88
148	141·97	—	—	48·67
149	141·97	—	—	47·67
150	141·97	—	—	46·67
151	141·97	11·83	·083333	45·67
152	130·14	23·66	·181818	48·77
153	106·48	11·83	·111111	58·50
154	94·65	—	—	64·75
155	94·65	—	—	63·75
156	94·65	—	—	62·75
157	94·65	—	—	61·75
158	94·65	—	—	60·75
159	94·65	—	—	59·75
160	94·65	—	—	58·75
161	94·65	—	—	57·75
162	94·65	—	—	56·75
163	94·65	—	—	55·75
164	94·65	—	—	54·75
165	94·65	—	—	53·75
166	94·65	—	—	52·75
167	94·65	—	—	51·75
168	94·65	—	—	50·75
169	94·65	—	—	49·75
170	94·65	—	—	48·75
171	94·65	—	—	47·75
172	94·65	—	—	46·75
173	94·65	—	—	45·75
174	94·65	11·83	·125000	44·75
175	82·82	11·83	·142857	50·07

Cage-age in days	l_x	d_x	q_x	e_x
176	70·99	—	—	57·33
177	70·99	—	—	56·33
178	70·99	—	—	55·33
179	70·99	11·83	·166667	54·33
180	59·16	—	—	64·09
181	59·16	—	—	63·09
182	59·16	11·83	·200000	62·09
183	47·33	—	—	76·48
184	47·33	—	—	75·48
185	47·33	—	—	74·48
186	47·33	—	—	73·48
187	47·33	—	—	72·48
188	47·33	—	—	71·48
189	47·33	—	—	70·48
190	47·33	—	—	
191	47·33	—	—	
192	47·33	—	—	
193	47·33	—	—	
194	47·33	—	—	
195	47·33	—	—	
196	47·33	—	—	
197	47·33	—	—	
198	47·33	—	—	
199	47·33	—	—	
200	47·33	—	—	
201	47·33	—	—	
202	47·33	—	—	
203	47·33	—	—	
204	47·33	—	—	
205	47·33	—	—	
206	47·33	—	—	
207	47·33	—	—	
208	47·33	—	—	
209	47·33	—	—	
210	47·33	—	—	
211	47·33	—	—	
212	47·33	15·78	·333333	
213	31·55	—	—	
214	31·55	—	—	
215	31·55	—	—	
216	31·55	—	—	
217	31·55	—	—	
218	31·55	—	—	
219	31·55	—	—	
220	31·55	—	—	
221	31·55	—	—	
222	31·55	—	—	
223	31·55	—	—	
224	31·55	15·78	·500000	
225	15·77	—	—	
226	15·77	—	—	
⋮				
340	15·77	—	—	
341	15·77	15·77	1·000000	

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Table V.

Exp. 2b. Life table for one mouse period (1. v. 23 *to* 30. viii. 24 *inclusive*).

All deaths. 549 mice.

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
0	10000·00	—	—	37·92	61	1872·68	36·36	·019417	56·19
1	10000·00	163·60	·016360	36·92	62	1836·32	—	—	56·30
2	9836·40	305·48	·031056	36·53	63	1836·32	18·18	·009901	55·30
3	9530·92	324·46	·034043	36·68	64	1818·14	36·36	·020000	54·85
4	9206·47	383·60	·041667	36·96	65	1781·78	—	—	54·95
5	8822·86	322·30	·036530	37·54	66	1781·78	37·12	·020833	53·95
6	8500·57	360·87	·042453	37·95	67	1744·66	75·04	·043011	54·09
7	8139·69	360·87	·044335	38·61	68	1669·62	37·52	·022472	55·50
8	7778·82	280·68	·036082	39·37	69	1632·10	18·76	·011494	55·76
9	7498·14	340·82	·045455	39·83	70	1613·34	18·76	·011628	55·41
10	7157·32	219·31	·030641	40·70	71	1594·58	—	—	55·05
11	6938·01	339·90	·048991	40·97	72	1594·58	57·64	·036145	54·05
12	6598·11	219·94	·033333	42·06	73	1536·94	19·21	·012500	55·06
13	6378·17	119·97	·018809	42·49	74	1517·73	57·64	·037975	54·75
14	6258·21	259·10	·041401	42·30	75	1460·10	19·21	·013158	55·89
15	5999·11	99·65	·016611	43·10	76	1440·88	—	—	55·63
16	5899·46	317·82	·053872	42·82	77	1440·88	18·71	·012987	54·63
17	5581·64	197·23	·035336	44·23	78	1422·17	—	—	54·34
18	5384·41	117·48	·021818	44·83	79	1422·17	37·92	·026667	53·34
19	5266·93	214·58	·040741	44·82	80	1384·25	—	—	53·79
20	5052·35	115·70	·022901	45·70	81	1384·25	37·92	·027397	52·79
21	4936·65	173·55	·035156	45·76	82	1346·32	—	—	53·27
22	4763·10	134·44	·028226	46·41	83	1346·32	19·23	·014286	52·27
23	4628·65	230·47	·049793	46·74	84	1327·09	18·96	·014286	52·02
24	4398·18	133·86	·030435	48·17	85	1308·13	56·88	·043478	51·76
25	4264·32	76·15	·017857	48·66	86	1251·25	37·92	·030303	53·09
26	4188·17	133·26	·031818	48·54	87	1213·34	18·96	·015625	53·74
27	4054·91	114·22	·028169	49·12	88	1194·38	18·96	·015873	53·58
28	3940·69	151·57	·038462	49·53	89	1175·42	37·92	·032258	53·44
29	3789·13	18·95	·005000	50·49	90	1137·50	18·96	·016667	54·20
30	3770·18	94·25	·025000	49·74	91	1118·55	18·96	·016949	54·11
31	3675·93	18·85	·005128	50·00	92	1099·59	—	—	54·04
32	3657·08	56·55	·015464	49·26	93	1099·59	19·29	·017544	53·04
33	3600·52	74·62	·020725	49·02	94	1080·30	19·29	·017857	52·97
34	3525·90	18·75	·005319	49·05	95	1061·01	77·16	·072727	52·93
35	3507·15	111·93	·031915	48·31	96	983·84	—	—	56·04
36	3395·22	92·77	·027322	48·89	97	983·84	—	—	55·04
37	3302·45	110·70	·033520	49·25	98	983·84	37·84	·038462	54·04
38	3191·75	147·60	·046243	49·94	99	946·00	37·10	·039216	55·18
39	3044·16	92·25	·030303	51·33	100	908·90	18·55	·020408	56·41
40	2951·91	55·00	·018634	51·92	101	890·35	37·10	·041667	56·58
41	2896·91	54·66	·018868	51·90	102	853·26	—	—	58·02
42	2842·25	54·66	·019231	51·89	103	853·26	18·15	·021277	57·02
43	2787·59	109·32	·039216	51·89	104	835·10	18·15	·021739	57·25
44	2678·27	36·69	·013699	52·99	105	816·95	18·15	·022222	57·51
45	2641·58	91·72	·034722	52·72	106	798·79	—	—	57·80
46	2549·86	92·39	·036232	53·60	107	798·79	18·15	·022727	56·80
47	2457·48	55·43	·022556	54·60	108	780·64	—	—	57·11
48	2402·04	91·68	·038168	54·84	109	780·64	—	—	56·11
49	2310·36	73·34	·031746	56·00	110	780·64	—	—	55·11
50	2237·02	145·50	·065041	56·82	111	780·64	—	—	54·11
51	2091·52	—	—	59·74	112	780·64	—	—	53·11
52	2091·52	55·04	·026316	58·74	113	780·64	36·31	·046512	52·11
53	2036·48	18·35	·009009	59·31	114	744·33	—	—	53·63
54	2018·13	54·54	·027027	58·85	115	744·33	54·46	·073171	52·63
55	1963·59	18·18	·009259	59·47	116	689·87	—	—	55·74
56	1945·41	18·18	·009346	59·02	117	689·87	18·15	·026316	54·74
57	1927·23	—	—	58·57	118	671·71	36·31	·054054	55·21
58	1927·23	—	—	57·57	119	635·40	—	—	57·34
59	1927·23	36·36	·018868	56·57	120	635·40	—	—	56·34
60	1890·86	18·18	·009615	56·65	121	635·40	18·15	·028571	55·34

Table V (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
122	617·25	—	—	55·95	187	253·73	42·29	·166667	30·22
123	617·25	—	—	54·95	188	211·45	—	—	35·17
124	617·25	18·15	·029412	53·95	189	211·45	23·49	·111111	34·17
125	599·09	—	—	54·57	190	187·95	—	—	37·38
126	599·09	—	—	53·57	191	187·95	—	—	36·38
127	599·09	—	—	52·57	192	187·95	—	—	35·38
128	599·09	18·72	·031250	51·57	193	187·95	—	—	34·38
129	580·37	37·44	·064516	52·22	194	187·95	—	—	33·38
130	542·93	—	—	54·78	195	187·95	—	—	32·38
131	542·93	18·72	·034483	53·78	196	187·95	23·49	·125000	31·38
132	524·21	18·72	·035714	54·69	197	164·46	—	—	34·79
133	505·49	—	—	55·69	198	164·46	—	—	33·79
134	505·49	—	—	54·69	199	164·46	—	—	32·79
135	505·49	—	—	53·69	200	164·46	23·49	·142857	31·79
136	505·49	18·72	·037037	52·69	201	140·96	—	—	36·00
137	486·76	—	—	53·70	202	140·96	—	—	35·00
138	486·76	—	—	52·70	203	140·96	—	—	34·00
139	486·76	—	—	51·70	204	140·96	—	—	33·00
140	486·76	18·72	·038462	50·70	205	140·96	—	—	32·00
141	468·04	—	—	51·71	206	140·96	—	—	31·00
142	468·04	18·72	·040000	50·71	207	140·96	—	—	30·00
143	449·32	—	—	51·80	208	140·96	—	—	29·00
144	449·32	—	—	50·80	209	140·96	—	—	28·00
145	449·32	18·72	·041667	49·80	210	140·96	—	—	27·00
146	430·60	—	—	50·94	211	140·96	—	—	26·00
147	430·60	—	—	49·94	212	140·96	23·49	·166667	25·00
148	430·60	—	—	48·94	213	117·47	—	—	28·90
149	430·60	—	—	47·94	214	117·47	23·49	·200000	27·90
150	430·60	18·72	·043478	46·94	215	93·98	—	—	33·75
151	411·88	—	—	48·06	216	93·98	—	—	32·75
152	411·88	—	—	47·06	217	93·98	—	—	31·75
153	411·88	—	—	46·06	218	93·98	—	—	30·75
154	411·88	18·72	·045455	45·06	219	93·98	23·49	·250000	29·75
155	393·16	18·72	·047619	46·18	220	70·48	—	—	38·50
156	374·43	—	—	47·46	221	70·48	23·49	·333333	37·50
157	374·43	—	—	46·46	222	46·99	—	—	55·00
158	374·43	—	—	45·46	223	46·99	—	—	54·00
159	374·43	—	—	44·46	224	46·99	—	—	53·00
160	374·43	—	—	43·46	225	46·99	—	—	52·00
161	374·43	18·72	·050000	42·46	226	46·99	—	—	51·00
162	355·71	—	—	43·67	227	46·99	—	—	50·00
163	355·71	—	—	42·67	228	46·99	—	—	49·00
164	355·71	—	—	41·67	229	46·99	—	—	48·00
165	355·71	—	—	40·67	230	46·99	—	—	
166	355·71	—	—	39·67	231	46·99	—	—	
167	355·71	—	—	38·67	232	46·99	—	—	
168	355·71	—	—	37·67	233	46·99	—	—	
169	355·71	18·72	·052632	36·67	234	46·99	—	—	
170	336·99	—	—	37·68	235	46·99	—	—	
171	336·99	—	—	36·68	236	46·99	—	—	
172	336·99	19·82	·058824	35·68	237	46·99	—	—	
173	317·17	—	—	36·88	238	46·99	—	—	
174	317·17	—	—	35·88	239	46·99	—	—	
175	317·17	—	—	34·88	240	46·99	—	—	
176	317·17	—	—	33·88	241	46·99	—	—	
177	317·17	—	—	32·88	242	46·99	—	—	
178	317·17	—	—	31·88	243	46·99	—	—	
179	317·17	42·29	·133333	30·88	244	46·99	—	—	
180	274·88	—	—	34·55	245	46·99	—	—	
181	274·88	—	—	33·55	246	46·99	—	—	
182	274·88	21·14	·076923	32·55	247	46·99	—	—	
183	253·73	—	—	34·22	248	46·99	—	—	
184	253·73	—	—	33·22	249	46·99	23·49	·500000	
185	253·73	—	—	32·22	250	23·49	—	—	
186	253·73	—	—	31·22	251	23·49	—	—	

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Table V (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
252	23·49	—	—		262	23·49	—	—	
253	23·49	—	—		263	23·49	—	—	
254	23·49	—	—		264	23·49	—	—	
255	23·49	—	—		265	23·49	—	—	
256	23·49	—	—		266	23·49	—	—	
257	23·49	—	—		267	23·49	—	—	
258	23·49	—	—		⋮				
259	23·49	—	—		303	23·49	—	—	
260	23·49	—	—		304	23·49	23·49	1·000000	
261	23·49	—	—						

Table VI.

Exp. 2*b*. *Life table for one mouse period* (1. v. 23 *to* 30. viii. 24 *inclusive*).

Specific deaths only. 549 mice.

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
0	10000·00	—	—	55·47	44	4118·34	56·42	·013699	64·97
1	10000·00	20·45	·002045	54·47	45	4061·92	141·04	·034722	64·86
2	9979·55	227·27	·022774	53·58	46	3920·88	113·65	·028986	66·18
3	9752·28	269·75	·027660	53·82	47	3807·23	85·88	·022556	67·14
4	9482·53	311·92	·032894	54·34	48	3721·35	85·22	·022901	67·68
5	9170·61	272·18	·029680	55·17	49	3636·13	28·86	·007937	68·25
6	8898·43	314·80	·035377	55·84	50	3607·27	175·96	·048780	67·79
7	8583·63	338·27	·039409	56·87	51	3431·31	—	—	70·24
8	8245·36	191·26	·023196	58·18	52	3431·31	60·20	·017544	69·24
9	8054·10	279·95	·034759	58·55	53	3371·11	60·74	·018018	69·47
10	7774·15	151·59	·019499	59·64	54	3310·37	30·65	·009259	69·74
11	7622·56	241·64	·031700	59·82	55	3279·72	30·37	·009259	69·38
12	7380·92	89·46	·012121	60·76	56	3249·35	30·37	·009346	69·03
13	7291·46	91·43	·012539	60·50	57	3218·98	—	—	68·67
14	7200·03	160·51	·022293	60·26	58	3218·98	—	—	67·67
15	7039·52	93·55	·013289	60·62	59	3218·98	60·74	·018868	66·67
16	6945·97	163·71	·023569	60·43	60	3158·24	—	—	66·95
17	6782·26	143·79	·021201	60·88	61	3158·24	61·32	·019417	65·95
18	6638·47	72·42	·010909	61·19	62	3096·92	—	—	66·24
19	6566·05	170·23	·025926	60·86	63	3096·92	30·66	·009901	65·24
20	6395·82	97·64	·015267	61·46	64	3066·26	61·33	·020000	64·89
21	6298·18	98·41	·015625	61·41	65	3004·93	—	—	65·20
22	6199·77	100·00	·016129	61·38	66	3004·93	62·60	·020833	64·20
23	6099·77	126·55	·020747	61·37	67	2942·33	94·91	·032258	64·56
24	5973·22	129·85	·021739	61·66	68	2847·42	63·99	·022472	65·70
25	5843·37	78·26	·013393	62·02	69	2783·43	31·99	·011494	66·19
26	5765·11	131·02	·022727	61·86	70	2751·44	—	—	65·96
27	5634·09	105·80	·018779	62·28	71	2751·44	—	—	64·96
28	5528·29	132·89	·024038	62·47	72	2751·44	66·30	·024096	63·96
29	5395·40	26·98	·005000	62·99	73	2685·14	33·56	·012500	64·52
30	5368·42	107·37	·020000	62·31	74	2651·58	67·13	·025316	64·34
31	5261·05	26·98	·005128	62·57	75	2584·45	34·01	·013158	64·99
32	5234·07	53·96	·010309	61·89	76	2550·44	—	—	64·85
33	5180·11	107·36	·020725	61·53	77	2550·44	—	—	63·85
34	5072·75	—	—	61·82	78	2550·44	—	—	62·85
35	5072·75	134·91	·026596	60·82	79	2550·44	34·01	·013333	61·85
36	4937·84	134·91	·027322	61·47	80	2516·43	—	—	61·68
37	4802·93	134·16	·027933	62·18	81	2516·43	34·47	·013699	60·68
38	4668·77	161·92	·034682	62·95	82	2481·96	—	—	60·52
39	4506·85	81·94	·018182	64·20	83	2481·96	35·46	·014286	59·52
40	4424·91	27·48	·006211	64·38	84	2446·50	34·95	·014286	59·37
41	4397·43	55·32	·012579	63·77	85	2411·55	104·85	·043478	59·23
42	4342·11	55·67	·012821	63·58	86	2306·70	34·95	·015152	60·90
43	4286·44	168·10	·039216	63·40	87	2271·75	35·50	·015625	60·83

Table VI (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
88	2236·25	70·99	·031746	60·78	153	943·21	—	—	47·73
89	2165·26	35·50	·016393	61·76	154	943·21	42·87	·045455	46·73
90	2129·76	35·50	·016667	61·78	155	900·34	42·87	·047619	47·93
91	2094·26	35·50	·016949	61·82	156	857·47	—	—	49·31
92	2058·76	—	—	61·88	157	857·47	—	—	48·31
93	2058·76	—	—	60·88	158	857·47	—	—	47·31
94	2058·76	36·76	·017857	59·88	159	857·47	—	—	46·31
95	2022·00	110·29	·054545	59·96	160	857·47	—	—	45·31
96	1911·71	—	—	62·39	161	857·47	42·87	·050000	44·31
97	1911·71	—	—	61·39	162	814·60	—	—	45·61
98	1911·71	73·53	·038462	60·39	163	814·60	—	—	44·61
99	1838·18	72·09	·039216	61·78	164	814·60	—	—	43·61
100	1766·09	36·04	·020408	63·28	165	814·60	—	—	42·61
101	1730·05	72·09	·041667	63·59	166	814·60	—	—	41·61
102	1657·96	—	—	65·33	167	814·60	—	—	40·61
103	1657·96	35·28	·021277	64·33	168	814·60	—	—	39·61
104	1622·68	35·28	·021739	64·72	169	814·60	42·87	·052632	38·61
105	1587·40	—	—	65·15	170	771·73	—	—	39·73
106	1587·40	—	—	64·15	171	771·73	—	—	38·73
107	1587·40	36·08	·022727	63·15	172	771·73	45·40	·058824	37·73
108	1551·32	—	—	63·61	173	726·33	—	—	39·06
109	1551·32	—	—	62·61	174	726·33	—	—	38·06
110	1551·32	—	—	61·61	175	726·33	—	—	37·06
111	1551·32	—	—	60·61	176	726·33	—	—	36·06
112	1551·32	—	—	59·61	177	726·33	—	—	35·06
113	1551·32	72·15	·046512	58·61	178	726·33	—	—	34·06
114	1479·17	—	—	60·44	179	726·33	96·84	·133333	33·06
115	1479·17	108·23	·073171	59·44	180	629·49	—	—	37·06
116	1370·94	—	—	63·09	181	629·49	—	—	36·06
117	1370·94	36·08	·026316	62·09	182	629·49	48·42	·076923	35·06
118	1334·86	72·15	·054054	62·76	183	581·07	—	—	36·94
119	1262·71	—	—	65·32	184	581·07	—	—	35·94
120	1262·71	—	—	64·32	185	581·07	—	—	34·94
121	1262·71	—	—	63·32	186	581·07	—	—	33·94
122	1262·71	—	—	62·32	187	581·07	96·85	·166667	32·94
123	1262·71	—	—	61·32	188	484·22	—	—	38·43
124	1262·71	37·14	·029412	60·32	189	484·22	53·80	·111111	37·43
125	1225·57	—	—	61·13	190	430·42	—	—	41·05
126	1225·57	—	—	60·13	191	430·42	—	—	40·05
127	1225·57	—	—	59·13	192	430·42	—	—	39·05
128	1225·57	38·30	·031250	58·13	193	430·42	—	—	38·05
129	1187·27	38·30	·032258	58·99	194	430·42	—	—	37·05
130	1148·97	—	—	59·94	195	430·42	—	—	36·05
131	1148·97	39·62	·034483	58·94	196	430·42	53·80	·125000	35·05
132	1109·35	—	—	60·02	197	376·62	—	—	38·99
133	1109·35	—	—	59·02	198	376·62	—	—	37·99
134	1109·35	—	—	58·02	199	376·62	—	—	36·99
135	1109·35	—	—	57·02	200	376·62	53·80	·142857	35·99
136	1109·35	41·09	·037037	56·02	201	322·82	—	—	40·90
137	1068·26	—	—	57·16	202	322·82	—	—	39·90
138	1068·26	—	—	56·16	203	322·82	—	—	38·90
139	1068·26	—	—	55·16	204	322·82	—	—	37·90
140	1068·26	41·09	·038462	54·16	205	322·82	—	—	36·90
141	1027·17	—	—	55·31	206	322·82	—	—	35·90
142	1027·17	41·09	·040000	54·31	207	322·82	—	—	34·90
143	986·08	—	—	55·55	208	322·82	—	—	33·90
144	986·08	—	—	54·55	209	322·82	—	—	32·90
145	986·08	—	—	53·55	210	322·82	—	—	31·90
146	986·08	—	—	52·55	211	322·82	—	—	30·90
147	986·08	—	—	51·55	212	322·82	—	—	29·90
148	986·08	—	—	50·55	213	322·82	—	—	28·90
149	986·08	—	—	49·55	214	322·82	64·56	·200000	27·90
150	986·08	42·87	·043478	48·55	215	258·26	—	—	33·75
151	943·21	—	—	49·73	216	258·26	—	—	
152	943·21	—	—	48·73	217	258·26	—	—	

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Table VI (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
218	258·26	—	—		262	64·56	—	—	
219	258·26	64·57	·250000		263	64·56	—	—	
220	193·69	—	—		264	64·56	—	—	
221	193·69	64·56	·333333		265	64·56	—	—	
222	129·13	—	—		266	64·56	—	—	
223	129·13	—	—		267	64·56	—	—	
224	129·13	—			268	64·56	—	—	
225	129·13	—	—		269	64·56	—	—	
226	129·13	—	—		270	64·56	—	—	
227	129·13	—	—		271	64·56	—	—	
228	129·13	—	—		272	64·56	—	—	
229	129·13	—	—		273	64·56	—	—	
230	129·13	—	—		274	64·56	—	—	
231	129·13	—	—		275	64·56	—	—	
232	129·13	—	—		276	64·56	—	—	
233	129·13	—	—		277	64·56	—	—	
234	129·13	—	—		278	64·56	—	—	
235	129·13	—	—		279	64·56	—	—	
236	129·13	—	—		280	64·56	—	—	
237	129·13	—	—		281	64·56	—	—	
238	129·13	—	—		282	64·56	—	—	
239	129·13	—	—		283	64·56	—	—	
240	129·13	—	—		284	64·56	—	—	
241	129·13	—	—		285	64·56	—	—	
242	129·13	—	—		286	64·56	—	—	
243	129·13	—	—		287	64·56	—	—	
244	129·13	—	—		288	64·56	—	—	
245	129·13	—	—		289	64·56	—	—	
246	129·13	—	—		290	64·56	—	—	
247	129·13	—	—		291	64·56	—	—	
248	129·13	—	—		292	64·56	—	—	
249	129·13	64·57	·500000		293	64·56	—	—	
250	64·56	—	—		294	64·56	—	—	
251	64·56	—	—		295	64·56	—	—	
252	64·56	—	—		296	64·56	—	—	
253	64·56	—	—		297	64·56	—	—	
254	64·56	—	—		298	64·56	—	—	
255	64·56	—	—		299	64·56	—	—	
256	*64·56*	—	—		*300*	*64·56*	—	—	
257	*64·56*	—	—		*301*	*64·56*	—	—	
258	64·56	—	—		302	64·56	—	—	
259	64·56	—	—		303	64·56	—	—	
260	64·56	—	—		304	64·56	64·56	1·000000	
261	64·56	—	—						

Table VII.

Exp. 3. *Life table* (14. ii. 24 *to* 27. vii. 24 *inclusive*).

Specific deaths only. 990 mice.

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
0	10000·00	20·20	·002020	39·03	10	7047·96	225·18	·031949	42·89
1	9979·80	91·65	·009184	38·11	11	6822·78	158·94	·023295	43·29
2	9888·15	113·42	·011470	37·46	12	6663·84	183·52	·027539	43·31
3	9774·73	365·11	·037353	36·89	13	6480·32	230·62	·035587	43·52
4	9409·62	443·05	·047085	37·30	14	6249·70	92·93	·014870	44·11
5	8966·57	491·61	·054827	38·12	15	6156·77	189·44	·030769	43·77
6	8474·96	487·06	·057471	39·30	16	5967·33	96·06	·016097	44·14
7	7987·90	372·55	·046639	40·66	17	5871·27	121·81	·020747	43·86
8	7615·35	231·77	·030435	41·63	18	5749·46	159·71	·027778	43·78
9	7383·58	335·62	·045455	41·92	19	5589·75	149·73	·026786	44·01

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Table VII (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
20	5440·02	112·81	·020737	44·21	85	1208·51	30·99	·025641	47·50
21	5327·21	114·43	·021480	44·14	86	1177·52	63·65	·054054	47·74
22	5212·78	128·71	·024691	44·09	87	1113·87	—	—	49·44
23	5084·07	169·90	·033419	44·20	88	1113·87	—	—	48·44
24	4914·17	131·40	·026738	44·71	89	1113·87	33·75	·030303	47·44
25	4782·77	185·48	·038781	44·92	90	1080·12	—	—	47·90
26	4597·29	147·44	·032070	45·71	91	1080·12	—	—	46·90
27	4449·85	81·15	·018237	46·21	92	1080·12	—	—	45·90
28	4368·70	124·03	·028391	46·06	93	1080·12	38·58	·035714	44·90
29	4244·67	69·36	·016340	46·39	94	1041·54	—	—	45·55
30	4175·31	70·77	·016949	46·16	95	1041·54	38·58	·037037	44·55
31	4104·54	71·26	·017361	45·94	96	1002·96	40·12	·040000	45·24
32	4033·28	57·83	·014337	45·75	97	962·84	—	—	46·11
33	3975·45	87·69	·022059	45·40	98	962·84	48·14	·050000	45·11
34	3887·76	29·45	·007576	45·42	99	914·70	—	—	46·45
35	3858·31	177·39	·045977	44·76	100	914·70	—	—	45·45
36	3680·92	89·41	·024291	45·89	101	914·70	—	—	44·45
37	3591·51	121·75	·033898	46·02	102	914·70	—	—	43·45
38	3469·76	61·41	·017699	46·62	103	914·70	—	—	42·45
39	3408·35	107·47	·031532	46·45	104	914·70	48·14	·052632	41·45
40	3300·88	61·41	·018605	46·95	105	866·56	—	—	42·73
41	3239·47	77·50	·023923	46·83	106	866·56	—	—	41·73
42	3161·97	47·43	·015000	46·96	107	866·56	—	—	40·73
43	3114·54	96·82	·031088	46·67	108	866·56	—	—	39·73
44	3017·72	32·62	·010811	47·15	109	866·56	—	—	38·73
45	2985·10	33·73	·011299	46·66	110	866·56	—	—	37·73
46	2951·37	51·48	·017442	46·19	111	866·56	57·77	·066667	36·73
47	2899·89	—	—	46·00	112	808·79	—	—	38·32
48	2899·89	129·29	·044586	45·00	113	808·79	—	—	37·32
49	2770·60	55·78	·020134	46·08	114	808·79	—	—	36·32
50	2714·82	56·56	·020833	46·01	115	808·79	—	—	35·32
51	2658·26	76·50	·028777	45·98	116	808·79	57·77	·071429	34·32
52	2581·76	19·71	·007634	46·33	117	751·02	—	—	35·92
53	2562·05	40·03	·015625	45·68	118	751·02	—	—	34·92
54	2522·02	80·70	·032000	45·40	119	751·02	—	—	33·92
55	2441·32	20·34	·008333	45·88	120	751·02	—	—	32·92
56	2420·98	—	—	45·26	121	751·02	—	—	31·92
57	2420·98	20·87	·008621	44·26	122	751·02	—	—	30·92
58	2400·11	42·48	·017699	43·64	123	751·02	—	—	29·92
59	2357·63	42·87	·018182	43·42	124	751·02	—	—	28·92
60	2314·76	45·39	·019608	43·22	125	751·02	—	—	27·92
61	2269·37	69·47	·030612	43·07	126	751·02	—	—	26·92
62	2199·90	46·31	·021053	43·42	127	751·02	—	—	25·92
63	2153·59	71·00	·032967	43·34	128	751·02	—	—	24·92
64	2082·59	23·94	·011494	43·80	129	751·02	—	—	23·92
65	2058·65	72·66	·035294	43·30	130	751·02	—	—	22·92
66	1985·99	24·52	·012346	43·87	131	751·02	—	—	21·92
67	1961·47	49·04	·025000	43·41	132	751·02	125·17	·166667	20·92
68	1912·43	98·07	·051282	43·51	133	625·85	—	—	24·00
69	1814·36	—	—	44·84	134	625·85	—	—	23·00
70	1814·36	75·60	·041667	43·84	135	625·85	—	—	22·00
71	1738·76	—	—	44·72	136	625·85	—	—	21·00
72	1738·76	76·71	·044118	43·72	137	625·85	—	—	20·00
73	1662·05	25·97	·015625	44·71	138	625·85	—	—	19·00
74	1636·08	53·64	·032787	44·42	139	625·85	—	—	18·00
75	1582·44	55·52	·035088	45·28	140	625·85	156·46	·250000	17·00
76	1526·92	55·52	·036364	45·52	141	469·39	—	—	21·50
77	1471·40	27·76	·018868	46·22	142	469·39	—	—	20·50
78	1443·64	28·31	·019608	46·10	143	469·39	—	—	19·50
79	1415·33	57·77	·040816	46·01	144	469·39	—	—	18·50
80	1357·56	28·88	·021277	46·95	145	469·39	—	—	17·50
81	1328·68	29·53	·022222	46·95	146	469·39	—	—	16·50
82	1299·15	90·64	·069767	47·01	147	469·39	—	—	15·50
83	1208·51	—	—	49·50	148	469·39	—	—	14·50
84	1208·51	—	—	48·50	149	469·39	—	—	13·50

Table VII (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
150	469·39	—	—	12·50	157	469·39	—	—	5·50
151	469·39	—	—	11·50	158	469·39	—	—	4·50
152	469·39	—	—	10·50	159	469·39	—	—	3·50
153	469·39	—	—	9·50	160	469·39	—	—	2·50
154	469·39	—	—	8·50	161	469·39	—	—	1·50
155	469·39	—	—	7·50	162	469·39	—	—	·50
156	469·39	—	—	6·50					

Table VIII.

Exp. 4. *Life table* (14. ii. 24 *to* 30. viii. 24 *inclusive*).
Specific deaths. 396 mice.

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
0	10000·00	101·01	·010101	39·53	48	3114·57	72·43	·023256	38·61
1	9898·99	25·45	·002571	38·93	49	3042·14	—	—	38·52
2	9873·54	231·42	·023438	38·03	50	3042·14	72·43	·023810	37·52
3	9642·12	209·61	·021739	37·93	51	2969·71	72·43	·024390	37·42
4	9432·51	211·37	·022409	37·76	52	2897·28	—	—	37·34
5	9221·14	374·19	·040580	37·62	53	2897·28	110·02	·037975	36·34
6	8846·95	322·68	·036474	38·19	54	2787·26	36·67	·013158	36·76
7	8524·27	327·86	·038462	38·61	55	2750·59	188·40	·068493	36·24
8	8196·41	220·04	·026846	39·14	56	2562·19	114·72	·044776	37·87
9	7976·37	194·54	·024390	39·21	57	2447·47	116·55	·047619	38·62
10	7781·83	167·96	·021583	39·17	58	2330·92	38·85	·016667	39·53
11	7613·87	139·96	·018382	39·03	59	2292·07	77·70	·033898	39·19
12	7473·91	451·25	·060377	38·75	60	2214·37	—	—	39·55
13	7022·66	84·95	·012097	40·21	61	2214·37	118·63	·053571	38·55
14	6937·71	114·67	·016529	39·69	62	2095·74	—	—	39·70
15	6823·04	232·28	·034043	39·35	63	2095·74	39·54	·018868	38·70
16	6590·76	176·54	·026786	39·72	64	2056·20	39·54	·019231	38·44
17	6414·22	299·73	·046729	39·80	65	2016·66	—	—	38·18
18	6114·49	149·87	·024510	40·73	66	2016·66	79·09	·039216	37·18
19	5964·62	182·59	·030612	40·74	67	1937·57	79·08	·040816	37·68
20	5782·03	215·29	·037234	41·01	68	1858·49	—	—	38·26
21	5566·74	155·50	·027933	41·57	69	1858·49	40·40	·021739	37·26
22	5411·24	31·10	·005747	41·75	70	1818·09	—	—	37·08
23	5380·14	62·56	·011628	40·99	71	1818·09	—	—	36·08
24	5317·58	94·96	·017857	40·47	72	1818·09	—	—	35·08
25	5222·62	127·38	·024390	40·19	73	1818·09	—	—	34·08
26	5095·24	161·24	·031646	40·19	74	1818·09	84·56	·046512	33·08
27	4934·00	128·99	·026144	40·48	75	1733·53	43·34	·025000	33·67
28	4805·01	193·49	·040268	40·56	76	1690·19	45·68	·027027	33·52
29	4611·52	98·12	·021277	41·24	77	1644·51	—	—	33·43
30	4513·40	164·72	·036496	41·12	78	1644·51	—	—	32·43
31	4348·68	99·59	·022901	41·66	79	1644·51	46·99	·028571	31·43
32	4249·09	67·45	·015873	41·63	80	1597·52	—	—	31·34
33	4181·64	236·06	·056452	41·29	81	1597·52	93·97	·058824	30·34
34	3945·58	134·89	·034188	42·73	82	1503·55	—	—	31·21
35	3810·69	—	—	43·23	83	1503·55	—	—	30·21
36	3810·69	102·07	·026786	42·23	84	1503·55	46·99	·031250	29·21
37	3708·62	68·05	·018349	42·37	85	1456·56	—	—	29·13
38	3640·57	34·35	·009434	42·16	86	1456·56	97·10	·066667	28·13
39	3606·22	103·03	·028571	41·55	87	1359·46	48·55	·035714	29·11
40	3503·19	69·37	·019802	41·76	88	1310·91	—	—	29·17
41	3433·82	69·37	·020202	41·59	89	1310·91	97·10	·074074	28·17
42	3364·45	106·25	·031579	41·44	90	1213·81	48·55	·04	29·38
43	3258·20	35·80	·010989	41·78	91	1165·26	48·55	·041667	29·58
44	3222·40	71·61	·022222	41·24	92	1116·71	—	—	29·85
45	3150·79	—	—	41·16	93	1116·71	—	—	28·85
46	3150·79	—	—	40·16	94	1116·71	50·76	·045455	27·85
47	3150·79	36·22	·011494	39·16	95	1065·95	—	—	28·15

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Table VIII (*continued*).

Cage-age in days	l_x	d_x	q_x	e_x	Cage-age in days	l_x	d_x	q_x	e_x
96	1065·95	—	—	27·15	121	452·84	—	—	19·50
97	1065·95	50·76	·047619	26·15	122	452·84	—	—	18·50
98	1015·19	—	—	26·43	123	452·84	—	—	17·50
99	1015·19	—	—	25·43	124	452·84	90·57	·200000	16·50
100	1015·19	—	—	24·43	125	362·27	—	—	19·50
101	1015·19	—	—	23·43	126	362·27	—	—	18·50
102	1015·19	—	—	22·43	127	362·27	—	—	17·50
103	1015·19	—	—	21·43	128	362·27	—	—	16·50
104	1015·19	59·72	·058824	20·43	129	362·27	—	—	15·50
105	955·47	—	—	20·68	130	362·27	—	—	14·50
106	955·47	127·40	·133333	19·68	131	362·27	—	—	13·50
107	828·07	—	—	21·63	132	362·27	—	—	12·50
108	828·07	—	—	20·63	133	362·27	—	—	11·50
109	828·07	69·01	·083333	19·63	134	362·27	—	—	10·50
110	759·06	69·01	·090909	20·37	135	362·27	—	—	9·50
111	690·05	—	—	21·36	136	362·27	—	—	8·50
112	690·05	69·01	·100000	20·36	137	362·27	—	—	7·50
113	621·04	—	—	21·56	138	362·27	—	—	6·50
114	621·04	—	—	20·56	139	362·27	—	—	5·50
115	621·04	—	—	19·56	140	362·27	—	—	4·50
116	621·04	—	—	18·56	141	362·27	—	—	3·50
117	621·04	77·63	·125000	17·56	142	362·27	—	—	2·50
118	543·41	—	—	19·00	143	362·27	—	—	1·50
119	543·41	90·57	·166667	18·00	144	362·27	362·27	1·000000	·50
120	452·84	—	—	20·50					

Table IX.

Exp. 2*a*. *Life table for three mouse period* (6. iii. 21 *to* 30. iv. 23 *inclusive*). All deaths.

Age x	Probability of dying in the next 5 days	Age x	Probability of dying in the next 5 days	Age x	Probability of dying in the next 5 days	Age x	Probability of dying in the next 5 days
0	·1969	31	·1316	61	·1197	91	·1429
1	·2316	32	·1270	62	·1102	92	·1200
2	·2580	33	·1175	63	·0970	93	·1333
3	·2709	34	·1172	64	·0818	94	·1021
4	·2731	35	·1070	65	·1456	95	·1345
5	·2774	36	·0961	66	·1439	96	·1082
6	·2653	37	·0980	67	·1569	97	·1395
7	·2551	38	·1031	68	·1409	98	·1587
8	·2543	39	·1020	69	·1370	99	·1173
9	·2562	40	·0947	70	·1037	100	·0887
10	·2567	41	·0970	71	·0909	101	·0887
11	·2870	42	·1092	72	·1323	102	·0556
12	·3002	43	·1014	73	·1653	103	·0192
13	·3111	44	·0961	74	·1682	104	·0385
14	·3190	45	·1085	75	·1759	105	·0392
15	·3200	46	·1042	76	·2114	106	·0392
16	·3062	47	·0965	77	·1909	107	·0784
17	·3007	48	·1179	78	·1524	108	·0980
18	·3014	49	·1194	79	·1456	109	·1000
19	·2815	50	·1354	80	·1020	110	·1020
20	·2607	51	·1384	81	·0864	111	·1633
21	·2321	52	·1420	82	·0453	112	·1915
22	·2088	53	·1300	83	·0794	113	·1739
23	·1876	54	·1409	84	·0920	114	·1556
24	·1826	55	·1238	85	·0920	115	·1591
25	·1785	56	·1368	86	·0833	116	·1463
26	·1783	57	·1259	87	·1071	117	·0789
27	·1677	58	·1397	88	·0741	118	·1053
28	·1551	59	·1490	89	·1266	119	·1579
29	·1317	60	·1314	90	·1392	120	·1892
30	·1295						

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Table X.

Exp. 2*a*. *Life table for three mouse period* (6. iii. 21 *to* 30. iv. 23 *inclusive*). Specific deaths.

Age x	Expectation of life limited to 60 days ahead	Probability of dying in the next 5 days	Age x	Expectation of life limited to 60 days ahead	Probability of dying in the next 5 days
0	22·49	·1433	63	32·83	·0735
1	21·82	·1830	64	32·90	·0696
2	21·31	·2178	65	32·37	·1278
3	21·05	·2328	66	32·24	·1307
4	21·28	·2361	67	31·69	·1449
5	21·48	·2410	68	31·55	·1346
6	21·86	·2273	69	31·43	·1306
7	22·32	·2153	70	32·96	·1037
8	22·57	·2132	71	32·94	·0909
9	23·00	·2122	72	32·95	·1245
10	23·48	·2071	73	32·46	·1495
11	23·55	·2370	74	32·21	·1604
12	23·76	·2509	75	32·78	·1682
13	24·04	·2568	76	32·29	·2040
14	24·54	·2661	77	33·53	·1815
15	24·96	·2713	78	34·02	·1509
16	26·12	·2540	79	34·25	·1360
17	26·98	·2442	80	35·24	·0920
18	27·65	·2449	81	36·38	·0761
19	28·75	·2266	82	36·85	·0427
20	29·62	·2084	83	36·11	·0567
21	30·44	·1885	84	35·77	·0695
22	31·18	·1744	85	35·02	·0695
23	32·13	·1528	86	35·50	·0363
24	32·76	·1437	87	34·73	·0488
25	33·12	·1378	88	34·35	·0374
26	33·32	·1391	89	34·41	·0919
27	33·64	·1294	90	33·61	·1051
28	33·86	·1230	91	32·82	·1314
29	34·23	·1114	92	32·45	·1200
30	34·41	·1077	93	31·62	·1333
31	34·73	·0989	94	33·48	·1021
32	34·72	·0938	95	33·12	·1041
33	34·75	·0884	96	33·27	·0770
34	34·69	·0852	97	32·42	·1093
35	34·74	·0763	98	32·07	·1291
36	34·72	·0726	99	32·80	·0863
37	34·51	·0743	100	32·51	·0887
38	34·32	·0759	101	31·69	·0887
39	34·11	·0744	102	32·00	·0555
40	33·81	·0725	103	32·39	·0192
41	33·64	·0776	104	31·58	·0192
42	33·46	·0932	105	31·38	·0200
43	33·29	·0916	106	30·56	·0200
44	33·02	·0859	107	29·75	·0600
45	32·63	·0944	108	28·94	·0800
46	32·61	·0933	109	28·13	·1000
47	32·98	·0816	110	27·88	·1020
48	32·77	·0834	111	27·07	·1429
49	32·30	·0885	112	27·40	·1718
50	32·23	·0997	113	27·19	·1538
51	32·18	·1027	114	26·99	·1350
52	32·14	·1059	115	27·81	·1386
53	31·97	·1086	116	27·23	·1464
54	31·67	·1151	117	28·52	·0790
55	31·70	·1102	118	27·70	·1053
56	32·03	·1184	119	26·88	·1579
57	32·09	·1117	120	26·76	·1622
58	32·00	·1302	121	27·43	
59	31·93	·1334	122	26·60	
60	32·06	·1155	123	26·51	
61	32·40	·1028	124	27·28	
62	32·21	·0932	125	27·29	

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Table XI.

Exp. 2*b*. *Life table for one mouse period* (1. v. 23 *to* 30. viii. 24 *inclusive*). All deaths.

Age x	Probability of dying in the next 5 days	Age x	Probability of dying in the next 5 days
0	·1177	61	·0485
1	·1499	62	·0499
2	·1725	63	·0908
3	·1838	64	·1023
4	·1856	65	·0945
5	·1888	66	·1051
6	·1838	67	·0860
7	·1894	68	·0795
8	·1801	69	·0701
9	·1654	70	·0950
10	·1618	71	·0964
11	·1497	72	·0964
12	·1541	73	·0747
13	·1558	74	·0630
14	·1584	75	·0519
15	·1578	76	·0393
16	·1632	77	·0657
17	·1466	78	·0533
18	·1404	79	·0669
19	·1649	80	·0550
20	·1560	81	·0961
21	·1516	82	·0988
22	·1487	83	·1129
23	·1486	84	·1143
24	·1385	85	·1304
25	·1159	86	·1061
26	·1223	87	·0938
27	·0981	88	·0794
28	·0863	89	·0809
29	·0695	90	·0673
30	·0698	91	·1204
31	·0764	92	·1053
32	·0970	93	·1053
33	·1135	94	·1243
34	·1366	95	·1434
35	·1583	96	·0950
36	·1468	97	·1327
37	·1394	98	·1327
38	·1266	99	·1172
39	·1202	100	·1012
40	·1051	101	·1028
41	·1198	102	·0638
42	·1354	103	·0851
43	·1383	104	·0652
44	·1374	105	·0444
45	·1532	106	·0227
46	·1798	107	·0227
47	·1489	108	·0000
48	·1522	109	·0465
49	·1265	110	·0465
50	·1222	111	·1163
51	·0699	112	·1163
52	·0786	113	·1395
53	·0536	114	·1463
54	·0450	115	·1463
55	·0370	116	·0789
56	·0374	117	·1053
57	·0472	118	·0811
58	·0472	119	·0286
59	·0566	120	·0571
60	·0577		

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Table XII.

Exp. 2*b*. *Life table for one mouse period* (1. v. 23 *to* 30. viii. 24 *inclusive*). Specific deaths.

Age x	Expectation of life limited to 60 days ahead	Probability of dying in the next 5 days	Age x	Expectation of life limited to 60 days ahead	Probability of dying in the next 5 days
0	34·33	·0829	65	40·27	·0844
1	33·64	·1102	66	39·68	·0844
2	33·02	·1399	67	39·93	·0649
3	33·10	·1545	68	40·68	·0570
4	33·36	·1506	69	41·03	·0474
5	33·81	·1523	70	40·93	·0607
6	34·16	·1434	71	40·35	·0731
7	34·74	·1401	72	39·76	·0731
8	35·49	·1157	73	40·14	·0502
9	35·68	·1060	74	40·07	·0381
10	36·30	·0945	75	40·51	·0263
11	36·37	·0888	76	40·48	·0133
12	36·92	·0811	77	39·91	·0268
13	36·74	·0896	78	39·33	·0268
14	36·57	·0881	79	38·75	·0408
15	36·76	·0914	80	38·69	·0417
16	36·62	·0933	81	38·10	·0833
17	36·87	·0859	82	38·04	·0847
18	37·04	·0811	83	37·45	·0990
19	36·84	·0903	84	37·38	·1150
20	37·19	·0864	85	37·33	·1169
21	37·17	·0846	86	38·44	·0921
22	37·15	·0912	87	38·45	·0938
23	37·15	·0937	88	38·49	·0794
24	37·34	·0967	89	39·19	·0492
25	37·58	·0813	90	39·30	·0506
26	37·49	·0874	91	39·42	·0872
27	37·75	·0710	92	39·55	·0714
28	37·88	·0630	93	39·01	·0714
29	38·20	·0598	94	38·47	·1071
30	37·80	·0551	95	38·62	·1266
31	37·96	·0614	96	40·27	·0950
32	37·55	·0824	97	39·72	·1327
33	37·33	·0987	98	39·17	·1327
34	37·52	·1116	99	41·18	·1172
35	36·92	·1277	100	41·28	·1012
36	37·32	·1094	101	41·63	·0825
37	37·74	·0959	102	42·92	·0426
38	38·22	·0819	103	42·41	·0643
39	39·00	·0862	104	42·83	·0440
40	39·12	·0820	105	43·28	·0227
41	38·75	·1084	106	42·80	·0227
42	38·63	·1232	107	42·31	·0227
43	38·52	·1318	108	42·81	·0000
44	39·47	·1171	109	42·34	·0465
45	39·40	·1119	110	41·85	·0465
46	40·21	·1249	111	41·34	·1163
47	40·81	·0987	112	40·84	·1163
48	41·16	·0941	113	40·32	·1395
49	41·54	·0896	114	41·75	·1463
50	41·29	·0908	115	41·24	·1463
51	42·84	·0530	116	43·99	·0789
52	42·29	·0619	117	43·52	·0789
53	42·50	·0451	118	44·23	·0541
54	42·73	·0276	119	46·30	·0000
55	42·57	·0370	120	45·84	·0294
56	42·41	·0280	121	45·34	
57	42·23	·0379	122	44·84	
58	41·64	·0379	123	44·32	
59	41·05	·0474	124	43·78	
60	41·23	·0485	125	44·56	
61	40·63	·0485	126	44·04	
62	40·83	·0499	127	43·51	
63	40·24	·0806	128	42·95	
64	40·05	·0922	129	43·72	

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Table XIII.

Exp. 3. *Life table* (14. ii. 24 *to* 27. vii. 24 *inclusive*).

Specific deaths only.

Age x	Expectation of life limited to 60 days ahead	Probability of dying in the next 5 days
0	29·03	·1033
1	28·32	·1508
2	27·80	·1922
3	27·34	·2209
4	27·61	·2153
5	28·18	·2140
6	29·02	·1949
7	30·00	·1658
8	30·70	·1490
9	30·90	·1536
10	31·60	·1264
11	31·89	·1254
12	31·90	·1189
13	32·05	·1128
14	32·48	·1056
15	32·13	·1164
16	32·49	·1073
17	32·28	·1122
18	32·20	·1157
19	32·36	·1209
20	32·49	·1208
21	32·43	·1370
22	32·37	·1464
23	32·43	·1407
24	32·78	·1362
25	32·92	·1270
26	33·48	·1072
27	33·83	·0936
28	33·71	·0900
29	33·94	·0841
30	33·77	·0759
31	33·60	·1032
32	33·46	·1095
33	33·20	·1272
34	33·22	·1233
35	32·73	·1445
36	33·56	·1199
37	33·66	·1196
38	34·10	·1024
39	33·98	·1146
40	34·36	·0957
41	34·28	0889
42	34·39	·0829
43	34·20	·0689
44	34·59	·0819
45	34·26	·0905
46	33·94	·0993
47	33·83	·1097
48	33·13	·1165
49	33·97	·0897
50	33·97	·1007
51	34·01	·0893
52	34·33	·0623
53	33·90	·0632
54	33·75	·0652
55	34·18	·0518
56	33·79	·0626
57	33·12	·0913
58	32·71	·1027
59	32·61	·1167
60	32·54	·1106
61	32·51	·1249
62	32·86	·1084
63	32·91	·1120
64	33·37	·1288
65	33·11	·1187
66	33·69	·1245
67	33·49	·1135
68	33·72	·1309
69	34·94	·0983
70	34·35	·1278
71	35·25	·1218
72	34·68	·1538
73	35·67	·1314
74	35·62	·1349
75	36·58	·1421
76	36·91	·1298
77	37·71	·1171
78	37·86	·1629
79	38·05	·1461
80	39·11	·1098
81	39·35	·1138
82	39·60	·1426
83	41·93	·0783
84	41·31	·0783
85	40·70	·1062
86	41·16	·0827
87	42·91	·0303
88	42·33	·0303
89	41·75	·0649
90	42·47	·0357
91	41·90	·0714
92	41·34	·1086
93	40·77	·1086
94	41·72	·1218
95	41·17	·1218
96	42·20	·0880
97	43·43	·0500
98	42·92	·0500
99	44·65	·0000
100	44·17	·0526
101	43·68	
102	43·19	

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Table XIV.

Exp. 4. *Life table* (14. ii. 24 *to* 30. viii. 24 *inclusive*).

Specific deaths only.

Age x	Expectation of life limited to 60 days ahead	Probability of dying in the next 5 days	Age x	Expectation of life limited to 60 days ahead	Probability of dying in the next 5 days
0	30·77	·0779	51	32·46	·1372
1	30·31	·1063	52	32·49	·1553
2	29·60	·1367	53	31·72	·1955
3	29·52	·1499	54	32·18	·1777
4	29·38	·1544	55	31·82	·1949
5	29·27	·1561	56	33·37	·1358
6	29·71	·1394	57	34·16	·1437
7	30·05	·1232	58	35·10	·1009
8	30·46	·1432	59	34·92	·1029
9	30·53	·1302	60	35·36	·0893
10	30·51	·1232	61	34·56	·0893
11	30·41	·1344	62	35·70	·0755
12	30·22	·1418	63	34·92	·1132
13	31·39	·1293	64	34·81	·0962
14	31·02	·1403	65	34·68	·0985
15	30·80	·1526	66	33·86	·0985
16	31·12	·1554	67	34·41	·0617
17	31·23	·1564	68	35·04	·0217
18	32·01	·1201	69	34·24	·0217
19	32·07	·1085	70	34·19	·0465
20	32·35	·0967	71	33·39	·0703
21	32·86	·0847	72	32·59	·0955
22	33·08	·0882	73	31·79	·0955
23	32·55	·1069	74	30·99	·0955
24	32·21	·1328	75	31·68	·0785
25	32·07	·1358	76	31·70	·0548
26	32·15	·1465	77	31·78	·0857
27	32·46	·1388	78	31·00	·0857
28	32·60	·1297	79	30·22	·0857
29	33·23	·1444	80	30·32	·0882
30	33·22	·1557	81	29·55	·0882
31	33·73	·1237	82	30·61	·0958
32	33·79	·1272	83	29·85	·1281
33	33·59	·1294	84	29·09	·1281
34	34·85	·0860	85		·1667
35	35·36	·0807	86		·2000
36	34·64	·0989	87		·1786
37	34·85	·0928	88		·1481
38	34·79	·1050	89		·1481
39	34·39	·1064	90		·1218
40	34·68	·1006	91		·0852
41	34·66	·0824	92		·0455
42	34·67	·0635	93		·0909
43	35·10	·0441	94		·0909
44	34·80	·0559	95		·0476
45	34·89	·0345	96		·0476
46	34·19	·0575	97		·0476
47	33·48	·0805	98		·0000
48	33·13	·0698	99		·0000
49	33·18	·0838	100		·0588
50	32·44	·0958			

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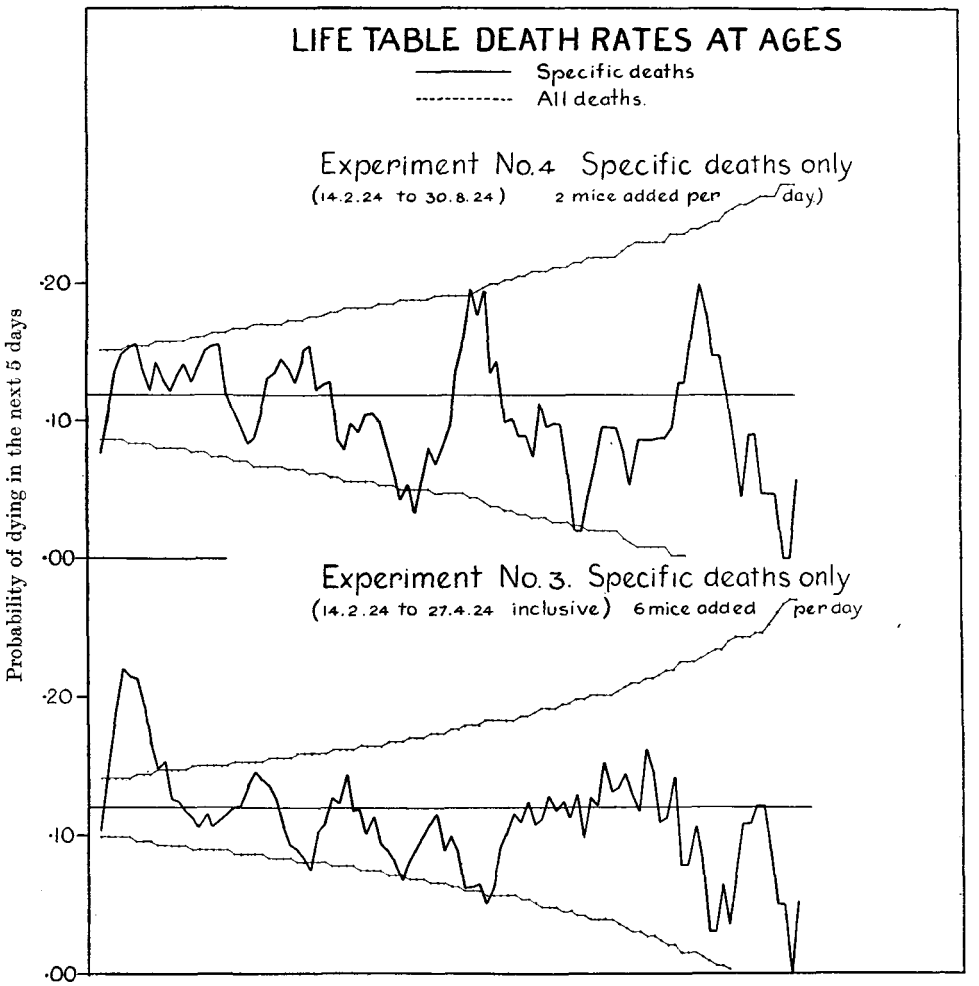
The most direct measure of the effect of different lengths of exposure is q_x, the probability of dying on day x after entering the cage (the day of entry is taken throughout as day 0). Let us examine first the q_x for specific deaths through the three-immigrant epoch of Exp. 2[1]. The probability of dying increases to day 6, then declines irregularly to day 10, increases to a second maximum on day 15, again falling irregularly to day 44. The course now becomes irregular, partly because the numbers exposed to risk are decreasing, having fallen to 103 by age 79 and 50 by age 109. In spite of this, there seems a tendency to increase after age 44, then to fall again at or about age 64 and then to rise once more. A somewhat clearer picture is given by the graph of ${}_5q_x$ (see Graph VIII and Tables IX and X), *i.e.* the probability of dying within the next 5 days of cage-age x. The rate of mortality is seen to



[1] The graphs of q_x for each day of age have not been reproduced, but the figures are given in Tables III to VIII.

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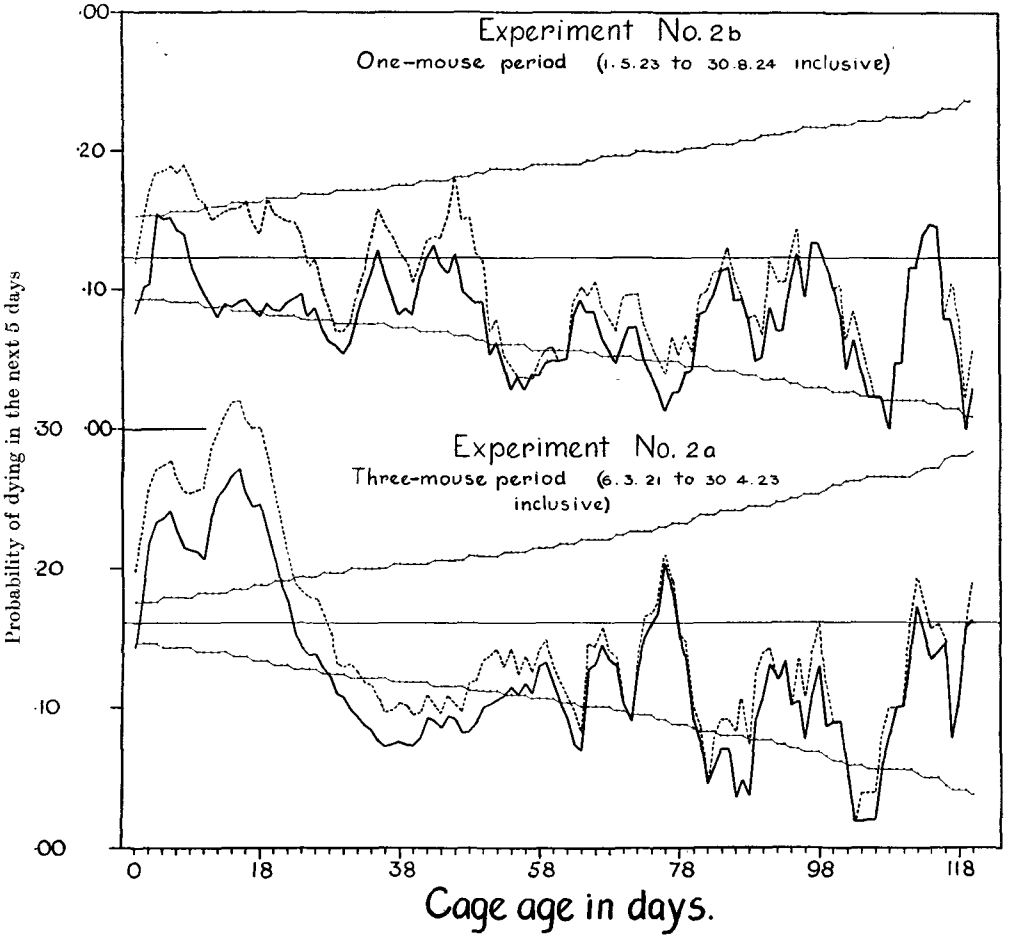

Graph VIII. Probability of dying in the next 5 days for Exps. 2*a*, 2*b*, 3 and 4.

Note. The straight line is the mean ${}_5q_x$ for all ages, and the line on either side of it marks ± 3 times the probable error of this mean for the appropriate numbers exposed to risk at each age.

increase rapidly during the first few days and has a secondary maximum between 5–9 days, a fall to 10–14, a rise to the highest maximum in 15–19, then a fairly steady decline to 36–40. After 30 days the general level is significantly lower than in the early days. After the minimum of 36–41 days, the death-rate fluctuates. The significance of these fluctuations has been tested by the usual statistical processes with the result that, while the smaller movements might well be due to errors of sampling, the larger ones, such as the rise between 36–40 and 76–80 and the fall in the period 86–90, cannot be so easily explained. This conclusion holds whether the individual q_x or an average be used to determine the standard deviation. But the test is a rough one; the true (unknown) standard deviation is larger than either value, since the secular trend clearly proves that the assumption of the conditions of simple sampling, in the usual statistical sense, is unwarranted.

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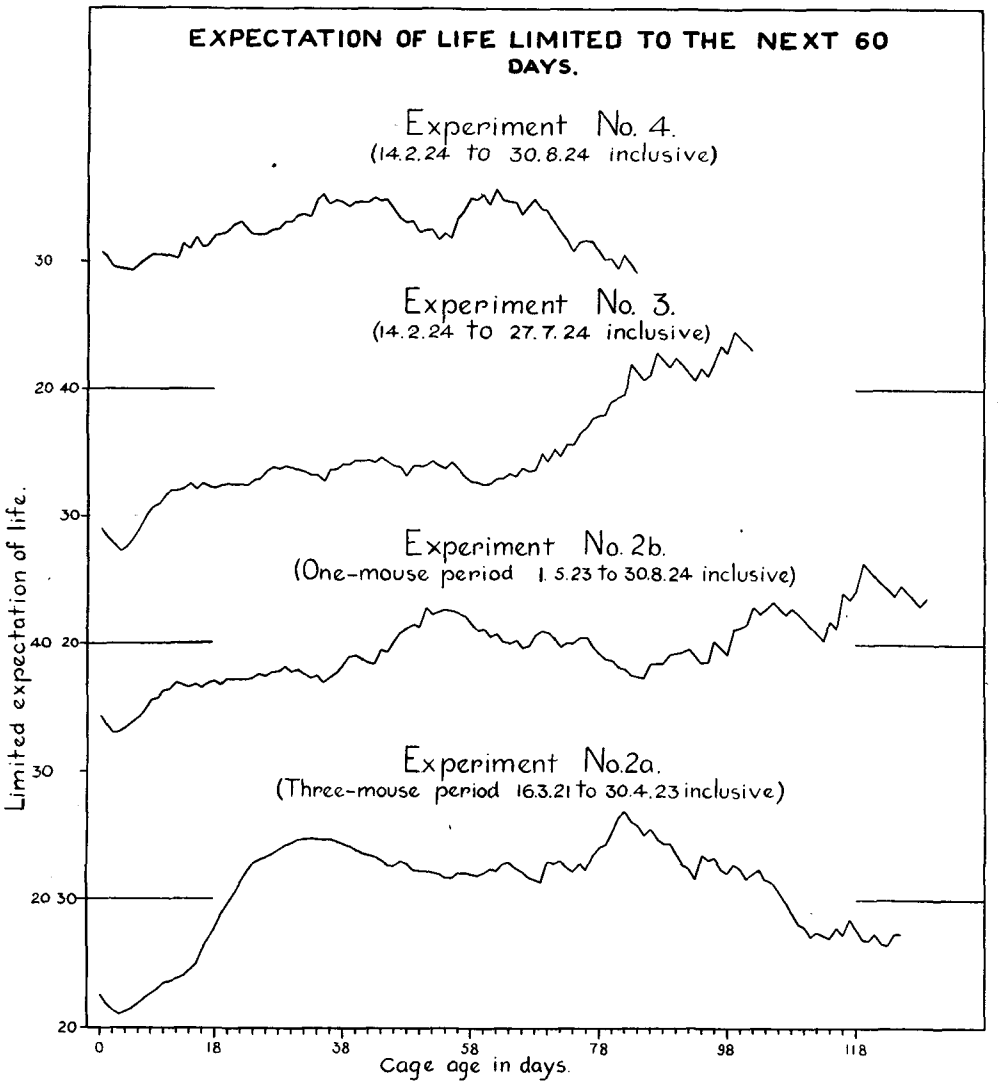
The practical conclusions are, we think, that the main features shown by these graphs down to age 40 are almost certainly real, that the subsequent general lowering of average mortality is also a true picture of events, but that, until we have a larger experience of rates of mortality at later (cage) ages, we must suspend judgment on the meaning of the fluctuations at later ages. The point is a very important one; on its elucidation depends judgment as to the permanent or transitory character of the immunity reached after long exposure. If the reality of the wave-like movement of later death-rates could be established, it would also be established that this immunity, at least in part, is an acquired immunity and not a mere consequence of the selection by survival of the fittest amongst normally variable immigrants. Passing now to the one mouse period of Exp. 2 (see Graph VIII and Tables XI and XII), one notes the same sharp initial increase; the first maximum is on day 7; there is a decline to days 12 and 13, then a fairly steady rate to day 28, then a further fall to day 35. The high maximum of day 15 in the first part of the experiment is not reproduced. After day 35 the death-rate increases more sharply than in the first part of the experiment, and, as in that experiment, then follows a wave-like course. The lowering of the general average of mortality at later (cage) ages is almost certainly significant, the fluctuations may not be. On the whole the picture is similar to that of the first period.

In Exp. 3 (see Graph VIII and Table XIII), the initial rise to a maximum, attained between days 5 and 6, is very steep; in this experiment, too, the decline to a lower level of mortality at later ages is significant. Oscillations of mortality at the longer durations again suggest a waxing and a waning but are not, statistically, significant. In Exp. 4 (Graph VIII and Table XIV), errors of sampling are still larger; nothing in the form of the graph modifies the impression conveyed by the others. Exp. 7 shows the rise to a maximum (7–11 days), a decline to the period 42–46 days and subsequent oscillations. Exps. 5 and 6 also exhibit the initial increases.

Although the precise details of the several pictures vary, we seem justified by a general study of the results in concluding that it is proven that immunity increases with exposure and probable that after an optimum has been reached this immunity fluctuates, but that the populations at risk are not large enough to warrant any definite statement of the measure or extent of such fluctuation. That no absolute immunity is ever created is, of course, proved by the fact that the deaths of the longest exposed mice are nearly all due to pasteurellosis. The expectation of life at different cage-ages is not so easy to interpret as the probability of dying, but it gives a smoother graph. Since the complete expectation might be dominated by the contribution of a small group of specially resistant mice, we have employed the partial expectation, limited to the next 60 days from each age (see Graph IX and Tables X, XII, XIII and XIV). The superiority of the one mouse period of Exp. 2 is evident, and the improvement after the first danger point is passed is a feature of all experiments. When the numerically more reliable phases of the two long

experiments are compared it is worth noticing that the first definite maximum is reached earlier in the three mouse epoch than in the one immigrant phase —at days 32–34 in the former, at day 56 in the latter. This is consonant with the greater selective stringency of the conditions in the former experiment,



Graph IX. Expectation of life limited to the next 60 days for Exps. 2*a*, 2*b*, 3 and 4.

but in Exp. 3 (six entrants), after a fairly constant level between ages 26 and 58, the expectation of life tends to increase with age.

The facts may be looked at from a different angle if we imagine a population of 10,000, suppose them all introduced to an environment representing the mean of the conditions obtaining at different times in the experiment,

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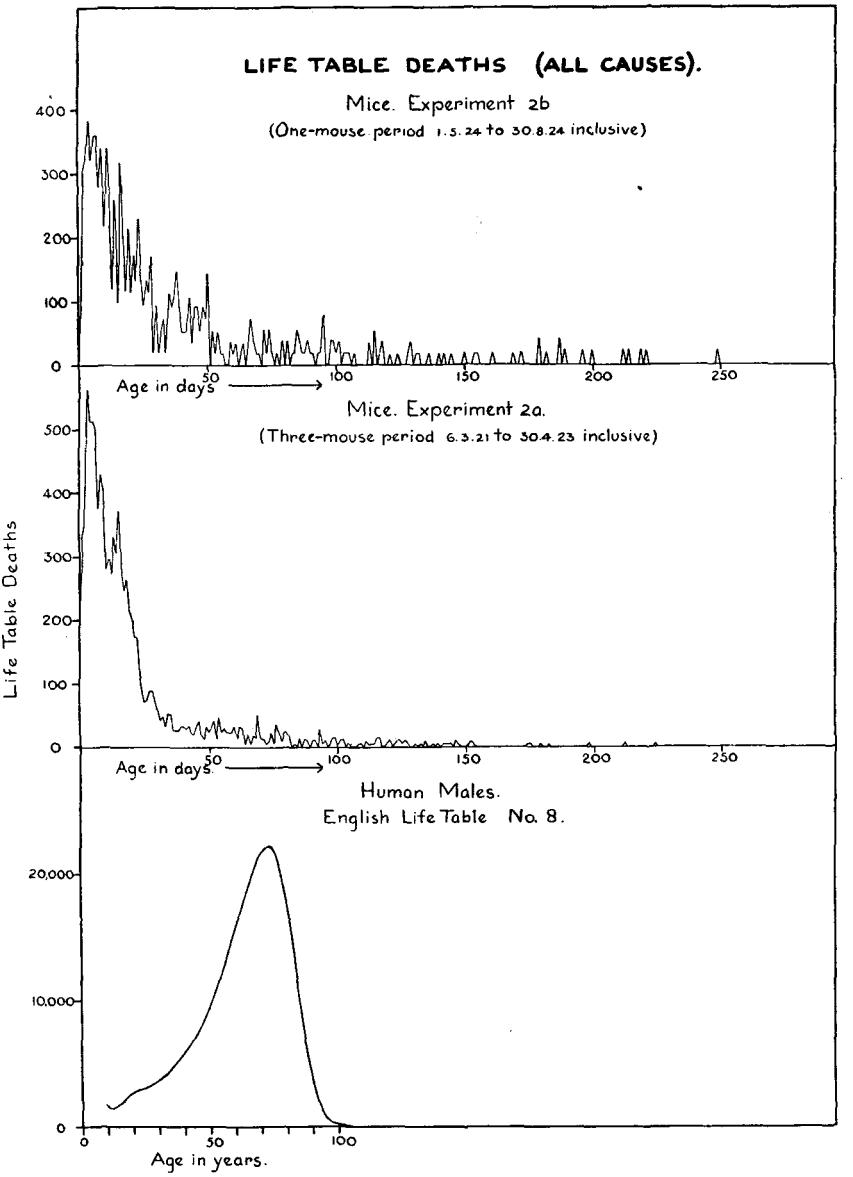
and examine the result. Such a population can be built up from the d_x columns, and the results plotted for both phases of Exp. 2 are shown in Graph X. The two curves are both alike in the steep ascent, much less steep descent



Graph X. Life table deaths of Exps. 2*a* and 2*b*, and of the English life table No. 8.

and long tail which extends to the right beyond the limits of the diagram. Below these graphs that of English Life Table No. 8 (Males, 1910–12) is drawn to show the contrast (we have no life table of normal mice). There is a reversal

of skewness. The mice curves have a steep ascent and very prolonged descent, the curve for men (omitting infant mortality) descends more sharply than it rises. This contrast suggests a matter for reflection. The causes of unequal life spans are of three classes:

(1) Variation in the environment of the cage, including of course any secular change in the infecting organism as well as concentration of carriers, etc.

(2) Differences of innate resistance of the immigrants.

(3) Change of resistance with exposure.

Effects under (1) play a leading part in a secular graph but are averaged out in a life table graph. They cannot, indeed, be completely effaced because mice entering during a long latent period, such as occurred in the early part of phase one of Exp. 2, do have an advantage; yet it is broadly true that immigrants did arrive at every secular phase and that mice entering on the same day differed very greatly in their survivorship records. Hence we are justified in ignoring (1) and holding that (2) and (3), smoothed out in a secular graph, are prominent in a life table graph.

If then there were a difference of innate susceptibility and that susceptibility were unaffected by exposure, would it be necessary to postulate an initial distribution as skew as that of the mortality? Let us, for a moment, include under the vague term resistance, which we will denote by U, any decrement of the potential rate of increase within the vulnerable tissues due to the defensive mechanism of the host, whether a mechanical means of elimination, or a chemico-physical power of destruction, which precluded multiplication. We will further suppose death to occur when the quantum of living organisms within the vulnerable tissue has reached a limit M. Then, if we suppose the conditions of infection and the potential rate of subsequent growth to be constant for all mice and at all lengths of exposure, t being the time of survival, U and t must increase together.

If δt be the increment of t corresponding to an increment δU of U the frequency of t between t and $t+\delta t$ is equal to the frequency of U between U and $U+\delta U$. If $t=F(U)$, then $\delta t=\frac{dF}{dU}\delta U$. Hence the frequency within the range δU of the U distribution is spread over the range $\frac{dF}{dU}\delta U$ in the t distribution. If therefore $\frac{dF}{dU}$ increase with U, the t distribution will be found from that of U by giving the latter a stretch to the right, and the faster $\frac{dF}{dU}$ increases with U, the more skew the distribution of t. So that we might start with a normal or even a left-hand skew distribution of innate resistance U in the mouse population and reach a distribution of deaths as abnormally skew as that found provided only that U and t are so connected that $\frac{dU}{dt}$ decreases with t, *i.e.* that $\frac{d^2U}{dt^2}$ is negative[1].

But if we assume, as seems necessary, that the organisms in the hosts' tissues increase by multiplication not, as in Dudley's theory (see footnote) by mere accumulation of doses, unless we likewise assume a corresponding increase in the opposing factor U, death will occur rapidly and the long tail of delayed deaths not be found.

[1] We have taken a hint from Dudley's paper (*M.R.C. Special Report*, 1923, No. 75), but Dudley defines U simply as the amount of infective material that the host can destroy in a unit of time, V as the amount of infective material received in the unit of time, and M as the minimum infective dose. All these are assumed constant, and he further assumes no multiplication of organisms. He has therefore $U=V-M/t$ giving $dU/dt=M/t^2$ which decreases with t increasing and in fact satisfies our skewness conditions. But his hypotheses do not seem applicable to our case.

For simplicity we have assumed M to be constant, the same for all mice, but this need not be assumed. We should merely have to replace the frequency distribution of U by a frequency volume of U, M, whence by applying the preceding argument to the U array for every value of M we should still reach a very skew distribution of t from a surface normal both in M and U.

It follows that an increase of immunity with exposure or amount of infection might explain adequately the form of the curves of death without the need to suppose any such distribution of innate resistance or lethal dosage.

VII. Seasonal Variation of Mortality.

Before returning to the question of immunity in relation to exposure, a word must be said on a possible disturbing factor, viz. a seasonal influence affecting all experiments.

The graphs of the shorter experiments suggested that the death-rates in different cages were for a time moving together. We accordingly correlated the death-rates of every possible pair of contemporaneous experiments for the 76 days from 14. ii. 24 to 29. iv. 24. In only five of the possible pairs, viz. 6 and 4, $r = 0{\cdot}72 \pm 0{\cdot}04$; 6 and 5, $r = 0{\cdot}35 \pm 0{\cdot}07$; 7 and 4, $r = 0{\cdot}27 \pm 0{\cdot}07$; 7 and 5, $r = 0{\cdot}34 \pm 0{\cdot}07$; and 4 and 5, $r = 0{\cdot}29 \pm 0{\cdot}07$, was the association significant. As all these experiments were started on the same day and in the same manner, as none was significantly associated with Exp. 2 (an experiment at a later phase); as, further, the latent periods of the long experiments did not tend to recur at the same times of year, we seem justified in concluding that seasonal periodicity has not been a disturbing factor.

VIII. Relation of Immunity to Previous Exposure and Time of Introduction.

In Section VI we have spoken of the relation between immunity and previous exposure to risk of infection. We now study the influence exerted by the severity of the risks endured and by the epoch of immigration. The rise and fall of the waves of mortality make this a most difficult problem to solve; the variations of death-rates from day to day, *within* each age group are large in comparison with the average differences *between* age group mortalities. In fact the standard deviations of the variations of the five days smoothed mortalities within age groups are all of order 77 per cent. to 107 per cent. of their means, while the *extreme* difference between any two age groups over the same period is only 70 per cent. of the mean; even taking single days of age, the maximum difference is only 180 per cent.

In other words, though a higher resistance is proved to exist amongst the survivors it cannot prevail against the full stress of epidemic waves, so that differences in the conditions of exposure in later cage-life may mask entirely the possible effect of conditions at the time of entrance.

These considerations are to be remembered in perusing the laborious and not fully conclusive arithmetical results now to be described.

It was noted in previous researches (Topley, 1921 *b*) that mice entering during the rise of a wave were usually not so long-lived as mice immigrating during a fall, while the latter had an advantage over immigrants arriving later in time but before a fresh wave began to rise.

Part of the explanation of this is that immigrants during the rise of a wave must be exposed to its maximum force. We have found that immigrants on a falling death-rate in the three mouse part of Exp. 2 lived on the average 19·92 days; entrants on a rising rate 17·08 days, not a very large advantage. The correlation (biserial method) of length of life with rise and fall (a rise taken as positive) is only $-0{\cdot}070 \pm 0{\cdot}02$, increased only to $-0{\cdot}075 \pm 0{\cdot}02$ by keeping the death-rate at day of entry constant. A similar method of analysis brings out no real advantage to mice which entered shortly after the crisis of an epidemic in comparison with later immigrants. The correlation between length of life and time elapsed since a maximum is (data of 8. iii. 21 to 30. ix. 23) only $0{\cdot}022 \pm 0{\cdot}029$, changed to $-0{\cdot}027 \pm 0{\cdot}029$ when the death-rate at day of entry is made constant. These are wholly inconclusive results.

Next, special pairs of samples were taken—a method having the advantage of eliminating differences of cage condition in later life as approximately the same period of exposure was taken. Our first pair consisted of: *A*, 31 mice which immigrated during the first large wave of the epidemic and lived until July 14, 1921, when the latent period began; *B*, 184 which entered immediately after July 14 and were not exposed to the first wave. Both samples were followed from July 14 until death, and for each sample the number of deaths expected according to our life table, for the appropriate days of exposure, was computed. The results were these:

Sample	Expected deaths	Observed deaths	Observed as percentage of expected	Mouse days at risk
A	93·3	31	33·2	3,131
B	394·7	184	46·6	10,124

This shows an advantage of 13·4 per cent. in favour of *A*.

Since many of the deaths occurred in the quiet period, when cannibalism was a sensible factor, another set of samples was taken, exposed to risk when the certainly specific mortality was higher.

Sample *A* (24 mice). These immigrated on or before 14. vii. 21, *i.e.* were exposed to the preceding wave, and were alive on 8. x. 21.

Sample *B* (83 mice). Immigrated between 14. vii. 21 and 31. viii. 21, and were still alive on 8. x. 21.

Sample *C* (72 mice). Immigrated between 31. viii. 21 and 7. x. 21, still alive on 8. x. 21.

Sample *D* (87 mice). Immigrated between 8. x. 21 and 5. xi. 21.

In all four samples the period of exposure was from 8. x. 21 onwards,

i.e. from the days about which the gradual rise of mortality at the end of the latent period took effect. The individuals were traced as before to death:

Sample	Expected deaths	Observed deaths	Observed as percentage of expected	Mouse days at risk
A	27·8	24	86·3	1067
B	59·8	83	138·9	2217
C	72·5	72	99·3	1967
D	91·5	87	95·1	2002

Here *A* and *B* contrast. They are alike in having been a fairly long time in the cage (at least 38 days) before the period of stress. *A*'s period of exposure extended back into a time when an epidemic was raging; *B*'s did not. The suggestion then is that it is only exposure to active disease which immunises.

One may also consider here the experience of the 62 survivors from the three mouse phase of Exp. 2 and their fate in the one mouse period. These are survivors from a time of stress placed under more favourable conditions; they ought, if exposure to risk is an advantage for survivors, to compare favourably with the average of either epoch. Such is the fact. Their mean length of life after the change was 50 days, while the average after-life time would be 29·5 days[1] according to the three mouse and 47·5 days according to the one mouse epoch.

Another line of enquiry is to see whether the correlations of death-rates in successive periods are negative, *e.g.* to see whether the death-rate at age 6–10 days for calendar day x is correlated with the death-rate for ages under 5 at day $x - 5$. This method was tried for the two middle cage-age groups over 978 days, from 6. iv. 21 to 27. xi. 23, but all the observed correlations were positive. For instance, the correlation between the mean q_x for cage-age 5–9 and the mean q_x for ages 0–4 at day $x - 5$ was $0{\cdot}199 \pm 0{\cdot}021$. This is not a surprising result; owing to the secular variation of death-rates there must be a high positive correlation of adjacent death-rates, perhaps sufficient to mask any selective action. The same difficulty has usually defeated any attempt to demonstrate a selective effect in human mortality rates. This method, therefore, has not succeeded. We return to the method of sampling and the case of Exp. 7.

The first period of this experiment (14. ii. 24 to 19. iii. 24), when the preliminary epidemic begun by addition of normal mice to a few infected animals was in progress, need not be examined. The second period (20. iii. 24 to 2. v. 24) began with the immigration of 80 healthy mice. There were three groups of inhabitants:

(1) The originally infected; called *O*'s below.
(2) Additions in stage 1; *A*'s.
(3) Immigrants at the end of stage 1; *B*'s.

[1] Calculated by taking the mean of the values of the expectation of life at the ages of the 62 survivors at the day of change.

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Their fates in the second period were as follows:

	No. alive at beginning of period	No. dying in the period	Percentage
O	6	1	16·7
A	14	4	28·6
O + *A*	20	5	25·0
B	80	24	30·0

The third period lasted from 3. v. 24 to 11. vi. 24. At the beginning 50 more healthy mice, *C*'s, were added. The results are:

	No. alive at beginning of period	No. dying in the period	Percentage
O + *A*	15	8	53·3
B	56	12	21·4
C	50	21	42·0

The *B*'s, which had passed through one wave, were more resistant than the *C*'s, but the survivors of the two waves, *O*'s and *A*'s, were no more resistant.

The fourth period extended from 12. vi. 24 to 1. vii. 24, and at the beginning 50 mice, *D*'s, were added. The results are:

	Periods passed through	No. at beginning of fourth period	Deaths	Percentage
O + *A*	3	7	5	71·4
B	2	44	9	20·5
C	1	29	7	24·1
D	0	50	22	44·0

The *O* + *A* group is very small; the *B*'s and *C*'s are relatively resistant, the *D*'s relatively susceptible. This period was shorter than the two previous ones, a fact which may explain the continued resistance of the *B*'s.

The fifth period lasted from 2. vii. 24 to 15. ix. 24. At the commencement 50 healthy mice were added, *E*'s. On the first day a mouse in the cage succumbed to *B. aertrycke* infection and thereafter the population was exposed to risk of both *Pasteurella* and *B. aertrycke* infections. The results are:

Table XV.

Samples shewing relative immunity.

Class	Exposure in periods	No. alive at start of period 5	No. of deaths due to					% of *P* deaths	% of *A* + *P* deaths	% of *A* deaths	% of *P* + *AP* deaths
			*P**	*A*	*O*	?	*A* + *P*				
O + *A*	4	2	0	1	1	0	0	—	—	—	—
B	3	35	5	11	10	6	2	14·3	5·7	31·4	20·0
C	2	23	2	10	6	0	2	8·7	8·7	43·5	17·4
D	1	28	2	8	10	2	0	7·1	0·0	28·6	7·1
E	0	50	8	14	11	7	5	16·0	10·0	28·0	26·0

* *P* = Pasteurellosis. *A* = *B. aertrycke* infection.
O = Not examined. ? = Examined but no definite infection found.

A + *P* and *AP* = deaths probably due to pasteurellosis. Such mice showed all lesions of that infection, but *B. aertrycke* as well as *Pasteurella* was isolated post-mortem.

Here the new immigrants, *E*'s, and the older survivors (*B*'s) are about

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equally resistant to *Pasteurella*, the *C*'s and especially the *D*'s more resistant. No consistent difference in respect of the new infection with *B. aertrycke* appears.

The numbers are small, too small to afford proof, but they are consistent with the hypothesis that mice which have survived exposure to the reigning infection are more resistant than newcomers but lose their advantage within 30 or 40 days, and that this increased resistance is to some extent specific.

The data of Exp. 3, in which an infection with *B. aertrycke* also occurred, have also been sampled. The periods chosen were from 14. ii. 24 to 12. vi. 24 and from 8. vii. 24 to 27. vii. 24. The fates of mice immigrating during these periods were followed; July 8, 1924, was the approximate date of emergence of a serious infection with *B. aertrycke* while immigration ceased on July 27. The immigrants of the former period, *A*'s, had been exposed to the risk of *Pasteurella* infection for at least 25 days by July 8, while at that date the others, *B*'s, had not been exposed at all. The subsequent fates are shown in the table.

Table XVI.

Samples shewing relative immunity.

Period	Class	No. at risk	Deaths					Percentage mortality		
			P	*A*	*O*	?	*AP*	*P*	*A*	*P*+*AP*
July 8–Aug. 1	*A*	117	16	7	14	5	6	13·7	6·0	18·8
	B	77*	19	4	17	8	6	24·7	5·2	32·5
Aug. 2–26	*A*	69	16	7	3	0	5	23·2	10·1	27·6
	B	66	12	17	13	2	5	18·2	25·8	25·8
Aug. 27–Sept. 20	*A*	38	12	8	3	1	7	31·6	21·1	50·0
	B	17	5	2	5	0	2	29·4	11·8	41·2

* In all other cases the number at risk is the number of mice in that class alive at the beginning of the period. The 77 is calculated on that basis allowing for addition at varying dates during period 1.

Between July 8 and Aug. 1, the *A*'s, with a history of previous exposure, die of pasteurellosis at a lower rate than the newcomers, *B*'s. *A*'s and *B*'s die at approximately the same rate from the *B. aertrycke* infection. In the second period, from Aug. 2 to Aug. 26, *A*'s and *B*'s are equally resistant, *B*'s perhaps have an advantage, to pasteurellosis, while *A*'s have a decided superiority in the matter of *B. aertrycke*. From Aug. 27 to Sept. 20, the groups are sensibly equal in response to *Pasteurella*, the *B*'s have an advantage against *B. aertrycke*. Here again the numbers are too small to give wholly trustworthy results, but —disregarding the inconsistency of the *B. aertrycke* results in the last period, dependent upon but two deaths—they are consonant with the hypothesis that a specific immunity is conferred, or that natural immunity is increased, by successful passage through an epidemic, but that this new property is lost or this improved power is deteriorated by a further lapse of time.

This matter of specificity is important, and we hope to throw more light upon it in a subsequent study, when the data available are rather more numerous. Webster (1924 *a*) has found that mice surviving preliminary doses

of *B. enteritidis* were more than normally resistant to subsequent infection with homologous or heterologous strains and even were more resistant to the exhibition of mercuric chloride. Webster found that the measure of resistance shown was more closely correlated with the virulence of the strain first administered than with its similarity to that subsequently used. On balance, our evidence points to these conclusions not being applicable to our data, but we think judgment ought to be suspended.

IX. AGE DISTRIBUTION AND EPIDEMICITY.

It will be remembered that one favourite theory of the periodicity of measles is that the disease becomes epidemic when the proportion of susceptibles accumulating by natural increase has reached a certain critical ratio to that of immunes. We have shown in the preceding pages—confirming earlier results—that the prevalence of the epidemic disease varies with the number of immigrants, the more numerous the immigrants the higher, on the average, the rate of mortality. The question must then be asked whether it is possible to predict in these populations the outbreak of an epidemic from a knowledge of the age composition of the population at risk at any moment. Can we say that when the proportion of mice of cage-age less than x reaches a critical value of y per cent. a wave of mortality will rise above the endemic level?

We have sought an answer to this question in various ways. In the first place, the numbers living in the four age groups, 0–4, 5–9, 10–29, 30 and over, were correlated with (*a*) the smoothed death-rate of that day (*Pasteurella* and ? deaths)[1], and (*b*) the length of life of each mouse entering on that day over the whole period 6. iii. 21 to 30. iv. 23. The results were inconclusive. The correlations between the length of life and the numbers in the age groups on the day of entry were all small and became negligible when the numbers of the remaining population and the mean death-rate were made constant. Correlations between the total number of the population and the death-rate or between the numbers in age groups and the death-rate were fairly large and all negative in sign. Keeping constant the number of the remainder hardly affected the values, rendering constant the death-rate of the second day before entry reduced them all to insignificance. The explanation is that a large population is a necessary consequence of a previous low death-rate and that adjacent death-rates are correlated; eliminating this factor by the method of multiple correlation leaves no sufficient scope for arithmetical variation or correlation.

A second attempt on the same general lines, but making allowance for the severity of the previous risks by weighting the numbers in each age group in accordance with the past death-rates, likewise failed to elicit any definite indications. These methods seem to be rendered nugatory by the necessary arithmetical relation between population and a previous death-rate and the equally stringent correlation of adjacent death-rates.

[1] See note 2 on p. 66 of § III.

Table XVII.

Age distributions of the population at the beginnings, maxima and ends of the chief waves in Exps. 2 a, 2 b and 3.

Exp. 2 *a* (three mouse period).

Age in days	Wave No. 1			2			3			4			5			6			7			8			9			10			Av. for whole period
	B	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	
Under 5	15	12	15	15	15	15	15	14	15	15	15	15	14	13	14	14	13	14	14	13	14	15	15	14	14	14	14	14	14	14	14·0
5–9	12	8	11	13	13	15	14	13	14	13	6	12	14	7	12	12	10	10	10	6	13	8	10	11	11	6	9	9	6	15	10·5
10–29	12	14	9	15	19	23	30	23	17	26	25	18	24	26	22	22	16	10	10	11	7	11	13	19	19	13	15	15	16	17	19·8
30–39	1	1	2	2	2	3	3	7	4	8	5	3	5	4	2	2	5	4	4	1	—	1	3	2	2	4	—	—	1	3	4·5
40–49	1	1	1	1	2	1	2	3	4	8	5	5	3	4	3	3	1	3	3	2	—	1	—	2	2	4	1	1	—	3	3·5
50–59	—	1	—	—	1	1	1	1	3	2	7	5	3	4	1	1	2	2	2	2	2	1	—	—	—	—	4	4	1	—	2·7
60–69	—	—	1	1	—	1	1	1	1	2	4	6	7	3	3	3	1	—	—	1	1	1	1	—	—	1	1	1	2	—	2·1
70 and over	—	—	—	—	1	1	1	2	3	5	6	7	9	11	3	3	4	4	4	4	—	1	1	1	1	1	—	—	—	—	6·3
All ages	41	37	39	47	53	60	67	64	61	79	73	71	79	72	60	60	52	47	47	40	37	39	43	49	49	43	44	44	40	52	63·5

Exp. 2 *b* (one mouse period).

Age in days	Wave No. 1			2			3			4			Av. for whole period
	B	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	
Under 5	5	4	5	5	5	5	5	4	5	5	5	5	4·9
5–9	5	2	5	5	1	4	4	3	4	4	2	2	4·2
10–29	18	5	4	16	7	3	13	6	6	14	9	4	11·1
30–39	3	4	1	5	—	2	1	3	2	8	4	2	3·8
40–49	7	1	—	1	3	—	1	3	2	2	6	4	3·0
50–59	2	3	—	—	4	—	2	—	3	4	2	3	2·3
60–69	2	3	1	—	1	1	—	—	—	5	4	2	2·0
70 and over	24	18	8	7	5	3	3	4	3	17	14	14	9·7
All ages	66	40	24	40	26	18	29	23	25	59	46	36	40·8

Exp. 3.

	1			2			3			4			5			6			Av. for whole period
	B	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	
Under 5	30	30	30	30	29	29	29	27	30	30	29	30	28	28	29	30	28	30	28·8
5–9	32	22	21	21	19	22	27	16	21	21	20	29	26	26	25	25	21	22	22·4
10–29	—	30	52	52	15	48	48	53	52	52	51	52	79	71	65	70	69	70	54·6
30–39	—	—	—	—	37	8	20	26	15	15	14	17	18	18	23	20	18	18	15·7
40–49	—	—	—	—	12	7	8	7	14	14	13	8	14	12	14	21	18	15	11·0
50–59	—	—	—	—	—	—	—	6	4	4	13	12	5	10	6	6	12	15	7·5
60–69	—	—	—	—	—	—	—	—	6	6	6	11	8	5	10	12	6	7	5·3
70 and over	—	—	—	—	—	—	—	—	—	—	4	6	14	15	14	15	21	23	10·4
All ages	62	82	103	103	112	114	132	135	142	142	150	165	192	185	186	199	193	200	155·7

Table XVIII.

Distribution of the numbers present at the beginnings, maxima and ends of the chief waves in Exps. 2 a, 2 b and 3, grouped according to the values of q_x for the observed cage-ages found in the appropriate life tables.

Exp. 2 *a* (three mouse period).

Death-rate	Wave No. 1			2			3			4			5			6			7			8			9			10		
	B	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*
·00–·05	3	3	3	3	3	3	3	3	4	6	3	4	3	3	4	4	3	5	5	3	3	3	3	3	3	3	3	3	3	3
·05–·10	4	4	7	6	7	7	9	12	14	20	16	12	16	14	9	9	11	9	9	7	4	6	5	7	7	10	5	5	5	8
·10–·15	5	6	3	4	4	7	8	9	6	10	17	20	17	14	7	7	8	8	8	8	5	6	7	5	5	6	7	7	6	5
·15–·20	3	3	3	4	6	8	7	6	3	4	5	7	7	8	7	7	5	3	3	4	4	4	4	5	5	4	3	3	5	4
·20–·25	24	15	19	25	27	30	30	26	30	29	22	26	25	24	29	29	19	19	19	14	19	15	18	25	25	15	22	22	16	29
·25–·30	2	6	4	6	6	5	10	8	4	9	8	1	10	8	4	4	6	3	3	4	2	5	6	4	4	5	4	4	5	3
Mice over* 150 days	—	—	—	—	—	—	—	—	—	1	2	1	1	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Total	41	37	39	47	53	60	67	64	61	79	73	71	79	72	60	60	52	47	47	40	37	39	43	49	49	43	44	44	40	52

Exp. 2 *b* (one mouse period).

Death-rate	Wave No. 1			2			3			4		
	B	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*
·00–·03	6	5	3	1	2	2	2	2	2	3	4	4
·03–·06	8	12	6	3	4	5	4	4	3	10	10	7
·06–·09	16	9	4	11	6	2	8	7	6	22	11	9
·09–·12	22	9	5	13	8	4	9	6	8	12	12	9
·12–·15	8	4	3	5	4	2	2	0	3	6	5	3
·15–·18	3	1	3	3	—	3	3	3	2	3	1	2
Mice over* 150 days	3	—	—	4	2	—	1	1	1	3	3	2
Total	66	40	24	40	26	18	29	23	25	59	46	36

Exp. 3.

Death-rate	Wave No. 1			2			3			4			5			6		
	B	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*	*B*	*M*	*E*
·00–·04	12	12	12	12	12	12	12	12	12	12	12	12	12	16	16	17	12	14
·04–·08	—	—	—	—	—	1	4	5	5	5	12	8	9	4	10	9	17	11
·08–·12	6	24	30	30	31	41	39	48	53	53	62	59	81	71	67	78	71	83
·12–·16	6	18	34	34	44	33	44	49	45	45	39	51	60	62	63	62	64	60
·16–·20	6	16	13	13	13	12	17	10	11	11	13	18	14	16	15	15	13	13
·20–·24	32	12	14	14	12	15	16	11	16	16	12	17	16	16	15	16	13	16
Mice over* 105 days	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2	3	3
Total	62	82	103	103	112	114	132	135	142	142	150	165	192	185	186	199	193	200

* The death-rates at these older ages are so unreliable that it seemed better to leave these few mice unclassified.

We then concentrated our attention upon simple inspection. Epidemic waves were chosen, and the age composition of the population at the beginning, the turning-point and the end of the wave was ascertained. All waves were first examined, then, in more detail, well-defined simple waves. This examination brings out one point very clearly. The numbers and proportions in age groups differ on the whole more at similar points of different waves than at dissimilar points of the same wave. This examination having failed to define any critical characters, the populations were re-grouped by death-rates (Table XVIII) without essential change of the picture. Returning to Table XVII it may be remarked that at the beginning of a wave the proportion of mice of low cage-age is greater than the average proportion. Thus in Exp. 2, for the ten waves shown in Table XVII, the observed proportion of mice older than ten days is smaller than the average proportion (and therefore, of course, the proportion of young mice larger) in eight of the ten instances. But this is also true at the turning-points of the waves, and this is hardly more than saying that in this particular experiment most of the epidemic waves tended to emerge when the proportion of young immigrants in the population was large. In a general way it may be said that the presence of a large proportion of young mice favours the development of an epidemic wave, but that more experiments of the type of No. 7 must be made before any definite conclusion can be reached. An important factor of perturbation in such experiments as these is the individual variability of resistance which our numbers are not large enough to average out. The data of Exp. 7 bring out this point. All the mice in one batch entered the same day and were subjected to the same environment conditions, but the coefficient of variation of, for instance, the second batch, with respect to age at death was 65 per cent. of the mean. The whole of this variability is not, of course, chargeable to innate differences—date of infection is involved—but with our present material we cannot determine how it should be allocated. There are elements of the evaluation of the critical factors of an outbreak which at present elude us. This, of course, is inevitable at the beginning of an investigation which can only be completed by the co-operation of many workers pursuing their inquiries for years.

Finally, we desire to express our indebtedness to Mr W. Bale, for his constant and attentive care of the normal and infected animals during the past four years, and for his assistance in many other ways.

X. General Conclusions.

We have now completed a detailed description of the researches at the stage reached in the autumn of 1924. We shall first set out the conclusions which are, with greater or less probability, deducible from these experiments and, finally, add some general reflections to which the whole study has given rise.

1. A pasteurellosis will continue as a fatal infectious disease within a

population of mice replenished wholly by additions of normal animals, not infected prior to immigration, over a period of more than $3\frac{1}{4}$ years, that is, through a period longer than a generation.

2. The rate of mortality experienced by such a population is not steady but exhibits wave-like reinforcements; the length of the wave and the interval between successive waves are not constant, but most frequently the length of a wave is 18–22 days.

3. For the reasons stated in (2), periodogram analysis cannot establish a regular short-period movement, but in the second part of Exp. 2 a period of 59 days is shown to exist.

4. The variations mentioned in (2) are so great that experiments of the kind here in question must be continued through many months if the risk of very serious error in interpretation is to be minimised.

5. In experiments where the conditions other than the rate of immigration are similar or identical, the average death-rate is higher the larger the proportion of immigrants.

6. The relatively low death-rate in the discontinuous experiment, No. 7, where large batches of immigrants were introduced, suggests that not absolute smallness but low circulation rate of non-immunes is the reason of the favourable death-rates in the herds with few immigrants.

7. Addition of immigrants in large batches is usually followed by an increased rate of mortality, but such increase is small in comparison with the wave movements found in populations receiving additions at regular short intervals.

8. The intervals between epidemic waves are usually longer when the numbers immigrating are small.

9. In the population receiving the largest number of daily immigrants, the wave form is more regular than in the others and the high average mortality is due not to the especial severity of the epidemic exacerbations, but to the shortness of interval between the waves. There is, indeed, a tendency to approximate to a steady (high) level of mortality.

10. When the varying secular conditions are averaged, by the method of the life table, the higher expectation of life of the population in the second (or slow additions) phase of the long experiment, Exp. 2, is clearly shown.

11. Death-rates at (cage) ages show always an initial increase to a first maximum between the fifth and seventh day of exposure (in the longest experiment there is a second maximum at age 15). In all cases the death-rate then declines and, in spite of subsequent increases, has a lower average level. A lower death-rate at older ages is proven. Indications of subsequent increase are numerous but not wholly conclusive.

12. Exposure to infection in the herd does not establish complete immunity; most of the longest-exposed animals died of the original infection in the herd.

13. The respective shares of innate and acquired resistance in the

immunity enjoyed cannot be determined; a balance of evidence is in favour of an acquired immunity being important.

14. There is evidence, but not conclusive evidence, that the immunity is at least partly specific.

15. The survivors of the first phase of the long experiment lived on the average longer than those mice whose whole experience was in the second phase, and much longer than those which died out in the first phase.

16. An epidemic does not inevitably break out when the proportion of young mice attains some critical value. At the commencement of a wave, young mice are usually more numerous than on the average of the whole population at all epidemic phases, but the interpretation is not simple.

Undoubtedly the most important result of this investigation is that stated in No. 1 of the preceding conclusions. It is not, so far as the whole of the investigations of this kind mentioned in the Introduction are concerned, novel, but the duration of this series, particularly of course of Exp. 2, gives it much weight. It will not be denied than an immense majority of prophylactic and controlling measures designed for coping with epidemic diseases in human and other herds assume that the admission to a herd of individuals free from the disease it is hoped to control is not a danger to the herd accepting them. So far as the animal here used, the mouse, and the *materies morbi*, *Pasteurella*, are concerned, this fundamental principle has been shown to be false. Argument from analogy is proverbially dangerous; there is only one thing more dangerous, wholly to ignore the suggestion conveyed by an analogy. It is not to be expected or even desired that the suggestions of this academic research be at once converted into terms of practice; it is, however, urged that a serious attempt ought to be made to determine whether the field data of herd sickness, in domestic animals as well as man, confirm or refute the teaching of this investigation.

Equally suggestive but less distinct are the indications of the mechanism of a natural immunising process within a herd, its waxing and waning. We have tried to make plain where we stand, how we see vaguely certain indications of an ordered sequence. We think that further experiment, of the same type as but on a larger scale than what is here described, will render this process manifest, by averaging out the variable factors which, in our small scale experiments, obscure the main features, or what we believe to be the main features. We have tried not to make the data bear more weight than they can fairly support; herein we may have failed, the psychologically open mind is a hard attitude to maintain. At least we hope to have succeeded in one thing, in showing what an attractive field for co-operative research experimental epidemiology offers to the experimenter and the statistician. In subsequent papers we hope to improve both our experimental and statistical technique, but we shall not be unrewarded if others by the use of a better experimental or statistical method can reach results which have been beyond our powers.

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