in dealing with sickness in civil life. The demands of war service, the urgent necessity for getting men back into the firing line, or of discharging them from hospital in order to make room for others, created a perfect orgy of exaggerated methods of treatment. Mr. Hamilton Russell, of Melbourne, truly wrote a few years ago: "The present methods of wound treatment have arisen largely by reason of the special character of war injuries as distinguished from those seen in civil practice. The injuries of civil life, however, remain what they were before, and it is necessary to exercise a wise discretion in introducing methods appropriate to war injuries into the much milder type of cases usual in civil life."

The whole war period brought into focus an exaggerated idea of the importance of surgical technique, and cramped the development of surgical judgment. The treatment of every injury and every disease became standardised, and each was passed through the same mill without consideration of qualifying circumstances. It was a bad training for the newly-qualified student of medicine. He was forced to deal with cases and not with patients, and my own personal experience convinced me that the loyal service which our young men so gladly gave to the nation impaired their subsequent usefulness in civil life. Each became a mere cogwheel in a great machine designed to fulfil a special purpose. During the most impressionable period of their career they worked amongst all the sensational excitement associated with military service, and "the daily round and common task" of civil practice is now an irksome experience for them. Hence is largely derived the widespread desire to practise some form of specialism. Specialism has become an idol which all and sundry worship. Not very long ago a well-known teacher in a great London school deplored this modern tendency in medicine. He said: "Everything is becoming divided into special classes and clinics, and the lecturer deals with his students as embryo specialists in the subjects in which he himself is expert. The necessary solid foundation of general knowledge upon which specialism should be built is receiving too scant attention, and the rising generation is being taught to run before it has learnt to walk." The late Sir William Macewen, whose recent death we deplore, once said, "No one can become a good surgeon unless he is first a good physician." It is an axiom which we should never forget, and it behoves every one to equip himself with a wide knowledge of general medicine before attempting to launch his boat upon the stormy sea of operative surgery. To the layman the term specialist has become a cabalistic word which he repeats upon every possible occasion. There is, however, one specialism which he frequently fails to appreciate at its proper value—the specialism of general practice. It requires more knowledge of human nature, and more experience over a wide field of observation, to make a really first-class general practitioner than the public has any cognisance of.

It would be absurd to depreciate the value of the many scientific methods of investigation which are available at the present time, but I am sure that a too ready appeal to them is doing much to destroy the initiative in the younger generation to think for themselves. Clinical observation threatens to become a lost art. Radiography and all the modern scientific methods are good servants but bad masters. There is a whole world of wisdom in an anecdote I heard recently. A patient presented himself before a surgeon, armed with a bundle of X ray photographs and reports of various kinds. The surgeon put them all on one side and said; "We will look at these presently, but in the meantime just get on to that couch and I will endeavour to find out what you are suffering from. After that, all these things *may* help to prove whether I am right or wrong."

I would insist, therefore, that our present failing is an over-confidence in modern technique and a lack of appreciation of the value of that wisdom which can only be obtained by personal observation and experience. I would urge the younger generation to think more and observe more for themselves, as their forefathers did, and not be so ready to bow the knee in a fanatical worship of so-called scientific methods of investigation and treatment. I would ask them to reflect on all the special methods which have been put forward during the past 35 years, from tuberculin down to deep X ray therapy for cancer, to realise how many have failed to stand the test of experience, and to reflect on all the bitter disappointments which have been inflicted by the thoughtless optimism with which each has been advocated. Our scientific knowledge has been greatly advanced, but knowledge avails us very little unless we cultivate the wisdom to gauge its practical value and apply it usefully:—

> "Knowledge and wisdom, far from being one
> Have oft times no connexion; knowledge dwells
> In heads replete with thoughts of other men,
> Wisdom in minds attentive to their own.
> Knowledge is proud that he has learned so much,
> Wisdom is humble that he knows no more."

What of the future? The day is coming when it will cease to be said that—

> "We are afflicted by what we can prove,
> We are distracted by what we know,"

because we shall obtain presently a truer perspective of the scientific methods of to-day. Experience, begotten by patient observation, will teach us their real value and their limitations. Some will be discarded, some may become a sheet anchor in times of doubt. Each will add their quota to our knowledge if they be wisely used, and not merely applied empirically just because they appeal to the popular craze of the moment. We must each play our part by developing our personal observation and experience, and not be content to invoke specialisms to solve those problems which we ought to decide for ourselves. If we do that we shall each add something to the sum of human happiness; and that, after all, is the one thing worth living for. Then when we have grown old, and the world has forgotten what we have done in the past, we shall find comfort in that consolation which has been given to every one who has striven to do his best:—

> "When earth's last picture is painted, and the tubes are twisted and dried,
> When the oldest colours have faded, and the youngest critic has died,
> We shall rest; and faith we shall need it, lie down for an æon or two
> Till the Master of all good workmen will put us to work anew.
> And only 'The Master' shall praise us, and only 'The Master' shall blame,
> And no one shall work for money, and no one shall work for fame,
> But each for joy of the working, and each in his separate star,
> Shall paint the things as he sees them for the God of things as they are."

An Address

ENTITLED

IS THE STATISTICAL METHOD OF ANY VALUE IN MEDICAL RESEARCH?

Delivered in the Institute of Pathology and Research, St. Mary's Hospital, on May 22nd, 1924,

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I RECOGNISE that there is a touch of disingenuousness in my choice of title; few human passions are stronger than vanity, and there are not many men whose love of truth is so compelling that they can stand up and confess to their fellows that the studies to which they have devoted many years are futile. I am not one of those rare spirits; the fact that I ask this question implies that I think I can answer it affirmatively, so I am an advocate, not a judge. But this I can plead in extenuation; my opinion of the statistical method has changed in the 20 years during which it has been my principal study; in some ways I value it more, in others less, than I did

as a youth; perhaps as candid an account of my present position as unconscious vanity will allow me to make will help others to assess fairly the value of the statistical method.

THE GENERAL CASE AGAINST MEDICAL STATISTICS.

It is generally agreed that statistics of a sort are useful to the medical profession; that, for instance, it is desirable to compute and publish death-rates and records of infectious diseases. But many research workers would deny that data of this kind either ever have been made or ever could be made the subject of a scientific investigation apt to reveal new and important truths, in the sense that the data of experiment can be made to disclose the secrets of nature. Let me try to state the grounds of such an opinion as forcibly as I can.

The medical statistics of any country can, at best, only reflect the opinions of its practitioners of medicine; at worst, they may be a mere translation into figures of the hearsay of laymen, possibly of drunken and venal old women—Graunt's view of the sources of vital statistics in the seventeenth century. Medical statistics between the best and the worst—that is to say, as they are compiled in most civilised countries—record not all the candid opinions of certifying practitioners, but some of their opinions. So long as medical practice is individualistic and death certificates are open to the inspection of the friends of the deceased—as they are in England and Wales—there is some motive to refrain from recording any opinion which may either hurt the credit of the practitioner in the eyes of his clients or do violence to common human sentiments. To subject documents of this order of accuracy to elaborate mathematical manipulation is surely trifling. "How and why did this man die?" is the most tremendous of interrogatories. To answer it fairly and fully may require knowledge and insight which no man has ever had, not Hippocrates, not Sydenham. Our medical statistics are the coding of answers given not by Hippocrates and Sydenham, but by men of only ordinary ability and insight, some ignorant, some biassed. "Dix millions d'ignorances," said Taine, "ne font pas un savoir." No calculus will transmute a million inaccurate verbal statements into an exact numerical appraisement. Can we deduce from this codification of half-truths anything at all which we might not have reached by plain good sense and observation without arithmetic? The Registrar-General tells us that 44,789 persons died of "influenza" in 1919, 112,310 in 1918, and only 7283 in 1917. We needed no statistics to convince us that "influenza" was a great pestilence in 1918, a serious cause of illness in 1919, and relatively unimportant in 1917. The Registrar-General does, indeed, tell us many things we did not know. He says that 29,777 persons were reported to have died of "old age" in 1919, and that four of these ancients were between 45 and 50, 14 between 50 and 55, and 59 between 55 and 60. We also learn from him that "old age" was epidemic in 1909; 33,975 people succumbed to it in that year, but it was much less virulent in 1913 when only 29,801 were cut off. Certainly we did not know these facts until the Registrar-General told us of them; indeed, we do not know them now. Putting it bluntly, what is true in his records is not new to any observant man, and what is new is probably not true. That, I think, is a fair statement of the objections many feel but few express, because, nowadays, statisticians, even medical statisticians, are quite respectable people. Now let us see whether the objection can be met, and met upon ground which is as unfavourable as can well be chosen—viz., the ground of the seventeenth century.

GRAUNT AND SYDENHAM.

Contemporaneously in London in the seventeenth century two men endeavoured to elucidate the natural history of disease. Each used the same figure of speech and supported it with the same authority. The one averred that "The Observations which I happened to make (for I designed them not) upon the Bills of Mortality, have fallen out to be both Political and Natural, some concerning Trade and Government, others concerning the Air, Countries, Seasons, Fruitfulness, Health, Diseases, Longevity, and the proportions between the Sex and Ages of Mankind. All which (because Sir Francis Bacon reckons his Discourses of Life and Death to be Natural History . . . .) I am humbly bold to think Natural History also, and consequently that I am obliged to cast in this small Mite into your great Treasury of that kind." [1] The other, desiderated, "primo Historia, sive morborum omnium descriptio quoad fieri potest graphica et naturalis," and said that, done so that "evitetur censura quam clarissimus Verulamius in nonnullos ejusmodi promissores vibravit," it would be a task not easy of fulfilment.[2]

One of the two was a London tradesman, John Graunt, the other, Thomas Sydenham, *medicus in omne cœvum nobilis.* One based his natural history upon tables of figures compiled from the reports of "ancient matrons" whose diagnostic powers were, he thought, affected by the "mist of a cup of Ale and the bribe of a two-groat fee." The other's data were his own careful observations through 20 years of practice in the capital.

Given two men so equipped for the discovery of truth, which was the likelier to find truth, to make known natural historical facts apt to stimulate further research and so lead to further discoveries? Surely the answer is, Sydenham. But if we were to select from the host of natural historical facts of mortality, a fact *now* trite enough, but a novelty 200 years ago, one fact which has inspired more sanitary effort and more laboratory investigation than perhaps any other, it would be, I think, the enormous excess of mortality in childhood in large cities. One of our two natural historians of disease revealed that fact. He said: "We shall find that about 36 *per centum* of all quick conceptions died before six years old." . . . "When I consider, that in the Country 70 are born for 58 buried, and that before the year 1600 the like happened in London, I considered, whether a city as it becomes more populous, doth not, for that very cause, become more unhealthful: and inclined to believe, that London now is more unhealthful than heretofore; partly for that it is more populous, but chiefly because I have heard, that 60 years ago few Sea Coals were burnt in London, which are now universally used."

These are the words not of Sydenham but of Graunt, and how "the observations which I happened to make" led, directly and immediately, to the foundation of scientific methods of life assurance and, indirectly, to the establishment of those national registers of life and death, without which the work of Simon, of Chadwick, of Buchanan, of Power, and of Shirley Murphy could never have been done, is an oft-told tale. To "the observations which I happened to make" may be traced the inspiration of bacteriological researches carried out by men who never heard the name of Graunt.

What inspiration have modern investigators derived from Sydenham? I do not ask what our debt to him might have been had we been wise enough to invest some of the intellectual money he gave us, but what we *actually* owe, what great discoveries made since the seventeenth century are to be directly traced to Sydenham's inspiration. I think the answer is—none whatever. No great intellect is wasted; Sydenham has, perhaps, a debtor still unborn who will make something of "Epidemic Constitutions."

> "That low man seeks a little thing to do,
> Sees it and does it;
> This high man, with a great thing to pursue,
> Dies ere he knows it."

Sydenham was the high man, if you please, and Graunt the low man, but what he sought to do he did do. It is fine to have a soul above mere shop arithmetic, but perhaps unless one does cloak the humanity of one's patients in the guise of mere ciphers and averages, flesh and blood will be too much for us and our interest in the individual happenings

will prevent us from discerning the general laws of the collectivity. Perhaps the old London tradesman might have used of his method the words of a physician whom Sydenham loved: "Ὅστις δὲ ταῦτα ἀποβαλὼν καὶ ἀποδοκιμάσας πάντα ἑτέρῃ ὁδῷ καὶ ἑτέρῳ σχήματι ἐπιχειρέει ζητέειν, καὶ φήσει τι εὑρηκέναι, ἐξηπάτηται καὶ ἐξαπατᾶται· ἀδύνατον γάρ. (He who, casting aside and rejecting all these methods, essays to find truth by another path and with another method and proclaims that he has discovered something is deceiving and deceived. The thing is impossible.)

IS THE STATISTICAL METHOD EXHAUSTED?

But my candid critic may accept all this and still refuse to recognise the modern statistician as a scientific investigator. He will say: "I am quite prepared to recognise that Graunt and those inspired by him did valuable work. I agree that it *was* necessary both for honest propaganda—for calling attention to the existence of great evils which might be remedied—and even for suggesting fruitful topics of *real* research, that systematic vital statistics should be compiled and published. But in the preparation and interpretation of these statistics, one needs no more than plain good sense. Because the results of their labours are useful, the compilers and analysers of these statistics are no more entitled to rank as scientific investigators than are the equally useful artisans who manufacture our laboratory apparatus. Indeed, when I glance at the pages of acrimonious dispute between rival statisticians touching the scientific claims of different 'coefficients' I am reminded of Sam Johnson's remark: 'Sir, there is no settling the point of precedency between a louse and a flea.'"

Let us consider these two perfectly reasonable contentions: (1) That there is, properly speaking, no special method or art of medical statistics, plain good sense is all that is required; (2) that there is no longer any scope for originality in statistical research, that now, after all these years of tabulation and publication, statistics are on the plane of repetitive semi-skilled manufacture.

THE TERRIBLE RESULTS OF COMMON SENSE.

Is it a fact that a man of good sense can be trusted to interpret statistical data without either special training or (as in Graunt's case) special ability? In 1801 Dr. William Heberden the Younger published "Observations on the Increase and Decrease of Different Diseases." Heberden was something more than a mere man of good sense; he was a scholar, an experienced physician, and had family interest in medico-statistical investigations. His father, one of the most famous of eighteenth century physicians, financed a continuation of Graunt's work by Corbyn Morris. Heberden, then, went over the ground fairly acquainted with his predecessor's work and reached a conclusion which attracted a good deal of attention; he said, "there is scarcely any fact to be collected from the bills of mortality more worthy the attention of physicians than the gradual decline of dysentery." Heberden took together the three titles, bloody flux, colic, and griping in the guts, he showed that the annual average was more than 1000 in the first decade of the eighteenth century, fell to 770, to 700, to 350, 150, 110, 80, 70, 40, and finally 20 in the decade 1790–1800. He attributed this decline to greater cleanliness and better ventilation. But, as Creighton pointed out,[3] Heberden had simply made a statistical mistake; he had supposed "griping in the guts" to be dysentery when it really meant infantile diarrhœa; he made this mistake by overlooking the age-incidence of the deaths assigned to griping in the guts and did not notice that the total had been gradually transferred to the rubric convulsions. He *did* notice that the numbers assigned to convulsions had increased, but explained it by the transfer to this heading of chrisomes and infants, but did *not* remark (*a*) that transfer had been made already while convulsions were still a small total, (*b*) the gross total of chrisomes and infants was never large enough to make a difference of the required order of magnitude. If you compare Heberden's treatment of this case with Graunt's treatment of the question of whether rickets were a "new disease" in or about 1634, I think you will have no difficulty in deciding that Graunt did have a critical faculty which is really something more than simple good sense, and that a very sensible man like Heberden may blunder badly.

It would be easy enough to mention examples more recent than that of Heberden. Such mistakes look very foolish *when they are pointed out;* but a dozen of them will be made by very intelligent men within a year. I think we may accept the proposition that there is a kind of statistical tact, which is rather more than simple good sense; some are born with it, like Graunt; the rest of us have to acquire it. The second point raised by my objector is worth more consideration.

I wish to consider it under two subdivisions—first, when we confine the scope of the statistical method to what Graunt modestly called his shop arithmetic or to developments of that shop arithmetic which would have been quite intelligible to him; secondly, when we bring into the account a modern calculus which would have been almost as hard for Graunt to understand as it is for many, even laboratory workers, in the twentieth century.

LIFE-TABLES.

I choose as an example under the first heading the case of life-tables. Graunt made the first life-table, and the difference between the last English life-table, with its serried ranks of numerals, and the few figures of Graunt is of detail, very important detail of course, not of principle. A life-table purports to tell us how many of a fictitious population born at the same instant will live, 0, 1, 2, &c., years and has been used for two main purposes. The first, to provide a basis for commercial transactions, to make it possible to buy and sell equitably life annuities, assurances upon lives, and other similar conditional payments; the second to effect a summary and graphic comparison between the states of mortality in different communities or different occupations. In *medical research*, in the sense in which most of this audience understand that term, it has been used by very few. In England, my friend, Dr. John Brownlee,[4] is perhaps the only medical man who has devoted close attention to its possibilities as an instrument of research. I am aware that Bardolph was not thought a good security for Falstaff, so I shall not dwell, as I should like to do, upon the researches of a fellow medical statistician but call a witness from the respectable and unstatistical pages of the *Zeitschrift für Allgemeine Physiologie.* In 1921, August Pütter,[5] of Bonn, published an essay in which he argued that the immense literature dealing with the physiology and pathology of the duration of life, a literature to which such men as Weismann and Rubner have contributed, suffers from the lack of any clear idea as to what really is being investigated. He observes that we know more about the course of life in man than in any other animal, and suggests that it would be just as well to start by learning what there is to be learned from life-tables.

Pütter brings to the subject a fresh mind, and, like an intelligent man, sets his imagination to work to discover a *law* of mortality—i.e., some mental shorthand which will describe the increase of mortality with age. He is interested in the physiological problem of senescence, and so he only considers increasing mortality—i.e., from adult age onwards. As a laboratory worker would naturally do, he first takes the analogy of the destruction of bacteria by a disinfectant and considers the law of decrement which describes that case, the logarithmic law, the expression of the waning of a population opposing a constant power of resistance to a constant force of destruction. He suggests the combination with this of a law of geometrically increasing destructive power, so the law of human mortality he finally reaches is compounded of two factors, (1) which measures a

constantly acting force, his *Vernichtungsfaktor*, (2) the other measures the increasing lability of the tissues and is the *Alternsfaktor*. He shows that the mere arithmetical average called the expectation of life or mean duration of life in any population must be a function of both these factors, but notes that it is only the second which is of importance in the physiological study of senescence. After displaying some arithmetical examples of his proposed formulæ, he writes: "These reflections suffice to make it clear that physiology has no use for the statistical concept of the mean after life-time, but that, on the other hand, from precisely the same data from which statistics draw the concept of a mean after life-time, that is, from the mortality or survival table, physiology can deduce an important concept, the concept of a factor of senescence" (op. cit., p. 25).

As I said at the beginning we are all vain, and it is hard, even for physiologists, to believe that their thoughts had passed through the minds of dead men who were perhaps not even physiologists. Pütter's idea *may* have occurred to de Moivre or one of the Bernouillis (most good statistical ideas have), and it was at least clearly and fully expressed 99 years ago by Benjamin Gompertz [6] who held "it possible that death may be the consequence of two generally coexisting causes; the one chance, without previous disposition to death or deterioration, the other a deterioration, or increased inability to withstand destruction." Gompertz had in mind a law of mortality to express both factors, although he actually proposed one only covering the second—Pütter's *Alternsfaktor*—and a formula, including both a *Vernichtungsfaktor* and an *Alternsfaktor*, was introduced into actuarial practice only 65 years ago by Makeham, and is now termed the Makeham-Gompertz law. It differs in technical detail—for the better—from Pütter's formula, but it seeks to embody precisely the same idea. But although the idea of Pütter, or Gompertz, has been public property for nearly a century, no *physiological* use has been made of it, save by Dr. Brownlee. Dr. Brownlee has pointed out the significance of the formula from the physico-chemical point of view, and made it the basis of reflections which I am too ignorant of physical chemistry to appraise. I have looked at it from a much humbler standing-point. My line of thought was this. Suppose one accepts the suggestion that mortality is fully determined by two factors in Pütter or Gompertz's sense, then are they sufficiently separated by the Gompertz-Makeham "law" for any useful comparison of the strength of the forces at different epochs to be possible? In a general way we know that the environmental conditions of this generation are more favourable than those of our great grandfathers, that many causes of death and illness which were powerful in the eighteenth century are now almost negligible; typhus is extinct, typhoid obsolescent, tuberculosis greatly less fatal than 100 years ago. The death-rate of 1924 will probably not be as much as 50 per cent. of that of 1774. But it does not follow that the natural rate of tissue senescence has changed; that if the environment were perfect men of our generation would live longer than men of the eighteenth century placed under ideal conditions would have lived.

Let us see whether we can test this by the life-table method. The earliest life-table for an English population which is suitable for comparison is that known as the Carlisle table, and was based upon the mortality of part of Carlisle in the years 1779–87; the most recent national table is English Life Table, No. 8, based on the mortality of 1910–12. The Makeham-Gompertz constants of these tables have been calculated, those of the Carlisle table long ago, those for English Life Table, No. 8, by Mr. Trachtenberg,[7] and if we compare the values of the *Vernichtungsfaktoren* in the two tables we find that of the Carlisle table no less than three times as large as that of English Life Table, No. 8. Now let us see how long life would have been under each experience had the *Vernichtungsfaktor* been obliterated. By the nature of the assumed law of senescence, a geometrical rate of increasing destruction, there is no point of age at which *all* will be dead; theoretically some of Mr. Shaw's immortals exist, but we may calculate the age at which the original population will be reduced to one-thousandth or one-millionth, or any desired fraction of its initial number. I find, then, that the age at which only one in a million of those who lived to be 20 would still be alive supposing only the *Alternsfaktor* operative is for the Carlisle experience 105·8 years. For the England and Wales (Makehamised) experience of 1910–12 it is 104·7 years—that is, almost the same. I repeated the experiment on the English Life Table, No. 5, experience of 1881–90 as Makehamised by Mr. Trachtenberg; this table has a *Vernichtungsfaktor* greater by 78 per cent. than that of 1910–12, but the *Alternsfaktor* is again sensibly equal to the others, the one in a million survival age, when the *Vernichtungsfaktor* is abolished is 105·2 years. I made a similar comparison of the national Swedish life-tables for the experiences of 1816–40 and 1901–10 (I obtained the Makeham-Gompertz constants by a rough but sufficiently accurate approximation). The change in the *Vernichtungsfaktor* was not so great, a difference of 21 per cent., but it was considerable, the ages of survival on the stated hypotheses were 104·7 years and 105·5 years. Having reached this point and having further noted the fact that the general run of the *Vernichtungsfakoren* for the Swedish life-tables (eight of which are available) is concordant with the fluctuations of the public health of that country through the nineteenth century, I might be tempted to assert categorically that by a study of life-tables one can (*a*) deduce the quantitative measure of improvement in environmental conditions; (*b*) conclude that the physiological rate of senescence is invariable and that the human span of existence is under no circumstances whatever likely to exceed 110 years. But a little wider induction shows how foolish such a statement would be. Returning again to Mr. Trachtenberg's useful collection of Makehamised tables, we note that although what I have called the *Vernichtungsfaktor* is usually smaller the more favourable the general mortality, it is not always so. Thus he has computed the constants for the 1911–12 experience of London, of the county boroughs, of the urban districts, and of the rural districts. In this series the lowest *Vernichtungsfaktor* is that of London, the highest that of the rural districts, 156 per cent. of the value for London. But London's mortality was not so favourable as that of the rural districts; the mean after life-time at age 20 was 47·08 years on the rural experience, 42·35 years on that of London, and, of course, no sensible person would believe that the general environmental conditions of the rural districts are half as bad again as those of London. There are, at least, two reasons for this discrepancy. The first, that the so-called law only approximates crudely to the description of the natural facts; the second, that we have not got the "facts." These life-tables are not, what some people still seem to think them, records of the way in which men have really died; they are records of the way in which men would have died had they been subjected to conditions to which no real men ever have been simultaneously subjected. The English life-table for the "experience" of 1901–10 does not record the way in which the males of England and Wales died in 1901–10, but the way a hypothetical population would have died out had it been subjected to the *average* forces of mortality prevalent in that epoch. This artefact possibly, indeed probably, does not differ very widely from the truth, only attainable if we had a life card for every person born—a perfectly attainable ideal. But it would not be very sensible to spend much ingenuity in inventing more complex mathematical "laws" of mortality for the sake of representing more closely such data. But even with our crude mathematical hypothesis and our imperfect material we have gained something—viz., a new point of view, and from that new point we see various possibilities of research. Sir Almroth Wright has spoken of the profound importance of a good technique in the

searching out of nature; the equivalent of technique in the mathematical sciences is *notation*, and the history of knowledge has shown that the discovery of a good notation is so important that, with a good notation a second-rate man may go further into the arcana of nature than a first-rate man can penetrate with a bad notation. Now the *notation* of the life-table is exceedingly good. One proof of that assertion is that the notation used in seemingly unrelated cases will help us to discovery. I may be permitted to give a trivial example. During the war there was a good deal of concern over the wastage of labour in munition factories, very wild statements were made as to the numbers of new hands it was necessary to engage in order to maintain a constant strength of workers, and as to the effect of various measures in increasing or diminishing the rate of loss. I was instructed to investigate the subject and thought that one might liken entrance to and exit from a factory to birth and death, and construct factory survival tables formally and notationally analogous to life survival tables.[8] Having once got the idea, its application was simple if laborious, and we not only solved the problem originally proposed—viz., to determine the actual rates of wastage and the effects upon such wastage of changing the environmental conditions—but we were able to show that when, as happened at one time, the output of munitions of a particular type exceeded the demand, there was no need either for dramatic discharges or curtailment of hours, that if merely the industrial birth-rate were reduced to zero by refraining from the engagement of new hands, the population would be reduced to the required dimensions by the operation of the industrial "death-rate" in such-and-such a time. By the application of the life-table method it was quite easy to solve what appeared to be an extremely complicated problem.

This is a trivial illustration; reference to the papers of Prof. W. W. C. Topley [9] suggests far more important applications. This is, indeed, the point to which I have been bringing you by devious paths. I said at the outset that my conception of the statistical method in medicine has changed in the last 20 years; this is especially so with regard to the bearing of statistical method upon experiment. I used to see in the statistician the critic of the laboratory worker; it is a rôle which is gratifying to youthful vanity, for it is so easy to cheat oneself into the belief that the critic has some intellectual superiority over the criticised. I do not think even now that statistical criticism of laboratory investigations is useless, but I attach enormously more value to direct collaboration, the making of statistical experiments, and the permeation of statistical research with the experimental spirit. In this matter Prof. Topley is the pioneer. Topley has endeavoured to study *under laboratory conditions* the genesis and development of epidemics. Down to his time the subject has been examined in absolutely isolated fields. We have had on the one hand historians, public health administrators, statisticians wholly occupied with the records of occurrences of epidemic disease in nature; we have had on the other laboratory workers sedulously investigating the biological properties of the *materies morbi* and searching out the immunological properties of the living tissues of men and other animals. Between these two groups there has been little coöperation, the sanitarians have often drawn on themselves the contempt of the trained laboratory worker by a certain rashness and even amateurishness in their exploitation of laboratory results; the laboratory workers have sometimes displayed an equal crudity in their interpretations of the facts of sanitary history. It has not been recognised that the complex of phenomena in the world of humanity is so vast and the accuracy of the historical record so poor that there is little hope of solving any epidemic problem by the statistical or historical analysis of records alone; there is equally little hope of solving it by the minutely accurate, small scale experiment which has been the fashion of the laboratory worker. We must observe a "population" less complex, less exposed to the play of varied influences than the world of men and women, but much more complex than any laboratory investigator before Topley and the staff of the Rockefeller Institute had dreamed of. But, from the moment that we envisage the possibility of studying an artificial epidemic, we are faced with the need of much greater knowledge of the physiology of the animals we shall use as our material, and of a notation to describe the results.

Topley has worked with populations of mice and has reached such tentative conclusions as these:—

"We were thus forced to the conclusion that mice, among which an epidemic was spreading, were subjected to an increased risk of death if they were allowed to mingle with normal members of their own species. This conclusion was confirmed by measuring the rate of extinction of a mouse population, among which a given bacterial disease was spreading, according as it was kept in isolation or was subject to a steady immigration of susceptible individuals of the same species. . . . It would seem, then, that the survivors from one epidemic, though in apparent health, are carrying the parasites which caused the disease from which their companions died, and that when they come into contact with any considerable number of susceptible individuals of their own species a process is set up which leads to a fresh outbreak of disease. It seems clear also that these mice which have passed through one epidemic wave are now possessed of some increased powers of resistance to the disease in question, for they tend regularly to outlive the new arrivals in the cage. But this resistance is relative and not absolute, for they tend to die during the later stages of the new epidemic which they themselves have started. . . . We are led to the view that the immigration of healthy but susceptible individuals into a population which has recently emerged from a considerable outbreak of disease is just as dangerous to the community they enter as it is to themselves" (op. cit., pp. 65–68).

Topley reaches these conclusions by treating his data on the lines of a life or survival table; it is evidently the proper way to treat them. Before we can fully profit by experimental studies of epidemics we must learn much more about the course of life, apart from epidemics, in our population. While "laboratory animals" are only used as living culture media or animated test-tubes, people have not bothered about their sociology! In Rössle's [10] vast *referat* on *Wachstum und Altern* one seeks in vain for *any* precise observations of the course of life in animals other than man. He cannot go beyond the cautious conclusion that in such animals as have been "tolerably" (leidlich) studied one finds "a uniform decay of many organs and tissues" rather than a senile central nervous system in a young body (op. cit., p. 569). We have a survival table for one animal other than man—*Drosophila melanogaster!*—made by Prof. Raymond Pearl [11] (*Metron*, 1923, ii., 697).

We know very little of the trend of life in mice. Yet this is important. Prof. Pearl suggests that we can make an exact comparison between the life-table of a fly and the life-table of a human population by merely altering the unit; one year of human life is equated to 1·1279 days in the life of a fly. Suppose we take the common opinion that the average life of a mouse is two years, then a year of human life is equivalent, taking an average human life as 50 years, to about a fortnight, so by that method of reckoning an attack of, say, mouse typhoid ending in recovery is a matter of (humanly speaking) years. We know what a different business, say, a pneumococcal pneumonia is between 40 and 50 and between 20 and 30 from the prognostic standpoint. We have not sufficiently considered the possibility that this factor may be of importance in populations of laboratory animals. We *must* consider this and many other histological factors on statistical lines, with the notation of the life-table and Graunt's shop arithmetic. Such is my answer to the first part of the second question proposed so long ago that you have forgotten it. Using no statistical methods which would not have been intelligible to John Graunt, applying those methods to the controlled populations handled by Topley, it is probable, it is almost certain, that we

shall reach a clearer insight into the phenomena of epidemic disease than generations of unintegrated experimental and statistical work have achieved; armed with that knowledge, we may be able to interpret the record, both minute and defective, of human history.

THE NEW STATISTICAL CALCULUS.

The second part of my question, what we are to hope from the new statistical calculus, I have left no time to answer fairly. I will only quote from an old book. Oesterlen[12] said:—

"It may be regarded as the established result of experience that scrofula, rachitis, the formation of tubercles, and similar affections, occur most frequently in the children of the poor. Statistical indications of the same circumstance are also not wanting, but our insight into its immediate or remote causes is not furthered by them because they merely give us a certain total result, and do not enlighten us, for nstance, as to whether those children fell sick from bad food and air, or from want of care, from hereditary predisposition, from bodily malformations, or from a syphilitic taint derived from their parents. All this we may hope to learn with more certainty as statistical comparison becomes more accurate and is better able to isolate some particular influence and determine its action upon any given case."

Oesterlen's prevision has been fulfilled. Even the most convinced adherents of the environmental as opposed to the genetic origin of ill-health will hardly deny that, for instance, Prof. Karl Pearson's investigations of the factors influencing the ill-being or well-being of children have given us a clearer insight into the rôles of different possible and probable causes of ill-health. Nature *does* present us with skeins not to be unravelled by the most habile experimenter, cases where the A, the B, and C *cannot* be studied in isolation. In these instances, the modern statistical calculus of correlations is, not indeed a key to all the mythologies, but a useful, an invaluable, tool.

As the immediate collaborator of the experimenter, collaboration implying that he will take pains to understand the work of the experimenter, even to do some of it himself, the medical statistician has, I submit, an important part to play in modern research. In the investigation of such phenomena as are, at first view, too complex for experimentation, he can do service, chiefly, I believe, in detecting by his calculus factors which might be made the object of a simpler but more exact experimental investigation. When I first took an interest in these matters, more than 20 years ago, there was some tendency to treat the statistician or biometrician as a pariah, and he acquired the virtues and vices of a minority, a certain courage and a certain trick of over-emphasis —they always characterise a fighting minority. Now, statistics and statisticians are perfectly respectable; there may even be a risk of putting the claims of the statistical expert too high. The time may perhaps come when a brilliant young mathematician, building higher on the mathematical foundations laid by Karl Pearson, will assert that in medical, or any other biological research, the judgment of the biometrician must be final; he must be the ultimate court of appeal. If that time comes, I shall be found enlisted under the banner of Sir Almroth Wright, and shall quote to the would-be dictator the words of Macaulay:—

"I tell the honourable and learned gentleman, that the same spirit which sustained us in a just contest for him will sustain us in an equally just contest against him. Calumny, abuse, royal displeasure, popular fury, exclusion from office, exclusion from Parliament, we were ready to endure them all, rather than that he should be less than a British subject. We never will suffer him to be more."

The statistician must be the equal not the predominant partner.

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(*Continued at foot of next column.*)

OBSERVATIONS ON THE USE OF INSULIN.

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INSULIN is employed in diabetes with the object of making good a deficiency in the supply of the natural hormone of the pancreas in these cases. The ideal method of administering the drug would be to imitate as closely as possible the normal supply of the substance in the body. Unfortunately we are ignorant of the rate of secretion of insulin by the pancreas and whether the process is continuous or intermittent. It would seem probable, however, that a small quantity of the hormone is constantly being poured out, and that an extra amount becomes available when required, for example, after a carbohydrate meal has been taken. In any case the supply of insulin in normal individuals is such that the blood-sugar remains about 0·1 per cent. and is only raised to a slight extent by ingested carbohydrates. Diabetic subjects respond to carbohydrate food less perfectly, the lack of insulin allowing a much greater and much more prolonged increase in the blood-sugar, the percentage often rising to 0·3 or 0·4. The mildest cases of the disease show this exaggerated hyperglycæmia only after feeding, and their blood-sugar may return to the normal level between meals and during the night. In such patients a sample of blood taken before breakfast will give a normal reading. When the case is more severe, the phase of hyperglycæmia persists longer after each meal and may not pass off completely during the night. The fasting blood-sugar level is therefore high, and glycosuria is present during the whole 24 hours. Such a patient starts his day with a handicap; the blood-sugar, which already stands above the renal threshold, is further raised by each meal, and does not have time to subside far before the next food is taken. It will be seen, then, that the morning blood-sugar value represents the lowest point in the daily cycle in such cases, and when the patient is on a standard diet, the height of the fasting sugar level gives a rough guide to the severity of the case *at the moment.*

Effect of Diet on Fasting Blood-sugar.

The character of the diet that the patient is taking is also a factor in determining the height of his fasting blood-sugar. When he passes from a more meagre to a larger diet, the level of the fasting blood-sugar gradually rises from day to day until a new equilibrium is reached. The full effect may not be evident for some days after the food increase has been made. In the same way reduction of the food intake lowers the fasting sugar levels, a principle that has been made use of in the well-known Allen system. Again, the new level only becomes definitely established after a certain interval. Some patients become sugar-free on slight restriction of diet, others must be deprived of food for two or three days before the blood-sugar falls below the renal threshold level. From this it follows that the state of the blood-sugar and the quantity of sugar lost by the kidney only correspond to the food intake when the patient has been on a constant diet for several days. This fact serves to explain the frequent failure to find a relationship between the food intake and the degree of glycosuria.

(*Continued from previous column.*)

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