in dealing with sickness in civil life. The demands of our war effort have made it necessary to get men back into the firing line, or of discharging them from war service, the urgent necessity for getting men back into the firing line, or of discharging them from war service, the urgent necessity for getting men back into the firing line, or of discharging them from war service.

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 forced to deal with cases and not with patients, and for the newly-qualified student of medicine. He was worked amongst all the sensational excitement of the day, and clinical observation threatens to become too ready appeal to them is doing much to destroy true appreciation of the value of that wisdom which is an over-confidence in modern technique and a lack of knowledge, 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, are of opposite character. Wisdom dwells in heads replete with thoughts of other men, and is a mental attribute to their own. Knowledge is proud that he has learned so much, but 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 the 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 that 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..."

We shall rest; and faith we shall need it, lie down for an acou..."

When the oldest colours have faded, and the youngest critic has..."

Till the Master of all good workmen will put us to work anew, And only ' The Master ' shall praise us, and only ' The Master '..."

And no one shall work for money, and no one shall work for..."

But each for joy of the working, and each in his separate star, Shall paint the things as he sees them for the Uod 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 32nd, 1924,

BY MAJOR GREENWOOD, F.R.C.P. LOND., MEDICAL OFFICER (MEDICAL STATISTICS), MINISTRY OF HEALTH.

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 aspirants; 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 of research, 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 be the attempt 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 related things. Depending on the disease, and 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 elementary school arithmetic tell us the relative weights or the distances of the planets 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 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.

We also learn from him that "old age" was epidemic in childhood in large cities. One of our two natural historians revealed that fact. He said: "When I thought, affected by the "mist of a cup of Ale 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 may be traced the inspiration of bacteriological 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 Murphy can be known for the first time, 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.

Graunt and Sydenham.

Contemporaneously in London in the seventeenth century two men endeavoured to elucidate the natural history of mortality. Each wrote a Bey, and what he set out to do he did. Sydenham set out to make "led, directly and immediately, to the establishment of those natural historical facts apt to stimulate further research and to lead to further discoveries? Surely not, for I have heard, that 60 years ago few Sea Coals were burnt in London, which are now universally used.

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 influenza in 1919, 112,310 in 1918, and only 7283 in 1917. We also learn from him 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 56, and 50 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 1915 when only 29,501 were cut off. Certainly we did not know these things 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 of us 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 objections can be validly raised and whether the ground on which they are based is as unfavourable as can well be chosen—viz., the ground of the seventeenth century.

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: 'Who knows but that the tickets ran by A. B. may more readily vanish than those run by wiser men.' Heberden made a mistake by over-valuing the observations of the twentieth century. He suggests the combination with this work of a continuation of Graunt's life-tables.

**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 his work. He concluded that the cause of the decrease in mortality was the greater cleanliness and better ventilation. But, as Creighton pointed out, Heberden had simply made a statistical mistake; he had supposed "griping in the guts" to be dysentery when it really meant colic, and griping in the guts and dysentery were as different to him as the difference between a logarithmic and normal law.

**The Statistical Method Exhausted?**

I choose as an example under the first heading the case of life-tables. Graunt made the first life-table, which was of the best form, but not of principle. A life-table purports to tell us the number of men who die during each year of age, and from this we can conclude that the mortality is increasing or decreasing. Heberden, however, made an error in his life-tables. He concluded that the mortality was increasing, but this was because he did not understand the problem of senescence, and so he only considered the mortality of the young. He concludes that the mortality of the young is increasing, but this is because he did not understand the problem of senescence.

**Life-tables.**

Heberden, then, went over the ground fairly acquainted with his predecessor's work and then published an essay in which he argued that the problem of senescence could be solved by a statistical method. He concludes that the mortality of the young is increasing, but this is because he did not understand the problem of senescence.

**The People's Clue.**

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constantly acting force, his Vernichtungsfaktor, (2) the other measures the increasing lability of the tissues and is the Alternsfaktor. He shows that the mere actuarial method of calculating the 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. To be 200 years old, he argues, 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 as repeated the experiment on the English Life Table, No. 5, 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 former, the age at which mean 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 experiences are 192 years and 104 years respectively. I reached this point and having further noted the fact that the general run of the Vernichtungsfaktoren for the Swedish life-tables (eight of which are available) is more or less concordant with the fluctuations of the public morality, whether of the homely or the more scientific kind, 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 indiction 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 in no case is the quality of life, as measured by the general environmental conditions of the rural districts 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 lived; they are mere figures 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 single males of England and Wales died in 1910, 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 does not wholly hide, indeed, the fact which we have discovered 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 apparatus to get at the forces of mortality hidden in the life-tables, when we can get at them by use of 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, that not to see how much we have failed in the early days 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
importance of a good notation is so important that, with a good
notation a second-rate man may go further into the
equivalents of technique than a first-rate man can penetrate
with a bad notation. Now the notation of the life-
tables 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
discussion about the value of the waste labour and
laboratory workers sedulously investigating the biological
properties of the materies morbi and searching out
the immunological properties of the living tissues of
the animals. We have known very little of the trend of life in mice.

The art of calculating life tables 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
kindred data of various measurest in increasing or diminishing the rate of loss. It was inevitable that
we must learn much more about the course of life,
among which a given bacterial disease was spreading, according as it was kept in isolation or was
exposed to a fresh outbreak of disease. It seems clear also
that these mice which have passed through one epidemic
disease are more likely to be exposed to the same disease in the future, for they are not immune to the
new arrivals in the cage. But this resistance is relative
and not absolute, for they tend to die during the later
stages of infection at a rate which is much lower than it was at the start. . . . We are led to the view that the immunity
of healthy but susceptible individuals into a population
which has recently emerged from a fresh 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
in this way that the problem was solved. We
can fully profit by experimental studies of epidemics
which must be the fashion of the twenty-first century.

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 labora-
tory workers sedulously investigating the biological
properties of the materies morbi and searching out
the immunological properties of the living tissues 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
hosts of their species they have an enormous advantage over a
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shall reach a clearer insight into the phenomena of epidemic disease than generations of uninitiated experimenters. And if we have achieved 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's quoted saying:—

"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 ill-health. Nature does present us with skeins not 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 roles of different possible and probable causes of ill-health. Cases where the A, the B, and C cannot be studied 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, 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 the work of the experimenter, 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 as a heretic 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. Nevertheless, the statistician and the biometrician must be final; he must be the ultimate court of appeal. If that time comes, I shall be found entitled 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 equal just contest for us. I tell him, that the appeal to the people, to the law, to the Press, to the public advantage of the people, to the public law, to the public safety, to the public health, to the public happiness, to the public welfare, abuse, royalty 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.

References.


Obervations on the Use of Insulin.

By D. Murray Lyon, M.D., F.R.C.P., Edin., Christison Professor of Therapeutics, University of Edinburgh.

Insulin is employed in diabetes with the object of making good a deficiency in the supply of the normal hormone of the pancreas. 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 instance of the disease is this exaggerated hyperglycaemia 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, however, the disease is advanced, the fasting blood-sugar level is therefore high, and glycosuria is present during the whole 24 hours. Such a patient starts each 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 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 the 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 seen for days after the increase in food intake 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, and some patients may return to the normal level only after feeding. 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.

References.

