pneumococcic, otitic, influenzal, an undoubted diagnosis can be made only by lumbar puncture and examination of the cerebro-spinal fluid.

As lumbar puncture is such an essential element in the diagnosis, it is well to insist that the risk of any harm from diagnostic puncture, provided the fluid is not withdrawn too rapidly or in excessive quantities, is almost negligible; some haemorrhage may occur, but this seldom causes serious damage.

The risk of introducing infection and setting up meningitis by diagnostic puncture may be practically dismissed, and is quite different from the danger of infection from repeated tapings.

Although it is simple enough to depend for the diagnosis of meningococcic meningitis on the examination of the cerebro-spinal fluid for meningococci, there are a number of cases in which a decision is still left in doubt. Cases certainly occur about which the purely clinical diagnosis appears unquestionable, but in which the cerebro-spinal fluid, though turbid from the presence of polymorphonuclear leucocytes, does not contain any micro-organisms. The occurrence of cases with a sterile polymorphonuclear fluid at the first lumbar puncture recalls Hort's contention that the meningococcus is only one of the phases in the life-cycle of the virus, and raises the unorthodox suggestion that in some of the phases the organism may be a filter-passer.

These cases should be treated, although they cannot be tabulated, as meningococcic; recovery is in favour of a meningococcic origin, not only from the point of view of this therapeutic test, but also because other forms of polymorphonuclear meningitis are usually fatal, recoveries in pneumococcic meningitis being most exceptional.

As already mentioned, the cerebro-spinal fluid, though characteristically polymorphonuclear, may, particularly in chronic cases, show a predominance of lymphocytes, and so resemble the cytology of the meningitis of tuberculosis, syphilis, mumps, malaria, acute lead poisoning, and of the meningitic form of acute poliomyelitis. Incidentally, some of the clinical differences from tuberculous meningitis have been referred to, and with regard to the others, though it is an interesting academic study, lumbar puncture will always be necessary, and more rapidly and surely decide the diagnosis and prognosis.

Meningism may be due to such a large number of acute infections that it would take too long to detail them. In particular, the lecturer mentioned pneumonia, otitis media, influenza, malaria, and salvarsan injection in this connexion.

Discussing the differential diagnosis, the lecturer mentioned tonsillitis, measles, rubella, rheumatic stiffness of the neck, and rheumatic fever as possible causes of difficulty.

Spirochaeta ictero-haemorrhagica may cause meningitis, and in some of these cases there may be little or no jaundice.

In the acute infective polyneuritis described by Bradford, Bashford, and Wilson, the initial symptoms of headache, vomiting, pain in the back, and moderate fever, are in rare instances sufficiently severe to suggest the possibility of cerebro-spinal fever, but lumbar puncture shows that there is not any meningitis. *Anthrax* with cerebral symptoms may imitate meningococcic meningitis.

The meningitic form of Acute Poliomyelitis.—Clinically the resemblance to cerebro-spinal fever is very close; thus in 1911 Reece found that a reputed outbreak of cerebro-spinal fever was really one of acute poliomyelitis without any admixture of meningococcic cases.

Encephalitis lethargica, when first seen in Paris and elsewhere, was thought to be meningococcic meningitis until lumbar puncture put this diagnosis out of court. The cerebro-spinal fluid is clear and the cell content usually normal; if there be any cytological change it is in the direction of a lymphocytosis. Another difference from meningococcic infection is the absence of a haemic leucocytosis. The striking features of the disease—lethargy and ocular paralyses, though the latter are not constant—should arouse suspicion.

Uraemia may be suggested by fulminating cases in an unconscious condition, especially as there may be albuminuria, or from collapse, suppression of urine, and a petechial rash which might be thought to be uraemic. In pregnant women convulsions during cerebro-spinal fever have been regarded as eclamptic.

The purpuric eruption of the fulminating and acute cases

may lead to confusion with fulminating and other forms of purpura, such as acute lymphocytic leukaemia, streptococcic septicaemia, Henoch's purpura, and the diagnosis may be cleared up only after death. *Haemorrhagic small-pox* occurring in connexion with cerebro-spinal fever may be regarded as the meningococcic infection. In the past the disease appears to have been confused with *malignant measles*, for in 1867 Gordon stated that haemorrhagic measles always accompanied cerebro-spinal fever.

Typhus, severe food poisoning, and acute osteomyelitis were also considered.

HOW TO READ STATISTICS.

BY

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It is a common but erroneous saying that statistics can prove anything; invaluable logical deductions can be drawn from complete statistical tables, but the conclusions drawn from incomplete tables are always fallacious. Every week one sees from insufficient data conclusions airily drawn that convince the simple reader; even the masters of the profession fail in this way: Gowers pointed out that among the lower classes 80 per cent. of the tabetics have been infected with syphilis, and therefore the preponderating cause of tabes was syphilis. Many people are so overwhelmed with a bald statistical statement of this sort that they seem to lose all their reasoning power. A moment's thought will show that the only logical conclusion that can be drawn from such a bald statement is that some syphilitics suffer from tabes. It is quite probable that less than 4 per cent. of syphilitics get tabes. It is not my intention to dispute the relation of tabes to syphilis, but to show what data are required before any association between two attributes can be inferred from statistical evidence.

Suppose that the following statement is made, and that it is known to be true of a certain assemblage: "99 per cent. of those who had red hair were Canadians." How many are apt to infer from this that the majority of Canadians had red hair! But a little thought will show that from the premiss it is impossible to say whether there is any association between Canadians and red hair; it is quite possible that 99 per cent. of the Canadians there had not red hair, as will be easily seen from the adjoining diagram.

Let the number of Canadians present be represented by the larger circle (A) and the number of those with red hair by the smaller circle (B). Let (N) denote the total number of observations, or in this case the total number of inhabitants in the place considered, say (N) = 12,000. Let capital letters denote the attributes to be investigated—for example, A denotes Canadians, B red hair. Further, let the number of those who possess the attribute of A, or the "class-frequency" of A, be denoted by (A); that is, let the class-frequency of an attribute be denoted by the attribute symbol enclosed in brackets. Similarly, let the class-frequency of the "not-A's" be denoted by (a), the corresponding small letter enclosed in brackets. Now suppose that the following five class-frequencies are given:

$$\begin{aligned} (N) &= 12,000 \\ (A) &= 11,880 \quad \text{and} \quad (B) = 100 \\ (a) &= 120 \quad \quad \quad (b) = 11,900 \end{aligned}$$

Of course it is always true that $(N) = (A) + (a) = (B) + (b)$, so that two of these data are redundant. For instance, if (A), (a) and (B) are given, (N) can be obtained by adding $(A) + (a)$; and (b) by finding the difference $(N) - (B)$. The above data are not sufficient to enable one to draw any conclusion as to the association of Canadians and red hair. For that we must know either how many Canadians have red hair—that is, the class-frequency (AB), or the class-frequency (A b), or some other associated class-frequency such as (a b).

Whenever two attributes are being investigated, 2² or 4 independent class-frequencies must be given in order that a valid conclusion may be drawn. It is well to remember that if n attributes are under consideration, valid conclusions as to their association can only be drawn when 2 ^{n} independent class-frequencies have been given. This point, if remembered, will prevent much waste of time in reading so-called statistical evidence which does not give the required number of independent class-frequencies.

To return to our original problem, whether there is any association between the attributes of red hair and Canadians, we must have 4 independent data. Suppose that they are—

$$(N) = 12,000, (A) = 11,880, (B) = 100, (AB) = 99.$$

From these data we can at once deduce the other five class-frequencies that are implicitly involved in these data; for the class (A), for instance, is composed of those that have red hair (AB) and of those that have not red hair (Ab), so $(A) = (AB) + (Ab)$, and similarly $(B) = (AB) + (aB)$.

All the nine class-frequencies can be arranged in a table like the following, where the attributes are placed above and on the left side, and the unassociated classes are denoted by their appropriate symbols in brackets.

	A	a	
B	99	1	100 (B)
b	11,781	119	11,900 (b)
	11,880	120	12,000 (N)
	(A)	(a)	

Now in order to determine the association, if any, that exists between Canadians and red hair, we must compare the proportion of the Canadians among those with red hair with that of the Canadians among those who have not red hair. Thus:

$$\frac{(AB)}{(B)} : \frac{(Ab)}{(b)}, \text{ or } \frac{99}{100} : \frac{11,781}{11,900}, \text{ i.e., } \frac{99}{100} : \frac{99}{100}.$$

Or we may compare the proportion of those with red hair among the Canadians with that of those with red hair among the non-Canadians:

$$\text{i.e., } \frac{(AB)}{(A)} : \frac{(aB)}{(a)}, \text{ or } \frac{99}{11,880} : \frac{1}{120}, \text{ i.e., } \frac{1}{120} : \frac{1}{120}.$$

Now whenever the ratios are equal (as in both the above examples) we may justly draw the conclusion that the attributes are entirely independent of each other in the assemblage considered.

It should be noted that the actual value of the ratio $\frac{(AB)}{(A)}$ or $\frac{(aB)}{(a)}$ alone gives no information; it must always be compared with its appropriate contrary ratio. Further, whenever $\frac{(AB)}{(A)} = \frac{(aB)}{(a)}$, it will also equal $\frac{(B)}{(N)}$. In the above case each of the first two ratios equals $\frac{1}{120}$ and $\frac{(B)}{(N)} = \frac{100}{12,000}$; and similarly when $\frac{(AB)}{(B)} = \frac{(Ab)}{(b)}$, each of them will also be equal to $\frac{(A)}{(N)}$. Hence it will save some arithmetical work if the ratios $\frac{(AB)}{(A)}$ and $\frac{(B)}{(N)}$ or $\frac{(AB)}{(B)}$ and $\frac{(A)}{(N)}$ are first compared; if they are found equal, the two attributes are quite independent.

The legitimacy of this short cut can be shown by very simple algebra.

$$\text{Let } \frac{a}{b} = \frac{c}{d} = k; \text{ then } k = \frac{k(b+d)}{b+d} = \frac{a+c}{b+d}$$

$$\text{If } \frac{(AB)}{(A)} = \frac{(aB)}{(a)}, \text{ each will be equal to } \frac{(AB) + (aB)}{(A) + (a)} \text{ or } \frac{(B)}{(N)}.$$

It is most important to realize that no conclusion whatever can be drawn as to the relation between A and B, if only (A), (B) and (AB) are given; the total number of observations must be also given, or be determinable from other data. This will be clear after studying the following examples, in which (A) = 40 deaf persons, (B) = 50 blind, and (AB) = 2 who are both deaf and blind. The number

(N) will be different in each example, and it will be found that the relation, or association, of deafness to blindness is different in each instance.

(1) Let (N) = 1000. Then

$$\frac{(AB)}{(A)} = \frac{2}{40} = 0.05, \text{ and } \frac{(B)}{(N)} = \frac{50}{1000} = 0.05.$$

As the two ratios are equal, it is unnecessary to examine it further; we can at once draw the conclusion that in this assemblage blindness and deafness are quite independent of each other.

(2) Now let (N) = 10,000. Then

$$\frac{(AB)}{(A)} = \frac{2}{40} \text{ or } 0.05, \text{ and } \frac{(B)}{(N)} = \frac{50}{10,000} \text{ or } 0.005.$$

This means that the proportion of the blind among the deaf in this assemblage is greater than the proportion of the blind among the whole population. In every case in which the ratios are unequal it is advisable to examine the relation more carefully—in this case to examine the ratio between the blind among the deaf, and that between the blind among those who are not deaf. In this way a more accurate degree of the association is obtained. We may make out a table as before:

	A	a	
B	2	48	50 (B)
b	38	9,912	9,950 (b)
	40	9,960	10,000 (N)
	(A)	(a)	

We see then that the proportion of the blind among the deaf is $\frac{(AB)}{(A)}$ or 0.05, but the proportion of the blind among those who are not deaf is $\frac{(aB)}{(a)} = \frac{48}{9,960}$ or 0.004819. In fact, among the deaf 5 per cent. are blind, while among the not-deaf less than 0.482 per cent. are blind.

Several methods have been suggested to define the measure of association. The following seems to me the simplest: When the ratios are equal the attributes are independent of each other, i.e., when the difference between the ratios is 0, there is no association. If now we multiply each ratio by the reciprocal R of the greater ratio, we shall not alter the relation of the ratios to each other, and the value of the greater ratio will become 1. If the association between the A's and B's be complete, there will be no B's among the not-A's, or $(aB) = 0$.

Consequently, $R \frac{(AB)}{(A)} : R \frac{(aB)}{(a)} = 1 : 0$, and the difference $1 - 0$, or 1 will denote complete association. When $R \frac{(aB)}{(a)}$ is a decimal, $1 -$ this decimal will be the measure of the incomplete association. For instance, in this case $\frac{(AB)}{(A)} : \frac{(aB)}{(a)} = 0.05 : 0.00482$ say; on multiplying both ratios by 20 and taking their difference we get $1 - 0.0964$ or 0.9036 as the measure of the association. However, those who have devoted their lives to the study of statistics have not agreed as to the best method of denoting the degree of association, so I merely offer this as a tentative suggestion.

We conclude that in this district there is a definitely strong association between blindness and deafness. On what this association depends may be the subject of a further inquiry. Deafness alone cannot cause blindness; there must be some other factor, which has not been noted in the tables given us, that is the cause of both conditions. It may, for instance, be that there are some steel works in the district, and that the observed association is due to the fact that some have become deaf from the attendant noise, while others have lost their sight from accidents in these works, or syphilis may be prevalent in this district.

(3) Now let (N) = 100. Let us suppose that in the annual report of an eye and ear hospital it is stated that there are 100 in-patients, of whom 40 are deaf, 50 blind, and 2 are both deaf and blind.

$$\text{Here as before } \frac{(AB)}{(A)} = 0.05 \text{ but } \frac{(B)}{(N)} = 0.5.$$

The ratio of the blind among the deaf is consequently less than that of the blind to all the inmates of the

hospital. On scrutinizing the data as $(aB) = (B) - (AB)$ or $50 - 2 = 48$, and $(a) = (N) - (A)$ or $100 - 40 = 60$, we have $\frac{(aB)}{(a)} = \frac{48}{60} = 0.8$. So $\frac{(AB)}{(A)} \cdot \frac{(aB)}{(a)} = 0.05 : 0.8$.

The proportion, therefore, of the blind among the deaf is 5 per cent., while that of the blind among the not-deaf is 80 per cent. The ratio of the two is 0.0625 : 1. To determine the measure of association by the proposed method we must remember that we are measuring the association of blindness and deafness, so we must find the value of $0.0625 - 1$, which gives the negative decimal -0.9375 , showing that there is a strong negative association, or a disassociation, between blindness and deafness in this assemblage.

A contentious director, if he were totally ignorant of medical etiquette, might say that "As blindness in this hospital protects from deafness, and deafness from blindness, it is obvious that the ophthalmic surgeon is a very good aurist but very inefficient at eyework, and vice versa"; and he might then move that the aurist and the ophthalmic surgeon should exchange their offices.

All aspersions on these worthy men would be removed if it were pointed out that an analogous instance occurred in the adjoining general hospital, where there were 10 cases of fractures and 20 cases of tonsillitis, and no patient suffered from both these affections. The last speaker would perhaps wish that the eminent surgeon and the no less distinguished physician should exchange their parts, on the ground that the surgeon was excellent at curing throats (which he had never seen) but no good for broken bones.

The above will give the reader some idea of the pitfalls that lie in a hasty generalization from statistical tables, unless great care is taken to consider the assemblage from which the tables are drawn. It must always be remembered that hospitals are artificial assemblages: for example, the patients of lock hospitals all suffer (it may be in very different ways) from one cause; whilst those of general hospitals suffer from causes that have little if any association with each other.

To avoid the peculiarities of special assemblages one may naturally turn to the census returns of the United Kingdom, but unfortunately these are useless for most medical purposes, for example, to determine the value of a certain course of treatment, for they do not give all the data required.

I have before me a paper written by an antivaccinationist; the statistics given are analogous to my first example: "99 per cent. of those who had red hair were Canadians." In no instance are we told the number (N) of the assemblage under consideration, we are frequently told the number (V S) of those who had been vaccinated that got small-pox, but never the number (v S) of those that had not been vaccinated that suffered from small-pox, and never the number of the vaccinated (V) or that of the unvaccinated (v) in a district. In 1887 we are told that in the neighbourhood of Sheffield "on they went, vaccinating and revaccinating, and still the small-pox epidemic spread. There were no less than 7,000 cases of small-pox, and alas! 600 deaths, and still the small-pox went on."

This is mere rant. What proportion of the 7,000 cases had been vaccinated? But even if this were given we could draw no conclusion as to the value, or want of value, of vaccination, unless we were given (N), (V) and (V S), as well as the (S) which is given as 7,000. If it is desired to consider the association of vaccination, small-pox, and fatal cases of small-pox, 8 class-frequencies must be given before any conclusion as to the value of vaccination could be drawn with reference to small-pox and its fatalities.

Statistics can be wielded effectively only by those who have taken the trouble to learn how to use them. In order to draw a conclusion about the association of two attributes A and B, it is necessary to compare the proportion, or the percentage, of the B's among the A's with that of the B's among the not-A's, or $\frac{(AB)}{(A)} \cdot \frac{(aB)}{(a)}$.

It is useless to compare the percentage of the B's among the A's with that of the not-B's among the A's, as is not unfrequently done by company promoters and antivaccinationists. If $\frac{(AB)}{(A)}$ and $\frac{(Ab)}{(A)}$ are compared, it is clear that the canon about the independence of the four class-frequencies has not been obeyed, for $(A) = (AB) + (Ab)$;

so only two independent class-frequencies have been given.

Enough has been said to guard the reader from being misled by conclusions drawn from insufficient statistical data.

REMARKS ON THE PATHOGENESIS OF DEFICIENCY DISEASES AND ON PELLAGRA.

BY

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HAVING seen the interesting report by Colonel McCarrison (of the Pasteur Institute of Southern India) on the changes in the organs of pigeons fed on polished rice and suffering from polyneuritis, I wish to call the attention of those interested in this very important group of researches to some results which I obtained several years ago when working on other forms of deficiency diseases; they were published in the summer of 1915, in the Italian review *Sperimentale*, but remained completely unnoticed.

After working for some years subsequent to 1911 on the pathogenesis of pellagra, this problem (at that time less known than now) was carefully examined by me from several points of view. In consequence I was unable to uphold the photodynamic theory of Raubitschek, because I found that the exposure to light of white mice fed on maize neither shortened their life nor did them more harm than maize feeding in the dark.¹ I could not find any precipitins in the serum of pellagra patients (for maize extracts or maize protein) as some had asserted, nor could I demonstrate any positive complement fixation between serums of pellagra patients and maize extracts.²

Other researches were directed towards the study of general and local reactions of pellagra patients to the injection of maize extracts under the skin. There was some positive expression of hypersensibility, owing, perhaps, to sensitization of those pellagra patients living on maize meal to maize proteins, through the intestinal tract. My countryman Volpino has worked much on the hypersensibility reactions of pellagra patients to maize extracts.³

Without reviewing further my former experimental work, I may say that later on I adopted the conclusion, which was rapidly gaining favour, that notwithstanding new theories on the infectious nature of the disease (I am thinking chiefly of Sambon's Simulium theory), pellagra must be regarded as a deficiency disease, and that the problem of its etiology ought to be studied as far as possible according to the new methods developed chiefly by American investigators. We have not yet succeeded in finding an animal in which pellagra can develop so rapidly and typically as, for example, polyneuritis (beriberi) in fowls and pigeons. The new researches of Chittenden and Underhill⁴ seem to show that dogs can become ill with pellagrous symptoms when fed on a special diet, and a long series of investigators have studied the effects of maize feeding on rabbits, and especially on guinea-pigs. I, too, have studied the maidism of guinea-pigs from different points of view, and these are the experimental researches which I think it would be useful to resume in order to make a comparison with the interesting data of McCarrison.

It is well known that exclusive maize feeding very quickly brings about a severe pathological condition in guinea-pigs, which die in a few weeks after having lost about one-third of their weight. In the last period of their life the animals suffer from loss of hair, weakness of the legs, and diarrhoea. We know also from the work of Holst and Fröhlich,⁵ and others after them, that guinea-pigs, when fed on cereal grains alone (oats, wheat), develop a typical scurvy-like condition with lesions of bones, bone-marrow, teeth, and blood vessels—these last occasioning a real haemorrhagic diathesis. This scurvy-like condition of guinea-pigs (which is most quickly produced by oat feeding) was considered by Fröhlich, Holst, Funk,⁶ and most scientists to be the result of lack of accessory food factors or vitamins. The features of the experimental diseases were compared to those of the scurvy of men, and chiefly to Barlow's disease. Recently