odds that are unlikely because they are too low. (A more direct algebraic method is available, but is rather complicated.) The reader should beware of a method sometimes recommended—namely, to calculate a standard deviation from the sample itself and then set off twice this standard deviation on each side of the odds given by the sample, to mark the likely upper and lower limits of the true odds. This method is fairly safe when the odds are nearly even, but is not safe otherwise.

The Number of Cases

It is obvious that, in general, the greater the number of cases in the sample the more accurate will be the odds estimated from the sample, but the bane of statistics in the hands of those unacquainted with ideas of sampling is the trust placed in large numbers, although it does not require profound knowledge to realize that if, for example, one wishes to estimate the incidence of an infectious disease in a whole population, a perfectly random sample of a dozen people or less from the whole population is safer than a sample of several hundreds taken from the slums only.

Various specific questions may be raised regarding the size of samples. A worker who has seven patients of whom six failed to recover from paralysis may ask: how many cases should I observe to prove that the odds against recovery are 2 to 1, or are unlikely to be 2 to 1? The answer is that it can never be proved, without examining all possible patients, what are the exact odds. Even if all existing and past patients were included the result would only be an estimate of the odds when the result had to be applied to new patients. However, by increasing the size of the sample it is quite possible to narrow the margin of error to any desired extent.

Therefore a more specific answer can be given to such a problem as the following.

An observer has a small sample, and suspects that the true odds are 2 to 1. He knows that he cannot prove this, but, assuming that it is so, he wishes to know how large a sample he would require so as to be reasonably sure that the odds are not 1 to 1 or 3 to 1. The answer, obtained by calculation that is rather too elaborate for this paper, is that the observer could expect a sample of 130 to be large enough to show that the odds are unlikely to be 1 to 1, and that he could expect a sample of 450 to be large enough to show that the odds are unlikely to be 3 to 1.

With regard to small numbers the probability tables referred to previously show that, in terms of cure and failure, a sample of less than six patients cannot show that the odds for (or against) cure are unlikely to be 1 to 1, even if all the patients in the sample are cured or all fail to recover. A sample of eight is necessary before it is possible to show that odds of 1 to 1 are highly unlikely, and even then all the patients must be cures or failures before such a judgement is safe.

A Caution Regarding Methods

Although only one type of problem has been discussed in this paper it should be repeated that the idea of variation between samples is essential in all clinical work that involves counting or measuring, and a general caution regarding methods may not be out of place—a caution against the older statistical methods, still often used and often safe enough with large samples, but by no means safe where application to small samples is necessary, as is very common in clinical work. It is to the methods of Fisher,⁴ his students and followers,⁶ that one must turn for safety in such cases.

The calculation necessary in applying the standard deviation test is very small. If many extractions of square roots are to be done Barlow's tables⁷ are to be recommended, but various smaller tables are often sufficient, and the direct arithmetical method is not very difficult. Finally, if a worker still hesitates to apply any tests to his results, he will, it is hoped, be prompted to observe the following rules:

1. To be sure that one's sample is the equivalent of a random sample of the material to be studied.

2. Never to express one's results as percentages without giving at least the totals from which *each* percentage was calculated.

3. Not to argue from samples unless they have been adequately tested by oneself or someone else. (An adequate test may, of course, entail only competent inspection of the data and results.)

Summary

In medical work there is serious neglect of highly important problems of chance and of variation between samples, exemplified in a recent estimate of chances of cure in facial paralysis where odds are wrongly estimated, and too great reliance is placed on samples.

What is required in clinical work is not elaborate mathematical tests, but an understanding of the meaning of chance, and adequate precautions that the samples, however small, are unbiased.

Recovery from disease, like most phenomena in life, commonly depends not only on a few important factors, but on numerous small independent factors, varying from patient to patient, and therefore, whatever may be the true odds for or against recovery, samples of patients must vary in the proportion of recoveries, and often give misleading ideas of the true odds. The simple standard deviation method, properly applied, is commonly adequate, even with a sample of three patients, to show what are likely to be the limits between which the true odds must lie.

The influence of sample-size is illustrated, and a caution is given against the use of old statistical methods that are specially unreliable with small samples.

I desire to acknowledge my indebtedness to Dr. R. A. Fisher, F.R.S., for inspecting this paper before it was offered for publication, and particularly for providing an alternative method of obtaining the numbers in the third paragraph of the section on the number of cases.

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THE VISSCHER-BOWMAN TEST FOR PREGNANCY

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The introduction of a new method in the diagnosis of pregnancy, particularly of simple chemical tests which can be performed by any practitioner and will give an immediate result, is always of great interest. The disadvantages of the Aschheim-Zondek test and its modifications are that it requires a laboratory with a stock of animals, and the result is not available for at least forty-eight hours. In 1929 Voge¹ described a chemical test, the bromine test, which was simple, cheap, and rapid, but had 25 per cent. error among pregnant patients and 13 per cent. among non-pregnant patients.²

More recently Visscher and Bowman³ have described another chemical test, for which they claim great accuracy. The test is performed as follows. To 1 c.cm. of urine are added one drop of 1 per cent. hydrogen peroxide, five drops of a 1 per cent. phenylhydrazine hydrochloride solution in water, five drops of a 5 per cent. methyl

cyanide solution in water, and five drops of concentrated hydrochloric acid. The mixture is heated in a water-bath for twenty-five minutes. After this time the reaction is said to be strongly positive if a russet colour develops with a thick flocculent precipitate. If a dark brown colour appears and there is a small, slightly flocculent precipitate the reaction is termed weakly positive. If the colour is brown and there is a slight powdery precipitate the reaction is regarded as suspect or negative. If the colour has not changed and there is no precipitate the result is negative.

Clinical Results

Vijscher and Bowman investigated 317 cases and found a correct result in 294, or 93 per cent. approximately correct. They compared forty tests with the Aschheim-Zondek test and found that thirty-three gave the same result. The clinical result of only one of the seven cases where the two tests did not agree is given; in this the chemical test was correct and the animal test wrong. Menken⁴ investigated a small number of cases, four in the early months of pregnancy. In three of these in which the reaction was positive on at least one occasion, and negative on another occasion some time later, one of the pregnancies terminated in an abortion. The fourth case in this series gave a positive result, and an abortion occurred a few days later. Menken also investigated eight cases in the last month of pregnancy; seven were positive. The negative one was from a patient who was delivered later of a healthy living child. He examined the urines of eleven non-pregnant patients, and found a negative reaction in all.

Dolff⁵ investigated the urines of seventy-eight pregnant patients and found the test correct in 95.26 per cent. Of eleven cases of extrauterine pregnancy nine were correct and two wrong. He investigated a certain number of non-pregnant cases, and found the results negative in urines of low concentration, but frequently positive in urines of high concentration. He regards the test as a valuable one, and believes that if the reducing substances present in highly concentrated urine could be eliminated the percentage of correct results would be raised.

I have investigated the urines from 100 pregnant patients who were attending the ante-natal clinic at the Obstetric Hospital, University College Hospital, and found the result correct in 90 per cent. of cases. The ten pregnant patients from whom a negative reaction was obtained were between the twelfth and thirty-fifth weeks of pregnancy. I have also investigated the urine from eighty non-pregnant (gynaecological) patients, and found the test correct in 88.8 per cent. The nine patients in this group with a positive reaction have all been investigated clinically, and the absence of pregnancy confirmed. Four patients were past the menopause; one of these had an ovarian cyst, two had fibroids, and one had a prolapse. The remaining five patients were of the child-bearing period. One had a carcinoma of the cervix, one had a retroversion of the uterus, two were suffering from dysmenorrhoea, and one had a prolapse.

Conclusion

It is clear that the percentage of error amongst the non-pregnant group is too high to make the test of any real value.

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Clinical Memoranda

A Case of Paradoxical Embolism

Cases of paradoxical embolism are of sufficient rarity to make the following one of interest. No case appears to have been recorded since 1930, when T. Thompson and W. Evans¹ described a number of cases and reviewed the literature on the subject. W. G. Barnard,² in the same year, added a further report on one case.

A married woman of 57 was operated on by Mr. A. G. Banks for acute appendicitis on March 11th, after twenty-four hours of abdominal pain. An acutely inflamed retro-caecal adherent appendix was removed. No drainage tube was inserted. Convalescence was uneventful except for a small stitch abscess, and the patient was discharged to the Bartlett Convalescent Home at Felixstowe on March 25th. Two days later, at 11 a.m., she suddenly developed severe pain in the right lower chest, and became very cyanosed and dyspnoeic. A pleural friction rub was heard at the right base. Next day, at 5.30 a.m., she developed a right hemiplegia and aphasia, and gradually sank into coma, which deepened until she died on April 8th.

POST-MORTEM FINDINGS

A post-mortem examination was made by Dr. E. Biddle, pathologist to the East Suffolk and Ipswich Hospital; the findings were as follows. The body was that of an obese female. Varicose veins were present in both legs. A recent operation wound in the right iliac fossa had healed satisfactorily. The brain was congested and showed slight flattening of the convolutions. On section in the left cerebral hemisphere beneath and slightly posterior to the Rolandic area was a soft, reddish, pultaceous mass about the size of a hen's egg. No other areas of infarction were found in the brain.

The air passages were clear, and the lungs well aerated and dry. No evidence of infarction or thrombosis was seen and the pleural surfaces showed no evidence of inflammation. The heart, about normal in size, showed no congenital or other defect, except for a patent foramen ovale. This opening, about one inch in diameter when lightly stretched, was partially closed by a crescentic valvular fold, leaving a circular aperture about the size of a lead pencil. In this orifice lay a thin cord of ante-mortem clot about 5 cm. long and 0.5 cm. in diameter. There were no vegetations on the healthy valves.

In the abdomen the caecum was adherent to the posterior abdominal wall, and the parietal peritoneum was injected in the region of the common iliac vein, but there was no evidence of any suppuration in or about the caecum. The common iliac vein had, however, a healthy wall, and the clot it contained was obviously post-mortem in origin. Both external iliac veins and the enlarged femoral veins were filled by tough, adherent ante-mortem clots. The spleen, liver, kidneys, pancreas, and other organs were normal, and no other areas of infarction were discovered. Sections of the various clots confirmed our opinion as to the time of their formation.

In view of the sudden and intense dyspnoea and cyanosis and the pleural friction rub we were surprised to find no evidence post mortem of pulmonary infarction or embolus. Thompson and Evans suggested that a rise of pressure in the right auricle following pulmonary embolism might be the cause of the passage of clot from the right auricle to the left auricle through a patent foramen ovale. It is difficult to see how this explanation could apply in this case.

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