skills. Drill diameters must be right and handling correct. The use of a bone tap and blunt-ended screws gives immeasurably better security than a self-tapping screw alone, although it takes a little longer. We must understand the liability of all metals to fatigue stresses—which are inevitable, predictable, and unavoidable unless fractures are perfectly reduced and compressed to take some of the load. Only then can we discard external splintage without risk of early mechanical failure of fixation. Progress in fracture care should demand raising our standards of expectation towards a return to complete normality—accepting no deformation, no weakness, and no joint stiffness. A nudge on such matters is clearly overdue and there is much evidence of complacency in fracture management in this country. We owe the ASIF much thanks for a greatly needed stimulus.

Nevertheless, in medicine, the “man with the method” needs to be watched. A substantial reduction in morbidity after fractures has been apparent in the developed world for the past fifty years or so. This may be the result of a general increase in care and attention, specialised fracture clinics, better physiotherapy, and better living standards. The role of more frequent internal fixation may be of minor importance. Overemphasising techniques blinds the eye to fundamentals. Biologically the truths of fracture healing are still elusive. Thus bone continues to exert a fascination in both its pathology and its changing patterns of behaviour through Jaques’s “seven ages of man.” We have not really made much progress in our understanding of fracture healing since Lucas Champonnière advocated minimal rigidity of fixation, and others, later, the opposite. We know that many fractures will unite without fixation and that most fractures will heal with a degree of rigidity of fixation which falls far short of that offered by the mechanical excellence of the ASIF system. It may well be that the perils of “fracture disease” are a tribal recollection of disasters from the days before specialised fracture clinics and rehabilitation facilities were in general use. Very early vigorous mobilisation may not be so important.

Conclusion

Progress has been made, however. There is no longer any excuse for bad internal fixation. Surgeons have the choice, depending on their circumstances, facilities, and inclination, to offer mechanically sound rigid internal fixation or to offer something less. As long as the surgeon is aware of what he is doing he can determine the correct aftercare of any given fracture after initial treatment and hazard a fair guess at the prognosis. If he has the time, the patience, and the necessary facilities and supporting staff he may even pursue excellence—by regular use of the ASIF system.

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Epidemiology for the Uninitiated

Aetiology of disease—selection of controls

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In last week’s article we gave a brief account of the two kinds of epidemiological study, cohort and case-control studies, which are used to test aetiological hypotheses. Crucial to these studies is the selection of appropriate controls—an exacting procedure that requires careful planning.

At the outset it must be noted that the word “control” is being used in a particular sense. A biochemist seeking to determine the normal range of values for a new blood test will require specimens from a group of “controls.” Ideally, he would obtain specimens from a random sample of the population, and his difficulty is the practical one of ensuring that the actual group of people he uses as controls—for example, patients or hospital staff—are not so unrepresentative of the population at large that measurements made on them will differ markedly from population values.

Cohort studies

In aetiological studies the difficulty is that the control groups required are not random samples of the population, because some form of matching of study and control groups is necessary. In cohort studies the principles of matching are readily identified. Consider, for example, a study of the association between oral contraceptives and deep vein thrombosis. Two groups of women, one using oral contraceptives (the study group) and one not doing so (the control group), are to be followed up over a period of time and the occurrence of thrombosis among them compared. This is analogous to a clinical trial except that the participants are not randomly allocated to the two groups, but are allocated by the many cultural and social influences that determine use of oral contraceptives. In so far as these factors influence and independently affect susceptibility to thrombo-embolic disease they will also affect the comparison between the two groups.

Clearly, the investigator must attempt to select two groups of women who, in so far as knowledge of the disease permits, are equally susceptible to the disease. The two groups must therefore be matched in respect of confounding variables, such as age and parity, which influence the frequency of deep vein thrombo-

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sis. Alternatively, the effect of confounding variables may be allowed for during the analysis.

Case-control studies

In case-control studies the theoretical basis for selection of controls is less clear. There is no experimental counterpart of the method, which is crude and is widely used only because studies are readily feasible and can often be carried out swiftly.

Suppose a doctor is recording each new case of deep vein thrombosis among women and wishes to carry out a case-control study, comparing the frequency of use of oral contraceptives among his patients with that in a control group who have not had thrombosis. A control group consisting of a random sample of women of childbearing age in the community would clearly be inappropriate. If more patients than controls used oral contraceptives there would be several possible explanations other than that contraceptives are causally related to thrombosis. There may be confounding variables, such as socioeconomic influences, that are associated with the occurrence of thrombosis and, independently, with the use of oral contraceptives. The cases and controls must be matched for confounding variables—or allowance for them made during analysis—before any conclusions about causality can be made.

If, within the community, there were a group of people—an ethnic group, for example—among whom thromboembolic disease did not occur, an investigator would conclude that they would be unsuitable as a source of controls. He would argue that in the context of an investigation into the causes of thrombosis the group belonged to a different population to the patients. Such an argument rests on the concept that a case-control study is, in effect, a retrospective analysis of a natural "experiment" on the link between a disease and a suspected cause, and groups who are not susceptible to the disease could not contribute to the results of such an experiment. Among the subjects who could contribute to the results there are likely to be varying levels of susceptibility. Nevertheless, it can be shown that if cases and controls are matched in respect of factors that influence the frequency of the disease independently of the suspected cause this will not alter the results of a case-control study, although it may greatly reduce the number of potential controls. Thus if the presence of varicose veins influences the likelihood of thrombosis, but not the likelihood of a woman electing to use oral contraceptives, there is no indication to match on this factor.

Also within the community, and usually more readily identifiable than variations in susceptibility to the disease, there are variations in the likelihood of individuals being exposed to the suspected cause. The investigator might identify a group of people who, because of religious beliefs for example, did not use contraceptives at all. Again, he would rightly argue that they could not contribute to the results of the natural "experiment" and he would exclude them as a source of controls. He might identify other factors which to some extent influence whether a woman uses oral contraceptives—her ease of access to a family planning clinic, for example. If all such influences were identified, and cases and controls matched on them, however, the results of the study would be nullified. The frequency of use of the contraceptive pill would be the same in the two groups. This is overmatching.

The principle of matching in case-control studies is that it is carried out only in respect of confounding variables, which independently influence both disease frequency and exposure to the suspected cause. It is not indicated for other variables, which influence only disease frequency or exposure.

CAUTION IN INTERPRETATION

A critical difficulty of the case-control method is that inadequate knowledge of the disease or suspected cause may make it impossible to identify with any certainty the dominant confounding variables. For this reason, the results of case-control studies must be interpreted with caution; and where, as often occurs, little is known about variables affecting disease frequency or the distribution of the suspected cause, no great importance can be attached to the results of any single study.

We know little about the magnitude of the errors which result, in practice, from inadequate matching, and studies of this, based on actual data, are needed. Clearly, the magnitude of the errors will be related to several factors—for example, the numbers and method of selection of cases in the study and the frequency and distribution of the suspected cause in the population.

METHODS OF MATCHING

Matching may be carried out either in groups, so that the overall distribution of confounding variables is the same among the cases and controls; or individually, so that each case is matched with one or more individual controls. Either way, some degree of protection against error is afforded by using several controls for each case.

Matching is sometimes most easily accomplished by using patients' relatives as controls—for example, it was found that the average IQ of children whose mothers were anaemic during pregnancy was below average, at 97.4. To investigate a possible connection between anaemia of pregnancy and brain impairment in the child, it was necessary to exclude confounding socioeconomic variables because anaemia of pregnancy occurs more often in families where the general level of education and measured intelligence are low. Matching to exclude these socioeconomic variables was most readily achieved by using a control group consisting of the brothers and sisters of the children. The mean IQ of the children born after pregnancies complicated by anaemia was the same as that of their brothers and sisters born after uncomplicated pregnancies.

When confounding variables are geographically localised—for example, variables relating to quality of housing—matching cases and controls may be most readily accomplished by using neighbours as controls.

In practice, the number of potential controls is often limited and the constraints of rigorous matching criteria may lead to insufficient being available. Sometimes, if individual matching is restricted to the dominant confounding variables, it is possible to allow for other variables by group matching during the analysis. At other times, the investigator may have to accept that the number of confounding variables is such that the case-control method is not feasible.

No matter how rigorously a case-control study is carried out the method is such that confirmation of the findings will usually be required from repeat studies. Although some of the case-control studies on smoking and lung cancer are open to criticism because of the method of selection of controls or cases, their results provided strong evidence of the association because they consistently showed higher smoking rates in the cases than controls, albeit the magnitude of the difference varied from study to study.

Eventually this series will be collected into a book and hence no reprints will be available from the authors.

What treatment, including diet, is advisable for a patient with haemorrhagic pancreatitis?

Haemorrhagic pancreatitis is a severe form of acute pancreatitis, with a high mortality rate. The very ill patient requires intensive nursing, cessation of oral feeding, intravenous fluid and electrolytes, gastric aspiration, and usually antibiotics. Surgical drainage of the sloughing pancreas may be required.