Epidemiology for the Uninitiated

Aetiology of disease—comparisons between individuals

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To test hypotheses about suspected causes of disease two kinds of epidemiological observations may be made on groups of individuals rather than whole populations. Using as an example the suspected relation between lack of dietary fibre and diverticulosis, these two kinds of observation are: (1) comparison of a group of people with diverticulosis and a group without, to show whether dietary fibre intake is lower in the former; and (2) comparison of groups of people taking diets of different fibre content to show whether diverticulosis is more prevalent among those on low-fibre diets.

The first kind of observation is made in a *case-control* study, comparing "cases" and a group of people without the disease. The second is made in a *cohort* study, comparing people exposed to the suspected cause and those not exposed. The case-control method is more widely used by doctors, since the starting point is a group of patients, rather than groups of "normal" people in the population.

Case-control studies

Possible sources of controls for case-control studies include groups of patients with other diseases, the general population, neighbours, and relatives. The choice of a source is partly determined by the need for cases and controls to be matched in respect of certain variables. The principles of matching will be described in next week's article. As a general rule, when patients with other diseases are used as controls it is wise to choose a variety of diseases. A study of the link between cigarette smoking and bladder cancer was rightly criticised because all the controls were drawn from a respiratory clinic. The atypical smoking habits of patients with respiratory disease make them unsuitable as controls. This association between the "control" diseases and the suspected cause could have been foreseen, but other such associations may be unforeseeable and selecting controls from a variety of patient groups mitigates this difficulty.

Matched controls drawn from the general population usually represent the ideal in a case-control study, but pose practical difficulties. Nevertheless, with the advent of patient registers general practitioners have a ready framework for sampling. Electoral rolls, school registers, employment registers, and other

listings may also be used, depending on the problems being investigated. Whatever source is used, the manner of selection of individual controls should be defined and orderly—for example, consecutive consultations or a formally drawn sample—rather than based on convenience. Using "healthy volunteers" is likely to introduce bias and is rarely satisfactory. The use of neighbours or relatives as controls is determined by the need to match out certain kinds of variables (see next week's article).

During the study observations should be made on the controls in the same conditions as the patients. Unavoidably the latter, because they are ill, may give more considered replies to questions about influences such as diet that might have caused their illness. But if dietary histories are obtained from patients while they are in hospital and from controls in their own homes additional bias may be introduced.

The finding that the dietary fibre intake of patients with diverticulosis was generally lower than that of the controls would suggest an association between the two. Interpretation of this requires that three questions be answered. Firstly, could this apparent association be the result of some bias in the investigation? Bias is rife in case-control studies and each investigation has its own possible sources. Secondly, is it likely that chance alone has produced the association? Significance tests may be used to help resolve this. Thirdly, if the association is real, is it most reasonably explained on the basis of cause and effect?

Cohort studies

In a cohort study two or more groups of people (the cohorts) are selected by reason of differences in their exposure to the suspected cause—in this instance, dietary fibre. The outcome—the frequency of diverticulosis—must then be determined among them. The starting point of the study is not, therefore, a group of patients, and the practical difficulties of cohort studies are generally much greater than in case-control studies. If a disease is an uncommon outcome of exposure then large cohorts will be necessary. If the latent period between exposure and disease is long, the study may have to continue for many years.

Fortunately, it is sometimes possible to carry out cohort studies without massive resources or a prolonged commitment. The method is widely used in studies of industrial hazards. Data on exposure to the hazards among a group of employees may be obtained retrospectively from factory records, and the occurrence of disease among the employees may be ascertained from routine hospital and mortality records.

Because cohort studies tend to be time-consuming and costly, they are usually reserved for testing precisely formulated hypotheses, while case-control studies are used for exploratory investigation. The cohort method is closer to the methods of experimental science and gives information that cannot be otherwise obtained. While the case-control method first showed the association between chronic renal failure and phenacetin ingestion, it could not, by its nature, give more than an indirect

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and approximate indication of the risk to an individual of developing chronic renal failure as a consequence of phenacetin ingestion. This risk, known as the *attributable risk*, is directly measurable by the cohort method—which showed that the difference in incidence of renal failure between cohorts with different phenacetin consumption was small, and that renal failure was an uncommon sequel to high analgesic consumption.

Associations between diseases

Another kind of study—that designed to reveal associations between diseases—must be mentioned. It has been argued that

if two diseases tend to be associated in individuals they must share one or more common causes, although other independent causes may also operate. In furtherance of the dietary fibre hypothesis, studies have been carried out to show whether or not patients with ischaemic heart disease have a higher frequency of other “diseases of civilisation,” such as diverticulosis, than is found in controls without ischaemic heart disease. Crucial to these studies is the selection and matching of the controls. This entails arguments similar to those used in selecting controls for case-control studies, the subject of our next article.

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

MATERIA NON MEDICA

Autumn in Lakeland

The fashion is for foreign travel, for sights and customs in lands afar. But for me it is autumn in Lakeland.

Colours change constantly. Light flashes and flickers in softer hues. Sunshine and autumn haze; trees are red, dappled with gold and yellow, olive and brown. But their trunks take on a silver sheen never before imagined; they glint through the shades in deep glades, majestically aligned, leading to the lake shore.

Saturday is market day. The top of the silver grass mound is reached on the outskirts of Keswick. Sharp shadows of purple hang curtain-like in smooth clefts of Skiddaw as its distant overhanging hillside fields and fences take on yet a greyer tint; the morning frost falls lightly from its rounded peaks casting a backcloth to church spire and rooftops of the town.

It's strangely silent after the departure of summer trippers. The light softens. Colours and contours change again. I stand rooted: watching; gazing; trying to fix the moment—to make the scene my own.

It will be different again in the spring.—J M S PEARCE (consultant neurologist, Hull).

Nimrod Dag

Four years ago we became obsessed by photographs and posters of Turkey which showed great stone heads of men and of gods, of lions and eagles, gazing from a mountain top across the mountains of eastern Turkey. It was relatively easy to find that this was the site created for their tombs by the kings of Comagene in the first century BC. The mountain of Nimrod Dag is over 2000 metres high, and the Comagenes cut artificial terraces near the top of the mountain, set huge statues there, and added an artificial pyramidal summit of stones over 50 metres high over the actual tombs. In 2000 years lightning has brought the great heads of the statues to the ground and they stand there each taller than a man. This year we travelled there.

In the evening before our ascent of Nimrod Dag I felt that we were indeed in a mountain base camp, in our little whitewashed room at the top of the mountain village hotel, where two holes high in the walls served as windows. At half past two on the following morning we set off and 14 of us crammed into a jeep-like vehicle for a journey of three to four hours. The sun was up when the jeep finally stopped two to three kilometres from the top of the mountain. The inevitable canvas tea house was there and we drank glasses of “chai” smelling of wood smoke.

This delay was a mistake since it allowed a party of French tourists to arrive and the mountain rang with their cries. The British had refused transport of two donkeys and a horse but two plump French ladies set off on the donkeys clinging to their wooden yokes and crying “Pardon Madame” as the donkeys made their way straight up the mountainside brushing everyone aside. I noted that far down the mountain a fat Frenchman had mounted the horse, to which he was clinging. On either side of him ran a Turk and as he fell to one side one pulled the opposite leg and as he fell to the opposite side the process was repeated. However, I had set off on my own pilgrimage up the mountain and forgotten his predicament when in a few moments I was ridden down by the horse, as if by Genghis Khan and his hordes. The

air was filled with cries in French, Turkish, and Scottish and I beat the horse back and rose from my knees, only to have the performance repeated. As I recovered I was passed by an elderly Frenchwoman dressed in summer frock, cardigan, and heel-less sandals. When this was over there was a sound of hyperventilation behind me, but, instead of the victim of mountain sickness whom I expected to see, a file of elderly Frenchmen jogged past me, wearing peaked caps and shouting “Hoo ha” in unison. At this point I realised that I had entered the world of one of Glasgow's favourite films, *Monsieur Hulot's Holiday*. The sacred pilgrimage had been lost in laughter.—I J M GIBSON (consultant in geriatric medicine, Glasgow).

Salmon leaping

I have seen the salmon leaping at Feughside near Aberdeen. I wish I could continue in that metrical fashion, for it is a subject worthy of poetry. Before the visit, on a fine windy Scottish day, it had rained for over a week. The water roared tumultuously down the fall and the race—foaming, banging, turbulent, and creamy brown.

It was awesome to view from the bridge, and imagination faltered at the thought of possibly fighting for survival in the seething maelstrom. And then the superb black shape of a salmon rose above the foam, apparently still trying to swim as it snaked through the unnatural element of the air. The creature failed as it slapped hard against the smooth rock face, feet short of its target, and was bundled back by the torrent. Others came too. There were pathetic little ones, possibly never able to overcome this vast obstacle, the task seeming quite insuperable. Occasionally there were majestic fish, sometimes sadly mistiming leaps, like pole vaulters and high jumpers do, then arcing, turning, and gyrating like Olympic divers, to fall slithering beneath the surface, ready to undertake the self-imposed work once more. The salmon are Olympian gods among fish in their performance of tasks against the odds, done with grace, concentration, strength, and singlemindedness.

What jostling goes on beneath the racing water, as first one and then another fish has a try, streaking amid its fellows and oblivious of them? Is there disappointment at failure, as there is among the watchers on the bridge? There develops an unspoken common will there that at least sometimes the biological power will triumph over the soulless physical forces of rock and water. If salmon could be recipients of extrasensory perception, and that could sustain them, they would be lifted clear of the fall into calmer places more often. They might be mesmerised as the spectators are. As I watch the water intently, the smooth-faced rocks appear to recede and rise up. It is a strange sensation as the normal standards fail. It is as if the eye would hold the water still to give the travellers below a better chance. But the rock will have none of this. It seems to conspire with the river to make sure that the obstacle is not lessened. Biological success must be wrested from physical matter, which strives not to yield.

As I turned away there was sadness that no fish had won its personal battle during my stay, and none seemed likely to do so until the spate had diminished. And yet the struggle would go on, which seemed appropriate in this land of Robert the Bruce and his spider. I was disposed not to believe that what I had witnessed could be explained in terms of atoms fortuitously bound to each other in ring formations.—PHILIP RHODES (postgraduate dean, Newcastle upon Tyne).