the temptation to crowd a lot of information into one slide should be resisted. Each slide should have only a few lines or numbers, displayed with large characters, easily seen by those in the back of the room.

Importance of Investigator Worry

Many things can go wrong and many errors can occur during a study. Therefore it is essential that, preferably, the investigator himself, or else a conscientious person responsible to the investigator, *worry about details.* The careful investigator might well adopt a questioning or even a suspicious attitude toward his study.

In addition to observing the process of data collection, as recommended above, the investigator should see to it that every data-recording form is checked carefully by someone other than the person who filled it out, to detect and correct omissions and obvious errors. Copies should be made of all completed data collection forms so that the original information will still be available if any forms are lost. Complete lists and counts of all study subjects should be maintained to provide a check against lost forms. It is surprising how often forms become misplaced or piles of punch cards fall behind a desk. Keypunching of data should be verified, which involves repeating the keypunching on a machine that detects discrepancies.

All mathematical calculations should be done twice by two different persons. The investigator should be sure to have his own work double-checked by a conscientious individual. Computer programs should be tested on small samples of data and the results compared with hand calculations.

Data tables should be checked to make sure that all the numbers are correct and add up to the totals shown. Surprising or inconsistent results should provoke redoubled efforts to check whether something has gone wrong.

Finally, it would be sad, indeed, if after all this work the resulting paper were to contain misleading typographical or printing errors. The manuscript and galley proofs should be proofread carefully.

Chapter 13

Epidemiology and Patient Care

Epidemiology is quite important in patient care. Clinical decisions are greatly affected by knowledge of the patterns of disease occurrence in populations. Some of the ways that diagnosis and treatment are, or should be, related to epidemiologic knowledge and principles will be discussed in this chapter.

Epidemiology and Diagnosis

In making a diagnosis, the physician must select from the hundreds of known diseases that one which most probably fits the patient's clinical picture. In assessing the probability of a given condition being present, the physician is strongly influenced by an awareness of what diseases are prevalent in his community at the time. During an influenza epidemic, for example, a patient exhibiting fever, headache, weakness, and myalgia would be promptly diagnosed as having influenza; whereas, with no such epidemic taking place,

laboratory tests would probably be ordered to rule out other explanations for the illness. Similarly, in the United States in the 1970's, if a patient presents with congestive heart failure, diphtheritic or Chagas' myocarditis need rarely be considered.

Descriptive epidemiologic findings indicating subgroups of the population in which a disease has a low or high prevalence are also useful for diagnosis. Knowing that a patient is of a particular age or sex or occupation, or that he comes from a certain part of the country, is very helpful in narrowing down the probable diseases he or she might have. For example, if a patient has lived in the San Joaquin Valley of California, coccidioidomycosis should be strongly suspected as the disease responsible for a nonspecific lung lesion seen on his chest x-ray.

The use of epidemiologic knowledge in the diagnosis of heart disease was well described by Dry (1943) who quoted "a cardiologist of long experience" as follows:

> When I am called to see a patient with heart disease that is not of almost self-evident nature I find out certain things before I enter the room. I know whether the patient is a baby, a child, an adolescent, or an adult. If he is an adult, I find out in what age range he falls. There are certain heart diseases found commonly in certain ages and rarely found in persons of other ages. I have made my first step in probable diagnosis right then.
>
> Then, particularly if the patient is an adult, I must know whether he is male or female, for there is a sex predilection for certain diseases of the heart. That's my second step and I have narrowed the probable diagnosis down further.
>
> Next, I find out from the history what he has been exposed to. What diseases has he had? What kind of life has he lived? Has he suffered important hardships, been a rounder? Is he or she a successful, hard driving person? How much does he eat, smoke and drink? In what condition is his general health? Such questions as these narrow the problem down further. I am pretty well along in logical diagnosis by exclusion before I cross the threshold.
>
> Then I do cross it but I'm in no hurry. I shake hands with the patient, feel his pulse. I get certain impressions that way. I look at him, talk to him and size him up as a man and a doctor rather than as a cardiologist. I ask him questions about his specific complaints and continue to ply him with questions until I have the picture in my own mind of just what he has been experiencing subjectively. It is not enough to know, for instance, that he has pain in his chest or shortness of breath because either may indicate serious heart disease or a condition that is relatively innocent. Thus I have secured further background and some of what already was in my mind when I was standing in the hall has been either reinforced or refuted.
>
> Then I put my hands and my stethoscope on his chest in the course of a complete and thorough examination. Next I review the x-ray and the electrocardiogram. I ought to get every bit of evidence I can, but I honestly doubt if any of it is usually as important as the thinking I did in the hall and at the bedside before I touched the patient or had any apparatus applied to him.

Analytic Studies to Improve Methods of Diagnosis

Population studies, quite analogous to analytic epidemiologic studies, have been used to refine diagnostic methods. Just as epidemiology traditionally studies the associations between a disease and etiologic or predictive factors, the same approach may be used to study the associations between a disease and symptoms, signs, or laboratory tests. These, after all, constitute the information that is used to make a diagnosis.

Because of the current popularity of laboratory tests, one need only glance through a volume of issues of any leading medical journal to find examples of studies showing how a particular test may be used to help distinguish between persons with and without a particular disease, or between different categories of patients with the same disease. Ordinarily, the test will be performed on different patient groups, plus some "normal controls." The distributions of the test results in each of these groups are then compared. When any two distributions appear quite different and show little overlap, the test is valuable in discriminating between the two groups; that is, the test is helpful in determining whether a patient belongs to one group or the other.

The value of a symptom in distinguishing between persons with and without a disease may be investigated similarly. Two recent

population studies are examples of great interest because they showed that certain traditional clinical teachings about the relationship between a disease and a symptom are probably incorrect.

One of these studies (Price, 1963) looked closely at the relationship between various types of indigestion or dyspepsia and gallbladder disease. It had long been taught by some authorities that chronic epigastric pain, flatulence, heartburn, and intolerance to fatty and other types of foods could often be due to a diseased gallbladder. A total of 204 women, ages 50–70, were identified in one urban general-practice patient roster in the United Kingdom. Of these women, 142, or 70 percent, agreed to be interviewed concerning these symptoms. Each patient later had an x-ray of the gallbladder, by means of which 24 were shown to have gallstones or a poorly functioning gallbladder.

The relative frequency of fatty-food intolerance and of each of the other "typical" symptoms was quite similar in the groups with normal and abnormal gallbladders. Altogether, dyspepsia was quite a common symptom, afflicting about half of each group. The type of indigestion experienced by the abnormal group did not differ appreciably from that reported by normals. The author concluded that among women, ages 50–70, the presence of both gallbladder disease and dyspepsia is coincidental, and that these symptoms can not assist in the diagnosis of gallbladder disease and should not influence its treatment.

In another study of this type, Weiss (1972) analyzed data from the 1960–1962 U.S. National Health Survey to explore the relationship between hypertension and certain symptoms, long regarded as being due to this condition. Responses to questions about these symptoms on a self-administered questionnaire were studied in relation to blood pressure subsequently measured by a physician. Headache, epistaxis, and tinnitus showed no relationship to either systolic or diastolic pressure. A history of dizziness was more prevalent only in those hypertensives with a very high diastolic pressure. Fainting was inversely related to blood pressure, being reported more frequently by those with lower pressures.

It is not surprising that many physicians have accepted the teaching that gallbladder disease produces fatty-food intolerance and hypertension produces headache. First of all, these relationships, particularly the former, can be "explained" physiologically. Secondly, these symptoms are quite common; thus it is not surprising to find patients complaining of them. Nevertheless, by examining these symptom-disease relationships in general population groups, the epidemiologic approach can put them in proper perspective.

"Normal" Values

Returning again to laboratory tests and other quantitative measurements, practicing physicians and laboratory directors are in the habit of dividing the distributions of these findings into two parts, the "normal" and the "abnormal." Having a clear dividing line or "normal limit" between the two alternatives makes it easier to make decisions. If the patient is normal, he can be reassured; if he or she is abnormal, some action must be taken. Thus, it is important to understand how normal limits are arrived at.

Unfortunately, much confusion surrounds this area because the term "normal" has more than one meaning. As used above it means "good" or "desirable" or "healthy." Another important meaning is "usual" or "frequent." In this sense, it is normal for an older person to have gray hair. This says that the occurrence is common but implies nothing either way about desirability. As if these two definitions did not cause sufficient confusion, there is a third meaning having to do with the shape of a distribution curve that is often observed in studies of human characteristics. This symmetrical, bell-shaped curve is referred to as the "Gaussian" or "normal" distribution curve.

One method that has been used to define the "normal-healthy" has been to determine the "normal-usual." That is, the particular test is applied to a large population. A cutoff point is applied to one or both ends of the distribution curve so that an arbitrary small percentage, say 5 percent or 1 percent of the population, will be called abnormal. Clearly, by this method, the normal range is merely the usual range; but it is easy to drift into the view that normal-usual means normal-healthy.

This method for determining normal-healthy limits can be improved upon by finding the normal-usual values in a population that is known to be healthy. Unfortunately, the healthy group studied

is often small and select—for example, a group of medical or nursing students. Thus it is hard to be sure whether test values associated with health in these groups would also be associated with health in persons of different ages and circumstances.

Even better than studying a healthy group alone is to determine the test values in two groups, one that is healthy and one which has the disease being tested for. The result will usually be two overlapping distributions as shown in Fig. 13-1. Outside the area where the distributions overlap, a test result clearly identifies the presence or absence of disease. If a patient's value falls into the area of overlap, he has a chance of belonging to either the normal or abnormal group. Choosing one cutoff point will thus result in errors in classification; that is, there will be some truly normal individuals on the abnormal side of the cutoff point who will, therefore, be called abnormal, and there will be some truly abnormal individuals who will be considered normal.

These two types of classification errors can be expressed quantitatively in terms of the *sensitivity* and the *specificity* of a test. Sensitivity is the proportion of truly diseased who are called diseased by the test. Specificity is the proportion of truly nondiseased persons who are so identified by the test. In the example shown in Fig. 13-1 it is apparent that these two measures are inversely related to one another. Shifting the cutoff point to the left will increase sensitivity at the cost of specificity. That is, a higher percentage of sick persons will be called sick but a smaller percentage of the well will be called well. Moving the cutoff point to the right will increase specificity while decreasing sensitivity. More of the well will be called well but less sickness will be detected.

In setting the normal cutoff point, then, attention must be paid to the purpose of the test. If it is very important not to miss a particular disease which is both treatable and serious, one usually favors sensitivity over specificity, hoping to correctly identify as many cases as possible. On the other hand, if detecting a disease results in little benefit while falsely labeling normal persons as sick results in much worry and cost, specificity is to be preferred.

Unfortunately, the physician's desire for a nice cutoff point has been dealt a rather serious blow by recent epidemiologic studies, particularly in cardiovascular disease. For important coronary risk

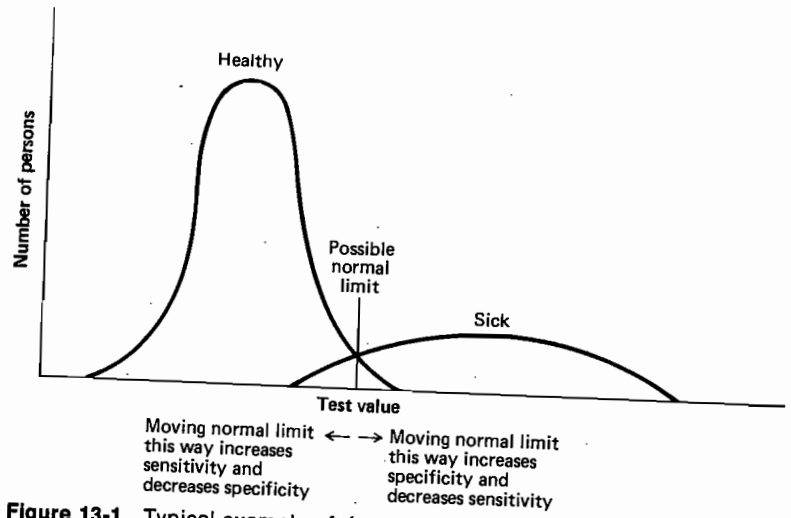

Figure 13-1 Typical example of the overlapping distributions of a test value in the healthy and the sick. Effects of shifting cutoff point on sensitivity and specificity.

factors such as blood pressure and cholesterol, it appears that within the range usually observed in this country there is no cutoff point between a safe and unsafe level. That is, the lower the level, the better off one is. There is no single level above which treatment should be given. Decisions to treat an elevated coronary risk factor must be based not only on the level of the risk factor itself but on the presence or absence of other indicators of risk. Thus, one is more apt to try to lower a serum-cholesterol level of 260 mg/100 ml if it is found in a middle-aged man who also smokes cigarettes and has a blood pressure of 150/95.

Serum cholesterol provides an excellent demonstration of the distinction between normal-usual and normal-healthy. It is not at all unusual to find a middle-aged man with a serum-cholesterol level which should hardly be considered as indicative of good health, even if the man feels well. Specifically, there is abundant epidemiologic evidence that *one-fourth* of men, i.e., those who happen to belong to the highest quartile of the cholesterol distribution, have three to four times the risk of developing clinical coronary heart disease as men in the lowest quartile. Knowing that about one in

every five men in this highest quartile will develop clinical coronary heart disease in the next 10 years hardly leads to confidence that they are normal-healthy, especially since there is mounting evidence that medical attention to their diet and living habits may reduce their high risk.

Epidemiologic studies have shown that many characteristics that have been regarded as normal because they are usual in persons who presently feel well are associated with a high probability of *future* disease. A preventive approach implies that these characteristics can no longer be regarded as consistent with good health.

Practicing Preventive Medicine in the Office or Clinic

Epidemiologic knowledge fosters the practice of preventive medicine in the medical office. Knowledge of the factors and characteristics which *cause* or *predict* the development of a disease permits identifying individuals who are at high risk of developing it. It may then be possible to prescribe measures for these patients that will prevent or at least delay the onset of the disease.

Nowadays, pediatricians are quite comfortable with the office practice of preventive medicine. Immunizations and well-baby care constitute an important phase of their work. However, in adult care the trend toward preventive medicine is only gradually taking hold. In the hope of hastening this process, the simplicity and ease of preventive care for one of the major threats to adult health, coronary heart disease, will be described.

Based on our current knowledge of coronary risk factors, identification of high-risk individuals requires little cost and effort. Age, sex, family history, and pertinent habits such as cigarette smoking and exercise are simple historical items that can be obtained by paramedical personnel or self-administered questionnaires. Likewise, height and weight or simple observation to detect obesity and a blood-pressure measurement can be done by anyone in the office with minimal training. All that remains is an electrocardiogram and the drawing of a blood specimen for measuring cholesterol and glucose. A fasting blood specimen for triglyceride might be

added, but there is some evidence suggesting that this adds little if the cholesterol is known.

Most authorities presently believe that persons with elevated levels of correctable risk factors should receive remedial therapy. As mentioned earlier, there is no safe cutoff point for each measure. The physician must form an overall impression of the patient's risk and act accordingly.

The remedial measures for the most part appear to be safe and consistent with good general health. Where appropriate, advice should be given to stop smoking, to eat less rich food in order to reduce weight and blood lipids, and to get more exercise without going to sudden extremes. Drugs that are apparently safe will lower blood pressure in most cases and will reduce lipid levels that do not respond sufficiently to diet.

The point that requires emphasis is that the detection and treatment of high coronary risk is simple and should be well within the scope of office medical practice. It would be naïve to assume that all high-risk patients will stop smoking, or eat less, or exercise more, if a doctor tells them to. Probably most will not. But some will, and it would be a shame if they were not given the opportunity and encouragement to lower their risk for a frequent, often fatal, disease.

CRITICAL READING OF THE MEDICAL LITERATURE

Most health-care professionals do not have enough time available for the careful reading and study of all the medical and scientific articles that come to their attention. It is important, however, to be able to evaluate critically reports and papers that can influence clinical decision or practice.

It is not intended, in this brief discussion, to cover all the errors and pitfalls that can occur in medical papers. Evaluating methods, observations, and interpretations in specialized fields such as surgery or biochemistry often requires knowledge and experience in the particular discipline.

An understanding of epidemiology does foster a critical approach to certain aspects of papers involving the study of populations or patient groups. The following discussion will focus primarily

on some common problems and fallacies of an epidemiologic or statistical nature. The basic principles involved should already be familiar to the reader as they have been mentioned in previous chapters.

Need for an Adequate Control Group or Basis of Comparison

Many papers report findings apparently showing the benefits of a preventive or treatment measure, based on what appear to be good results, when the measure has been used on a study group. In viewing these "good results" the reader should always ask, *Compared to what?* This initial question will usually imply others such as, *Was there a control or comparison group? Who constituted the control group? Were they similar to the treated group in all important aspects other than the treatment?* The author should have provided clear and satisfying answers to these questions in the paper. If not, there is good reason to doubt the claimed benefits.

It might be found, for example, that 95 percent of those given a certain hypnotic drug reported the next day that they slept soundly. Although, at first glance, this in itself sounds like impressive evidence for the efficacy of the drug, we must know what percentage of similar but untreated persons would report sleeping soundly on the previous night. Furthermore, to rule out a placebo effect, we need to know what percentage, given an inactive "sleeping pill," would similarly report sound sleep.

The demonstration of harmful effects also requires a basis of comparison. It may be recalled from Chap. 7 that it was not sufficient to show that a large proportion of fatally injured pedestrians have high blood-alcohol levels to incriminate alcohol as a contributor to being struck and killed by a motor vehicle. It was also necessary to demonstrate that noninjured pedestrians, otherwise similar to those killed, had, on the average, *less* alcohol in their blood.

Requirement of Denominators for Statements Comparing Risks

Statements implying that a factor involves greater or less risk of a certain outcome are often made using only "numerator" data. The

reader should "think epidemiologically" and remember that statements concerning risk should be based on *rates*, which require *denominators* as well as numerators. An example, again regarding motor-vehicle accidents, comes from a radio advertisement of a few years ago promoting the use of auto seat belts. A statement was made to the effect that 75 percent of all motor-vehicle fatalities occurred within 25 miles of home. The implication seemed to be that it was especially risky to drive on short trips close to home. However, note that motor-vehicle fatalities constitute only the numerator of a mortality rate, which needs also an appropriate denominator, such as passenger-miles. If, say, 95 percent of all passenger miles were driven within 25 miles of home, it could easily be shown that the *risk* of getting killed per passenger mile is *less* within 25 miles of home than it is farther away.

Failure to choose the appropriate denominator in drawing conclusions about risk is an easy error to fall into. One might note that the age distribution of a large series of 500 myocardial infarction cases observed at a particular institution was as shown in Table 13-1.

It would be tempting but erroneous to conclude on the basis of these data that the risk of myocardial infarction rises with age into the sixties and then falls sharply. Statements about risk at various ages must be related to the underlying population from which the cases are drawn. Incidence rates should be constructed by using the number of cases at each age as the numerator and the number of

Table 13-1 Hypothetical Age Distribution of Myocardial Infarction Cases

Age	Number of cases	Percent
20–29	10	2
30–39	40	8
40–49	75	15
50–59	125	25
60–69	175	35
70–79	50	10
80+	25	5
Total	500	100

persons at risk in the denominator. These will permit an appropriate comparison of risk at different ages. Fallacious inferences about risk, of the type illustrated here, are frequent and should be watched for.

Other Problems

A variety of special problems involving particular concepts, measurements, or study designs have been discussed in previous chapters. Examples are the possibility for spurious correlations due to uncontrolled variables, the need to distinguish statistical from biological significance (Chap. 11) and the likelihood of biased comparisons of survival when the starting point for follow-up is different in two groups (Chap. 10). Perhaps the reader's attention should again be called to the discussions in Chap. 3 on the limitations of medical observations, to the sections in Chaps. 4 through 10 concerning the conduct and interpretation of various types of studies, and to the interpretation of statistical associations as described in Chap. 11. In addition, much of the advice on conducting a study in Chap. 12 is also pertinent to evaluation the studies of others. Further discussion of problems and fallacies can be found in Ludwig and Collette (1971), Schor and Karten (1966), Hill (1971), and Huff (1954).

Although they are not solely epidemiologic concerns, some other general points deserve consideration in reading critically. These are discussed below.

Possibilities for Bias

The possibilities for biased comparisons are many. Misleading differences between groups may result from differences in the way they were selected, differences in the way data were collected from them, different follow-up durations, different criteria for judging outcome, and so on. The critical reader should try to think of these sources of bias and should note whether the author has taken them into account in his study methods or data analysis. Important potential biases should at least be mentioned in the Discussion section of a paper, if they could not be excluded.

Need for Adequate Information

It is important to determine whether the author has described his methods of selecting subjects, and of collecting and analyzing data in enough detail so that they can be evaluated and so that others can try to repeat the study or understand why their findings might differ. By close attention to these methods, the critical reader may also be able to determine whether the study was done with care or rather haphazardly.

Evidence of Objectivity

Some attempt should be made to determine whether the author appears to be objective or whether he is an advocate of a particular point of view. Is the presentation slanted toward a particular viewpoint? Would the author have published the paper if the opposite findings had been observed? Some knowledge of his previous work may be helpful in answering these questions.

One way that lack of objectivity may affect study results is through a selection process. Without intending to be misleading, an investigator may emphasize those observations which support his point of view and discard those that do not. Referring again to Fig. 11-1, page 152, which shows a moderate correlation between coronary heart disease mortality and per capita cigarette consumption in 44 states, note that the points for Utah, Arkansas, Kentucky, Indiana, and Connecticut fall along a straight line. If one wanted to show that the two variables had a nearly perfect correlation, one could prepare a graph showing these five states only. These five points would indeed present an impressive picture, if it were not mentioned that they were selected out of all the available data.

Selection for Publication

Viewing the medical literature as a whole, it is clear that positive findings are more apt to appear than negative findings. It must be remembered that positive findings may occur by chance where there is no relationship. Even when the authors are objective, chance positive findings are more apt to find their way into the literature

than truly negative findings, at least until controversy makes negative findings just as important and interesting as positive findings.

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Chapter 14

Epidemiology, Medical Care, and the Health of the Community

Health and disease in the community are important concerns not only of medical and public health professionals but of the general public as well. To illustrate the important role of epidemiology in community health, two types of epidemiologic investigations will be described briefly—the time-honored investigation of infectious-disease epidemics and some recent efforts to detect unsuspected environmental hazards. Then, the limited effects of medical care on community health will be discussed. Screening for disease and other methods for increasing the beneficial effects of health care on the community will then be described.

Investigation of Epidemics of Infectious Disease

Until a few decades ago, epidemiology had focused primarily on the infectious diseases, which have been the major scourges of mankind. Recently, in the more affluent nations, most infectious diseases