GUEST EDITORIAL

USING EPIDEMIOLOGY IN CLINICAL MEDICINE

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EPIDEMIOLOGY, the study of disease in population, is traditionally the concern of physicians doing public health and has been paid little attention by those caring for individual patients. Yet most of the facts we use as clinicians are drawn from populations, and the decisions we make concerning individuals depend on the groups into which we categorize them, often subconsciously. There is thus increasing interest in "clinical epidemiology" and in applying the logic of epidemiologic inquiry to general medical practice.

When a physician evaluates a patient presenting with fever, he typically considers such features as occupation, age, race, sex, and place of living or travel, along with the presence or absence of other symptoms, physical signs, and laboratory findings. This categorization places the patient in a series of overlapping subgroups of the population which have differential chances of having certain diseases and of benefiting from certain courses of action or therapy. In epidemiologic terms, he establishes the patient *characteristics* which influence the probability of having, or not having, certain *conditions*. If the febrile patient also has chills and headache and is a young male working on a new oil palm land scheme, the chances increase that he may have a rickettsial or malarial infection, and indeed might be cured by a single dose of doxycycline or pyrimethamine-sulfadoxine. One would then pay particular attention to lymph nodes and spleen on physical exam and probably seek a thick blood film and hemaglutination titer. What is transpiring in the course of such clinical judgment, often in only a few minutes time in a busy practice, is the estimation of a series of "conditional probabilities" — the likelihood of D given the existence of A and B but not C. The basis for making these quick decisions — for assigning the relative probabilities on which we must act — is a cumulative set of associations observed in previous patients, from our own practices and those reported by others, which suggest that people with certain characteristics are likely to have (or not have) a certain condition.

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Unfortunately, apparent relationships are often misleading. Epidemiologic experience suggests several questions worth asking when evaluating associations that seem clinically important. 1) Is there a problem with false labelling or *bias* in the observations used? 2) Are the data being compared with an appropriate *denominator group?* 3) Is it a *secondary association*, not a direct one? 4) Could the association be simply due to *chance* or sampling variation?

The pervasive problem of *bias* simply refers to the fact that the symptoms, signs, and tests we rely on clinically often do not represent what they purport to. There may be problems with *reliability* — patients recall selectively what they think is important, and observers in both the laboratory and the examining room tend to find what they expect to find and to have idiosyncratic preferences in the classifications they use. There are also problems with *validity* — we can rarely measure directly the phenomena of interest and must use tests and criteria that though *sensitive* may have frequent false positives, or though *specific* have frequent false negatives. The enlarged spleen is a sensitive criterion for malaria in that, at least by the second week of infection, it occurs in the great majority of patients. However, it may be falsely positive, i.e. enlarged due to prior infection unrelated to the current fever, or falsely negative early in the infection. If reliably performed the thick film will be positive only when malaria parasites are in the blood and is thus a

specific test; however it may be falsely negative if taken at a low point in the parasitemia cycle. Another bias problem, termed *selection*, refers to patients coming under study in ways that may give results unrepresentative of other populations. For example, the character of malaria as seen in a teaching hospital differs from that seen in an estate dispensary which in turn differs from an urban general practice. The critical physician must constantly evaluate the effects of these various biases on the data he uses — whether in a published report or in his own set of clinical impressions.

One of the most common fallacies in associations drawn from clinical work comes from examining only cases without an appropriate comparison or denominator group. One may be impressed that most babies with colic are being bottle-fed. But to draw an association between bottle-feeding and colic one must then examine what proportion of babies one sees without colic are also bottle-fed. It may be that one is simply seeing more bottle-fed babies. Simple as this sounds, this fallacy occurs often in subtle forms. For example, a distinguished clinical observer reported data from his practice showing that most men with chronic bronchitis were smokers whereas most female bronchitics were non-smokers. He concluded thus that something other than smoking underlay bronchitis in the female. What was lacking? The denominator data as to the proportion of non-bronchitic women who smoked, which would likely be smaller than that for those with bronchitis. One thus needs regularly to ask, when examining an interesting set of numbers, what is the relevant denominator with which the numerator data should be compared?

Another recurrent problem is that the association may be real but only a secondary one. For example, one might well find an association between refrigerators and coronary heart disease because both are associated with affluent, stressful modern life, not because cold drinks bring on heart attacks. The following is a more clinically important example of the same problem. Hookworm infection in Malaysia is common but usually does not involve enough worms to cause anemia. Yet one might find an association between the presence of hookworm eggs in the stool and anemia because the infection is a marker for living amidst poor sanitation and hence for lower economic status, which in turn is related to the poor nutritional status which likely produces the anemia. Thus one must ask if the characteristic studied (hookworm infection) is likely leading directly to the condition (anemia) or if it is simply a proxy indicator of some other characteristic (economic status and nutrition) which may be the direct (and actionable) association.

Finally there is the problem of whether the observed association could happen by chance alone. This determination of course is the main function of statistics, and there are many tests used. However, the $p < 0.05$ often seen in articles usually says simply that the observed difference in means between groups (most commonly using that t test) or in distribution of individuals among categories (with the chi squared test) would occur by chance with the numbers given less than one time in twenty. The most commonly useful do-it-yourself statistical assessment is to make a two by two ("contingency") table cross-tabulating the number of individuals with and without the characteristic and condition of interest. Looking at the association of bottle-feeding (BF) with colic (CL) as suggested above, we would tabulate:

		Colic YES	Colic NO	Total
Bottle-feeding	YES	a	b	t_1
Bottle-feeding	NO	c	d	t_2
	Total	t_3	t_4	T

and calculate: $X^2 = \frac{(ad-bc)^2 T}{t_1 t_2 t_3 t_4}$

If the result is four or greater the chances are only 1 in 20 that the distribution would occur by chance. Often just putting the data in the tabular form will give a sense of likely significance, but the calculation is simple enough with the generally available pocket calculators. If any of the numbers a, b, c, or d are smaller than five statisticians prefer a more exact test, but still this one will give an approximate estimate. "Statistical significance" is largely dependent on the numbers studied and should not be confused with "clinical significance". If four out of five patients treated for a rare fatal disease with medicine A live, and four out of five treated with medicine B die, the clinical

significance may be quite impressive even though the statistical significance will be marginal due to the small sample size. Of more general importance, clinicians should not be cowed by the complexity of the mathematics in a report. The math will usually be done properly; what requires scrutiny is the logic of the data put into the computation.

Epidemiology is basically a disciplined way of asking questions, and most of its rules are simply an organized form of common sense. Unfortunately, like most common sense, it is anything but common. The physician thus needs to develop his own critical sense for assessing the logic of associations on which his clinical decisions are based.

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