

## Lecture

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### Epidemiology and Clinical Psychiatry\*

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The Maudsley Bequest lectures have traditionally been intended for trainee psychiatrists. No previous lecture in the series has been concerned directly with epidemiology, and the trainee who seeks enlightenment in the British textbooks of psychiatry is likely to be disappointed or misled, for the standard view of the subject is epitomized in the statement which appears in their weightiest representative: 'In this field the epidemiological approach concerns itself with investigation of the frequency with which definable forms of psychiatric disorder occur in carefully delineated populations' (Slater and Roth, 1969). While this aspect of the discipline is central to the interests of workers in the field of public health and administration, the notion of epidemiology as primarily an exercise in head-counting is unlikely to suggest the relevance of the discipline to clinical activities, especially if these are conceived as being focused primarily on the individual patient. In this lecture I propose to try and correct this impression and indicate the provenance and scope of epidemiology as a major branch of scientific inquiry which is indispensable to clinical psychiatry.

Epidemiology, meaning literally no more than 'on the people', is a term used in medicine to designate the study of populations rather than individuals. It is instructive to recall, as a point of departure, the remarkable monograph, *The Epidemics of the Middle Ages*, first published almost 150 years ago, in which J. F. C. Hecker traced the course and effects of three major calamities (Hecker, 1859). Two of them, the Black Death and the Sweating Sickness, might

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have been expected but the third, and in many ways most interesting, study is of an epidemic of disordered behaviour, the Dancing Mania, to which Hecker later added another example in the form of a long essay on Child-Pilgrimages. In these accounts Hecker makes no distinction between epidemics of infectious disease and those of morbid behaviour, whose cause he identified as an abnormal emotional state. This view was maintained by many influential medical scientists, not least among them Rudolf Virchow, and was not to be disputed until much later in the nineteenth century, when the rise of the germ theory and the establishment of bacteriological science led to the claim that the notion of 'epidemic' be confined to the designation of infectious disease, based squarely on the establishment of host, agent and vector as the triad of key factors.

With the identification of individual organisms and the therapeutic use of antibiotics the trend became more pronounced and the terminological issue more acrimonious, the debate over words concealing, as so often, a major issue of substance which continued for some 50 years. As late as the early 1950s an eminent professor of bacteriology was moved to write to the *British Medical Journal*, condemning 'an undoubted debauchery of a precise and essential word, "epidemiology", which is being inflated by writers on social medicine and similar subjects to include the study of the frequency or incidence of diseases whether epidemic or not. The right and, as I thought, obvious meaning of epidemiology is given by the shorter *O.E.D.* as "the study of epidemics", and an epidemic is "a disease prevalent among a people or a community at a special time, and produced by

some special causes not generally present in the affected locality". Therefore, to speak of the epidemiology of coronary thrombosis, or of hare lip, or diabetes, or of any non-epidemic disease is a debasement of the currency of thought. It is of no use saying that the word is being used in its wider sense. It has no wider sense' (Gardner, 1952).

The snide reference to social medicine was understandable as a response to the challenge which had been issued by its first and foremost representative in this country: 'Public health', wrote John Ryle, 'has been largely preoccupied with the communicable diseases, their causes, distribution and prevention. Social medicine is concerned with all diseases of prevalence, including rheumatic heart disease, peptic ulcer, cancer, the psychoneuroses, the psychoses and accidental injuries—which also have their epidemiologies and their correlations with social and occupational conditions and must eventually be considered in greater or less degree preventable' (Ryle, 1948). To support his contention in the field of mental disorder Ryle might have cited the example which illustrates *par excellence* the place of epidemiology in psychiatry, namely the contribution of Joseph Goldberger to the problem of pellagra. This outstanding but still surprisingly neglected work repays consideration in some detail.

#### **Elucidation of Pellagra: an impressive achievement**

In the early years of the twentieth century pellagra was a disease which evoked great concern, especially in Italy and the southern states of North America. Here is a brief description from an Italian textbook of mental diseases at this time: 'Pellagra is an endemic disease of remittent course, and generally afebrile, which sooner or later proves fatal. It is dependent upon a specific cause—namely, the eating of maize (commonly used in the form of polenta and pan giallo) that has been damaged by moulds. Its clinical picture is that of a cachexia from intoxication, and when fully established includes not only intestinal, gastric, and cutaneous symptoms, but also motor and psychic phenomena' (Tanzi, 1909). Other authorities favoured other views, including

genetic transmission and, above all, the spread by an unknown organism. In the U.S.A. two influential Commissions in 1911 and 1913 had declared themselves in favour of an infectious aetiology, and a year later Joseph Goldberger was assigned by the Surgeon-General to the task of identifying the organism and eradicating the disease.

Goldberger himself was then a professional epidemiologist in the U.S. Public Health Service (Parsons, 1943). In this capacity he had rapidly acquired the reputation of an outstanding investigator and had made a number of important contributions to the elucidation of various infectious diseases, including yellow fever, dengue, typhus, measles, diphtheria and Schamberg's disease. In early 1914 Goldberger visited the State hospital for the insane in Jackson, Mississippi, knowing almost nothing about mental disorder. In June of the same year he published the first of his papers on pellagra. Only three pages long, it is entitled *The Etiology of Pellagra: the Significance of certain Epidemiological Observations with Respect Thereto* (Goldberger, 1914). The following extract demonstrates how he approached the problem in his own clear-sighted way:

The writer desires to invite attention to certain observations recorded in the literature of pellagra, the significance of which appears entirely to have escaped attention.

At the National Conference on Pellagra held in Columbia, S.C., November 3, 1909, Siler and Nichols in their paper on the 'Aspects of the pellagra problem in Illinois' stated that certain facts would seem to indicate that the exciting cause of the disease is present within the institution (Peoria State Hospital), and added that 'at the same time no nurses, attendants, or employees have shown the disease'.

The results of personal inquiry at some of our State asylums in which pellagra occurs confirm the reported observations above cited. Thus at the South Carolina State hospital for the insane, where Babcock (1910 Ann. Rept.) states that while cases of pellagra develop in patients who have been there for years, no case so far as the writer was able to ascertain has occurred in the nurses or attendants. It may be of interest to recall in this connection that in his annual report for 1913 Babcock states that a total of about 900 pellagrins had been admitted to his institution during the preceding six years.

At the State hospital for the insane at Jackson, Miss., there have been recorded 98 deaths from pellagra for the period between October 1, 1909 and July 1, 1913. At this institution cases of institutional origin have occurred in inmates. Dr. J. C. Herrington, assistant physician and pathologist, told me at the time of my visit of a case in an inmate after 15 and in another after 20 years' residence at the institution. No case, so far as I was able to learn, has developed in a nurse or attendant, although since January 1, 1909 there have been employed a total of 126 who have served for periods of from 1 to 5 years.

In considering the significance of such observations it is to be recalled that at all of these institutions the ward personnel, nurses, and attendants spend a considerable proportion of the 24 hours on day or night duty, in close association with the inmates; indeed at many of these institutions, for lack of a separate building or special residence for the nurses, they live right in the ward with and of necessity under exactly the same conditions as the inmates.

It is striking therefore that although many inmates develop pellagra after varying periods of institutional residence, some even after 10 to 20 years of institutional life and therefore, it seems permissible to infer, as the result of the operation within the institution of the exciting cause or causes, yet nurses and attendants living under identical conditions appear uniformly to be immune. If pellagra be a communicable disease, why should there be this exemption of the nurses and attendants?

To the writer this peculiar exemption or immunity is inexplicable on the assumption that pellagra is communicable. Neither 'contact' in any sense nor insect transmission is capable of explaining such a phenomenon, except on the assumption of an incubation or latent period extending over 10 to 20 years. In support of such an assumption there exists, so far as the writer is aware, no satisfactory evidence.

The explanation of the peculiar exemption under discussion will be found in the opinion of the writer in a difference in the diet of the two groups of residents. At some of the institutions there is a manifest difference in this regard; in others none is apparent.

The latter would seem to be a fatal objection to this explanation, but a moment's consideration will show that such is not necessarily the case. The writer from personal observation has found that although the nurses and attendants may apparently receive the same food, there is nevertheless a difference in that the nurses have the privilege—which they exercise—of selecting the best and greatest variety for themselves. Moreover, it must not be overlooked that nurses and attendants have opportunities for supple-

menting their institutional dietary that the inmates as a rule have not.

In this connection brief reference must be made to two other epidemiological features of pellagra. It is universally agreed (1) that the disease is essentially rural, and (2) associated with poverty. Now there is plenty of poverty and all its concomitants in all cities, and the question naturally arises—why its greater predilection for rural poverty? What important difference is there between the elements of poverty in our slums and those of poverty in rural dwellers? It is not the writer's intention to enter at the time into a detailed discussion of these questions; he wishes to point out one difference only. This difference relates to the dietary. Studies of urban and rural dietaries (Walt, Office of Experiment Stations, *Bulletin*, 221, 1909) have shown that on the whole the very poor of cities have a more varied diet, than the poor in rural sections. 'Except in extreme cases, the city poor . . . appear to be better nourished than the mountaineers of Tennessee'.

In view of the great uncertainty that exists as to the true cause of pellagra, it may not be amiss to suggest that pending the final solution of this problem it may be well to attempt to prevent the disease by improving the dietary of those among whom it seems most prevalent. In this direction I would urge the reduction in cereals, vegetables, and canned foods that enter to so large an extent into the dietary of many of the people in the South and an increase in the fresh animal food component, such as fresh meats, eggs, and milk.

From these initial observations Goldberger set out the implications of his own hypothesis. These were, in his own words, 'first, that a difference in diet as between pellagrins and non-pellagrins be demonstrable; second, that the disease must be curable by a proper diet; third, that it must be preventable by such a diet, and, fourth, that it may be experimentally produced by diet'. The way in which he proceeded to sustain these propositions is to be found in more than 50 papers which contain the essence of his work over the remaining 15 years of his life (Terris, 1964). First, he established that the distribution of early pellagra was related to dietary deficiencies in other institutions, notably orphanages. Then he showed that a diet of milk, eggs, meat, beans and peas prevented the occurrence of pellagra in institutions where it had been rife. And, to clinch the case, he went on to induce pellagra among

the inmates of a prison by dietary deprivation, a procedure which would probably upset the members of most ethical committees today.

Next, he moved from the institution to the community in his famous field-survey of cotton-mill villages in South Carolina. This is one of the great examples of 'shoe-leather' epidemiology, which entailed fortnightly house-visits to all members of the population from whom he obtained detailed socio-demographic, personal and dietary information. From the mass of data which he collected Goldberger was able to clinch the association between pellagra and low animal protein food (*not* corn), home food-supplies and, above all, selective poverty. Working with the economist, Edgar Sydenstricker, he constructed the 'ammain', a socio-economic unit for measuring variation in gross demand for articles of consumption which, they demonstrated, was significantly related to the incidence of pellagra. The detail of their painstaking inquiry is legendary:

(1) Statements were obtained from households as to the immediate source of every article of food entering into their half-month's supplies. Thus it was ascertained, for example, whether the fresh milk used by the household was produced at home, purchased from another mill worker's household in the village, or from some specific farmer, dairy or store, or donated by a relative, neighbour, or other person. In the event that a household had a source of supply not common generally to households in the village, inquiries were directed with a view to ascertaining the length of time the household had had such a supply, particularly with respect to the period after January 1, 1916.

(2) From farmers, hucksters, or 'peddlers' selling from house to house, statements were secured relating to the quantities sold, prices, frequency of selling, and character of produce sold since January 1, 1916.

(3) From managers and clerks in the stores, markets, and other retail establishments at which mill workers' households largely dealt, data were secured relating to (a) prices during the 15-day period and price changes during 1916; (b) sources of each food sold, whether direct from near-by farms or through middlemen from local agricultural territory or from other sections of the United States; (c) names of brands and quantities of the foods sold; (d) practices with respect to credit to mill workers' households, especially as affected by the amount of earnings by the mill workers.

As the facts accumulated it became abundantly clear that the prevalence of pellagra was related to the availability of supplies of certain foods but that this in turn was closely influenced by the one-crop type of agriculture with its lack of diversification. Characteristically, therefore, Goldberger and Sydenstricker undertook what amounted to a full-scale economic analysis of tenant-farming in the cotton-producing area of the deep south. They concluded: 'The situation is manifestly one which calls for study with a view of working out practicable solutions of the economic and agricultural problems involved. In such study, however, the needs of health must be held in mind as of controlling importance'.

At the same time as he adopted this macro-sociological approach, however, Goldberger became increasingly aware of the need to study the micro-behaviour of individuals and family-units, if only to account for the apparent exceptions to the general rule which he was formulating. The following passage illustrates how well he appreciated the role of personal factors:

Reference may be made to the group of factors that tend to determine the amount and proportion of family income available for the purchase of food, an example of which is the occurrence of sickness or injury, making an unusual draft on the family income. Related to such factors are the general spirit of the household with respect to thrift (which, when unwisely directed, may be harmful) and the intelligence and ability of the housewife in utilizing the available family income.

More tangible than these, and perhaps of more immediate practical importance in its effect on the household diet, is the difference among households with respect to the availability of food supplies.

Even granting what is not necessarily the case, that financial ability to provide may be assumed to be invariably synonymous with the actual provision of a good diet and that a liberal diet was actually available to the individual, it by no means follows that such diet was in fact consumed. For such assumption would totally ignore the existence of individual likes and dislikes, more or less marked examples of which may be observed at almost any family table.

Further, a great variety of causes may operate to bring about individual peculiarities of taste with respect to food. They may have their origin in the seemingly inherent human prejudice against the new

and untried food or dish; they may date from some disagreeable experience associated with a particular food; they may arise as the result of ill-advised, self-imposed or professionally directed dietary restrictions in the treatment of digestive disturbances, kidney disease, etc.; they may originate as a fad; and in the insane they may arise because of some delusion such as the fear of poisoning, etc.

And, as if all this were not enough, towards the end of his life, Goldberger took another, paradigmatic step. He abandoned the epidemiological method altogether because, as he pointed out, it had confirmed the hypothesis that pellagra was a deficiency-disease but had also reached the limits of its own potential. He therefore turned to the laboratory and the experimental method and set himself two different objectives: (a) to determine the pellagra-preventive action of various foods, and (b) to identify the nature of the specific deficiency involved. He had already disposed of the infection-theory by injecting first Rhesus monkeys and then himself and his wife with biological fluids derived from pellagrins. Having gone on to establish an animal model in canine black-tongue he began by working on the hypothesis of an amino-acid deficiency, possibly tryptophan, then on the unknown pellagra-preventing factor in water-soluble vitamin B which was to be identified in 1937 as nicotinic acid, of which tryptophan is a precursor.

This brief summary of one of the most impressive medical achievements of the century illustrates the role of epidemiology in one of its several spheres of application—the investigation of the causation of disease. Essentially it proceeded by establishing an hypothesis through observation, supporting it by ecological inquiry, tracing the multifactorial genesis of individual cases and then providing experimental confirmation. Not the least remarkable feature of the work is that Goldberger succeeded in combining what Griesinger had called the study of aetiology, i.e. the patterns of the associations of disease, with the study of pathogeny, i.e. the mechanisms of disease. In *sensu strictu* the epidemiologist addresses himself to finding causal factors rather than elucidating their mode of

action. Goldberger did both, and eliminated a major scourge in the process.

This example is now more than 50 years old but, with the possible exception of kuru, it remains the most elegant demonstration of the way in which the epidemiological method can be applied to elucidate the causes of a neuro-psychiatric disorder. Why should this be so? The answer, I would suggest, is twofold. First, Goldberger was an investigator of exceptional ability and very few men of his calibre have concerned themselves with any aspect of mental disorder. Secondly, as a disease entity pellagra might be regarded as having been riper for investigation than the great majority of conditions which are included in the formal category of mental illness. Goldberger himself indicated as much when, towards the end of his life, he was made a financially attractive offer to direct a research unit for the study of dementia praecox. He took his time to consider the proposition, studied the current literature and then declined in a letter which gave his reasons: 'In 5 or more years I could probably find out nothing. Much work will be needed on the physiology of the central nervous system and on many collateral problems before dementia praecox can be understood'. After half a century these words remain still uncomfortably relevant to the contemporary situation.

But the role of epidemiology in psychiatry is far from confined to basic research. It has at least two other major spheres of application. One of these is in the sphere of the workings of health services which, important as they are, chiefly affect the administrative aspects of psychiatry. The other function of the subject, by contrast, concerns all trainee psychiatrists, namely its direct links with clinical psychiatry.

### Clinical epidemiology in psychiatry

#### 1. *The transmission of mental disorder*

This is historically the oldest sphere of epidemiological concern and activity, and extends to the current interest in so-called 'socially shared psychopathology' (Gruenberg, 1957). The induction of schizophreniform states with paranoid features, for example, is a well-recognized clinical phenomenon, described by various authors as 'communicated



specific virus' (Böök, 1961). It is significant that in recent years geneticists have come to speak of the 'transmission' of mental illness (Rosenthal and Kety, 1968), but the contribution of genetics to the clinician concerned with individual cases of mental disorder, as opposed to mental subnormality, still remains exiguous. In Lionel Penrose's words—'When the classical work of Sjögren on amaurotic idiocy is compared with the monumental surveys of Rüdin and his school on psychosis, it is like comparing the movements of a cat with those of a rhinoceros' (Penrose, 1971).

In clinical practice every psychiatrist must, of course, clearly pay close attention to the environment, or milieu, in which morbid ideas can be transmitted and mental illness induced. On a large scale this has been well documented at times of social upheaval and natural disaster, when aberrant conduct and frank mental disorder are often prominent. Fig 2 tells its own story (Glass and Bernucci, 1966). The detailed study of such phenomena, however, is usually limited by chance and opportunity, as in the observations of Rawnsley and Loudon on the inhabitants of Tristan da Cunha whom they

were able to study after a volcanic eruption, comparing their results with data obtained from a survey carried out 25 years before (Rawnsley and Loudon, 1964).

More often the clinical study of environmental factors which bear on the transmission of mental disorder are on a smaller scale, and tend to be focused on the nuclear family. In the sphere of general morbidity the clustering of illness-episodes within families has been well documented. This phenomenon has now been shown to apply to non-infectious disorders, including emotional illness. In a careful study extending over a period of two years, Brown was able to make a continuous assessment of two matched groups of families: one with and the other without a mother suffering from neurotic disability (Shepherd *et al.*, 1966). During the period of observation the neurotic women exhibited significantly more illness, physical as well as psychological, than their controls, and by the same criteria a similar difference was recorded for the husbands and the children of the index patients. The factors contributing to such family interaction are complex, including as they do genetic influence, assortative mating,

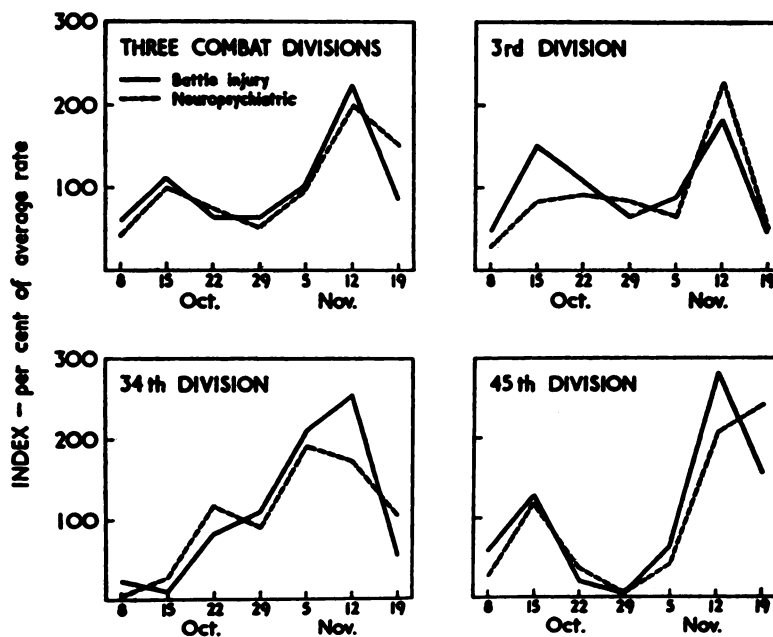


FIG 2.—Relation between trend of battle injury and neuropsychiatric admissions, selected divisions, Fifth U.S. Army (Glass and Bernucci, 1966).

socio-cultural determinants and the intra-familial milieu, and though some relevant work has been carried out much more research is needed to estimate their relative significance.

## 2. *The phenomena of illness*

(a) First among these may be placed what has been called the completion of the spectrum of disease (Morris, 1957). In psychiatry the extension of epidemiological inquiries focused on the extra-mural dimensions of morbidity has radically modified our view of the nature and distribution of mental illness in the population at large. The model is indicated in Fig 3.

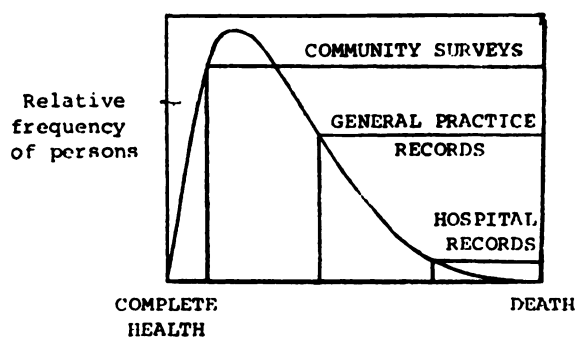


FIG 3.—Coverage of sickness continuum achieved by the major sources of morbidity statistics (Kalton, 1968).

To elaborate on just one example. We now know from epidemiological inquiries that psychiatric illness in the community is composed largely of minor affective disorders (Shepherd, 1977). From a clinical standpoint it is apparent that this large pool of affective illness not only extends the spectrum of the concept of such disorders but also bears pointedly on the aetiology of these illnesses and on the sterility of much work on their classification based on hospital cases. Further, it seems that in the middle-aged groups these disorders are associated with a raised expectation of physical morbidity, including major disease (Eastwood, 1976); that the more chronic forms are also associated with long-term problems of social adjustment (Cooper, 1972); and that new episodes are often precipitated by events in the family and social orbit (Brown and Harris,

1978). These findings are in conformity, both with the theoretical concept of 'illness-proneness' and with much recent work on the significance of life-change. They point to the need for co-ordination between mental health, general medical and social services in the management of patients with a consistently high experience of morbidity.

(b) Next we come to outcome and prognosis. Concerned as they are with the manifold associations of disease, the methods of epidemiological inquiry are central to the study of the natural history of mental disorders, a concept whose bearing on diagnosis and classification has been generally appreciated since the work of Kraepelin. The numerous follow-up studies of the schizophrenias, for example, have for the most part been conducted within the Kraepelinian framework and have tended to incorporate outcome as an axis for diagnostic classification in the absence of a clear aetiology and pathogenesis. Outcome has been defined in several ways, including the length of illness, the recurrence of attacks, the presence or absence of defect states and the chances of acquiring an hereditary disorder. These measures have in turn been related to such clinical features as abruptness of onset, the occurrence of particular symptoms, the pre-morbid personality and the body-build.

More recently, the impact of social factors on the course of schizophrenia has also been demonstrated in a series of epidemiological studies, focusing initially on mental hospital patients (Wing and Brown, 1970) and thence extending to the community through consideration of discharged patients and their families (Brown *et al*, 1962). Research on institutionalism and schizophrenia has been supplemented by studies of discharged patients whose subsequent progress has been related to their type of living-group, their degree of emotional involvement with relatives, their occupational adjustment and the experience of stressful events. It seems clear that the course and outcome of schizophrenic illness are heavily influenced by social factors which have to be taken into account in assessing individual prognosis. These studies are important, not merely in that they render prediction more accurate but because they



point to relatively specific social measures for improving the long-term outcome.

(c) Closely related to outcome studies are two other spheres of enquiry, each of which I can do no more than mention. The first is the actuarial assessment of individual morbid risk, either to calculate illness-expectancy among the relatives of patients with established mental disorder or to assess the risk for the patient himself in conditions where the occurrence of one or more previous attacks is held to influence the probability of future episodes (Strömngren, 1950). The second is nothing less than the whole area of therapeutic evaluation by means of the controlled clinical trial, which is itself essentially no more than an exercise in applied epidemiology (Shepherd, 1975).

(d) And finally—underlying all these endeavours—is the basic issue of the diagnosis and classification of mental disorder. For the epidemiologist, representing as he does what has been called the science of denominators, it becomes imperative to attain diagnostic precision to ensure that he can add or subtract or compare like with like. For the clinician, even though his primary concern be the individual case, this same objective becomes the springboard for his central function, which Sir James Spence has defined as ‘the knowledge of disease as a predictable sequence of events, the understanding of which becomes the basis, the only basis, by which the process of disorder in the living patient can be rationally interpreted’ (Spence, 1954). And just as Molière’s M. Jourdain is unaware of the fact that he is talking prose, so the clinician does not always appreciate that he is talking epidemiology. By way of illustration we may take two examples of the end-product of clinical assessment, the diagnostic formulation: ‘A 19-year-old single student of good pre-morbid personality and a family history of affective illness, suffering from a depressive reaction to work and domestic stresses which should respond to medication and supportive psychotherapy’; and: ‘A 45-year-old unmarried university professor with paranoid personality traits and a history of heavy consumption of alcohol who has developed delusional ideas of grandeur. No evidence of physical disease. Prognosis uncertain’.

Both statements, neither of them unusual of their kind, are impregnated with the epidemiological perspective which, if given due consideration, provides the trainee clinician with perhaps its most important contribution, namely a constant reminder of what he does *not* know about the individual patient under his care. With this awareness he can be both protected from self-deception and, perhaps, prompted to explore the general implications of the particular case, alive to the fact that while every patient is in some measure unique he also exemplifies Sir Aubrey Lewis’s dictum that ‘considered as an isolated unit, the behaviour of any single human being is much like a lost piece of a complete jigsaw puzzle carrying little meaning in itself’. The epidemiological approach does not, of course, embrace all issues of clinical significance. It would not, for example, furnish necessary information about biological mechanisms, therapeutic techniques or the art and ethos of the medical role. All of them depend, however, on a clear-sighted awareness of the logical infra-structure of the clinical method. This, I would maintain, is very close to epidemiology and in no branch of medicine is it needed more than in psychiatry.

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#### Further Reading

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