BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 29 1938

STATES OF DEPRESSION: THEIR CLINICAL AND AETIOLOGICAL DIFFERENTIATION *

BY

AUBREY LEWIS, M.D., F.R.C.P.

Clinical Director and Lecturer on Psychiatry, Maudsley Hospital

Classification and diagnosis have been so derided in psychiatry that the subject of our discussion to-day is almost a shady one. No doubt the shadow under which it lies comes also from the solid difficulties, which are plain when any of the current ways of differentiating between depressions are applied to a series of cases. It is, I think, at all events correct to say that (although a fair amount has been written) no fresh light has been cast on the subject for several years, since it is much easier to show the inadequacy of proposed methods than to substitute for them a useful and valid one. Useful and valid are the two epithets which any classification should deserve. In considering them the opportunities and difficulties can be brought into clearer view.

Valid Classification

The usefulness of a classification will vary according to who uses it. One that serves the clinician well may be of little value to the research worker: it may even make his task harder. The clinician wants classes into which he can put his patient's illness after a reasonably brief period of investigation, and which will assist him to make a prognosis and decide on treatment. So long as the classes do this, it does not matter how illogical, psychologically or pathologically unsound, and expressive of his own idiosyncrasies they may be: they provide him with extra knowledge of the sort he wants, and he does not care whether they represent his own, more or less incommunicable, experience or the fruits of others' study. The man who treats patients only in private practice may find a classification useful which the physician in the mental hospital regards as illusory, and the latter may use one which the consulting-room psychotherapist detests or cannot understand: both these classifications may be useless to the general practitioner. If all three physicians had the same clinical material and problems they would no doubt come to use the same classification; but at present they do not, although they may use the same words for their classes: to realize this one has only to compare the letters sent by each of them when referring depressed patients to an out-patient clinic. Because of the peculiar phenomena of mental disorder, so much harder to describe in agreed conventional terms than those of other illnesses,

it is customary for clinicians to use their words, and their classes, with an individual twist. This is what distinguishes them from those of the research worker. He wants his classes, and his words, to have some fixity, so that he can generalize and summarize and communicate his observations: he cannot work in circumstances where the case that he calls an endogenous melancholia another man may call a reactive depression, and a third man call a paranoid schizophrenic. He may be satisfied if he can delimit a class of depressions in which the only distinguishing feature common to all members of the class is some chemical anomaly, even though for the clinician this turns out to be a woefully heterogeneous group. Many quarrels about the justness of classifications in psychiatry are usually due to these differing needs of the clinician and the research worker. In an ideal state of knowledge the schism would end, but that is still a distant time.

It might seem that validity is here merely a synonym for usefulness. But classifications may be useful for the wrong ends: they may be used to separate off cases which are regarded—wrongly—as hopeless, or as needing a particular type of treatment; the clinician may never come to see how vicious are the uses to which he has been, contentedly, putting his classification. The research worker, on his side, may have delimited classes of which the characteristic is irrelevant to his problem, much as though he were to divide depressives into those with and those without naevi, or those whose parents had hernia and those who had not. A valid classification is one which is not only useful, but useful for sound medical or scientific ends. It is necessary to see how far the available classifications are valid in this sense.

The first task of classification is obviously to recognize the depression itself. This is too often taken to be a diagnostic act. It should be concerned with nothing further than description of the emotional state. Any person who is unhappy, and ill with his unhappiness, may properly be said to be in a state of depression. To lay down other criteria for a depression is to raise fundamental problems. For convenience we may restrict the term to those states of depression in which we cannot discover any other significant illness—for example, schizophrenia, cerebral tumour, arteriosclerosis. But the elimination of these is the second task. It is common ground that depression may be the conspicuous or the only clinical evidence of almost any mental illness at some stage: everyone will

* Read in opening a discussion in the Section of Neurology and Psychological Medicine at the Annual Meeting of the British Medical Association, Plymouth, 1938.

aim at spotting the G.P.I., say, or cerebral tumour, or schizophrenia which hides behind a depressive front. What is more, the psychiatrist cannot dismiss this depressive front as a false one, a screen, but has to consider how far it stands for an independent contribution to the total illness. It is at this point that the clinician's private notion of depression creeps in, bringing confusion. If he regards "true" depression as an endogenous illness, of good prognosis, and itself recognizable, he will be interested to see whether this patient's depression conforms to his notion of "true" depression, in which case, if there is also another disorder present, such as a schizophrenic or an obsessional one, he says, "We have here a mixed picture": or he may regard this depression as the normal response to the abnormal situation created by the concomitant, or screened, illness, and may dismiss it as secondary and rather irrelevant. In short, the moment description is deserted, at the second stage of the classifying process, influences get to work which are often only in part consciously recognized as such by the clinician, though they may greatly modify his decisions.

Hereditary and Environmental Factors

The most popular classification is, on the surface, an aetiological one. It says that there are depressions due to heredity (autonomous, autogenous, endogenous, manic-depressive, cyclothymic, vital, constitutional, are among the words employed) and others due to the environment (psychogenic, exogenous, extraneous, reactive, psychoneurotic). But this is purely theoretical. We have no means of detecting such causes satisfactorily, except in a minority of cases. Moreover, as theory it is bad. It derives from the days when Nature and nurture could be contrasted in an epigram. It assumes that heredity commonly operates with that high probability of manifestation which we see in Huntington's chorea or the height of sweet peas: and that environment can work on an almost illimitably plastic and responsive human organism. As biology has moved beyond these excessively simple views, and recognizes that hereditary and environmental factors commonly interact, it is reactionary to uphold them in the case of a depressive illness, especially when it is so extremely difficult to determine the relative importance of hereditary and environmental factors in any such case. It is probably true that in some depressions the hereditary factor vastly outweighs the environmental, and that in others the reverse is the case, but to detect such cases we have only dubious means—study of the parentage and sibship, observation of the bodily habit, assessment of the relation between the outbreak of the illness and the external factors which might have conducted to it. In the present state of knowledge these are dubious means when applied to the individual case, though they serve well enough for the analysis of a collection of cases, statistically. The number of cases in which critical and experienced psychiatrists with different theoretical standpoints would be found to agree that the hereditary factors were almost certainly responsible for the attack (or, in the alternative instance, that environmental ones were) is, I believe, so small that the subjectiveness of many of our judgments on this matter can scarcely be gainsaid. There are some cases in which a recent distress seems to account for the depression, which is then properly called a reactive one, but since profound melancholia or mania may likewise ensue upon a sorrow, reactivity does not mean only psychogenesis. The more thorough the analysis that can be made of the life of the patient, and of his responses to circumstances, the stronger is one's inclination to attribute his morbid behaviour mostly to post-natal influences;

genetic studies have the opposite effect. There is no reliable evidence as to the heredity of so-called psychogenic depression; and as for the other varieties, what has been reported does not justify distinctions upon a hereditary basis.

Differentiation by Study of Symptoms

A differentiation that can be made by study of the symptoms is of value to the practising physician. When he sees a patient who has fits it is more convenient for him to run over in his mind the differential points given in the textbook tables than to inquire at length into the previous personality, make an encephalogram, etc. At any rate he tries the short method first, preparatory to further search. If he could similarly separate forms of depression he would not be put off by any uncertainty about causes. I have taken a very recent table of the sort: the author says that the differences between neurotic and manic-depressive depression are usually clearly marked: they lie in the constancy of the depression during the attack; the patient's ability to be amused by a joke, to weep, or to appreciate beauty; his interest in himself and his surroundings, his self-reproach, his good health in the period before or between attacks, and his admission that he is ill. Also it is said that in manic-depressive depression "the patient gets well obviously spontaneously. He has been unresponsive to all therapeutic efforts, and the doctor is never given the impression that he has done anything." Nothing could better illustrate what I said earlier about the personal and partly incommunicable value of the classification which a particular clinician may find useful. The psychiatrist quoted works very satisfactorily with a scheme which to me is useless: when I try to apply it it fails, because the same cases will fall on one count into the left-hand side of the table and on another count into the right-hand side. It is true that when first seen in the out-patient department cases often seem to me to fall readily into one or the other category, but when they are gone into more fully in the course of treatment this facility of classification turns out to have been spurious. And I take it that this is partly because my notions of spontaneous or aided recovery, of variability and responsiveness in the depression, and so forth, are not those of the author of the table. Also it is because of a disagreement about facts: patients with severe self-reproachful depression sometimes weep, sometimes even laugh, sometimes worry about their relatives, are mildly depressed and anxious between attacks, or admit that they are ill; patients with chronic reactive depression may be self-reproachful, incapable of appreciating beauty, and never weep. Moreover, in a series of cases I have lately looked through for the purpose, illnesses that fulfil all these clinical requirements of a reactive depression have occurred preceding an acute mania and a severe involutional melancholia, either as an initial stage or as a previous attack (in my earlier published series the same sequence can be found): some of them have been treated as such psychotherapeutically, and with benefit, in previous attacks. Even this shows only how useless the scheme is to me: not that it is generally useless. Actually it is a question of how many patients fit comfortably into either group, so characterized. As is fairly plain in the series I reported, I find that few do; Curran reaches the same conclusion. I think these groups are extreme types rather than clinical realities: a few others, however, find good reason to hold the contrary view. Clouston, who believed in the importance of a distinction (between "melancholy" and "melancholia"), put the matter quite simply in 1904: "Typical cases exhibiting these two conditions are totally different and distinguishable, and the only excuses for confounding them are that they shade off

into each other, that we have no absolutely definite scientific test to distinguish them, that they are both in many cases the outcome of the same temperament and diathesis, and that they both have something of the same nature, both psychologically and physiologically." These are good excuses. Probably there are genuine differences between cases of mainly hereditary causation and those in which environmental causes predominate, possibly also between cases with different kinds of hereditary causation, but the clinical differences given in such tables as I have mentioned do not at present serve to distinguish them. And it is well to remember, as Newman has recently concluded from his studies, that in many ways what heredity can do environment can also do.

There is another such table which includes bodily features—anorexia, constipation, loss of weight. Muncie has stressed the sleep disturbance. Various writers have thought that metabolic variations, especially in respect of nitrogen and carbohydrate metabolism, occur in manic-depressive depression and not in reactive depression. Such claims have not been substantiated as yet. When classes can be separated which are marked by significant somatic differences, it will have the advantage that trained observers will presumably be able to agree as to the presence or absence of these somatic characteristics in any patient.

In recent contributions to the subject emphasis is variously laid upon periodicity, concomitant depersonalization or anxiety and tension, sleep, personality, heredity, psychopathology, and somatic pathology (Rouart, Muncie, Titley, Schnitzenberger, Brockhausen, Montassut, Anthonisen, Schilder, Armenise, Lorand, Baruk and Gevaudan, Georgi, etc.). But periodicity would be more valuable if it could be demonstrated to be a frequent characteristic, whereas actually it is rare; recurrence is of course a different thing, and may be no more indicative of an intrinsic rhythm, a biological periodicity, than is a series of colds in the head; it may indicate recoverability only. As for the anxiety or tension depressions, they cannot be made to form a homogeneous group, for they have only the phenomena of the anxiety attack in common, all the rest being expressible in terms of mild and severe, or proportions of fear and misery. Personality and heredity have not so much cast light on involutional melancholia as left it in a penumbra. Twin studies should, of course, elucidate the whole problem, but until Dr. Slater's material is published nothing is available on this aspect of the classification of depressive states. Psychopathology is as variable as ever in its voices, and no somatic changes are of sufficient definiteness and constancy to be the basis or the buttress of a differentiation.

Distinction between Reactive and Manic-depressive Varieties

Apart from some English writers, it is difficult in the literature of the last five or even ten years to find support for any sharp distinction between reactive and manic-depressive varieties of depression. But a distinction of this sort is often implied in what is written, especially (if it may be said without offence) in the more elementary presentations, in which an almost entirely hereditary psychosis is kept remote from the "neurasthenia" of year-long neurotics and the mourning and unhappiness of those who have lost something of immense emotional value to them. Moreover, in many writings the intelligibility of the occurrence is taken as a criterion: if the physician can enter into the patient's feelings and understand the illness as the natural outcome of situations in which the patient has been, then he calls it psychogenic or reactive; if he

cannot, then he calls it autonomous (thus Adolf Meyer talks of a "true simple melancholia, or 'unjustified depression'"). No doubt this too is a personally valuable way of reviewing the illness, but it has the disadvantages already mentioned as attaching to such subjective judgments. For psycho-analysts it is out of the question, because of the universally explanatory value of their views and method.

There could be no more convincing evidence of the way classifications epitomize theory, and can be serviceable for very limited groups while worthless to others, than the psycho-analytical classification put forward by Glover. Psycho-analytical work in the field of depression during the last few years (for example, Schilder, Klein) has shed as little light on the topic of this discussion as have published studies in heredity, psychology, or somatic pathology.

It is very probable that all the tables and classifications in terms of symptoms are nothing more than attempts to distinguish between acute and chronic, mild and severe: and where two categories only are presented, the one—manic-depressive—gives the characteristics of acute severe depression, the other of chronic mild depression. I am using acute and chronic as temporal words, and mild and severe as indicating the degree of the overt mental disturbance. This, if recognized for what it is, is a useful division, provided the vulgar error is avoided of thinking that every manic-depressive should get well inevitably and spontaneously, and that every case of reactive depression calls for intensive psychotherapy which, if well given, should bring recovery. It also rather fails to provide for the acute mild and the severe chronic cases, which are numerous.

The danger of these classifications, for the clinician, lies in two directions. First there is the assumption, just alluded to, that when a patient's illness seems to fit into the manic-depressive category there is nothing to be done but to fold one's arms in resignation, or, at most, to employ "reassurance and safeguarding" until he gets better of his own accord; and, alternatively, that if it falls into the other group, psychotherapy, and nothing but psychotherapy, will restore him to active life. Treatment should be based on a knowledge of the patient's constitutional qualities and the stresses he has met, not on a schematic and rigid plan, a short cut to the wrong shop. Secondly, it is dangerous because it says, as one of these tables does, that in reactive depression suicide is "sometimes talked but not attempted." Now and again there appears in the account of some inquest the evidence of the doctor who had concluded that it was "only a neurotic depression," and had his views confirmed by a psychiatrist, who found no sign of a "genuine psychosis." Of course, everyone makes mistakes in assessing the likelihood of suicide, and it is quite possible that in these cases the suicide would have occurred anyhow, since one cannot send into a mental hospital every doubtful case of suicidal risk. And, again, it may be conceded that in the hands of some clinicians this method of assessing the risk of suicide works very well. But it is surely bad when that immensely important question of suicide can be disposed of in the practitioner's mind by reference to a classification that creaks at the joints, and is applied differently by different people. Classifications cannot take the place of experience, or of knowledge of one's patient, of the depth of his despair, and the strength of his impulses.

Involutional Depression

These are the two varieties of depression chiefly dwelt upon in textbooks and articles. Attention is also paid to

involuntional depression. Thus, one authority speaks of five varieties: constitutional depression, prolonged neurasthenic malaise, true simple melancholia, depressive delusion with intense fear, and catatonic melancholia (but the last two are, of course, usually involuntional, and the first covers Reiss's group of 1910, now swallowed up in the reactive group). It is true that some features common in involuntional melancholia are rare in other forms of depression, but since these probably depend on the patient's age and on degenerative cerebral disease (often of the vessels), or on schizophrenic admixture, it does not seem necessary for classification to stress them as such, but rather to use the patient's age as the sole reason for calling the depression "involuntional," and to seek for further data which will illuminate the prognosis and treatment.

The necessity for making sure that a depression is not due to G.P.I., pernicious anaemia, or other organic disease is present to everyone's mind. But it is less often remembered that the discovery of hysterical, obsessional, or other psychopathic trends in the patient may be important too. A very depressed young woman may be troubled by the thought that she has injured her child through leaving pins about which he could swallow; the obsessional component in this needs examination. A depression in a patient aged 50 may be accompanied by many hysterical symptoms; if the patient has most of his life shown nothing hysterical in his behaviour the possibility of a cerebral arteriosclerosis must then be reckoned with. Or a depression may be found to have developed in a person of schizoid personality, and to be ushering in a schizophrenia. Depression is a very ready psychic response; hence it cannot be evaluated and pigeon-holed without a survey of the patient's life. It was not for lack of instances to support their view that the psychiatrists of the last century believed that most mental diseases began with a stage of depression.

Conclusion

The classification, or avoidance of classification, which I would propose is: first, to determine whether the depression is severe or mild—melancholia or neurasthenia, descriptively speaking; and, of course, there are many grades. Next, does it depend on physical disease, and, if so, how completely? What happened in any previous attacks? On what discoverable influences does it depend: age; constitutional morbid trends; lifelong environmental factors, recent more acutely disturbing ones? What, in sum, is the presumptive balance of environmental forces responsible for the illness as against inherited ones; and what is the balance between environmental influences that may be modified for the better and those that are irremediable? Has the morbid condition been going on long enough to have, so to speak, established an autonomy, set up bodily and mental habits that are inveterate? Have the patient's character and surroundings worked to his advantage or disadvantage during the illness? These are points to weigh rather than points on which to classify; matters of clinical judgment, not solely of observation. A classification can, however, be built upon them. It is because we have no sure means of distinguishing exactly the numerous causes in each case, and their effects, that we must deny ourselves the ease of a simple classification: I think it is a deceptive ease and a deceptive simplicity. No doubt increasing knowledge will bring an improved, eventually even a stable, classification based on aetiology, and pointing, it may be hoped, to treatment: whether it comes by way of genetics, psychology, or somatic pathology, it will be welcome so long as it is useful and valid.

THE CLINICAL SIGNIFICANCE AND ESTIMATION OF BLOOD VITAMIN B₁

BY

EIRWYN N. ROWLANDS, M.D., B.Sc.

Assistant Director, Department of Clinical Investigations and Research, Royal Infirmary and University of Manchester

AND

**JOHN F. WILKINSON, M.Sc., Ph.D., M.D.,
F.R.C.P., F.I.C.**

Honorary Physician and Director, Department of Clinical Investigations and Research, Royal Infirmary and University of Manchester

Vitamin B₁ has been used therapeutically in many diseases, but only in beriberi is there overwhelming evidence of its importance. Therapeutic successes, however, have been claimed in nearly all forms of neuritis; thus, Russell (1936) and others have reported dramatic improvement in patients with subacute combined degeneration of the spinal cord following parenteral administration of vitamin B₁ concentrates. We, however, have failed to obtain such striking responses in a series of patients suffering from the disease in varying degrees of severity, although partial relief was noted in a few; a similar series of patients treated in the usual way with liver extracts or preparations of hog's stomach showed much more satisfactory improvement.

Writers on nutrition differ noticeably in their views of the incidence of vitamin B₁ deficiency; thus, whereas Hutchison and Mottram (1936) state that "it is in the perversity of things that food faddists have raised more to-do about vitamin B₁, which few, if any of us, lack," Vorhaus (1937) and McCarrison (1936) have remarked on the relative frequency of this deficiency, McCarrison writing that "the insufficient ingestion of vitamin B₁ is a common food fault."

Our disappointing results in subacute combined degeneration of the cord, the difficulty of assessing the value of vitamin B₁ in this disease, and the many statements that these patients are deficient in vitamin B₁ led us to investigate the possibility of estimating satisfactorily the state of vitamin B₁ nutrition in a series of normal subjects and in patients. The vitamin B₁ content of a diet is not easily estimated from a list of its constituents, and Williams (1938) considers that it is impossible to do so from the available data with an error of less than 50 per cent. Biological assay and the chemical methods so far employed are not sensitive enough to measure the minute quantities present in blood. Roscoe (1936) attempted to estimate the urinary excretion of the vitamin, using for a test the cure of neuritis in rats, but concluded that the method was of little value, while Harris and Leong (1936) have used the rat bradycardia technique.

Test for Vitamin B₁ in Blood

It appeared possible that a satisfactory test for vitamin B₁ in blood might be based upon Schopfer's discovery (1935) that the growth of the mould *Phycomyces blakesleeanus* was proportional within certain limits to the amount of vitamin B₁ present in the medium. By plotting the weight of mycelium obtained against the quantity of vitamin B₁ added, a smooth curve could be produced, and Schopfer used this as a quantitative test for vitamin B₁ in foodstuffs and animal tissues. We have employed Schopfer's technique and applied it to the