

SOME REFLECTIONS ON THE NATURE OF AFFECTIVE DISORDERS,
ARISING FROM THE RESULTS OF PREFRONTAL LEUCOTOMY.*

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FOR the use of the term " affective disorder " there is good literary warrant. Shakespeare, writing in the last decade of the sixteenth century, or just before it, uses the word thus :

" Necessity will make us all forsworn
Three thousand times within this three years' space ;
For every man with his affects is born,
Not by might mastered, but by special grace " (92).

This use is evidently taken from the Latin word " affectus," and is here used in the sense of " disposition." But Spenser, who, there is evidence to suggest, owed neither his use nor his coinage of this same word to Shakespeare, has given it a more specifically emotional connotation. In *Astrophel*, a collection of elegies on Sir Philip Sydney published in 1595, some of which are by Spenser and some by friends and imitators, there appear the words, attributed to Spenser himself :

" But thou (O blessed soule) doest haply not respect
These teares we shead, though full of loving pure affect " (94).

In Book VI of the *Faerie Queene*, published in 1599, the Lady Briana's emotional reactions are described when she learns that the lewd and wicked Crudor, to whom she is devoted, has been magnanimously spared by Sir Calidore, who has revoked his original intention to put Crudor to death :

" Whereof she now more glad than sorry earst,
All overcome with infinite affect
For his exceeding courtesie, that pearst
Her stubborn hart with inward deepe effect,
Before his feet herself she did project . . . " (95).

And Robert Greene, in his last play, " The Scottish Historie of James the Fourth," published in 1598, has borrowed the word :

" My gracious father, gouerne your affects " (46).

After the 1590's use of the word seems to have been abandoned until it was revived in the pursuit of psychiatry (101). Its lineage is thus respectable, its meaning is clear, its use is warranted by distinguished precedent, and in these respects it differs from many psychiatric terms. For our present purposes, however, it is somewhat too wide ; and it may be possible, by subdividing the affective disorders, to do something in the way of consolidating such knowledge

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as we have of the effects of prefrontal leucotomy on these conditions. It is to these considerations that we now turn.

The occurrence of mania and melancholia in the same patient at different times had long been recognized before Kahlbaum formulated the two as different phases of the same disease process, under the term "cyclothymia." Kraepelin, in 1896, extended this concept, under the term "manic-depressive psychosis," which he regarded as a disease entity, with a course and an underlying pathology of its own.

There has been prolonged discussion of the matter since. Dana (21) preferred to recognize three groups of depressive illness: (a) involuntional melancholia, a condition occurring in chronic worriers at the climacteric, together with pre-involuntional conditions, akin to it in symptoms but occurring earlier in life, all characterized by agitation and worry; (b) simple recurrent melancholic states, which he said seemed "quite different," characterized by profound depression, apathy with loss of interest and psycho-motor sluggishness, which he considered apart from manic-depressive psychosis, though like it; and (c) simple recurrent melancholic states associated with intervening manic bouts, which he considered true manic-depressive psychosis.

Meyer (68) urged abandonment of the term "melancholia" in favour of the more noncommittal "depression," later to be amplified so as to denote the type of depression in the light of aetiology, symptom-complex and course of illness. Always in favour of concepts in terms of "more or less" rather than "either/or," he shifted the emphasis away from considerations of disease entities in themselves, and towards illness in terms of reaction and the interplay between the patient and his environment (67). His great influence and the good sense implicit in such a view have led to the persistence of this trend since.

But at once there arise questions which have never been fully answered. Allowing that all illnesses are coloured by the impact of the environment, and by the way in which the patient reacts, are there in fact affective disorders as disease entities *per se*? If so, can we separate these entities from illnesses merely reactive in type? If so, are the differences differences in kind or only of degree?

Schools of thought have developed as different answers to these questions have been framed. Although Kraepelin was driven to extend his original concept more and more inclusively, the German school, with its tendency to formalism and categorization, has been the main exponent of separation of "endogenous" and "reactive" conditions. Thus Muncie (76) says: ". . . the impression is gained that modern German psychiatric thought has not abandoned the disease entity, an impersonal something which attacks its victims, diagnosed by its pathognomonic signs, and places little value for diagnosis or treatment on attempts to reconstruct the story as a dynamic individual biography gone wrong. The disease process is either exogenic or endogenic in origin." And indeed, Bleuler (5), while admitting the occurrence of mixed psychotic pictures which transgress the bounds of formal categories says, "I follow, as far as possible, Kraepelin's classification, which is now pretty well understood in the whole world . . ." and goes on to say,

“ recently an attempt was made to place the classification of the psychoses on an entirely different basis by emphasizing the various factors participating in the causation, development, and course. I made the effort to initiate these viewpoints also here but had to desist from it.” In France, the United States and in this country more elastic concepts have tended to prevail, but it is still customary, however fallacious, to speak and to think in terms of “ endogenous ” or “ reactive ” depression, and, raising the same problem in a different aspect, in terms of “ psychosis ” or “ neurosis.”

Thus, Mapother (65), in 1926, having declared that Kraepelin had “ come to the conclusion that it is simplest to include all cases showing the affective excesses and also the syntonics types of intellectual and conative disorder ” under the heading manic-depressive psychosis, startled his hearers into acrimonious indignation by refusing to admit any clinical distinction between a neurosis and a psychosis. “ The distinction between neuroses and psychoses has grown out of practical difficulties particularly as regards certification and asylum treatment.” He could “ find no other basis for the distinction ; neither insight, nor co-operation in treatment, nor susceptibility to psychotherapy will serve.” As regards the notion that there were “ neurotic ” conditions which were purely psychogenic, and “ psychotic ” conditions dependent on structural change, he argued that “ to assume that an enduring physical basis for habitually abnormal behaviour is probably non-existent because at present its exact nature is not demonstrable, seems to me a flat defiance of all relevant experience in medicine.” His view, therefore, seemed to be that any “ attack ” of depression from whatever cause, whether seemingly reactive or seemingly endogenous, is mediated by essentially the same means. “ The essence of an attack is the clinical fact that emotions for the time have lost enduring relation to current experience, and whatever their origin and intensity they have achieved a sort of autonomy.” Much the same view has been expressed elsewhere by Symonds (98).

His hearers were able to tolerate this with varying degrees of equanimity. Buzzard (10) objected to a view which would not distinguish between manic-depressive psychosis and anxiety states. He regarded the recovery of the manic-depressive as more or less assured (if uncertain as to time) in the presence of adequate custodial care ; but he thought that anxiety states, for recovery, needed and were susceptible to direct attack, the prognosis depending on the ease with which the anxiety could be disclosed and removed. The proper differentiation between psychoses and neuroses was prognostically and therapeutically important, as well as for academic accuracy. Ross (86), more indignantly, said that of a group of 66 patients diagnosed as manic-depressive, 12 had since been certified, whereas of 355 psychoneurotic patients admitted over the same period only 3 had since been certified, and two of those had been wrongly categorized against his better judgment ; this alone made the distinction prognostically and therapeutically important. But further, between neurotic and psychotic depression there were differences in kind : remorse was not a feature of psycho-neurosis but was common in psychotic depression : the psychotic blamed himself, the neurotic blamed others. The pre-morbid personalities were different : for example, the manic-depressive

often overworked, the neurotic said that he did, but did not : and there was a difference in reaction to environment in that the psycho-neurotic was capable of enormous improvement if reorientated, whereas psycho-therapy could achieve little with the manic-depressive.

Gillespie (41) between acid parentheses stressed the differences in heredity between manic-depressive and psycho-neurotically depressed patients, the differences in personality and body-build, that the accompanying physical disturbances differed in kind as well as in quantity, and that the psycho-neurotic varied topically according to stimuli, whereas the manic-depressive did not.

In 1930 there was a second debate, less of a foray, in which Buzzard, seemingly unpersuaded by Mapother, put forward certain criteria for distinguishing between psychotic and neurotic depression. He stressed the type of depression, its diffuseness colouring the whole outlook, though often centred on some event inadequate to justify it, its continuity, its independence of environment, its phasic morning-evening variation, its association with detachment from reality, loss of interest, loss of affection and of the power to grieve, with an apparent memory defect really due to inattentiveness leading to lack of concentration and indecision, and with a positive family history in which suicide and alcoholism were especially frequent. He contrasted this with neurotic conditions, in which responsibility for the trouble was thrown on to other people, in which the insomnia was more difficult to overcome, in which there was preoccupation with the heart and bowels as opposed to concern over the brain, in which the possibility of recovery was acknowledged and not rejected, in which distraction from morbid thoughts was easier, and in which the characteristic psychotic-depressive physical disturbances (dull eyes, lack-lustre hair, sallow and pigmented complexion, anorexia, constipation, furred tongue, failure of growth of the nails and lassitude) were absent (11).

Riddoch (84) stressed that the depressive attacks of the manic-depressive were often externally precipitated, and that the presenting complaint might be anything other than depression. But the depression was there, and specially characterized by its continuity, so that, although it might "lift" a little, it never disappeared except in convalescence. To the diagnostic criteria mentioned by others he added the possible occurrence of hallucinations and a special emphasis on the psycho-motor sluggishness (which Dana had also stressed).

Crichton Miller (17) considered the basic feature of the manic-depressive condition (which he preferred to call cyclothymia) to be a variability of affective response independent of external stimulus. Cyclothymic variation was an integrated one, in two contrasted forms (manic and depressive) and endogenously determined, comparable with the swinging of a pendulum; neurotic variation was a disintegrated one, depending on external stimuli and their associations, comparable with the motion of a boat with insufficient keel. Since no psychological theory explained cyclothymia and no psychological treatment influenced it, an explanation must be looked for outside psychological medicine. Its phasic nature suggested a physiological solution :

the similarity between the euphoria of alcoholic intoxication and the exaltation of the manic phase suggested a chemical action on the thalamus ; the similarity between the depressive phase and depressive states due to chronic intestinal absorption suggested an endogenous chemical factor ; the frequency of abnormal sex lives in cyclothymics, and the frequency of cyclothymic variation in relation to menstruation suggested a hormonal factor. Cyclothymia, unlike neurotic states, was a metabolic disease.

Boyle (6), thinking also in metabolic terms, urged that the frequency of thyroid disturbance in manic-depressive psychosis was beyond coincidence, and stressed the suggestiveness of what might be expected in the way of mood disturbance in hyper- and hypo-thyroidism, together with the similarity of age of incidence, and the higher incidence in women of both Graves' disease and manic-depressive psychosis.

Yellowlees (107) considered the difference between manic-depressive and neurotic depression essentially one of kind. He claimed that the cardinal feature of the neurasthenic was excessive fatigability, and that the neurotic was a person of active emotional reactions who bewailed the limitations imposed upon him by the illness, whereas the psychotic depressive was the reverse. Finally, somewhat strangely, he invoked the presence of insight in the neuroses and its absence in the psychoses as "a touchstone which he had never known to fail."

Reynell (83), on the other hand, claimed that manic-depressives might well have the fatigability of neurasthenics, and regarded the difference only as one of degree, with preponderant occurrence of mixed types.

Strauss (96) insisted on the inclusion of diagnostic criteria of physique and character (on Kretschmerian lines). He regarded it as "unthinkable" that a person of schizoid make-up could develop a typical attack of manic-depressive psychosis, and depression in such a subject should arouse suspicions of catatonic schizophrenia, or of a mixed psychosis with accordingly different prognosis. Viewed in this light, manic-depressive psychosis was a much rarer condition than was commonly supposed.

These views were, of course, clinical impressions. In the meantime Gillespie, stimulated no doubt by the debate of 1926, had sought facts in his own support. In his "Clinical Differentiation of Types of Depression" (42) he set out conclusions drawn from immediate scrutiny of case material. From 25 cases studied with detailed regard to the heredity, life history, precipitating factors, symptom-complex of the illness and its course, he formed three groups of depressive cases.

Group I (14 cases).

Distinguished by its affective variability, especially in response to ascertainable factors, whether these last were external to the patient or were topics of preoccupation. In addition to depression there might be anxiety, but the depression was "as a rule" the leading feature and indicated something more than, and not essential to, anxiety states. The chief topic of preoccupation was almost always the patient's health, and usually the depression (with or without anxiety) itself. The preoccupations led to impaired attention and

concentration, but not to retardation. And there was usually a reduction of motor activity, though of a selective kind in which the patient's wishes could be discerned.

The depression in this group was causally related to conscious factors, though such relationship was not fully, if at all, understood by the patient. Thus, there was insight into the abnormal nature of the affect, but not into its cause.

Group II (7 cases).

A group of autonomous depressions in whom the (admittedly considerable) affective variation was spontaneous and independent of ascertainable inter-current stimuli. Remorse and apprehension were frequently but not invariably added, but there was no tendency to blame the environment (which had been found in 7 out of 14 of Group I). As regards topics of preoccupation, self-accusatory trends were common (almost absent in Group I) and ideas of unworthiness more frequently expressed, but both were in fact found in each group. Complaints as to cerebration were more complex in this group and did not appear directly related to the topics of preoccupation, thus differing from Group I. This was in line with the "impression" that the autonomous illness was more extraneous and less closely identified with the patient's personality. The insight in this group was, therefore, to that extent better.

Physical signs and symptoms were not helpful in differentiation. Precipitating causes and suicides were found in both groups. But a family history of psychoses, specially depressive, was more common in the second group, and the general personality traits differed from the predominantly quiet, shy, sensitive, timid, worrying types of Group I.

Group III (4 cases).

This small group was distinguished chiefly by hypochondriacal preoccupation overshadowing (but co-existent with) the depression: by the lack of insight both into the affective disorder and the hypochondriasis: by the number of accompanying symptoms, and by the actual rejection of explanation and re-assurance. In personality they were much closer to Group I than to Group II, and the form of illness had an involuntal stamp.

Cases of the first group were the only ones accessible to psychotherapy in any noteworthy degree, and they showed the shortest illnesses and the highest degree of recovery.

Gillespie concluded that no one sign could serve as a diagnostic, prognostic or therapeutic indication, but "of all the single criteria employed, it is probable that reactivity in the sense of this paper is the one of greatest practical value." The number of cases was surely far too small, but that he still felt confident of there being sufficient of a trend to allow of distinction between psychotic and neurotic depression is shown by a further paper. In this, a contribution intended to illumine an obscure subject for the comparatively uninitiated rather than for the expert clinician, he set down criteria for the differential diagnosis more or less in the light of what he had found from study of the 25 cases (43).

The next stage in the controversy was marked by the appearance of three papers by Lewis, which remain the most scholarly and authoritative productions on the subject in English. They annihilated that little hope of orderliness in a confusing subject which Gillespie had held out. The first (60) was a historical survey of melancholia setting the matter in due perspective. The second was a clinical survey of depressive states derived from a minutely detailed scrutiny of 61 cases. The third was a prognostic study on the same material (62). The outcome of this research must have been disconcerting to the separative school, for not only were the clinical impressions propounded by them in the debates of 1926 and 1930 not borne out by examination of actual case-material, but no separative criteria emerged at all. Lewis concluded that it was impossible to place the majority of cases in either group, and that "the term reactive depression and the grouping it denotes" would be better done away with. The prognostic study which followed was equally ideoclastic: no unequivocal prognostic signs emerged at all. A certain trend towards uniformity in the cases who died was spoiled by their being too few for statistical significance. In the other cases, while certain features seemed on the whole favourable or unfavourable, there was no constancy, so that cases with favourable outcome not infrequently showed unfavourable features, and vice versa. Nor did the remissions become shorter as time went on (as had been held by the German school), and though there was some trend towards lengthening of the attacks themselves, this was irregular. It had been implied in the debates that complete recovery was the rule, but complete recovery—even including those cases which had a second attack, again to be followed by complete recovery—occurred in only 18 of the 61 cases. And heredity had no special significance. Lewis, who describes himself as "chagrined" at the somewhat negative results of this laborious and painstaking enquiry, concluded, "Short cuts and clear sign-posts do not exist," and that manic-depressive psychosis is "a provisional group of heterogeneous disorders."

It remained for Curran, in a paper pregnant with sarcasm (18), to apply Gillespie's differential criteria. He found the criteria ambiguous and the application extremely difficult, but with the best attempt on a series of 25 depressive patients he found, not without gusto, an almost incredible variety of combinations of "neurotic" and "psychotic" features occurring in each case. No differentiation on such a basis could be made.

It seemed that the wheels of Juggernaut had passed over the separative school. But in 1940, Rogerson (a pupil of Gillespie and a successor to Ross, just as Lewis was a successor to Mapother, in whose school Curran also served) revived the argument (85). He reasserted the prognostic and therapeutic desirability of distinction between neurosis and psychosis, and maintained that it had clinical validity, quoting three illustrative cases. "The only method of arriving at the diagnosis is to study the history and day-to-day behaviour of the patient with minute care. It may then be possible to decide whether or not the mood change observed is dependent upon the preoccupations of the patient, themselves related in a proper manner on the one hand to external reality, and on the other to his instinctual strivings." This is the same as Gillespie's concept of reactivity. He quoted Ross (87) that out of 1,043

patients with a diagnosis of neurosis followed over three to fifteen years, less than 5 per cent. developed psychotic illness; that is to say, their pattern of reaction remained essentially the same, which, if the difference between neurosis and psychosis were merely one of degree, is not to be expected.

It will be noted that both Rogerson and Ross seem to have been quite confident not only that there is some essential difference between psychosis and neurosis, but that they could recognize this difference when they saw it. If there are no valid criteria of differentiation Ross's figures are meaningless.

Curran and Mallinson, in an analysis of 99 depressive states occurring in sailors in the second world war, were again unable to find any division between endogenous and reactive depressions. They did, however, find it possible to make some distinction between affective and hysterical disorders, although the latter involved affective components; and they regarded this distinction as of some therapeutic and prognostic importance (19).

Tredgold (100) found similarly with soldiers that the differences were of degree rather than kind, that some passed from what might be called psychotic depression to "neurotic" depression and vice versa, and that no sharp classification could be achieved.

Reviewing the matter at this point, one sees clearly what is the aim of the separative school, however impossible it may be of achievement. The standpoint taken by its opponents is not so clear. Mapother was certainly liable to the construction that all the affective disorders arose on an anatomical and physiological basis which in all instances was essentially the same. This view is rather difficult to accept.

Whitehorn, on the other hand, though not approving the separation in any clear-cut form of endogenous from reactive depressions, views the matter in terms of personality rather than in terms of anatomy, physiology and pathology. It is his view that a psychiatrist who decides whether a depressive condition can or cannot be legitimately considered due to a given set of circumstances is—in reaching such a decision—revealing more of himself than of the patient. He claims that the more is known of the patient the more are "reactive" features in the illness likely to be detected, and that patients who show manic and/or depressive reactions develop these through some special predisposition of the personality, which causes them to be "specially sensitive to praise and blame, to feel a strong obligation to control themselves, and to find in situations certain elements, not obtrusive to the outside observer but of special personal significance to themselves, which lead to excessive inhibitory reactions, and ruminations involving self-blame or features of inadequacy, self-justifying and self-assertive counter-currents, of which the manic or depressive reactions are the symptomatic expression." He says, however, that he finds "depressive reactions too diversified to fit a unitary formula. Quite different importance has to be given in different cases to obsessional trends, to fatigue, to boredom, to loss of supporting persons, loss of dependent persons, etc." (105).

The analytic school, also, would seem to regard all depressive states as reactive; and mainly to some form of loss, not merely in the material sense,

but of something, whether a person, a cause or an idea, which had long been identified with the ego: and the loss of which love-object brings out the ambivalence felt towards it so that an attack is launched upon it, depreciatory and hostile: but that attack is turned inwards on the self, owing to the identification that has long existed between that love-object and the ego. Hence, self-depreciation, unworthiness and suicide.

Here, indeed, we are a long way from Kraepelin, who, seeking for causes in terms of altered metabolism, disturbances of vaso-motor innervation or diseases of vaso-motor pathways, or auto-intoxication, has said that such external influences as bereavements are "possibly sparks for the discharge of individual attacks, but that the real cause of the malady must be sought in permanent internal changes."

Where the opinions as to causes are so widely disparate as these, one cannot but be suspicious that the different observers are describing different things, and that, from a heterogeneous group, each has selected an aspect for description.

Curran, after showing the impossibility of differentiation between psychotic and neurotic depressions, remarks: "Because the types of reaction which are recognized at present are also recognized as neither being clearly cut, nor accurately and rigidly differentiated and defined, it does not follow that they cease to have any meaning or use." But later he says, "No sharp division appears to be achieved. It is argued that it does not in fact exist . . ." Elsewhere, however, he writes of "a classical manic-depressive psychosis and its opposite, an allegedly typical neurosis" (20), and "of the small classical manic-depressive group, which does combine a persistent abnormality of mood with an essentially endogenous origin." This, however continuous the series between one extreme and the other, necessarily implies some possibility of separation, and accords with the fact that of Lewis's 61 cases, there were 10 in which no environmental cause could be found, and 9 in which he was "almost satisfied" that the precipitating factors were an adequate cause for the illness: at any rate the situation had been an "indispensable efficient cause." These factors do not lead one to suppose that possibilities of differentiation are necessarily dead, which view is strengthened by other considerations.

First, the arguments on either side are based (apart from the clinical impressions which are so dangerous) on very small numbers of cases. It is quite possible that a survey on a wide scale (which might well be a life work) would show broad general trends in favour of the contentions of the separative school. This would constitute a contribution to knowledge, and although Lewis's work suggests that such broad trends would be quite unhelpful when it came to dealing practically with an individual case, that would not necessarily be so if some form of treatment were to be discovered, efficient in some affective conditions but not in others.

Second, one is struck by a certain uniformity (in a subject which lends itself to uniformity so little) in the concepts propounded by the discussants of 1930 of the depressive phase of manic-depressive psychosis as they saw it: and that they agree pretty well with Dana's description of a quarter of a century before. There is no doubt that such states occur. It would appear

that, attractive through their relative simplicity, they were taken as a paradigm of depressive conditions, and were thus thought to occur more often than they really do. Perhaps they represent the depressive phase of manic-depressive psychosis in pure culture. But in the great majority of cases the illness is coloured by the reaction of the individual to it, as well, perhaps, as by the addition of genes of minor effect. Such a combination of added factors may alter the picture entirely, giving the appearance of a condition different in kind as well as in degree, though the fundamental mechanisms may be just the same.

This brings us to our third consideration, the genetic aspect. Here, indeed, lie possibilities that the appearance of a condition different in kind may not be fictitious, and that there is a difference in kind, in fact. How is it possible, if there is no differentiation between different types of depression, for Lewis to write in another place (59) of the genetics of manic-depressive psychosis, "The figures conform broadly to expectation if one assumes that there are three genes concerned, of which two are recessive and one dominant." If everyone who has a fit of the blues is to be considered liable later to develop an attack of mania, no such figures could ever have been compiled. Slater has observed (93), "In an investigation of manic-depressive insanity only the indisputable cases should be included as part of the working material," and enough such cases have been found for a probable estimate of the genetic basis of the condition. And a hint, at least, of further differential possibilities is evident when Slater remarks, "It is one of the services of psychiatric genetics to have shown that what is commonly called involuntional melancholia has nearer connections with the schizophrenic psychoses than with the manic-depressives."

Finally, we come to considerations arising out of recent advances in treatment. It is noteworthy that the bulk of the papers we have been considering were written before there was any great experience of convulsive therapy. The latter has come to be directed more and more specifically towards affective states, and especially to states of depression. Cook, in reviewing the literature (15), says, "It may be said at once that no doubt exists as to the efficacy of convulsion treatment in affective psychoses." But he issues a warning that "the presence of anxiety in a depressive setting" is according to the general trend of opinion an unfavourable prognostic feature as regards application of this treatment, and says, "It is possible that much of the success reported in treating psycho-neurotics with convulsions consists in clearing up essentially depressive symptoms, which may often simulate neurotic anxiety." Sargant and Slater (91) say, "Some neurotic types of depression may be aggravated by very few convulsions," and "The only patients with "anxiety neuroses" who will benefit from convulsions are those who are wrongly so called, who are in fact suffering from a depressive illness in which anxiety and agitation are to the fore." Sands (90) states unequivocally that it is the "psychotic depressions" who gain with electroplexy. It is his opinion that the mood disturbance may not be the most important feature in the differentiation of these cases; more so are "the diminishing state of awareness with movement away from reality, increasing introspection with narrowed range of thought

and repetitive preoccupation with a few ideas." (This concept is reminiscent of the French School of thought, as indicated by Lewis (61).) He goes on to say that some cases show agitation, but that this depends mainly on the conflicts, and unlike "neurotic tension," is not easily heightened by outside influences. He finds cases with neurotic depression "quite different" with their hypersensitiveness and awareness, and he notes, as did Gillespie, the lack of identification of the illness with the personality. He concludes by observing that the effect of this treatment shows that the problem of neurosis or psychosis is less academic than ever before, since the decision whether to employ a drastic treatment depends on the answer.

If such a distinction, in the light of response to electroplexy, is valid, and is of importance in deciding the suitability of a case for treatment, how much the more important must it be when considerations arise of a far more drastic treatment of irreversible kind?

It is desirable, therefore, to examine the effects of prefrontal leucotomy from a special aspect. The detailed results in a series of 300 cases all investigated and personally followed by the writer (at the suggestion of Dr. Thomas Tennent and under the aegis of St. Andrew's Hospital, Northampton) are in course of preparation. In this series there were 82 cases of affective disorder which survived the operation sufficiently long for study. It is these 82 cases that we are now going to consider, not so much as regards post-operative function or post-operative deficits, but as regards the degree of recovery achieved in relation to the type of disorder present, so far as we are able to determine it.

Of these 82 cases we may make the following classification:

- (1) One patient had had recurrent attacks of mania, but without attacks of depression.
- (2) 15 were essentially in the manic-depressive group in that they had shown evidence both of mania and of depression.
- (3) 27 had had recurrent depressive illnesses but without manic attacks.
- (4) 36 had had single depressive illnesses, and were operated on at one stage or another of the only attack to which they had been subject.

That leaves three other cases for consideration:

- (5) One of these may be considered to have shown an essentially reactive depression in that his disturbance of mood was clearly related to, and caused by, intractable pain—by difficulties in the diagnosis and treatment of which he had become increasingly demoralized.
- (6) The other two were fundamentally obsessional patients, whose mood disturbance was considered essentially based upon, and arising from, their obsessiveness.

We will consider these groups *seriatim*.

- (1) The patient subject only to manic attacks continued to be manic after operation in that he still showed great push of talk with distractibility and

undue cheerfulness of mood. His spontaneity, excitement and activity were, however, reduced, so that the condition persisted in a modified form.

(2) Of the 15 manic-depressive cases, 8 showed the illness in classical form. One, operated on in a depressive phase characterized by agitated self-reproach with feelings of guilt, remained depressed in so far as he retained depressive delusions (which he had lost during previous remissions) with some fundamental lowering of the mood; but he had lost his agitation, was able to tolerate his condition, and was quite well enough to be discharged from hospital.

One swung very slowly and almost from the moment of operation from a state of unvarying depression of 12 years' duration into a state of gradually increasing animation, which culminated in frank mania 18 months later.

One, operated on in a depressive phase, swung quickly into a state of hypomania which gradually settled to a vivacity within normal limits.

One, operated on in a depressive phase, returned to normal but relapsed 21 months after operation into a hypomanic state (in which co-existent depressive features were discernible), which rapidly subsided.

One, whose attacks (constantly recurring over a period of 14 years) had only twice demanded hospital care, and were over a period of 11 years compatible with earning his living, was improved to the extent that his mood remained equable over the ensuing 2 years.

Of the other three, in whom manic phases (in which they were operated on) had predominated, 2 were substantially unchanged, and the other has relapsed, though here again the post-operative state showed some modification in that the subsequent states were of milder form.

The other 7 manic-depressive cases showed atypical features, both in the content and behaviour, while otherwise conforming generally to a manic-depressive pattern. For example, incoherence and inappropriateness of replies, odd posturings, Messianic ideas, impulsive violence, etc., were noted at one time or another. Of these 7, 1 was noteworthy in that he had an almost unvarying cycle of depression and mania on alternate days (though that had not always been so), the rhythm of which was unchanged by operation. But in him, as in 2 other cases, the intensity of the disturbance has been modified. One case remained free from attacks for the abnormally long period of 10 months before dying from an obscure cause. The other 3 cases have remained well for periods much in excess of any remission that they had previously enjoyed.

Thus, out of these first 16 cases that we have considered, in the manic-depressive group or closely allied to it, the symptoms have either persisted or recurred in no fewer than 11, while of the 5 who "recovered," 1 survived only for 10 months after operation. Now, of these 16 cases there were only 7 in whom it was felt that psychological mechanisms played any serious contributory part in the development of the illness. It is striking that the 5 "recovered" patients are to be found among those 7; the 2 cases in the development of whose illness psychological mechanisms appeared to play a serious part, but who did not recover, were (*a*) an unstable epileptic dullard whose psychotic phases could be construed as a reaction to the frustration engendered by his handicaps, and whose handicaps remained unchanged by

operation, and (b) a 52-year-old woman whose personal and family histories suggested a heavy constitutional loading, and who became markedly deteriorated in the course of a 3-year illness of such severity and turbulent course that any original psycho-dynamics had become lost in a psychotic deluge, so that the final phase bore no relation to anything that had gone before.

The length of time over which the various attacks had been distributed had no influence on the outcome, but all the recovered cases had had remissions of good quality (if brief) within two years of operation. None of the unrecovered cases had had such remissions. These figures suggest that the more the illness appears to be autonomous and constitutionally determined, the less effect does the operation have; and the more the illness appears to be reactive, in the sense that psychic conflicts may precipitate, or prolong the attacks through influencing the mood, the better are the chances that operation affords.

(3) Of the 27 cases with recurrent depressions, 14 had had severe illnesses characterized by an unremitting chronicity. In 6 of these cases there were situational factors which might have helped to precipitate the condition. But it was impossible, on common sense grounds, to consider these as adequate causes either for the severity or duration of the illnesses that followed. These last appeared in those respects truly autonomous, though it is felt that the reactions shown by the patients towards the illnesses themselves may have prolonged the latter and militated against early recovery.

Of these 14, one entered a curious post-operative state (which we shall see paralleled in another case later), in which she giggled, was facetious to the point of fatuousness, made sharp sallies, played Puckish jokes and was thoroughly irresponsible. But when she could be got to discuss how she felt, she said that she was still depressed, that she wished she were dead, that she had no feelings or interest, but experienced—in parallel with her affective lack—a lethargy for life which was in fact evident in her behaviour. Her statement carried much conviction, and it is believed that the essential nucleus of the 12-year illness remained, although her attitude towards it had been altered. She has remained much the same for more than 2 years.

Another, markedly agitated and ill for 8 years, took 15 months to recover from his depression, although meanwhile his lamentations and expressions of hopelessness had been markedly reduced. Both these cases show what has also been observed by Mixter, Tillotson and Wies (72), and what has been referred to by them as "affective de-sensitization," i.e. a more tranquil attitude leading to better tolerance of the persistent symptoms. Another case, though able to live at home, was still depressed with affective loss at 6 months after operation, though by the end of a year she was fully well.

A fourth took 9 months to recover from his depression, though his agitation had been at once reduced after operation; 2 years after operation, at the age of 60, he entered a state of hypomania, of which there had previously been no history.

A fifth, a chronic alcoholic, was recovered from his depression within 6 months, but entered another, though milder, depressive phase, complicated by alcohol, 2 years after operation.

A man of 81, who had been very severely depressed and suicidal, largely recovered but was post-operatively labile. The picture was complicated by senile changes.

The other 8 patients all recovered fully from their depressions, and have remained free from relapse for periods between 1 and 2½ years.

Thus, in these 14 cases, there was post-operative persistence of depression over considerable periods of time in 4 cases, with relapse into hypomania of one of those, and recurrence of depression in a fifth.

Now, of these 14 cases, 6 had been continuously ill for more than 2 years, and there were only 2 of those 6 cases who did not show this slow improvement. Of the 8 cases who had been ill for less than 2 years, none showed a slow recovery. There seems to be some relation, therefore, between the speed of recovery, on the one hand, and the severity and duration of the symptoms on the other. It might be thought that those cases who showed persistence of symptoms with slow improvement might have shown the latter anyway, even in absence of operation. Yet the balance of the evidence seems against this, since the attitude of the patients towards the illness was in all cases altered to a more favourable one. It may be that the restriction of interest to the symptoms, the agitation and self-absorption, all tend to prolong the attack, so that moderation of these helps to facilitate a spontaneous recovery.

Next, there were 4 patients who showed persistent depression with little variation, but marked by accompanying obsessional symptoms, and in two of them also by compulsive thoughts of violence, which were absent when the patient was well. In 3 cases there were some situational factors. All 4 showed a rapid and satisfactory recovery without relapse over a period of 2 years. All had been ill for less than 2 years.

Then there were 5 patients who had shown repeated attacks of depression between brief remissions of good quality extending over periods of 17, 15, 9, 6 and 4 years, the attacks lasting for a few months and the remissions for a few weeks or longer. In 2 cases there were never adequate precipitating factors; in the other 3 there were no adequate precipitating factors for any attack except the first one. All 3 patients lost their symptoms and, although one of them has since entered a mental hospital on account of personal inadequacies, none has had a recurrence of actual depression in the 2 years since operation.

There remain 4 cases whose illnesses seemed quite different. All were chronically inadequate people with a tendency to hysterical reactions: all were immature, dependent, dissatisfied with themselves and, through past experience and awareness of their own deficiencies, more or less constantly expectant of misfortune. Their illnesses seemed clearly related to their dissatisfactions and their fears: both the symptoms shown and the course of illness could be so interpreted without straining the facts; further, their states could be markedly influenced at a given time by appropriate stimuli, so that they showed variation to outside events as well as to their own thoughts. They could be brought to brightness and animation, could be removed from self-absorption, could be induced to show a wider interest. In fact, all showed reactivity. All 4 cases lost their depression rapidly, though one—12 months

after operation—went through a remarkable paranoid phase which seemed to be enabled to reach expression through a post-operatively increased confidence and outspokenness, which enhanced her resentment over certain changes which had occurred to her disadvantage in her work situation during absence through illness.

Thus, while in our recurrently depressed cases the rate of recovery with absence of relapse is markedly better than in our frankly manic-depressive cases, there is evidence of persistence of symptoms after operation, with consequently slow recovery in 4 out of the 23 cases considered to be ill on a constitutional basis, with relapse into depression or mania in 2 more. Four out of the 23 cases, therefore, have shown a delayed recovery, and this was apparent only in those cases who had been ill for more than 2 years. In the 4 cases who were considered to be ill on an essentially reactive basis, in the sense that the illness was determined by the reaction of the personality to events outside the physical structure there were no cases of delayed recovery, although all had been continuously under treatment for depressive states for more than 2 years. It may be that here there is a hint of some difference in kind between two forms of depressive illness.

(4) We come now to consider our group of 36 cases who have had single depressive illnesses. But of these there are 18 who seem to form a rather special group bearing a resemblance to what is often described as "involitional melancholia." The status of involitional melancholia has long been a matter of dispute. Kraepelin considered it "quite different" from manic-depressive psychosis in 1904 (56), defined it in the seventh edition of his text-book as including "all pathological states of anxiety in more advanced age which are not episodes in the course of other forms of insanity," but in the eighth edition grouped it together with manic-depressive conditions as part of the same disease process (57, 58). This *volte face* arose largely from some remarks made by Dreyfus (27) after examination of some of the patients and of the case-records on which Kraepelin's original view had been founded. But Dreyfus' criticisms have themselves been strongly criticized, notably by Hoch and MacCurdy (52) and by Henderson and Gillespie (51). Lewis objects to the independent status of involitional melancholia on the ground that precisely similar cases also occur early in life (61). Farrar and Franks (32) have also concluded that depressions around the menopause show no distinctive characteristics other than can be accounted for by the age factor. On the other hand, Strecker and Ebaugh consider involitional melancholia, though probably a subdivision of manic-depressive psychosis, to merit special separate description by virtue of (1) its special age incidence, (2) its lengthy course, (3) its distinctive symptomatology (97), and substantially the same view is expressed by Henderson and Gillespie, while Noyes (77) observes that "in addition to its affective characteristics there are special physiological and psychological factors of such dynamic importance and so peculiar to that period of the individual's life during which the mental disturbance occurs that separate consideration is justified." Hoch and MacCurdy, in a classical paper on the subject (52), also regard the concept as worth retention, remarking that between the extremes of the depressive phase of manic-depressive psychosis and in-

volitional melancholia there is a marked contrast, though between them there are also innumerable transitions. They conceive of two types: (1) with a marked emotional reaction, usually anxiety and restlessness, with prominent delusions of death and poverty, to which peevishness and hypochondria may be added, though not sufficiently well developed to be consistently dominant features in the psychosis; (2) with, instead of frank fear reactions, much moaning, whining, surliness, seclusiveness, together with restriction of interest in about half the cases, while though death and poverty ideas are present in much the same proportion as in the first type, hypochondria is in this second type more prominent. They regard the first type as related to manic-depressive psychosis, and the second as related to schizophrenia. The prognosis is correspondingly considered by them to be worse in the second group than in the first. This view was to a large extent borne out by a later study of 68 cases by Drobnes (28), except that his figures seem to show that introverted personalities carry a better prognosis than extraverted. A somewhat different view is put forward by Davidoff and Brew (24), who consider the condition to be compounded of the personality changes and neurotic symptoms which arise at this catabolic phase of life, together with the "previously more specific individual personality attitudes and adaptations," so that the psychosis takes different forms according to its being primarily a matter of psycho-neurotic states imposed on the involuntional symptoms (the "involuntional symptoms" intended presumably in a more purely physical sense), or primarily of the involuntional symptoms colouring the pre-existing state, or of its being some essential compound of the two. It is their opinion, contrary to that of Hoch and MacCurdy and of Drobnes, that though the early personality influences the occurrence of the psychosis, it does not influence its outcome.

Palmer and Sherman (79), on the other hand, viewing the condition as a definite entity and chiefly of psychic origin, consider that there is a definite personality type which predisposes to the development of involuntional melancholia; this is characterized by introversion, strong conscious repression, obsessional characteristics, sado-masochistic tendencies, sexual maladjustment, hyper-religious trends leading to chronic worrying, undue meticulousness, denial of pleasure, pathological inhibition and rigidity. To this formidable list a later paper by Palmer, Hastings and Sherman (78) adds narrowness, poverty of affect and absence of normally warm relationships.

Titley (99) has also mentioned pre-morbid rigidity, and constriction of interests as characteristic.

Malamud, Sands and Malamud (64) likewise regard this condition as a clinical entity occurring in persons of a particular personality type, but they have a conception of the pre-psychotic personality somewhat wider than that of Palmer and Sherman, and include the (1) hard-driving, aggressive, over-conscientious and stubborn; (2) seclusive, autistic, under-active, prudish; (3) sensitive, timid and hypochondriacal, but all with rigidity and constriction of interest as the keynote. Noyes (77) would add to these persons who have been disappointed.

A catalogue of personality traits of this sort would seem to constitute an illness in itself, apart from the addition of melancholia, but Eyman and Rivers

and their associates (30), surveying 300 cases of involuntional melancholia, did find that the significant factors in the pre-psychotic personality were obstinacy, parsimony and perfectionism, while their series had an unduly high incidence of educated patients, and gross sexual maladjustments were present in a minimum of 25 per cent. of females and 16 per cent. of males. As regards precipitating factors, they found that in women, bereavements figured three times as often as any other, and in men financial worry occurred twice as often as any other. They note that Farquharson (31) had also found these the most prominent situational factors. Doty (26) has made a similar observation, but adds that reduced physical fitness, or the threat of it, are also of importance.

It seems, on the whole, legitimate to include involuntional melancholia among our diagnostic subdivisions, and to regard it as an entity, with affinities both to manic-depressive psychosis and to schizophrenia, occurring in the later life of persons not previously subject to affective disturbance: characterized by depression with agitation and hypochondriacal features, and with a special tendency to be precipitated by bereavements, financial anxiety and the threat of poor health, in persons of rigid personality with inadequate social adjustments.

Eighteen out of our 36 patients with single depressive illnesses may be considered involuntional melancholics. Of these, 10 may be best assigned to Hoch and MacCurdy's Group I (those more allied to manic-depressive psychosis) and 8 to their Group II (those more allied to schizophrenia and with a worse prognosis). Of these:

One patient, aged 70, was substantially unchanged after a 14-year illness of Group II type.

One patient, after a 10-year illness of Group I type, showed a post-operative state similar to that which we have already considered in one of our recurrently depressed patients. With every appearance of euphoria, he was giggly, flippant, and given to smart repartee, instead of being intolerably tormented, agitated and wretched. But he was quick to point out that his giggling was automatic, beyond his control, and provoked by silly things; such fatuousness, he added, was proof that he was an imbecile, as he had always said. His other self-depreciatory beliefs, such as that he was getting sillier and sillier, had ruined himself by masturbation, and was a "rotting mass of secondary syphilis," still persisted unshakeably, though he no longer cried them aloud. As to his mood, he would make no comment beyond saying that he hadn't one. "I don't feel anything at all; I'm not human; I see jam and I know it's jam, but it doesn't make my mouth water. I don't feel anything at all." That he was cheerful he emphatically denied: "I ought to be dead, and I wish I were." "It's queerer than anything in Edgar Allen Poe. Here I am; I'm not human, I'm useless, it's a tragedy, yet I laugh at it and see it has a funny side, but I haven't any feeling, and I ought to be dead." He was quite responsible, and able to do meticulously accurate work in the hospital office. Yet no one could say that he was well, or near it. It seems that here again is an instance of the "affective desensitization" of Mixter, Tillotson and Wies (72): that the central core of this illness persisted, that it was

through a reduction in the elaboration of his emotions and thoughts and therefore of his agitation, that his attitude towards the illness had been altered. In 2½ years he has shown little further change.

Three other patients, ill for 7, 4 and 3 years (one of Group I and 2 of Group II type), were also improved by operation but not recovered. In 2 the depressive symptoms persisted for nearly 2 years, while the third (still unrecovered) died of a stroke in the tenth post-operative month.

The other 13 involuntional melancholics recovered more rapidly. With regard to the time factor, 9 patients had been ill for more than 2 years, and 9 had been ill for less. The 5 patients who showed persistence of symptoms after operation were among the 9 who had been ill for more than 2 years. Of the 4 who, though ill for more than 2 years, recovered quickly, 2 had been comparatively mildly depressed with spontaneous fluctuations and some reactivity which had always stopped short of recovery, in a third the depression had also been mild but overlaid by a querulous hypochondriacal anergia, while the fourth (who had responded very well but always transiently to electroplexy) had actually been ill for 12 years with little spontaneous fluctuation.

Despite this last case, however, the evidence suggests on the whole that the longer a depressive illness persists in severe form without fluctuation or reactivity, the less good are the chances of relief by operation. For of 9 cases ill for longer than 2 years there were 4 (the most severely ill and the least reactive) who were still not recovered by 2 years after operation, and a fifth had died unrecovered in the tenth post-operative month; whereas, of 9 cases with illnesses of at least comparable severity but of less than 2 years' duration, none failed to recover. Two of the unrecovered cases were in Hoch and MacCurdy's Group I (with the more favourable prognosis), and 3 were in their Group II (with the less favourable prognosis). But in all of them, with or without situational factors, endogenous mechanisms were considered to have been paramount in the development and persistence of the illness.

Next in this group of patients with single depressive illnesses come 12 cases who were not involuntional melancholic. There were notable outside contributory factors in 8 of these 12 cases. Yet it seemed difficult, on common-sense grounds, to attribute the illness entirely to such cause. It was impossible to assign them definitely to one group or the other. All these 8 cases showed rapid relief of depressive symptoms after operation, though 2 of them later relapsed, again in situations which appeared contributory.

In the remaining 4 of these 12 cases it was felt that outside factors did little to precipitate the illnesses and contributed virtually nothing to their persistence. These were the cases with the least reactivity, in which the illnesses appeared autonomous. In 2 of these 4 cases there was only partial relief after operation, and the depressive symptoms persisted, though one of those 2 became fully recovered between the 12th and 24th post-operative months.

The time relationships here are also of significance. Three out of these 12 patients had been ill for 10 years. Of these 3, one who had been ill on an essentially endogenous basis did not recover, but the other 2 (who had shown reactivity) lost their depressive symptoms forthwith.

Seven patients had been ill for between 2 and 4 years. Of those, the one who had been unreactive and appeared ill on an essentially endogenous basis retained depressive symptoms for more than a year; the others (who had all shown reactivity) showed no post-operative persistence of depression.

Two patients had been ill for less than 2 years: they lost their depressive symptoms after operation.

Here again, then, it would appear that reactivity is a favourable prognostic sign, and it was only in the cases considered essentially endogenous that depressive symptoms persisted after operation.

This leaves us with 6 other cases who showed single depressive illnesses. All of these were considered to have been ill on a neurotic as opposed to a psychotic basis, in the sense that their states of depression seemed explicable solely in terms of the reaction of their particular personalities to their environmental stresses. These depressions were reactive; they were not autonomous; they were themselves a part of and identical with the patients' personalities. In none of these cases was there persistence of depression after operation, but all lost such symptoms. Two of them, it is true, showed later some degree of relapse. One had so far alienated her relatives that they could not tolerate her, so that when solitary and with nowhere to live, she easily fell back into a querulous and self-pitying ("Nobody wants me") state, and flung herself back on the hospital. The other found his powers of adjustment overtaxed by a marriage into which he had been persuaded when at his worst, and which he came to regret.

Thus, among the 6 neurotic cases with single depressions there was no post-operative persistence of depressive symptoms, despite the fact that all 6 had been ill for more than 2 years and 2 of them had been ill for more than 7 years.

(5) There was one case in which the depression appeared to be purely secondary to intractable pain from an atypical trigeminal neuralgia. After operation the depressive symptoms disappeared, although the pain persisted unchanged.

(6) There were 2 cases in which the illness appeared based upon, and essentially secondary to, obsessional characteristics. Neither patient was markedly ritualistic, but both were ruminative, unable to relinquish distressing trains of thought, and inextricably enmeshed in obsessional preoccupations of a frightening and gloomy nature. Both cases showed reactivity and could lose their depression if sufficiently beguiled, but neither could be beguiled for long. In both instances the illnesses were of many years' duration, and the depression had gradually come to be the clamant feature as a result of which hospital care became necessary. Both cases recovered without persistence of depressive symptoms after operation.

CONCLUSIONS.

We may summarize our findings as regards the recovery in these 6 groups as follows:

(1) In the manic and manic-depressive groups there was persistence of manic-depressive symptoms after operation in 9 out of 16 cases.

(2) In the group with recurrent depressions there was persistence of depressive symptoms after operation in 4 out of 23 cases, all considered to have been ill on an endogenous basis.

(3) In the group with single depressions there was persistence of depression after operation in 7 out of 22 cases considered to have been ill on an endogenous basis.

(4) In 8 cases in which it was considered that situational factors certainly, and endogenous factors probably, played a part, there was no persistence of depressive symptoms after operation.

(5) In 13 cases in which it was felt that endogenous mechanisms had played no appreciable part in influencing the depression (4 of them with recurrent depressions, 6 of them with single depressions, 1 of them reacting to intolerable pain, and 2 depressed secondarily to obsessional preoccupations), there was no persistence of depressive symptoms after operation.

(6) Thus, out of 61 cases believed to have been ill on an endogenous basis, there was post-operative persistence of symptoms in 20 cases. Out of 21 cases in which the illnesses were considered mainly reactive (in 13 of them entirely reactive) there was post-operative persistence of symptoms in none.

(7) With regard to relapse, as opposed to persistence of symptoms after operation, this occurred in 4 out of 51 cases considered to have been ill on an essentially endogenous basis.

(8) Relapse also occurred in 4 out of 21 cases in which the illnesses were considered to be largely or entirely reactive.

(9) The figures suggest that while reactivity carries a favourable prognosis as regards the immediate effects of operation, it carries also a greater likelihood of relapse. This is in accord with expectation, since the effect of the operation is but to modify, and not basically to change, the personality (81).

(10) The duration of illness, also, appears to exert less adverse influence on the effects of operation in those conditions that are mainly or entirely reactive than in those conditions which are more essentially endogenous.

It is the significance, if any, of these conclusions that we will now consider.

DISCUSSION.

It is necessary, of course, to consider first how far these figures can be accepted. The diagnoses themselves must be considered to some extent open to question, like many other psychiatric diagnoses. The distinction between endogenous and reactive conditions is not a matter that can be decided by measurement, or that is susceptible of proof. It must depend on an impression, and impressions are dangerous. The family histories were, on the whole, unhelpful in the differentiation. The principal criteria in attempting to distinguish between the endogenous and the reactive illnesses have been, as regards the former, the shape and massive form disproportionate to the situational factors and to what has gone before; and, as regards the latter,

the intelligibility of the condition in terms of psycho-dynamics, and the reactivity. But apart from this, the illnesses seemed different in quality, though to convey the difference in words would tax the abilities even of a professional writer of long experience. The "neurotic" illnesses were of a quality much more personal to the patient, and more intimately bound up with those individual patterns of reaction which arose from their particular personal characteristics. The illnesses did not have the same stamp, as did the others, of having struck the patient from without, and of being alien to their normal states. There was about them a curious note of acceptance by the patients, so that they were described in a fashion showing the patient to have difficulty in explaining what symptoms were normal for himself, and which were not. The symptoms themselves varied widely, not only from case to case but from time to time in the same case, so that the clinical picture was inconsistent, though all complained of depression. The illnesses seemed to have merged out of the personalities, and the patients to have acquiesced in—almost to have encouraged—their development.

In this difficult exercise of projecting oneself into the patient's situation and judging it in the light of common sense, there are so many imponderables and uncertainties, as well as biases arising from the observer's own personality, that exception may be taken even to attempting it as being too far fraught with possibilities of fallacy. But the histories were taken with care, the patients were interviewed at length, discussion was held with the responsible doctors and nurses, much indispensable help was obtained from the relatives. In the writer's opinion, a reasonable judgment is not necessarily as impossible as many recent writers in the literature would lead one to suppose. In so far as it is a matter of opinion, the conclusions cannot be more than speculative, and to make further speculations arising from them may be to invite that criticism so trenchantly voiced by Halstead (48) that studies of prefrontal leucotomy have resulted only in the "pyramiding of unknowns." Yet the advancement of science has been due to the formulation of postulates, which have later been corrected as the development of knowledge has proved them to be wrong.

Now that it has been found possible to relieve affective disorders, in a number of cases at least, by interference with neural pathways, it seems that the future holds a real possibility that we shall be able to relate symptoms to lesions, in terms of disordered function of anatomically localizable structures, as in other branches of medicine. Here we are again reminded of Mapother's remark (65): "To assume that an enduring physical basis for habitually abnormal behaviour is probably non-existent because at present its exact nature is not demonstrable seems to me a flat defiance of all relevant experience in medicine."

Now, the operation of prefrontal leucotomy has shown that, as part of the changes which it may effect, it is possible to alter the patient's attitude towards an underlying condition without altering the condition itself. The best example of this is in the case already cited, where the patient post-operatively had still the same intractable pain, but did not suffer to the same degree. If, then, there exist endogenous affective disorders for which there

is an underlying physical basis, it should be possible to alter the attitude of the patient towards such a condition without removing the disorder itself. In fact, this seems to have happened in 20 out of our 82 cases. Here we would seem to have examples of "an enduring physical basis." But that the physical basis is not always enduring in a permanent sense is indicated by the fact that, notwithstanding incomplete relief immediately after operation, many of these 20 cases have shown a slow and gradual tendency towards post-operative recovery, sometimes over a period of nearly 2 years. Further, it may be borne in mind that—largely owing to geographical exigencies—few of these 82 patients were personally seen by the writer until 6 months had elapsed since operation. There is thus the possibility that a number of other cases may have shown the same slow, but less slow, trend towards recovery with persistence of post-operative depression for some part of that 6 months.

Where is this "enduring physical basis" to be located?

ANATOMICAL CONSIDERATIONS.

Both the underlying concepts and the technique of prefrontal leucotomy have changed much since the bold but naïve ideas of Moniz (73) first led him to begin this work in 1935. The severance, to a greater or less extent, of the thalamo-frontal radiation is now the avowed object of the procedure. This is the stream of fibres which runs forward from the dorsal medial nucleus of the thalamus to the frontal poles. The work of Meyer and his collaborators (70, 71) makes it now seem certain that, despite early doubts (69), section of these fibres is of major importance in achieving the post-operative effects. This is in line with the contention originally put forward by Freeman and Watts (36, 37, 38) that the beneficial results of operation were in some way dependent on that degeneration of the dorsal medial nucleus of the thalamus which they had noted in their own post-mortem material, and which occurred as a result of cutting the thalamo-frontal fibres. Recognition of the fact that the changes resulting from this manifest themselves mainly in the emotional sphere has done much to clarify the confusion of thought that previously surrounded the problem of the functions of the frontal lobes. It used to be held by clinicians that these were association areas on the integrity of which the intellectual life depended. But the unrivalled opportunities afforded by the 1914-18 war for observing the clinical effects of head injuries brought no definite evidence in favour of such a view. Both Forster (34) and Feuchtwanger (33) concluded that, though injury to the frontal lobes was followed by lack both of initiative and of emotional control, primary intellectual impairment did not occur. Kleist (55) believed that there was some localization in that emotional disturbances followed injury to the orbital surface, while intellectual and hypokinetic changes followed damage to the convexity. In the former conclusion he echoed the observations of Leonore Welt in 1888 (103), and in the latter he has to some extent been confirmed by the recent findings of Penfield (82). With the development of intracranial surgery, enormous resections of frontal lobe tissue without gross changes of purely intellectual kind have been reported by Dandy (22, 23), Ackerley (1) and Brickner (7, 8), while Jefferson's results (53) indicated that as long as one side

only was affected no deficits resulted from a unilateral lobectomy. Indeed, Lidz (63) with detailed tests was unable to demonstrate any intellectual impairment on one of Jefferson's later cases. Finally, Hebb and Penfield (49) reported a case with bilateral removal of the frontal lobes, allegedly with no intellectual deficits at all, and this view was re-affirmed by Hebb (50) on re-examination 6 years later. Goldstein (44, 45), on the other hand, has always maintained that a particular form of intellectual impairment does follow frontal damage, though special methods of examination are required for its demonstration; and Rylander's admirably detailed studies of 32 cases with various excisions of the frontal lobes render it hard to escape the conclusion that the more thorough the examination the more is something in the way of deficits likely to be found, though these may not be such as to form any notable handicap in the life situation (89).

Thus, though it is improbable that the frontal lobes are of no importance in intellectual function, they would seem less essential in that connection than used to be supposed, and attention has come to be focused more on the role that they play in the emotional life. This is in line with the suggestion of von Bonin (102) that, on comparative grounds, it is the temporo-parietal region, rather than the frontal lobes, which shows the greatest evolutionary development in man, and which is probably responsible for his intellectual ascendancy. Such a view also brings clinicians into more agreement with anatomists, who have long regarded the frontal lobes as receptor areas for hypothalamic stimuli rather than as association areas (14). Certainly the anatomical arrangements suggest this, and it would appear that the hypothalamic stimuli reach the frontal cortex via the thalamus, and mainly via the dorsal medial nucleus of that structure. The hypothalamus, thalamus and cortex are thus to be regarded as the component parts of a co-ordinated system, mutually interdependent and reciprocally influencing each other. Colour is lent to this view by the further discovery by Meyer (14) not only of fronto-thalamic connections, but of direct connections between the frontal cortex and the hypothalamus itself. It is with this co-ordinated system that the operation of pre-frontal leucotomy interferes by dividing the thalamo-frontal radiation, and thus (to a greater or less extent, according to the size of the incision) isolating the frontal poles, on the one side, from the thalamus and the hypothalamus, on the other. The effect of this must be to abolish, or to reduce, the passage of stimuli from the hypothalamus and thalamus to the frontal poles.

There is evidence that these stimuli must be concerned with the conscious experience of emotion.

PHYSIOLOGICAL CONSIDERATIONS.

The importance of the autonomic system and its connections in the mediation of emotion had long been apparent as the result of observations by Cannon (12), before Bard (4), by a series of painstaking experimental ablations of progressively larger areas of brain tissue in animals, showed that the posterior nuclei of the hypothalamus were indispensable for the appearance of those bodily emotional changes which Cannon had called "sham rage." Ranson

(88) further showed that "sham rage" was producible to order by electrical stimulation of the hypothalamus, while the work of Gellhorn (40), attempting an even more precise localization, suggested that this reaction was mediated essentially by the mammillary bodies.

But that these states producible by interference with the hypothalamus are the bodily expressions of emotion only, and with a qualitative difference from emotion as experienced in consciousness, has been most ingeniously shown by Masserman (66), who, just as Cannon called his effects sham rage, calls these "pseudo-affective." He introduced electrodes into the hypothalami of cats and left them there, so that the animals walked about with them as part of their permanent anatomy. When electrical stimuli were applied the cats would show all the outward appearances of rage, but, somewhat like our more irritable patients after leucotomy, would be immediately tranquil on cessation of the stimulus and would continue what they had been doing as though nothing had happened. This evidence was suggestive, but it was clinched by further experiment. Attempts were made to establish conditioned reflexes in these animals by presenting them, immediately before electrical stimulation of the hypothalamus, with such outside stimuli as noises, lights and currents of air; it was expected that, under the influence of conditioning, exhibition of the outside stimulus would produce the sham rage without need for electrical stimulation. But nothing of the sort happened, and the cats looked on these outside stimuli unmoved: it appeared that they had not associated the stimuli with any *feeling* of emotion. Similarly, when conditioned reflexes had been established in the cats in the ordinary way, it was found that these could be obliterated by presenting outside stimuli designed to make the cat annoyed: but they were not obliterated by mere stimulation of the hypothalamus. In fact, the outside stimuli annoyed the whole cat; the hypothalamic stimuli alone annoyed only the cat's autonomic system. Or, more accurately, the hypothalamus mediated the somatic expression of the emotion, but without the subjective experience.

Further, the hypothalamus appears to exert decisive influences on the bodily economy as a whole—on the pulse and respiration rate, the level of the blood pressure and blood sugar, the degree of hydration and dehydration, the general endocrine state (via the pituitary body, with which it is connected by the supra-optico-hypophyseal tract), and the wakefulness or sleepiness of the person. In fact, it is hypothalamic activity that determines the tensions at which we live, and that provides the milieu within which conscious experience becomes possible.

As to the means by which conscious experience becomes possible we know nothing, though we have a glimmer of knowledge as to the level at which this occurs. It appears to take place in the thalamus, which, as the great receptor centre for afferent stimuli, seems somehow to integrate these stimuli into percepts, and to endow them with feeling tone. Papez (80) suggested in 1937 that the integration took place through the receptive nuclei in the ventral part of the thalamus (lateral geniculate body receiving optic stimuli, part of the reticular nucleus receiving stimuli from the spino-thalamic and trigemino-thalamic tracts, nuclei in the mammillary peduncles receiving stimuli from the

medial lemniscus) and their connections with the pars optica and tuber cinereum of the hypothalamus, which in their turn connect with the mammillary body, which in its turn receives afferents from the fornix, mammillary peduncle and medial bundle of the fore-brain. He conceived that after integration in the thalamus the stream divides, so that those components relating to (1) the stream of movement, pass through the dorsal thalamus and internal capsule to the corpus striatum; (2) the stream of thought, pass through the internal capsule to the lateral cortex; (3) the stream of feeling, pass through the ventral thalamus to the hypothalamus, via the mammillary nuclei to the anterior thalamic nuclei, and thence to the gyrus cinguli. Incoming stimuli of cortical origin, having passed along a neural chain via the hippocampus and fornix to the mammillary body, are likewise relayed via the anterior thalamic nucleus to the gyrus cinguli. It is in the cingular gyrus, he concluded, that experience is endowed with emotional consciousness. But that conscious experience, if of a primitive kind, can occur actually at the thalamic level has been shown by animal experiment, for a decorticate cat will show rage at a barking dog (14a). Further, the results of prefrontal leucotomy would suggest that the post-operative changes in the affective life of the patient must be associated with the division of the thalamo-frontal fibres, and resultant degeneration of the dorsal medial nucleus of the thalamus. It would therefore appear that consciousness is possible at the thalamic level, but is elaborated at the cortical level, and—although the cingular gyrus is likely to play some important part—that this is also achieved through the relay to the frontal cortex of stimuli passing from the dorsal medial nucleus.

We might then summarize the matter by saying that it seems probable that the hypothalamus, thalamus and cortex function together in a co-ordinated relationship. The hypothalamus provides the milieu within which it becomes possible to experience in consciousness those integrations of stimuli into percepts, with their accompanying emotional investments, which are the products of thalamic function. The enlivening effects of hypothalamic activity are made felt through these integrations, are relayed through the dorsal medial nucleus to the frontal lobes, where, with ever-widening chains of association, and with modifications or elaborations according to those associations, the affective life finds its most mature and richest expression. The process, it must be presumed, is a reciprocal one in which both cortex and lower centres function as a unit with interplay and mutual influence. Feelings thus mediated will arouse other feelings, and these will form promptings to activity, which, translated into action, will result in movement and speech of every grade of complexity. Such a process may, perhaps, find its fullest expression in persons who are the subjects of mania; its greatest reduction in those akinetic depressions which Kraepelin considered typical of the depressive phase of manic-depressive psychosis.

INFERENCES AS TO THE NATURE OF AFFECTIVE DISORDERS.

That some such sequence does, in fact, occur in manic-depressive psychosis seems probable. It is well known that affective changes can occur as a result of lesions at hypothalamic levels. Fulton and Bailey (39) in 1929 drew atten-

tion to the fact that "manic attacks" occur with tumours at the base of the brain, but not in cases of tumour of the hemispheres, and recorded having seen three cases of maniacal excitation after operation for hypophyseal adenoma. Guttmann and Hermann (47) tell of a woman who had a manic attack with recovery at 27, followed by a phase of severe anxiety, excitement, irascibility and aggressiveness at 49, after which she died; autopsy disclosed a tumour of the third ventricle invading the hypothalamus from the chiasma to the corpora mammillaria. Foerster and Gagel (35) and Bumke and Foerster (9) describe how manic responses (manifested by push of talk, clang associations and flight of ideas) could be elicited by manipulation (while operating for its removal) of a suprasellar craniopharyngioma which compressed the floor of the third ventricle; and manic excitement, in a patient who had never before shown such tendencies, on attempts being made to remove a blood clot in the third ventricle; and a "manic reaction with euphoria" (push of talk, flight of ideas, psycho-motor over-activity) in a patient with a hypophyseal tumour compressing the hypothalamus. Alpers (2) has vividly described the behaviour (which he conservatively and correctly prefers to call "manic-like" rather than manic) of a patient with a teratoma involving the third ventricle. Cox (16) has recorded attacks of "mania" occurring in a racehorse later found to have a basal lesion, and more significantly, phases of apathy with affective loss in a woman in whom autopsy revealed a pinealoma.

Here, then, we have suggestive evidence of an "enduring physical basis" for affective disorders. It would seem probably to be located in the hypothalamus, but to make its effects felt also at the thalamic level, on account of the intricacy and intimacy of the anatomical connections. It would thus appear to be a dysfunction of those cell groups which mediate the somatic and subjective components of emotion. Such a dysfunction would account for the chronicity and apparently autonomous nature of some of the cases that we have considered. It would account also both for the persistence of symptoms after operation and for their recurrence. For, if the enduring physical basis be thalamic and/or hypothalamic in site, to operate on the thalamo-frontal radiation is to operate above the level of the lesion.

If we are correct in our conception that the thalamo-frontal radiation relays to the frontal poles what we may call for convenience "emotional stimuli" which are the products of thalamic and hypothalamic activity, and that these are elaborated, enriched and prolonged by the awakening of associations in the frontal cortex, then it follows that to divide the thalamo-frontal radiation is merely to reduce—by limiting the number of available pathways and by partly destroying the dorsal medial nucleus—the extent of the elaboration that can occur. The underlying disorder, however, would be left unchanged. It seems that this is, in fact, what has happened in many of our cases. Some of the manic cases persisted in mania, but in a less elaborate mania, while those who showed recurrences showed them in a modified form. Some of the depressive cases persisted in depression, but with a great reduction of agitation, distress and complexity, so that they tolerated the disturbance of mood in simpler fashion.

It is therefore tentatively concluded that this may be the sequence of

events in manic-depressive psychosis. It would seem that such a dysfunction can occur in the absence of psychic stimuli from the higher centres, or at any rate where such stimuli play an essentially secondary part in the development of the disorder. It is, for example, exceedingly difficult to think that certain regularly recurrent affective conditions (such as that described by Klein and Nunn (54), which underwent a regular weekly manic-depressive cycle with 5 days of depression and 2 of mania; and the instance already mentioned in our own case-material in which the patient alternated on alternate days) can be so rhythmically influenced by their psychic stimuli. But it would also seem that, though such dysfunction may start in the absence of psychic stimuli, it is, in fact, precipitated by the latter more often than not, and that, once it has started, it can be maintained by them. It is possible that here lies the explanation of the ordinary recovery, as well as of those curiously slow recoveries that we have noted in some instances to follow operation, where the agitation and distress having been post-operatively reduced, it seemed that by that very removal the patient was enabled to make spontaneous improvement. It might be that, by the comparative isolation (through operation) of the lower centres from the higher, the former were released from noxious influences transmitted before operation, perhaps by the fronto-thalamic and fronto-hypothalamic connections which, it has been noted already, Meyer has recently shown to exist. Such a conception has something in common with Cid's original suggestion that the *modus operandi* of leucotomy might lie in "putting the injured part at rest" (13).

As to the nature of this dysfunction, and to what, in its turn, it may be a reaction, we are in the dark, and much patient work has failed to solve the difficulty, though—taking into account that it is possible to postulate a genetic basis for such conditions as involuntional melancholia and manic-depressive psychosis—it must be presumed to arise from a constitutional predisposition. Whitehorn (104) was unsuccessful in finding any abnormality in the blood chemistry of manic-depressive patients. Baird (3) has sought to explain this by a conception of mania as a massive over-action of the entire autonomic system with both sympathetic and parasympathetic components functioning powerfully but equally, and thus maintaining homoeostasis, while he explains its prolongation by postulating a sustained alteration of the vascular bed in the way that Wolff and Wolf (106) consider to happen more transiently in states of rage. Although he failed to produce changes in a depressed patient by transfusion of 500 c.c. of blood from a manic one, he produced striking changes, and claims to have, in adrenalectomized cats and rats by transfusion of blood from human manics, which did not follow transfusion of blood from human normals. It is possible, therefore, that the metabolic changes so often stressed by Kraepelin may be factors of influence in affective disorders, possibly through an altered relation between the hypothalamus and the anterior pituitary, with secondary effects on other endocrine structures. This is the merest speculation, but even altered behaviour in cats and rats in such experimental circumstances shows that the possibility of metabolic changes, whether arising from hypothalamic dysfunction or leading to it, must not be overlooked.

The work also of Elvidge and Reed (29), who found suggestive changes in the oligodendroglia both of schizophrenic and manic-depressive cases when sections taken from living subjects were compared with controls, is a further indication that metabolic or physio-chemical changes may be at work.

It remains for us to note, however, that post-operative persistence of depression (which we have inferred to be evidence of an "enduring physical basis" for the affective disorder) was found in none of our cases except those considered to be ill on an endogenous basis. This raises the question of whether there is or is not a difference in kind between these patients and those whom we considered to be ill as a reaction to stimuli lying outside the physical structure. It would seem that there are some cases in which the patient reacts to disagreeable events (whether present in the outside world, or having arisen there as the result of his own behaviour, or whether they are more subjective in the form of feelings of inadequacy or conflict) by having disagreeable sensations, and that these are mediated by neural circuits from the cortex via thalamus and hypothalamus and back to the cortex again. This is a procedure of outside cause and inward effect, and the effects vary with the causes in a more rather than less physiological way. As the patient makes his adjustment (whether to the outside world or within himself) the effects cease as the causes no longer continue to operate. It is felt that this might be the sequence of events in "reactive depression" and in depressions of neurotic origin, and there seems no need in such cases to postulate any pathological process. The absence of the latter would constitute the difference between the reactive depression and the endogenous one, which last may not involve reaction to events outside the physical structure (at any rate at the onset), may be mediated by the same sort of neural circuits, but is more rather than less pathological, with some essential morbid process in the structure shown by dysfunction (to which the patient is genetically predisposed), mainly at the hypothalamic level and not essentially dependent on cortical impulses. Unlike the reactive depression, therefore, it is not necessarily resolved when the precipitating factors outside the physical structure are removed.

SUMMING UP.

In this way we conceive of two types of depression, and such a concept goes some way towards explaining the different results achieved by pre-frontal leucotomy in different kinds of affective disorder. Our considerations suggest that the operation is likely to prove of most immediate value in those cases in which the psycho-dynamics play a decisive part, whether they do this by themselves determining the condition without the development of any structural pathological change (as we believe to happen in reactive states), or by precipitating such through their action on hypothalamic centres constitutionally predisposed to dysfunction, or by maintaining, through repeated stimuli, such dysfunction once it has begun (as we believe happens in endogenous states). They suggest further that in some cases, but not in all, there is a more or less enduring physical basis for affective disorders. This is apparent in many of those cases here considered to have been endogenous, but in none of those cases considered to have been reactive. In the endo-

genous conditions, presumably by virtue of this physical basis, there seems to be a time factor which militates against recovery. In the reactive conditions there was no evidence of such a time factor. The apparent existence of this physical basis for the symptoms in some conditions but not in others suggests that it is not merely permissible, but desirable, to conceive of affective disorders in terms of endogenous, on the one hand, and reactive, on the other, though it is recognized that the clinical differentiation may in some cases be impossible, and that in many cases both factors may operate, probably to varying extents.

If there is truth in this concept, however, it should be pursued both in the interests of academic accuracy and in the hope of more precise observation yielding future contributions to knowledge. With one of Lewis's conclusions it is difficult to agree, namely that the term reactive depression and the grouping it denotes would be better done away with: from another, which he shares with Schultz, it is impossible to differ, namely, that we should always ask, "How far are reactive processes, in the widest sense, concerned in this case, and how far obscure hereditary or somatic determinants of a fateful sort?" (61).

As to the future, it would seem worth while to correlate the results of two different forms of treatment which, despite some similarity of effect, probably secure those effects in ways more widely different than would superficially appear, namely, electroplexy and prefrontal leucotomy. Where one succeeds and the other fails, or where one succeeds after the other where it had failed before (the occurrence of which has been pointed out by Dax and Radley-Smith (25)), some differential points might emerge which have hitherto eluded our notice. It is possible, with these modern treatments, that we have attended too much to the mood and too little to the general behaviour. We might pay more regard, on the one hand, to such aspects as sensitiveness and responsiveness with wider range of thought and action, with vacillation and indecisiveness amounting sometimes to what Muncie (75), quoting Meyer, has called "a poorly directed strenuousness with a certain restless chafing"; and, on the other hand, as Sands (90) has suggested, to "the diminishing state of awareness with movement away from reality, increasing introspection with narrowed range of thought and repetitive preoccupation with a few ideas," with which is associated Kraepelin's "impediment of volition," and sometimes an apparent reduction of affect. (For Lewis's contention that in the melancholic there is an increase of affective excitability for painful affect, though it contains of course much truth, does not seem always to be true.)

Finally, although the most highly reactive disorders are those likely to receive most immediate benefit from prefrontal leucotomy, it does not follow that this is the treatment of first choice. Since it appears that in them the time factor is of least importance, there is the more indication for giving alternative methods of treatment an extended trial, in view of the irreversibility of the operative procedure and the risk of undesirable sequelae.

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