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Melancholia

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M.B. Ch.B.

Abstract

An Extract from a Dissertation read before the Royal Medical Society on Friday, 27th January, 1961.

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MELANCHOLIA

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"Melancholy," meaning "black bile" or "black despair," designates aptly that spiritual blight which has vexed mankind from the earliest time. Playwrights and philosophers have long been intrigued by the spectacle of causeless melancholy, and, more recently, pathological melancholy, rechristened "psychotic depression" has been the subject of clinical definition.

The indaquacy of our language is recognised as a major stumbling-block in many spheres to-day where rapid progress is being made and this is particularly the case in psychiatry. While awaiting improvements, one must try to name conditions as accurately as possible with existing terms. In describing the condition in question, "melancholia" seems a preferable word to "depression." "Depression" is part of the common coinage of everyday speech and, as such, has an individual meaning for every member of the public. In their experience, it constitutes a normal, if undesirable state of mind, and to give the same name to a recognised pathological condition is as confusing as calling angina pectoris, heartache. Furthermore, not all patients who may be diagnosed as suffering from depression will admit to feeling depressed. To call a disease after one of its symptoms and not an invariable one at that, seems irrational and very liable to mislead.

Burton in "The Anatomy of Melancholy" defines melancholy as "a kind of dotage without a fever having for his ordinary companions fear and sadness without any apparent occasion." This, written at the time when the humoral concept of physiology was unchallenged, served admirably as a nidus on which later definitions might grow.

Kraeplin, in his classification of the psychoses, regarded melancholia as a disorder of mood and a form of manic-depressive insanity. He stressed the periodic nature of attacks and their propensity for spontaneous cure.

In summary melancholia may be described as a disorder of emotion inexplicable in terms of external events and without apparent organic cause, which is characterised by a sad anxious mood and psychomotor retardation. The condition usually remits spontaneously and completely but there is a tendency to recur.

As so often happens, what begins as a definition ends as a description. This emphasises the truth that until we know the cause, we cannot accurately define the disease. What then is the cause? Essentially it is unknown. However, from a devious and intensive study of its actiology has emerged what Einstein called "the feeling for order behind appearance." It is this feeling which

suggests that soon the disease will yield its secrets and its exact nature be known.

It has long been felt that the tendency to affective instability is inherited. Kallmann collected statistics of morbidity from manic-depressive psychoses in Europe and America. His conclusions were that in no case did the incidence in the general population exceed one per cent. Yet it had been shown that morbidity rates for parents, siblings or children of manic-depressive index cases were of the order of twelve per cent or more. In a series of 27 monozygotic twin pairs. Kallmann reported a hundred per cent incidence of affective psychosis. Among these twins it is interesting that there was no concordance of form or timing in the mood swings. It seems from this that the genotype sets the balance but some other as yet undetermined factors determine which way and when it will swing.

The form of this genetic transmission remains undecided. Slater and Kallmann contend that it is inherited as a single autosomal dominant while others postulate a multifactorial genetic determination. Much remains to be clarified, perhaps the outcome of investigations into the molecular structure of genes will be a more exact understanding of the disease and even a hint as to its cure. Even the facts which are established indicate that it is essential to take a full family history in all cases of this kind.

Kretschmer's types have become part of our psychological tradition and from his studies he has shown that the pyknic habitus is more frequent in patients suffering from affective disorders than could be expected by chance. Such typing although an absorbing exercise has proved of little practical value. When chromossome maps have been plotted it may be found that the predispositions to pyknic appearance and affective disorders are genetically linked.

A passing acquaintance with European history makes it clear that it is impossible to speak of racial characteristics in any meaningful way. However, it is reported that the Jews show a higher incidence of affective psychosis than average. The disease is commoner in Britain and Bavaria than in Norway and Prussia. An incidence of 0.3/1000 was reported in a Finish population of 400,000 and one of 3.5/1000 in a Scottish rural population of 56,000.

These figures have not been explained. It must always be borne in mind that each community has its own criteria for normal and abnormal behaviour and the pressure exerted from without to encourage a sick man to seek treatment will vary accordingly. Moreover, the difficulty in finding any uniformity of diagnosis must affect the interpretation of results.

Manic-depressive insanity is commoner in the female, the ratio being 3 : 2. Any conclusions drawn from these figures have met with a certain scepticism because the male is notoriously liable to show atypical features, particularly alcoholism which mask diagnosis.

Periodicity is a feature of the female metabolism and this cycle of hormonal activity produces changes of temperament in even the normal woman. The occurrence of menstrual and premenstrual depression is well established, as are the affective aberrations of the puerperium and menopause. It is also worth noting that amenorrhea is a frequent feature of depression. All this naturally prompted a search for some hormonal key to the aetiology of affective disorder. To counteract this enthusiasm, it has been pointed out that puberty and adolescence, times when the hormones are at their liveliest, rarely show an affective psychosis.

Many of the cyclic variations in human behaviour are initiated by the influence of the hypothalamus on the prefrontal cortex. Furthermore, it has been shown that in animals with both cerebral hemispheres removed, the periodic discharges affecting all divisions of the vegetative system persist.

Foerster produced elation by stimulating the hypothalamus in a patient under local anaesthetic. This and the effect of leucotomy which severs connections between the primitive brain and the cortex both augment the view that the diencephalon has some role in determining the affective disorders.

It is perhaps in the light of damage to the primitive brain that we should regard the various neurological diseases commonly associated with affective upset. Among such are general paralysis of the insane, arteriosclerosis, disseminated sclerosis and Parkinson's disease. In persons predisposed, affective illness is not an uncommon sequel of infections such as pneumonia and particularly, influenza.

To support the view that melancholia represents a regional disorder of brain function we may quote Hughlings Jackson in his essay on "The Factors of Insanities":—

"In every insanity, more or less of the highest cerebral centre is out of action temporarily or permanently from some pathological process; for my present purpose it matters little what that process be. It only matters as the pathological process produces loss of function, that is, dissolution of more or less of the highest centres. I do not use the term 'function' in the sense often given to it in clinical accounts of nervous maladies as for example, when it is said of a patient that his case is entirely functional. I do not believe that there is such a thing as loss or defect of function of any nervous elements without a proportionate material alteration of their structure and nutrition."

This essay written in 1894 which was referred to at the 1960 Gowers Memorial Lecture retains its relevance to the present day.

To attempt the elucidation of this disorder of function whose presence we feel but cannot see, we must journey to the world of the biochemist. Here we may cull from their intricate geometries a pattern which seems both comprehensible and hopeful.

It is well known that many drugs such as alcohol, opium or mescalin can alter our mental state. More particularly, certain drugs, notably reserpine, can produce a condition clinically similar to melancholia. Brodie (1957) showed that reserpine caused the depletion of brain serotonin—this is thought to be due to the release of bound serotonin. Vogt has shown that the concentrations of nor-adrenalin and serotonin in the hypothalamus, midbrain and floor of the fourth ventricle were higher than elsewhere in the C.N.S. Both these substances are concerned in the transmission of nerve impulses. Furthermore, reserpine has also been shown to liberate adrenalin and related amines from these areas of high concentration.

Such revelations naturally led workers to speculate that depletion of brain serotonin and catechol amines was in some way associated with depression. Apparent confirmation of this view arose when it was shown that the monoamine oxidase inhibitors were clinically effective in depression. These drugs inhibit the enzymes which are at least in part responsible for the breakdown of serotonin and adrenalin.

In recent years it has become increasingly well recognised that it is the subcortical brain which is concerned with our awareness and response to surroundings. This activating system co-ordinates autonomic, somatic and psychological activity. It has been suggested that this system has two components, one sympathetic and promoting active go-getting behaviour, the other akin to the parasympathetic and largely responsible for recuperation causing drowsiness and loss of interest (a state likened by some to hibernation). It is hinted that some of the afore-mentioned amines play a part in arousing these systems.

From all this confusion emerge certain trends, none of them universally

accepted, which hint at the possible nature of melancholia. We have a disorder which appears to be genetically determined. It appears predisposed by a biochemical lesion centred in the activating system of the primitive brain. As in so many physiological systems normality is a precariously held equilibrium and release of inhibiting forces or overstimulation of the opposing system results in the appearance of a pathological state. What seems so difficult to explain is the periodicity of the disease—why does the balance tilt when it does, without apparent occasion?

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SYLLABUS 1961-1962

OCTOBER 1961

13. INAUGURAL ADDRESS
8 p.m. Sir Walter Mercer, F.R.C.S.E. "The Edinburgh Influence on Early American Medicine."
20. Dissertation: J. A. R. Friend, Esq., B.A.(Cantab.): "The Failing Heart."
27. Dissertation: J. S. Kelly, Esq., B.Sc. "Chemical Transmission."

NOVEMBER

3. Dissertation: R. Butler, Esq. "Sir Charles Bell."
10. Dissertation: J. F. Peutherer, Esq. "Malabsorption."
17. ADDRESS: Professor A. G. R. Lowdon, O.B.E., M.A., F.R.C.S.E. "Acute Ischaemia of the Limbs."
23. PRESIDENTS' ANNUAL DINNER
Royal College of Surgeons, 7.15 for 7.30 p.m. Guest of Honour: Professor Sir Derrick Dunlop, B.A., M.D., F.R.C.P.E., F.R.C.P.
24. Dissertation: C. E. Hope, Esq. "Respiratory Inadequacy."

DECEMBER

1. TALK: Dr. W. I. Card, M.D., F.R.C.P.E., F.R.C.P. "Gastro-intestinal Hormones."
8. Dissertation: J. A. Calvert, Esq., B.Sc. "The Treatment of Renal Diseases."

JANUARY 1962

12. ADDRESS: Professor W. L. M. Perry, O.B.E., M.D., D.Sc. "Laboratory Investigation of Hypersensitivity."
19. Dissertation: P. J. Swarbrick, Esq. "Congenital Dislocation of the Hip."
26. Dissertation: M. C. Grayson, Esq. "Why Medicine?"
31. Film Show.

FEBRUARY

2. Dissertation: W. H. Leach, Esq. "Atherosclerosis."
7. ANNUAL BALL, in Carlton Hotel.
9. TALK: Mr J. H. S. Scott, F.R.C.S.E. "Evolution—the Orthopaedic Excuse."
16. Dissertation: N. A. Boyle, Esq. "Physiology, Neuropharmacology, and Therapeutic Use of the Monoamine Oxidase Inhibitors."
22. Debate with the Glasgow Medico-Chirurgical Society, in Edinburgh. Motion to be arranged.
23. ADDRESS: Professor Ian Donald. "The Development of a New Diagnostic Technique by Ultrasonic Echo Sounding."

MARCH

2. Dissertation: R. A. Bailey, Esq. "Mongolism."
9. PRESIDENT'S VALEDICTORY ADDRESS.
14. Annual Extraordinary General Meeting.

PRIVATE BUSINESS at 7 p.m. PUBLIC BUSINESS at 8 p.m.

Clinical Meetings, Film Meetings, and Industrial Visits will be arranged during the Session.