BASAL METABOLISM IN MANIC-DEPRESSIVE PSYCHOSES

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The estimation of basal metabolism in manic-depressive psychoses is helpful in detecting somatic disorders, particularly of endocrine origin, whose existence may have an important bearing on the etiology and treatment of the mental condition. It is useful also in evaluating the influence of emotion on the metabolic rate, from a purely physiological point of interest.

Whether or not the oxidative activities of the body are influenced by an emotional psychosis has been the subject of much controversy. Grafe[1] and Bornstein[2] were among the first to investigate this problem and contended that manic reactions had no appreciable effect on the basal metabolism. This contention was supported by the researches of later writers. Thus Fischer,[3,4,5] in a small group of manic-depressive cases, found uniformly normal values, and observed that basal metabolism might be used as a means of differentiating between dementia præcox, in which there was a lowering of the basal metabolic rate, and manic-depressive psychosis, in which metabolism was normal. Walker,[6] Janowska,[7,8] Whitehorn and Tillotson,[9] and Baumann[10] were similarly of the opinion that in the affective psychoses the basal metabolism fell within physiological limits.

In contrast to these negative findings, there have been reported definite deviations from the normal in the metabolism of manic-depressives.

Among the first researches reporting abnormalities of metabolism were those of Bowman and his co-workers,[11,12] who revealed a distinct tendency toward low readings. The existence of pathologically low basal metabolisms in manic-depressive psychoses was further substantiated by the investigations of Gibbs and Lemcke,[13] Farr,[14] Schou,[15] Badonnel,[16] Zeckel and Posthumus,[17] Massaut,[18] Lauzier,[19] and Langfeldt.[20] The latter writer, contradicting Fischer (*q. v.*), contended that the basal metabolism could not be used as a differentiating point between manic-depressive pyschosis and dementia præcox since low rates existed in both conditions.

Table I is a compilation of reported basal metabolic determinations in manic-depressives. A casual analysis reveals a tremendous disparity in the reported findings. Even in those cases where a marked tendency to low readings has been claimed, it is seen that the majority of tests fall within normal limits. It is evident also that in some cases there is actually an elevation of metabolism.

It is deplorable that in a number of researches the material has been so inadequately handled as to vitiate a proper evaluation of the results obtained. In many instances a single basal metabolism is considered a representative determination and no attempt has been made to tabulate the metabolic variations during the evolution of the psychosis. There is furthermore a general acceptance of average predicition values as normal and a total disregard of the metabolic rate of the individual after restoration to his normal mental state. In most cases information is lacking regarding the emotional, psychomotor, and nutritional status at the time of the test, and there is no indication of the type of mental reaction, the depth of the psychosis, state of muscular tonus, nor of existent endocrine, vegetative and other physical disturbances. The absence of this correlative information would seem to make the metabolic results barren and unconvincing.

A review of the literature on the effect of emotion on basal metabolism shows it to be similarly replete with apparent contradictions.

In normal individuals emotional states, especially apprehension and fear, are said to have a profoundly stimulating effect on metabolism,[21] due probably to the calorigenic action of liberated adrenalin,[22, 23, 24, 25] the rise in metabolism being proportionate to the intensity of the emotion.[26]

Experimental attempts to excite emotion artificially and to measure the resulting change of metabolism have yielded somewhat conflicting results. The most notable experiments are those in which emotional states have been induced by suggestion during hypnosis. Grafe and his co-workers[27, 28] found that while in some cases metabolism was uninfluenced by emotion, in other cases there was an increase in metabolic rate ranging from 5 to 25 per cent, without a corresponding increase in respiration or heart action. Whitehorn, Lundholm, and Gardner[29] discovered that the moods of depression

and elation hypnotically induced had no effect on the basal metabolism, whereas the moods of anxiety or apprehension hypnotically induced had a markedly elevating effect.

TABLE I. REPORTED BASAL METABOLISMS IN MANIC-DEPRESSIVE PSYCHOSES

Author	Total number of cases reported	Number of cases above +10%	Number of cases between +10% and —10%	Number of cases below —10%
Fischer[3]	15	0	15	0
Fischer[5]	9	0	9	0
Janowska[8]	16	4	11	1
Whitehorn and Tillotson[9]	17	2	14	1
Baumann[10]	12	0	11	1
Bowman and Grabfield[11]	6	3	2	1
Bowman and Fry[12]	25	3	16	6
Gibbs and Lemcke[13]	15	2	8	5
Farr[14]	38	3	26	9
Schou[15]	34	0	21	13
Badonnel[16]	6	0	1	5
Zeckel and Posthumus[17]	13	1	5	7
Lauzier[19]	6	2	2	2
Total	212	20	141	51

That metabolism may be depressed instead of elevated through the influence of emotion was demonstrated by Crile[30] in rabbits frightened by dogs. The work of Deutsch[31] is noteworthy in this reference in bringing out the fact that collapse due to extreme emotion is apt to cause a drastic fall in basal metabolism.

The associated mood abnormalities of psychoses would appear to offer a convenient means of investigating the problem of metabo-

lism in emotional states. That mental disturbances are capable of disrupting the biochemical equilibrium of the body was observed by Gordon,[32] who reported in psychoses with intense emotional changes the existence of hyperglycemia and increased adrenalin output. It is not unreasonable therefore to anticipate a change of metabolism in the manic-depressive psychoses, in which pathological mood disturbances notoriously prevail.

Changes of metabolism have actually been reported by Henry,[33] who discovered that acceleration of basal metabolism occurred in elated, over-active and over-talkative patients, as well as in apprehensive, tense and agitated patients, unless counteracted by depression. Retardation of metabolism occurred in depressed, under-active and under-talkative patients. Henry concluded that basal metabolism could be altered pathologically by intense emotions, and conjectured that the so-called normal variation in metabolic rate was due to different emotional states presented by the same person.

A detailed study of emotional changes in manic-depressive psychoses was conducted by Janowska.[8] The basal metabolism was first tested, following which the patient was told particularly unpleasant news. Feelings of anxiety and occasionally states of desperation, irritation, and rage resulted during which the metabolism was again determined. After the crisis had passed, the basal metabolic rate was again obtained. The conclusions reached were that metabolism was increased in states of fright, desperation and rage, as well as in pathological depressions; that reactions were more evident if there was an increased activity of the thyroid gland; and that the change in metabolism under the influence of emotion was greater in depressed than in normal cases.

On the other hand Landis,[34] after reviewing the literature on the subject, and as a result of his own experiments, decided that an altered emotional state did not necessarily have an effect on the basal metabolism, and concluded that manic-depressive psychosis, with its supposedly altered emotional content, might or might not affect the metabolic rate.

In anxious, agitated states one would ordinarily expect an increase of metabolism. Nevertheless there is evidence that the me-

tabolism may not be affected in this manner. Thus Carey and Brumfield[35] found a low metabolic rate in 28 anxious and agitated psychoneurotics; and Gibbs and Lemcke[13] reported normal metabolisms in two depressed and agitated cases who cooperated satisfactorily. Obregia[36] and Padeano[37] denied that the basal metabolic rate was influenced by psychomotor agitation. The latter writer found an approximately equal percentage of normal, increased, and decreased readings for calm as well as for agitated cases. Extreme psychomotor agitation necessitating immobilization of the subject seemed to increase the metabolism merely because of the muscular efforts of the patient to free himself and because of the increased amplitude of the respiratory movements.

The conclusions that we are therefore forced to adopt from the work which has been done on the subject of basal metabolism in emotional states is that emotion potentially may increase or decrease or may have no effect on the metabolic rate.

The Present Study

Repeated basal metabolic determinations were performed in 105 manic-depressive patients for the purpose of investigating as completely as possible the following problems: (1) How does the basal metabolism during the active phase of a manic-depressive psychosis vary from prevailing standards for normal metabolism? (2) What fluctuations, if any, occur during the course of the psychosis? (3) Is there any appreciable difference in metabolism between manic and depressed phases of the psychosis? (4) Does the basal metabolic rate bear any relation to the severity of the psychosis? (5) How does the basal metabolism, following the recovery from the psychosis, vary from the metabolism existing during the psychosis? (6) What are the effects of psychomotor agitation or retardation on the metabolic rate? (7) How do emotions such as anxiety, elation and depression influence the basal metabolism? (8) What effects have abnormalities in muscle tonus, and nutritional and physical disturbances on the validity of the metabolic readings?

The patients selected for study were those residing on the female reception service at the Kings Park State Hospital. Only benign emotional cases in which the diagnosis of manic-depressive psycho-

sis was obvious were considered. Excluded from the group were all cases exhibiting malignant features.

The apparatus used was a Sanborn Graphic basal metabolism machine, in which the metabolism is measured indirectly by determining the oxygen consumption of the body on the basis of a respiratory quotient of .82 and the assumption that 4.825 calories of heat are produced by the body for each liter of oxygen utilized.[38] Under ordinary conditions the error involved by this method is said to be rarely greater than two per cent. The standards used were the Aub-DuBois (Sage Institute) normals. The machine was tested at frequent intervals for circulation, leakage, carbon-dioxide removal, and correctness of timing. The thermometer on the apparatus and the metabolism barometer were similarly checked. In addition a normal subject was tested regularly to check on the accuracy of the machine.

Only patients conforming with the standard requirements for basal metabolic tests were tested. A 14-hour fast and an 8-hour rest period in bed on the evening before the test were imposed. Because of the effect they might have on the readings, sedatives[39] were avoided for several days preceding the determinations. The patients were obliged to walk down a flight of stairs to the basement where the apparatus was kept, but since a further rest period of one-half to one hour was enforced prior to the test, this muscular activity was not considered significant. The patients were comfortably clothed, the room temperature was normal, and there were no drafts. Noises and other disturbing influences were absent.

To obtain a uniformity of technique all metabolic determinations were conducted by myself. No difficulty was experienced in testing the patients except in cases of violently disturbed manic patients who refused to remain quiet during the test. By means of constant reassurance most moderately hyperactive patients remained sufficiently relaxed for satisfactory determinations. The majority of depressed and agitated patients cooperated satisfactorily. Determinations complicated by muscular activity on the part of the patient were discarded. However, isolated minor muscular movements, which Benedict[40] and Lefevre[41] have shown insignificant, were not considered important. Other unsatisfactory determina-

tions were those during which the patient laughed, talked, or purposely forced respiration. A careful watch was kept for leaks due to poorly adjusted noseclip and mouthpiece.

Each test consisted of at least two consecutive determinations. Where there was a difference of more than five or six per cent between the two readings, a third determination was obtained. At the time of the test the patient's temperature, pulse and blood pressure were recorded. Patients with fever were, of course, not tested. The patient's general physical and mental condition were tabulated at the time of the test, and the psychomotor and emotional condition recorded. The objective evidences of emotion prior and subsquent to the test, and the patient's own account of her feelings during the test, constituted the data from which the emotional status was estimated.

The group of 105 manic-depressive patients consisted of 45 manic cases, 54 depressed cases, 5 mixed manic cases, and 1 circular manic case. During the course of study 57 patients recovered, 31 patients improved, 14 patients remained unimproved, and 3 patients died from intercurrent illness. Eleven patients who had recovered and had been discharged or paroled were readmitted, and of this group two patients recovered, three patients improved, five remained unimproved, and one patient died.

Basal Metabolisms During the Active Psychosis

Figure 1 represents the frequency distribution of the readings in the entire series of 441 tests taken during the active stages of the psychoses. The black area represents readings within the generally accepted normal range of +10 per cent and —10 per cent. The largest number of readings, 68.7 per cent, fell within this normal area. The unshaded areas contain the abnormal readings, 8.6 per cent of these being pathologically high, and 22.7 per cent pathologically low.

The manic group of patients, as shown in Figure 2, demonstrated the following dispersion of readings: 67.9 per cent within the range of +10 per cent and —10 per cent, 12.8 per cent pathologically elevated, and 19.3 per cent pathologically depressed.

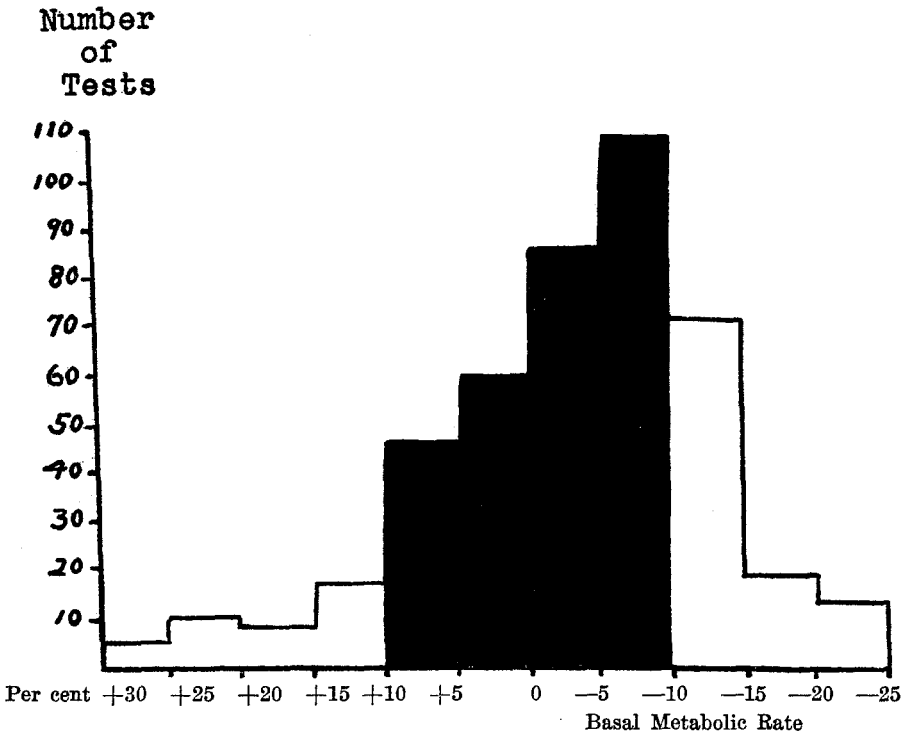

Fig. 1. Distribution of basal metabolic rates during active psychosis—all cases
Total number of metabolic tests—441
The unshaded areas represent abnormal readings

In the depressed group, illustrated by Figure 3, 70 per cent of the readings were normal, 4 per cent high, and 26 per cent low.

The 31 basal metabolic tests conducted in the five mixed manic patients revealed 20 tests within normal limits, 5 tests with high readings, and 6 tests with low readings. The circular manic patient demonstrated 3 tests with normal rates and 3 tests with abnormally low rates.

It is obvious, therefore, that while the majority of basal metabolic rates were within normal limits in the entire series of cases, a greater number of abnormal readings were obtained than one would expect in a similar group of "normal" individuals. The distribution of readings was slightly more uniform in the manic than in the depressed group, and in the former group there was relatively a greater number of elevated readings than in the latter

group. There was a general tendency toward minus readings, especially pronounced in the depressed cases. Pathologically low metabolic rates occurred rather frequently in both manic and depressed groups, but a relatively greater percentage of low readings prevailed in the depressed patients.

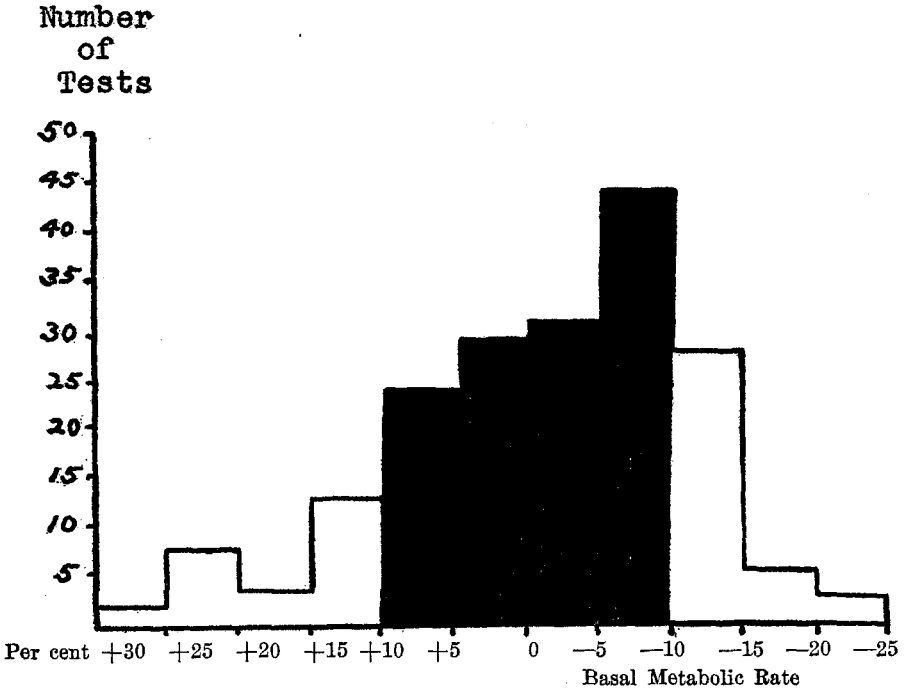

Fig. 2. Distribution of basal metabolic rates during active psychosis—manic phases
Total number of metabolic tests—187
The unshaded areas represent abnormal readings

Metabolic Fluctuations During the Course of the Psychoses

Under normal conditions the basal metabolism, like the temperature, pulse rate, and blood pressure, is fairly constant for the individual. Variations nevertheless do occur from day to day, even hourly, although Magnus-Levy,[42] Benedict and Carpenter,[43] Zuntz and Loewy[44] have shown that the deviations from the average are rarely more than 10 per cent.

Basal metabolisms obtained at various stages during the psychosis in the present study revealed in many cases variations over a wider range than is considered normal.

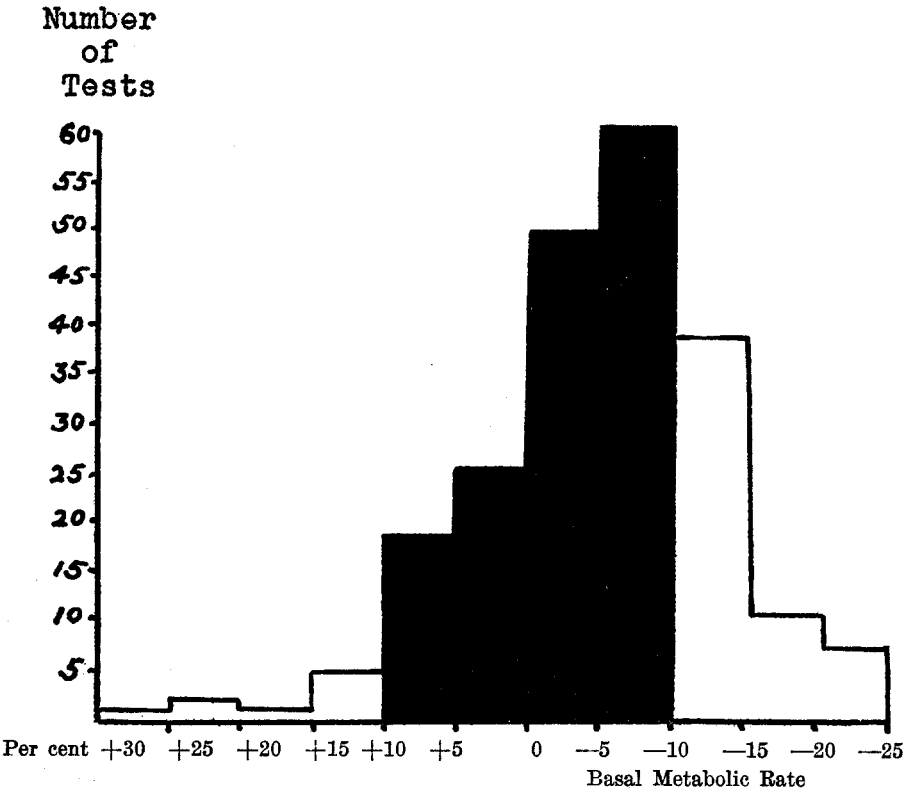

Fig. 3. Distribution of basal metabolic rates during active psychosis—depressed phases
Total number of metabolic tests—223
The unshaded areas represent abnormal readings

Changes in the depth of the psychotic reaction had no constant or sustained action on the metabolic rate. Similarly no definite influences on metabolism could be attributed to either mild or marked improvement in the mental condition, in many cases there appearing to be no change in metabolic rate, but in some instances an elevation and in others a depression of metabolism was associated.

Effects of Emotion, Agitation and Retardation on Metabolism

One of the most outstanding observations in the group of patients studied was the minimal effect of states of elation and depression on the basal metabolism. This was best illustrated in

seven cases in which there were phasic changes in emotional reaction, from elation to depression or vice versa. In all of these cases there was no pathological variation in metabolism. The fact that the mean metabolic rate tended to be higher in the manic than in the depressed patients was not believed due to emotional influences, but rather to associated muscular disturbances. In the manic series hyperactivity and elation were more commonly associated with mild muscular movements and increases of muscle tension than in the depressed series. In those depressed cases where muscle tension was increased or where tremors or mild muscular movements existed, the basal metabolism was abnormally elevated regardless of the depth of depression. The fact that reactions of anxiety and fear are frequently accompanied by muscular disturbances may similarly explain the associated high readings reported in these states. In relatively few cases was an increased adrenalin output believed provocative of rises in metabolism, although it was difficult to establish definitely this fact apart from observing the absence of noteworthy changes in pulse rate and blood pressure.

Psychomotor agitation unaccompanied by gross muscular disturbances had no discernible effect on the metabolic rate. Where an elevation of metabolism was present there was almost inevitably associated some muscular involvement. Psychomotor retardation similarly had no characteristic influence on the readings, except where muscle tonus was extraordinarily diminished as in the stuporous cases.

Effect of Mental Recovery on Basal Metabolism

The basal metabolism of the psychotic patient upon mental recovery presumably would be a better indication of his true metabolic rate than average prediction standards. A comparison of the metabolic rate during the active psychosis with the metabolism upon recovery might perhaps indicate the effect of the psychosis on metabolism. Table II is a comparison of the basal metabolic rates during the active psychosis with the rate upon recovery.

TABLE II. COMPARISON OF METABOLIC RATES DURING THE PSYCHOSIS AND UPON RECOVERY

Case number	Diagnosis	Range variation BMR in psychosis, per cent	Mean BMR, in psychosis, per cent	Mean BMR, in recovery, per cent
1	manic	— 8.6 to —13.0	—10.8	— 6.3
2	mixed	+18.2 to —10.6	— 1.7	— 0.8
5	manic	+29.1 to — 4.7	+14.6	— 7.2
6	manic	—15.9 to —22.3	—19.2	—23.8
10	manic	+14.7 to — 3.5	+ 2.4	— 2.9
12	depressed	+ 2.0 to — 6.7	— 3.6	— 8.2
13	manic	+ 9.7 to —14.7	— 4.2	— 8.4
15	manic	+12.2 to —14.6	— 4.9	— 7.7
17	manic	+18.1 to —14.6	— 4.5	— 4.6
18	manic	+10.3 to — 8.3	+ 2.9	— 7.9
20	depressed	+ 2.1 to —13.2	— 6.9	+ 8.3
21	manic	+11.6 to + 4.1	+ 7.9	+ 1.3
22	depressed	0 to —18.2	—12.9	— 6.4
23	manic	+ 3.5 to — 4.3	— 0.6	+ 8.1
25	manic	+12.7 to + 4.8	+ 8.1	+ 0.2
26	manic	+ 6.2 to —14.7	— 5.2	—10.1
27	depressed	+ 7.9 to + 3.1	+ 5.6	+ 0.3
28	manic	— 1.8 to —18.3	— 9.8	+ 6.8
29	manic	+ 5.0 to — 7.4	+ 0.7	+12.1
31	depressed	—14.1 to —22.3	—17.8	—18.2
32	depressed	+22.7 to + 3.8	+10.9	+ 0.1
33	manic	+22.8 to —11.5	+ 6.5	— 0.7
34	depressed	— 2.1 to —14.6	— 9.7	— 5.2
35	depressed	+ 5.2 to — 1.7	+ 2.4	— 8.9
36	manic	+24.1 to — 6.3	+ 6.4	+ 5.2
40	manic	+ 5.2 to —12.7	— 0.5	+11.4
41	manic	+12.6 to — 2.3	+ 6.9	— 5.9
42	manic	+14.7 to + 3.5	+ 8.5	+ 6.5
43	depressed	— 3.4 to — 7.8	— 5.6	+ 5.5

TABLE II. COMPARISON OF METABOLIC RATES DURING THE PSYCHOSIS AND UPON RECOVERY—(*Concluded*)

Case number	Diagnosis	Range variation BMR in psychosis, per cent	Mean BMR, in psychosis, per cent	Mean BMR, in recovery, per cent
44	manic	— 2.9 to —11.6	— 7.0	— 0.1
48	depressed	— 2.1 to — 8.6	— 6.0	— 3.9
50	manic	+ 3.2 to — 8.1	— 0.8	+ 5.3
51	depressed	+ 6.3 to —18.6	— 6.9	+11.6
52	depressed	+ 7.3 to + 4.0	+ 5.6	+ 1.6
54	manic	—10.1 to —13.2	—11.6	— 8.6
55	depressed	—12.9 to —16.5	—14.7	— 4.0
59	depressed	—12.1 to —16.1	—13.2	— 4.3
60	manic	+12.3 to —11.3	— 2.8	+ 6.1
62	depressed	— 3.2 to —21.8	—11.5	— 8.1
63	depressed	+22.0 to — 3.0	+ 5.6	— 7.2
65	depressed	+ 9.2 to — 9.4	+ 2.1	— 8.6
66	depressed	+ 1.2 to —11.4	— 5.9	— 3.5
67	manic	+ 1.3 to — 5.0	— 2.6	— 2.9
69	depressed	— 3.7 to — 9.0	— 7.1	— 6.2
70	manic	— 5.3 to —10.2	— 7.6	— 6.5
71	depressed	— 3.5 to — 9.0	— 7.0	— 0.6
72	manic	— 5.9 to — 7.1	— 6.5	— 2.0
76	depressed	+ 3.6 to — 2.1	+ 0.7	— 7.5
78	depressed	— 7.2 to — 8.5	— 7.9	— 5.6
80	manic	+ 3.8 to — 7.4	— 3.4	+ 2.6
81	depressed	—11.6 to —23.6	—17.2	—16.3
85	manic	+12.3 to —11.8	+ 3.1	+ 1.0
88	manic	+ 9.0 to — 8.6	— 1.9	+ 5.8
91	manic	— 4.3 to — 6.1	— 4.9	+ 1.9
95	depressed	— 2.0 to — 7.3	— 5.3	—10.6
96	depressed	+32.2 to —14.2	+ 8.2	+20.6
100	manic	— 8.7 to —16.1	—12.3	— 6.4

Although individual tests showed numerous abnormal readings, mean metabolic rates were abnormal in only 12 patients. The cases fell roughly into the following groups: First, those in which all metabolic tests during the psychosis yielded normal readings; second, those in which at least one test was elevated; third, those in which at least one test was low; and fourth, those in which both pathologically low and high rates were obtained. In the first group there were 20 patients, 18 of whom demonstrated normal metabolic rates upon recovery, 1 an increased rate, and 1 a decreased rate. In the second group of 11 patients, there were 10 cases in whom the recovery metabolism was normal, and 1 case in whom there was no change in metabolism. There were 20 patients in the third group, 14 of whom showed normal metabolisms on recovery, 2 an increased rate, and 4 no change. In the fourth group there were 6 patients, all of whom demonstrated normal rates upon recovery.

Factors of Physical Illness and Nutrition

Approximately 13 patients suffered from an associated physical illness, the various diagnoses being hypertension, emphysema, arteriosclerosis, mitral regurgitation, carcinoma of the uterus, hypertrophic arthritis, cardiac arrhythmia, ulcerative colitis and sciatic neuralgia, hypertension and hypertensive heart disease. Except perhaps for one case who demonstrated a terminal cardiac decompensation, the basal metabolic rates were not believed significantly affected by the physical illness.

Objective evidence of endocrine disease was lacking in all except five cases. The first, who demonstrated constant low basal metabolisms, had had a thyroidectomy performed some years before for an exophthalmic goitre, and apparently was suffering from a hypothyroid condition. Two other cases showed physical signs of hypothyroidism along with lowered metabolic rates. The fourth case demonstrated a girdle obesity and male hair distribution, but the basal metabolism was normal. The fifth patient had the physical stigmata of acromegaly, but there were no abnormalities in the basal metabolism.

Although undernutrition occurred in 20 patients of the group, basal metabolisms were depressed in only eight cases. In five cases

the readings were normal, and in seven cases they were actually elevated. It is interesting to speculate that in those undernourished patients with normal or elevated metabolic rates, factors which increased metabolism were coexistent, although it must be frankly admitted that in most instances such factors were not discernible. In five patients in whom metabolism was reduced, presumably on the basis of undernutrition, mental improvement or recovery was associated with a rise in metabolism; and in each case a gain in weight and improved nutritional condition was present. Eighteen of the patients were obese; but the condition of adiposity itself appeared to have no influence on the basal metabolism.

Discussion

In attempting to interpret the results obtained in the present study, it may be expedient to discuss in brief the factors which govern and regulate the basal metabolism of the body. It must be confessed, however, that our present knowledge of metabolic processes is relatively limited and that we are still ignorant of many important metabolic determinants.

Basal metabolism is the measure of the basal rate of oxidation in the body—the measure of the minimum chemical and physical changes compatible with life. Twenty-five per cent of the total basal metabolism, according to Krogh,[45] is accounted for by the activities of various organs of the body, and 75 per cent of the total heat produced under basal conditions is derived from cellular oxidation. The digestive tube is said to account for one-fifth of the metabolism and the muscular system for one-third; the remainder is accredited to the other tissues of the body.

The evaluation of any single basal metabolic rate involves a consideration of associated factors which may have stimulated or depressed the metabolism. Paradoxically several conditions may coexist which may simultaneously raise or lower the metabolic rate. The rate itself, therefore, is not significant of any single condition, but is merely the resultant of a number of complex factors which have varying effects on the oxidative processes.

There are four glands of internal secretion which influence the metabolic rate—namely, the thyroid, suprarenals, gonads, and ante-

rior pituitary. The principal autacoid is thyroxin, which has a slow, regular and sustained action on metabolism. Total extirpation of the thyroid gland causes a fall in metabolism of approximately 40 per cent. Overactivity of the thyroid causes a tremendous rise in metabolic rate. The suprarenal glands also have a powerful metabolic action. Adrenalin acts independent of thyroxin and its effects are immediate, irregular, and unsustained. Extirpation of the adrenals has been shown to cause a considerable depression of metabolism.[46, 47] The effects of gonadal and pituitary secretions are less definite. Removal of the gonads is often associated with a fall in metabolic rate.[48, 49] Korenchevski[50] suggests the metabolic interrelation of the gonads with the thyroid gland. The exact mode of operation is still somewhat problematic. The metabolic activities of the anterior pituitary have within recent years been thoroughly explored and it has been established that the gland is related to the thyroid and suprarenals through thyrotropic and interrenotropic hormones.

Other important factors in metabolism are muscle tonus and the nutritional status of the individual.

Muscle tone, according to DuBois,[51] is responsible for much of the basal metabolism. Clinically it is often observed that increases of muscle tonus are associated with elevations in metabolism.[52] In conditions of marked muscular relaxation, as in sleep, the basal metabolism drops below normal limits. Due to the active protoplasmic mass involved other muscular disturbances may profoundly affect the basal metabolism. The influence of muscle tremors on metabolism has been pointed out by Grafe[53] and Magnus-Levy,[54] and muscular contractions are known to raise the metabolic rate in proportion to the degree of muscular activity.

The effects of nutrition and previous diet on basal metabolism are fairly well established. Lusk[55] believes that undernutrition as a factor in itself may reduce the basal rate by as much as one-third. Starvation has a depressing influence on metabolism but even a low caloric or low protein diet may have the same effect.[56, 57, 58] Furthermore a drastic loss of weight is generally accompanied by a fall in metabolism.

It is important to realize that the basal metabolism is a labora-

tory test and as such is subject to many limitations. A number of variables are always present, such as mechanical errors, technical errors, and errors due to variations in the clinical condition of the patient at the time of the test. With technical competence, errors due to mechanical sources and errors of technique may be reduced to negligible proportions.

By far the most potent source of errors is in the patient himself. In manic-depressive conditions such errors may be considerable since a true basal state is frequently difficult to achieve. Unless carefully watched, hyperactive patients may successfully evade the preliminary rest requirements, or manage to obtain and imbibe food on the morning of the test. Uncooperativeness on the part of the patient during the test, indulgence in muscular movements, attempts to talk or to write or to laugh, voluntary holding of the shoulder girdle and abdomen taut, forced breathing, and increased tension of muscles may entirely corrupt the accuracy of the readings. Extraneous factors such as physical exhaustion and associated transitory endocrine and other somatic derangements may interefere with the validity of the determinations.

Assuming that mechanical errors have been eliminated, that technical errors have been reduced to a minimum, that the basal state is as nearly perfect as possible, and that no physical disease or abnormality is present, the basal metabolic rate in normal individuals will almost always be within the ranges of +10 per cent and —10 per cent.

Pathologically high metabolism rates are found most frequently in hyperthyroidism, hyperadrenalism, and in febrile states, and less frequently in leukemia, pernicious anemia, polycythemia, certain forms of hyperpituitarism, diabetes, terminal pregnancy, and cardiac decompensation.

Pathologically low metabolisms are found in myxedema, cretinism, cachexia strumipriva, hypoadrenalism, marked undernutrition, and certain types of pituitary insufficiency.

In each of 32 cases in the present series there was present at least once an elevated metabolic reading. Muscular disturbances, such as increased muscle tonus, muscular tremors and contractions were present in the great majority of these elevated tests. In a

few instances an increased output of adrenalin was suggested by transitory rises in blood pressure and pulse rate. In four cases elevated readings followed mental improvement or recovery and were associated with a gain in weight and improved nutritional status. Only in one case could the elevated rate be attributed to actual physical disease. Emotional conditions appeared to have no definite action in elevating metabolism, except perhaps by increasing muscle tonus, by producing other muscular disturbances, or by stimulating endocrine activity.

Not so easily explainable are the pathologically low metabolism tests obtained at least once in each of 47 cases. Eliminating the 8 undernourished cases and the 3 hypothyroid cases, there remain 36 patients who demonstrated lowered basal metabolic rates without apparent reason. Thorough physical examinations revealed in these cases no somatic disease to account for the metabolic abnormalities. This is in opposition to the contention of Fischer,[4, 5] who alleges that low metabolic readings are present only in those manic-depressive patients in whom there is associated physical disease.

Especially in retarded depressed and physically exhausted patients are decreases in muscle tonus and physical inactivity suggested as possibilities. That mental and physical inactivity may decrease the basal metabolism was demonstrated by the hypnotic experiments of Goldwyn.[59] Furthermore, it has been pointed out by Benedict[60] that profound relaxation as in sleep has a depressing action on the metabolic rate. However, in all except three stuporous cases in the present series the factors of decreased muscle tonus and physical inactivity did not seem especially prominent.

Thyroid involvement is another possibility, especially hypothyroidism without classical symptoms of thyroid deficiency, which condition Smith[61] believes not uncommon. That evidence of subnormal thyroid function is lacking in most cases of subnormal metabolisms without myxedema has been pointed out by Thurmon and Thompson,[62] McKinlay,[63] Carey and Brumfield,[64] who found that few cases responded favorably to thyroid therapy. There appears to be no real evidence that the thyroid gland is responsible for the lowered metabolism in manic-depressive conditions.

Deficiencies of the suprarenal glands as the cause of low basal

metabolisms in states of exhaustion following mental and physical strain have been suggested by Koehler,[65] and perhaps might apply to those extremely hyperactive manic patients who work themselves into states of exhaustion. However, physical signs of hyposuprarenalism were absent in all suspected cases in the present group.

Reports by various writers show that low basal metabolic rates are not uncommon even in individuals who are apparently normal. Thus McKinlay[63] examined 155 normal students, aged 17 to 35 years, at the University of Minnesota and found 27.9 per cent of the readings below normal. Boothby and Sandiford[66] discovered 103 out of 8,614 normal subjects with metabolic rates below —15 per cent, without evidence of hypothyroid disease. Wishart[67] and Means[68] have emphasized the fact that there is a group of individuals who during health habitually show metabolic rates between —15 per cent and —20 per cent without evidence of disease, whose metabolisms are apparently normal for the individual. It is therefore necessary to keep in mind the fact that the low metabolic rates obtained in some patients during the present study might have been normal for those patients. Especially suggestive are those cases in which the recovery metabolism remained subnormal.

A number of other theories have been suggested to explain pathologically low metabolic rates and fluctuations in metabolism in manic-depressives. Pötzl, Eppinger and Hess postulate a reduction of excitability of the vegetative nervous system; Stransky believes the cause to lie in an auto-intoxication by glandular products; Walker[6] attributes the reason to a decreased function of the autonomic nervous system; Wuth,[69] to disturbances of the neuro-vegetative mechanism and endocrine system; and Landis,[34] to vascular changes involving the volume-flow of blood.

Our inability to explain adequately pathologically low metabolic rates may perhaps be due to our ignorance of a great many metabolic processes and determinants. It is possible that when our knowledge of these determinants is more complete we shall be able to arrive at more satisfactory explanations.

It may be opportune at this point to emphasize the inadequacy of our present prediction standards. There is a general consensus of opinion that the Aub-DuBois standards,[70, 71] probably the most

widely used, are too high, since most of the variations within the so-called normal zone are below zero rather than above. Jenkins,[72] in a group of 34 apparently normal male university students found the mean metabolic rate to be —5 per cent. Using the same apparatus at the University of Chicago clinics, determinations on 1,126 men and 2,994 women were made and a mean metabolic rate of—9 per cent was obtained. MacLeod and Rose[73] have emphasized their opinion that metabolic standards for women are much too high. In 33 normal women Benedict,[74] using the Aub-DuBois standards, found 10 cases below —10 per cent, and an average of —7.3 per cent. Benedict concludes that the present prediction standards for women are too high and should be lowered by 5 per cent.

If we were to lower our normal zone to —15 per cent, as has been suggested, there would naturally be a larger number of tests in the present study within normal limits. Only 8 of 187 tests in the manic group and 19 of 223 tests in the depressed group would be pathologically low. In each of 17 patients a basal metabolism below —15 per cent would be present at least once. If we were to simultaneously raise the upper normal limit to +15 per cent, 12 tests in the manic group and 4 tests in the depressed group would be pathologically high. In each of 16 patients a basal metabolism above +15 per cent would be present at least once.

Conclusions

1. Repeated basal metabolism determinations in a group of 105 manic-depressive patients revealed a majority of tests within normal limits; however, the percentage of abnormal readings was greater than one would expect in a similar number of "normal" individuals.

2. In the manic group of 45 patients, 12.8 per cent of the tests were pathologically elevated, while 19.3 per cent were pathologically lowered. In the depressed group of 54 patients, 4 per cent of the tests were elevated and 26 per cent were lowered. In 5 mixed manic patients, 20 tests were normal, 5 tests were high, and 6 tests were low. In one circular manic patient 3 tests were normal and 3 tests were pathologically low. There was a general tendency

toward minus readings especially pronounced in the depressed cases.

3. Fluctuations in metabolism during the course of the psychosis were in many cases over a wider range than is considered normal.

4. The severity of the mental reaction appeared to bear little relation to the metabolic rate.

5. Psychomotor agitation and retardation, and the emotions of elation and depression had no discernible influence on the basal metabolism except in cases where muscular disturbances, such as increased muscle tonus and muscle tremors, were associated and caused increases in metabolism.

6. The emotions of anxiety and fear were occasionally accompanied by an increased basal metabolism, due probably to associated muscle disturbances and perhaps to increased adrenalin output.

7. Basal metabolism upon the advent of mental recovery tended to more normal figures than readings during the active psychosis.

8. Factors of undernutrition, physical inactivity, endocrine disorders and somatic illness accounted for a very small percentage of abnormal metabolic rates.

9. A great many abnormally elevated readings were associated with increases in muscle tonus, muscular tremors and contractions, and improved nutritional condition.

10. Although adequate explanations for the majority of depressed readings and for metabolic fluctuations were lacking, in a few cases decreases in muscle tonus, transitory endocrine abnormalities, and depression of neuro-vegetative function were suggested.

11. That a pathologically low metabolic rate may be normal for a few patients in the group is probable.

12. Average prediction standards in present use are perhaps too high and this factor may account for the tendency to minus readings. It is suggested that the Aub-DuBois standards be reduced five per cent.

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