THE SERUM CHOLESTEROL IN MENTAL DISORDERS.

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In view of the fact that cholesterol is one of the principal constituents of nervous tissue and presumably plays an important part in the functioning of that tissue, it is surprising that comparatively little attention has been given to the study of the variations of the blood cholesterol in disorders of the brain and mind. Such researches as have been published do not appear to have been based, as a rule, on any extensive number of cases, and there is rarely any attempt to analyse the results according to the actual mental state of the patient, apart from the diagnosis. It is therefore not remarkable that the conclusions of different observers have been somewhat contradictory.

Cruickshank and Tisdall (1) published their estimations of the serum cholesterol of forty psychotic patients, but the method of extraction then used is now known to be unreliable. Targowla, Badonnel and Berman (2) recorded the cholesterol content of sixty sera taken from various cases of mental disorder. They found it to be above the normal in general paralysis, chronic alcoholism and agitated melancholia, variable, but usually raised, in epilepsy and confused states, and low or below normal in mental deficiency. It was also diminished in epilepsy with marked confusion. They suggested an association between hypercholesterinæmia and vagotonia, and between hypocholesterinæmia and sympatheticotonia. Parhon, C. J., and Parhon, M. (3), found the serum cholesterol to be increased in chronic alcoholism and senile states, variable in general paralysis; variable in dementia præcox, but lowered in the chronic forms, and diminished in melancholia and also in a young imbecile. They emphasized the possibility that the serum cholesterol might be influenced by the endocrine glands. Tinel, Dupouy and Schiff (4) considered hypercholesterinæmia to be practically constant in senile conditions. Ducceschi (5) found an increase in blood cholesterol in a series of chronic alcoholics, and showed that this also occurred in dogs poisoned by alcohol. Jacobi (6) agreed with de Crinis (7) that in epilepsy the blood cholesterol is raised, and that the occurrence of a fit is associated with a further increase. Robinson, Brain and Kay (8) found that it was diminished in epileptics,

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especially within twenty-four hours of a fit, and that there was a fall in the cholesterol content of the blood during the pre-convulsive period. Goodall (9) was unable to find any marked difference between the pre-paroxysmal blood and that taken between the paroxysms. Gibbs (10) estimated the blood cholesterol in 38 cases of dementia præcox and found the figure to be low, especially when associated with a recent acute mental state. Forsyth (11) also considered it to be lower in dementia præcox than in other psychotic cases.

Stenberg (12) has recently published a review of the literature on this subject, together with the results of his own investigations on 76 female and 15 male psychotic patients. He found the blood cholesterol to be above the normal in 14 manic-depressive cases with a decrease to a normal value during a remission. In dementia præcox the value was also raised, but normal during remissions. Emotionally dulled cases had a low blood cholesterol, and in emotionally heightened cases it was raised. Only 13 cases, however, appear to have been investigated when improved as well as during the acute state.

My own investigations have been carried out during the last three years at Severalls Mental Hospital, and I am indebted to Dr. R. C. Turnbull for permission to publish the results. They are the records of male patients only, thus eliminating the fallacies introduced by the variation which occurs in blood cholesterol before, during and after menstruation. Serum was used, as the cholesterol present in blood-cells is not susceptible to metabolic variations, and the use of an anti-coagulant for the purpose of procuring plasma introduces the risk of hæmolysis. The blood was taken 2½ to 3 hours after breakfast. The estimation was carried out by drying 1 c.c. of serum in plaster-of-paris, which was then powdered, transferred to a thimble, and percolated by chloroform in an all-glass fat extractor. In all cases duplicate estimations were made, one sample being extracted for at least two hours, the other for an hour longer. The chloroform percolated the plaster at the rate of about 750 c.c. per hour, and control experiments showed that 1½ hours' extraction was sufficient. The solution of cholesterol in chloroform was transferred to a graduated test-tube, made up to 15 c.c. in volume, and estimated by the Liebermann reaction. In order to bring the unknown near to the strength of the standard, a preliminary estimation was carried out on 5 c.c. and the remaining 10 c.c. diluted as indicated. With the usual precautions taken to ensure dry reagents and the balancing of the colorimeter each time

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it was used, this method gives sufficiently accurate comparative results. No estimation was accepted in which the two results differed from their average by more than 2½%.

A series of estimations on 26 normal men gave figures varying from 145 to 199, with an average of 172. The limits of normal serum cholesterol are therefore taken as 140 and 200 mgrm. per 100 c.c. The ages of these subjects varied between 18 and 55.

Dementia Præcox.

89 cases of dementia præcox were examined. Quite early in the investigation it was observed that patients in states of confusion, excitement, agitation or depression tended to have a lower serum cholesterol content than those who were quiet or apathetic. Efforts were therefore made to carry out repeated tests on patients whose mental states showed these variations, whatever the diagnosis. The following are the main conclusions:

1. Dementia præcox patients in a dull or quiet mental state have a high serum cholesterol value. It was found to average 214 in 76 cases, and to be above the limit of normal in 47 of these.

2. In states of confusion or excessive emotion the figure is much lower—average 179 in 38 cases.

3. Of 25 patients in whom repeated estimations in varying mental states could be made, the serum cholesterol was found in 21 cases to be lower when the patient was confused, excited or agitated, than when he was quiet or apathetic; in the remaining four it was raised. The average figures for all 25 were 224 and 185, an average fall in cholesterol value of 17% accompanying the acute phase.

4. The duration of the disorder and the age of the patient (up to 54 years) have little or no influence on the serum cholesterol.

Two cases of dementia præcox may be quoted in detail:

1. Dementia præcox with recurrent confusional state:

3.1.28.	Mental state clear	Cholesterol	260
24.1.28.	Very confused	,,	145
6.2.28.	Clear	,,	245
28 2.28.	Recovering from confusion	,,	271
6.3.28.	Clear	,,	264
20.3.28.	Confused	,,	199
2.4.28.	Clear	,,	255
17.4.28.	Confused	,,	190
19.4.28.	Improving	,,	201
30.4.28.	Clear	,,	217
5.5.28.	Becoming confused	,,	172
14.5.28.	Confused	,,	173
22.5.28.	Clear	,,	256
10.7.28.	Slightly confused	,,	193

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2. Dementia præcox with recurrent state of excitement:

29.11.27.	Excitement . . .	Cholesterol	200
9.1.28.	Just recovered . . .	,,	215
24.1.28.	Clear	,,	230
6.2.28.	Excitement . . .	,,	135
28.2.28.	Clear	,,	240
22.5.28.	,, ...	,,	237

Mood Psychoses.

The cases of mood psychosis—manic-depressive insanity and involutional melancholia, excluding senile manic and depressive states—numbered 50 in all. It was found from the results in these cases that—

1. The average serum cholesterol content during the acute phase of mood psychoses was higher than the normal; the figures are 199 in 32 cases of manic-depressive insanity, 216 in 18 cases of involutional melancholia, and 205 in the whole group of 50 cases.

2. Of the 20 patients tested during a remission or on recovery, as well as during the acute phase, a rise in serum cholesterol accompanied improvement in 17 cases, a fall occurred in 1 case, and in 2 the change was insignificant. The average figures were 206 and 247 for the acute phase and improved period respectively in the series of 20 cases, 207 and 229 in the 6 involution cases, and 206 and 255 in the 14 manic-depressives. Counting one patient tested only during a remission—cholesterol 326—and not included in this group, 18 out of 21 cases were found to be above the normal limit when improved or recovered.

3. There was no constant relationship between the age of the patient and the cholesterol value during a remission or in the acute phase.

General Paralysis.

39 cases of general paralysis were examined. The figure was within normal limits in 9 cases, low in 1, and above the normal in 29. The average was 222. In only 12 cases was the estimation made both in the acute stage and during a remission after treatment; it was found that the cholesterol increased with improvement in 5 cases and was diminished in 7. This series is too small to allow any attempt to associate the cholesterol variation with the different mental abnormalities observed in general paralysis, and with the results of treatment.

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Organic Mental Disorder.

All cases of mental disorder associated with gross organic disease other than general paralysis are included in this series. The average for the 30 cases was 230. The figure was above the normal limit in 23 cases. Cerebral syphilis and organic nervous disease consequent on arterio-sclerosis are the two principal groups in this series; in the former the average figure was 256, in the latter it was 231. In one case which recovered, after prolonged arsenical treatment, from a condition of stupor associated with cerebral syphilis, the cholesterol was observed to fall from 329 to 198.

Alcoholic Psychoses.

The average figure for the 22 cases in this group was found to be 211; in the acute emotional states it was 195, and in the cases without marked emotional changes it was 225. In only 2 cases could the test be made on recovery as well as in the acute phase; in one the cholesterol value rose from 193 to 225 on recovery from a state of agitated melancholia, and in the other from 179 to 233 on recovery from a manic condition.

Imbecility.

The results in 35 imbeciles give an average figure of 178. In only 9 patients was the cholesterol value above 200, and these were nearly all very dull or else over 55 years old. In one case there was a rise from 153 to 180 on recovery from a state of excitement.

Senility.

The average in 15 cases of senile mental disorder was found to be 228. In 9 cases the figure was abnormally high.

Epilepsy.

Epileptics in a mental hospital show two important variations in mental state; they are the fit, with its loss of consciousness, and confusion, or clouding of consciousness, which may be permanent, or occasional and independent of fits, or associated with seizures. Serum cholesterol estimations were made in 20 cases of imbecility with epilepsy, and 32 cases of insanity with epilepsy. The average for the former class was 204, for the latter 217, and for the 52 cases, 212. These estimations were made

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during the patient's usual mental condition, which is distinguished as clear or confused. They show an average of 209 for the 17 cases of confusion and 213 for the 35 cases in which consciousness was clear. Imbeciles differ from other epileptics only in having a slightly lower average. 14 cases were investigated in a state of temporary confusion not associated with fits, for comparison with the figure obtained in the usual mental state. The averages were 223 for a clear mental state and 182 for the confused. In 2 cases the serum cholesterol was increased when the patient was confused; in the other 12 it was lowered, the average fall being 51, and the extremes of the fall 7 and 132. 21 cases were tested on 38 occasions within twenty-four hours of a fit; on 24 the cholesterol was diminished in association with the fit, on 12 it was increased, and on two the change was insignificant. The figures offer no definite evidence to associate the cholesterol variation with the fit or with the pre-paroxysmal phase, owing to the difficulty of arranging for the blood test to be made shortly before a seizure. On only one occasion was this possible; in this case the serum cholesterol was 217 twenty-five minutes before a fit, 152 ninety minutes after the attack, when there was no confusion, and 161 on the following day when confused, 4½ hours after another fit. The next day, when the mental state had cleared, it was 250, and on the following day it was 192. The inter-paroxysmal figure was 213.

It is of interest to ascertain whether any variation occurs in association with epileptiform seizures in cases other than those of so-called idiopathic epilepsy. Two such cases have been under observation.

1. A case of fits and intermittent confusion caused by cerebral cysts:

1.1.29.	Mental state clear . .	Cholesterol	232
4.2.29.	Confused	,,	228
5.2.29.	More confused . . .	,,	236
7.2.29.	Clear	,,	236
22.2.29.	Very confused, 40 min. after fit	,,	228
28.2.29.	Confused for last six days .	,,	197
5.3.29.	Still confused, but less so .	,,	198
9.10.29.	After numerous seizures .	,,	248

2. A case of epidemic encephalitis:

26.3.29.	In a hypomanic state . .	Cholesterol	219
12.12.29.	In *status epilepticus* . .	,,	290

Conclusions cannot be drawn from the second case, on account of the long interval between the two tests, but the first showed that neither confusion nor a fit affected the cholesterol content, except that after prolonged confusion it was lowered.

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These records are completed by the inclusion of two cases of delusional insanity of unknown cause, the serum cholesterol being 164 and 174, and of one case of obsessional state, cholesterol 188.

Summary and Conclusions.

This investigation was carried out on 336 cases of mental disorder of various types. It shows that in the dull, quiet group of dementia præcox cases the serum cholesterol is high, surpassing the normal limit in the majority of cases. It is also raised in most cases of manic-depressive insanity and involution melancholia, and still more so in these cases during a remission. In general paralysis it is variable, but much more frequently above than below the normal, and there is no constant change as the result of treatment. It is high in the majority of cases of psychosis associated with gross organic disease, in alcoholic mental disorders, and in most cases of senile psychosis. It is usually within normal limits in imbeciles, except when complicated by epilepsy. An increase is also found in "insanity with epilepsy." It appears that a high serum cholesterol value is to be expected in all types of mental disease, but not in imbecility.

The variations which occur with changes in the mental state are equally definite. Patients in a confused condition, or with excessive emotional reaction, have a lower serum cholesterol content than others in the same psychiatric group, unless the confusion is of very long duration, as in those epileptics who are always confused, when there is little difference. This diminished cholesterol is observed in the confusion or mood changes of dementia præcox, manic-depressive insanity, involutional melancholia and alcoholic psychoses, in the occasional confusion of epileptics, and frequently in association with the epileptic fit. By repeated tests on the same patient in varying states the fall in cholesterol associated with the acute condition was demonstrated in 52 out of 61 cases of dementia præcox, mood disorder, alcoholic psychosis and epilepsy (exclusive of the fit). It was also found in one imbecile thus investigated. It is not dependent on a high initial cholesterol value, since similar fluctuations occur when the cholesterol during the remission is within the normal limits. It is probable that such variations occur in all types of mental disorder, and it appears likely that a fall in blood cholesterol accompanies emotional reaction in the healthy individual.

So slight is our knowledge of cholesterol metabolism that it is

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impossible to do more than speculate on the cause of the increased blood cholesterol in mental diseases. The fall observed in acute mental states, and here suggested to be a normal accompaniment of emotion, indicates that the blood cholesterol is influenced by the central nervous system, probably by way of the sympathetic and endocrine gland systems. The nature of this influence and its biological value offer a wide field for research in cholesterol variations, not only in the insanities, but in the neuroses and in sound mental health. Further investigations are being carried out, and will be made the subject of a future communication.

References.—(1) Cruickshank and Tisdall, *Journ. Ment. Sci.*, 1916.—(2) Targowla, Badonnel and Berman, *L'Encéphale*, 1923.—(3) Parhon, C. J., and Parhon, M., *ibid.*, 1925.—(4) Tinel, Dupouy and Schiff, *ibid.*, 1925.—(5) Ducceschi, *Annali d'Igiene*, 1920.—(6) Jacobi, *Monats. f. Psych. u. Neur.* 1926–27.—(7) De Crinis, *Monog. aus dem Gesamtgebiete der Neur. u. Psych.*, 22.—(8) Robinson, Brain and Kay, *Lancet*, 1927, ii.—(9) Goodall, *ibid.*, 1929, i.—(10) Gibbs, *Amer. Journ. of Psychiat.*, 1925.—(11) Forsyth, *Journ. Ment. Sci.*, 1926.—(12) Stenberg, *Acta Med. Scand.*, 71 and 72.

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