# SERUM CHOLINE ESTERASE AND DEPRESSION.

By DEREK RICHTER, M.A., B.Sc.Oxon., Ph.D.Munich, and MARGARET LEE, M.Sc.Manitoba.

From Mill Hill Emergency Hospital, London, and the Central Pathological Laboratory (L.C.C.), West Park Hospital, Epsom.

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WHILE investigating the serum choline esterase activity in anxiety states, a series of successive new admissions to the Neurological Section of the Mill Hill Emergency Hospital were tested with a view to obtaining further information as to the types of cases giving abnormally high or low esterase activities.

Sera giving abnormally high esterase activity were generally found to come from patients who had been diagnosed on admission as anxiety states, but an exception was noted particularly in the case of one patient (P. M—) with the very high esterase activity of 169. This patient was described on admission as " always emotional ; he feels like weeping when the National Anthem is sung ; not afraid of dangers." He complained of uncontrollable weeping in company and he had considered suicide. Both from our own observation and from that of others it appeared that he was not a particularly anxious person, but he was extremely depressed. This observation raised the question of whether anxiety is the only emotional condition in which the serum esterase activity is raised or whether it may not also be raised in severe depression.

It appeared that information on this point might be obtained by analysing the data which had accumulated in testing the new admissions, which consisted of a varied collection of patients suffering from anxiety states, depressive states, hysteria and other neurological and mixed conditions. The possibility of subsequent analytical treatment was not considered at the time when the data were collected and the diagnoses were made by more than 12 different physicians who were known to differ to some extent in their diagnostic criteria. For this reason it was hardly expected that the results would be extremely clear-cut, but in actual fact the analysis brought out surprisingly clearly the differences in serum choline esterase activity in different types of neurotics. The diagnoses were made without a previous knowledge of the esterase activities and were therefore unbiased in this respect ; we are indebted to the physicians for their permission to make use of them.

*Methods.*—The method of estimating the serum choline esterase was the same as was described in the preceding paper (Richter and Lee, 1942), except that venous blood from the arm was used instead of capillary blood. In some of the estimations acetylcholine bromide was used instead of the chloride. The bromide ion caused a slight inhibition of the enzyme which was corrected by multiplying by the factor 1·06, which was determined empirically by carrying out estimations on the same sample of serum with the chloride and bromide at the same time. The control group consisted of the 12 normal and 12 surgical patients described in the preceding paper ; the mean serum esterase activity for the 24 controls was 75 units. The various esterases occurring in blood have been described by Richter and Croft (1942).

## STATISTICAL ANALYSIS.

The most promising method of analysis appeared to be to divide the patients into groups that would be as homogeneous as possible from a diagnostic point of view and compare the mean esterase activities of the different groups. Out of the total of 169 patients who were tested at random as unselected new admissions there were 27 who were given the main diagnosis of " Hysteria " or " Hysterical amnesia,



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aphonia, etc." In 4 of these hysterics, anxiety or other complicating features were mentioned in the diagnoses; these were therefore discarded, leaving a group of 23 hysterics in whom no other features were specifically mentioned in the diagnoses. The mean esterase activity for this group was 86, which was slightly higher than the value 75 obtained for the control group, but which did not differ significantly from it when examined statistically by Fisher's "*t*" test. The mean activity of 86 found for the hysterics was very close to the mean activities of 77 and 83, which were previously found by Tod and Jones (1937) for hysterics and normals respectively.

TABLE I.

| Number of cases. | Diagnosis. | Mean esterase activity. | Per cent. above normal. | Range. | S.D. | *t*. | *P*. |
|---|---|---|---|---|---|---|---|
| 24 | Normal and surgical | 75 | 0 | 35–112 | 21 | — | — |
| 23 | Hysteria | 86 | 15 | 61–108 | 17 | 1·55 | 0·15 |
| 41 | Miscellaneous neurological, etc. | 85 | 13 | 44–136 | 22 | 1·79 | 0·08 |
| 7 | Mild depressive state | 85 | 13 | 69–104 | 11 | 1·15 | 0·25 |
| 53 | Anxiety state | 95 | 27 | 35–137 | 20 | 3·9 | <0·01 |
| 27 | Depressive state | 96 | 28 | 65–169 | 23 | 3·29 | <0·01 |
| 11 | Anxiety and depression | 103 | 37 | 59–126 | 19 | 3·59 | <0·01 |
| 7 | Post-concussional state | 108 | 44 | 66–126 | 23 | 3·4 | <0·01 |

Differences from the normal mean are taken as significant when $P<0.01$, which means that the probability is greater than 100 to 1 that the observed difference is real and not due to chance.

There were 53 patients in whom the main diagnosis was "Anxiety state" or "Anxiety" without any mention of depression; the mean esterase activity for this group was 95, which showed a considerable increase over the control group. The difference was significant by Fisher's "*t*" test. A small group of 7 patients diagnosed as "Mild depressive state" gave a mean activity of 85, which was only slightly above the normal; but a group of 27 patients diagnosed simply as "Depressive state" or "Depression," without any mention of anxiety or other complicating factors, gave a mean activity of 96, which was significantly higher than the normal. A group of 11 patients diagnosed as both anxious and depressed gave the very high mean of 103. These figures gave clear evidence of a tendency for the serum esterase activity to be high in depression.

Of the remaining patients it was noted that several who were diagnosed as "Post-concussional state" came out with prominently high esterase activities. It therefore appeared justifiable to consider these "post-concussive states" together in a separate group which gave a mean again significantly above the normal. Some of those with post-concussional states were definitely anxious and depressed, but there were not sufficient data to decide whether the high esterase activities in this group should be attributed to the emotional state or whether it was a more direct consequence of the cerebral damage.

The finally remaining 41 patients who were left over from the groups already discussed consisted of a heterogeneous collection of those with diagnoses such as "Psychopathic personality" and mixed neurological conditions; they gave a mean esterase activity of 85, which did not differ significantly from the control group.

### *Groups of Highest and Lowest Esterase Activities.*

An alternative method of analytical approach is to take two groups of subjects with the highest and lowest esterase activities and compare them with respect to their emotional state. This method is less reliable and more subject to error than the preceding method, but nevertheless it brings out certain facts which might otherwise not be clear and helps to define the types of patients that tend to give the highest esterase activities.

Of the total of 205 subjects who were examined (12 normals, 12 surgical controls, 12 selected anxiety neurotics and 169 new admissions taken at random) there were 8 with serum choline esterase activities below 50 and 10 with activities above 130. These two levels were therefore taken as arbitrary limits since they gave high and low groups of approximately equal size.

*High activity group.*—In the group of 10 with esterase activities above 130 there

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were 9 who were diagnosed as anxious or depressed or both. The remaining one was diagnosed as " Psychopathic personality with hysterical features," but he was apparently not free from anxiety, since it was stated in describing his mental condition on admission—" He is an anxious, unstable type of man." Apart from the

TABLE II.—*Group with High Serum Esterase Activity.*

| No. | Diagnosis. | C.E. | Complaint. | Mental condition on admission. |
|---|---|---|---|---|
| 1. | Anxiety state with depressive features | 153 | Enuresis; nervousness; anxiety dreams | " Mood is one of depression, without self-deprecation, and considerable anxiety. He is preoccupied with war experiences and family worries." |
| 2. | Depression | 169 | Afraid to be alone; weeping in company | " Always emotional; he feels like weeping when the National Anthem is sung; not afraid of dangers. Has considered suicide." |
| 3. | Anxiety state and mild depression. Not typical effort syndrome | 168 | Breathlessness; palpitations | " Mentally depressed. Thin, ill-looking man; serious tending to anxious expression." |
| 4. | Anxiety state with hysterical features. | 130 | Sleepless in air raids. Shakes when bombs drop. Fits | " Anxious and somewhat depressed with facile weeping." |
| 5. | Depressive state | 132 | Depression | " Depressed, tearful, over-conscientious, easily worried." |
| 6. | Psychopathic personality with hysterical features | 135 | Headaches, dizziness, loss of consciousness, feels anxious | " Consistently complaining of some pain or ache. He is an anxious, unstable type of man." |
| 7. | Acute anxiety neurosis with depressive and hysterical features | 134 | Jumpiness; anxiety; depression; tremor | " Shows marked anxiety at any loud noise and will weep and run out of the room at the sound of gunfire. He appears depressed." |
| 8. | Effort syndrome. Angina pectoris. Anxiety | 131 | Praecordial pain; breathlessness; palpitations; giddiness | " Nervous type of man. Patient is worried re family. Bangs of guns startle patient. Often feels he is going to die with palpitations." |
| 9. | Anxiety state originating from head injury | 132 | General nervousness | " He is mildly depressed and anxious. Worried over financial difficulties. Anxious expression and tendency to stutter." |
| 10. | Anxiety state with hysterical features | 137 | Stammering; stiffness of right leg; general shakiness; fainting attack | " Very agitated and apprehensive in his behaviour. Mood one of some anxiety, but most of the agitation appears to be hysterical." |

diagnoses, the descriptions of the mental condition on admission gave evidence of a marked general tendency towards anxiety or depression in this group. The condition was also generally severe, as was shown by the fact that 8 of the 10 patients in this group were recommended for discharge from the Army (Category " E ").

*Low activity group.*—In the group of 8 subjects with low esterase activities there came two of the normal and two of the surgical controls. Only one of this group, diagnosed as " Anxiety state after bombing," was described as being anxious. He was discharged after 20 days in hospital with the recommendation, " He should be fit for work in a few weeks."

Patient No. 7, who was diagnosed as " Endogenous depression," differed from the other depressed patients in that his condition was of long standing, and he had previously been admitted to a mental hospital with a depressive illness some 6 years before the war. He was depressed in the sense of being retarded, but he was not acutely emotional like most of the patients in the " Depressive state " group.

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TABLE III.—*Group with Low Serum Esterase Activity.*

| No. | Diagnosis. | C.E. | Complaint. | Mental condition on admission. |
|---|---|---|---|---|
| 1. | Normal | 41 | *Nil* | Normal. |
| 2. | ,, | 35 | ,, | ,, |
| 3. | Surgical | 46 | Surgical | ,, |
| 4. | ,, | 47 | ,, | ,, |
| 5. | Addisonian anaemia | 49 | Loss of appetite; headaches; indigestion; weakness | *Nil* abnormal mentioned. |
| 6. | Cerebral tumour | 48 | No complaints; referred for observation | "Mood one of apathetic listlessness with periods of depression." |
| 7. | Endogenous depression | 44 | Nervousness; depression | "Co-operative but depressed, retarded and vaguely suspicious. Takes little interest in his surroundings." |
| 8. | Anxiety state after bombing | 35 | Memory defect; headaches; nervousness | "Irritable. Jumps with noises. Feels he can do his work now except for remembering details." |

In spite of the few exceptions that have been discussed, it was clear that the two groups selected on the grounds of their high or low choline esterase activities were extremely different when judged from a psychiatric point of view. The group with high esterase activity was characterized by a marked predominance of patients who were anxious or depressed.

## DISCUSSION.

The data presented in the present paper give evidence that the serum choline esterase activity tends to be raised (*a*) in acute depressive states and (*b*) in certain "post-concussional states" as well as in anxiety. Groups of hysterics, mildly depressed neurotics and mixed neurological patients did not differ significantly from the normal in their serum esterase activity.

The high esterase activities found in depressed cases might at first appear to disagree with the results of Tod and Jones (1937), who reported normal esterase activities in depressive states; but their work was done with different material in that they used depressed psychotics (involutional melancholics and manic-depressives) in their investigation. It must be concluded that either (*a*) the emotional condition in the acutely depressed neurotics that we have investigated differed significantly from that of the depressed psychotics examined by Tod and Jones, or (*b*) that the serum esterase activity reverts again to the normal in depressive states of very long standing. It has frequently been pointed out (Whitehorn, 1938) that the main physiological concomitants of emotion are closely similar in anxiety, depression, anger and fear; these physiological reactions depend for the most part on the visceral and circulatory changes due to the increased activity of the autonomic nervous system, particularly in the sympathetic division, and the finding of an increased serum esterase activity in anxiety and depression agrees with many other observations as to the similarity of the physiological changes in these emotions.

From a statistical point of view the most significant of the correlations was that between high serum esterase activity and the combination of anxiety and depression which was generally described in such terms as "Anxiety state with depressive features." The summarized notes included in Table II under the heading "Mental condition on admission" give a fair indication of the types of patients in whom the serum esterase activity tended to be high, but this point would appear to require further and more detailed investigation. The high esterase activities found in the seven "Post-concussional states" was not anticipated, and it is not yet clear whether this is to be related to the emotional condition or whether it is a more direct result of injury to the central nervous system.

Stedman and Russell (1937) regarded the serum choline esterase as serving the purpose of destroying any acetyl choline that may escape into the blood from the tissues. Tod and Jones (1937) suggested that the raised serum esterase activity in anxiety might act as a physiological mechanism to combat the increased output of acetyl-choline due to the increased autonomic activity. Against this very

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attractive hypothesis it must be pointed out that the esterase activity of the serum is small in comparison with the activity of the tissues, where most of the acetylcholine destruction would be expected to occur; it is therefore unlikely that the relatively small increase in serum esterase activity in anxiety can be significant in acting in this way.

High serum esterase activities have hitherto been found in (*a*) severe anxiety, (*b*) acute depressive states, (*c*) thyrotoxicosis and (*d*) " post-concussional states." The most obvious factor which is common to all these conditions is the over-action of the autonomic nervous system, and it seems reasonable to infer that the high serum esterase activity may be related to this. Randall and Jellinek (1939) found that the serum choline esterase activity in schizophrenics was increased significantly by " shock " therapy with insulin and this result again supports the view that the serum esterase activity is related to the autonomic activity, since it is believed that the sympathetic activity is increased as a result of insulin " shock " therapy (Gellhorn, 1938). The evidence at present available is insufficient to justify any conclusions being drawn as to the reason for the observed changes in esterase activity or the way in which these changes are brought about, but there is considerable evidence that a high serum esterase level tends to be associated with conditions in which there is an abnormally high autonomic activity. Apart from thyrotoxicosis or cerebral damage the serum choline esterase activity tends to be high in conditions of severe emotional tension, which may be either anxious or depressive in character.

The serum choline esterase activity is influenced by a number of different factors, which account in part for the large range of activities found in normal individuals. In view of the considerable extent of the normal range (35–112) it cannot be expected that individual values will correspond closely with the intensity of the emotional state; but the correlation between high serum choline esterase activity and emotional state becomes evident in those individuals with activities that are well above the normal range, and in groups which are large enough for the individual variations to cancel out so that they give a satisfactory mean.

## SUMMARY.

(1) A statistical analysis has been made of the data obtained from estimating the serum choline esterase activity in 205 neurotic patients and controls.

(2) High serum esterase activities, differing significantly from the normal, were observed in (*a*) acute depressive states and (*b*) " post-concussional states " as well as in anxiety states. Groups of hysterics, mildly depressed neurotics and mixed neurological cases did not differ significantly from the normal in esterase activity.

(3) The significance of these results is discussed.

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## REFERENCES.

GELLHORN, E. (1938), *Arch. Neurol. Psychiat., Chicago*, **40**, 125.
RANDALL, L. O., and JELLINEK, E. M. (1939), *Endocrinology*, **25**, 279.
RICHTER, D., and CROFT, P. G. (1942), in press.
RICHTER, D., and LEE, M. (1942), preceding paper.
STEDMAN, E., and RUSSELL, W. R. (1937), *Biochem. J.*, **31**, 1987.
TOD, H., and JONES, M. S. (1937), *Quart. J. Med.*, **6**, 1.
WHITEHORN, J. C. (1939), *Interrelationships of Mind and Body*, p. 256.

https://doi.org/10.1192/bjp.88.372.435 Published online by Cambridge University Press