The Alkalinity of the Blood in Mental Diseases.(1) By ROBERT PUGH, M.D.(Edin.), Assistant Medical Officer, London County Asylum, Claybury.

DURING the past year I have been engaged in a research on the reaction of the blood in various forms of mental disease. Whilst this and previous similar researches by other workers have not so far contributed largely to our knowledge of the pathology of mental diseases, several important results have been obtained which have a direct bearing upon the treatment of these diseases, especially that of epilepsy. I will shortly describe the method used in the research, the physiology and pathology of the blood-serum, and the variations which the alkalinity of the blood undergoes in various forms of mental disease.

Method.—Under normal conditions the reaction of the human blood is alkaline. The alkalinity is due to the presence of two salts, bicarbonate of soda, $NaHCO_3$, and disodic phosphate, Na_2HPO_4. These two salts are acid salts, and are readily dissociated when brought in contact with litmus, forming a coloured salt. Thus the blood is an alkaline fluid in virtue of these two salts, which are bases in combination with very weak acids.

Up to the present time various investigations have been carried out and different methods used to estimate the alkalinity of the blood. The earlier investigators used the titration method with the organic acids. Zuntz (1) titrated with phosphoric acid, Lassar (2) with oxalic acid. These methods were improved upon by Landois (3) and this has been in extensive use; the objections to this method are that for clinical purposes it is too elaborate, that too much blood is required, and it takes too much time. The method used in this investigation is that introduced by Wright (4). This method has obvious advantages over the others, and these are, the quantity of blood required is small; the red blood-corpuscles are completely separated from the serum; the alkalinity can be tested in a few hours, during which time the stable equilibrium of the serum and plasma is fixed—and from a clinical point of view the alkalinity of the serum is the more important, because it comes into such close contact with the tissues, and

may be taken as an index to the changes taking place in the circulating blood.

The method requires a brief description. The necessary apparatus consists of a couple of glass tubes for receiving the blood, which is drawn off from the thumb; of one or two capillary pipettes for measuring and mixing the serum with the titrating acid; and of half a dozen watch-glasses. The blood-tubes and the capillary pipettes are made by drawing out pieces of ordinary glass tubing, after heating in a flame. The necessary reagents consist of (*a*) red litmus paper; and (*b*) a series of dilutions of a standardised solution of sulphuric acid.

The thumb is cleansed with soap and water, and sterilised with a 5 *per cent.* solution of formalin; a solution of carbolic acid is inadmissible, as it interferes with the reaction of the blood. The thumb is pricked with a blunt-pointed instrument, and a copious supply of blood is obtained.

The tube must be filled in such a manner that one of the ends may remain perfectly free from the blood. The ends of the tube are then sealed up in the blowpipe flame; the tube is inverted and suspended for a period varying from three to twenty-four hours. A capillary pipette is inserted into the serum, and the serum is allowed to flow in until it occupies 2 cm. of the stem of the capillary pipette; then a mark is made with a blue pencil. The end of the pipette is now quickly inserted into a solution of acid of a known strength, and the acid solution allowed to run in until the lower end of the serum column runs up to the blue mark. In this way an equal quantity of serum and an acid of known strength is obtained. The contents of the tube are blown out on to a clean watch-glass and thoroughly mixed with the end of the pipette. This process is repeated until the contents of the tube are thoroughly mixed. Finally, a series of drops is blown on to the surface of the litmus paper, the reaction is noted, and if the neutral point has not been accurately estimated, fresh titrations are carried out with acids of greater or less strength until the neutral reaction is obtained.

The alkalinity has been returned as the amount of H_2SO_4 in 1 c.c. of acid, which would exactly neutralise 1 c.c. of blood-serum. Thus, by the result, alkalinity 1·385, is meant, that 1000 c.c. of a solution containing this amount of H_2SO_4

would exactly neutralise the alkaline properties of 1000 c.c. of the blood-serum.

Physiology.—The alkalinity undergoes a diurnal variation, being lowest in the morning, gradually rising in the afternoon, becoming less again in the evening (5). It is *increased* during digestion owing to the passage into the circulation of sodium carbonate, which is formed by the production of HCl acid from the sodium chloride in the cells of the stomach. It is *decreased* after severe muscular exercise, owing to the entrance into the circulation of the acid products of muscular metabolism, *e. g.*, sarco-lactic and carbonic acids. Apart from these two conditions, the alkalinity is maintained at a constant level, and may be taken as an index to the amount and activity of oxidation within the tissues, between the blood and the various tissues; also upon it depends the activity, the well-being, and the fighting power of the leucocyte. Recent observations tend to suggest that there is a relationship between the alkalinity and immunity, that the higher the alkalinity the more resistent is the individual to disease from bacterial infection.

Pathology.—Numerous observations are recorded noting the changes in the alkalinity in disease. These changes are constant, and manifest themselves in a lowering of alkalinity, probably owing to the presence in the blood of acid products, lactic, uric, and butyric acids.

1. *In diseases of the blood.*—Simple anæmia; pernicious anæmia; leucocythæmia.

2. *In febrile and cachectic conditions.*—The diminution in fevers is probably due to the insufficiently oxidised acid products formed by the tissue destruction.

3. *In all toxic conditions.*—In diabetes, and especially in diabetic coma; in uræmia, jaundice, gout, and rheumatism.

4. *In certain mental diseases.*—Especially in epilepsy (6) and general paralysis (7).

In obtaining the normal alkalinity, control cases have been selected from the staff of Claybury Asylum—the physicians, clerks, and attendants. Care was taken to avoid the times during which the alkalinity is said to vary, *e. g.*, after food and after severe muscular exercise. Blood was taken at a stated time, 11 a.m., on successive days from each case; the highest value obtained was 1·806, the lowest 1·538. In all, twenty

cases were examined, and these cases showed an average of 1·662. The reason why the control cases are not taken from one class is to show the constancy of the alkalinity—that in spite of the different conditions of living, such as diet, habits, etc., the alkalinity is maintained at a constant value, and varies within physiological limits.

Epilepsy.—Blood was taken from each patient at 11 a.m. on successive days.

a. During the inter-paroxysmal period. (By this is meant a minimum interval of seven days between the seizures.)

b. During the aura.

c. After the paroxysm, a period varying from ten minutes to twenty-four hours after a fit.

Forty cases were examined.

I will select one case, and describe shortly the changes in the alkalinity:

A. B—, æt. 18. Duration of epilepsy, four years; bodily condition fair.

Family History.—Father intemperate, died of acute Bright's disease, aged 36; mother alive and healthy; six children, four boys, two girls. Patient is the fifth child; the youngest child is also an epileptic.

History of Fits.—Developed his epilepsy when nine years of age. His mother states that he had a fall on his head when six. On an average has seven fits a month; grand mal; two minutes before a fit his right eyelids twitch. Recovery from mental confusion takes place in two hours.

Inter-paroxysmal alkalinity, 1·538. Fit, 8 a.m.; blood taken at 11 a.m.; alkalinity, 1·385; blood taken at 2.30 p.m.; alkalinity, 1·538.

Blood taken	60 seconds	before a fit—alkalinity,	1·26
„	½ hour	after a fit „	1·18
„	1 „	„ „	1·26
„	2 hours	„ „	1·43
„	4 „	„ „	1·48
„	24 „	„ „	1·58

These results show clearly that the alkalinity of the blood undergoes marked variations in epilepsy. These variations are constant, and manifest themselves in a diminution.

1. The average alkalinity during the inter-paroxysmal period is lower than the average of the control cases.

2. There is a sudden and pronounced fall immediately prior to the onset of the fit.

3. There is a further diminution after the fit is over.

The Diminution in the Inter-paroxysmal Period.—All the cases studied showed this diminution, with the exception of two senile cases. The lowest values of the alkalinity obtained during this period were from cases suffering from gastric catarrh and constipation. This diminution may be explained by the gradual accumulation of toxines of an acid nature in the blood, or it may be the result of deficient metabolism of the body tissues generally.

The fall *immediately prior to the onset of the fit* is difficult to account for, also the time at my disposal is too short to deal with the matter fully.

The *further diminution after the fit is over* is easily explained; it is apparent soon after the fit is over, and lasts for some hours. The alkalinity gradually rises, the rise being more marked in the first hour; the return to the normal varies in the different cases, and on an average takes from five to six hours. This diminution is directly due to the acid products of muscular metabolism, *e.g.*, carbonic and sarco-lactic acids generated during the violent tonic and clonic spasms of the epileptic seizure. This phenomenon is physiological, and is seen, though in a less degree, after muscular exercise. The diminution is scarcely perceptible in cases of petit mal. The variations in the fall met with in the different cases depend upon the number of fits, and the duration and severity of the muscular spasms. These facts, together with the appearance of the fall after the spasms are over, and the gradual rise to normal, seem to prove that this diminution is muscular in origin.

Dementia Paralytica.—Twenty-three cases were examined, and these were classified according to the different clinical types of the disease.

1. *Juvenile General Paralysis.*—Two cases.

2. *Ordinary Chronic General Paralysis.*—Cases with diminished knee-jerks, dilated pupils, and not subject to convulsive seizures. Eight cases.

3. *Acute General Paralysis.*— Cases which run a rapid course, pupils contracted, knee-jerks exaggerated, and subject to convulslve seizures. Eight cases.

4. *Tabetic General Paralysis.*—Five cases.

The examination of the blood of these groups of cases was very instructive, and all showed a low value of alkalinity, much below the average of the control cases; in fact, the highest value obtained in some of these cases, and these were the juvenile general paralyses, was below the lowest physiological limit of the normal alkalinity. The diminution varied in the different groups; the acute cases (Group 3) showed the greatest diminution, the juvenile cases (Group 1) the least. The lowering of the alkalinity in this disease is constant, well marked, and varies according to the type, duration, and progress of the disease.

The lowering of alkalinity by concurrent diseases, and by the products of muscular metabolism, is ruled out in this disease, although these factors may cause a slight and transient diminution in the early stages. The diminution may be regarded as a phenomenon directly associated with general paralysis, due to bio-chemical, abnormal metabolic and degenerative changes taking place in the central nervous system. This persistent lowering of alkalinity may have a different origin from the various degrees of diminution met with in epilepsy, though the factors referred to in the case of the former probably act in the latter. The additional factor in the diminution is probably the general auto-toxæmia which occurs in the progress of this disease. This general auto-toxæmia manifests itself by the presence of choline, neurine and glycero-phosphoric acid in the circulation. This is supported by the fact that more choline is found in the blood of cases suffering from acute neuronic degeneration, in which class of cases the alkalinity is lower than in the more chronic variety of the disease. Other factors which tend to maintain a low value of alkalinity are—deficient excretion of the neuronic products by the kidneys; deficient neutralisation by the secretions of glands; and the relative incompetence of the leucocytes. The most marked diminution in this disease occurs in connection with the convulsive seizures, and the more acute the case the greater the diminution. In two of the cases, where the blood was taken after seizures occurring a short time before death, the alkalinity was found to be very low compared with the reduction found in cases of *status epilepticus*. The cause of this somewhat marked lowering before death is probably the terminal auto-intoxication which occurs in

practically all the cases of the disease which do not die suddenly from some accidental cause, such as pneumonia and cardiac failure alone, or following a sudden series of seizures.

Dementia.—Ten cases were examined. These included the different varieties of dementia. All the cases were in good bodily condition.

Secondary Dementia.—Six cases. Alkalinity, 1·662, 1·731, 1·662, 1·59, 1·662, 1·662.

Senile Dementia.—Three cases. Alkalinity, 1·59, 1·662, 1·662.

Organic Dementia.—One case. Alkalinity, 1·662.

The alkalinity in these cases does not undergo any marked variation, but varies within physiological limits. Observations were carried out on the blood of these patients after manual labour. They were sent out to work on the farm, and immediately on their return their blood was taken and tested; the alkalinity was found to be lowered below the lowest physiological limit.

Mania.—In this disease fifteen cases were examined, of which ten were cases of acute mania and the remaining five were cases of chronic mania.

In the acute cases, and especially those who suffered from intense motor restlessness, the alkalinity was reduced. This diminution varied according to the restlessness of the case; the more restless the patient the greater the fall, and as the patient became quiet there was a gradual rise of the alkalinity to normal. During comparative repose the alkalinity remained within its normal limits.

The chronic cases did not show a lowering of alkalinity, and it was maintained at a fairly constant value, except during periods of excitement, when there was a slight lowering of alkalinity.

Melancholia.—Ten cases were examined. Of these eight were acute cases; they were very miserable and depressed; the remaining two were chronic cases.

The alkalinity in these cases was fairly constant, and varied within the normal limits. One case showed a persistent diminution; the writer is of opinion that this bears no relation to the disease, and is explained by the fact that the patient suffered from mitral disease and chronic rheumatism.

Conclusions.

1. The alkalinity of the blood is physiological in *chronic mania*, *melancholia*, and *dementia*.

2. It is lowered in cases of *mania*, during the period of excitement.

3. It undergoes marked variations in *epilepsy*, *e. g.*:

a. It is below normal during the inter-paroxysmal period.

b. It undergoes a sudden and pronounced fall immediately prior to the onset of the fit.

c. It undergoes a further diminution after the fit is over. This after-diminution depends upon the length of time, the severity of the muscular spasms, and the degree of the alkalinity in the inter-paroxysmal period.

d. There is a gradual return of the blood to its normal alkalinity, which takes place in five to six hours.

e. There is a relationship between the degree of the alkalinity and the onset of fits, *e. g.*, the higher the alkalinity the less liable is the patient to have a fit.

f. It is impossible to elevate and maintain the alkalinity within physiological limits for any appreciable length of time by the administration of drugs.

4. It undergoes a diminution in *dementia paralytica*. This diminution is constant and well marked, and is probably due to the products of neuronic degeneration in the circulation. The variations in the diminution met with depend upon the type, progress, and duration of the disease.

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TABLE I.—*Showing the Alkalinity during the Aura and varying periods after the Epileptic Seizure.*

Case.		Aura.	10 to 30 minutes.	1 hour.	2 hours.	3 hours.	4 hours.	5 to 12 hours.	12 to 24 hours.
1	7 fits	—	1·0387	1·26	1·385	1·43	—	—	1·43
	5 „	—	—	1·18	—	1·43	1·48	1·48	—
2	1 „	1·26	1·18	1·385	—	—	—	1·43	—
3	1 „	—	—	—	—	1·385	—	1·538	—
	2 „	—	—	1·26	1·385	1·48	—	1·59	—
4	8 „	—	·831	1·26	1·385	—	1·48	—	—
	15 „	—	·831	1·26	—	—	—	—	1·538
5	1 „	—	1·0387	1·26	1·43	—	—	1·538	—
6	5 „	—	·831	1·26	1·385	—	1·48	—	1·662
	1 „	1·26	—	—	—	—	—	—	—
7	4 „	1·385	1·12	—	1·385	—	1·48	1·59	—
8	1 „	1·18	—	1·26	1·385	—	1·538	—	1·59
9	6 „	—	—	—	—	—	—	1·48	1·59
10	3 „	—	·831	1·12	1·26	—	1·43	1·48	—

TABLE II.—*Showing the Alkalinity in the various Clinical Types of Insanity and of Dementia Paralytica.*

Case.	Type.	Alkalinity.	Alkalinity.	
1	Chronic G.P.	1·48	1·48	
2	,,	1·538	1·48	
3	,,	1·48	1·43	
4	,,	1·43	1·43	
5	,,	1·59	1·538	
6	,,	1·43	1·43	
7	,,	1·385	·831	After a severe convulsive seizure.
8	,,	1·48	1·48	
9	Juvenile G.P.	1·662	1·662	
10	,,	1·662	1·662	
11	Acute G.P.	1·43	1·43	
12	,,	1·385	·6925	After numerous seizures.
13	,,	1.385	1·385	
14	,,	1·26	·5935	After seizures, and just before death.
15	,,	1·385	·5935	,, ,, ,,
16	,,	1·43	1·26	
17	,,	1·26	1·26	
18	,,	1·18	·831	After a slight seizure.
19	Tabetic G.P.	1·48	1·48	
20	,,	1·59	1·538	
21	,,	1·43	1·43	
22	,,	1·48	1·48	
23	,,	1·48	1·48	
		DEMENTIA.		
1	Secondary D.	1·662	1·48	After severe muscular exercise.
2	,,	1·731	1·538	,, ,, ,,
3	,,	1·662	1·48	,, ,, ,,
4	,,	1·59	1·385	,, ,, ,,
5	,,	1·662	1·48	,, ,, ,,
6	,,	1·662	1·48	,, ,, ,,
7	Senile D.	1·59	1·48	,, ,, ,,
8	,,	1·662	1·43	,, ,, ,,
9	,,	1·662	1·48	,, ,, ,,
10	Organic D.	1·662	1·48	,, ,, ,,
		MANIA.		
1	Acute Mania	1·662	1·48	After a period of excitement.
2	,,	1·662	1·662	
3	,,	1·731	1·59	24 hours after a period of excitement.
4	,,	1·662	1·662	
5	,,	1·59	1·48	Acutely maniacal.
6	,,	1·662	1·662	
7	,,	1·59	1·59	
8	,,	1·662	1·48	
9	,,	1·59	1·43	3 hours after a period of excitement.
10	,,	1·59	1·59	
11	Chronic Mania	1·731	1·731	
12	,,	1·662	1·662	
13	,,	1·662	1·48	After a period of excitement.
14	,,	1·662	1·662	
15	,,	1·59	1·59	

TABLE II—*continued.*

Case.	Type.	Alkalinity.	Alkalinity.	
				MELANCHOLIA.
1	Acute Mel.	1·662	1·662	
2	,,	1·59	1·48	Mitral disease chronic rheumatism.
3	,,	1·662	1·731	
4	,,	1·731	1·662	
5	,,	1·59	1·59	
6	,,	1·59	1·59	
7	,,	1·662	1·731	
8	,,	1·662	1·662	
9	Chronic Mel.	1·662	1·662	
10	,,	1·59	1·662	

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The Abnormalities of the Palate as Stigmata of Degeneracy.

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THE study of, in many cases trivial, bodily variations and deformities has for many years attracted much attention from a large field of workers, and in no part of this sphere has this study been more elaborated than in that including the criminal and the lunatic. As examples of these studies may be mentioned the numerous papers which have been written, giving copious and precise details concerning the anatomical configuration, the complexion, the shape of the ear, nose, etc., and the physiological eccentricities in certain types of criminal. Of these variations and deformities none have been more thoroughly studied, and at the same time been the subject of more discussion and difference of opinion, than those connected with the shape, size, and general development of the palate.

Owing to the exceptional opportunities enjoyed by the author at Claybury during the past few months, it has been possible for him to add a further contribution to this subject which, owing to difference of method, etc., has, in his opinion,

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