VIII. STUDIES IN EXPERIMENTAL TETANY.

III. ON ALKALOSIS AND ACIDOSIS.

IV. ON THE HYDROGEN ION CONCENTRATION OF THE BLOOD.

V. ON THE ALVEOLAR CARBON DIOXIDE TENSION.

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THE problem, the results of the investigation of which are here presented, was to determine the changes in the acid-base balance of the blood in experimental tetany and to attempt to decide what was the essential nature of these changes; to arrive at a conclusion as to the extent of the change, if any, in the reaction of the blood; and to note the tension of CO_2 with which the arterial blood was in equilibrium in the lungs. The further question of the variability in the acidity of the haemoglobin molecule was also borne in mind as an integral part of the problem, but is not here discussed.

III. THE QUESTION OF THE ASSOCIATED CONDITIONS OF ALKALOSIS AND ACIDOSIS IN TETANY.

The question as to whether or not tetany is associated with a condition of alkalosis has been a subject of investigation for some considerable time, the general trend of opinion being that alkalosis may be produced by parathyroid extirpation, intravenous injections of sodium bicarbonate solutions, gastric lavage and hyperpnoea. The question, however, as to whether this condition of alkalosis is due to an uncompensated alkali excess or an uncompensated CO_2 deficit has not been answered. It can only be answered by an investigation of the time relations of the changes in the acid-base balance of the blood occasioned by any of the above mentioned procedures.

That parathyroid extirpation results in a condition of alkalosis, an alkalosis due to increase in base, was suggested by Wilson and others [1915] and McCann [1918]. On the other hand the work of Hastings and Murray [1921] and that of Underhill and Nellans [1921] would indicate that there was no change in the alkalinity or in the CO_2 -combining power of the blood in parathyroid

tetany. In a recent paper Greenwald [1922] states that tetany produced by the administration of sodium bicarbonate is not due to alkalosis but is due to the toxic effect of large doses of sodium salt, this effect being essentially of the nature of a sudden and marked disturbance of the relationship between the sodium ion and other cations. This idea has also been emphasised by Collip [1921].

After a long series of experiments upon the reaction of the blood of dogs and rabbits following parathyroid and thyroparathyroid extirpation, we came to the conclusion that a high p_H was not a necessary concomitant of parathyroid tetany and that the condition of alkalosis, due to increased production of alkali in the blood, if it existed, did so to a comparatively small extent, and that only during the short period preceding the acute attack of tetany; and further, the results obtained suggested that the condition of alkalosis was due, not to an uncompensated increased production of alkali, but to an uncompensated increased loss of acid. Since it was also noted that, with the appearance of those marked physical signs of tetany to which reference has already been made [Cruickshank, 1923], the p_H , which had increased slightly, fell to, and passed below, the normal figure, we had further to conclude that the acute tetany was associated with a condition, in which the reaction of the blood changed from the alkaline to the acid side of normality. It was also thought that the muscular tremors, which in many cases were very marked indeed, might by the production of acid bodies be responsible for a definite alteration from alkalosis to acidosis in the associated blood condition, and that they constituted a sign of the commencement of a new phase of the condition produced by lack of parathyroid substance. As considerable emphasis has in the past been laid upon the fact that tetany is a condition associated with alkalosis, with a high CO_2 -combining power of the blood with a p_H as high as 7.8, it was deemed expedient, in order to decide to what extent this change to the alkaline side of the normal occurred, to secure data on the acid-base balance of the blood and to determine the hydrogen ion concentration of the blood during the period after operation in which no signs of tetany were present, or at least no excessive respiratory movements, no marked muscular tremors and no sickness. It was to prove or disprove these ideas that the present work was undertaken.

Methods.

As in previous work, total thyroparathyroidectomies were performed. Blood samples were drawn, under cocaine, from the femoral arteries, and as the femoral arteries can be readily exposed at any point in their course, blood could be obtained with ease on at least four consecutive occasions. The blood for the immediate estimation of the total CO_2 by the Van Slyke method [Van Slyke and Stadie, 1921] was drawn under liquid paraffin, in a small centrifuge tube coated with potassium oxalate to make a 0.3 g. % solution; the blood to be equilibrated with various tensions of CO_2 was collected in a

50 cc. centrifuge tube, also coated with oxalate; both tubes were placed in a rack surrounded with ice. A little difficulty was experienced in obtaining potassium oxalate which gave a reaction between p_H 7.0 and 7.4; the oxalate supplied by Merck, Darmstadt, was found to be satisfactory. For obtaining approximate carbon dioxide tensions in the tonometers, the gas manifold described by Austin and others [1922] was used. To obtain the necessary equilibration data, four large and four small tonometers, connected by a short rubber tube, were used; the capacity of each of the former being 300 cc., that of the latter 20 cc. Ten cubic centimetres of blood were drawn into each of the large tonometers, equilibration was carried out at 38°, the period of equilibration extending for not more than 40 minutes. After equilibration the blood samples were sealed with mercury in the small tonometers and the estimation of their CO_2 content proceeded with immediately, while the air, with which the blood had been equilibrated, was sealed with mercury in the large tonometers and set aside in a water-bath at room temperature (28°–32°) for subsequent examination with the latest form of the Haldane-Henderson [Henderson 1918] gas analysis apparatus.

Calculations. The abbreviations used are those suggested by Van Slyke and others [1922]: namely mM for millimolecular, $[CO_2]$, $[H_2CO_3]$, $[BHCO_3]$ for their respective millimolecular concentrations, p_{CO_2} for the CO_2 tension in millimetres of mercury. From the equilibration data a curve, relating $[CO_2]$ or $[BHCO_3]$ to p_H , was constructed. By fixing four points to obtain a curve which has an approximately linear character, it is possible to determine with a considerable degree of accuracy the position of the curve, and by interpolating upon this curve the $[CO_2]$ value of the blood as drawn, the p_H of the circulating blood is determined. From this p_H and the known $[CO_2]$, the $[BHCO_3]$, $[H_2CO_3]$, p_{CO_2} and alveolar CO_2 were calculated by use of Hasselbalch's [1917] equation,

$$p_H = p_{K_1} + \log \frac{BHCO_3}{H_2CO_3},$$

where $p_{K_1} = 6.18$. Other equations used in the calculations are:

$$[BHCO_3] = \frac{[CO_2] \times R}{(R+1)},$$

$$p_{CO_2} = \frac{[CO_2]}{0.03(R+1)} \text{ or } p_{CO_2} = \% CO_2 (B - 49)$$

where $R = \frac{BHCO_3}{H_2CO_3}$ and $\log R = p_H - p_{K_1}$,

$$[H_2CO_3] = \frac{\alpha CO_2 \times p_{CO_2}}{760 \times 0.0224}$$

$$= 0.03 \times p_{CO_2}$$

where $\alpha = 0.511$ [Bohr, 1905].

Changes in the acid-base ratio have been noted, while all the changes in $[H_2CO_3]$ and $[BHCO_3]$, p_H and alkali reserve have been related as percentage changes from their respective normal amounts. Changes in the alkali reserve are measured at the normal p_H , because at a constant p_H the change in the

blood bicarbonate expresses directly the change in excess of base over acids, other than H_2CO_3 . Since equilibration data were obtained in all these experiments, one could, by extrapolation of the $[\text{CO}_2]$ values of the blood drawn upon each succeeding day to the value which would obtain at the normal p_{H} , calculate the corresponding $[\text{BHCO}_3]$ value and thus determine directly the change in the alkali reserve.

Discussion of Results.

It has been the general result in this laboratory to find all animals develop signs of tetany in the course of the second or third day after operation. This then afforded the opportunity to determine what was the blood condition existing prior to the development of symptoms of acute tetany, and for this purpose the acid-base balance, the p_{H} , and the alkali reserve of the blood were determined 24, 48 and 72 hours after operation.

Table I.

Dog No. I. Tetany on third day after operation.

Fine tremor of muscles of head, neck, shoulder girdle and abdomen.

Respiration rate—200 per minute, with apnoeic pauses.

Time in hrs.	Atmosphere		Alveolar air	Blood		$[\text{H}_2\text{CO}_3]$	$[\text{BHCO}_3]$	R	p_{H}	Remarks
	% CO_2	p_{CO_2}	CO_2	% CO_2	$[\text{CO}_2]$					
0	5.503	39.33	5.17	40.95	18.28	1.180	17.10	14.45	7.34	Normal
24	3.630	25.30	3.29	31.75	14.16	0.760	13.40	17.38	7.42	Tetany A
					16.20		15.15			At normal p_{H}
48	3.23	22.66	2.98	27.40	12.23	0.680	11.55	19.05	7.46	Tetany B
					14.30		13.38			At normal p_{H}

Tetany A				Tetany B			
		Total changes	% changes			Total changes	% changes
p_{H}	=	0.08 +	1.09	p_{H}	=	0.12 +	1.63
p_{CO_2}	=	14.03 -	—	p_{CO_2}	=	16.67 -	—
$[\text{BHCO}_3]$	=	3.70 -	21.62	$[\text{BHCO}_3]$	=	5.55 -	32.45
$[\text{H}_2\text{CO}_3]$	=	0.420 -	35.60	$[\text{H}_2\text{CO}_3]$	=	0.50 -	42.40
Alkali reserve	=	1.95 -	11.40	Alkali reserve	=	3.72 -	21.75

Table II.

Dog No. II. Tetany on third day after operation—very mild.

Muscular tremors very faint.

Respiration rate—120 per minute.

Time in hrs.	Atmosphere		Alveolar air	Blood		$[\text{H}_2\text{CO}_3]$	$[\text{BHCO}_3]$	R	p_{H}	Remarks
	% CO_2	p_{CO_2}	CO_2	% CO_2	$[\text{CO}_2]$					
0	4.710	47.33	6.22	51.80	23.12	1.420	21.70	15.14	7.360	Normal
24	4.470	31.66	4.18	38.00	16.97	0.940	16.03	17.02	7.412	Tetany A
					18.25		17.12			At normal p_{H}
48	4.430	31.33	4.12	39.40	17.59	0.940	16.65	17.78	7.430	Tetany B
					19.10		17.92			At normal p_{H}

Tetany A				Tetany B			
		Total changes	% changes			Total changes	% changes
p_{H}	=	0.062 +	0.842	p_{H}	=	0.07 +	0.951
p_{CO_2}	=	15.67 -	—	p_{CO_2}	=	16.00 -	—
$[\text{BHCO}_3]$	=	5.67 -	26.11	$[\text{BHCO}_3]$	=	5.05 -	23.25
$[\text{H}_2\text{CO}_3]$	=	0.48 -	33.77	$[\text{H}_2\text{CO}_3]$	=	0.48 -	33.77
Alkali reserve	=	4.58 -	21.11	Alkali reserve	=	3.78 -	17.42

Table III.

Dog No. III. Tetany developed on fourth day after operation.

Legs spastic, with muscular twitching of hind legs. Tremor produced by moving, as in lifting, the dog.

Time in hrs.	Atmosphere		Alveolar	Blood				R	p_H	Remarks
	% CO_2	p_{CO_2}	air CO_2	% CO_2	$[CO_2]$	$[H_2CO_3]$	$[BHCO_3]$			
0	4.320	30.33	3.99	36.70	16.380	0.910	15.47	17.18	7.415	Normal
24	3.730	26.33	3.47	33.92	15.150	0.790	14.36	21.88	7.520	Tetany A
					16.602		15.69			At normal p_H
48	3.216	32.66	2.98	31.62	14.12	0.68	13.44	19.95	7.48	Tetany B
					15.75		14.88			At normal p_H

Tetany A			Tetany B		
	Total changes	% changes		Total changes	% changes
p_H	= 0.105 +	1.55	p_H	= 0.065 +	0.87
p_{CO_2}	= 4.00 -	—	p_{CO_2}	= 3.67 -	—
$[BHCO_3]$	= 1.110 -	7.12	$[BHCO_3]$	= 2.03 -	13.11
$[H_2CO_3]$	= 0.12 -	13.18	$[H_2CO_3]$	= 0.23 -	25.29
Alkali reserve	= 0.220 +	1.42	Alkali reserve	= 0.59 -	3.83

In Tables I, II and III are given details of the results obtained on three dogs in which the tetany was of a comparatively mild character. The first of these dogs showed fine tremors of the abdominal and shoulder muscles and marked contractions of the neck and head muscles on the third day after operation, while in the others the tremor was much less marked. The respiration rate increased in the first to a maximum of 200 per minute; in the other two the maximum did not exceed in either case 120 per minute. There seems to have been a delay in the development and a diminution in the severity of the symptoms in these animals which may be accounted for by the daily withdrawal of 60 cc. of blood. It will be seen that in the case of animals 1 and 2 there is a definite fall in the alkali reserve in the first 24 hours, a

A—X = Fall in Alkali reserve in Tetany A.
 B—X = " " " Tetany B.

fall which is maintained throughout the second day, while in the case of number 3 the fall in alkali reserve is delayed until the second day. This change in the alkali reserve is shown in the dissociation curves for the blood of dog number II (Fig. 1) and in the graphs in Figs. 2, 3 and 4. From the graphs it will be seen that in all these cases the fall in H_2CO_3 exceeds that in

Fig. 2.

BHC0_3 , thus creating a condition of alkalosis, extending throughout the second day after operation. It is evident from these results that in mild cases of experimental tetany there is a definite though small change in the reaction of the blood, which probably reaches its maximum sometime during the second

day of the disease, and that with this slight change there is a condition of alkalosis, of no great severity it is true, which is occasioned by the fact that there is a greater loss of H_2CO_3 than of BHCO_3 (Figs. 2, 3 and 4).

In those cases, however, in which there is a more rapid production of parathyroid tetany and in which the animal shows within 48 hours a definite change from an active, well-conditioned though abnormal individual to one that is manifestly ill and whose *exitus fatalis* is clearly a matter of three or

Fig. 3.

four days, the picture obtained is of a type in which one can almost state from the graph the time at which a change from a condition of alkalosis to one of acidosis takes place. An examination of Tables IV, V and VI and of the graphic representation of certain of their details in Figs. 5, 6 and 7, showing the change in alkali reserve on the initial p_{H} lines and in Figs. 8, 9 and 10, showing the relative percentage changes, will disclose the fact that a primary condition of alkalosis is followed towards the end of the second day by the

opposite condition of acidosis. This swing of the acid-base balance is due to rapid alterations in the H_2CO_3 content. The change in the reaction of the blood is very small, the greatest alteration being 0.163, but small though it is, it would be possible with very accurate and facile methods for p_{H} estimation to indicate the point in time at which the change from alkalosis to acidosis takes place, namely the point at which the acid and base losses are accurately balanced. In the diagrams, this point is seen to be slightly in advance of the point at which the p_{H} line crosses the zero or normal line. All of these results indicate consistently that the increase in p_{H} is small,

Fig. 4.

that the primary condition is one of alkalosis due to a CO_2 deficit and that this picture is altered to one of acidosis during the development of the signs of acute tetany.

The extreme fall in the alkali reserve in these cases indicates that there is a production of acid or acids other than H_2CO_3 . The work of Greenwald [1922] would indicate that lactic acid is produced before muscular tremor is evident and that it is greatly increased when this becomes marked, and further that the increase in lactic acid in the blood is not large enough to account for the total fall in blood alkali. It must be noted that these animals did not show the violent muscular twitchings, with involuntary snapping of the jaws, which

Table IV

Dog No. IV. On the second day after the operation no tremors of the shoulder muscles were visible: slight tremor of legs present with slight spasticity of hind legs. Respiration 70 per minute. Appetite impaired, drinking copiously. Perspiration visible: condition excellent.

On third day after operation, tremor of shoulder, fronto-orbital and leg muscles visible: attempt to move produced coarse spasmodic twitchings of limb muscles. Legs spastic. Respiration rate not increased.

Time in hrs.	Atmosphere		Alveolar air CO ₂	Blood				R	p _H	Remarks
	% CO ₂	p _{CO₂}		% CO ₂	[CO ₂]	[H ₂ CO ₃]	[BHCO ₃]			
0	4.00	28.00	3.685	39.60	17.67	0.840	16.83	18.20	7.44	Normal
24	2.18	15.33	1.975	28.90	12.89	0.460	12.43	26.30	7.603	Tetany A
					17.80		16.87			At normal p _H
48	3.62	25.33	3.340	31.49	14.05	0.760	13.29	17.78	7.430	Tetany B
					13.70		12.98			At normal p _H
72	3.88	23.66	3.115	25.68	11.45	0.710	10.74	15.14	7.360	Tetany C
					9.70		9.20			At normal p _H

Table V

Dog No. V. Marked tetany developed towards the end of the second day. Respiration 240 per minute. Muscle tremor well marked.

Time in hrs.	Atmosphere		Alveolar air CO ₂	Blood				R	p _H	Remarks
	% CO ₂	pCO ₂		% CO ₂	[CO ₂]	[H ₂ CO ₃]	[BHCO ₃]			
0	3.910	27.33	3.61	35.95	16.05	0.820	15.13	16.22	7.391	Normal
24	2.647	18.66	2.46	42.62	19.04	0.560	18.48	33.88	7.710	Tetany A
					26.40		24.88			At normal p _H
48	3.642	25.67	3.37	31.26	13.95	0.770	13.18	16.98	7.410	Tetany B
					14.20		13.38			At normal p _H
72	3.595	25.33	3.33	22.30	9.96	0.760	9.20	12.02	7.260	Tetany C
					6.80		6.52			At normal p _H

Tetany A				Tetany B				Tetany C			
Total changes		% changes		Total changes		% changes		Total changes		% changes	
p _H	=	0.319 +	4.32	p _H	=	0.019 +	0.257	p _H	=	0.131 -	1.77
pCO ₂	=	8.67 -	—	pCO ₂	=	1.66 -	—	pCO ₂	=	2.00 -	—
[BHCO ₃]	=	3.35 +	22.15	[BHCO ₃]	=	1.95 -	12.89	[BHCO ₃]	=	5.93 -	39.20
[H ₂ CO ₃]	=	0.26 -	31.7	[H ₂ CO ₃]	=	0.05 -	6.10	[H ₂ CO ₃]	=	0.06 -	7.32
Alk. res.	=	9.75 +	64.45	Alk. res.	=	1.75 -	11.56	Alk. res.	=	8.71 -	57.50

was so marked a feature in those animals which formed the subjects of the experiments carried out last year. This may be due as mentioned before to the daily withdrawal of blood. Still, in all of these experiments here quoted in detail the animals developed definite tetany and the general uniformity of the results obtained inclines one to the opinion that the first stage of tetany is associated with a condition of alkalosis due to a CO₂ deficit, and that previous to the development of the second phase of the disease, there is a fall in the

A—X = Fall in Alkali reserve in Tetany A.
B—X = " " " Tetany B.

Fig. 9.

Fig. 10.

Table VI

Dog No. VI. Definite mild tetany with visible fine muscle tremor.
Respiration rate did not exceed 140 per minute.

Time in hrs.	Atmosphere		Alveolar air	Blood				R	p_H	Remarks
	% CO ₂	p_{CO_2}	CO ₂	% CO ₂	[CO ₂]	[H ₂ CO ₃]	[BHCO ₃]			
0	5.880	42.50	5.53	41.60	18.57	1.275	17.27	13.54	7.302	Normal
24	2.840	20.00	2.64	25.41	11.35	0.600	10.75	18.20	7.440	Tetany A
					14.60		13.60			At normal p_H
48	4.58	32.66	4.30	29.00	12.95	0.98	11.97	13.33	7.271	Tetany B
					12.10		11.18			At normal p_H

Tetany A				Tetany B			
		Total changes	% changes			Total changes	% changes
p_H	=	0.138 +	1.89	p_H	=	0.031 -	0.43
p_{CO_2}	=	22.0 -	—	p_{CO_2}	=	9.84 -	—
[BHCO ₃]	=	6.52 -	37.73	[BHCO ₃]	=	5.30 -	30.70
[H ₂ CO ₃]	=	0.675 -	52.92	[H ₂ CO ₃]	=	0.295 -	23.11
Alkali reserve	=	3.67 -	21.25	Alkali reserve	=	6.09 -	35.26

alkali reserve, and a balancing of base and acid, which ultimately results in an increase of acid over base, both being lower than normal, and thus a condition of acidosis is introduced which is steadily increased up to the time of the death of the animal. As to whether or not the alkali reserve of the blood becomes encroached upon during the first 24 hours after operation depends upon the severity and the rate of development of tetany, upon the previous diet of the animal, and also upon the type of the animal. Diet undoubtedly plays a very important part in determining the nature of the subsequent tetany. Here it has been found that all dogs do not develop those signs which are generally regarded as pathognomonic of tetany. It may be that accessory parathyroid tissue is responsible for this. Our experience has been such that we find it possible almost to predict whether the tetany will be accompanied in an active alert dog by violent spasmodic muscular contractions, rapid respiration, profuse perspiration, cardiac irregularity, or in a rather lethargic dog by slight fine tremors, at times difficult to detect, a respiration rate never exceeding 100 per minute and slight perspiration, the dog becoming less and less inclined to move about. The former condition is obtained in short-haired animals of the fox or Irish terrier type; the latter condition, in long-haired animals of the collie type, though usually of very indefinite breed. In all our experiments it has been our constant endeavour to secure animals of the former type.

IV. THE HYDROGEN ION CONCENTRATION OF THE BLOOD IN TETANY.

Reference has already been made to previous work, in which estimations of the p_H of the blood of parathyroidectomised dogs indicated a slight change to both sides of the normal, the average increase being 0.143. The average figure given by Grant and Goldman [1921] for the change in reaction produced by hyperpnoea was 0.160.

Table VII. *The p_H of the blood of normal and thyroparathyroidectomised dogs, determined from CO_2 dissociation curves.*

Dog	Normal p_H	p_H 24 hrs. after operation	Change in p_H	p_H 48 hrs. after operation	Change in p_H	p_H 72 hrs. after operation	Change in p_H
1	7.370	7.590	0.22 +	—	—	—	—
2	7.340	7.420	0.08 +	7.460	0.120 +	—	—
3	7.440	7.603	0.163 +	7.480	0.010 —	7.360	0.080 —
4	7.391	7.710	0.319 +	7.410	0.019 +	7.260	0.131 —
5	7.360	7.420	0.062 +	7.430	0.070 +	—	—
6	7.415	7.520	0.105 +	7.480	0.065 +	—	—
7	7.302	7.440	0.138 +	7.271	0.031 —	—	—
8	7.330	7.480	0.150 +	—	—	—	—
Average	7.369	7.523	0.154 +	7.413	0.044 +	7.310	0.059 —

The range of the change of p_H in the present series with its time relations is shown in Table VII. The average normal p_H obtained was 7.369; the average p_H 24 hours after operation was 7.523, an increase of 0.154; after 48 hours it had fallen to 7.413, an increase above the normal of 0.044; after 72 hours it was 7.301, a decrease of 0.059. It seems justifiable, therefore, to conclude that there is a slight change in the reaction of the blood in parathyroid tetany. The following are average figures from several observers, showing alterations in the p_H of the blood in cases of experimental tetany:

Grant and Goldman [1921]	0.150
Collip and Backus (calculated 1920)	0.240
Cruickshank (colorimetric 1922)	0.146
Cruickshank (dissoc. curve 1923)	0.154

These indicate a rise in p_H , but if the reaction of the blood be followed throughout the period of acute tetany it will be found as shown in the accompanying graphs that it ultimately falls below the normal for the blood under investigation.

V. ALVEOLAR CO_2 TENSION IN TETANY.

That hyperpnoea will produce tetany has been demonstrated by Davies, Haldane and Kennaway [1921], Collip and Backus [1920], Bazett and Haldane [1921], and Grant and Goldman [1921]. The forced breathing, which is a sign of parathyroid tetany, causes a reduction in the alveolar CO_2 and by this so-called washing out of CO_2 alters the ratio $BHCO_3/H_2CO_3$ thereby inducing a condition of alkalosis. The theory that the washing out of the CO_2 is a sufficient cause of tetany is not tenable. The causative mechanism, which has as its basis a disturbance of parathyroid function, is more likely to be the nature of a disturbance of the equilibrium of certain ions both in the blood and tissue cells, a disturbance which includes alterations in the stability of the oxyhaemoglobin molecule. It is because of this latter that the tension of O_2 and CO_2 both in alveolar air and in the tissues is of importance. Any mention of the variations of the CO_2 tensions of the alveolar air, without further correlation, can be merely one of interest and it is from that aspect at present that the averages of the CO_2 tensions stated as percentages of dry alveolar air, at 760 mm. Hg., in the various tables are here stated.

Percentage of CO₂ in the alveolar air of normal and tetany dogs.

Normal	Tetany 24 hours	Tetany 48 hours
4.493	2.935	3.49

These figures will indicate, as have the others, that there is a return from a primary phase towards the normal, and it is quite probable that, with the loss of alkali reserve and with the increase in some non-volatile acids or some alterations in the acidity of the haemoglobin molecule, the alveolar CO₂ will increase, keeping pace with the increasing H ion concentration of the circulating blood.

Whatever may be the factors in the production of tetany, the results given in this paper suggest that the essential condition is one of alkalosis only in the first phase of the disturbance and that in fully developed parathyroid tetany the disturbance in the equilibrium of the electrolytes is associated with a reaction of the blood, which is on the acid side of the normal.

CONCLUSIONS.

1. The change in the acid-base balance in parathyroid tetany is, in the primary or quiescent stage, such that a condition of alkalosis, due to CO₂ deficit, is produced.
2. During the development of acute tetany, the condition of alkalosis changes to one of acidosis, due to a continuous loss of BHCO₃ and an increase in H₂CO₃.
3. Depending upon the rapidity of the development of tetany, the alkali reserve will begin to fall on the first or second day after operation and will continue to fall steadily until the death of the animal.
4. The reaction of the blood, as determined from CO₂ dissociation curves, changes very slightly, the p_H increasing above normal for the animal by an average of 0.154, during the stage of alkalosis, and falling with the introduction of the stage of acidosis.
5. The change towards acidosis is probably hastened but not produced by muscular tremor.
6. The alveolar CO₂ may fall as low as 1.975 % but with the continued loss of base there is a tendency for it to return towards the normal figure.

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