XLVI. THE EFFECT OF INGESTION OF UREA, SODIUM LACTATE AND SODIUM BICARBONATE ON THE REACTION OF THE BLOOD AND THE COMPOSITION OF THE ALVEOLAR AIR IN MAN.

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The present paper records an attempt to test the question whether certain substances taken by the mouth have the effect of making the blood in the body more alkaline.

Some preliminary experiments on the subject were made by Wolf and Barcroft [1915], who in a few experiments on dogs and on Barcroft himself found that blood exposed to oxygen at 17 mm. pressure took up somewhat more of the gas after ammonium citrate or urea had been taken. This suggested increased alkalinity of the blood.

Toyojiro Kato [1915, 1] recently observed that addition of certain alkaline substances to the blood, NaOH , Na_2CO_3 , NaHCO_3 , Na_2HPO_4 , accelerates the oxidation and retards the reduction of blood. Accepting this, one would expect that alkali would increase the percentage saturation of oxygen in blood exposed to a given oxygen pressure, just as acid reduces the percentage saturation [Barcroft and colleagues, 1914]. We have then used this measurement as a test for the changed reaction.

The method of exposing blood to a standard gas mixture is that described by Kato [1915, 2], in which 1–2 tenths of a cc. is put into the bulb of a small pipette, gas is then passed over it from a gas holder, the pipette being rotated in a water bath at $37^\circ\text{--}38^\circ\text{C}$. for about ten minutes. This suffices to secure

complete equilibrium between the blood and the gas. The blood is then transferred to the differential gas analysis apparatus designed by Barcroft [1914, p. 300] for the analysis of 0.1 cc. of blood. In this its percentage saturation is determined.

On account of the novelty of Kato's tonometer I thought it desirable to test the method rigorously. The following are the results of two sets of determinations in which I tried to see whether on repeated analysis the same blood yielded similar values for the percentage saturation.

Percentage Saturation of Oxygen in Blood.

No. of exp.	Number of determinations	Animal	Maximal result	Minimal result	Mean
I	7	Sheep	58.8	53.3	55.3
II	7	Rabbit	43.8	39.8	41.1

To these results I added some on the percentage saturation of Barcroft's normal blood when exposed to 17 mm. O₂ pressure. They are as follows:

Experiment III.

Percentage saturations					
(1)	77.1	75.1	79.6	—	mean 77.3
(2)	74.5	71.7	67.8	—	„ 71.3
(3)	71.0	74.0	73.4	73.9	„ 73.8
(4)	67.6	67.6	71.7	—	„ 69.1

These results shew that, so far as the method of gas analysis is concerned, any individual sample of blood gives very concordant results. They suggest that the blood of the same person varies to a trifling extent from day to day. This result must however be received with great caution, lest it should be due to a slight want of uniformity in the gas used on different occasions.

Results on my own blood were slightly more uniform:

Experiment IV.

Percentage saturations			
(1)	72.8	72.5	mean 72.7
(2)	73.1	69.6	„ 71.4
(3)	74.0	72.1	„ 73.0

In no case do the above observations include cases in which substances for investigation such as urea, sodium lactate etc. have been taken by the patient so recently as the day before the observation.

*Experiments on the percentage saturation of human blood at
17 mm. O₂ pressure.*

The following experiments shew that urea taken by the mouth causes the blood to become more alkaline, i.e. causes the percentage saturation in the blood to rise when exposed to the standard mixture.

Effect of Urea on Percentage Saturation of Blood.

No. of exp.	Dose	Percentage saturation				
		Before	After			
			1 hour	2 hours	Approximate time	
					5 hours	Next day
V	15 g. urea in 250 cc. water	77.3	82.0	—	84.2	—
VI	„	71.3	—	—	76.7	72.0
VII	„	73.1	—	80.2	—	—

Poulton and Ryffel [1913], who performed experiments on the percentage saturation of blood in uraemic patients, state that the addition of urea, in small concentrations, to blood does not change its affinity for oxygen. This I verified:

Experiment VIII. Rabbit's Blood.

	Urea added to 1 cc. blood	Percentage saturation with oxygen at 17 mm.			
(1)	Nil	48.8	Mean of 2 observations		
(2)	0.1 cc. N/10 CON ₂ H ₄	48.1	„	„	„
(3)	0.2 cc. „	47.1	„	„	„
(4)	0.3 cc. „	49.4	„	„	„

The solution of urea was normal in reaction. Since the urea itself does not affect the affinity of blood for oxygen, the inference is that urea taken by the mouth becomes partially converted into ammonia in the body [Wolf, 1912].

Exp. IX. It therefore became of interest to ascertain the concentration of ammonia, which, if added directly to blood, would produce the same change as the urea which was given by the mouth. This proved to be 0.2 cc. of N/10 NH₃ per cc. of blood or 0.017 %. This quantity changed the percentage saturation at 17 mm. from 73 to 83.7 %. (Mean of two determinations: 81.8 and 85.5.)

Sodium lactate was suggested by Sir Almroth Wright on the ground of its rapidly causing the urine to become alkaline. It does not follow that

the blood would become appreciably alkaline for the sodium might be rapidly eliminated.

The preparation of sodium lactate which we used was slightly acid in reaction and when added to defibrinated blood it caused the percentage saturation at 17 mm. O_2 to drop, when added in dilute solutions; after 0.2 cc. N/10 lactate further addition had no effect, presumably because the degree of ionisation does not increase.

Experiment X. Rabbit's Blood.

	Sodium lactate added to 1 cc.	Percentage saturation with oxygen at 17 mm.
(1)	Nil	48.8 Mean of 2 determinations in each case
(2)	0.1 cc. N/10 $NaC_2H_3O_2$	41.8 " " "
(3)	0.2 cc. " "	32.2 " " "
(4)	0.3 cc. " "	32.9 " " "

Given by the mouth however sodium lactate has precisely the opposite effect.

Experiments XI, XII and XIII. Effect of Sodium lactate.

No. of exp.	Dose	Percentage saturation with oxygen					
		Before	After				
XI	5 g. in about 10 cc. of water	72.7*	74.7	83.9	78.6	—	—
XII	"	74.4	75.5	—	77.5	72.5	72.6
XIII	"	72.6	76.2	88.0	74.1	75.0	—

* Each of these results is the mean of two determinations.

These figures indicate that the maximal effect is obtained at the end of about two hours. The question then arises, to how much alkali does this correspond? On this point I obtained the following data by the addition of NaOH directly to defibrinated blood.

Experiment XIV. Addition of NaOH to Human Blood (Barcroft).

	NaOH added to 1 cc. of blood	Percentage saturation with oxygen at 17 mm.
(1)	Nil	69.3 Mean of 8 determinations
(2)	0.1 cc. N/10 NaOH	80.1 " 4 "
(3)	0.2 cc. "	80.7 " 3 "

The effect of adding urea, sodium hydroxide, sodium lactate and ammonia to defibrinated blood is shewn in Fig. 1.

A third substance which I tried was sodium bicarbonate.

Fig. 1.

Ordinates = Percentage saturation of blood at 17 mm. oxygen pressure.

Abscissae = Quantity of drug added.

(1) N/10 NaOH (Blood of Barcroft)	(3) N/10 CON ₂ H ₄ (Blood of Rabbit)
(2) N/10 NH ₃ („ Momose)	(4) N/10 NaC ₃ H ₅ O ₃ („ „)

Fig. 2.

(3), (2). Exp. XVII.
(1), (4). Exp. XVIII.

 Ordinates: (a) mm. pressure of CO₂ (dotted line).

(b) Percentage saturation of blood at 17 mm. oxygen pressure (continuous line).

Abscissae = Time after taking dose in hours.

Fig. 3.

(1), (4). Exp. XIX.
(2), (3). Exp. XX.

It might be expected that the addition of substances which would raise the percentage saturation at 17 mm. would also raise the alveolar carbonic acid. I made numerous measurements of the alveolar CO_2 , therefore, before and after taking sodium lactate with the following results:

Alveolar CO_2 pressure in mm. (Momose).

No. of exp.	Dose of sodium lactate	Before	After		
			1 hour	2 hours	3 hours
XV	5 g.	40.1	40.9	40.1	40.2
XVI	"	40.2	42.4	41.0	40.5

The change in the alveolar CO_2 is extremely slight, but such as it is it reaches a maximum at the end of the first hour.

In order to see whether the change in the CO_2 really reaches its maximal value in a different time from the change in the percentage saturation at 17 mm. a series of observations of the two were undertaken concurrently in the same experiment.

Effect of Sodium lactate on Percentage Saturation and Alveolar Carbonic Acid.

No. of exp.	Dose of sodium lactate		Before	After		
				1 hour	2 hours	3 hours
XVII	5 g.	% sat.	73.1	73.1	83.3	72.2
		Alv. CO_2 mm.	39.5	43.0	42.3	40.1
XVIII	"	% sat.	74.0	80.5	85.3	74.0
		Alv. CO_2 mm.	40.1	41.9	39.7	39.4

These figures bear out what I found in the earlier observations, namely, that the trifling change in CO_2 pressure is most evident at the end of the first hour and the change in percentage saturation at the end of the second (Fig. 2).

It was a matter of some interest to ascertain whether a similar result would be obtained when sodium bicarbonate was taken (Fig. 3).

Effect of Sodium bicarbonate on Percentage Saturation and Alveolar Carbonic Acid.

No. of exp.	Dose of NaHCO_3		Before	After		
				1 hour	2 hours	3 hours
XIX	4 g. (3.8 g. equivalent to 5 g. sodium lactate)	% sat.	78.2	83.5	90.3	83.9
		Alv. CO_2 mm.	40.4	40.3	40.9	40.5
XX	"	% sat.	73.9	81.5	83.9	76.9
		Alv. CO_2 mm.	40.6	40.9	40.7	41.0

CONCLUSIONS.

Two points seem to be established.

(1) Urea, sodium lactate and sodium bicarbonate, in the doses taken, produce little change on the alveolar CO_2 .

(2) These substances produce an appreciable change on the affinity of blood for oxygen in the presence of CO_2 .

It remains to investigate the question: Do these compounds affect the percentage saturation of the blood with oxygen in the presence of the alveolar pressure of CO_2 ? So far as sodium lactate in 5 gram doses is concerned the effect does not appear to be appreciable:

Effect of Sodium lactate on Percentage Saturation in the Presence of 27.7 mm. of Oxygen and 40 mm. CO_2 .

No. of exp.	Dose	Before	After 2 hours
XXI	5 g. sodium lactate	57.4 (Alv. CO_2 =40)	58.5 (Alv. CO_2 =39)
XXII	„	47.1 (Alv. CO_2 =40)	45.8 (Alv. CO_2 =39)

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