XXXIX. THE EFFECT OF ALKALIS ON THE RATES OF OXIDATION AND REDUCTION OF BLOOD.

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The effect of the addition of acids to blood, in altering the rate at which it can be oxidised or reduced under given conditions, has been studied in this laboratory by Mathison [1911] and by Oinuma [1911], whilst some observations of a similar nature on haemoglobin have been made by Barcroft [1914]. Mathison found that acids accelerated the rate of reduction of blood with a stream of inert gas and that their effect was proportional to the alteration of hydrogen ion concentration produced by them in serum. Oinuma found that, in addition to the acceleration of reduction observed by Mathison, carbonic acid rendered reduced blood less rapidly oxidised by a stream of gas containing oxygen.

No similar observations exist concerning the effect of alkalis. I therefore determined to undertake a research on this subject. The results are given in the following paper.

After testing a number of methods, each of which seemed to promise some improvement on that used by Mathison, I returned to his as being the most satisfactory. Briefly this consists in bubbling gas from a gas holder through a given quantity of blood for a given time. The blood is contained in a tube tilted at an angle of about 15° to the horizontal in a water bath of a given temperature. The tube which I have used has the length of 41 cm. measured from the top to the first bend and the bore is 1 cm. In order to

prevent "frothing," the greatest difficulty presented by this method, a spiral of wire covered with vaseline is inserted into the tube at a convenient distance above the surface of the blood. Sometimes, especially when the concentration of the added alkali is high, the bubbles are not easily broken and the successive films remain unbroken in the tube; thus the streaming of gas is retarded and it is longer in contact with the blood. Accordingly the reduction or oxidation is accelerated at a given rate and duration of bubbling. In order to get uniform results therefore great attention must be paid to this frothing. Slight frothing often makes an experiment useless.

The actual measurement is that of the percentage saturation of the blood with oxygen after gas (either for the purpose of oxidising or reducing the blood) has been passed through for a measured time. The measurements of the percentage saturation have been made with Barcroft's differential blood gas apparatus, the form used being that designed for 1 cc. of blood and described by Barcroft [1914, p. 291]. The shaking of the apparatus has been carried out by the apparatus used by Barcroft for this purpose.

Whilst it is not necessary to go into further detail here as to the apparatus used, I may state the degree of accuracy which it has afforded me. In the present paper there are more than 170 double determinations of the percentage saturation of blood with oxygen. The divergence observed may be tabulated as follows:

Divergence	1 % and under	1-2 %	2-3 %	3-4 %	4-5 %	5-6 %	6-7 %	7-8 %
Number of determinations	43	39	34	18	15	7	3	1

Data given below in the following form:

$$\begin{array}{l} 42.5 \\ 40.0 \end{array} \left. \vphantom{\begin{array}{l} 42.5 \\ 40.0 \end{array}} \right\} 41.3 \%$$

signify that gas was bubbled through one sample of blood and that two determinations were made of the resulting blood; but where they are given with a double bracket as follows:

$$\begin{array}{l} (a) \ 18.5 \\ (b) \ 18.2 \\ (c) \ 20.4 \\ (d) \ 19.3 \end{array} \left. \vphantom{\begin{array}{l} (a) \ 18.5 \\ (b) \ 18.2 \\ (c) \ 20.4 \\ (d) \ 19.3 \end{array}} \right\} \begin{array}{l} 18.4 \\ 19.2 \end{array}$$

the meaning is that the blood was divided into two portions. The gas was bubbled through the first, and determinations (a) and (b) were performed, then in an exactly similar way through the second, (c) and (d) being the

determinations obtained from it. The divergence between (a) and (b) therefore is simply that caused by errors in the measurement of the percentage saturation, that between the figures in the second column (18·4 % and 19·9 %) includes the errors due to inequality in the rate of bubbling and similar causes. There are four sets of determinations of this character given below, in none of which do the figures in the second bracket differ by as much as four per cent. from one another.

The blood used was always from animals recently killed without use of any narcotics or drugs. When the blood is not fresh enough the sensitiveness to alkali suffers to a considerable extent. In the case of oxen and sheep the animals were usually killed at the slaughter house about one or two o'clock, in which case the experiment was finished that day. Occasionally the butcher killed the animals late in the evening; the blood was then kept in ice till the next morning. When rabbit's blood was used, the animal was killed just before the experiment; the blood was always defibrinated by whipping.

The addition of alkali to the blood. The same routine has been adopted throughout for the addition of alkali to the blood; 4·5 cc. of blood have been taken and 0·5 cc. of a solution of the alkali in physiological saline (0·9–1 % NaCl) added, the alkali in the portion added being ten times the strength to which it was desired to bring the blood. Thus in the tables, if the blood is described as having alkali added to the extent of M/100 NaOH, 0·5 cc. of M/10 NaOH in physiological saline was added to 4·5 cc. of blood. For each control experiment ("normal blood"), to 4·5 cc. of blood 0·5 cc. of physiological saline was added.

The reduction of the blood was always carried out with commercial nitrogen, this was never quite free from oxygen, containing just under 0·5–0·8 % of that gas. The blood was always thoroughly shaken up with air before the reduction commenced, thus ridding it of carbonic acid and saturating the haemoglobin with oxygen.

The oxidation of the blood was carried out with gas which consisted of approximately 12 % oxygen and 88 % nitrogen; as there were slight differences in the quantity of oxygen present in different experiments, the oxygen sometimes rising as high as 12·6 %, the analysis is given at the head of the tables.

The oxidation experiments have, of course, to be carried out on previously reduced blood. This reduction was effected by the bubbling of nitrogen through the blood for an adequate time. This proved to be 40–50 minutes

at 39–40°, the more alkaline the blood the longer did it take for reduction. A few examples will serve to illustrate the complete reduction.

Blood	Alkali added	Duration of bubbling in minutes	Number of bubbles per min.	Temperature C.	Percentage saturation of blood with O ₂ after reduction
Calf	M/200 NaOH	40	60	38°	-1.0 } 0.2 1.3 }
Ox	M/50 NaOH	50	72	39°	-2.4 } -0.6 1.2 }
Rabbit	M/50 NaHCO ₃	50	80	39°–40°	0.8 } -0.2 -1.2 }

The correction necessary for the exchange of gases in physical solution. In theory this correction differs with each sample of blood. In practice we have applied a uniform correction to our whole series of experiments which is sufficiently accurate for the purpose.

To consider the simplest case. Suppose the blood in the tube at the end of the experiment is completely reduced.

(a) 1 cc. of blood will have no oxygen in solution; it will take up from the air in the blood gas analysis apparatus $0.031 \times 21/100 = 0.0065$ cc. oxygen, since the blood absorbs at 15° about 0.031 cc. of oxygen.

(b) It has been in contact with nitrogen at about 710 mm. pressure (that of the atmosphere less the pressure of aqueous vapour at 38°). The amount of gas which it can absorb at 710 mm. pressure and 38° is 0.0103. In the blood gas bottle it is in equilibrium with nitrogen at approximately 600 mm. pressure and at a temperature of about 15°. The amount of nitrogen, which 1 cc. of blood absorbs at 600 mm. pressure and 15° is 0.013. Therefore on shaking up in the blood gas apparatus it gains $0.013 - 0.0103 = 0.00207$ cc. nitrogen. Thus the total amount of gas physically taken up by the blood in the blood gas bottle is $0.0065 + 0.002 = 0.0085$ cc. If the oxygen capacity of 1 cc. blood (diluted with 1/10 of its volume of fluid) be 0.16 cc., then the gas taken up is about 5 % of the oxygen capacity, which must be added as a correction to the observed value of percentage saturation. A similar correction should be made to each experiment for the physical gas exchange.

THE BLOOD GAS OF DIFFERENT ANIMALS.

The blood of different species.

It is clear that the blood of different species of animals presents very different properties both in relation to oxidation and reduction [Barcroft and King, 1909, man and rabbit; Barcroft and Camis, 1909, man and dog].

That some such difference must exist is the necessary corollary to the fact that when in equilibrium with gas of a uniform partial pressure of oxygen the blood of different species exhibits different percentage saturations. Three animals have been studied in this respect, the ox, the sheep and the rabbit. Of these the properties of ox blood and sheep's blood are very similar, but they differ markedly from rabbit's blood which is on the one hand more readily reduced and on the other less readily oxidised. These facts are shown in the following tables:

SERIES 1. *Comparison of ox and sheep's blood, oxidised with*
 N_2 (87.4 %) + O_2 (12.6 %).

Animal	Duration of bubbling in minutes	Number of bubbles per minute	Temperature C.	Percentage saturation
Ox	5	60	39	50.2 } 52.4 } 51.3
Sheep	5	60	39	53.8 } 53.2 } 53.5

SERIES 2. *Comparison of ox and sheep's blood, reduced with N_2 .*

Ox	15	60	38	23.5 } 23.2 } 23.4
Sheep	15	60	38	26.8 } 27.6 } 27.2

SERIES 3. *Comparison of sheep's and rabbit's blood oxidised with*
 N_2 (88 %) + O_2 (12 %).

Sheep	10	60	38	62.3 } 60.5 } 61.4
Rabbit	10	60	38	47.2 } 45.2 } 46.2

SERIES 4. *Comparison of sheep's and rabbit's blood, reduced with N_2 .*

Sheep	10	60	38	52.2 } 54.2 } 53.4
Rabbit	10	60	38	43.0 } 44.2 } 43.6

The blood of different animals of the same species.

The fresh blood from different animals of certain species which we have tested presents much the same properties as regards both oxidation and reduction.

Percentage saturation of blood with O₂ after reduction with N₂.

Series	Animal	Duration of bubbling in minutes	Rate of bubbling per minute	Percentage saturation of blood with O ₂ after reduction		
1	ox 1	7½	60	49.7 50.9	49.9	
		12	60	32.1 33.0		32.6
		10	(interpolated)		39.8	
		ox 2	10	60	39.6 39.7	39.7
	2	sheep 1	5	72	60.0 60.7	
sheep 2		5	72	65.2 62.0	63.6	
sheep 1		10	72	40.8 38.8		39.8
sheep 2		10	72	42.4 38.6	40.5	
sheep 1		15	72	22.8 22.6		24.1
sheep 2		15	72	28.8 25.4	27.1	
sheep 1		20	72	16.1 —		16.1
sheep 2		20	72	19.4 13.2	16.3	
sheep 1		30	72	— 0.2		
sheep 2		30	72	0.6 4.6	2.6	
3		rabbit 1	10	60		45.1 44.2
					43.0 44.2	43.6
	rabbit 2	10	60			

Percentage saturation of blood with O₂ after oxidation with N_2 (= 88 %) + O₂ (= 12 %).

Series	Animal	Duration of bubbling in minutes	Rate of bubbling per minute	Percentage saturation of blood	
1	ox 1	5	72	54.8)	53.1
				51.4)	
	ox 2	5	72	52.4)	52.6
				52.8)	
	ox 1	10	72	84.5)	84.8
				85.2)	
	ox 2	10	72	82.8)	81.5
				80.2)	
	ox 1	15	72	94.3)	95.2
				96.0)	
	ox 2	15	72	91.7)	91.7
				91.7)	
2	sheep 1	5	72	53.8)	53.5
	sheep 2	5	72	53.2)	
				50.2)	51.3
				52.4)	

However there are many exceptions. Not seldom the blood of animals of the same species has shown a definitely different value of oxygen capacity and also great divergence of percentage saturation with regard both to oxidation and to reduction. It is certain that in man there are slight differences in the percentage saturation of the blood which is in equilibrium with gas containing a uniform partial pressure of oxygen [Barcroft, 1914]. Similar differences have been observed in the blood of different mice with reference to carbon monoxide [Douglas, Haldane, J. S., and Haldane, J. B. S., 1912]. There are no data to show whether these differences are sufficiently large to show themselves in experiments similar to those quoted above.

THE INFLUENCE OF ALKALI UPON THE REDUCTION AND OXIDATION OF BLOOD.

Series I. Reduction. The first series of experiments which were rather of a preliminary character consisted in reducing blood made alkaline with NaOH always to the extent of M/200 and varying the circumstances under which the reduction took place, namely, the duration and rate of the bubbling and the animal from which the blood was taken. In every case the more alkaline blood was reduced to a less extent than the control blood to which alkali was not added.

(a) Ox blood, 60 bubbles of N₂ per min. at 38°:

Blood	Duration of bubbling in minutes	Percentage saturation after reduction
Normal	7½	49·7 50·0 } 49·9
+ M/200 NaOH	7½	61·0 59·2 } 60·1
Normal	12	32·1 33·0 } 32·6
+ M/200 NaOH	12	41·1 43·3 } 42·2

(b) Sheep's blood, 64 bubbles of N₂ per min. at 38°:

Normal	10	41·5 36·3 } 38·9
+ M/200 NaOH	10	45·6 46·7 } 46·2

(c) Ox blood, 60 bubbles of N_2 per min. at 38° :

Blood	Duration of bubbling in minutes	Percentage saturation after reduction
Normal	10	39.6 } 39.7 39.8 }
+ M/200 NaOH	10	47.5 } 48.4 49.2 }
Normal	15	23.5 } 23.4 23.2 } 25.4 } 24.9 24.3 }
+ M/200 NaOH	15	32.2 } 31.1 30.0 } 33.1 } 34.0 34.8 }

(d) Sheep's blood, 60 bubbles of N_2 per min. at 38° :

Normal	15	26.8 } 27.2 27.6 }
+ M/200 NaOH	15	35.0 } 32.8 30.6 }

(e) Rabbit's blood, 72 bubbles of N_2 per min. at 38° :

Normal	10	21.8 } 19.3 16.7 }
+ M/200 NaOH	10	29.6 } 27.8 26.0 }

(f) Sheep's blood, 72 bubbles of N_2 per min. at 38° :

Normal	10	40.1 } 38.6 37.1 } 39.9 } 41.8 43.6 }
+ M/200 NaOH	10	50.0 } 49.6 49.1 } 50.0 } 49.1 47.2 } 48.6

Series II. Oxidation. The second series consists of a corresponding set of experiments not on the reduction but on the oxidation of blood. The result shows that blood made alkaline to the extent of M/200 NaOH is more rapidly oxidised than is normal blood.

The gas used for the oxidation in this series consisted of O_2 , 12 % + N_2 , 88 %:

(a) Ox blood, 60 bubbles per min. at 38° :

Blood	Duration of bubbling in minutes	Percentage saturation at end of oxidation
Normal	10	80.1 } 80.0 79.9 }
+ M/200 NaOH	10	89.1 } 88.8 88.5 }

(b) Rabbit's blood, 72 bubbles per min. at 38°:

Blood	Duration of bubbling in minutes	Percentage saturation at end of oxidation
Normal	20	91.8 } 91.3 } 91.6
+ M/200 NaOH	20	94.3 } 92.8 } 93.6

(c) Rabbit's blood, 48 bubbles per min. at 39°:

Normal	5	43.7 } 40.1 } 41.9
+ M/200 NaOH	5	54.8 } 48.0 } 51.4

(d) Sheep's blood, 48 bubbles per min. at 39°:

Normal	5	41.4 } 36.7 } 39.1
+ M/200 NaOH	5	48.3 } 43.3 } 45.8

The above tables give the percentage saturations attained by the alkaline and normal bloods in a given time. This measurement is of much less theoretical interest than the relative times taken to attain a given percentage saturation, since this latter measurement gives the relative velocities of the two reactions. Some idea of this may be derived in the case of reduction from figures given in Series I. Let V_A/V_N be the ratio of the velocities of reduction of the alkaline and normal blood.

In Series I (a), the alkaline blood gives the following data:

	Alkaline blood			Normal blood	V_A/V_N
	Observed	Interpolated		Observed	
Time	7.5	12	9.8	7.5	0.77
Percentage saturation	60.1	42.2	50	49.9	
	Normal blood			Alkaline blood	V_A/V_N
	7.5	12	9.4	12	
Percentage Saturation	49.9	32.6	42.2	42.2	0.78
From Series I (c),					
	Alkaline blood			Normal blood	V_A/V_N
	10	15	12.6	10	
Percentage Saturation	48.4	32.6	39.7	39.7	0.78
	Normal blood			Alkaline blood	V_A/V_N
	10	15	12.0	15.0	
Percentage saturation	39.7	24.2	32.6	32.6	0.79

As the second decimal place in the ratio V_A/V_N is probably valueless, we may conclude that the addition of alkali to the extent of M/200 NaOH reduces the velocity of the reduction to 0.75 – 0.8 of its normal value.

THE COURSE OF REDUCTION AND OXIDATION OF ALKALINE BLOOD.

Reduction. As it seemed desirable to test this result over a much greater range of the whole process of reduction, both in percentage saturation and time, a second series of experiments was performed in which fair curves were obtained representing the course of the reaction from the fifth to the thirtieth minute of the reaction (there is always some uncertainty about the first minute or two as it is not clear that a steady condition has established itself). The results of two experiments are as follows:

EXP. A. Sheep's blood. 72 bubbles per minute of nitrogen at 38°:

Time in minutes		5	10	15			
Percentage saturation of blood with O ₂ after reduction	Normal	62.7	61.7	40.8	39.8	22.8	24.2
		60.7		38.8		25.6	
	+ M/200 NaOH	70.4	71.3	48.9	50.8	32.0	30.8
		72.2		52.6		29.5	
Time in minutes		20	25	30			
Percentage saturation of blood with O ₂ after reduction	Normal	16.1	16.1	10.9	7.0	-0.2	-0.2
		—		3.0		—	
	+ M/200 NaOH	15.8	17.6	12.7	11.5	7.2	5.4
		19.4		10.3		3.6	

EXP. B. Sheep's blood. Ditto:

	Time in minutes	5	10	15	
Percentage saturation of blood	Normal	65.2	42.4	28.8	27.1
		62.0	38.6	25.4	
	+ M/200 NaOH	75.0	53.7	27.8	31.0
		70.6	51.1	34.2	
	Time in minutes	20	25	30	
Percentage saturation of blood	Normal	19.4	—	0.6	2.6
		13.2	—	4.6	
	+ M/200 NaOH	19.1	—	5.8	8.0
		18.4	—	10.2	

Figure 1 is a graphic representation of the data furnished by the first of the two experiments given above, which are very concordant. From it the following values for V_A/V_N may be obtained:

Percentage saturation	60	50	40	30	20
V_A/V_N	0.73	0.73	0.78	0.84	0.84

It is not quite clear from these figures whether the ratio V_A/V_N remains constant in the strict sense of the term over the whole course of the reaction, but clearly it remains approximately so.

Oxidation. To turn to the corresponding data which have been obtained with regard to the relative velocities of the oxidation process in the normal blood and that made alkaline to the extent of M/200 NaOH, the following data enable us to construct curves for the purpose of comparison (Fig. 2).

Fig. 1. Rate of reduction of blood with N_2 (Exp. A). Ordinates = percentage saturation of blood with O_2 . Abscissae = time in minutes. — normal blood. ..... blood containing M/200 NaOH.

Fig. 2. Rate of oxidation of blood with N_2 (88 %) + O_2 (12 %) (Exp. A). Ordinates = percentage saturation of blood with O_2 . Abscissae = time in minutes. — normal blood. ..... blood containing M/200 NaOH.

EXP. A. Ox blood. 72 bubbles of N_2 (88 %) + O_2 (12 %) per min. at 38° :

Time in minutes		5		7½		10		
Percentage saturation of blood	{	Normal	52.4	} 52.6	67.8	} 67.2	82.8	} 81.5
			52.8				66.5	
	{	+ M/200 NaOH	61.0	} 62.4	79.1	} 77.1	90.1	} 88.9
			63.7				75.0	
Time in minutes		15		20		30		
Percentage saturation of blood	{	Normal	91.7	} 91.7	96.1	} 96.1	97.2	} 98.0
			—				96.1	
	{	+ M/200 NaOH	94.6	} 95.0	96.6	} 99.4	100.8	} 100.8
			95.3				102.2	

The relative velocities of the oxidation process work out from these figures as follows:

Percentage saturation	30	40	50	60	70	80	90
V_A/V_N ...	1.29	1.29	1.27	1.29	1.29	1.27	1.32

The following data, so far as they go, confirm the value of V_A/V_N obtained above, so far as ox blood is concerned.

EXP. B. Ox blood. 72 bubbles of N_2 (88 %) + O_2 (12 %) per min. at 38° :

Time in minutes		5		10		15	
Percentage saturation of blood	Normal	54.8	} 53.1	84.5	} 84.8	94.3	} 95.7
		50.4		85.2		96.0	
	+ M/200 NaOH	68.3	} 65.7	92.6	} 92.3	101.0	} 99.2
		63.0		92.0		97.0	

from which may be deduced:

Percentage saturation	60	70	80	90
V_A/V_N ...	1.30	1.27	1.27	1.28

Taking 1.28 as being the mean value of V_A/V_N for the oxidation process and 0.78 for the reduction process it is worth noting that the one is the reciprocal of the other. That this is not necessarily the case is shown by similar data on the effect of temperature on the oxidation and reduction process [Oinuma, 1911]. Bubbling experiments such as are dealt with in this paper show that the lowering of temperature *greatly* retards the reduction process (i.e., the dissociation of oxygen from haemoglobin) whilst it *scarcely* accelerates the oxidation process, indeed if correction is made for the fact that the oxidation curves at different temperatures reach different final equilibrium points [Oinuma, 1911, Fig. 2], the effect of temperature on the oxidation process becomes negligible.

The following consideration, however, prevents us from attaching too much importance to the reciprocal relation existing between the values of

V_A/V_N obtained for the oxidation and reduction processes. In the first place one set of experiments was performed on sheep's blood and the other on ox blood. Later it will appear that the bloods of these two species agree closely in their properties, nevertheless it would have been more satisfactory had the two curves been obtained on the same blood. Moreover there seems to be some evidence that V_A/V_N differs in different species. In the rabbit we get a markedly lower value as regards the oxidation process than in the ox:

Exp. C. Rabbit's blood. 60 bubbles of N_2 (88 %) + O_2 (12 %) per min. at 38°:

Time in minutes		5	10	20
Percentage saturation of blood	Normal	41.6	65.0	86.0
		—	62.5	88.1
	+ M/200 NaOH	48.2	70.0	90.0
		47.0	72.0	89.6

from which may be deduced:

Percentage saturation	60	70	80
V_A/V_N	1.25	1.19	1.17

Similar experiments on calf's blood gave figures of 1.23–1.26 for calf's blood, slightly below that of ox blood, but on this difference we cannot, without further research, lay any stress.

THE EFFECTS OF VARIOUS CONCENTRATIONS OF ALKALI ON THE REDUCTION AND OXIDATION OF BLOOD.

Reduction. So far all the experiments of which I have treated have taken the form of contrasting normal blood with that made alkaline to the extent of M/200 NaOH. I have, however, used both stronger and weaker alkalis than this. Thus the effect of M/400 NaOH is quite appreciable.

The effect of alkali does not seem to be the same at all concentrations. Thus in rabbit's blood NaOH seems to have its maximal effect in retarding the reduction of the blood at some concentration of the order of M/50. With concentrations of NaOH higher than this the blood appears to regain its power of reducing, as is shown by the following table in which the percentage saturation of the blood is given after periods of reduction of 10 and 7.5 minutes respectively.

*The effect of various concentrations of NaOH
on the reduction of blood.*

EXP. A. Rabbit's blood. 60 bubbles of N_2 per min. for 10 minutes at 38° :

Blood	Normal	+ M/400 NaOH	+ M/200 NaOH	+ M/100 NaOH
Percentage saturation	39.7	45.0	49.5	54.8
after reduction	41.1	46.2	50.9	56.5
Blood		+ M/50 NaOH	+ M/33 NaOH	+ M/20 NaOH
Percentage saturation		66.5	55.1	48.3
after reduction		66.7	53.2	45.7

EXP. B. Rabbit's blood. 60 bubbles of N_2 per min. for $7\frac{1}{2}$ minutes at 38° :

Blood	Normal	+ M/400 NaOH	+ M/200 NaOH
Percentage saturation	55.4	63.0	67.6
after reduction	55.7	62.4	66.8
Blood	+ M/100 NaOH	+ M/50 NaOH	+ M/33 NaOH
Percentage saturation	73.0	80.4	68.9
after reduction	71.5	79.6	70.0

As the spectroscope shows no alkaline haematin in the blood which contains NaOH to the extent of M/20 (for this confirmation I am indebted to Mr Hartridge) this diminished effect of alkali in higher concentration than M/50 is probably due to the laking of blood which occurs to some extent in the course of reduction with this concentration of alkali.

The fact that increased alkali up to M/100 NaOH retards the rate of reduction of blood with nitrogen is shown also for ox blood by the following figures:

EXP. C. Ox blood. 60 bubbles of N_2 per min. for 10 minutes at 38° :

Blood	Normal	+ M/200 NaOH	+ M/100 NaOH
Percentage saturation	39.6	47.5	52.7
after reduction	39.7	48.4	53.1

When sodium bicarbonate is used instead of sodium hydroxide, the data are somewhat different as shown in the following table:

*The effect of various concentrations of $NaHCO_3$
on the reduction of blood.*

EXP. D. Sheep's blood. 60 bubbles of N_2 per min. for 10 minutes at 38.5° :

Blood	Normal	+ M/200 $NaHCO_3$	+ M/100 $NaHCO_3$	+ M/33 $NaHCO_3$	+ M/20 $NaHCO_3$	+ M/200 NaOH
Percent. saturation	53.1	54.8	57.0	59.7	60.2	60.2
after reduction	51.8	53.7	56.6	58.8	59.2	59.9

EXP. E. Rabbit's blood. 60 bubbles of N_2 per min. for 10 minutes at 38° :

Blood	Normal	+ M/200 $NaHCO_3$	+ M/100 $NaHCO_3$	+ M/33 $NaHCO_3$	+ M/20 $NaHCO_3$	+ M/200 NaOH
Percent. saturation	45.1	49.8	52.3	63.7	68.5	56.9
after reduction	44.7	48.5	51.2	62.5	68.1	54.7

We see now that the retardation of reduction caused by sodium bicarbonate steadily increases with the increased concentration and, unlike the case of sodium hydroxide, also in higher concentration than M/50, even in M/20.

Oxidation. Increased concentration of alkali seems to increase the power of alkali in accelerating the velocity at which reduced blood is oxidised by gas consisting of nitrogen and oxygen in the mixture which I have used. I have worked up to concentrations equal to M/33. This fact is true not only of NaOH but also of NaHCO_3 as is shown by the following table:

The effect of various concentrations of alkalis on oxidation of blood.

EXP. A. Sheep's blood. 60 bubbles of N_2 (87.4 %) + O_2 (12.6 %) per min. for 5 minutes at 39°:

Blood	Normal	+ M/400 NaOH	+ M/200 NaOH	+ M/100 NaOH	+ M/50 NaOH	+ M/33 NaOH
Percent. saturation	53.8	59.2	65.3	68.0	73.2	77.2
after oxidation	53.2	56.6	61.0	63.6	74.0	73.8

EXP. B. Ox blood. 60 bubbles of N_2 (87.4 %) + O_2 (12.6 %) per min. for 5 minutes at 38°:

Blood	Normal	+ M/400 NaOH	+ M/200 NaOH	+ M/100 NaOH	+ M/33 NaOH
Percent. saturation	49.2	57.5	62.0	60.3	65.0
after oxidation	52.4	54.4	57.0	61.3	71.9

EXP. C. Rabbit's blood. 60 bubbles of N_2 (88 %) + O_2 (12 %) per min. for 7½ minutes at 39°:

Blood	Normal	+ M/200 NaHCO_3	+ M/100 NaHCO_3	+ M/33 NaHCO_3	+ M/200 Na_2CO_3	+ M/200 NaOH
Percent. saturation	54.7	59.2	61.7	67.4	62.1	66.0
after oxidation	56.5	57.6	59.7	67.5	61.3	61.2

EXP. D. Sheep's blood. 60 bubbles of N_2 (88 %) + O_2 (12 %) per min. for 10 minutes at 39°:

Blood	Normal	+ M/200 NaHCO_3	+ M/100 NaHCO_3	+ M/50 NaHCO_3	+ M/200 Na_2CO_3	+ M/200 NaOH
Percent. saturation	63.3	64.1	68.2	74.1	69.5	71.5
after oxidation	61.5	65.2	66.8	72.8	68.2	69.0

On adding NaOH to the extent of M/33 there is no fall of the power of alkali to accelerate the rate of oxidation of blood as in the case of reduction. I repeated similar experiments several times but could prove no definite fall of the effects of alkali. Any higher concentration of alkali than M/33 caused intense frothing in the tube towards the end of the preliminary reduction of blood, which must last about 50 minutes or more, and made the experiment useless.

THE EFFECT OF DIFFERENT ALKALIS ON THE RATE OF REDUCTION
AND OXIDATION OF BLOOD.

I have compared a number of alkaline salts of sodium, under similar conditions. Of these it appears that sodium hydroxide and sodium carbonate in equimolecular proportion do not differ materially in their effects, and that they are more potent both in retarding reduction and in accelerating oxidation than are either dibasic sodium phosphate or sodium bicarbonate, which in turn have approximately equal effects.

*Comparison of the effect of different alkalis of equimolecular concentration
upon the rate of reduction.*

EXP. A. Sheep's blood. 72 bubbles of N_2 per min. for 10 minutes at 38° :

Blood	Normal	+ M/200 Na_2HPO_4	+ M/200 $NaHCO_3$	+ M/200 Na_2CO_3	+ M/200 NaOH
Percent. saturation	39.5	41.2	42.6	45.8	47.8
after reduction	41.4 } 40.5	41.1 } 41.2	43.2 } 42.9	45.9 } 45.9	48.5 } 48.2

EXP. B. Rabbit's blood. 72 bubbles of N_2 per min. for 10 minutes at 38° :

Blood	Normal	+ M/100 Na_2HPO_4	+ M/100 $NaHCO_3$	+ M/100 Na_2CO_3	+ M/100 NaOH
Percent. saturation	34.3	36.9	41.2	49.4	50.3
after reduction	33.8 } 34.1	36.2 } 36.6	39.1 } 40.2	50.5 } 50.0	49.9 } 50.1

*Comparison of the effect of different alkalis of equimolecular concentration
upon the rate of oxidation.*

EXP. C. Sheep's blood. 60 bubbles of N_2 (88 %) + O_2 (12 %) per min. for 10 minutes at 39° :

Blood	Normal	+ M/200 Na_2HPO_4	+ M/200 $NaHCO_3$	+ M/200 Na_2CO_3	+ M/200 NaOH
Percent. saturation	—	72.5	72.2	78.0	79.4
after oxidation	69.1 } 69.1	70.8 } 71.7	71.5 } 71.9	77.1 } 77.6	77.4 } 78.4

EXP. D. Rabbit's blood. 60 bubbles of N_2 (88 %) + O_2 (12 %) per min. for $7\frac{1}{2}$ minutes at 38° :

Blood	Normal	+ M/100 Na_2HPO_4	+ M/100 $NaHCO_3$	+ M/100 Na_2CO_3	+ M/100 NaOH
Percent. saturation	47.4	50.0	50.1	60.0	61.3
after oxidation	44.0 } 46.2	49.3 } 49.7	51.1 } 50.6	58.2 } 59.1	57.1 } 59.2

THE INTERFERENCE OF CARBON DIOXIDE WITH THE EFFECT OF ALKALI ON
THE RATE OF OXIDATION OF BLOOD.

As shown by Bohr, Hasselbalch and Krogh [1907] and also by Mathison [1911] and Oinuma [1911], the presence of carbon dioxide hastens the rate of reduction of blood and slows that of oxidation. We see now that alkali acts in just the opposite way. The last series of the present investigation was undertaken to see the extent to which carbon dioxide and alkali counteract each other with regard to the oxidation of blood. As oxidising gas two mixtures were employed at body temperature: each consisted of nitrogen containing 12·8 % oxygen, but one with 5·6 % CO₂ added, the other without CO₂. The partial pressures of oxygen and carbon dioxide in the former roughly correspond, at body temperature and with the tension of aqueous vapour corrected, to 100 mm. and 40 mm. of mercury respectively; the mixture is therefore approximately equivalent to alveolar air. The following data were obtained after passing a stream of each gas mixture through normal and alkaline blood which had been previously entirely reduced.

Interference of CO₂ with the effect of alkali upon the rate of oxidation.

EXP. A. Rabbit's blood. 60 bubbles of gas mixture at 39° for 10 minutes:

Gas mixture	Percentage saturation of blood					
	Normal		+ M/100 NaHCO ₃		+ M/100 NaOH	
N ₂ (87·2 %) + O ₂ (12·8 %)	63·5	63·8	75·5	69·3	74·7	73·5
	64·0		68·0		72·3	
N ₂ (81·6 %) + O ₂ (12·8 %) + CO ₂ (5·6 %)	56·2	55·6	61·9	60·9	67·3	65·7
	55·0		58·8		64·0	

EXP. B. Rabbit's blood. 60 bubbles of gas mixture at 39° for 10 minutes:

Gas mixture	Percentage saturation of blood					
	Normal		+ M/200 NaOH		+ M/100 NaOH	
N ₂ (87·2 %) + O ₂ (12·8 %)	64·7	65·9	73·7	72·8	75·1	76·2
	67·0		71·8		77·3	
N ₂ (81·6 %) + O ₂ (12·8 %) + CO ₂ (5·6 %)	57·1	56·8	65·8	64·8	68·5	67·4
	55·6		63·7		66·3	

From these results it is obvious that blood made alkaline by adding M/100 NaOH is oxygenated to a greater degree by a gas containing 5·6 % CO₂ than normal blood is oxidised by a similar gas which contains no CO₂, and blood with NaOH added to M/200 to a slightly smaller degree. Thus the depressing action of CO₂ at the same partial pressure as in the alveolar air

on the rate of oxidation of blood is counteracted by the addition of NaOH to the blood to some concentration between M/200 and M/100. The addition of NaHCO₃ to M/100 does not wholly counteract the effect of CO₂ of the percentage mentioned above.

If we compare the figures in any one line, we find another fact worthy of mention, i.e., the differences between the percentage saturation of normal blood and that of alkaline blood are practically equal in the cases in which the oxidising gas contained CO₂ and in those in which no CO₂ was contained. Accordingly it may be asserted that the alkali exerts an accelerating effect of about equal extent on the oxidation of blood both in cases where the oxidising gas used contains CO₂ and where no CO₂ is present.

It is clear that these results concerning the effect of alkali on the gas exchange of blood have a certain clinical significance. Numerous observers, Poulton and Ryffel [1913], Peabody [1914], Lewis, Barcroft and their collaborators [1913], have described acid conditions of the blood associated with dyspnoea probably of renal origin. Such conditions might conceivably be treated by the addition of alkali in some form or other to the blood; the line of argument being (1) that the alkali by reducing the hydrogen ion concentration of the blood would relieve the dyspnoea; (2) that it might be added in sufficient quantity to do this in spite of a possible rise in the CO₂ occasioned by the slower respiration. The results given show that the alkali would assist the taking up of oxygen in the lung and would probably not retard the reduction process, in the case of patients resting in bed, sufficiently to impair the respiration in the tissues to an extent which would be really injurious.

SUMMARY.

(1) The rate at which arterial blood gives up its oxygen at low oxygen tensions or the venous blood takes up the gas at high oxygen tensions is influenced to an appreciable degree by the presence of alkali in small quantity. The oxygenation is hastened and the reduction slowed.

(2) The addition of alkali to the extent of M/200 NaOH reduces at body temperature the velocity of reduction of blood on an average to 0.78 of its normal values and increases that of oxidation approximately to 1.2-1.3. Of these two values one is nearly the reciprocal of the other.

(3) The above effect of alkalis (NaOH, NaHCO₃) upon the rate of oxidation and reduction increases with increased concentration up to about M/50.

The power of NaOH in retarding the velocity of reduction appears to fall at a concentration higher than M/50.

(4) In equimolecular concentrations, NaOH and Na_2CO_3 have an equivalent effect. The same is true of Na_2HPO_4 and NaHCO_3 but their effect is less than that of NaOH and Na_2CO_3 .

(5) In the rabbit the effect of carbon dioxide, which is contained in the oxidising gas in such a proportion as is found in the alveolar air, upon the rate of oxidation of blood is counteracted by the addition of NaOH of concentration between M/200 and M/100.

(6) Blood of animals of different species is reduced or oxidised at different rates. In the same species the rate of reaction is generally similar in different animals. There are, however, many exceptions.

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