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Experimental Study on the Disturbance of Acid-Base Balance during and after Bilateral Thoracotomy and on its Prevention

By

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Introduction

When we operated inside the thoracic cavity in old days, sometimes bilateral thoracotomy was forced to perform and the patient was confronted with death. In the earlier part of this century (1904), Sauerbruch, Brauer and others invented " Ueberdruck-Verfahren " (high pressure gas machine) which prevented the above mentioned danger. This apparatus became popular and a great progress in thoracic surgery was established. It has been, however, looked over for a long time that, when this apparatus is used, beside an advantage that the blood O_2 content increases, there occurs a great disadvantage that CO_2 accumulates in blood due to disturbance of expiration.[1)-6)] The first object of this study is to elucidate the condition to cause the accumulation of CO_2 and to clarify the mechanism of disturbance of acid-base balance encountered during and after the operation. To find out the counter measure to prevent such disturbance is the second object of this research.

Experimental

(I) The Disturbance of Acid-base Balance during and after Bilateral Thoracotomy with Constant Flowing of O_2 under Positive Pressure

Method

Rabbits and dogs were used for this experiment. In rabbits the chest wall was incised bilaterally, 3 to 4 cm. long under local anesthesia, and in dogs an incision of 20 cm. long was made also under local anesthesia, barbiturate having been administered previously. After thoracotomy, an air-tight tube was inserted in the trachea and was connected

to an apparatus of continuous O_2 flow under positive pressure (semi-closed system).

Chemical analysis of blood samples. Blood samples which were taken from A. femoralis with oiled syringe containing a small quantity of potassium oxalate sufficient to prevent coagulation were centrifuged to separate plasma. The plasma samples thus obtained were analysed as soon as possible. CO_2 content was measured by Van Slyke and Neill's method[7] with 0.5 cc. samples. The pH of the plasma was measured with Hasting and Sendroy's phenol red bicolor standard method[8]. The CO_2 tension, pCO_2 was read from Peters and Van Slyke's Nomogram[9] by the observed pH and the total plasma CO_2. When the data in question fell outside the scales of the nomogram, pCO_2 was calculated directly by Henderson-Hasserbalch's equation:

$$pCO_2 = \frac{[\text{Total } CO_2]p}{0.1316 \times 0.510\,(10^{pH-6.10}+1)}$$

Blood Hb (in g. per 100 cc.) was measured by Acid Hematin method (Sahli-Komiya).

$[HCO_3]$ corrected for pH 7.4, (mM/L. of plasma) was computed by the formula:[10][11]

$$\text{Hb mM/L.} = \frac{\text{Hb in g. per 100 cc.} \times 10}{16.7}$$

$$\beta = 8.6 + 2.3\ (\text{Hb mM/L.})$$

$$\therefore\ [HCO_3]p \text{ cor.} = [HCO_3]p \text{ obs.} + \beta\ (pH_s \text{ obs.} - 7.4)$$

Result

1) *The factors contributing to the accumulation of CO_2 during long standing opening of chest and constant flow of O_2 under positive pressure (semi-closed system)*

The CO_2 showed an ascending curve resembling hyperbola (See Table I). The CO_2 tension increased sharply making almost a straight line, while the pH values decreased also linearly. R_2 died 6 hours after opening the chest, when the pH dropped to 6.85 and the CO_2 tension ascended to 207 mm. Hg. As soon as the chest was opened, the respiratory rate was about 50 per minute, though the respiratory depth was not remarkably increased. The breathing got deeper with the lapse of time and the strained ventilation became gradually evident. 4 hours after operation the respiration decreased by and by. 5 hours later great spastic respiration appeared occurring about 20 times per minute and the pulse slowed down. The general condition got so worse that 6 hours later the heart stopped in diastole.

TABLE I

Changes in CO_2 during Long-timed Opening of Chest with Constant Flow of O_2 under Positive Pressure in Rabbits

Case Number	Item	Before thoracotomy	Time after start of thoracotomy					Remark	
			5 (min.)	1 (hour)	2 (hour)	5 (hour)	6 (hour)	Continuous press.	Intermitt. press
R_1	CO_2 vol %	35.9 (0.0)	52.6 (+16.7)	62.0 (+26.1)			58.1 (+22.1)	4 cm. H_2O	P=4/0 cm. H_2O R=40/Min.
R_2	CO_2 vol %	53.0 (0.0)	56.8 (+ 3.8)	69.2 (+16.2)	77.8 (+24.8)		59.9 (+16.9)	do	do
R_3	CO_2 vol %	49.1 (0.0)	57.3 (+ 8.2)	71.2 (+22.1)	75.4 (+26.3)		70.8 (+21.7)	do	do
R_5	CO_2 vol %	41.6 (0.0)	55.0 (+13.4)	54.5 (+12.9)	54.0 (+12.4)		56.5 (+14.9)	12 cm. H_2O	P=12/2 cm. H_2O R=40/Mim.
R_6	CO_2 vol %	38.5 (0.0)	41.6 (+ 3.1)	52.9 (+14.4)	69.3 (+30.8)		68.5 (+30.0)	do	do
R_7	CO_2 vol %	49.3 (0.0)		70.9 (+21.6)	82.5 (+33.2)	91.3 (+42.0)	92.0 (+42.7)		
	pHs	7.32		7.28	7.18	7.00	6.85		
	pCO_2 mm. Hg.	41.5		66.0	94.8	155.2	207.1		
	HCO_3^- obs. mM/L.	21.3		29.8	34.4	36.4	34.1		
	Hb mM/L.	8.7		7.5	7.8	6.8	6.7		
	HCO_3^- cor. mM/L.	19.0		26.7	28.6	26.7	20.9	8 cm. H_2O	
	change in fixed acid mM/L.	—		−7.7	−9.6	−7.7	−1.9		
Average	CO_2 vol %	44.5 (0.0)	52.6 (+ 9.1)	63.5 (+19.1)	71.8 (+25.5)				

* The figures shown are the CO_2 vol % obtained when intermittent positive pressure was applied for 10 minutes after the bilateral thoracotomy was performed for 2 hours under constant flow of O_2 positive pressure (see Remark).

TABLE II

Changes in CO_2 Content, pH, pCO_2, Fixed Acid during and after Pleura Opened, in Dogs

Case Number	Item	Before thoraco-tomy	1 Hour after pleura opened	30 Min. after pleura closed	Time after end of operation	
					2 (day)	5 (day)
D_7	CO_2 vol %	56.5 (0.0)	57.6 (+ 1.1)		49.3 (− 7.2)	54.9 (− 1.6)
	pH_s	7.30 (0.0)	7.17 (− 0.13)		7.03 (− 0.29)	7.38 (+ 0.08)
	pCO_2 mm. Hg.	49.5 (0.0)	67.5 (+18.0)		71.5 (+22.0)	41.0 (− 8.5)
	HCO_3^- obs. mM/L.	27.5 (0.0)	28.0 (+ 0.5)		20.3 (− 7.2)	23.3 (− 4.2)
	Hb mM/L.	6.9 (0.0)	7.0 (+ 0.1)		9.6 (+ 2.7)	7.4 (+ 0.5)
	HCO_3^- cor. mM/L.	25.1 (0.0)	22.4 (− 2.7)		9.9 (−15.2)	18.2 (− 6.9)
	change in fixed acid mM/L.	−	+ 2.7		+15.2	+ 6.9
Average of D_1 D_2 D_3 D_4 D_5 D_6 & D_7	CO_2 vol %	47.9 (0.0)	52.0 (+ 4.5)	45.8 (− 0.7)	39.1 (−11.7)	
	pH_s	7.39 (0.0)	7.15 (− 0.24)	7.24 (− 0.16)	7.23 (− 0.13)	
	pCO_2 mm. Hg.	35.1 (0.0)	65.2 (+28.7)	46.3 (+13.6)	41.3 (+ 3.0)	
	HCO_3^- obs. mM/L.	21.5 (0.0)	22.5 (+ 1.0)	18.7 (− 0.9)	16.1 (− 8.8)	
	Hb mM/L.	7.0 (0.0)	7.1 (+ 0.1)	7.1 (+ 0.1)	7.2 (+ 0.4)	
	HCO_3^- cor. mM/L.	21.2 (0.0)	16.2 (− 5.0)	14.3 (− 5.1)	11.4 (−12.2)	
	change in fixed acid mM/L.	−	+ 5.0	+ 5.0	+12.2	

2) *Changes in CO_2 content, pH, CO_2 tension, concentration of bicarbonate and fixed acids during and after the opening of chest*

Table II shows the results of experiments on dogs. When both pleurae were opened during the course of operation, the CO_2 tension showed a tendency to rise and pH to fall as shown in Table I. This tendency was observed in the greatest degree in D_5; CO_2 tension increased to 47.9 mm. Hg. and pH fell 0.40 compared with the preoperative value. The average increase of pCO_2 was 28.7 mm. Hg. and decrease of pH was 0.24. Obviously this was due to respiratory acidosis. The change

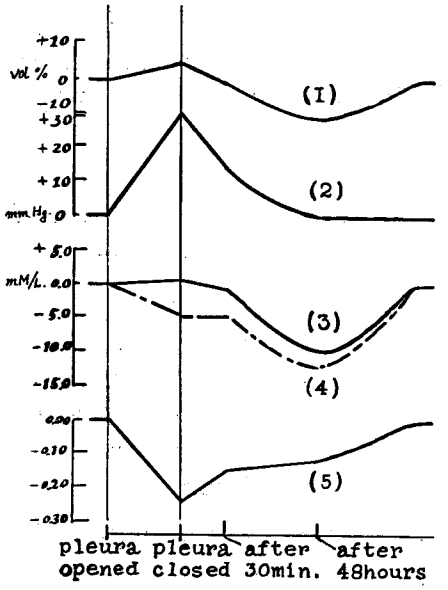

Fig. 1. Graph based on Table II shows the average changes of values of (1) total CO_2 (vol %), (2) pCO_2 mm. Hg., (3) $[HCO_3]$ mM/L., (4) $[HCO_3]$ corrected for pH, mM/L. and (5) pH_S. during and after operation.

of fixed acids was variable depending upon the individuals. In some increase and in others no change was found, the change being 5.0 mM/L. in average. Generally speaking, respiratory acidosis became complicated, more or less, with metabolic acidosis during the course of opening the chest. After the pleura was opened for an hour, the chest was closed by inflating the lungs sufficiently under about 20 cm. H_2O positive pressure. The CO_2 which increased during the course of operation returned to the preoperative value and the pH showed a tendency to increase 30 minutes after the closure of the pleura.

Concerning the postoperative course, all cases did not show any increase of pCO_2, except D_7 which suffered obviously from anoxic anoxia due to insufficient closure of the chest; no symptom indicating the respiratory acidosis was observed. In all cases, however, alkali reserve decreased remarkably (12.2 mM/L.) (metabolic acidosis). While pH in almost all cases were in the compensatory area, that in D_7 dropped to as low as 7.03 which was a dangerous area for the animal. It seems that this metabolic acidosis was due to postoperative anoxia which often produces a large amount of fixed acids by the disturbance in metabolism of the tissue cells.

(II) Prevention against the Respiratory Acidosis Accompanying the Opening of Thorax

In order to prevent the respiratory acidosis the ventilation of alveolar gas was considered. To improve the above mentioned constant flowing procedure under positive pressure the following two modifications were studied experimentally (A & B).

(A) Intermittent administration of O_2 under positive pressure

Method

The compressed O_2 was supplied from the O_2-bomb to a positive pressure machine (semi-closed system). The apparatus was regulated so as to allow the constant flow of O_2 at the rate of one liter per 30 seconds, and the pressure was rhythmically changed.

Result

Rabbits R_8 and R_9 were observed under positive pressure of 8 cm. H_2O. The hydrolic pressure was regulated to synchronize with the natural rythm of respiration. While the pressure in the alveolar cavity fluctuated between 8 cm. H_2O in inspirium and 4 cm. H_2O in expirium, the accumulation of CO_2 was hardly prevented. R_{10} was experimented, so that the rate of respiration was 20 per minute and pressure swinged between 8 cm. H_2O and 0 cm. H_2O. The blood CO_2 decreased, but the result was not yet satisfactory. R_{11} and R_{12} were conditioned to the rate of respiration of 20 per minute, and the pressure between 10 cm. H_2O and 0 cm. H_2O. The CO_2 got lower than the preoperative level, showing that the condition was satisfactory. R_{13} and R_{14} were examined for acid-base balance under the same condition. The decrease of CO_2 accompanied with the fall of pCO_2; the respiratory acidosis was completely under control. But I have to point out that there was a tendency of an increase of fixed acid, and a slight fall of pH during the course of this method (see Fig. 2 (A)). Judging from the recovery of the metabolic acidosis after the closure of pleura, this phenomenon seems to be related to this mode of artificial respiration. It may have been resulted from the production of ketone substances due to hyperventilation.

(B) Constant flowing under positive pressure by intermittent insufflation of excessive O_2

Method

Both pleural cavities were opened under certain positive pressures (P.) and insufflated with O_2 at a constant speed of flowing (Insufflation

TABLE III

Changes in CO_2 when the Intermittent Administration of O_2 under Positive Pressure was used on Various Conditions in Rabbits

Case number	Item	Before thoracotomy	After pleura-opening: 30 (min.)	After pleura-opening: 1 (hour)	After pleura-opening: 2 (hour)	1 Hour after pleura-closing	Remark: Intermitt. pressure	Remark: Rate of respiration
R_8	CO_2 vol %	41.2	53.8	58.4	65.5	46.0	P=8/4 cm. H_2O	R=40
R_9	CO_2 vol %	45.3	56.5	66.0	63.7	50.0	do	do
R_{10}	CO_2 vol %	50.2	53.3	57.7	61.8		P=8/0 cm. H_2O	R=20
R_{11}	CO_2 vol %	51.0	44.1	40.8	40.4	51.3	P=10/0 cm.H_2O	R=20
R_{12}	CO_2 vol %	35.0	30.6	32.7	34.4	45.6	do	do
R_{13}	CO_2 vol %	44.4	40.3	34.9		51.6	do	do
	pH_s	7.33	7.30	7.28		7.25		
	pCO_2 mm. Hg.	36.5	35.0	32.1		51.0		
	HCO_3^- obs. mM/L.	18.8	17.1	14.6		21.5		
	Hb mM/L.	6.9	6.9	7.5		6.6		
	HCO_3^- cor. mM/L.	17.1	14.7	11.5		17.9		
	change in fixed acid mM/L.	—	+2.4	+5.6		−0.8		
R_{14}	CO_2 vol %	55.8	43.7	32.3		38.4	do	do
	pH_s	7.30	7.27	7.28		7.25		
	pCO_2 mm. Hg.	49.5	41.7	30.0		37.8		
	HCO_3^- obs. mM/L.	23.6	18.5	13.6		16.2		
	Hb mM/L.	7.5	7.2	7.2		7.2		
	HCO_3^- cor. mM/L.	21.0	15.2	10.6		12.4		
	change in fixed acid mM/L.	—	+5.8	+10.4		+8.6		
Average of R_{13} & R_{14}	CO_2 vol %	50.1	42.0	33.6		45.0	do	do
	pH_s	7.32	7.29	7.28		7.25		
	pCO_2 mm. Hg.	43.0	38.4	31.1		44.4		
	HCO_3^- obs. mM/L.	21.2	17.8	14.1		18.9		
	Hb mM/L.	7.2	7.1	7.4		6.9		
	HCO_3^- cor. mM/L.	19.1	15.0	11.1		15.2		
	change in fixed acid mM/L.	—	+4.1	+8.0		+3.9		

of O_2 at the rate of 1 liter per 30 seconds from the O_2-bomb to the positive pressure machine). Then, during the course of opening of chest, a certain amount of O_2 (5 liters) was insufflated at a high speed (at the rate of one liter per 4 seconds) intermittently (frequency F.). Subsequently the positive pressure rose by 2 cm. H_2O higher than given positive pressure

TABLE

Changes in CO_2 when Constant Flowing under Excessive O_2 was used on

Case number	Item	Before thoraco-tomy	After pleura-opening		
			30 (min.)	1 (hour)	2 (hour)
R_{16}	CO_2 vol %	34.5	42.0	51.5	55.8
R_{17}	CO_2 vol %	47.6	57.6	56.8	62.7
R_{20}	CO_2 vol %	29.6	29.0	27.6	29.4
R_{21}	CO_2 vol %	48.9	44.0	44.8	44.6
R_{22}	CO_2 vol %	60.2	59.8	59.2	
	pH_s	7.33	7.33	7.35	
	pCO_2 mm. Hg.	49.9	49.0	46.2	
	HCO_3^- obs. mM/L.	25.3	25.1	25.0	
	Hb mM/L.	8.1	8.5	8.5	
	HCO_3^- cor. mM/L.	23.4	23.1	23.6	
	change in fixed acid mM/L.	—	+ 0.3	− 0.2	
R_{23}	CO_2 vol %	43.8	43.8	39.7	
	pH_s	7.33	7.33	7.30	
	pCO_2 mm. Hg.	36.0	36.0	35.0	
	HCO_3^- obs. mM/L.	18.5	18.5	16.8	
	Hb mM/L.	7.2	7.2	7.5	
	HCO_3^- cor. mM/L.	16.7	16.7	14.3	
	change in fixed acid mM/L.	—	0.0	+ 2.4	
Average of R_{22} & R_{23}	Co_2 vol %	52.0	51.8	44.5	
	pH_s	7.33	7.33	7.33	
	pCO_2 mm. Hg.	43.0	44.5	40.6	
	HCO_3^- obs. mM/L.	21.9	21.8	20.9	
	Hb mM/L.	7.7	7.9	8.0	
	HCO_3^- cor. mM/L.	20.1	19.9	19.0	
	change in fixed acid mM/L.	—	+ 0.2	+ 1.1	

followed by the expansion of lungs.

Result

R_{16} was under the condition of P.=4.0 cm. H_2O, F.=one time per 15 minutes. The increase of CO_2 was lower than that observed in the constant flowing under positive pressure (Table I), but the removal of CO_2 was not yet satisfactory. R_{17} was under the condition of P.=6 cm. H_2O, F.=2 times per 5 minutes. The results were also not good. R_{20}

IV

Positive Pressure by Intermittent Insufflation of Various Conditions in Rabbits

After pleura-closing			Remark	
1 (hour)	2 (day)	3 (day)	Positive press.	Frequency
			P=4 cm. H_2O	F=1/15 Min.
80.7			P=6 cm. H_2O	F=2/5 Min.
41.9			P=4 cm. H_2O	F=2/5 Min.
50.9			do	do
62.0		59.9		
7.33		7.42		
51.8		42.7		
26.1		25.4	do	do
8.5		6.8		
24.1		25.4		
− 0.7		− 2.0		
44.0	46.8			
7.28	7.35			
41.0	36.3			
18.5	19.7		do	do
7.5	6.5			
15.4	18.5			
+ 1.3	− 1.8			
53.0				
7.31				
46.4				
22.3			do	do
8.0				
19.8				
+ 0.3				

and R_{21} were under the condition of P.=4 cm. H_2O, F.=2 times per 5 minutes. The CO_2 did not increase and satisfactory results were thus obtained. R_{22} and R_{23} were examined for acid-base balance under the same condition. The pCO_2, pH and alkali reserve did not show significant changes. Therefore, the respiratory acidosis was to be considered completely prevented, not causing also the metabolic acidosis. An ideal condition was found (see Fig. 2 (B)). Furthermore, R_{22} was killed 10 days after the operation, and its lungs were examined histologically. No

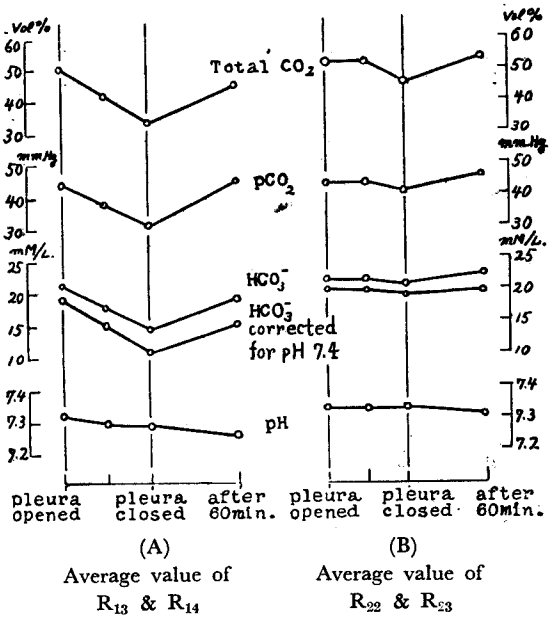

Fig. 2. Comparison of (A) intermittent administration of O_2 under positive pressure & (B) constant flowing under positive pressure by intermittent insufflation of excessive O_2. Experiments on rabbits.

pathologic processes were detected.

Comment

Little significance has been given clinically to the respiratory acidosis. This fact may be explained as follows: the respiratory acidosis in diseases treated ordinarily in clinic is almost always accompanied with anoxia, because the rate at which CO_2 diffuses through animal membranes is 20 to 30 times as great as the rate at which O_2 diffuses (Krogh),[11] in any individual breathing the usual atmosphere, interference with the gas exchange results in death from O_2 want before CO_2 accumulation becomes dangerous[11)-13)]. When both pleurae of animals are opened under positive pressure of O_2, a peculiar condition is recognized. That is, anoxia doesn't appear because of sufficient supply of O_2, but the accumulation of CO_2 develops severe respiratory acidosis and the animal is exposed to death. In clinical cases, however, this kind of acidosis develops usually so gradually, that it will be followed at first by a shift of the CO_2 absorption curve, then by a change in the concentration of plasma bicarbonate. Both of them are the compensatory mechanism and bring the pH which has fallen for a while back to within the normal range. Whereas the respiratory acidosis which will occur during thoracotomy has not enough time to

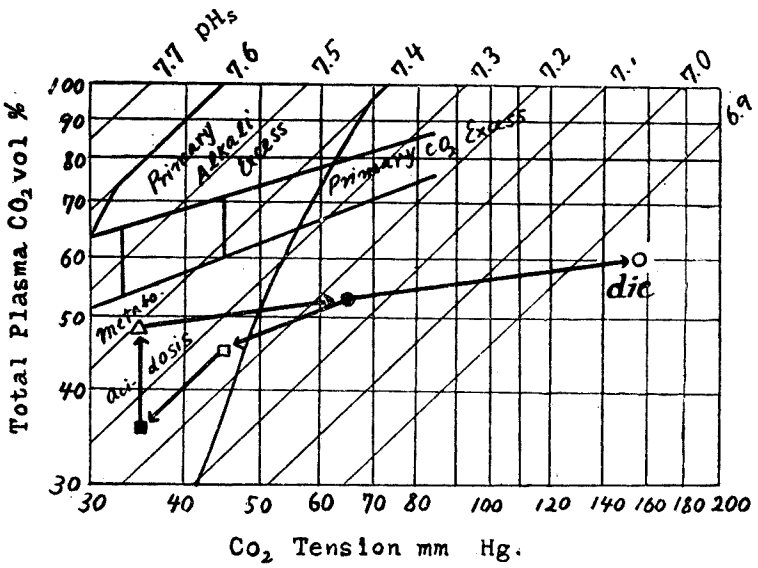

Fig. 3. The changes of acid-base balance during and after bilateral thoracotomy drawn in a logarithmic chart after Peters based on the data of table I and table II.

△—Values preoperative and after complete recovery.

●—Values during bilaterally open chest.

○—Values of cases of death from severe respiratory acidosis caused by long standing open chest.

□—Values immediately after closure of chest.

■—Values a few days after operation.

be alleviated by compensatory mechanism, the respiratory acidosis develops rather acutely along with the shift of the CO_2 absorption curve. Consequently, the pH drops sharply and the circulatory collapse becomes imminent (see Fig. 3). The respiratory acidosis during the opening of chest under the special condition of using O_2 flow under positive pressure, is characterized by the lack of tachypnea and cyanosis which are the sole symptoms of respiratory acidosis ordinarily observed in clinic. Therefore, a danger of acidosis would be doubled. A method to prevent its occurrence *during* the operation should be considered important.

A method of intermittent administration of O_2 under positive pressure following the similar principle of Crafood[5] was performed, and the accumulation of CO_2 was successfully prevented. Though the prevention of respiratory acidosis is possible while the prevention of metabolic acidosis is impossible by such a procedure, it seems judging from the patterns of acid-base balance, that the hyperventilation will be followed by a metabolic acidosis due to overproduction of ketone substances or the increased fixed

acid by the overwork of respiratory muscle, as the artificial respiration interfers with normal respiration (see Fig. 2 (A)). This is the reason why unnecessary hyperventilation should be avoided. When thoracotomy with the method of constant flowing under positive pressure by intermittent insufflation of excessive O_2 is performed, the metabolic acidosis as well as respiratory acidosis is completely prevented and more suitable condition can be obtained by this means than the above mentioned method (see Fig. 2 (B)).

No papers concerning the development of metabolic acidosis postoperatively have been so far reported as far as they are accessible to me. Anemic, stagnant and other types of anoxia which can develop frequently after operation seem to play a great role in metabolic acidosis and if it complicates with anoxic anoxia the danger of acidosis will be exaggerated. The prevention of such untoward factors is an urgent problem besides the usual postoperative care for fluid and O_2 supply.

Summary

An experimental study on disturbances of acid-base balance encountered during operations of opened chest was carried out in dogs and rabbits. Special attention was given to the effects of methods for continuos O_2 supply under positive pressure. The following results were obtained:

1. When bilateral thoracotomy is performed with constant flowing of O_2 under positive pressure, the removal of CO_2 is hindered, the respiratory acidosis sets in with the lapse of time and the danger ensues. In fact, in spite of enough supply of O_2, the animal dies due to the acidosis.
2. The respiratory acidosis during operation will be relieved by closing the chest.
3. The respiratory acidosis during operation is often complicated by metabolic acidosis.
4. Metabolic acidosis appears few days after operation and it tends to increase.

Concerning the research how to prevent the occurrence of acidosis during operation the following results were obtained:

5. When the intermittent administration of O_2 under positive pressure or the constant flowing under positive pressure by intermittent insufflation of excessive O_2 is used to expedite the exchange of the alveolar gas, the respiratory acidosis is prevented.
6. The partial pressure of CO_2 is not increased by the type of intermittent administration of O_2 under positive pressure, but the alkali reserve decreases and the pH falls.
7. Metabolic acidosis as well as respiratory acidosis do not occur by the type of constant flowing under positive pressure by intermittent

insufflation of excessive O_2. More physiologic, accordingly more suitable condition can be obtained by this means than by the above mentioned method.

Kind advices were given by Prof. K. Matsuda, of applied physiology I should like to express my gratitude to him.

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