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PNEUMOTHORAX GASES.

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ABSTRACT.

Analyses of the gas mixtures from 15 pneumothoraces in dogs and from 62 human patients reveal a striking difference between the human and dog results. The human patients as a rule have a much lower concentration of oxygen and a somewhat higher concentration of carbon dioxide than do the dogs.

Possible reasons for this divergence are discussed and attempts have been made with dogs to bring their results into line with human figures. The duration of the pneumothorax is not a factor. A large pneumothorax may result in a slight change in the analysis in this direction, as may depression of respiration by morphine, but these are not the chief factors. Results in dogs approximating human analyses are obtained when pleural irritation and inflammation is induced.

The typical composition of a human pneumothorax is therefore apparently due to a concomitant pleural inflammation.

INTRODUCTION.

The induction of an "artificial pneumothorax" is now a common practice in the treatment of certain forms of lung disease such as pulmonary tuberculosis, and the occurrence of a "spontaneous pneumothorax" is not an uncommon development of these same diseases. The term pneumothorax means merely the presence of gas in the pleural cavity, that is, within the chest but outside the lungs, and unless qualified its full significance is not indicated.

If the pneumothorax is artificially induced, care is taken to avoid infection of the pleura or lining of the pleural cavity,

and the air put in displaces the lung thereby allowing it to shrink or collapse and putting it at rest. If the pneumothorax is of spontaneous origin, the usual cause is a small tear of the surface of the lung, opening into the smaller branch bronchi and allowing air to enter the pleural cavity through the respiratory tubes. The effect towards collapse of the lung would be the same, but as the trachea and bronchi are by no means always bacteriologically sterile, infection of the pleural surface with later development of pleurisy and perhaps empyema is only too likely to result. A spontaneous pneumothorax may develop in a person who already has an artificial and the desirability of knowing when this has happened is apparent. Sometimes it cannot be detected by ordinary clinical examination. The primary purpose of this work was to provide a test which would aid the clinician in his diagnosis. Partial success has been noted in this regard, but these more clinical features are not being discussed in this paper. In the course of the work certain results presented themselves for explanation, and the further investigation of these results constitute the bulk of this publication which really is a preliminary report of work still in hand.

Pneumothorax in Dogs and Humans.

Air is injected into the pleural cavities by a syringe with an attached hypodermic needle inserted through the thoracic wall. The amount injected varies from about 100 cc. to 500 c.c. This is all absorbed from the cavity within a day or two unless air is repeatedly injected and, when this is done, the absorption rate apparently becomes slower after a time. The total gas pressure within the pleural cavity is subatmospheric, being in the order of -10 to -20 mm. Hg during inspiration and 0 to -10 mm. Hg during expiration.

This gas is in a closed cavity the walls of which are moist so that the components of the mixture (O_2, CO_2, and N_2) will presumably go into solution in the fluid of the pleural surfaces according to their partial pressures. The pleural and thoracic walls behind them contain circulating blood which is also

carrying these gases. If air is injected, one would expect oxygen to be absorbed through the pleura and carried away by the blood as the O_2 tension of the blood is less than that of the injected air. Similarly as the CO_2 tension of the blood is greater than the negligible value for the injected air, one would expect carbon dioxide to diffuse out from the blood into the pleural cavity. In time the gases in the cavity should reach or at least approach an equilibrium with the tensions of the blood. Equilibrium would appear to be attained (Table 6) in the case of CO_2 in less than 30 minutes but in the case of O_2 not for 8 to 12 hours.

The pressures of the gases in the pleural cavity are readily determined by analysis in the ordinary Haldane apparatus. Thus if 10% of the gas is O_2 then the pressure of O_2 would be of the order of,

$$\frac{10}{100} \times (745\text{-}45) = 70 \text{ mm. Hg.}$$

(745 = total gas pressure)
(45 = tension aqueous vapor)

The tensions in the blood cannot be accurately obtained as it is the capillary blood in the pleura (parietal and visceral) which is significant. The gas tensions of capillary blood will lie somewhere between those of the arterial and venous bloods supplying and draining the region. However an attempt has been made below to calculate probable values (Table 1). Arterial and mixed venous blood tension figures are given,

TABLE 1.

Blood Gases.

	Tension	See Text
	(mm. Hg.)	%
Oxygen—Normal Arterial	90	13
Normal Venous	40	6
Very low Venous	20	3
CO_2 —Low Arterial	35	5
Normal Venous	46	6.5
Very High Venous	56	8
Maximum Endurable	70	10

and in the second column the percentage figures represent the analysis of pleural gas which would approximate these tensions.

A consideration of these figures leads to the conclusion that the pneumothorax gas if in equilibrium with capillary blood should ordinarily consist of about 8-10% O_2 and about 5.5-6.5% CO_2. The figures actually obtained are given in Table 2, in which the means of analyses of gases of 15 separate pneumothoraces induced in normal dogs, the standard deviation of the means and the extreme range of figures are given. Also given is the distribution of the 62 human pneumothorax cases according to their analysis figures.

TABLE 2.

Pleural Gases.

Dogs		Humans			
Mean	Range	$\%O_2$	Cases	$\%CO_2$	Cases
$\%CO_2$ 5.8±0.2	5.0- 6.6	0- 2.9	20	7.1 up	22
$\%O_2$ 10.2±0.3	8.4-12.5	3- 4.9	27	7-5	33
		5-10.0	9	4.9-0	7
		10.1 up	6		

The figures show that the results in the dogs conform very closely to the predicted values but that a great divergence is observed in the human results. About ¾ of the human cases showed an O_2 concentration of less than 5% and indeed less than 1% was the value for several. About ½ of the cases, too, showed a higher CO_2 percentage than did any of the dogs. These results conform to those reported from time to time since 1823. In the more recent literature[1-6], the workers have for the most part been interested in the clinical application of the results or have reported them incidental to other work,

1 Davy, *Phil. Trans.*, 1823, p. 496.
2 Demarquay and Leconte, *Compt. rend de l'acad. sc.*, Vol. 56, (1860).
3 Rist and Strohl, *Annals de Med.*, 8, 233, (1920).
4 L. Hill and J. A. Campbell, *Brit. Med. Journal*, 1, 752, (1923).
5 J. A. Campbell, J. Physiol, 57, 273, (1923).
6 P. N. Corylios, H. Konterwitz and E. R. Levine, *Am. Rev. Tbc.*, 26, 153, (1932).

without explanation. Possible causes of these divergences of the human figures from the predicted composition seemed well worthy of investigation.

One might ask at this point what differences in conditions, if any, may be present in these two series which could possibly tend to cause these results. Some at least of the human cases with high O_2 concentrations are those with spontaneous or open pneumothoraces; these also have a low CO_2 concentration. Those cases with the low O_2 concentrations, usually also with high CO_2 figures, are of particular interest in that they are more difficult to explain.

Duration of the Pneumothorax.

The human figures as a whole are not strictly comparable to the dog figures in that the dogs were normal animals and the humans were patients under treatment. Some were ill, some were apparently well, but all were breathing normally and none showed any signs of respiratory difficulty. They had had pneumothoraces for a considerable time, years in some cases. Specimens for analysis were taken when they came in for a routine refill, which ranged from a few days to a month or more from the last refill. The dogs on the other hand had pneumothoraces of relatively short duration, a week or so, and they required refilling every day or two in order to keep gas in the pleural space. Analysis figures of dogs, unless otherwise indicated, are of specimens taken 24 hours after injection of air. However, the duration of the pneumothorax does not seem to be responsible for the difference between the animal and human figures. In two dogs, pneumothoraces were maintained continuously for two months and throughout this period the analysis remained constant. There was no tendency with time for the O_2 figures to become lower or for the CO_2 concentrations to rise. Furthermore consideration of the few figures obtainable of human cases early in the course of a pneumothorax failed to show any correlation between duration of pneumothorax and the analysis results.

THE DEGREE OF OXYGENATION OF ARTERIAL BLOOD.

The possibility arises that with a considerable degree of collapse of lung consequent upon a pneumothorax, the gaseous exchanges between lung and blood would be sufficiently impaired to cause low O_2 and high CO_2 tensions in the arterial, and hence capillary, blood. That this is not so in the ordinary human cases such as those being reported is well established[7]. In our dogs on eight occasions the oxygen content and oxygen capacity of arterial and venous bloods have been determined. The bloods were taken by cardiac puncture and the determinations done with the Haldane Blood Gas apparatus. By referring these figures to a standard oxygen dissociation curve[8] the oxygen tensions were estimated. It must be stressed that the oxygen tensions as estimated by this method must be very inaccurate and can only give a rough approximation of the true value. The arterial oxygen tensions averaged 70 mm. Hg and the venous 32 mm. Hg. Typical normal figures are 90 and 40 mm. Hg respectively so these figures do suggest a somewhat lowered oxygen tension. However it is to be noted that the tensions of oxygen in the pleural spaces of these dogs lay in every case between the arterial and venous figures.

A different approach to this question has been used also. After induction of a large pneumothorax, specimens were taken for analysis during the period of absorption. Dogs which had had a moderate pneumothorax for some time were chosen, so that the absorption rate would not be too rapid. 600-1000 c.c. air were injected, and absorption was not complete for about a week.

A typical example is given in Table 3.

A slight rise in oxygen concentration and slight fall in carbon dioxide concentration with the diminution of the pneumothorax is noted and was similarly noted in six of the seven trials. The change however is slight and would seem to be far too small to account for the great difference between

[7] J. C. Meakins, "*Practice of Medicine*", C. V. Mosby, 1936.
[8] Peters, J. P. and Van Slyke, D.D., "*Quantitative Clinical Chemistry*", Vol. 1. Williams and Wilkins 1932.

the animal and human figures. This is especially true when it is remembered that specimens from the human cases were taken when they had come in for a refill and X-ray observations made at the time frequently showed a considerable degree of re-expansion of the lung to be present.

TABLE 3.

	Composition of gas in pleural cavity	
Days from induction	% O_2	% CO_2
2	8.6	6.0
5	9.5	5.5
8	10.0	4.9

An attempt was also made to depress respiration in two dogs by keeping them for several days continuously under the influence of morphine. It was thought that this might reduce the degree of oxygenation of the arterial blood and hence cause a lowered oxygen concentration in the pneumothorax. The results are given in Table 4. Sufficient morphine was given daily to keep the animals in a lethargic condition.

TABLE 4.

Dog A					Dog B.			
Control		Morphine			Control		Morphine	
$\%O_2$	$\%CO_2$	$\%O_2$	$\%CO_2$		$\%O_2$	$\%CO_2$	$\%O_2$	$\%CO_2$
10.2	5.5	8.1	8.5		11.2	6.0	8.4	7.7
9.4	6.6	9.0	7.7		10.2	6.0	8.0	8.3
9.1	6.1	9.5	6.0		10.4	6.5	9.3	6.4
9.0	6.6	8.8	6.7		9.3	6.6	7.8	7.5
9.5	6.3	...	...		....	...	...	...
10.7	5.6	...	...		....	...	...	...
9.6	6.1	8.9	7.2	Averages	10.3	6.3	8.4	7.5

The control figures consist of all the ordinary pneumothorax analyses made on the dog in question and the morphine figures are those obtained during four days of morphine.

It will be seen from these figures that there does seem to be some reduction in the oxygen concentration in the pneumothorax gases following the administration of morphine. The change however is relatively slight and is not nearly enough to bring the dog figures into line with the human analyses.

The State of the Pleura.

As the duration of the pneumothorax, or a defective gaseous exchange between the alveoli and the blood do not account for the unexpectedly low oxygen or high carbon dioxide concentration of the pleural gases in human cases, some possible change in the state of the pleural membranes must be considered as a possible cause.

Coryllos[9] has reported that a pneumothorax analysis of less than 1% O_2 will be found in cases of empyema, if between 1 and 2% O_2 are found a non purulent fluid will be present and that if more than 3% O_2 is present the case is a simple pneumothorax. In our series it is certainly true that most of the lowest figures are found in empyema cases but no such sharp differentiation as Coryllos suggests was found. For example four cases with no demonstrable pus in the pleural cavities gave analyses of less than 1% oxygen, and on the other hand, five cases with pus gave analyses of more than 3% oxygen.

Severe pleural irritation has been induced in three dogs by the injection of 1-2 cc. of Monsel's solution (Ferric Subsulphate) and in one dog by the injection of 1 cc. of 5% solution of iodine in 10% potassium iodide. The injection material in each case was diluted to 20-30 cc. with saline. The injections are transiently very painful and morphine or an anaesthetic must be given with the injection. Following the injection there is a small effusion of clear pleural fluid, the composition of the pleural gas mixture changes over a period

[9] Coryllos, P. N., *J. Thorac. Surg.*, 7, 48, (1937).

of several days, and the rate at which the pneumothorax is absorbed becomes very much slower. Gas may remain in the pleural cavity for weeks without need for refilling. Analysis of this gas is given in Table 5. Specimens for these analyses were taken 3-5 days after injection of irritant solution and air.

TABLE 5.

Material Injected	Pneumothorax Analysis	
	% O_2	% CO_2
Ferric Subsulphate	4.0	7.8
" "	4.8	8.9
" "	2.6	7.4
Iodine	5.8	7.9

These are the first results of this type of experiment and it is this work which is now being subjected to further investigation. However the figures are of great interest in that the figures are of the same order as those from human cases. It seems to be significant that the only cases of pneumothoraces in dogs that have given analyses comparable to those of the majority of human cases are those in which pleural irritation was present. If the pleural inflammation were merely acting so as to delay the diffusion of gases through the membrane, equilibration of the pleural gases with the blood would be delayed perhaps but equilibrium should eventually be attained at the normal levels. A thickening of the pleurae and an outpouring of pleural fluid, both of which occur, would reasonably account for this. Equilibrium is however attained in a reasonably normal time but at a different level than that commonly found.

That this is true, is shown by the following figures. In Table 6 are grouped the results of "normal" animals and a "pleurisy" animal which had had Monsel's solution injected. As is seen from the figures, after the injection of air or nitrogen into the pleural space, specimens were taken at intervals

and analysed. The "normal" results are each compiled from four curves. The final levels in the four animals were not exactly the same, nor were the intervals, so that the figures given are not averages but are typical figures. The figures for the "pleurisy" animal are the actual results in a single animal obtained nine days after the first injection of irritant. In this case it was known (Table 5) that following the injection of air, oxygen would be absorbed until a concentration of about 5% is reached. It was desired to find out whether oxygen would also pass in the reverse direction, from blood into pleural cavity, and hence for the purposes of this experiment nitrogen was used. The nitrogen was obtained from a cylinder and as actually injected contained about 2% oxygen.

TABLE 6.

Equilibration Curves of Pneumothoraces.

Normal Animals (4)					Pleurisy Animal		
	Air		Nitrogen		Nitrogen		
Time since induction	CO_2	O_2	CO_2	O_2	Time since induction	CO_2	O_2
0 min....	1.5%	20.0%	1.5%	2.5%	0 min.	2.1%	2.4%
10 " ...	4.5	19.0	4.5	3.0	5 "	5.0	2.4
30 " ...	6.0	17.0	6.0	5.0	15 "	6.9	2.5
1 hour...	6.0	15.5	6.0	6.5	1 hour	7.6	3.0
3 " ...	6.0	13.0	6.0	7.5	3 "	7.8	4.0
6 " ...	6.0	11.0	6.0	8.5	6 "	...	...
1 day....	6.0	10.0	6.0	10.0	1 day	8.1	5.0
2 days...	6.0	10.0	6.0	10.0	2 days	8.0	4.8

Thus it is clear that both in "normal" and "pleurisy" dogs, if air is injected into the pleural cavity, oxygen is removed presumably into the blood and carbon dioxide enters the cavity presumably from the blood. If nitrogen is injected, both carbon dioxide and oxygen diffuse into the cavity and the ultimate gas concentrations are the same no matter whether air or nitrogen is injected. This certainly suggests that the pleural gas is equilibrating with blood gases. In the case

of the pleurisy dog the final concentration for oxygen is lower and for carbon dioxide it is higher, and the rate of the attaining of the equilibrium is not greatly delayed.

A similar curve made two months later in the same dog revealed that equilibrium was not attained with CO_2 for 1-3 hours and with O_2 for 24-48 hours. At this time the pleura was a thick tough fibrous layer 2 mm. thick instead of the normal gossamer thin membrane. Even though there is now obvious delay in the equilibration process, it is apparently complete in a relatively short period while the total removal of all gases from the cavity is not complete for a matter of weeks. Coryllos and Birnbaum[10] have reported that the absorption of nitrogen, hydrogen, or helium from a pleural cavity or an obstructed pulmonary lobe is very much slower than the absorption of oxygen or carbon dioxide. This observation is in keeping with our findings as the complete absorption of the pleural gases would be controlled by the absorption rate of the nitrogen present while equilibrium with regard to O_2 and CO_2 would be much more rapidly attained.

Two hypotheses are being used as guides for further work in this problem. The first is that the inflammatory condition has markedly altered the capillary circulation of the pleural surfaces in such a way that the capillaries contain a more poorly oxygenated or more greatly reduced blood than is usual. Some degree of stagnation or stasis of the blood in the capillaries would cause this and is quite within reason. Possibly the best indication of this is the analysis of pleural gases but some other means of approach, possibly histological, will be needed for proof. The second is that the pleural fluid, purulent or not, and/or the thickened pleura utilises oxygen which is partially at least obtained from the pleural gases. Against this conception is the demonstration that even in these cases oxygen diffuses into the pleural cavity if pneumothorax is induced with nitrogen. Only one experiment has been performed to directly attack this problem. About 100 cc. purulent fluid from a human case was placed in a closed vessel with about

[10] Coryllos, P. N. and Birnbaum, G. L., *Am. J. Med. Sc.*, *1932*, 183, Pp. 317, 326, 347.

50 c.c. air and this was shaken from time to time and left for three days at room temperature. On analysis the air then contained 2.0% CO_2 and 17.9% O_2. This does suggest some respiratory activity of the purulent fluid. Its significance would seem to be small but can hardly be judged on the basis of this one determination.

Conclusions.

The gas mixture in a pneumothorax rapidly reaches an equilibrium and its composition depends upon the individual. In most dogs it is about 6% CO_2 and about 10% O_2 while the figures in human cases vary widely; in the majority it is less than 5% O_2 and in many, less than 1% O_2, with more than 7% CO_2.

Pleural inflammation in dogs causes the composition of their pleural gases to become similar to human figures.

A pneumothorax with a low oxygen and high carbon dioxide concentration is indicative of pleural inflammation.