612.221.3:536.423

THE PRESSURE OF AQUEOUS VAPOUR IN THE ALVEOLAR AIR.

By RONALD V. CHRISTIE and ALFRED L. LOOMIS.

(From the Department of Medicine, McGill University Clinic, Royal Victoria Hospital, Montreal, Canada, and The Loomis Laboratories, Tuxedo Park, New York.)

The pressure of aqueous vapour of the alveolar air is generally accepted to be a physiological constant. In calculations of alveolar gas pressures the value 47 mm. Hg is used, a value which represents the pressure of aqueous vapour in air saturated with moisture at 37·2° C. To our knowledge no direct measurement of the pressure of water vapour in the alveolar air has ever been made, and even from theoretical considerations it would seem probable that the figure which has been accepted is too high. It would also seem possible that this value might readily show physiological variations. This is evident when we consider the assumptions made in assuming a vapour pressure of 47 mm.—It is assumed that (*a*) the osmotic pressure of the pulmonary epithelium is equal to that of the blood; (*b*) the alveolar air is always saturated with moisture; (*c*) the temperature of the alveolar air is 37·2° C. and does not vary. The validity of these assumptions will be discussed later.

Methods.

Various volumetric, gravimetric and dew-point methods were tried, but we have only found the two which are described to be satisfactory.

(*a*) *Dew-point method.*

To obtain an accurate measurement of the temperature at which condensation of the water vapour in the alveolar air takes place, we have found the simple arrangement shown in Fig. 1 entirely satisfactory. A 500 candle-power parallel beam of light (*A*) is made to traverse a 1 litre pyrex flask (*B*) filled with water, the temperature of which can be accurately read to ± 0·02° C. After traversing the flask the beam is reflected by a mirror (*C*) in such a way that it just misses a second mirror

(*D*) which is placed to one side of its path. The faintest trace of moisture condensing on the pyrex flask at the point of exit of the beam of light (*E*) will cause some scattering of the light rays, and some of these will impinge on the second mirror (*D*). This will show as a bright flash if the condensation be only transitory or as a steady glow if the condensation remains. The surface of the flask must be scrupulously clean (we have found that the use of concentrated nitric acid and distilled water is sufficient) and the water in the flask distilled. At the beginning of the experiment the water is heated to approximately 40° C. and then

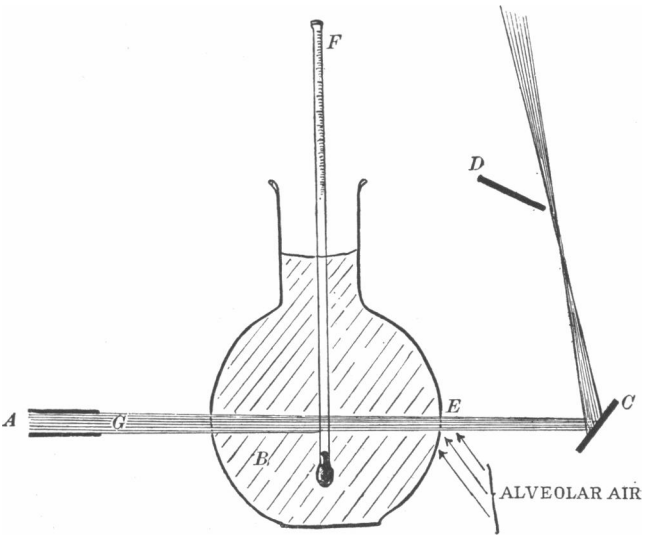

Fig. 1. Dew-point method. *A*, 500 candle-power light; *B*, pyrex flask filled with distilled water; *C*, mirror; *D*, mirror; *E*, clean surface of flask on which alveolar air is made to impinge; *F*, thermometer; *G*, parallel beam of light.

allowed to cool slowly, temperature equilibrium being ensured by continuous stirring with the thermometer. At frequent intervals samples of alveolar air are made to impinge on the pyrex flask at the point of exit of the beam of light. Whenever a flash of light is observed on the second mirror (*D*) a temperature reading is made. This temperature represents the dew point of alveolar air and from this the vapour pressure can be calculated directly. The alveolar air is made to impinge on the pyrex flask simply by making a forced expiration with the mouth close to the point of exit of the beam of light. The expiratory act should take about 3 sec., and with a little practice it is easy to stir the water, observe the mirror (*D*), and expire forcibly, at the same time.

With this system, successive measurements of the vapour pressure of the alveolar air will not vary by more than $\pm$ 0·2 mm. of Hg. To form some estimate of the absolute accuracy of the method we have measured the vapour pressure of air artificially saturated with moisture. Air is passed through a water pumice stone tower, its temperature is accurately measured, and it is then allowed to impinge on the pyrex flask. The temperature of the air was always found to be somewhat higher than the temperature of the flask at which condensation was observed (Fig. 2), the discrepancy amounting to an average of 0·23° C. in 57 observations. Unfortunately, since the evaporation of water produces an appreciable lowering of the temperature in the saturating chamber, it is impossible with this system to have complete temperature

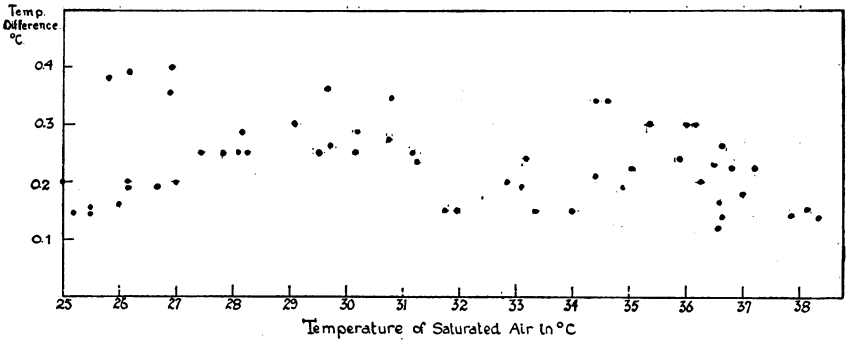

Fig. 2. Calibration of dew-point method. Showing difference between temperature of dew formation and temperature at which air was saturated with moisture.

equilibrium between the air saturated with moisture and its environment. For this reason we strongly suspect that some at least of the variations shown in Fig. 2 are due to unsaturation of the air caused by increase in temperature after saturation. This supposition is strengthened by the fact that a much smaller variation was obtained when air saturated with water vapour in the lungs was used. However, the factor 0·23° C. certainly represents the maximum difference between the true dew point and the observed dew point by this method, and as such has been used as a constant correction factor.

(*b*) *Gravimetric method.*

To measure the weight of water in a known volume of alveolar air we have passed successive Haldane-Priestley samples of alveolar air through a chain of P_2O_5 tubes and then carefully measured the total volume of alveolar air by water displacement.

A three-way glass tap of 4 mm. bore is wound with several yards of insulated German silver wire and the whole bound with asbestos string. By passing a 12-volt current through the wire the tap can be heated to well above body temperature. One limb of the tap is covered with rubber so as to serve as a mouthpiece and so placed that by turning the tap expiration may take place through one or other of the airways. One of these is left open to the atmosphere and the other directly connected to two large P_2O_5 tubes in series, filled with P_2O_5 and glass-wool. After having traversed these tubes the air is led through a gas sampling tube of 1 cm. bore and 25 cm. length, followed by a tower filled with pumice stone saturated with 1 p.c. sulphuric acid to saturate with water and avoid absorption of CO_2, and finally a graduated cylinder capable of measuring the gas volume to within $\pm$ 2 c.c. by water displacement. This cylinder is equipped with a thermometer to measure the temperature of the gas, and a water manometer to ensure pressure equilibrium between the gas whose volume is being measured and the atmosphere. Instead of water, 1 p.c. H_2SO_4 is used for displacement to avoid absorption of CO_2. The technique of analysis is as follows. The P_2O_5 tubes are carefully dried and weighed to $\pm$ 0·1 of a mg. The gas chain is then assembled as described above and the mouthpiece tap heated by passing sufficient current through the German silver wire. The mouthpiece tap is turned so that the airway is from mouthpiece to room air. The H_2SO_4 reservoir is lowered so that a negative pressure of 20 cm. of H_2O is developed in the system. Flow of water between the reservoir and the graduate cylinder is then prevented and, by observing the level in the water manometer, the presence of any leak detected. If no leak occurs the experiment is begun and a negative pressure of 20 cm. of H_2O throughout the system maintained. A deep breath is taken and the lips firmly applied to the mouthpiece on the three-way tap, which is heated to a temperature which can just be tolerated. The breath is held for 20 sec. and a slow expiration lasting from 3 to 5 sec. made, so as almost but not completely to expel the complementary and reserve air. The three-way tap is then turned so that from 100 to 150 c.c. of the air from the lungs are drawn through the gas chain. This procedure is repeated until 5 litres of alveolar air have been measured by the measuring cylinder. The P_2O_5 tubes are again weighed and the vapour pressure calculated from the usual formula $PV = \frac{W}{M}RT$. The following points are important. As the sample of alveolar air which is drawn through the gas chain remains in the mouth for several seconds, breathing must be through the nose during and prior to each deep breath. No saliva must

be allowed to touch the limb of the three-way tap in the mouthpiece. There must be no condensation of moisture in the arm of the P_2O_5 tube within 2 cm. of its termination.

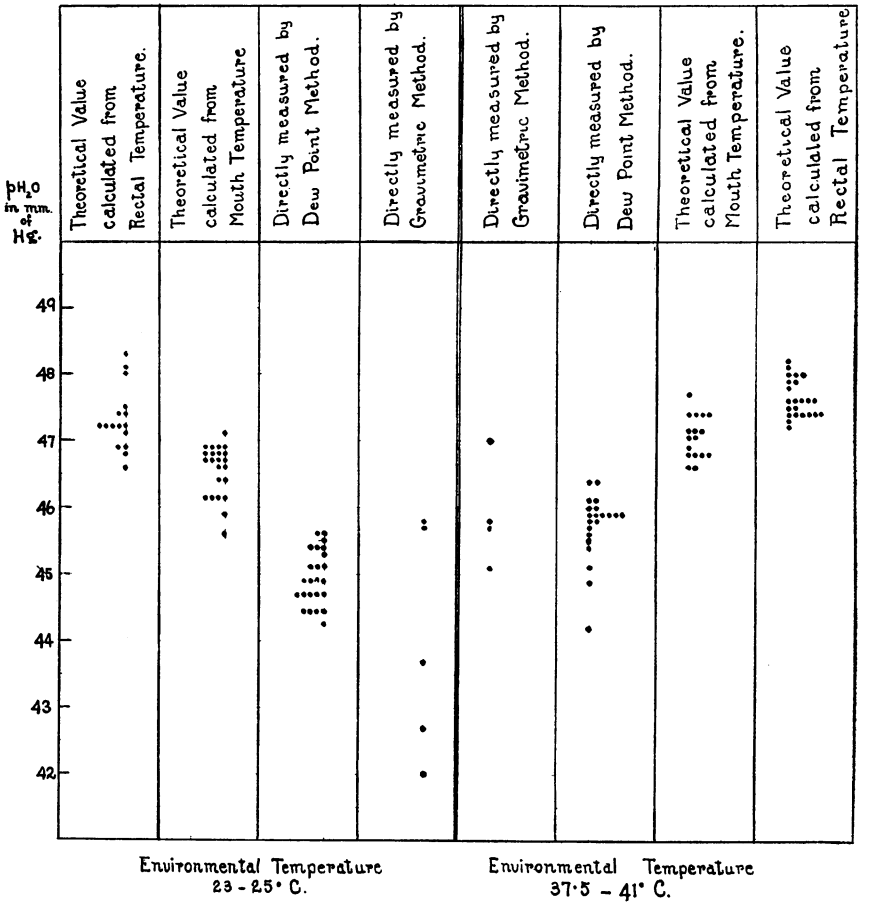

Fig. 3. The vapour pressure of the alveolar air by direct measurement and by calculation from the rectal and mouth temperatures.

In spite of the utmost care the figures obtained for the vapour pressure of the alveolar had a range of almost 3 mm. of Hg, which compares unfavourably with those obtained by the dew-point method (Fig. 3). Also an observation by this method takes 2 hours or more, while by the dew-point method only from 2 to 5 min. are required.

Results.

As might be expected the vapour pressure of the alveolar air was found to follow closely changes in the systemic temperature. For the sake of clarity we have calculated the vapour pressure of air saturated with moisture at the rectal and mouth temperatures, and compared these pressures with those obtained by direct measurement on the alveolar

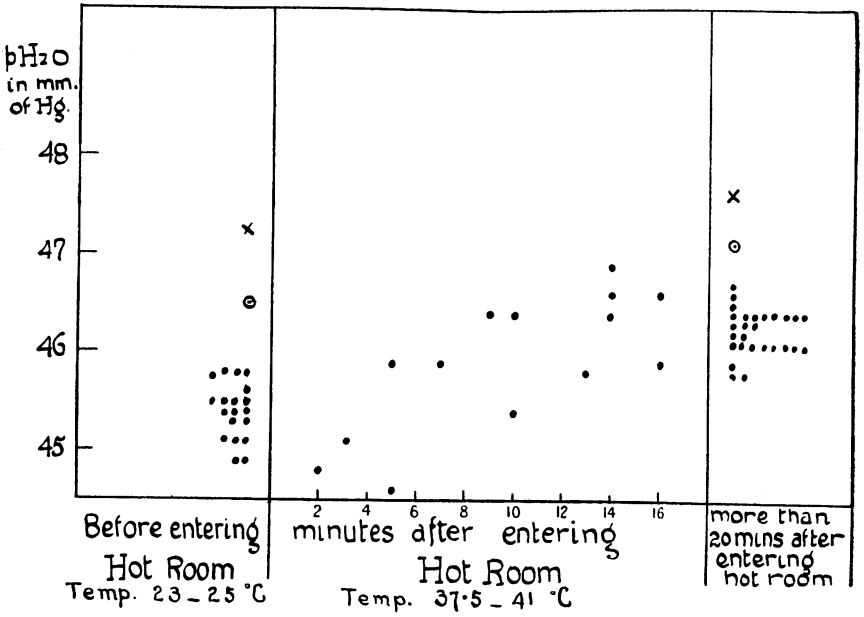

Fig. 4. The vapour pressure of alveolar air brought into equilibrium with the venous blood by 45 sec. apnœa. Measured before and after entering hot room, by dew-point method.

× = vapour pressure calculated from average rectal temperature.
⊙ = vapour pressure calculated from average mouth temperature.
• = vapour pressure measured by dew-point method.

air. The results are shown in detail in Fig. 3. The theoretical values calculated from the rectal and mouth temperatures average 47·26 and 46·55 mm. respectively, whereas the measured values average 44·91 mm. by the dew-point method and 44·0 by the gravimetric. When the temperature of the environment was raised to between 37·5 and 41° C. the vapour pressure calculated from the rectal and mouth temperatures rose to average values of 47·65 and 47·16 mm. respectively, followed by the alveolar air which rose to 45·81 mm. by the dew-point method and 45·9 by the gravimetric (Fig. 3).

Effect of voluntary apnœa.

When complete equilibration between blood and alveolar air was ensured by holding the breath for a period of 45 sec., the same change was found to take place, the vapour pressure rising from an average of 45·43 mm. in the cold environment to 46·26 in the hot (Fig. 4). In both hot and cold environment the apnœa produced *per se* an average rise of 0·5 mm. in the alveolar vapour pressure (Figs. 3 and 4).

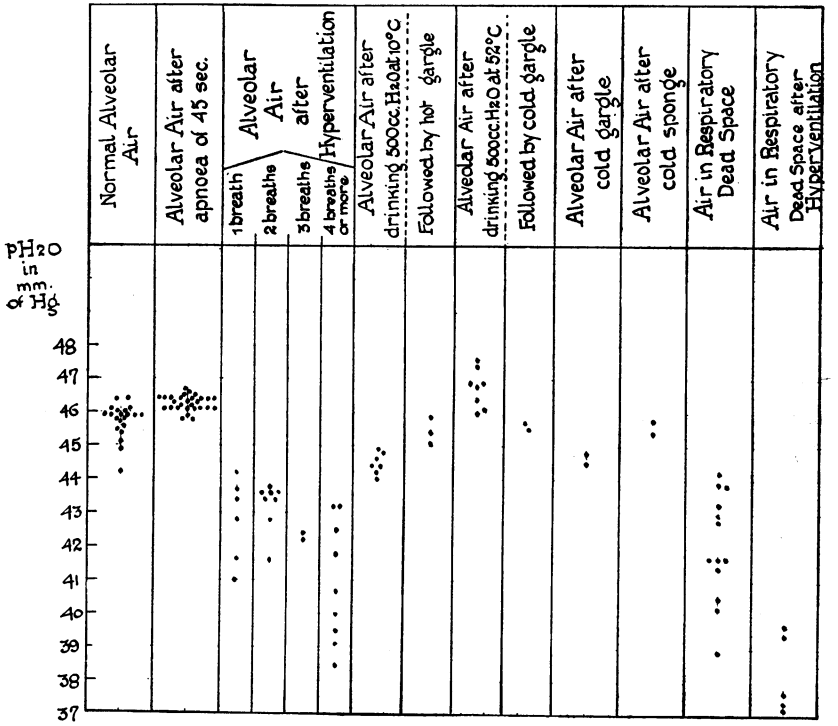

Fig. 5. Variations in the vapour pressure of the alveolar and dead space air. Dew-point method. Temperature of environment 37·5–41·0° C.

Effect of hyperventilation.

One full inspiration immediately followed by a forced expiration is sufficient to produce a perceptible lowering of the vapour pressure of the alveolar air as measured by the dew-point method (Fig. 5). The average values found were 42·8 mm. after one deep breath, 43·2 mm. after two breaths, 42·3 mm. after three breaths and 40·9 mm. after four

or more breaths. The lowest value obtained was 38·5 mm. after eight deep breaths. These experiments were all conducted in an environmental temperature of from 39 to 41° C.

Rapid and shallow breathing.

After voluntary tachypnœa of 45 sec. duration with a respiratory rate of 60 a minute and depth of approximately 200 c.c., the vapour pressure of the expired air at the end of such a shallow breath amounted to an average of 38·3 mm. (Fig. 5). These experiments were also conducted in an environmental temperature of from 39 to 41° C.

Effect of cooling mouth and naso-pharynx.

If the vapour pressure of the alveolar air is measured before and after 500 c.c. of water at 12° C. are drunk, a slight but definite fall is observed, amounting to an average of 1·3 mm. (Fig. 5). In the same way the imbibition of hot water causes an average rise of 1·0 mm. Similar changes were observed on air held in the lungs for 45 sec. Either of these effects can be eliminated by a hot or cold gargle following the cold or hot drink respectively (Fig. 5). The duration of this apparent lowering of the alveolar vapour pressure was followed on four occasions after cold water was drunk and it was found that 8, 8, 6 and 4 min. respectively had to elapse before a normal reading could be obtained on either the alveolar air, or air held in the alveoli for 45 sec.

Vapour pressure of air in the respiratory dead space.

The vapour pressure of the expired air after only 100 c.c. had been expired was found to average 42·1 mm. (Fig. 5). After an apnœa of 30 sec. the vapour pressure of this air was found to have mounted to 44·4, 44·9, 45·1 and 45·1 mm. on four estimations.

Criticisms.

These experiments, especially those with hot and cold water, immediately suggest that under any conditions, whether with quiet respiration or with hyperventilation, the alveolar air may be cooled during its passage from the alveoli to the mouth. Were this true any application of the dew point as measured by this method to the vapour pressure of the alveolar air would be entirely fallacious. One purpose of the experiments which have been described was to prove or disprove this possibility, and, when we analyse the evidence, it would seem to be entirely against such a supposition.

(*a*) Rapid and shallow breathing produces no lowering of the vapour pressure of the true alveolar air. Neither rapid and shallow breathing nor hyperventilation produced any lowering of the vapour pressure of air subsequently held in the lungs for 45 sec. With cold water, on the other hand, the lowering of the dead space temperature sufficient to produce a fall in vapour pressure of only 1 mm. persisted over a period of from 4 to 8 min.;—obviously a different mechanism from that which produced a very much greater but purely transitory fall in vapour pressure.

(*b*) Were the alveolar air being cooled by the respiratory passages one would expect this effect to be greater when breathing cold air than hot. It follows that a greater rise in the vapour pressure of the alveolar air is to be expected from a period of apnœa after breathing cold air than after breathing hot air. Within the limits of experimental error this was not found to be the case, the rise with cold air amounting to an average of 0·5 mm. and with hot air to an average of 0·45 mm., in twenty observations.

(*c*) With the exception of the group of observations on the normal vapour pressure of the alveolar air, all the experiments described were performed in an environmental temperature above that of the body. The bronchi were covered with mucous of high viscosity, and it would indeed be surprising if under these circumstances they could be perceptibly cooled by any form of respiratory gymnastics.

Discussion.

This is the first attempt, as far as we know, which has been made to measure directly the vapour pressure of the alveolar air. Mainly in the course of studies on water balance several attempts have been made to measure the total amount of water excreted by the lungs over a given length of time. In all some gravimetric method has been used in none of which is the possibility of condensation of moisture outside the weighing system completely excluded. From this point of view each method has its own particular possibility of error and we will only discuss in brief the conclusions which have been drawn. All are agreed that the expired air is far from saturated with moisture [Galeotti, 1912 and 1915; Loewy and Gerhartz, 1914; Jacquot and Mayer, 1925, 1926], but that the saturation rises with the temperature of the environment [also Rubner, 1898], and is unaffected by the humidity of the environment [also Levi, 1925, *a*, *b*]. Viale [1926] has shown that deep breathing increases water excretion of the lungs, and Galeotti

and Signorelli [1912] have shown the water excretion is increased at high altitudes. From our own results these conclusions would seem to be perfectly reasonable, but it must be remembered that water excretion is largely a function of the volume of air expired, and does not necessarily bear any relationship to the vapour pressure in the alveoli.

Evidently the vapour pressure of the alveolar air is lower by some 2 mm. than the generally accepted value of 47 mm. of Hg. From the experiments described we are able to analyse in some detail the factors responsible for this discrepancy. (*a*) Holding the breath for 45 sec. raises the vapour pressure of the alveolar air by 0·5 mm. irrespective of the temperature of the environment. The possibility of any significant cooling of the alveolar air while passing through the respiratory dead space has been excluded, so we can assume that 0·5 mm. represents the lack of equilibrium between the blood and the alveolar air. Such a gradient seems very reasonable when we consider that Bock and his associates [1924, 1929–30] have shown that with CO_2 a measurable gradient exists between the plasma and the alveolar CO_2. (*b*) The difference between the osmotic pressure of the blood and that of water could only account for a lowering of the vapour pressure of at the most 0·15 mm. (*c*) Binger and Christie [1927] in a large number of observations have shown that, in the anæsthetized dog at least, the lung temperature is always lower than that of the rectum. We have taken 50 such observations at random and have found that the lung temperature is on an average 0·24° C. lower than the rectal temperature. The temperature was measured by thermocouples accurate to ± 0·02° C. In the same way we found that the blood passing through the lungs was cooled by an average of 0·08° C. on seven simultaneous measurements of the temperature of the right and left heart blood [Binger and Christie]. We have ample evidence then for the assumption that the temperature of the lung is somewhat lower than that of the rectum. If we accept a difference of 0·24° C. as also applying to the human subject, this would represent a fall of 0·6 mm. in the vapour pressure.

These three factors could account for 70 p.c. of the discrepancy between the vapour pressure of the alveolar air, as measured by us, and that which has been assumed in the past. When we consider that there is a difference of about two atmospheres between the osmotic pressure of the yolk and white of an egg [Straub, 1930; Hill, 1931], it would indeed be remarkable if all the factors influencing even the vapour pressure at the surface of a living cell could be analysed.

Effect of environmental temperature.

Even with extreme changes in the temperature of the environment the vapour pressure of the alveolar air was found to follow closely the temperature of the rectum. The same was found to be true with air retained in the lungs for 45 sec. In both the vapour pressure reaches an equilibrium after some 5 to 10 min., while 15 min. or more is necessary for constant readings of the rectal temperature (Figs. 4 and 5). This early rise in the vapour pressure, unaccompanied by any change in the rectal temperature, at first deceived us into the rather attractive hypothesis that a change in the osmotic pressure of the blood and pulmonary epithelium was being reflected. However, the rise in vapour pressure is far greater than could be produced by any such change, and when we take into consideration the lag of the rectal temperature, the phenomenon can be explained more simply by a rise in the temperature of the lung.

Effect of cold and hot water.

It has been suggested [Galeotti, 1912, 1915; Jacquot and Mayer, 1926] that there is some reflex mechanism in the lungs to increase or decrease water excretion, the stimulus being a sensation of cold or warmth. We have been unable to find any evidence for such a reflex. The changes in vapour pressure which we observed with changes in the environmental temperature have already been discussed, and the changes after imbibition of cold or hot water have been shown to be due probably to changes in the temperature of the respiratory dead space.

Effect of hyperventilation.

The lowering of the alveolar vapour pressure which was found after hyperventilation might either be due to cooling of the lungs or to an increased gradient between the alveolar air and the blood. The possibility of cooling the respiratory air passages has already been disposed of, and it seems inconceivable that cooling of the lung could account for the change observed. During the 10–15 sec. period of hyperventilation certainly not more than 0·4 g. of water is excreted, which represents a maximum heat loss of 230 calories, a quantity quite insufficient to lower the temperature of the lung and blood circulating through it by the 3° C. necessary for such a fall in vapour pressure. The lung probably is cooled to a slight extent, but the factor mainly responsible for the fall in vapour pressure must be lack of equilibrium between the alveolar air and the blood, the gradient probably being one of temperature as

well as saturation. Whatever factors may be responsible, the fact remains that the alveolar vapour pressure may be lowered by as much as 9 mm. of Hg by hyperventilation, even in an atmosphere which is warmer than that of the lungs.

This observation would seem to have a direct bearing on any accurate analysis of hæmo-respiratory exchange during work or at high altitudes. With a fall of the alveolar vapour pressure to 39 mm. an error of 0·5 mm. in the pressure of CO_2 and of 1·1 mm. in the pressure of oxygen would result from the use of the standard value of 47 mm. At an altitude of 15,000 ft., with an alveolar oxygen tension of 50 mm. and CO_2 tension of 30 mm. [*Report of the Peru High-Altitude Committee*, 1923], this would result in an error of 0·5 p.c. in the calculated saturation of the arterial blood and an error of 0·01 in the *p*H calculated from the Henderson-Hasselbach equation.

Rapid and shallow breathing.

With a respiratory rate of 60 a minute and depth of 200 c.c. the pressure of water vapour at the end of such a breath was found to average 38·3 mm. Hg, the pressure in the alveoli remaining unchanged. Under similar conditions the tension of CO_2 was found to be 23·2, 22·4 and 20·1 mm. on three occasions, with a CO_2 tension of the expired air of 8·9, 10·0 and 7·8 mm. respectively. The alveolar pCO_2 of this subject averaged 41 mm. on eight observations.

It follows that rapid and shallow breathing is a very efficient mechanism for the elimination of heat by the evaporation of water with CO_2 loss reduced to a minimum. Were the loss of CO_2 to parallel the loss of H_2O a gaseous alkalosis would soon result. In cases of lobar pneumonia with rapid and shallow breathing this does not occur and a dog does not develop tetany when he pants. Presumably this lack of parallelism is to be explained on the score of evaporation in that region where the dead space ends and the alveolar air commences. The evidence we have presented is certainly against any significant lowering of temperature in the respiratory tract and, *a priori*, it would seem that heat loss must be from the pulmonary vascular bed, the whole structure of which, with its amazingly efficient "water-cooled" system, would lend itself to the evaporation of moisture without any significant fall in temperature. When we consider the lack of agreement which exists between what might be called the Haldane school on the one hand, and the Krogh school on the other, as to the boundaries and even significance of the respiratory dead space, it is easy to conceive an area between the

anatomical dead space and the alveoli, hyperventilation of which would produce a loss of water out of proportion to the loss of CO_2. Indeed, if we accept the evidence of Krogh and his associates against homogeneity throughout the alveolar air, such a possibility seems likely, since more H_2O vapour than CO_2 can be given off by a cubic centimetre of blood when hyperventilated. Moreover, in this area heat loss would be from the pulmonary blood itself and not from the bronchial capillaries. Such a mechanism would fully explain the absence of gaseous alkalosis in such conditions as lobar pneumonia, the panting of dogs and any form of thermal polypnœa. It would also explain the subnormal temperature usually found in cases of emphysema with chronic rapid and shallow breathing, with impairment of the function of CO_2 excretion. In repeated observations on five such cases we have found an average temperature of 36·4° C.

Summary and conclusions.

1. A method for the accurate measurement of the vapour pressure of the alveolar air is described.

2. The vapour pressure of the alveolar air is some 2 mm. Hg lower than the value generally accepted. An explanation for this discrepancy is given.

3. The vapour pressure of the alveolar air can be lowered by hyperventilation by as much as 7 mm. Hg. The significance of these observations with regard to hæmorespiratory exchange during conditions of work and at high altitudes is discussed.

4. Changes in the alveolar vapour pressure with the temperature of the environment can be fully accounted for by changes in the systemic temperature.

5. The efficiency and specificity of rapid and shallow breathing as a mechanism for the elimination of heat and conservation of carbon dioxide is described. The application of this mechanism to thermal polypnœa, lobar pneumonia and emphysema is discussed.

REFERENCES.

Binger, C. A. L. and Christie, R. V. (1927). *J. exp. Med.* **46**, 571, 585, 595.
Bock, A. V., Dill, D. B., Edwards, H. T., Henderson, L. J. and Talbott, J. H. (1929–30). *J. Physiol.* **68**, 277.
Bock, A. V. and Field, H. (1924). *J. biol. Chem.* **62**, 269.
Galeotti, G. (1912). *Biochem. Z.* **46**, 173.
Galeotti, G. (1915). *Pflügers Arch.* **160**, 27.
Galeotti, G. and Signorelli, E. (1912). *Biochem. Z.* **41**, 268.
Hill, A. V. (1931). *Adventures in Biophysics*, pp. 55–60. Univ. of Pennsylvania Press, Philadelphia.
Jacquot, R. and Mayer, A. (1925). *C. R. Soc. Biol.*, Paris, **93**, 1471.
Jacquot, R. and Mayer, A. (1926). *Ann. Physiol. Physicochem. Biol.* **2**, 153.
Levi, M. (1925 *a*). *Arch. Ital. Biol.* **74**, 229.
Levi, M. (1925 *b*). *Ber. ges. Physiol.* **32**, 872.
Loewy, A. and Gerhartz, H. (1914). *Pflügers Arch.* **155**, 231.
Report of the Peru High-Altitude Committee (1923). *Philos. Trans.* **211**, B, 351–480.
Rubner, M. (1898). *Arch. Hyg.*, Berl. **33**, 151.
Straub, J. (1930). *Trans. Faraday Soc.* **26**, 673.
Viale, G. (1926). *Ber. ges. Physiol.* **36**, 826.