

ANOXIA, OXYGEN CONSUMPTION AND CARDIAC OUTPUT IN NEW-BORN LAMBS AND ADULT SHEEP

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(Received 10 October 1958)

It has been shown that the oxygen consumption of new-born animals of many different species (babies, Cross, Tizard & Trythall, 1955, 1958; puppies and kittens, Moore, 1956*a, b*; lambs, Acheson, Dawes & Mott, 1957; rabbits, Dawes & Mott, 1959*a*) falls during moderate anoxia. The oxygen consumption of adult mammals (man, dog and cat) does not appear to fall to the same extent, even in extreme anoxia, except in species which are small in size (mouse, rat, guinea-pig; see discussion in Acheson, Dawes & Mott, 1957; Hill, 1958). It seemed to us desirable to examine the effects of anoxia in the new-born animal and the adult of the same species, using so far as possible identical methods of investigation under the same laboratory conditions, in order to establish whether this difference was real and to try to discover its cause. As oxygen absorption is primarily dependent on pulmonary ventilation and blood flow, these also have been measured during anoxia. The sheep is a convenient experimental animal for this purpose because the new-born lamb is sufficiently large to allow the withdrawal of a moderate number of blood samples. Preliminary accounts of some of these experiments have been published (Cross, Dawes & Mott, 1958*a, b*).

METHODS

Sixteen adult ewes and forty-eight lambs varying in age from a few hours to 60 days from birth were used. Most of them were a Clun-Hampshire cross, but a few were Welsh, Suffolk or Kerry Hill. The sheep was laid on its side, a polyethylene catheter was introduced into an external jugular vein under local anaesthesia, and chloralose was administered in doses which varied according to the age and weight of the animal.

The blood pressure was measured with a condenser manometer from a systemic artery, the femoral in new-born lambs and a branch of the radial in adult sheep. The pulse wave was used to operate a heart-rate meter (Wyatt, 1956, 1957), and both mean blood pressure and heart rate were recorded on a Cambridge Instrument Co. Slow Recorder. The catheter in the external jugular vein, used for giving the first dose of anaesthetic, was replaced by a longer one which was passed into the right ventricle. The pulse shape, recorded from a condenser manometer, indicated

when it reached its correct position, which was verified post mortem. Blood samples (0.8 ml.) were withdrawn simultaneously from this catheter and from one introduced into a systemic artery (usually a branch of the radial in both new-born lambs and adult sheep) for calculation of the cardiac output by the Fick principle. They were analysed for their O_2 content and capacity by a modification of the Barcroft-Haldane method, using Warburg manometers (Born, Dawes & Mott, 1955). Blood lactate was estimated by the method of Barker & Summerson (1941) and pH by a glass electrode and pH meter. Rectal temperature was recorded at intervals.

Measurement of oxygen consumption and breathing. The tracheal cannula was attached to a closed circuit, whence the carbon dioxide was removed by soda-lime, and to which oxygen was supplied by a roller pump driven by a velodyne motor-generator (Williams & Uttley, 1946) at a rate just sufficient to keep the volume constant at the end of expiration. The apparatus is illustrated in Fig. 1. A volume recorder (*A*) attached to the closed circuit registered the tidal volume

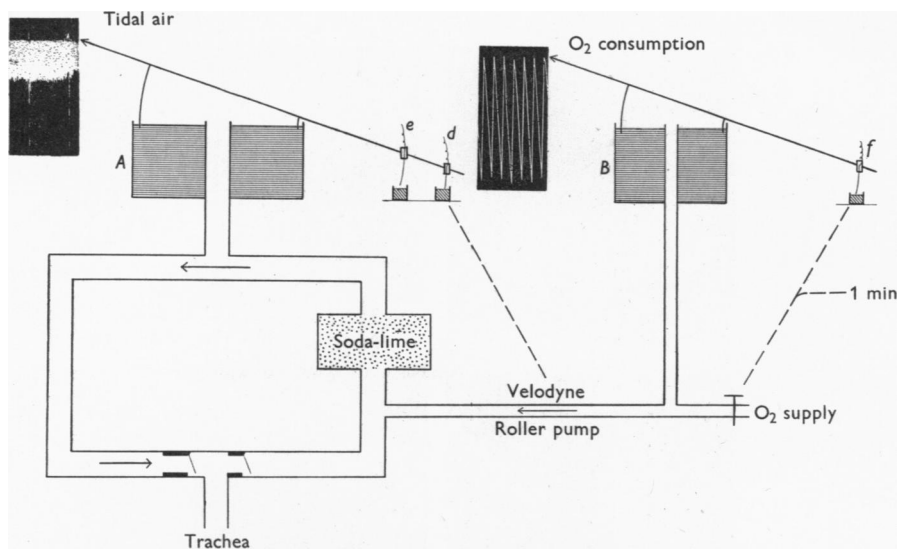


Fig. 1. Diagram of apparatus used for measuring O_2 consumption. Volume recorder *A* measures the tidal air. Oxygen is admitted by the velodyne roller pump at a rate just sufficient to maintain the position of this volume recorder constant at the end of expiration (see Methods). Oxygen is supplied from a volume recorder *B* which is automatically refilled after an interval of 1 min and gives a record of O_2 consumption.

of each breath on a smoked drum revolving at about 0.5 cm/min. To the end opposite from the writing lever was attached a lever carrying two electrodes. One of these (Fig. 1*d*) made contact with a reservoir of mercury at the end of expiration, and thus stopped the roller pump. The other electrode (Fig. 1*e*) was of platinum and dipped into saline when the lever descended a few millimetres further. The resistance between the platinum and the saline was in parallel with one arm of an a.c. bridge designed to control the speed of rotation of the velodyne roller pump, to which it was connected through a circuit having a time constant of 0.5–1.0 sec. The bridge was adjusted so that the roller pump introduced oxygen into the circuit at a rate somewhat greater than that which the animal required; when the lever descended too far at the end of expiration, the platinum-saline contact was made, and the roller pump rotated at a slower speed during the next respiratory cycle (a ratchet prevented the pump from reversing its direction of rotation). The writing point of the volume recorder (*A*) therefore did not deviate in position by more than a few millimetres at the end of expiration, except after large gasps or sudden movements, when it rapidly regained

its equilibrium position (Fig. 2*A*). Oxygen was supplied to the roller pump from a second volume recorder (*B*), which was refilled automatically from a cylinder to a level determined by the contact labelled *f* in Fig. 1, after an interval of 1 min or more, as convenient. In this way a continuous graphic record of O_2 consumption per minute was obtained. In some experiments the mean current output of the velodyne generator, which is directly proportional to the rate of revolution of the roller pump, was also used as a measure of O_2 consumption, and was displayed on the Cambridge Slow Recorder. At each breath, when contact *d* (Fig. 1) was made, the relay which stopped the roller pump also actuated an impulse counter (Thorp, 1948), which thus provided a record of respiratory rate. Examples of kymograph records of O_2 consumption, tidal air and respiratory rate thus obtained are shown in Figs. 2 and 15.

The apparatus described above contains a negative feed-back loop between the tidal air volume recorder and the velodyne motor-generator which drives the roller pump. Figure 2*B* shows that even during periodic breathing the system operates rapidly and effectively, and indicates a periodic

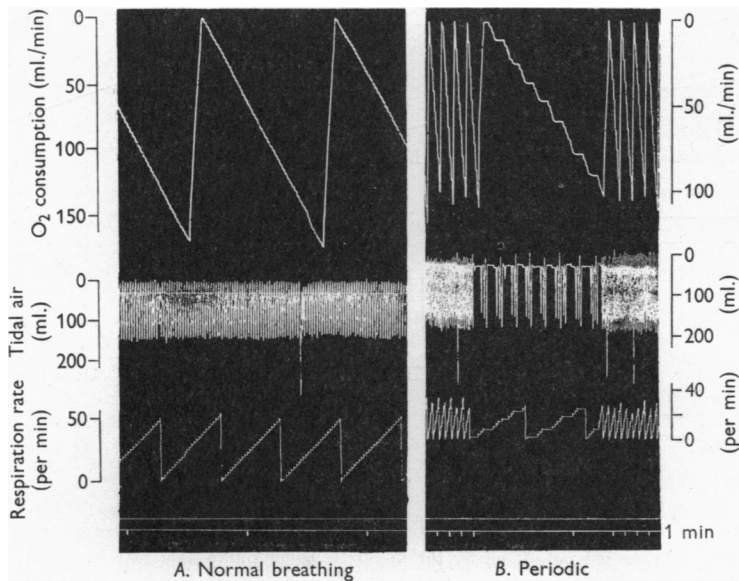


Fig. 2. Using the apparatus illustrated in Fig. 1, *A* is a record of normal breathing with the kymograph drum running fast, to illustrate the method for measuring O_2 consumption; note the gasp. *B* is a record of periodic breathing to show the intermittent uptake of oxygen.

consumption of oxygen. A severe test of its properties was instituted as follows. A Starling 'Ideal' pump was connected in place of the animal and another roller pump was attached to the closed circuit in such a way that it withdrew gas from the system, and thereby simulated the consumption of oxygen. Figure 3 indicates that when the rate of withdrawal of gas was instantaneously reduced to less than half there was a small change in the level of the 'tidal air' trace and the new equilibrium position was reached during the subsequent minute. The period of arrest at the end of expiration is very short in this artificial system and approximates to the least favourable conditions encountered during severe hyperpnoea.

The same basic apparatus was used for experiments on adult sheep and on new-born lambs, but some minor modifications were necessary for the latter. Thus the cross-sectional area of the tidal air volume recorder was $27 \times 25 \text{ cm}^2$ for sheep and $19 \times 14 \text{ cm}^2$ for lambs; it also proved convenient to use either of two volume recorders for O_2 consumption of 19×14 or $11 \times 9 \text{ cm}^2$ area

respectively. The volume of the closed circuit was about 9 l. for adult sheep, including a 5 l. flask, which was removed for experiments on lambs. The temperatures of the gas in the closed circuit and of the oxygen entering the circuit were recorded, and the rate of O_2 consumption was corrected to dry gas at s.t.p. With adult sheep the tracheal cannula was connected to a respiratory valve constructed of Perspex the dead space of which was small, modified from the design published by Cunningham, Johnson & Lloyd (1956). End-expiratory gas was withdrawn by a roller pump at a rate of about 100 ml./min, through a heated mica non-return valve from the further end of the expiratory valve, using the principle described by Rahn & Otis (1949). Samples were withdrawn

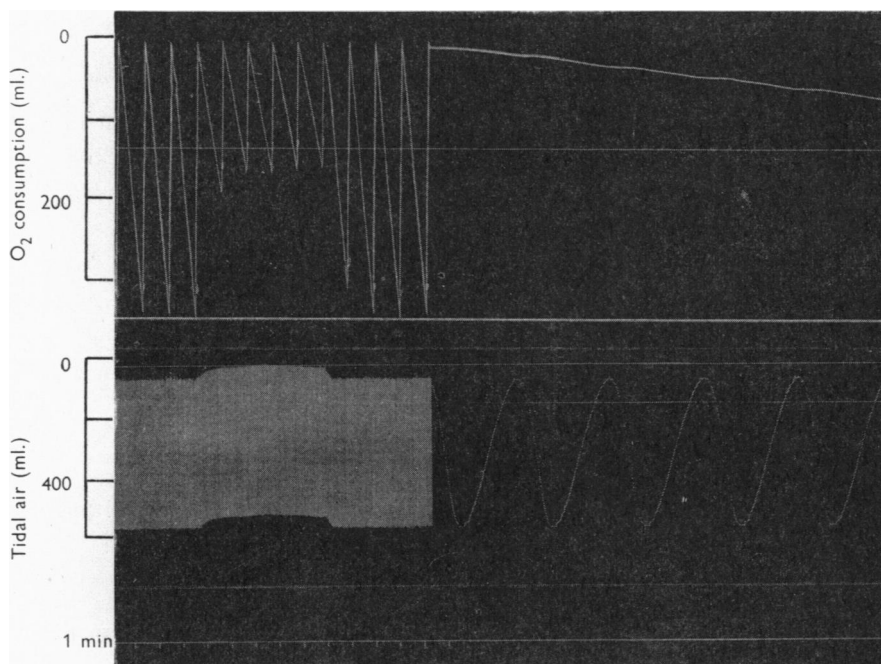


Fig. 3. Model experiment as a test of the O_2 consumption apparatus. O_2 consumption was abruptly reduced for 5 min during the first part of the record. Although the period of arrest at the end of expiration was very brief, as seen in the latter part of the tidal air record, the system responds rapidly with only a small change in the level of the tidal air trace (below).

for analysis for O_2 and CO_2 by Haldane's apparatus; otherwise it was returned to the closed circuit. When the apparatus was used for new-born lambs the tracheal cannula was attached to it by a T-tube, and the gas in the system was circulated by means of a roller pump at 4–5 l./min. This had the advantage that the resistance to breathing was low, but it was no longer possible to collect end-expiratory samples. During some experiments the lamb was connected to the closed circuit by a respiration pump, so that O_2 consumption could be measured after respiration had failed.

Oxygen consumption was also measured in a few unanaesthetized lambs. The lamb was placed in a gas-tight box with a transparent lid. Gas was circulated at about 5 l./min through the box, which was connected in series with the closed-circuit apparatus described above. Tidal air was not measured; respiratory rate was counted by observation through the lid.

Measurement of oxygen content of inspired gas. The inspired gas was sampled for its O_2 content by a roller pump at a constant rate of about 60 ml./min, using a modification of the polarographic

method described by Davies & Brink (1942). The gas was sucked through a sintered glass distributor into about 10 ml. sodium chloride solution 0.9% (w/v) and thence returned to the closed circuit. The gas bubbled round a platinum electrode immersed in the saline and the current, passed between this and a silver chloride electrode at a potential difference of 0.7 V, was registered by a damped galvanometer. The current was directly related to the O₂ content of the gas over the range in which we were interested, but the instrument was temperature-sensitive and also, over many hours, showed a slow decrease in sensitivity which was attributed to polarization. Therefore observations during which air was circulated through the instrument for 2 min (which was sufficient to ensure equilibrium) were interpolated between observations of the current passed when the inspired gas was circulated. The apparent O₂ content of the inspired gas was then calculated as

$$\frac{\text{galvanometer current during passage of inspired gas}}{\text{galvanometer current during passage of air}} \times 20.9\%$$

Calibration (Fig. 4) was performed with gas mixtures analysed by Haldane's apparatus, and remained constant over many weeks provided that the electrodes were cleaned regularly.

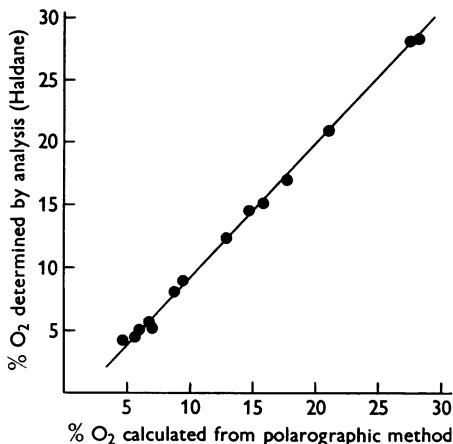


Fig. 4. Calibration of the polarographic method for analysis of O₂ content of inspired air against Haldane's method; pooled results on three different days.

Changes in the oxygen content. The oxygen content of the gas in the closed circuit, and therefore of the inspired gas, was reduced by replacing with air the oxygen consumed by the sheep (i.e. by disconnecting the velodyne roller pump of Fig. 1 from the oxygen supply); the rate of fall was usually 1% in 1–2 min. During this procedure O₂ consumption was not recorded by the volume recorder (Fig. 1B). At the end of the period of anoxia the oxygen content of the closed circuit was raised in one of two ways. In some experiments the closed circuit was flushed with room air; this took several minutes, during which O₂ consumption was not measured. Alternatively a small reservoir filled with oxygen, and of volume such that the oxygen content of the system was raised to rather more than 21%, was introduced in series with the closed circuit for a few minutes and then removed.

Inferior vena caval flow. Blood flow through the inferior vena cava in new-born lambs was measured by inserting a velodyne flowmeter (Dawes & Mott, 1959b). The lamb was placed on its left side, and the vena cava was approached retroperitoneally through a lateral incision. Small branches were tied and the lamb was heparinized. The vena cava was then divided below the entry of the renal veins and the flowmeter was connected between the two cut ends. The largest possible cannulae were used; these were connected to the flowmeter by double-lumen tubes, the inner core of which was connected to the pressure-sensing part of the instrument. The flowmeter was then adjusted so that the mean drop in pressure between the cannulae was negligible.

RESULTS

A general description of the results of experiments upon adult sheep will be given first. This is followed by an account of similar observations on new-born lambs, during which the physiological behaviour of the two groups of animals is compared.

Adult sheep

Experiments have been carried out on sixteen adult sheep, but detailed results will only be presented from five sheep which were in a satisfactory physiological condition, and in which all the measurements were made con-

TABLE 1. Results obtained on five sheep which were in a satisfactory physiological condition

Breed	No.	762	764	765	766	767
				Welsh	Kerry Hill	Kerry Hill	Hampshire	Welsh
Age (years)				7	6	6	1.7	5
Weight (kg)				31	55	80	57	33
Surface area (m ²)				0.98	1.17	1.49	1.07	0.75
Chloralose (mg/kg)				71	55	60	63	49
O ₂ inspired (%)				20.0	22.4	21.7	21.0	22.4
O ₂ saturation (%)								
Arterial				80	95	84	83	90
Venous				50	55	46	32	49
End-expiratory								
pO ₂ (mm Hg)				99	120	111	118	114
pCO ₂ (mm Hg)				32	30	33	33	37
Minute volume (l./min, B.S.P.T.)				9.7	9.9	8.4	8.8	4.5
Respiration rate per minute				34	30	28	26	16
B.F. (mm Hg)				132	135	147	102	140
Cardiac output (l./min)				5.6	6.0	5.1	5.1	4.4
O ₂ consumption (ml./min)				209	257	234	252	149

currently and over a long period of time. However, the incomplete results on the eleven sheep excluded from detailed consideration were similar, and substantiate the general conclusions reached. Table 1 shows the results of various observations on the five sheep mentioned above, at the beginning of the experiment while they were breathing a gas mixture containing 20% O₂ or more. These measurements were all begun about 2 hr after administration of the dose of chloralose indicated. The rectal temperature ranged from 38.6–40.4 °C.

Each sheep was subjected to two periods of anoxia, lasting 1–1½ hr. During the first period of anoxia the sheep were more deeply anaesthetized than subsequently, when it was usually necessary to give additional small doses of chloralose. Sheep 762 (Table 1), with the lowest arterial O₂ saturation (80%) had had the highest dose of chloralose initially (71 mg/kg). In the three sheep which had the lowest initial arterial O₂ saturation (80–84%), the saturation rose, some 2–3 hr later and after the first period of induced anoxia, to a value of 86–91% with an end-expiratory pO₂ of 111–127 mm Hg when they were once more breathing 20.5–22.6% O₂. These measurements are described in

some detail in order to show what we believe to be reasonably satisfactory physiological criteria for experiments upon adult sheep.

In order to make the sheep anoxic, the oxygen content of the inspired air was reduced stepwise as shown in Fig. 5; it was then rapidly restored to about 21%. At least once during each experiment anoxia was carried to a point at which respiratory failure occurred. As Fig. 5 shows, the rate of oxygen consumption of an adult sheep during this procedure was hardly affected until terminal respiratory failure on 7.8% O₂, even though the arterial O₂ saturation fell to less than 20%, and though there was hardly any oxygen in

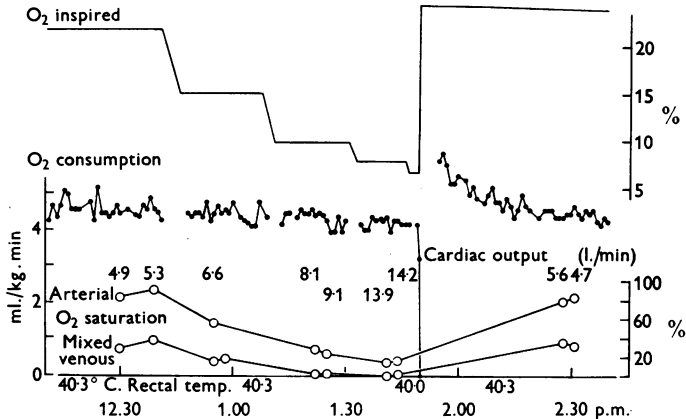


Fig. 5. Adult sheep, 1.7 years old, 57 kg, chloralose 63 mg/kg. A reduction in the O₂ content of the inspired air caused only a comparatively small fall in O₂ consumption; there was a large increase in cardiac output.

the mixed venous blood. The end-expiratory pO₂ fell from 118 mm Hg while breathing 21.8% O₂ to 35 mm Hg on 7.8% O₂; the pCO₂ fell from 33 to 19 mm Hg. Anoxia caused a large increase in tidal air, but only a small change in respiratory rate. The minute volume of breathing increased 2.3 fold during this period of anoxia, and cardiac output increased nearly threefold. The oxygen carrying capacity of the blood increased from 9.6 to 11.0 ml./100 ml. There was little change in mean arterial pressure; heart rate rose from about 130 to 190 beats/min at the maximum. The rectal temperature fell slightly during anoxia, in this as in other adult sheep. When the anoxia was relieved, O₂ consumption increased considerably during the subsequent 20 min, as if a substantial O₂ debt were being eliminated. In this sheep it amounted to approximately 1.5 l.O₂.

After an interval of 2 hr this sheep was subjected to a second period of anoxia, not shown in Fig. 5, during which breathing did not cease until the O₂ content of the inspired air was lowered to 6%. On this occasion the end-expiratory pO₂ fell to 25 mm Hg, pCO₂ to 13 mm Hg and the minute volume

increased sixfold. Cardiac output increased fourfold (to 22 l./min) and the O_2 carrying capacity of the blood increased to 13.1 ml./100 ml. These changes are all greater than those observed during the first period of anoxia, in spite of the fact that an additional 10 mg/kg chloralose had been given during the intervening recovery period. The increased ability to withstand oxygen lack is attributed to the lightening of anaesthesia at the time of the second period of anoxia. This conclusion is supported by observations on the other sheep. In one of these a large additional dose of chloralose (56 mg/kg) was given between the first and second periods of anoxia, with the result that the minute volume of breathing was increased less and breathing ceased at a higher inspired pO_2 than on the previous occasion. Every adult sheep tolerated a period of breathing 6% O_2 or less (corresponding to an end-expiratory pO_2 of 20–26 mm Hg), providing it was lightly anaesthetized; this period was as long as 50 min in one experiment. Under these conditions both the minute volume of breathing and the cardiac output were increased on the average 3.5 fold. It was notable that in no adult sheep was there any significant increase in O_2 consumption (Figs. 5, 9). The fall in O_2 consumption during anoxia was greatest in the sheep which had had the most anaesthetic, and which showed the least increase in respiratory minute volume and cardiac output.

New-born lambs

Anaesthesia. Our experience with adult sheep had led us to believe that a dose of chloralose of 40–80 mg/kg might be required for general anaesthesia. After we had performed a number of experiments on new-born lambs with this dose, we became aware that lambs less than 3 days old, and particularly within the first 24 hr after birth, require less anaesthetic. Indeed, as little as 10 mg/kg was sometimes sufficient to produce good general anaesthesia, lasting for some hours, in a vigorous new-born lamb. In seventeen lambs less than 3 days old, which received 10–30 mg/kg chloralose, the arterial O_2 saturation exceeded 90% in all but one.

In order to confirm our impression that light chloralose anaesthesia did not seriously modify the resting O_2 consumption of new-born lambs, we measured the O_2 consumption of three lambs which were not anaesthetized, but which were lying quietly at rest (see Methods). These lambs were 1–12 hr old and had an O_2 consumption of 9–13 ml./kg. min, i.e. within the range for anaesthetized lambs. Two of them were then anaesthetized with progressively increasing quantities of chloralose from 5 to 30 mg/kg, but showed no significant change in O_2 consumption. In other experiments we have increased the dose of chloralose from 10 to 50 mg/kg, also without any change in O_2 consumption.

O_2 consumption. The following experiments were carried out in the absence of shivering or panting, and at a rectal temperature of 38.5–40.5° C, maintained if necessary by external warmth. Oxygen lack was induced as in the adult

sheep by lowering the oxygen content of the inspired air stepwise, over a period of $\frac{1}{4}$ –2 hr, usually until breathing stopped.

Almost all new-born lambs showed some decrease of O_2 consumption during anoxia. The magnitude of this decrease depended not only on the degree to which the arterial O_2 saturation was reduced before breathing stopped, but also, and to a much greater extent, on the initial O_2 consumption. Fig. 6 illustrates an experiment in which anoxia caused a large decrease in O_2 consumption in a lamb which was 18 hr old, and whose initial oxygen consumption was high. In this, as in several other new-born lambs, there was

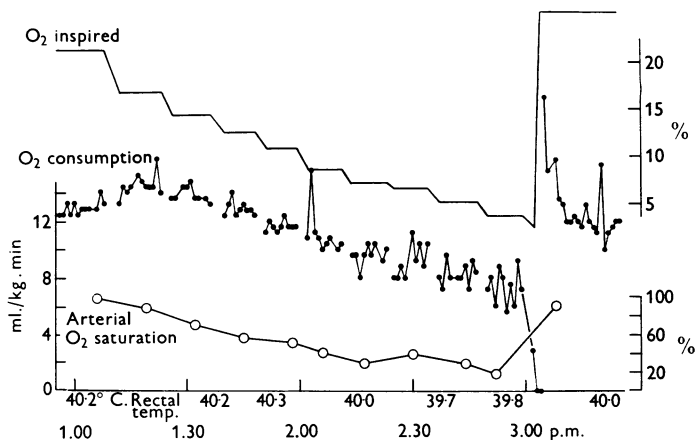


Fig. 6. New-born lamb, 18 hr old, 4.8 kg, chloralose 30 mg/kg. A reduction in the O_2 content of the inspired air caused a large fall in O_2 consumption.

also a small initial *increase* in O_2 consumption, at a time when the O_2 content of the inspired air was about 15%, and breathing was increasing in rate and depth.

Figure 7 shows the change in oxygen consumption with arterial oxygen saturation in lambs which were *less than 1 day old*. The observations depicted in Fig. 6 are represented as triangles (\blacktriangle) in Fig. 7. The initial oxygen consumption when the lambs were breathing air was 6–15 ml./kg. min. As we have explained in a previous paper, the oxygen consumption of the lamb rises rapidly during the first 24 hr after birth, from the foetal level of 4–5 ml./kg. min to 12–15 ml./kg. min (Dawes & Mott, 1959*b*). Of the thirteen lambs, experiments on which are depicted in Fig. 7, eleven had an initial O_2 consumption ranging between 6 and 8.5 ml./kg. min; when these lambs were made anoxic there was only a comparatively small fall in O_2 consumption when the arterial O_2 saturation fell below 50%. In the other two lambs of this group, which had an initial O_2 consumption of 13–15 ml./kg. min, there was a very large fall in oxygen consumption down to a level of about 6 ml./kg. min.

Figure 8 shows observations on eleven lambs, 1-9 days after birth. Of this group there was only one which started with an O_2 consumption of less than 9 ml./kg. min. There was a comparatively small fall in oxygen consumption during anoxia in this lamb. The remainder all showed large falls in oxygen consumption, which in some instances exceeded 40%. Moreover in several

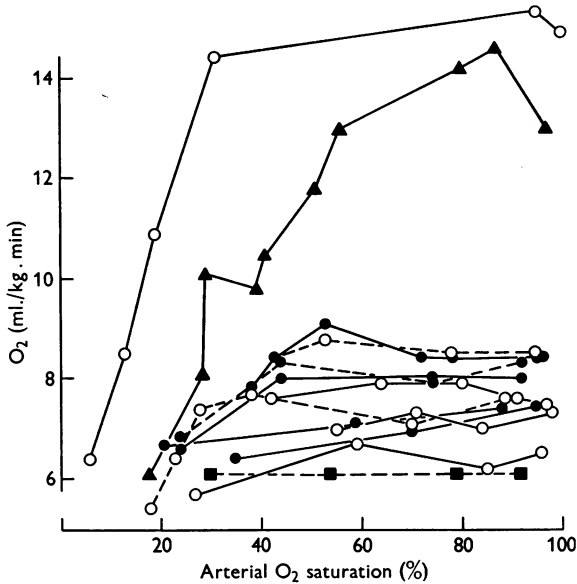


Fig. 7. O_2 consumption/kg body weight plotted against arterial O_2 saturation for thirteen lambs less than 1 day old. The observations from the experiment shown in Fig. 6 are depicted as triangles (▲), and those from the experiment of Fig. 14 as squares (■).

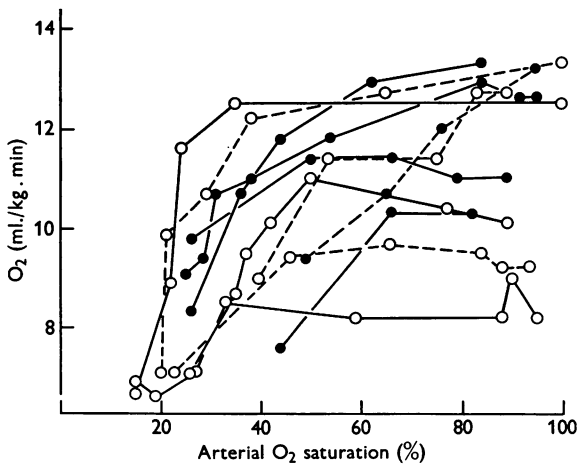


Fig. 8. O_2 consumption/kg body weight plotted against arterial O_2 saturation for eleven lambs 1-9 days old.

of these experiments a substantial decrease in oxygen consumption had already occurred when the oxygen saturation of the arterial blood reached 40–50%.

Figure 9 shows for comparison similar observations on the five *adult sheep*; the experiment illustrated in Fig. 5 is shown here as open circles joined by a interrupted line (○---○). Their weight was 31–80 kg and their initial oxygen consumption 2.9–6.7 ml./kg. min. The fall in oxygen consumption during anoxia was usually trivial and in no instance did it exceed 20%. Some additional observations were made on six *lambs of 20–60 days*, weighing 7.9–14.5 kg. Their initial oxygen consumption was 8.1–11.9 ml./kg. min. These

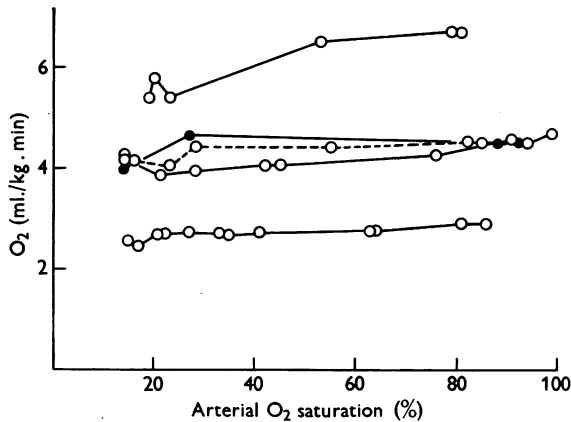


Fig. 9. O₂ consumption/kg body weight plotted against arterial O₂ saturation for five adult sheep. The observations from the experiment shown in Fig. 5 are depicted as open circles joined by interrupted lines (○---○).

lambs behaved like adult sheep so far as their oxygen consumption was concerned, that is to say the fall in oxygen consumption as the arterial O₂ saturation fell was comparatively small and never exceeded 20%.

We may, therefore, summarize the position by saying that some new-born lambs show a very large fall in oxygen consumption during anoxia. This fall is best seen in lambs which have an oxygen consumption of 9 ml./kg. min or more, and within the first 10 days of life. After 20 days from birth a comparable change is not observed even though the resting oxygen consumption, in the absence of shivering, exceeds 9 ml./kg. min.

We have also reduced to 8% the O₂ content of the air breathed by an unanaesthetized lamb which was 7 hr old. The O₂ consumption fell from 13.0 to 7.7 ml./kg. min. This demonstrates that the phenomenon is not dependent on anaesthesia.

In Figs. 7 and 8 the rate of O₂ consumption is plotted against the arterial O₂ saturation, rather than the O₂ content of the inspired air, because the

change in the minute volume of breathing during anoxia varied from lamb to lamb. The changes in O_2 consumption during anoxia in new-born animals of other species have been expressed in terms of the O_2 content of the inspired air (Cross, Tizard & Trythall, 1955, 1958; Moore, 1956*a, b*; Hill, 1958). In order that the observations on lambs may be compared with those on other species, the arterial O_2 saturation has been plotted (Fig. 10) against the O_2 content of the inspired air for the twelve lambs, 9 days old or less, of Figs. 7 and 8 which had an initial O_2 consumption greater than 9 ml./kg. min, i.e. those lambs in which a large fall in O_2 consumption was observed during

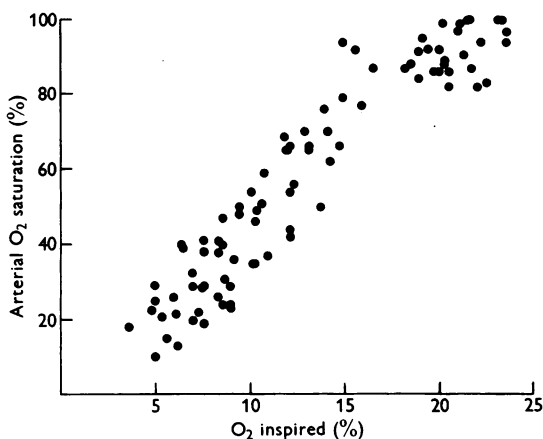


Fig. 10. The arterial O_2 saturation has been plotted against the O_2 content of the inspired air for twelve lambs, 9 days old or less, whose O_2 consumption exceeded 9 ml./kg. min.

anoxia. When breathing 15% O_2 the arterial O_2 saturation was above 70%; on 10% O_2 it was 35–55%. In this group of lambs, and under these experimental conditions, there was little fall in O_2 consumption until the O_2 content of the inspired air was reduced below 12%. In Fig. 6 there was no significant fall in O_2 consumption until the O_2 content of the inspired air was reduced to 10.7%; and in Fig. 15 there was no fall even when breathing 9.6% O_2 .

Overventilation during anoxia. The minute volume of breathing in new-born lambs increased during anoxia, but to a variable extent. Fig. 11*A* shows that the minute volume while breathing air ranged from 0.12 to 0.45 l./kg in lambs up to 10 days from birth. The older lambs and adult sheep had had a larger dose of chloralose than the younger ones; their minute volume per kilogram covered a similar range. The quantity of gas breathed for each millilitre of O_2 consumed was rather greater in lambs of 20–60 days and adult ewes than it was for younger lambs. Although the new-born lambs which were less than 12 hr old had required less anaesthetic, their maximum minute volume per kilogram during anoxia was somewhat smaller than that observed

in older lambs and adults (Fig. 11*B*). Some of the observations shown in this figure suggest that there is an inverse relation between the minute volume of breathing and the dose of chloralose, as is only to be expected.

Cardiac output. Whereas cardiac output in the adult sheep increased very greatly during anoxia, in the new-born lamb it was doubtful in many experiments whether there was any change at all. In Fig. 12*A* is shown the change in cardiac output (in l./m².min) in five adult sheep. When the arterial oxygen saturation fell below 40% there was a very large increase. By contrast, in only four out of ten experiments on lambs of 4 hr-60 days of age was there any evidence of a significant increase in cardiac output during anoxia (Fig. 12*B*).

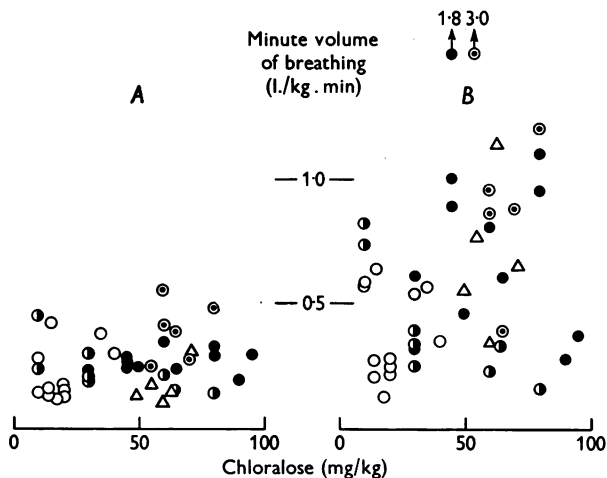


Fig. 11. Minute volume of breathing plotted against dose of chloralose (*A*) while breathing air, and (*B*) in extreme hyperpnoea during anoxia, for lambs < 12 hr old (○), 12 hr-2 days old (●), 2-10 days old (●), 20-60 days old (⊙) and for adult sheep (△).

In each of these four experiments the apparent increase depended upon one single observation. This difference is the most striking single difference between the new-born lamb and the adult sheep in their response to partial oxygen lack.

Oxygen-carrying capacity, blood pressure and heart rate. The oxygen-carrying capacity of the blood varies with age. In the mature foetal lamb it ranges from about 12 to 18 ml./100 ml. under our conditions of anaesthesia and delivery (Born, Dawes & Mott, 1956; Dawes, 1957). The oxygen-carrying capacity falls progressively after birth, as is shown in Fig. 13, towards the adult value of 8-13 ml./100 ml. Oxygen lack of a degree sufficient to reduce the arterial O₂ saturation below 25% caused a large increase in the oxygen-carrying capacity of adult sheep (mean 37%) and a relatively and absolutely smaller increase (mean 9%) in new-born lambs. The latter, however, started with a higher oxygen-carrying capacity.

The blood pressure before anoxia ranged from 62 to 100 mm Hg within the first 2 days after birth, and up to 120 mm Hg within 10 days. Anoxia was induced slowly, and in only three experiments was there any significant rise

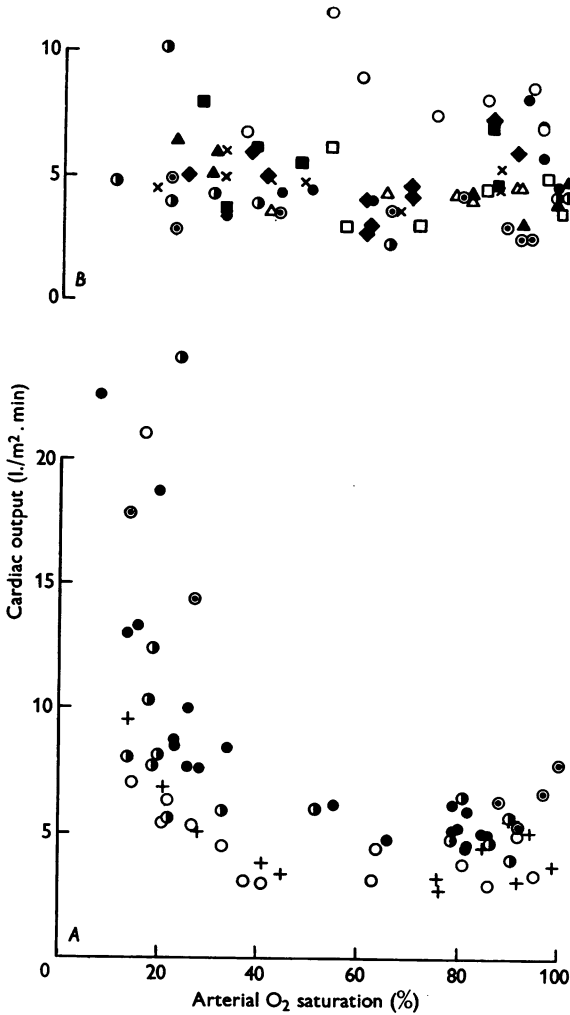


Fig. 12. Cardiac output per m² body surface has been plotted against the arterial O₂ saturation, A for adult sheep, and B for new-born lambs < 12 hr old (\square , \circ , \triangle), 2-7 days old (\odot , \bullet , \times), and 20-60 days old (\blacktriangle , \blacksquare , \bullet , \blacktriangle).

of blood pressure before breathing slowed and stopped, when there was sometimes a terminal rise. Usually there was no change in blood pressure or a gradual fall. There was often an increase in heart rate (Fig. 14) and always a rise in the mean pressure difference between the cavity of the right ventricle and the atmosphere.

Blood lactate, pH and temperature. In five lambs 1½–5 days old the blood lactate and pH were measured. The blood lactate was under 10 mg/100 ml. and pH was 7·2–7·5 when the lambs were breathing air. We were surprised to observe the wide range in pH values, for which we are unable to account. When the lambs were made progressively more anoxic, the blood lactate began to rise as the arterial O₂ saturation fell below 50%. Thus in a typical experiment the O₂ content of the inspired air was reduced stepwise to 8·3% over a period of 1½ hr in a lamb 5 days old. The O₂ consumption fell from 13·6 to 8·5 ml./kg.min and the blood lactate rose from 7·5 to 82 mg/100 ml. The

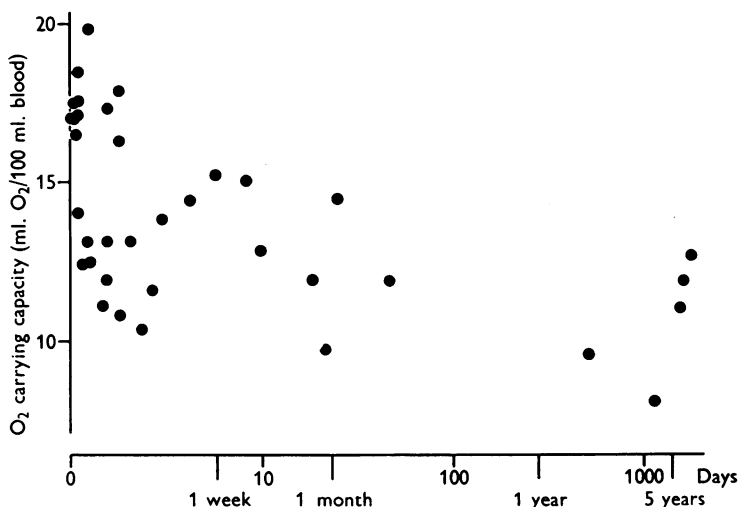


Fig. 13. The O₂ carrying capacity of the blood has been plotted against age (on a logarithmic scale) for lambs and sheep.

lamb was then given room air to breathe and the O₂ consumption returned to its previous level. An hour and 2 hr later the blood lactate was 69 and 18 mg/100 ml. respectively. The changes in pH were less consistent. In some lambs there was a small fall and in others a small rise; there was no clear association with the simultaneous hyperpnoea. The rectal temperature tended to fall during hypoxia (Fig. 6).

Respiratory failure and resuscitation. Most new-born lambs did not stop breathing until the O₂ content of the inspired air was reduced considerably below 10%. Twelve of thirty-three lambs less than 10 days old continued breathing 6% O₂ or less. Usually, if the lamb was still gasping when once more given room air to breathe, recovery was rapid. Respiratory rate and depth eventually returned to pre-anoxic levels, though many lambs continued to over-ventilate for as long as an hour afterwards. In three lambs we failed to restore adequate oxygen sufficiently rapidly, and we were unable to revive these lambs by artificial respiration. In all the others in which breathing had

stopped artificial respiration was effective, though occasionally breathing was periodic in character for a short while thereafter.

Six lambs 4–18 hr from birth stopped breathing when the O_2 content of the inspired air was high, 9.4–15.1%. Three of these lambs had been delivered naturally, three by Caesarean section at 142–145 days gestation. Their birth weights (3.8–5.7 kg), and O_2 consumption (7.0–12.0 ml./kg. min) were in the normal range, and they had received 18–35 mg/kg chloralose. O_2 consumption did not fall in any of these lambs before breathing suddenly stopped (Fig. 14). Arterial blood samples taken shortly before this ranged from 30–58%. Of these six lambs one recovered completely when given air to breathe; one did

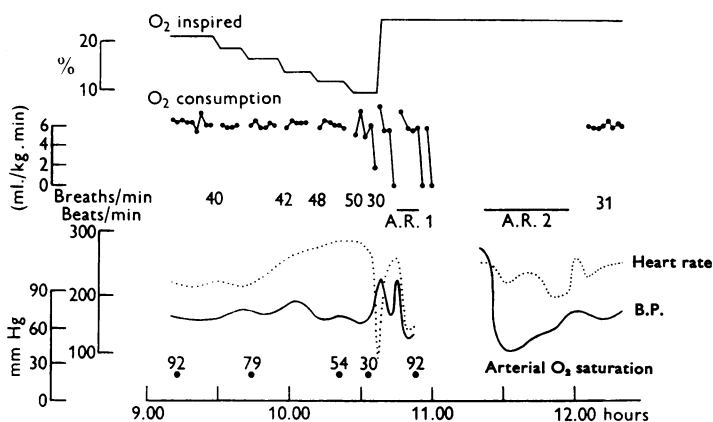


Fig. 14. Lamb 3.75 kg delivered by Caesarean section at 4.45 p.m.; chloralose 20 mg/kg at 8.20 p.m. Progressive anoxia caused respiratory failure when the arterial O_2 saturation fell below 30%. The O_2 content of the inspired air was then raised, but in spite of this, and of a short period of artificial respiration (A.R. 1) at 10.45 p.m., breathing did not recover. It required artificial respiration (A.R. 2) for more than half an hour before normal breathing could be re-established.

not breathe even after 2 hr artificial ventilation with a respiration pump. In the other four breathing appeared to recover after a short period of artificial respiration, fully adequate to restore the arterial O_2 saturation to normal, only then to fail once more (Fig. 14). A prolonged period (15–60 min) of artificial ventilation then led to a rapid fall of blood pressure to a low level, followed by a gradual rise to a level not very different from that immediately preceding respiratory failure. At the same time heart rate fell towards the pre-anoxic value (Fig. 14). In all four lambs discontinuation of artificial ventilation was then followed by the establishment of normal breathing. In the experiment, part of which is illustrated in Fig. 14, the same sequence of respiratory failure during anoxia, and resuscitation only by prolonged artificial ventilation, was repeated after an interval of three hours; no additional anaesthetic was given.

In another of these lambs breathing stopped suddenly on 11.6% O₂ when the arterial O₂ saturation was 58% and without any previous reduction in O₂ consumption. It was only re-established after artificial ventilation for 1 hr. Half an hour later the O₂ content of the inspired air was lowered *during artificial ventilation* to 6.2%, when the arterial O₂ saturation was only 25%; O₂ consumption fell from 11 to 6 ml./kg. min. Spontaneous breathing was then re-established on air; it failed subsequently when the inspired O₂ was decreased to 10.7%. On this occasion, however, normal breathing began on air once more, without any prolonged period of artificial ventilation. This experiment shows that the phenomena described above are due to primary respiratory failure. It is interesting that it should occur at a relatively high arterial O₂ saturation, and only in such very young lambs. The fact that prolonged artificial ventilation was sometimes necessary to re-establish normal breathing suggests that in these lambs the metabolic consequences of anoxia may have added to a depressant action of the anaesthetic upon the respiratory centre.

Blood flow and O₂ consumption in the hind quarters. The fact that anoxia caused a large decrease in O₂ consumption in many new-born lambs raised the question as to whether this decrease was general throughout the body, or whether it was greater in some tissues than in others. In order to decide between these two alternatives, blood flow was measured in the hind quarters by inserting a velodyne flowmeter into the inferior vena cava just caudal to the entry of the renal veins. Oxygen consumption in the area drained was calculated by multiplying flow and the arteriovenous oxygen difference.

Four successful experiments were performed in lambs 4–12 days old, with a total O₂ consumption while breathing room air of 10–12 ml./kg. min. The flow in the inferior vena cava under these conditions was 94–126 ml./min and the oxygen consumption of the hind quarters was 1.3–1.5 ml./kg. min, i.e. 9.4–12.5% of the total. In all four lambs, when the arterial O₂ saturation was reduced to 31–43% by lowering the O₂ content of the inspired air, the O₂ consumption of the hind quarters was reduced relative to that of the whole lamb. Figure 15 illustrates such an experiment, in which the arterial O₂ saturation fell to 41% and the venous to 10%. The O₂ consumption of the whole lamb was hardly reduced at all, but that of the hind quarters fell by about 25% in spite of an increased blood flow in the inferior vena cava. Before and after anoxia the O₂ consumption of the hind quarters was 12.2–12.9% of that of the lamb; during anoxia it was 10.5 and 8.7%. The minute volume of breathing doubled, heart rate increased from 240 to 370 beats/min and blood pressure rose by less than 5%.

These observations appear to establish a *prima facie* case for believing that the decrease in O₂ consumption during anoxia in the new-born lamb is considerably greater in some tissues than in others. Indeed, one would expect

that the O_2 consumption of the respiratory muscles might even be increased. There is one alternative explanation of these observations which has to be considered, namely, the possibility that the quantity of venous blood returning from the hind quarters to the heart through anastomotic channels other than the inferior vena cava is altered during anoxia. Calculation suggests that this is unlikely, particularly in view of the large decrease in arteriovenous O_2 difference during anoxia, and the small changes in flow in the inferior vena cava which were observed when using the velodyne flowmeter, the mean pressure drop across which is negligible. Thus, using the values in Fig. 15, it can be shown that if the apparent decrease in the O_2 consumption of the

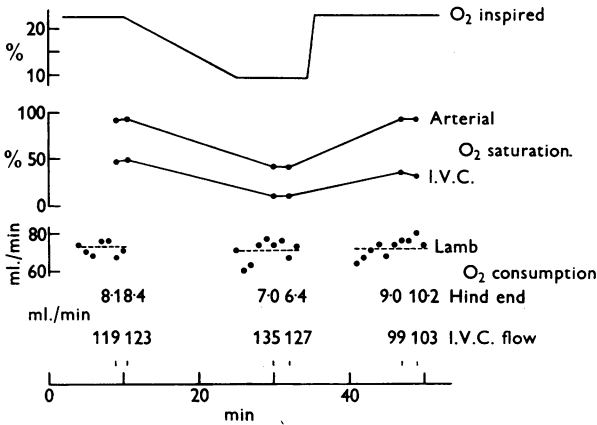


Fig. 15. Lamb 7 days old, 5.6 kg, chloralose anaesthesia. The O_2 consumption of the whole lamb was measured with the apparatus shown in Fig. 1, and that of the hind quarters was calculated from measurement of inferior vena caval flow and the arteriovenous O_2 difference. During anoxia there was no significant fall in total O_2 consumption, but that of the hind quarters decreased considerably.

hind quarters during anoxia were wholly to be accounted for by a change in anastomotic flow, that flow would have to be at least one-third of the flow in the inferior vena cava during anoxia. It would also have to increase by at least 50% from its initial value, in circumstances under which the flow in the inferior vena cava increased less than 10%. The evidence is therefore in favour of the conclusion that there was a real, and substantial, decrease in the O_2 consumption of the hind quarters.

The effect of anoxia on shivering and on O_2 consumption. All the preceding experiments were carried out on lambs which were not shivering, and at rectal temperatures of 38.5–40.5° C. Lambs which were 2 or more days old were almost all able to maintain their rectal temperature at 39–40° C, without shivering, in the laboratory at 17–20° C; their resting O_2 consumption, and so their metabolic rate, was sufficiently high. Many younger lambs had an O_2

consumption of less than 9 ml./kg. min at rest and in the absence of shivering; their environmental temperature had to be raised above 20° C by placing them on a warm table and by radiant heat in order to prevent shivering. Some of these lambs were able to raise their O₂ consumption to as much as 25 ml./kg. min by shivering. Shivering was always abolished by warming to a rectal temperature of 39.5° C or above; it was sometimes abolished at a lower rectal

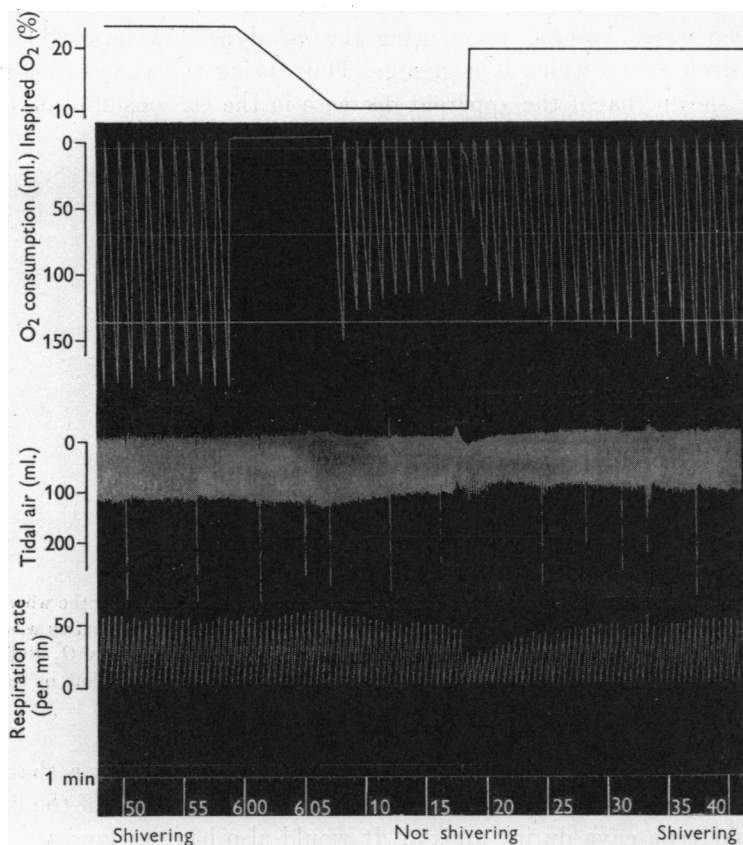


Fig. 16. Lamb 60 days old, 12.7 kg, chloralose 50 mg/kg. The lamb was cooled and during the period covered by the record its rectal temperature was 37° C. Lowering the O₂ in the inspired air to 10% caused a fall in O₂ consumption and cessation of shivering. Note the transient increase of tidal air and respiration rate while the inspired O₂ was decreasing.

temperature and occasionally, on warming with radiant heat, before any change in rectal temperature had been observed. When lambs were warmed still more, so that their rectal temperature rose above 40.5° C, they began to pant, respiration rate increased to 200/min or more, and at a rectal temperature of 41° C O₂ consumption had risen by 15–20% above the minimum value. These observations demonstrate that the preceding experiments had

been conducted at the neutral temperature, at which the rate of O₂ consumption was minimal.

It is well known that anoxia abolishes shivering in the adult animal or, put into other terms, that below the neutral temperature anoxia reduces O₂ consumption. This phenomenon was readily seen in lambs in which shivering was induced by cooling. Figure 16 illustrates such an experiment in a 60-day-old lamb of 12.7 kg body weight. The O₂ consumption at the start of the experiment, when it was breathing air at an environmental temperature of 19° C and with a rectal temperature of 39.7° C, was 120 ml./min. The lamb was then cooled by the use of ice, wet cloths and a fan, and at the beginning of the record shown in Fig. 16 its rectal temperature was 37.0° C and O₂ consumption about 190 ml./min. When the O₂ content of the inspired air was reduced to 10 %, shivering gradually ceased and the O₂ consumption fell to 110 ml./min. When the O₂ content of the inspired air was raised, shivering began again and O₂ consumption increased.

There are two interesting features of these experiments. First, under such conditions a large fall in O₂ consumption was often seen with a comparatively small reduction in the O₂ content of the inspired air, to between 10 and 15 %; the arterial O₂ saturation was often well in excess of 50 %. Secondly, the effect of anoxia upon breathing was different when the lamb was cool from that observed when it was warm. Figure 16 shows that there was an initial increase in tidal air and respiration rate, but this was not maintained. As shivering ceased and oxygen consumption decreased, there was a concomitant fall in the minute volume of ventilation. When the oxygen content of the inspired gas was raised once more, breathing became slow and periodic for a short while, and thereafter increased towards its initial level as shivering reappeared and oxygen consumption rose.

DISCUSSION

In the preceding account of the experimental results the depth of anaesthesia has been given particular prominence. One of the most useful guides to the sheep's condition was the end-expiratory pO₂, which can be measured rapidly, and was 111–127 mm Hg while breathing air under *light* anaesthesia; the arterial O₂ saturation was 86–95 %. It was evident that a comparatively small increase in the dose of anaesthetic had a large effect on the ability of the adult sheep to withstand anoxia, as judged by the cardiac output, the breathing and the O₂ carrying capacity of the blood. New-born lambs required less anaesthetic to produce surgical anaesthesia; even 10 mg/kg chloralose was sometimes sufficient in the first day after birth. Similarly new-born puppies require less pentobarbitone or chloralose for anaesthesia than do adult dogs. This greater sensitivity of new-born animals to anaesthetics made the execution

of the experiments and comparison with the results observed in adult ewes more difficult.

Oxygen consumption during anoxia

In previous papers (Acheson *et al.* 1957; Dawes & Mott, 1959*b*) it was shown that the O_2 consumption of foetal and new-born lambs falls substantially during anoxia. The foetal lambs were still attached to their mothers by the placentae and were not breathing; the new-born lambs were artificially ventilated. In the present paper all the new-born lambs and adult sheep were breathing spontaneously. The primary object of the experiments was achieved, that is, it was established, using the same methods of investigation, that the

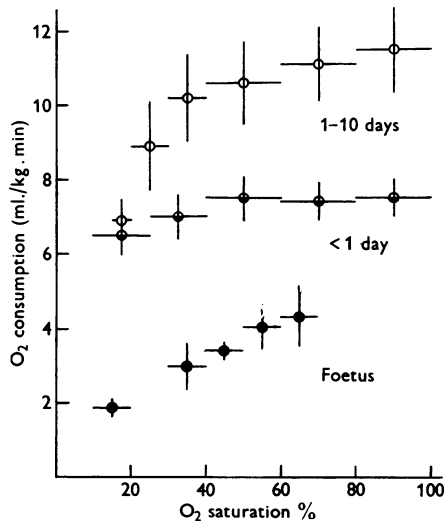


Fig. 17. The O_2 consumption/kg body weight has been plotted against the arterial O_2 saturation for ten foetal lambs (●, from the data of Dawes & Mott, 1959*b*) and for eleven lambs more than 1 day old (○, from Fig. 8) and for eleven lambs less than 1 day old with an initial O_2 consumption of 6–9 ml./kg.min (◐, from Fig. 7). The vertical lines indicate the 95% confidence limits of the means and the horizontal lines the range of observations.

O_2 consumption of many new-born lambs fell during anoxia to a greater extent than that of adult sheep. It is also evident, however, that the situation is more complicated than was at first appreciated.

The resting O_2 consumption of an anaesthetized foetal lamb is 4–5 ml./kg.min when the arterial O_2 saturation exceeds 50%. When the arterial O_2 saturation is reduced to 20%, O_2 consumption falls to about 2 ml./kg.min (Fig. 17, ●). Within a few hours of birth the resting O_2 consumption begins to rise. In many lambs which are less than 1 day old it is about 7.5 ml./kg.min while breathing air, and as the arterial saturation falls to 20% during anoxia there is a small fall of O_2 consumption, but only to 6.5 ml./kg.min

(Fig. 17, \ominus). Some change has therefore already taken place since birth, as a consequence of which the lamb maintains its consumption of oxygen at a higher level than under foetal conditions. Within 1–2 days of birth, and sometimes within 4–5 hr, O_2 consumption rises even further, to a mean of about 11 ml./kg. min; in these lambs anoxia causes a larger fall of O_2 consumption than that seen immediately after birth, but not below 6.5 ml./kg. min (Fig. 17, \circ). Finally, during the next 2–3 weeks a further change occurs, so that lambs 20–60 days old maintain their O_2 consumption at an even higher level during extreme anoxia, to an extent comparable with that seen in adult sheep.

Now Hill (1958) has observed in new-born kittens and in adult guinea-pigs, which are relatively small in size, that at low environmental temperatures O_2 consumption is increased even in the absence of visible shivering, and it is this increase in O_2 consumption which is also particularly susceptible to hypoxia. The phenomenon of a fall in O_2 consumption during anoxia should therefore be considered under two heads. First, in any new-born animal below its neutral temperature (and it is to be noted that this may be high, above normal laboratory temperatures, for small animals) a small degree of oxygen lack (e.g. an inspired O_2 of 10–15%) may reduce oxygen consumption approximately to that at the neutral temperature (Fig. 16). Secondly, and even at the neutral temperature, a rather more severe degree of anoxia (inspired O_2 < 12%) may cause a reduction in oxygen consumption in the new-born lamb (Fig. 17, \circ). So far as babies are concerned, the observations of Cross, Tizard & Trythall (1955, 1958) will have to be reconsidered from this point of view, since it is not known whether the babies were at or below their neutral temperatures.

When there was a large fall of O_2 consumption in new-born lambs during hypoxia, the rectal temperature tended to fall. This would be consistent with a reduction in metabolic rate, in spite of anaerobic glycolysis. In two experiments the rate of energy production by anaerobic glycolysis (calculated from the rise of blood lactate, assuming that the lactate ion was evenly distributed throughout the entire body mass) was less than the energy deficit associated with the fall in O_2 consumption.

Changes in cardiac output at birth

The measurements of cardiac output were based upon the Fick principle. In the new-born animal the foetal channels are not fully closed for some days after birth, and it is necessary to consider what the quotient of O_2 consumption and arteriovenous O_2 difference represents in the presence of an open foramen ovale and/or ductus arteriosus. Table 2 indicates these possibilities. It was assumed, in compiling this Table, that the valve of the foramen ovale prevents a left-to-right shunt through it. The combination of a left-to-right shunt

through the ductus arteriosus with a right-to-left shunt through the foramen ovale (Table 2, 6) is improbable; if the pulmonary vascular resistance is sufficiently low to permit a left-to-right shunt through a patent ductus arteriosus, then pulmonary flow will be large and it is unlikely that inferior vena caval pressure will then exceed left atrial pressure. The only circumstance likely to lead to this combination is primary right-sided heart failure. Apart from this, Table 2 shows that when there is a left-to-right shunt through the ductus, application of the Fick principle results in measurement of right ventricular flow only; and where there is a right-to-left shunt through the ductus arteriosus or foramen ovale, it measures left ventricular flow only.

TABLE 2. Application of the Fick principle to the measurement of cardiac output when the foetal channels are patent

	Ductus arteriosus	Foramen ovale	Meaning of O_2 consumption A-V O_2 difference
1.	Closed	Closed	R.V. = L.V. output = systemic flow.
2.	Closed	R → L shunt	L.V. output = systemic flow.
3.	R → L shunt	Closed	L.V. output = systemic flow - D.A. flow.
4.	R → L shunt	R → L shunt	L.V. output = systemic flow - D.A. flow.
5.	L → R shunt	Closed	R.V. output = systemic flow.
6.	L → R shunt	R → L shunt	R.V. output + F.O. flow = systemic flow.

R.V., L.V., right and left ventricle respectively; D.A., ductus arteriosus; F.O., foramen ovale.

In either event the *lower* of the two ventricular outputs is the one calculated. In the new-born lamb, soon after birth, the ductus arteriosus is usually open; a murmur characteristic of left-to-right flow is usually heard for up to 2 days. As a lamb is made more and more anoxic the right ventricular pressure rises, and there is sometimes a tendency for systemic arterial pressure to fall. We must therefore envisage the possibility (Born, Dawes, Mott & Rennick, 1956) that during extreme anoxia, flow through the ductus may revert to the foetal direction, right-to-left. In such circumstances we would have calculated right ventricular output initially, while the lamb was breathing air, and left ventricular output towards the end of the period of anoxia. The results must be discussed with these considerations in mind.

First, there is apparently evidence of a considerable change in cardiac output at birth. In the mature foetal lamb, within 10 days of term, umbilical blood flow is about 130 ml./kg.min (Cooper, Greenfield & Huggett, 1949; Acheson *et al.* 1957). As about 55% of the combined output of *both* ventricles goes to the placenta (Dawes, Mott & Widdicombe, 1954), the output of both ventricles together is about 235 ml./kg.min. Barcroft & Torrens (1946), as a result of experiments using a cardiometer on three lambs of 129-141 days gestation age, calculated a combined ventricular output of 240 ml./kg.min. The evidence suggests that the output of the two ventricles is unequal, that of the left being 58% of the total (130 ml./kg.min) and that of the right 42%

(100 ml./kg. min). The cardiac output (one ventricle only) of sixteen new-born lambs *breathing air* was 325 ± 30 ml./kg. min. There was no significant difference between the cardiac output of six lambs which had an O_2 consumption of 7.0–8.5 ml./kg. min and that of the remainder which had an O_2 consumption of 10.5–16.0 ml./kg. min. We can be reasonably sure that this is a measurement of right ventricular output, and that within the first few hours of life the output of the left ventricle is considerably greater by reason of the left-to-right shunt through the ductus arteriosus (Dawes, Mott & Widdicombe, 1955), which may indeed be almost as large as the output of the right heart.

These changes are even more remarkable when considered in relation to the volume of blood flow through the lungs and through the other tissues of the lamb. To take the lungs first, our previous calculations suggested that about 12% of the combined ventricular output should pass through the foetal lungs (which would amount to 28 ml./kg. min). The observations on the cardiac output of new-born lambs therefore indicate that pulmonary blood flow has increased 11.5 fold at birth. Our previous direct measurements of flow through the left lung gave a 3–10 fold increase on artificial ventilation for 1–2 hr (Dawes, Mott, Widdicombe & Wyatt, 1953).

Some 33% of the combined ventricular output was calculated to pass through the foetal tissues, other than the lungs (Dawes *et al.* 1954); this would amount to about 75 ml./kg. min. It is therefore evident, taking these figures at their face value, that there has been an increase of more than fourfold in systemic blood flow at birth. There may have been a small increase in blood pressure, as between the foetus and the 1–2-day-old lamb, but this certainly does not amount to more than 40% at the very outside. We can therefore deduce that there has been a very large decrease in peripheral vascular resistance.

The conclusions arrived at in the preceding three paragraphs derive from estimations of foetal cardiac output which are based on measurements of umbilical blood flow and of the distribution of oxygenated blood within the foetal lamb with an open chest. Future experiments may show that the present estimates of foetal cardiac output are too low. There are two considerations which might lead to this suspicion. First, cardiometer measurements on open-chest adult animals give figures for cardiac output which are far below those based on the Fick method (Kenney, Neil & Schweitzer, 1951); our calculations of foetal cardiac output agreed well with the cardiometric measurements of Barcroft & Torrens (1946). Secondly, it has been shown that new-born lambs require much less chloralose for general anaesthesia than do adult sheep; the foetal lambs which are still attached by the umbilical cord to their mother may therefore have been very deeply anaesthetized. However, if future experiments should show that foetal cardiac output has been underestimated, say by a factor of 3–4, this would certainly entail a very

considerable change from the present view as to the normal rate of blood flow within the different parts of the foetal circulation.

Changes in cardiac output during anoxia

We must now return to a comparison of the effects of anoxia on the cardiac output of the new-born lamb and the adult sheep. In the latter, cardiac output increased up to fourfold when the arterial O_2 saturation fell below 40% (Fig. 12A). As this was accompanied by no significant change in arterial blood pressure, it must be associated with systemic vasodilatation. In the 20–60-day-old lambs we are certain that the foramen ovale and ductus arteriosus were anatomically closed; there was no significant increase in cardiac output, and no great change in blood pressure. Systemic vasodilatation cannot therefore have taken place to a comparable extent or, alternatively, if it did do so, cardiac failure must then have occurred so rapidly that we were unable to make the appropriate measurements. In the younger lambs we are on less certain ground because of the possible patency of the foetal passages. There was certainly no positive evidence of any increase in left or right ventricular output (whichever was least) during anoxia, up to the time at which breathing stopped. Further than that it is not possible to go.

There is one further point. We have concluded that there is a large increase in cardiac output, pulmonary blood flow and systemic blood flow at birth. Now Figs. 12A and B relate the cardiac outputs of new-born and adult lambs to their surface areas, and it will be seen that they are approximately equal, ranging from about 4–8 l./m². min. But when cardiac output is expressed in terms of body weight, that of the new-born lamb is three times that of the adult sheep (Fig. 18). Therefore not only has the cardiac output of the lamb increased greatly at birth, but it has increased to a value much in excess, per unit body weight, of that of an adult sheep breathing air.

Breathing

Even the youngest lambs showed an increase in the minute volume of breathing during anoxia, but in general the increase was rather greater in older lambs and adults. A similar difference has been observed in rats (Adolph, 1957). However, there was no evidence that the fall in O_2 consumption during anoxia in young lambs, which was greater than that in older lambs or adult sheep, was dependent on this difference. In new-born infants Cross & Oppé (1952) showed that administration of 15% O_2 caused hyperpnoea, which was maintained for a few minutes only. They concluded that the failure to maintain hyperpnoea might be due to a depressant effect of oxygen lack upon the respiratory centre. It has been shown that this phenomenon can be produced in the new-born rabbit placed in a cool environment, but not in a warm environment (Dawes & Mott, 1959a). The same is true of the new-born

lamb (Fig. 16). The ability of an animal to maintain hyperpnoea during anoxia is therefore related to its environmental temperature, and once again it may be relevant that it is not known whether the observations of Cross & Oppé (1952) on new-born babies were executed at or below the neutral temperature.

In some very young lambs respiration stopped when breathing 10–15% O₂, and spontaneous breathing was not restored until a period of as much as an

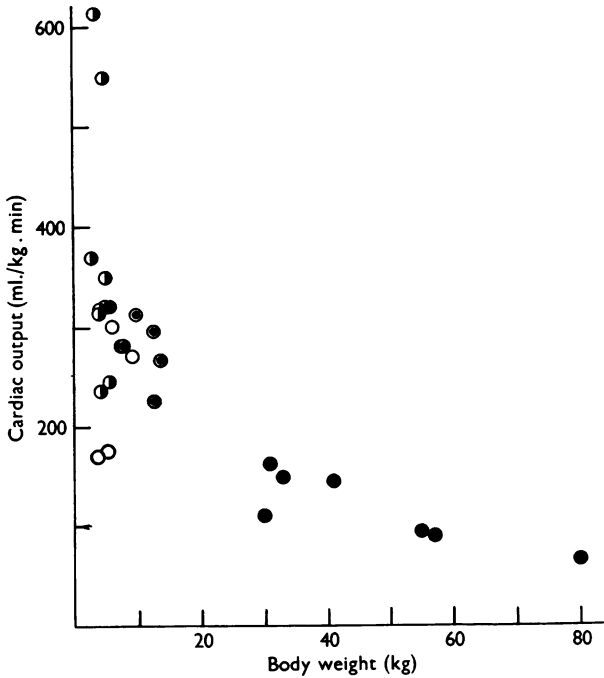


Fig. 18. The cardiac output per kg body weight has been plotted against body weight for lambs < 1 day old (●), 2–12 days old (○), 20–60 days old (⊙) and for adult sheep (●), all while breathing air.

hour had elapsed, during which time the lamb was artificially ventilated. The implication of this observation is that, under anaesthesia, it is possible for a period of lack of oxygen to result in some change in the central nervous system or elsewhere which is reversible, but which in the absence of artificial respiration would lead to death.

SUMMARY

1. The new-born lamb required less chloralose to produce surgical anaesthesia than the adult sheep, particularly in the first day after birth.
2. The oxygen consumption of lightly anaesthetized adult sheep was well maintained, when the O₂ content of the inspired air was reduced to 6%.

In the new-born lamb at the neutral temperature and in the absence of shivering, there was a fall of up to 40%, varying according to the age of the lamb and the initial rate of O₂ consumption.

3. Calculation suggests that cardiac output and systemic blood flow as well as pulmonary flow may have increased after birth.

4. Cardiac output per kilogram body weight was greater in the new-born lamb than in the adult sheep. Anoxia caused no significant increase in cardiac output in new-born lambs; there was a 3–5 fold increase in adult sheep.

5. In a few very young lambs in which respiratory failure had suddenly occurred while breathing 10–15% O₂, prolonged artificial ventilation with air was required before spontaneous breathing was re-established.

6. The flow in the inferior vena cava was measured in new-born lambs; the calculated O₂ consumption of the hind quarters decreased proportionately more than that of the whole lamb during anoxia.

7. When a new-born lamb was cooled so that it began to shiver, O₂ consumption and the minute volume of respiration increased. A small reduction in the O₂ content of the inspired air to 10–15% suppressed shivering and reduced O₂ consumption to just below its initial level. In these circumstances there was only a transient increase in tidal air and respiration rate.

We wish to thank the Nuffield Foundation for a grant in support of this work; the Medical Research Council for travelling expenses of K.W.C.; and J. Farrant Esq. and H. B. Parry Esq. for supplying sheep. We are also indebted to Dr D. J. C. Cunningham for advice about the construction of respiratory valves and to J. Bricknell, W. Dodson, H. Elvidge, A. Ryder and G. K. Smith for technical assistance.

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