J. Physiol. (1953) 122, 66–80

CHANGES IN ALVEOLAR CARBON DIOXIDE TENSION BY NIGHT AND DURING SLEEP

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(*Received* 16 *February* 1953)

Stanbury & Thomson (1951) tentatively suggested that the diurnal variations in renal excretion of acid and salt might be due to changes in ventilation and consequent change of carbon dioxide content of alveolar air and blood. Criticizing this suggestion, Longson & Mills (1952, 1953) showed that exposure to CO_2 often failed to increase the renal acid output and never decreased the salt excretion. It was, however, uncertain how large a fluctuation of alveolar CO_2 tension might be expected during sleep; and since the renal rhythm persists during 24 hr without sleep (Longson, Mills & Stanbury unpublished), we wished to know whether alveolar CO_2 tension showed a similar habitual rhythm.

No claims for a spontaneous rhythm in alveolar CO_2 tension have been found in the literature, and the existence of such is specifically denied by Haldane & Fitzgerald (1905). The tensions plotted by Cohen & Dodds (1924) upon two fasting subjects awake for 24 hr do, however, show a regular variation, although this is not commented upon by the authors. Such a spontaneous rhythm might be responsible for some of the changes ascribed to sleep. Others may be ascribable to posture, since recumbency (Mackay, 1943) leads to a rise in alveolar CO_2 tension.

In the course of other work (Longson, Mills & Stanbury, unpublished) many series of alveolar CO_2 determinations were made upon subjects either fasting or with minimal hourly food intake, sometimes for 24 hr or more, and these provide data for consideration of diurnal rhythms. These were supplemented with other determinations during sleep, either throughout the night or during short afternoon naps. To facilitate afternoon sleep, hexobarbitone gr. 4 orally was usually taken. A further interest in the tensions reached during nocturnal sleep comes from the claim of Doust & Schneider (1952) that arterial oxygen saturation may fall during sleep as low as 86%, which suggests a much more profound respiratory depression than any previously claimed.

Alveolar sampling during sleep presents obvious difficulties, and in previous work a variety of techniques have been employed. Since none is quite unobjectionable, several methods have here been used.

METHODS AND MATERIAL

All determinations during sleep have been performed upon the author, aged 38. For study of the diurnal rhythm in subjects awake, six other healthy males, aged 17–34, have also been used.

Except for a few early experiments with the Haldane apparatus, gas analysis has been carried out with the commercial infra-red analyser made by the Infra-Red Development Co. Ltd. This was frequently calibrated against a CO_2 mixture taken from a cylinder, and analysed with the Haldane apparatus. The analyser gives a dial reading of CO_2% on a nearly linear scale whose smallest calibration marks represent 0·1 %. If the pointer were perfectly steady, the same accuracy could be obtained as with the Haldane apparatus. This was sometimes so. Sometimes, however, small fluctuations of the pointer, even when a slow stream of gas of constant composition was passing through from a cylinder, made it impossible to read with a greater accuracy than 0·05 %, or half a scale division.

Alveolar samples were mostly collected by the method of Henderson & Haggard (1925), whereby during each inspiration 1–3 ml. of air from the end of the previous expiration is automatically sucked from just beyond the expiratory valve. These are referred to as 'end-tidal' samples. By insertion of the analysis chamber of the infra-red machine in place of the sampling tube, alveolar air was sucked continuously through the analysis chamber, with a slight delay since the capacity of the chamber is 5 ml., and only 1–3 ml. entered at each breath. With a steady barometer, conversion of alveolar CO_2 percentage to tension merely involves multiplication by a constant factor. The sensitivity of the apparatus was therefore so adjusted that the scale reading of 4 % corresponded to 40 mm Hg, and the alveolar CO_2 tensions were read directly from the scale to, at best, 0·1 mm Hg.

A few early determinations were of end-inspiratory Haldane-Priestley samples collected in evacuated tubes; when these were collected in the laboratory three or four samples were collected in the same tube by successive partial evacuation; at home, only single samples were collected.

For estimation of the alveolar tension during sleep, three methods have been used: Haldane-Priestley samples on being awakened by an alarm clock, or occasionally on spontaneous waking; end-tidal sampling; and the application of suction.

In the suction method the alveolar samples were collected exactly as in the Haldane-Priestley method but without the co-operation of the subject, as with the apparatus described by Lambie & Morrissey (1948). Forced expiration was achieved by connecting the subject abruptly to a 20 l. flask of air at a suitable negative pressure by means of a slide tap. This tap could be operated very rapidly, had no dead space, and did not—as do standard respiratory three-way taps—connect all three channels at some moment of its excursion. Just beyond the tap from the subject were two apertures to which evacuated tubes were connected for sampling.

If the subject is breathing from a closed-circuit spirometric system before the collection, and is re-connected to it afterwards for a sufficient time for his respiration again to become steady, it is possible to estimate from the change in volume recorded on the spirometer how much air has been sucked out of the lungs by this device. When an initial negative pressure of around 100 mm Hg was used in eighteen collections, a mean volume of 1047 ml. was sucked out with a standard deviation of 93 ml., at ambient temperature and pressure, a volume surprisingly constant and sufficient to satisfy the strict Haldane & Priestley (1905) requirements for alveolar air. With smaller or larger suction pressures, a smaller volume was collected; the higher pressures appeared to cause spasm of the glottis. Initial suction pressures of around 100 mm Hg below atmospheric were therefore always used.

RESULTS

Diurnal fluctuations

Upon four subjects, alveolar air was collected and analysed hourly during 24 hr without sleep, occupied by sedentary work, and with the subjects either fasting or taking 10 g glucose hourly. The samples from *M* and *S* were three pooled Haldane-Priestley samples, analysed with the Haldane apparatus; those from *B* and *J* were end-tidal samples, passed through the infra-red analyser; neither of these last two subjects had extensive experience of giving alveolar samples; but the end-tidal sampling needed no co-operation from the

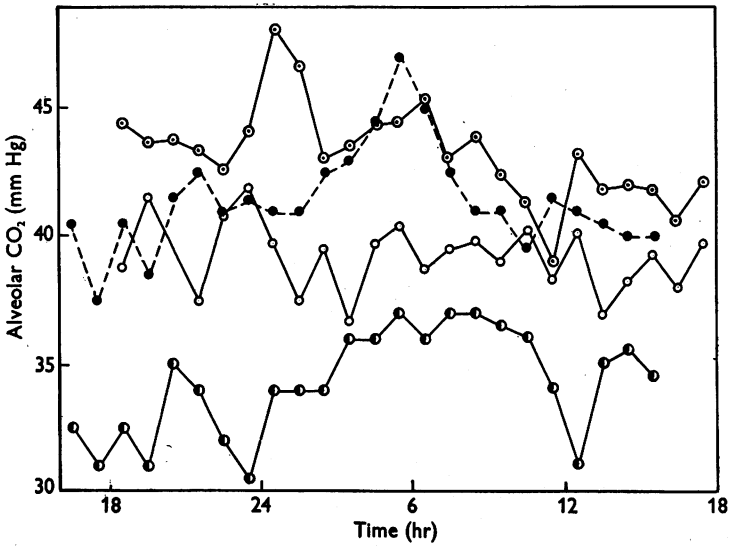

Fig. 1. Alveolar CO_2 tensions during 24 hr without sleep or solid food; subjects engaged in light laboratory work. ⊙, *M*, ○, *S*, Haldane-Priestley samples analysed with Haldane apparatus. ◐, *J*, ●, *B*, end-tidal samples passed continuously through infra-red analyser.

subject, and was continued for about 5 min to make certain that respiration was steady and that the tension recorded remained fairly constant; occasionally the subject gave a Haldane-Priestley sample at the end, to make sure that the dead space was being adequately washed out by the tidal air; this procedure never gave values for the CO_2 tension above the end-tidal value.

The results are seen in Fig. 1. Some show a considerable random scatter, probably due in part to faulty sampling technique, but in part to physiological variation; slow fluctuations over a range of 1–2 mm have often been observed when end-tidal samples were drawn continuously through the infra-red analyser for 10 min or more. Superimposed upon these random variations from sample to sample are obvious fluctuations over the 24 hr in all subjects except *S*, in whom if they exist they are obscured by random error. The time of

maximum tension differed widely, however, being about 01.00–02.00 hr in *M*, 05.30 hr in *B*, and 05.30–08.30 hr in *J*. Since the random scatter among these determinations was considerable the mean square successive difference ratio test (Hart, 1942) was applied to the data. This test measures whether each value is more closely related to the previous value than to the mean, that is, whether there is any trend or fluctuation over periods longer than the interval between determinations. For subject *S*, $\delta^2/s^2 = 2{\cdot}35$, $P > 0{\cdot}05$, indicating that in this subject any fluctuation is obscured by random error; for subjects *B*, *J* and *M* this ratio is 0·70, 0·80 and 0·89, values which differ significantly from the expected value of 2 for a random series ($P < 0{\cdot}01$). There was thus in all

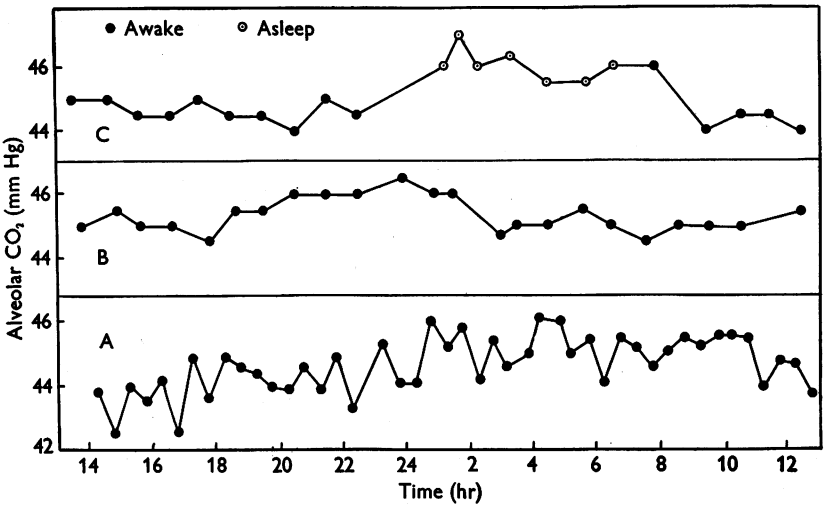

Fig. 2. Alveolar CO_2 tensions during 24 hr complete bed rest. A: subject *T*, sleeping between samples during the night; B: subject *M*, awake; C: subject *M*, following immediately upon B, sleeping during night. All analyses by passing end-tidal samples continuously through infra-red analyser.

these three subjects a real fluctuation, giving maximal values of alveolar CO_2 tension in the night or early morning. More recently, a similar experiment on *M* has shown no rhythm, hourly determinations giving values between 42·8 and 44·2 mm Hg throughout 24 hr.

Two similar series, shown in Fig. 2, curves A and B, were obtained from subjects at rest and semi-recumbent for 24 hr, with similar regular hourly alimentation, and collection of alveolar samples hourly or half-hourly by the end-tidal sampler. The existence of a diurnal rhythm, independent of sleep, was again obvious, and again the maximal tensions were reached at different times by the two subjects, about midnight by *M* and between 04.00 and 05.00 hr by *T*.

Many series of end-tidal samples were obtained from *M*, and a few from

three other subjects, in the course of other experiments when the subject remained at complete rest in an easy chair from about 06.00 or 09.00 hr for the greater part of the day; in some of these no food was taken, and in others light sandwich meals. Four such series on *M* fasting are shown in Fig. 3. From 09.00 hr onwards there was no trend upwards or downwards, in any single experiment or in the pooled results, as measured by absence of a significant linear regression on time. Results were similar but more irregular in the non-fasting experiments. In one experiment on subject *T* there was however a significant fall, calculated from linear regression on time as equal to 0·3 mm/hr

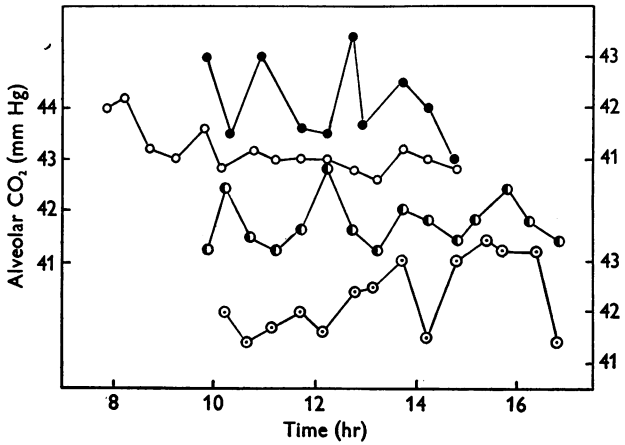

Fig. 3. Alveolar CO_2 tensions during days spent fasting at complete rest. Subject *M*. All analyses by passing end-tidal samples continuously through infra-red analyser. For clarity, the top and bottom curves have been respectively raised and lowered 2 mm Hg, as indicated in scales on right.

from 09.00 to 17.00 hr. The usual absence of any steady trend over a period when the renal excretion of most electrolytes is steadily falling strengthens the argument of Longson & Mills (1953) that these spontaneous variations in renal behaviour cannot be ascribed to changes in blood CO_2 tension.

In three experiments starting early in the morning, eight alveolar air analyses were performed between 06.45 and 09.00 hr, and the mean tension found, 44·7 mm, exceeded the mean of twenty-seven samples collected on the same days between 09.00 and 17.00 hr, 42·9 mm. The difference was, however, only just significant, $0{\cdot}05 > P > 0{\cdot}02$.

It would appear that when sleep, activity and meals do not interfere, the alveolar CO_2 tension often rises spontaneously by a few mm Hg at some period of the late evening, night or early morning, but that throughout the day it maintains a steady level.

Changes during sleep

Observations during sleep were confined to subject *M*, who with the longest experience of respiratory experimentation was least likely to have his sleep disturbed by the procedures or their anticipation, and most likely to respond correctly immediately on waking, when that was required.

Upon seven nights he slept at home with the mouth-piece of a Haldane-Priestley tube close to his mouth and an alarm clock wound so that it would only ring for 15 sec. Immediately on being awakened he delivered a Haldane-Priestley sample; this had always been collected in the gas sampling tube

TABLE 1. Alveolar CO_2 tensions, mm Hg, in Haldane-Priestley samples collected either immediately on being awakened ('asleep') or after subject had lain awake at least 20 min

Night	Time (hr)	Awake or asleep	CO_2 tension
1	23.33	Awake	48·9
	01.27	Asleep	53·9
	03.08	Asleep	46·5
	07.41	Asleep*	49·5
2	23.56	Awake	48·9
	01.35	Asleep	47·8
	03.35	Asleep	53·7
	05.28	Asleep	44·5
	07.25	Awake	37·9
3	03.00	Asleep	53·2
	03.20	Awake	44·7
4	02.05	Asleep	48·3
	02.25	Awake	47·9
5	04.05	Asleep	45·0
	04.25	Awake	48·4
6	21.50	Asleep	49·6
	22.10	Awake	49·4
	06.15	Asleep	48·4
	06.35	Awake	45·2
7	02.05	Asleep	47·5
	02.25	Awake	47·6

* On waking spontaneously.

before the alarm stopped ringing. Twelve such samples were collected, including one on spontaneous waking; for comparison he delivered nine waking samples, usually by remaining awake for 20 min after giving a 'sleeping' sample. The results are shown in Table 1. It will be seen that three of the sleeping samples had very high tensions, 53–54 mm Hg, but that out of eleven samples with tensions between 47½ and 50 mm six were waking and only five sleeping. There is some evidence here that the tension rises during the night, whether the subject is awake or asleep, and that the tension is still higher in the sleeping subject.

In an endeavour to obtain more information about the nocturnal course of the alveolar CO_2 tension, two nights were spent sleeping in the laboratory with

the subject connected to the mouth-piece of the end-tidal sampler. Contrary to Magnussen's (1944) experience, it was found that a carefully adjusted nose-clip did not impede sleep, and that the mouth-piece was often well retained during deep sleep; but it was never retained indefinitely, and the subject never slept continuously for much beyond 1 hr. The mouth-piece was sometimes strapped on, but this added to the difficulties of sleep.

One of these nights, represented in Fig. 2, curve C, formed the second 24 hr of a continuous 48 hr period of recumbency with minimal alimentation; during the first night (Fig. 2, curve B) the subject remained awake, so during the second night sleep was very sound. Comparison of the two 24 hr periods shows, however, a very similar range of variation of alveolar CO_2 tensions in both, though in the first the high values were found between 18.00 and 02.00 hr, when the subject had the greatest difficulty in keeping awake, and in the second they occurred during the actual period of sleep, between midnight and 09.00 hr. It will also be seen that the first waking sample had as high a tension as most of the sleeping ones.

In the other experiment, the top curve of Fig. 4, alveolar air was sampled during wakeful intervals as well as during sleep, and it will be seen that although the CO_2 tension was high between 02.00 and 04.00 hr this rise bore no relation to sleep; samples collected when the subject was awake had tensions as high as had sleep samples at the same time of night.

The end-tidal technique would be invalid if the tidal volume diminished too much during sleep; this was measured and was actually slightly higher during than just before sleep.

It was owing to uncertainty over the validity of end-tidal sampling at low tidal volume that the suction sampler was devised. This had the disadvantage that it almost always woke the subject, so that frequent sampling was impracticable. Tensions obtained on two nights are shown in the middle and bottom curves of Fig. 4. To ensure sound sleep on the second of these (bottom curve), the subject slept for only $1\frac{1}{2}$ hr on the previous night, and spent the previous day in fairly continuous open-air exercise. This had the desired effect: he sometimes even slept through the operation of the sampler, was described by the observer as being more nearly comatose than sleeping and was completely disorientated upon being awakened; next morning he had very little memory for the events of the night.

During neither of these nights was there much indication of a high CO_2 tension due to sleep. On the first night the highest value was reached immediately before sleep and on the second night the variations were similar to those observed on sleepless nights.

To determine further whether sleep *per se* was accompanied by any change in CO_2 tension, observations were made during a series of short naps during the day. Three such are shown in Fig. 5, all with the end-tidal sampler. The

subject lay down 45 min before the readings started to allow for the initial postural changes. Periods of sleep were associated with no change in alveolar

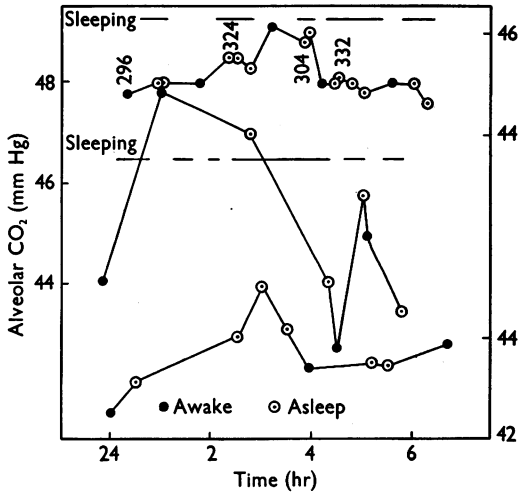

Fig. 4. Alveolar CO_2 tensions of subject *M* during three nights. The periods of sleep are indicated for the top and middle curves by the discontinuous lines; in the bottom curve sleep was almost continuous. Top curve, end-tidal sampler; figures beside this curve are tidal vol. at 37° C saturated. Middle and bottom curves, suction sampler. All analyses by infra-red analyser. For clarity, the top and bottom curves have been raised and lowered, as indicated by the scales on right.

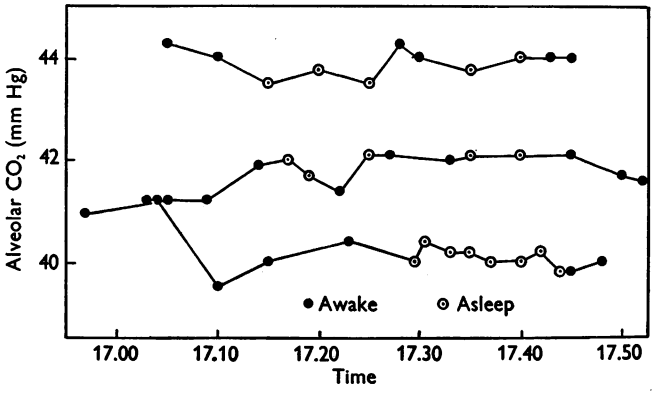

Fig. 5. Alveolar CO_2 tensions of subject *M* during three afternoon naps, aided by hexobarbitone. All analyses by passing end-tidal samples continuously through infra-red analyser.

CO_2 tension. Less complete data from seven other similar naps are in agreement with this conclusion that sleep *per se* causes little if any change in tension. The data of one such are included in Table 4.

DISCUSSION

The existence of a diurnal rhythm in alveolar CO_2 tension does not appear to have been explicitly reported before, despite its obvious presence in the curves of Cohen & Dodds (1924) and a brief mention of Straub (1915) that tension is often high about 21.00–22.00 hr. Its most likely cause is a respiratory depression forming part of the habitual wakefulness and sleepiness rhythm (Kleitman, 1939) of which the subject is so well aware in any experiments in which he is awake for 24 hr. It forms another piece in the somewhat perplexing jig-saw of human 24 hr rhythms, of which account must be taken when trying to explain other components. Since the variations of tension are not large, and may be absent, the argument of Longson & Mills (1953) that the rhythm of urinary electrolyte excretion cannot be due to any such respiratory rhythm appears valid.

It is also of importance in any study of the nature, or the physiological concomitants, of sleep. Most of the claims that alveolar CO_2 tension is high during sleep are based upon nocturnal sleep, and may in fact have been merely studies of the rhythm here reported.

The validity of the different methods of alveolar sampling during sleep needs critical consideration. Rahn (1949) gives evidence that end-tidal sampling gives the closest approximation to 'ideal' alveolar air, with a R.Q. almost identical with that derived from whole expired air, whilst Haldane-Priestley samples give a low R.Q. and a CO_2 tension too high by about 2 mm Hg. Fowler (1949), continuously analysing single breaths with the nitrogen meter, found that a wash-out volume of 325 ml., S.D. 65 ml., was necessary before pure alveolar air was obtained; results as satisfactory as those of Rahn must presumably depend upon a sufficient tidal volume, and it is possible that during sleep this volume may become too small.

Most of those workers who have used end-tidal sampling have found rather small rises of tension. Thus, Bass & Herr (1922), who appear to be the first to have used the method, found a rise of up to 2 mm Hg at the onset of sleep, and thereafter the tension followed a course that could be paralleled by sleepless nights. This method has the great advantage that numerous readings can be taken without waking the subject; but it is sometimes hard to secure an air-tight fit at mouth or nose with occlusion of the other passage; moreover the method may at any time be vitiated by a decrease in tidal air sufficient for the dead-space to be no longer washed out. Thus the finding by Rabinowitsch (1929) of tensions as low as 21–24 mm Hg in subjects in chloral hydrate narcosis was presumably due, as Magnussen (1944) suggests, either to shallow breathing or to leakage. These difficulties are largely obviated by Regelsberger's (1934) technique of aspirating air from the pharynx through a nasal tube. Here the difficulty is to ensure that samples are aspirated only during the terminal part of each expiration.

Magnussen (1944) has published the largest series of results by the end-tidal method, and claims a mean increase of tension of a little over 2 mm Hg during sleep. Only one experiment is recorded fully, and for the others it is not even indicated whether sleep was continued throughout the night. However, every precaution appears to have been taken to secure an air-tight fit of the mouthpiece, and the tidal air was always at least 2½ times the dead space. When the same technique was used in the present investigation there was no difference between sleeping and waking samples, either in afternoon (Fig. 5) or nocturnal sleep. The tidal air in the night experiment was somewhat greater when the subject was asleep than awake, so the failure to find any rise in alveolar CO_2 tension cannot be ascribed to imperfect washing out of the dead space. In the afternoon experiments the tidal air was not measured; but the tensions were so steady that it is hard to believe that an increase of CO_2 tension was exactly balanced by a diminished tidal air and consequent imperfect washing out of dead space.

Of those who have used the Haldane-Priestley method on waking or being awakened, Douglas (1914, p. 356) found a tension raised by 2–2½ mm Hg, but this was apparently on waking in the morning. Straub (1915) never found the tension higher than 43·4 mm Hg, but this was probably not during deep sleep. Leathes (1919) compared sleep values with ones with the subject awake and standing, so the differences he observed may merely have been due to posture. Endres (1922, 1923) found increases of as much as 10 mm Hg during sleep, which are as big as any reported.

This technique of collection of Haldane-Priestley samples immediately on waking seems to have fallen into disfavour, although it has the great advantage that sleep is quite unencumbered and so is much more likely to be natural and deep. Magnussen (1944), discussing the technique, wrote: 'Awakening is presumably associated with a considerable output of carbon dioxide. This may reasonably be assumed to contribute considerably to the increased alveolar carbon dioxide tension "during sleep" in these experiments. So the "sleep" values recorded may safely be assumed to have been artificially increased.' There appears here to be a confusion between high tissue production of CO_2 and a high rate of liberation of the gas in the lungs; the latter is probable, the former improbable and never demonstrated on waking. A high lung evolution of CO_2 would result from a low alveolar tension and not, as Magnussen apparently supposes, cause a high alveolar tension.

There are many reasons why the 'sleep' samples, collected from a somewhat confused subject, may have been lowered artificially; but they could hardly have been artificially increased unless the subject held his breath. To discover an outside limit for any such spurious rise, subject *M* gave a series of Haldane-Priestley samples after breath-holding for 15 sec, preceded by a few minutes of continuous end-tidal analysis. The results, shown in Table 2, show that a rise

of about 4 mm Hg may thus be produced. This figure is somewhat lower than the increase of 4·9–7·7 mm Hg found in 15 sec breath-holding by DuBois, Britt & Fenn (1952). There is, however, no reason to suppose that during the period of up to 15 sec between the start of the alarm and the completion of Haldane-Priestley sampling the subject did not breathe. Upon seven occasions stethograph tracings were obtained while the subject was awakened from barbiturate sleep by an alarm bell. His respiration maintained its previous rhythm until the large artifact occurred as he put his mouth to the sampling tube.

TABLE 2. Alveolar CO_2 tensions in mm Hg before and after breath-holding for 15 sec in the recumbent posture

Before	After
45·1	49·4
45·0	48·0
44·3	48·4
43·2	48·0

It is unlikely, then, that the high tensions sometimes found in Haldane-Priestley samples by Endres and in the present paper were due to apnoea just before sampling; but the rather high tensions, of 47–50 mm Hg, sometimes found by night with the subject awake and even before sleep, suggest that the rise is partly due to a habitual rhythm.

A disadvantage of the Haldane-Priestley technique is that the subject is thoroughly awakened, so that it is impossible to obtain information about a normal night's sleep if more than one or two samples are collected.

The suction sampler avoids the difficulties of both other methods in that no co-operation is needed from the subject, and a diminished tidal volume does not invalidate the results. It does, however, necessitate sleeping with a mouth-piece, and this was never achieved throughout the night. On the night when sleep was soundest, that represented in the bottom curve of Fig. 4, there were two periods of an hour each when no samples could be collected as the subject failed to retain the mouth-piece when asleep. There is no doubt that when the samples were collected he was very soundly asleep, especially as he was not always awakened by the procedure, and even so the highest tension was only some 2 mm above the waking value at 03.55 hr. Deep sleep can thus occur, in conformity with the findings of other workers with end-tidal sampling, with at most a very small elevation of alveolar CO_2 tension.

Empirical validation of the techniques was attempted by performing all three in quick succession in a series of collections by day on the recumbent subject (Table 3), and during an afternoon and a night's sleep (Table 4). The end-tidal samples gave the lowest tension in both, in agreement with Rahn (1949), but the mean differences from tensions found in suction samples were small, 0·7 and 1·7 mm Hg in the two series. There was no consistent difference between suction and Haldane-Priestley samples.

In a further series of fifteen paired comparisons between suction samples and Haldane-Priestley samples collected 1–2 min later, the Haldane-Priestley samples were lower by a mean value of 0·5 mm Hg. A very similar mean drop, 0·8 mm Hg, was observed in six similar paired collections in which the suction

TABLE 3. Consecutive series of alveolar CO_2 collections by end-tidal and suction samplers and Haldane-Priestley technique; all determinations by infra-red analyser. The first five determinations were over the space of 1 hr, the second five over another hour with an interval of 2 hr. Subject awake

	Alveolar CO_2 tensions (mm Hg)		
	End-tidal	Suction	Haldane-Priestley
	41·5–42·5	42·1	43·1
	41·5–42·5	43·0	44·1
	42·0–42·2	42·2	—
	41·0–41·5	41·4	39·5
	41·5–42·0	42·3	42·5
	44·1–43·8	44·1	44·9
	42·5	43·8	41·9
	42·6	44·3	44·8
	42·0	43·4	43·0
	42·6	43·5	42·7
Mean	42·28	43·01	42·94

The mean difference between suction and end-tidal samples, though small, is highly significant, $P < 0{\cdot}01$.

TABLE 4. Alveolar CO_2 tensions during sleep, by end-tidal and suction sample and Haldane-Priestley technique; all determinations by infra-red analyser. Haldane-Priestley samples collected 1–2 min after suction samples, whose collection always woke the subject. One afternoon and one night sleep

	Alveolar CO_2 tension (mm Hg)			
Time (hr)	End-tidal	Suction	Haldane-Priestley	State
17.05	43·7	47·2	47·0	Dozing
17.20	43·7	44·8	46·9	Asleep
17.35	44·0	44·4	—	Asleep
23.50	43·1	44·1	44·9	Awake
01.00	45·3	47·8	46·2	Awake
02.45	45·2	47·0	—	Asleep
03.30	47·2	—	46·2	Asleep
04.20	—	44·1	44·9	Asleep
04.30	—	42·8	43·8	Awake
05.00	—	45·8	45·1	Asleep
05.05	—	45·0	43·6	Awake
05.45	—	43·5	42·5	Lightly asleep

Mean difference, suction – end-tidal = 1·7 mm; $0{\cdot}02 > P > 0{\cdot}01$.

sample was collected from the sleeping subject, who was awakened by the procedure. When a suction sampling from the sleeping subject was followed in 1–2 min by another suction sampling, a drop in tension of 0–0·5 mm Hg was found in five experiments. When the subject was awakened by an alarm and gave a Haldane-Priestley sample, and 1–2 min later gave another, a non-significant mean fall of tension of 0·5 mm Hg was found in fourteen experiments. It thus appears not only that these two techniques give virtually

identical results, but also that the alveolar CO_2 tension does not change considerably within a minute or two of waking.

It is possible that there occur during the night periods of exceptionally deep sleep when the tension rises, in the subject here investigated, to around 54 mm Hg, but that sleep is then so deep that a mouth-piece cannot be retained. In this way can best be explained the very high tensions found somewhat erratically by the Haldane-Priestley technique by the present author, as well as by earlier workers such as Endres (1922, 1923).

Since respiratory depression will both lower alveolar oxygen and elevate alveolar CO_2 tension, measured changes in either can give an approximate indication of changes in the other. Doust & Schneider (1952) report figures for arterial oxygen saturation during sleep which suggest a profound respiratory depression. For the precise calculation of alveolar CO_2 tension from their data it would be necessary to know the barometric pressure, respiratory quotient, and oxygen dissociation curves at a variety of CO_2 tensions of the individual subjects. An approximate calculation may be made, however, assuming barometric pressure = 760 mm Hg, using the dissociation curves for his own blood published by Barcroft (1914), and assuming a R.Q. of 0·7, since any higher quotient would give a higher value for alveolar CO_2 tension. Only a rough approximation is possible, since Barcroft published no O_2 dissociation curves between 40 and 90 mm CO_2 and none appears to have been published since; wide interpolation is therefore necessary. In order to attain the 86% O_2 saturation recorded in deep sleep the alveolar CO_2 tension would have to be at least 60–70 mm Hg, and even to attain 90% saturation, the alveolar CO_2 tension would have to rise to 55 or 60 mm Hg. Since oxygen saturations of below 90% were claimed by these authors for considerable fractions of a night's sleep, the validity of the oximetric determinations must be viewed with caution, particularly as the waking saturation of 96% is considerably below the figure of 98–99% found by Drabkin & Schmidt (1945). The general pattern of change is, however, probably a qualitative representation of the extent of respiratory depression and hence the elevation of alveolar CO_2, and to that extent supports the conclusion of the present paper, that periods of exceptionally deep sleep occur with respiratory depression greater than any found during the greater part of a night's sleep. The considerable respiratory depression claimed by Doust & Schneider during even the lightest sleep—'pre-sleep' of these authors —is at variance with any results here recorded.

SUMMARY

1. Alveolar carbon dioxide tension sometimes shows a diurnal rhythm, with high values during the night even in subjects who remain awake fasting in constant conditions of rest or light activity.

2. Alveolar samples collected by suction or by an end-tidal sampler during nocturnal sleep show a rise of tension no greater than that shown during sleepless nights.

3. During afternoon sleep, assisted by hexobarbitone, the tension does not rise.

4. Some of the Haldane-Priestley samples collected from a subject awakened by an alarm clock had tensions as high as 53–54 mm Hg.

5. It is concluded that sleep *per se*, even deep sleep, may cause at most a trifling change in alveolar carbon dioxide tension, but that periods of very deep natural sleep occur when a mouth-piece is not retained and the tension rises considerably.

I wish to thank the subjects for their fortitude, Dr D. Longson and Mr P. J. Conlon for watching while I slept, the Medical Research Council for an Apparatus Grant, and Mr A. M. Walker, of the Department of Mathematics, for drawing my attention to the mean square successive difference ratio test.

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