Respiration Physiology (1982) **50**, 177–185
Elsevier Biomedical Press

THE CONTRIBUTION OF HEART BEAT TO GAS MIXING IN THE LUNGS OF DOGS

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Abstract. The mixing efficiency for two gases of different gaseous diffusivity, helium (He) and sulphur hexafluoride (SF_6) have been studied in anaesthetised dogs, closed and open chested, with and without the heart beating. Equilibration of He and SF_6 was studied during rebreathing at a frequency of 0.5 Hz and a tidal volume of either 0.3 or 0.5 L. Circulation and gas exchange were taken over by a complete heart and lung bypass circuit during the periods when the heart was stopped. The number of breaths required to reach 99% equilibration (n99) ranged from 4 to 14 for He and from 6 to 17 for SF_6.

There was no significant change in mixing efficiency in any situation. Stopping the heart increased the n99 for He by only 0.4 ± 11% (1 SD) (n = 21). Opening the chest increased n99 by 1.4 ± 13% with the heart beating and 2.5 ± 19% with the heart stopped. The n99 for SF_6 was 30 ± 22% higher than that for He with the chest closed with or without the heart beating. This increased to 37% with the chest opened but was not altered by stopping the heart. The findings for the final phase equilibration rate constant were similar. We conclude that the beating action of the heart does not affect gas mixing in the lungs in the tidal breathing range.

Cardiopulmonary bypass
Gas diffusion
Helium
Inert gas equilibration
Respiratory mass spectrometry
Sulphur hexafluoride

Oscillations in concentrations of injected argon were demonstrated in 1959 and 1961 by West and Hugh-Jones in the lobar and segmental bronchi of both dog and human lungs. These oscillations were in phase with the heart beat. More recently oscillations in nitrogen concentration have been demonstrated in airways during a single inspiration of pure oxygen, and mixing in the airways has been studied with and without the heart beating (Engel *et al.*, 1973a,b). Fukuchi *et al.* (1977) have shown in the living animal that an injection of saline into the pericardial sac diminishes these oscillations in nitrogen concentration measured in 5 mm airways

Accepted for publication 19 July 1982

and also that the concentration of nitrogen in these airways during inspiration of pure oxygen falls to zero in the absence of oscillations and only to 10% when the heart is more effectively in contact with the lungs, implying an enhanced mixing of gas in the anatomical deadspace. Some predictions from a theoretical model set up by Slutsky (1981) are that the heart should enhance mixing in the lungs by about ten-fold and that SF_6 will be affected to a greater extent than He.

We have carried out a study to see whether the action of the heart aids mixing of gases in the lungs as a whole or whether the effect is restricted to the airways.

Methods

Four dogs (mean weight 23 kg) were anaesthetised with thiopentone sodium (5 mg/kg) and pentobarbitone sodium (3–6 mg/kg/h). The surgical preparation is shown in fig. 1. The tidal volume and frequency of the ventilator were set at 20 ml/kg and 15 breaths/min. Systemic arterial and right ventricular pressures were recorded from catheters introduced into the carotid artery and right ventricle. For

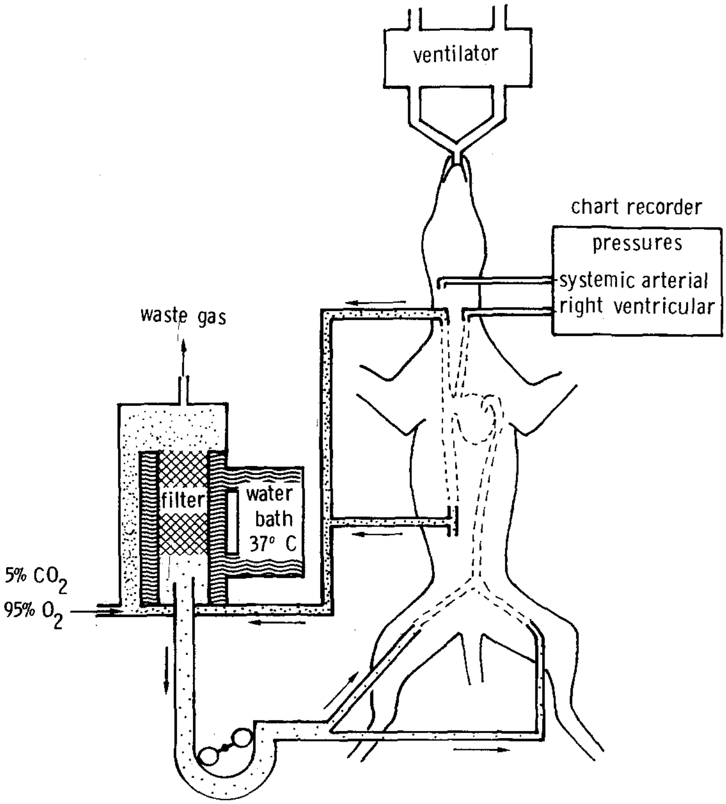

Fig. 1. Diagram of heart and lung bypass preparation in anaesthetised dog.

cardiopulmonary bypass, blood was withdrawn through wide-bore catheters in the superior and inferior vena cavae, pumped through an oxygenator and heat exchanger and returned through both femoral arteries. The bypass circuit was used whenever the animal's heart was stopped. The heart was stopped by passing an electrical current between metal plates on either side of the chest, and the voltage was increased until the right ventricular pressure pulsations ceased. The heart was restarted with a defibrillator, and the bypass circuit was turned off. An initial measurement of gas mixing efficiency was made with the heart beating and subsequent measurements made with the heart stopped and restarted repeatedly. Following this, the chest was opened and the chest wall retracted. Positive end-expiratory pressure was instituted and adjusted to give the same functional residual capacity as with the chest closed. Further measurements of gas mixing efficiency were made with and without the heart beating. In one dog a final measurement was made 20 min after death with the heart still.

The measurements of gas mixing efficiency were made using a rebreathing technique shown diagrammatically in fig. 2. A syringe which contained a gas mixture made up of 10% each of He and SF_6 with 30% oxygen (balance argon) was connected to the endotracheal tube in place of the ventilator. The syringe volume was 0.5 L in the first dog and 0.3 L for the other three. The lungs were rebreathed for 20 breaths with the test mixture, emptying and filling the syringe at a rate of

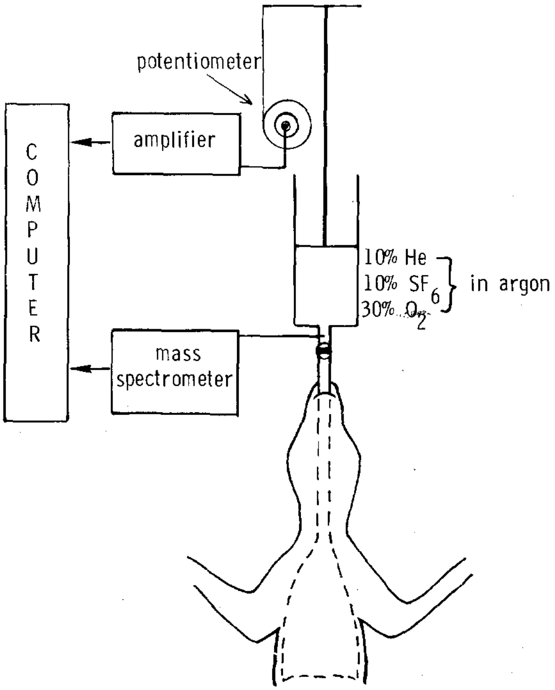

Fig. 2. Diagram of apparatus used for rebreathing measurements.

30/min. At the end of the rebreathing manoeuvre the animal was reconnected to the ventilator. During rebreathing the concentrations of all gases present in the syringe–lung system were measured continuously by a mass spectrometer (Centronic MGA 200) which sampled 40 ml/min of gas. This mass spectrometer was linked via an analogue to digital converter to a digital computer (Digico μ16). The gas concentrations were volume weighted over every 20 msec from the signals from a potentiometer connected to the syringe which were delayed to match the measured delay time of the mass spectrometer from sample line tip to detector. This delay was the same for He and SF_6. The computer then printed out the time and volume of each breath and then the volume-weighted mean inspired concentration of all gases. The concentrations of the insoluble gases were corrected for any net loss in volume of the syringe–lung system to give the concentration that would have been present in the absence of soluble gas uptake. For each breath we plotted the difference between the corrected mean inspired (*i.e.*, bag) concentration and the final equilibrium level normalised to the difference on the first breath in (100%).

The number of breaths required to reach 99% equilibration was calculated for He and SF_6 together with the individual rate constants for the final approach to the equilibrium value. A straight line was drawn by eye through the data points for breaths 7–15 on the semi-logarithmic plot constructed as in fig. 3, from which the slope (λ) was calculated. For each rebreathing manoeuvre the functional residual capacity (FRC) was calculated from the insoluble gas dilution using the corrected values.

Results

An example of the He and SF_6 mixing is shown in fig. 3 with and without the heart beating. The difference between mixing for the He and the SF_6 is unaffected by whether the heart is beating or not. The number of breaths required to reach 99% equilibration (n99) is 7 for He and 9.5 for SF_6. Table 1 shows the mean values for FRC and n99s in each of the dogs. Figure 4 shows all the data points for all of the dogs. Each point represents the n99 related to the mean n99 for He for each dog with the chest closed and the heart beating. Thus the scatter around 1.0 shows the repeatability of the measurements. Neither the mean values indicated by horizontal bars in fig. 4 nor the means in table 1 deviate significantly from 1.0 for He with the heart stopped in either the closed or open chest situation. The mean values for SF_6 are always about 30% higher than those for He and this difference is unaffected by opening the chest or stopping the heart.

The rate constants (λ) for the approach to equilibrium for He and SF_6 are plotted in fig. 5 with each λ being related to the mean baseline λ for He for each dog (chest closed and heart beating) as for n99. In this case the mean λ is slower for SF_6 than for He by approximately 30% and again there is no significant difference in the values obtained with the heart beating or stopped, in the open or closed chested preparation.

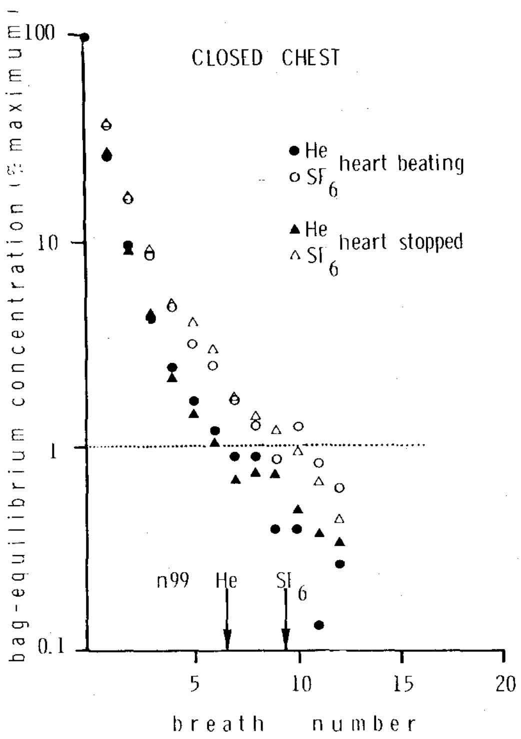

Fig. 3. Comparison of He (closed symbols) and SF$_6$ (open symbols) washins, as a concentration difference (bag minus final equilibrium level normalised to the first inspiration; 100%) against breath number, with the heart beating (circles) and with the heart stopped (triangles) with the chest closed.

TABLE 1

Closed circuit He and SF$_6$ equilibration with mean number of breaths (n99) required for 99% equilibration. FRC (end-expiratory volume, in litres) measured from He dilution; n = number of measurements. Also shown is the mean for all measurements of n99 normalised to the n99 for He with the heart beating and chest closed in each dog with 1 SD.

Dog No.		Closed chest					Open chest				
		FRC (L)	Heart beating		Heart stopped		FRC (L)	Heart beating		Heart stopped	
			He n99	SF$_6$ n99	He n99	SF$_6$ n99		He n99	SF$_6$ n99	He n99	SF$_6$ n99
1		1.61	6.75	8.25	6.63	8.00	1.60	7.00	8.75	10.00	12.50
	n	8	4	4	4	4	3	2	2	1	1
2		1.93	11.20	13.33	12.33	15.00	2.10	12.70	15.53	13.10	15.25
	n	7	3	3	4	4	5	3	3	2	2
3		1.14	5.13	7.31	5.19	7.67	1.07	4.50	7.90	4.56	7.16
	n	15	8	8	7	7	8	3	3	5	5
4		1.49	6.67	8.23	6.30	7.65	1.73	6.85	7.65	6.60	6.85
	n	12	6	6	6	6	4	2	2	2	2
Total n			21	21	21	21		10	10	10	10
Mean n99/n99He			1.00	1.30	1.00	1.31		1.01	1.37	1.03	1.36
SD			0.14	0.22	0.11	0.24		0.13	0.18	0.19	0.28

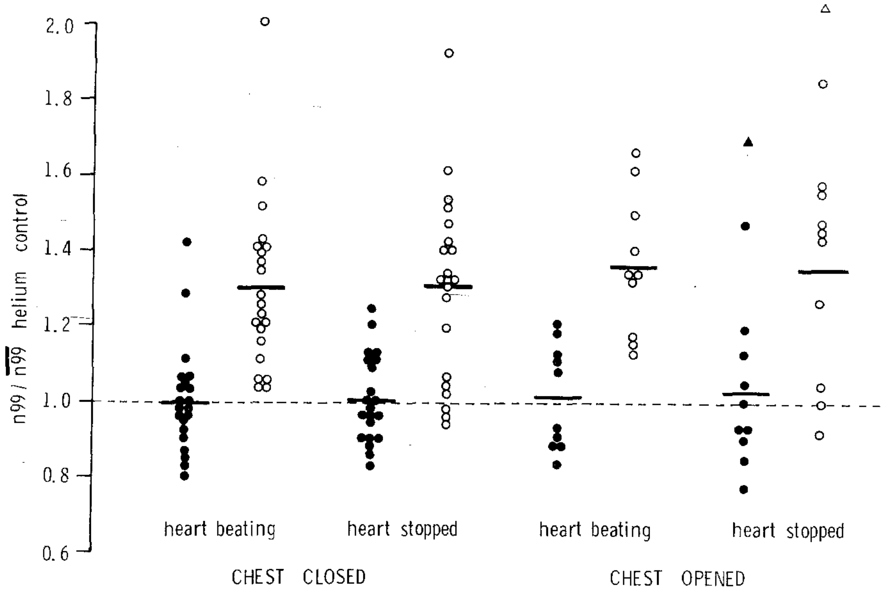

Fig. 4. n99 values for He (●) and SF_6 (○) normalised to the mean n99 for He with the chest closed and the heart beating for all measurements. ▲△ represent measurements after death. Horizontal bars represent the mean value for each group.

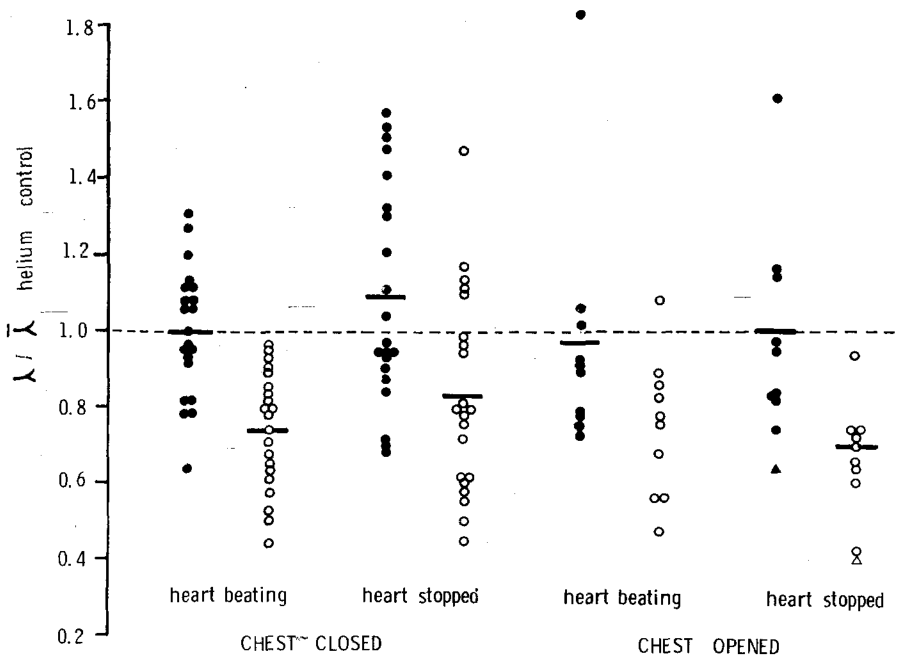

Fig. 5. Rate constant (λ) for the final phase of mixing for He and SF_6 normalised to the mean λ for He with the chest closed and the heart beating for all measurements (symbols as in fig. 4).

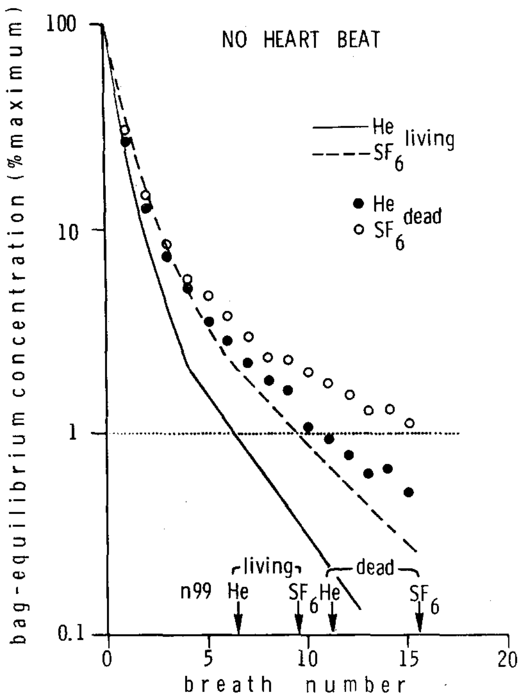

Fig. 6. Comparison of He and SF_6 washins (as in fig. 3) before and after death in the absence of heart beat.

A measurement made 20 min after death in one animal with open chest, gave n99 values for He and SF_6 greater than in any other situation, the n99 for He being delayed by 5 breaths and for SF_6 by 7 breaths (fig. 6). Similarly, the rate constants for both gases were the lowest obtained. In this case the FRC was 1.5 L living and 1.48 L after death.

Discussion

The theory of the kinetics of gaseous equilibrium between a bag (or spirometer) in closed circuit with a multicompartment lung has been explored by Visser (1957) and Nye (1961a,b). In outline, equilibration consists of two distinct phases; the initial phase leads rapidly to a final phase representing a dynamic balance of gas mixing between all compartments, a situation in which all units of the lung (fast and slow) are approaching equilibrium with the same rate constant. This situation occurs because in closed-circuit no unit can reach equilibrium before the slowest unit.

In most cases the initial phase can be represented by a single exponential superimposed on the final phase. This first rapid phase of mixing is determined by units with a very high ventilation per unit lung volume ($\dot{V}/V_A$), which in normal lungs is predominantly the anatomical and instrumental deadspace. However, when the dispersion of $\dot{V}/V_A$ is gross it may be multiexponential (Nye, 1961a). Nevertheless, the final phase is always effectively monoexponential, both in normal and abnormal human lungs and mathematical models with up to five compartments with differing $\dot{V}/V_A$ (Jones *et al.*, 1982; Hughes *et al.*, 1982).

The model simulations have shown that the rate constant of the final phase is determined by the dispersion of $\dot{V}/V_A$ among all the lung units, whereas the intercept is dependent on the relative volumes of these different $\dot{V}/V_A$ units (Davies *et al.*, 1979).

In these closed-circuit experiments we have analysed the rate constant (λ) of the final phase in terms of a single exponential. In addition, we have calculated a parameter, n99, the time for 99% equilibration of the whole system. While λ would be changed by the appearance of a relatively small number of units with a very low $\dot{V}/V_A$, n99 would be affected less since it is weighted by the intercept (volume dispersion) as well as λ (ventilation dispersion). Thus n99 is arguably the fairer estimate of overall mixing efficiency. Taken together, n99 and λ provide a reasonably comprehensive description of the overall kinetics of bag–lung equilibration.

Table 1 and figs. 4 and 5 show no difference for either helium or SF_6 mixing efficiency with the heart beating or stopped. These results do not exclude the possibility that the heart may assist gas mixing at lower frequencies or during apnoea. Although rebreathing was carried out at a frequency (0.5 Hz) and tidal volume (0.3 or 0.5 L) well within the normal range for resting spontaneously breathing (masked) greyhound dogs (Amis, 1979), further studies using different breathing patterns would be helpful. Nevertheless, large changes in respiratory frequency (0.33–1.66 Hz) and inspiratory flow pattern have relatively little effect on the n99 for helium in normal man (Jones *et al.*, 1982).

The studies of Fukuchi *et al.* (1977) in dogs, using retrograde catheters, demonstrated that gas mixing in small airways was less effective after the introduction of fluid into the pericardial sac, but that elimination of nitrogen by open-circuit washout was unaffected. It is possible, as these authors suggest, that multibreath N_2 washout is not a sufficiently sensitive measure of gas mixing under these circumstances. If the enhancement of gas mixing by the heartbeat is confined to the anatomic deadspace, that is a reasonable explanation. Our closed-circuit He–SF_6 studies confirm the open-circuit results of Fukuchi *et al.* (1977) assuming that a pericardial effusion acts in a similar manner on gas mixing as stopping the heart beating. Both multibreath techniques (open- and closed-circuit) should be sensitive enough to detect important changes in mixing efficiency in the alveolar compartment of the lung. Indeed, the rebreathing technique we have used can detect a 30% change in mixing efficiency in normal human (Jones *et al.*, 1982) and dog lungs for gases with a six-fold difference in gaseous diffusivity.

There is a definite change in mixing efficiency immediately after death in retrograde catheter (Engel *et al.*, 1973a,b) multibreath washout (Ronchetti *et al.*, 1980) and multibreath washin studies (fig. 6). It is unlikely that these changes can be attributed solely to stopping the heart but must be due to other factors, such as an increase in anatomic deadspace or to the formation of fluid menisci in small airways. *In vivo*, the heart beat plays a limited role in assisting gas mixing in the tidal breathing range.

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