Cardiogenic oscillations of nitrogen and argon concentration in expired gas in man

G. W. BRADLEY, A. K. HENDERSON AND R. J. MILLS
Centre for Respiratory Investigation, Glasgow Royal Infirmary

(Received 28 May 1974)

Summary

1. The cardiogenic oscillations in the concentration of nitrogen and argon in expired gas, which are seen after the inspiration from residual volume of pure oxygen or a bolus of argon, have been studied in normal subjects and in patients with atrial fibrillation.

2. In the upright position of the subject, the peaks of nitrogen and argon concentration coincide with ventricular systole, although there is a transit delay along the tracheobronchial tree before any change of concentration occurs at the mouth.

3. Studies in different postures demonstrated that the effect of the heart is predominantly due to a reduction in cardiac volume during systole with a decrease in airflow from regions adjacent to the heart. These areas contain a different concentration of nitrogen and argon in the alveolar air from the more apical regions.

4. It has been shown that the results are consistent with the present concepts of the influence of gravity on the distribution of inspired air.

Key words: cardiogenic oscillations, nitrogen, argon, respiratory air flow.

Introduction

Cardiogenic oscillations in the concentration of nitrogen were noted by Fowler (1951) in gas sampled from lung lobes in dogs and more recently by Engel, Menkes, Wood, Utz, Joubert & Macklem (1973) in gas sampled from small airways. Similar oscillations have been described in a number of gases sampled at the mouth during expiration, particularly during closing volume manoeuvres (Collins, 1973). Changes in pulmonary vascular volume resulting from the pulsatile action of the heart have been suggested as a cause of the oscillations detected at the mouth (Dahlstrom, Murphy & Roos, 1954; Langer, Bornstein & Fishman, 1960). On the other hand, Fowler & Read (1961) attributed these oscillations to the rapid fall in ventricular volume during systole with consequent reduction in gas flow from adjacent lung regions.

Recent work on regional lung volumes (Kaneko, Milic-Emili, Dolovich, Dawson & Bates, 1966; Milic-Emili, Henderson, Dolovich, Trop & Kaneko, 1966) has clarified the mechanism by which gravity-dependent regional differences in gas concentration are formed throughout the lungs. The present work was undertaken to re-examine the cause of cardiogenic oscillations of expired gases in the light of this information.

Methods

The apparatus shown in Fig. 1 was used in most experiments. The seated subject initially breathed room air through a mouthpiece and valve box system. After a few normal breaths the subject expired to residual volume and the tap was then turned into the position shown in Fig. 1. 100% oxygen was then slowly inspired until total lung capacity was reached. A 100 ml bolus of argon could be injected into the inspired gas at any time during the inspiration. In the present work the argon bolus was given either at residual volume (early argon bolus) or to-
G. W. Bradley, A. K. Henderson and R. J. Mills

FIG. 1. Apparatus used for obtaining and measuring nitrogen and argon oscillations.

Towards the very end of inspiration (late argon bolus) when the subject signalled that his lungs were nearly fully expanded. The flow rate was monitored from the pneumotachograph by the box–bag system and maintained below 30 l/min during inspiration of the oxygen.

On reaching total lung capacity the subject then breathed out to residual volume, the flow rate being kept constant, usually at 20 l/min. Expired air was sampled at the mouthpiece and nitrogen and argon concentrations were measured by a respiratory mass spectrometer (20th Century Electronics) with a transit time of 100 ms. The flow rate, electrocardiograph (ECG), nitrogen and argon concentrations were recorded on a Devices M4 recorder.

A simpler system had to be used when the subject changed posture from the erect position. The subject breathed air through a large three-way tap, which could be turned at residual volume to allow inspiration from a previously closed loop containing 150 ml of argon, which was followed by atmospheric air. Air flow rate was measured by a pneumotachograph attached to this loop, and argon concentration was measured from air sampled at the mouthpiece. The tap, loop and pneumotachograph were fixed to a board which could easily be held by the subject. Nitrogen oscillation could not be studied by this technique.

None of the seven subjects had a history of pulmonary disease, but two subjects were in atrial fibrillation due to rheumatic heart disease. All subjects readily consented to the procedures.

The oscillations in expired gas concentration were studied in the following circumstances: (1) with different expiratory flow rates; (2) with the argon bolus given at the beginning and near the end of inspiration; (3) in the erect position and with the thorax inverted by hanging over the end of a high couch (the legs being firmly held to the couch by an assistant and the head supported by a pillow on the floor); (4) on inspiration of the argon bolus in the erect position but with expiration in the supine position.

Results

Time relationship between the ECG and oscillations

Fig. 2 shows the effect of different expiratory flow rates on the time relationship between the nitrogen oscillations and the ECG. It can be seen that the QRS complexes are related to different phases of the cardiogenic oscillations depending on the expiratory flow rate. Assuming that at the higher flow rate of 40 l/min a QRS complex is related to the next up-going phase of the nitrogen concentration, it is possible to relate the QRS complex to the oscillations at the lower flow rates (when the delay may be more than one cardiac cycle) by following the gradual
lengthening of this interval as the flow rate is reduced. A plot of this interval against the reciprocal of flow rate (Fig. 3) can be extrapolated to infinite flow, and

![Graph](image)

**Fig. 3.** A graph of the reciprocal of expired flow (1/\(\nu_E\)) against the interval between the Q wave of the ECG and the start of the resulting increase in nitrogen concentration (delay), corrected for the transit delay of the mass spectrometer. At infinite flow (1/\(\nu_E = 0\)) the remaining delay is 150 ms.

... the remaining interval gives a measure of the delay between the electrical change in the heart and the consequent change in gas concentration within the thorax. This calculation was performed on five normal subjects, and, when sampling delay due to the mass spectrometer line was subtracted, the values obtained were 200, 180, 200, 240 and 150 ms (mean = 190). The correlation coefficients were 0.998, 0.994, 0.993, 0.873 and 0.998.

The time relationship between the ECG and the oscillations was further studied in two patients with atrial fibrillation. The irregular heart beat allows a direct correlation between a particular QRS complex and the resulting change in concentration of expired gas. Fig. 4 shows an ECG and a record of argon concentration in a patient with atrial fibrillation. It can be seen that there are two obvious periods of lengthy diastole which can be correlated with two periods of a slowly falling argon concentration. This confirms that ventricular systole must be associated with a rise in concentration. By this means of comparing the ECG with the resulting change in gas concentration it was found in the two patients that the delay between the Q wave and the resulting argon oscillation (with correction due to sampling delay) varied between 400 and 800 ms with an expiratory flow rate of 20 l/min.

**Comparison of nitrogen and argon oscillations**

Fig. 5 shows that, with the subject in the erect position, the nitrogen and argon oscillations are in phase when the argon bolus is given early in the preceding inspiration (bolus first). However, the oscillations are 180° out of phase when the argon bolus is given late (bolus last), suggesting that cardiac systole is now associated with a fall in argon concentration. It can also be seen that the terminal rise in argon concentration which takes place when the argon bolus is given early (bolus first) is converted into a falling concentration when the argon bolus is given late (bolus last). However, the terminal rise in nitrogen concentration is uninfluenced.

**Effect of changes in posture**

The effect of changes in posture was studied in three subjects by means of the simplified apparatus described in the Methods section. The argon bolus was inspired from residual volume in all cases. Fig. 6 shows that, in the erect position of the subject, QRS complexes coincided with peaks of the argon oscillations. However, at the same flow rate of 20 l/min, with a manoeuvre performed in the upside-down position, QRS complexes coincided with troughs in the argon oscillations. This corresponds to a phase shift of 180° between the ECG and oscillations in the two postures.

Inspiration of argon in the erect posture followed by expiration performed in the supine is of interest for reasons described in the Discussion section. With this modification to the manoeuvre the oscillations...
Fig. 5. Two records, each consisting of an ECG, expired nitrogen and argon concentration and expiratory flow rate. The argon bolus was either (a) given early on in the inspiration (bolus first) or (b) towards the very end of inspiration (bolus last). Vertical bars demonstrate equivalent points on the nitrogen and argon records. The flow rate was kept as near to 20 l/min as possible in both cases and the mean values can be seen to be similar in the two cases.

Fig. 6. Two records, each consisting of an ECG, expired argon concentration and expiratory flow rate. (a) Record obtained in the sitting position after inspiration of an early argon bolus. (b) Record obtained in the upside-down position after inspiration of an early bolus.
Oscillations in expired gas concentration

Fig. 7. Records of an ECG, expired argon concentration and expiratory flow rate after inspiration of an early argon bolus in the sitting position with expiration performed in the supine position.

not only persisted but sometimes increased in size (Fig. 7). The phase relationship between the ECG and oscillations remained the same as when the subject stayed in the erect position throughout the procedure.

Discussion

Engel et al. (1973) sampled gas from small airways (2.5–16 mm in diameter) in dogs and detected cardiogenic oscillations in nitrogen concentration. These oscillations were thought to result from longitudinal displacement of the nitrogen gradient between alveolar air and dead space due to flow pulsations. When the dead space has been washed out during expiration they will no longer be obtained, and, as pointed out by Engel et al., they are not to be confused with similar oscillations detected at the mouth. These latter oscillations presumably result from the mixing gas streams coming from areas of the lung containing different concentrations of nitrogen, but there will be a delay before any resulting change in gas concentration is detected at the mouth.

This transit delay obscures the correlation between the activity of the heart and the resulting effect on expired gas concentration. Dahlstrom et al. (1954) overcame this problem by measuring the interval between the Q wave and the resulting increase in nitrogen concentration at different flow rates. By plotting the reciprocal of the flow against this interval, a linear relationship was obtained, which could be extrapolated to infinite flow rate, so abolishing the effect of transit delays. When the instrumental delay was subtracted, they found an interval of 350–380 ms, which presumably is the time-interval between the beginning of ventricular depolarization and the start of the resulting increase in nitrogen concentration. Using the same technique Langer et al. (1960) obtained an interval of 150 ms and, in the present work, a mean interval of 190 ms was obtained. Since there is a delay of about 80 ms between ventricular depolarization and the start of right ventricular ejection (Braunwald, Fishman & Cournand, 1956), it appears that the increase in nitrogen concentration within the thorax correlates well with the maximum phase of ventricular ejection.

However, this method necessitates the choice of equivalent points on the ECG and nitrogen curve and makes a number of assumptions. It is presupposed that the peak in nitrogen concentration results from cardiac systole, and although this would seem a reasonable assumption when the rise in nitrogen concentration takes the form of a definite pulse-like deviation from the base line (Fig. 5), it is less obvious when the oscillation is sinusoidal (Fig. 6). The method also assumes that the delay is no greater than one cardiac cycle at the higher expiratory flow rates and, furthermore, necessitates extrapolation beyond the experimental data. The use of patients with irregular pulses allows a more direct correlation of electrical changes of the heart with the resulting gas changes at the mouth. The present work has shown that, in patients with atrial fibrillation, long periods of diastole are associated with a fall in nitrogen concentration. This confirms the above assumption that the peak in nitrogen concentration coincides with ventricular systole. However, it has also been shown that, with an expiratory flow rate of 20 l/min, the delay between the Q wave and resulting rise in argon concentration varies between 400 and 800 ms, which may mean a delay of more than one cardiac cycle.

Miloc-Emili et al. (1966) demonstrated a lower gas volume in the dependent regions of the lung than in the upper regions at residual volume, and it follows that inspiration of 100% oxygen from residual volume to total lung capacity leads to a greater dilution of the nitrogen in these dependent regions. When total lung capacity is reached, therefore, the nitrogen concentration is greater in the uppermost part of the lung than in the dependent region. A similar non-uniform distribution of inert gas can be produced in the lung by inspiring a bolus of the gas during inspiration from residual volume. Dollfuss et al. (1967)
have shown that the distribution of the gas depends upon the point at which, during inspiration, the bolus is taken in; early inspiration of the gas would distribute the bolus to the uppermost regions of the lung, whereas late inspiration of the gas would distribute it to the dependent regions. Both these phenomena are gravity-dependent.

Cardiogenic oscillations in expired gas concentration can be explained on the basis of the heart beat influencing the relative rates of emptying of these regions containing different concentrations of gases. The present results have shown that, when the argon bolus is inspired early, the nitrogen and argon oscillations are in phase. The peaks of the oscillations result from preferential emptying of regions containing a higher argon and nitrogen concentration. According to the above-named workers this region will be in the uppermost part of the lungs. Conversely, a late bolus of argon is distributed to the dependent regions and this results in the oscillations being 180° out of phase. These findings are consistent with an uneven distribution of nitrogen and argon due to gravity-dependent phenomena. On the other hand, Langer et al. (1960) postulated that the rise in nitrogen concentration resulted from expulsion of air from poorly ventilated peri-hilar regions of the lung, and Dahlstrom et al. (1954) were of the opinion that poorly ventilated peripheral regions were responsible for the peaks in nitrogen concentration.

There are two possible mechanisms that could explain the influence of the heart beat on air flow from different lung regions. Since the pulmonary artery pressure is low the effect of gravitational forces are large and this results in poor perfusion at the lung apices in the erect position (West & Dollery, 1960). Therefore vessels in these regions will be much less distended than vessels in the dependent regions. It is therefore possible that the systolic increase in pulmonary artery pressure produces a greater volume change in non-distended vessels in the uppermost regions of the lungs, with consequent displacement of air and increase in air flow from this region. Alternatively, the sudden reduction in cardiac volume during systole may expand the lung tissue in adjacent regions. This will cause a fall in intra-alveolar pressure in these regions with a decrease in air flow.

Study of the cardiogenic oscillations in different postures has helped to clarify the relative importance of the two mechanisms. An argon bolus taken in early during inspiration will pass to the uppermost regions of the lungs whether the thorax is upright or inverted. Pulsatile volume changes due to gravitational influence would cause a peak in argon concentration with the heart beat independently of the posture. The present work has shown, however, that there is a phase shift of 180° in the relationship between the ECG and argon oscillations between the two postures. In the inverted position the heart lies uppermost and the adjacent part of the lung will contain a high argon concentration, which is in contradistinction to the situation in the erect posture. If changes in cardiac volume are directly influencing regional air flow, then the phase shift mentioned above would be expected.

Clarke, Jones & Glaister (1969) demonstrated an inversion of nitrogen oscillations when oxygen was inspired with the subject upside-down but the subsequent expiration was recorded when the subject was upright. This manoeuvre produces a relatively high nitrogen concentration at the lung bases but does not differentiate between the two possible causes of the oscillations mentioned. It is equivalent to giving a bolus of argon late on in inspiration when, in the erect posture, the argon passes to the lung bases. The present work has demonstrated that the relationship between nitrogen and argon oscillations depends on whether the argon bolus is given early or late in the inspiration. Clarke et al. (1969) also showed that the oscillations appeared to be inverted when the whole procedure was performed in the upside-down position, which agrees with our finding.

Further confirmation of the importance of direct influences of changes in cardiac volume on adjacent lung tissue has been demonstrated by the persistence of oscillations when an argon bolus is inspired from residual volume in the erect position but expiration is performed in the supine position. In this case argon will be distributed to the lung apices and will remain in the lung apices on lying supine. The argon concentration will now be similar in both the upper and lower part of the lungs (i.e. in the ventral and dorsal aspects), and gravity-dependent pulsatile volume changes in pulmonary vessels should not influence the expired argon concentration. In fact, the oscillations not only persisted but sometimes increased in size. The direct influence of a changing cardiac volume is not changed by this manoeuvre since the regions adjacent to the heart remain in contact with the lung bases, which contain little argon.

There is therefore strong evidence for the predominant importance of the direct effect of changes in heart size with cardiac systole. However, in the
erect posture, it is possible that this mechanism is potentiated by gravity-dependent pulsatile volume changes.

References


