The retention of lung secretions during the night in normal subjects

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Summary

1. Mucociliary clearance has been measured over a 6 h period by using the radioaerosol technique in seven normal male subjects lying supine, both during the day when awake, and during the night when asleep.

2. The percentage of radioaerosol cleared during the night, when asleep, was significantly less than during the day when awake (P < 0.02).

3. A comparison of radioaerosol clearance before and after the time of onset of sleep demonstrates that reduced clearance occurred during sleep, indicating that this is probably a sleep-related phenomenon and not merely a result of diurnal variation.

4. This finding has important implications for patients with chronic bronchitis or asthma, in whom early morning cough or wheeze may be a predominant feature.

Key words: asthma, chronic bronchitis, gamma-emitting radionuclide, mucociliary clearance, sleep.

Introduction

Bronchial secretions and foreign particles inhaled into the tracheo-bronchial tree are removed by three processes: mucociliary clearance (Kilburn, 1967), cough (Leith, 1968) and alveolar clearance (Green, 1973). In the normal human subject secretions and small particles deposited upon the conducting airways are predominantly removed by the mucociliary process with cough acting as a reserve mechanism. Two basically different methods have been employed to assess the function of the mucociliary apparatus in man: the clearance of inhaled radioactive particles from the lung and the transport of markers placed on the tracheo-bronchial mucosa (Wanner, 1977). The former technique has been used in the present study.

The efficiency of mucociliary clearance may be impaired by several factors, including infection with influenza A virus in normal subjects (Camner, Jarstrand & Philipson, 1973), and drugs such as hyoscine (Pavia & Thomson, 1971) and atropine (Annis, Landa & Lichtiger, 1976), and improved by β-adrenoreceptor agonists (Foster, Bergofsky, Bohning, Lippman & Albert, 1976; Camner, Strandberg & Philipson, 1976) and mucolytic agents (Dulfano & Glass, 1969; Thomson, Pavia & McNicol, 1973). Patients with lung disease causing sputum production often state that expectoration is greatest in the early morning after sleep. Furthermore, patients with asthma sometimes suffer from nocturnal and early morning wheezing, which may awaken them from sleep (Turner-Warwick, 1977). In both retention of lung secretions appears to occur during sleep. We have determined the effect of nocturnal sleep upon mucociliary clearance in healthy subjects.

Methods

Seven healthy volunteer male subjects, two non-smokers and five current smokers, with normal lung function (Cotes, 1975) were studied. Each
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TABLE 1. Physical characteristics, tobacco consumption and ventilatory function in the seven subjects

Mean values, with ranges, are shown.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Height (m)</th>
<th>Weight (kg)</th>
<th>Tobacco consumption (pack-years)</th>
<th>FEV₁,O (l)</th>
<th>FVC (l)</th>
<th>PEFR (l/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>32.5</td>
<td>1.70</td>
<td>74.4</td>
<td>9.1</td>
<td>4.32</td>
<td>5.10</td>
<td>610</td>
</tr>
<tr>
<td>(19.0–25.0)</td>
<td>(1.60–1.83)</td>
<td>(59.5–87.6)</td>
<td>(0–42.0)</td>
<td>(2.60–5.35)</td>
<td>(3.00–6.15)</td>
<td>(520–725)</td>
</tr>
</tbody>
</table>

gave their informed consent. Their physical characteristics, cigarette consumption and ventilatory function are shown in Table 1. We used the radioaerosol technique for monitoring whole lung clearance, as described by Thomson & Short (1969), Thomson & Pavia (1973) and Thomson et al. (1973). Polystyrene particles (5.0 ± 0.7 μm in diameter) permanently tagged with the gamma-emitting radionuclide ⁹⁹mTc (Few, Short & Thomson, 1970) were generated by a spinning disc (May, 1949) and inhaled through the mouth by the upright seated subjects. Each subject inhaled known volumes of radioaerosol (450 ml), from functional residual capacity, in eight single breaths automatically cut off by a solenoid valve at the preset volume, followed by breath-holding for 3 s before exhaling. The subjects rinsed their mouths and swallowed some water after the inhalation of the radioaerosol to remove any particles deposited in the mouth, pharynx or oesophagus. The initial distribution of the deposited particles was determined by rectilinear gamma scanning (Dawson, Douglas, Pavia, Reeves, Short & Thomson, 1971) across the right lung in vertical columns 1 inch in width. Radioaerosol clearance from both lungs was subsequently monitored by a single scintillation detector [NaI (Tl) crystal 3.8 cm diameter; 2.5 cm thick] placed anteriorly 1.3 cm from the chest at the mid-point of the sternum in the supine subject. The detector was inserted within a heavy lead-shield assembly (I.D.L. type 2220) with a short, wide-angle collimator 9 cm in diameter. Counts corrected for radioactive decay and background were collected over 100 s at 13 half-hour intervals over the next 6 h with a final count over 300 s at 24 h. The radioactivity count rate was continuously charted by a pen recorder. Radioactivity counts were expressed as a percentage of the initial count (mean 40351; range 3066–181338/100 s) to adjust for differences in the radioactive dose, which did not exceed 30 μCi in each study. The field of view of the collimated detector included most of both lungs but excluded the stomach (Thomson & Pavia, 1973). The subjects neither smoked nor took food or drink for 1 h before inhaling the radioaerosol, and for the following 6 h. Studies in each subject included one when awake by day, and one when asleep by night, in a randomized order. The inhalations were given at midday and midnight. Subjects remained supine throughout each study, without use of hypnotics. The onset of sleep was judged clinically. All studies were conducted in a temperature-controlled room (20°C) at constant relative humidity (53%).

As the number of subjects studied is small and a normal distribution cannot be assumed Wilcoxon’s test for pair differences was used for comparisons (Snedecor & Cochran, 1968).

Results

The group mean radioactivity count, expressed as a percentage of the total count for each individual for each vertical traverse across the right lung, is shown by the height of the columns for day and night (Fig. 1). There was no significant difference (P > 0.3) in paired comparisons between the day and night studies for each traverse, in all seven subjects. The ratio of the sum of the two peripheral to the sum of the two innermost traverse counts has been used as a radioaerosol distribution (or penetration) index. These mean ratios did not differ significantly between the day (0.56; range 0.30–0.95) and night (0.47; range 0.17–1.07) studies.

Fig. 1. Mean initial horizontal distribution of radioaerosol particles, across the right lung, for the seven subjects.
Fig. 2. Mean lung clearance curves for the day (○, awake) and night (▲, asleep) studies for the seven subjects.

Fig. 3. Radioaerosol clearance for each of the seven subjects during both 6 h study periods.

Fig. 4. Comparison of radioaerosol clearance for each subject: (a) from the start of the night study to the onset of sleep and the equivalent period during the day study; (b) for the period during sleep and the equivalent period awake during the day.

Discussion

Our studies show that mucociliary clearance in the normal human lungs is considerably reduced during sleep at night. Furthermore, the relative retention of tracheo-bronchial secretions appears to be associated with sleep and not to be a feature of a diurnal variation alone. This observation, however, requires confirmation by a study when the subjects are awake at night.

The mucociliary apparatus of the airways contributes to defence of the lungs by moving inhaled particulate matter and secretions from the tracheo-bronchial mucosa. The reduction of this action during nocturnal sleep implies that it is under homeostatic control, as exists, for example, with cardiac output, body temperature, urine output and plasma cortisol concentrations. Host defence mechanisms are either continuously active or respond to an appropriate stimulus. Mucociliary clearance has previously been considered to be continuous, with no diurnal variation but with a wide reserve.
capacity for the removal of secretions and inhaled particulate matter from the tracheo-bronchial tree. Tracheo-bronchial deposition of inhaled particulate matter is probably reduced during sleep. The ambient surroundings are stable, the nose acts as an efficient filter under resting conditions (assuming non-mouth breathing), and ventilation remains at a basal level. Reduction in activity of the mucociliary escalator during nocturnal sleep may thus not unduly endanger host defence. The efficiency of the normal mucociliary apparatus depends upon the volume and rheological characteristics of bronchial secretions and the morphological and functional integrity of the ciliated epithelium lining the tracheo-bronchial tree, but the role of both are unknown in sleep at present. Cilia are believed to be under cholinergic control (Kordik, Bülbring & Burn, 1952; Gosselin, 1966; Corssen Allen, 1959). They possess intrinsic activity and rhythmicity (Bidder, 1923), and beat independently of the central nervous system (Gosselin, 1966; Brody, Waldhausen & Kuhl, 1971). Furthermore, they continue to be active in the cadaver for up to 36 h after death (Hilding, 1957). Except for circumstantial evidence drawn from animal experiments under barbiturate anaesthesia (Bridger & Proctor, 1972), there are no data on the modification of ciliary action by sleep.

A homeostatic mechanism for the mucociliary apparatus of the tracheo-bronchial tree has not been elucidated. However, many pharmacological agents including cholinergic and adrenergic drugs can modify mucociliary action either by altering the volume or rheological characteristics of the secretions, or by a direct effect on the cilia (Wanner, 1977). On this basis homeostasis may be maintained by neurohumoral control via cholinergic and adrenergic mediators.

The retention of lung secretions during nocturnal sleep may have important implications for patients with lung disease, such as chronic bronchitis, where patients often complain of early morning cough and sputum, possibly due to retention of bronchial secretions during sleep. Adrenergic agents have been reported to enhance mucociliary clearance in such patients (Santa Cruz, Landa, Hirsch & Sackner, 1974) and should perhaps be administered during the sleep period. It is well known that asthma has a marked diurnal variation and some patients present with symptoms arising largely during sleep. Furthermore, death from asthma is more likely to occur during the night (Cochrane & Clark, 1975), which may be related to certain phases of sleep (Clark & Hetzel, 1977). Retention of lung secretions may underlie the diurnal variation of asthma, and this may be reduced by ensuring therapeutic concentrations of sympathomimetic drugs throughout the night.

Further studies are necessary to confirm that retention of lung secretions during nocturnal sleep is intimately related to sleep, and to ascertain whether this also occurs in patients with chronic bronchitis, or asthma.

References


Retention of lung secretions at night
