Patients with chronic airway obstruction show a diurnal variation of bronchial responsiveness to histamine (de Vries et al Int Arch All 1962) with greatest responsiveness at 4 am. Whether such diurnal variability exists in normal subjects is unknown. We have measured methacholine (M) responsiveness of five normal and four asthmatic subjects at 8 am and 6 pm on the same day. M was administered by Wright's nebuliser for 2 mins at each concentration with the subject breathing tidally.

Concentration was progressively doubled every 7 min until a response was obtained. Airway calibre was assessed by partial and maximal flow-volume loops. From the partial loop we derived Fd0P and from the maximal loop we derived FEV1. At 8 am the mean M concentration causing a 40% fall in V0.4 was 2.25 ± 0.08 and at 6 pm was 7.4 ± 0.1. The decrease of responsiveness was as great in normal as in asthmatic subjects. For a 20% fall in FEV1 the M concentration (PC20) was 58 ± 22.1 at 8 am but at 6 pm PC20 was above our maximum M concentration of 200 mg/ml in 5 subjects and was unobtainable in a further subject due to unacceptable symptoms. In the remaining 3 subjects PC20 was 61 ± 14, which represented a 10 fold increase from the 8 am value in these subjects. In conclusion, partial flow-volume loops provide a sensitive method for measuring bronchial response. The responsiveness to methacholine is approximately 3 x more in the morning than in the early evening.

**242 ARTERIAL DESATURATION, HYPERINFLATION AND CHANGES IN REGIONAL LUNG VENTILATION CAN DEVELOP DURING HISTAMINE INDUCED BRONCHOCONSTRICTION IN CHRONIC ADULT ASTHMATICS**

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To study the mechanism of the variable fall in arterial oxygen saturation (SaO2) following histamine induced bronchoconstriction we measured FeV1, SaO2, tidal volume (VT), functional residual capacity (FRC) and minute ventilation (VE) before and during bronchoconstriction induced by inhaled histamine (to PC20 or above) in 9 chronic stable asthmatics (8M, 1F, 28-56yr), initial FEV1 61-100% predicted. We simultaneously measured regional VT and regional FRC in the upper, mid and lower third of both lungs when seated before a computer linked LFOV gamma camera (Siemens). For this we used a new respiratory gated Xe ventilation scan technique correcting for changes in regional lung geometry during tidal breathing by simultaneous recording of Tc133 counts from labelled MAA lodged in lung capillaries after an initial perfusion scan. (Muir et al, Nucl. Med. Com. 1985; 6: 127). FEV1 fell by 0.45-1.875 as SaO2 (ASaO2) fell by 0-4% (derived PaO2 fell by 2-2.9 kPa). VE rose (1.2 to 6%) in 5 subjects, fell (by 0.25 to 0.5%) in 2 and was unchanged in the others, whereas FRC rose in all with histamine. The fall in FEV1 was related to ASaO2 (r=0.62) but this relationship in a given subject depended upon VE, FRC and initial SaO2. In 7/9 subjects regional VT/regional FRC of the lung bases was reduced with histamine, and the variability in regional VT/regional FRC of the six zones within each subject was exaggerated in every patient with histamine challenge. This study shows that non-specific bronchial hyperreactivity to histamine in chronic asthmatics varies between different parts of the bronchial tree, even within the same subject.

This variable change in regional ventilation in response to histamine, which presumably thereby increases V/Q imbalance, could be the basis of the hypoxaemia following histamine, if this is not compensated by any increase in overall ventilation.

**243 EFFECT OF RESPIRATION ON VENTRICULAR RATE IN ATRIAL FIBRILLATION**

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The electrocardiogram was recorded for 3 minutes during spontaneous respiration in 50 subjects in atrial fibrillation. In 13 (26%) subjects the first order autocorrelation coefficient was statistically significant (p<0.05) indicating that the rhythm was non-random. This could have been due to modulation of ventricular rate by cardio-regulatory reflexes and we attempted to demonstrate variation of ventricular rate with respiration as independent evidence of reflex activity.

Statistically significant (p<0.05) variation in ventricular rate with reference to respiration was found in 27 (54%) and 7 (14%) cases by time-sampling and cosinor analysis respectively. When the analyses were repeated with reference to an arbitrary time marker the corresponding figures were 6 (12%) and 2 (4%), and the distribution of phase angles was random.

The distribution of phase angles with respect to respiration was non-random (p<0.05) and different from that in sinus rhythm (p<0.01). In atrial fibrillation, in contrast to sinus rhythm, maximum ventricular rate occurred around the time of end-expiration. These results indicate that the beat-to-beat ventricular rate may be under the influence of cardio-regulatory reflexes, and they provide additional evidence that the pulse in atrial fibrillation is often not irregularly irregular.