

## RESPIRATORY RESPONSES OF HYPERTHERMIC SUBJECTS.

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### INTRODUCTION

Hyperpnoea in man associated with elevated core temperature was first described by Haldane<sup>(1)</sup> and has been documented more recently (Saxton, 1981)<sup>(2)</sup>. The increase in pulmonary ventilation (VE) has been found to be associated with a reduction in end tidal partial pressure of carbon dioxide ( $P_aCO_2$ ). This hyperventilation in heat stressed subjects may be due to either; a change in sensitivity of the central chemoreceptor response (i.e. a greater increase in VE for a set increase in partial pressure of CO<sub>2</sub> ( $PCO_2$ ), or a change in the threshold of that response (i.e. the level above which  $PCO_2$  increases VE). In exercising heat stressed subjects the first manifestation of any problem is failure to adopt a steady rhythm of breathing, progressing to frank hyperventilation (Oakley, 1987). In heat trials carried out at the Institute, hyperpnoea has frequently been observed, occasionally leading to tetany, resulting in withdrawal of the subject. The present investigation was designed to examine the effect of hyperthermia upon the sensitivity of the central chemoreceptors to CO<sub>2</sub> and explore the mechanisms which cause heat induced hyperventilation.

### METHOD

The experiment was completed in two parts. In the first part six subjects performed rebreathing tests according to Read<sup>(4)</sup> during normo & hyperthermic core temperature conditions (measured by aural thermistors,  $T_{au}$ ) whilst seated in a temperature controlled water bath up to level of the shoulders. Secondly a further eight subjects performed the same experiment using a 100% Oxygen (O<sub>2</sub>) rebreathing method with prior voluntary hyperventilation to reduce the subjects  $P_aCO_2$  to below 20 mmHg for 1 minute. This was carried out in an attempt to measure pre-threshold responses of the central chemoreceptors. Each subject was instructed to breathe through a mouthpiece and 3 way valve (Rudolph Valves, USA) with a pneumotachograph on the expiratory outlet to measure ventilation. Inspiratory & Expiratory gases were analysed breath by breath using a mass spectrometer (Centronics, USA). After a period of a few minutes resting ventilation (or 1 minute of voluntary hyperventilation) the subject was switched to a 6 litre rebreathing bag containing either the Read mixture (7% CO<sub>2</sub>, 43% O<sub>2</sub> bal. N<sub>2</sub>) or 100% O<sub>2</sub> until the  $P_aCO_2$  reached a maximum of 9% or the O<sub>2</sub> fell below 21%. When ventilation returned to normal this subject was passively heated whilst ventilatory variables were measured to a maximum  $T_{au}$  of 38.8°C by raising the temperature of the water up to a maximum of 39.5°C. When a stable hyperthermic core temperature was reached the rebreathing procedure was repeated (without prior voluntary hyperventilation). Graphs of  $V_E$  vs.  $P_aCO_2$  were drawn to produce a response curve of the central chemoreceptors to CO<sub>2</sub>. During the second group of experiments graphs were also drawn of  $V_E$ ,  $P_aCO_2$  & ventilatory equivalent ( $V_E O_2$ ) against  $T_{au}$  during the heating phase.

### RESULTS

In the first group two subjects were removed from the bath before completing the experiment due to considerable hyperventilation. Two subjects had a  $P_aCO_2$  which was identical under normo & hyperthermic conditions and showed no change in sensitivity of the chemoreceptor response. The remaining four subjects started rebreathing during hyperthermia with a  $P_aCO_2$  up to 10 mmHg lower than that measured during normothermia. Three of these subjects showed an increase in the sensitivity of the chemoreceptor response. The largest changes were seen in subjects with the greatest increase in core temperature. The other subject showed a change in the threshold of the response without a change in sensitivity however this may be due to the inclusion of pre-threshold data as the subject was hyperventilating. Without this pre-threshold data, the sensitivity would appear to have increased similarly to the other three subjects.

During the second group of experiments in which pre-threshold data was measured, two subjects did not show any ventilatory response to hyperthermia and no changes in thresholds or sensitivity of the chemoreceptor response. Three subjects exhibited a linear increase in ventilation together with a linear decrease in  $P_aCO_2$  as  $T_{au}$  increased. Three subjects did not exhibit this response until an apparent temperature threshold was reached, beyond which the response was linear. The responses were shown to be true hyperventilation as  $V_E O_2$  rose linearly in response to hyperthermia following the same time course as the  $V_E$  &  $P_aCO_2$  responses.

The  $V_E$  vs.  $P_aCO_2$  curve for the two subjects who showed no change in ventilatory variables showed no changes in either threshold or sensitivity of the response. The remaining subjects had lines of best-fit-by-eye drawn for the  $V_E$  vs.  $P_aCO_2$  curve one of which is shown in the diagram. Three phases were apparent in four subjects. The subjects who did not show three phases had fewer data points which made it much more difficult to distinguish phases. It is clear that each of the three phases are at an increased gain during hyperthermia i.e. the ventilation was greater and in four of the subjects was more than double that measured at normothermic temperatures. There did not appear to be any changes in sensitivity of any of the responses.

### CONCLUSIONS

Jeyaranjan *et al* (1987)<sup>5</sup> demonstrated a 3 phase response of  $V_E$  to  $P_aCO_2$  during hypoxia and considered this to be the threshold and sensitivity curve of both the peripheral and central chemoreceptors. Between thresholds the ventilation is driven only by the peripheral chemoreceptors although Dejours *et al* (1958)<sup>6</sup> suggested that the peripheral chemoreceptors are suppressed in hyperoxic conditions. The 3 phase response was not seen during the initial experiments as

the method used the Read<sup>7</sup> gas mixture and was therefore above both thresholds. The gain increase in ventilation measured during the second group of experiments rather than increased sensitivity of the central chemoreceptors as measured in the initial experiments suggests that perhaps one way the increase in ventilation due to hyperthermia is caused is a change in the way afferent input is handled centrally. However it has been shown<sup>8</sup> that hyperoxic conditions reduce the sensitivity of the central chemoreceptors by as much as 15%. Thus if the elevated core temperature does increase the sensitivity of the respiratory centre, our method also reduces it. Further work is required to investigate this aspect and would require subjects to breathe a normoxic gas mix in which a linearly rising  $pCO_2$  is introduced to simulate rebreathing. This would yield information regarding the sensitivity of both types of chemoreceptor in normoxic conditions.

### REFERENCES

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