Ventilatory responses to carbon dioxide in four ethnic groups in Cape Town

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Summary

Ventilatory responses to carbon dioxide (ScO₂) were measured in 80 healthy adult subjects from four ethnic groups living in Cape Town. The mean ScO₂ was 1,77 ± 0.14 l/min/mmHg in whites, 1,13 ± 0.09 l/min/mmHg in mixed race people, 0.99 ± 0.11 l/min/mmHg in Indians and 0.87 ± 0.10 l/min/mmHg in blacks. The difference between whites and the other three ethnic groups was highly significant (P < 0.0001), whereas the differences between blacks, mixed race subjects and Indians were not. However, correction of ScO₂ for differences in lung size, i.e. ScO₂/vital capacity, eliminated the differences between whites and the other groups.

Of the various stimuli known to affect the control of breathing, chemical factors such as hypoxia and hypercapnia are most important. Although the carbon dioxide tension in the blood is maintained within narrow limits, differences exist between healthy individuals in the responsiveness of their respiratory centres to hypercapnia. A variety of factors are known to modify this, including ethnic influences.

In order to determine whether potentially important differences could be detected in the four different ethnic groups living in Cape Town, ventilatory responses to hypercapnia were measured.

Patients and methods

Twenty subjects from each of four ethnic groups, i.e. blacks, mixed race people, Indians and whites, were studied. They were drawn from staff and medical students at Groote Schuur Hospital, Cape Town, and both men and women under the age of 40 years were selected. A short questionnaire and spirometry were used to exclude individuals with past or present chest disease. All subjects gave informed consent.

The ventilatory response to inhaled carbon dioxide was determined using the rebreathing method of Read. The test was performed approximately 2 hours after any meal or beverages, including tea or coffee, and with extraneous noise kept to a minimum. Seated comfortably with the mouthpiece in place and nose clips applied, the subjects breathed room air for 2 - 3 minutes through one outlet of a 3-way valve making sure that there were no leaks at the mouthpiece. Once the end-tidal partial arterial carbon dioxide pressure (PeCO₂) was steady, the subjects were instructed to breathe out to residual volume and then switched into a 6 l anaesthetic bag containing 7% CO₂ and 93% O₂. To facilitate gas mixing between the bag and the lungs, the subjects took three deep breaths followed by spontaneous rebreathing from the bag for about 4 minutes. Ventilation was assessed by the bag-in-the-bottle method using a Wedge spirometer (Med Science, St Louis, Missouri, USA). End-tidal PCO₂ was recorded at the mouthpiece by a rapidly responding infra-red analyser (Capnograph, Godart, Bilthoven, The Netherlands). Simultaneous recordings of ventilation and end-tidal PCO₂ were made. Care was taken to ensure that an adequate mixed venous plateau was achieved shortly after rebreathing. Results during the first 30 seconds of rebreathing were discarded and a plot of minute ventilation (corrected for body temperature, prevailing atmospheric pressure and water vapour saturation) against end-tidal PCO₂ was constructed. The slope of the regression line, indicating the ventilatory response to carbon dioxide, ScO₂ in l/min/mmHg, was calculated by the least-squares regression method. This was subsequently corrected for differences in vital capacity (VC). Mean values for ScO₂ and ScO₂/VC for each group were compared using analysis of variance.

Results

The mean value and range for ScO₂ in the four ethnic groups are shown in Table I and Fig. 1. The difference between the white group and the other three groups was highly significant (P < 0.0001), whereas the differences between blacks, mixed race subjects and Indians were not. However, for each of the groups there was a wide range of values and considerable overlap.

Table II shows the mean ± SEM and the range for the vital capacities in each group. The value in white subjects was significantly higher than in each of the other three groups (P < 0.001).
### TABLE I. VENTILATORY RESPONSES (Sco₂, l/min/mmHg) IN FOUR ETHNIC GROUPS

<table>
<thead>
<tr>
<th>Ethnic Group</th>
<th>Mean ± SEM</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whites</td>
<td>1.77 ± 0.14</td>
<td>0.79 - 2.88</td>
</tr>
<tr>
<td>Mixed race</td>
<td>1.13 ± 0.09</td>
<td>0.66 - 1.92</td>
</tr>
<tr>
<td>Indians</td>
<td>0.89 ± 0.11</td>
<td>0.48 - 1.97</td>
</tr>
<tr>
<td>Blacks</td>
<td>0.87 ± 0.10</td>
<td>0.35 - 1.80</td>
</tr>
</tbody>
</table>

W = whites; C = mixed race; I = Indians; B = blacks.

When the differences in VC were allowed for, the mean corrected value for Sco₂ (Sco₂/VC) in the white group was 0.33 ± 0.02 which, although higher than in the other three ethnic groups, no longer reached statistical significance.

Corrected values for Sco₂ were 0.24 ± 0.04 in blacks, 0.30 ± 0.03 in the mixed race group and 0.28 ± 0.04 in the Indians (Table III).

### Discussion

Despite the CO₂ tension in the blood being maintained within narrow limits, studies on healthy white subjects have shown up to a 16-fold variation in responsiveness of their respiratory centres to hypercapnia. Re buck and Read found a range of Sco₂ in healthy white subjects of 0.57 - 8.16 l/min/mmHg. Saunders et al. have shown that 80% of subjects will have a response between 1.0 and 3.99 l/min/mmHg. The frequency of distribution of the ventilatory response is not normally distributed but is skewed to the left, with more subjects having lower responses than higher ones. Most of the variation is due to differing tidal volumes although low responders do not increase respiratory frequency as much as high responders do during the rebreathing procedure.

Just why there should be such a wide variation is unclear. In some individuals low responses may offer a biological advantage, as for example in endurance athletes. On the other hand, such low responses may be deleterious in patients with chronic obstructive airways disease, predisposing them to early onset respiratory failure with CO₂ retention.

A number of factors are known to modify the ventilatory response. These include drugs, familial and personality factors, athleticism, altitude and ethnic factors. Genetic factors also seem to have some influence on ventilatory response, particularly in terms of the tidal volume response.

Possible differences between ethnic groups have not received a great deal of attention. They were first suggested by Beral and Read, who measured responses in a group of 13 Enga tribesmen in New Guinea and found considerably lower responses in the New Guineans, i.e. 1.37 l/min/mmHg compared with 2.51 l/min/mmHg in a control group of white subjects. In a later study, Patrick and Cotes reported low ventilatory responses to hypercapnia in 140 New Guinean highlanders and lowlanders compared with a white control group.

Other workers, however, have not found such ethnic differences. Edwards et al., studying subjects of East Indian and West African backgrounds living in Jamaica, found no significant differences from a white control group. Similarly no differences were reported between Nigerian men and white subjects.

In this study we found that mixed race, black and Indian subjects had low responses compared with a white group. However, intergroup comparisons of ventilatory responses must make allowance for differences in lung size between the groups. Of the size-dependent variables, the VC is the best, since it is linearly related to the ventilatory response. Correction for...
Cancer — approaching a universal molecular mechanism?

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Summary

Accumulating evidence strongly suggests that cancer is a genetic disease, arising from mutations in DNA. These mutations alter the function or synthesis of two groups of proteins, which are the products of either proto-oncogenes or anti-oncogenes. Of the more than 30 proto-oncogenes identified, ras proto-oncogenes are most frequently found to be mutationally activated (to oncogenes) in human tumours. Developments leading to current understanding of the function of ras proto-oncogenes and of the retinoblastoma anti-oncogene are reviewed. Based on the involvement of all known oncogenes and anti-oncogenes in cellular signal transduction pathways, it is suggested that a general model for cancer at the molecular level may become a reality.

The term 'cancer' indicates any of the various types of malignant neoplasms; cancer cells are characterised by loss of normal growth control and the ability to metastasise. Accumulating evidence suggests that cancer is a genetic disease; mutations in DNA affecting the expression of certain genes are almost certainly necessary for the transition of a normal cell to tumorigenicity. These mutations ultimately alter the activity of proteins involved in cellular chemical communication. The rapid advances being made in understanding these complex communication pathways and their role in cellular transformation is set to change our understanding and treatment of cancer.

Proto-oncogenes are normal cellular genes. They code for the synthesis of certain proteins (proto-oncoproteins or oncoproteins), all of which appear to be important in the communication of extracellular signals to the cell nucleus. However, certain mutations or rearrangements can cause these proteins to be modified in function or to be produced in inappropriate amounts, thereby contributing to cell transformation and tumour development.

Some oncogenes are initially identified as the transforming genes of animal tumour retroviruses. These genes were acquired by transduction and mutation of normal cellular proto-oncogenes from the host cell (Fig. 1). For example, the cellular homologue of the v-sis oncogene is platelet-derived growth

REFERENCES

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