OXYGEN UTILIZATION BY DOGS AFTER ADMINISTRATION OF POTASSIUM PERCHLORATE, DURING HYPOTHERMIA, AND AT A PRESSURE OF 2 ATMOSPHERES

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Many reports concerning the physiology of the hypothermic state have appeared during the past decade. Most of the authors have shown that oxygen consumption diminishes consistently with decreasing body temperature. Bigelow and associates, for example, in their excellent early study in dogs found a steady decrease in oxygen consumption as body temperature was lowered.

Another method of lowering oxygen uptake has been the utilization of procedures which limit activity of the thyroid gland. Leidig and Gray found that thyroidectomized rats used less oxygen than they did under control situations, both groups being subjected to lowered ambient temperatures. Godley and Stanbury observed that administration of potassium perchlorate was followed by a decrease in metabolic rate of human subjects, chiefly because it blocked accumulation of iodine in the thyroid gland.

A third method of attempting to make one's internal oxygen supply sufficient for a prolonged period has been to do the surgical procedure within a tank at 3 atmospheres pressure of oxygen. Boerema and co-workers reported some success in prolonging the safe period of circulatory occlusion by this method.

This study was undertaken to find whether a combination of two or three of these modalities might produce a sufficient decrease of oxygen demand so that the safe period of occlusion of circulation might be substantially extended. The level of 30 C. was chosen because it seems that the heart is reasonably protected from ventricular fibrillation at this temperature. Potassium perchlorate was used because it had been found to be effective in several cases that were refractory to thiocyanate. Two atmospheres of pressure were employed because slow decompression from this pressure is unnecessary.

METHODS

Thirteen mongrel dogs were anesthetized with 25 mg./kg. of thiopental intravenously. Endotracheal intubation was performed and a cuff was inflated around the tube. A Water's to-and-fro carbon dioxide absorber was inserted into the system. Oxygen uptake was measured with the Collins Vitalometer while each dog breathed spontaneously. When the dog began to awaken after the first administration of thiopental, 0.2 mg./kg. of succinylcholine chloride was injected intravenously. This, of course, produced apnea and oxygen uptake was again measured. Assisted respiration was used during each period of diminished spontaneous respiratory activity. When spontaneous respiration returned, oxygen consumption was again recorded. One hundred milligrams of thiopental and 0.2 mg./kg. of succinylcholine were then given simultaneously, and during the apneic period another measurement of oxygen uptake was made.

The animals were cooled in an ice water bath to 30 C. and a second similar series of measurements were made. The dogs were allowed to warm and to awaken.

After obtaining the above control values, potassium perchlorate 60 mg./kg. was administered to each dog three times daily with some food for a period of a week. The entire series of measurements of oxygen uptake was then repeated both at normal temperatures and at 30 C.

Protein-bound iodine was determined before and after the medication with potassium perchlorate in 4 of the 13 dogs.

In each of two experiments a dog was anesthetized with thiopental, electroencepha-
lographic leads were attached, provision was made for intravenous injection of succinylcholine, a thoracotomy was performed and tapes were placed around the aorta. The thorax was then closed with retention sutures. The animal was put into a chamber and the pressure was raised to 2 atmospheres with oxygen. Each dog was given succinylcholine and its lungs were artificially ventilated with oxygen for 30 minutes before occlusion of circulation. Circulation was stopped suddenly by tightening the tapes around the aorta while an electroencephalogram was recorded.

RESULTS

Table 1 presents average values of oxygen consumption for the 13 dogs, both at normal temperatures and at 30 C., before and after administration of potassium perchlorate. The combination of thiopental and succinylcholine reduced oxygen uptake to a value which was lower than with either thiopental or succinylcholine alone (table 1). This was true whether the animal was at normal temperature or at 30 C. Hypothermia significantly reduced oxygen uptake below the values observed at normal body temperature. (Columns 1, 4 and 7 compared to columns 5, 6 and 8, respectively.) While average values of oxygen utilization were lower after than before administration of potassium perchlorate, the degree of diminution was not great enough to be of statistical significance. (Columns 1, 5 and 6 compared to 7, 8 and 9 respectively.) Potassium perchlorate diminished protein-bound iodine by approximately 30 per cent.

The maximum dose of potassium perchlorate was given, because anorexia, vomiting and diarrhea occurred in several of the animals receiving the drug. The animals returned to normal immediately after withdrawal of medication.

After occlusion of circulation of the animals in the pressure chamber, the electroencephalogram became isoelectric (flat) within less than 30 seconds on each occasion.

DISCUSSION

The presently accepted safe limit for occlusion of circulation at 30 C. is perhaps 8
minimize. If one could administer potassium perchlorate to a patient and thereby diminish his metabolic rate (oxygen requirement) it would be possible to occlude circulation for a longer period for cardiac operations. This might eliminate the necessity for the use of extracorporeal circulation under some circumstances. The dog is a suitable animal in which to carry out these experiments because his heart fibrillates more easily than that of man at low temperatures. Also, the dog’s basal metabolic rate is perhaps diminished less by potassium perchlorate than is that of man. If favorable results were obtained on both counts, then it would seem that the human being might have even more favorable results from these procedures. Our present results, however, do not show statistical significance for the lowering of oxygen uptake by potassium perchlorate, although the average metabolic rate was lessened by this drug and was diminished significantly further by hypothermia. The values for potassium perchlorate (table 2) indicate that potassium perchlorate definitely suppressed thyroid activity in the 4 animals utilized. One could not obtain more striking results from larger doses, for the potassium perchlorate in doses used upset the intestinal activity of some animals. It would seem that a relatively small benefit could be obtained as far as oxygen uptake is concerned by the clinical use of this drug. Its trial in man does not seem to be warranted.

Evidence is available by comparison of columns 1 and 3 of table 1 to show the effect of muscle activity on the basal metabolic rate. The values of column 3 indicate that although temperatures were equivalent, oxygen usage was much greater in an active animal than after the animal had had thiopental (column 1). Shivering was visible in none of these animals, but results of occult shivering were apparent on the electrocardiogram of several dogs. A greater contrast is seen by comparing the values before relaxation (column 3) with those after complete relaxation (column 4). Leidig and Gray* reported that stress in the form of external cold which caused shivering in rats increased their oxygen uptake 43 per cent even though it decreased the temperature of the animals from 38.4 C. to 35.8 C. Thus, relaxation must be sufficient to offset both gross muscular activity and shivering to obtain a minimal oxygen demand.

The period for the electroencephalogram to become flat after occlusion of the aorta at 2 atmospheres pressure of oxygen was nearly 30 seconds in each of two cases. Our results with human beings indicate that at 1 atmosphere pressure the time for the electroencephalogram to become isoelectric was approximately 30 seconds. The difference, if any, was certainly not favorable enough to warrant further experiments.

**Summary**

The oxygen uptake of 13 dogs was measured (1) after thiopental anesthesia, (2) after being paralyzed with succinylcholine, (3) after returning to a nearly awake stage, and (4) after administration of a combination of thiopental and succinylcholine. The animals were then cooled to 30 C. Oxygen consumption was measured (5) after intravenous injection of thiopental and (6) after further administration of both thiopental and succinylcholine. Oxygen utilization was greatest when the animal was nearly awake and lowest after both thiopental and succinylcholine had been given. Lowering the temperature to 30 C. significantly diminished oxygen demand.

The same 13 dogs were fed potassium perchlorate 60 mg./kg. three times daily for a week. They were anesthetized with thiopental and their oxygen uptake measured (7). They were cooled to 30 C., given thiopental (8) and then thiopental plus succinylcholine, and the oxygen utilization again determined (9). The average usage of oxygen per

<table>
<thead>
<tr>
<th>Dog</th>
<th>Before KClO₄</th>
<th>After KClO₄</th>
<th>Decrease Per Cent</th>
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<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>44</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>77</td>
<td>51</td>
<td>34</td>
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<td>3</td>
<td>70</td>
<td>49</td>
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<tr>
<td>4</td>
<td>58</td>
<td>44</td>
<td>24</td>
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<tr>
<td>Average</td>
<td>67.5</td>
<td>47</td>
<td>30</td>
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minute was lower in the potassium perchlorate-treated dogs, but not statistically significant. Determination of protein-bound iodine in 4 of the 13 animals, before and after ingestion of potassium perchlorate, revealed a 30 per cent decrease of thyroid activity.

Two dogs were kept 30 minutes in a chamber at 2 atmosphere pressure of oxygen. Sudden occlusion of their aortas resulted in production of flat electroencephalographic records within 30 seconds.

The results suggest clinical trials of potassium perchlorate feeding and high pressure oxygen exposure to obtain more efficient oxygen usage unwarranted.

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REFERENCES


TETANUS Tetanus may be mild with some patients recovering on treatment only to reduce discomfort; may be moderate, with patients recovering on treatment with sedatives and phenothiazine derivatives; may be severe, requiring the use of mechanical respirators after total paralysis has been induced; and may be inevitably fatal due to overwhelming dosage of toxin. Severe cases are judged to be those having muscle spasms that stop respiration. In 2 out of 10 patients treated by paralysis with curare and mechanical respiration, recovery occurred. One other patient died of pneumonia. The remaining patients died of causes unknown, but an important factor in their demise appears to have been a toxic myocarditis which produced hypotension, electrocardiographic changes and histological changes. The conception of tetanus as a self-limiting disease may not be a true one in view of the evidence for myocarditis. (Alhady, S. M. A., and others: Total Paralysis Regime in Secere Tetanus, Brit. Med. J. 1: 540 (Feb. 20) 1960.)