Maximum oxygen consumption and heat loss facilitation in small homeotherms by He-O₂

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ALTHOUGH ANIMALS IN NATURE spend the majority of their time resting or at low levels of activity, some functions critical for survival such as fighting, escaping, or predation greatly increase the energy demand. The maximum capability to increase metabolism is the main factor in limiting the intensity of such physical activity and, as well, sets the limit for cold tolerance. Evaluations of maximum metabolism (Mₘₐₓ) in moderate cold in species ranging from 7-g pygmy mice (Baiomys taylori) to 250-g white rats, including redpolls (Acanthis flammea), two vesper mice (Calomys ducilla, C. callosus), tundra voles (Microtus oeconomus), and four strains of Mus musculus. Values slightly exceeded those in similar animals using other methods to confirm the low metabolic ratio (Mₘₐₓ/Mₘᵢₐ) in rodents (4-8 X). Submaximal values at higher temperatures defined thermal conductance in He-O₂ and air. In different species the ratios of these conductances ranged from 1.4 to 2.6, differences which relate to the extent and quality of the respective insulation. Mₘₐₓ was obtained at 13-70°C warmer in He-O₂ than required in air for the same metabolic effort. Avoidance of low-temperature technology and freezing injury, elimination of treadmills and training in running, prompt attainment of Mₘₐₓ (3-10 min after He-O₂ exposure), and obviation of shaving or wetting procedures are advantages of the present technique.

Maximum oxygen consumption and heat loss facilitation in small homeotherms by He-O₂. Am. J. Physiol. 226(3): 490-495. 1974.—The high thermal conductance of an 80% He-20% O₂ atmosphere was used to elicit maximum metabolism (Mₘₐₓ) in moderate cold in species ranging from 7-g pygmy mice (Baiomys taylori) to 250-g white rats, including redpolls (Acanthis flammea), two vesper mice (Calomys ducilla, C. callosus), tundra voles (Microtus oeconomus), and four strains of Mus musculus. Values slightly exceeded those in similar animals using other methods to confirm the low metabolic ratio (Mₘₐₓ/Mₘᵢₐ) in rodents (4-8 X). Submaximal values at higher temperatures defined thermal conductance in He-O₂ and air. In different species the ratios of these conductances ranged from 1.4 to 2.6, differences which relate to the extent and quality of the respective insulation. Mₘₐₓ was obtained at 13-70°C warmer in He-O₂ than required in air for the same metabolic effort. Avoidance of low-temperature technology and freezing injury, elimination of treadmills and training in running, prompt attainment of Mₘₐₓ (3-10 min after He-O₂ exposure), and obviation of shaving or wetting procedures are advantages of the present technique.

METHODS

Tests were conducted on two laboratory species, the white mouse and the white rat, previously assessed for Mₘₐₓ by various other procedures. Three further strains of Mus musculus, a hairless mutant (HRS/J), and feral house mice from 15,000 feet at Morococha, Peru and from Arkansas were also compared. In addition, measurements were made on wild species native to different habitats: arctic (Microtus oeconomus from Fairbanks), alpine (Calomys ducilla from 13,000 feet near Puno, Peru), and subarctic (Calomys callosus from San Joaquim, Beni Province, Bolivia), and the pygmy mouse Baiomys taylori. The final species was a small arctic bird, the redpoll (Acanthis flammea), also native to Fairbanks. We are indebted to Dr. Oliver P. Pearson and Dr. Karl M. Johnson for the respective Calomys, to Dr. Hermann Pohl for the redpolls, and to Dr. John Sealander for the lowland Mus. These rodents were maintained in our animal facility at a neutral T₀ of 20-24°C. Three to eight individuals of each type were tested at 735-750 torr.

O₂ consumption was measured in a closed-circuit manometric respirometer (28). Since the oxygen consumed by the animal is replaced by successive aliquots, the inert component maintains its concentration as established. The metabolic chambers of stainless steel were submerged in a thermoregulated water-glycol bath. After a variable length of time (1-3 h) in which the metabolic rate in air was measured, the chambers were flushed with 5-6 times their volume of an 80% He-20% O₂ mixture from a proportioning gas mixing pump or from a gas tank. Use of the gas tanks with premixed He-O₂ reduced the purging time to only 2 min as compared with 7-9 min with the mixing pumps. To avoid temperature changes, the He-O₂ mixture was admitted through a submerged copper coil.
Food as apple, carrot, and sunflower seed was generally available during the tests. Regardless of the duration and temperature of the metabolic measurements, the animals were tested about 4 times a week, and generally 2 days were allowed between consecutive tests at high submaximal rates.

RESULTS

Immediately after the substitution of He-O2 for air, O2 consumption increased well above the resting levels in air, as shown in Fig. 1 for M. oeconomus. Of interest also is the suppression in He-O2 of the metabolic cycles reflecting changes in activity or posture, an effect also seen at lower T in air. These relations are shown in Fig. 2 for a series of T between 26 and 7°C again for M. oeconomus. The respective values in air and in He-O2 lie along two straight lines which extrapolate to the T at 39°C to fit the relations:

\[ M = C(T_b - T_a) = C\Delta T \]
\[ M = C^{He} \Delta T \]

The constant C usually designated as the (minimum) conductance actually includes a component of evaporative/respiratory heat loss, but at these T below thermal neutrality this represents a constant (small) fraction of the thermal loss through the surface—a cost of "chemical" thermoregulation. Accordingly, C is a measure of the overall facility for heat loss from the body and will reflect changes in the properties of the insulative layers. In this example the substitution of He-O2 increased conductance from 0.178 to 0.377 ml O2 (g·h·°C)-1, a factor of 2.12 (C/He/C).

At temperatures below the thermoneutral zone, heat production more than doubled in He-O2 until at about 6°C (in this species) a limit was reached, indicating maximum metabolic capability for temperature regulation (Mmax). In fact, at 1°C in He-O2 the maximum heat production could only be maintained for approximately 5 min, and longer exposure under these conditions resulted in decreased O2 consumption and hypothermia. Exposure to lower temperatures in He-O2 did not seem to modify their maximum response, but the highest rates were held for a shorter time. The quotient, Mmax/C, provides an estimate of the maximum temperature differential tolerable by the animal, in this case -7°C. This has been shown graphically by extrapolation of \( M = C \Delta T \) to the value Mmax = 12.5 ml O2 (g·h)-1 at -31°C. It may be noted that we have observed limiting values of cold tolerance of this species (neutral acclimation) at -25 to -30°C (unpublished observations).

A somewhat lower ratio was observed in white rats (Fig. 3). Maximum rates in He-O2 were attained within 6-10 min at -3°C. Exposure at -10°C in He-O2 resulted in reduced O2 consumption and hypothermia.

The effects of He-O2 on highland house mice and white mice are shown in Fig. 4. The ratio CHe/C was 2.3 in the house mice as compared to 2.1 in white mice and Mmax was 24% higher, 13.8 vs. 11.1 ml O2 (g·h)-1. In lowland...
FIG. 4. Oxygen consumption of feral house mice (circles) and of white mice (squares) in air (open symbols) and in He-O\(_2\) (solid symbols) as a function of \(T_\text{a}\).

FIG. 5. Oxygen consumption of hairless mice in air (open symbols) and in He-O\(_2\) (solid symbols) as a function of \(T_\text{a}\). Reference curves compare function for normal mice.

house mice the \(M_{\text{max}}\) was intermediate at 12.3 mlO\(_2\) (g·h\(^{-1}\)).

To gain insight into the relation between the surface insulation and the effects of He-O\(_2\), hairless mice were also tested (Fig. 5). The ratio of the thermal conductance in air of hairless versus normal mice was 1.9, close to a previously reported ratio of 2.2 for these strains (29). However, in He-O\(_2\), the conductance ratio hairless versus normal was only 1.3 due to the much smaller response of the hairless mice to helium (\(C^{\text{He}}/C = 1.40\)). \(M_{\text{max}}\) in hairless mice was 13% higher than in the normal white mice (12.5 vs. 11.1 mlO\(_2\) (g·h\(^{-1}\)) but still 10% lower than in the feral mice. Similarly, the metabolic expansivity of the hairless mice (10.5 mlO\(_2\) (g·h\(^{-1}\)) lay between those of the two other strains. \(M_{\text{max}}/M_{\text{min}}\) ratios were 6.3 in both the white and the hairless mice as compared with 7.2-7.3 in both feral groups.

Results of He-O\(_2\) exposure in Calomys ducilla, a highland species, and Calomys callosus, a tropical species, are shown in Fig. 6. \(M_{\text{max}}\) of 14 mlO\(_2\) (g·h\(^{-1}\)) was found in the 16-g C. ducilla and 6.8 mlO\(_2\) (g·h\(^{-1}\)) in the 3 times larger C. callosus.

Redpolls (Acanthis flammea) were treated in a similar way to the rodents with the exception of a wooden perch in the cages and an aluminum cover to maintain a dark environment and so diminish spontaneous activity. O\(_2\) consumption values in air and in He-O\(_2\) are shown in Fig. 7. The highest ratio, \(C^{\text{He}}/C = 2.6\), was observed in the redpoll and a \(M_{\text{max}}\) of 21.8 mlO\(_2\) (g·h\(^{-1}\)) was elicited at -5°C.

Table 1 summarizes the thermogenetic effects of He-O\(_2\) in the experimental species, the temperatures at which \(M_{\text{max}}\) was elicited in He-O\(_2\), the extrapolated air temperatures for these rates, and the thermal conductance values in relation to the He-O\(_2\) atmosphere and to the animal's surface area. In general, \(M_{\text{max}}\) in the rodent species was obtained in He-O\(_2\) at 13-30°C warmer temperatures than expected in air, but in the hairless mice the difference was only 7°C. In contrast, a 70°C warmer temperature for \(M_{\text{max}}\) elicitation in He-O\(_2\) was estimated for the redpolls.
HEAT LOSS AND MAXIMUM OXYGEN CONSUMPTION IN HE-O₂

DISCUSSION

A comparison of our data on Mₘₐₓ of mice, rats, and of the pygmy mouse with reported values for the same species but obtained with different methodologies is shown in Table 2. Our values for white mice are equal or higher than reported figures from mice kept at neutral or warm temperatures but are 8% lower than from cold-acclimated mice (12). Similarly in white rats, Mₘₐₓ values in He-O₂ are the same or higher than reported capabilities in normal mice (12). Similarly in white rats, Mₘₐₓ values in He-O₂ temperatures but are 8% lower than from cold-acclimated ones (32).

Published data for the rest of our wild species seem to be unavailable, but some values have been reported in references shown in Table 2. Our values for white mice are equal or higher than reported figures from mice kept at neutral or warm temperatures but are 8% lower than from cold-acclimated ones (32). Our value for 32-g Microtus oeconomus was 5.2.

In summer birds, exposure of house sparrows to -30 to -65°C resulted in Mₘₐₓ of 15 mlO₂ (g·h)⁻¹ and Mₘₐₓ/Mₘᵢₙ of 3.3 (14). In the goldfinch, exposure to 0°C after removing the feathers gave Mₘₐₓ of 18.9 mlO₂ (g·h)⁻¹ and Mₘₐₓ/Mₘᵢₙ of 4.2 (8). By comparison Mₘₐₓ of summer redpolls in He-O₂ was 21.8 mlO₂ (g·h)⁻¹ with a Mₘₐₓ/Mₘᵢₙ ratio of 5.6.

In previous studies of white mice and rats, considerably smaller effects of He have been reported (34, 36). Examination shows that those measurements, sometimes on groups of animals rather than individuals, gave reference values in air which clearly include a considerable activity component which is then suppressed under the cooling influence of the He (compare Fig. 1). Nor will measurements made within the thermoneutral zone show as large an increase in metabolism with He-O₂.

Free/forced convection and radiation present major routes for heat loss from bare skin with little or no involvement of simple conduction. Convective heat transfer in He-O₂ as compared with air has been described by Epperson et al. (5), in relation to the ratios of their thermal conductivities, densities, specific heats, and viscosities, together representing a ratio of 2.1. A somewhat larger value has been calculated for conductive-convective effects (7). By contrast to bare skin, conductive heat transfer should be of greater importance through fur (11), and a facilitation of fourfold is indicated (air → He-O₂). However, it is not easy to assess the effective thickness of a fur, which will depend on the density, length, erection angle, and uniformity of the fibers which modify convective mixing in the outer layers. Neither is it easy to assess the amount of radiative heat loss from the outer layers.

### Table 1. Metabolic ratios and conductance factors in He-O₂ and air

<table>
<thead>
<tr>
<th>Species</th>
<th>Weight, g</th>
<th>Acclim.</th>
<th>Mₘₐₓ/Mₘᵢₙ</th>
<th>Mₘₐₓ/Mₘᵢₙ</th>
<th>Cₘₐₓ/ Cₘᵢₙ</th>
<th>Cₘₐₓ/ Cₘᵢₙ</th>
<th>Cₘₐₓ/ Cₘᵢₙ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rattus norvegicus</td>
<td>18.5</td>
<td>c</td>
<td>10.75</td>
<td>3.5</td>
<td>(8) Cold water wetting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>26.5</td>
<td>c</td>
<td>10.10</td>
<td>5.2</td>
<td>(13) Run 6 m/min at 2°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>26.7</td>
<td>c</td>
<td>12.15</td>
<td>6.5</td>
<td>(12) Run 5 m/min at -10°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>33.0</td>
<td>c</td>
<td>10.50</td>
<td>4.2</td>
<td>(32) Run 23 m/min at -10°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>34.0</td>
<td>c</td>
<td>9.30</td>
<td>3.1</td>
<td>(32) Run 19 m/min at -3°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>33.4</td>
<td>c</td>
<td>7.40</td>
<td>3.5</td>
<td>(18) Noradrenaline, 1.7 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>29.5</td>
<td>n</td>
<td>11.10</td>
<td>6.3</td>
<td>(1) He-O₂ at 7°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>21.0</td>
<td>n</td>
<td>12.50</td>
<td>6.3</td>
<td>(1) He-O₂ at 14°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>17.5</td>
<td>n</td>
<td>13.80</td>
<td>7.3</td>
<td>(1) He-O₂ at 2-5°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R. n.</td>
<td>17.0</td>
<td>n</td>
<td>12.30</td>
<td>7.2</td>
<td>(1) He-O₂ at 10°C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Comparison of maximum metabolism and Mₘₐₓ/Mₘᵢₙ ratios obtained with different techniques

<table>
<thead>
<tr>
<th>Species</th>
<th>Weight, g</th>
<th>Acclim.</th>
<th>Mₘₐₓ, mlO₂/g·h</th>
<th>Mₘᵢₙ, mlO₂/g·h</th>
<th>Reference and Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mus musculus albino</td>
<td>380</td>
<td>w</td>
<td>3.20</td>
<td>2.7</td>
<td>(19) Cold exposure at -35°C</td>
</tr>
<tr>
<td>R. n.</td>
<td>385</td>
<td>w</td>
<td>2.76</td>
<td>2.7</td>
<td>(4) Cold exposure down to -33°C</td>
</tr>
<tr>
<td>R. n.</td>
<td>290</td>
<td>w</td>
<td>4.83</td>
<td>3.3</td>
<td>(27) Swim with 2% load</td>
</tr>
<tr>
<td>R. n.</td>
<td>115</td>
<td>w</td>
<td>4.81</td>
<td>3.6</td>
<td>(8) Cold water wetting</td>
</tr>
<tr>
<td>R. n.</td>
<td>300*</td>
<td>w</td>
<td>3.20</td>
<td>2.7</td>
<td>(17) Run at 0°C or rest at -35°C</td>
</tr>
<tr>
<td>R. n.</td>
<td>300*</td>
<td>c</td>
<td>5.05</td>
<td>4.2</td>
<td>(17) Run at -30°C or rest at -45°C</td>
</tr>
<tr>
<td>R. n.</td>
<td>286</td>
<td>c</td>
<td>4.90</td>
<td>3.1</td>
<td>(32) Run 35 m/min at 6°C</td>
</tr>
<tr>
<td>R. n.</td>
<td>334</td>
<td>c</td>
<td>5.40</td>
<td>3.5</td>
<td>(32) Run 27-37 m/min at b to -3°C</td>
</tr>
<tr>
<td>R. n.</td>
<td>253</td>
<td>n</td>
<td>5.20</td>
<td>4.9</td>
<td>(1) He-O₂ at -3°C</td>
</tr>
<tr>
<td>R. n.</td>
<td>371</td>
<td>c</td>
<td>(-5.53)</td>
<td>(-5.0)</td>
<td>(22, 25) Cytochrome oxidase activity</td>
</tr>
<tr>
<td>Baiomys taylori</td>
<td>7.8</td>
<td>n</td>
<td>10.40</td>
<td>5.3</td>
<td>(20) Exposure at 15°C</td>
</tr>
<tr>
<td>R. n.</td>
<td>6.9</td>
<td>n</td>
<td>12.30</td>
<td>4.3</td>
<td>(1) He-O₂ at 23°C</td>
</tr>
</tbody>
</table>

* Assumed.       † Acclimation: cold, warm, neutral, Tₐ.   ‡ This study.
The relation between conductance and He facilitation was con-
later suggested by lower skin temperatures in He-O2 (34).

evaporation and tissue insulation, with involvement of the
radiant loss either from the outer layer of fibers or from
more thinly covered areas as on the face, feet, or tail. Other factors not directly influenced by He are surface
and tissue insulation, with involvement of the latter suggested by lower skin temperatures in He O₂ (34).

Although the increase in conductance in the He-O₂ mix-
ture cannot define all these factors quantitatively, it should
give us some measure of the relative importance of con-
duction (f = 4) as compared to convection (f = 2)
radiation, tissue insulation, and surface evaporation (f = 1).

As noted in Table 1, CHe/C ranged from 1.4 in the hair-
less mouse to 2.6 in the redpoll. Since a thick layer of fur
or feathers will emphasize conductive transfer as compared
to other modes, CHe/C ratio should vary directly with the
insulation. That such is the case may be seen in Fig. 8 for
species from 7 to 32 g. The larger C. callosus and white rat,
however, do not conform to this pattern, perhaps because of
greater reliance on tissue insulation. Similarly, induction of
hypothermia in He-O₂ has been also reported to be re-
lated to body size in rats of 100 to over 200 g (31). The
relation between conductance and He facilitation was con-
firmed experimentally by observations of cooling rates in
air and He-O₂ in preserved Microtus oeconomus with differ-
ent degrees of insulation (Fig. 9). These results show con-
ductance ratios of 1.83 when the fur was intact, 1.62 when
the fur was clipped to 1 mm, and 1.32 when the fur was
totally removed.

As heat dissipation is seen to be much more affected by
insulation in air than in He-O₂ (3 times), a simple way of
describing the metabolic effects of helium in different
species is in terms of the functional removal of the surface
insulation, regardless of its degree or quality, the meta-
bolic increase then being proportional to the magnitude
of the insulation so “removed.” Thus, well-insulated ani-
imals, sensitive to small changes of skin temperature (15),
would show a larger response.

Among the many applications of inert gases, He-O₂ at-
mospheres have been used for therapeutic reasons (2, 9),
also for prevention of nitrogen narcosis in divers (1), and in
recent years for induction of hypothermia in small mam-
als (6, 30, 31). The elicitation of maximum O₂ consump-
tion in small homeotherms may prove to be another prac-
tical application. The rapidly attained Mₘₐₓ values (3–10
min), the simplicity of operation, the avoidance of extreme
cold temperatures and of treadmills and training tests are
definite advantages of the present technique over the cur-
rent conventional methods.

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