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VENTILATION AND PULMONARY GAS EXCHANGE DURING EXERCISE IN THE SAVANNAH MONITOR LIZARD (*VARANUS EXANTHEMATICUS*)

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Summary

During exercise, pulmonary gas exchange in reptiles was predicted to differ from that in mammals because of their less complex lung structure, which might reduce ventilation–perfusion heterogeneity ($\dot{V}/\dot{Q}_L$) at the expense of pulmonary diffusion limitation. To investigate this, the multiple inert gas elimination technique was used in six *Varanus exanthematicus* at rest and during maximal exercise. Trace amounts of six inert gases were infused into the external jugular vein and blood samples were collected from the pulmonary artery and the left atrium. Mixed expired gas samples and ventilatory and metabolic data were acquired. Indices of $\dot{V}/\dot{Q}_L$ heterogeneity, calculated using a 50-compartment model, were low at rest (log standard deviation of perfusion distribution, $\log SD_{\dot{Q}}=0.39$) and increased significantly with exercise ($\log SD_{\dot{Q}}=0.78$). Oxygen diffusion limitation was apparent during exercise and was comparable to reported mammalian values. A molecular-mass-dependent limitation, suggesting limited intrapulmonary gas mixing, was evident only at rest. An increase in left atrial P_{O_2} from 82 mmHg at rest to 96 mmHg during exercise was associated with a corresponding decrease in P_{CO_2}. These data indicate adequacy of pulmonary ventilation and gas exchange for metabolic demands in exercising varanid lizards and suggest that less complex lung structures are not necessarily linked to increased pulmonary diffusion limitation.

Key words: *Varanus exanthematicus*, ventilation, inert gas, ventilation–perfusion heterogeneity, exercise, diffusion limitation, molecular-mass-dependent intrapulmonary gas mixing.

Introduction

Among reptiles, monitor lizards (genus *Varanus*) have one of the highest aerobic scopes (Gleeson *et al.* 1980; Mitchell *et al.* 1981), supported by one of the most mammalian-like cardiopulmonary systems. They have multicameral lungs that are subdivided into many chambers, and the surface area for gas exchange is three times greater than that of other lizards (Perry, 1983). The varanid heart has a well-developed muscular ridge that facilitates functional separation of pulmonary and systemic circulations, and reduces intracardiac shunting (Burggren and Johansen, 1982). Despite this, the mass-specific gas-exchanging surface area of the lung is less than one-quarter of that of a mammal (Perry, 1983), and when oxygen transport is stressed, gas-exchange limitations can occur, as shown by effective lung–arterial P_{O_2} differences of over 30 mmHg in *Varanus exanthematicus* during maximal running exercise (Mitchell *et al.* 1981).

The physiological factors that can increase an effective lung (or alveolar)–arterial P_{O_2} difference, and therefore limit oxygen uptake, are (1) incomplete diffusion equilibration, (2) spatial mismatching of pulmonary ventilation and perfusion, (3) intrapulmonary and intracardiac shunting. The first two factors have been shown to be important limitations in many mammals during maximal exercise (Hammond *et al.* 1986; Hopkins *et al.* 1994; Wagner *et al.* 1989). We hypothesized that, in varanid lizards compared with mammals, (1) diffusion limitation would be more important because of a smaller gas-exchange surface area and the greater thickness of the blood–gas barrier, and (2) ventilation–perfusion mismatching would be less important because the lungs are divided into fewer functional subunits. To test these hypotheses and to determine the mechanisms limiting pulmonary gas exchange during exercise in a highly aerobic reptile, we applied the multiple inert gas elimination technique (Hlastala, 1984; Wagner *et al.* 1974*a*,*b*) to *Varanus exanthematicus* at rest and during running exercise.

Materials and methods

This study was approved by the Animal Subjects Committees of the University of California, Irvine and San Diego, USA. Six savannah monitor lizards (*Varanus exanthematicus* Bosc) were obtained from a commercial dealer, housed in large cages

in a temperature-regulated room (30 °C) and fed on snails. The animals were trained to run on a treadmill for periods of up to 10 min at a time. They were encouraged to run by taping the cardboard enclosure from their cage at the front of the treadmill, and the animal was gently prodded with a blunt rod when it approached the back of the treadmill. The maximum treadmill speed that would allow steady-state running for at least 4 min was determined for each animal.

The animals were prepared for surgery by placing them in crushed ice until they could be handled easily. They were then intubated with rubber tubing and artificially ventilated with a mixture of 95 % O_2, 5 % CO_2 passed through a halothane vaporizer set to 3 %. After induction of anesthesia, the halothane level was reduced to 2 % for the duration of the surgery. A mid-ventral incision was made over the heart, and the pericardium and great vessels were exposed. The common pulmonary artery was non-occlusively cannulated using a 22 gauge intravenous catheter connected to PE 50 tubing. The left atrium was non-occlusively cannulated with PE 90 tubing for blood sampling (Ishimatsu *et al.* 1988). The tubing was sutured in place, filled with heparinized saline, looped loosely to avoid traction, and led to the exterior through small holes in the skin on the animal's back. The pericardium was closed, and wound closure was achieved by suturing the deep layers and sealing the skin with cyanoacrylate tissue glue (Nexaband; S/C-Tri-Point Medical Raleigh, NC, USA). We chose these blood sampling sites to exclude any cardiovascular shunts. Venous access for infusion of the inert gas solution was obtained through a small incision over the neck. The jugular vein was occlusively cannulated with PE 50 tubing, sutured in place and led to the exterior adjacent to the other tubing. The animals were then allowed to recover for 3 days prior to further testing.

A respiratory circuit was constructed as follows. PE tubing (size 120) was inserted in the animal's nares and secured with fast-drying epoxy resin to the top of the head. The PE tubing was then attached to a Y-connector, which in turn was connected to the mouth port of a miniature two-way non-rebreathing valve (Hans Rudolph 2300). Spiral plastic tubing (Vacuumed, 10 mm i.d.) connected the expiratory port of the valve to a pneumotachometer (Fleisch no. 00). Flow was measured using a differential pressure transducer (Validyne MP45), and the signal was digitized (Biopac, Goleta, CA, USA) and flow was integrated later to obtain volume. We checked for mouth-breathing in these animals by placing them in a sealed metabolic chamber and passing a continuous bias flow through the chamber to determine oxygen consumption ($\dot{V}_{O_2}$) and carbon dioxide production ($\dot{V}_{CO_2}$). These results were checked against simultaneously obtained values using the arrangement described above, with excellent agreement. Additionally, we placed a small piece of tubing connected to the CO_2 analyzer in front of the animal's mouth at rest and during exercise. No CO_2 production was detected during these measurements. Mixed expired gases were collected in a Mylar gas-impermeable bag, and oxygen and carbon dioxide concentrations were determined (Beckman OM-11, Sensormedics LB2 respectively).

Ventilation–perfusion distributions were obtained using the multiple inert gas elimination technique (Hlastala, 1984; Wagner *et al.* 1974*a*,*b*). A mixture of sulfur hexafluoride (SF_6), ethane, cyclopropane, enflurane, diethyl ether and acetone, dissolved in normal saline, was infused *via* the jugular vein (rate 0.2–0.6 ml min^{-1}). Mixed expired gases (to give a measure of $P\bar{E}$) were collected using the respiratory circuit previously described and transferred into gas-tight glass syringes. Duplicate 3 ml blood samples for the inert gas analysis were taken from the pulmonary artery (mixed venous blood, $P\bar{v}$) and left atrium (P_{LA}). Solubilities, retentions (equal to $P_{LA}/P\bar{v}$) and excretions (equal to $P\bar{E}/P\bar{v}$) for the inert gases were determined using gas chromatography (Hewlett-Packard 5890) (Wagner *et al.* 1974*a*,*b*). Hematocrit was measured for each sample.

$\dot{V}/\dot{Q}_L$ (ventilatory volume per unit time/blood flow through the lung) distributions were calculated from the inert gas data assuming an alveolar lung model. Using the multiple inert gas elimination technique, compartmental ventilation or blood flow to areas of different $\dot{V}/\dot{Q}_L$ ratios can be calculated and represented graphically. If $\dot{V}/\dot{Q}_L$ matching were perfect and no $\dot{V}/\dot{Q}_L$ heterogeneity were present, then all ventilation and blood flow would be at the overall $\dot{V}/\dot{Q}_L$ ratio and the standard deviation of the distributions would be zero. Since a wide range of $\dot{V}/\dot{Q}_L$ ratios are examined, it is conventional to use a logarithmic scale to represent these data, and the standard deviation of the perfusion distribution ($\log SD_{\dot{Q}}$) is used as an indicator of the degree of $\dot{V}/\dot{Q}_L$ heterogeneity. Arterial P_{O_2} (Pa_{O_2}) decreases and the alveolar–arterial P_{O_2} difference increases with increasing $\log SD_{\dot{Q}}$ (West, 1969).

Additional blood samples were obtained from the left atrium and pulmonary artery for measurement of the partial pressures of blood gases. Left atrial and pulmonary mixed venous P_{O_2}, P_{CO_2} and pH were measured at 35 °C (Radiometer BMS MK2). Blood-gas correction factors were determined by tonometry (IL213) of each animal's blood on the day of the experiment.

The animals were studied in a walk-in environmental chamber maintained at 35 °C. Resting samples were measured after leaving the animal covered and undisturbed on the treadmill described above for 30 min. A second set of measurements was made during exercise after the third minute of exercise at the highest speed that the animal could maintain for 4–5 min (0.8–1.0 km h^{-1}).

Data were analyzed for differences between rest and exercise with Student's *t*-test for paired groups. Student's *t*-test for single groups was used to test whether measured minus predicted left atrial P_{O_2} (P_{LAO_2}) was different from zero. Significance was accepted at $P<0.05$ (two-tailed). Results are reported as means ± S.E.M.

Results

Metabolic and ventilatory data

Mean metabolic and ventilatory data for all six animals are presented in Table 1. Treadmill exercise increased oxygen consumption by a factor of more than three and doubled

Table 1. *Ventilatory and metabolic data for* Varanus exanthematicus *at rest and during exercise*

	Rest	Exercise
Ventilation ($ml\,kg^{-1}\,min^{-1}$)	38.6±13.5	199.8±44.9**
Respiratory frequency (breaths min^{-1})	3.6±2.0	21.1±2.8**
Tidal volume ($ml\,kg^{-1}\,min^{-1}$)	14.3±2.8	11.8±3.6
Cardiac output ($ml\,kg^{-1}\,min^{-1}$)	51.6±13.1	98.1±24.9**
$\dot{V}_{O_2}$ ($ml\,kg^{-1}\,min^{-1}$)	0.92±0.19	3.33±0.77**
$\dot{V}_{CO_2}$ ($ml\,kg^{-1}\,min^{-1}$)	0.76±0.17	3.76±1.02**

Values are means ± S.E.M., N=6.
**Significant change from resting condition, P<0.01.

Table 2. *Effective lung* P_{O_2} *and arterial and mixed venous blood gas variables at rest and during exercise*

	Rest	Exercise
P_{LO_2} (mmHg)	110±5.3	127±4.3**
P_{LAO_2} (mmHg)	82±7	94±5
P_{LACO_2} (mmHg)	29.4±1.6	23.3±2.5*
pH_{LA}	7.40±0.05†	7.32±0.02†
$P\bar{v}_{O_2}$ (mmHg)	43±4	26±3
$P\bar{v}_{CO_2}$ (mmHg)	30.5±1.7	40.1±3.3*
$pH\bar{v}$	7.38±0.04†	7.20±0.05†

Values are means ± S.E.M., N=6.
†N=4 animals.
Significant changes from resting conditions are indicated by asterisks: *P<0.05, **P<0.01.
P_{LO_2}, effective lung P_{O_2}; P_{LAO_2}, left atrial P_{O_2}; P_{LACO_2}, left atrial P_{CO_2}; pH_{LA}, left atrial pH; $P\bar{v}_{O_2}$, mixed venous P_{O_2}; $P\bar{v}_{CO_2}$, mixed venous P_{CO_2}; $pH\bar{v}$, mixed venous pH.

Table 3. *Blood gas partition coefficients measured at 35 °C*

Sulfur hexafluoride, SF_6	0.00312±0.0003
Ethane	0.044±0.002
Cyclopropane	0.27±0.01
Enflurane	1.09±0.08
Diethyl ether	15.0±0.5
Acetone	753±107

Values are means ± S.E.M., N=6.

cardiac output. Mean respiratory exchange ratio increased from 0.81 at rest to 1.03 during exercise, indicating a heavy level of work for these animals. Tidal volume was unchanged, but there were significant increases in respiratory frequency (P<0.01) and ventilation (P<0.01).

Blood gases

Blood gas data are summarized in Table 2. There was a borderline increase in left atrial P_{O_2} (P_{LAO_2}) with exercise (P=0.06), associated with a significant fall in P_{LACO_2}, indicating hyperventilation and adequate gas exchange despite increasing metabolic demands. Effective lung P_{O_2} (P_{LO_2}) was calculated from the alveolar gas equation:

$$P_{LO_2} = P_{IO_2} - [1 - (1 - R)F_{IO_2}](P_{ACO_2}/R),$$

where R is the respiratory exchange ratio, P_{IO_2} is the partial pressure of inspired oxygen, F_{IO_2} is the fractional oxygen content of inspired air and P_{ACO_2} is the ideal lung P_{CO_2} (taken to be the same as left atrial P_{CO_2}). P_{LO_2} increased significantly with exercise to over 127 mmHg.

Ventilation–perfusion relationships

Blood gas partition coefficients for the six inert gases measured in each animal at 35 °C are presented in Table 3. The lower solubilities for SF_6, ethane and cyclopropane and higher solubilities for the remaining gases, compared with mammalian values, are probably an effect of the low hematocrits in these animals (18±6 %). Fig. 1 shows a typical measured $\dot{V}/\dot{Q}_L$ distribution at rest (Fig. 1A) and during exercise (Fig. 1B). Complete inert gas data were obtained on five animals and are summarized in Table 4. In one animal, the resting inert gas data were lost for technical reasons and therefore we report inert gas data for five animals only. The overall $\dot{V}/\dot{Q}_L$ ratio was 0.71 at rest and increased to 2.13 during exercise, reflecting a greater increase in ventilation than perfusion with exercise.

$\log_{S.D.}\dot{Q}_L$ increased with exercise, indicating increased heterogeneity of blood flow. Perfusion to areas of the lung with a low $\dot{V}/\dot{Q}_L$ ratio ($\dot{V}/\dot{Q}_L$ ratio less than 0.1) was less than 3 % of total cardiac output at rest and decreased further with exercise to 1.2 %. The intrapulmonary shunt was significantly reduced with exercise from 5.8 % at rest to 1.9 %, accompanied by a significant reduction in venous admixture. Inert gas dead space includes anatomical dead space and instrument dead space in contrast to physiological dead space, which also includes ventilation to some areas with a high $\dot{V}/\dot{Q}_L$ ratio. Inert gas dead space was corrected for the dead space of the rebreathing valve (0.8 ml); it averaged 25 % at rest and showed a trend towards reduction with exercise (P=0.08).

Pulmonary diffusion limitation

Left atrial P_{O_2} was predicted for each of the five animals for which complete inert gas data had been obtained, at rest and during exercise, based on the observed $\dot{V}/\dot{Q}_L$ distribution and intrapulmonary shunt and assuming diffusion equilibrium. We used the data of Wood *et al.* (1977) and Hicks *et al.* (1987) to modify the computer subroutines of the inert gas program to allow for the differences in shape between the varanid lizard oxygen–hemoglobin dissociation curve and that of mammals. When observed P_{LAO_2} is less than the predicted value, this can be argued to represent pulmonary diffusion limitation (Hopkins *et al.* 1994; Torre-Bueno *et al.* 1985). No evidence of pulmonary diffusion limitation was observed at rest because the measured–predicted P_{LAO_2} was not significantly different from zero. During exercise, however, observed P_{LAO_2} averaged 13.9 mmHg less than predicted P_{LAO_2} and was

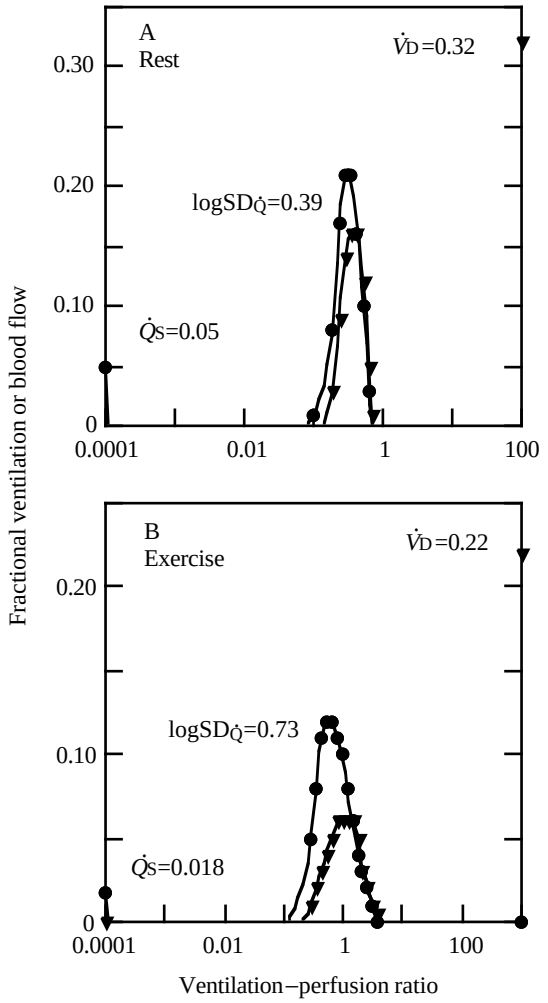

Fig. 1. Fractional ventilation (filled triangles) and blood flow (filled circles) *versus* ventilation–perfusion ratio at rest (A) and during exercise (B). These are representative distributions measured in one animal. $\dot{V}_D$, fractional dead space ventilation; $\dot{Q}_S$, fractional shunt; logSD$_{\dot{Q}}$, standard deviation of the perfusion distribution (log scale).

significantly different from zero (P<0.01). This indicates diffusion limitation at high workloads (see Table 4).

Incomplete intrapulmonary gas mixing

The goodness of fit of the retention and excretion data to the predicted $\dot{V}/\dot{Q}_L$ distribution is given by the residual sum of squares (RSS; Table 4). This averaged 17.5 at rest, which is higher than that predicted for six inert gases from random experimental error. As we address in the Discussion, this may be a result of incomplete intraregional gas mixing in the lung (stratified inhomogeneity). The error (ϵ) between the measured retention and best-fit retention, for enflurane, the heaviest gas, and cyclopropane, the lightest gas, is predicted to be positive with incomplete intrapulmonary gas mixing (Powell and Gray, 1989). ϵ was always positive in data sets with high sums of squares and was significantly greater at rest than during exercise.

Table 4. *Inert gas data at rest and during exercise*

	Rest	Exercise
Residual sum of squares	17.5±3.9	3.1±1.2
ϵ enflurane minus ϵ cyclopropane	4.92±0.78	1.84±0.30**
Intrapulmonary shunt (% of cardiac output)	5.8±1.0	1.9±0.5*
Inert gas dead space (% of ventilation)	25±9	9±4
Standard deviation of perfusion distribution	0.39±0.06	0.78±0.05**
P_{LAO_2} predicted by inert gas analysis (mmHg)	73±4	106±5**
P_{LAO_2} observed minus P_{LAO_2} predicted (mmHg)	0±2.3	–13.9±5.6†

Values are means ± S.E.M., N=5.

Significant changes from resting conditions are indicated by asterisks: *P<0.05, **P<0.01.

†Significantly different from zero, P<0.01.

ϵ, error between the measured retention and best-fit retention, an index of incomplete gas mixing.

P_{LAO_2}, left atrial P_{O_2}.

Discussion

This study reports the first investigation of pulmonary gas exchange using the multiple inert gas elimination technique and the first direct measurements of expired ventilation ($\dot{V}_E$) in awake, unrestrained resting and maximally exercising lizards. The multiple inert gas elimination technique allows us to distinguish between spatial $\dot{V}/\dot{Q}_L$ heterogeneity, intrapulmonary shunting and diffusion limitation as causes of decreased O_2 transfer across the lung in a variety of experimental situations including exercise. On the basis of differences in lung structure, we hypothesized that lizards would have a greater pulmonary diffusion limitation during exercise than that observed in mammals and that the ventilation–perfusion heterogeneity would be correspondingly smaller. However, this was not observed. Although the varanid lung is subdivided to a smaller extent than alveolar mammalian lungs, we did not observe appreciably better or worse spatial $\dot{V}/\dot{Q}_L$ matching compared with that in mammals.

Although oxygen consumption during exercise is less than reported by Gleeson *et al.* (1980), we were able to elicit an almost fourfold increase in oxygen consumption, associated with a doubling of pulmonary blood flow, at similar treadmill speeds (0.8–1.0 km h^{-1}). However, these speeds were not sustainable speeds for our animals as they were for Gleeson *et al.* (1980). Our animals could only run at these speeds for 5 min. Lower $\dot{V}_{O_2}$ in our animals may reflect the prolonged period of captivity prior to the study, resulting in detraining. As explained above, the low $\dot{V}_{O_2}$ was not due to loss of ventilatory gases through the mouth.

Ventilation during exercise

We found increasing pulmonary ventilation adequate for the metabolic demands of heavy exertion in these animals. Carrier

(1987) suggested that the pulmonary system of varanid lizards may be mechanically limited by locomotion during exercise, as shown by a decreasing tidal volume with increasing running speed. In our animals, the tidal volume was unchanged and ventilatory frequency increased with exercise, resulting in an increase in $\dot{V}_E$. In a series of preliminary experiments, we measured ventilation and $\dot{V}_{O_2}$ in four animals at different treadmill speeds. In all cases, ventilation increased with increasing treadmill speed up to the maximal speed that the animal could sustain for 1 min. Also, if a mechanical constraint limited ventilation, then an increase in P_{LACO_2} and decrease in P_{LAO_2} would be expected as a result of relative hypoventilation. Such was not the case, as hypocapnia during exercise confirmed hyperventilation. Mitchell *et al.* (1981) also observed an increase in arterial P_{O_2} (Pa_{O_2}) and a fall in arterial P_{CO_2} (Pa_{CO_2}) in their animals during exercise.

Ventilation–perfusion heterogeneity and intrapulmonary shunts

One of the most striking aspects of this study is the remarkable similarity of ventilation–perfusion matching in these exercising reptiles compared with exercising mammals. In mammalian lungs, $\log SD_{\dot{Q}}$ at rest is approximately 0.4 (Gale *et al.* 1985; Wagner *et al.* 1975, 1989). During exercise, $\log SD_{\dot{Q}}$ increases to almost 0.7 in highly athletic humans (Hopkins *et al.* 1994). However, such marked increases in heterogeneity have not been reported for some species, such as the horse (Wagner *et al.* 1989) and the dog (Sylvester *et al.* 1981).

The reason for the development of $\dot{V}/\dot{Q}_L$ heterogeneity during exercise in any species is unknown. It has been postulated to represent decreased hypoxic pulmonary vasoconstriction, secondary to increased pulmonary blood flow or representing early or subclinical pulmonary edema (Schaffartzik *et al.* 1992). We cannot rule out pulmonary edema as an explanation for the increased $\dot{V}/\dot{Q}_L$ heterogeneity with exercise in these reptiles. Low-frequency breathing, such as we observed at rest, would be expected to cause temporal $\dot{V}/\dot{Q}_L$ heterogeneity and would be interpreted as spatial $\dot{V}/\dot{Q}_L$ heterogeneity by the inert gas analysis. However, this would very slightly overestimate the $\dot{V}/\dot{Q}_L$ heterogeneity at rest and underestimate the increase with exercise.

The only substantive difference between the $\dot{V}/\dot{Q}_L$ distributions obtained from these lizards and mammalian distributions was a modest intrapulmonary shunt of about 5 % at rest, which decreased to less than 2 % during exercise. The resting intrapulmonary shunt is much smaller than the values obtained by Hlastala *et al.* (1985) in the anesthetized tegu lizard *Turinambis nigropunctatus*, and the values of almost 30 % obtained by Powell and Gray (1989) in anesthetized, pump-ventilated alligators. Since we found that the intrapulmonary shunt decreased when pulmonary blood flow increased in our animals, the higher intrapulmonary shunt observed in the alligator and tegu lizard may be a result of the lower cardiac output and pulmonary flows in those prior studies. Seymour (1983) quantified the intrapulmonary shunt in the turtle breathing 100 % O_2 at about 10 % of total pulmonary blood flow, which is similar to values obtained in the present study. Note that the left atrial sampling site for arterial blood in the present study excludes any contribution of intracardiac shunting to these measurements.

Pulmonary diffusion limitation

Pulmonary diffusion limitation is detected as the difference between the measured P_{LAO_2} and the P_{LAO_2} predicted for the $\dot{V}/\dot{Q}_L$ distribution assuming diffusion equilibrium. This difference represents that portion of the observed lung–arterial difference not explained by $\dot{V}/\dot{Q}_L$ heterogeneity or intrapulmonary shunting and it is used to quantify pulmonary diffusion limitation (Torre-Bueno *et al.* 1985). Although we found no discrepancy between observed and predicted values for P_{LAO_2} at rest, the difference was about 14 mmHg during exercise, suggesting pulmonary diffusion limitation with heavy exercise. This value is similar to that observed in humans capable of sustaining high metabolic rates, in which rapid pulmonary transit times are considered to be an important factor determining end capillary diffusion equilibrium (Hammond *et al.* 1986; Hopkins *et al.* 1994). In varanid lizards, the lower surface area for diffusion and the increased thickness of the blood gas barrier (Perry, 1983) are additional contributors. An alternative explanation for the discrepancy between the observed and predicted P_{O_2} is the extrapulmonary shunt (e.g. bronchial arteries and thebesian veins). This effect is very small (Hlastala *et al.* 1975).

Incomplete intrapulmonary gas mixing

Incomplete intrapulmonary gas mixing at rest was suggested by high residual sum of squares (RSS). The RSS, the difference between the measured retention and the predicted retention for the $\dot{V}/\dot{Q}_L$ distribution, is expected to be less than 5 for six gases, given random experimental error (Powell and Wagner, 1982). The high RSS we calculate for our animals at rest is not likely to be due to technical problems with processing the inert gas samples since the RSS values (mean 3.1±1.2) during exercise were always within the expected range. The error (ϵ) between the measured retention and the best-fit retention for enflurane, the heaviest gas, and cyclopropane, the lightest gas, is expected to increase in the presence of incomplete intrapulmonary gas mixing, as the retention of the heaviest gas will be increased in contrast to gases of low molecular mass (Downs and Wagner, 1983). An acceptable approach to determine whether ϵ enflurane minus ϵ cyclopropane is suggestive of incomplete intrapulmonary gas mixing is to compare the recovered errors with a similar data set in which the data do fit the model. Such was the case with the data obtained during exercise, where mean ϵ enflurane minus ϵ cyclopropane was 1.84, not significantly different from zero. At rest, however, the difference averaged 4.92, which was significantly different from rest ($P<0.005$), suggesting the presence of inhomogeneity of gas mixing within the lung.

Incomplete intrapulmonary gas mixing can be expected to distort the recovered $\dot{V}/\dot{Q}_L$ distributions such that $\log SD_{\dot{Q}}$ is reduced in the main $\dot{V}/\dot{Q}$ mode, with increases in perfusion to

areas of low and high $\dot{V}/\dot{Q}_L$ (Hlastala *et al.* 1981; Scheid *et al.* 1981). To determine the effect of incomplete intrapulmonary gas mixing on the recovered distribution, we repeated the analysis with the elimination of enflurane. Although the RSS was reduced to 11.9±3.9 (N=5), the change altered the recovered distributions only slightly and log S.D.$\dot{Q}_L$ at rest increased from 0.39 to 0.41 and the intrapulmonary shunt increased by 0.2 %. Therefore, the effect of incomplete intrapulmonary gas mixing under these conditions is minimal and does not alter the conclusions reached. Oxygen and carbon dioxide, which have molecular masses an order of magnitude smaller than that of enflurane, would probably not be affected by this small, albeit detectable, degree of incomplete intrapulmonary gas mixing.

The difficult experimental conditions might also affect the RSS, particularly because of problems in maintaining steady-state conditions at rest as a result of the long sampling time. Samples were collected over 3 min to allow for adequate expired gas samples to be obtained, and it is possible that pulmonary flows could have changed over the collection period.

Arterial blood gases and effective lung–left atrial P_{O_2} *difference*

During exercise, left atrial P_{O_2} was maintained, or even increased, in the face of worsening $\dot{V}/\dot{Q}_L$ heterogeneity and diffusion limitation. This was accomplished by a reduction in venous admixture, by a reduction in perfusion to areas of low $\dot{V}/\dot{Q}_L$ and intrapulmonary shunt and by increasing effective lung P_{O_2} through hyperventilation. At rest, an effective lung–left atrial P_{O_2} of 27 mmHg was observed, which did not increase appreciably with exercise. Similar results to those of the present study were obtained by Mitchell *et al.* (1981), who measured blood gas levels and calculated effective lung ventilation in *Varanus exanthematicus* and *Iguana iguana.* They postulated that the wide effective lung–arterial difference observed during exercise was related to pulmonary diffusion limitation and cardiac shunting. No information on cardiac shunting was obtained in the present study, as the placement of the catheters was designed to exclude cardiac shunts. However, evidence of diffusion limitation, as shown by a discrepancy between observed and predicted P_{LAO_2}, was seen during exercise. Also, as previously noted, marked $\dot{V}/\dot{Q}_L$ heterogeneity was observed during exercise and, together with intrapulmonary shunting, it can be considered to be an important contributor to the effective lung–left atrial P_{O_2} difference observed, with the relative contributions from each varying with the experimental condition.

In conclusion, we found mammalian-like ventilation–perfusion distributions at rest and with exercise in varanid lizards. The main difference was a 5 % intrapulmonary shunt in lizards at rest, which was reduced significantly with exercise. Arterial oxygenation was maintained during heavy exercise and relative hypocapnia was present, indicating adequate ventilation. These findings indicate the lung structure is well matched to metabolic capacity in varanid lizards and they suggest that pulmonary gas exchange does not limit their active behavior patterns in the wild any more than it does in mammals.

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