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Hypoxic pulmonary vasoconstriction in reptiles: a comparative study of four species with different lung structures and pulmonary blood pressures

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Skovgaard, Nini, Augusto S. Abe, Denis V. Andrade, and Tobias Wang. Hypoxic pulmonary vasoconstriction in reptiles: a comparative study of four species with diverse lung structures and pulmonary blood pressures. Am J Physiol Regul Integr Comp Physiol 289: R1280–R1288, 2005. First published June 16, 2005; doi:10.1152/ajpregu.00200.2005.—Low O₂ levels in the lungs of birds and mammals cause constriction of the pulmonary vasculature that elevates resistance to pulmonary blood flow and increases pulmonary blood pressure. This hypoxic pulmonary vasoconstriction (HPV) diverts pulmonary blood flow from poorly ventilated and hypoxic areas of the lung to more well-ventilated parts and is considered important for the local matching of ventilation to blood perfusion. In the present study, the effects of acute hypoxia on pulmonary and systemic blood flows and pressures were measured in four species of anesthetized reptiles with diverse lung structures and heart morphologies: varanid lizards (Varanus exanthematicus), caimans (Caiman latirostris), rattlesnakes (Crotalus durissus), and tegu lizards (Tupinambis merianae). As previously shown in turtles, hypoxia causes a reversible constriction of the pulmonary vasculature in varanids and caimans, decreasing pulmonary vascular conductance by 37 and 31%, respectively. These three species possess complex multicameral lungs, and it is likely that HPV would aid to secure ventilation-perfusion homogeneity. There was no HPV in rattlesnakes, which have structurally simple lungs where local ventilation-perfusion inhomogeneities are less likely to occur. However, tegu lizards, which also have simple unicameral lungs, did exhibit HPV, decreasing pulmonary vascular conductance by 32%, albeit at a lower threshold than varanids and caimans (6.2 kPa oxygen in inspired air vs. 8.2 and 13.9 kPa, respectively). Although these observations suggest that HPV is more pronounced in species with complex lungs and functionally divided hearts, it is also clear that other components are involved.

hypoxia; pulmonary circulation; systemic circulation

LOW OXYGEN LEVELS IN THE LUNGS of birds and mammals cause constriction of the pulmonary vasculature that elevates resistance to pulmonary blood flow (Q̇_{pul}) and increases pulmonary blood pressure (3, 14, 43). This hypoxic pulmonary vasoconstriction (HPV) diverts Q̇_{pul} from poorly ventilated and hypoxic areas of the lung to more well-ventilated parts. Therefore, HPV is considered important for local matching of ventilation to blood perfusion, which improves pulmonary gas exchange and maintains arterial P_{O₂} (4, 12, 43). The primary site of the hypoxic vasoconstriction is the precapillary muscular pulmonary arteries (45).

HPV is a locally mediated response that persists in isolated and perfused lungs with no neurohumoral influences and also occurs in isolated rings of vascular smooth musculature (15, 37). The constriction is intrinsic to the vascular smooth muscle surrounding the small resistance vessels and is likely to be mediated by inhibition of one or several different types of K⁺ channels, with various endothelium-derived vasoactive compounds acting as modulators (25, 44, 45, 46). In contrast, the systemic circulation of most vertebrates responds to hypoxia by vasodilatation (10, 13, 38, 41).

The need for local matching of ventilation and perfusion is likely to increase as the lung structure becomes more complex (36). Hence, it is possible that, in the transition from the structurally simple lungs of reptiles to more complex lungs in mammals, local and humoral regulations of the pulmonary circulation are increasingly important. In contrast to mammals, the role of humoral and local factors in cardiovascular control remains largely unknown in reptiles. Recent studies, nevertheless, indicate that the pulmonary circulation is much less responsive to humoral and local factors than the systemic circulation (8, 9, 11, 16, 35, 40).

Lung structure and heart morphology vary substantially among reptiles. Most snakes and many lizards have unicameral and simple lungs, whereas the multicameral lungs in turtles, varanid lizards, and crocodilians are more complex and compartmentalized (26, 31, 32, 34). The higher complexity allows for smaller gas exchange units and increased surface area, which increases pulmonary diffusive capacity for O₂ but may also render the lungs more prone to local mismatching of ventilation to perfusion [ventilation-perfusion (V̇_{A}/Q̇_{pul}) inhomogeneity] (36). Turtles exhibit HPV (10), but no other reptiles have been studied. In most noncrocodilian reptiles, the ventricle is anatomically and functionally undivided, so blood pressures are equal in systemic and pulmonary circulations (e.g., Ref. 20). Therefore, blood flow distribution between pulmonary and systemic circulations is primarily determined by pulmonary and systemic vascular resistances, respectively (10, 20), and HPV would increase the right-to-left cardiac shunt in animals with an undivided heart. This would reduce the ability to exploit the pulmonary oxygen reserve, which would be further aggravated in animals with periodic ventilation, where P_{O₂} decreases in the lung during breath hold. Thus we hypothesize that HPV has evolved in groups of reptiles that have functionally divided hearts and morphologically complex lungs.

In the present study, the effects of acute hypoxia on pulmonary and systemic blood flows and pressures were measured in four species of anesthetized reptiles with diverse lung struc-
tasures and heart morphologies: rattlesnakes (Crotalus durissus) and tegu lizards (Tupinambis merianae), which possess an undivided ventricle and a simple lung structure; caimans (Caiman latirostris), which have an anatomically divided ventricle and complex lung structure; and varanid lizards (Varanus exanthematicus), which possess functionally divided ventricles and morphologically complex lungs. The study was performed on anesthetized animals to reduce cardiovascular reflexes involving the central nervous system and therefore to reduce the possibilities that the observed responses are due to stimulation of, for example, vascular chemoreceptors. To investigate whether changes in vagal tone on the pulmonary vasculature (e.g., Refs. 5, 28) were altered during hypoxia, we characterized the hypoxic responses before and after a pharmacological blockade of the muscarinic receptors by atropine.

MATERIALS AND METHODS

Experimental Animals

Experiments were performed on six tegu lizards (Tupinambis merianae), six rattlesnakes (Crotalus durissus), seven caimans (Caiman latirostris), and seven varanid lizards (Varanus exanthematicus). The tegu lizards were captive bred at UNESP (Rio Claro, Brazil) and freighted to the Department of Zoophysiology, University of Aarhus (Aarhus, Denmark), where experiments were conducted. They had body masses ranging between 0.83 and 3.0 kg (1.36 ± 0.34 kg, mean ± SE). Varanid lizards with body masses between 0.33 and 1.02 kg (0.66 ± 0.12 kg) were obtained from Danish commercial suppliers, and experiments were performed at the University of Aarhus. Studies on rattlesnakes and caimans were carried out at UNESP. Rattlesnakes with body masses ranging from 0.53 to 1.5 kg (0.81 ± 0.16 kg) were obtained from the Butantan Institute (São Paulo, Brazil) and transported to UNESP. Caimans were captive bred at UNESP and had body masses between 0.73 and 1.4 kg (0.94 ± 0.08 kg). Rattlesnakes were held in vivaria and caimans in outdoor pens at 27 ± 5°C, with free access to water. Food was withheld 3 days before experiments. All animals appeared healthy, and experiments were carried out according to Danish and Brazilian federal regulations.

Anesthesia

Tegu lizards, rattlesnakes, and caimans were anesthetized with an intramuscular injection of pentobarbital sodium (30 mg/kg for rattlesnakes and 50 mg/kg for tegu lizards and caimans; Mebumal, Syeghusapotekerne, Denmark). Corneal and pedal withdrawal reflexes disappeared within 15–45 min. Because of their low tolerance of hypoxia, varanid lizards were rapidly anesthetized by inhalation of isoflurane vapor (Isofluran, Baxter, Denmark) by placing a plastic bag over their heads. During the initial surgery, the varanid lizards were ventilated with room air containing 1% isoflurane; however, when the first cannulation was finished, an intra-arterial injection of pentobarbital sodium (Mebumal; 50 mg/kg) was given, and the isoflurane was turned off. Tegu lizards and caimans were intubated, whereas rattlesnakes and varanid lizards were tracheotomized for artificial ventilation using a Harvard Apparatus mechanical ventilator at 15–20 breaths/min and a tidal volume of 50–100 ml/kg with 3% CO2 balance air.

Surgery and Instrumentation

Because of anatomical differences among the different species and because experiments were performed at different places, the surgeries and instrumentation differed slightly between the four species.

Varanid lizards. To access the central vascular blood vessels, a 5-cm incision was made through the sternum. The left carotid artery was occlusively cannulated with a PE-50 catheter containing heparinized saline for measurement of systemic arterial blood pressure, and a branch of the left pulmonary artery was occlusively cannulated (PE-50) for measurement of pulmonary arterial blood pressure. Transit-time ultrasonic blood flow probes (25 or 2R; Transonic System) were placed around the left pulmonary and the left aortic arch for measurements of blood flows.

Tegu lizards. A 5-cm ventral incision was made through the sternum, leaving the pericardium intact. For measurement of pulmonary blood pressure, a branch of the left pulmonary artery was occlusively cannulated, and a blood flow probe was placed around the common pulmonary vein for measurement of total Qpul.

Rattlesnakes. A small incision was made cranial to the heart, and a PE-50 catheter was advanced into the right aortic arch through the vertebral artery for measurement of systemic blood pressure. For measurement of pulmonary blood pressure, a small branch of the pulmonary artery supplying the lower part of the lung was occlusively cannulated. In addition, for measurement of right and left atrial pressures (PRAI and PLa), the right atrium and left atrium were cannulated in three animals using a flared PE-60 catheter containing heparinized saline, which was advanced into the atrium through a small incision in the atrial walls and secured with a suture. Transit-time ultrasonic blood flow probes (25 or 2R; Transonic System) were placed around the left aortic arch and the pulmonary artery.

Caimans. A 5-cm ventral incision was made through the sternum. For measurement of systemic blood pressure, the right carotid artery was occlusively cannulated using a PE-50 catheter containing heparinized saline. To measure pulmonary blood pressure, the common pulmonary artery was nonocclusively cannulated with a flared PE-60 catheter advanced through a small incision in the artery wall and secured with a suture. PRAI and PLa, respectively were measured in three animals using a flared PE-60 catheter, which was advanced into the atrium through a small incision in the atrial walls and secured with a suture. For measurements of blood flows, probes were placed around the left pulmonary arch and the left subclavian artery.

All catheters were connected to disposable pressure transducers (model PX600; Baxter-Edwards, Irvine, CA), and signals were amplified using an in-house-built preamplifier. Acoustical gel was infused around the blood flow probes to enhance the signal. Flow probes were connected to a Transonic dual-channel flow meter (T206). The pressure transducers were positioned at the level of the heart of the animal and were calibrated daily against a static water column.

Signals from the pressure transducer and the blood flow meter were recorded with a Biopac MP100 data-acquisition system (Biopac Systems, Goleta, CA) at 100 Hz.

Calculation of Blood Flows, Stroke Volumes, and Vascular Conductances

Measurements of blood flow in the common pulmonary vein in the tegu lizard represent total Qpul. Because there is only one pulmonary artery in the rattlesnake, measurements of blood flow in the pulmonary artery represents Qpul. Total systemic blood flow (Qsys) in the rattlesnake can be estimated as 3.3 times blood flow in the left aortic arch (17). Qpul in caimans and varanid lizards was calculated as two times blood flow in the left pulmonary artery under the assumption that Qpul is distributed evenly between the left and right pulmonary artery. Total cardiac output was calculated as Qsys + Qpul. Heart rate (fh) was calculated from the instantaneous blood flow trace, and total stroke volume (pulmonary + systemic) was calculated as total cardiac output/fh.

When baseline blood flow changes more than baseline blood pressure, which is the case in most in vivo situations, conductance provides a better index for comparing vascular tone than resistance (24, 29). Pulmonary and systemic conductance (Gpul and Gsys, respectively) were calculated from mean blood flow and mean blood pressure (Gpul = Qpul/Ppul and Gsys = Qsys/Psys, where Ppul and Psys were obtained using a pressure transducer placed around the left pulmonary artery and the left aortic arch, respectively).
are pulmonary and systemic pressure, respectively), assuming that central venous blood pressures are negligible.

Experimental Protocols

During experiments, the animals were artificially ventilated using a Harvard Apparatus mechanical ventilator at 15–20 breaths/min and a tidal volume of 50–100 ml/kg. Because the animals were hyperventilated, Pco2 of inspired air was maintained at 0.03 kPa during all experiments to keep arterial pH constant. Gases of desired composition were delivered to the ventilator by a Cameron Instrument gas mixer or a Wösthoff (Bochum, Germany) gas-mixing pump. Hemodynamic variables stabilized over a period of 30–45 min after instrumentation, and the animals were then exposed to progressive levels of hypoxia through a reduction in PO2 of inspired air (Poxi) (turtles: 13.7, 10.3, 8.2, 6.2 kPa; varanid lizards: 13.9, 10.3, 8.2, 6.2, 5.6 kPa; turtles and caimans: 13.9, 9.2, 7.4, 5.5, 3.7, 1.8 kPa). Each gas mixture was administered for 20 min, and the animals were then returned to normoxia.

After hypoxic exposures, atropine (3 mg/kg) was administered through the systemic catheter in caimans and rattlesnakes and was allowed to take effect for 30 min. The lowest levels of hypoxia (turtles: 3.7, 1.8 kPa; caimans: 5.5, 3.7, 1.8 kPa) were then repeated. Experiments were carried out at 25 ± 3°C.

Data Analyses and Statistics

We analyzed data using AcqKnowledge data analysis software (version 3.7.1; Biopac). Mean pressure and mean blood flow were taken over a 3-min period, at the end of each period of treatment. All data are presented as means ± SE. Effects on hemodynamic variables were assessed by a one-way ANOVA for repeated measures followed by a Dunnett’s post hoc test to identify values that were significantly different from values obtained during normoxia. Differences between resting values and recovery values were assessed using paired t-tests. A limit for significance of P < 0.05 was applied.

RESULTS

In the tegu lizards, hypoxia led to a decrease in Gpul from 7.2 ± 0.9 to 4.9 ± 1.3 ml·min⁻¹·kg⁻¹·kPa⁻¹ (32%) when Pto2 was reduced to 6.2 kPa (Fig. 1C). This pulmonary constriction was reverted when the animals were returned to normoxia (Fig. 1C). There were no changes in Ppul and Qpul, but fH was significantly reduced at 6.2 kPa and did not recover at return to normoxia (Fig. 1).

In the rattlesnakes, inhalation of hypoxic gas mixtures increased Gsys, attended by a decrease in Psys and a rise in Qsys (Fig. 2, A–C). The dilation, however, persisted on return to normoxia. Hypoxia had no effect on Gpul, but there was a decrease in Ppul and Qpul, indicating an increased right-to-left cardiac shunt caused by the systemic vasodilatation (Fig. 2, D–F). This is also apparent from the reduction in the shunt fraction (Qpul/Qsys), which decreased from 0.8 ± 0.2 to 0.4 ± 0.1 at 1.8 kPa (Fig. 3D). The fH increased progressively during hypoxia, but there were no changes in total stroke volume or total cardiac output (Fig. 3, A–C). Infusion of atropine, following the exposure to hypoxia, did not affect any of the hemodynamic variables in normoxia. During subsequent exposure to hypoxia, most responses were not affected, but the progressive decline in Psys and rise in Gsys were no longer manifested.

Table 1 shows the Pkai and Plai in three turtles that breathed normoxic air and then were exposed to progressive levels of hypoxia. The low n values did not allow for statistical analysis, but it appears that the atrial pressures remained unchanged during hypoxia (mean Pkai of 0.52 ± 0.01 kPa and mean Plai of 0.63 ± 0.01 kPa).

In the caimans, Psys decreased during hypoxia, although there were no changes in left subclavian blood flow, Gsys, and fH (Figs. 4, A–C, and 5). Hypoxia caused a pulmonary vasoconstriction, apparent as a decrease in Gpul from 12.9 ± 1.9 to

![Fig. 1. Effects of hypoxia on the pulmonary circulation in the tegu lizard (Tupinambis merianae). Pulmonary arterial blood pressure (Ppul; A), pulmonary blood flow (Qpul; B), pulmonary vascular conductance (Gpul; C), heart rate (fH; D), and inspired PO2 (Poxi) results are shown. *Significantly different from the normoxic results; †significant difference between recovery values and initial normoxic values (P < 0.05). Values are means ± SE (n = 6).](image-url)
8.9 ± 0.6 ml·min⁻¹·kg⁻¹·kPa⁻¹ (31%); this was attended by an increase in Ppul, whereas Q˙pul remained stable (Fig. 4, D–F). The threshold for the vasoconstriction was 13.9 kPa. Infusion of atropine did not affect hemodynamic variables in normoxia and during subsequent exposure to hypoxia.

Table 2 shows that PLA in three caimans did not change in normoxic air and progressive hypoxia.

In the varanid lizards, hypoxia decreased Psys and fH, whereas there were no changes in blood flow in the left aortic arch or Gsys (Figs. 6, A–C, and 7). Psys and fH did not recover when the animals were put back on normoxia. Hypoxia elicited a decrease in Gpul from 16.8 ± 3.3 to 10.6 ± 1.8 ml·min⁻¹·kg⁻¹·kPa⁻¹ (37%) followed by a decrease in Qpul but no changes in Ppul (Fig. 6, D–F). The threshold for HPV was 8.2 kPa, and Gpul recovered to basal values when the lizards were returned to normoxic air.

**DISCUSSION**

The present study describes HPV in four different species of reptiles with different lung structure and heart morphologies. These species were selected to investigate the hypothesis that HPV is most pronounced in reptilian species with structurally complex lungs where VA/Q inequalities are more likely to occur. At the same time, we hypothesized that animals with an undivided ventricle, where the blood flow distribution between the systemic and pulmonary circulations is determined by the vascular resistances and constriction of the pulmonary vasculature would induce a right-to-left cardiac shunt, are less likely to exhibit HPV.

As previously shown in turtles (10), hypoxia caused a reversible constriction of the pulmonary vasculature in varanids and caimans. These three species possess complex multicameral lungs where HPV would aid to secure VA/Q homogeneity. There was no response in rattlesnakes, which is consistent with the view that species with structurally simple lungs are less prone to VA/Q inhomogeneities and therefore are less dependent on local responses for proper VA/Q matching. However, tegu lizards that also have simple unicameral lungs did exhibit HPV, albeit at a lower threshold than varanids and caimans. Thus, although the data support our general hypothesis that HPV is more pronounced in species with complex lungs and divided hearts, it is also clear that other factors are involved.

In mammals, it is well established that HPV is locally mediated and that the primary site of constriction is the small resistance arteries (15, 37, 46). In reptiles, Gpul can also be

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Fig. 2. Effects of hypoxia before and after a bolus injection of atropine (3 mg/kg) on hemodynamic parameters in the rattlesnake (Crotalus durissus). Systemic arterial blood pressure (Psys; A), systemic blood flow (Q˙sys; B), systemic vascular conductance (Gsys; C), Ppul (D), Qpul (E), and P02 results are shown. *Significantly different from the normoxic results; †significant difference between recovery values and initial normoxic values (P < 0.05). Values are means ± SE (n = 6).
altered through a vagally mediated constriction of the pulmonary artery (e.g., Refs. 5, 28); however, vagal tone is normally low or even absent in reptiles anesthetized with barbiturates (e.g., Refs. 10, 16). Furthermore, because the hypoxic responses persisted after muscarinic receptor blockade by atropine in caimans (Fig. 4F) and in turtles (10), it is reasonable to conclude that the decrease in $G_{\text{pul}}$ during hypoxia in our study does reflect a local vasoconstriction of resistance vessels in response to low oxygen.

In mammals, it is well documented that acute exposure to hypoxia causes a sustained rise in pulmonary arterial pressure (42). Nevertheless, it is conductance of the pulmonary vasculature that is the determining factor. In fact, pressure alone cannot reveal HPV because cardiac contractility or other factors could affect pulmonary pressure without conductance being changed. Furthermore, in reptiles, where the ventricle of most species is undivided, pulmonary pressure is also determined by systemic resistance. Thus, during hypoxia, when the systemic vasculature normally dilates, it is quite conceivable that pulmonary pressure could decline, even though this part of the pulmonary circulation constricts.

**Critique of Methods**

To calculate vascular conductance as conductance = flow/pressure, we assumed that central venous pressures are negligible. This assumption is potentially problematic in low pressure systems and could underestimate systemic and pulmonary conductances if atrial pressures are high; the higher the atrial pressures, the higher the conductances (2). We measured $P_{\text{LAt}}$ in three rattlesnakes and three caimans (Tables 1 and 2). In caimans, the $P_{\text{LAt}}$ of 0.7 kPa does significantly underestimate $G_{\text{pul}}$; however, because it was only measured in three of the seven animals, we did not subtract $P_{\text{LAt}}$ in the calculation of $G_{\text{pul}}$. Importantly, $P_{\text{LAt}}$ did not change during hypoxia in either caimans or rattlesnakes; therefore, the changes in $G_{\text{pul}}$ in response to hypoxia are not due to altered atrial pressures but a change within the pulmonary circulation.

**HPV in Reptiles**

Both varanid lizards and caimans have functionally divided ventricles with mammalian-like high pressures in the systemic circulation and low pulmonary pressures (7, 23); furthermore, they have highly complex multicameral lungs with multiple subdivisions, but a fairly shallow edicular respiratory parenchyma (32, 33, 34). In both species, hypoxia elicited a 35% decrease in $G_{\text{pul}}$, which led to an increase in pulmonary pressure in the caiman, whereas $Q_{\text{pul}}$ decreased in the varanid lizards. Millard and Johansen (27) previously showed that pulmonary arterial pressure increases when nonanesthetized *Varanus niloticus* were breathing hypoxic gases. In our experiment, the threshold for the response was lower in the varanids compared with the caimans (8–10 and 14 kPa $P_{O_2}$, respectively). The threshold for the caiman is certainly within the range of normal lung $P_{O_2}$ values during breath hold (e.g., Refs. 18, 19). Anesthetized turtles (*Trachemys scripta*) also exhibit a marked HPV, but this response only occurred in severe hyp-
oxia (1.5–3 kPa PO2) (10). Turtles have structurally complex lungs (31), but, contrary to the caimans and varanid lizards, their ventricles are undivided, and HPV, accordingly, increases the right-to-left cardiac shunt (10). During normoxia, V/A/Q inhomogeneity decreases with increased Qpul in anesthetized turtles (21); therefore, it is possible that the lower pulmonary blood flow that occurs as a consequence of HPV could, in itself, affect V/A/Q matching.

The rattlesnake and the tegu lizard have undivided ventricles and, consequently, equal pressures in systemic and pulmonary circulation (Ref. 16; N. Skovgaard and T. Wang, unpublished observations on tegus). Their lungs are unicameral with a central air-filled cavity that opens radially into the parenchyma (26, 32). The faveolar parenchyma has deep honeycomb-shaped respiratory units, which are heterogeneously dispersed in the lung (26, 32). Although the gross anatomy of these lungs

Fig. 4. Effects of hypoxia before and after a bolus injection of atropine (3 mg/kg) on hemodynamic parameters in the caiman (Caiman latirostris). Psys (A), left subclavian blood flow (Qsub; B), Gsys (C), Ppul (D), Qpul (E), Gpul (F), and P02 results are shown. *Significantly different from the normoxic results; †significant difference between recovery values and initial normoxic values (P < 0.05). Values are means ± SE (n = 7).

Fig. 5. Effects of hypoxia before and after a bolus injection of atropine (3 mg/kg) on fH in the caiman (Caiman latirostris). Values are means ± SE (n = 7). P < 0.05.

Table 2. Left atrial pressure measured in the caiman, Caiman latirostris, when breathing normoxic air and progressive levels of hypoxia

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<tr>
<th>PO2, kPa</th>
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<tr>
<td>19.3</td>
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<td>3</td>
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<td>13.9</td>
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<td>1.8</td>
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is simple, the respiratory parenchyma is structurally complex, and it is possible that the HPV expressed in the tegu lizards represent local regulation of blood flows within individual faveoli. In this case, HPV may be expressed in the tegus but not in the rattlesnakes because of their relatively higher maximal metabolic rates (1, 22). In any event, the very low threshold of the HPV (6 kPa O₂) is close to the minimum level of PŒ₂ that tegu lizards can tolerate (39).

Powell and Hopkins (36) recently reviewed V˙A/Q˙ distributions, measured by the multiple inert gas elimination technique, in vertebrates. Surprisingly, they observed that some species with structurally simple lungs, such as the tegu lizard, were characterized by high inhomogeneity compared with reptiles with high complexity. It is possible that the low threshold for HPV in tegus may contribute to the relatively high V˙A/Q˙ inhomogeneity. Along these lines, it would be of interest to investigate whether other local vasoactive substances (e.g., regulatory peptides and metabolites) exert stronger effects in species with complex lungs.

Although increased lung complexity is likely to require HPV for V˙A/Q˙ matching, other structural and physiological aspects are also likely to determine whether HPV is expressed. Many reptiles, particularly aquatic species, have an intermittent breathing pattern with long periods of breath hold where lung and blood PŒ₂ decline (e.g., Ref. 6). If the heart is undivided, HPV during long breath holds would induce right-to-left cardiac shunts where the pulmonary circulation is bypassed,
which would reduce the ability to exploit pulmonary oxygen stores. This may explain the low threshold for HPV in turtles compared with caimans and the tegu and varanid lizards. Lung oxygen stores, however, can be fully exploited during breath hold if the heart is functionally divided, which may explain why caimans exhibit HPV at very modest hypoxia. In animals with a divided heart, HPV during breath hold will, nevertheless, cause pulmonary hypertension that may disturb pulmonary fluid balance (47). It is not surprising, therefore, that varanid lizards that normally have a continuous breathing pattern and that are unlikely to experience environmental hypoxia exhibit strong HPV.

Responses of the Systemic Circulation to Hypoxia

In rattlesnakes, hypoxia induced a dilation in the systemic circulation and a rise in $f_{v}$, which is consistent with the mammalian response to hypoxia (13, 38). There was also a trend toward higher $G_{3ys}$ during hypoxia in caimans and turtles (10), and the systemic vasculature of teleost fish generally vasodilates during hypoxia (41). The hypoxia-induced systemic vasodilation facilitates oxygen delivery to hypoxic tissue, but the evolution of vascular responses to hypoxia is not well known. It has recently been shown that hypoxia leads to constriction of vascular smooth muscles in systemic tissues of cyclostomes, and it was proposed that hypoxic constriction rather than dilation is the original response among vertebrates (10), and the systemic vasculature of teleost fish generally responds to hypoxia with a divided heart, HPV during breath hold if the heart is functionally divided, which may explain why caimans exhibit HPV at very modest hypoxia. In animals with a divided heart, HPV during breath hold will, nevertheless, cause pulmonary hypertension that may disturb pulmonary fluid balance (47). It is not surprising, therefore, that varanid lizards that normally have a continuous breathing pattern and that are unlikely to experience environmental hypoxia exhibit strong HPV.

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