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Blood Oxygen Transport and Delivery in Reptiles[1]

F. HARVEY POUGH

Section of Ecology and Systematics, Langmuir Laboratory, Cornell University, Ithaca, New York 14850

SYNOPSIS. Cenozoic reptiles are characterized by physiological, morphological, and ecological systems with low energy requirements compared to those of mammals. Ectothermy and low resting rates of metabolism are the primary physiological adaptations of reptiles that produce low energy demand. Adjustments of the oxygen-transport system to different thermoregulatory characteristics among reptiles may be reflected in blood viscosity, oxygen capacity, oxygen affinity, and the temperature sensitivity of oxygenation. Other adaptations reduce the energy cost of oxygen transport. Reptiles have low hematocrits and large, widely spaced capillaries that contribute to a low fluid resistance in the vascular system, but also limit the oxygen-transport capacity. The low oxygen affinity characteristic of the blood of most reptiles appears to facilitate diffusion of oxygen to the tissues, overcoming the intrinsic limitations imposed by the morphological specializations of the cardiovascular system. The low blood oxygen affinity permits virtually all of the oxygen carried by the blood to be delivered to the tissues during periods of stress. It may also help to maintain a relatively high arterial Po_2 even when a right-to-left shunt occurs in the heart. Reptilian erythrocytes are capable of reducing methemoglobin rapidly. The high concentrations of methemoglobin and polymerized hemoglobin that occur *in vivo* may indicate that these compounds have a functional role. In their blood physiology, as in other aspects of their biology, reptiles are specialized animals that reflect selective forces quite different from those that have shaped the evolution of mammals.

INTRODUCTION

The living orders and suborders of reptiles are the products of many tens of millions of years of separate evolution. The phylogenetic lineages of the three orders of living reptiles have been separated from each other as long as they have been from the phylogenetic line that led to mammals (Carroll, 1969, 1977). Because of this long separation it is likely that physiological characteristics shared by living reptiles reflect similar functional adaptations rather than retention of patterns shared at the time of separation.

The general adaptation that characterizes reptiles appears to be a low-energy approach to the life of a tetrapod (Pough, 1980). Two interlocking features of reptilian physiology in particular distinguish them from mammals and contribute to their low energy requirements. These features are their ectothermy and their low resting rates of metabolism that force them to rely upon anaerobic metabolism to sustain high levels of activity. As ectotherms, reptiles rely upon external sources of energy to raise their body temperatures to the levels required to carry out their biological activities. During their periods of activity, reptiles maintain their body temperatures within a span called the Activity Temperature Range (ATR). When they are not active, reptiles allow their body temperatures to fall to ambient levels. The precision of thermoregulation varies among reptiles. Two extremes of reptilian thermoregulatory patterns are useful contrasts for generalizations provided that their abstract nature is appreciated. Thermal specialists have narrow ATRs that often extend nearly to the upper lethal temperatures for the species whereas thermal generalists have broader ATRs usually well below their lethal temperatures (Huey and Slatkin, 1976).

The second major difference between reptiles and mammals is their response to activity. Instead of maintaining the very high resting metabolic rates required for high levels of aerobic energy production during activity many reptiles rely upon anaerobic metabolism to sustain exercise. (For a review see Bennett, 1978.) In consequence these animals can continue activ-

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TABLE 1. *Summary of blood measurements of reptiles.**

Taxon	Hematocrit (percent)	Hemoglobin (g/100 ml blood)	Oxygen capacity (ml/100 ml blood)	Bohr effect (Δ log P_{50}/Δ pH)
Turtles (28 species)	27 (n = 38, 21 species)	8.5 (n = 29, 16 species)	7.6 (n = 21, 13 species)	−0.47 (n = 10, 9 species)
Crocodilians (5 species)	25 (n = 10, 5 species)	7.6 (n = 2, 1 species)	9.5 (n = 5, 3 species)	−0.74 (n = 3, 3 species)
Snakes (52 species)	28 (n = 42, 33 species)	8.8 (n = 29, 27 species)	8.4 (n = 26, 20 species)	−0.44 (n = 9, 9 species)
Lizards (60 species)	29 (n = 30, 20 species)	8.8 (n = 36, 32 species)	9.2 (n = 49, 38 species)	−0.50 (n = 5, 4 species)
All reptiles (145 species)	28 (n = 120, 83 species)	8.7 (n = 96, 76 species)	8.7 (n = 101, 74 species)	−0.49 (n = 27, 26 species)

* The data summarized here are presented in full by Pough (1979). Copies are available from the Division of Reptiles and Amphibians, National Museum of Natural History, Smithsonian Institution, Washington, D.C. 20560.

ity for only a few minutes before they become exhausted. This exhaustion is accompanied by a depletion of oxygen stores in the metabolizing tissues and blood and by metabolic acidosis.

A view of reptiles as tetrapods specialized for a low energy flow in contrast to the high energy flow of mammals integrates diverse features of their ecology, physiology, morphology, and behavior (Gans, 1978; Pough, 1978; Regal, 1980). In this review I will concentrate on those aspects of the oxygen-transport system that appear to reflect this general adaptation of reptiles. Recent reviews have treated the biochemistry of reptilian blood (Dessauer, 1970) and hemoglobin (Sullivan, 1974), and the morphology of blood cells (Duguy, 1970; Saint Girons, 1970). I will concentrate on functional aspects of oxygen transport and delivery in relation to the variation of body temperature and plasma pH experienced by reptiles.

BLOOD OXYGEN CAPACITY

The volume of oxygen carried to the tissues by a unit volume of blood depends upon a number of factors including the amount of hemoglobin present in the blood and the proportion of that hemoglobin that is actually functioning in oxygen transport. Differences in hematocrit between species do not necessarily correspond to the differences in hemoglobin content or oxygen capacity of the blood (Table 1). There is significant variation in hematocrit among reptiles ($F_{3,98} = 2.97$, $P < 0.05$), but not in hemoglobin content ($F_{2,78} < 1$, $P > 0.05$) or oxygen capacity ($F_{3,90} = 2.13$, $P > 0.05$).

In addition to interspecific variation in the factors that determine blood oxygen capacity, there is intraspecific variation in many of them. Increased erythrocyte counts during natural or artificial exposure to cold have been reported in a number of species of reptiles. This topic was reviewed by Maclean *et al.* (1975). High hematocrit, hemoglobin content, or oxygen capacity has been reported in some lizards from high altitudes (Vinegar and Hillyard, 1972; Ballinger and Newlin, 1975; Newlin and Ballinger, 1976). Ontogenetic changes in hematocrit or erythrocyte counts have been reported (Duguy, 1970, and references therein; Frair, 1977; Pough, 1977*c*, 1978). Parasitic infections, prolonged periods of weather unfavorable for activity, or prolonged starvation changed the character of circulating erythrocytes in *Cordylus* (Villiers Pienaar, 1962).

As a consequence of this background of

inter- and intraspecific variation, generalizations about reptile blood involve a degree of uncertainty that cannot yet be fully evaluated. Nonetheless, comparisons of blood properties of reptiles with those of birds and mammals show that in most cases reptiles have lower hematocrits and lower cell counts, lower hemoglobin contents, and lower blood oxygen capacities than the endotherms.

Blood viscosity

The ability of blood to transport oxygen to the tissues depends upon its viscosity and oxygen content. Increasing the hematocrit increases the oxygen capacity of blood, but simultaneously increases its viscosity. The optimum hematocrit is defined as the hematocrit that yields maximum oxygen transport under a given set of circumstances. Blood viscosity also increases as temperature falls. These relationships could affect reptiles on both short-term and evolutionary time scales.

The optimum hematocrits of species with high ATRs should be higher than those of species with low ATRs (Snyder, 1970). This hypothesis may account for some of the variation in hematocrit among reptiles at the ordinal and subordinal levels. Snakes, turtles, and crocodilians have similar ATRs whereas lizards are active at somewhat higher body temperatures (Brattstrom, 1965). Analysis of the data summarized in Table 1 indicates that the hematocrits of lizards are significantly higher than those of the other reptiles ($F_{s\ 1,100} = 4.91$, $P < 0.05$). There is no significant correlation between the midpoint of a species' ATR and its hematocrit within any of the groups of reptiles, however. Thermophilic species of lizards (midpoint of ATR above 35°C) do not have higher hematocrits than species with lower ATRs ($F_{1,15} = 3.46$, $P > 0.05$). Clearly adjustment of blood viscosity is not the only factor that sets the hematocrit of a species of reptile, and hematocrit is not the only determinant of viscosity. Differences in the size, shape, and rigidity of erythrocytes affect their properties of flow and thus the viscosity of blood (Braasch, 1971). The sizes and shapes of reptilian erythrocytes are extremely variable, and lizards alone include a range as great as all other reptiles combined (Saint Girons, 1970). The functional properties of reptilian erythrocytes are an attractive field for study.

Many reptiles experience daily and seasonal changes in body temperature that can alter blood viscosity. The viscosity of reptile blood may have an inherently lower temperature sensitivity than mammalian blood (Snyder, 1971), and short-term adjustments of hematocrit can compensate for daily changes in body temperature (Maclean *et al.*, 1975). Other examples of changes in hematocrit of reptiles with change in body temperature and of the possible involvement of anticoagulent substances in regulating blood viscosity and thrombus formation at low temperatures are reviewed in that paper.

Direct effect of temperature on blood oxygen capacity

In addition to the *in vivo* adjustment of hematocrit in response to changes in body temperature, there is a direct effect of temperature on blood oxygen capacity that can be demonstrated *in vitro*. The quantity of oxygen bound by whole blood from 17 species of reptiles was reversibly decreased as much as 40% at the extremes of the temperature ranges the animals normally encounter (Pough, 1976). For most species the temperature producing the maximum blood oxygen capacity fell within the ATR. It seems probable that this reduction in blood oxygen capacity at high and low temperatures is produced by mechanisms that regulate the function of the hemoglobin molecule in the face of changing temperatures and blood pH.

Ontogenetic changes in hematocrit and blood oxygen capacity

An ontogenetic increase in blood oxygen capacity has been described in *Iguana iguana, Sauromalus hispidus, Nerodia sipedon,* and *Thamnophis sirtalis* (Pough, 1976, 1977*d*, 1978). The mechanism of the ontogenetic change has been investigated in only a few species of reptiles. There is an ontogenetic increase in the hematocrit of five species of sea turtles produced by an approximate

TABLE 2. *Apparent heats of oxygenation of reptilian blood.**

Taxon	ΔH (kcal/mole)		
	Mean	Modal range	Total range
All lizards (43 species)	−3.6	−2 to −3	−0.8 to −11.8
Thermophilic species			
Agamidae (3 species)	−2.4	−2 to −3	−1.0 to −4.0
Iguanidae (14 species)	−3.5	−2 to −3	−0.8 to −10.5
Teiidae (3 species)	−4.0	—	−2.7 to −5.2
Thermophobic species			
Anguidae (2 species)	−2.2	—	−1.0 to −4.4
Gekkonidae (3 species)	−5.5	—	−2.4 to −7.6
Scincidae (3 species)	−7.7	—	−5.1 to −11.8
Snakes (18 species)	−7.3	−5 to −6	−3.8 to −12.8
Turtles (4 species)	−7.6	—	−5.9 to −10.6

* The data include only measurements of whole blood. Sources: Burggren *et al.*, 1977; Greenwald, 1971; Pough, 1977*c* and unpublished; Wood and Johansen, 1974; Wood and Moberly, 1970; Wood *et al.*, 1978.

doubling in cell volume (Frair, 1977). There is no information about changes in the hemoglobin content or oxygen capacity of the blood of these turtles.

In garter snakes (*Thamnophis sirtalis*) and water snakes (*Nerodia sipedon*) the hematocrit and oxygen capacity more than doubled between birth and maximum size (Pough, 1977*c, d,* 1978, and unpublished data). In garter snakes the total hemoglobin increased by 80% whereas functional hemoglobin increased by 160%, as the result of a reduction in the proportion of inactive hemoglobin from more than half the total hemoglobin in newborn snakes to less than 3% in snakes of 50 cm snout–vent length or more. The ability of garter snakes and water snakes to sustain activity increased as the blood oxygen capacity increased. This increased endurance was accompanied by ontogenetic changes in ecology and behavior. A similar ontogenetic increase in endurance occurs in the snakes *Opheodrys vernalis, Storeria occipitomaculata, S. dekayi,* and *Diadophis punctatus* (Pough, unpublished).

BLOOD OXYGEN AFFINITY

Measurements of the oxygen affinity of whole blood under conditions approximating the temperatures, pH, and gas tensions that obtain in a living animal are clearly necessary as a basis for inferences about the adaptive significance of the functional properties of blood. In the absence of specific information about the proper conditions for reptiles, most workers have made measurements at room temperature or at 37°C and have used mammalian values of P_{CO_2}. These conditions are not appropriate for all the reptiles studied (Pough, 1969; Burggren *et al.*, 1977).

Reptile blood hemolyzes readily when it is equilibrated with gas in a tonometer (Pough, 1976). Because the oxygen affinity of hemolyzed blood is very much higher than that of whole blood, even a small amount of hemolysis in a sample can produce a spuriously high oxygen affinity measurement. Polymerization of hemoglobin molecules and formation of methemoglobin *in vitro* and *in vivo* are additional potential sources of difficulty (Sullivan, 1974).

Effect of temperature on oxygen affinity of reptile blood

In reptiles, as in other animals, an increase in temperature normally shifts oxygen-loading curves to the right, representing a reduction in the oxygen affinity of the blood. The apparent heat of oxygenation, ΔH, is a measure of the sensitivity of oxygen affinity to temperature. Oxygen affinity of whole blood of turtles and snakes is more temperature-sensitive than that of most lizards (Table 2). The relative merits of high and low temperature sen-

sitivity for reptiles have been debated (Wood and Johansen, 1974; Burggren *et al.*, 1977). Low temperature sensitivity would help to stabilize blood function, especially in the face of a rapid change in body temperature, whereas high temperature sensitivity would facilitate delivery of oxygen to the tissues at high temperatures. Both views may apply if the contrasting thermoregulatory patterns of thermal specialists and generalists are considered separately.

Thermal specialists may have lower apparent heats of oxygenation than thermal generalists. Twenty species of thermal specialists in three families of lizards have an average ΔH value of -3.3 kcal/mole whereas eight species of thermal generalists from three families have an average value of -5.1 kcal/mole (Table 2). Snakes and turtles, two groups with lower and broader ATRs than lizards, have more negative apparent heats of oxygenation. This pattern is the opposite of that postulated for fishes (Johansen and Lenfant, 1972) and contrary to that based upon a comparison of reptiles with mammals (Wood, 1980). This paradox emphasizes the extent to which reptiles are physiologically specialized in ways that may be quite different from those of mammals. The mechanisms that determine the temperature sensitivity of whole blood are complex. In a number of species of fishes the temperature sensitivity of whole blood in the presence of CO_2 is less than that of blood without CO_2 or of hemoglobin solutions (Powers *et al.*, 1979).

The oxygen affinity of lizard blood appears to show adaptation among species such that a characteristic P_{50} value is observed within a species' ATR. The variances of P_{50} values for 30 species of lizards at 25°C, an arbitrary temperature that is below the ATR of most species, are 1.5 to 3 times the variances observed for the same species when each is measured within its ATR. There is a significant correlation between body mass and P_{50} in the ATR for iguanid lizards, but no significant relationship exists at 25°C for the same species ($r = 0.02$, $n = 49$, $P > 0.05$) (Pough, 1977*a*, and unpublished data).

Blood oxygen affinity in relation to body size and ecology

Turtles. There is surprisingly little information about the oxygen affinity of turtle blood considering turtles' traditional role as "the reptile" in comparative physiology. The data tabulated in a recent summary do not reveal a relationship between body mass and P_{50} but many of these were measured at inappropriate gas tensions (Burggren *et al.*, 1977; see also Palomeque *et al.*, 1977, for additional data). Fourteen P_{50} values measured at 15 and 25°C range from 12 to 40 mm Hg and seven of them lie between 25 and 32 mm Hg. These values are approximately the same as the P_{50} values of mammals in the body size range of the turtles (0.5 to 13 kg); they are considerably lower than the P_{50} values of snakes or lizards of equivalent size. I believe that the temperatures at which these determinations were made were unrealistically low, however. Both terrestrial and aquatic turtles bask in the sun and body temperatures above 30°C have frequently been reported (Mayhew, 1968; Cloudsley-Thompson, 1971). The high temperature sensitivity of turtle blood would raise their P_{50} values at these temperatures to levels similar to those of squamate reptiles. Active species of turtles may have lower oxygen affinities and higher oxygen capacities than sedentary species. There does not appear to be any direct correlation of oxygen affinity with terrestrial or aquatic habits (Burggren *et al.*, 1977).

Crocodilians. I have been able to find only three reports of the oxygen affinity of whole blood of crocodilians. In their pioneering studies of comparative blood physiology, Dill and Edwards (1931, 1935) measured a P_{50} value of 49 mm Hg for *Crocodilus acutus* at 29°C and values of 28 and 56 mm Hg for *Alligator mississippiensis* at 20 and 37.5°C respectively. A P_{50} value of 32 mm Hg at 20°C has been reported for *C. porosus* (Bauer and Jelkman, 1977). The alligators weighed 1–2 kg, the weights of the crocodiles were not stated. These P_{50} values are similar to those expected for lizards at those temperatures.

Lizards. Lizards have lower blood oxygen

affinity than birds or mammals of the same body size. Bennett (1973) reported that the P_{50} of blood from 11 species of lizards in six families at 37–38°C was described by the equation

$$\log P_{50} \text{ (mm Hg)} = 1.973 - 0.0936 \log m$$

where m = mass in g. Pough (1977*a*) presented a similar relationship derived from measurements of 20 species of iguanid lizards. Body masses ranged from 2.9 g to 2.7 kg and each species was measured in its own ATR. Oxygen affinity was related to body size by the equation

$$P_{50} \text{ (mm Hg)} = 68.88 - 1.79 \log m.$$

Both equations predict similar P_{50} values, which are higher than those of birds or mammals of similar body mass by factors of 1.4 to 1.8. Lizards from four other families had P_{50} values in their own ATRs that were the same as those of iguanid lizards of similar size. Only geckos and the sole xantusiid lizard measured had inherently higher blood oxygen affinities than iguanids. Geckos and xantusiids are nocturnal, secretive, and relatively inactive. In contrast to those families, small teiids, which are active predators, appeared to have lower oxygen affinities than iguanids of the same body sizes. It is possible that a low oxygen affinity facilitates oxygen delivery to the tissues, but varanid lizards are also active predators and have blood oxygen affinities equivalent to iguanids of equal size (Bennett, 1973; Wood and Johansen, 1974; Pough, 1977*a*).

Snakes. The relationship of blood oxygen affinity to body size in snakes differs from that seen in all other vertebrates. In 15 species of colubrid snakes P_{50} at 25°C increased with increasing adult body mass by the relationship

$$P_{50} \text{ (mm Hg)} = 21.54 + 7.39 \log m$$

(corrected from misprinted form in Pough, 1977*b*). Ontogenetic change in P_{50} also shows a pattern of decreasing oxygen affinity with increasing body size (Pough, 1977*c*). The P_{50} values measured under similar conditions for snakes in seven other families are the same as those of colubrids of similar body size (MacMahon and Hamer, 1975; Seymour and Webster, 1975; Seymour, 1976; Pough, 1977*b*). The anomalous pattern of oxygen affinity in snakes may reflect the morphological and functional specializations of the single lung that is retained in most snakes. Lung morphology differs among snakes and the sites of breathing movements may shift in response to the demands of various activities. The tidal volumes of snakes are more than twice those of lizards of similar body size (Pough, 1977*b*). Variable pulmonary blood shunts and gradients in pulmonary gas tensions have been measured in snakes at rest and during activity (Donnelly and Woolcock, 1978; Gratz *et al.*, 1978; Seymour, 1978).

Ontogenetic change in oxygen affinity

Fetal hemoglobins, or oxygenation properties different from those of adults, have been described in turtles, lizards, and snakes (McCutcheon, 1947; Manwell, 1960; Pough, 1969, 1977*a, c,* 1978). Ontogenetic change in hemoglobin and oxygen affinity have been investigated most extensively in snakes. Manwell (1960) reported an ontogenetic decrease in the oxygen affinity of the whole blood of garter snakes (*Thamnophis sirtalis*), but there was no change in the oxygen affinity of hemoglobin in solution. Electrophoretic analysis revealed a continuous shift of hemoglobin into faster migrating fractions during ontogeny (Pough, 1977*c*). The P_{50} at 25°C increased from 21 mm Hg in newborn snakes to 45 mm Hg in adults. A similar ontogenetic increase in P_{50} occurs in northern water snakes (*Nerodia sipedon*) and milk snakes (*Lampropeltis triangulum*) (Pough, 1977*b, c*). A recent study has revealed an ontogenetic increase in P_{50} in diamondback water snakes (*N. rhombifera*) equivalent to that of *N. sipedon* (A. Hughes and V. H. Hutchison, personal communication).

There was no change in the oxygen affinity of hemoglobin solutions of garter snakes, confirming Manwell's conclusion that some component of the intraerythrocytic environment is responsible for the change. Addition of ATP to hemoglobin solutions in molar ratios equalling or ex-

ceeding those measured in erythrocytes decreased the oxygen affinities of the solutions, but did not bring them to the P_{50} values of whole blood. An ontogenetic decrease in the methemoglobin concentration may contribute to the ontogenetic decrease in oxygen affinity (Pough, 1977*c*).

Modifiers of oxygen affinity

Bohr effect. The wide variation in plasma pH experienced by reptiles as a consequence of change in body temperature or bouts of activity complicates interpretation of Bohr effects. Plausible reasoning can ascribe physiological advantages to large or small Bohr effects for reptiles, and both patterns may be represented in the class. Turtles, lizards, and snakes have smaller Bohr effects than mammals of the same body size (Table 1). The average Bohr effect for 23 species in these groups is −0.46. In contrast, the average Bohr effect of nine species of mammals weighing 2 kg or less (the approximate maximum size of the reptiles included in the survey) is −0.66 (data from Table 74 in Altman and Dittmer, 1971, and Table 8-3 in Prosser, 1973). The small Bohr effect of the reptiles may be related to the low oxygen affinity of their blood. The chuckwalla, with a Bohr effect of −0.65, may be unable to saturate its blood with oxygen when the plasma pH is lowered by metabolic acidosis following activity (Bennett, 1973).

The large Bohr effect of crocodilians may be a specialization associated with their diving (Andersen, 1961). Hemoglobin from some aquatic turtles shows a larger Bohr effect than hemoglobin from terrestrial species, but there are many exceptions to this generalization (Sullivan and Riggs, 1967). The aquatic snake *Acrochordus* has an enormous Bohr effect (Johansen and Lenfant, 1972), but the equally specialized sea snakes have very small Bohr effects (Seymour and Webster, 1975; Seymour, 1976). *Acrochordus* also has an exceptionally high hematocrit and blood oxygen capacity, characters not shared by sea snakes (M. E. Feder, personal communication in Pough, 1979).

Intracellular metabolites. Erythrocytic organophosphates of reptiles vary quantitatively and qualitatively during ontogeny and in a daily cycle correlated with photoperiod (Barlett, 1978; V. H. Hutchison, personal communication). Parallel and convergent evolution have clearly occurred in the organophosphates of reptilian erythrocytes because the phylogenetic distribution of the compounds described by Bartlett (1978) bears no resemblance to the evolutionary relations of the groups involved. Different organophosphates are differentially effective in modifying oxygen affinity, and the organophosphate present at highest concentration in erythrocytes is not necessarily the one with the greatest effect (Coates, 1975). Different hemoglobin fractions may have different sensitivities to organophosphates (Schwantes *et al.,* 1976). Inorganic ions and carbon dioxide interact with organophosphates in modifying the oxygen affinity of hemoglobin (see Kilmartin and Rossi-Bernardi, 1973, for a review). Modification of the oxygen affinity of crocodile hemoglobin appears to depend upon the formation of carbamate compounds rather than the effects of phosphates (Bauer and Jelkman, 1977).

In garter snakes (*Thamnophis sirtalis*) and water snakes (*Nerodia sipedon*) intracellular compounds are responsible for the differences in oxygen affinity of blood from adults and juveniles, but in diamondback terrapins (*Malaclemys terrapin*) a difference persists in hemoglobin solutions (McCutcheon, 1947; Manwell, 1960; Pough, 1977*c*). The oxygen affinity of reptilian blood increases during storage as does that of human blood. In both cases the mechanism is probably depletion of erythrocytic organophosphates (Pough, 1977*b*). Alteration of the quantity or quality of phosphates may also be involved in the short-term changes in oxygen affinity that result from acclimation to different temperatures and photoperiods (MacMahon and Hamer, 1975). The role of phosphates in acclimation is not limited to their allosteric effects. Acclimation to low temperature increased intracellular phosphates and blood oxygen affinity in a tortoise as a result of the effect of the nondiffusible ATP anions on intracellular pH (Wood *et al.,* 1978).

Ions and osmotic changes can alter the shape and flexibility of erythrocytes and affect the functional properties of hemoglobins directly and indirectly (Braasch, 1971; Kilmartin and Rossi-Bernardi, 1973). Several species of lizards nearly double plasma sodium and potassium concentrations during dry seasons (Bentley, 1976). A study of the responses of erythrocytes and hemoglobin to these changes in plasma salt concentrations would be instructive.

Multiple hemoglobins and polymerization of hemoglobin. Most reptiles have multiple hemoglobins (Dessauer, 1970; Sullivan, 1974). The presence of two or more hemoglobin fractions offers the possibility of stabilizing blood function if two hemoglobin fractions respond in offsetting fashion to changes in physical or chemical conditions. Examples of this sort of regulation have been described in fishes but not in reptiles (Riggs, 1970; Schwantes *et al.*, 1976). In addition to the multiple hemoglobins found in all members of a species, individual hemoglobin variants with different oxygenation properties have been described in a turtle (Manwell and Schlesinger, 1966).

Polymerization of hemoglobin by formation of disulfide bridges occurs *in vivo* and *in vitro* in some, but not all, species of turtles and has been described in one species of snake, two lizards, and two crocodilians (Sullivan, 1974; Reischl and Diefenbach, 1976; Bauer and Jelkman, 1977). One of the hemoglobin fractions of the turtle *Kinixys erosa* (not "*crosa*") forms dimers or octamers whereas the second does not (Aboderin and Obidairo, 1976). The oxygenation properties of hemoglobin *in vitro* are apparently not altered by polymerization (Sullivan, 1974), but its effect *in vivo* requires clarification. The disulfide bridges may have a functional role in regulation of pH (Dessauer, 1970) or the phenomenon may be a biochemical artifact (Sullivan, 1974). Dimerization could play a role in adjustment of oxygen affinity via subunit exchange in the methemoglobin form (Pough, 1976).

Methemoglobin. High concentrations of methemoglobin (MetHb) have been reported in a variety of reptiles including freshly captured animals (reviewed by Sullivan, 1974). In contrast, Board *et al.* (1977) reported MetHb values <3% in the animals they studied. In garter snakes (*Thamnophis sirtalis*) MetHb decreased from an average of 29.7% in newborn snakes to 2.6% in snakes longer than 30 cm body length (Pough, unpublished). Activities of NADH-methemoglobin reductase and NADPH-methemoglobin reductase are higher in reptiles than in mammals and intact erythrocytes are able to reduce MetHb rapidly (Board *et al.*, 1977). Thus the hypothesis that high levels of MetHb in reptiles are the result of deficiencies in the enzyme systems of the cells lacks an experimental basis as well as being intuitively unsatisfactory. A functional role for MetHb during anaerobic metabolism has been suggested (Pough, 1969) and the observation that MetHb reduction proceeds more rapidly with lactate as a substrate than with glucose (Board *et al.*, 1977) lends it some support. Reptiles might also adjust the oxygen affinity of hemoglobin in response to varying body temperatures by changing the MetHb concentration (Pough, 1976). These hypothetical functional roles for MetHb could be complementary.

THE REPTILIAN OXYGEN-TRANSPORT SYSTEM

To this point I have emphasized the diversity of structural and functional characteristics of reptilian blood. Some of this diversity can plausibly be viewed as adaptation to particular ecological specializations. Other sorts of variation do not appear to be related to particular adaptations. A broader perspective illuminates some of these puzzling features and provides a framework for the formulation of hypotheses.

There is a clear distinction between the modal blood characteristics of reptiles, particularly squamate reptiles, and mammals. These two classes of vertebrates, both composed primarily of terrestrial forms, share the same habitats and eat the same foods, but differ in a host of phys-

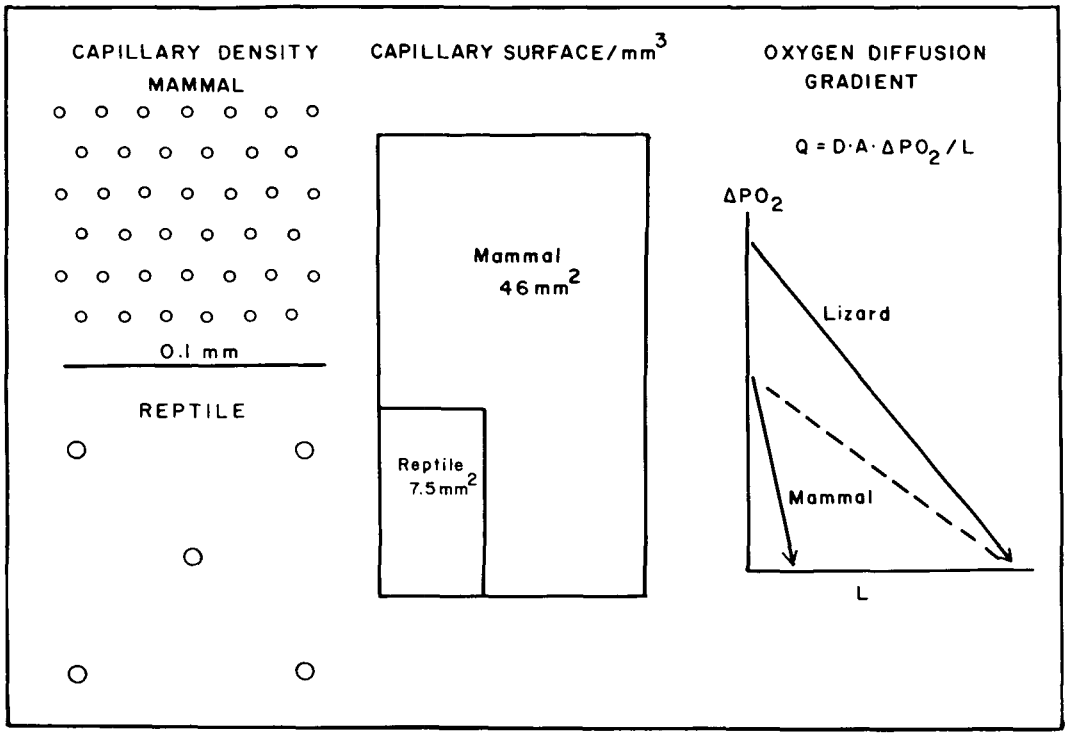

FIG. 1. Comparison of oxygen delivery in a mammal and a reptile. Left: The diameter of reptilian capillaries is greater than that of mammals' and the capillary density in tissues is lower. Middle: As a consequence of the large diameter and wide spacing of their capillaries, reptiles have far less capillary surface per unit volume of tissue than mammals. Right: The average diffusion distance from capillary to cell in reptiles is double that of mammals. If reptile blood had the same oxygen affinity as mammalian blood the gradient for diffusion would be very low (dashed line). Because the oxygen affinity of reptilian blood is low, oxygen is released at a high partial pressure and the gradient for diffusion to the cell ($\Delta Po_2/L$) is steep. Thus the low oxygen affinity of reptile blood helps to overcome the handicaps of limited surface area for diffusion (A in the Fick equation), and the long diffusion distance (L). (Diagrams are drawn to scale for a comparison of a 20 g mouse and lizard. Anatomical information from Tables 171 and 173 in Altman and Dittmer [1971], oxygen affinities calculated from formulae in Schmidt-Nielsen and Larimer [1958] and Pough [1977*a*].)

iological and behavioral features. Among the characters directly associated with oxygen transport and delivery, most reptiles have lower hematocrits, lower blood oxygen capacity, and lower oxygen affinity than mammals of the same body size. How are these differences between reptiles and mammals reflected in the function of their oxygen-transport systems, and what is the ecological significance of those physiological differences?

The basic pattern of adaptation that characterizes reptiles in comparison to mammals is their specialization as a low energy flow system (Pough, 1980). The specializations that permit this low energy flow are interlocking features of morphology, physiology, and behavior. Examples of these interlocking mechanisms can be found in the oxygen-transport system. The following discussion is based upon limited data and will certainly require modification when more information is available. Nonetheless I believe that there is sufficient information to construct an hypothesis that will have heuristic value.

Fluid resistance is the force against which the heart works. Adatation to a low-energy life should be facilitated by low fluid resistance in the vascular system, and low vascular resistance is characteristic of reptiles. Systolic blood pressure is 30–50 mm Hg in those animals compared to 80–100 mm Hg in birds and mammals (Table 4 in Altman

and Dittmer, 1971). The low fluid resistance of the vascular system of reptiles is a consequence of their low hematocrits and widely spaced capillaries with diameters nearly 50% larger than those of mammals. These same characteristics of the cardiovascular system also reduce the oxygen-transport ability of the blood of reptiles in comparison to mammals. There is less than one-fifth the capillary surface area for diffusion of gases per unit volume of muscle tissue, and the average distance from a cell to the nearest capillary is 2.5 times greater (Fig. 1). A number of features of reptilian blood facilitate oxygen delivery *in spite of the intrinsic handicaps* of the reptilian vascular system. The adjustment of hematocrit and blood viscosity to yield maximum oxygen transport at a species' ATR or in response to changes in body temperature, and the maximization of blood oxygen capacity in the ATR are examples of physiological adaptations that promote oxygen transport in these ectotherms, despite their relatively low hematocrits.

Delivery of oxygen to the tissues is facilitated by low oxygen affinity of blood. In dogs an experientally produced increase in the P_{50} of 2 mm Hg increased the arteriovenous concentration difference and allowed maintenance of the same metabolic rate with a reduced cardiac output (Krall *et al.*, 1978). This experimental manipulation duplicates on a lesser scale the difference in oxygen affinity of the blood of reptiles and mammals. Oxygen is released from hemoglobin at a higher pressure in the blood of crocodilians, lizards, and of snakes larger than 50 to 150 g, than it is in the blood of mammals of the same mass. This increased oxygen pressure may compensate for the greater diffusion distance from capillary to tissues by increasing the gradient for diffusion of oxygen from blood to tissue in reptiles (Fig. 1). Furthermore, the displacement of the oxygen-loading curve to the right in reptiles should increase the proportion of oxygen that can be given up to the tissues, especially during periods of recovery from activity when tissue oxygen pressures should be very low. Under stress reptiles can unload virtually all of the oxygen bound to the blood reducing the oxygen content of mixed venous blood to 1 ml oxygen/100 ml blood or less (White, 1959; Berkson, 1966; Tucker, 1966). As long as circulation is maintained, reptiles can withstand complete and prolonged deoxygenation of their blood (Belkin, 1968). In contrast, mammals are not tolerant of very low venous oxygen tensions. Even in maximum exercise the oxygen content of mixed venous blood does not fall below 5 ml oxygen/100 ml blood (calculations based on Tables 63 and 65 in Altman and Dittmer, 1971). *The ability to tolerate low venous oxygen* tensions allows reptiles to compensate for the low oxygen capacity of their blood by delivering almost all of the bound oxygen to the tissues. The significance of this adaptation probably lies in speeding repayment of an oxygen debt incurred during activity.

The sorts of morphological and physiological adaptations exemplified by the oxygen-transport system of reptiles are complex and specialized, and similar examples can be found in other physiological systems. White (1976) reviewed the adaptative significance of other aspects of the reptilian circulatory system, including the thermoregulatory role of the cardiovascular shunts permitted by the specialized heart morphology. The respiratory systems of recent reptiles integrate a variety of morphological and behavioral features that produce a system with low energy expenditure (Gans, 1978). Reptilian activity and behavior patterns, like the morphological and physiological characters discussed here, appear to be specializations associated with low energy flow (Regal, 1978).

This perspective suggests that features *of the reptilian oxygen-transport system* that appear to be nonadaptive, or even maladaptive, are more likely to be adaptations that we do not yet understand. Modern reptiles are most appropriately viewed as animals with specializations that are quite different from those of mammals, reflecting different selective forces.

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