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Form and Function in Reptilian Circulations[1]

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SYNOPSIS. Consistent with the great variation in their circulatory morphology, there are distinct variations in the cardiovascular physiology of extant reptiles. The chelonian and squamate reptiles have a complexly structured heart that includes three partially separated ventricular cava. In most species (under most conditions), the ventricle acts as a single pressure pump perfusing both the pulmonary and systemic circuits. However, the varanid lizards provide a striking exception. Subtle evolutionary changes in cardiac morphology allow the ventricle of the varanid lizard to divide functionally during systole into a low pressure, pulmonary pump and a high pressure, systemic pump. The crocodilians represent yet another anatomical and physiological pattern. The ventricle is completely divided into left and right chambers as in homeotherms, but the systemic and pulmonary circuits may still communicate through the left aorta that arises from the right ventricle.

A fundamental feature of all reptilian circulations is the ability to regulate the distribution of cardiac output between systemic and pulmonary circuits via central vascular blood shunts. Regardless of species, mechanisms for regulating intracardiac shunting involve changes in the balance between peripheral resistance of the pulmonary and systemic circulations, and adjustments in cardiac performance per se. Several hypotheses are presented that suggest selective advantages for central vascular shunting in intermittent breathing reptiles with variable body temperature and metabolic rate.

INTRODUCTION

This paper will briefly review the cardiovascular anatomy and physiology of reptiles. The first section will emphasize cardiac hemodynamics, the regulation of cardiac output and the adjustment in distribution of blood to the pulmonary and systemic circulation. The second section will include a discussion of why these cardiovascular patterns, and shunt regulation in particular, may have evolved and how they may serve as useful adaptations for reptiles. Through this discussion I hope to demonstrate that:

1) the reptilian heart in its various forms does not fit into a direct morphological continuum between the heart of amphibians and the homeotherms, and

2) "efficiency" of function must be examined in a context appropriate for each vertebrate class, and not in the sole context of homeotherms.

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PATTERNS AND PRESSURES IN REPTILIAN CIRCULATIONS

Extant reptiles exhibit more variation in circulatory structure and function than all other living tetrapods combined. Three general cardiovascular patterns appear to have emerged, although a consensus has certainly not been formed by all researchers for all species studied. Interestingly, these patterns cut quite sharply across phylogenetic lines, suggesting that "lifestyle" might be as important as systematics in predicting cardiac form and function in reptiles.

Chelonians and squamates

The heart of "typical" chelonians (turtles, tortoises) and squamates (snakes, lizards) has two discrete atrial chambers, with a ventricle subdivided into three anatomically interconnected cava (Fig. 1A). The ventricular cavum receiving oxygenated left atrial blood (cavum arteriosum) has no direct output into an arterial arch, while the ventricular cavum perfusing the pulmonary artery (cavum pulmonale) has no direct input of relatively deoxygenated right atrial blood. Blood flowing from the

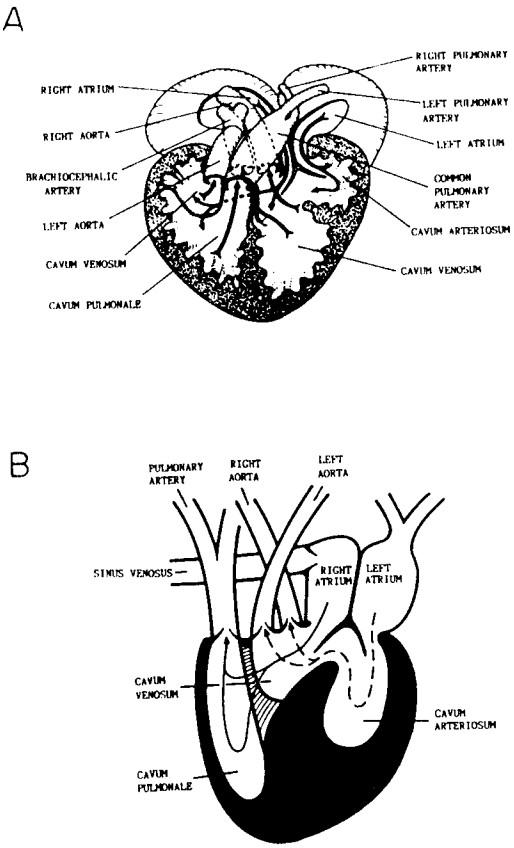

FIG. 1. (A) Diagrammatic illustration of the chelonian heart shown in a ventral aspect. The solid arrows indicate pathways of blood from the ventricular chambers into the arterial arches, but are not intended to illustrate the flow of separate bloodstreams through the ventricle. From Shelton and Burggren (1976). (B) Highly schematic two-dimensional presentation of the heart chamber and vessel arrangement of the savannah monitor lizard, *Varanus exanthematicus*. The muscular ridge (striped area) between cavum venosum and cavum pulmonale is projected onto the outer heart wall for clarity. From Heisler *et al.* (1983).

two atria not only comes into contact, but must undergo considerable redistribution within and between the three ventricular cava before systolic ejection into the two or more systemic arteries and single pulmonary artery can occur. Varying degrees of admixture of oxygenated and deoxygenated blood occur during this redistribution, constituting the so-called "intracardiac shunt" (see below, also White [1976], Johansen and Burggren [1980], and Burggren [1985] for reviews). When pulmonary venous blood flows directly through the heart into the pulmonary artery, then a so-called "left-to-right" shunt occurs. Conversely, a "right-to-left" shunt or "pulmonary bypass" results from systemic venous blood flowing directly into the systemic arteries. Shunts can occur simultaneously in both directions in this cardiac arrangement, with the direction of the net shunt determined by whether the systemic or pulmonary circulation receives the majority of total cardiac output.

What are the hemodynamics of this relatively complexly structured heart of chelonians and squamates? Very similar, if not identical, systolic and diastolic pressures are usually recorded from all three ventricular cava (Fig. 2A; Steggerda and Essex, 1957; Johansen, 1959; Shelton and Burggren, 1976; Burggren, 1977*a*, *b*), suggesting that the ventricular cava are in anatomical connection during both isometric and isotonic phases of systole as well as diastole. Thus, the ventricle is a single pressure pump whose output is directed into multiple arterial outlets leaving the heart. In such a system the pulmonary and systemic vascular beds reside in parallel, rather than in series as in the avian or mammalian circulation. Intracardiac shunting potentially can occur during diastole and systole.

As a consequence of being perfused by a single pressure source, the pulmonary and systemic circuits experience very similar systolic arterial pressures, commonly ranging from 20–50 mm Hg (see Burggren [1985] for values). A variable resistance to blood flow resides in the pulmonary outflow tract of some chelonians and squamates and is manifested as a depression of pulmonary arterial pressure relative to that in systemic arteries (see below). Differences in peripherally-measured arterial pressures thus are not necessarily indicative of pressure separation within the ventricle.

It is important to emphasize that exceptions (in both measurements and their interpretations) to the general pattern outlined above almost certainly occur. For example, small (<2 mm Hg) differences in systolic pressures between ventricular cava have been measured during both lung ventilation and voluntary periods of apnea in

garter snakes (Burggren, 1977*b*). These small regional differences, which are still quite compatible with the notion of a single pressure pump, are probably attributable either to pressure gradients required to drive flow both within and between cava or to phenomena involving potential/kinetic energy conversions in rapidly accelerating or decelerating blood. Substantial differences in blood pressures between the ventricular cava have been recorded in rare instances during intermittent breathing in the turtle *Chrysemys* (=*Pseudemys*) *scripta* (Shelton and Burggren, 1976). Heisler *et al.* (1983) have recorded both identical and disparate intraventricular systolic pressures in different individuals of *C. scripta*. Apparently, under some as yet undefined circumstances, the chelonian ventricle can generate regional pressure separation.

Varanid lizards

The monitor lizards (*Varanus*) are an interesting group that includes the largest living lizards. This very old family diverged from close ancestry with snakes as early as the Upper Cretaceous. Varanid lizards depart markedly from the "typical" squamate cardiovascular pattern. Although phylogenetically very distant from the therapsid ancestors of the mammals or the archosaur ancestors of birds, varanid lizards show cardiovascular adaptations which fall on a physiological continuum between the single pressure ventricle of most reptiles and the completely divided, dual pressure circulation of birds and mammals.

As in other squamates, all varanid ventricular chambers are anatomically patent, and the systemic and pulmonary circuits reside in parallel rather than in series. The cavum venosum of the varanid ventricle is considerably reduced in size, and essentially forms a narrow "interventricular" channel connecting the prominent cavum arteriosum on the left and the cavum pulmonale on the right of the ventricle (Fig. 1B; Webb *et al.*, 1971; Burggren and Johansen, 1982; Heisler *et al.*, 1983). Redistribution of left and right atrial blood between ventricular chambers must occur before ejection into the pulmonary and systemic arteries. Thus, the potential for intraventricular mixture or shunting of oxygenated and comparatively deoxygenated blood still exists in varanids as in other squamates. At least during systole, however, the cavum pulmonale of all varanids examined to date is functionally isolated from the regions of the ventricle associated with perfusion of the systemic circulation (cavum arteriosum and cavum venosum), and generates a systolic pressure of only 50–60 mm Hg compared with 110–120

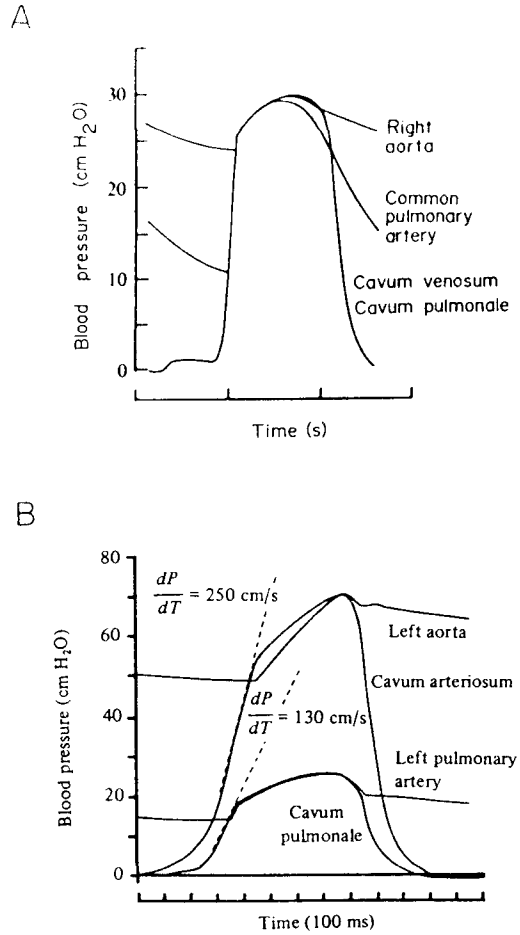

FIG. 2. (A) Blood pressures measured simultaneously in the cavum pulmonale, cavum venosum, right aorta, and common pulmonary artery, of a turtle, *Chrysemys* (=*Pseudemys*) *scripta*. From Shelton and Burggren (1976). (B) Blood pressures measured simultaneously in the ventricular cava and pulmonary and systemic arteries of a savannah monitor lizard, *Varanus exanthematicus*. From Burggren and Johansen (1982).

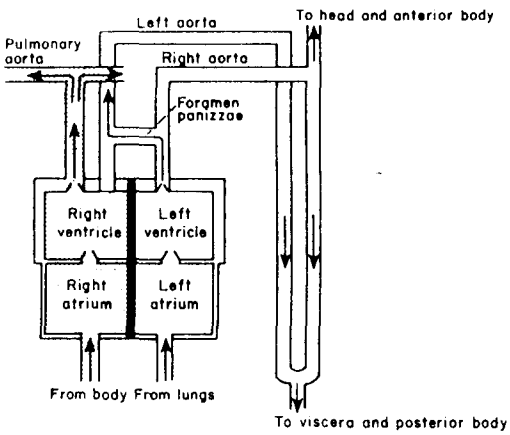

FIG. 3. Diagrammatic illustration of the cardiac chambers and greater vessels of the crocodilian heart. Arrows show the course of blood through the heart during lung ventilation. Shaded regions of the heart convey deoxygenated blood to the lungs. From Johansen and Burggren (1980), after White (1968).

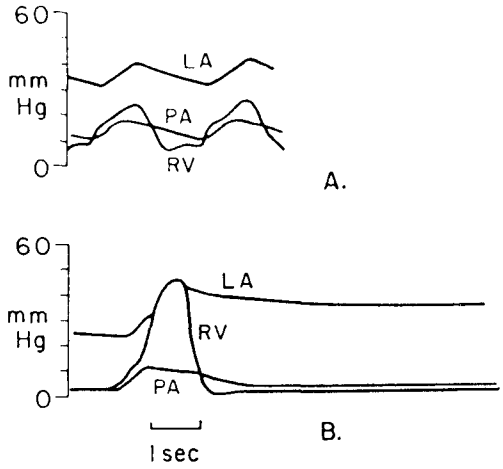

FIG. 4. Simultaneously recorded pressures from an unanesthetized alligator. Pressures were recorded during lung ventilation (A) and after 12 min of apnea (B). Left aortic arch (LA), pulmonary arch (PA), and right ventricle (RV). From White (1969).

mm Hg in the cavum arteriosum and cavum venosum (Fig. 2B). The varanid heart appears to be best represented as a dual pressure pump (Millard and Johansen, 1973; Burggren and Johansen, 1982; Heisler *et al.*, 1983; Johansen and Burggren, 1984).

Crocodilians

The cardiac anatomy of crocodiles and alligators is in many respects more similar to that of homeotherms than to other reptilian families. In addition to two atrial chambers, the heart is completely divided into a thick-walled left ventricle, from which the right aorta arises, and a thinner-walled right ventricle, from which the pulmonary artery arises (Fig. 3). Unique to the Crocodilia, however, is a left aorta arising from the right ventricle. Left and right aorta merge distally, providing a potential avenue for deoxygenated blood from the right ventricle to bypass the lungs and enter the systemic arterial circulation (*i.e.*, "right-to-left" shunt). A more proximal passage, the Foramen Panizzae, connects the bases of the two aortae.

Pressure and flow events in the crocodilian heart are closely related to ventilation patterns (Fig. 4). During periods of lung ventilation, systolic pressure in the left ventricle (40–50 mm Hg) exceeds that in the right ventricle (25–30 mm Hg) (White, 1969). Because the comparatively high left ventricular pressure is transferred to the base of the left aorta via the Foraman Panizzae and the conjugation of the two aortae, systolic pressure in the left aorta at all times will exceed systolic pressure in the right ventricle. Consequently, the valves at the base of the left aorta remain closed throughout the cardiac cycle, and all blood ejected from the right ventricle must enter the pulmonary circulation. Under these conditions, the crocodilian heart operates as a dual pressure pump with complete anatomical and functional separation of oxygenated and comparatively deoxygenated blood, and with equal output from left and right ventricles. The crocodilian circulation during lung ventilation is thus qualitatively indistinguishable from the heart of a bird or mammal.

During long periods of apnea, however, there is a convergence of systolic pressures in the left and right ventricles, and the pressure gradient keeping the valves at the base of the left aorta closed disappears (White, 1969). Under these circumstances, blood ejected from the right ventricle may enter the left aorta as well as the pulmonary artery, providing a potential route for

a partial bypass of the pulmonary circulation (right-to-left shunt).

BLOOD SHUNTING: THE DISTRIBUTION OF CARDIAC OUTPUT

Considerable anatomical and physiological diversity occurs in reptilian circulations, but the potential for a regulated redistribution of cardiac output between systemic and pulmonary circuits is a common feature linking all reptilian circulations. Moreover, there appears to be a common degree of evolutionary conservativeness, in that regulatory mechanisms appear very similar in the three common patterns of circulation in reptiles.

Regulation through adjustment in peripheral resistance

When systemic and pulmonary circulations are arranged in parallel, as in chelonian and squamate reptiles (excluding varanid lizards), the proportions of cardiac output entering the pulmonary and systemic circulation (*i.e.*, the magnitude of the net intracardiac shunt) will be dictated by the relative resistances offered by these two circuits. When lung ventilation begins after a period of apnea in the turtle *C. scripta*, for example, both pulmonary and systemic arterial resistance decrease, but the decrease in pulmonary resistance is generally much greater than in systemic circulation at this time (Shelton and Burggren, 1976; Burggren, 1985). Consequently, the pulmonary circuit becomes the most favored route for blood ejected from the ventricle. When apnea is resumed, there is a greater increase in pulmonary resistance than in systemic resistance, and thus pulmonary flow is most affected. Under these conditions, blood flow to the lungs may account for less than 30% of total cardiac output as a net right-to-left shunt develops (White and Ross, 1966; Burggren and Shelton, 1979; Shelton and Burggren, 1976).

What are the mechanisms affecting these changes in resistance in the chelonian circulation? As in other vertebrates, vasomotor activity at the level of very small arteries and the arterioles will profoundly affect vascular resistance. In contrast to mammals, in chelonians at least one-half of the variable resistance of the pulmonary arterial tree lies proximal to the lung parenchyma (Burggren, 1976, 1977*a*). The major pulmonary artery leading to each lung of the turtle is approximately equally divided into a highly compliant, poorly muscularized proximal segment and a relatively non-compliant, highly muscularized distal segment (Burggren, 1977*a*; Milsom *et al.*, 1977; White, 1976). *In situ* perfusion of the distal pulmonary artery of the turtle indicates that neurally mediated vasomotor responses of this vascular segment increase and decrease arterial resistance during apnea and lung ventilation, respectively (Burggren, 1976, 1977*a*).

The pulmonary outflow tract of the ventricle is an additional site for regulation of pulmonary resistance, and thus for regulation of the intracardiac shunt. In chelonians a smooth muscle sphincter underlying the bulbus cordis (March, 1961; Burggren, 1977*a*) is adrenergically dilated and cholinergically constricted (Burggren, 1977*a*). When constricted, either pharmacologically or by vagal stimulation, this sphincter generates a large resistance to blood ejection into the pulmonary circuit, manifested by a significant drop in blood pressure across the site of resistance. In chelonians there is usually little tonus of this sphincter (see Burggren, 1985). However, White and Ross (1966) reported a considerable decrease in pulmonary relative to systemic arterial blood pressure during lung ventilation in a freshwater turtle. While pressure separation of the ventricle may account for these observations, it is more likely that a constriction of the pulmonary outflow tract produced a depressed pulmonary arterial pressure.

In squamates, as in chelonians, cardiac output is distributed between the systemic and pulmonary circulation by adjustments in vascular smooth muscle in the lung parenchyma, the extrinsic pulmonary arteries, and the pulmonary outflow tract. It is noteworthy, however, that in garter snakes there is a constant, vagally mediated tonus of the smooth muscle sphincter in the pulmonary outflow tract. This tonus results in a significant reduction in pul-

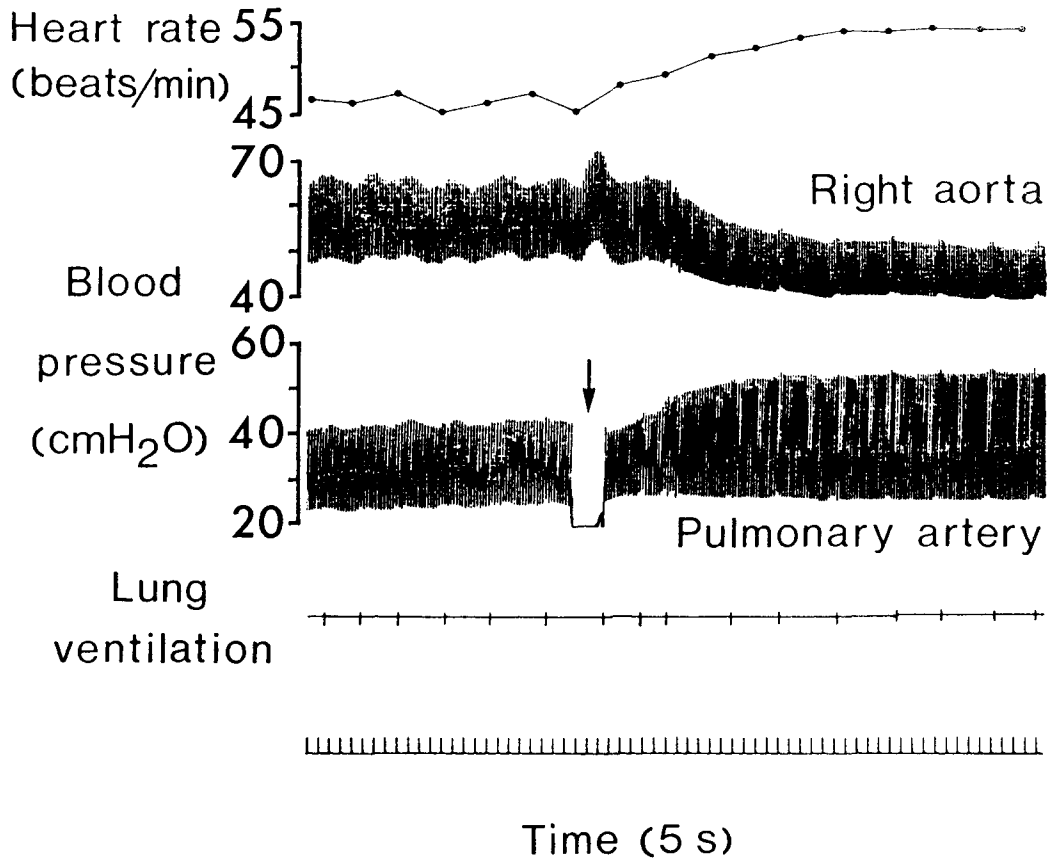

FIG. 5. Systemic and pulmonary arterial blood pressures in an unrestrained, unanesthetized garter snake, *Thamnophis sirtalis*. Atropine (1.0 mg/kg body weight) was injected at the arrow. From Burggren (1977*b*).

monary arterial pressures relative to that in the cavum pulmonale (Fig. 5). Consequently, pulmonary arterial pressure is lower than aortic pressure even though both systemic and pulmonary circuits of the garter snakes are being perfused by a common, single pressure pump (Burggren, 1977*b*). A large resistance in the pulmonary outflow tract (or, less likely, pressure separation of the ventricle) may occur in other snakes, as a depressed pulmonary relative to systemic arterial pressure has also been reported for *Boa constrictor* (Johansen, 1985).

The distribution of cardiac output between the systemic and pulmonary arteries of *Varanus* is similarly dependent on the balance in peripheral resistance of the two arterial circuits. The analysis is much more complex than in other squamates and chelonians, however, because of the functional division of the varanid ventricle during contraction. Briefly, intraventricular admixture of left and right atrial blood occurs primarily during diastole when ventricular filling and blood redistribution occur. Both end-systolic and end-diastolic volumes of all three ventricular cava are of crucial importance to the distribution of cardiac output.These volumes will be directly dictated by the resistance of the pulmonary and systemic vascular beds (see Heisler *et al.* [1983] and Burggren [1985] for more details).

The magnitude and direction of intracardiac shunting in varanid lizards are not clear. Millard and Johansen (1973) described marked and independent adjustments in pulmonary and systemic arterial pressures associated with hypoxia, hyper-

capnia and voluntary diving in *V. niloticus*, which suggests that intracardiac shunting occurs. Highly variable, but usually very small, shunts were measured with electromagnetic flow meters in *V. exanthematicus* during constant artificial lung ventilation (Burggren and Johansen, 1982). Most recently, Heisler *et al.* (1983), using microsphere techniques, reported for *V. exanthematicus* that shunting was unaffected by voluntary intermittent lung ventilation. Intracardiac shunts in reptiles can reverse direction in seconds, however (see Shelton and Burggren, 1976; Burggren *et al.*, 1977). Microsphere techniques, with their "single snapshot" timing, are unlikely to differentiate brief adjustments in intracardiac shunting.

In the Crocodilia, cardiac output either can be equally distributed between the systemic and pulmonary circuits (as during lung ventilation), or redistributed during apnea such that there is a partial or full lung bypass (White, 1969, 1970). A net left-to-right shunt is an anatomical impossibility in these reptiles. The pathway for central vascular shunting during apnea resides entirely in the derivation of the left aorta from the right ventricle, with the magnitude of the shunt regulated by peripheral vascular resistance. The rise in pulmonary relative to systemic vascular impedance during periods of apnea (White, 1969, 1970) contributes to the convergence of pressures in the left and right ventricles. When left aortic pressure is surpassed by right ventricular pressure, a proportion of right ventricular blood will perfuse the systemic arterial circulation via the left aorta. During prolonged apnea the rise in pulmonary resistance is particularly great, and the ensuing right-to-left shunt can produce a nearly complete pulmonary bypass (White, 1969). The pulmonary outflow tract of crocodilians is also actively involved in adjustment of pulmonary vascular resistance during intermittent lung ventilation (White, 1969, 1976). The wide phylogenetic representation of a vasoactive pulmonary ventricular outflow tract suggests that it is probably a general morphological trait of extant reptiles, rather than an adaptation by a few genera.

Regulation through adjustments in cardiac excitation

Adjustments in cardiac muscle excitation and performance *independent* of peripheral vascular events can also affect central cardiovascular shunting in reptiles. For example, in intact, conscious *C. scripta* and *Testudo graeca*, two totally different patterns of ventricular activation develop, with the particular pattern highly dependent upon whether the animal is breathing or breath holding (Fig. 6). During lung ventilation, the activating wave of depolarization spreads from the right side to the left side of the ventricle at a velocity of approximately 0.07–0.08 m/sec. Within one to two heart beats after the onset of apnea, however, the activation pattern is completely altered, with depolarization spreading from the left to the right side of the ventricle at a considerably increased velocity of approximately 0.15 m/sec! This pattern switch is regulated by the cardiac vagus nerve, since the pattern typical during lung ventilation is abolished by vagotomy and induced by vagal stimulation (Burggren, 1978). Importantly, when the pattern typical of lung ventilation is experimentally induced during a period of apnea, pulmonary arterial P_{O_2} immediately falls by 10 mm Hg and left aortic P_{O_2} rises by a similar amount, indicating a reduction in intraventricular mixing of oxygenated and deoxygenated blood (see Burggren, 1978). Reversals in the direction of cardiac biopotentials may also develop during stress such as activity or fright in the lizard *Sauromalus hispidus* (A. Smits, unpublished). The phenomenon of variable activation and contraction patterns of the heart is clearly worthy of further investigation.

Blood shunts—what purpose do they serve?

A fundamental premise of gas exchange theory is that gas transfer is most efficient when perfusion and ventilation of the respiratory organ are optimally matched. In animals with continually high metabolic rates (*e.g.*, homeotherms), lung ventilation tends to be a continuous process, variable within comparatively narrow limits. Consequently, lung perfusion also tends to be

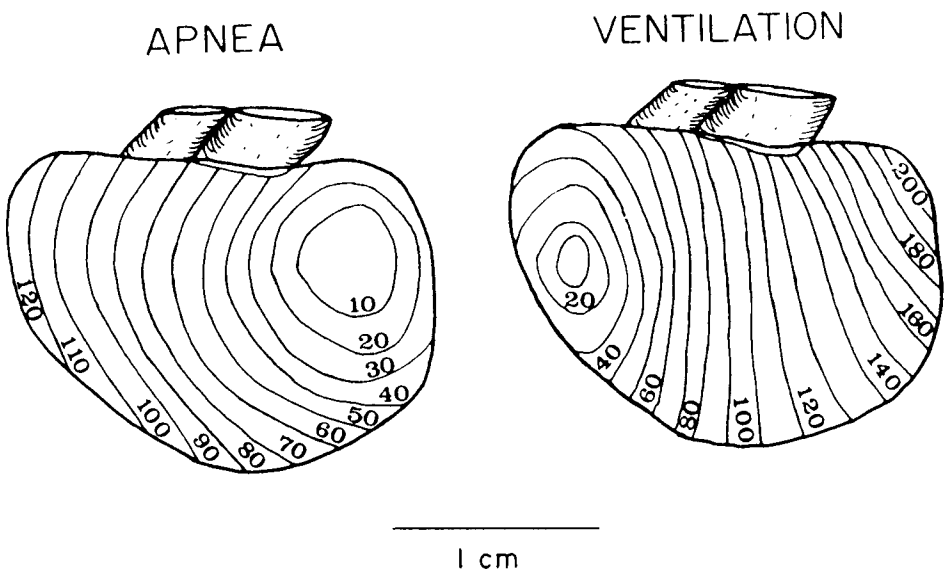

FIG. 6. Patterns of normal *in vivo* depolarization propagation over the ventral and dorsal surfaces of the ventricle of the tortoise *Testudo graeca* during apnea and during lung ventilation. The sequence of epicardial depolarization is indicated by 10 msec interval isochronal lines. The numbers indicate msec after the initial appearance of depolarization on the ventral surface of the ventricle. From Burggren (1978).

continuous and comparatively non-variable. Air breathing poikilotherms, on the other hand, tend to have considerably lower metabolic rates and can often serve their respiratory demands using non-continuous breathing patterns. Optimal matching of perfusion with this intermittent ventilation is produced by large adjustments in blood flow to the gas exchange organs.

In reptiles exhibiting intermittent breathing, cardiac output (and thus pulmonary flow) tends to be highest during periods of lung ventilation and lowest during apnea, the result of changes in both heart rate and stroke volume of the heart (Shelton and Burggren, 1976; White, 1976; Johansen and Burggren, 1980). Thus, lung ventilation and perfusion remain matched in spite of profound changes in breathing rate. It is important to emphasize that perfusion nominally could be matched with ventilation simply through adjustment in cardiac output. For example, a straightforward reduction in cardiac output during apnea *without any change in the magnitude or direction of intracardiac shunting* certainly would reduce pulmonary blood flow. Of course, systemic blood flow also would be reduced, but presumably the demand for systemic perfusion in a poikilotherm with low metabolic rate could be sufficiently supplied by intermittent perfusion, just as gas exchange is achieved with intermittent ventilation.

Why, then, has the ability to adjust perfusion of the lungs *independent* of perfusion of the other body tissues—a situation simply unattainable by homeotherms—been so universally selected for during the evolution of divergent reptilian lineages? Why have the exquisite regulatory mechanisms controlling intracardiac shunting persisted in reptiles while animals with higher metabolic rates evolved completely divided circulations in which equivalent flow must occur? Unfortunately, differing opinions among researchers are many, while testable hypotheses are few (see Johansen and Burggren, 1985)! To determine whether the development of a net left-to-right or right-to-left shunt under a certain set of respiratory conditions constitutes a cardiovascular "adaptation" requires assigning physiological costs and benefits to these shunts. Several hypotheses assigning physiological benefits to the development of

cardiovascular shunting during intermittent breathing have been advanced during the last two decades of the study of cardiovascular shunts in reptiles. One perspective has emphasized the net right-to-left shunt during apnea (Hypotheses #1–3, below), while the other has emphasized the net left-to-right shunt during lung ventilation (Hypothesis #4). Additionally, blood shunting may be involved in thermoregulation (Hypothesis #5).

Hypothesis #1—pulmonary bypass saves cardiac energy during apnea

This hypothesis suggests that, as apnea proceeds and lung gas partial pressures move towards pulmonary venous levels, the respiratory "benefit" of continued lung perfusion does not outweigh the circulatory "cost." Thus, cardiac energy is conserved by reducing pulmonary perfusion during apnea.

This hypothesis is fairly easily falsified. Firstly, right-to-left shunts often begin to develop within a few heart beats of the termination of lung ventilation when pulmonary P_{O_2} is still high (and P_{CO_2} quite low) and, thus, the benefits of pulmonary perfusion are still high relative to the metabolic cost of lung perfusion. Secondly, energetic arguments based on the metabolic cost of pulmonary perfusion simply do not hold up to close scrutiny. Table 1 presents preliminary calculations for the energetic costs associated with intracardiac shunting in the turtle *C. scripta*. Cardiac work can be calculated from blood pressure and cardiac output and an assumed muscle efficiency of 10%, and then expressed as an O_2 uptake (see Burggren, 1985). The metabolic cost of the circulation during peak cardiac output in the turtle (*i.e.*, during lung ventilation) amounts to less than 5% of total aerobic metabolism at rest. During brief apnea in the turtle, when cardiac output is normally reduced by at least ½, the cost of heart metabolism falls to about 2% of the total aerobic metabolism. (This assumes that total metabolic rate remains constant during brief alternating periods of apnea and ventilation.) Now, the metabolic cost of pulmonary blood flow per se is easily calculated from the metabolic cost of total cardiac output and of the fraction of cardiac output that pulmonary flow represents. During lung ventilation (net 65% left-to-right shunt) and during apnea (net 49% right-to-left shunt) the cost of lung perfusion as a percentage of total metabolic rate can be estimated at about 3% and 1% of total metabolic rate, respectively. Reduced perfusion of the lung during apnea thus saves only about 2% of the total aerobic energy expenditure of the turtle during this period. It should be emphasized that much of the reduction in lung perfusion is achieved by the considerable reduction in cardiac output, and *not* by the changing shunt fractions (Table 1). In fact, the reduction in pulmonary blood flow specifically attributable to right-to-left shunting during apnea accounts for only 0.5% of the aerobic metabolic rate of turtles. Although these calculations for *C. scripta* are admittedly quite simple and make many assumptions, they have been corroborated independently by others (N. Heisler, unpublished).

Given the extremely low metabolic costs and savings of shunting in reptiles like the turtle, it is unlikely that metabolic cost has been the major factor in the evolution of intracardiac shunting and of mechanisms serving to regulate it.

Hypothesis #2—pulmonary bypass allows "metering" of lung O_2 store

This hypothesis suggests that, by reducing the rate of pulmonary perfusion at the onset of apnea, the O_2 store of the lung can be conserved to be slowly "metered" out to the blood and tissues during apnea. Experimental evidence from the turtle *C. scripta* supports the notion that the rate of transfer of O_2 from the lung to arterial blood can be regulated by adjustment in blood flow. During most dives of relatively short duration, the P_{O_2} of lung gas and arterial blood decrease at similar rates from the outset of apnea (Fig. 7A), suggesting a relatively constant rate of O_2 transferal from lung to blood. During about ⅛ of all dives, and particularly if the dive lasts more than 30 min, the pattern of O_2 depletion is characterized by pulsatile transfer of O_2

TABLE 1. *Estimated metabolic costs of circulation in the turtle* Chrysemys (=Pseudemys) scripta *at 20°C.* *

	Lung ventilation	APNEA
Aerobic metabolic rate ($ml\ O_2 \cdot kg^{-1} \cdot h^{-1}$)	41.4	41.4
Heart rate ($beats \cdot min^{-1}$)	23	11
Cardiac output ($ml \cdot min^{-1} \cdot kg^{-1}$)	57	27
% of cardiac output directed to lungs	65% (left-to-right)	49% (right-to-left)
"Cost" of cardiac output (% of aer. met. rate)	4.8%	2.2%
"Cost" of lung perfusion (% of aer. met. rate)	3.1%	1.0%
Metabolic "saving" due to reduced lung perfusion (% of aer. met. rate)	2.1%	
Metabolic "saving" due specifically to reduced cardiac output (% of aer. met. rate)	1.6%	
Metabolic "saving" specifically due to right-to-left shunting (% of aer. met. rate)	0.5%	

* Data are from studies by Jackson (1973), Shelton and Burggren (1976) and Burggren and Shelton (1979). These calculations assume that: total metabolic rate remains constant during intermittent breathing, cardiac muscle efficiency is 10%, and the complete metabolism of 1 ml of O_2 yields 20.80 Joules.

from lung to arterial blood (Fig. 7B). These data strongly suggest that, during long dives typified in Figure 7B, a large pulmonary bypass develops immediately upon apnea. Little, if any, O_2 stored in the lung is transferred to the blood, since pulmonary perfusion has been greatly reduced. At several points during the dive, however, it appears that pulmonary perfusion rises as the right-to-left shunt is diminished (perhaps even transiently replaced with a left-to-right shunt) and O_2 is rapidly transferred from lung gas to arterial blood.

It is not intuitively obvious (to me) what the specific physiological advantage of a particular pattern of O_2 depletion from the lung during apnea might be. Provided the O_2 stores of lung, blood and tissue fluids have been replenished by a period of lung ventilation of sufficient duration, then each store will contribute O_2 during apnea according to their volumes and O_2 capacitances (Piiper, 1982; Shelton, 1985). While the position of the store, blood flows and gas partial pressure differences will dictate the rate and timing of the contribution of a particular O_2 store, the net result during a long period of apnea will be depletion of all three sources of O_2. Whether the O_2 stores of arterial blood and lung gas are depleted simultaneously (Fig. 7A) or whether the blood O_2 is depleted before the lung gas store is tapped (Fig. 7B) ultimately should not affect the duration of the aerobic period of the dive.

Perhaps the O_2 partial pressure gradients driving oxygen diffusion under the two sets of circumstances outlined in Figure 7 are of importance. When a severe depletion of the oxygen store of the blood is allowed to occur (Fig. 7B), then the P_{O_2} gradient from lung to pulmonary capillary blood will be much larger during subsequent lung perfusion than when a steady

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FIG. 7. (A) Lung gas O_2 and CO_2 partial pressures ($P_{A_{O_2}}$ and $P_{A_{CO_2}}$) and femoral arterial blood O_2 and CO_2 partial pressures ($P_{A_{O_2}}$ and $P_{A_{CO_2}}$) during intermittent breathing in a freely diving, unrestrained turtle, *Chrysemys (=Pseudemys) scripta.* Periods of lung ventilation are indicated by the shaded vertical bars. In (A) a turtle showed a typical pattern of frequent episodes of lung ventilation. In (B) a turtle voluntarily made an extended dive. From Burggren and Shelton (1979). Similar phenomena occur in the Australian freshwater turtle, *Chelodina longicollis* (W. Burggren, A. Smits, and B. Evans, unpublished).

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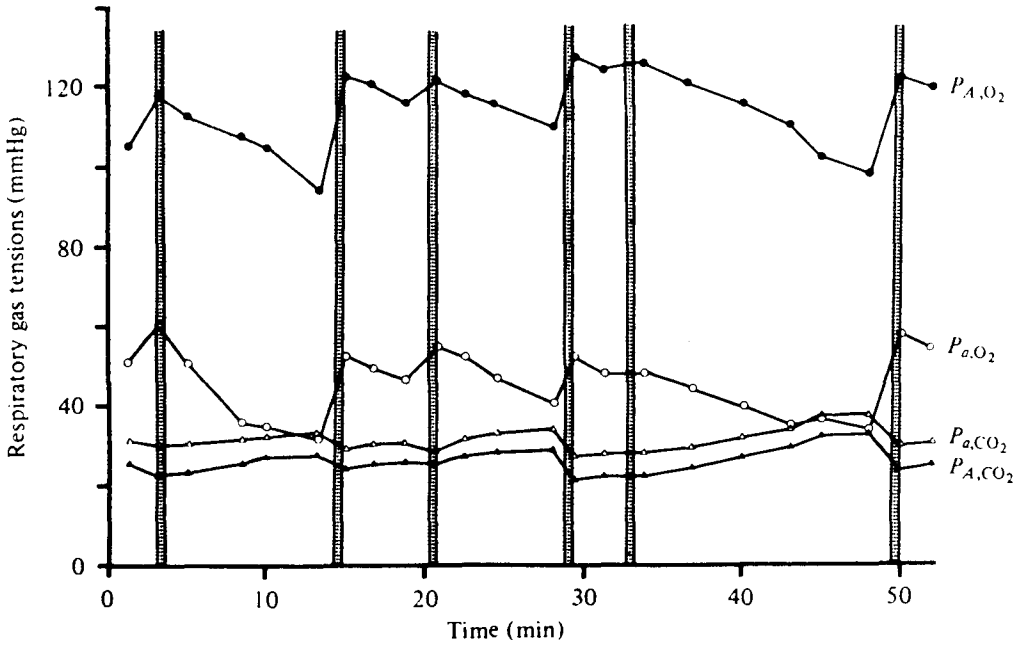
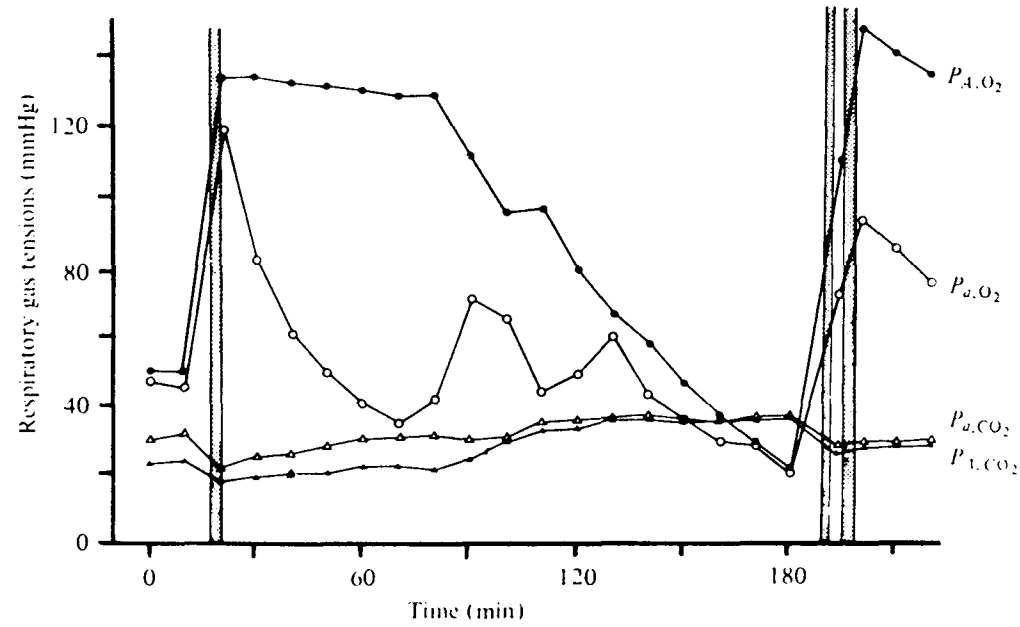

Respiratory gas tensions (mmHg)
120
80
40
0
0
10
20
30
40
50
Time (min)
P_{A,O_2}
P_{a,O_2}
P_{a,CO_2}
P_{A,CO_2}

B


Respiratory gas tensions (mmHg)
120
80
40
0
0
60
120
180
Time (min)
P_{A,O_2}
P_{a,O_2}
P_{a,CO_2}
P_{A,CO_2}

reduction in both pulmonary gas P_{O_2} and arterial P_{O_2} is allowed to develop (Fig. 6A). Thus, the rate of O_2 transferral from lung to blood for a given rate of lung perfusion will be higher. Why, then, is this pattern of intermittent lung perfusion during apnea, with its apparently greater rate of O_2 transfer, not commonly practiced in the more frequent, short dives of turtles? The implication is that high rates of pulmonary perfusion attending left-to-right shunt during apnea might have disadvantages as well as advantages. This idea is explained in the next hypothesis.

Hypothesis #3—pulmonary bypass reduces plasma filtration into lungs

The plasma flux between pulmonary capillaries and lung interstitium is proportional to pulmonary blood flow in the turtle *C. scripta* (Burggren, 1982). At high blood flows characteristic of left-to-right shunting during lung ventilation, net plasma filtration occurs at a rate 10–20 times that in the mammalian lung. However, at low pulmonary blood flows characteristic of apnea, a net reabsorption of fluid from lung interstitium into the pulmonary capillaries occurs (Fig. 8). Because high and low pulmonary blood flows alternate frequently during normal patterns of intermittent lung ventilation, the turtle lungs remain, in the long term, in a state of fluid balance (Burggren, 1982). The phenomenon of high and reversible rates of transcapillary fluid fluxes may be quite widespread in lower vertebrates. Work in progress in our laboratory (A. Smits, unpublished) indicates that high rates of transcapillary fluid flux can also occur in the lizard *Sauromalus hispidus* and the marine toad *Bufo marinus.*

Mechanisms for reducing pulmonary blood flow during apnea, including the development of a right-to-left blood shunt, may have evolved in part to reduce plasma filtration into the lung. Because the diffusion of respiratory gases is several orders of magnitude slower through liquid compared to gas, the accumulation of fluid in the lung from plasma filtration can have extremely serious consequences to gas exchange if this fluid interposes into the gas diffusion pathway. By reducing blood flow through the lung, particularly during long periods of apnea when partial pressure gradients for O_2 and CO_2 are not particularly favorable for gas exchange, the respiratory membranes are kept relatively "dry" in preparation for the next period of lung ventilation and attendant high blood flow.

Hypothesis #4—left-to-right shunt facilitates CO_2 elimination

A corollary of hypotheses that assign physiological advantages or disadvantages to shunts on the sole basis of O_2 transport is that a net left-to-right shunt during lung ventilation conveys no advantage to O_2 transport, and is simply a non-functional consequence of the undivided nature of the chelonian and squamate circulation. After all, once blood has been O_2-saturated in passage through the lungs, what could be achieved by subsequent transits of that same blood through the lung during net left-to-right shunting, especially since O_2 content (or saturation) is more important to blood O_2 transport than blood O_2 partial pressure in vertebrates with intracardiac shunts (Wood, 1984). Thus, *from the perspective of O_2 transport* net left-to-right shunting has been considered to be a non-functional consequence of the undivided chelonian and squamate circulation.

Recently, intracardiac shunting has begun to be examined in the context of CO_2 elimination rather than O_2 uptake. The elimination of CO_2 into the lungs is quite pulsatile. Relatively little CO_2 is transferred into lung gas during apnea, but during the relatively brief period of lung ventilation a large pulse of CO_2 is eliminated into the lungs (Ackerman and White, 1979; Burggren and Shelton, 1979). Important relationships between CO_2 elimination and left-to-right shunting during lung ventilation in intermittently breathing turtles are emerging (Ackerman and White, 1979; White, 1985). Since these analyses are beyond the scope of this paper, suffice it to say that the left-to-right shunt during lung ventilation enhances CO_2 excretion in two ways. Firstly, repeated recirculation of pulmonary venous blood

back to the lung (*i.e.*, net left-to-right shunt) will result in continued elimination of CO_2 as long as the P_{CO_2} gradient from capillary blood to lung gas exists. Clearly, this situation of continual CO_2 elimination during left-to-right shunting is *not* the mirror image of O_2 transport, where there is a pigment that reaches saturation and can achieve no further saturation even though recirculated through the lungs. Secondly, the Haldane effect on the CO_2 dissociation curve of the blood decreases blood CO_2 capacitance at the lung, and so increases transpulmonary CO_2 conductance. A net left-to-right shunt during lung ventilation will produce maximal O_2 saturation and thus assure minimal blood CO_2 capacitance.

While this hypothesis assigns a respiratory "benefit" to a net left-to-right shunt in chelonians and squamates exhibiting intermittent patterns of ventilation, it should be emphasized that intermittently breathing crocodilians, in which there can be no left-to-right shunt, nonetheless eliminate CO_2 adequately. A left-to-right shunt appears to be a cardiovascular adaptation to intermittent breathing, but clearly is not an absolute requisite in all reptiles showing these ventilatory patterns.

Hypothesis #5—shunting affects body warming and cooling

Most reptiles warm up to their preferred core temperature much faster than they cool to temperatures below it, indicating the involvement of active physiological processes. One of the most effective thermoregulatory processes in ectotherms involves regulation of internal heat transport through a highly selective distribution of blood between the periphery (which may be exposed to the warming influence of sunlight, for example) and the body core. In squamates and turtles there are reciprocal vasomotor responses of the cutaneous and deep muscle and visceral vascular beds in response to both general elevation of core temperature and localized heating of the skin (see White [1976] and Johansen and Burggren [1980] for references). In addition, elevation of core temperature (as opposed to localized skin temperature) in squamates is accompanied by an increase in right-to-left intracardiac shunting, as well as an increase in heart rate and cardiac output (Baker and White, 1970). This redistribution of "cooler" blood from the core away from the lung to the "warmer" periphery of the systemic vasculature (especially the skin) will greatly facilitate the rate of body temperature increase associated with basking in warm environments.

Since respiratory membranes can be an important route of heat loss, large changes in the flow of blood to these membranes might affect body temperature. Tucker (1966) suggested that, by reducing heat loss from the lung, a right-to-left shunt would speed the increase in body core during basking in squamate reptiles. Alternatively, the development of a large left-to-right shunt in conjunction with the well documented panting (Crawford and Gatz, 1974) might facilitate rapid transferral of heat from body core to the environment.

Recent studies by Wood and his colleagues (see Wood *et al.*, 1987) have indicated that the extent of central vascular shunting may be closely associated with temperature regulation in a variety of ectotherms. They hypothesize that central vascular shunting is modified to align with the changing needs for respiratory gas transport produced by changes in body temperature, rather than (or in addition to) the use of the circulation as a physical conduit for heat.

The five groups of hypotheses outlined above ascribe physiological advantages to intracardiac shunting in reptiles. In most instances the regulated distribution of cardiac output relates to intermittent breathing. Therefore, it follows that the longer the periods of apnea exhibited by a particular species, the greater should be the perceived benefits of cardiovascular shunting and the stronger the selection pressures for mechanisms allowing shunt regulation. This corollary remains untested, since the very limited quantitative data on central vascular shunting is primarily from reptiles which characteristically show lengthy periods of apnea (*e.g.*, turtles, alligators). A systematic study of cardiovascular physi-

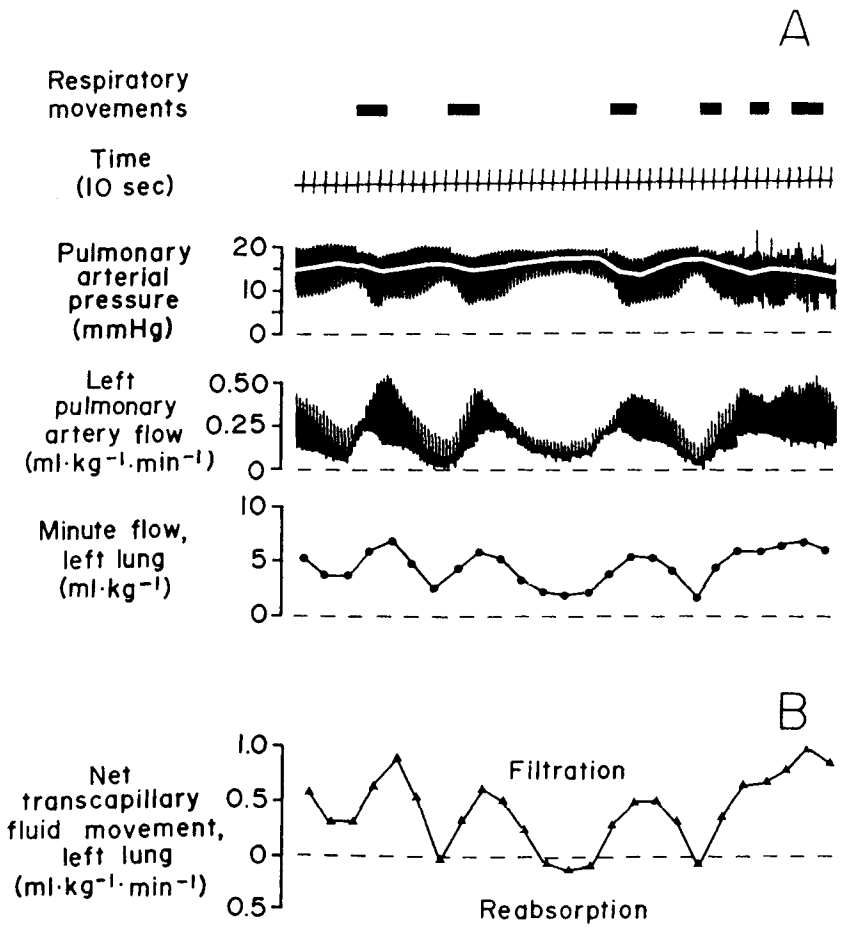


FIG. 8. (A) Pulmonary arterial blood pressure and flow to the left lung of an unanesthetized turtle *Chrysemys* (=*Pseudemys*) *scripta* during normal intermittent breathing. Mean pulmonary blood pressure is indicated on the blood pressure trace by the white line. Lung ventilation is indicated by black bars. (B) Net plasma filtration and reabsorption in the lung during the period depicted in (A). From Burggren (1982).

ology within a reptilian family spanning many different ventilatory patterns would be a welcome addition to the literature.

SUMMARY

Extant reptiles exhibit great interspecific variability in both cardiovascular structure and function. There are frequent and major departures from the common (but incorrect!) view of the evolution of the vertebrate circulation that places a primitive and inefficient reptilian heart on a direct and ascending continuum between that of extant amphibians and homeotherms. This erroneous view, historically rooted in the supposed superiority of the completely divided avian and mammalian circulation, implies that intracardiac shunts in the reptilian heart are the unfortunate consequence of an undivided circulation unable to separate oxygenated and deoxygenated blood entering the heart. In fact, the redistribution of cardiac output between systemic and pulmonary circulation via central vascular shunting is a carefully regulated physiological process, and allows for effective matching of lung perfusion to lung ventilation during intermittent breathing.

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