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Role of the Central Circulation in Regulation of Cutaneous Gas Exchange[1]

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SYNOPSIS. Although primarily limited by the rate of diffusion of oxygen and carbon dioxide across the integument, cutaneous gas exchange is also affected by adjustments in the absolute flow of blood to the skin, the pattern of distribution of blood within the cutaneous vascular bed, and the effects of central vascular shunting on gas partial pressures of arterial blood perfusing the skin. The interplay of these various factors, particularly in animals with heterogeneous arterial supply to the skin and/or with highly variable intracardiac shunts, potentially is complex, only poorly understood, and worthy of considerable future experimentation.

INTRODUCTION: PERFUSION *IS* IMPORTANT IN A "DIFFUSION LIMITED" GAS EXCHANGE ORGAN

The exchange of respiratory gases across the skin of vertebrates is limited by proximate factors that affect gas diffusion—skin diffusion coefficient, skin surface area, gas diffusion distance and transcutaneous gas partial pressures. That cutaneous gas exchange is primarily "diffusion limited" in vertebrates has been verified repeatedly both by theoretical models and experimental data (see reviews by Feder and Burggren, 1985*a*, *b*, 1986; Piiper, 1988).

A description of the skin as primarily "diffusion limited" is generally taken to imply that limitations due to "perfusion" (*i.e.*, blood convection) are unimportant and thus that increased perfusion will not augment gas exchange. While such a perspective is appropriate when interpreting events *at the level of individual capillaries* in the skin, it must be emphasized that changes in the rate of blood perfusion at the *tissue level* can alter variables important to gas diffusion and so potentially can play a pivotal role in regulating exchange of gases.

The rate of perfusion of the skin can affect cutaneous gas exchange in several ways. First, and most obviously, the blood serves as the bulk transporter for oxygen and carbon dioxide. Thus, irrespective of local conditions for gas diffusion across the skin, the absolute volume of blood perfusing the skin will influence the absolute quantity of respiratory gases that can be carried away following exchange by diffusion. Importantly, blood flow to the skin is rarely, if ever, in a steady-state condition. If blood flow (and thus blood velocity in the vessels) decreases, capillary blood will have more time to equilibrate with the surrounding medium. Under such conditions of reduced blood flow, the *rate of perfusion* will then dictate the total amount of gas exchange. Low blood flow states are particularly important in fishes, amphibians and reptiles that depend heavily on cutaneous gas exchange, for many such animals characteristically exhibit a normally very large range in cardiac output. In the bullfrog *Rana catesbeiana*, for example, intermittent breathing, activity and hypoxic exposure can all produce many-fold changes in bulk flow of blood to the skin (Moalli, 1980; Boutilier *et al.*, 1986; A. Pinder, unpublished).

A second general aspect of perfusion that can influence cutaneous gas exchange in a diffusion-limited vascular bed relates to the *gas composition* of afferent arterial blood. The skin of all vertebrates is located in parallel with the arterial supplies to other systemic vascular beds. (As described below, there are circulatory specializations for cutaneous gas exchange in many fishes and in anuran amphibians—however, this gross characterization of the skin circulation remains accurate.) Thus, any of a number

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of perfusion-related physiological factors that result in an alteration of the P_{O_2} or P_{CO_2} of arterial blood (*e.g.*, intracardiac shunting, change in blood flow to perfusion-limited gas exchange organs such as the lungs) will affect the transcutaneous partial pressure gradient for diffusion and, consequently, cutaneous gas exchange.

The third aspect of perfusion influencing cutaneous gas exchange in diffusion-limited vascular beds involves capillary recruitment. Historically, the skin has been modelled as consisting of a single vascular compartment—*i.e.*, a single "capillary" (Gatz *et al.*, 1975; Piiper *et al.*, 1976). Such a model does not incorporate capillary recruitment, which has recently been implicated in the regulation of cutaneous gas exchange in amphibians (Burggren and Moalli, 1984; Pinder, 1985; Burggren and Feder, 1986). Even though gas exchange in each individual capillary may be primarily limited by gas diffusion, the absolute number of capillaries that are actually perfused will directly dictate the amount of gas exchange achieved, since changes in capillary recruitment will alter the total capillary surface area across which gas exchange can occur (Burggren and Moalli, 1984). Of course, a major adjustment of the perfused proportion of the total cutaneous vascular bed will demand either major adjustment of the bulk flow of blood to the skin or a substantial alteration of blood velocity in perfused capillaries. Either situation can affect cutaneous gas exchange. (Details of capillary recruitment and how this might influence cutaneous gas exchange are dealt with in detail by Malvin [1988] later in this symposium.)

To summarize, changes in cardiovascular performance affect cutaneous gas exchange by modifying the absolute volume of blood perfusing the skin, by adjusting the gas composition of arterial blood, and by changing the pattern of capillary perfusion. This paper will now consider in detail how bulk transport (*i.e.*, the absolute amount of flow) and gas composition of afferent blood could affect the cutaneous exchange of oxygen and carbon dioxide in vertebrates.

REGULATION OF CUTANEOUS BLOOD FLOW

As with any other vascular bed, blood flow to the skin varies directly with the blood pressure gradient along the length of the vessels in the skin and varies inversely with the vascular resistance presented by the cutaneous vessels. The interplay of these factors is quite complex, however, and involves hemodynamic adjustments in both the peripheral and central circulation.

Peripheral microvascular adjustments

Marked changes in the local pattern and distribution of blood in the skin occur in all vertebrate classes (Feder and Burggren, 1985*a*, *b*). Less well understood is how these changes occur, although they certainly involve localized adjustments in vascular resistance. In the skin of mammals, the role of the pre-capillary sphincter in distributing blood between exchange capillaries and arterio-venous anastomoses that bypass the capillaries has been long known (see Hales, 1985). In mammals, which use adjustments in skin perfusion to regulate exchange of heat rather than of respiratory gases, peripheral adjustments in cutaneous perfusion are affected by vasomotion in small arteries and arterioles (neurally regulated) and in the pre-capillary sphincters (mediated by localized metabolites).

In spite of renewed interest in cutaneous exchanges in non-mammalian animals (witness this symposium), surprisingly little is known of the local mechanisms and structures that influence the pattern of blood distribution in the skin of lower vertebrates. Early studies by Poczopko (1957) indicated that localized adjustments in skin perfusion occurred in the frog *Rana esculenta* in response to hypercapnia. The recruitment of cutaneous capillaries in bullfrogs is altered both by alpha-adrenergic blockade (Burggren and Moalli, 1984; Pinder, 1986) and muscarinic, cholinergic blockade (A. Pinder, unpublished), but the precise site of action in the microcirculation has yet to be determined. Malvin (1988, this volume) discusses the conse-

quences to gas exchange of these localized changes in cutaneous perfusion.

Central "macrovascular" adjustments

As indicated earlier, a change in cutaneous blood flow from no flow to a flow at which all capillaries are recruited can occur. Under the latter conditions, maximal surface area for gas diffusion is presented. Numerous structures and processes located in the central circulation potentially can regulate the total flow of blood to the skin (as distinct from the distribution of this flow within the skin). In a few vertebrate groups anatomical specializations of the arterial blood to the skin facilitate cutaneous gas exchange.

Skin-breathing vertebrates with "non-specialized" cutaneous blood supply. In non-anuran amphibians and reptiles the afferent blood supply to the skin is typical of other vertebrates—the cutaneous vascular bed is "just another systemic tissue" located in parallel with the vascular beds of the central nervous system, the visceral organs, muscle, etc. Can perfusion of the skin in these animals be preferentially adjusted to regulate cutaneous gas exchange? Unfortunately, experimental data relating to gas exchange are limited, but several studies indicate the potential for altering cutaneous flow. A major redistribution of blood flow between the various systemic vascular beds, resulting in a relative increase or decrease in cutaneous perfusion, occurs in response to thermal stress. In lizards, for example, an excessive elevation of body temperature triggers a disproportionate increase in cutaneous perfusion, resulting in enhanced convective heat loss from the body core (for review see Bartholomew, 1982). For example, Weathers *et al.* (1970), studying the lizards *Iguana* and *Tupinambis*, found that a sympathetically mediated vasoconstriction occurs in muscle of the hind limbs and tail upon heating, resulting in a preferential shunting of blood away from this muscle and to the skin. Adjustment of cutaneous perfusion for regulation of heat loss is also consistent with differential rates of heating and cooling in the Galapagos marine iguana (Bartholomew and Lasiewski, 1965) and with hysteresis in the relationship between heart rate and body temperature during heating and cooling in the soft-shelled turtle *Trionyx spinifer* (Smith *et al.*, 1981). Changes in cutaneous blood flow in response to dehydration stress occur in the salamander *Aneides* (Brown, 1972). Thus, cardiovascular mechanisms for preferentially perfusing the skin, which potentially could be utilized to regulate cutaneous gas exchange, exist in non-anuran amphibians and reptiles.

Little is known of how redistribution of blood flow between the skin and other vascular beds within the systemic circulation is actually achieved in non-anuran amphibians and reptiles, but redistribution almost certainly involves a neurally mediated adjustment in the relative balance of resistances offered by each of the parallel systemic circuits.

Skin-breathing vertebrates with "specialized" cutaneous blood supply. At least two groups of vertebrates have discrete, specialized vessels supplying blood to the skin in addition to the "typical" systemic arterial supply derived from vertebral vessels. First, I will discuss such vascular specializations in fishes.

Recent morphological studies by Vogel and his colleagues (Vogel, 1981*a*, *b*; Vogel and Claviez, 1981; Vogel, 1985) have revealed that an entire population of small vessels, regarded literally for centuries as lymphatic vessels (see Kampmeier, 1969, for references), in fact constitute a "secondary" arterial supply that lies parallel to the "primary" circulation (Fig. 1A) in cyclostomes, elasmobranchs and teleosts. The vessels of the secondary circulation, which derive from interarterial anastomoses from primary arteries, invariably have a much smaller diameter than the primary vessels (Fig. 1B). The secondary arterial vessels in trout, carp and *Tilapia* are extremely vasoactive and highly sensitive to any experimental manipulation (Vogel, 1985). Because of their very small diameter, experimentally induced vasoconstriction can result in exclusion of the comparatively large red cells from the secondary circulation, a phenomenon doubtlessly

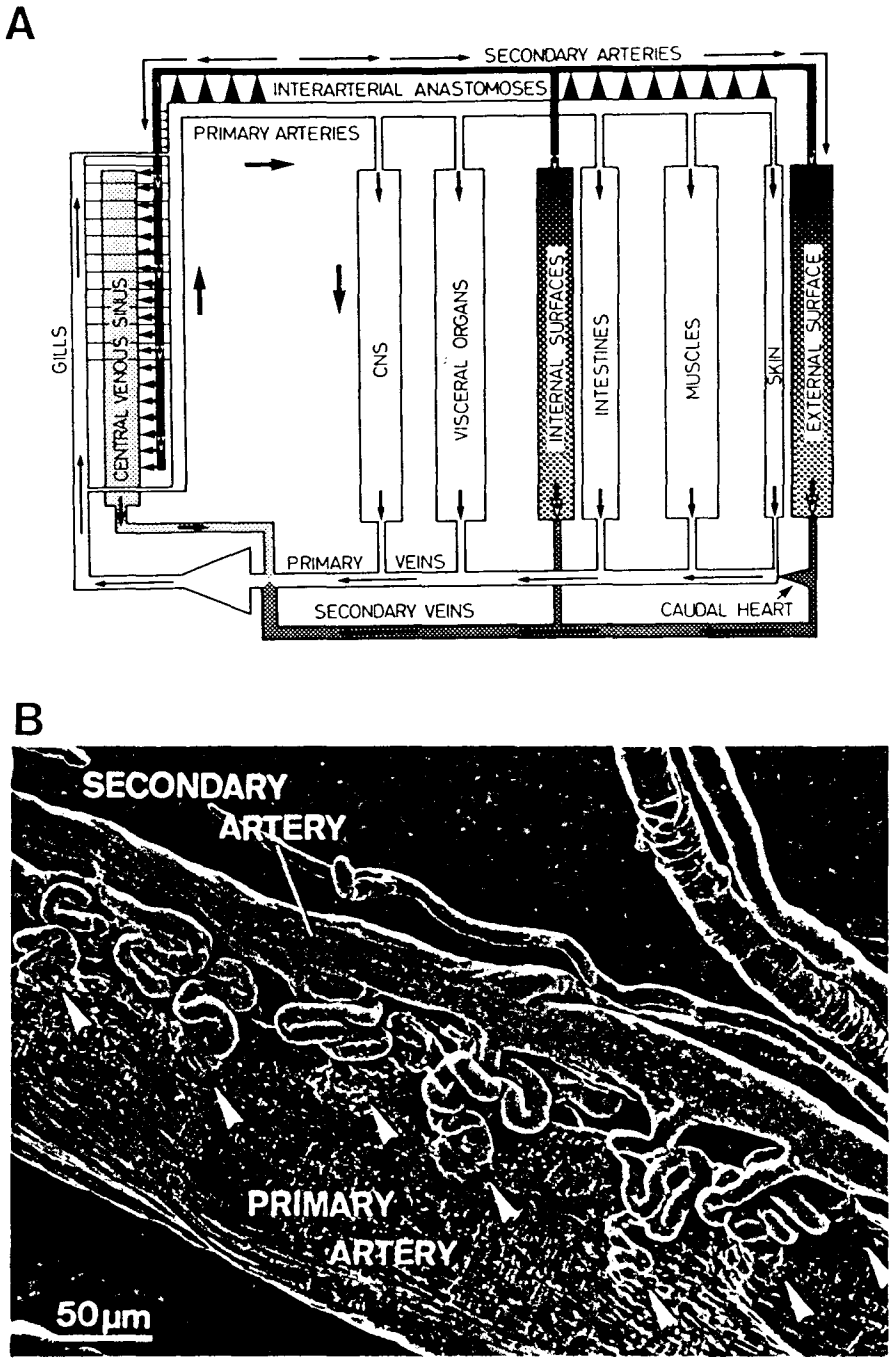

FIG. 1. A) Highly schematic diagram of the cardiovascular system of a typical water breathing fish. The vessels of the secondary circulation are shaded. B) Scanning electron micrograph of the vascular cast of arteries from the rainbow trout, *Salmo gairdneri*. The origins of interarterial anastomoses connecting a primary and secondary artery are indicated by arrows. From Vogel, 1985.

leading to their long-standing mistaken identification as lymphatic vessels. The strong vasoactivity of the secondary circulation suggests a considerable capacity for active regulation of blood flow in this circulation.

The skin of fishes, in particular, is heavily invested with secondary vessels that form a dense capillary network (Vogel, 1985). This secondary capillary network lies significantly closer to the surface than the primary vessels, and in scaled fishes is located mainly above the scales, immediately below the skin epithelium. This reduced blood/water (or blood/air) barrier almost certainly facilitates exchange of gases and ions in the cutaneous secondary circulation of fishes. Many fishes—both aquatic and air breathers—routinely depend upon cutaneous gas exchange to supplement ongoing branchial exchange (see Feder and Burggren, 1985*a*). An additional, nonbranchial exchange site for ions and gases also may be crucial for those aquatic fishes that ventilate their gills only intermittently (see Burggren *et al.*, 1986; Roberts and Rowell, 1988). Finally, some air breathing fishes leave the water briefly to forage on land. In *Erpetoichthys* (=*Calamoichthys*) *calabaricus*, for example, oxygen consumption triples during brief periods of air exposure, even though branchial gas exchange is greatly reduced under these conditions (Sacca and Burggren, 1982). The increased need for gas exchange during air exposure is met by increases in both pulmonary and cutaneous gas exchange.

A secondary capillary network available for recruitment under conditions of increased demand for gas exchange would appear to be particularly advantageous if blood flow through it could be finely regulated. Unfortunately, very little is known of how blood flow through the secondary circulation of the skin in fishes is regulated and, consequently, the physiological role of the secondary circulation remains enigmatic. The secondary circulation of the gills of fishes has recently come under considerable scrutiny (see Randall, 1985), and circulating catecholamines have been implicated in regulation of blood entering the central venous sinuses from the secondary arterial circulation of the gills.

Anuran amphibians also have specializations of the vasculature supplying the skin. Anurans possess a systemic arterial supply to the skin similar to that of other vertebrates. In addition, however, the skin of anurans receives a separate, substantial blood supply from a pair of discrete cutaneous arteries (Fig. 2). These arteries are derived from a proximal bifurcation of paired pulmocutaneous arteries. The pulmocutaneous arteries receive a greater proportion of deoxygenated blood from the heart than do the systemic arteries (see below) and thus the skin of anurans is heterogeneous in terms of both anatomical origin and gas composition of blood perfusing it. At least two studies have used radioactive microspheres to map the distribution of these two separate arterial supplies to the skin of the bullfrog *Rana catesbeiana* (Moalli *et al.*, 1980; Boutilier *et al.*, 1986). Although differences in the experimental preparations doubtlessly led to the differences in details of blood flow distribution that emerged, these studies collectively reveal that 1) all regions of the skin receive some blood supply from both arterial sources, and 2) the distribution of the pulmocutaneous blood supply is very heterogeneous (Fig. 3).

Numerous recent studies have examined how anurans regulate blood flow to the skin (for references see West and Burggren, 1984; Feder and Burggren, 1985*a*). First, consider flow regulation in the systemic arterial supply to the skin. Unfortunately, the systemic supply to the skin of anurans consists of numerous small and mostly inaccessible arteries, and to date few hemodynamic data for this particular vascular bed are available. The use of miniaturized ultrasonic pulsed Doppler transducers has allowed some recording of blood flow in systemic vessels supplying the skin of a curarized *Rana catesbeiana* at 10°C (A. Pinder, unpublished, see figs. 7 and 8 in Feder and Pinder [1988] in this symposium). Blood flow in these systemic cutaneous arteries can be regulated in concert with blood flow in the cutaneous arteries.

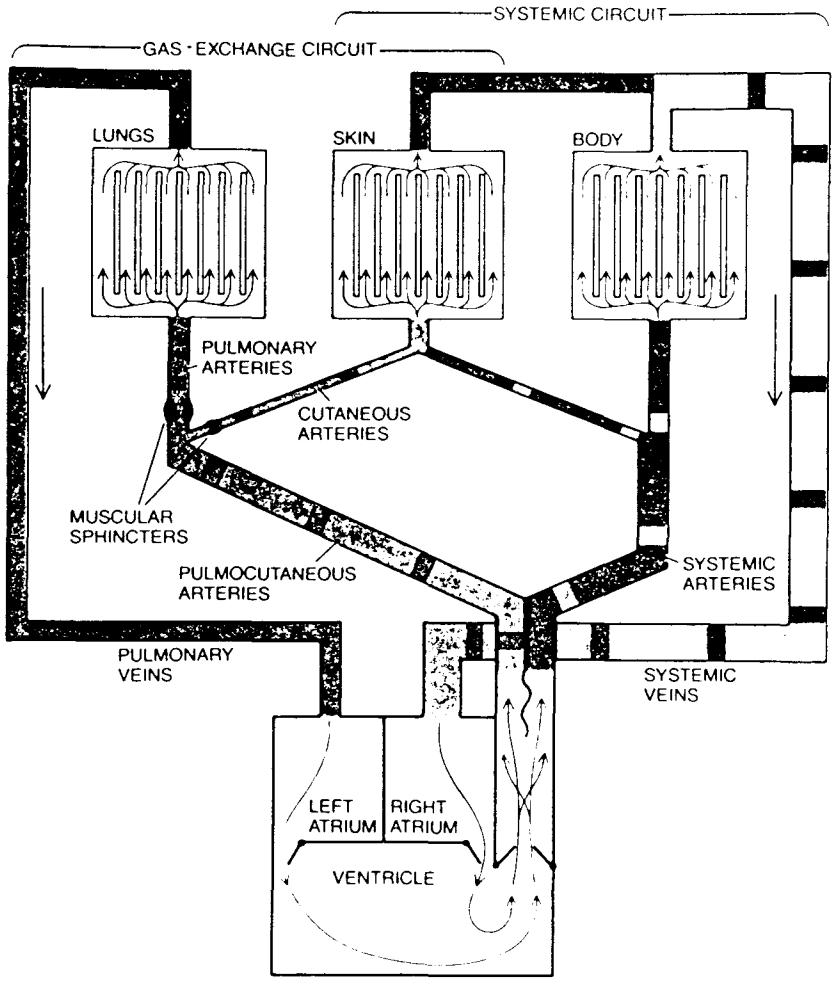

FIG. 2. Diagram of the circulation of an anuran amphibian. Heavy shading indicates oxygenated blood. From Feder and Burggren, 1985*b*.

Higher vertebrates can preferentially divert an increased systemic cardiac output to active muscle beds at the expense of cutaneous and visceral perfusion. Whether such redistribution within the systemic arterial circulation occurs in actively exercising anurans currently is unknown. A sympathetically mediated redistribution of arterial blood within the systemic circulation of anurans occurs in response to a challenge to water balance (Hillman and Somerfeldt, 1982; Burggren and Moalli, 1984). In Burggren and Moalli's (1984) study, a few hours of air exposure in bullfrogs with surgical ligation of the cutaneous branch of the pulmocutaneous arteries resulted in a significant decrease of systemic arterial blood flow to the skin with no significant change in blood flow to a variety of other tissues, including brain, muscle, stomach, liver, kidney, etc. During diving in frogs, when heart rate and presumably total cardiac output fall markedly (Jones, 1967; Lillo, 1979; Burggren and Doyle, 1986), blood flow in the systemic arteries supplying the skin actually increases substantially (Moalli, 1980). Interestingly, Moalli (1980) reported that changes in systemic arterial blood flow to the skin associated with intermittent breathing were cholinergically mediated, although he did not determine whether this resulted from

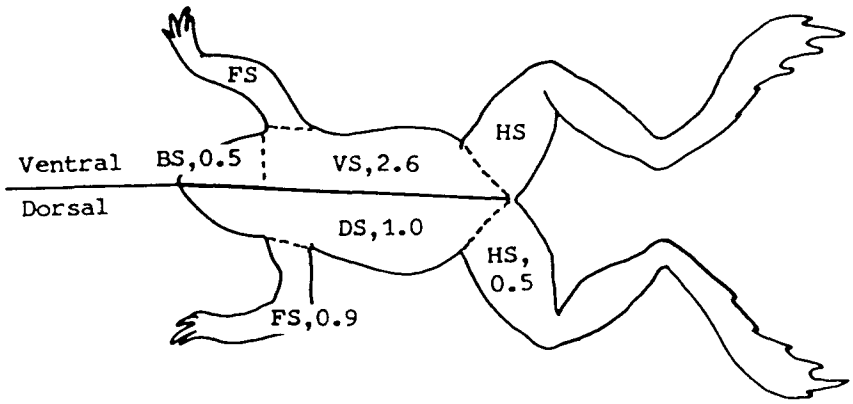

FIG. 3. The regional distribution of the cutaneous arterial blood supply to the dorsal and ventral skin of the conscious, unrestrained bullfrog, *Rana catesbeiana*. Data were collected at 10 min into a voluntary dive under normoxic conditions. The numbers reflect the ratio of mass-specific blood flow from the cutaneous artery serving a particular region to total mass-specific flow in the entire cutaneous vascular bed, for the blood source shown in the drawing. Ratios greater than 1 indicate a greater than average supply to that region of skin from the cutaneous arteries. DS, dorsal skin; VS, ventral skin; BS, buccal skin; HS, hindleg skin; FS, foreleg skin. Modified from Boutilier *et al.*, 1986.

an active adjustment of the cutaneous vascular bed or a passive redistribution of blood away from vasoactive muscle. In summary, several lines of evidence suggest that anurans can actively regulate the blood flow through the systemic arterial component of the cutaneous vascular bed independent of other systemic vascular beds.

In contrast to the anatomy of the systemic arterial supply to the skin, the cutaneous arterial supply consists proximally of a pair of large, relatively accessible arterial trunks. Consequently, most physiological and pharmacological experiments have concentrated largely, if not exclusively, on regulation of cutaneous arterial blood flow, as will now be described. The central vascular arrangement of anurans essentially places the two gas exchange organs—lungs and skin—in parallel with each other (Fig. 2). In turn, this combined gas exchange circuit lies in parallel with the systemic circulation. The proportion of total pulmocutaneous blood flow that is distributed into the cutaneous vascular bed is dictated not only by the resistance offered by the skin, but also by the resistance resident in the pulmonary vasculature. Within limits, it is the *balance* between pulmonary and cutaneous resistance that dictates the peripheral distribution of pulmocutaneous blood flow. Thus, cutaneous blood flow in anurans can be altered not only by increases in absolute levels of pulmocutaneous blood flow, but also by independent or orchestrated changes in resistance of the skin and of the lungs. This unique circulatory arrangement provides numerous potential "control points" in both pulmonary and cutaneous circuits that ultimately can regulate cutaneous blood flow (Couvreur, 1889; Arthaud and Butte, 1890).

Pulmonary vascular resistance in anurans is quite labile, both *in vivo* and *in vitro* (Shelton, 1970; Campbell, 1971; Emilio and Shelton, 1972; Smith, 1976, 1978; De Saint-Aubain and Wingstrand, 1979; De Saint-Aubain, 1982; West and Burggren, 1984). The anatomical basis for regulation of pulmonary vascular resistance is not fully understood. In addition to vasomotor activity within the lung parenchyma, the extrinsic segment of the pulmonary artery of anurans is highly vasoactive, constricting strongly in response to either vagal stimulation or application of acetylcholine (Smith, 1976, 1978; De Saint-Aubain and Wingstrand, 1979). In the frog *Rana temporaria* and the toad *Bufo bufo*, at least, a vagally innervated muscular sphincter is located at the base of the pulmonary artery just distal to the point at which it arises

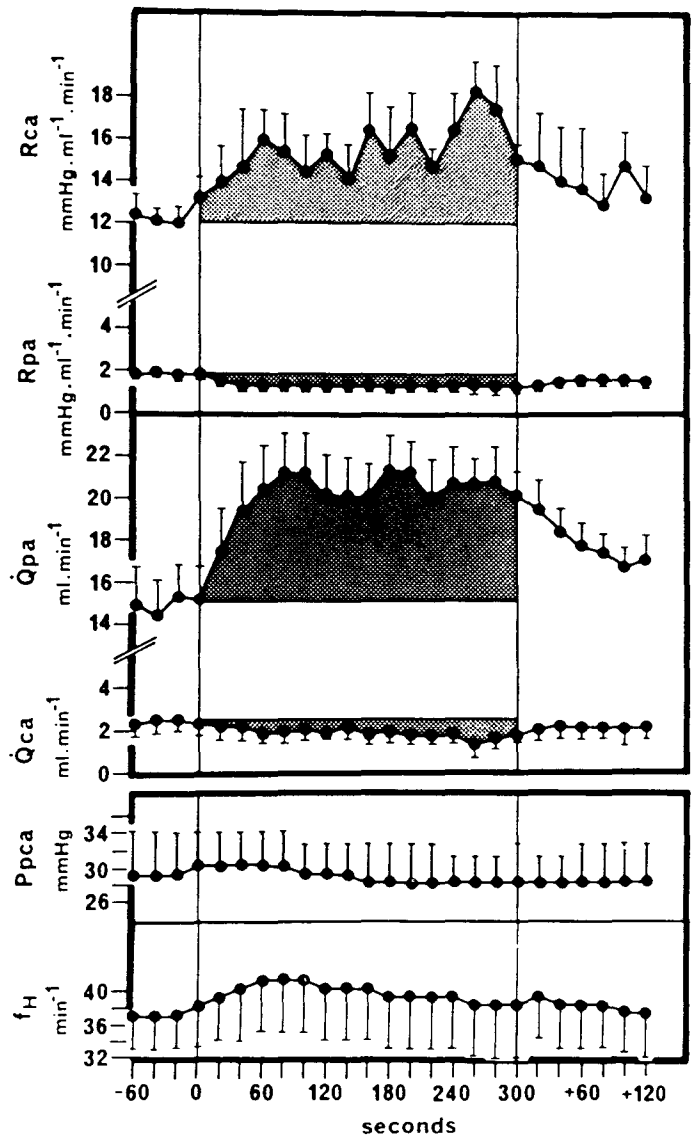

FIG. 4. Responses to lung inflation from 0 up to 3 cm H_2O in unidirectionally ventilated, anesthetized toads, *Bufo marinus*. Vertical bars = SE; n = 5, mean mass = 468 ± 29 g. Rca = cutaneous arterial resistance; Rpa = pulmonary arterial resistance; Qpa = pulmonary arterial minute flow; Qc = a cutaneous arterial minute flow; Ppca = mean pulmocutaneous arterial pressure; f_H = cardiac frequency. From West and Burggren, 1984.

from the pulmocutaneous artery (De Saint-Aubain and Wingstrand, 1979; De Saint-Aubain, unpublished; Fig. 2). Adjustments in pulmonary vascular resistance occur during voluntary intermittent ventilation (see Shelton, 1986, for review) and artificial inflation of the lungs produces a decrease in pulmonary resistance accompanied by a large increase in pulmonary blood flow (Fig. 4). The magnitude of the inflation response depends in a complex fashion upon the O_2 and CO_2 composition of the gas used for lung inflation (West and Burggren, 1984), and has been interpreted by these authors as mediation of the reflex by chemo-sensitive mechanoreceptors known to exist in

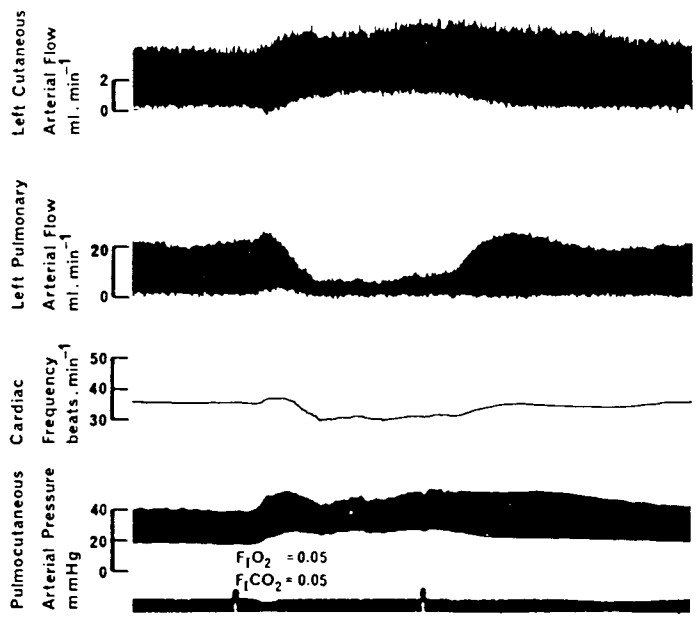

FIG. 5. Pulmonary and cutaneous blood flow, pulmocutaneous arterial pressures and cardiac frequency in a unidirectionally ventilated, anesthetized toad, *Bufo marinus*. At the point indicated on the time marker, a step-wise change in lung gas composition from air to 5% O_2 and 5% CO_2 was initiated. This mixture was used to unidirectionally ventilate the lungs for 5.0 min, after which unidirectional ventilation with air was resumed. Note the reciprocity of pulmonary and cutaneous blood flow. From West and Burggren, 1984.

amphibian lungs (see Burggren, 1988, for references).

Cutaneous vascular resistance is also very labile, but the anatomical basis for these adjustments is less clear than for the pulmonary circulation. The cutaneous artery in *Bufo marinus* is innervated by excitatory adrenergic nerve fibers from the vagosympathetic trunk—there appears to be considerably less cholinergic innervation (Smith, 1976; West and Burggren, 1984).

The same factors that reflexly adjust pulmonary vascular resistance (*e.g.*, spontaneous ventilation, artificial lung inflation, hypercapnia, hypoxia) also reflexly alter cutaneous vascular resistance. Importantly, however, a stimulus such as lung inflation with hypoxic, hypercapnic gas causes *reciprocal* changes in cutaneous and pulmonary blood flow (Figs. 4, 5). Thus, if pulmonary blood flow is reflexly increased due to mechanical distension of the lungs, cutaneous blood flow reflexly decreases. These changes, achieved by changes in peripheral resistance, are due to active adjustments in vessel diameter produced by vasomotion, rather than by "passive" changes in the diameter of compliant vessels resulting from changes in transmural pressure.

The reciprocal nature of pulmonary and cutaneous arterial blood flow in anurans, achieved by alterations in the balance of vascular resistances, appears to facilitate effective matching of perfusion with the changing potential for gas exchange by the lungs and skin (Smith, 1976; West and Burggren, 1984). During periods of lung ventilation, the P_{O_2} of lung gas is highest, as is the gas exchange potential of the lungs (Boutilier and Shelton, 1982). Pulmocutaneous blood is distributed away from the heavily diffusion-limited skin and into the pulmonary circuit, facilitating gas exchange in the lungs. During prolonged breath holding, however, the gas exchange potential of the lungs falls. Relative to the lungs, the skin assumes a greater role in gas exchange, facilitated by the distribution of blood away from the lungs and to the skin.

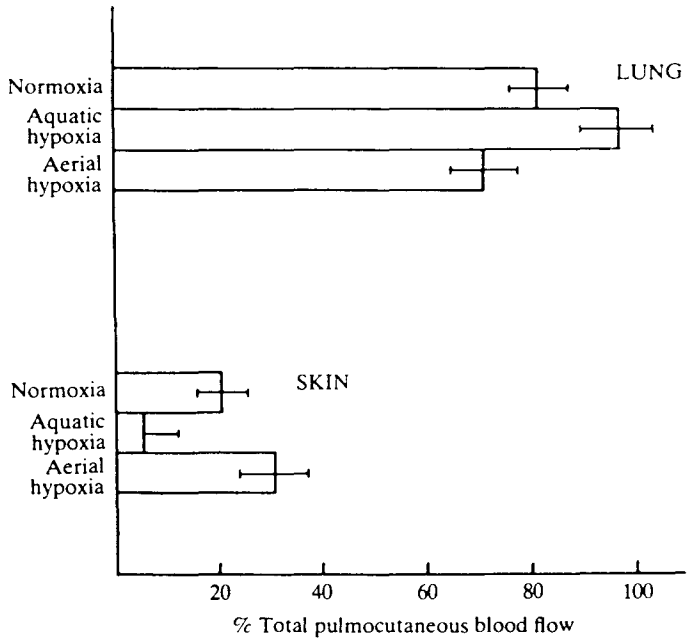

FIG. 6. The relative distribution to the lungs and skin of pulmocutaneous blood in conscious, unrestrained bullfrogs (*Rana catesbeiana*) 10 min into a voluntary dive. Frogs were subjected to normoxia (P_{O_2} = 155 mmHg), aquatic hypoxia (P_{O_2} = 40 mmHg) only, and aerial hypoxia (P_{O_2} = 40 mmHg) only. From Boutilier *et al.* (1986).

A recent study of Boutilier *et al.* (1986) has advocated an additional rationale for the reciprocity of blood flow to the lungs and skin. Using microspheres to examine blood flow in intact, unrestrained bullfrogs (*Rana catesbeiana*) during voluntary dives, these investigators found that the usual distribution of pulmocutaneous blood flow (80% to lungs, 20% to skin) could be altered significantly by aquatic hypoxia to favor lung perfusion, or by aerial hypoxia to favor skin perfusion. Boutilier *et al.* (1986) suggest that blood flow to the lungs or skin may be adjusted to prevent loss of oxygen from blood in the capillaries to an hypoxic respiratory medium (Fig. 6).

REGULATION OF O_2 AND CO_2 COMPOSITION OF CUTANEOUS ARTERIAL BLOOD

A second major mechanism by which central cardiovascular adjustments alter cutaneous gas exchange involves short-term alterations in the P_{O_2} and P_{CO_2} of arterial blood perfusing the cutaneous vascular bed, and thus in the transcapillary partial pressure gradient for gas diffusion.

Many different factors ultimately will influence the gas composition of arterial blood leaving the heart, including the extent of diffusion or perfusion limitations in non-cutaneous gas exchange organs, the absolute levels of ventilation and perfusion of these other exchangers, composition of the respiratory medium, etc. These phenomena do not specifically affect the blood supply to the skin, but rather cause equivalent changes in gas composition of blood distributed to each systemic arterial bed.

The oxygen and carbon dioxide partial pressures of arterial blood perfusing the skin can also be influenced by intracardiac admixture of pulmonary venous and systemic venous blood. In reptiles, intracardiac shunting can range from virtually no admixture to nearly complete bypass of the lungs (approaching 100% right-to-left shunt), resulting in a direct recirculation of systemic venous blood in the systemic arterial circulation (for reviews see White,

1976; Burggren, 1985; White, 1985; Burggren, 1987). However, few studies have specifically addressed the effects of such shunting on the movement of oxygen and carbon dioxide across the skin. Presumably, an increased right-to-left shunt, which results in decreased systemic arterial P_{O_2} and increased P_{CO_2}, would increase the transcutaneous partial pressure gradients and facilitate movement of gases between cutaneous capillary blood and the ambient medium. In reptiles, a right-to-left shunt is most likely to develop during prolonged periods of apnea, when the potential demand for non-pulmonary gas exchange would be highest (see Burggren, 1987). On the other hand, both stroke volume and, in particular, heart rate are the very lowest during prolonged periods of apnea, and so cardiac output and skin perfusion also are probably at their lowest. To what extent the increased transcapillary partial pressure gradient is offset by a reduced cutaneous arterial blood flow has not been assessed.

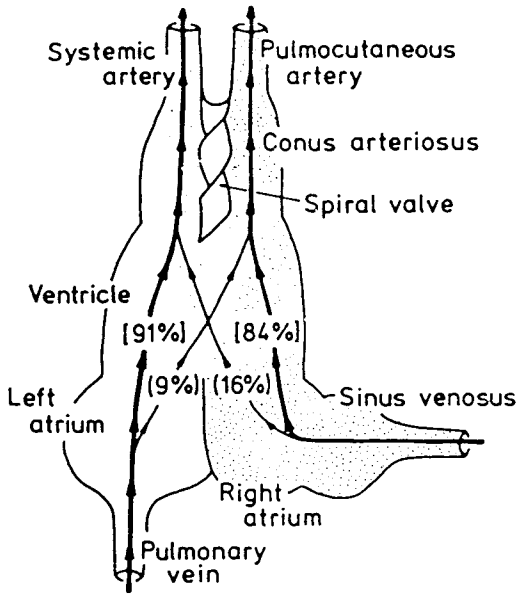

FIG. 7. Mean intracardiac shunt fractions in the bullfrog, *Rana catesbeiana*. Data were collected from repeated blood sampling from anesthetized frogs with opened chest and pericardium. From Tazawa *et al.*, 1979.

Intracardiac shunting also occurs in amphibians (see reviews by Shelton, 1985; Malvin, 1985). In these vertebrates, however, the analysis is even more complex than in reptiles, since systemic venous blood is composed not only of relatively deoxygenated blood draining muscle, viscera, etc., but also contains considerable quantities of oxygenated blood draining the skin (Fig. 7; Tazawa *et al.*, 1979). Thus, a given proportion of recirculation of systemic venous blood into the systemic arteries (*i.e.*, a right-to-left shunt) will not reduce systemic arterial P_{O_2} to the same extent as in reptiles.

In anuran amphibians, in which the skin receives both systemic and cutaneous arterial blood (Fig. 2), the analysis of the effect of intracardiac shunting on gas exchange is particularly complex. In anesthetized bullfrogs with an open pericardium, surprisingly little intracardiac admixture occurs (Tazawa *et al.*, 1979). More than 90% of all pulmonary venous return (which is about 96% O_2 saturated) is directed to the systemic arteries, while more than 80% of systemic venous return (which is only 44% O_2 saturated) is directed to the pulmocutaneous circulation (Fig. 7). A similarly highly selective passage of oxygenated and deoxygenated blood through the heart occurs in intact, unrestrained anurans (see Shelton, 1985, for references).

Ironically, the lack of a major intracardiac shunt will *reduce* the transcutaneous partial pressure gradient and thus the potential for cutaneous gas exchange in those capillaries perfused from systemic arteries. At the same time, however, the lack of an intracardiac shunt results in a greater gas partial pressure gradient between the ambient medium and blood perfusing the skin that originated from the pulmocutaneous arteries. The net effect on cutaneous gas exchange will thus depend on the proportion of total cutaneous blood flow that is supplied from each arterial source. Unfortunately, a quantitative analysis of the effect of shunting on cutaneous gas exchange has yet to be made.

Additional complexity results from the increasing intracardiac shunt in both directions during progressive apnea in anurans (Shelton, 1976, 1985). An increased shunt fraction will progressively reduce the dif-

ference in gas partial pressures in systemic and cutaneous arterial blood, leading towards functional homogeneity with respect to the gas composition of blood perfusing the skin perfusion. Apnea may influence cutaneous exchange by altering the total amount of skin blood flow according to mechanisms discussed earlier. While Moalli *et al.* (1980) have documented the heterogeneous nature of the vascular supply to the skin of anurans under steady-state conditions, if and how the contribution of the two different arterial sources changes during intermittent breathing is not clear.

CONCLUDING REMARKS

Although primarily limited by the rate of diffusion of oxygen and carbon dioxide across the integument, cutaneous gas exchange in vertebrates is affected by adjustments in 1) the absolute flow of blood to the skin, 2) the pattern of distribution within the cutaneous vascular bed of this blood, and 3) the gas partial pressures of arterial blood perfusing the skin. The interplay of these various factors, particularly in animals with heterogeneous arterial supply to the skin and/or with intracardiac shunts potentially influencing arterial gas partial pressures, is complex and in many instances not fully understood.

Particularly fruitful areas for further research include: 1) establishing the role of capillary recruitment in adjusting skin gas exchange, 2) identification of mechanisms and structures responsible for distribution of blood flow within the cutaneous vascular bed, 3) ascertaining how and to what extent bulk flow to the skin can be varied independently of general systemic perfusion. Those vertebrates with specializations of the cutaneous arterial supply—fishes and anuran amphibians—present additional challenges, including: 4) determining the physiological role of the extensive secondary circulation of the skin of fishes and 5) elaborating upon our fragmentary knowledge of the heterogeneous character of cutaneous vasculature in anuran amphibians.

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