

CUTANEOUS GAS EXCHANGE IN VERTEBRATES: DESIGN, PATTERNS, CONTROL AND IMPLICATIONS

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I. INTRODUCTION

Most accounts of the evolution of gas exchange organs in vertebrates have emphasized the gills, air bladder and lungs as allowing progressively increasing access to diverse aquatic and terrestrial environments. The role of the skin as a gas exchange organ has received comparatively little attention, and then mainly as an evolutionary relic in a few primitive or bizarre species. In this review we emphasize several seldom appreciated aspects of cutaneous gas exchange in vertebrates: its widespread occurrence, its versatility, its control, and the many problems and several advantages associated with breathing with the body surface. We emphasize general principles in cutaneous gas exchange and delineate productive areas for future research.

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The skin is an unusual respiratory organ in vertebrates because it is not dedicated solely to the exchange of gases with the environment. Although the gills of vertebrates often function in osmoregulation and feeding, and the lungs or air bladder function in sound production, sound reception, buoyancy regulation and metabolic regulation (Randall *et al.*, 1981; Feder & Wassersug, 1984), the primary function of these structures is gas exchange. The skin of vertebrates, by contrast, has many important functions in addition to gas exchange (protection from mechanical injury, support, locomotion and thermoregulation) but no obvious 'primary' function. In some vertebrates, skin functions in feeding, predator defence, communication, courtship and reproduction as well. At first consideration, these functions seemingly conflict with cutaneous gas exchange. Moreover, the skin poses special problems as a gas exchanger because it is not confined to a discrete anatomical locality; its ventilation and regulation as a gas exchanger are thus potentially difficult.

The physical laws that govern the exchange of gases through the lungs and gills apply equally to cutaneous gas exchange. These laws suggest that gas exchange via the skin will be constrained in certain ways, but that means exist by which an animal may partially circumvent these constraints. The occurrence of cutaneous gas exchange in diverse vertebrates testifies that cutaneous gas exchange is effective despite such constraints, and that vertebrates have used diverse but related solutions to the common problems inherent in cutaneous gas exchange. Cutaneous gas exchange contributes significantly to tissue respiration in various fishes, nearly all amphibians, many reptiles, and certain mammals. Vertebrates that rely on cutaneous gas exchange occur in marine, fresh water, intertidal and terrestrial habitats. Although cutaneous gas exchange typically is integrated with branchial or pulmonary gas exchange in most animals that breathe through their skin, some fishes, amphibians and reptiles rely solely on cutaneous gas exchange in certain circumstances. Many salamanders either lack or do not use lungs and gills, and thus always breathe solely through their skin. We first consider these potential physical and physiological constraints upon cutaneous gas exchange, possible remedies and which of these remedies have actually been employed.

II. DESIGN CONSTRAINTS OF CUTANEOUS GAS EXCHANGE

Gas exchange across the skin of vertebrates is governed by three separate processes. The first is ventilation, the delivery of the respiratory medium (air or water) to the skin's surface. This process is crucial to the effective functioning of lungs and gills. Most models of cutaneous gas exchange in vertebrates assume that the skin is in contact with an 'infinite pool' of air or water; presumably the lack of active ventilation places negligible constraints upon cutaneous gas exchange given this circumstance. We discuss the reality of this assumption below. The second and third processes are diffusion, in which gas passes through the skin, and convection, in which gas dissolved in blood or bound to haemoglobin is carried to or away from the skin via bulk flow.

The quantity of O_2 and CO_2 that is exchanged through the skin and hence the utility of the skin as a gas exchange organ depends on both morphological and physiological variables. Diffusion is proportional to the skin surface area, the skin permeability to gases and the difference in gas concentration (or, more appropriately, the gas partial pressure) on either side of the skin, and is inversely proportional to skin thickness. Fick (1870)

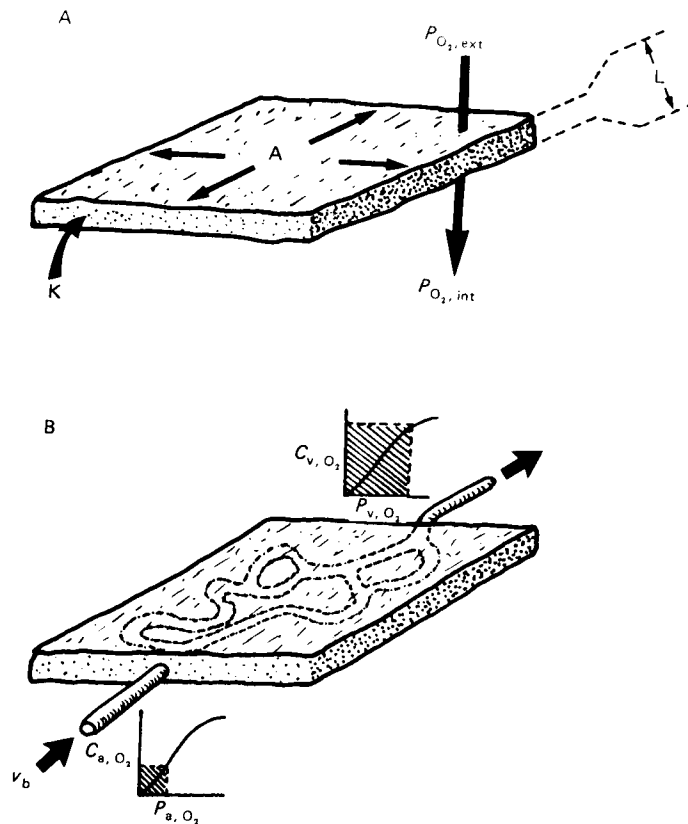


Fig. 1. Diagram representing physical variables that influence the rate of O₂ transfer across a patch of skin of surface area A and thickness L . Symbols: $P_{O_2, ext}$ and $P_{O_2, int}$, partial pressure of O₂ external and internal to the skin, respectively; K , Krogh's diffusion coefficient, the product of O₂ diffusivity in skin (D) and skin capacitance for O₂ (β) (Krogh, 1919); \dot{V}_b , the rate of blood flow through the skin; C_{a, O_2} and C_{v, O_2} , the concentration of O₂ in arterial blood entering the skin and venous blood leaving the skin, respectively; P_{a, O_2} and P_{v, O_2} , arterial and venous P_{O_2} . (A) Factors that influence diffusion across the skin. (B) Factors that influence carriage of O₂ to or from the skin. Note that the functional surface area, the area of the capillary across which O₂ passes into the blood, can be less than the total surface area of the patch of skin.

first described the relationship between these factors as it governs gas diffusion through membranes, and formally stated the 'law' as:

$$\dot{M}_x = D_x \cdot A \cdot (C_{ext, x} - C_{int, x}) / L, \quad (1a)$$

where \dot{M}_x is the mass of gas x transferred per unit time, A is the surface area for diffusion, $(C_{ext, x} - C_{int, x})$ is the concentration difference of x across the skin, L is the barrier width or membrane thickness, and D_x is the diffusion coefficient of x . These elements are shown diagrammatically in Fig. 1. Because the measurement of gas concentrations in tissues is often difficult or impossible, the equation may be expressed similarly as:

$$\dot{M}_x = K_x \cdot A \cdot (P_{ext, x} - P_{int, x}) / L, \quad (1b)$$

where K is defined empirically and is equivalent to the product of D_x and the skin capacitance for gas x (Dejours, 1981). Convective transport of gas is proportional to the rate of bulk flow and the difference in blood gas concentration as the blood enters and leaves the skin. Fick (1870) characterized this relationship as:

$$\dot{M}_x = \dot{V}_b \cdot (C_{a,x} - C_{v,x}) \quad (2a)$$

or

$$\dot{M}_x = \dot{V}_b \cdot \beta_x \cdot (P_{a,x} - P_{v,x}), \quad (2b)$$

where \dot{V}_b is the rate of blood flow, β_x is the blood capacitance for gas x , and $(C_{a,x} - C_{v,x})$ and $(P_{a,x} - P_{v,x})$ represent the difference in blood gas concentration and partial pressure, respectively, as blood enters and leaves the skin.

Either diffusion or convection alone may limit cutaneous gas exchange. Moreover, cutaneous gas exchange is most effective when the rate of diffusion approximately matches the rate of convection. Thus, the relative magnitude of both processes and all of their components can limit cutaneous gas exchange.

In skin, as in other gas-exchange organs, all diffusion variables may fluctuate independently. These variations may be the subject of natural selection in the evolution of a species and also may occur rapidly in an individual animal. This flexibility, often unappreciated by biologists, affords vertebrates that breathe through their skin an enormous number of ways to meet changing respiratory demands. Unfortunately, it also makes the study of the process extremely complex. Here we discuss how each variable in the Fick equation has been modified to meet changing needs for gas exchange across the skin.

(1) *Surface area*

Fick's equation (1) suggests that animals can modify cutaneous gas exchange by changing the *functional* surface area through which diffusion occurs. This may occur in at least three ways: by (1) changing the total amount of skin surface, (2) changing the proportion of capillaries that are perfused at any given time; and (3) changing the number of respiratory capillaries per unit skin surface.

(a) *Total surface area*

Many vertebrates that rely upon cutaneous respiration have undergone evolutionary changes in shape that increase the total surface area available for gas exchange. One common change in shape consists of the skin being thrown into a series of well vascularized folds, which increase the surface area of the animal while retaining the general body form. These range from simple skin folds in the aquatic salamander *Cryptobranchus alleganiensis* (Guimond & Hutchison, 1973a) and the tail fin in many amphibian larvae (Medvedev, 1937; Strawinski, 1956) to dedicated dermal papillae in several species of 'hairy' frogs (Fig. 2; Noble, 1925, 1931; Parker, 1936) and enormous flaps of skin in some frogs (Fig. 2; Hutchison, Haines & Engbretson, 1976; W. Duellman, personal communication). The gross body form may also facilitate or retard cutaneous gas exchange. Whereas many fish have a relatively globose body form, some species that rely heavily upon cutaneous respiration (e.g. the eel, the reedfish *Calamoichthys*, the mudfish *Neochanna* (Berg & Steen, 1965; Meredith, Davie & Forster, 1982; Sacca & Burggren, 1982)) are elongate and thus have a large surface: volume ratio.

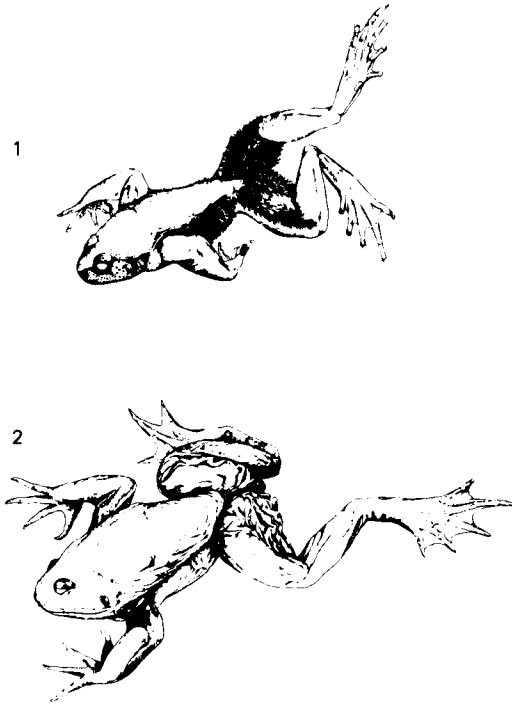


Fig. 2. Increased cutaneous surface area for gas exchange in amphibians (Noble, 1925). (1) In *Astylosternus robustus* (the 'hairy' frog), the hind limbs bear dermal papillae. (2) In *Batrachophrynus macrophthalmus* and *Telmatobius culeus* (not shown), the skin is loose and highly folded.

Individual animals may also alter their surface area during their lives. The tail fin of male newts enlarges during their breeding season (Czopek, 1959*b*, 1965), when metabolic demands are likely to increase (Bennett & Houck, 1983). This hypertrophy probably promotes tolerance of hypoxia and successful mating (Bannikov, 1948; Halliday & Sweatman, 1975). Also, the large tail fin of bullfrog tadpoles, *Rana catesbeiana*, degenerates as the lungs enlarge during metamorphosis (Burggren & West, 1982).

(b) Skin capillarization and surface area

Increasing the numbers of blood vessels per unit area (i.e. skin capillary density) can also enhance the functional surface area of the skin. Changes in capillary density are associated with interspecific differences, developmental changes in individual animals, and environmental effects on a particular individual at a particular developmental stage.

The skin of amphibians, which almost always rely on cutaneous gas exchange, is heavily vascularized, with capillary densities of 30–200 capillary meshes per mm² of skin (Fig. 3; Czopek, 1965). Between 20–95% of total respiratory capillarization may reside in the skin, even in species that also breathe with lungs and gills (Czopek, 1965). Many studies (Bethge, 1898; Ficalbi, 1899; Noble, 1925; Czopek, 1965; Ultsch, 1974*a*) have related interspecific variation in the capillary density of amphibians to dependence upon cutaneous gas exchange. These features are not highly correlated. For example, in the lungless plethodontid salamanders, which rely almost entirely on cutaneous exchange,

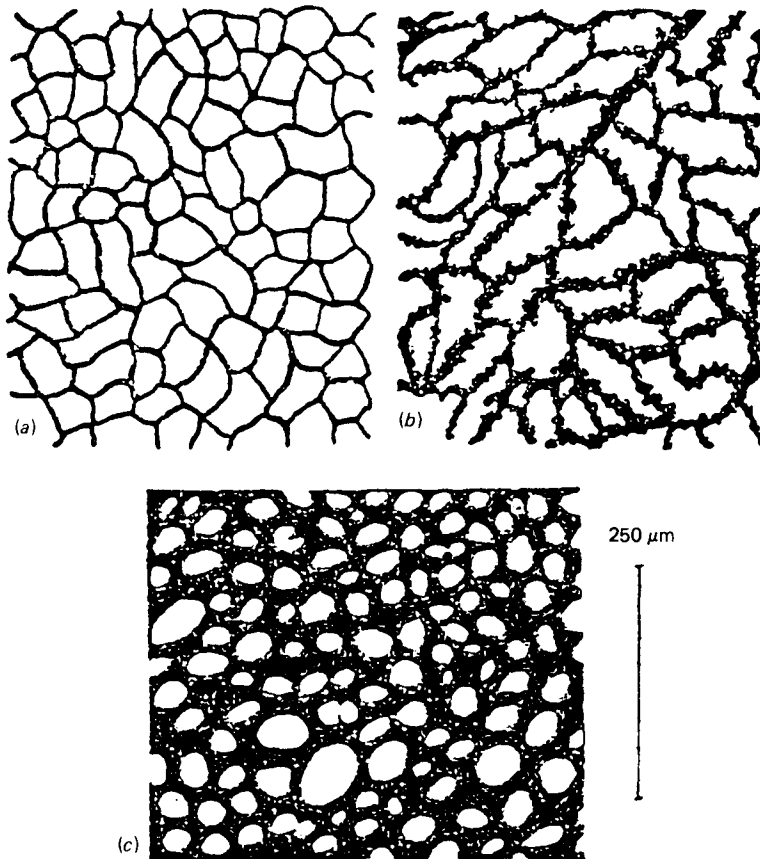


Fig. 3. Capillaries in the skin (a), palate (b), and lungs (c) of *Rana esculenta* L., a frog (from Czopek, 1955).

skin capillary networks are no more dense than in anurans or salamanders with lungs (Czopek, 1965). The lack of correlation is not especially surprising because so many other variables are related to diffusion of gas across the skin. Also, interspecific variation in skin capillary density may be more closely related to non-respiratory functions of the skin. In anurans, for example, the ventral surface is often the most heavily capillarized region of the skin (Czopek, 1965), but is most generally in contact with the substrate and thus may be ineffective in gas exchange. This heavy capillary density in the ventral skin of frogs may relate more to water balance (particularly cutaneous water uptake) than to cutaneous respiration (Shoemaker & Nagy, 1977). Urodeles as a group generally lack a dense ventral capillary network.

Skin capillary density, and thus functional surface area, also change ontogenetically (Strawinski, 1956; Czopek, 1957, 1959a; Burggren & Mwalukoma, 1983), although no consistent trend is apparent. While Czopek (1957) associated the decreased numbers of skin capillaries after metamorphosis in salamanders (*Ambystoma*) with the increasing importance of pulmonary gas exchange, either no change (Burggren & Mwalukoma, 1983) or an increase (Strawinski, 1956; Saint-Aubain, 1982) in capillary density occurs with metamorphosis in anurans. In most adult amphibians examined, the role of the skin in CO_2 excretion remains constant or increases after metamorphosis, with pulmonary function related mainly to oxygen uptake (see Section IV, 2).

Skin capillary density can vary markedly when environmental changes such as hypoxia are imposed upon individuals of a single species of a specific mass at a single developmental stage. Such changes may indeed relate to changes in the functional surface area for respiration. In larval bullfrogs, *Rana catesbeiana*, chronic exposure to moderate hypoxia increases the capillary mesh density of the skin by nearly 150% (Burggren & Mwalukoma, 1983).

Accordingly, with the possible exception of short-term adjustment to a specific environmental stress affecting gas exchange, variations in the extent of skin capillarization, and thus variations in the respiratory surface area of the skin, appear to relate as much to other skin functions as to gas exchange.

(c) Capillary recruitment and surface area

All capillaries in the skin of fishes or amphibians are seldom perfused all the time. In the most precise usage, the surface area A in Fick's equation (1) represents not the *total* surface area of the gas exchange organ, but rather the *functional* surface area; i.e. that proportion of the total surface area that actually is both ventilated and perfused at a given time. Thus, while A is usually portrayed as a fixed value in Fick's equation, this value will in fact undergo rapid and large changes if capillary recruitment or derecruitment occurs. Since gas diffusion is directly proportional to the surface area term A in Fick's equation (1), considerations of capillary recruitment, its effect on functional surface area and its regulation are therefore extremely important in an analysis of cutaneous gas exchange.

Many investigators have described rapid and large changes in skin perfusion, based on observations of 'blushing' of formerly less perfused skin patches (M. Feder, D. Quinn, R. Wassersug, W. Burggren – all independent, unpublished observations; Connolly, 1926; Heatwole & Seymour, 1978). Thus, additional skin capillaries may potentially open and accommodate blood flow (capillary recruitment). If at any given time the skin contains non-perfused capillaries, then the surface area across which cutaneous gas exchange can occur will be some fraction of the total surface area of the skin. Non-perfused regions of the skin thus experience a 'physiological' blood shunt, which reduces total gas conductance in a fashion analogous to the reduction in gas transfer accompanying the physiological shunt common in the under- or non-perfused alveoli of the upper zones of mammalian lungs (West, 1979).

Despite this potential for significant physiological shunts in the skin, quantitative analyses of cutaneous respiration in vertebrates have invariably assumed full capillary recruitment – i.e., all capillaries that can be identified morphologically are assumed to be open and perfused. For example, in their calculations of cutaneous gas exchange in the lungless salamander *Desmognathus fuscus*, Gatz, Crawford & Piiper (1975) and Piiper, Gatz & Crawford (1976) used Czopek's (1961) morphological estimate of *total* cutaneous and buccopharyngeal capillary surface area, reduced by one-half to designate gas exchange across the outer half of each capillary (i.e. that half facing the external environment).

In many lower vertebrates, however, the proportion of capillaries that are perfused, and hence the functional surface area, is under active control. Connolly (1926) described adrenergically mediated vasodilation of the skin and fin rays of the teleost *Fundulus*. Alterations in skin perfusion and subsequent changes in the depth of skin colour in this fish were stimulated by changes in substrate colour; no consideration of changes in gas

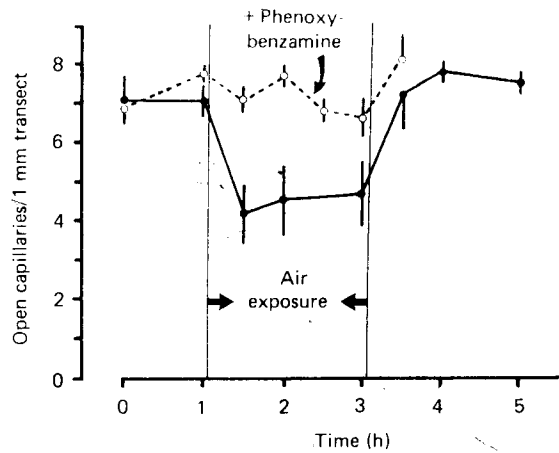


Fig. 4. Numbers of perfused capillaries in the hind foot web of *Rana catesbeiana*, a frog, before, during and after complete air exposure. Dashed line indicates data collected after injection of phenoxybenzamine, an alpha adrenergic blocker (after Burggren & Moalli, 1984).

exchange was made. In air-breathing fishes such as *Calamoichthys*, cutaneous O_2 uptake increases during brief periods of air exposure (Sacca & Burggren, 1982). These authors inferred that cutaneous perfusion probably increased, and certainly the recruitment of capillaries in response to local irritation of the scales occurs in this species (Burggren, unpublished). In amphibians, in which cutaneous gas exchange (particularly CO_2 excretion) is of major importance, recruitment of skin capillaries is well documented. Poczopko (1957) reported that in the frog *Rana esculenta*, the number of skin capillaries perfused increased by 30% when frogs breathed a 5% CO_2 -air mixture, or when pulmonary ventilation was prevented by blocking the glottis. Szarski (1959) has also shown that gross variations in the P_{O_2} and P_{CO_2} of gas in contact with the skin alters the number of skin capillaries open in adult frogs. An increase in the functional respiratory surface area of the skin during diving would be appropriate in amphibians, particularly during long periods of breath-holding, when the potential for pulmonary gas exchange is lowest. An increase in blood flow into the cutaneous artery concomitant with a decrease in pulmonary blood flow during voluntary diving has been observed in *Rana catesbeiana* (Moalli *et al.*, 1980) and the pharmacological and physiological basis for reciprocal changes in pulmonary and cutaneous arterial flow has been described for *Bufo marinus* (Smith, 1978; Saint-Aubain & Wingstrand, 1979; West & Burggren, 1984). For functional surface area to change, however, changes in the actual number of capillaries perfused must accompany adjustments in cutaneous perfusion rate. Alpha-adrenergic regulation of capillary recruitment occurs in *Rana catesbeiana* (Burggren & Moalli, 1984). In this species, the number of perfused skin capillaries decreases by nearly one-half during several hours of total air exposure, and restoration of capillary blood flow occurs after the animal returns to floating on the water's surface (Fig. 4). Considerable disruption of cutaneous CO_2 elimination accompanies capillary derecruitment, which is blocked by the alpha-antagonist phenoxybenzamine. These authors speculate that reduced cutaneous blood flow during total air exposure may be important in minimizing water loss, although at the temporary expense of CO_2 elimination.

Large adjustments in cutaneous blood flow in response to local or general heating of the skin occur in crocodylians, lizards, snakes and turtles (Bartholomew, 1982). Courtice (1981) has shown that localized exposure of the skin of the water dragon, *Physignathus lesueurii*, to 5% CO₂ increases blood flow through the underlying skin. Critical information is still unavailable regarding whether these vascular responses in reptiles represent increased blood flow through capillaries already perfused, or actual recruitment of previously stagnant capillaries.

(2) Diffusion path length (L)

Decreases in the thickness (L) of the skin overlying the cutaneous capillaries should result in an increase in cutaneous gas exchange, whether considering the growth of an individual animal or interspecific differences. Only in a few vertebrates has thinning of the skin evolved in conjunction with cutaneous respiration (Czopek, 1965), perhaps because of the multi-faceted function of skin. Whereas the gas diffusion barrier of dedicated internal gas-exchange organs such as lungs or gills can often be as little as 0.1–10 μm (Dejours, 1981; Randall *et al.*, 1981), the evolution of a similarly thin skin might well compromise the mechanical and support functions of the skin or lead to the unbridled loss of water and various osmolytes. Thus, the epidermis of amphibians is rarely less than 20 μm thick (Czopek, 1965).

Many vertebrates, however, accommodate the respiratory and non-respiratory functions of skin simultaneously by possessing discrete patches of thick and thin skin, which serve different needs. For example, in snakes, lizards and many teleosts, relatively thick scales (which protect the skin) alternate with patches of skin. The relatively thin skin between the scales is richly invested with capillaries (see Section IV). The eeltrid fish *Dormitator* has a highly vascularized epithelial surface on top of its head, which it exposes to the air when in hypoxic water; the remainder of the fish's skin is unremarkable (Todd, 1972, 1973). A similar phenomenon may have evolved in reverse to curtail water loss from the skin; cutaneous capillaries are deep to the skin of xeric 'waterproof' frogs (*Chiromantis*), but are superficial in most other amphibians (Drewes *et al.*, 1977).

In cutaneous gas exchange, respiratory gases must transit the skin overlying the respiratory capillaries, any mucus that is present on the skin, and a 'diffusion boundary layer' of stagnant respiratory medium immediately adjacent to the outermost layer of the skin and mucus. The thickness of the skin is fixed at any one time. The thickness of the mucus covering the skin will vary, but little is known about how this mucus affects cutaneous gas exchange. The mucus covering the skin of the carp, *Cyprinus carpio*, has an O₂ diffusivity about 30% lower than water itself, and clearly represents an added diffusion barrier (Ultsch & Gros, 1979).

The thickness of the diffusion boundary layer may change with ventilation (see Section II, 4(a)). Changes in skin thickness and thus in L can also occur in a single individual in response to developmental changes or environmental conditions. Some specialized amphibians and fish construct 'cocoons' about their body during prolonged aestivation. These cocoons may consist of shed epidermis, mucus and dried soil, and generally reduce water loss. In constructing cocoons, such animals may change both D_x and L, which in turn alters the partitioning of gas exchange between lungs and skin (Loveridge & Withers, 1981).

increases in the thickness of the gas-diffusion barrier of the skin may also occur during metamorphosis in anurans (Burggren & Mwalukoma, 1983) and urodeles (Czopek, 1957, 1959a). Chronic exposure to mild hypoxia causes the gas diffusion barrier in the skin of larval *Rana catesbeiana* to decrease from 45 μm to just 15 μm (Burggren & Mwalukoma, 1983), presumably enhancing cutaneous oxygen uptake. Under identical conditions, however, the arrangement of skin capillaries remains unchanged in adult bullfrogs (Burggren & Mwalukoma, 1983). Seasonal changes in the gas diffusion barrier of the skin of amphibians have also been described (Czopek, 1959b, 1965; Kun, 1959).

(3) Diffusivity (D_x or K_x)

Adaptive variation in diffusivity is somewhat constrained because diffusivity is related mainly to the composition of a substance and the skin is always constructed from basically the same set of biochemical substances. However, different body tissues may vary severalfold in diffusivity. For example, K for muscle is 22% greater than that for connective tissue and more than ten times that for chitin (Krogh, 1919). Thus, differences in skin composition among vertebrates may result in differing permeabilities to respiratory gases. This possibility has not been examined; it remains to be seen whether vertebrate skin composition actually varies sufficiently to affect cutaneous gas exchange and whether the skin diffusivity of vertebrates is correlated with their reliance upon cutaneous gas exchange. However, as recent work with 'scaleless' reptiles has emphasized, direct measurements are required to relate skin structure to skin permeability (Licht & Bennett, 1972; Bennett & Licht, 1975). Much long-established speculation in the absence of such measurements (e.g., that reptilian scales reduce skin permeability) may be unfounded.

All else being equal, respiratory gases will diffuse at rates approximately in inverse proportion to their molar masses (Dejours, 1981); i.e., O_2 will diffuse slightly more rapidly than CO_2 . However, both biological tissue and water have a far greater CO_2 capacitance than O_2 capacitance. When differences in capacitance are taken into account, CO_2 will diffuse through tissue and water 20–40 times more rapidly than will O_2 (Dejours, 1981). Moreover, the size of the diffusion boundary layer will be greater for O_2 than for CO_2 (see Hitchman, 1978). Consequently, on the basis of diffusivity considerations alone, the skin of aquatic vertebrates should be far more effective in excreting CO_2 than in extracting O_2 from the water, all other factors being equal. Indeed, in vertebrates that rely on cutaneous gas exchange, the skin typically is more important in CO_2 excretion than in O_2 uptake (see Section IV).

A potential drawback of cutaneous gas exchange is that if the skin promotes a large flux of respiratory gases, it may also promote large fluxes of other substances as well and thereby hinder osmoregulation. This possibility is discussed more fully below. However, in at least one group of vertebrates (sea snakes), the skin is more permeable to respiratory gases and water than to ions (Dunson, 1975, 1978; Lillywhite & Maderson, 1982). The basis for this selective resistance to ion flux is enigmatic (Lillywhite & Maderson, 1982), but presumably lies in differing diffusivities for each solute species. In any event, independence of gas, water, and ion diffusivities in skin could obviously be advantageous to vertebrates that rely on cutaneous gas exchange.

(4) *Partial pressure gradient*(a) *Ventilation*

In the lungs and gills of vertebrates, the process of ventilation renews the air or water with which gas exchange occurs. This maintains a large partial pressure gradient across the gas exchanger, and thereby promotes gas exchange. The skin of vertebrates, by contrast, lacks a dedicated ventilatory pump. One beneficial but seldom recognized aspect of cutaneous respiration is that animals can use environmental flow and routine body movements to 'ventilate' the skin with little energetic cost attributed specifically to the respiratory process (see Vogel, 1981*a*, and Section V). If environmental flux or animal movement is infrequent, however, diffusion of gases through the skin creates a hypoxic or hypercapnic boundary layer about an animal. Such stagnant, unstirred boundary layers may limit cutaneous gas exchange. For example, Hills & Hughes (1970) have calculated that the diffusion boundary layer about the secondary lamellae of fish gills accounts for 80–90% of the total resistance to diffusion of respiratory gases.

The severity of such limitation is related to the thickness of the diffusion boundary layer (T), which is in turn related to the velocity (V) and kinematic viscosity (ν) of the respiratory medium about the skin, diffusivity of the gas in question (D), and the linear dimension (X) of the animal across which the respiratory flow may occur, as follows (Hitchman, 1978):

$$T = D^{0.33} \nu^{0.66} (X/V)^{0.5}. \quad (3)$$

For diffusion of O_2 in water:

$$T \text{ (cm)} = 0.01357 [X \text{ (cm)}/V \text{ (cm} \cdot \text{sec}^{-1})]^{0.5}. \quad (4)$$

All else equal, the thickness of the diffusion boundary layer is inversely proportional to the square root of the velocity of the respiratory medium across the skin. For respiratory gas exchange not to be limited by a diffusion boundary layer, the following condition must hold (Hitchman, 1978):

$$T \ll D_{\text{water}} \cdot T_{\text{skin}}/D_{\text{skin}}. \quad (5)$$

where D_{water} and D_{skin} are the diffusivity of a gas in water and skin, respectively, and T_{skin} is skin thickness. Substituting the values of Dejours (1981, table 2) for O_2 and equation (5) into equation (3), and solving for V yields

$$V' \text{ (cm} \cdot \text{sec}^{-1}) = 1.743 \times 10^{-5} X \text{ (cm)} \cdot [T_{\text{skin}} \text{ (cm)}]^{-2}. \quad (6)$$

V should exceed this value (V') to avoid incipient limiting effects of the diffusion boundary layer on cutaneous O_2 uptake. For a typical lungless salamander ($T_{\text{skin}} = 25 \mu\text{m}$; $X = 1.5 \text{ cm}$; Czopek, 1965) in water, V' is approximately $4 \text{ cm} \cdot \text{sec}^{-1}$. This flow rate corresponds well to the current speed at which a diffusion boundary layer begins to limit O_2 excretion from photosynthesizing plants in water (Wheeler, 1980). All of the above equations are for laminar flow; diffusion boundary layers are likely to be less thick in turbulent flow (Hitchman, 1978).

Implications of these equations are severalfold. Krogh's constant of diffusion (the product of D and gas capacitance) is much greater for CO_2 in water than for O_2 in water, suggesting that a smaller V' than is required for O_2 will dissipate the CO_2 diffusion boundary layer about skin. Both D and ν are far greater in air than in water, necessitating

only a low V' for skin in air. Because air movement is seldom less than 10 cm. sec⁻¹ even in 'still' air (Nobel, 1974), diffusion boundary layers should seldom affect cutaneous respiration in air. V' is greater for large animals than for small animals, and is greater when the long axis of an animal or limb is parallel to the ventilatory flow than when the long axis is perpendicular to the ventilatory flow. Finally, because V' is proportional to $(T_{\text{skin}})^{-2}$, boundary layer formation should be of greatest consequence to animals with thin, highly permeable skins.

Despite the potential significance of diffusion boundary layers, measures of water and air flow rates about the cutaneous gas exchangers of vertebrates in their natural habitats are few (Vogel, 1981a). Thigmotrophic responses that orient an animal's body in a water current, or even locomotor movements while in unstirred water, may well increase gas diffusion across the skin. Amphibians of several species wave parts of the body or the entire body in the water, thereby ventilating the skin; these movements are more frequent in hypoxia and hypercapnia (Guimond & Hutchison, 1973a; Hutchison *et al.*, 1976; Boutilier, McDonald & Toews, 1980; Boutilier & Toews, 1981).

At any one moment, significant portions of an animal's integument may contact the substrate or be folded together, thereby reducing the potential for cutaneous gas exchange. Often bottom sediments in water are hypoxic or anoxic. Minor adjustments in posture and locomotor movements may well have dramatic effects on cutaneous gas exchange, but have not been investigated in this regard.

Perfusion

Oxygen and carbon dioxide partial pressure gradients across the skin are influenced not only by the diffusive properties of the skin and boundary layer and convection of the respiratory medium, but also by the gas partial pressures of the blood perfusing the skin. Partial pressures of blood perfusing the skin are dictated by a complex interaction of factors including (1) the respiratory quality of the environment, (2) the efficacy of gas transfer of other gas exchange organs (gills, lungs, gas bladder), (3) the derivation of the cutaneous blood supply, (4) the rate of cutaneous blood perfusion, and (5) the respiratory properties of the blood. The derivation of the cutaneous blood supply from the central circulation is probably the single most important factor affecting blood partial pressure gradients across the skin. Obviously, the difference in P_{O_2} between blood leaving gills or lungs and that draining systemic tissues is large, and so the relative proportions of 'venous' and 'arterial' blood entering the arteries leading to the skin will have major implications for cutaneous gas exchange.

The fishes generally perfuse the skin with blood derived from the dorsal aorta. The gills are located in series with and proximal to the general systemic circulation, including the skin. Since the gills with their countercurrent flow of water and blood are highly effective organs for gas exchange, blood perfusing the skin will already have a substantially higher P_{O_2} and lower P_{CO_2} compared with venous blood draining the tissues (Randall, 1970). This anatomical arrangement does not particularly favour effective cutaneous gas exchange. Nonetheless, cutaneous gas exchange represents a significant proportion of total gas exchange in many fishes (see Section IV). Interestingly, in bony fishes an extensive secondary vascular system parallels much of the regular (primary) vessels in the peripheral vasculature (Vogel, 1978, 1981b, 1982). In particular, this previously undescribed vascular system forms an extensive network in the skin and the

rins, and has been implicated in both gas exchange and osmoregulation (Vogel, 1982). However, this secondary vascular network, like the primary one, derives its blood supply from the dorsal aorta, and so P_{O_2} and P_{CO_2} gradients between cutaneous blood and the environment will still be lower than if the skin received venous blood before transit through the gills. Steffensen, Lomholt & Johansen (1981), reporting a considerable cutaneous uptake in the plaice *Pleuronectes platessa*, speculated that the skin micro-circulation might involve a second capillary arrangement in series with the nutritive capillaries of the skin. This 'portal-like' skin vascular bed would considerably enhance cutaneous O_2 uptake, since the P_{O_2} gradient across the walls of these capillaries would be larger than in other skin capillaries. Such a micro-circulation remains to be documented, however.

Major morphological adaptations of the circulation occur in many air breathing fishes, but such specializations preferentially direct deoxygenated blood to a gas bladder or lung rather than to the skin (see Johansen, 1970; Satchel, 1976; Johansen & Burggren, 1980). While considerable cutaneous gas exchange may occur in air breathing fishes (Graham, 1976; Sacca & Burggren, 1982), the partial pressure gradients across their skin are nonetheless smaller than would be the case if venous rather than arterial blood perfused the skin.

The amphibians are the only vertebrate class in which the central circulatory morphology favours cutaneous gas exchange by preferentially directing deoxygenated, venous blood towards the skin. In addition to a 'conventional' intersegmental arterial supply perfusing the skin with blood derived primarily from the left atrium, all regions of the skin also receive arterial blood primarily from the right atrium via the cutaneous arteries (Fig. 5). The cutaneous arteries carry blood similar in quality to that conveyed in the pulmonary arteries (i.e. primarily right atrial blood with low P_{O_2} and high P_{CO_2}), since they all branch distally from the paired pulmo-cutaneous arteries. The skin is thus a mosaic with respect to derivation of its blood supply and the gas partial pressure gradients, with the largest transcapillary gradients for O_2 and CO_2 occurring in capillaries perfused from the cutaneous artery. Recently, Moalli *et al.* (1980) have used microspheres to quantify the relative contributions of aortic and cutaneous arterial blood to skin perfusion in *Rana catesbeiana*. The skin covering the flanks and dorsal surface of the body receives primarily deoxygenated blood from the cutaneous artery (Fig. 6). In contrast, the systemic arterial supply is greatest to the skin of the limbs and approximately equally distributed to all other regions. The partial pressure gradients driving oxygen uptake and CO_2 removal thus will be greatest on the dorsal surfaces and the flanks, though of course other factors such as functional surface area and skin thickness will influence the actual amount of gas exchanged. Since much of the ventral surface of amphibians is occluded when these animals rest on the substrate, the pulmocutaneous supply may in fact perfuse most of the functional cutaneous respiratory surface.

No vestige of the cutaneous branch of the amphibian pulmocutaneous circuit remains in reptiles. In this class the intersegmental arteries exclusively supply the skin. Aortic blood is usually derived largely from left atrial blood and is near O_2 saturation during periods of lung ventilation and all but the most prolonged apnoea (see White, 1976; Burggren & Shelton, 1979; Seymour, 1982). Thus, transcutaneous gas partial pressure gradients will normally be small. Intracardiac shunting in reptiles can redistribute

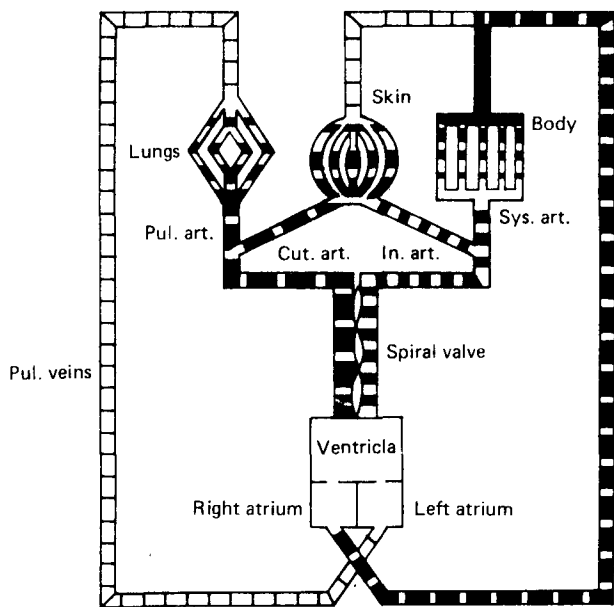


Fig. 5. A highly diagrammatic representation of the amphibian circulation. Oxygenated blood, white; deoxygenated blood, black. Cut. art., cutaneous artery; In. art., intersegmental arteries; Pul. art., pulmonary arteries; Pul. veins, pulmonary veins; Sys. art., systemic arteries; Sys. veins, systemic veins.

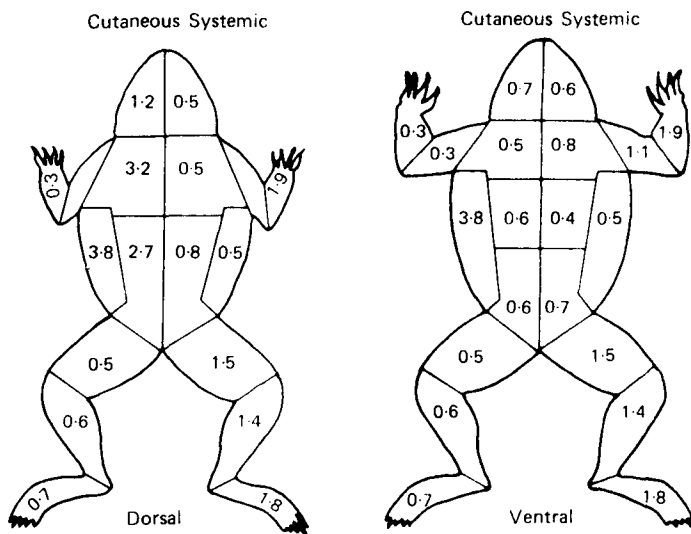


Fig. 6. The relative distribution of cutaneous and systemic circulation for various skin regions in the dorsal and ventral skin of the bullfrog, *Rana catesbeiana*. The numbers reflect the ratio of blood flow per gramme of skin in a particular region to total blood flow per gramme of skin for the entire body surface, for the blood source shown above the drawing. Ratios greater than 1 indicate a greater than average supply to that region of skin from the particular blood source (from Moalli *et al.*, 1980).

blood output such that the lungs are substantially bypassed and the cutaneous circulation is perfused primarily with right atrial blood with a low P_{O_2} and a high P_{CO_2} (see Johansen & Burggren, 1980). Sea snakes use this mechanism to great advantage (Seymour, 1982). A large right-to-left shunt during diving ensures a low arterial P_{O_2} , which favours the diffusion of oxygen across the skin from the water. Thus, some diving aquatic snakes obtain one-third or more of their oxygen via the skin (see Section IV (3)). Irrespective of intracardiac shunting, prolonged apnoea (e.g. during diving or dormancy) may be accompanied by extreme values of arterial P_{O_2} (less than 20 Torr) and P_{CO_2} (greater than 60 Torr) (Seymour & Webster, 1975; Burggren & Shelton, 1979; Ultsch & Jackson, 1982). In these exceptional circumstances, transcutaneous pressure gradients may increase sufficiently to promote significant O_2 uptake and CO_2 elimination via the skin in reptiles that might otherwise rely entirely on pulmonary gas exchange.

Blood respiratory properties will also affect transcutaneous gas partial pressure gradients, particularly in the presence of venous-arterial shunts, either in the central vascular circulation or in the gas exchange organs themselves. If significant admixture of 'arterial' and 'venous' blood does occur, then the P_{O_2} of the resulting mixed blood is a function of blood O_2 content and blood O_2 affinity (P_{50}) (Wood, 1984). Under such conditions, the higher the blood O_2 affinity (the lower the P_{50}), the lower will be the resulting blood P_{O_2} after blood admixture. In amphibians, for example, left and right atrial blood mix in the single ventricle and in the base of the pulmocutaneous and systemic arches. For the same ratio of left and right atrial admixture, the resulting P_{O_2} of both pulmocutaneous and systemic arterial blood will be lower (and thus the transcutaneous P_{O_2} gradient higher) if the blood oxygen affinity is higher. Thus, in animals with significant central vascular shunts (i.e. amphibians, most reptiles) blood oxygen affinity may greatly influence the transcutaneous P_{O_2} gradient and thus cutaneous gas exchange. Lenfant & Johansen (1967) have compiled extensive blood gas and O_2 affinity data for a series of amphibians (*Necturus*, *Amphiuma*, *Rana*) with an increasing dependence on aerial respiration (Guimond & Hutchison, 1976). Interestingly, while all three species have a systemic arterial saturation of about 90%, the blood P_{50} s for *Necturus*, *Amphiuma* and *Rana* are 14, 27 and 39 Torr, respectively (Fig. 7). Given these sets of independent variables, the dependent variable, arterial P_{O_2} , is 35, 81 and 95 Torr, respectively. According to these P_{O_2} values for arterial blood, *Necturus* should have the greatest transcutaneous P_{O_2} gradient and so the greatest cutaneous O_2 uptake, while *Rana* should have the least. Gas partitioning experiments have supported this contention (Guimond & Hutchison, 1972, 1974, 1976; Gottlieb & Jackson, 1976; Burggren & West, 1982; Burggren & Moalli, 1984).

An enhanced Bohr shift is another adjustment in blood characteristics that might favour cutaneous gas exchange. As in any gas exchange organ, elimination of CO_2 will increase O_2 affinity through the Bohr shift, and thus facilitate O_2 uptake. A significant Bohr shift might be particularly appropriate in some amphibians, in which the skin is the major site of CO_2 elimination and thus the release of CO_2 in the capillary should be high.

The rate of cutaneous blood flow and hence velocity of blood movement (independent of changes in numbers of perfused capillaries; see Section II, 1(c)) can affect transcutaneous partial pressure gradients and thus cutaneous gas exchange. If the blood velocity through cutaneous capillaries is very slow, then capillary blood gases will

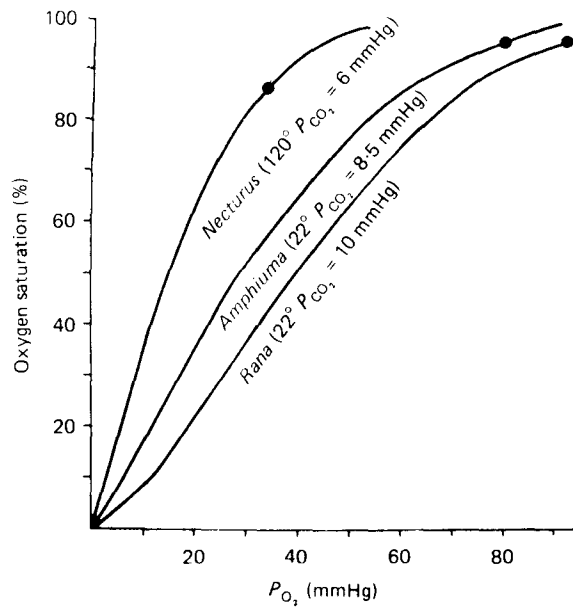


Fig. 7. Oxygen equilibrium curves for whole blood of the aquatic salamanders, *Necturus* and *Amphiuma*, and the bullfrog, *Rana catesbeiana*. Typical levels of arterial blood saturation for each species are indicated by the points on the curves (after Lenfant & Johansen, 1967).

equilibrate with the respiratory medium well before leaving the capillary. From this point until the efferent end of the capillary, no additional gas will be exchanged; this portion of the capillary is functionally 'wasted'. If the velocity of capillary flow is very fast, then the blood in cutaneous capillaries may lack sufficient time to equilibrate with the respiratory medium, and the gas content of this blood will change but little along the entire length of the capillary. A large cutaneous gas transfer may occur overall, but the incremental change in gas partial pressure and content of blood draining the skin may be quite small, and certainly smaller than in the optimal situation in which capillary blood approaches equilibrium with the respiratory medium only towards the end of its transit through the capillary. Unfortunately, virtually nothing is known of transit times through cutaneous capillaries in vertebrates, or of the direct effects of changes in blood velocity on transcutaneous partial pressure gradients.

(5) Conclusion

The ways that vertebrates may adjust cutaneous gas exchange are of two types. Some elements of the Fick relationship are constrained by morphological and physiological properties of organisms, and are more or less fixed at any one time. Skin diffusivity cannot be increased above certain limits because the skin is composed of protoplasm and membranes, whose composition fixes its diffusivity. Likewise, selective distribution of deoxygenated blood to the skin is impossible unless the necessary cardiac and arterial constructs are present. Skin thickness, area, and capillary density, although subject to acclimatory and evolutionary modification, cannot be altered instantaneously when gas exchange needs change. By contrast, several related components of the Fick equation

minutes from minute to minute. These include ventilation of the skin, blood flow to the skin, the number of cutaneous capillaries that are perfused, and the partial pressure gradient across the skin. These components may also undergo acclimatory and evolutionary modification. Thus, cutaneous gas exchange should be viewed as extremely plastic and subject to adaptive modification on a long-term basis. In the short term, however, cutaneous gas exchange is governed by two resistances: the fixed and the variable elements of the Fick relationship. Several questions pertain to this dual governance of cutaneous gas exchange. Can vertebrates effectively manipulate the variable resistances so as to modify the skin to meet changing needs for gas exchange? Are the fixed resistances sufficiently great to constrain gas exchange in vertebrates regardless of any short-term adjustments, or can short-term adjustments compensate for the fixed resistances? How do the major groups of vertebrates differ in their dependence upon cutaneous gas exchange and the efficacy of their control of this process? What, if any, are the consequences of constraints upon cutaneous gas exchange?

III. CONTROL OF CUTANEOUS RESPIRATION

Vertebrates that breathe through lungs and gills can generally regulate the rate at which gases are exchanged with the respiratory medium; this regulation typically occurs through adjustments in ventilation and perfusion. Thus, vertebrates that breathe through lungs and gills can increase, decrease, or hold constant their O_2 intake and CO_2 elimination while maintaining a relatively constant P_{O_2} and P_{CO_2} in the arterialized blood. As Section II emphasizes, vertebrates that use cutaneous gas exchange can also vary ventilation and perfusion of the skin. However, there is some question as to whether changes in ventilation and perfusion *can* alter cutaneous gas exchange significantly and whether vertebrates that breathe through their skin are ever able to increase or decrease cutaneous gas exchange while maintaining relatively fixed P_{O_2} and P_{CO_2} in arterialized blood, as is the case with pulmonary and branchial gas exchange. Our aim in this section is to consider first whether cutaneous gas exchange in vertebrates *can* be regulated (i.e. increased, decreased, or held constant) short of gross changes in internal gas pressures, and secondarily how such regulation might be accomplished.

Several models suggest that adjustments in ventilation and perfusion have relatively little effect on cutaneous gas exchange. In an extensive analysis of cutaneous gas exchange in *Desmognathus fuscus*, Gatz *et al.* (1975), Piiper & Scheid (1975), and Piiper *et al.* (1976) assessed the relative roles of diffusion and perfusion in cutaneous gas exchange. Their calculations were based on a model with a single blood compartment experiencing variable blood flow. By estimating the fractional decrease in gas transfer rate (\dot{M}) from the actual measured value when no diffusion limitation was present (i.e. $D = \infty$), an index for diffusion limitation was established, and defined as

$$L_{\text{diff}} = \frac{\dot{M}_{(D=\infty)} - \dot{M}}{\dot{M}_{(D=\infty)}}. \quad (7)$$

Similarly, comparison of the measured gas transfer with that calculated for when no perfusion limitation existed (i.e. $\dot{V}_b \cdot \beta = \infty$) yielded the perfusion limitation, defined as

$$L_{\text{perf}} = \frac{\dot{M}_{(\dot{V}_b \cdot \beta = \infty)} - \dot{M}}{\dot{M}_{(\dot{V}_b \cdot \beta = \infty)}}. \quad (8)$$

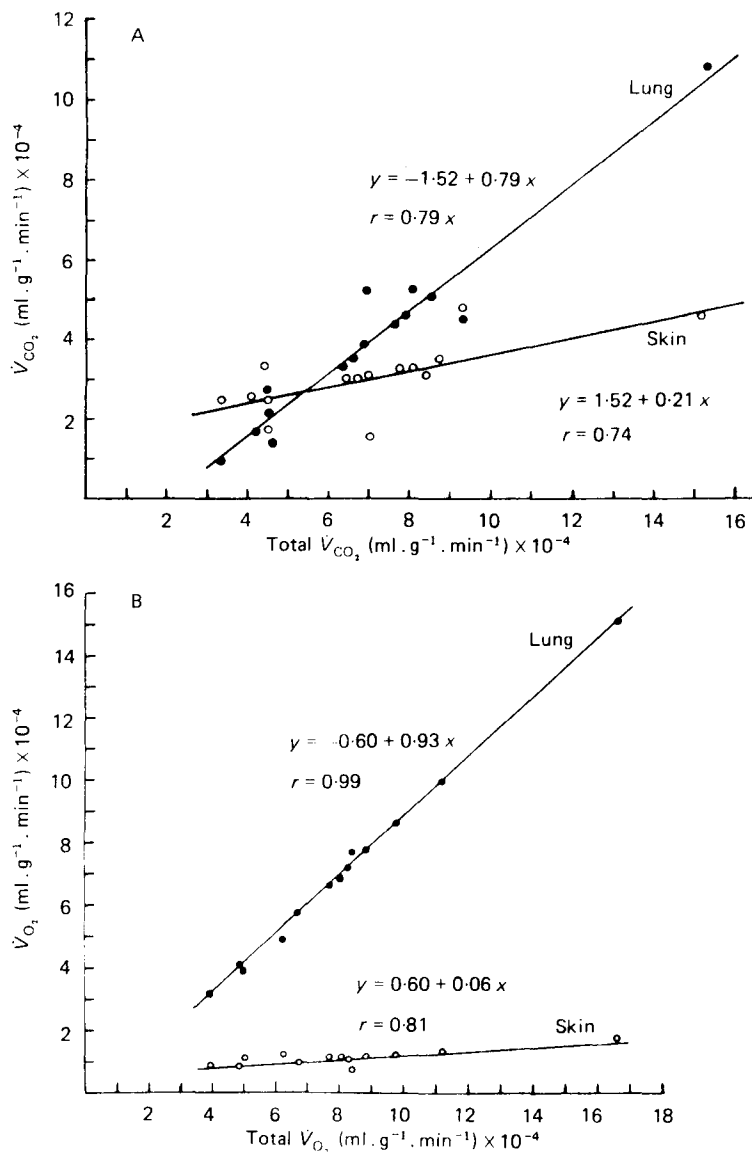


Fig. 8. Relationships between lung and skin with regard to total carbon dioxide production (A) and oxygen consumption (B) in the bullfrog *Rana catesbeiana* (from Gottlieb & Jackson, 1976).

For mass transfer of both O₂ and CO₂, L_{perf} was less than 0.2, while L_{diff} was greater than 0.7. Essentially, factors regulating diffusion (changes in the P_{O_2} gradient across the skin, the P_{CO_2} gradient, D_x , L or A) had a much greater effect on cutaneous gas exchange in *Desmognathus* than even quite gross changes in the rate of skin perfusion. Because D_x , L and A are assumed to be more or less fixed at any one time, the only option available to regulate cutaneous gas exchange is to change the P_{O_2} and P_{CO_2} gradient by altering internal P_{O_2} and P_{CO_2} . Similarly, according to a one-blood-compartment model of cutaneous gas exchange in adult bullfrogs, *Rana catesbeiana* (Moalli *et al.*,

1980; Moalli, 1981; Burggren & Moalli, 1984), diffusion is also more likely to limit cutaneous gas exchange than perfusion.

Most published experimental evidence supports these theoretical predictions. For example, cutaneous gas exchange in adult bullfrogs floating in water is influenced primarily by changes in the transcutaneous partial pressure gradients, with skin diffusion capacity remaining relatively constant (Gottlieb & Jackson, 1976; Moalli, 1981). Because of diffusion limitation, cutaneous CO_2 excretion declines in importance relative to that via the lungs if blood CO_2 is increased experimentally (Gottlieb & Jackson, 1976; Jackson, 1978; Mackenzie & Jackson, 1978; Jackson & Braun, 1979; Moalli *et al.*, 1981). In addition, cutaneous O_2 loss and CO_2 gain occur in hypoxic and hypercapnic environments, respectively (Heisler *et al.*, 1982; Feder, 1983*a, c*; Feder & Wassersug, 1984), further suggesting little regulation of cutaneous gas exchange, if any.

These models and experimental data are problematic in several respects. Most models explicitly ignore the possibility of ventilation limitation, and assume that the skin is in contact with an 'infinite pool' of respiratory medium. Most experimental data have been gathered in circumstances in which the respiratory medium is well mixed, either by design or by natural convection. In doing so, these experiments and models have eliminated the potential resistance of a diffusion boundary layer (see Section II, 4(*a*)). Both fishes and amphibians ventilate the skin, an unlikely behaviour if it were valueless. These points suggest that vertebrates should be able to regulate cutaneous gas exchange through modification of skin ventilation, especially in water, although ventilation should not allow vertebrates to exceed the 'ceiling' imposed by diffusion limitation in the skin.

Second, many of the experimental studies have been conducted in circumstances in which cutaneous gas exchange is relatively unimportant, such as when total metabolic rates are high (Fig. 8; Gottlieb & Jackson, 1976; Mackenzie & Jackson, 1978). Regulation of cutaneous gas exchange might well be more evident in animals with low metabolic rates. For example, in resting bullfrogs with metabolic rates equivalent to the very lowest reported by Gottlieb & Jackson (1976), and thus presumably with a high dependence on cutaneous gas exchange, cutaneous gas exchange seems subject to regulation by variation in skin perfusion (Burggren & Moalli, 1984). When bullfrogs were totally exposed to air (as opposed to floating in water with partial air exposure, as in all previously published experiments on this species), then both the rate of CO_2 elimination (\dot{M}_{CO_2}) and RE, the ratio of \dot{M}_{CO_2} to the rate of O_2 consumption (\dot{M}_{O_2}), were severely reduced (Fig. 9). After a return to water several hours later, \dot{M}_{CO_2} and RE increased above pre-exposure levels for several hours. Given that at least 60–80% of total \dot{M}_{CO_2} is via the skin, these data indicate strong regulation of cutaneous gas exchange by *Rana catesbeiana*. Microsphere injections subsequently revealed that cutaneous blood flow decreased during air exposure. This result clearly contradicts estimates of L_{perf} based on a one-blood-compartment model, which suggest that adjustment in overall blood flow to the skin should have a negligible effect on cutaneous gas exchange. Further experimentation revealed that decreases in the actual number of capillaries perfused (i.e. changes in capillary recruitment), strictly accompanied decreases in blood flow. In essence, adjustments of the surface area (A) in Fick's equation were regulating cutaneous gas exchange. Klocke, Gurtner & Farhi (1963) reached a similar conclusion regarding CO_2 excretion by human skin. Reduction in capillary recruitment also occurs in the salamander *Aneides* in dehumidified air (Fig. 10; Brown, 1972). This response

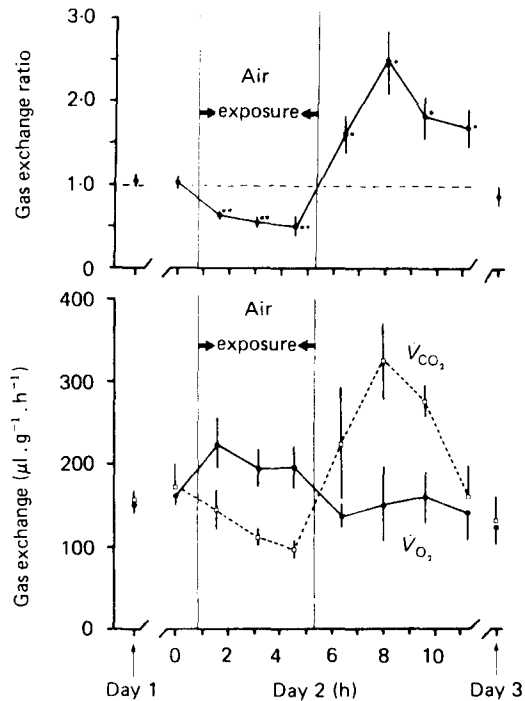


Fig. 9. Oxygen uptake, carbon dioxide elimination and the gas exchange ratio of juvenile *Rana catesbeiana* before, during and after complete air exposure: Bullfrogs were allowed to float at the water's surface and voluntarily breathe air before and after the 4–5 h period of air exposure (after Burggren & Moalli, 1984).

is appropriate for reducing cutaneous water loss, but also indicates the potential for adjusting cutaneous gas exchange when circumstances dictate. Blushing of the ventral skin surface of anuran larvae following exercise has been described, as have changes in capillary recruitment with localized hypoxic or hypercapnic exposure of the skin (see Sections II, 1(c), II, 4(b), and III).

These observations support the contention that regulation of cutaneous gas exchange by changes in perfusion can occur in response to changing needs for cutaneous respiration. However, these changes apparently occur not by changes in blood flow within individual respiratory capillaries (as in lungs and gills), but by changes in the number of capillaries through which blood flows. In other words, functional surface area (A in Fick's equation) can undergo short-term variation to regulate cutaneous gas exchange, contrary to the assumptions of models of diffusion limitation.

While we would not dispute the elegance of regulation of gas exchange of gills and lungs through subtle adjustment in air or water and blood convection, we do maintain that equally subtle adjustment in skin ventilation and perfusion, and most particularly in the distribution of blood flow, can provide a means for precise regulation of cutaneous gas exchange. Certainly, much more information is required to understand the overall role of convective changes in cutaneous respiration.

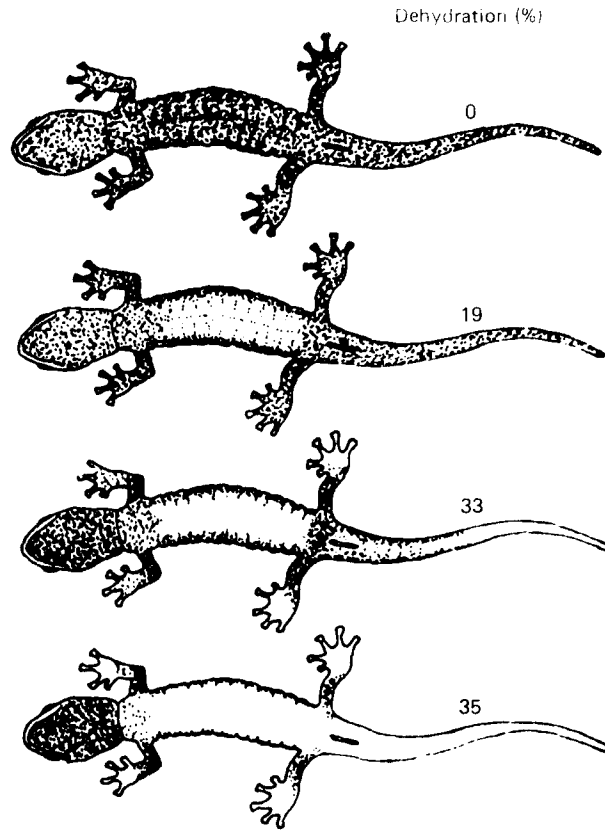


Fig. 10. Effect of progressive dehydration on cutaneous perfusion in the lungless salamander *Aneides*. Stippling indicates cutaneous capillaries that are filled with blood. The dehydration deficit, the number alongside each outline, indicates the amount of water (as a percentage of body mass) that the animal has lost (from Brown, 1972).

IV. PATTERNS OF CUTANEOUS GAS EXCHANGE IN VERTEBRATES

As a consideration of Fick's equations demonstrates, many aspects of both the skin and the circulatory system may facilitate cutaneous gas exchange. How effective is the skin as a gas exchanger? One can envisage various degrees of reliance upon cutaneous gas exchange: a negligible role in overall gas exchange; meeting the needs of the skin and other superficial tissues alone and not meeting the needs of other portions of the body; as an accessory gas exchanger used under special circumstances or satisfying a minority of the respiratory requirement; as the primary gas exchanger; or as the sole gas exchanger. Under what circumstances do vertebrates fall into each of these categories and are they fixed for each species?

Research to date provides two different perspectives on this question. The first is from studies in which other modes of gas exchange are abolished experimentally, and the capacity of animals to maintain normal levels of gas exchange is determined. The second is from studies in which cutaneous gas exchange is experimentally partitioned from other modes of gas exchange and the relative contribution of cutaneous exchange is measured

under various experimental conditions. Both perspectives testify to an extraordinary diversity in vertebrates' use of cutaneous gas exchange, ranging from negligible to complete dependence. Of special interest is the large number of species and environmental circumstances for which cutaneous gas exchange plays a primary or major role.

Studies involving 'deletion' of particular gas-exchange organs are valuable not so much for indicating the actual importance of a gas-exchange organ as the maximum respiratory requirement that the remaining gas exchangers may satisfy (Bentley & Shield, 1973). Such studies have used two different methodologies: (1) direct surgical or pharmacological intervention; and (2) transfer of an animal to an unusual respiratory medium (fish to air or terrestrial vertebrate submerged in water).

Before discussing such studies, some cautionary notes are necessary. When a respiratory organ is experimentally rendered functionless, non-respiratory as well as respiratory functions may be abolished. Hence intolerance of its deletion may well stem from factors other than respiratory failure. For example, the gills of fish are important in the transfer of ions and nitrogenous wastes as well as O₂ and CO₂; if the gills are incapacitated, a fish may die from osmotic imbalances even if the skin can compensate for the lost respiratory functions of the gills. The time course of such experiments is important; for example, the skin may compensate briefly for the loss of other respiratory organs but fail ultimately. Many experiments have interfered with the function of either lungs or gills but few with both. The failure of animals to survive such experiments clearly demonstrates the skin's inability to suffice for all gas exchange; however, survival in such experiments may be due to the combined gas exchange of the skin and the remaining respiratory organ(s) rather than the skin alone.

(1) *Fishes*

Cutaneous gas exchange in fishes was first described by Krogh (1904), and numerous studies have subsequently reported on this phenomenon in a variety of fresh water, intertidal, and marine fishes (Table 1). Although considerable data are now available, no clear phylogenetic correlation with the ability of fishes to exchange gases across the skin has emerged, nor do morphological factors such as increased surface area: volume ratios evidently enhance cutaneous gas exchange, with the fusiform eel and the globose tench exhibiting a somewhat similar dedication to cutaneous gas exchange. Even the gross morphology of the integument (e.g. presence or absence of scales) appears to have little bearing on cutaneous gas exchange. Cutaneous O₂ exchange is approximately 30% of total O₂ exchange in both the scaleless plaice (Steffensen *et al.*, 1981) and the very heavily scaled reedfish (Sacca & Burggren, 1982). The scales of fish are generally covered by a layer of living, non-keratinized dermal cells (Mittal & Datta Munshi, 1971), an arrangement that places perfused tissue *between* the environment and the scale itself (Fig. 11). The acquisition of scales during morphogenesis of larval herring and plaice greatly reduces cutaneous respiration (de Silva & Balbontin, 1974). However, this could also arise from the increased diffusion distances through the thicker skin of larger fish, rather than the presence or absence of scales (cf. Ultsch, 1973).

Although many fishes achieve an unusually large O₂ uptake across the skin, reliance upon cutaneous gas exchange seems unrelated to the gross habitat of fish; i.e. marine or fresh water (Table 1). However, every air-breathing fish – marine, intertidal or fresh water – that has been examined uses the skin as an accessory organ for O₂ exchange (e.g.

TABLE 1. Cutaneous oxygen uptake as a percentage of total oxygen uptake in fishes

Species	Temperature (°C)	Total M_{O_2} (%)	Reference
Fresh water			
<i>Carassius carassius</i>	13	10	Nonotte (1981)
<i>Perca fluviatilis</i>	13	10	Nonotte (1981)
<i>Esox lecius</i>	13	10	Nonotte (1981)
<i>Salvelinus fontinalis</i>	13	6	Nonotte (1981)
<i>Salmo trutta</i>	13	7	Nonotte (1981)
<i>Ictalurus melas</i>	13	20	Nonotte (1981)
<i>Anguilla anguilla</i>	13	28	Kirsch & Nonotte (1977)
<i>Salmo gairdneri</i>	13	15	Kirsch & Nonotte (1977)
<i>Tinca tinca</i>	13	22	Kirsch & Nonotte (1977)
<i>Misgurnus fossilis</i>	?	10-30	Jeuken (1957)
Marine			
<i>Chaenoccephalus aceratus</i>	?	40	Hemmingsen & Douglas (1970)
<i>Platichthys flesus</i>	13	33	Nonotte & Kirsch (1978)
<i>Blennius pholis</i>	13	10	Nonotte & Kirsch (1978)
<i>Ciliata mustela</i>	13	7	Nonotte & Kirsch (1978)
<i>Gadus morhua</i>	13	6	Nonotte & Kirsch (1978)
<i>Pholis gunnellus</i>	13	23	Nonotte & Kirsch (1978)
<i>Pleuronectes platessa</i>	13	27	Steffensen <i>et al.</i> (1981)
<i>Scyliorhinus canicula</i>	15	5	Toulmond, Dejourns & Truchot (1982)
Air Breathing			
<i>Calamoichthys calabaricus</i>	27	32	Sacca & Burggren (1982)
<i>Amphipnous cuchia</i>	?	33	Lomholt & Johansen (1976)
<i>Anguilla vulgaris</i>	15	12	Berg & Steen (1965)
<i>Periophthalmus cantonensis</i>	20	48	Tamura <i>et al.</i> (1976)
<i>Boleophthalmus chinensis</i>	20	36	Tamura <i>et al.</i> (1976)
<i>Neochanna burrowsius</i>	17	43	Meredith <i>et al.</i> (1982)

Tamura, Morii & Yuzuriha, 1976). In fact, significant skin respiration has so frequently been described for air breathing fishes that most authors routinely include the integument as a gas-exchange organ (see Johansen, 1970; Singh, 1976; Graham, 1976; Randall *et al.*, 1981, for reviews). Cutaneous respiration seems particularly important in air breathing fishes because their gills tend to collapse when these fishes emerge from water (Randall *et al.*, 1981). The reduced boundary layer in air as compared to water would also facilitate cutaneous gas exchange (see Section II, 4(a)). Relatively few experiments on air breathing fishes have partitioned gas exchange among respiratory organs (gills, skin, lung/air bladder/pharyngeal diverticula) as opposed to between air and water (see Graham, 1976; Singh, 1976; Randall *et al.*, 1981). In studies in which cutaneous gas exchange has been quantified, however, it increases consistently upon exposure to air (Table 2).

While significant (albeit variable) O_2 uptake by the skin of fishes clearly occurs, it is much less evident to what extent the O_2 taken up by the skin is used in skin metabolism itself, as opposed to being conveyed away from the skin in venous blood for transport to other sites for metabolism. Kirsch & Nonotte (1977), Nonotte & Kirsch (1978), and Nonotte (1981) have surveyed cutaneous gas exchange in fresh and seawater teleosts. *In vivo* oxygen uptake across the skin was compared with the oxygen

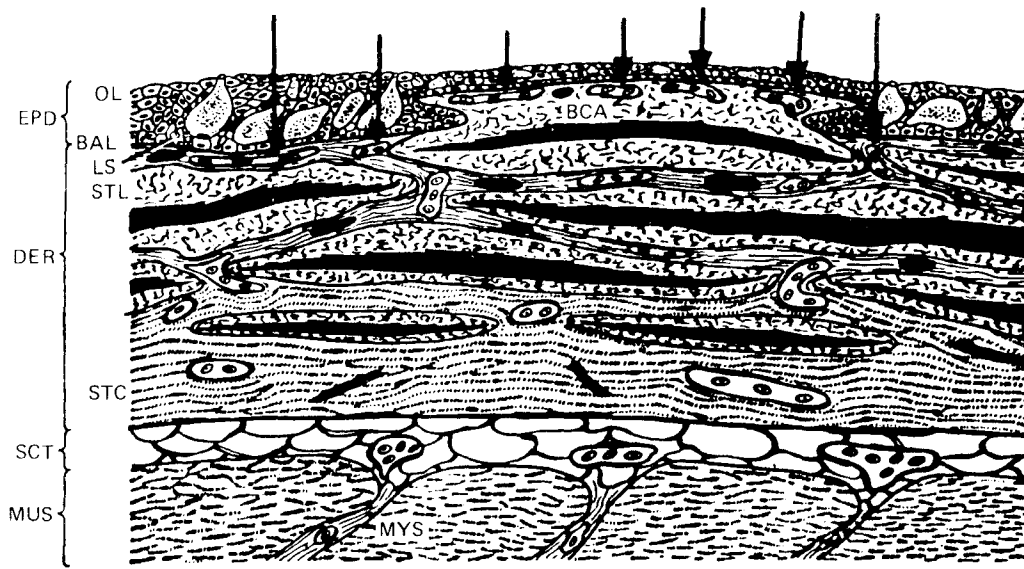


Fig. 11. Anatomy of the skin of a fish, *Mastacembelus pancalus* (Hamilton), indicating the position of the cutaneous capillaries (Mittal & Datta Munshi, 1971). Scales are indicated by solid black; note that cutaneous capillaries (indicated by arrows) lie *between* the scales and the epidermis. Abbreviations: BAL, basal layer; BCA, blood capillary; DER, dermis; EPD, epidermis; MUS, muscles; MYS, myoseptum; SCT, subcutis; STC, stratum compactum; STL, stratum laxum.

Table 2. Partitioning of oxygen uptake in air-breathing fish when in water with access to air and when completely in air

Species	Temperature (°C)	In water: % \dot{M}_{O_2} via			In air: % \dot{M}_{O_2} via			Reference
		Skin	Gills	Other	Skin	Gills	Other	
<i>Anguilla vulgaris</i>	7	12	88		43	57		Berg & Steen (1965)
	15	12	88		33	67		
<i>Boleophthalmus chinensis</i>	20	36	59	5	43	52	5	Tamura <i>et al.</i> (1976)
<i>Calamoichthys calabaricus</i>	27	32	28	40	41	0	59	Sacca & Burggren (1982)
<i>Neochanna burroensis</i>	17	43		57*	43		57*	Meredith <i>et al.</i> (1982)
<i>Periophthalmus cantonensis</i>	20	48	52	0	76	27	0	Tamura <i>et al.</i> (1976)

* Gas exchange via the animal's head (including gills and skin).

consumption of excised skin tissue. Cutaneous oxygen consumption was equal to or exceeded cutaneous O_2 uptake from water in the eel, rainbow trout, tench, crucian carp, yellow perch, northern pike, brook trout, brown trout, butterfish, cod and rockling. Thus, in this diverse group of fish, the skin is not serving as "an oxygen exchanger for the benefit of other organs" (Nonnotte, 1981). On the other hand, in the catfish, shanny, flounder and sole, cutaneous O_2 uptake significantly exceeded cutaneous O_2

... suggesting that the skin was adding to gas exchange by the gills for the benefit of other tissues (Graham, 1976; Nonnotte & Kirsch, 1978). The basis for such a large cutaneous O_2 consumption may lie in the non-respiratory functions of the skin. The skin of teleost fishes has an important role in hydromineral balance, either directly through active transport of ions (Fromm, 1968; Kirsch, 1972) or more indirectly through the secretion of a protective mucus boundary (Bert, 1871; Duval, 1925; Marshall, 1977). Both metabolic processes demand considerable O_2 .

Regardless of whether O_2 taken up by the skin of fishes is involved in local metabolism or is transported to other body tissues, there must be at least crude regulation of this process. Few experiments on fishes have specifically addressed this problem. Cutaneous O_2 uptake in the plaice and the crucian carp remains constant over a very wide range of ambient O_2 , even when branchial O_2 uptake begins to fail (Privolnev, 1945; Steffensen *et al.*, 1981). Cutaneous gas exchange in the reedfish can increase two to three times when branchial gas exchange stops upon emersion from water (Sacca & Burggren, 1982). These rather surprising findings suggest either that (1) changes in skin blood flow can influence capillary surface area and/or the O_2 partial pressure across the skin, or (2) that convective forces move ambient water across the skin surface. Interestingly, the larval stages of several fishes have ciliated epithelia capable of generating a convective flow of water over the skin surface (Kryzanowsky, 1934; Balon, 1975; Lanzing, 1976; Whiting & Bone, 1980). In the exclusively aquatic larvae of *Monopterus*, an air-breathing teleost, movement of the pectoral fins generates a discrete flow of water in a direction countercurrent to capillary blood flow (Liem, 1981). Disruption of this countercurrent flow of water and blood by placing the larvae in an artificially generated water flow concurrent with blood flow significantly reduces total O_2 consumption of the larvae. Exposure to hypoxic water increases the frequency of pectoral fin movements.

Cutaneous gas exchange clearly occurs in both larval and adult fishes. However, little is known of regulatory mechanisms for this process, particularly in those fishes in which O_2 actually crosses the skin into the blood. While the intricacies of countercurrent gas exchange in fish gills has rightfully received considerable attention, an unfortunate consequence has been diversion of attention from gas exchange across fish skin, a process begging further investigation.

(2) *Amphibians*

In the Amphibia, the skin has a major role in gas exchange in every species for which measurements are available (Table 3; Foxon, 1964; Whitford & Hutchison, 1965; Hutchison, Whitford & Kohl, 1968). The magnitude of cutaneous gas exchange varies both among and within species of amphibians, and is related to several factors: skin morphology, the presence of alternative gas exchangers (i.e. lungs and gills), the respiratory medium (air and water), environmental levels of O_2 and CO_2 , and temperature. These effects illustrate both the 'design constraints' upon skin as a gas exchanger and the utility of cutaneous gas exchange in diverse circumstances.

The morphology of amphibian integument facilitates cutaneous gas exchange. The skin of amphibians lacks hair, feathers, and typically scales and other barriers to diffusion. The epidermis is thin, typically 10–50 μm (Czopek, 1965). Cutaneous capillarization accounts for a relatively high proportion of total respiratory capillarization in species in which the skin is thin. For 22 species of anurans between 0.6–53 g body

Table 3. Cutaneous gas exchange as a percentage of total gas exchange in amphibians breathing both air and water

Species	Temperature (°C)	% of total		Reference
		\dot{M}_{O_2}	\dot{M}_{CO_2}	
URODELES				
<i>Ambystoma tigrinum</i> (adult)	15	23	—	Whitford & Sherman (1968)
	25	29	—	Whitford & Sherman (1968)
<i>Amphiuma means</i>	5	92	100	Guimond & Hutchison (1974)
	15	59	78	Guimond & Hutchison (1974)
	25	44	77	Guimond & Hutchison (1974)
<i>Cryptobranchus alleganiensis</i>	5	94	97	Guimond & Hutchison (1973a)
	15	89	98	Guimond & Hutchison (1973a)
	25	92	98	Guimond & Hutchison (1973a)
<i>Necturus maculosus</i>	5	37	42	Guimond & Hutchison (1972)
	15	30	32	Guimond & Hutchison (1972)
	25	30	27	Guimond & Hutchison (1972)
<i>Notophthalmus viridescens</i>	25	82	—	Wakeman & Ultsch (1975)
<i>Siren lacertina</i>	15	33	54	Guimond & Hutchison (1973b)
	25	24	29	Guimond & Hutchison (1973b)
<i>Taricha torosa</i>	25	58	—	Wakeman & Ultsch (1975)
ANURANS				
<i>Rana berlandieri</i> (larvae)	15	73	—	Burggren <i>et al.</i> (1983)
	25	66	—	Burggren <i>et al.</i> (1983)
	33	80	—	Burggren <i>et al.</i> (1983)
<i>R. catesbeiana</i> (larvae)	15	77	—	Burggren <i>et al.</i> (1983)
Larvae	25	59	—	Burggren <i>et al.</i> (1983)
Larvae	33	65	—	Burggren <i>et al.</i> (1983)
'Water-breathing' larvae (bimodal larvae)	25	58	60	Burggren & West (1982)
	25	67	58	Burggren & West (1982)
(postmetamorphic)	25	12	91	Burggren & West (1982)
(adults)	25	18	82	Burggren & West (1982)
(adults)	20	14	46	Gottlieb & Jackson (1976)
(adults)	10	—	48	Mackenzie & Jackson (1978)
(adults)	20	—	38	Mackenzie & Jackson (1978)
(adults)	30	—	29	Mackenzie & Jackson (1978)
(juveniles)	25	30	70	Burggren & Moalli (1984)
(adults)	25	20	80	Burggren & Moalli (1984)
<i>Telmatobius culeus</i>	10	100	—	Hutchison <i>et al.</i> (1976)
<i>Xenopus laevis</i>	20	24	—	Emilio & Shelton (1974)
	15	46	—	Hutchison & Miller (1979)
	25	40	—	Hutchison & Miller (1979)
	25	29	86	Emilio & Shelton (1980)
CAECILIANS				
<i>Siphonops annulatus</i>				
(intact vs. tracheotomized)	?	42	58	Mendes (1945)
(intact vs. anesthetized)	?	51	86	Mendes (1945)
<i>Typhlonectes compressicauda</i>	19–25	6	60	Sawaya (1947)

mass (Czopek, 1965), the partial correlation coefficient of epidermal thickness and the proportion of total capillarization residing in the skin (controlling for mass and capillary density) is -0.465 ($P = 0.019$). The sub-epidermal capillary network of amphibians is unusually extensive (30–200 capillary meshes per mm^2) and accounts for 20–96% of total respiratory capillarization (Czopek, 1965; Saint-Aubain, 1982).

The significance of these features to cutaneous gas exchange is illustrated by several exceptional species that depart from typical amphibian patterns of cutaneous morphology. Respiratory capillaries of some caecilians and anurans lie deep to the dermis instead of superficial to it as in most other forms (Bennett & Wake, 1974; Drewes *et al.*, 1977). In one such animal, the caecilian *Typhlonectes compressicauda*, cutaneous O₂ uptake is the lowest reported for an amphibian (Sawaya, 1947). Some amphibians secrete a 'cocoon' of sloughed epidermis and mucous secretions when dormant; cocoons decrease cutaneous water loss but pose an additional barrier to diffusion of gas through the skin (Loveridge & Withers, 1981). In the African frog *Pixicephalus adspersus*, 84% of total gas exchange is via the skin under most circumstances but only 56% is cutaneous in cocooned individuals (Loveridge & Withers, 1981). In other anurans the dermis of the head is poorly vascularized and co-ossified with underlying bone, presumably as a barrier to water loss (Seibert, Lillywhite & Wassersug, 1974); the consequences of co-ossification for gas exchange have not been determined. Large amphibians typically have thicker skin than small ones (Czopek, 1965; Ultsch, 1973). Increasing skin thickness during ontogeny results in a 60% decrease in cutaneous permeability to O₂ in the aquatic salamander *Siren lacertina* (Ultsch, 1973).

Some amphibians have cutaneous specializations that increase cutaneous gas exchange. These include the vascularized papillae of the 'hairy frog' *Astylosternus robustus*, large skin folds in the montane frogs *Batrachophrynus* and *Telmatobius* (Fig. 2), minute skin folds in aquatic salamanders *Cryptobranchus*, expansion of the tail fin in newts and tadpoles, and thinning of the skin during hypoxia acclimation in tadpoles (Noble, 1925; Foxon, 1964; Czopek, 1965; Hutchison *et al.*, 1976; Burggren & West, 1982; Burggren & Mwalukoma, 1983).

Amphibians' reliance upon cutaneous respiration reaches its zenith in several lineages of salamanders (*Chioglossa*, *Salamandrina*, *Rhyacotriton*, and the entire family Plethodontidae) in which neither gills nor lungs are present in adults. However, most amphibians have lungs, gills or both in addition to skin, and partition gas exchange between the skin and these alternative respiratory surfaces. Although the skin almost always accounts for at least 20% of total oxygen consumption, it often accounts for a minority of oxygen uptake except in lungless salamanders (Table 3; Whitford & Hutchison, 1965; Hutchison *et al.*, 1968). By contrast, the skin almost always accounts for a majority of CO₂ excretion in amphibians. Thus, the gas exchange ratio (RE) for amphibian skin is typically well above unity. As body temperature increases, both O₂ uptake and CO₂ excretion increase; typically, the Q₁₀ of these processes is 2–3. The cutaneous fraction of CO₂ excretion remains loosely fixed despite changes in temperature. Temperature effects upon cutaneous O₂ uptake are varied. In most terrestrial forms, the lungs (if present) assume a progressively greater proportion of oxygen uptake as temperature increases; the cutaneous fraction declines correspondingly (Whitford & Hutchison, 1965; Hutchison *et al.*, 1968; Whitford, 1973). Similar patterns occur in some bimodally respiring aquatic species, but in many others the cutaneous contribution to O₂ uptake remains constant or increases with temperature (Table 3; Burggren, Feder & Pinder, 1983). The fraction of gas exchange via the skin differs little in air-breathing and bimodally respiring amphibians, when each are measured in their respective respiratory media (cf. Table 3 and data of Hutchison *et al.*, 1968). However, aquatic amphibians can extract O₂ from water via the skin more readily than can terrestrial

amphibians (Hutchison & Dady, 1964; Wakeman & Ultsch, 1975). After vigorous physical activity, most amphibians repay a large oxygen debt. Payment of the O_2 debt is almost entirely via the lungs (i.e. not via the skin) in bimodally respiring amphibians (Preslar & Hutchison, 1978; Hutchison & Miller, 1979; Miller & Hutchison, 1979). Similarly, the cutaneous fraction of CO_2 elimination is lower in bullfrogs with high metabolic rates than in frogs with low metabolic rates (Fig. 7; Gottlieb & Jackson, 1976; Mackenzie & Jackson, 1978; Burggren & Moalli, 1984). To summarize, the skin plays an important role in exchange of both CO_2 and O_2 in amphibians. In species with multiple gas-exchange organs, the cutaneous fraction of O_2 exchange is often smaller than the fraction of CO_2 exchange, and typically (but not always) decreases at high temperatures or during activity.

All of the above generalizations are for amphibians in air or in air-equilibrated water. As environmental gas tensions surrounding a gas exchanger vary, so should its effectiveness (see Section II, 4). Accordingly, aquatic hypoxia or hypercapnia greatly limit cutaneous gas exchange with water or render it counterproductive. As the aquatic P_{O_2} declines, aquatic amphibians extract progressively less O_2 from the water and resort increasingly to aerial respiration. Severe hypoxia actually promotes the loss of O_2 to the water in some tadpoles (Feder, 1983*a*, 1983*c*; Feder & Wassersug, 1984). Likewise, environmental hypercapnia prevents CO_2 loss and, if severe, induces substantial respiratory acidosis in amphibians breathing through their skin (Jackson & Braun, 1979; Heisler *et al.*, 1982; Stiffler, Tufts & Toews, 1983). With few exceptions (Wakeman & Ultsch, 1975), these data are from aquatic species for which branchial and cutaneous gas exchange have not been partitioned and thus combine effects upon gills and skin. Effects of hypoxia and hypercapnia upon cutaneous gas exchange may be especially pronounced because aquatic amphibians can seldom shield the skin from the water. By contrast, amphibians can curtail branchial and buccopharyngeal O_2 loss to hypoxic water by decreasing ventilation of the internal gills (West & Burggren, 1982, 1983; Feder, 1983*a*, 1983*c*; Feder & Wassersug, 1984).

Is the cutaneous contribution to overall gas exchange in amphibians more or less constrained by morphology and environment, or does the skin have extra capacity for gas exchange that is not exploited in some circumstances? In relatively favourable circumstances (normoxia, normocapnia, moderate temperatures, in air or in water with access to air), the skin can support higher rates of gas exchange than are typically observed in amphibians. Thus, some lungless salamanders have high maximum rates of O_2 consumption (Feder, 1977, 1978; Hillman *et al.*, 1979), partial pneumectomy has minimal consequences for maximum O_2 consumption of anurans (Hillman & Withers, 1979), the tadpoles and at least one adult anuran maintain high rates of O_2 consumption in normoxic water when prevented from breathing air (Hutchison *et al.*, 1976; Feder, 1983*c*; Feder & Wassersug, 1984). Moreover, when pulmonary respiration is abolished pharmacologically or surgically, total O_2 consumption in air is unaffected in several species (Krogh, 1904; Bentley & Shield, 1973). The many factors underlying these increases in cutaneous gas exchange in amphibians are reviewed in Section II and seem at variance with the 'diffusion-limited' status of cutaneous respiration in amphibians assumed by Piiper (1982).

In less favourable circumstances (hypoxia, hypercapnia, high temperatures, in water with no access to air, during or after activity), the skin of amphibians is often unable to respond to changing respiratory needs. For example, if many varieties of air-breathing

Table 4. Measurements of diffusive conductance in amphibians.
Units are nmoles gas . cm⁻² . hr⁻¹ . Torr⁻¹

Species	Temperature (°C)	Conductance		Reference
		O ₂	CO ₂	
<i>Cryptobranchus alleganiensis</i> *	5-25		142-166	Moalli <i>et al.</i> (1981)
<i>Desmognathus ochrophaeus</i>	13-22	4-7	62-178	Piiper <i>et al.</i> (1976)
<i>Rana catesbeiana</i>	10		38	Mackenzie & Jackson (1978)
	20		47	
	30		42	
<i>Siren lacertina</i>	25	2-7	--	Ultsch (1974b)

* Calculated in part from surface area-mass regression of Whitford & Hutchison (1967)

species are immersed in water without access to air, oxygen consumption decreases abruptly and death often ensues (Hutchison & Dady, 1964; Shield & Bentley, 1973; Ultsch, 1973, 1974a, 1976b; Preslar & Hutchison, 1978). Ligation of the gills of aquatic amphibians decreases oxygen uptake in some species, especially in hypoxic water (Boell, Greenfield & Hille, 1963; Bentley & Shield, 1973; Shield & Bentley, 1973). Forced immersion in air-breathing forms and forced exposure to air in water-breathing amphibians disturbs arterial P_{O_2} and P_{CO_2} greatly. These perturbations require several hours to be remedied (Lenfant & Johansen, 1967). In each case, the skin fails to compensate for decreases in gas exchange when other respiratory organs are removed.

A second approach towards demonstrating the limitations of cutaneous respiration in amphibians has been to compare animals of different morphologies in so-called 'natural experiments'. For example, Boutilier *et al.* (1980) and McDonald, Boutilier & Toews (1980) have compared responses to physical activity in a toad (*Bufo*) and an exclusively skin-breathing salamander (*Cryptobranchus*), and found that the salamander recovers from acidosis much more slowly than the toad. However, the aquatic larva of *Rana catesbeiana*, which relies greatly on the skin for cutaneous gas exchange, recovers from exhausting activity much more quickly than the adult, which relies more heavily on pulmonary respiration (Quinn & Burggren, 1983). Many workers have compared large and small amphibians. On a mass-specific basis, large amphibians have less cutaneous capillarization than small individuals of the same species; in many cases the same is true of large and small species (Czopek, 1965; Ultsch, 1973, 1974a). In amphibians that either lack lungs or in which pulmonary respiration has been abolished experimentally, large individuals have greater critical P_{O_2} s and succumb to hypoxia more readily than small individuals (Ultsch, 1973, 1974a, 1976a, b; Beckenbach, 1975; Withers, 1980). Moreover, exclusively skin-breathing salamanders have lower rates of oxygen consumption after activity or stress than salamanders breathing via both lungs and skin (Whitford & Hutchison, 1967; Feder, 1977, 1978).

A third and most direct approach is to quantify conductance of the skin to respiratory gases (Table 4). The diffusive conductance of amphibian skin is much lower than the convective conductance associated with blood flow to the skin, suggesting that diffusion of gas through the skin is the limiting factor to gas transport, and that increases in the rate of cutaneous perfusion (as opposed to changes in perfusion pattern) will do little to augment cutaneous gas exchange (see Section III and references cited in Table 4).

However, as recognized by most of the above workers, behavioural and circulatory

adjustments of ventilation and perfusion may nonetheless have profound effects on 'diffusion limitation' in amphibian skin and have not received adequate attention in this regard. For these reasons, definitive conclusions about the inadequacy of cutaneous gas exchange in amphibians must await future studies.

(3) *Reptiles*

Cutaneous gas exchange in reptiles has recently been the subject of excellent reviews by Seymour (1982), Lillywhite & Maderson (1982), and Gatten (1984). To summarize their conclusions, cutaneous gas exchange in reptiles appears 'diffusion limited and subject to little physiological control', in the same sense that this phrase has been applied to amphibians. As in amphibians, reptiles may be able to increase cutaneous gas exchange by perfusing additional cutaneous capillaries or by ventilating the skin through movements of the body. Shunting of blood to the skin of reptiles, although best documented in the context of thermoregulation (White, 1976; Bartholomew, 1982), occurs in many reptiles. In diving sea snakes, shunting of blood past the lungs to the skin may be particularly important for gas exchange; the skin may literally turn pink from increased perfusion in some circumstances (Heatwole & Seymour, 1975, 1978; Seymour, 1978, 1982). Some cutaneous exchange of O₂ or CO₂ occurs in every species of turtle, lizard and snake that has been studied, although the cutaneous contributions are sometimes quite low. The proportional contribution of cutaneous gas exchange is related to four factors: body size, respiratory medium, aquatic hypoxia and temperature. As in amphibians, large reptiles have thicker skins, relatively less cutaneous surface area, and lower rates of cutaneous gas exchange than small reptiles. Aquatic reptiles, especially species that dive for long periods, typically have higher rates of cutaneous gas exchange than terrestrial reptiles, which must curtail cutaneous water loss. However, in snakes that routinely encounter aquatic hypoxia, cutaneous O₂ consumption resembles that of terrestrial forms. A low cutaneous conductance in these snakes would presumably forestall O₂ loss to the environment.

The 'naked skin' of amphibians has long been associated with cutaneous respiration, and the scaled skin and greater pulmonary capacities of reptiles supposedly accompany a transition from cutaneous to pulmonary respiration. Thus, the wide use of cutaneous gas exchange in reptiles is unexpected. Obviously, reptilian skin and cutaneous gas exchange are not mutually exclusive. In fact, some aspects of reptilian skin may facilitate cutaneous gas exchange. In species with high levels of cutaneous respiration, the blood vessels may underlie the scale hinges or skin between the scales rather than the scales themselves (Jammes & Grimaud, 1976; Rauch, 1978) and are relatively superficial (Rosenberg & Voris, 1980). Cutaneous blood vessels partially penetrate the scales in some species (Fig. 12; Rauch, 1978). Skin composition also has profound effects on cutaneous transfer of substances. Roberts & Lillywhite (1980) documented the importance of skin lipids as a barrier to cutaneous water loss, and suggested that keratin and scale morphology were only of nominal importance in limiting water loss. Water loss in scaleless snakes is the same as in scaled snakes (Bennett & Licht, 1975). Dunson (1978) reported that the skin of aquatic snakes allows a large flux of water but not of sodium. The relationship between these properties of skin and cutaneous gas flux is poorly understood and should be a fruitful area for future investigation.

Reptiles use the skin as a route for O₂ uptake and CO₂ excretion during prolonged

Table 5. Cutaneous gas exchange in reptiles

Species	Medium*	Temperature (°C)	% of total		Reference
			\dot{M}_{O_2}	\dot{M}_{CO_2}	
TURTLES					
<i>Chelodina expansa</i>	AW	25	3	—	Gatten & Legler (1984)
<i>Chelydra serpentina</i>	AW	4	11	—	Gatten (1980)
	WV	4	3	—	Gatten (1980)
	AW	20	5	—	Gatten (1980)
<i>Eseya latisternum</i>	AW	25	5	—	Gatten & Legler (1984)
<i>Emydura canni</i>	AW	25	10	—	Gatten & Legler (1984)
<i>Geochelone denticulata</i>	AW	20	—	3	Jackson <i>et al.</i> (1976)
<i>Malaclemys terrapin</i>	AW	20	—	20	Jackson <i>et al.</i> (1976)
<i>Pseudemys scripta</i>	WF	22	4	—	Belkin (1968)
	WF	24	6	—	Jackson & Schmidt-Neilsen (1966)
	WF	24	—	20	Jackson (1976)
	AW	24	—	10	Jackson (1976)
	AW	20	—	11	Jackson <i>et al.</i> (1976)
<i>Rheodytes leukops</i> †	AW	25	25	—	Gatten & Legler (1984)
<i>Sternotherus minor</i>	AW	22	12	—	Gatten (1984)
	AW	20	—	31	Jackson <i>et al.</i> (1976)
	WF	22	32	—	Belkin (1968)
<i>S. odoratus</i>	WF	25	9	—	Root (1949)
<i>Terrapene carolina</i>	AW	20	—	6	Jackson <i>et al.</i> (1976)
<i>Trionyx mutica</i>	AW	20	—	65	Jackson <i>et al.</i> (1976)
<i>T. spiniferus</i>	WF		> 1	—	Gage & Gage (1886)
	WF		> 1	—	Dunson (1960)
<i>T. triunguis</i>	WF	24	> 1	—	Girgis (1961)
SNAKES					
<i>Acalyptophis peronii</i>	WF	26	11	—	Heatwole & Seymour (1975)
<i>Acrochordus granulatus</i>	WF	26	13	—	Heatwole & Seymour (1975)
<i>A. javanicus</i>	AW	21	7	33	Standaert & Johansen (1974)
<i>Aipysurus duboisii</i>	WF	26	11	—	Heatwole & Seymour (1975)
<i>A. laevis</i>	WF	26	22	—	Heatwole & Seymour (1975)
<i>Cerberus rhynchops</i>	WF	26	10	—	Heatwole & Seymour (1978)
<i>Constrictor constrictor</i>	AW	21	3	21	Standaert & Johansen (1974)
<i>Hydrophis belcheri</i>	WF	26	32	—	Heatwole & Seymour (1978)‡
<i>H. cyanocinctus</i>	WF	26	32	—	Heatwole & Seymour (1978)‡
<i>H. inornatus</i>	WF	26	34	—	Heatwole & Seymour (1978)‡
<i>H. melanocephalus</i>	WF	26	5	—	Heatwole & Seymour (1975)
<i>H. ornatus</i>	WF	26	29	—	Heatwole & Seymour (1978)‡
<i>Lapemis hardwickii</i>	WF	26	6	—	Heatwole & Seymour (1975)
<i>Laticauda colubrina</i>	WF	26	13	—	Heatwole & Seymour (1978)
<i>L. laticaudata</i>	WF	26	12	—	Heatwole & Seymour (1978)
<i>Natrix rhombifera</i>	AE	29	8	12	Gratz (1978)
<i>Pelamis platurus</i>	AW	27	19	—	Graham (1974)
	WF	27	38	74	Graham (1974)
LIZARDS					
<i>Lacerta viridis</i>	AE	20	10	16	Jammes & Grimaud (1976)
<i>Physignathus lesueurii</i>	AW	23	5	15	Courtice (1981)
<i>Sauromalus obesus</i>	AE	25	2	4	Crawford & Schultetus (1970)

* AW = in water with access to air; AE = in air; WF = in water, forcibly submerged without access to air; WV = in water, voluntarily submerged.

† Cloacal bursae are presumed to be the major 'cutaneous' gas exchanger in this species.

‡ Percentage of total O₂ consumption predicted by regression equations of Bennett & Dawson (1975) for snakes, assuming mass equal to median mass of sample.

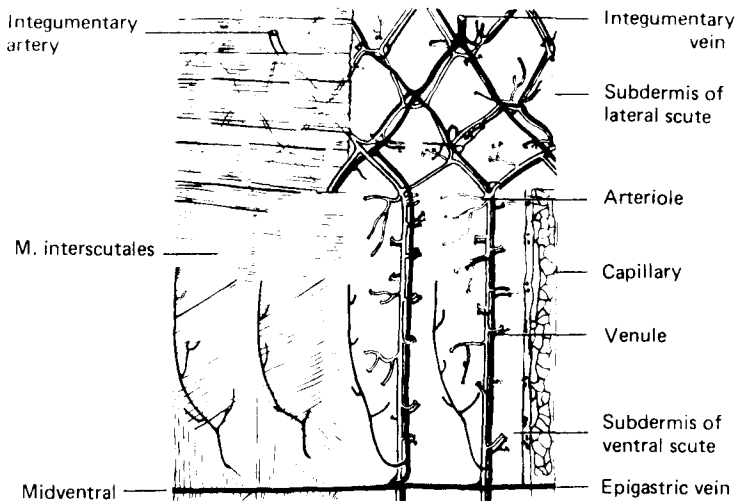


Fig. 12. A lateral view of integumentary blood vessels in the skin of a snake (Rauch, 1978).

dives. Unlike other vertebrates, marine snakes may use the skin as an avenue for nitrogen excretion during prolonged, deep dives (Seymour, 1974, 1978, 1982). Loss of nitrogen from the skin is thought to prevent decompression sickness in diving sea snakes.

(4) *Endotherms*

Although cutaneous respiration frequently makes significant and even crucial contributions to gas exchange in vertebrate ectotherms, the skin is rarely considered as a possible avenue for gas exchange in the birds and mammals. The relatively impervious cornified skin of the endotherms, coupled with frequently thick layers of skin or feathers and a substantially reduced capillary density in the dermis, constitutes a formidable barrier to gas exchange. Moreover, the metabolic rate of an endotherm is typically 5–15 times greater than that of an ectotherm with similar mass and, more importantly, similar cutaneous surface area. Thus, even if the furred or feathered integument of birds or mammals were as permeable as that of a frog, for example, the much greater metabolic rate of endotherms could nonetheless be supported only by effectively designed and ventilated lungs with large surface area.

Yet, in a few notable situations cutaneous gas exchange is significant in endotherms. The thin, highly perfused wing membranes of bats provide for a very large surface area. As in other mammals, little or no oxygen uptake can be measured across the skin of bats with involuntarily extended wings (Herreid, Bretz & Schmidt-Nielsen, 1968). However, up to 12% of total \dot{M}_{CO_2} can occur via the wings in such bats (Herreid *et al.*, 1968). This compares with an almost negligible 1.4% of total \dot{M}_{CO_2} for man (Fitzgerald, 1957; Alkalay *et al.*, 1971) and 1.2% for the pigeon (Krogh, 1904). Of course, the large surface area of the bat wing is lost when the wings are folded about the body, potentially relegating gas exchange to the lungs during roosting.

Although the “cutaneous gas exchange of man amounts to less than the error inherent in the measurement of total gas exchange” (Fitzgerald, 1957), exchange of gases between skin and air may be much more important for local skin metabolism in

mammals with naked skin (such as man) than is generally appreciated. Fitzgerald (1957) has reviewed the earlier literature on cutaneous gas exchange in man. He calculated that all of the O_2 consumed by the skin in man, all of the CO_2 produced by the skin, and an undetermined quantity of CO_2 from capillary blood perfusing the skin can be exchanged directly between skin and air. Cutaneous gas exchange in man varies with the ambient P_{O_2} and P_{CO_2} as in other gas exchangers. Interestingly manifold increases in cutaneous gas exchange accompany increases in cutaneous perfusion, such as is induced by a rise in temperature or application of vasodilators (Fitzgerald, 1957; Klocke *et al.*, 1963). Other factors affecting cutaneous gas exchange in man are regional variation in skin thickness and pathological conditions resulting in skin cornification. The effects of age on cutaneous gas exchange in man are equivocal, but most often cutaneous gas exchange decreases with increasing age (Ernstene & Volk, 1932; Schulze, 1943). Many newborn mammals and newly hatched birds have reduced or absent layers of fur or feathers and apparently well vascularized, thin skin. Cutaneous respiration may well be more important in these animals than in adults, but clearly must be a short-lived phenomenon associated with development. Diffusion through the shell and shell membranes is the major means of gas exchange in bird and reptile eggs (Rahn, Ar & Paganelli, 1979; Feder, Satel & Gibbs, 1982), and some 'cutaneous' gas exchange undoubtedly occurs in the mammalian embryo and fetus (Walsh, Meyer & Lind, 1974). Typically, however, accessory chorioallantoic or placental structures become associated with embryonic gas exchange as development ensues.

V. CONSEQUENCES OF CUTANEOUS GAS EXCHANGE

In a functional evaluation of respiration, cutaneous gas exchange emerges as effective or ineffective depending on how it compares with alternative gas exchangers or an idealized model in physiological performance trials. In an evaluation based on evolutionary considerations, cutaneous gas exchange is successful or unsuccessful depending on whether its practitioners are less prone to extinction (as indicated by ecological versatility, geographic range, population size, and fitness) than animals that rely on alternative gas exchangers, all else being equal. These two approaches differ fundamentally in philosophy, application, parameters and criteria for success. It is especially important to avoid misapplying the results of one to the questions of the other. For example, a gas exchanger may have limited performance capabilities based on physiological measurements and yet be completely adequate to meet an animal's needs in any environmental circumstance it is likely to encounter (e.g. Withers & Hillman, 1983). Nonetheless, both approaches are valid, and each can yield important insights into the overall significance of cutaneous gas exchange.

(1) *Functional consequences*

Cutaneous respiration plays an important role in a great diversity of vertebrates. However, its value is greatest only in certain circumstances, generally where conditions for gas exchange are close to ideal (e.g. normoxia and normocapnia) and demands for gas exchange are small (e.g. in resting animals). As circumstances temporarily depart from the ideal, cutaneous gas exchange becomes increasingly inadequate; either the skin is supplanted by other gas exchangers, overall gas exchange decreases, or both. Thus, reliance on cutaneous gas exchange can be viewed as posing a number of significant

'functional' problems for vertebrates by restricting the range of gaseous environments in which gas exchange can be regulated at routine levels and by restricting the duration of sojourns into less favourable gaseous environments.

Many of these problems stem from the multiple functions of the skin in both respiratory and non-respiratory roles. The skin must support and protect the organism; it cannot be as thin or as permeable as the well protected alveolar-capillary membranes within the lungs or the membrane of the secondary lamellae in fish gills. Diffusion limitation is one result. Because the skin covers the entire body, ventilation of such a diffuse surface is difficult or impossible without gross movement of the entire body. Because the skin of many aquatic vertebrates is a major site of CO_2 release, it must remain permeable at all times to prevent acidosis. However, continual and unregulated permeability will lead to the transcutaneous loss of O_2 in hypoxic water and transcutaneous water loss whenever an animal is exposed to air. Similarly, significant fluxes of water and solutes may occur across the skin whenever concentration gradients dictate. Unless specific mechanisms are employed to compensate for these fluxes, animals breathing through their skin will accumulate undesirable substances that are at high concentrations in the environment and lose desirable substances (water, solutes, etc.) from within the body, thereby enhancing environmental toxicity or complicating osmoregulation.

As skin-breathing animals increase in mass, both the cutaneous surface area and total cutaneous capillarization decrease relative to the mass of the animal; skin thickness, by contrast, increases in proportion to mass (Fig. 13; Ultsch, 1973, 1974*a*). As a result, mass-specific gas exchange capacity of the skin decreases in proportion to body mass, scaling in one study as $\text{mass}^{-0.46}$ (Ultsch, 1973). Mass-specific O_2 consumption and CO_2 excretion also decrease with body size; however, this decrease (typically scaling as $\text{mass}^{-0.25}$) is less steep than the decrease in exchange capacity (Ultsch, 1973, 1974*a*, 1976*b*). Similar differences often exist between large and small species as well. Accordingly, as body size increases in ontogeny or evolution, the skin should become increasingly inadequate for gas exchange, and alternative gas exchangers should become increasingly important. Many studies have directly documented the increasing inadequacy of cutaneous respiration as the body size of fishes, amphibians, and reptiles increases (Dunson, 1960; Whitford & Hutchison, 1967; Ultsch, 1973, 1974*a*, 1976*a, b*; Beckenbach, 1975; Jordan, 1976; Feder, 1977, 1978; Seymour, 1982), although limitation is not apparent in every case (Feder, 1976; Hillman & Withers, 1979).

Other features of skin that reduce its effectiveness are related to the respiratory medium. The low diffusivity and capacitance of O_2 in water make hypoxia much more likely than in air. Accordingly, aquatic animals breathing through their skin may frequently be forced to resort to pulmonary respiration as a supplement or an alternative, while the reverse is seldom true because the air is generally hypoxic only at high altitude.

Surprisingly, many of these apparent inadequacies may be beneficial in other contexts. The energetic savings associated with a reduction in O_2 consumption and lack of ventilation can be large; see below. Jackson and his co-workers (e.g., Mackenzie & Jackson, 1978; Moalli *et al.*, 1981) suggest that cutaneous gas exchange is deficient because the CO_2 conductance of the skin does not change with temperature, resulting in increased P_{CO_2} at high temperatures. However, this fixed conductance results in 'regulation' of pH and P_{CO_2} at precisely the level required for each temperature without

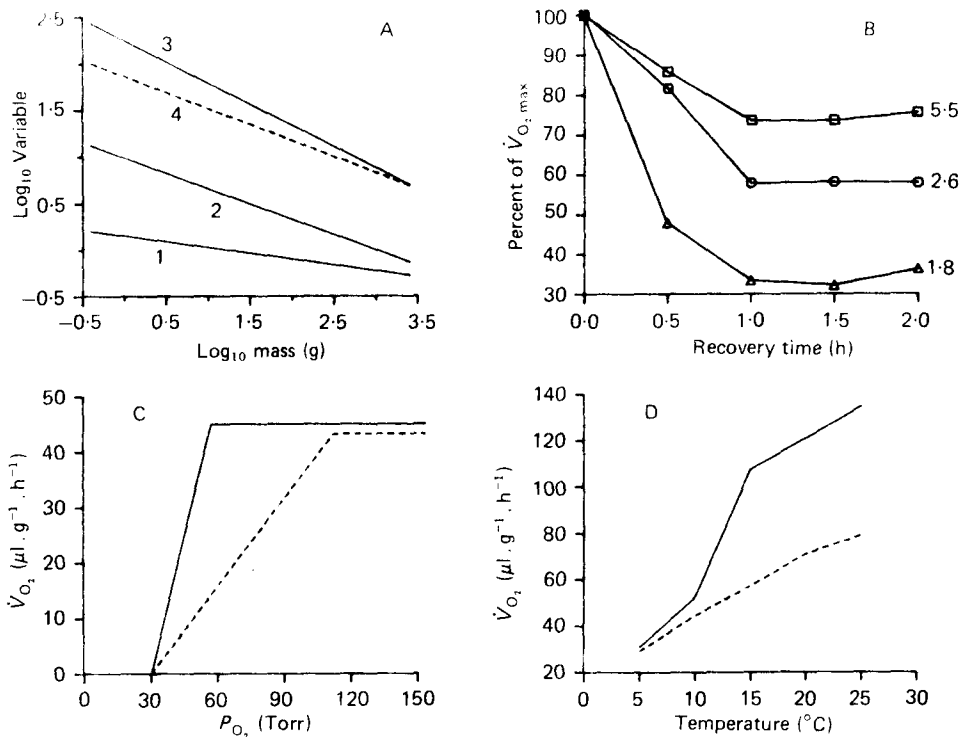


Fig. 13. Scaling of skin diffusion capacity and its consequences for the scaling of cutaneous gas exchange in amphibians. (A) Scaling of (1) cutaneous surface area in $\text{cm}^2 \cdot \text{gram body mass}^{-1}$, (2) cutaneous permeability to $\text{O}_2 \times 10$ in $\mu\text{l O}_2 \cdot \text{h}^{-1} \cdot \text{cm}^{-2} \cdot \text{Torr}^{-1}$, (3) O_2 exchange capacity in $\mu\text{l O}_2 \cdot \text{g}^{-1} \cdot \text{hr}^{-1}$, and (4, broken line) the metabolic rate in $\mu\text{l O}_2 \cdot \text{g}^{-1} \cdot \text{hr}^{-1}$ in aquatic salamanders, *Siren lacertina*, breathing through their skin (Ultsch, 1973). Skin thickness increases, permeability and relative surface area decrease, and thus gas exchange capacity becomes increasingly inadequate, as body size increases. (B) After cessation of activity, the metabolic rates of small exclusively skin-breathing salamanders (Plethodontidae) decline much more rapidly from maximal levels than do rates of larger plethodontids (Withers, 1980). Body mass (g) is given alongside each line. (C) In an exclusively skin-breathing salamander, *Desmognathus quadramaculatus*, hypoxia reduces the metabolic rate of large individuals (10.4 g, broken line) at relatively high P_{O_2} ; small conspecifics (2.2 g, solid line) are unaffected until the P_{O_2} is relatively low (Beckenbach, 1975). (D) The rate of O_2 consumption in a species with lungs (*Ambystoma maculatum*, solid line) increases at high temperatures, while the metabolic rate of an exclusively skin-breathing species (*Desmognathus quadramaculatus*, broken line) does not (Whitford & Hutchison, 1967).

the extensive ventilatory adjustments necessary in gill-and lung-breathing animals. Piiper *et al.* (1976) view the low arterial P_{O_2} of lungless salamanders as a deleterious consequence of cutaneous respiration. However, low blood gas tensions may be inconsequential if the blood oxygen affinity is high (as it is in many amphibians, including lungless salamanders) and may actually promote gas exchange across the skin.

Limited O_2 exchange in skin-breathing animals may be especially valuable because it is equivalent to a reduction in metabolic costs (assuming, of course, that anaerobic metabolism does not increase to offset reduced aerobic metabolism). Although forced reliance upon cutaneous respiration seems deleterious to many aquatic salamanders because it decreases the rate of O_2 consumption (Ultsch, 1976b), this metabolic

depression slows depletion of energy stores. Salamanders and turtles can live for months in this condition (Ultsch, 1976*b*; Seymour, 1982; Ultsch & Jackson, 1982). Similarly, depression in metabolism associated with cocoon formation in amphibians increases the time animals can remain dormant within the cocoon.

Although it may promote the formation of a diffusion boundary layer, lack of a ventilatory pump also conserves energy. Estimates of ventilatory costs for lungs and gills range from 1–50% of the oxygen that is extracted by these organs (White, 1978). Even the lowest cost can be substantial when accrued throughout the lifetime of an animal. Animals breathing through their skin are spared this cost. Moreover, if skin-breathing animals live in a current of air or water, their skin is ventilated at no cost to themselves (Vogel, 1981*a*).

(2) *Evolutionary consequences*

From a functional perspective, reliance upon cutaneous respiration places severe constraints on vertebrates, although it confers certain unique advantages as well. In an evolutionary evaluation, however, the skin need not be absolutely effective as a gas exchanger; it only need be adequate as a gas exchanger and have relatively small costs associated with its function in this role. From this perspective, the skin is usually a good gas exchanger and places relatively few respiratory constraints upon vertebrates. Its interaction with water flux, however, is a serious drawback for terrestrial vertebrates.

The diversity of vertebrates that use cutaneous gas exchange is perhaps the best testament to its evolutionary efficacy. Our perception as we began this review was that, except in amphibians, cutaneous gas exchange is relatively uncommon and something of a curiosity. In actuality, cutaneous gas exchange is very common in reptiles and fishes, occurs in both air and water, and frequently accounts for a large proportion of total gas exchange. Thus, the occurrence of cutaneous gas exchange in so many species and in so many circumstances is fundamentally inconsistent with the supposed 'functional' deficiencies of cutaneous gas exchange.

The application of laboratory studies to explain the distributional patterns of skin-breathing vertebrates is problematic. The properties of skin may very well limit its maximum gas-exchange capacity. However, if vertebrates seldom need the maximum capacity of the gas exchanger, they may seldom be restricted by its inadequacies. Even if the capacity of cutaneous gas exchange is approached, most lower vertebrates have alternative gas exchangers that can compensate for any deficit in cutaneous gas exchange. Perhaps cutaneous gas exchange is best regarded as an energetically inexpensive respiratory process that is of primary value in resting animals in normoxia and normocapnia. In this sense cutaneous respiration is of variable benefit but is seldom a liability. However, cutaneous respiration can impose a significant ecological restriction if water loss or solute influx, possible correlates of a permeable skin, are themselves limiting.

Lungless salamanders, of course, have no alternative gas exchangers to compensate for deficiencies in skin breathing; it is in these forms that respiratory restrictions in an evolutionary sense should be most evident. Several studies have examined possible consequences of lunglessness for salamanders by correlating the geographical ranges, habitats or sizes of plethodontids with their patterns of gas exchange, inferring that cutaneous respiration is responsible for ecological restrictions that are observed (Whitford & Hutchison, 1965, 1967; Beckenbach, 1975). These studies suggest that

lungless salamanders are restricted to small body sizes and cool temperatures because of the functional inadequacy of cutaneous gas exchange in large animals or at high temperatures. In reality, lungless salamanders attain maximum body sizes far greater than those of most terrestrial salamanders with lungs, and experience warm temperatures (Feder, 1982; Feder, Papenfuss & Wake, 1982). One of the largest salamanders, *Cryptobranchus alleganiensis*, is aquatic and breathes almost exclusively through its skin (Guimond & Hutchison, 1973a). Thus, the ecological and morphological data do not bear out the predicted restrictions.

Cutaneous gas exchange clearly has restricted the ecological range and evolutionary potential of amphibians in terrestrial and marine environments, although not through its inadequacy as a respiratory process. The necessity for cutaneous respiration has endowed nearly all amphibians with a skin that offers little resistance to flux of water (Shoemaker & Nagy, 1977). As a result, amphibians readily lose water to air and to hyperosmotic environments. High rates of water loss restrict terrestrial amphibians to moist microhabitats most of the time, and limit the duration of forays into dry microhabitats (Feder, 1983b). Although amphibians evidence ecological versatility within this constraint, terrestrial forms clearly cannot forage widely during the day in the manner of many reptiles, birds and mammals. Even foraging at night is severely limited by hydric constraints (Feder, 1983b). For similar reasons, few amphibians are able to tolerate saline water. In reptiles, reliance upon cutaneous gas exchange is inversely related to the dryness of the environment (Crawford & Schultetus, 1970; Jackson, Allen & Strupp, 1976; Seymour, 1982). Obviously, reptiles must sacrifice cutaneous gas exchange to achieve an integument that is relatively impermeable to water loss.

Some obvious questions are whether amphibians are able to do without cutaneous respiration, thereby limiting cutaneous water loss, and why they (unlike xeric reptiles) have not done so. Several experiments (Hutchison *et al.*, 1968; Preslar & Hutchison, 1978; Hutchison & Miller, 1979; Jackson & Braun, 1979; Miller & Hutchison, 1979) suggest that the lungs of terrestrial amphibians are by themselves capable of meeting most of the gas exchange requirement. The energetic cost of ventilating these structures, however, is greater than the cost of ventilating the skin. Gans (1970a, b) has suggested that energetic inefficiencies in lung ventilation obligate anurans to use the skin to excrete CO₂. Perhaps the energetic savings of cutaneous respiration justify its retention in terrestrial amphibians. Alternatively, the importance of amphibian skin in water uptake may more than offset its drawback as a site of water loss.

VI. SUMMARY

1. The exchange of oxygen and carbon dioxide between skin and environment is commonplace in the vertebrates. In many lower vertebrates, the skin is the major or even sole avenue for respiration.
2. As implied by the physical laws governing diffusion of gases, the skin diffusion coefficient, surface area, gas diffusion distance and transcutaneous gas partial pressures may independently or jointly affect cutaneous respiration. In vertebrates, each of these variables has undergone modification that may be related to dependence upon cutaneous gas exchange.
3. Both theoretical models and experimental data suggest that cutaneous gas exchange

is limited by the rate of diffusion. However, changes in convection of the respiratory medium and of blood may partially compensate for diffusion limitation, and potentially function in the regulation of cutaneous gas exchange.

4. Typically, the skin is one of several gas exchangers, although many salamanders and some species in other vertebrate groups breathe solely through the skin. The cutaneous contribution to overall gas exchange is often most important in small animals, at cool temperatures, at low levels of activity and in normoxic and normocapnic conditions. Branchial and pulmonary respiration increasingly predominate in other circumstances.

5. Often, the skin figures more prominently in CO₂ excretion than in O₂ uptake.

6. Cutaneous gas exchange emerges in vertebrates as a process perhaps less effective and more constrained than branchial or pulmonary exchange but also less energetically costly. Its utility is indicated by its wide and successful exploitation in vertebrates occupying a diverse array of habitats.

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