Pulmonary fluid balance following pulmocutaneous baroreceptor denervation in the toad

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SMITS, ALLAN W., NIGEL H. WEST, AND WARREN W. BURGGREN. *Pulmonary fluid balance following pulmocutaneous baroreceptor denervation in the toad.* J. Appl. Physiol. 61(1): 331–337, 1986.—Pulmonary hemodynamics and net transcapillary fluid flux (NTFF) were measured in conscious toads before and following bilateral denervation of the recurrent laryngeal nerves (rLN), which contain afferents from baroreceptors located in the pulmocutaneous arteries. Denervation caused an acute doubling of the arterial-venous pressure gradient across the lung and a threefold increase in pulmonary blood flow. Calculated pulmonary vascular resistance fell and remained below control values through the period of experimentation. NTFF increased by an order of magnitude (0.74–7.77 $ml \cdot kg^{-1} \cdot min^{-1}$), as filtration increased in response to the hemodynamic changes caused by rLN denervation. There was a better correlation between NTFF and pulmonary blood flow than between NTFF and pulmonary driving pressure. Our results support the view that tonic neural input from pulmocutaneous baroreceptors protects the anuran lung from edema by restraining pulmonary driving pressure and blood flow and perhaps by reflexly maintaining vascular tone in the extrinsic pulmonary artery, therefore tending to increase the pre-to-postpulmonary capillary resistance ratio and biasing the Starling relationship in the pulmonary capillaries against filtration.

Bufo marinus; lung; fluid filtration; denervation; pulmonary hemodynamics

THE NET FLOW OF FLUID between blood and the interstitial fluid spaces is of crucial importance in organs such as the lung, where interstitial edema may lengthen the diffusion path for O_2 and CO_2, whereas further fluid movement into alveoli may impair ventilation. In mammals, at least, the forces controlling microvascular filtration and absorption are balanced so that the net movement of fluid from intravascular to interstitial spaces within the normal lung is very low. In addition, lymphatic drainage promptly removes excess filtrate, and consequently the lung interstitium does not normally accumulate fluid (30). The maintenance of relatively "dry" lungs in mammals is predicted on the basis of *1*) constant and comparatively low pulmonary arterial pressures (10–15 mmHg), and 2) relatively high plasma oncotic pressures (~28 mmHg), both of which favor absorption of fluid from the lung interstitium (30).

In marked contrast, pulmonary blood pressure in lower vertebrates may be two to three times higher than in mammals (4), whereas plasma oncotic pressure is substantially lower (11, 33). Furthermore, pulmonary blood flow in lower vertebrates may be highly variable, changing with an intermittent pattern of ventilation and the presence of central (and in some cases peripheral) shunts (15, 31). This, at least in turtles, results in a net filtration of fluid into the lung parenchyma at rates 10–20 times those in mammals during ventilation, whereas in apneic periods characterized by low pulmonary blood flow net absorption occurs (3). It is not known if such transient lung filtration in turtles impairs pulmonary gas exchange or whether such a phenomenon is characteristic of other lower vertebrates that demonstrate similar adjustments in pulmonary hemodynamics.

In anuran amphibians (frogs and toads), the functional characteristics of pulmocutaneous baroreceptors and their location in the pulmonary outflow tract have led recent investigators to propose that the end organ primarily at risk from inappropriate changes in blood pressure is the lung (1, 32). Increases in pulmonary arterial pressure could increase the rate of fluid filtration from pulmonary capillaries and perhaps cause pulmonary edema (32).

Therefore we set out to test the hypothesis that the elevated pulmonary arterial-venous pressure gradient and pulmonary blood flow resulting from the denervation of pulmocutaneous baroreceptors would also result in an elevated rate of fluid filtration from pulmonary capillaries in anurans. To this end we compared pulmonary fluid filtration rates in unanesthetized conscious toads during a resting control state and after bilateral denervation of the recurrent laryngeal nerves, which contain the afferents of pulmocutaneous arterial baroreceptors.

MATERIALS AND METHODS

Animals. The experiments were performed on toads, *Bufo marinus* (body mass, 288 ± 14 g), obtained from commercial suppliers. Animals were maintained at 20–22°C for 1–3 wk before the experiments and were fed newborn mice during this period.

Surgical preparations. All experiments were performed at 20–22°C. Toads were anesthetized by immersion in tricaine-methanesulfonate (MS 222, Sandoz; 1:1,000) adjusted to pH 7.0 with NaOH, before implantation of pressure cannulas and electromagnetic flow probes. The

surgical procedures were similar to those used by West and Burggren (31). The toad was placed ventral side up, and a cannula was inserted past the glottis into the trachea to allow artificial lung ventilation with a Harvard Apparatus respirator. The pectoral girdle was then split in the midventral line, revealing the heart and central vessels. A 40-cm length of polyethylene tubing (PE-50) was used to nonocclusively cannulate the left pulmocutaneous artery in the truncus arteriosus before this vessel separated from the systemic arteries. The cannula tip faced downstream. The apex of the left atrium was nonocclusively cannulated with a second 40-cm length of tubing (PE-50). Cannulas were filled with heparinized saline (200 USP U/ml, 0.65% NaCl).

With the exception of unusually large toads over 350 g, pulmonary blood flow cannot be measured reliably with an electromagnetic flow transducer (31). To circumvent this problem, the cutaneous artery was ligated close to its point of origin from the pulmocutaneous artery, and an electromagnetic flow probe with 1.5-mm lumen was placed on the pulmocutaneous artery proximal to the point of ligation. Care was taken to pass the cutaneous artery ligature between the artery and the recurrent laryngeal nerve (rLN), with which it is associated at this point (32). After ligation, all flow in the left pulmocutaneous artery was directed to the left lung. To ensure symmetry in the preparation, the right cutaneous artery was also ligated at its point of origin from the right pulmocutaneous artery. Ligation of the cutaneous arteries in anuran amphibians does not eliminate blood flow to the skin, as a substantial component of cutaneous blood flow is derived from the systemic aortas (10). In preliminary experiments, a second 1.5-mm electromagnetic flow probe was placed on the right pulmocutaneous artery to determine bilateral equality of pulmonary flow, but this was not performed routinely.

Both left and right rLN were cleared and encircled with hydrophylic cotton thread at a location close to the origin of the cutaneous artery and central to their passage over the pulmocutaneous artery. Extreme care was taken to avoid stretching or otherwise damaging the nerves (see Ref. 32). These nerves contain pulmocutaneous baroreceptor and laryngeal mechanoreceptor afferents (14, 28). All cannulas, leads, and nerve snares were exteriorized anteriorly and attached securely to the skin at the point of exit from the body cavity. The sternum was then closed with sutures and the skin closed with stainless steel wound clips. Toads were placed dorsal side up in a dimly lit, moist container to allow recovery from anesthesia and surgery. Cannulas, leads, and nerve snares were led out of the container.

Arterial and atrial cannulas were connected to Narco P-1000B pressure transducers, and transducer output displayed on a four-channel Narco MK-IV rectilinear chart recorder. The pulsatile pressure signal was fed to a Narco 7320 biotachometer to give an instantaneous measurement of cardiac frequency. Pressure transducers were calibrated frequently throughout the experimental period. Blood flow was measured with a Zepeda SWF-4 electromagnetic blood flow system. Occlusion zero was determined on implantation of the flow probe and magnetic zero set to coincide. Magnetic zero was determined frequently during the course of the experiments. After termination of the experiments flow transducers were calibrated in situ using saline or heparinized *Bufo* blood delivered via an infusion pump at five different flow rates that were determined gravimetrically. The P_{O_2}, P_{CO_2}, and pH of blood sampled from the cannulas were measured at 22°C using an Instrumentation Laboratory Micro 13 blood gas analyzer.

Experimental protocol. Continuous recording of the following variables was begun immediately after surgery: pulsatile blood pressures in the left pulmocutaneous artery and left atrium; pulsatile left pulmonary blood flow; and instantaneous heart rate. Unrestrained toads were allowed to recover from anesthesia, and animals were considered to be in a control state when all of the following criteria were met: *1*) tactile reflexes present; *2*) spontaneous lung ventilation occurring in a typical intermittent pattern (19); *3*) pulmonary blood flow changing during alternating periods of pulmonary apnea and ventilation (31); and *4*) heart rate below 40 beats/min. Recovery reflecting these criteria usually required 4–8 h. Toads were very sensitive to noise or vibration even though screened from movements of the investigators, responding to these disturbances with transient but large increases in heart rate and pulmonary blood flow. Thus great care was taken to ensure that toads were in an undisturbed resting condition at control.

After recovery, as defined above, a series of blood samples was drawn simultaneously from the left atrium and left pulmocutaneous artery. Approximately 200 μl of blood were drawn up into each cannula to flush through its dead space, following which 250 μl of blood were drawn into a 1-ml tuberculin syringe and refrigerated for later analysis (see below). Generally, two to five blood samples, separated by at least 10 min, were made over a 1- to 2-h period and were designated as controls. Pulmocutaneous artery and left atrial blood pressure, pulmocutaneous blood flow, and heart rate corresponding to the time of blood sampling were identified on the chart records. During the sampling periods, mean pulmocutaneous flow was recorded for ease of analysis.

Following establishment of control values, the snares around the left and right recurrent laryngeal nerves were pulled, instantaneously severing these nerves. Denervation induced progressive increases in blood pressure and flow, which peaked within 5–30 min (13, 14). A single pair of simultaneously drawn blood samples was taken at peak levels of blood flow and pressure and designated "denervation" samples. A third series, consisting of two to four pairs of samples, was taken 15–30 min after control samples and designated "early postdenervation." A final series of one to three pairs of blood samples was taken 1.5 h after denervation and designated "late postdenervation."

Calculation of net transcapillary fluid flux in lungs. The net transcapillary fluid flux (NTFF) of the lungs (expressed as $ml \cdot kg^{-1} \cdot min^{-1}$) was calculated from the change in concentration during transit through the lungs of a nonmetabolized "marker" confined to the vascular spaces. Rather than using introduced foreign materials

(6) or erythrocytes (3) as the markers, calculations of NTFF were based on blood hemoglobin concentration. The concentration of hemoglobin in pulmocutaneous artery and left atrial blood was assayed colormetrically by measuring cyanmethemoglobin absorbance at 530 nm (Sigma Procedure 525). The rate of fluid filtration or absorption in both lungs was calculated according to the following equation

$$\text{net transcapillary fluid flux } (\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}) = \frac{2\cdot\dot{Q}_{\text{left lung}}(1-[\text{Hb}]_{\text{pa}}/[\text{Hb}]_{\text{pv}})}{\text{body mass}}$$

These calculations necessarily assume complete equality of the left and right lung with respect to blood flow and hemoglobin concentration of pulmonary arterial and venous blood. Measurements in preliminary experiments showed that there was a bilateral equality of pulmonary blood flow in the conscious toad (Fig. 1). The further assumption was made that there was no sequestration of erythrocytes within the lung. Reflexive changes in heart rate and bilateral pulmonary blood flow with lung ventilation (31), under control conditions, indicated that the innervation of the pulmonary vasculature was not compromised by surgery.

Statistical analysis. The arithmetic mean of all "control" values for each variable in each animal was calculated, as were means for denervation and early and late postdenervation. A one-way analysis of variance was performed on the assembled set of means. Where significant treatment effects were indicated, multiple comparisons of means (LSD test) were performed to assess differences between means. All data were then pooled for product-moment correlations to determine which variables best accounted for changes in NTFF within the lung. A fiducial limit of 0.05 was adopted for all tests. Average values are expressed as means ± SE.

RESULTS

Control period. Toads recovering from surgery demonstrated gradual reductions in heart rate and pulmonary blood flow and pressure, stabilizing within 4–8 h. The animals were fully conscious and alert and showed reflexive changes in cardiopulmonary function in response to both voluntary lung ventilation (Fig. 1) and disturbances by the investigators. Measurement of P_{O_2}, P_{CO_2}, and pH in pulmonary arterial (57.0 ± 3.2 Torr, 14.8 ± 0.8 Torr, 7.59 ± 0.03) and pulmonary venous (91.0 ± 6.7 Torr, 14.2 ± 1.1 Torr, 7.59 ± 0.01) blood, respectively, indicated that pulmonary gas exchange was not significantly impaired by the surgery, although the pH values indicated an acidosis. Mean values for bilateral pulmonary blood flow, heart rate, and hemodynamic driving pressure (mean arterial pressure minus mean venous pressure) across the lung were 70 ± 18 $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, 40 ± 1 beats/min, and 20 ± 1 mmHg. NTFF within the lung was 0.74 ± 0.41 $\text{ml}\cdot\text{kg}\cdot^{-1}\cdot\text{min}^{-1}$, indicating a state of net filtration of fluid out of the pulmonary vasculature (Fig. 3).

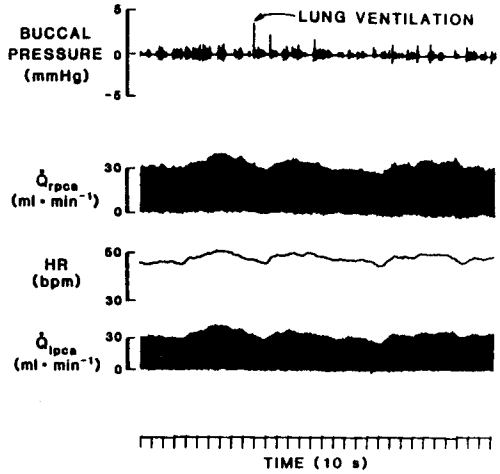

FIG. 1. Spontaneous changes in heart rate (HR) and blood flow in right pulmocutaneous artery ($\dot{Q}$rpca) and left pulmocutaneous artery ($\dot{Q}$lpca). Note bilateral equality of flow.

Effects of denervation. Bilateral denervation of the recurrent laryngeal nerves resulted in dramatic changes in pulmonary hemodynamics and NTFF (Figs. 2 and 3). Within 5 min of denervation, toads typically showed a doubling in pulmonary vascular driving pressure and three- to fourfold increases in pulmonary blood flow. Calculated pulmonary vascular resistance, therefore, fell. Following a transient decrease immediately on denervation, heart rate also increased significantly above control levels to 55 ± 2 beats/min. Associated with these hemodynamic changes was a concomitant increase in NTFF to an order of magnitude greater (7.77 ± 2.09 $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) than that observed during the control state. Hematocrit measured in blood from the pulmocutaneous artery showed a significant elevation (21.7 to 25.2%) during this time. Comparisons of these and associated cardiopulmonary variables and levels of statistical significance are illustrated in Fig. 3.

Postdenervation. Early postdenervation was characterized by significant decreases in the magnitudes of both NTFF and pulmonary blood flow from peak levels despite the unchanged elevated levels in heart rate and blood pressure (Fig. 3). Increases in pulmonary vascular resistance (Rpca) during this time must have accounted for the decrease in pulmonary blood flow, although changes in Rpca were quite variable and thus statistically invariant. By late postdenervation all measured cardiopulmonary variables had returned to levels that were statistically similar to those in the control period; in particular, this represented a decrease in both heart rate and pulmonary driving pressure (Fig. 3).

Correlations between 12 measured and calculated variables across all experimental conditions (control through late postdenervation) indicated that changes in net fluid filtration within the lung were primarily influenced by pulmonary blood flow ($P < 0.01$) (Table 1) and secondarily by variables that altered cardiac output (heart rate and arterial blood pressure; $P < 0.05$). Pulmonary blood flow, in turn, was best correlated with changes in heart rate, lung peripheral resistance, and venous blood pressure. Surprisingly, NTFF was poorly correlated with the vascular driving pressure across the lung ($r = 0.282$, $P > 0.1$), since both heart rate and arterial systolic blood

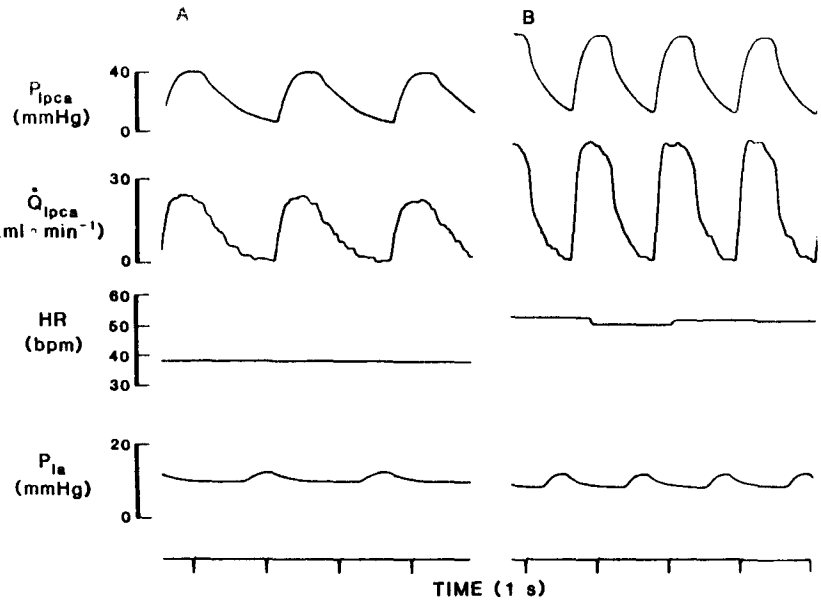

FIG. 2. *A*: left pulmocutaneous arterial pressure (Plpca), blood flow ($\dot{Q}$lpca), left atrial pressure (Pla) and heart rate (HR) before bilateral recurrent laryngeal nerve denervation in a conscious toad (280 g). *B*: same variables 5 min after denervation.

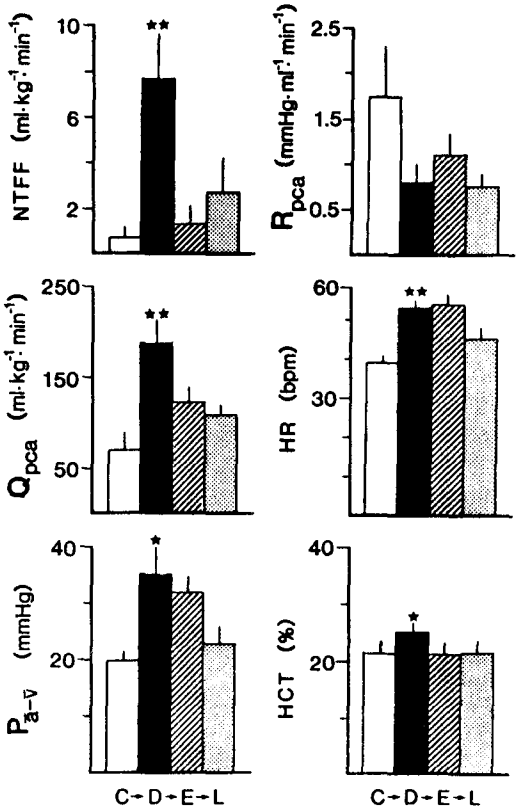

FIG. 3. Average changes in 6 cardiovascular variables measured in 7 conscious toads during control periods (C), 5 min following bilateral recurrent laryngeal nerve denervation (D), and during early (E) and late (L) postdenervation ~0.5 and 1.5 h following denervation, respectively. Variables represented are net transcapillary fluid flux (NTFF), pulmocutaneous arterial flow ($\dot{Q}$pca), mean driving pressure across the lung (P_{a-v}), pulmonary vascular resistance (Rpca), heart rate (HR), and pulmocutaneous arterial hematocrit (Hct). *Vertical lines* above histograms represent SE. Significant differences between control and denervation values are indicated by $^*P < 0.05$ and $^{**}P < 0.01$.

pressure contribute significantly ($P < 0.01$) to that factor.

A direct comparison between the influence of pulmonary blood flow and pressure on NTFF in the toad lung is illustrated in Fig. 4 where the responses of individual toads to denervation are plotted. With the exception of no. 5, all animals demonstrated increases in NTFF when either mean vascular driving pressure or pulmonary blood flow increased. However, the proportional changes in NTFF in response to increased blood flow ($r = 0.82$, $P < 0.01$) were much more uniform than those in response to increased driving pressure ($r = 0.36$, $P > 0.05$) suggesting that NTFF was more directly related to the magnitude of blood flow through the lung than to the pressure gradient across it.

DISCUSSION

Bilateral denervation of the rLN, which contain afferents from baroreceptors located in the proximal pulmocutaneous artery (14, 28), and laryngeal mechanoreceptors (28, 29) resulted in acute increases in heart rate, pulmonary driving pressure, and pulmonary blood flow in conscious *B. marinus* (see also Refs. 12–14, 24, 32). Electrical stimulation of the rLN in conscious toads has been shown to cause a fall in heart rate and arterial blood pressure (13, 29), whereas distension of the pulmocutaneous artery has a similar result (14, 32). Collectively, these data suggest that tonic input from pulmocutaneous baroreceptors contributes to the regulation of pulmocutaneous pressure and flow in the toad (1, 32).

The present study has determined the acute hemodynamic effects of rLN denervation in the pulmonary circulation and the resulting consequences for the rate of pulmonary fluid filtration. Under control conditions, conscious toads had a net transcapillary filtration within their lungs, averaging a loss of ~1% of pulmonary blood flow (Fig. 3). This rate of fluid loss is substantially greater than that estimated by pulmonary lymph flow in the mammalian lung (2, 26) and is consistent with the previous accounts of high rates of lymph flow in anurans (16). However, our measurements may represent a slight overestimate of lung filtration in the normal toad. Because the cutaneous artery normally receives ~10% of

TABLE 1. *Changes in net fluid filtration within the lung*

	NTFF, ml·kg^{-1}·min^{-1}	Cardiovascular Variables										
		1	2	3	4	5	6	7	8	9	10	11
$\dot{Q}$, ml·kg^{-1}·min^{-1}	0.744†	1.000†										
$\dot{Q}$, ml/min	0.669†	0.967†	1.000									
Stroke flow, ml	0.532†	0.900†	0.959†	1.000								
Heart rate, beats/min	0.511*	0.554†	0.514*	0.291	1.000							
Pa systolic, mmHg	0.458*	0.472*	0.434*	0.253	0.768†	1.000						
Pv systolic, mmHg	0.361	0.445*	0.572†	0.576†	0.172	0.034	1.000					
Rpca, mmHg·ml^{-1}·min	−0.315	−0.641†	−0.664†	−0.727†	−0.229	−0.047	−0.484*	1.000				
Hematocrit, %	0.290	0.083	0.150	0.033	0.348	0.241	0.255	0.216	1.000			
Ppa-v, mmHg	0.282	0.153	0.117	−0.043	0.604†	0.855†	−0.252	0.228	0.318	1.000		
Pa diastolic, mmHg	0.276	0.100	0.131	0.004	0.510*	0.680†	0.017	0.202	0.471*	0.900†	1.000	
Pv diastolic, mmHg	0.267	0.438*	0.568†	0.603†	0.085	−0.089	0.969†	−0.531†	0.161	−0.410*	−0.157	1.000

Correlation coefficients (r) between 12 cardiovascular variables potentially affecting pulmonary fluid balance measured in seven conscious toads. Variables are named along the left margin and numbered across the top of table. NTFF, net transcapillary fluid flux; $\dot{Q}$, pulmocutaneous arterial flow; Pa, arterial pressure; Pv, venous pressure; Rpca, pulmonary vascular resistance; Ppa, pulmonary arterial pressure. Levels of significance: * $P < 0.05$; † $P < 0.01$.

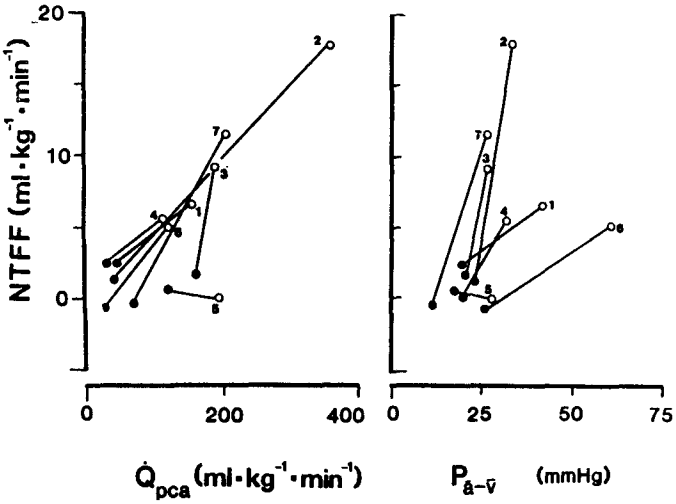

FIG. 4. Changes in net transcapillary fluid flux (NTFF) plotted as a function of pulmonary vascular driving pressure (P_{a-v}) and pulmocutaneous blood flow ($\dot{Q}$pca) in response to bilateral recurrent laryngeal nerves denervation. *Numbered lines* represent same individuals on both *left* and *right*.

the pulmocutaneous blood flow (31), ligation of the cutaneous arteries in our experiments may have redirected significantly more blood to the lungs.

Pulmonary fluid filtration increased to 4–5% of the pulmonary blood flow following the increases in blood flow and pressure associated with rLN denervation. Despite estimates of a large blood volume in the toad (~7–14% body mass) (22, 27), this increased fluid efflux is equivalent to a loss of 5–10% of the toad's plasma volume per minute in this condition, which may explain the transient increase in arterial hematocrit (Fig. 3).

The proportionate rise in pulmocutaneous arterial blood flow on denervation was greater than the increase in pulmonary driving pressure, and therefore calculated vascular resistance fell. Such a change in resistance may have active components due to a reduction in the tone of vascular smooth muscle and passive components due to changes in the transmural pressure across distensible or recruitable vessels (21). However, Van Vliet and West (29) found that pulmocutaneous arterial resistance was unchanged by elevations in pulmonary driving pressure between 20 and 35 mmHg in anesthetized toads, suggesting that a passive decrease in vascular resistance on denervation due to an increased transmural pressure is unlikely.

We do not know whether the site of the fall in pulmonary vascular resistance we observed was arterial or venous, or the resulting change in pre- to postcapillary resistance ratio. Maloney and Castle (20) concluded that the majority (50–70%) of the pulmonary vascular resistance in anuran lungs resided on the venous side of the circulation. However, this estimate must be considered a measure of passive resistance only as their experiments were performed on pithed animals in which vascular tone was probably minimal. On the other hand, the extrinsic segment of the pulmonary artery is vasoactive in intact anurans. It receives cholinergic vagal motor innervation (18) and reflexively alters vascular tone in response to both the degree of lung inflation and to intrapulmonary gas composition (31). Furthermore, electrical stimulation of the recurrent laryngeal nerves results in increases in pulmocutaneous arterial resistance (29), whereas interruption of the pulmonary vagal motor outflow causes the extrinsic pulmonary artery to dilate maximally and permanently (18). Thus the decrease in pulmonary vascular resistance on pulmocutaneous baroreceptor denervation may have been due to a reduction in resistance upstream of the gas exchange capillaries, resulting from a dilatation of the extrinsic pulmonary artery (8) and a greater transmission of arterial pressure directed toward the pulmonary capillaries. If this scheme is correct, recruitment of parallel capillaries or distension of already patent capillaries may be favored. Because the toad lung is a unicameral organ, all lung capillaries probably experience similar alveolar pressures. Further, the size of the toad lung prohibits the formation of substantial hydrostatic gradients within the lung, thus hydrostatic pressures within the capillaries are probably also quite uniform. Because left atrial pressures following denervation (avg = 7.9/5.5 mmHg) exceed normal intrapulmonary pressures measured in toads (1–3 mmHg) (19), a redistribution of blood flow due to the Starling resistor effect also seems unlikely. Unlike the situation in mammals, obvious arterial-venous shunts are not apparent in the

toad pulmonary circulation (25). Thus distension of already patent capillaries might best explain the increased filtration following denervation. However, Smith (23) has shown that electrical stimulation of the pulmonary vagus causes a vasoconstriction of intrinsic vessels in the isolated toad lung sufficient to eliminate perfusion of two-thirds of the pulmonary vasculature. Because recurrent laryngeal nerve denervation in the toad apparently reduces vagally induced tone of the extrinsic pulmonary artery, as stated above, it may also cause a vasodilation of the intrinsic pulmonary vasculature, which results in capillary recruitment and an increased surface area for transcapillary fluid flux.

Transcapillary filtration rate was more closely related to the magnitude of pulmonary blood flow in all conditions (control, denervation, early and late postdenervation) than to the pressure gradient across the lung. This suggests that the relative contributions of pre- and postcapillary resistance were variable and, therefore, pulmonary capillary pressure (a major determinant of fluid movement into the interstitium) may have varied under conditions in which the pressure gradient across the lungs was similar (e.g., control and late postdenervation). If our hypothesis is correct however, the large increases in pulmonary blood flow on denervation were also associated with a reduction in precapillary (extrinsic pulmonary artery) resistance, and, therefore, a greater transmission of arterial pressure to the capillaries, whereas parallel capillaries may have become patent. Under these conditions, it is perhaps not surprising that fluid filtration correlates highly with pulmonary blood flow (see also Ref. 3).

The efficacy of pulmonary lymphatics of anurans (9) remains in question although somatic lymph flow is copious. The whole volume of circulating plasma is filtered some 50 times/day in the frog (16). It is difficult however, to see how such high rates of fluid loss to the pulmonary interstitium following denervation might be tolerated, unless these filtration rates were transient. Filtration did decrease substantially by early postdenervation concomitant with reduced pulmonary blood flow, but pulmonary driving pressure across the lung was unchanged (Fig. 3). As in mammals the alveolar epithelium of anurans rather than the endothelium of the pulmonary capillaries represents the major resistance to water and solute flow across the blood-gas interface (5, 7). In *Rana* lungs 96% of the epithelial pores are of very small size (0.5-nm radius), which represent a relatively impermeable barrier to fluid and solute flux (17). Because transcapillary fluid movement depends on the Starling forces and the permeability characteristics of the capillary, the fall in NTFF during early postdenervation could be due to an increase in hydrostatic pressure within an interstitial space that is bounded by the permeable capillary endothelium and a relatively impermeable alveolar epithelium.

It is clear from our results that elimination of baroreceptive afferent traffic from the pulmocutaneous artery by recurrent laryngeal nerve denervation results in acute elevations in pulmonary blood flow and pressure sufficient to initiate substantial transcapillary filtration within the toad lung. Therefore it appears that pulmocutaneous arterial baroreceptors in anurans may play a part in protecting the anuran lung from the deleterious effects of pulmonary edema by buffering changes in circulatory hemodynamics in the pulmocutaneous circulation (1, 32).

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