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CONTROL OF NASAL VASCULATURE AND AIRFLOW RESISTANCE IN THE DOG

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SUMMARY

1. Nasal vascular and airflow resistances have been measured in dogs, simultaneously on both sides separately.

2. Vascular resistance was measured either by constant flow perfusion of the terminal branch of the maxillary artery (which supplies, via the sphenopalatine artery, the nasal septum, most of the turbinates and the nasal sinuses) or by measuring blood flow through this artery, maintained by the dog's own blood pressure.

3. Airflow resistance was assessed by inserting balloon-tipped endotracheal catheters into the back of each nasal cavity via the nasopharynx, and measuring transnasal pressure at constant airflow through each side of the nose simultaneously.

4. Preliminary experiments indicated that there was 5–10 % collateral anastomosis between the two sides.

5. Close-arterial injection of drugs showed different patterns of response.

6. Adrenaline, phenylephrine, chlorpheniramine and low doses of prostaglandin $F_{2\alpha}$ increased vascular resistance and lowered airway resistance.

7. Salbutamol, methacholine and histamine lowered vascular resistance and increased airway resistance.

8. Dobutamine decreased airway resistance with a small increase in vascular resistance.

9. Prostaglandins E_1, E_2 and $F_{2\alpha}$ (high dose) decreased both vascular and airway resistances.

10. Substance P, eledoisin-related peptide and vasoactive intestinal polypeptide lowered vascular resistance with little change in airway resistance.

11. The results are interpreted in terms of possible drug actions on precapillary resistance vessels, sinusoids and venules, and arteriovenous anastomoses. It is concluded that nasal airway resistance cannot be correlated with vascular resistance or blood flow, since the latter has a complex and ill-defined relationship with nasal vascular blood volume.

INTRODUCTION

The nose is the primary airway to the lung and accounts for about half of the total airways resistance in man (Proctor, 1977). Nasal airway resistance varies with changes in posture, exercise, ambient air conditions, pharmacological agents and disease (Runderantz, 1969; Takagi, Proctor, Salman & Evering, 1969; Rao & Potdar, 1970; Salman, Proctor, Swift & Evering, 1971; Krausz, 1977). The degree of vascular congestion in the nose has been postulated as the most important physiological factor affecting nasal airway resistance (Proctor, 1977). Measurements of nasal blood flow or vascular resistance are rare and are usually performed by indirect methods, using temperature or colour changes (Malcolmson, 1959; Drettner, 1963) or the disappearance rate of an easily diffusible tracer (Anggard & Edwall, 1974; Bende, Flisberg, Larsson, Ohlin & Olsson, 1983). Any change in nasal blood volume is usually derived indirectly from nasal patency measured by rhinomanometric methods (Eccles & Wilson, 1974; Matson, Welter and Kvam, 1978). However, direct measurement of nasal venous outflow as a reflexion of the total nasal blood flow has been described (Malm, 1973).

The nasal vascular bed includes precapillary resistance vessels which supply the blood to rich sub-epithelial and periglandular capillary networks, a plexus of large venous sinusoids draining into venules, both of which are relatively muscular (Temesrekasi, 1969), and numerous arteriovenous anastomoses which may allow the blood to bypass the sinusoid–capillary networks (Cauna, 1982). We assume that nasal airway resistance depends upon the volume of blood in the mucosa (as well as upon the volumes of interstitial fluid and of intraluminal secretions). A decrease in blood volume in nasal capacitance vessels may be caused either by (1) an increase in the arterial resistance to inflow via active vasoconstriction of the arterioles; (2) an opening of arteriovenous anastomoses; or (3) a decrease in the vascular outflow resistance by vasodilation of the venules. The first mechanism would increase total vascular resistance while the last two would decrease it, but each would increase nasal airway resistance. Thus, depending on the vascular site(s) of action of drugs, it should be possible to obtain any combination of changes in vascular and airway resistances simultaneously.

We have developed techniques to measure directly and simultaneously both nasal vascular and airway resistances. We have related changes in these variables in response to various pharmacological agents. Some of the results have been presented in an abstract (Lung, Wang & Widdicombe, 1982).

METHODS

The experiments were carried out with greyhounds (body weight $27 \pm 0{\cdot}6$ kg; $n = 26$) and mongrels (body weight $20 \pm 0{\cdot}8$ kg; $n = 23$) of either sex. The animals were anaesthetized with intravenous injections of either sodium pentobarbitone (25 mg kg^{-1}) or chloralose (80 mg kg^{-1}). Body temperature (rectal) was maintained at 37 °C by means of an electric heating pad placed underneath. Both femoral arteries were catheterized (8FG, Portex). One catheter was connected to a pressure transducer (P231D, Gould) for the measurement of systemic arterial blood pressure. The other catheter was used to supply blood to the nasal perfusion circuit. A femoral venous catheter (3FG, Portex) was inserted for administration of heparin (1000 u. h^{-1}) and supplementary

doses of anaesthetic. A low cervical tracheostomy was performed and the tracheal cannula was connected to a Fleisch pneumotachograph to give airflow and tidal volume by electrical integration.

Measurement of nasal vascular resistance

Nasal vascular resistance was determined by measuring either nasal arterial pressure at constant perfusion flow, or nasal arterial inflow at the dog's own arterial pressure.

An infra-orbital incision was made along the zygomatic arch. The zygomatic bone was removed to expose the internal maxillary artery and its infra-orbital and terminal branches (shown as M, O and S respectively in Fig. 1). A catheter (5FG, Portex) was inserted retrogradely into the infra-orbital artery for administration of drugs or connexion to the perfusion circuit. The terminal branch is the main arterial supply to the nasal mucosa.

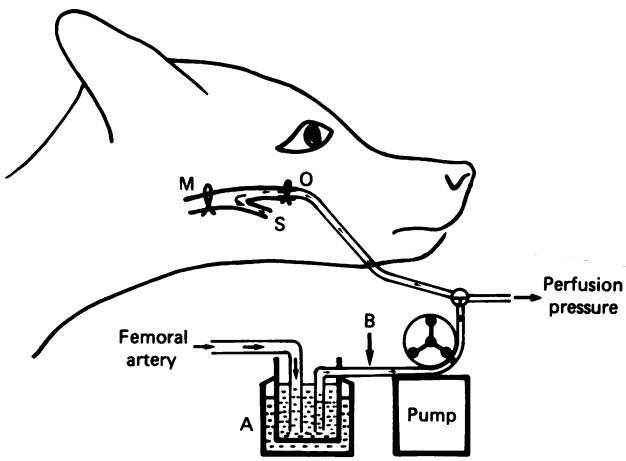

Fig. 1. Diagram of nasal arterial perfusion preparation. The zygomatic bone was removed to expose the internal maxillary artery (M) and its infra-orbital (O) and terminal (S) branches. A: thermostat water bath and blood reservoir. B: site for administration of drugs.

For perfusion of the nasal mucosa, a nylon thread loop was placed around the internal maxillary artery just proximal to the origin of its terminal branch and passed through plastic tubing. Before the onset of perfusion, the nylon thread was tightened and the terminal branch of the internal maxillary artery was then perfused via the infra-orbital artery with blood from a reservoir filled from the femoral artery; perfusion was at a constant rate by a peristaltic pump (MHRE, MK4, Watson-Marlow). The perfusion pressure was measured by a pressure transducer (F231D, Gould) from a point between the peristaltic pump and the infra-orbital catheter. The perfusion flow rate was adjusted so that the nasal perfusion pressure was close to the systemic arterial pressure. Nasal vascular resistance was calculated as the ratio of the mean nasal arterial perfusion pressure (mmHg) to its related blood flow (ml min^{-1}). In a series of preliminary studies, nasal venous pressure was measured and found to be close to zero and therefore it was neglected in the calculation of the nasal vascular resistance. Nasal vascular perfusions were performed on both sides simultaneously with separate pumps. The constant flow perfusions were performed with greyhounds.

For measurement of the nasal arterial inflow, an electromagnetic flow probe (SL7515, Statham) of suitable size was placed around the internal maxillary artery just proximal to the origin of its terminal branch. Changes in nasal arterial inflow represented changes in nasal vascular resistance provided that systemic arterial blood pressure (being monitored) remained unchanged. The flow measurement experiments were performed on mongrels.

Measurement of nasal airway resistance

Two cuffed endotracheal tubes (No. 5, Portex) were tied together and inserted into the nasopharynx via an incision in the upper part of the oesophagus in the neck. Both tubes were

advanced until the tip of each was located in the posterior opening of each nasal cavity. The cuffs were inflated to produce air-tight seals. Continuous flows of humidified air were passed through both tubes and hence through the nasal cavities in the direction of expiration. The airflow rates were measured by two rotameters (No. 1100, GEC-Elliott). The pressure differentials between the back of each nasal cavity and the atmosphere were measured with differential pressure transducers (PE5, Gould). Nasal airway resistances were expressed as the ratios of the pressure differential (mmH_2O) to its related airflow ($l\ min^{-1}$). The independence of each airflow system was tested by occluding each nostril and confirming that the pressure on only the appropriate side was increased.

All flows and pressures were recorded on magnetic tape (Racal) and an ultraviolet oscillograph (Model 6008, SE) or on a Dynograph (Beckman).

TABLE 1. Average values of nasal perfusion pressure, perfusion flow rate, vascular resistance, nasal airway pressure, airflow rate and airway resistance of one side of the nose. Values are means ± S.E. of means

	Greyhounds ($N = 26$)	Mongrels ($N = 15$)
Perfusion pressure (mmHg)	160 ± 5·5	126 ± 3·8
Vascular flow ($ml\ min^{-1}$)	18·7 ± 0·96	15·8 ± 0·95
Vascular resistance ($mmHg\ ml^{-1}\ min$)	8·6 ± 0·53	7·0 ± 0·70
Airway pressure (mmH_2O)	11·2 ± 0·94	6·5 ± 0·22
Airflow ($l\ min^{-1}$)	2·9 ± 0·23	2·1 ± 0·14
Airway resistance ($mmH_2O\ l^{-1}\ min$)	3·9 ± 0·27	3·1 ± 0·25

Drugs were injected directly into the nasal vascular bed in 0·1 ml saline either via the infra-orbital arterial catheter or into the perfusion circuit. They include adrenaline (Macarthys), phenylephrine (Boots), salbutamol (Ventolin, Allen & Hanburys), dobutamine (Dobutrex, Lilly), histamine dihydrochloride (Sigma), chlorpheniramine (Piriton, Allen & Hanburys), cimetidine (Tagamet, Smith, Kline & French), methacholine chloride (Sigma), prostaglandin E_1 (Sigma), prostaglandin E_2 and $F_{2\alpha}$ (Upjohn), substance P, eledoisin-related peptide (ERP) and vasoactive intestinal polypeptide (VIP) (Cambridge Research Chemicals). Doses of drugs are expressed as weights of salts. Controls were given as injections of 0·1 ml saline into the nasal vascular bed. The results are given as means ± S.E. of means. Paired t tests were used to determine the level of significance of difference between the means. For simplicity, only peak changes have been analysed, although the latency and timing of some of the changes can be seen in the Figures.

Drugs were injected at intervals of at least 15 min on alternate sides, always after complete recovery from the effects of the previous injection. N values apply to numbers of injections, rarely more than two (one on each side) per dog for each drug.

RESULTS

Nasal collateral anastomoses

Nasal arterial pressures were measured from the infra-orbital catheters before the perfusion of the nasal vascular beds. The mean nasal arterial pressures were 160 ± 5·5 mmHg in greyhounds and 126 ± 3·8 mmHg in mongrels (Table 1); they were not significantly different from the femoral arterial blood pressures.

In fourteen dogs, when the right internal maxillary artery was occluded, the nasal arterial pressure on the same side fell from 120 ± 9·5 to 47 ± 4·0 mmHg, whilst the pressure on the contralateral non-occluded side was not measurably changed. With additional occlusion of the left internal maxillary artery, there was a further drop in the right nasal arterial pressure and the nasal arterial pressures on both sides decreased to the same value of 30 ± 2·4 mmHg (Fig. 2). In four other dogs, bilateral

occlusion did not result in equal pressures on the two sides. For these dogs right internal maxillary artery occlusion lowered the right nasal arterial pressure to 10, 25, 65 and 68 mmHg respectively. With additional occlusion to the left side, the pressure on the right side fell to 0, 0, 40 and 50 mmHg, while that on the left side became 25, 30, 25 and 35 mmHg respectively. As will be discussed later, these results suggest that for most dogs there were collateral anastomoses between the two sides.

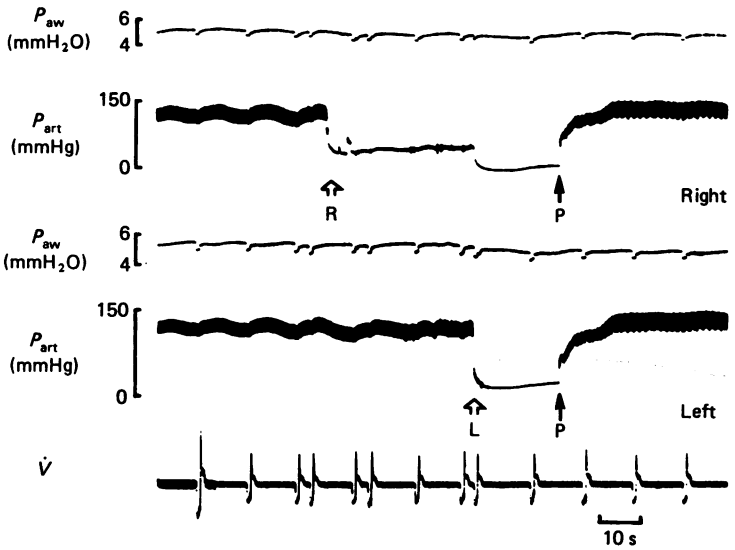

Fig. 2. Effects of unilateral and bilateral occlusions of the internal maxillary arteries on nasal arterial pressure before the start of perfusion. Traces from above downwards: right nasal airway pressure (P_{aw}), right nasal arterial perfusion pressure (P_{art}), left nasal airway pressure, left nasal arterial perfusion pressure and tracheal airflow ($\dot{V}$). R: occlusion of the right internal maxillary artery. L: occlusion of the left internal maxillary artery. P: onset of nasal arterial perfusion on both sides.

The effect of internal maxillary artery occlusion on the nasal airway resistance was insignificant. With right internal maxillary artery occlusion, right nasal airway pressure fell slightly from $10{\cdot}2 \pm 0{\cdot}86$ to $9{\cdot}6 \pm 0{\cdot}74$ mmH$_2$O ($n = 14$), while the nasal airway pressure on the opposite side remained unchanged. With additional occlusion on the left side, both nasal airway pressures dropped to $9{\cdot}2 \pm 0{\cdot}92$ mmH$_2$O.

When 0·1 μg adrenaline was injected into one side of the perfused vascular bed, there was an increase in the nasal perfusion pressure from 150 to 250–300 mmHg on the same side as well as an increase in the nasal perfusion pressure from 150 to 170–180 mmHg on the other side (Fig. 3). This result indicated that a small amount of adrenaline had crossed over to the contralateral side, causing an increase in its perfusion pressure. The increase in pressure on the contralateral side could be reproduced by administration of a smaller dose of adrenaline intra-arterially on that side (0·005–0·01 μg). Therefore about 5–10% of the nasal arterial flow could cross over the anastomoses linking the vascular beds on both sides even though the perfusion pressures were initially equal. The average nasal blood flow to each side was about 16–19 ml min^{-1} (Table 1). Therefore the flow across the anastomoses of the nose would be about 1 ml min^{-1}.

Nasal vascular and airway resistances

Table 1 gives the average nasal perfusion pressures, flow rates and vascular resistances for each side of the nose for greyhounds and for mongrels and the corresponding average values for airway measurements. It will be noted that, although the greyhounds weighed more than the mongrels, they had somewhat higher vascular and airway resistances.

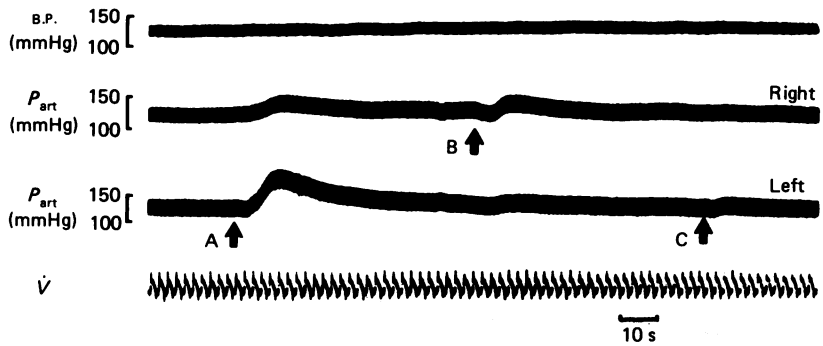

Fig. 3. Effects on nasal arterial perfusion pressures after intra-arterial injection of adrenaline. Traces from above downwards: systemic arterial blood pressure (B.P.), right and left nasal perfusion pressures (P_{art}), and tracheal airflow ($\dot{V}$). The letters indicate the tests performed. A, 0·1 μg adrenaline in 0·01 ml saline injected on the left side. B, 0·01 of adrenaline in 0·1 ml saline injected on the right side. C, 0·001 μg adrenaline injected on the left side.

Effects of drugs

Tables 2 and 3 summarize the results, Table 2 referring to constant flow infusions in greyhounds and Table 3 to flow measurements at near-constant pressure in mongrels. Responses to representative drug doses are given, although for most drugs ranges of doses were used without qualitative differences unless stated.

α-Adrenoceptor agonists, adrenaline and phenylephrine, increased nasal vascular resistance and decreased nasal airway resistance (Tables 2 and 3; Fig. 4). However, adrenaline compared to phenylephrine was far more effective on vascular resistance for similar airway resistance changes.

The β_2-adrenoceptor agonist, salbutamol, decreased nasal vascular resistance and increased airway resistance. Dobutamine, a β_1-adrenoceptor agonist, did not significantly change vascular resistance at constant flow but decreased nasal airway resistance (Tables 2 and 3; Fig. 5). At constant pressure infusion, dobutamine decreased nasal blood flow.

Methacholine decreased vascular resistance and increased airway resistance (Table 2).

Histamine decreased vascular resistance and increased airway resistance (Table 2; Fig. 6). Compared with methacholine, histamine had a relatively greater effect on airway resistance than on vascular resistance. Both drugs usually caused the secretion of mucus that appeared at the nares.

The H_1-receptor antagonist, chlorpheniramine, increased nasal vascular resistance

and decreased airway resistance. The H_2-receptor antagonist, cimetidine, caused no significant change in either vascular or airway resistance.

Prostaglandins (PG) E_1 and E_2 decreased both nasal vascular and airway resistances with a large increase in blood flow at constant pressure (Tables 2 and 3; Figs. 7 and 8). The responses to PGE_1 and PGE_2 were qualitatively similar whatever

TABLE 2. Action of drugs on nasal vascular and airway resistances in the dog, with constant blood perfusion rate. Values are given as percentage changes of the controls. Means ± S.E. of means. Number of tests in parentheses. $P < 0.05$*, $P < 0.01$**

	Nasal vascular resistance (% change)	Nasal airway resistance (% change)
Adrenaline (0·05 μg)	+69·5 ± 12·62 (5)**	−30·4 ± 6·71 (5)*
Phenylephrine (0·5 μg)	+29·4 ± 6·31 (5)**	−33·5 ± 6·71 (5)**
Salbutamol (5 μg)	−13·7 ± 3·52 (6)*	+21·7 ± 4·85 (6)**
Dobutamine (5 μg)	+4·2 ± 2·25 (6)	−27·8 ± 5·23 (6)**
Methacholine chloride (1 μg)	−37·2 ± 5·04 (8)**	+21·8 ± 6·78 (4)*
Histamine dihydrochloride (5 μg)	−18·8 ± 3·43 (9)**	+34·0 ± 13·61 (9)*
Chlorpheniramine (100 μg)	+41·8 ± 14·58 (6)*	−26·1 ± 9·26 (6)*
Cimetidine (100 μg)	−3·4 ± 2·61 (4)	+3·6 ± 1·69 (4)
PGE_1 (0·6 μg)	−19·1 ± 2·92 (8)**	−16·3 ± 3·16 (8)**
PGE_2 (1 μg)	−22·9 ± 3·21 (5)**	−11·9 ± 3·34 (5)*
$PGF_{2\alpha}$ (0·1 μg)	+13·2 ± 3·57 (7)**	−12·2 ± 2·66 (7)**
(1·0 μg)	−17·4 ± 6·76 (4)	−17·8 ± 4·47 (4)*
Substance P (10 ng)	−32·0 ± 2·94 (11)**	+3·5 ± 1·64 (5)
ERP (100 ng)	−29·3 ± 3·31 (4)**	+8·4 ± 3·49 (4)
VIP (100 ng)	−29·0 ± 3·10 (10)**	+9·3 ± 3·51 (5)

TABLE 3. Action of drugs on nasal arterial blood flow in the dog, at near-constant arterial blood pressure. Mean ± S.E. of mean. $P<0.05$*, $P<0.01$**, N = number of tests

	N	Control nasal arterial blood flow (ml min^{-1})	Nasal vascular resistance (% change)	Nasal airway resistance (% change)
Adrenaline (0·05 μg)	8	30·6 ± 1·05	+58·5 ± 9·30**	−21·3 ± 1·34**
Salbutamol (5 μg)	5	30·6 ± 2·59	−36·6 ± 5·44**	+18·5 ± 4·52*
Dobutamine (5 μg)	7	27·4 ± 1·98	+26·2 ± 4·02**	−13·8 ± 2·26**
PGE_1 (0·6 μg)	5	24·0 ± 2·09	−48·8 ± 6·03**	−19·0 ± 3·77**
$PGF_{2\alpha}$ (0·1 μg)	5	28·2 ± 1·43	+27·0 ± 9·13*	−8·1 ± 1·51**
(1·0 μg)	5	27·8 ± 2·07	−39·6 ± 6·05**	−14·6 ± 0·75**
Substance P (10 ng)	5	27·8 ± 2·56	−39·3 ± 13·21*	+7·2 ± 2·99

the dose. The same effect was seen with high doses of $PGF_{2\alpha}$, but low doses of $PGF_{2\alpha}$ increased vascular resistance with a fall in airway resistance (Tables 2 and 3).

Substance P, ERP and VIP each decreased nasal vascular resistance with statistically insignificant increases in airway resistance (Tables 2 and 3; Fig. 9).

Injections of 0·1 ml saline into the perfusion circuit caused small, transient (*ca.* 5–10 s) decreases in the perfusion pressure, presumably due to a lowering of blood viscosity. This was taken into account in assessing the actions of drugs.

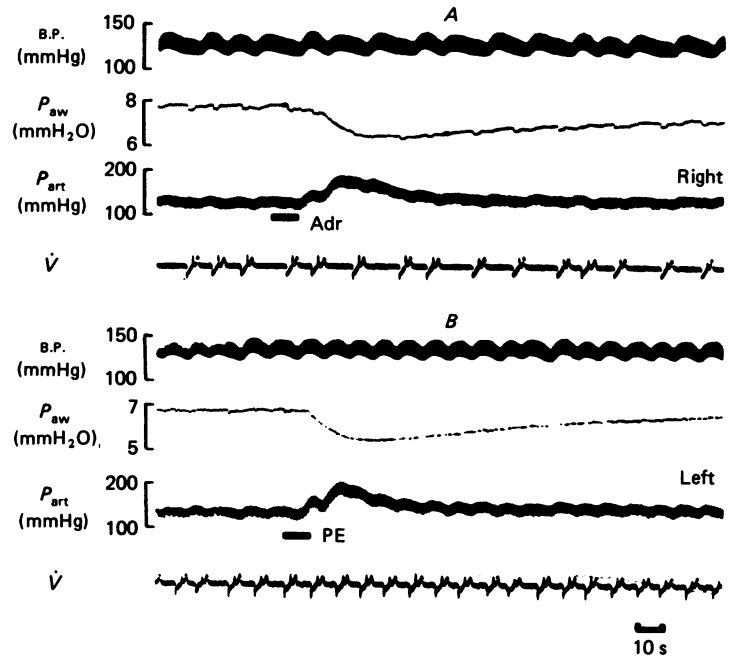

Fig. 4. Effects on nasal arterial perfusion pressure and airway pressure after intra-arterial injection of *A*, adrenaline (Adr; 0·05 μg in 0·01 ml saline) and *B*, phenylephrine (PE; 0·5 μg in 0·1 ml saline), injected at signal bars. Traces from above downwards in each record: systemic arterial blood pressure (B.P.), nasal airway pressure (P_{aw}), nasal perfusion pressure (P_{art}), and tracheal airflow ($\dot{V}$).

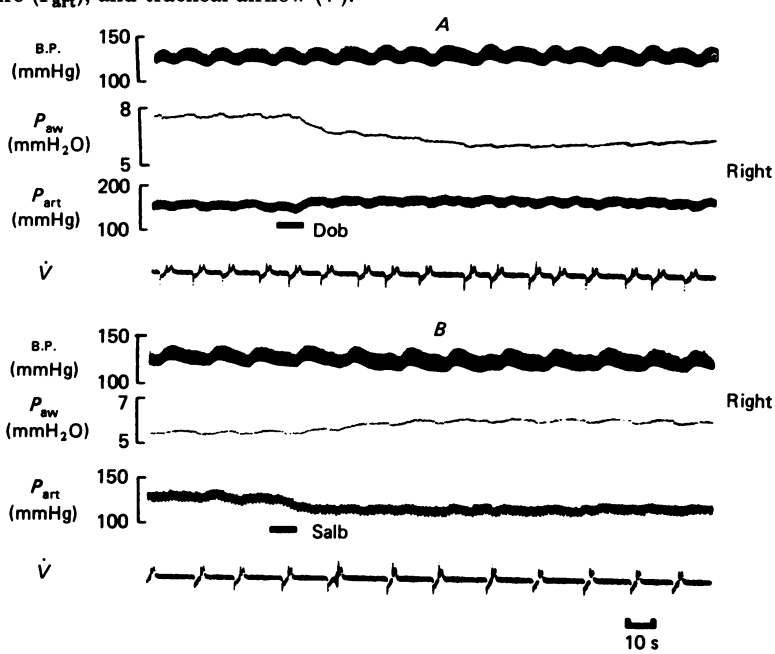

Fig. 5. Effects on nasal arterial perfusion pressure and airway pressure after intra-arterial injection of *A*, dobutamine (Dob; 5 μg in 0·1 ml saline) and *B*, salbutamol (Salb; 5 μg in 0·1 ml saline), injected at signal bars. Traces from above downwards in each record: systemic arterial blood pressure (B.P.), nasal airway pressure (P_{aw}), right nasal perfusion pressure (P_{art}), and tracheal airflow ($\dot{V}$).

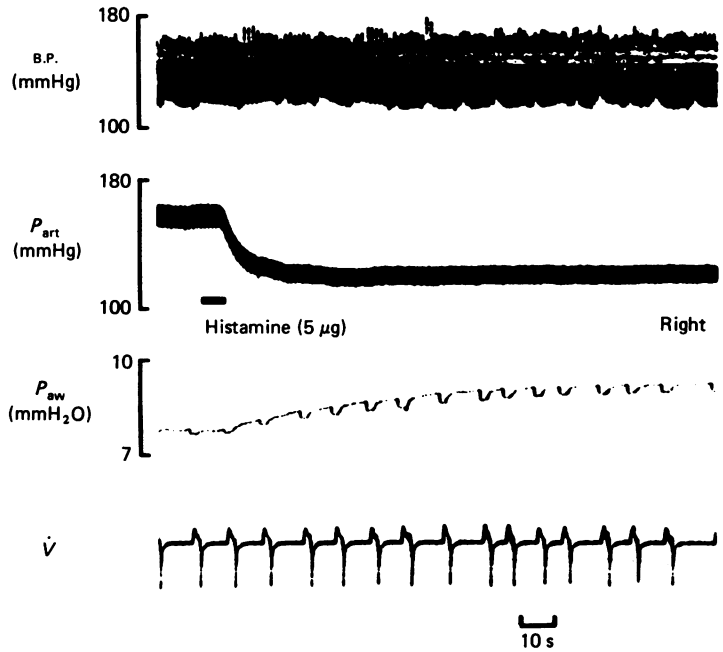

Fig. 6. Effects on nasal arterial perfusion pressure and airway pressure after intra-arterial injection of histamine (5 μg, injected at signal bar). Traces from above downwards: systemic arterial blood pressure (B.P.), right nasal perfusion pressure (P_{art}), right nasal airway pressure (P_{aw}), and tracheal airflow ($\dot{V}$).

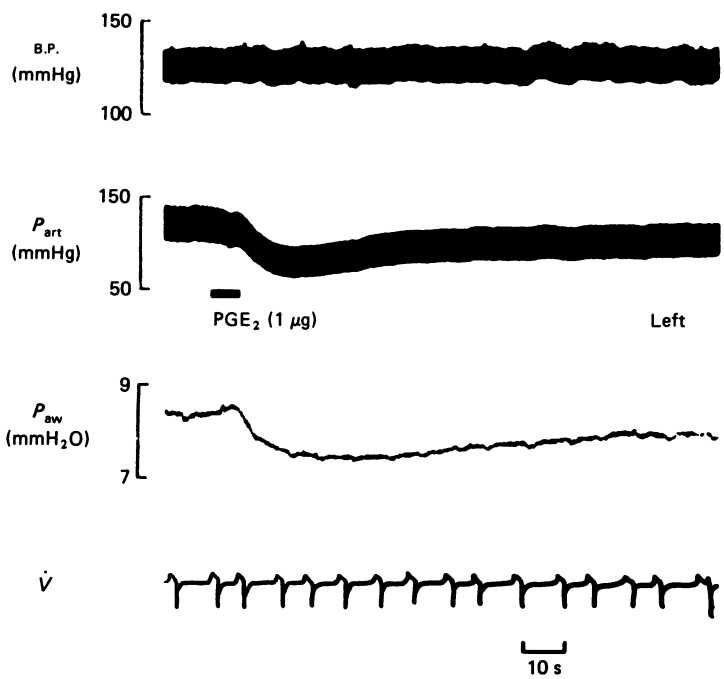

Fig. 7. Effects on nasal arterial perfusion pressure and airway pressure after intra-arterial injection of PGE_2 (1 μg, injected at signal bar). Traces from above downwards: systemic arterial blood pressure (B.P.), left nasal perfusion pressure (P_{art}), left nasal airway pressure (P_{aw}), and tracheal airflow ($\dot{V}$).

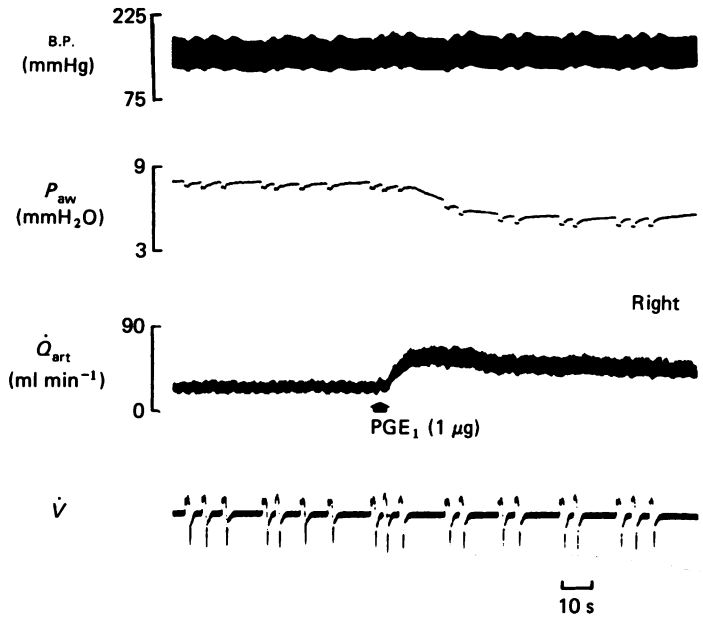

Fig. 8. Effects on nasal arterial inflow and airway pressure after intra-arterial injection of PGE_1 (1 μg, injected at signal bar). Traces from above downwards: systemic arterial blood pressure (B.P.), right nasal airway pressure (P_{aw}), right nasal arterial flow ($\dot{Q}_{art}$) and tracheal airflow ($\dot{V}$).

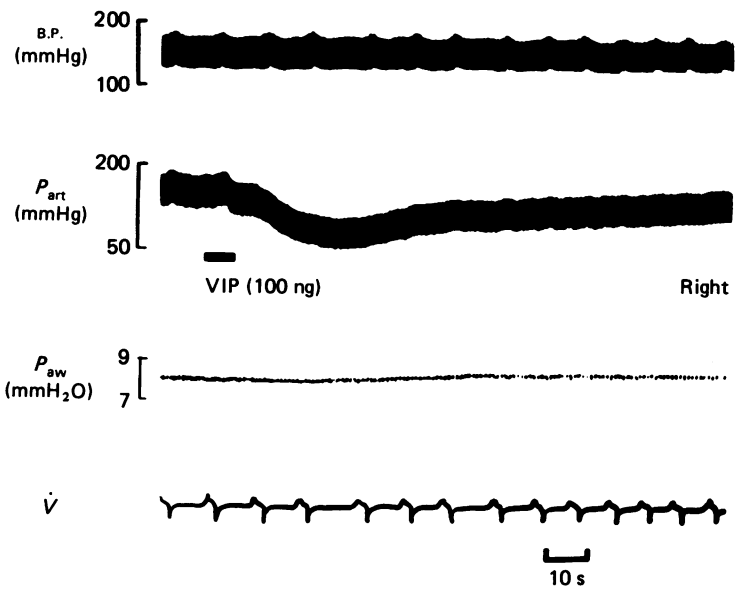

Fig. 9. Effects on nasal arterial perfusion pressure and airway pressure after intra-arterial injection of VIP (100 ng, injected at signal bar). Traces from above downwards: systemic arterial blood pressure (B.P.), right nasal arterial perfusion pressure (P_{art}), right nasal airway pressure (P_{aw}), and tracheal airflow ($\dot{V}$).

DISCUSSION

As far as we know, our method is the first to describe direct measurements of nasal vascular and airway resistances simultaneously. Previous indirect methods include the changes in pressure or volume in the closed nasal cavities, assumed to be due to changes in blood volume (Tschalussow, 1913; Eccles & Wilson, 1974). Alternatively, changes in nasal airway resistance are thought to reflect changes in mucosal blood volume (Malcolmson, 1959). Nasal blood flow has been directly measured by Malm (1973) by collecting the outflow from the pterygopalatine vein in the cat. However, since blood drains also to the angular and facial veins anteriorly and to the ethmoidal vein posteriorly (Dawes & Prichard, 1953), that via the pterygopalatine vein is only a small fraction of the total outflow and cannot represent the total arterial inflow.

In the dog the perfused terminal branch of the internal maxillary artery supplies the septum, most of the turbinates, and the ethmoidal, frontal and maxillary sinuses (Dawes & Prichard, 1953), which was confirmed in our preparation by injections of dye. The terminal branch of the internal maxillary artery includes the sphenopalatine, and the minor and major palatine arteries, which supply the palate and anastomose with the sphenopalatine. In addition the anterior portions of the superior and middle turbinates and meatuses and a small area of the septum are supplied by the anterior and posterior ethmoidal branches of the ophthalamic artery, and the olfactory region is supplied by the ethmoidal artery; these vessels were not included in our perfusions.

Nasal collateral anastomoses

Anastomoses between the two sides of the nose were shown when the internal maxillary arteries were occluded in turn just proximal to their terminal branches. When the second maxillary artery was occluded, arterial perfusion pressure fell on both sides. The responses to unilateral adrenaline injections while both sides were perfused at approximately equal pressures indicates that the collateral flow in either direction was about 5–10 % of the nasal arterial blood flow for one side (Fig. 3). Eccles & Eccles (1981) with pigs and Malm (1974*a*) with cats have previously demonstrated nasal collateral circulation. The fact that unilateral occlusion caused little change in resistance on the contralateral side suggests that the anastomoses were distal to the main resistance vessels.

Bilateral occlusion of the internal maxillary arteries led to only slight decreases in nasal airway resistance on both sides of the nose. Thus in control conditions nasal blood volume is not greatly decreased by removal of blood flow, presumably because there is a high arteriolar resistance and/or high arteriovenous anastomotic blood flow bypassing the main capacitance vessels. Blocking arterial flow does not empty the capacitance vessels as effectively as do vasoactive drugs like adrenaline.

Nasal vascular resistance

The control spontaneous nasal arterial inflow for one side of the nose ranged from 24 to 31 ml min^{-1} (Table 3). The flow rates in the perfusion experiments were about 16–19 ml min^{-1}. These flow rates are much higher than those reported by other workers, so that the calculated nasal vascular resistances are much lower. Using labelled microspheres, Abe & Jackson (1972) found that the total nasal blood flow

in the dog was about 2–3 ml min^{-1}, but the presence of arteriovenous anastomoses would result in an artificially low value. Malm (1974*a*) reported that the resting venous outflow from the pterygopalatine vein in the cat was about $0{\cdot}6 \pm 0{\cdot}1$ ml min^{-1}, but the pterygopalatine vein is only part of the total venous drainage.

Nasal airway resistance

McCaffrey & Kern (1979) measured the dog's total upper airway resistance (larynx, pharynx and both nasal passages in parallel) with the mouth sealed; their values of about 30–40 $cmH_2O\ l^{-1}s$ are consistent with ours (20 $cmH_2O\ l^{-1}s$ for each nasal passage). We used airflows and pressures within the physiological range of the dog (Proctor, 1977), and respiratory oscillations were often seen superimposed upon the pressure records (Figs. 2, 6 and 8), as described by Eccles & Lee (1981*b*); that they were seldom seen on the perfusion pressure or blood flow records suggests that they are not due primarily to changes in tone of the main resistance vessels.

The effects of drugs

α-Adrenoceptor agonists such as adrenaline and phenylephrine decrease nasal airway resistance (Hall & Jackson, 1968; Jackson, 1970) and decrease venous outflow (Malm, 1974*a*). In man the vasoconstrictor action may be due primarily to α_2- rather than α_1-receptors (Andersson & Bende, 1983). The action is probably due to constriction of the arteriolar resistance vessels since both drugs decreased airway resistance, indicating a decrease in mucosal blood volume. The importance of arteriolar constriction is supported by our finding that adrenaline and phenylephrine caused a decrease in spontaneous nasal arterial inflow. That the decrease in airway resistance was considerably greater than that seen when the internal maxillary artery was occluded may indicate that adrenaline and phenylephrine also contract the smooth muscle of sinusoids and venules, thus emptying the capacitance vessels.

The existence of β-adrenoceptors in the nasal vasculature is controversial. Hall & Jackson (1968) could not demonstrate their presence in the dog. Anggard & Edwall (1974) stated that they were absent in the cat. Later, Malm (1974*b*) demonstrated the presence of β_2-adrenoceptors in the resistance vessels of the cat, but his results for the capacitance vessels were inconclusive. Hiley, Wilson & Yates (1978) reported that β_2-adrenoceptors were present in the feline capacitance vessels. In man, topical administration of isoprenaline or terbutaline results in either a variable response (McLean, Mathews, Ciarkowski, Brayton & Solomon, 1976), an increase in airway pressure (Grobler, 1966) or no effect (Cohen, 1970; Svensson, Hegardt & Lofkvist, 1980). Our results suggest that β_1- and β_2-adrenoceptors are present in the nose of the dog. Dobutamine, a β_1-agonist, significantly decreased airway resistance with a small increase in the vascular resistance of the perfused nose in greyhounds and a decrease in spontaneous arterial inflow in mongrels. Thus, at constant flow, any weak arteriolar constriction due to dobutamine may be compensated by an increase in arteriovenous anastomotic flow, and the decrease in the vascular volume could be due to venular dilatation and emptying of sinusoids. Salbutamol, mainly a β_2-adrenoceptor agonist, decreased vascular resistance of both the spontaneously and pump-perfused noses and increased airway resistance. Thus salbutamol probably dilates arterioles and increases volume of capacitance vessels. Adrenaline also

stimulates β-receptors, but its α-effect seems dominant in the dog nose at the doses used.

Electrical stimulation of parasympathetic nerves to the nose and application of parasympathomimetic drugs cause a decrease in nasal patency and an increase in the blood content of the mucosa as well as a watery secretion (Jackson & Rooker, 1971; Eccles & Wilson, 1974; Anggard, 1977). This vasodilator action of the parasympathetic nerves is consistent with our findings that methacholine decreased vascular and increased airway resistances.

Histamine decreases nasal patency and increases nasal airway resistance (Jackson, 1970; Salem & Clemente, 1972: Hiley *et al.* 1978; Matson *et al.* 1978), and it relaxes nasal mucosal strips (Jackson, 1979). It increases nasal blood flow in man (Bende, Elner & Ohlin, 1983). Our results confirm these observations; the action is presumably mainly due to opening of precapillary resistance vessels.

Antihistamines may prevent the action of histamine on the nasal vascular bed (Jackson, 1970; Salem & Clemente, 1972; Hiley *et al.* 1978), although Bentley & Jackson (1970) could not demonstrate this effect in the dog. Antihistamines have a wide spectrum of pharmacological activity, including sedative, anticholinergic and vasoconstrictive actions (Goodman & Gilman, 1980). In our experiments chlorpheniramine, an H_1-antagonist, increased vascular resistance and decreased airway resistance, suggesting either a high degree of histaminergic tone in healthy dogs, or a direct vasoconstrictor action of chlorpheniramine not involving H_1-receptors. Since cimetidine, an H_2-antagonist, had little effect on either vascular or airway resistances, any predominant histamine receptors in the dog nasal vasculature may be H_1 rather than H_2.

Prostaglandins are present in the nasal mucosa of normal subjects and in the secretions of allergic rhinitis (Toh & Mohiuddin, 1958; Chow, Salmon, Karim & Kunaratnam, 1976; Okazaki, Reiman & Arbesman, 1977). PGE_2 occurs in the nasal mucosa of the pig (Bedwani, Eccles & Jones, 1983). Early experiments by Stovall & Jackson (1967) and recent clinical trials by Anggard (1969) and Karim, Adaikan & Kunaratnam (1978, 1979) suggest that prostaglandins, especially $PGF_{2\alpha}$, are nasal vasoconstrictors since they cause an increase in nasal patency. However, effects on the nasal vascular bed have not been directly assessed, and in general the PGEs relax vascular smooth muscle (Nakano, 1973; Goodman & Gilman, 1980). Our results show that PGE_1, PGE_2 and high doses of $PGE_{2\alpha}$ decrease both nasal vascular resistance and airway resistance. This may be explained by a decrease in both arterial and venous resistances, presumably more the latter, and/or the opening of arteriovenous anastomoses, leading to a decrease in mucosal blood volume. Low doses of $PGF_{2\alpha}$ increased nasal vascular and decreased airway resistance, suggesting a constriction of precapillary resistance vessels.

In the feline nasal mucosa, fine varicose VIP-containing nerves surround small blood vessels and the acini of submucosal glands (Uddman, Alumets, Densert, Hakansson & Sundler, 1978; Uddman, Malm & Sundler, 1980). VIP administered intra-arterially increases nasal venous outflow and increases nasal airway resistance, indicating a vasodilator action on both resistance and capacitance vessels of the nose (Malm, Sundler & Uddman, 1980). This view is supported by our findings that VIP induced a dose-dependent decrease in nasal vascular resistance. However, the small

increase in the nasal airway resistance was not significant. Thus VIP in the dog may dilate both arterioles and arteriovenous anastomoses with little change in vascular volume.

Substance P-containing sensory fibres surround small blood vessels in the nasal mucosa in the cat (Anggard, Lundberg, Hokfelt, Nilsson, Fahrenkrug & Said, 1979), and substance P is a very potent dilator of precapillary resistance vessels of various other vascular beds (Eklund, Jogestrand & Pernow, 1977; Burcher, Atterhog, Pernow

TABLE 4. Summary of types of response to drugs

	Change in:	
	Vascular resistance	Airway resistance
(1) Adrenaline, Phenylephrine, Chlorpheniramine, $PGF_{2\alpha}$ (low dose)	↑	↓
(2) Salbutamol, Methacholine, Histamine	↓	↑
(3) Dobutamine	(↑)	↓
(4) PGE_1, PGE_2, $PGF_{2\alpha}$ (high dose)	↓	↓
(5) Substance P, ERP, VIP	↓	=

& Rosell, 1977). Our results show that both substance P and its related peptide (ERP) decrease vascular resistance with little change in airway resistance. Thus the over-all action of substance P is similar to that of VIP.

In this study several drugs have been tested and Table 4 groups them according to their patterns of response. Those of the first group ('vasoconstrictors') increased nasal vascular resistance and decreased nasal airway resistance. Those of the second group ('vasodilators') had the opposite actions. These results support the general contention that nasal vascular and airway resistances always change in opposite directions. However, the prostaglandins E_1, E_2 and $F_{2\alpha}$ (high dose) each decreased both nasal vascular and airway resistances, while dobutamine decreased nasal airway resistance and spontaneous arterial inflow without inducing appreciable changes in perfused nasal vascular resistance. Substance P, ERP and VIP significantly decreased nasal vascular resistance without affecting airway resistance much. The results suggest that a change in nasal vascular resistance is in itself of little predictive value for changes in nasal airway resistance, and vice versa. This view is supported by the observations of Andersson & Bende (1983) that α_2-adrenoceptor agonists lower nasal blood flow in man, whereas α_1-agonists do not, although both are effective 'decongestants'.

The results presumably depend on the complicated vascular structure of the nose, including arteriovenous anastomoses, sinusoids and muscular venules, on which drugs

may have different actions. In order to interpret changes in the nasal vascular bed it is important to develop methods of measuring simultaneously nasal blood flow, anastomotic flow, resistance and blood capacity.

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