Eur Respir J
1988, 1, 711–715.

Pulmonary artery pressure - flow plots in hyperoxic and in hypoxic dogs: effects of prostaglandin E_1

M. Leeman, P. Lejeune, C. Mélot, R. Naeije

Pulmonary artery pressure: flow plots in hyperoxic and in hypoxic dogs: effects of prostaglandin E_1. M. Leeman, P. Lejeune, C. Mélot, R. Naeije.
ABSTRACT: The effects of prostaglandin E_1 on mean pulmonary artery pressure ($\bar{P}pa$):cardiac index ($\dot{Q}$) relationships were investigated in eight anaesthetized dogs, ventilated in hyperoxia (fraction of inspired oxygen (Fio_2) 0.4) and in hypoxia (Fio_2 0.1). Cardiac output was increased by opening an arterio-venous femoral bypass or reduced by stepwise inflations of a balloon in the inferior vena cava. Five-point $\bar{P}pa$:$\dot{Q}$ relationships were found to be linear in all experimental conditions. Hypoxia increased $\bar{P}pa$ over the entire range of $\dot{Q}$ studied (1–5 $l \cdot min^{-1} \cdot m^{-2}$). Prostaglandin E_1 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ intravenously decreased hyperoxic $\bar{P}pa$ for $\dot{Q}$ ranging from 3–5 $l \cdot min^{-1} \cdot m^{-2}$, hypoxic $\bar{P}pa$ for $\dot{Q}$ ranging from 2–5 $l \cdot min^{-1} \cdot m^{-2}$ and attenuated hypoxia-induced increases in $\bar{P}pa$. These results show that prostaglandin E_1 is a pulmonary vasodilator in both hyperoxic and hypoxic conditions. At the dose of 0.4 $\mu g \cdot kg^{-1}$, prostaglandin E_1 partially inhibits hypoxic pulmonary vasconstriction.
Eur Respir J., 1988, 1, 711–715.

Laboratory of Cardiovascular and Respiratory Physiology, Erasme University Hospital, Brussels, Belgium.

Correspondence: Dr. M. Leeman, Dept of Intensive Care, Erasme University Hospital, 808 route de Lennik, 1070 Brussels, Belgium.

Keywords: Hypoxic pulmonary vasoconstriction; prostaglandin E_1.

Received: September 6, 1987; accepted after revision June 3, 1988.

Prostaglandin E_1 (PGE_1) is known to be one of the most potent pulmonary vasodilating prostaglandins [1]. However, depending on the experimental model and the dosage used, reports of the pulmonary circulatory effects of this compound have varied. PGE_1 has been shown either to inhibit [2] or not to affect [3] canine hypoxic pulmonary vasoconstriction (HPV). PGE_1 reduced pulmonary vascular resistance (PVR) in patients with pulmonary hypertension secondary either to decompensated chronic obstructive pulmonary disease [4] or to the adult respiratory distress syndrome [5]. In healthy subjects, PGE_1 at the same dosage did not inhibit hypoxia-induced increases in PVR [4]. We recently reported that PGE_1 (0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ intravenously) significantly reduced the pulmonary hypertension secondary to oleic acid lung injury in dogs [6]. A possible explanation is the inhibition of HPV. We therefore investigated the effects of this dosage of PGE_1 in intact dogs with strong hypoxia-induced increases in pulmonary artery pressure.

In the present experiments, the influence of PGE_1 on hyperoxic and hypoxic pulmonary vascular tone was evaluated by constructing multipoint mean pulmonary artery pressure ($\bar{P}pa$):cardiac index ($\dot{Q}$) plots. Pulmonary vascular tone in the intact animal and in human studies is commonly evaluated by PVR calculation as $\bar{P}pa$ minus pulmonary capillary wedge pressure (Pw, assumed equal to left atrial pressure) divided by $\dot{Q}$. This approach rests on the assumptions that the $\bar{P}pa$:$\dot{Q}$ relationship is linear over a physiological range of flows and that the extrapolation of the $\bar{P}pa$:$\dot{Q}$ relationship crosses the pressure axis at a level equal to the left atrial pressure. The second of these assumptions is incorrect in most experimental circumstances [6–14]. In isolated lungs, the $\bar{P}pa$:$\dot{Q}$ relationship is linear over a physiological range of flows but becomes curvilinear at low flow with a convexity to the pressure axis [7, 13, 14]. The linear extrapolation of such $\bar{P}pa$:$\dot{Q}$ lines has a positive pressure intercept which represents the mean closing pressure, *i.e* the effective out-flow pressure, of the pulmonary circulation [7, 13, 14]. If left atrial pressure is higher than the closing pressure, the extrapolated pressure intercept should equal left atrial pressure. However, in certain conditions like hypoxia, the extrapolated outflow pressure has been reported to exceed left atrial pressure [10, 13]. Thus, when flow and/or closing pressure have been altered, assessment of pulmonary vascular tone by PVR calculation is misleading and could account for some discrepancies in the literature about the reported effects of PGE_1 on HPV. Therefore, in the present study, $\bar{P}pa$:$\dot{Q}$ plots were constructed in order to discriminate active (tone-dependent) from passive (flow-dependent) changes in $\bar{P}pa$.

Methods

Eight mongrel dogs (21–26 kg, mean 24 kg) were anaesthetized with sodium pentobarbital (25 $mg \cdot kg^{-1}$ *i.v.*), paralysed with pancuronium bromide (0.2 $mg \cdot kg^{-1}$ i.v.) and ventilated with a servo-ventilator Elema 900 B

(Siemens Elema, Solna, Sweden) *via* a cuffed endotracheal tube; the inspired fraction of oxygen (Fio_2) being 0.4, the respiratory rate 12·min^{-1} and the tidal volume 15–20 ml·kg^{-1} adjusted to maintain an arterial carbon dioxide tension (Pco_2) between 30 and 35 mmHg. No positive end-expiratory pressure was used. Injections of pentobarbital (2 mg·kg^{-1}) and pancuronium (0.2 mg·kg^{-1}) were repeated hourly to maintain anaesthesia and to prevent spontaneous respiratory efforts. Pentobarbital is a long-acting barbiturate that does not affect pulmonary haemodynamics [15]. All measurements were performed during stable conditions at least 10 min after anaesthetic injections. Throughout the experiment, sodium chloride 0.9% was infused (4 ml·kg^{-1}·h^{-1}) into the left external jugular vein. Temperature was maintained at 37–38°C by use of an electric heating pad.

A thermistor-tipped Swan-Ganz catheter (93A-131-7F, Edwards Laboratories, Santa Ana, CA) was inserted *via* the right external jugular vein and advanced under pressure monitoring in a branch of the pulmonary artery for measurements of $\bar{P}pa$, Pw, right atrial pressure and for mixed venous blood sampling. The catheter was positioned so that Pw could be measured by fully inflating the balloon. A polyethylene catheter was placed in the abdominal aorta, *via* the right femoral artery, for systemic blood pressure measurement and for arterial blood sampling. A balloon catheter (Percor 45, Datascope, Paramus, NJ) was advanced into the inferior vena cava through a right femoral venotomy. Inflation of this balloon allowed us to continuously decrease cardiac output by reducing venous return. A large-bore polyethylene cannula was inserted into the left femoral artery and vein to act as an arterio-venous bypass. Opening this bypass resulted in an increase in cardiac output by an average of 0.4 *l*·min^{-1}·m^{-2}. Thrombus formation along the catheters was prevented by sodium heparin 100 U·kg^{-1} i.v. just before the insertion and 50 U·kg^{-1} *i.v.* every 2 h thereafter.

Pulmonary and systemic artery pressures were measured using Bentley transducers and the HERES computer system (ACEC, Charleroi, Belgium) and were recorded on a 4-channel Gould recorder (2400 S, Gould Inc., Instruments Division, Cleveland, OH). The pressure transducers were zero referenced at mid-chest and vascular pressures measured at end-expiration. Heart rate was determined from a continuously monitored electrocardiographic lead. Cardiac output was measured by thermodilution using injections of 10 ml of sodium chloride 0.9% at 0°C, a computer (9520-A, Edwards Laboratories) and an automated pneumatic pump electronically synchronized to the ventilatory cycle, and was calculated as the mean of at least three determinations. Arterial and mixed venous blood gases were measured immediately after drawing the samples by an automated analyser (ABL2, Radiometer, Copenhagen, Denmark) and corrected for temperature. Body surface area was calculated in m^2 as 0.112 x weight (kg)$^{2/3}$.

After ensuring steady state conditions for 20 min at Fio_2 0.4 (stable systemic blood pressure, $\bar{P}pa$ and heart rate), a first 5-point $\bar{P}pa$:$\dot{Q}$ plot was generated from $\bar{P}pa$ and cardiac output measurements at baseline (1 point), after opening the arterio-venous bypass (1 point) and after stepwise incremental inflations of the inferior vena cava balloon with occluded bypass (3 points). The same procedure was repeated after 10 min at Fio_2 0.1. One $\bar{P}pa$:$\dot{Q}$ plot was generated in 20–25 min.

We selected eight dogs with vigorous hypoxic pulmonary pressor responses, defined as at least a 20% hypoxia-induced increase in $\bar{P}pa$ at $\dot{Q}$ equal to the first hyperoxic baseline $\dot{Q}$. A second sequence of $\bar{P}pa$:$\dot{Q}$ plots at Fio_2 0.4 and at Fio_2 0.1, successively, was generated after 15 min of a continuous infusion of PGE_1 0.4 μg·kg^{-1}·min^{-1} using a calibrated pump (Infusomat II, Braun Melsungen AG, Melsungen, Germany).

Arterial and mixed venous blood gases, systemic blood pressure, Pw and right atrial pressure were measured at the highest and the lowest $\dot{Q}$ of each $\bar{P}pa$:$\dot{Q}$ plot (hyperoxia, hypoxia, before and after PGE_1 infusion).

Visual inspection of the individual $\bar{P}pa$:$\dot{Q}$ plots showed them to be essentially linear and thus a least squares regression analysis was used to compute the slopes and extrapolated pressure intercepts for each $\bar{P}pa$:Q relationship. To obtain composite $\bar{P}pa$:Q plots for each experimental condition, $\bar{P}pa$ interpolated from the regression equations from each individual dog were averaged at 1 *l*·min^{-1}·m^{-2} intervals of $\dot{Q}$ from 1–5 *l*·min^{-1}·m^{-2} and presented as mean±SE in the figure. A two-way analysis of variance for repeated measurements was used to assess: 1) the effects of reducing $\dot{Q}$ from the highest value to the lowest on haemodynamics and blood gases; 2) the effects of hypoxia and PGE_1 on haemodynamics and blood gases at the highest $\dot{Q}$; 3) the effects of hypoxia and PGE_1 on $\bar{P}pa$ over the entire range of $\dot{Q}$ studied. Paired t-tests were used when the F-ratio of the analysis of variance reached a $p<0.05$ critical level to compare two specific conditions [16].

Results

Manipulation of cardiac output

Haemodynamic and blood gas determinations at the highest and lowest $\dot{Q}$ are shown in table 1. Reduction in $\dot{Q}$ decreased systemic blood pressure, $\bar{P}pa$, Pw, right atrial pressure and mixed venous oxygen tension (Po_2). Mean correlation coefficient of the least squares analysis was 0.97 (range 0.88–0.99). The $\bar{P}pa$:$\dot{Q}$ relationships from one typical experiment are illustrated in figure 1.

Hypoxia

Hypoxia markedly decreased arterial and mixed venous Po_2 with no change in arterial pH and $Paco_2$. Systemic blood pressure and $\bar{P}pa$ increased at the highest flow while Pw and right atrial pressure remained unchanged (table 1). Hypoxia increased $\bar{P}pa$ over the entire range of $\dot{Q}$ studied, 1–5 *l*·min^{-1}·m^{-2} (fig. 2).

Table 1. – Effects of prostaglandin E_1 (0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$) on haemodynamics and blood gases (mean±SE) in eight dogs

		Base		PGE_1	
		Fio_2 0.4	Fio_2 0.1	Fio_2 0.4	Fio_2 0.1
$\dot{Q}$ $l \cdot min^{-1} \cdot m^2$	H	4.06±0.45	4.94±0.48	5.62±0.68*	6.98±0.68*
	L	1.22±0.15+	1.58±0.14+	1.82±0.24+	1.93±0.17+
pHa	H	7.36±0.01	7.35±0.02	7.32±0.02	7.34±0.02
	L	7.36±0.02	7.33±0.03	7.33±0.02	7.35±0.02
Pao_2 mmHg	H	213±11	38±2*	210±10	39±1
	L	215±14	43±2	119±16	41±1
$Paco_2$ mmHg	H	35±1	35±2	33±1	32±1
	L	30±1+	33±3	31±1	29±1+
$P\bar{v}o_2$ mmHg	H	57±2	29±2*	63±4	32±1
	L	34±1+	24±1+	42±4+	25±1+
HR beats·min^{-1}	H	158±11	159±7	166±10	171±8
	L	165±7	164±10	173±9	161±8
BP mmHg	H	106±5	139±4*	95±3	115±7*
	L	62±7+	17±6+	63±5+	58±6+
$P\bar{p}a$ mmHg	H	14±1	27±1*	14±1	26±2
	L	7±1+	13±1+	7±1+	11±1+
Pw mmHg	H	4±1	5±1	5±1	6±1
	L	2±1+	2±1+	2±1+	2±1+
Pra mmHg	H	3±1	3±1	3±1	3±1
	L	1±1+	2±1+	1±1+	1±1+

$\dot{Q}$: cardiac index; pHa: arterial pH; Pao_2: arterial oxygen tension; $Paco_2$: arterial carbon dioxide tension; $P\bar{v}o_2$: mixed venous oxygen tension; HR: heart rate; BP: mean systemic artery pressure; $P\bar{p}a$: mean pulmonary artery pressure; Pw: pulmonary capillary wedge pressure; Pra: right atrial pressure; H: highest $\dot{Q}$; L: lowest $\dot{Q}$; *: $p<0.05$ second and third column *vs* the first, and fourth column *vs* the second; +: $p<0.05$ lowest $\dot{Q}$ *vs* highest $\dot{Q}$.

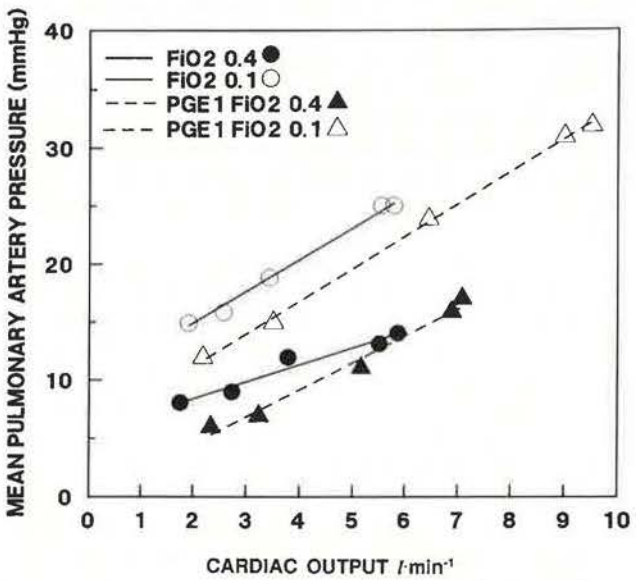

Fig. 1. – Typical experiment showing mean pulmonary artery pressure:cardiac output plots in a dog ventilated alternatively in hyperoxic (Fio_2 0.4) and in hypoxic (Fio_2 0.1) conditions, before and after prostaglandin E1 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion.

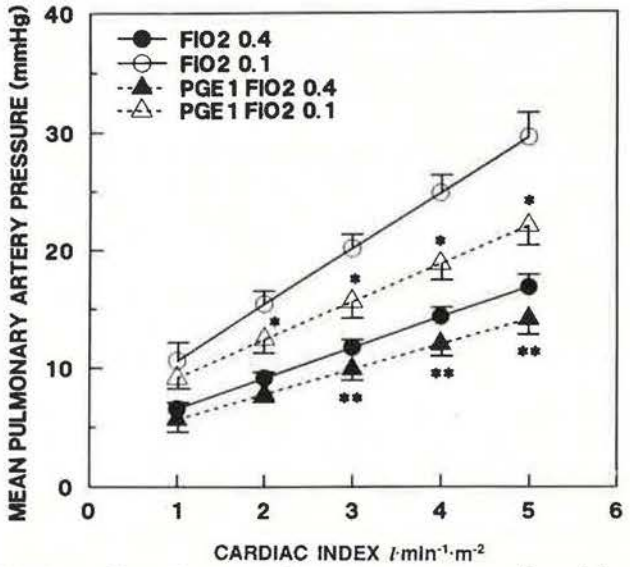

Fig. 2. – Composite mean pulmonary artery presssure (mean±SE): cardiac index plots for eight dogs before and after prostaglandin E_1 (PGE_1) at 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in hyperoxic (Fio_2 0.4) and in hypoxic (Fio_2 0.1) conditions. *, **: $p<0.05$; PGE_1 compared to control at the same Fio_2. PGE_1 decreased hyperoxic and hypoxic Ppa at identical flow.

Prostaglandin E_1

At the highest $\dot{Q}$, PGE_1 decreased systemic blood pressure by 10% in hyperoxia (non-significant) and by 17% in hypoxia ($p<0.005$). PGE_1 increased $\dot{Q}$ in both these ventilatory conditions. pH, Pao_2, $Paco_2$, mixed venous Po_2, and Pw and right atrial pressure were not affected by PGE_1 administration (table 1). PGE_1 decreased hyperoxic Ppa for $\dot{Q}$ ranging from 3–5 $l \cdot min^{-1} \cdot m^{-2}$ and hypoxic $\bar{P}pa$ for $\dot{Q}$ ranging from 2–5 $l \cdot min^{-1} \cdot m^{-2}$ (fig. 2). The hypoxic pressor response was partially inhibited by PGE_1 administration (fig. 3).

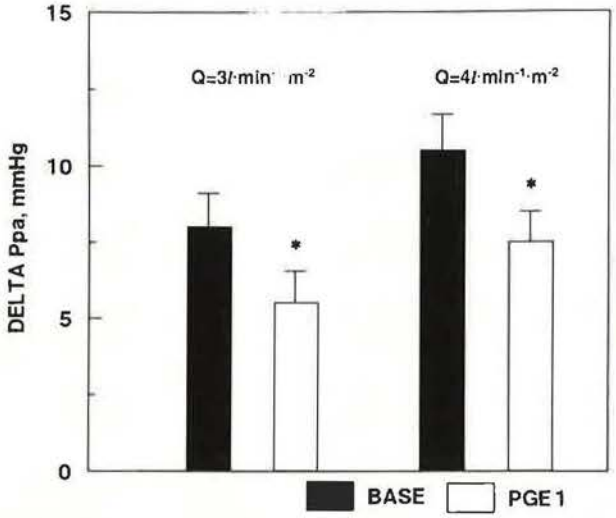

Fig. 3. – Mean±SE delta $\bar{P}pa$ (Ppa at Fio_2 0.1 minus $\bar{P}pa$ at Fio_2 0.4) for a normalized cardiac index (Q) of 3 $l \cdot min^{-1} \cdot m^{-2}$ (left) and 4 $l \cdot min^{-1} \cdot m^{-2}$ (right) in eight dogs without drug (base) and during prostaglandin E_1 (PGE_1) at 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion. *: $p<0.02$; PGE_1 compared to base. PGE_1 partially inhibited hypoxic pulmonary vasoconstriction.

Discussion

In the present study, $\bar{P}pa$:$\dot{Q}$ relationships were characterized in intact anaesthetized and ventilated dogs. PGE_1 decreased hyperoxic and hypoxic pulmonary vascular tone and inhibited HPV.

The $\bar{P}pa$:$\dot{Q}$ plots in our dogs were linear in all experimental conditions, in keeping with previous studies on isolated lungs [7, 13, 14], intact conscious dogs [10, 11] and intact anaesthetized and ventilated dogs [6, 8, 9, 12]. Individual pressor responses to hypoxia consisted of variable increases in slopes and/or pressure intercepts of the $\bar{P}pa$:$\dot{Q}$ plots, also in agreement with reports on isolated lungs [13], conscious dogs [10] and anaesthetized ventilated dogs [8, 9, 12].

We have recently shown that $\bar{P}pa$ remained stable during 30 min at constant $\dot{Q}$ (the maximum time required to construct a $\bar{P}pa$:Q plot) in hyperoxia and in hypoxia and that two consecutive hypoxic challenges induced the same increase in $\bar{P}pa$ at identical $\dot{Q}$ [8, 12]. A sequence of alternating hyperoxic and hypoxic $\bar{P}pa$:$\dot{Q}$ plots were reproducible up to two times without a change in slope or pressure intercept [9]. Our experimental model thus appears suitable for the study of the acute effects of physiological and pharmacological interventions on the pulmonary vascular tone in intact dogs.

Changes in blood gases, baroreflex stimulation and neurohumoral activity may have influenced pulmonary vascular tone, along with the decrease in $\dot{Q}$. The $\bar{P}pa$:$\dot{Q}$ plots in intact animals probably represent an integrated response of the pulmonary circulation to multiple vasoactive stimuli rather than truly passive pressure:flow relationships [11]. These methodological limitations inherent in our intact animal model led us to compare the changes in $\bar{P}pa$ at several levels of flow instead of analysing slopes (taken as incremental resistance) and extrapolated pressure intercepts (taken as mean closing pressure) of the $\bar{P}pa$:$\dot{Q}$ plots.

PGE_1 is generally considered as a pulmonary vasodilatator [1]. However, variable data on its pulmonary vascular actions during normoxia and hypoxia have been reported [2, 3] and few studies have investigated its effects on HPV [2, 4]. In anaesthetized dogs, PGE_1 did not affect normoxic $\bar{P}pa$ and PVR but inhibited the increase in $\bar{P}pa$ and in PVR induced by hypoxia [2]. Inhibition of HPV occurred at a dose of 5 $\mu g \cdot kg^{-1} min^{-1}$ but not at 1.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$. On the other hand, in conscious dogs, PGE_1 at 1 $\mu g \cdot kg^{-1} min^{-1}$ decreased $\bar{P}pa$ in normoxia but not in hypoxia, and produced a similar decrease in PVR under normoxic and hypoxic conditions, so that HPV was probably not inhibited [3]. PGE_1 reduced the pulmonary vasoconstriction associated with lobar pneumonia in dogs [17] as well as the pulmonary hypertension secondary to endotoxin infusion in pigs [18] and in sheep [19], or secondary to oleic acid lung injury in dogs [6]. In septic primates with shock and respiratory failure, however, PGE_1 at 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ failed to reduce pulmonary vascular pressure and resistance [20].

At the maximum doses tolerated in clinical practice, 0.02–0.04 $\mu g \cdot kg^{-1} \cdot min^{-1}$ PGE_1 did not affect normoxic and hypoxic $\bar{P}pa$ and PVR and did not inhibit HPV in healthy subjects [4]. The same dosage, however, was associated with a decrease in pulmonary hypertension in patients with decompensated chronic obstructive pulmonary disease [4] as well as in patients with adult respiratory distress syndrome [5]. Since blood gas indices of pulmonary gas exchange in these studies did not deteriorate after PGE_1, it could be hypothesized that local adaptation of pulmonary vascular tone to regional hypoxia was preserved [4].

In the present study, PGE_1 at 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ decreased hyperoxic and hypoxic pulmonary vascular tone and attenuated HPV. This dose was chosen because it decreased systemic blood pressure and was based on a previous report [6]. Since exogenous PGE_1 is efficiently inactivated during one single passage through the lung vascular bed [21], a fall in systemic blood pressure probably indicates that the drug fully saturates the pulmonary circulation. However, the pulmonary vascular effects of PGE_1 might be dose-related, so that more significant vasodilatation and stronger inhibition of HPV could possibly occur with larger doses.

In summary, our data show that PGE_1 dilates pulmonary vessels in hyperoxic and hypoxic conditions and partially inhibits hypoxic pulmonary vasoconstriction.

Acknowledgements: The authors are grateful for the technical assistance of M.T. Gautier. P. Lejeune, M. Leeman and C. Mélot were fellows of the Erasme Foundation and recipients of the Therabel Research Fellowship, in 1985, 1986, 1987, respectively.

References

1. Hyman AL, Spannhake EW, Kadowitz PJ. – Prostaglandins and the lung. *Am Rev Respir Dis*, 1978, 117, 111–136.
2. Weir EK, Reeves JT, Grover RF. – Prostaglandin E_1 inhibits the pulmonary vascular pressor response to hypoxia and prostaglandin F_2. *Prostaglandins*, 1975, 10, 623–631.
3. Alpert JS, Beller GA, Giamber SR, Saltz SB. – Effects of hypoxia on the hemodynamic actions of prostaglandin E_1. *Prostaglandins*, 1976, 11, 783–797.
4. Naeije R, Mélot C, Mols P, Hallemans R. – Reduction in pulmonary hypertension by prostaglandin E_1 in decompensated chronic obstructive pulmonary disease. *Am Rev Respir Dis*, 1982, 125, 1–5.
5. Shoemaker WC, Appel PL. – Effects of prostaglandin E_1 in adult respiratory distress syndrome. *Surgery*, 1986, 99, 275–282.
6. Leeman M, Lejeune P, Mélot C, Naeije R. – Pulmonary vascular pressure:flow plots in canine oleic acid pulmonary edema. Effects of prostaglandin E_1 and nitroprusside. *Am Rev Respir Dis*, (in press).
7. Graham R, Skoog C, Macedo W, Carter J, Oppenheimer L, Rabson J, Goldberg HS. – Dopamine, dobutamine and phentolamine effects on pulmonary vascular mechanics. *J Appl Physiol.* 1983, 54, 1277–1283.
8. Leeman M, Naeije R, Lejeune P, Mélot C. – Influence of cyclooxygenase inhibition and of leukotriene receptor blockade on pulmonary vascular pressure:cardiac index relationships in hyperoxic and in hypoxic dogs. *Clin Sci*, 1987, 72, 717–724.
9. Lejeune P, Naeije R, Leeman M, Mélot C, Deloof T, Delcroix M. – Effects of dopamine and dobutamine on hyperoxic and hypoxic pulmonary vascular tone in dogs. *Am Rev Respir Dis*, 1987, 136, 29–35.
10. Lodato RF, Michael JR, Murray PA. – Multipoint pulmonary vascular pressure-cardiac output plots in conscious dogs. *Am J Physiol*, 1985, 249, H351–H357.
11. Murray PA, Lodato RF, Michael JR. – Neural antagonists modulate pulmonary vascular pressure-flow plots in conscious dogs. *J Appl Physiol*, 1986, 60, 1900–1907.
12. Naeije R, Lejeune P, Leeman M, Mélot C, Deloof T. – Pulmonary arterial pressure:flow plots in hyperoxic and in hypoxic dogs. Effects of isoflurane and of nitroprusside. *J Appl Physiol*, 1987, 63, 969–977.
13. Rock P, Patterson A, Permutt S, Sylvester J. – Nature and distribution of vascular resistance in hypoxic pig lung. *J Appl Physiol*, 1985, 59, 1891–1901.
14. Shoukas AA. – Pressure-flow and pressure-volume relations in the entire pulmonary vascular bed of the dog determined by two-part analysis. *Circ Res*, 1975, 37, 809–818.
15. Mathers C, Benumof JL, Wahrenbrock EA. – General anesthetics and regional hypoxic pulmonary vasoconstriction. *Anesthesiology*, 1977, 46, 111–114.
16. Winer BJ. – *In:* Statistical principles in experimental design. 2nd edition, McGraw-Hill, New York, 1971.
17. Goldzimer EL, Konopka RG, Moser KM. – Reversal of the perfusion defect in experimental canine lobar pneumococcal pneumonia. *J Appl Physiol*, 1974, 37, 85–91.
18. Modig J, Samuelsson T, Sandin R. – Treatment with prostaglandin E_1 in a porcine model of early adult respiratory distress syndrome. *Acta Chir Scand*, 1986, 152, 569–575.
19. Smith ME, Gunther R, Zaiss C, Demling RH. – Prostaglandin infusion and endotoxin-induced lung injury. *Arch Surg*, 1982, 117, 175–180.
20. Brockmann DC, Stevens JH, O'Hanley P, Shapiro J, Walker C, Mihm F, Collins JA, Raffin TA. – The effects of prostaglandin E_1 on the adult respiratory distress syndrome in septic primates. *Am Rev Respir Dis*, 1986, 134, 885–890.
21. Piper PJ, Vane RJ, Wyllie JH. – Inactivation of prostaglandins by the lung. *Nature*, 1970, 225, 600–604.

RÉSUMÉ: Les effets de la prostaglandin E_1 sur la relation pression artérielle pulmonaire ($\overline{Ppa}$): index cardiaque ($\dot{Q}$) ont été étudiés chez huit chiens anesthésiés et ventilés alternativement en hyperoxie (fraction inspiratoire en O_2, Fio_2 0.4) et en hypoxie (Fio_2 0.1). Le débit cardiaque a été réduit en gonflant un ballon dans la veine cave inférieure ou augmenté en ouvrant une fistule artério-veineuse, de manière à construire des relations la $\overline{Ppa}$:$\dot{Q}$ à 5 points. La linéarité de ces relations a été vérifiée dans toutes les conditions expérimentales. L'hypoxie a augmenté la $\overline{Ppa}$ à tous les niveaux d'index cardiaques étudiés (1–5 $l \cdot min^{-1} \cdot m^{-2}$). Une perfusion continue de prostaglandine E_1 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ a diminué la $\overline{Ppa}$ en hyperoxie pour des index cardiaques variant de 3–5 $l \cdot min^{-1} \cdot m^{-2}$, en hypoxie pour des index cardiaques variant de 2–5 $l \cdot min^{-1} \cdot m^{-2}$ et a atténué la réponse vasculaire pulmonaire à l'hypoxie. Ces résultats montrent que la prostaglandine E_1 est un vasodilatateur pulmonaire en hyperoxie et en hypoxie. A la dose de 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$, la prostaglandine E_1 inhibe partiellement la vasoconstriction pulmonaire hypoxique.