

## Effect of PEEP Ventilation on Renal Function, Plasma Renin, Aldosterone, Neurophysins and Urinary ADH, and Prostaglandins

G. Annat, M.D.,\* J. P. Viale, M.D.,† B. Bui Xuan, M.D.,† O. Hadj Aissa, M.D.,‡ D. Benzoni, Pharm. D.,§ M. Vincent, Pharm. D.,¶ C. Gharib, M.D.,\*\* J. Motin, M.D.††

To explore the main factors which could be involved in the fluid retention induced by continuous positive pressure ventilation (CPPV), hemodynamic, renal, and hormonal parameters were measured in seven intensive care patients during three consecutive 60-min periods: one of intermittent positive pressure ventilation (IPPV), one of CPPV (PEEP 10 cmH<sub>2</sub>O), and finally one of IPPV. During CPPV, a 15% decrease in cardiac output was observed, without alteration in arterial pressure or right atrial transmural pressure. In addition, decreases were observed in urinary output by 34%, glomerular filtration rate by 19%, renal blood flow by 32%, sodium excretion by 33%, and potassium excretion by 26%. There was no change in the fractionnal excretion of sodium and free water. Institution of PEEP also led to a significant increase in plasma renin activity, plasma aldosterone, and urinary antidiuretic hormone, without significant variation in plasma neurophysins and urinary prostaglandins E and F<sub>α</sub>. All of the changes that occurred during CPPV were reversed when PEEP was withdrawn. It is concluded that the short-term antidiuretic effect of PEEP is mainly due to a hemodynamic impairment of renal function. The water- and sodium-retaining hormonal systems also are stimulated and could participate in the fluid retention during more prolonged respiratory support with PEEP. (Key words: Heart: cardiac output. Hormones: aldosterone; antidiuretic; prostaglandins. Kidney: blood flow; function; urine output. Polypeptides: renin-angiotensin. Ventilation: positive end-expiratory pressure.)

IN PATIENTS treated with intermittent positive pressure ventilation (IPPV), the addition of positive end-expiratory pressure (PEEP) leads to a decrease in urinary output.<sup>1-3</sup> Two main factors have been suggested to account for this effect: changes in renal hemodynamics<sup>1</sup> and increase in antidiuretic hormone (ADH) release.<sup>3</sup> But the contribution of at least two other hormonal

factors acting on the kidney also must be considered. The first is the renin-angiotensin-aldosterone system (RAAS), a major determinant of urinary sodium excretion, the second is the prostaglandins (PG<sub>s</sub>) produced by the kidney, which are currently thought to play modulating roles in the regulation of renal water and electrolytes elimination.<sup>4</sup>

The present study was designed to explore simultaneously the main factors which could be involved in the fluid retention induced by continuous positive-pressure ventilation (CPPV). This was achieved by measuring glomerular filtration rate (GFR), renal blood flow (RBF), plasma renin activity (PRA), aldosterone (PA), and immunoreactive neurophysins (iNp), and urinary excretion of ADH, PGE, and PGF<sub>α</sub> during the application of 10 cmH<sub>2</sub>O PEEP in intensive care patients.

### Methods

#### PATIENTS

The study was carried out in seven patients undergoing ventilatory treatment with IPPV (Servo Model 900 B), according to a protocol approved by the ethical committee on human research at the University Claude Bernard of Lyon. Informed consent concerning the nature and purpose of the study was obtained in each case from the patient's closest relative.

Clinical data are given in table 1. Patients were spontaneously stuporous lapsing into sleep if undisturbed (patients 1, 2, 3, and 5) or deeply stuporous requiring strong pain to provoke appropriate movements (patients 4, 6, and 7). Cerebral edema and intracerebral hematoma were eliminated by computerized tomography. At the time of the examination, all the patients were normovolemic and had normal cardiovascular and renal functions. None were receiving diuretic, analgesic, or anti-inflammatory drugs. They were fed via a nasogastric tube.

#### PROTOCOL

From the beginning of the study, each patient received an inulin and PAH infusion: the priming injec-

\* Chef de Travaux de Physiologie.

† Assistant d'Anesthésie-Réanimation.

‡ Assistant de Physiologie.

§ Maître Assistant de Physiologie.

¶ Chef de Travaux de Physiologie.

\*\* Professeur de Physiologie.

†† Professeur d'Anesthésie-Réanimation.

Received from the Department of Physiology, at University Lyon I, Faculté de Médecine Grange-Blanche, 69373 Lyon Cédex 08, France, and the Intensive Care Unit, Hôpital E. Herriot, Place d'Arsonval, 69374 Lyon Cédex 03 France. Accepted for publication July 8, 1982. Presented in part at the meeting of the French Society of Intensive Care Medicine, Paris 1981.

Address reprint requests to Dr. Annat: Université Claude Bernard, Laboratoire de Physiologie A, 8 avenue Rockefeller, 69373 Lyon Cédex 08, France.

TABLE 1. Clinical Characteristics of Patients at Study Date. All the Patients Were Ventilated with IPPV

Patient Number	Age (yr)	Sex	Diagnosis	Number of Days Intubated at Time of Study	F <sub>IO<sub>2</sub></sub>	P <sub>aO<sub>2</sub></sub> (mmHg)	P <sub>aCO<sub>2</sub></sub> (mmHg)
1	18	M	Multiple trauma	10	0.30	120	33
2	17	M	Multiple trauma	8	0.25	109	33
3	19	M	Multiple trauma	5	0.30	103	40
4	46	M	Anoxic coma	13	0.30	123	35
5	19	M	Multiple trauma	30	0.40	94	36
6	65	F	Multiple trauma	15	0.35	102	36
7	19	M	Quinine intoxication	8	0.40	114	38

tion was 0.03 g/kg inulin and 0.05 g/kg PAH, followed by a sustaining infusion of 0.04 g/kg inulin and 0.03 g/kg PAH diluted to 120 ml with 10% mannitol and infused at a constant rate of 1 ml/min. In addition, 5% glucose in water containing 34 mM sodium and 26 mM potassium per liter was infused at a constant rate of 1.5 ml/min, and 6 mg of pancuronium bromide and 1 mg of flunitrazepam were given intravenously at 60-min intervals.

After a 60-min equilibration period, three consecutive examination periods were performed: one hour of IPPV (IPPV<sub>1</sub>), then one hour of CPPV (PEEP 10 cmH<sub>2</sub>O), and finally, one hour of IPPV (IPPV<sub>2</sub>). In the middle of each period, a 10-ml arterial blood sample was drawn to determine hematocrit (Ht), plasma osmolality, and inulin and PAH concentrations. At the end of the period, an additional 20-ml arterial blood sample was taken for the measurement of P<sub>aO<sub>2</sub></sub>, P<sub>aCO<sub>2</sub></sub>, PRA, PA, iNP, sodium, and potassium concentrations. At the same time, heart rate, cardiac output (CO), and intraarterial, esophageal (P<sub>es</sub>), and right atrial pressures were evaluated. Urine was collected through an intravesical catheter and urinary volume, osmolality, inulin, PAH, sodium, potassium, ADH, PGE, and PGF $\alpha$  were measured at the end of each examination period.

#### MEASUREMENTS AND CALCULATIONS

Catheters were placed into the right atrium and a radial artery. Intravascular and esophageal pressures were measured with standard pressure transducers and monitoring equipment. For P<sub>es</sub>, we used a saline-filled catheter passed through the nose into the esophagus for a distance of 40 cm and perfused continuously at a rate of 0.1 ml/min. All transducers were positioned at the midaxillary level, and atmospheric pressure was used as the zero reference point. The mean right atrial transmural pressure (P<sub>TRA</sub>) was calculated by subtracting the mean esophageal pressure from the intracavitary pressure. Cardiac output was determined by the thermodilution technique (GOULD SP 1425). All the hemo-

dynamic parameters analyzed were simultaneous observations at end expiration (v waves for right atrial pressure curve), and were measured in triplicate.

Standard laboratory techniques were used for the measurement of plasma and urine osmolality (FISK® osmometer), sodium and potassium concentrations (IL photometer), P<sub>aO<sub>2</sub></sub>, and P<sub>aCO<sub>2</sub></sub> (Corning® 175). Inulin and PAH were analyzed as described previously.<sup>5</sup> Clearances of inulin and PAH (CPAH), and fractional excretion of sodium (FE Na) and of free water (FE fH<sub>2</sub>O) were calculated.<sup>1</sup> Renal blood flow was estimated as CPAH/100-Ht. Specific radioimmunoassays were used to measure PRA,<sup>6</sup> PA,<sup>7</sup> iNP,<sup>8</sup> and urinary ADH,<sup>9</sup> PGE, and PGF $\alpha$ .<sup>10</sup>

Results are presented as the means  $\pm$  SE, and further statistical analysis used the Wilcoxon signed test for paired data. Correlations were calculated using regression analysis.

#### Results

During the three examination periods, the seven patients who were studied exhibited similar changes in the measured hemodynamic, renal, and hormonal variables.

#### HEMODYNAMIC AND RENAL EFFECTS OF CPPV

As shown in table 2, PEEP did not significantly alter heart rate, arterial blood pressure, or P<sub>TRA</sub>, but did induce a 15% decrease in CO. During CPPV, decreases in urinary output by 34%, GFR by 19%, RBF by 32%, sodium excretion by 33%, and potassium excretion by 26% were observed (table 3). No significant variations were observed in the other measured variables (table 3). All the changes that occurred during CPPV were reversed when PEEP was withdrawn. The calculated RBF/CO ratio was  $18.7 \pm 1.4\%$  before PEEP  $16.6 \pm 1.2\%$  during PEEP ( $P < 0.023$ ), and  $19.3 \pm 2.2\%$  after PEEP.

#### HORMONAL EFFECTS OF CPPV

As shown in figure 1, institution of PEEP led to a marked increase in PRA, PA, and urinary ADH, with-

TABLE 2. Hemodynamic Effect of CPPV (Means  $\pm$  SE)

	IPPV <sub>1</sub>	CPPV	IPPV <sub>2</sub>
Heart rate (beats/min)	111.0 $\pm$ 6.0	117.0 $\pm$ 6.0	115.0 $\pm$ 5.0
Mean arterial pressure (mmHg)	92.7 $\pm$ 4.4	90.1 $\pm$ 3.6	92.3 $\pm$ 4.3
Cardiac output (l/min)	6.9 $\pm$ 0.3	5.9 $\pm$ 0.4*	7.1 $\pm$ 0.3
Right atrial pressure (cmH <sub>2</sub> O)	7.8 $\pm$ 1.1	12.6 $\pm$ 1.1*	7.3 $\pm$ 0.8
Esophageal pressure (cmH <sub>2</sub> O)	5.5 $\pm$ 1.8	9.2 $\pm$ 1.7*	5.6 $\pm$ 2.4
Right atrial transmural pressure (cmH <sub>2</sub> O)	2.3 $\pm$ 1.2	3.4 $\pm$ 1.7	1.7 $\pm$ 1.9

\*  $P < 0.016$  by comparison with the corresponding IPPV<sub>1</sub> value.

out significant variations in iNP and urinary PGE and PGF $\alpha$ . Values found after IPPV<sub>2</sub> were the same as those found after IPPV<sub>1</sub>. There was a positive correlation between PRA and PA ( $r = 0.76$ ,  $n = 21$ ,  $P < 0.001$ ), and a negative one between PRA and urinary sodium excretion ( $r = -0.8$ ,  $n = 21$ ,  $P < 0.001$ ).

### Discussion

Although the effects of alterations in airway pressure on urinary output have been widely documented, in humans as well as in laboratory animals, most of the previously published data were limited to the study of only one of the possibly involved mechanisms, *i.e.*, variations in renal function, general hemodynamics, or hormonal secretions. As recently claimed by Berry,<sup>11</sup> the results obtained are often difficult to interpret and to compare, due to marked differences in study designs, particularly choice of patients or animals with various thoracopulmonary distensibility and cardiovascular status, level of PEEP employed, duration of CPPV and nature of drugs administered. We therefore measured in the same patients simultaneous hemodynamic, renal, and endocrine variables during short-term changes in their ventilatory status.

For the selection of our study group the positive inclusion criteria were normal cardiovascular and renal functions, without drug therapy likely to directly modify the activity of the studied hormonal systems. In addition, our patients were free from lung diseases known to alter lung distensibility, and received sedative and muscle relaxant drugs to attenuate eventual interindividual variations in their chest-wall compliance.

Our patients were suffering from head trauma of various degrees of seriousness, and coma itself could possibly modify the activity and/or the reactivity of the neuroendocrine system. We did find wide interindividual differences in the basal levels of the studied hormonal systems (see fig. 1). However all the measured variables changed in the same direction when PEEP was instituted, and changed again when PEEP was withdrawn. Thus, we assume that the physiologic reactions induced in our patients by changes in their ventilatory status were not affected strongly by variability in their neurologic status.

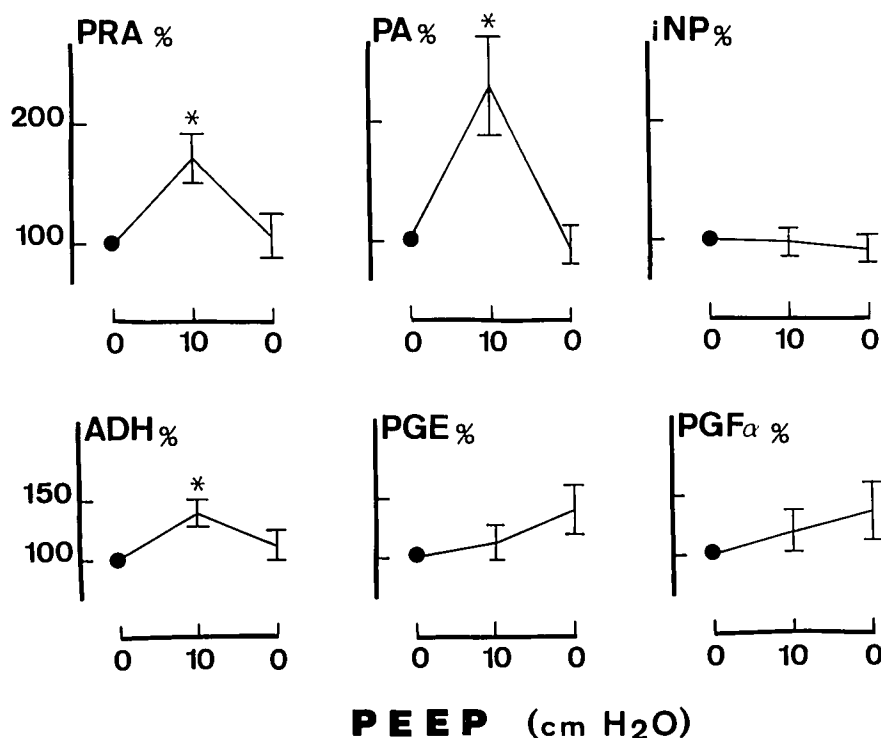
The decrease in CO which we measured during CPPV is a well-known effect of increased intrathoracic pressure. It is conventionally ascribed to impairment in venous return, leading to decreased preload for the

TABLE 3. Effect of CPPV on Some Plasma, Urinary, and Renal Parameters (Means  $\pm$  SE)

	IPPV <sub>1</sub>	CPPV	IPPV <sub>2</sub>
PaO <sub>2</sub> (mmHg)	108.00 $\pm$ 8.00	109.00 $\pm$ 9.00	109.00 $\pm$ 10.00
PaCO <sub>2</sub> (mmHg)	35.00 $\pm$ 3.00	33.00 $\pm$ 3.00	33.00 $\pm$ 4.00
Plasma			
Sodium (mmol/l)	142.00 $\pm$ 2.00	143.00 $\pm$ 2.00	142.00 $\pm$ 3.00
Potassium (mmol/l)	4.5 $\pm$ 0.2	4.5 $\pm$ 0.3	4.4 $\pm$ 0.3
Osmolality (mosm/kg)	279.00 $\pm$ 4.00	277.00 $\pm$ 5.00	280.00 $\pm$ 5.00
Urinary			
Output (ml/min)	2.75 $\pm$ 0.28	1.79 $\pm$ 0.18*	2.51 $\pm$ 0.21
Sodium (mmol/min)	165.00 $\pm$ 20.00	111.00 $\pm$ 22.00*	172.00 $\pm$ 26.00
Potassium (mmol/min)	125.00 $\pm$ 21.00	94.00 $\pm$ 17.00*	119.00 $\pm$ 19.00
Osmolality (mosm/kg)	706.00 $\pm$ 62.00	738.00 $\pm$ 65.00	731.00 $\pm$ 69.00
Glomerular filtration rate (ml/min)	164.00 $\pm$ 14.5	134.00 $\pm$ 10.00*	192.00 $\pm$ 18.4
Renal blood flow (ml/min)	1212.00 $\pm$ 73.00	935.00 $\pm$ 82.00*	1340.00 $\pm$ 115.00
Fe Na (%)	0.91 $\pm$ 0.2	0.67 $\pm$ 0.3	0.72 $\pm$ 0.3
Fe fH <sub>2</sub> O (%)	1.83 $\pm$ 0.7	2.02 $\pm$ 0.4	2.03 $\pm$ 0.1

\*  $P < 0.016$  by comparison with the corresponding IPPV<sub>1</sub> value.

FIG. 1. Effect of changes in PEEP level on PRA, PA, iNP, and urinary ADH, PGE, and PGF $\alpha$ . The results are expressed as percentages of values found after IPPV, which were as follows (means  $\pm$  SE): PRA =  $226 \pm 132$  pmol  $\cdot$  l $^{-1}$   $\cdot$  min $^{-1}$  (range 50.1–1,006); PA =  $371 \pm 122$  pmol/l (range 43–860); iNP =  $2 \pm 0.3$  ng/l (range 1–3); UADH =  $0.33 \pm 0.08$   $\mu$ U/ml GFR (range 0.15–0.76); UPGE =  $19.3 \pm 5.9$  ng/h (range 6.5–39); and UPGF $\alpha$  =  $121 \pm 46.6$  ng/h (range 52–300). \* $P < 0.016$ .



right ventricle. However, we did not observe a decrease in  $P_{TRA}$  as would be expected to occur in these conditions. But, as recently demonstrated by Skarvan *et al.*,<sup>12</sup> esophageal pressure probably underestimates pericardial pressure changes during PEEP ventilation. Other factors such as a restriction in left ventricular filling caused by a leftward displacement of the interventricular septum<sup>13</sup> also could participate in this PEEP-induced reduction of CO. Unlike CO, arterial pressure did not change during CPPV, thus indicating an appropriately enhanced peripheral vascular resistance during these circumstances.

In the present study, institution of 10 cmH<sub>2</sub>O PEEP for one hour led to a 34% decrease in urinary output, which is in agreement with observations made by others in patients undergoing comparable changes in their ventilatory status.<sup>1,2</sup> We also measured a consistent drop in RBF, GFR, and RBF/CO ratio. This strongly suggests onset of renal vasoconstriction during the application of PEEP, which probably was a major determinant in the antidiuretic effect observed. In favor of this hypothesis, Fewell *et al.*<sup>14</sup> demonstrated in the dog that complete renal denervation prevents the decrease in RBF, GFR, and urinary output induced by PEEP. In patients with acute respiratory failure sedated with diazepam and meperidine, Jarnberg *et al.*<sup>1</sup> measured a 12% decrease in RBF, but not in GFR during applica-

tion of PEEP. On the other hand, Kaukinen *et al.*<sup>2</sup> observed a consistent decrease in GFR in sedated and curarized patients requiring ventilatory support for various medical or surgical reasons. Unequal transmission of PEEP due to differences in lung or chest wall distensibility could, at least in part, account for these discrepancies.

We found urinary electrolyte excretion to be correlated with variations in urinary volume. In particular, FE Na did not change significantly during the application of PEEP, which is contrary to the increase in sodium tubular reabsorption reported by Jarnberg *et al.*<sup>1</sup> in similar conditions.

Besides hemodynamic impairment, CPPV leads to changes in the activity of different hormonal systems acting on the kidney. We evaluated neurohypophyseal reactivity by measuring urinary ADH and plasma neurophysins. The cumulative measurement of ADH in urine for a given time interval is a reliable index of ADH secretion, provided that eventual variations in renal function are taken into account.<sup>15,16</sup> This peptide is removed from plasma essentially by glomerular filtration,<sup>15</sup> and urinary ADH concentration is most often expressed in mU/mg of urinary creatinine. In our study, GFR was measured precisely by the calculation of inulin clearance, and it was more appropriate to express urinary ADH in mU/ml of glomerular filtration.

In these conditions, we observed a significant increase in urinary ADH during CPPV, which confirms the previously published studies in humans<sup>3</sup> and dogs.<sup>17</sup> Several authors failed to observe a corresponding change in free water clearance,<sup>1,2</sup> which led them to conclude that ADH probably did not play a primary role in the antidiuretic effect of PEEP. In our study, we found no significant variation in FE  $\text{H}_2\text{O}$ , a theoretically more reliable index of free water reabsorption, which confirms the results obtained by Jarnberg *et al.*<sup>1</sup> However, the significance of free water clearance as an index for the action of ADH in the collecting tubule is questionable in studies like ours where there are significant changes in renal hemodynamics. Otherwise, under these circumstances, it has been suggested that ADH acts rather as a vasoconstrictor than as an antidiuretic factor.<sup>18</sup> A number of mechanisms could be involved in the PEEP-induced elevation of the ADH levels<sup>17</sup>: decrease of thoracic blood volume acting via left atrial stretch receptors or via arterial baroreceptors, hypoxia, angiotensin release, raised plasma osmolality, and elevation of intracranial pressure. It is not possible to draw any conclusion from our results concerning these hypotheses. We only can observe that plasma osmolality and arterial pressure did not change, that hypoxia did not occur, and that no correlation was found between ADH and PRA levels.

Neurophysins are central nervous carriers of ADH and oxytocin. They have no biologic activity. There is now some evidence that neurophysins are released from neurosecretory granules together with these two hormones by exocytosis.<sup>19</sup> Therefore, the measurement of their plasma concentration, which is technically less complicated than that of the hormonal peptides has been proposed as an index for neurohypophyseal activity. In humans, under circumstances such as water load or nicotine injection, parallel variations of ADH and iNP have been demonstrated.<sup>19</sup> Our results are not conclusive in this respect since the iNP levels were not affected by the changes in ventilatory conditions, unlike urinary ADH. One possible explanation for this result may be related to the radioimmunoassay used here. This assay measures the total immunoreactive neurophysins and, thus, ADH-neurophysins and oxytocin-neurophysins cannot be measured separately. Therefore, subtle fluctuations in the ADH-neurophysins concentration may not be detected.

We found basal PRA levels to be inversely correlated to urinary sodium excretion. Thus, in spite of possible variability in neurologic status and sympathetic tone, our patients' renin secretion remained largely dependent on their sodium balance, as is usually observed in normal subjects.<sup>20</sup> In all of the patients, PRA levels increased after PEEP. This is in agreement with obser-

vations in the dog,<sup>17,21</sup> but is in contrast with those of Kaukinen *et al.*<sup>2</sup> who reported that PEEP did not alter PRA levels in his ventilated patients. The positive correlation that we calculated between PRA and PA indicates that the renin-angiotensin system plays a major role in the control of aldosterone secretion in these circumstances. An eventual PEEP-induced decrease in aldosterone metabolic clearance rate is certainly insufficient to account for the PA values reported here; in addition, we found no correlation between PA and plasma potassium. The renal sodium sparing effect of the RAAS was not apparent during our short-term experiment, but probably becomes significant during a long-term application of CPPV. Moreover, a direct vasoconstrictor effect of angiotensin on the kidney, whose vessels are extremely sensitive to this peptide cannot be excluded during the application of PEEP.

The stimulating effect of PEEP on the RAAS could be mediated by several mechanisms, mainly decreased renal perfusion pressure, changes in sodium delivery to the Macula Densa, or increased renal neural activity.<sup>20</sup> Whether one or more of these factors are brought into play cannot be stated with certainty. In the dog, Bark *et al.*<sup>17</sup> recently found that prior administration of propranolol completely blocked the elevation of PRA induced by PEEP, thus suggesting an important participation of a beta-adrenergic mechanism. In fact, a number of experiments in the dog have established the existence of a reflex control of renin release originating from atrial volume receptors, which are sensitive to changes in intrathoracic blood volume, such as those induced by CPPV.<sup>22,23</sup> Whether such a mechanism is present in humans remains to be proved.

To our knowledge, this is the first report of urinary  $\text{PG}_s$  during PEEP ventilation in humans. The urinary excretion of  $\text{PGE}$  and  $\text{PGF}\alpha$  is a reliable index for  $\text{PG}_s$  synthesis by the kidney.<sup>24</sup> The local actions of renal  $\text{PG}_s$  are particularly complex and are still not fully elucidated. They have been reported to antagonize the effect of ADH in the collecting tubule, to decrease urea reabsorption and salt transport, to increase medullary blood flow, and finally to modulate the renal vasoconstrictor effect of angiotensin.<sup>4</sup> It has been suggested recently by Epstein *et al.*<sup>25,26</sup> that the renal secretion of  $\text{PG}_s$  could be affected by changes of intrathoracic blood volume. Epstein has studied normal subjects undergoing water immersion to the neck, a stimulus known to induce a central blood volume expansion resulting in a diuretic and natriuretic response. After only one hour of immersion, a significant increase of urinary  $\text{PGE}$  excretion was observed, which was attenuated by indomethacin pretreatment. Since indomethacin also attenuated the natriuretic response of immersion in sodium-depleted subjects, it was suggested that renal  $\text{PGE}$  may participate

in the renal response observed. By comparison with water immersion, PEEP ventilation leads to an opposite redistribution of circulating blood volume, *i.e.*, a central hypovolemia, and to an opposite variation of urinary output *i.e.*, an antidiuresis. Therefore, we speculated that an opposite change might occur in the secretion rate of renal  $\text{PG}_s$ . However, no significant variations of urinary  $\text{PGE}$  and  $\text{PGF}\alpha$  were observed in our patients, suggesting little or no involvement of renal  $\text{PG}_s$  in the PEEP-induced impairment of renal function. To gain insight into this question it would be interesting, although ethically questionable, to observe the effects of blocking  $\text{PGs}$  synthesis with indomethacin in similar conditions.

In conclusion, the present data suggest that the short-term antidiuretic effect of PEEP is mainly due to a hemodynamic impairment of renal function. In addition, the water- and sodium-retaining hormonal systems, ADH and RAAS, are stimulated, and probably participate in the fluid retention observed during more prolonged respiratory support with PEEP.

The authors thank Prof. Bizollon, Prof. Legros, and Dr. Degueurce for their advice. They also thank the nursing staff of Prof. Motin Unit and Mrs. Sempore, Augoyard, Laurent, Gallo-Bona, and Seon for their excellent technical assistance.

## References

1. Jarnberg PO, Dominguez De Villota E, Eklund J, Granberg PO: Effects of positive end-expiratory pressure on renal function. *Acta Anaesthesiol Scand* 22:508-514, 1978
2. Kaukinen S, Eerola R: Positive end expiratory pressure ventilation, renal function and renin. *Ann Clin Res* 11:58-62, 1979
3. Hemmer M, Viquerat CE, Suter P, Vallotton MB: Urinary antidiuretic hormone excretion during mechanical ventilation and weaning in man. *ANESTHESIOLOGY* 52:395-400, 1980
4. Dunn M: Prostaglandins and the kidney. *Am J Physiol* 233:F169-F184, 1977
5. Pozet N, Hadj Aissa A, Pellet M, Traeger J: Activity of a new high efficiency diuretic in man: Piretanide (Hoe 118). *Br J Clin Pharmacol* 9:577-583, 1980
6. Sassard J, Vincent M: Comparaison des dosages radioimmunologique et biologique de l'activité rénine du plasma. *Clin Chim Acta* 41:321-327, 1972
7. Bizollon CA, Riviere JF, Franchimont P, Favre A, Claustrat B: A solid phase radioimmunoassay for plasma aldosterone. *Steroids* 23:809-821, 1974
8. Legros JJ, Franchimont P: Human neurophysine blood levels under normal, experimental and pathological conditions. *Clin Endocrinol* 1:99-133, 1972
9. Allevard AM, Geelen G, Sempore B, Zebidi A, Gharib C: Dosage radioimmunologique de l'ADH dans les urines chez l'Homme. *Ann Endocrinol (Paris)* 40:99-110, 1979
10. Benzoni D, Vincent M, Sassard J: Radioimmunoassay for urinary prostaglandins E and  $\text{F}\alpha$ : Normal values in different age groups. *Clin Chim Acta* 111:9-16, 1981
11. Berry AJ: Respiratory support and renal function. *ANESTHESIOLOGY* 55:655-667, 1981
12. Skarvan K, Hasse J, Wolff G: Myocardial transmural pressure in ventilated patients. *Intensive Care Med* 7:277-283, 1981
13. Jardin F, Farcot JC, Boissante L, Curien N, Margairaz A, Bourdarias JM: Influence of positive end-expiratory pressure on left ventricular performance. *N Engl J Med* 304:387-392, 1981
14. Fewell JE, Bond GC: Renal denervation eliminates the renal response to continuous positive pressure ventilation. *Proc Soc Exp Biol Med* 161:574-578, 1979
15. Shade RE, Share L: Renal vasopressin clearance with reductions in renal blood flow in the dog. *Am J Physiol* 232:F341-F347, 1977
16. Thibonnier M, Marchetti JP, Corvol P, Menard J, Milliez P: Advantages and drawbacks of AVP radioimmunoassay in plasma and urine in normal subjects. *Horm Metab Res* 13:300-301, 1981
17. Bark H, Le Roith D, Nyska M, Glick SM: Elevations in plasma ADH levels during PEEP ventilation in the dog: mechanisms involved. *Am J Physiol* 239:E474-E481, 1980
18. Hall SV, Steinman TJ: Alterations in renal function during acute respiratory failure. *Int Anesthesiol Clin* 14:179-213, 1976
19. Legros JJ: Les neurophysines. *Ann Endocrinol (Paris)* 39:319-339, 1978
20. Davis JO: Control of renin release. *Am J Physiol* 55:333-350, 1973
21. Ziegler M, Janzik W, Miksche L, Möhring H, Weigand W, Gross F: Effects of positive and negative pressure breathing on plasma renin concentration in the dog. *Pfluegers Arch* 348:185-196, 1974
22. Brennan LA, Malvin RL, Jochim KE, Roberts DE: Influence of right and left atrial receptors on plasma concentrations of ADH and renin. *Am J Physiol* 221:273-278, 1971
23. Annat G, Grandjean B, Vincent M, Jarsaillon E, Sassard J: Effect of right atrial stretch on plasma renin activity. *Arch Int Physiol Biochim* 84:311-315, 1976
24. Frolich JC, Wilson TW, Sweetman BF, et al: Urinary prostaglandins: Identification and origin. *J Clin Invest* 55:763-770, 1975
25. Epstein M, Lifschitz MD, Hoffman DS, Stein JH: Relationship between renal prostaglandin E and renal sodium handling during water immersion in normal man. *Circ Res* 45:71-80, 1979
26. Epstein M, Lifschitz R, Haber E: Dissociation of renin-aldosterone and renal prostaglandin E during volume expansion induced by immersion in normal man. *Clin Sci* 59:55-62, 1980