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Effects of Expiratory Positive Airway Pressure vs Continuous Positive Airway Pressure in Conscious, Spontaneously Breathing Dogs[1–3] (41305)

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Abstract. The purpose of this study was to compare the cardiopulmonary effects of expiratory positive airway pressure (EPAP) and continuous positive airway pressure (CPAP) in conscious, spontaneously breathing dogs. Nine conscious dogs with electromagnetic flow probes on their pulmonary arteries, catheters in their left atria and pulmonary arteries, and chronic tracheostomies, stood partially supported by slings, and breathed 100% oxygen through endotracheal tubes, pneumotachographs, and nonrebreathing valves which were part of either an EPAP or CPAP system. The effects of EPAP only were studied on four dogs while five were exposed to both EPAP and CPAP. After a 20-min control period, they breathed through either the EPAP or CPAP system for 10 min each under 5-, 10-, 15-, and 20-cm H_2O airway pressure. The mean pulmonary artery pressure, mean left atrial pressure, pulmonary vascular resistance, and minute ventilation were found to be significantly higher in the CPAP-treated group. Stroke volume and cardiac output were significantly higher in the EPAP-treated group. Both groups showed a significant carbon dioxide retention.

Positive end-expiratory pressure, in conjunction with mechanical ventilation, is often used in the treatment of patients with pulmonary edema and adult respiratory distress syndrome. One potential disadvantage of this therapy is a decrease in cardiac output (1–3).

This study was done to determine if decreases in cardiac output accompany positive airway pressure breathing in normal awake spontaneously breathing dogs. Two different modes of therapy were used in comparing the effects on cardiac output. Since there is no generally accepted terminology for the various treatment modalities utilizing positive airway pressure ventilation, we have adopted Grenvik's (4) terminology in this study. EPAP is defined as expiratory positive airway pressure when the individual is breathing spontaneously. CPAP is defined as continuous positive airway pressure during spontaneous breathing. Therefore, this study compared the cardiopulmonary effects of EPAP and CPAP in healthy, awake, mongrel dogs. The effects of EPAP and CPAP on cardiovascular parameters in animals have never been compared to our knowledge. Gherini (15) compared the effects of CPAP and EPAP on the work of breathing and functional residual capacity in humans, but not the cardiovascular effects.

Materials and Methods. Nine heartworm-free mongrel dogs, weighing between 15.2 and 23.3 kg (average weight 18.3 kg) were anesthetized with intravenous sodium pentobarbital (30 mg/kg). The surgical techniques employed were a modification of those previously described (5). A left thoracotomy was performed via the fourth intercostal space for placement of noncannulating electromagnetic flow probes (Biotronex type 5000) on the main pulmonary artery. At this time, a Silastic cath-

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eter was placed into the left atrial appendage. A chest tube was inserted and was used to reestablish expansion of the lung upon closure of the surgical wound.

After approximately one week of recovery, a second surgical procedure was performed. The dogs were premedicated with atropine (0.4 mg intraatrially) and anesthetized with sodium methohexital (3 to 4 mg/kg intraatrially). A chronic tracheostomy was performed and a large-bore Silastic catheter (0.132-in. i.d. × 0.183-in. o.d.) was placed into the right external jugular vein. After surgery the dogs were trained to stand partially supported by slings and breathe through endotracheal tubes inserted into their tracheostomies.

During the experiments, the main pulmonary artery blood flows were obtained using a Biotronex Model 613 EZ flow meter. Mean flows were used to determine cardiac output (CO). The left atrial catheter was connected to a Statham blood pressure transducer for monitoring mean left atrial pressure (MLAP). A Swan-Ganz catheter was inserted into the pulmonary artery via the right external jugular Silastic catheter. The Swan-Ganz catheter was connected to a Statham blood pressure transducer for monitoring mean pulmonary artery pressure (MPAP). The transducers were calibrated prior to the experiment with a mercury manometer and zero pressure was referenced to the level of the left atrium. Air flow was measured by using a pneumotachograph (size 0) connected to an endotracheal tube and a Statham Model PM 15E differential air pressure transducer. A needle was inserted into the endotracheal tube and connected via iv tubing to a Statham blood pressure transducer for monitoring airway pressure. The outputs of the three Statham blood pressure transducers, differential air pressure transducer, and the main pulmonary artery blood flow transducer were recorded continuously on an eight-channel Beckman Dynagraph.

The EPAP system utilized a Rudolph nonrebreathing valve. The inhalation port of the Rudolph valve was connected to a 5-liter reservoir bag which received a continuous oxygen supply. The exhalation port of the Rudolph valve was connected to wide-bore tubing which was submerged under water to produce expiratory positive airway pressure. The breathing port of the Rudolph valve was connected to the pneumotachograph and endotracheal tube of the dog.

The CPAP system utilized two Hudson nonrebreathing valves, one on the inspiratory limb and one on the expiratory limb. A gauge was used to measure pressure and a 5-liter reservoir bag, located on the inspiratory limb, was connected to the source of oxygen and the bag was kept distended to generate inspiratory positive airway pressure. The inspiratory valve was located between the reservoir bag and a T tube which was connected to a pneumotachograph and endotracheal tube of the dog. The expiratory valve was located between the T tube and a wide-bore tubing which was submerged under water to produce expiratory positive airway pressure.

The dogs first breathed 100% oxygen for 20 min through either the EPAP or CPAP system; this served as the control period and was termed 0 cm H_2O EPAP or CPAP. Following this, the dogs breathed through either of the systems for 10 min each under 5, 10, 15, and 20 cm H_2O EPAP or CPAP. This order was varied in several experiments to rule out the effects of fatigue. Then the dogs breathed for 10 min at 0 cm H_2O EPAP or CPAP. At the end of each period, MPAP, MLAP, cardiac output (CO), pulmonary vascular resistance (PVR), arterial and mixed venous blood gases, and ventilatory parameters were determined.

Blood gases were analyzed at 37° using standard electrodes. Pulmonary vascular resistance was calculated using the equation: $PVR = P_1 - P_2/CO$. P_1 was MPAP. P_2 was the greater of either MLAP or end-expiratory pressure. End-expiratory pressure was used when it was greater than MLAP because "waterfall" conditions were assumed to exist at those times (6). Tidal volume (V_T) was calculated by determining the area under the air flow curves with a planimeter. This included mechanical dead space, which was identical for both

systems. Minute ventilation ($\dot{V}_E$) was calculated by multiplying V_T by ventilatory frequency.

The electromagnetic flow probes were calibrated *in vitro* using whole blood which flowed by gravity from an elevated reservoir through freshly excised sections of blood vessels similar to those used in the experiments. While a period of flow was timed, a measured volume of one liter of blood was allowed to flow through the vessels. Each flow probe was subjected to three calibration runs. The results of this method of determining CO compares favorably with the results of the dye dilution cardiac output determination method (7).

The results are expressed as the mean ± the standard error of the mean. Data within each group were tested for significance by analysis of variance: single classification data and a *t* test. Comparison of data between EPAP and CPAP were tested for significance by analysis of variance: single classification data with subgroups and a *t* test (8). Values of $P < 0.05$ were considered significant.

Fourteen CPAP experiments were performed on five dogs and sixteen EPAP experiments were performed on nine dogs. Each experiment consisted of two periods of O PAP and one period of 5-, 10-, 15-, and 20-cm H_2O PAP. The order of exposure to the different PAPs was changed in some of the experiments. One dog in the EPAP group developed a clot in the right external jugular catheter and it was not possible to measure MPAP, PVR, and mixed venous blood gases on this animal. Five dogs participated in both groups. Their results followed the general trend in each of the two groups of experiments.

Results. *EPAP.* Table 1 shows the data collected in the EPAP-treated dogs. There were no significant differences at any level of EPAP in PVR, CO, stroke volume (SV), heart rate, P_aO_2, mixed venous oxygen tension (P_vO_2), $\dot{V}_E$, V_T, and ventilatory frequency.

MPAP increased significantly at 10, 15, and 20 cm H_2O EPAP. The MLAP also increased significantly at every level of EPAP equal to or greater than 10 cm H_2O EPAP.

Arterial carbon dioxide tension (P_aCO_2) tended to increase at each level of EPAP and was increased significantly at 20 cm H_2O EPAP. It is interesting to note that the ventilatory parameters, $\dot{V}_E$, V_T, and ventilatory frequency did not increase significantly despite this increase in P_aCO_2. The mixed venous carbon dioxide tension (P_vCO_2) was significantly elevated at 15 and 20 cm H_2O EPAP.

The arterial pH (pH_a) decreased significantly at 15 and 20 cm H_2O EPAP. There was a significant decrease in the venous pH (pH_v) at 10, 15, and 20 cm H_2O EPAP.

CPAP. The results of the CPAP experiments are depicted in Table 2. There were no statistical differences at any level of CPAP in heart rate, P_aO_2, P_vO_2, pH_a, or in ventilatory frequency.

The MPAP increased in direct proportion to increases in CPAP, and was significantly increased at 5, 10, 15, and 20 cm H_2O CPAP. The MLAP also was significantly increased at all levels of CPAP. There was a significant increase in PVR at 10, 15, and 20 cm H_2O CPAP.

There was a significant decrease in CO at levels of CPAP equal to or greater than 10 cm H_2O CPAP (Fig. 1). This decrease in CO was accompanied by a significant decrease in SV at 15 and 20 cm H_2O CPAP.

P_aCO_2, P_vCO_2, and pH_v were significantly elevated at 20 cm H_2O CPAP. There was a significant increase in $\dot{V}_E$ at 10 and 20 cm H_2O CPAP. The V_T was increased significantly at each and every level of CPAP when compared to control.

EPAP vs CPAP. The MPAP was significantly greater in the CPAP group at 10, 15, and 20 cm H_2O of positive airway pressure breathing when compared with the EPAP group.

In comparing the EPAP and CPAP groups, the MLAP was significantly greater in the CPAP group at all levels of positive airway pressure. The CPAP group had a significantly higher PVR than did the EPAP group at 10, 15, and 20 cm H_2O.

The CO was significantly lower in the CPAP group at 10, 15, and 20 cm H_2O pressure when compared with the EPAP group (Fig. 1). The CPAP group had a signifi-

TABLE I. THE CARDIOVASCULAR EFFECTS OF EPAP

	0 cm H_2O	5 cm H_2O	10 cm H_2O	15 cm H_2O	20 cm H_2O	0 cm H_2O
MPAP (Torr)	12.2 ± 0.8	14.8 ± 1.0	17.2 ± 0.7**	19.1 ± 0.9**	23.2 ± 1.2**	13.0 ± 0.9
MLAP (Torr)	2.3 ± 0.5	3.6 ± 0.5	4.4 ± 0.6**	5.3 ± 0.8**	7.7 ± 0.8**	1.5 ± 0.4
PVR (Torr/ml/min)	0.0038 ±0.0004	0.0047 ±0.0006	0.0053 ±0.0006	0.0064 ±0.0007	0.0059 ±0.0006	0.0045 ±0.0005
CO (ml/min)	2530 ± 148	2536 ± 126	2491 ± 184	2504 ± 141	2264 ± 132	2493 ± 152
SV (ml)	25.0 ± 2.9	23.9 ± 2.0	23.6 ± 2.1	22.4 ± 1.9	19.5 ± 1.7	24.0 ± 2.5
Heart rate (beats/min)	115.5 ± 8.7	115.2 ± 8.7	111.1 ± 7.6	118.4 ± 8.7	122.8 ± 6.8	113.9 ± 7.9
P_aO_2 (Torr)	460.6 ± 17.9	445.9 ± 10.4	432.8 ± 12.9	443.8 ± 9.3	446.3 ± 11.2	452.2 ± 15.7
P_vO_2 (Torr)	42.5 ± 1.5	40.4 ± 1.8	40.2 ± 1.4	40.3 ± 1.7	41.7 ± 1.5	39.5 ± 1.7
P_aCO_2 (Torr)	31.9 ± 0.9	32.7 ± 0.8	33.4 ± 1.0	34.4 ± 0.8	37.2 ± 1.1**	31.3 ± 0.8
P_vCO_2 (Torr)	38.0 ± 0.9	38.7 ± 0.9	39.8 ± 1.1	41.0 ± 1.0*	43.6 ± 1.2**	38.3 ± 1.1
pH_a	7.42 ± 0.01	7.41 ± 0.01	7.41 ± 0.01	7.39 ± 0.01*	7.37 ± 0.01**	7.43 ± 0.01
pH_v	7.37 ± 0.01	7.35 ± 0.01	7.34 ± 0.01*	7.33 ± 0.01**	7.31 ± 0.01**	7.36 ± 0.02
$\dot{V}_E$ (ml/min)	5478 ± 606	5595.4 ± 461	5609.7 ± 515	5429.2 ± 490	4750 ± 717	5951.4 ± 529
V_T (ml)	249 ± 21	277 ± 28	271 ± 22	277 ± 21	250 ± 19	218 ± 16
Vent. rate	22.0 ± 1.7	20.2 ± 1.3	20.7 ± 1.8	19.6 ± 1.4	19.0 ± 2.2	27.3 ± 3.4
$\overline{AirP}$	0	2.2 ± 0.3**	3.0 ± 0.5**	4.5 ± 0.8**	6.4 ± 0.8**	0

Note. Mean values ± SEM. MPAP (mean pulmonary artery pressure), MLAP (mean left atrial pressure), PVR (pulmonary vascular resistance), CO (cardiac output), SV (stroke volume), $\dot{V}_E$ (minute ventilation), V_T (tidal volume), $\overline{AirP}$ (mean airway pressure).

* Significantly different from control ($P < 0.05$).

** Significantly different from control ($P < 0.01$).

cantly higher $\dot{V}_E$ when compared with the EPAP group.

Discussion. In this study we have demonstrated that there are differences in the cardiopulmonary effects of the two different modes of positive airway pressure in conscious spontaneously breathing dogs. CPAP elevated the MPAP, MLAP, PVR, and $\dot{V}_E$ to a greater extent than did EPAP. The cardiac output and stroke volume were maintained with EPAP but decreased with CPAP. The reported heart rate, SV, CO, and P_aCO_2 during the control period compare favorably with those reported by Kontos *et al.* (13) in the awake dog. The other parameters in the control period are similar to those reported by Levitzky (5).

Our determination of MPAP and MLAP were referenced to atmospheric pressure. Our attempts to measure intrapleural pressure in this preparation failed. We did not monitor esophageal pressure since the awake dog would not have tolerated the presence of an esophageal monitoring device. We hoped to monitor intrapleural pressure via the chest tube but we were unable to obtain data consistently.

Airway pressures were negative during inspiration in the EPAP group; the airway pressures were always positive in the CPAP group. The dogs treated with EPAP had to generate negative airway pressure in order to open the valve during inspiration. Therefore, in EPAP the intrapleural pressure during inspiration is assumed to be as negative or more negative than that which would be generated with spontaneous quiet breathing. Mean airway pressures were less positive during EPAP than CPAP at corresponding levels as would be expected.

The increase in MPAP in both groups was probably due to mechanical factors. The positive pressure in the airway was transmitted to the tracheobronchial tree, to the alveoli, and to the intrapleural space. The increased pressure in the alveoli compressed (9) the alveolar vessels and, at the same time, there was a compression of the

TABLE II. THE CARDIOVASCULAR EFFECTS OF CPAP

	0 cm H_2O	5 cm H_2O	10 cm H_2O	15 cm H_2O	20 cm H_2O	0 cm H_2O
MPAP (Torr)	13.4 ± 1.0	18.1 ± 1.4**	19.9 ± 0.5**	26.5 ± 1.4**	30.5 ± 0.8**	12.5 ± 0.8
MLAP (Torr)	3.4 ± 0.4	5.2 ± 0.4**	6.9 ± 0.5**	9.1 ± 0.4**	10.5 ± 0.5**	2.6 ± 0.4
PVR (Torr/ml/min)	0.0044 ±0.0005	0.0058 ±0.0006	0.0074** ±0.0008	0.0108** ±0.0011	0.0141** ±0.0011	0.0053 ±0.0005
CO (ml/min)	2388 ± 140	2237 ± 222	1911 ± 133*	1797 ± 184**	1562 ± 110**	1975 ± 112
SV (ml)	21.4 ± 2.1	19.9 ± 2.0	17.6 ± 1.9	15.4 ± 1.6*	13.3 ± 1.4**	19.6 ± 2.0
Heart rate (beats/min)	119.2 ± 8.4	117.3 ± 8.5	117.6 ± 9.3	122.4 ± 9.8	126.4 ± 8.4	109.9 ± 9.4
P_aO_2 (Torr)	447.5 ± 11.1	453.9 ± 12.1	434.6 ± 8.7	427.1 ± 7.0	439.3 ± 12.1	425.7 ± 8.0
$P_{\bar{v}}O_2$ (Torr)	39.9 ± 1.8	38.4 ± 1.8	38.7 ± 1.8	38.5 ± 1.6	37.7 ± 1.5	39.9 ± 1.6
P_aCO_2 (Torr)	32.1 ± 0.7	31.3 ± 0.5	32.0 ± 0.6	33.6 ± 0.8	34.7 ± 0.9**	29.7 ± 0.6*
$P_{\bar{v}}CO_2$ (Torr)	40.2 ± 0.8	39.0 ± 1.1	40.1 ± 0.9	42.5 ± 1.1	44.4 ± 0.8**	39.0 ± 0.9
pH_a	7.43 ± 0.02	7.43 ± 0.02	7.43 ± 0.01	7.41 ± 0.02	7.38 ± 0.02	7.43 ± 0.02
$pH_{\bar{v}}$	7.35 ± 0.01	7.36 ± 0.01	7.36 ± 0.01	7.33 ± 0.01	7.31 ± 0.01**	7.35 ± 0.01
V_E (ml/min)	6652.1 ± 304	7913.2 ± 480	8006.9 ± 589*	7669.2 ± 592	8872.3 ± 929**	6880.4 ± 436
V_T (ml)	221 ± 12	271 ± 22*	319 ± 18**	308 ± 15**	307 ± 15**	206 ± 13
Vent. rate	30.1 ± 2.5	29.2 ± 3.1	25.1 ± 2.1	24.9 ± 1.9**	28.9 ± 2.7	33.4 ± 3.7
$\overline{\text{Air P}}$	0	3.5 ± 0.4**	8 ± 0.5**	12.5 ± 0.4**	16.5 ± 0.5**	0

Note. Mean values ± SEM. MPAP (mean pulmonary artery pressure), MLAP (mean left atrial pressure), PVR (pulmonary vascular resistance), CO (cardiac output), SV (stroke volume), V_E (minute ventilation), V_T (tidal volume), $\overline{\text{Air P}}$ (mean airway pressure).

* Significantly different from control ($P < 0.05$).

** Significantly different from control ($P < 0.01$).

extraalveolar vessels exposed to positive intrapleural pressure: during expiration with EPAP; at all times with CPAP.

The increase in MLAP seen in both the CPAP- and EPAP-treated groups also was due in part to mechanical compression of the left atrium by the increased intrathoracic pressure. The increase in MLAP could also reflect left ventricular depression (10).

The increase in PVR in the CPAP-treated group was due in part to mechanical compression of the alveolar vessels. As the cardiac output decreased, there was also probably a derecruitment of pulmonary vessels which could increase PVR.

Most studies of positive airway pressure with mechanical ventilation have shown a decrease in cardiac output (10–12). Various reasons have been given as to the cause of the decreased cardiac output, including the release of a negative inotropic agent (11) and right ventricular enlargement interfering with left ventricular filling (10). Cournand (3) speculated that a decreased venous return may act to decrease cardiac output. Since our dogs generated negative inspiratory pressure during EPAP, they must have generated negative intrapleural pressure which would tend to augment venous return. There was no significant change in CO at any level of EPAP employed in this experiment. Thus, it is possible that CO was maintained in the EPAP group because of a relatively uncompromised venous return. There was a significant decrease in CO and SV with increased levels of CPAP in this study. With CPAP, during both inspiration and expiration, there was positive airway pressure which must have reflected positive intrapleural pressure which may have decreased venous return. However, the mechanism causing the differences in CO during equal levels of CPAP and EPAP were not revealed by this study.

Berryhill and Benumof (14) reported an increase in end tidal CO_2 during spontaneous ventilation with PEEP. In the present

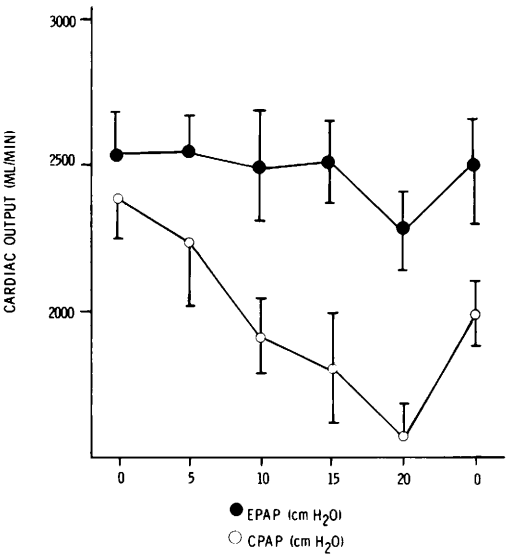

FIG. 1. Changes (mean ± SEM) in cardiac output with increasing positive airway pressure breathing. There was no significant difference in cardiac output at any level of EPAP (n = 16). The cardiac output decreased significantly in the CPAP group at 10, 15, and 20 cm H_2O CPAP (n = 14). The CPAP group had a significantly lower cardiac output at 10, 15, and 20 cm H_2O airway pressure when compared to the EPAP group.

study, P_aCO_2 increased steadily with increased EPAP. It has been reported by Gherini *et al.* (15) that there is a significant increase in the work of breathing with EPAP. Gherini also found that functional residual capacity did not increase with PEEP but rose in proportion to the level of CPAP. In the present study, this increase in the expiratory work of breathing with EPAP was indicated by increased expiratory efforts. Although elevated P_aCO_2 would be expected to increase minute ventilation, there was no increase in $\dot{V}_E$ at any level of EPAP. The increased P_aCO_2 with unchanged $\dot{V}_E$ may be due to an increase in $\dot{V}_{CO_2}$ from increased respiratory efforts or an increase in physiological deadspace.

The elevated resistance to breathing is also reflected in the finding that these dogs displayed brief pauses in respiration for increased periods of time with increased EPAP. For example, at 20 cm H_2O EPAP, the dogs became apneic for about one minute at the beginning of breathing against the pressure. No other periods of apnea were noted after this initial episode at each level of elevated airway pressure. Other investigators report similar apneic periods (16) or reduced respiratory drive (17) with positive end-expiratory pressure. It is also possible that the Hering–Breuer inflation reflex played some role in the elevated P_aCO_2, since an increase in functional residual capacity has been reported with positive end-expiratory pressure (1). This reflex may be overriding the CO_2 drive to ventilation and in so doing it may bring about CO_2 retention. Either this or some other unexplained mechanism was responsible for the lack of an adequate response by the chemoreceptors or central controller to an elevated P_aCO_2.

Although there was an increase in P_aCO_2 in the CPAP-treated group, it appears that the response was different. The P_aCO_2 was essentially unchanged at 10 cm H_2O CPAP, but $\dot{V}_E$ increased. There is also an increase in the work of breathing with CPAP when compared to normal breathing (15). The apnea that occurred at the beginning of each change in CPAP did not appear to be quite as long as the apnea associated with EPAP. However, with 20 cm H_2O CPAP there was an increase in P_aCO_2 despite an increase in $\dot{V}_E$ and V_T. This compared with 20 cm H_2O EPAP where there was an increase in P_aCO_2 and no change in $\dot{V}_E$ and V_T. Thus, it appears that the CPAP-treated dogs were able to partially respond to increased P_aCO_2 and thereby increased $\dot{V}_E$.

In conclusion, this study demonstrates several different effects on cardiopulmonary dynamics when CPAP is compared with EPAP. Even though both groups had elevated MPAP and MLAP with increased airway pressure, the increase was greater in the CPAP group. Only the CPAP group had a significantly elevated PVR with increased airway pressure. The stroke volume and cardiac output were decreased in the CPAP-treated group but there was no significant difference in the EPAP group. The increase in P_aCO_2 was greater in the EPAP group and this elevated P_aCO_2 apparently did not stimulate the chemoreceptors to in-

crease minute ventilation. The CPAP group responded to the elevated P_aCO_2 with an increase in minute ventilation and tidal volume. Since CPAP is widely used clinically and there is some interest in using EPAP clinically (18), these differences should be considered in choosing the mode of therapy to be employed on a particular patient.

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