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Intracranial Responses to PEEP

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Elevated intrathoracic pressure due to positive end-expiratory pressure (PEEP) has the potential for increasing intracranial pressure (ICP) and reducing arterial blood pressure (BP). Such changes could critically reduce cerebral perfusion pressure (CPP = BP − ICP). This possibility was investigated in 15 cats with artificially-produced expanding intracranial masses (intracranial balloon). The interrelationships among ICP and central venous and arterial pressures were observed during application and removal of graded levels of PEEP (5, 10, 15 cm H_2O). The electroencephalogram and pupillary diameters were monitored. At various levels of ICP, nine of the cats were given oleic acid intravenously to embolize the lung and cause pulmonary dysfunction.

In cats not given oleic acid, PEEP caused a maximal reduction in cerebral perfusion pressure of 45 ± 4 torr (SEM), accompanied by variable changes in ICP. PEEP application in the absence of oleic acid embolization of the lungs caused electroencephalographic abnormalities in 77 per cent of these cats, while pupillary diameters increased in 56 per cent. Animals embolized with oleic acid had significantly less ($P < .001$) severe CPP reductions (mean 21 ± 4 torr) than did the non-embolized animals, and developed no EEG change due to PEEP. However, increases in pupillary diameter still occurred in 33 per cent of cats given oleic acid when PEEP was applied.

In 82 per cent of the PEEP applications (n = 44) in both experimental groups only insignificant increases in intracranial tension occurred (average peak ICP gain < 1.5 torr). Abrupt increases in ICP exceeding 11 torr (15 cm H_2O) occurred in four animals in each group. This happened most frequently (63 per cent) when the intracranial tension before PEEP was above 15 torr. Sudden removal of or reduction in PEEP was accompanied by increases in arterial and intracranial pressures in both groups, although this response was attenuated in the cats given oleic acid.

The results indicate a potential for PEEP to evoke neurologic complications in patients who have intracranial disease and that the presence of pulmonary disease may attenuate these deleterious side effects. Monitoring of neurologic function as well as blood-gas and cardiovascular effects of PEEP in patients who have intracranial disease is suggested. (Key words: Brain, intracranial pressure: Ventilation, positive end-expiratory pressure.)

POSITIVE END-EXPIRATORY PRESSURE (PEEP) impedes thoracic venous flow and may increase cerebral venous and intracranial pressures (ICP).[1] While improving arterial oxygenation, PEEP can also reduce cardiac output and blood pressure (BP).[2] These side effects of PEEP (BP and/or ICP changes) could potentially summate to produce critical reductions in cerebral perfusion pressure (CPP = BP − ICP).

Our observations in neurosurgical patients revealed highly variable clinical responses to PEEP and other respiratory care maneuvers elevating intrathoracic tension.[1] In a minority of cases, PEEP treatments have initiated episodes of intracranial hypertension and/or changes in neurologic function. In some patients, PEEP treatments appeared to precipi-

ABBREVIATIONS

BP = arterial pressure
CPP = cerebral perfusion pressure (BP-ICP)
CVP = central venous pressure
EEG = electroencephalogram
ICP = intracranial pressure
PEEP = positive end-expiratory pressure

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tate neurologic deterioration without inducing increases in ICP. The initial clinical manifestations of intracranial responses due to PEEP in individual patients were difficult to predict. The variability of these side effects of PEEP in the clinical setting led to the present experiment, wherein the effects of PEEP on cardiovascular and intracranial responses were examined in cats with induced intracranial mass lesions with or without acute pulmonary dysfunction caused by oleic acid embolization.

Methods

General Preparation

Fifteen cats (3.0 to 3.5 kg) were anesthetized with pentobarbital (30 mg/kg, ip) and tracheostomies performed. Catheters for pressure measurement, blood-gas sampling, and fluid infusion were threaded via the femoral vessels into the descending thoracic aorta and inferior vena cava. Catheters were also inserted into the tracheal tube for airway pressure measurement and sampling of end-tidal CO_2 by a Godart capnograph. Vascular and airway pressures were measured with Statham model P23Db transducers, and all pressure transducers were zeroed to heart level to permit computation of CPP from a common reference point. Mean pressures were obtained intermittently by electrical integration, or calculated by adding a third of the systolic–diastolic difference to the diastolic pressure.

ICP Measurement—Control and Electroencephalography

The cat's head was positioned in a holder with the dorsum of the cranial vault 15 cm above heart level. This was done to compensate partially for the hydrostatic pressure head developed by the maximal experimental PEEP level of 15 cm H_2O. An intracranial epidural pressure-recording balloon (volume < 0.2 ml) and an expansion balloon (variable volume) were positioned on opposite sides of midline, just caudad to the coronal suture, through bilateral trephinations (12 mm diameter). The cranial vault was then reconstructed with a rapidly-curing methyl methacrylate polymer. Only observations from animals with intracranial balloons certified leak-proof after termination of the experiment are included in this report.

The volume of the intracranial expansion balloon was increased by progressive additions of approximately 0.1 ml of saline solution and adjusted to produce ICP levels about 5 torr apart within each animal. When a stable ICP was attained (baseline drift < 2 torr/5 min) each progressively higher ICP, PEEP was sequentially applied in 5-cm H_2O increments to 15 cm H_2O. This was followed by PEEP reductions to 10 and 0 cm H_2O. All observations, including assessment of pupillary diameter, were continued at each PEEP for 5 minutes. Recovery observations were made during a 10-minute period following completion of a PEEP run. This cycle was then repeated following ICP stabilization at a higher level.

Few animals could be stabilized at ICP levels above 10–15 torr without developing a unilateral fixed–dilated pupil, usually ipsilateral to the expanding balloon. Pupillary and EEG changes directly consequent to balloon inflation and occurring prior to PEEP application were not considered to be caused by PEEP within the context of our experiment. When both pupillary dilation and EEG changes were irreversible during the 10-minute recovery interval the experiment was terminated. The times from onset of balloon inflation to termination of data collection ranged from 3 to 4 hours.

The electroencephalogram (EEG) was recorded from two epidurally situated brass electrodes placed at the anterior–lateral margins of the trephinations. EEG recordings were made at a gain of 50 microvolts/7.5 mm and usually recorded at a speed of 0.4 mm/sec. Faster recordings were occasionally obtained to improve time resolution of the EEG tracing.

Production of PEEP and Oleic Acid Embolization

Following intravenous administration of gallamine (10 mg/kg, and then 20 mg, *p.r.n.*) ventilation was maintained with a constant-volume respirator (Harvard dual-phase) at 15 cycles/min. The tidal volume was adjusted to produce a steady expiratory phase stream of bubbles from the opening of the exhalation hose of the ventilator situated at a depth of

15 cm H_2O. Different PEEP levels (5, 10, 15 cm H_2O) were obtained by positioning the exhalation hose at the appropriate level below the water surface. Variable amounts of carbon dioxide were added to the inspiratory gases to obtain constancy of Pa_{CO_2} throughout the experiment. Arterial blood gases and pH during each pre-PEEP control period were determined. Pa_{O_2} and Pa_{CO_2} were subsequently determined at 10, 15, and 10 cm H_2O PEEP. In all animals $F_{I_{O_2}}$ was always more than 95 per cent.

In nine cats, following variable adjustments in intracranial tension, oleic acid (U.S.P.) in a dose of 0.15 ml/kg was administered intravenously. Three of these cats had one PEEP cycle, at variable intracranial tensions, prior to embolization of their lungs with oleic acid. All cats given oleic acid rapidly developed a pink, frothy pulmonary exudate and cardiovascular instability. Dextran 40 with dextrose 5 per cent, saline solution, and small doses of bicarbonate (1 mEq/kg) were given to support the blood pressure. When an embolized animal could not survive an entire range of PEEP application due to irreversible shock, the data from that PEEP run were not included in our analysis. Under these conditions the number of completed PEEP cycles in oleic acid-embolized cats was 18. Twenty-six PEEP runs were accomplished in non-embolized animals before a fixed–dilated pupil and non-reversible EEG changes developed. Unpaired t tests were employed in the statistical comparisons between the non-embolized and oleic acid-embolized groups. Significant differences were considered to be present when $P < .05$.

Results

Airway Pressure, Arterial Oxygenation and Acid–Base Changes

Prior to PEEP, peak airway pressure was significantly higher ($P < .001$) in the embolized cats (table 1). As PEEP was increased to 10 and 15 cm H_2O, peak airway pressures in the non-embolized and embolized cats increased as indicated in table 1. However, the peak airway pressures at these higher PEEP levels were not significantly different between the two experimental groups.

TABLE 1. Peak Airway Pressures and Arterial Blood Gases before and after PEEP in Non-embolized and Oleic Acid-embolized Cats Ventilated with More Than 95 Per Cent O_2*

	Control				PEEP 5 cm H_2O	PEEP 10 cm H_2O				PEEP 15 cm H_2O			
	P_{aw} (mm)	pH_a	Pa_{O_2} (mm)	Pa_{CO_2} (mm)	P_{aw} (mm)	P_{aw} (mm)	Pa_{O_2} (mm)	Pa_{CO_2} (mm)		P_{aw} (mm)	Pa_{O_2} (mm)	Pa_{CO_2} (mm)	
Non-embolized cats (±1 SEM)	11.8 ± 0.6	7.43 ± .02	367 ± 14.9	26.3 ± 1.5	16.7 ± 0.8	31.0 ± 2.1	37.4 ± 14.0	29.9 ± 1.84		40.2 ± 2.3	358 ± 11.1	28.3 ± 1.18	
Embolized cats (±1 SEM)	18.6 ± 0.9	7.31 ± .02	146 ± 17.5	30.7 ± 1.6	20.7 ± 1.0	31.2 ± 1.7	349 ± 18.6	26.0 ± 1.43		43.2 ± 2.1	368 ± 1.99	28.0 ± 1.85	
Significance (P value)	<.001	<.001	<.001	NS	<.01	NS	NS	NS		NS	NS	NS	

* Mean (±1 SEM) peak airway pressures (P_{aw}), pH_a, and Pa_{CO_2} obtained in cats with and without prior intravenous oleic acid embolization subsequently treated with positive end-expiratory pressure (PEEP). pH_a was determined during the pre-PEEP control period only, while the blood gases were also measured during PEEP applications. Results of unpaired t tests between embolized and non-embolized groups are listed below each column (NS = $P > .05$).

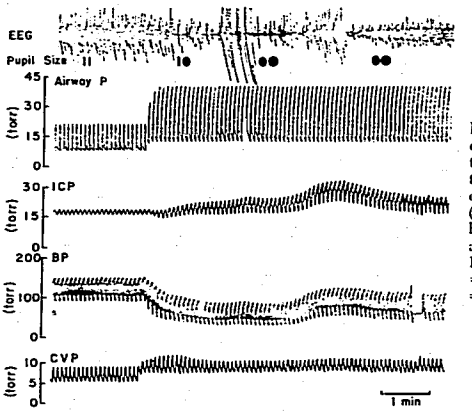

FIG. 1. Polygraph recording of vascular and intracranial pressure changes occurring during a 3.7-torr gain in positive end-expiratory pressure (from 10 to 15 cm H_2O) in a cat not given oleic acid. The electroencephalogram (EEG) and superimposed changes in bilateral pupillary configuration are also shown. P_{aw} = airway pressure; ICP = intracranial pressure; BP = arterial blood pressure; CVP = central venous pressure.

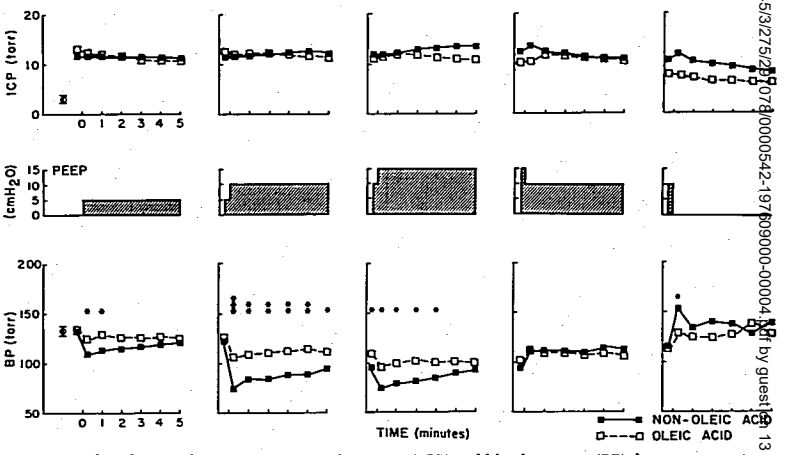

FIG. 2. Grand mean changes in intracranial pressure (ICP) and blood pressure (BP) during progressive application and removal of PEEP in groups of cats with and without prior pulmonary oleic acid embolization. The pattern of the PEEP application is indicated in the middle panel. Control pressures (±1 SEM) obtained prior to inflation of the expansion balloon are indicated by circles on the left in the first panels. Significance as shown by results of unpaired t tests between the two groups at each time point is: * = $P < .05$; ** = $P < .01$; *** = $P < .001$.

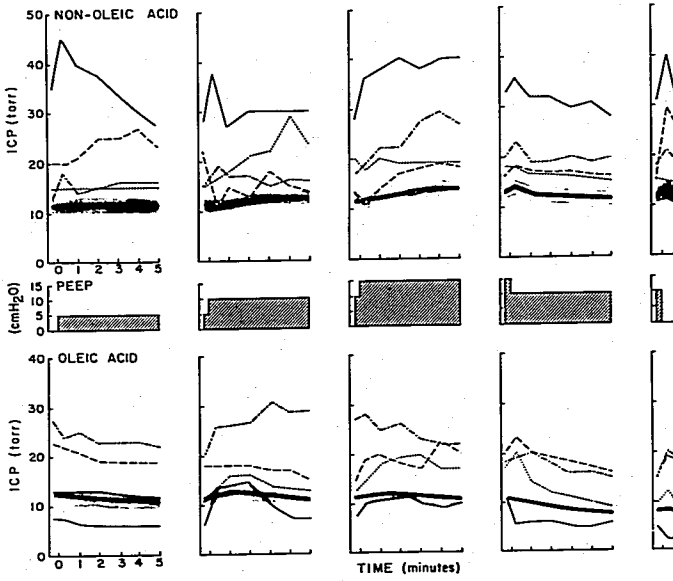

FIG. 3. Extreme individual intracranial pressure (ICP) changes (ΔICP > 11 torr) due to PEEP in cats with and without prior pulmonary oleic-acid embolization. The heavy solid line indicates the mean ICP as taken from figure 2 and the shaded area about this line shows ± 1 SEM.

Table 1 also indicates that animals given oleic acid developed significant systemic acidosis and increased alveolar–arterial oxygen differences ($P < .001$) compared with non-embolized cats. PEEP reduced the alveolar–arterial oxygen difference in the embolized cats such that their Pa_{O_2}'s were the same as those measured in cats not given oleic acid.

PEEP Effects on ICP and Vascular Pressures

Figure 1 is a polygraph record that demonstrates ICP and vascular alterations observed during PEEP application. Accompanying changes in the EEG and pupillary diameters are also shown. The recording indicates an initial (first 2 minutes) decrease in arterial pressure, accompanied by minor increases (about 4 torr) in ICP and central venous pressure, as PEEP was increased from 10 to 15 cm H_2O. This was accompanied by changes in neurologic function as discussed below. After approximately 3 minutes of 15 cm H_2O PEEP, BP began to recover and ICP further increased without additional alterations in central venous pressure. At this juncture, mean peak ICP gained about 15 torr, while mean BP remained 35 torr below its respective pre-PEEP control level.

For the purposes of this experiment, we defined two types of ICP increases consequent to PEEP. In the first (Type I), the change in ICP due to PEEP was always less than the increase in end-expiratory pressure. In some cases ICP could decrease in a Type I response if severe arterial hypotension occurred. In the Type II ICP response to PEEP, the gain in ICP exceeded the highest PEEP level applied during

the experiment, *i.e.*, 15 cm H_2O or 11 torr. In figure 1 the initial ICP elevation represents a Type I response, while the ICP elevation occuring after 3 minutes is a Type II response.

Figure 2 shows the average ICP and BP responses for all embolized and non-embolized animals. It does not differentiate between Type I and Type II responses. However, the data in figure 2 are mainly representative of Type I intracranial responses to PEEP, since Type II responses occurred in only eight of a combined total of 44 PEEP runs. Below 15 cm H_2O PEEP no change in intracranial tension occurred, while BP declined. The reduction of BP was less severe in oleic acid-embolized cats, providing they could experience and recover from a full cycle of PEEP. At 15 cm H_2O PEEP, a further 12-torr reduction in BP occurred in the oleic acid group, while BP's in the non-embolized animals remained stable at the low level (75 torr) already established by exposure to 10 cm H_2O. Very slight increases in mean peak ICP occurred at 15 cm H_2O in both groups. These ICP changes were out of phase with each other, with the oleic acid group peak increase (1.0 torr) occurring after 1 minute of exposure to PEEP, and the non-embolized peak ICP gain (1.5 torr) after 5 minutes. The peak intracranial tension increase in the non-embolized group at 15 cm H_2O coincided with a slow compensatory increase in mean BP in these cats, while BP in the embolized group remained stable.

The presence or absence of pulmonary disease resulting from oleic acid embolization of the lungs influenced the appearance of Type I ICP increases (of at least 1 torr). As PEEP was increased to 5, 10, and 15 cm H_2O in cats not given oleic acid, Type I responses were observed in 23, 85, and 58 per cent of the respective PEEP levels. In those receiving oleic acid the corresponding Type I changes were 6, 44, and 61 per cent. These percentages are based on the total number of PEEP runs within each experimental group and do not include responses wherein ICP decreased.

Figure 3 shows that Type II responses could occur in animals with pre-PEEP "control" intracranial tensions within, below, and above the average control range of ICP's for both groups. However, five of the eight Type II responses occurred in cats that had pre-PEEP exposure ICP levels greater than 15 torr. As shown in figure 3, Type II responses could occur at any time during application of a new PEEP level. In the embolized group, no Type II response was observed at PEEP below 10 cm H_2O, while Type II responses were elicited at 5 cm H_2O PEEP in the cats not given oleic acid.

Increases in BP always accompanied PEEP reduction in both experimental groups, as shown in figure 2. When PEEP was reduced from 10 to 0 cm H_2O, the rapid BP gain in the cats not given oleic acid (42 ± 4 torr SEM) was significantly ($P < .001$) greater than that in animals given oleic acid (23 ± 3 torr). BP increases due to reduction of end-expiratory pressure were frequently accompanied by variable increases in ICP in both experimental groups (figs. 2 and 3).

Besides altering the ICP and BP responses to positive end-expiratory pressure, oleic acid embolization of the lungs also modified the response of central venous pressure to PEEP. Non-embolized cats had greater increases in central venous pressure during PEEP. The changes in central venous pressure during PEEP in both experimental groups are indicated in figure 4.

Figure 5 shows the overall effects of BP and ICP alterations on the net changes in CPP due to PEEP in both groups. Oleic acid-embolized cats had significantly less CPP perturbation during application and removal of PEEP.

Neurologic Function and PEEP

As previously mentioned, figure 1 indicates that neurologic function can be altered by PEEP in the presence of an intracranial mass lesion. Tables 2 and 3 summarize the intracranial and cerebral perfusion pressures associated with alterations in the EEG pattern or pupillary diameter due to PEEP. EEG changes (table 2) occurred only in cats not given oleic acid. Seven of the nine cats exposed to PEEP in the absence of pulmonary oleic acid embolization developed EEG changes at some time during the application of PEEP. In three of these instances, EEG's remained abnormal during 10-minute recovery periods following removal of PEEP.

Table 3 indicates conditions associated with changes in pupillary diameter. These changes were either unilateral or bilateral and were

observed in both embolized and non-embolized animals. In three of the animals not given oleic acid, EEG and pupillary changes occurred simultaneously. One cat (4B) developed persistent fully dilated non-light-reactive pupils bilaterally following a peak ICP increase of 19 torr as PEEP was removed. As shown in tables 2 and 3, not all cats with EEG abnormalities had accompanying pupillary changes.

Discussion

A Model for Intracranial Responses to PEEP

Our principal findings show that PEEP can initiate changes in intracranial pressure and systemic hemodynamics that can cause neurologic dysfunction in the presence of an intracranial space-occupying lesion. Figure 6 presents a schematic outline of the pathophysiologic sequence we believe to be operative in this situation. In this model the transmission of PEEP into the thoracic cavity is variable and depends upon the elastic properties of lung tissue, which can be altered by disease.[3,4] When PEEP increases intrathoracic pressure, central venous pressure will increase (relative to atmospheric pressure) and cardiac filling pressure will be reduced.[2] Systemic circulatory adaptation to these changes may be incomplete,[2] especially in volume-depleted states, and cerebral perfusion pressure may be critically reduced as BP falls.

The elevated central venous pressure due to PEEP can also impede cerebral venous out-

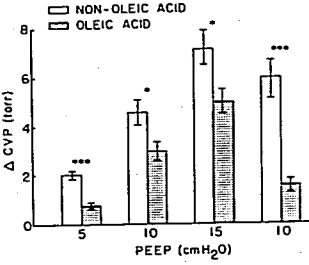

FIG. 4. Mean changes (± 1 SEM) in central venous pressure (CVP) from pre-PEEP run control values in the non-oleic acid and oleic acid-embolized cats during increase and reduction of PEEP. Asterisks indicate significance levels as defined in figure 2.

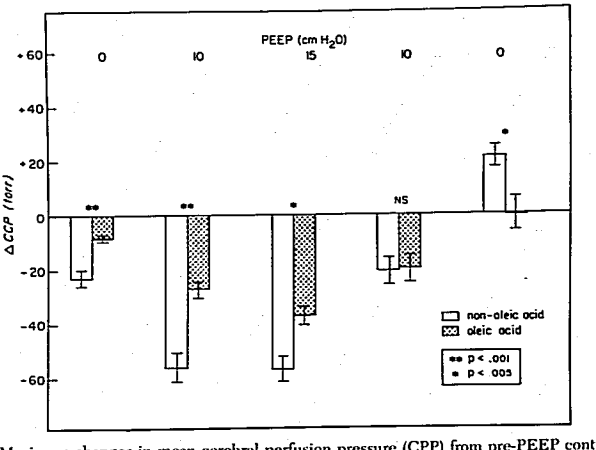

FIG. 5. Maximum changes in mean cerebral perfusion pressure (CPP) from pre-PEEP control values in cats with and without prior pulmonary embolization with oleic acid. Vertical bars indicate ± 1 SEM. Significant differences between groups are indicated by asterisks as defined in figure 2.

TABLE 2. PEEP-induced ICP and CPP Changes Associated with Alterations in Electroencephalographic Activity*

	Control			EEG Change			Recovery				
	PEEP (cm H_2O)	ICP (torr)	CPP (torr)	PEEP (cm H_2O)	ICP (torr)	CPP (torr)	PEEP (cm H_2O)	ICP (torr)	CPP (torr)	EEG	Recovery of EEG
Cat 1	5	15	113	10	16	64	10	20	65	Decreased amplitude with isoelectric periods	Yes
Cat 2	5	7	131	10	8	52	10	8	84	Decreased amplitude with isoelectric periods	Yes
Cat 3	5	18	85	10	14	26	0	19	131	Decreased amplitude with isoelectric periods	Partial
Cat 4	5	11	86	10	12	30	0	18	100	Decreased amplitude with isoelectric periods	Partial
Cat 5	5	20	82	10	8	34	0	15	95	Decreased amplitude	Partial
Cat 6	10	5	108	15	4	54	15	5	77	Decreased amplitude	Yes
Cat 7	10	8	84	15	6	64	10	6	87	Decreased amplitude	Yes

* Electroencephalogic changes were determined by gross changes in the amplitude and activity pattern as recorded on the polygraph at a speed of 0.42 mm/sec. None of the animals in this table received oleic acid. Data in this table represent the first PEEP-induced abnormalities observed within single animals and do not include changes that repeated themselves on subsequent PEEP runs. Pressures are reported as mean values. PEEP levels in Cats 1, 2, and 6 were unchanged because the EEG change was transient and recovery occurred within 5 minutes at the new PEEP level. Absence of full recovery was determined after 10 minutes at 0 cm H_2O PEEP.

TABLE 3. PEEP-induced ICP and CPP Changes Associated with Changes in Pupillary Diameter*

	Control			Pupillary Change					Recovery of Pupils				
	PEEP (cm H_2O)	ICP (torr)	CPP (torr)	PEEP (cm H_2O)	ICP (torr)	CPP (torr)	OD (mm)	OS (mm)	PEEP (cm H_2O)	ICP (torr)	CPP (torr)	OD (mm)	OS (mm)
No oleic acid													
Cat 1	5	15	113	10	29	68	4	2	10	20	65	4	2
Cat 2	5	7	131	10	8	52	2	2	15	7	85	.5	.5
Cat 3	5	18	85	10	14	26	10	10	0	3	147	0	0
Cat 4A	10	10	47	15	12	28	1	3	10	16	96	0	0
Cat 4B	10	16	76	0	29	106	10	10	0	27	60	10	10
Cat 7	10	8	84	15	6	64	3	3	10	4	101	1	0
Oleic-acid-embolized													
Cat 10	10	10	115	15	10	95	3	1	0	9	141	.5	0
Cat 13	5	15	110	10	19	63	4	2	0	9	131	1	0
Cat 15	5	13	107	10	12	73	3	2	0	5	130	.5	.5

* Configurations of pupils were observed and their diameters measured in the horizontal axis and traced onto the polygraph record. The normal configuration is slit-like and has a diameter of 0.1 to 0.5 mm; this was present in all animals prior to recording of the changes shown. Maximal dilation is 9–10 mm/ul diameter. The response of Cat 4B occurred with PEEP removal, while the other responses were due to increased PEEP. OS = left eye; OD = right eye. Recovery of pupillary diameter was defined to occur when at least one dilated pupil returned to 0.5 mm in diameter with PEEP maintained or after 10 minutes without PEEP.

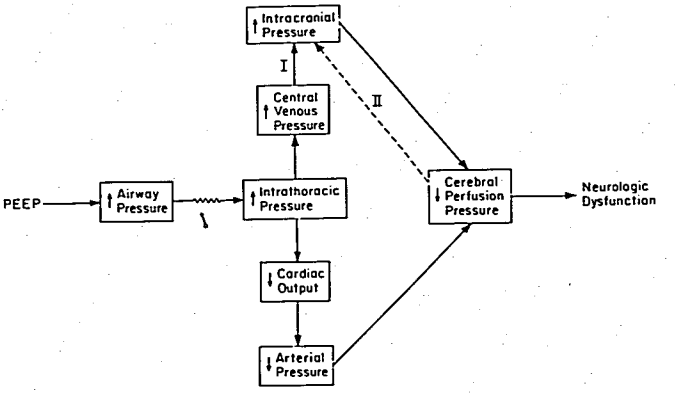

FIG. 6. Schematic representation of the pathophysiologic events leading to changes in intracranial hemodynamics and pressure in cats with intracranial mass lesions subjected to PEEP. The zigzag arrow indicates the introduction of a variable pulmonary impedance to pressure transmission into the thoracic cavity. I and II indicate Type I and Type II ICP responses. In a Type I response, the ICP increase is equal to or less than the mean increase in airway pressure. Type II ICP increases are greater than PEEP-induced gains in airway pressure and probably are due to reflex cerebrovasodilation. Dashed line indicates potential for a cyclic increase in ICP. See text for further elaboration.

flow and increase intracranial tension. When intracranial compliance is reduced, *e.g.*, by a mass lesion, even small increases in cerebral blood volume can significantly elevate ICP.[1,6,7] However, when the intracranial tension is very high (*i.e.*, 10–15 torr above central venous pressure), the pressure response of the intracranial compartment to a central venous pressure elevation should theoretically be reduced. In this circumstance the added extracranial impedance to cerebral venous outflow is minor in comparison with the extrinsic pressure exerted upon the collapsible intracranial venous system. In effect, this situation models the Starling resistor. Even if the Starling resistor effect develops during advanced intracranial hypertension, an initial period when PEEP-related central venous pressure increases can directly influence ICP (Type I response) will exist.

The ICP and BP contributions to reduction in the cerebral perfusion pressure described above may result in cerebral ischemia. Such ischemia can then initiate reductions in cerebrovascular resistance, and, providing BP remains high enough, this will cause increases in cerebral blood volume and ICP.[11] Changes like these may be responsible for the Type II ICP responses observed in our experiment, and can lead to the establishment of the pathologic cycle shown in figure 6. If the CPP reduction is severe, signs of cerebral ischemia such as pupillary dilation and EEG changes occur.

PEEP and Cerebral Ischemia

Normally, intracranial tension elevation and blood pressure reduction can be tolerated without development of cerebral ischemia. This depends on an intact cerebral blood flow autoregulation response and the absence of an overall cerebral perfusion pressure decline below 50 to 60 torr.[1] Intracranial vascular and mass lesions modify autoregulation.[8] When autoregulation is lost, cerebral blood flow, brain blood volume, and intracranial pressure become blood pressure-dependent. This means that one might expect a patient with a normal brain to have an adequate capacity to compensate for the intracranial hemodynamic and ICP stresses of PEEP, whereas the presence of intracranial disease should alert one

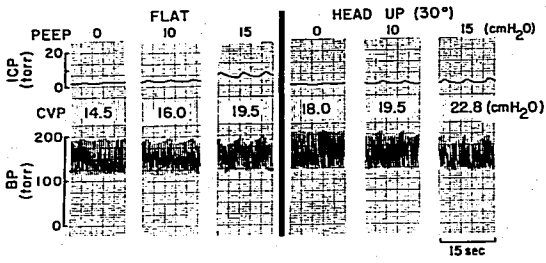

FIG. 7. Attenuation of the intracranial pressure (ICP) effect of PEEP by elevation of a patient's head. BP = blood pressure; CVP = central venous pressure.

to an enhanced possibility of neurologic complications due to PEEP therapy. Sudden arterial pressure declines, similar to those that occurred in the cats not given oleic acid, can transiently pose a severe stress to cerebral blood flow autoregulation even when BP remains above 60 torr. Evidence for this phenomenon is found in the cats developing transient EEG abnormalities at blood pressures above 50–60 torr (table 2).

ICP Responses to PEEP

Two kinds of ICP responses to PEEP were defined in the present experiment. The ICP change in the Type I response was negative or less than the end-expiratory pressure applied to the airway. We attempted to modify Type I ICP increases by elevating the cat's head 15 cm above heart level to offset PEEP-induced venous hydrostatic pressure changes. Greater Type I ICP increases might have occurred if this had not been done. Figure 7 demonstrates modification of the ICP response to PEEP by postural changes in a patient given PEEP therapy. Although elevating the head of the bed might seem to be an effective way of combating Type I ICP increases, there is evidence that the combination of upright posture and increased intrathoracic pressure causes an earlier loss of cerebral blood flow autoregulation (*i.e.*, cerebral ischemia occurs at BP's above 50–60 torr).[9]

In a Type II ICP response the intracranial tension gain exceeds the highest PEEP level applied to the airways and may occur at any time after PEEP application. In these responses there is a sudden ICP increase (second ICP gain in figure 1) that may be variably accompanied by a BP elevation. Lundberg found similar ICP waves in his neurosurgical patients in association with abrupt neurologic changes.[10] It is thought that these reflex-based increases in CBV and ICP are due to brainstem ischemia and/or distortion.[11-13] Under our experimental conditions, we were not able to predict when reflexive Type II ICP responses would occur. This is similar to our clinical experience and remains a problem in applying PEEP to patients who have intracranial mass lesions or hydrocephalus.

The absolute increases in ICP Type I and II responses to PEEP might have been higher and longer-lasting if BP (which provides a major force generating ICP) had not simultaneously decreased during application of PEEP. Further attentuation of ICP increases in response to higher PEEP levels probably occurred as a result of intracranial volume compensation. This compensation requires time and is effected by translocation of cerebrospinal fluid and brain tissue from the supratentorial to the infratentorial space. As no additional volume was added to the expansion balloon during PEEP, the lower ICP following PEEP (figs. 2 and 3) provides evidence for ongoing volume compensation in our cats.

PEEP Removal

A complex series of systemic and intracranial hemodynamic events can ensue when previously established PEEP levels are reduced. Abrupt removal of thoracic impedance to venous inflow initiates variable autotransfusion from peripheral to central circulation. Depending on the extent of autotransfusion and state of myocardial contractility, augmentation or depression of circulatory indices can occur when PEEP is reduced.[2,7] The increase

in BP associated with PEEP removal in the cats given oleic acid was less than that occurring in the non-embolized group. This may be partially due to circulatory buffering caused by the embolized lungs, as well as the greater systemic acidosis in the oleic acid-embolized cats (figs. 2 and 3). Coupling of the PEEP-reduction BP overshoot with defective cerebral blood flow autoregulation and reduced intracranial compliance can result in brisk increases in cerebral blood volume and intracranial pressure. This combination of events also predisposes to cerebral edema.[1,14]

Clinically, blood volume augmentation may be necessary to support cardiovascular function when PEEP is applied.[2,4] This may be more frequently needed in neurosurgical patients treated with therapeutic dehydration regimes. When PEEP is reduced in such patients, autotransfusion and subsequent changes in cardiovascular indices are likely to be greater. We suggest that abrupt reductions in PEEP levels, like those associated with tracheal suctioning, be avoided or modified when possible in management of neurosurgical patients who have recognized abnormal cerebral blood flow autoregulation and reduced intracranial compliance.

Neurologic Changes and PEEP

The EEG provided an index of cerebral ischemia related to PEEP-caused reductions in CPP (table 2). No EEG change was seen in the non-embolized group, possibly because CPP was better maintained in this group. In some instances, full recovery to the pre-PEEP EEG pattern did not occur even though CPP was restored after relatively brief periods of hypotension. This indicates that neurologic damage may occur when PEEP is first applied to patients who have intracranial disease. Although systemic and intracranial circulatory adaptation to PEEP stresses may occur with time, our study indicates the possible pitfalls in initially establishing PEEP therapy.

Often concurrent changes in pupillary dimensions and the EEG occurred in cats not given oleic acid. However, there were instances in which isolated changes in either the EEG or the pupils occurred. Development of unilateral pupillary dilation as a sign of cerebral herniation (excluding that directly due to balloon expansion) in the absence of intracranial hypertension (ICP < 15 torr) suggests that the previously mentioned tissue shifts provided some intracranial volume compensation in our cats. Additionally, this provides evidence that a combination of direct pressure on the third cranial nerve and decline in BP can suffice to cause local ischemia and produce clinically apparent neurologic dysfunction (pupillary dilation) in the absence of a very high ICP.

PEEP and Neurologic Patients

Because PEEP may be administered to patients who have a broad spectrum of intracranial and pulmonary abnormalities, the neurologic changes in our study assume clinical importance. Is PEEP then contraindicated in the presence of intracranial hypertension? We believe the answer to this question is a qualified "no." When PEEP ameliorates severe hypoxia or permits reduction of high inspired oxygen concentrations, it should not be withheld.[15] However, since PEEP can potentially accelerate or cause neurologic abnormalities in the presence of intracranial disease, this therapy must be titrated against neurologic as well as cardiopulmonary status. When PEEP is needed for patients who have a potential for developing intracranial hypertension, monitoring should probably include, in addition to blood-gas and blood pressure measurements, assessment of neurologic status and intracranial and cerebral perfusion pressures. Inclusion of continuous monitoring of the EEG in patients given sedatives and muscle relaxants to facilitate mechanical ventilation and PEEP therapy should improve our ability to detect cerebral ischemia in these patients. With this monitoring approach, PEEP levels can be titrated to meet various organ system requirements simultaneously.

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Critical Care

COST-BENEFIT IN THE CRITICALLY ILL Increasing amounts of medical resources are being devoted to the care of the critically ill. What can be learned from an objective evaluation of the costs and benefits involved in this area? The authors report data derived from the consecutive treatment of 226 patients during a year. The average duration of hospitalization was 35 days. At the end of a month, 123 patients (54 per cent) had died. Of patients surviving a month, almost a third had returned home. The remainder progressed in two different ways: some showed gradual improvement to full recovery, while others declined and died within the year. At the end of a year, 164 patients (73 per cent) had died. Evaluation of all patients surviving during the first year showed that 26 (12 per cent of the entire study group) were functioning normally. This had been accomplished at a total hospital cost (excluding physician fees) of $3,232,647. The cost of blood and blood products represented 21 per cent of the total cost. The authors conclude that the data "document the use of increasingly limited resources in the management of critically ill patients. The medical profession must make difficult decisions to allocate these resources effectively." (*Cullen DJ, and others: Survival, hospitalization charges and follow-up in critically ill patients. N Engl J Med 294: 982–987, 1976.*)