POSTANESTHETIC HYPOTENSION FOLLOWING CYCLOPROPANE: ITS RELATIONSHIP TO HYPERCAPNIA * †

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THE initial enthusiasm accorded cyclopropane following its discovery (1) and introduction into clinical anesthesia (2) abated somewhat as the respiratory and circulatory abnormalities consequent to the use of this anesthetic became more evident. Waters and Schmidt (3) stressed the profound respiratory depressant action of the agent. Subsequent investigations of this property and its effect on acid-base balance soon appeared (4, 5, 6). Stormont and others (7) in 1942 described severe respiratory acidosis in 17 patients anesthetized with cyclopropane. In 1947 Dripps (8) presented data of a similar nature; in one instance cited, the pH fell as low as 6.99 and the carbon dioxide tension rose to 120 mm. of mercury.

As the use of cyclopropane became widespread, a clinical syndrome termed "cyclopropane shock" was recognized. This entity was characterized by a pronounced fall in blood pressure occurring immediately after the cessation of the anesthesia. Often this fall was precipitous and out of all proportion to the amount of surgical trauma inflicted. Usually it was associated with marked pallor, weak slow pulse and a cold clammy skin. Occasionally the fall in blood pressure was more gradual and less profound and the patient exhibited few, if any, untoward clinical signs. There arose considerable interest concerning the etiology of this phenomenon. Some early writers (4) thought that it was related to the sudden withdrawal of the oxygen-rich atmosphere accompanying cyclopropane anesthesia; others (9) held that it resulted from the manipulative stimuli occurring during operation, the effects of which remained suppressed until the anesthetic was withdrawn. In recent years, emphasis has been placed on the concept that the syn-

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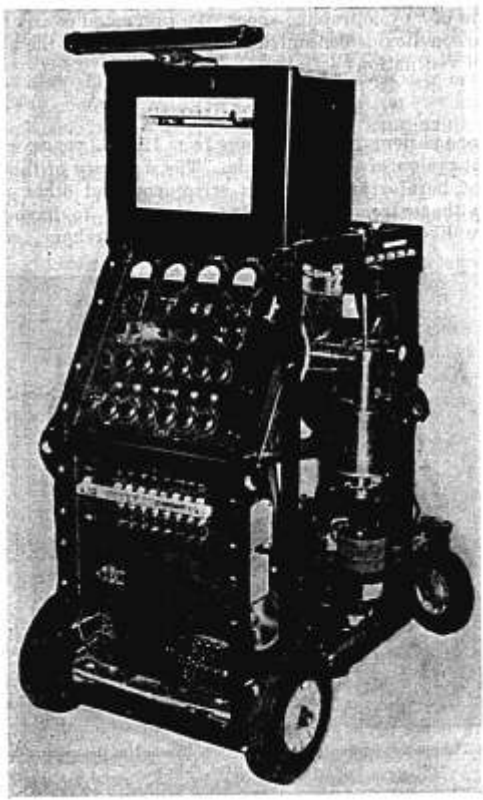

FIG. 1. The portable mass gas spectrometer.

drome may be the result of hypercapnia secondary to the respiratory depression produced by cyclopropane. Dripps (8) studied 11 patients undergoing cyclopropane anesthesia and was able to show a direct relationship between the degree of hypercapnia developed and the severity of the subsequent postoperative hypotension.

Development of the portable mass spectrometer (fig. 1) for the continuous measurement of alveolar gas tensions (10, 11, 12) afforded an opportunity to study the carbon dioxide elimination in subjects anesthetized with cyclopropane. The following question arose: Can the

phenomenon of "cyclopropane shock" be prevented consistently if the alveolar carbon dioxide concentration is maintained at the normal level by artificial ventilation?

METHODS AND PROCEDURES

Thirty-one patients, varying in age from 12 to 83 years, were studied during light cyclopropane anesthesia. The majority of the operations consisted of herniorrhaphies, vein strippings and other minor procedures on the extremities. Patients who were to have operations which were likely to be accompanied by hemorrhage, considerable

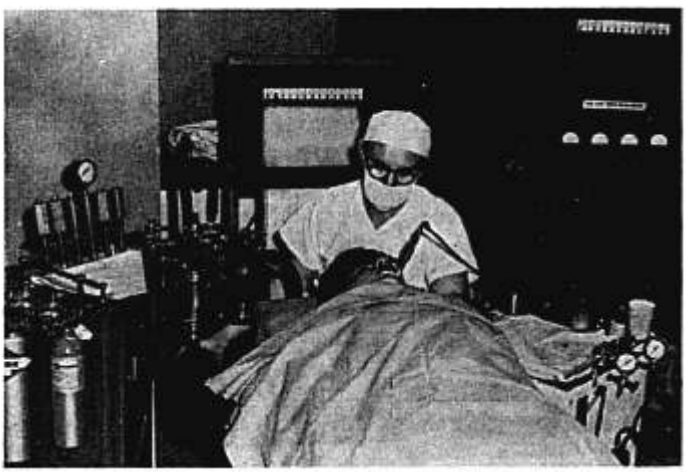

FIG. 2. The mass spectrometer sampling tube attached to the endotracheal tube of an anesthetized patient.

trauma, or peritoneal or pleural manipulation were avoided. All patients had normal respiratory systems.

In most cases premedication consisted of the subcutaneous administration of morphine sulfate, 10 mg., and atropine sulfate, 0.4 mg., ninety minutes before operation. The patients were placed in the *supine* position and an intravenous infusion of 5 per cent dextrose in distilled water was started before induction of anesthesia. Following induction with cyclopropane, intubation was performed and light anesthesia was maintained during the entire operative procedure utilizing a closed circle carbon dioxide absorption system. The sampling tip of the mass spectrometer was attached to the endotracheal tube in the manner

previously described (12) and a continuous analysis of the alveolar carbon dioxide concentration was recorded throughout the operation (fig. 2). At the conclusion of the operative procedure, the anesthesia machine was disconnected and the patient was allowed to breathe room air through the endotracheal tube while the spectrometer sampling tip was still in place. In this way, the alveolar carbon dioxide concentration was recorded during emergence from anesthesia, at least to the point at which the patient no longer tolerated the endotracheal tube.

Frequent blood pressure readings were taken by the oscillometric method during the operation, in the immediate postoperative period and for twelve hours or more following recovery.

The patients were divided into two groups. Fifteen were managed without benefit of assisted respirations, while 16 were assisted by manual compression of the breathing bag in synchrony with their spontaneous exchange. The recorder of the mass spectrometer was stationed outside the operating room where it could not be viewed by the anesthesiologist during the conduct of the anesthesia of the unassisted group. During anesthesia of the group in whom respiration was assisted, the recorder was placed in the operating room, thereby enabling the anesthesiologist to maintain a normal alveolar carbon dioxide concentration at all times.

RESULTS

Unassisted Cases. All of the 15 patients who were allowed to breathe spontaneously (unassisted) during cyclopropane anesthesia showed significant accumulations of alveolar carbon dioxide. It is interesting to note that elevated values were observed very soon after induction of anesthesia, often before the operation had commenced. The highest levels recorded during operation in each case ranged from 7.5 per cent to 20.0 per cent, the average being 12.3 per cent (approximately equivalent to 85 mm. of mercury tension) (table 1, column 4).

These cases likewise showed a uniform arterial blood pressure response during anesthesia. The average elevation of the systolic and diastolic pressures above the preoperative level was 32.9 and 7.0 mm. of mercury, respectively (table 1, columns 6 and 7). The magnitude of the hypertensive response varied considerably from case to case, however, and was not related to the degree of hypercapnia; this possibly may indicate some variability in the sensitivity of the vascular system to cyclopropane.

Upon cessation of the anesthesia, these cases in which respiration was unassisted exhibited an immediate decrease in alveolar carbon dioxide tension; this was accompanied by a prompt and sometimes alarming fall in arterial blood pressure. The maximal systolic decrease *below the preoperative level* was 108 mm. of mercury. The average decrease *below the preoperative level* was 47.1 mm. of mercury

in the systolic and 30.6 mm. of mercury in the diastolic pressure (table 1, columns 9 and 10). A direct relationship was noted between the *degree* of hypercapnia developed and the severity of the postanesthetic hypotensive reaction. There seemed to be no such correlation between the *duration* of the hypercapnia and the severity of the hypotension. In fact, the 2 patients who exhibited the most profound and prolonged decrease in blood pressure were anesthetized for only eighty-five minutes. An equally startling feature of this postanesthetic period was the duration of the hypotensive state. In several instances the arterial

TABLE 1

CIRCULATORY RESPONSE DURING AND AFTER CYCLOPROPANE ANESTHESIA, RESPIRATIONS UNASSISTED

Pt.	Age	Normal B/P	Highest CO_2 Attained, per cent	During Anesthesia			After Anesthesia			Remarks
				Highest B/P Attained	Systolic Rise Above Preop. Level, mm. Hg	Diastolic Rise Above Preop. Level, mm. Hg	Lowest B/P Attained	Systolic Fall Below Preop. Level, mm. Hg	Diastolic Fall Below Preop. Level, mm. Hg	
F. T.	60	170/80	18.0	195/100	25	20	72/30	98	50	Hypotensive 48 hrs.
C. H.	60	110/65	8.5	155/80	45	15	110/65	0	0	
A. H.	81	210/100	8.0	215/100	5	0	118/70	92	30	Hypotensive 48 hrs.
R. F.	18	124/88	11.0	170/90	46	2	105/30	19	58	
M. G.	67	140/80	15.0	170/80	30	0	105/55	35	25	
V. Z.	39	140/80	11.5	165/90	25	10	102/50	38	30	
G. W.	64	170/80	8.5	186/80	16	0	124/70	46	10	
E. E.	22	130/80	9.0	160/84	30	4	102/60	28	20	
E. P.	64	142/84	12.5	205/90	63	6	90/60	52	24	
M. B.	42	110/66	7.5	140/80	30	14	76/0	34	66	
D. S.	33	160/90	15.0	235/100	75	10	110/60	50	30	
L. M.	19	138/80	20.0	168/94	30	14	105/64	33	16	Hypotensive 18 hrs.
G. T.	16	130/80	13.0	174/80	44	0	96/70	34	10	Anuric 28 hrs.
J. W.	50	140/70	7.5	160/80	20	10	100/70	40	0	
F. T.	69	180/90	20.0	190/90	10	0	72/0	108	90	Hypotensive 12 hrs.
Average			12.3		32.9	7.0		47.1	30.6	

blood pressure did not return to normal for twelve to forty-eight hours (fig. 3).

Clinically, several of these patients became delirious, cold and clammy and had weak, thready pulses. In some cases, marked suppression of urine formation was a prominent feature of the postoperative period (fig. 4). Several continuous electrocardiographic tracings were recorded during emergence from anesthesia. Although the alveolar carbon dioxide tension was reduced sharply and the blood pressure fell at that time, no abnormalities of cardiac rhythm were observed.

Assisted Cases. As in the unassisted group, the carbon dioxide

levels of the 16 cases to be assisted were found to be elevated immediately following induction and intubation. This initial rise accounts for the slightly abnormal average value shown in column 4, table 2. This situation was remedied promptly through manually assisted respiration and the alveolar carbon dioxide tensions were maintained thereafter within the normal range by this means.

The arterial blood pressure rose during the anesthetic period in all 16 assisted cases. The rise usually occurred in the early minutes of

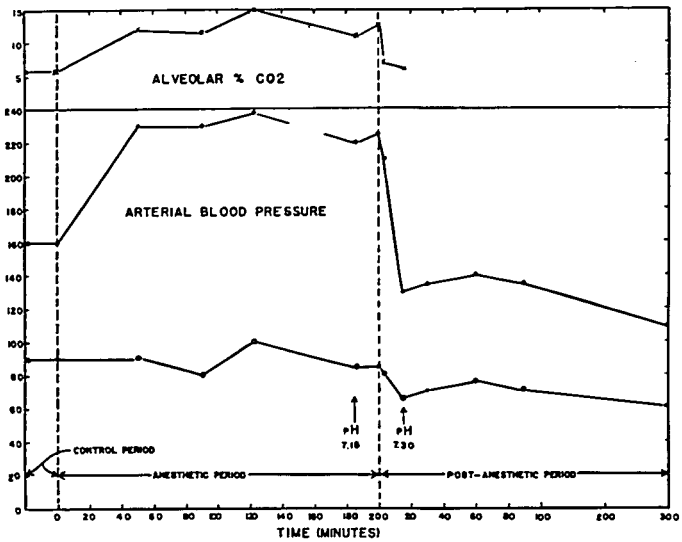

FIG. 3. Chart on patient D. S., age 33, illustrating the rapid development of hypercapnia during light cyclopropane anesthesia when respiration is not augmented. Observe the profound hypotension in the early minutes of the postanesthetic period.

the anesthesia and was not always maintained. Here again considerable variability was noted from case to case. There did not seem to be any correlation between the blood pressure elevation and the alveolar carbon dioxide level since the 2 patients who exhibited the most marked increases in the blood pressure had no elevation of alveolar carbon dioxide tension. From these data and that previously cited for the unassisted group, it would appear that the hypertension often encountered with cyclopropane is not related exclusively to carbon dioxide accumulation.

Upon cessation of the anesthesia, 14 of the 16 patients so managed (assisted) exhibited no significant decrease in the blood pressure during the postanesthetic period (columns 9 and 10, table 2). The 2 remaining patients experienced falls of systolic pressure of 44 mm. and 24 mm. of mercury, respectively, the cause of which is not apparent from this study. All patients in this group had smooth recovery periods and were easier to manage in all respects. Figures 5 and 6 are typical examples of the cases in the assisted group.

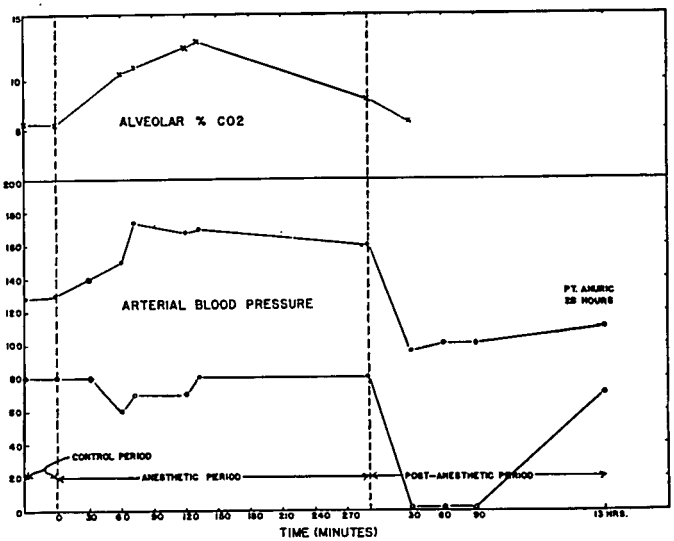

FIG. 4. Chart on patient G. T., age 16, again illustrating the inadequacy of carbon dioxide clearance during light cyclopropane anesthesia, respirations unassisted. Hypotension and prolonged anuria are features of the postanesthetic period.

DISCUSSION

The above findings substantiate the belief that the syndrome of "cyclopropane shock" is directly related to hypercapnia. The underlying basis for the development of this respiratory acidosis is the depression of tidal exchange occasioned by the anesthesia. The acidosis progresses steadily during the anesthetic period, the carbon dioxide tension often reaching startling levels. It should be emphasized that the severe degrees of hypercapnia observed in this series were not the result of extreme depth of anesthesia; on the contrary, in

all cases the anesthesia was "light," yet respiratory exchange was inadequate.

The development of severe degrees of hypercapnia is not limited to those patients who receive cyclopropane anesthesia. This complication has been described by several authors (19, 20) during ether anesthesia, a concept contrary to the generally accepted belief that ether is a respiratory stimulant. Certainly, intravenous barbiturate anesthesia and those inhalation technics supplemented by curare given intravenously are exceptionally prone to cause respiratory depression unless specific preventative measures are employed. Furthermore, in-

TABLE 2

CIRCULATORY RESPONSE DURING AND AFTER CYCLOPROPANE ANESTHESIA, RESPIRATIONS MANUALLY ASSISTED

Pt.	Age	Normal B/P	Highest CO_2 Attained, per cent	During Anesthesia			After Anesthesia			Remarks
				Highest B/P Attained	Systolic Rise Above Preop. Level, mm. Hg	Diastolic Rise Above Preop. Level, mm. Hg	Lowest B/P Attained	Systolic Fall Below Preop. Level, mm. Hg	Diastolic Fall Below Preop. Level, mm. Hg	
J. S.	42	140/80	8.0	160/90	20	10	132/70	8	10	6¼ hr. anesthesia
G. U.[g]	30	120/70	6.0	128/70	8	0	125/70	0	0	
W. L.[i]	12	120/50	9.0	130/80	10	30	116/54	4	0	
C. P.[j]	38	120/70	5.5	190/70	70	0	124/70	0	0	
L. G.[k]	83	120/70	4.5	180/80	60	10	130/52	0	18	
F. B.	65	135/90	6.0	150/80	15	0	136/64	0	26	
R. W.	25	112/78	7.0	140/74	28	0	105/70	7	4	
W. H.	24	110/80	7.5	170/90	60	10	104/70	6	10	
E. V.	60	164/86	6.5	180/90	16	4	120/80	44	6	"Failure" case
W. M.	26	105/80	6.5	140/80	35	0	110/68	0	12	
L. H.	50	140/60	7.5	162/76	22	16	116/70	24	0	"Failure" case
H. H.	35	118/70	6.5	130/80	12	10	110/60	8	10	
J. I.	32	106/64	7.5	150/80	44	16	102/60	4	4	
J. I.	32	106/64	6.0	116/70	10	6	120/70	0	0	
A. P.	40	116/70	7.5	140/80	24	10	104/62	12	8	
W. B.	23	120/70	7.5	150/80	30	10	124/70	0	0	
Average			6.8		29.0	8.1		7.3	6.7	

trathoracic surgical procedures have been shown to result in severe respiratory acidosis in a high percentage of cases (21).

Clearly, inadequate pulmonary ventilation consequent to impairment of respiratory exchange is the common denominator in the production of these acidotic states. This may be traceable to mechanical factors such as unfavorable positioning upon the operating table or collapse of the lung during surgical pneumothorax, or it may be the result of pharmacologic impairment of the respiratory center or musculature, or both, by anesthetic or relaxant drugs.

The effect of increased carbon dioxide in the blood upon the vaso-

motor center by way of the aortic and carotid chemoreceptors (13), resulting in peripheral vasoconstriction, is well known. Conceivably, when this high concentration of carbon dioxide is allowed to persist, an elevation of the threshold governing vascular homeostasis results. If the carbon dioxide subsequently is eliminated rapidly, the activity of the medullary cells concerned with peripheral vascular tone is reduced and a fall in blood pressure results.

The possibility that this hypotensive phenomenon might be related to the type of intravenous fluid administered, as suggested by O'Malley

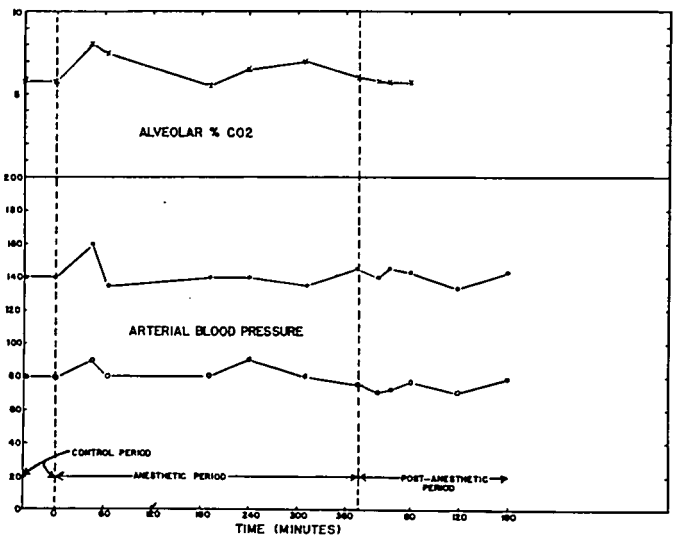

FIG. 5. Chart on patient J. S., age 42, cyclopropane anesthesia. Alveolar carbon dioxide level was maintained within the normal range by manual assistance to respiration. Note that the blood pressure remained unaltered in the postanesthetic period.

and Frumin (14), was considered. Although all patients in this study received infusions of 5 per cent dextrose in water, said by the above authors to produce postoperative hypotension in a significant number of subjects, the postoperative hypotensive syndrome herein considered consistently developed only in the patients in the unassisted hypercapneic group.

The practical significance of such hypercapnia becomes apparent in the light of recent investigations. Miller *et al.* (15) produced serious or fatal cardiac irregularities in 18 of 19 dogs breathing high concen-

trations of carbon dioxide by suddenly withdrawing the carbon dioxide-rich atmosphere. The only technic by which these investigators consistently were able to avoid electrocardiographic abnormalities and salvage their animals was that of gradual reduction of the blood carbon dioxide tension over a fifteen to thirty minute period. Waters (16) in 1937 suggested that some of the fatalities occurring upon the operating table and in the immediate postoperative period, popularly attributed to hypoxia or the anesthetic agent, might be the result of just such a sequence of events. Hypercapnia is known to potentiate vagal activity (17, 18), with the result that otherwise insignificant stimuli (for

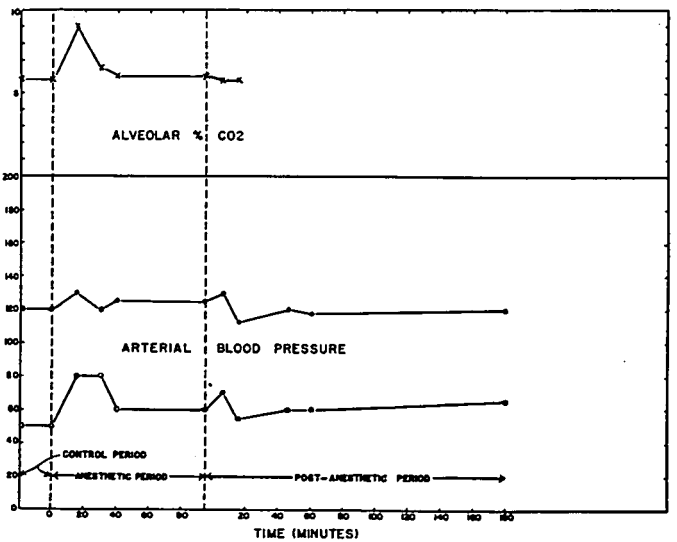

FIG. 6. Chart on patient W. L., age 12, cyclopropane anesthesia, respirations manually augmented throughout. No postanesthetic decrease in blood pressure was observed.

example, suctioning within the tracheobronchial tree, hilar manipulation, endotracheal extubation) may set up fatal cardiac reflexes. Furthermore, such severe hypotensive episodes which can occur render the patient more prone to vascular thrombosis. When such hypercapnia is superimposed upon the common complications of surgical disease such as infection, toxemia, dietary deficiency, dehydration or hemorrhage, it is not surprising that tragedies occasionally ensue. Finally, bouts of oliguria or anuria render more complex the management of the postoperative fluid and electrolyte therapy.

CONCLUSION

Avoidance of such serious postoperative sequelae is the aim of every competent anesthesiologist. This end can be accomplished best by meticulous attention to the maintenance of adequate pulmonary ventilation. The present data illustrate vividly the necessity for such vigilance during cyclopropane anesthesia; studies now in progress in this clinic indicate a similar requirement during ether-oxygen anesthesia. Intravenous methods, especially when curare is employed, are equally prone to produce inefficient pulmonary ventilation. Until an analyzer somewhat less complex than our mass spectrometer has been developed to aid us in detecting immediately the acidotic trend, we believe that *all* patients under general anesthesia, regardless of the agent employed, require augmentation of their spontaneous respiration. Several clinics have employed mechanical devices to provide this artificial ventilation, especially during thoracic procedures. It is our belief that rhythmic manual compression of the breathing bag by the anesthesiologist, provided he is experienced and skilled in this practice, provides more adequate ventilation than can be produced by any machine yet devised.

SUMMARY

The syndrome of "cyclopropane shock" and current etiologic theories are outlined.

Continuous mass spectrometric analyses of alveolar carbon dioxide tensions in 31 patients undergoing cyclopropane anesthesia are recorded; simultaneous arterial blood pressure readings were correlated with the above values.

Fifteen patients allowed to breathe unassisted showed an accumulation of alveolar carbon dioxide during anesthesia with a concomitant rise in blood pressure. Upon cessation of the anesthesia these patients exhibited a prompt and sometimes severe fall in blood pressure.

Of 16 patients given assisted respiration to maintain an approximately normal alveolar carbon dioxide tension only 2 showed a significant fall in blood pressure upon termination of the anesthesia.

The practical significance of hypercapnia is considered.

Prophylaxis of this syndrome by maintenance of normal alveolar carbon dioxide tension by manually augmented respiration is demonstrated.

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