Cyclopropane–Carbon Dioxide Arrhythmic Threshold in Patients with Cardiovascular Disease

M. Jerome Strong, M.D., Cornelia P. Lukban, M.D.,† Arthur S. Keats, M.D.‡*

The threshold for arrhythmias produced by hypercarbia during cyclopropane anesthesia was determined during 50 operations in 47 elderly patients with cardiovascular disease. Arterial carbon dioxide tension and alveolar cyclopropane concentrations were measured simultaneously in the presence and absence of arrhythmias. The arrhythmic threshold observed was considerably higher in these patients than the threshold previously reported for young healthy adults. In patients in whom anesthesia was induced with thiopental, arrhythmias were less frequent than in patients in whom anesthesia was induced with cyclopropane alone. In addition, the rapid intravenous administration of 150 mg. of thiopental caused a disappearance of arrhythmias in six of eight patients. The results of this study suggest that elderly patients are more resistant to cyclopropane-carbon dioxide arrhythmias than young healthy adults and that thiopental has antiarrhythmic actions.

PRICE, Lurie, and their associates,[1,2] in a series of experiments in man, demonstrated a relationship between alveolar cyclopropane and carbon dioxide concentrations necessary to produce ventricular arrhythmias in unpremedicated healthy subjects not undergoing operation. An increase in the concentration of either cyclopropane or carbon dioxide tended to increase the incidence of arrhythmias; values for an "arrhythmic threshold" were obtained in terms of combinations of cyclopropane and carbon dioxide. Their subsequent studies indicated that hypercarbia increased cardiac sympathetic stimulation, thus precipitating ventricular arrhythmias in the presence of cyclopropane.

We recently reported an anesthetic technique which utilizes deliberate hypercarbia during cyclopropane anesthesia to increase cerebral blood flow during carotid endarterectomy.[3] Since the patients studied were elderly and many had hypertensive or coronary heart disease, we anticipated a high incidence of ventricular arrhythmias during hypercarbia. Unexpectedly, arrhythmias occurred only twice during 66 operations at alveolar carbon dioxide tensions estimated to be between 48 and 60 mm. Hg.[3] To explore the reasons for this low incidence of arrhythmias, we undertook a systematic study of the arrhythmic threshold in a patient population which differed markedly from the healthy subjects studied by Price and Lurie *et al.* During these studies the effect of thiopental on the arrhythmias produced was investigated also.

Methods

The study was carried out during 50 operations on 47 patients. Forty-one patients had carotid endarterectomy with patch angioplasty. Three of these had a second carotid endarterectomy on the opposite side five to seven days after the first operation. Cyclopropane with deliberate hypercarbia was used as the anesthetic technique. Five patients were studied during resection of an abdominal aneurysm and one patient during the insertion of a femoral popliteal bypass graft. These six patients served as controls for the operative procedure. Pertinent characteristics of the patients, divided into two groups on the basis of anesthetic management, are summarized in table 1. No patient had an arrhythmia before operation. All had at least one preoperative electrocardiogram. No patient received digitalis or an antiarrhythmic drug before operation.

* Assistant Professor.
† Instructor.
‡ Professor and Head of Division of Anesthesiology.

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TABLE 1. Patient Characteristics by Groups

	Group (Number of Patients)		
	I	II	Total
Number in group	25	22	47
Mean age (years)	63	65	64
Age range (years)	41–81	53–77	41–81
Male	15	14	29
Female	10	8	18
Previous myocardial infarction	7	4	11
Previous stroke	4	15	19
Abnormal ECG without infarction	3	6	9
Hypertension*	6	13	19

*Systolic or diastolic pressure greater than 150/90 mm. Hg.

The basic anesthetic management for all patients was as follows. Patients were given morphine (6–8 mg.) or meperidine (50–75 mg.) intramuscularly with 0.2 mg. of atropine or scopolamine 60–90 minutes before induction of anesthesia. Anesthesia was induced with 100–200 mg. thiopental and cyclopropane in Group I patients and with cyclopropane alone in Group II patients. Endotracheal intubation was accomplished following the intravenous administration of 50–100 mg. succinylcholine. Atropine, 0.2 mg. was given intravenously before the succinylcholine to decrease the incidence of bradycardia. A 16-gauge plastic catheter was placed in the lumen of the endotracheal tube and fixed so that it projected 1 cm. beyond the distal end of the tube; the proximal end was passed through the nipple of a Rovenstine elbow as the source of end-tidal gas samples. After tracheal intubation, cyclopropane was administered at a rate of 200–300 ml. with 1,000 ml./min. of oxygen in a closed-circle system, with periodic emptying of the rebreathing bag. In all patients an infusion of 0.2 per cent succinylcholine was administered to control respiration. An indwelling needle was placed in the radial artery; electrocardiographic leads were attached. Lead II of the ECG and arterial blood pressure as transduced by a Statham strain gauge were displayed on an oscilloscope, and records were made at 2-minute intervals on a Grass recorder. Hypercarbia was induced by hypoventilation using a controlled respiratory rate of 6–8 breaths per minute at a tidal volume not exceeding 500 ml. If arrhythmias did not appear within 10–15 minutes, the CO_2 absorber was eliminated from the circle system. The period of hypoventilation varied from 10–40 minutes depending on the appearance of arrhythmias. An arrhythmia was defined as the appearance on the electrocardiogram of two or more abnormal ventricular complexes occurring within a two-minute period. Whenever an arrhythmia appeared, arterial blood and alveolar gas were sampled simultaneously and ventilation was increased until the arrhythmia disappeared. In all patients undergoing carotid endarterectomy, the carotid bifurcation was infiltrated with 4 ml. 1 per cent lidocaine just after exposure to prevent reflex bradycardia and hypotension secondary to manipulation. Reflex bradycardia with hypotension did not occur in any patient.

The initial group of 25 patients who had 26 operations (Group I) was managed as described. Arterial blood and alveolar gas were sampled after five minutes of hypoventilation; just before clamping of the carotid artery; just before release of the carotid clamp; and at any time an arrhythmia appeared during the hypoventilation. In the second group of 22 patients who had 24 operations (Group II), induction of anesthesia by thiopental was omitted. Instead, anesthesia was induced with 50 per cent cyclopropane and arterial blood and alveolar gas were sampled simultaneously whenever an arrhythmia appeared. In the absence of an arrhythmia, samples were taken after 20 minutes of hypoventilation and at the end of the hypoventilation period (up to 40 minutes). Eight patients in Group II who developed arrhythmias were given 150 mg. 2 per cent thiopental intravenously over a 30-second period to observe the effect of thiopental on the arrhythmia. Ventilation was not altered during this period.

Arterial samples were collected anaerobically in heparinized syringes and iced immediately. Carbon dioxide tension (Pa_{CO_2}) was determined within 30 minutes at 38° C. using a modified Severnighaus electrode calibrated with known gas mixtures. Pa_{O_2} was measured with a modified Clark electrode, and arterial *p*H with a glass electrode. End-tidal gas samples were collected in 10-ml. glass syringes by

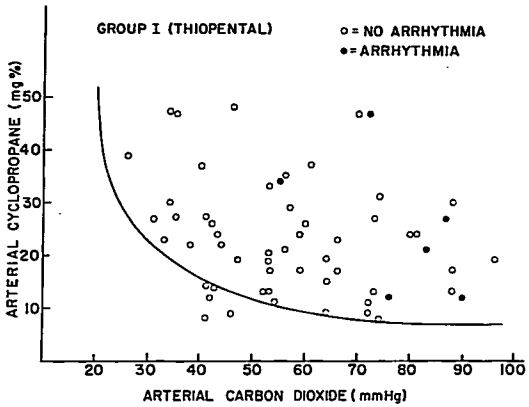

FIG. 1. Fifty-eight paired values of Pa_{CO_2} and arterial cyclopropane taken from 25 patients who received thiopental for induction of anesthesia, plotted in relation to the cyclopropane-hypercarbia arrhythmia threshold determined for young adults by Lurie *et al.*[1] Six patients developed arrhythmias at a mean Pa_{CO_2} of 77.2 ± 5.2 mm. Hg and a mean cyclopropane of 25.5 ± 1.9 mg./100 ml. Eight paired values fell at or below the previously-described threshold; none of these were associated with an arrhythmia. Forty-four of the 50 paired values which exceeded this threshold were not associated with arrhythmias.

aspirating the catheter within the endotracheal tube at the end of an expiration and during manual compression of the chest. The first 5 ml. of the sample were discarded and the remaining 5 ml. injected into a Scholander analyzer containing 31 N sulfuric acid.[1, 4] Four minutes were allowed for cyclopropane absorption and the percentage of cyclopropane was calculated from the unabsorbed gas volume. The accuracy of this method was determined by analysis of more than 100 samples of known concentrations of cyclopropane in oxygen ranging from 2 per cent to 80 per cent cyclopropane. Mixtures of cyclopropane were made up by water displacement. Cyclopropane concentrations as determined did not deviate more than 2 volumes per cent from the known concentration. Volumes per cent of cyclopropane in end-tidal air were converted to mg./100 ml. in blood using a solubility coefficient of 0.42 at 37° and a density of 1.65 mg./100 ml. at 37° C.[1, 5] Values of Pa_{CO_2} and mg./100 ml. of cyclopropane were rounded to whole numbers because of the wide range of values observed. Mean arterial blood pressure (MABP) was estimated by taking one third of the sum of systolic pressure plus twice the diastolic pressure.[6] In the statistical evaluation of the data, the conventional *t* test and chi-square were used. Results are reported as means ± standard error of means.

Results

Patients Who Received Thiopental (Group I)

During 26 operations in 25 patients, arrhythmias appeared in only six operations, or 23 per cent. During these operations, alveolar air and arterial blood were sampled simultaneously on 58 occasions. The paired values were plotted in relation to the arrhythmic threshold described by Lurie *et al.*[1] (fig. 1). Only eight combined values of arterial cyclopropane and Pa_{CO_2} fell at or below this threshold and none of these was associated with an arrhythmia. Of the 50 values which exceeded the threshold, only six, or 12 per cent, were associated with an arrhythmia, although 38 of the Pa_{CO_2} values exceeded 50 mm. Hg and 33 cyclopropane values exceeded 20 mg./100 ml. The highest values of cyclopropane and Pa_{CO_2} during which no arrhythmia appeared in each of 20 operations are presented in table 2, with the values at which arrhythmias appeared during the other six operations.

Patients Without Thiopental (Group II)

Thiopental was omitted in the second group of 22 patients studied during 24 operations. In five patients (26–30, inclusive) all preanesthetic drugs were omitted as well. Arrhythmias appeared during 20, or 83 per cent, of the operations in this group at the values for

TABLE 2. Highest $Paco_2$ and Arterial Cyclopropane in 25 Patients Who Received Thiopental (Group I)

Patient	$Paco_2$ (mm. Hg)	Cyclo. (mg./100 ml.
No Arrhythmia (20 Operations)		
1	72	11
2*	64	15
4†	64	9
5*	60	26
6†	42	26
7†	56	35
8	40	37
10†*	59	24
11*	88	30
12*	88	13
13†	53	19
14	47	19
15	66	17
16*	52	13
17	53	33
18	74	8
22	81	24
23a	96	19
24†	59	17
25	88	17
Mean ± SE	65.1 ± 3.7	20.6 ± 1.9
Arrhythmia (6 Operations)		
3	76	12
9	72	47
19†	90	12
20	83	21
21	55	34
23b	87	27
Mean ± SE	77.2 ± 5.2	25.5 ± 5.5
All patients Mean ± SE	67.9 ± 3.2	21.7 ± 1.9

† Previous myocardial infarction.
* Operation other than carotid endarterectomy.

cyclopropane and Pa_{CO_2} listed in table 3. The mean cyclopropane concentrations was significantly lower in Group II than in Group I ($P < 0.05$). There was, however, no significant difference in mean Pa_{CO_2} between the two groups. In those patients of Group II who developed arrhythmias, the arrhythmias appeared at a significantly lower mean cyclopropane concentration (16.5 ± 1.3 mg./100 ml.) than in those of Group I who developed arrhythmias (25.5 ± 5.5 mg./100 ml.) ($P < 0.05$). Although the mean Pa_{CO_2} of Group II patients who developed arrhythmias was also lower (71.6 ± 3.5 mm. Hg) than that of arrhythmia patients of Group I (77.2 ± 5.2 mm. Hg), the difference was not significant. The difference in incidence of arrhythmias for Group II (83 per cent) compared with Group I (23 per cent) was highly significant ($P < 0.01$). Although arrhythmias were more frequent when thiopental was omitted, the combined values of cyclopropane and Pa_{CO_2} still exceeded the previously-reported threshold of Lurie *et al.*[1] in 19 of 20 samples obtained in the absence of an arrhythmia (fig. 2).

TABLE 3. Highest $Paco_2$ and Arterial Cyclopropane in 22 Patients Who Did Not Receive Thiopental (Group II)

Patient	$Paco_2$ (mm. Hg)	Cyclo. (mg./100 ml.
No Arrhythmia (4 Operations)		
26†	96	11
30*†	86	10
33†	99	14
38	73	22
Mean ± SE	88.5 ± 5.9	14.3 ± 2.7
Arrhythmia (20 Operations)		
27*	64	21
28*	74	14
29*	83	14
31	61	31
32a	46	14
32b	84	13
34	93	16
35	74	15
36	40	19
37	52	7
39	73	25
40	83	10
41a†	76	21
41b†	86	17
42	55	20
43	70	16
44	72	16
45	61	21
46	86	8
47	100	12
Mean ± SE	71.6 ± 3.5	16.5 ± 1.3
All patients Mean ± SE	74.5 ± 3.3	16.1 ± 1.1

* No preanesthetic medication.
† Previous myocardial infarction.

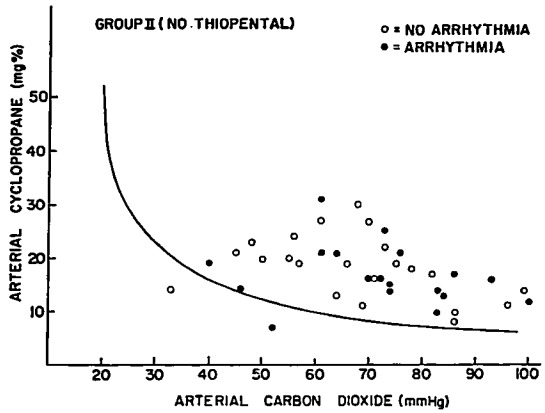

FIG. 2. Forty paired values of Pa_{CO_2} and arterial cyclopropane taken from 22 patients who did not receive thiopental, plotted in relation to the cyclopropane-hypercarbia arrhythmia threshold previously determined for young adults by Lurie *et al.*[3] In contrast to the group which received thiopental (fig. 1), arrhythmias occurred during 83 per cent of the operations. With one exception, the paired values of Pa_{CO_2} and arterial cyclopropane at which arrhythmias occurred fell to the right of the previously determined threshold. Nineteen of the 20 paired values not associated with arrhythmias also exceeded the threshold.

TREATMENT OF ARRHYTHMIAS WITH THIOPENTAL

During eight operations in seven patients of Group II, 150 mg. thiopental was given intravenously three to five minutes after the onset of an arrhythmia. Neither the respiratory pattern nor the tidal volume was altered during this time. Five of these patients had a bigeminal rhythm, two had multifocal ventricular extrasystoles and one had ventricular extrasystoles. In six of eight patients cardiac rhythm reverted to a sinus mechanism within 45 seconds after thiopental administration. There was no marked alteration in arterial blood pressure. The data for these eight patients, including Pa_{CO_2} and arterial cyclopropane values obtained at the time the arrhythmia disappeared, are summarized in table 4. No consistent changes in Pa_{CO_2} or arterial cyclopropane levels could account for the disappearance of the arrhythmia. Unless ventilation was increased, the arrhythmia tended to recur approximately five minutes after thiopental.

TYPES OF ARRHYTHMIAS

The arrhythmias observed during 26 operations were rarely of a single type in any patient. Most patients had more than one arrhythmia. Earliest to appear were ventricular extrasystoles or bigeminal rhythm. Ventricular extrasystoles tended to progress to bigeminal rhythm or multifocal ventricular extrasystoles, whereas bigeminal rhythm tended to remain as the established rhythm. On one occasion, atrial fibrillation, and on two occasions, ventricular tachycardia, appeared transiently. The predominant arrhythmia was bigeminy in 58 per cent of operations, ventricular extrasystoles in 15 per cent and multifocal ventricular extrasystoles in 27 per cent.

ROLE OF BLOOD PRESSURE

Hypercarbia during cyclopropane anesthesia consistently produced an increase in blood pressure. Mean arterial blood pressure (MABP) for all patients who did not develop an arrhythmia rose from a preanesthetic value of 111 ± 3.0 mm. Hg to a maximum of 127 ± 5.0 mm. Hg during anesthesia. In patients who developed an arrhythmia, MABP increased from 113 ± 2.4 mm. Hg before anesthesia to 130 ± 3.2 mm. Hg at the time an arrhythmia appeared. The differences in blood pressure between the arrhythmia and nonarrhythmia groups were not significant. Further comparisons within groups led to equivocal results. In Group I, the maximum MABP recorded in patients who did not develop arrhythmias was 125 ± 6.8 mm. Hg, compared with 140 ± 2.8 mm. Hg for MABP at the time an arrhythmia developed in the other patients. Although this difference was significant ($P < 0.05$) in Group I, a similar comparison for

TABLE 4. Effect of Intravenous Thiopental on Arrhythmias Precipitated by Hypercarbia During Cyclopropane Anesthesia

Patient	During Arrhythmia				After Thiopental			
	$Paco_2$ mm. Hg	Cyclo. mg./100 ml.	MABP mm. Hg	Arrhythmia	$Paco_2$ mm. Hg	Cyclo. mg./100 ml.	MABP mm. Hg	Arrhythmia
40	83	10	133	VEX	85	11	133	NSR
41a	76	21	133	Bigem	76	21	130	NSR
41b	86	17	125	Bigem	92	15	125	NSR
42	55	20	114	Bigem	73	10	116	NSR
44	72	16	—	MFVX	72	16	—	MFVX
45	61	21	107	Bigem	78	8	90	NSR
46	86	8	117	Bigem	86	8	118	Bigem
47	100	12	110	MFVX	100	12	110	NSR

VEX = ventricular extrasystole; Bigem = bigeminy; MFVX = multifocal ventricular extrasystoles; NSR = normal sinus rhythm.

Group II was not. Maximum MABP for patients in Group II who did not develop arrhythmias was 133 ± 2.7 mm. Hg; for those with arrhythmias, 131 ± 5.4 mm. Hg.

In Group I no patient with essential hypertension (preoperative blood pressure 150/90 to 200/100 mm. Hg) developed an arrhythmia. All 13 patients with hypertension in Group II (preoperative blood pressure 140/100 to 220/130 mm. Hg) developed arrhythmias. A relationship between MABP and the appearance of arrhythmias could not be identified.

ROLE OF OTHER FACTORS IN DEVELOPMENT OF ARRHYTHMIAS

Although arterial oxygen tensions were determined for all blood samples, the results are not reported, since the lowest value of any one sample was 160 mm. Hg. Thus, hypoxia could not have played a role in these arrhythmias. Similarly, *p*H values are not reported, since they were correlated strongly with Pa_{CO_2} and their separate consideration provided no additional information.

Infiltration of the carotid bifurcation with lidocaine was performed during all carotid endarterectomies. The possible effect of this procedure on arrhythmias was examined in the six patients having operations other than carotid endarterectomy. All six patients were in the group who received thiopental; none developed an arrhythmia (table 2). The mean Pa_{CO_2} (68.5 ± 6.4 mm. Hg) and mean arterial cyclopropane (20.2 ± 3.0 mg./100 ml.) of these six patients were not significantly different from the means of the other patients in this group who did not develop arrhythmias (Pa_{CO_2} 63.3 mm. Hg and C_3H_6 20.8 mg./100 ml.). There was no evidence that these patients behaved differently than those undergoing carotid endarterectomy.

Separate analysis of the data for the five patients in Group II who did not receive preoperative narcotic or anticholinergic drugs led to a similar conclusion. Three (60 per cent) developed arrhythmias at a mean Pa_{CO_2} of 73.6 mm. Hg and mean cyclopropane concentration of 16.3 mg./100 ml. The mean values were similar to those of the other patients in Group II who received preanesthetic drugs and developed arrhythmias.

Since most patients had more than one arterial sample drawn during the development of hypercarbia, the rate of rise of Pa_{CO_2} could be estimated. Since carbon dioxide was not added to the circle system and carbon dioxide absorption was used at times, the rate of rise of Pa_{CO_2} was uniformly low, ranging from 0.22 to 2.30 mm. Hg/min. (mean 1.19 ± 0.12 mm. Hg/min.). Within this narrow range no correlation was found between the appearance of arrhythmias and rate of rise of Pa_{CO_2}.

Attempts to relate a history of myocardial infarction, a history of cerebrovascular accident, preoperative electrocardiographic abnormalities, age and sex to the incidence of arrhythmias, differences in arrhythmic thresholds, or differences between Groups I and II were unsuccessful. These subgroups possibly were too small for correlations. It was of interest, however, that 82 per cent of the pa-

tients with histories of myocardial infarction did not develop arrhythmias. Only one hospital death occurred among the patients studied. A 72-year-old man (Patient 11) died on the second postoperative day after resection of an abdominal aneurysm, as a result of acute myocardial infarction.

Discussion

These data demonstrate a higher threshold for cyclopropane-hypercarbia arrhythmias in elderly patients with known disease of the cardiovascular system than in young healthy adults. The data also suggest that thiopental may protect against rather than precipitate arrhythmias during cyclopropane anesthesia as has been suggested by studies in animals.[7, 8, 9, 10] Several major differences exist between the circumstances of this study and the studies of Lurie *et al.*[1] and Price *et al.*[2] These differences should be examined to identify their possible roles in effecting the observed lower incidence of arrhythmias.

Apart from the obvious differences in age and the presence of cardiovascular disease, the patients in this study differed from those of Lurie *et al.*[1] in that they received a narcotic, atropine or scopolamine, thiopental, succinylcholine and lidocaine during operations on the carotid artery. In addition, hypercarbia was developed by endogenous accumulation rather than by addition of carbon dioxide to the breathing circuit.

The effect of preoperative narcotic and anticholinergic drugs on the arrhythmic threshold was examined in five patients, who were found to behave no differently from those who received preanesthetic drugs. It might be anticipated, however, that narcotics and succinylcholine, by increasing vagal tone,[11, 12] and atropine or scopolamine, by decreasing vagal tone,[13] could affect the incidence of arrhythmias during cyclopropane anesthesia. In all animals studied by Dresel and his associates,[9, 10] bilateral vagotomy was performed to facilitate the appearance of cyclopropane-induced arrhythmias. Jones, Deutsch and Turndorf[13] demonstrated that rapid intravenous administration of 0.2–0.6 mg. of atropine during cyclopropane anesthesia in man often precipitated ventricular arrhythmias. Williams *et al.*,[14] in a similar study, showed that rapid administration of succinylcholine during cyclopropane anesthesia precipitated ventricular arrhythmias in a high percentage of patients. Although similar studies with a narcotic have not been performed, Orth, Wangeman and Meek[15] suggested that preoperative use of morphine increased the incidence of arrhythmias during cyclopropane anesthesia. Their observations, however, were made before the role of hypercarbia in cyclopropane arrhythmias was generally recognized. In the present study, all drugs were given either in small doses intramuscularly or by slow intravenous administration. If these drugs altered the incidence of arrhythmias, they would be expected to increase the observed incidence. The converse, a lower-than-expected incidence of arrhythmias, was observed.

The role of infiltration of the carotid bifurcation with lidocaine was more difficult to assess, beyond the assessment attempted by study of six patients undergoing operations other than carotid endarterectomy. It is likely that 40 mg. lidocaine injected directly into the exposed carotid sheath could block the vagus nerve on that side and increase the incidence of arrhythmias.[9, 10, 13] It is unlikely, however, that this small volume of lidocaine solution injected in exposed tissues would spread to the stellate ganglion and protect against ventricular arrhythmias.[2] On the other hand, systemic absorption of 40 mg. lidocaine conceivably could exert an antiarrhythmic effect.[16] Some protection against arrhythmias by infiltration of the carotid bifurcation, therefore, cannot be excluded, although it is unlikely.

In the study of Lurie *et al.*,[1] carbon dioxide was added to the breathing circuit and the arrhythmic threshold, expressed in terms of alveolar carbon dioxide tension ($P_{A_{CO_2}}$), was directly related to the rate of rise of $P_{A_{CO_2}}$. Since alveolar rather than arterial carbon dioxide tension was measured during administration of carbon dioxide, a positive gradient of carbon dioxide tension existed from alveolus to blood. This gradient would be expected to be proportional to the rate of rise of $P_{A_{CO_2}}$ and the arrhythmic threshold in terms of $P_{A_{CO_2}}$ would be overestimated in proportion to the gradient. In the present study, arterial rather than alveolar carbon dioxide tension was measured. The rate of rise of $P_{a_{CO_2}}$ was low com-

pared to those of Lurie *et al.*,[1] and was within the range expected from studies of diffusion respiration.[17] For these reasons arrhythmic threshold values were expected to be lower in this study than those reported by Lurie *et al.*[1] The converse, a high threshold, was observed.

It seems reasonable, therefore, to conclude that differences in patient population account primarily for the differences in arrhythmic thresholds, and that elderly patients are more resistant to cyclopropane-hypercarbia arrhythmias than younger patients. Unfortunately, no precise information is available to document differences in cardiovascular responses to most drugs with increasing age. Possibly with age the myocardium becomes less excitable and less susceptible to arrhythmias in the absence of specific cardiac disease. Since stimulation of the cardiac sympathetic nerves is a major factor in the production of cyclopropane-hypercarbia arrhythmias, it is possible that with increasing age there is less sympathetic response to stimuli such as those induced by cyclopropane. This, too, could explain the difference in threshold. Unfortunately, data to support either postulate are lacking.

Of special interest is the apparent protective and therapeutic effect of thiopental as an antiarrhythmic agent. Robbins, Baxter and Fitzhugh[20] reported that dogs anesthetized with cyclopropane but given an oxybarbiturate before anesthesia had a lower incidence of arrhythmias than when the oxybarbiturate was omitted. They were also able to abolish some arrhythmias in these dogs by the intravenous administration of sodium amytal. Johnstone[18] produced arrhythmias by deliberate hypercarbia in two patients during thiopental anesthesia; these were abolished by administration of an additional 250 mg. of thiopental. In another patient with ventricular extrasystoles before anesthesia, the induction of anesthesia by thiopental caused disappearance of the extrasystoles. Seuffert and Urbach[19] recently reported a lower incidence of arrhythmias during cyclopropane anesthesia in patients in whom anesthesia was induced by thiopental, compared with a similar group of patients induced by cyclopropane alone.

These reports suggesting an antiarrhythmic action of thiopental are in direct contrast to those of several investigators who studied the effect of thiopental on arrhythmias in dogs.[7-10] In dogs lightly anesthetized with ether, Gruber, Haury and Gruber,[7] and Gruber and Lonergan[8] observed that intravenous thiopental produced a pressor response and precipitated arrhythmias. Thiopental also increased the incidence of arrhythmias which followed carotid compression. Arrhythmias appeared only when a pressor response was induced by the thiopental, however, and they could be made to disappear if additional thiopental reduced blood pressure. They concluded that the level of arterial blood pressure was the critical factor in the initiation of arrhythmias by thiopental. Their observation that thiopental elicits a pressor response in dogs has not been confirmed by others.[9, 10, 20] MacCannell and Dresel[9] found that smaller doses of epinephrine were required to produce arrhythmias in dogs during cyclopropane anesthesia when they had received thiopental for induction of anesthesia. A bilateral vagotomy was performed prior to study, since Dresel and Sutter[10] previously had observed that the intact vagus appeared to exert a "protective" effect against epinephrine–cyclopropane arrhythmias. They also observed that stimulation of the peripheral end of the cut vagus nerve could abolish epinephrine-induced arrhythmias during cyclopropane anesthesia.

The mode of action of thiopental as an antiarrhythmias agent can only be speculated upon. It is possible that clinical doses exert a direct depressant effect upon the myocardium[21] and that this action outlasts its hypnotic effects. It is also possible that thiopental, by its central nervous system action, increases vagal tone or decreases cardiac sympathetic stimulation in response to cyclopropane. This modification of the response of cyclopropane may be specific for thiopental or simply secondary to an increase in depth of anesthesia not apparent clinically. Finally, the ability of cyclopropane to "sensitize" the myocardium may be altered by thiopental.

Conclusions and Summary

Simultaneous measurements of arterial carbon dioxide and cyclopropane concentrations, during 50 operations in 47 elderly patients with cardiovascular disease, indicated that in the patient population studied the threshold for cyclopropane-carbon-dioxide-induced arrhythmia was considerably higher than that

of the young, healthy adult. A further increase in arrhythmic threshold was observed in those patients in whom anesthesia was induced by thiopental. Thiopental also appeared to possess anti-arrhythmic activity, because in six of eight patients who had not received thiopental previously, intravenous administration of thiopental converted arrhythmias to normal sinus rhythm.

These data suggest that in this particular patient population, deliberate hypercarbia may be given with impunity. Carbon dioxide long has been held responsible for many adverse effects of general anesthesia. Deliberate hypercarbia may find other areas of use in anesthesiology.

That thiopental exerts an antiarrhythmic action has been suggested previously. The mode of action of thiopental as an antiarrhythmic agent is not known. The divergent results from comparative pharmacologic studies of thiopental in the dog and man suggests a need for a careful reappraisal of the pharmacology of this agent in man.

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