The Effects of Halothane Anesthesia on Reflex Cardiovascular Responses to Simulated Diving and the Valsalva Maneuver

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The authors studied the effects of halothane on the simulated diving reflex and the Valsalva maneuver in man. Arterial blood pressure, heart rate, cardiac output by ballistocardiogram and other measurements of cardiovascular function were recorded. Diving was simulated by application of a wet cloth at 0 C to the face with simultaneous apnea. The Valsalva maneuver was effected by raising the airway pressure to 25–30 torr for 25–30 sec. Simulated diving in the conscious subject decreased heart rates as much as 29 per cent from the lowest control heart rate, compared with a 3.6 per cent decrease during halothane anesthesia. Bradycardia was associated with increases in systolic and diastolic blood pressures in conscious and anesthetized subjects. The decrease in cardiac output observed in conscious subjects did not occur during anesthesia. Anesthesia apparently abolishes the parasympathetic component of the simulated diving reflex and interferes with the sympathetic component of this reflex. During phases II, III, and IV of the Valsalva maneuver greater decreases in blood pressure and increases in heart rate were observed during anesthesia. Halothane reduces or abolishes the circulatory reflex responses to diving and to the Valsalva maneuver in man. (Key words: Halothane; Valsalva maneuver; Ballistocardiogram; Diving reflex; Cardiac output; Apnea.)

ANESTHESIA modifies man's responses to many stimuli. Pain and other noxious stimuli no longer arouse him[1]; his respiratory response to carbon dioxide (and probably to hypoxia as well) is reduced or abolished.[2,3] Although circulatory regulatory mechanisms in animals generally are altered by anesthetics,[4,5] alterations of circulatory reflexes by anaesthesia are more difficult to assess. The difficulty arises because of the subtlety of these reflexes in man and the complexity of precise measurements of cardiovascular function. During studies of the effects of halothane on the circulation of human volunteers we had the opportunity to measure the effects of halothane on two circulatory reflexes. The results of these studies are reported.

The cardiovascular response of diving mammals (seals, porpoises) to submersion include bradycardia, decreased cardiac output, and decreased peripheral blood flow.[6] Land mammals such as man appear to have an attenuated diving reflex. Diving may be simulated in man by application of a cold (0 C) wet cloth to the face of an apneic subject.[7] Pentobarbital anesthesia has been shown to abolish the bradycardia of simulated diving in dogs and seals.[5]

In 1707, Valsalva described the effects of a sudden, voluntary sustained increase in intrathoracic pressure, which became known as the Valsalva maneuver. The cardiovascular response to the Valsalva maneuver has five phases. The first phase, lasting 1–2 sec, consists of an abrupt increase in peripheral arterial pressure caused by the increase in intrathoracic pressure. Since there is little change in heart rate or pulse pressure, transmural pressure changes within the aorta are not altered and the aortic baroreceptors are not stimulated. The transmural pressure (the intra-

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TABLE 1. Baseline Heart Rates and Blood Pressures Prior to Simulated Diving at Different Levels of Anesthesia

	Prior to Breath-holding Alone	Prior to Cold Alone	Prior to Cold + Apnea
	$\bar{X} \pm$ SE	$\bar{X} \pm$ SE	$X \pm$ SE
Preanesthesia			
Lowest systolic blood pressure (torr)	129 ± 3.17	129 ± 4.01	134 ± 3.38
Lowest diastolic blood pressure (torr)	80.7 ± 3.63	76.8 ± 4.33	80.2 ± 3.19
Highest systolic blood pressure (torr)	142 ± 2.93	139 ± 3.68	146 ± 3.14
Highest diastolic blood pressure (torr)	89.3 ± 3.53	82.0 ± 4.22	86.7 ± 3.80
Lowest heart rate (beats/min)	73.2 ± 3.27	73.7 ± 4.11	74.8 ± 3.55
Highest heart rate (beats/min)	89.7 ± 4.70	83.8 ± 2.56	88.0 ± 3.42
MAC 1.0–1.2			
Lowest systolic blood pressure (torr)	83 ± 4.72	84 ± 4.28	85 ± 4.90
Lowest diastolic blood pressure (torr)	52 ± 3.13	53 ± 2.59	54 ± 2.92
Highest systolic blood pressure (torr)	87 ± 4.48	101 ± 4.23	94 ± 4.42
Highest diastolic blood pressure (torr)	55 ± 3.38	63 ± 2.85	58 ± 2.30
Lowest heart rate (beats/min)	73 ± 1.09	73 ± 1.56	71 ± 1.14
Highest heart rate (beats/min)	79 ± 1.77	80 ± 2.07	81 ± 0.61
MAC 1.9			
Lowest systolic blood pressure (torr)	71 ± 5.76	77 ± 4.77	73 ± 4.45
Lowest diastolic blood pressure (torr)	49 ± 3.93	51 ± 3.21	49 ± 3.02
Highest systolic blood pressure (torr)	77 ± 5.44	87 ± 4.52	81 ± 4.60
Highest diastolic blood pressure (torr)	51 ± 3.79	55 ± 2.93	54 ± 3.03
Lowest heart rate (beats/min)	75 ± 3.04	79 ± 3.24	78 ± 3.45
Highest heart rate (beats/min)	79 ± 3.28	83 ± 2.98	87 ± 3.38

luminal minus the extravascular pressure) in the periphery, including the carotid sinus, is increased, but apparently has little or no effect on the heart rate. In the second phase the sustained intrathoracic pressure impairs venous return to the thorax, reducing cardiac output, pulse pressure and mean arterial pressure to normal or less. This reduction in mean arterial pressure lasts only a few seconds because it is due to barostatic reflex vasoconstriction in response to reduced arterial pressure. Transmural and intraluminal pressures may then rise in the third phase of the Valsalva maneuver. In the fourth phase, lasting 1–2 sec, the intrathoracic pressure is released and the arterial pressure decreases in an amount equal to the decrease in thoracic pressure. Venous return increases and produces the fifth phase, in which arterial pressure and pulse pressure increase to above control levels and heart rate decreases. Persistence of the vasoconstriction of phase II probably accounts for the pressure overshoot, and the bradycardia probably results from concomitant cardiac inhibition by baroreceptors.[9] Price *et al.* found that profound cyclopropane anesthesia alters the effects of the Valsalva maneuver. A positive intrapulmonary pressure of 22–25 cm H_2O failed to reduce arterial blood pressure, and did so only slightly at lower levels of anesthesia. This altered response to increased airway pressure appeared to result from marked increases in intrathoracic venous and right atrial pressures produced by cyclopropane.[10]

Methods

Eight male volunteers ranging in age from 21 to 36 years served as subjects. An informed consent was obtained from each individual. The protocol for these procedures was approved by both the Stanford University and the University of California Committees on Human Experimentation. Each subject lay supine on an ultralow-frequency air-supported honeycombed aluminum ballistocardiograph bed (weight: 6.5 pounds, fn—0.18 Hz).[11] A foot brace aided in coupling the subject to the bed. Acceleration was transduced in the head–foot direction with a variable-capacitance accelerometer. Cardiac output (COB) was determined from the ballistocardiogram (Bcg). Under local anesthesia a catheter was passed percutaneously into a brachial artery. Blood pressure (BP) was transduced with a Statham P23Gb strain gauge. Mean arterial pressure ($\overline{AP}$) was obtained by electrical damping. A

TABLE 2. Maximum Percentage Changes in Blood Pressure and Heart Rate during the Three Tests of Simulated Diving at Different Anesthetic Levels

	Breath-holding Alone		Cold Alone		Cold + Apnea	
	X ± SE	Time in Seconds*	X ± SE	Time in Seconds*	X ± SE	Time in Seconds*
Preanesthesia						
Lowest systolic blood pressure	+0.30 ± 2.72	25.9	− 3.54 ± 2.20	38.3	+ 2.60 ± 1.97	15.8
Lowest diastolic blood pressure	−2.36 ± 2.64	25.9	− 0.84 ± 2.71	38.3	+ 2.26 ± 2.14	15.8
Highest systolic blood pressure	+9.71 ± 2.19	71.8	+19.2 ± 4.63	85.3	+17.7 ± 2.67	89.0
Highest diastolic blood pressure	+6.64 ± 2.54	71.8	+19.5 ± 5.61	85.3	+20.8 ± 4.13	89.0
Lowest heart rate	−6.26 ± 5.03	50.2	−26.4 ± 5.68	54.6	−29.1 ± 7.56	62.4
Highest heart rate	+3.80 ± 2.94	27.8	+ 5.93 ± 3.75	33.9	+ 5.46 ± 3.33	19.7
MAC 1.0–1.2						
Lowest systolic blood pressure	−1.25 ± 2.58	25.7	− 0.87 ± 1.61	11.3	− 2.07 ± 0.37	27.0
Lowest diastolic blood pressure	−1.60 ± 1.13	25.7	− 0.10 ± 0.78	11.3	+ 1.20 ± 1.86	27.0
Highest systolic blood pressure	+3.55 ± 0.04	56.5	+11.7 ± 5.15	94.3	+ 8.03 ± 6.12	82.7
Highest diastolic blood pressure	−1.60 ± 1.13	56.5	+18.5 ± 10.1	94.3	+11.5 ± 8.46	82.7
Lowest heart rate	−5.10 ± 1.27	88.0	+ 0.80 ± 0.65	10.8	− 3.40 ± 1.56	37.5
Highest heart rate	−3.13 ± 2.09	14.5	+10.7 ± 4.75	115	+ 4.73 ± 3.38	62.5
MAC 1.9						
Lowest systolic blood pressure	+0.16 ± 1.09	40.6	− 1.74 ± 0.75	23.7	− 0.25 ± 0.67	30.6
Lowest diastolic blood pressure	−0.53 ± 0.71	40.6	− 1.38 ± 1.00	23.7	− 0.19 ± 0.63	30.6
Highest systolic blood pressure	+1.64 ± 2.18	56.6	+ 7.60 ± 2.24	99.1	+ 2.95 ± 1.42	106
Highest diastolic blood pressure	+2.51 ± 1.91	56.6	+ 6.07 ± 2.36	99.1	+ 9.66 ± 2.46	106
Lowest heart rate	−5.11 ± 1.09	34.9	− 0.25 ± 0.49	13.0	− 3.60 ± 1.28	19.6
Highest heart rate	−1.41 ± 1.44	32.9	+ 4.45 ± 1.77	112	+ 7.97 ± 1.11	96.6

* Average time after application of stimulus (breath-holding and/or cold).

polyethylene catheter was inserted percutaneously under local anesthesia into the basilic vein and guided blindly into the right ventricle as determined by the ventricular pressure tracing. The catheter was then withdrawn into the right atrium, as indicated by an abrupt change in the ventricular pressure tracing, and left in this position to record right atrial pressure (RAP). A catheter was inserted into a forearm vein also. Forearm blood flow (FBF) was measured by occlusion plethysmography using a Whitney mercury in Silastic strain gauge. The strain gauge was placed about the greatest circumference of the forearm. A cuff at the wrist was inflated throughout the period of FBF measurement to occlude both arterial and venous blood flows. The cuff on the arm was then inflated to occlude venous outflow. The resulting change in forearm circumference was determined from the change in the electrical resistance of the mercury. Flow per 100 ml of tissue per minute was computed as 200 $\Delta C/C$, where C was the forearm circumference and ΔC was the change in circumference per minute. All data were recorded simultaneously on an Offner recorder and a seven-channel FM magnetic tape recorder.

The data were played back from the tape recorder into a general-purpose analog computer. The computer was programmed to calculate stroke volume (SV) from the Bcg with the Starr formula:

$$SV = K\sqrt{(2\,I_{dt} + J_{dt})}\sqrt{C}$$

in which K = a constant programmed into the computer, C = cardiac cycle (R-R interval of the electrocardiogram), I_{dt} = area under the I wave, and J_{dt} = area under the J wave. The computer program used operational relay logic to select the I and J waves of the Bcg. The desired operations of integration, addition, multiplication and square-root extraction were simultaneously performed beat by beat. Each R wave of the electrocardiogram (ECG) reset the computer and began a new calculation. Stroke volume rather than aortic flow was obtained by this method. The computer was programmed further to compute COB from heart rate (HR) and SV as well as left ventricular minute work (LVW) and total peripheral resistance (TPR) from $\overline{AP}$, RAP and COB. The ECG, SV, COB, HR, $\overline{AP}$, LVW and TPR were recorded from the computer onto a rectilinear oscillograph (Brush Instruments, Cleveland, Ohio). To validate the Bcg–computer system, cardiac output determinations were made with a dye-injection apparatus. Following intravenous injection of Cardio-green, blood was withdrawn from the brachial artery with an infusion-withdrawal pump and passed immediately through a Cardiodensitometer. A disc integrator permitted calculation of cardiac output from the resultant dye-dilution curve by forward triangulation. The withdrawn blood was reinfused after each determination. The densitometer was calibrated after each study with serial dilutions of dye in a sample of each subject's blood obtained before injection of the dye.[12]

TABLE 3. Comparisons of Percentage Changes in Heart Rate and Blood Pressure during Different Levels of Anesthesia*

MAC 1.0–1.2	P NS†
MAC 1.9	
Slowest rate	
BA *vs.* CA	NS
BA *vs.* C + A	NS
CA *vs.* C + A	NS
Fastest rate	
BA *vs.* CA	<0.05
BA *vs.* C + A	<0.001
CA *vs.* C + A	NS
Preanesthesia	
Highest systolic blood pressure	
BA *vs.* CA	<0.10
BA *vs.* C + A	<0.05
CA *vs.* C + A	NS
Highest diastolic blood pressure	
BA *vs.* CA	<0.10
BA *vs.* C + A	<0.025
CA *vs.* C + A	NS
Slowest heart rate	
BA *vs.* CA	<0.05
BA *vs.* C + A	<0.05
CA *vs.* C + A	NS

* BA denotes breath-holding alone; CA denotes cold alone; C + A denotes cold plus apnea.

† NS = No significant difference found.

Simulated diving and the Valsalva maneuver were studied with the subjects conscious and during halothane anesthesia. Each subject lay supine and breathed either oxygen or oxygen-halothane through a mouthpiece (while conscious) or an endotracheal tube (while anesthetized) while baseline arterial BP, $\overline{AP}$, RAP, HR, and COB were recorded for two minutes. To test the diving reflex we repeated these measurements during 1) cessation of respiration in midinspiration (breath-holding alone) for two minutes; 2) application of a wet cloth at 0 C to the subject's face (the cloth encircled the mouthpiece or endotracheal tube) during spontaneous respiration for two minutes (cold

TABLE 4. Baseline Values Prior to Diving Simulated by Cold Plus Apnea at Different Levels of Anesthesia

	Preanesthesia	MAC 1.0–1.2	MAC 1.9
Cardiac output (1/min)	7.03 ± 0.50	5.00 ± 0.42	4.12 ± 0.63
Stroke volume (ml)	77.7 ± 11.0	59.2 ± 12.9	46.9 ± 10.5
Heart rate (beats/min)	94.5 ± 5.14	84.5 ± 0.99	87.8 ± 2.93
Left ventricular minute work (kg-m/min)	9.5 ± 1.0	4.8 ± 0.61	3.4 ± 0.54
Mean arterial pressure (torr)	109 ± 4.25	71.5 ± 3.17	61.2 ± 3.77
Central venous pressure (torr)	1.93 ± 2.39	7.25 ± 3.40	7.42 ± 3.20
Total peripheral resistance (dynes/sec/cm^{-5})	1,735 ± 262	1,026 ± 59.0	1,044 ± 34.7

TABLE 5. Percentage Changes from Baseline Values during the Five-second Period of Diving (Simulated by Cold Plus Apnea) Having the Lowest Cardiac Output

	Preanesthesia		MAC 1.0–1.2		MAC 1.9	
	X ± SE	Time in Seconds*	X ± SE	Time in Seconds*	X ± SE	Time in Seconds*
Cardiac output	−23.0 ± 10.2	96.8	−2.85 ± 1.83	53.3	−1.94 ± 7.11	82.1
Stroke volume	−0.61 ± 5.42	96.8	+1.98 ± 9.40	53.3	−4.21 ± 7.19	82.1
Heart rate	−27.2 ± 6.69	96.8	−0.83 ± 2.64	53.3	+1.08 ± 1.15	82.1
Left ventricular minute work	−19.5 ± 10.4	96.8	+1.11 ± 7.50	53.3	−0.81 ± 6.25	82.1
Mean arterial pressure	+12.9 ± 3.26	96.8	+7.05 ± 5.22	53.3	+3.4 ± 4.57	82.1
Central venous pressure (torr) (absolute difference)	+7.35 ± 1.40	96.8	+2.75 ± 0.87	53.3	+1.35 ± 0.81	82.1
Total peripheral resistance	+52.8 ± 15.0	96.8	+7.41 ± 5.82	53.3	+10.4 ± 8.99	82.1

* Time after application of cold plus apnea in which the measurements were obtained.

alone); 3) application of a wet cloth as in 2 while respiration was stopped in midinspiration for two minutes (cold plus apnea). In a fourth test, we measured forearm blood flow immediately before and then during application of a wet cloth at 0 C to the face during two minutes of apnea in midinspiration.

Baseline arterial BP, CVP and HR were re-

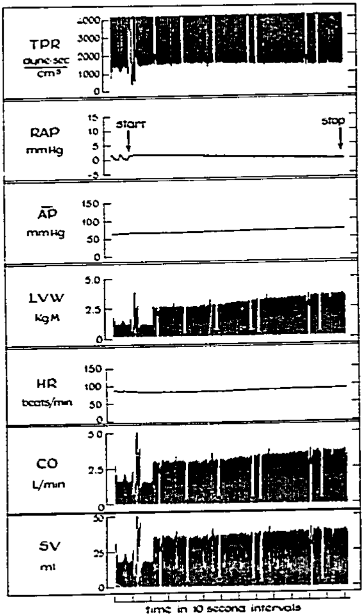

FIG. 1. Ballistocardiograph of diving reflex simulated by cold plus apnea at MAC 1.0 (0.8 per cent halothane).

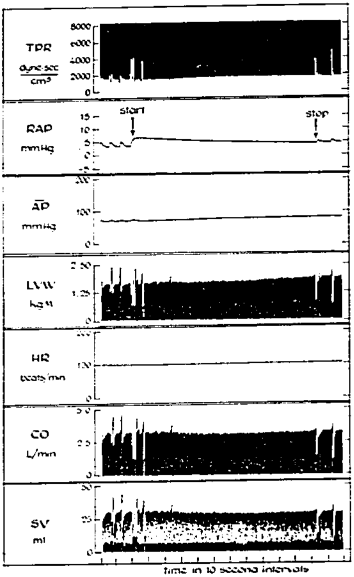

FIG. 2. Ballistocardiograph of diving reflex simulated by cold plus apnea at MAC 1.9 (1.6 per cent halothane).

corded continuously immediately prior to, during, and after the Valsalva maneuver. After baseline measurements had been obtained, the airway pressure was raised to 25–30 torr, measured with a mercury manometer by squeezing the reservoir bag, and apnea was maintained at this pressure for 25–30 sec. The airway pressure was then released and regular respirations resumed.

We induced anesthesia by mask with halothane and oxygen. When anesthesia reached a sufficient depth we intubated the trachea with a cuffed endotracheal tube. Except during the periods of apnea, ventilation was controlled to maintain arterial P_{CO_2} between 35 and 40 torr. Each subject was studied with alveolar halothane concentrations held at 0.8–1.0 per cent (1.0–1.2 MAC) (light anesthesia) and at 1.6 per cent (1.9 MAC) (deep anesthesia).[13, 14]

Results

DIVING REFLEX

Arterial BP and HR changes were recorded as: lowest systolic BP, lowest diastolic BP, highest systolic BP, highest diastolic BP, lowest HR, and highest HR. Baseline values for 1.0–1.2 MAC and 1.9 MAC are given in table 1. The percentage changes effected by each test at 1.0–1.2 MAC and 1.9 MAC are recorded in table 2, except for CVP, for which the absolute difference from baseline was used. Significant differences between percentage changes effected by each test at the two levels of anesthesia are recorded in table 3.

TABLE 6. Percentage Changes from Baseline Values during the Five-second Period of Simulated Diving Which Had the Highest Mean Cardiac Output*

	MAC 1.0–1.2 $\bar{X} \pm$ SE	MAC 1.9 $\bar{X} \pm$ SE
Cardiac output	18.1 ± 5.2	5.9 ± 4.3
Stroke volume	17.0 ± 4.6	7.2 ± 3.8
Heart rate	−1.8 ± 1.2	1.07 ± 0.83
Left ventricular minute work	20.6 ± 7.5	8.6 ± 7.9
Mean arterial pressure	−2.7 ± 2.3	4.2 ± 3.8
Central venous pressure	+0.3 ± 1.13	+1.2 ± 0.4
Total peripheral resistance	−15.6 ± 5.7	−2.1 ± 1.8

* Diving simulated by cold plus apnea.

Absolute baseline COB, SV, HR, LVW, $\overline{AP}$, CVP, and TPR values were obtained from averages of values during the five seconds before

TABLE 7. Blood Pressures, Heart Rates and Central Venous Pressures during the Valsalva Maneuver before and after Anesthesia*

	Baseline Values	Changes from Baseline Values				
	X ± SE	Phase I $\bar{X} \pm$ SE	Phase II $\bar{X} \pm$ SE	Phase III $\bar{X} \pm$ SE	Phase IV $\bar{X} \pm$ SE	Phase V $\bar{X} \pm$ SE
Preanesthesia						
Systolic blood pressure	132 ± 2.73	+2.12 ± 0.97	−7.87 ± 2.29	+3.85 ± 1.55	−3.09 ± 1.80	+7.49 ± 1.38
Diastolic blood pressure	77.7 ± 3.13	+0.54 ± 1.95	−8.28 ± 1.78	+8.02 ± 2.81	+4.29 ± 2.71	+9.64 ± 2.69
Heart rate	76.9 ± 2.85	+4.24 ± 2.49	−11.3 ± 2.27	−13.6 ± 6.12	−9.06 ± 2.75	−8.69 ± 4.32
Central venous pressure (torr) (absolute)	1.56 ± 0.90	+3.19 ± 0.49	+6.12 ± 0.95	+6.87 ± 0.87	+3.50 ± 0.71	+2.14 ± 0.88
Time (absolute)	—	1.69 sec†	7.12 sec†	24.2 sec†	1.81 sec‡	5.71 sec‡
MAC 1.0–1.2						
Systolic blood pressure	90.0 ± 4.09	+6.70 ± 1.05	−17.1 ± 4.59	−12.6 ± 4.87	−22.0 ± 5.87	+5.20 ± 1.49
Diastolic blood pressure	56.0 ± 3.39	+7.69 ± 0.84	−10.4 ± 2.48	−6.45 ± 3.09	−14.0 ± 4.00	+7.62 ± 1.67
Heart rate	76.6 ± 1.93	+2.87 ± 0.93	+5.85 ± 1.51	+4.62 ± 2.34	+2.66 ± 1.86	+3.18 ± 1.95
Central venous pressure (torr) (absolute)	2.14 ± 0.91	+3.64 ± 0.19	+6.57 ± 0.75	+6.71 ± 0.85	+4.07 ± 0.97	+0.50 ± 0.28
Time (absolute)	—	0.34 sec†	9.28 sec†	22.8 sec†	1.64 sec‡	7.33 sec‡
MAC 1.9						
Systolic blood pressure	77.7 ± 3.79	+1.20 ± 3.45	−13.1 ± 2.96	−12.0 ± 2.58	−24.6 ± 3.09	−4.95 ± 1.94
Diastolic blood pressure	52.5 ± 2.95	+1.91 ± 3.05	−7.20 ± 1.88	−7.28 ± 1.95	−19.3 ± 2.63	−1.61 ± 2.06
Heart rate	78.3 ± 1.41	+0.48 ± 1.24	+3.07 ± 2.01	+2.56 ± 1.73	+1.03 ± 1.53	+3.02 ± 1.33
Central venous pressure (torr) (absolute)	3.37 ± 0.79	+31.9 ± 0.63	+6.25 ± 0.53	+6.25 ± 0.53	+3.25 ± 0.64	+0.87 ± 0.56
Time (absolute)	—	0.64 sec†	16.2 sec†	24.0 sec†	3.00 sec‡	6.00 sec‡

* Percentage changes are given for blood pressure and heart rate; changes in central venous pressure and time are absolute values.

† Seconds after onset of breath-holding.

‡ Seconds after release of breath-holding.

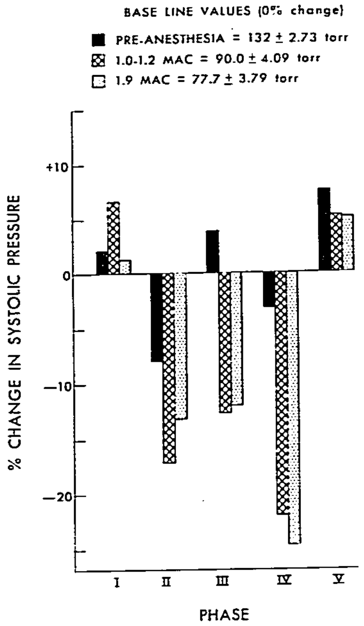

FIG. 3. Valsalva maneuver: Comparison of percentage changes of systolic blood pressure from baseline in the five phases.

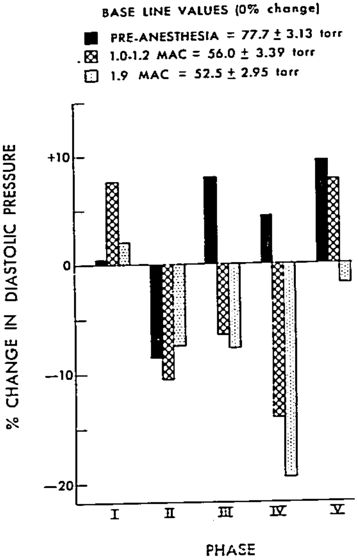

FIG. 4. Valsalva maneuver: Comparison of percentage changes of diastolic blood pressure from baseline in the five phases.

cold plus apnea at 1.0–1.2 MAC and 1.9 MAC levels of anesthesia (table 4). Mean percentage changes from baseline were calculated for the lowest value for any five-second period (table 5, fig. 1, fig. 2) and for the five-second period which had the highest cardiac output (table 6).

Percentage changes in venous blood flow due to cold plus apnea were studied, with a comparison of preanesthesia values and values at 1.0 MAC. Cold plus apnea resulted in decreased venous blood flow, but there was no significant difference between preanesthesia and 1.9 MAC values.

VALSALVA MANEUVER

Absolute baseline BP, HR and RAP values were recorded and the percentage changes from baseline were recorded at each of the five phases of the Valsalva maneuver for preanesthesia, 1.0–1.2 MAC, and 1.9 MAC. The five phases of the Valsalva maneuver were defined as follows: phase I, the peak BP immediately after increase in airway pressure; phase II, the lowest BP after the increase in airway pressure; phase III, the BP immediately before release of increased airway pressure; phase IV, the lowest BP immediately after release of increased airway pressure; phase V, the highest BP (overshoot) following release of increased airway pressure. Most notable are the results during phases II, III, and IV. Both levels of anesthesia caused greater percentage decreases in BP and higher HR's during these phases (table 7, fig. 3, fig. 4). RAP values for all phases were comparable at all levels of anesthesia, and confirm the maintenance of intrathoracic pressure values consistent with the Valsalva maneuver. Significant comparisons of percentage changes in BP and absolute changes in RAP during the five phases of the Valsalva maneuver at different levels of anesthesia are shown in table 8. Some of the blood pressure differences were significant. It should be noted that systolic and diastolic pressures were lower under anesthesia and that a significant percentage change represented a smaller absolute change compared with changes while the subject was conscious.

TABLE 8. Comparisons of Percentage Changes in Pressure and Absolute Changes in Central Venous Pressure during the Five Phases of the Valsalva Maneuver at Different Levels of Anesthesia

	Systolic Blood Pressure *P*	Diastolic Blood Pressure *P*	Central Venous Pressure *P*
Phase I			
PA *vs.* MAC 1.0–1.2	<0.02	<0.02	NS
Phase II	NS	NS	NS
Phase III			
PA *vs.* MAC 1.0–1.2	<0.02	<0.01	NS
PA *vs.* MAC 1.9	<0.001	<0.005	NS
Phase IV			
PA *vs.* MAC 1.0–1.2	<0.02	<0.005	NS
PA *vs.* MAC 1.9	<0.001	<0.001	NS
Phase V			
PA *vs.* MAC 1.9	<0.005	<0.02	NS
MAC 1.0–1.2 *vs.* MAC 1.9	<0.005	<0.01	NS

Discussion

Bradycardia and vasoconstriction in dogs and seals during diving have been shown to be abolished by pentobarbital anesthesia.[8] Our results led us to similar conclusions for halothane anesthesia in man.[7] In the conscious subject simulated diving produced a 26 per cent (cold alone) to 29 per cent (cold plus apnea) decrease in HR from the lowest baseline HR, as opposed to decreases no greater than 3.6 per cent in HR during halothane anesthesia with cold alone and cold plus apnea. Anesthesia apparently abolishes the parasympathetic response to simulated diving which slows the HR so markedly in conscious man. Under anesthesia, simulated diving increased the highest HR observed. Stimulation of temperature, pain, or even touch sensory nerve endings by the cold cloth on the face could cause sympathetic nervous stimulation not abolished by anesthesia, with an associated chronotropic effect on the heart. Another source of sympathetic stimulation might be the carbon dioxide retained during breath-holding. Under anesthesia, reductions from the lowest systolic and lowest diastolic BP's were minimal and did not differ from changes when the subjects were conscious. There were increases in the highest systolic and diastolic BP's with the subjects either conscious or anesthetized. In contrast to the abolition of the parasympathetic slowing of heart rate, anesthesia apparently did not abolish the sympathetic response to simulated diving, although the increase in TPR was markedly reduced.

During phases II, III, and IV of the Valsalva maneuver, anesthesia resulted in greater decreases in BP, accompanied by higher HR's, than those observed prior to anesthesia. At 1.9 MAC, the phase V "outshoot" did not occur, and diastolic BP was less than baseline. This suggests that under anesthesia the circulatory depression induced by elevation of intrapulmonary pressure will be greater, and that responsiveness of the peripheral vascular system to lowered arterial pressure will be less. Price *et al.* found similar results during cyclopropane anesthesia.[10]

Our results show that halothane anesthesia reduces or abolishes the normal circulatory responses of conscious man to diving and the Valsalva maneuver. The body's ability to respond to related stresses (vigorous controlled respiration) or more distantly related stresses (asphyxia or hypotension from arrhythmia or hypovolemia) also may be reduced by halothane. Such a reduction may result from other general anesthetics also.

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Pediatrics

PULMONARY FUNCTION IN CYSTIC FIBROSIS Eighteen children (mean age 8 years) with cystic fibrosis underwent studies of pulmonary diffusing capacity by the carbon monoxide method at rest, sitting, head down, and after exercise to exhaustion. In contrast to eight normal children of comparable ages, none of the children with cystic fibrosis were able to increase their diffusion rates for carbon monoxide in the head-down position or during severe exercise. Lung volumes, mechanics of breathing and gas mixing were normal in half of the children with cystic fibrosis. The inability of the child with cystic fibrosis to increase the diffusion rate with exercise or gravity represents a profound loss of adaptability, and may be responsible for the poor exercise tolerance, dyspnea, and cyanosis observed in these children during physical activity. Further studies will be necessary to determine whether the limitation of diffusion capacity results from loss of membrane surface area or from abnormalities in the pulmonary capillary bed. (*Zelkowitz, P. S., and Giammona, S. T.: Effects of Gravity and Exercise on the Pulmonary Diffusing Capacity in Children with Cystic Fibrosis, J. Pediat. 74: 393 (March) 1969.*)

Surgery

GOODPASTURE'S SYNDROME Resolution of the pulmonary changes in Goodpasture's syndrome may occur after bilateral nephrectomy. Hemophthisis disappeared, infiltrates resolved, and arterial P_{O_2} increased from 51 to 90 torr in a group of patients in whom this operation was performed. (*Siegel, R. R.: The Basis of Pulmonary Disease Resolution after Nephrectomy in Goodpasture's Syndrome, Amer. J. Med. Sci. 259: 202 (March) 1970.*)