Changes in Respiratory Dead Space During Halothane, Cyclopropane, and Nitrous Oxide Anesthesia

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The influence of halothane, cyclopropane and nitrous oxide anesthesia on respiratory dead space has been measured in 18 surgical patients. Dead space was found to increase progressively in each patient, with the anatomical dead space remaining relatively unchanged. The progressive increase was in alveolar dead space. Similar measurements in 5 normal awake volunteers failed to reveal appreciable changes. Arterial oxygen tensions did not fall in spite of rhythmical mechanical ventilation.

DURING INHALATIONAL anesthesia associated with deliberate hypotension, it was observed [1] that gas exchange in the lungs was impaired even with apparently adequate minute volume of ventilation. Other investigators [2-5] have found uneven ventilation with an increase in physiological dead space in anesthetized volunteers. It has been shown that intermittent deep breaths assist in maintaining adequate ventilation [6, 7, 8] but information concerning changes in pulmonary dead space during anesthesia is limited. No one has reported the changes occurring during controlled ventilation with a constant inspiratory pressure.

The purpose of this study is to demonstrate some of the changes in respiratory dead space and pulmonary gas exchange following mechanical ventilation without intermittent deep breaths in patients anesthetized with halothane, cyclopropane or nitrous oxide.

Methods

Observations were made in 23 subjects, 18 of whom were undergoing surgical procedures; the remainder were healthy volunteers who served for comparison. The age distribution, sex and operation performed are listed in table 1.

The patients for operation were given 100–150 mg. secobarbital and 0.2–0.4 mg. atropine intramuscularly approximately one hour before being brought to the operating room. Anesthesia was induced with an average of 150 mg. thiopental intravenously. Six patients each were then anesthetized with cyclopropane, nitrous oxide and halothane through a Copper Kettle, and nitrous oxide alone. Their tracheas were intubated with the aid of an average dose of 50 mg. succinylcholine intravenously. All but one patient was given *d*-tubocurarine to assist in providing muscular relaxation, and prevent respiratory efforts (table 1). The level of anesthesia with cyclopropane and halothane was estimated clinically to be in upper plane 2, and that for nitrous oxide upper plane 1. Four liters of nitrous oxide were used along with 2 liters oxygen.

Following tracheal intubation a Bird Mark 4 pressure-limited respirator was connected to the endotracheal tube as represented schematically in figure 1 and respiration was controlled at a constant rate and pressure throughout the entire procedure with particular care to avoid hyperinflation or sudden changes in lung volume.

The breathing system was of the circle carbon dioxide absorbing type, incorporating undirectional valves near the endotracheal tube, non-expandable plastic corrugated tubing, and an expired air mixing chamber (fig. 1). The adequacy of the valves could be checked by visual observation through the plastic housing or by observing the continuous record of end-tidal CO_2 concentrations. The total dead space of the valve system was 15 ml.

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An Emerson breathometer served both as a mixing chamber for expired air, thereby permitting determination of mixed expired CO_2 and as a device for measuring tidal and minute volumes of respiration. The breathometer was calibrated repeatedly at the beginning of the investigation with a Tissot spirometer. Respired volumes were corrected for BTPS. A shunt was introduced between the inspiratory and expiratory sides of the system, distal to the breathometer (fig. 1–15).[9] In the absence of this shunt, there is continuous passage of gas through the unidirectional valves from the inspiratory to the expiratory side of the system due to slight inflow from the anesthesia machine. This continuous inflow of gas does not contribute to pulmonary ventilation.

End-tidal air was obtained via a small plastic catheter from the distal end of the endotracheal tube. Samples were led to an infrared CO_2 analyzer at the rate of 600 ml./minute. A three-way stopcock permitted alternate measurement of airway pressure with a Statham strain gauge calibrated in cm. of water. A second stopcock placed near the infrared analyzer allowed measurement of P_{CO_2} either in the mixed expired air or end-tidal air. After passing through the analyzer, the sampled air was returned proximal to the endotracheal tube. The data from the infrared analyzer and the strain gauge were recorded on a Grass polygraph. The values obtained for P_{CO_2} in mixed and end-tidal air were corrected for the broadening effect of nitrous oxide and cyclopropane.[10]

Intra-arterial blood pressure was measured by means of a 19-gauge needle placed in a brachial artery, transduced via a Statham strain gauge calibrated in mm. of mercury and recorded on the polygraph. A three-way stopcock at the needle permitted withdrawal of arterial blood samples into heparinized 10 ml. Luer Lok syringes. These were placed immediately in iced water until analyzed in duplicate for P_{O_2}, P_{CO_2} and *p*H by means of an electrode system consisting of a Clarke oxygen electrode, a Severinghaus P_{CO_2} electrode and a *p*H microelectrode (E.I.L. model SIH33). In three patients, 9 duplicate samples of blood were withdrawn and analyzed on a "blind" basis; the values corresponded within 0.5 mm. of mercury P_{CO_2} and 2 mm. P_{O_2}.

Experimental procedure: After anesthesia was induced, the patient's trachea intubated and respirator connected, a needle was placed

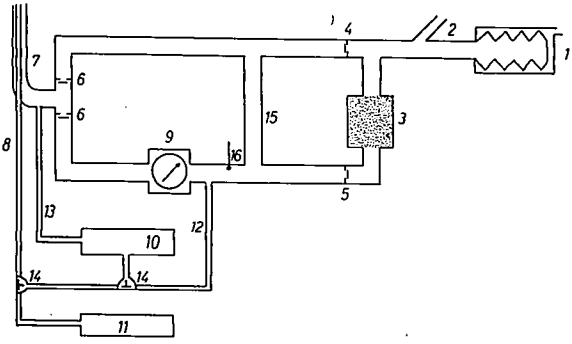

FIG. 1. Schematic representation of breathing circuit: (*1*) Bird Mark 4 respirator; (*2*) anesthetic gas inlet; (*3*) CO_2 absorber; (*4*) inspiratory valve; (*5*) expiratory valve; (*6*) unidirectional valve; (*7*) endotracheal tube; (*8*) catheter for sampling end-tidal air or measuring airway pressure; (*9*) Emerson breathometer; (*10*) infrared CO_2 analyzer; (*11*) strain gauge for measuring airway pressure; (*12*) tube to CO_2 analyzer for sampling mixed expired air; (*13*) return from CO_2 analyzer (*14*) threeway stopcock; (*15*) shunt; (*16*) thermometer.

into the brachial artery. This required an average of 15 minutes. Approximately 10 minutes later the first arterial blood sample was withdrawn and simultaneously respiratory minute volume was measured. The carbon dioxide tensions of mixed expired air and end-tidal air were recorded alternately and continuously throughout the procedure. Minute volume of respiration was measured and arterial blood samples were obtained every 30 minutes during the remainder of the operation; in most cases 4–6 sets of samples were obtained. The infrared analyzer was calibrated with 3, 5 and 7 per cent CO_2 mixtures after each measurement period.

The 5 normal volunteers received only seco-

TABLE 1. Measured and Calculated Respiratory

Expt.	Cyclopropane	d-Tubo. (mg.)	Time on Respirator (min.)	B.P. (mm.Hg)	Pulse/ min.	Airway Pressures (cm.H_2O)	f	MV (ml. BTPS)	Vt (ml. BTPS)
C-1	W F 47 yrs.	6	10	110/80	65	2/14	19	7,940	416
	61″ 141 lbs.	0	45	130/90	60	2/13	20	7,090	353
	Subtotal gastrectomy	6	75	150/95	60	2/11	22	7,230	328
		0	105	145/90	60	1/12	25	10,730	429
C-2	W F 47 yrs.	0	10	110/60	52	−2/9	20	6,750	337
	62½″ 130 lbs.	0	35	120/70	64	2/11	20	6,700	335
	Vein stripping	0	65	120/70	55	1/9	20	5,710	286
		0	90	120/80	60	1/10	20	5,760	288
C-3	W M 72 yrs.	6	10	180/90	78	0/8	21	8,760	453
	67″ 150 lbs.	0	45	160/90	80	0/8	20	8,000	403
	Subtotal gastrectomy	6	70	150/90	72	0/8	21	7,880	382
		0	100	150/90	72	0/8	20	8,170	410
		0	130	175/95	72	0/8	20	7,930	403
		0	150	155/90	72	0/8	20	8,300	420
C-4	W M 60 yrs.	6	10	150/90	84	−1/6	18	7,670	457
	74″ 209 lbs.	0	35	190/110	80	−2/12	19	8,190	456
	Subtotal gastrectomy	6	65	190/110	75	−2/11	18	8,070	471
		0	95	190/110	90	−2/11	17	7,910	471
		0	125	160/100	90	−2/11	18	8,050	497
C-5	W M 63 yrs.	0	10	150/90	66	−1/12	14	9,030	659
	72″ 175 lbs.	6	35	140/80	66	−1/11	15	8,650	635
	Vein stripping	0	60	150/90	66	−1/12	15	8,620	615
		0	85	150/95	66	−2/9	14	9,060	690
C-6	N F 58 yrs.	6	20	100/60	65	−1/10	12	6,000	575
	63″ 133 lbs.	0	45	130/80	72	−1/13	12	5,440	488
	Hemicolectomy	0	65	110/70	78	−1/12	13	5,960	536
		0	95	140/90	60	−1/12	12	6,450	556
		0	125	160/100	60	−1/11	12	6,180	529
	Halothane								
H-1	W F 74 yrs.	0	60	175/100	90	5/18	27	9,760	359
	60″ 188 lbs.	6	90	160/100	80	4/15	30	10,200	340
	Total hysterectomy	0	115	150/100	90	4/15	27	10,200	378
		0	130	150/100	90	4/15	30	11,700	390
		0	150	150/100	90	7/19	30	11,700	390
H-2	W F 42 yrs.	6	35	100/75	80	−1/10	19	8,650	455
	64″ 140 lbs.	0	60	100/75	90	0/10	19	8,760	461
	Vein stripping	0	90	100/75	60	−1/10	19	8,600	452
		0	120	100/60	60	−1/10	19	8,180	430
		0	150	100/60	60	−1/10	19	8,940	470
H-3	W F 33 yrs.	6	20	100/80	54	2/8	20	7,010	350
	65″ 145 lbs.	0	50	105/80	60	3/9	20	7,060	353
	Axillary dissection	0	80	100/80	58	3/9	21	7,060	336
		0	150	100/90	59	4/8	20	6,610	331
H-4	W F 38 yrs.	6	20	100/80	66	−1/7	18	7,820	434
	61″ 139 lbs.	0	50	100/80	66	−1/7	18	7,950	439
	Total hysterectomy	0	80	100/80	68	−1/7	17	8,050	450
		0	150	100/80	68	−1/6	18	8,300	474
H-5	W M 60 yrs.	0	40	100/90	66	1/15	17	7,468	351
	66½″ 159 lbs.	6	70	140/90	96	−1/10	18	6,970	383
	Subtotal gastrectomy	0	100	120/90	90	1/12	12	7,570	349
		0	130	120/90	84	1/12	21	7,930	381
		0	150	110/80	72	1/12	21	7,740	372
H-6	W M 68 yrs.	6	10	120/80	84	0/7	14	9,488	664
	65″ 145 lbs.	0	35	120/80	80	0/10	14	9,330	653
	Inguinal herniorrhaphy	0	60	120/80	80	0/10	14	9,171	642
		0	90	120/80	84	0/10	14	9,488	664

barbital were not anesthetized but were placed supine on an operating table and breathed through the same equipment used for the anesthetized patients. Their respiration was not controlled, nor were their tracheas intubated. They breathed 20 per cent oxygen in air; otherwise the study was completed in the same way as in the anesthetized groups.

Physiological (V_{D_P}) and anatomical ($V_{D_{(anat)}}$) dead spaces were calculated from the data obtained with Bohr's equation. No correction was made for the equipment dead space.

Results

The measured and calculated respiratory data from the 18 patients and 5 volunteers are

Data from the 18 Patients and 5 Volunteers

$P_{E_{CO_2}}$ (mm.Hg)	$P_{A_{CO_2}}$ (mm.Hg)	$P_{a_{CO_2}}$ (mm.Hg)	$P_{a_{CO_2}}$ (mm.Hg)	pH	a-A P_{CO_2} Diff. (mm.Hg)	V_{DP} (ml.)	$V_{D_{(anat)}}$ (ml.)	V_{DA} (ml.)	V_{DP}/V_T	Mean V_T	Slope
20.6	30.5	275	30.7	7.390	0.2	137	136	1	0.329		
20.6	33.2	321	34.7	7.381	2.5	143	134	9	0.406		
20.6	35.1	433	36.7	7.380	1.6	144	135	9	0.439		
19.2	20.3	376	32.4	7.384	3.1	175	147	28	0.407	380	0.34
18.9	27.7	132	27.7	7.432	0.0	107	107	0	0.292		
17.0	27.4	130	30.5	7.356	3.1	148	127	21	0.443		
18.1	28.5	142	28.9	7.375	0.4	107	104	3	0.373		
18.1	29.7	213	34.6	7.399	4.9	138	112	26	0.480	310	0.34
17.2	23.3	203	25.6	7.396	2.3	148	119	29	0.328		
16.0	23.5	233	30.1	7.374	6.6	188	129	59	0.468		
16.0	25.7	313	30.5	7.356	4.8	182	144	38	0.476		
16.5	25.4	321	31.0	7.356	4.6	192	143	49	0.468		
16.0	23.5	375	31.8	7.352	8.3	200	129	71	0.497		
16.5	24.3	320	32.2	7.350	7.9	205	134	71	0.488	412	0.36
28.6	39.3	129	43.1	7.308	3.8	154	124	30	0.336		
27.6	37.3	141	43.4	7.338	6.1	166	119	47	0.364		
26.4	34.6	177	44.7	7.302	10.1	193	112	81	0.409		
28.6	40.4	184	52.4	7.238	12.0	213	137	76	0.473		
27.6	35.6	184	48.9	7.234	13.3	216	112	104	0.436	470	0.59
21.6	28.6	236	30.5	7.364	1.9	192	161	31	0.292		
19.3	24.9	241	32.3	7.373	7.4	255	143	112	0.402		
19.6	27.6	201	34.5	7.388	6.9	266	177	89	0.432		
18.6	25.4	298	32.6	7.417	7.2	296	184	112	0.429	650	1.17
23.5	29.1	143	34.1	7.447	5.0	179	110	69	0.311		
23.5	32.5	172	37.4	7.437	4.9	182	134	48	0.372		
24.5	31.5	188	40.0	7.425	8.5	208	119	89	0.388		
22.6	30.1	115	38.4	7.418	8.3	229	138	91	0.411		
24.2	34.4	112	47.0	7.412	12.6	257	156	101	0.485	537	0.79
10.8	17.2	461	23.3	7.570	6.1	192	134	58	0.536		
10.1	17.2	536	24.0	7.513	6.8	197	150	57	0.579		
10.1	17.7	507	20.9	7.543	3.2	195	162	33	0.517		
8.5	15.5	550	20.6	7.533	5.1	228	175	53	0.587		
8.0	15.5	586	20.5	—	5.0	237	188	49	0.609	370	0.48
18.8	23.3	146	26.9	7.539	3.6	136	88	48	0.301		
16.6	21.3	137	24.8	7.542	3.5	152	101	51	0.330		
15.5	19.1	112	25.3	7.588	6.2	174	85	89	0.387		
13.9	20.4	132	24.4	7.600	4.0	185	126	59	0.430		
13.9	19.0	143	24.2	7.603	5.2	200	136	64	0.425	450	0.55
18.6	25.0	205	26.5	7.450	1.5	104	89	15	0.298		
19.0	25.0	203	27.8	7.458	2.8	112	85	27	0.316		
19.0	25.0	236	28.9	7.468	3.9	115	81	34	0.343		
17.4	25.4	214	29.4	7.456	4.0	135	103	32	0.408	340	0.22
19.3	26.4	214	28.1	7.455	1.7	135	117	18	0.313		
18.6	26.7	199	28.3	7.451	1.6	150	133	17	0.342		
18.3	25.9	193	28.3	7.440	2.4	159	132	27	0.353		
17.6	25.9	199	28.5	7.430	2.6	181	151	30	0.382	450	0.35
20.4	31.5	122	37.0	7.392	5.5	157	124	33	0.448		
21.2	34.1	106	38.0	7.350	3.9	169	144	25	0.442		
19.7	30.6	117	38.5	7.346	7.9	170	124	46	0.488		
18.3	29.1	114	38.9	7.323	9.8	201	141	60	0.530		
17.6	29.1	119	39.1	7.312	10.0	204	146	58	0.519	370	0.41
22.7	30.3	123	33.4	7.458	3.1	212	167	45	0.320		
19.7	26.5	133	31.5	7.479	5.0	244	168	76	0.374		
18.3	25.5	137	30.8	7.460	5.3	260	181	79	0.405		
17.1	24.0	115	30.2	7.468	6.2	288	191	97	0.434	660	0.86

TABLE 1.—(*Continued*)

Expt.	Nitrous Oxide d-Tubo.	d-Tubo. (mg.)	Time on Respirator (min.)	B.P. (mm.Hg)	Pulse/ min.	Airway Pressures ($cm.H_2O$)	f	MV ml. (BTPS)	V_T ml. (BTPS)
N-1	W F 43 yrs. 68" 155 lbs. Total hysterectomy	12 9 15 0	30 60 75 100	120/80 120/80 120/80 140/90	84 84 72 60	0/10 −1/10 −1/10 0/10	13 12 12 13	12,400 13,100 12,300 11,900	915 915 900 915
N-2	W F 75 yrs. 64" 156 lbs. Cholecystectomy	15 9 6 0	10 40 70 100	110/60 130/70 110/60 120/60	90 78 78 66	4/13 5/16 5/16 6/18	13 14 14 15	15,200 15,150 17,100 17,100	1,176 1,189 1,187 1,187
N-3	W M 62 yrs. 128 lbs. Subtotal gastrectomy	18 9 15 6 0	10 40 70 100 130	150/80 150/80 140/80 190/100 175/95	63 63 60 63 63	3/20 3/20 3/20 2/19 2/18	12 13 13 13 13	7,424 6,980 7,235 7,179 7,238	569 568 579 574 594
N-4	W M 44 yrs. 66½" 168 lbs. Aortic graft	12 12 9 6 0	10 40 70 100 130	90/70 90/60 90/50 100/80 100/80	84 90 90 84 78	0/15 0/16 0/17 0/16 0/17	11 11 11 12 12	9,507 8,838 8,689 7,755 8,834	818 769 756 720 769
N-5	W M 64 yrs. 68½" 172 lbs. Subtotal gastrectomy	15 12 6 9 0	10 40 70 100 130	120/80 200/95 200/100 120/60 140/80	50 54 54 78 78	2/16 1/18 1/18 1/17 1/18	12 13 13 13 12	9,283 9,167 8,276 8,776 8,295	755 678 631 685 664
N-6	N F 19 yrs. 63½" 105 lbs. Axillary dissection	12 6 6 0 0	3 40 70 100 130	110/80 100/70 90/70 90/70 90/70	96 84 84 78 90	1/15 2/19 1/18 0/17 0/17	12 11 12 12 12	9,167 9,690 10,300 10,195 10,732	770 814 847 836 880

listed in table 1. Minute ventilation is seen to have been reasonably constant for each patient during the period of study.

Respiratory Dead Space. The physiological dead space increased during the 2½ hour period of observation in every patient in all

TABLE 1.—(*Continued*)

Expt.	Awake Volunteers	Time on Breathing System (min.)	B.P. (mm.Hg)	Pulse/ min.	f	MV ml. (BTPS)	V_T ml. (BTPS)	$P_{E'CO_2}$ (mm.Hg)
A-1	M 27 yrs. 73" 151 lbs.	20 50 80 110 140	110/80 110/80 110/80 110/80 110/80	66 66 66 66 66	16 16 17 16 17	7,104 6,830 7,104 6,450 7,104	444 427 418 503 417	27.5 26.5 26.5 26.8 26.5
A-2	M 32 yrs. 66" 155 lbs.	20 50 80 110 140	100/70 100/70 100/70 100/70 100/70	60 60 60 60 60	9 9 9 9 8	4,225 4,635 4,635 4,525 4,084	503 515 515 503 511	30.0 30.0 30.0 30.0 30.0
A-3	M 32 yrs. 74" 200 lbs.	20 50 80 110 140	100/75 100/75 100/75 100/75 100/75	54 54 54 54 54	5 7 7 6 7	3,539 4,313 4,977 4,424 5,087	708 616 711 737 726	34.0 31.7 34.0 34.0 34.0
A-4	M 27 yrs. 68" 170 lbs.	20 50 80 110 140	110/75 110/75 110/75 110/75 110/75	63 63 63 63 63	5 6 6 6 6	4,424 4,977 4,977 5,198 4,977	885 830 830 866 830	36.2 36.2 36.2 36.2 36.2
A-5	M 31 yrs. 74" 175 lbs.	20 50 80 110 140	110/70 110/70 110/70 110/70 110/70	63 63 63 63 63	9 9 9 9 9	5,212 5,212 5,328 5,267 5,489	579 579 591 585 610	32.2 32.2 32.2 32.2 32.2

TABLE 1.—(*Continued*)

$P_{E_{CO_2}}$ (mm.Hg)	$P_{A_{CO_2}}$ (mm.Hg)	$P_{a_{O_2}}$ (mm.Hg)	$P_{a_{CO_2}}$ (mm.Hg)	*p*H	a-A P_{CO_2} Diff. (mm.Hg)	V_{DP} (ml.)	$V_{D(anat)}$ (ml.)	V_{DA} (ml.)	V_{DP}/V_T	Mean V_T	Slope
20.7	23.6	158	24.5	7.514	0.9	141	112	29	0.154		
19.4	22.1	116	24.0	7.511	1.9	175	112	63	0.191		
19.4	22.2	147	24.9	7.522	2.7	199	113	86	0.221		
18.6	21.3	157	24.5	7.556	3.2	220	115	105	0.240	911	1.08
14.3	17.4	125	18.9	7.606	1.5	275	209	66	0.243		
12.2	15.5	122	17.0	7.585	1.5	333	250	83	0.282		
11.0	13.2	103	16.4	7.652	3.2	390	198	192	0.329		
10.1	12.9	104	16.1	7.656	3.2	441	257	184	0.372	1,183	1.85
19.1	24.9	143	32 2	7.459	7.3	231	132	99	0.406		
17.8	23.0	125	30.3	7.462	7.3	234	128	106	0.412		
17.1	24.0	126	31.8	7.439	7.8	267	166	101	0.462		
16.0	24.0	130	31.1	7.424	7.1	278	191	87	0.485		
16.0	20.3	132	31.1	7.454	10.8	288	126	162	0.485	580	0.53
21.9	30.3	152	34.5	7.443	4.2	298	226	72	0.365		
21.6	29.3	99	34.9	7.445	5.6	293	202	91	0.381		
20.5	27.4	83	36.4	7.388	9.0	330	191	139	0.436		
22.1	31.2	83	41.4	7.375	10.2	336	210	126	0.467		
20.5	29.3	113	39.0	7.368	9.7	364	230	134	0.474	760	0.59
18.7	22.0	78	23.2	7.596	1.2	147	113	34	0.191		
16.4	22.1	69	24.1	7.529	2.0	216	174	42	0.319		
15.7	21.3	84	25.5	7.523	4.2	243	167	76	0.384		
15.2	21.0	77	26.0	7.495	5.0	284	189	95	0.415		
15.2	19.0	65	25.7	7.463	6.7	271	133	138	0.408	680	1.05
15.3	18.3	165	18.8	7.551	0.5	143	126	17	0.186		
14.0	16.5	156	18.4	7.552	1.9	195	124	71	0.239		
12.4	14.6	163	17.2	7.570	2.6	236	128	108	0.279		
12.2	14.6	156	17.4	7.526	2.8	250	137	113	0.299		
12.7	14.9	156	19.0	7.506	4.1	292	130	162	0.332	830	1.17

three anesthetized groups. In those anesthetized with halothane-nitrous oxide a mean increase of 33 per cent was recorded (fig. 2). In the cyclopropane group the average increase was 33 per cent (fig. 3), and in the nitrous oxide group an average increase of 52 per cent

TABLE 1.—(*Continued*)

$P_{A_{CO_2}}$ (mm.Hg)	$P_{a_{O_2}}$ (mm.Hg)	$P_{a_{CO_2}}$ (mm.Hg)	*p*H	a-A P_{CO_2} Diff. (mm.Hg)	V_{DP} (ml.)	$V_{D(anat)}$ (ml.)	V_{DA} (ml.)	V_{DP}/V_T	Mean V_T	Slope
42.3	191	43.0	7.343	0.7	160	155	5	0.36		
41.5	188	42.3	7.362	0.8	159	154	5	0.37		
41.5	204	42.2	7.350	0.7	156	151	5	0.37		
41.5	227	43.1	7.349	1.6	153	143	10	0.37		
41.5	192	42.1	7.346	0.6	155	150	5	0.37	420	
42.0	174	42.6	7.346	0.6	149	143	6	0.296		
41.0	166	41.6	7.378	0.6	144	138	6	0.279		
41.8	164	41.9	7.379	0.1	146	145	1	0.284		
41.6	169	42.2	7.378	0.6	145	140	5	0.289		
41.6	169	42.2	7.378	0.6	148	143	5	0.289	509	—
48.0	161	48.6	7.332	0.6	213	206	7	0.301		
48.2	177	48.7	7.329	0.5	214	210	4	0.349		
47.5	183	48.2	7.336	0.7	210	202	8	0.295		
47.1	177	48.0	7.338	0.9	215	205	10	0.292		
47.5	179	48.4	7.346	0.9	216	206	10	0.298	600	—
44.8	194	45.9	7.347	1.1	186	170	16	0.212		
45.4	173	46.0	7.340	0.6	177	168	9	0.213		
45.4	167	46.1	7.339	0.7	178	168	10	0.215		
45.4	175	46.0	7.340	0.6	184	175	9	0.213		
45.4	195	46.0	7.330	0.6	177	168	9	0.213	850	—
44.0	182	45.1	7.344	1.1	166	155	11	0.286		
44.0	199	44.7	7.333	0.7	162	155	7	0.280		
44.0	182	44.8	7.342	0.8	166	158	8	0.281		
44.0	211	44.7	7.342	0.7	164	157	7	0.280		
42.9	199	44.4	7.350	1.9	168	152	16	0.275	590	—

B.P. = arterial blood pressure, f = respiratory rate/minute, M.V. = respiratory minute volume, V_T = tidal volume, $P_{E_{CO_2}}$ = mixed expired P_{CO_2}, $P_{A_{CO_2}}$ = end tidal P_{CO_2}, $P_{a_{CO_2}}$ = arterial P_{CO_2}, $P_{a_{O_2}}$ = arterial P_{O_2}, a-A P_{CO_2} diff. = arteria-end tidal P_{CO_2} difference, V_{DP} = physiological dead space, $V_{D(anat)}$ = anatomical dead space, V_{DA} = alveolar dead space, V_{DP}/V_T = ratio of physiological dead space to tidal volume.

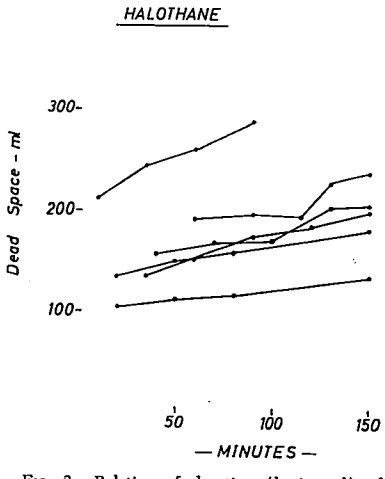

FIG. 2. Relation of duration (horizontal) of halothane anesthesia to change in physiological dead space (vertical). Lines connect observations in the same patient.

was observed (fig. 4). The regression lines for each of these three groups is shown in figure 5 which presents the average change for each of the agents. ($V_{D(anat)}$ as calculated from the Bohr equation remained nearly constant during the study period, whereas V_{D_A} increased progressively.

In the five unanesthetized volunteers, the physiological dead space did not change appreciably. An average initial value of 174 ml. remained unaltered and two hours later the average was still 174 ml. (fig. 6).

V_{DP}/V_T Ratio. The ratio between physiological dead space and the tidal volume of respiration (V_{D_P}/V_T) representing that part of the inspired gas which does not participate in gas exchange, increased gradually during the study period. In the halothane group the average increase was 26 per cent. In the cyclopropane group, the mean increase was 44 per cent and in the nitrous oxide group, 49 per cent. No change was noted in the control group.

One patient (C-2, table 1) in the cyclopropane group has been excluded from the average calculations since the operating table was tilted 20 degrees head-down. However, this patient demonstrated the effect of body position on dead space.[11, 12] Physiological dead space decreased from 148 to 107 ml. and the arterial–end-tidal P_{CO_2} difference was reduced from 3.1 to 0.4 mm. of mercury.

Arterial–End-Tidal P_{CO_2} Difference. The difference between arterial and end-tidal P_{CO_2} increased during the study as did the physiological dead space and the V_{DP}/V_T ratio. The average increase was from 3.6 to 5.5 mm. of mercury in the halothane group, 2.2 to 8.2 mm. of mercury in the cyclopropane group, and 2.6 to 6.3 mm. of mercury in the nitrous oxide group. A change was not found in the awake volunteers.

The last two columns in table 1 list the mean tidal volume for each study and the slope for the regression line of V_D on time. Table 2 shows the mean tidal volume and mean slopes for each group. The nitrous oxide group had the steepest slope and also the largest average tidal volume, whereas the halothane group had the smallest slope and the lowest mean tidal volume. This suggests a relation between tidal volume and the increase in dead space. The slopes for all 18

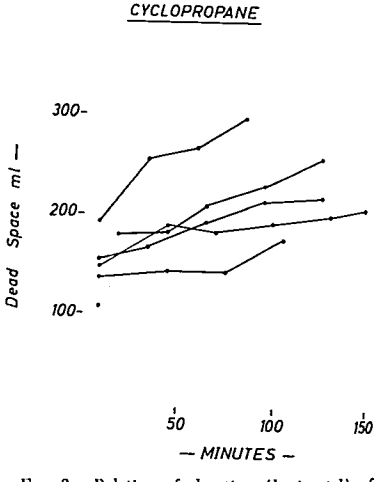

FIG. 3. Relation of duration (horizontal) of cyclopropane anesthesia to changes in physiological dead space (vertical). Lines connect observations in the same patient.

patients with their corresponding tidal volumes are plotted in figure 7. The calculated regression line is shown and a Rank correlation reveals a coefficient of 0.88 for the entire study.

Discussion

The major change we have recorded with three different anesthetic agents or techniques was a gradual increase in physiological dead space, in the ratio V_{DP}/V_T and in arterial–end-tidal P_{CO_2} difference. These increases were nearly linear during the period of study. It is possible that ultimately a plateau might be reached but there was no evidence of this during the first 2½ hours of anesthesia.

The initial values for the ratio V_{DP}/V_T in both anesthetized and awake subjects were in the range of 0.3—that usually reported in anesthetized patients.[3, 13, 14] Our first determination was 25 minutes after induction of anesthesia and 10 minutes after the onset of controlled ventilation. No correction was made for instrument dead space. The average arterial–end-tidal P_{CO_2} difference was 0.77 mm. of mercury found in the awake volunteers corresponds closely to that of 0.80 mm. of

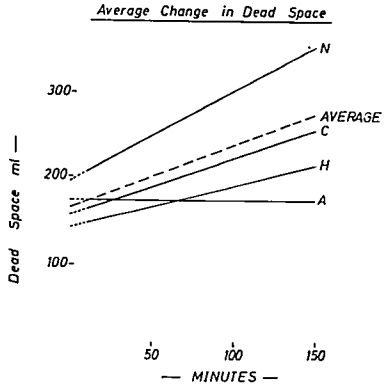

FIG. 5. Regression lines showing the average change in dead space (vertical) with duration of anesthesia (horizontal). N = nitrous oxide group; C = cyclopropane group; H = halothane group; A = awake volunteer group.

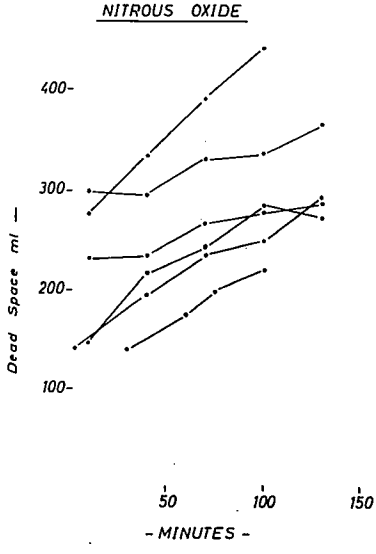

FIG. 4. Relationship of duration (horizontal) of cyclopropane anesthesia to change in physiological dead space (vertical). Lines connect observations in the same patient.

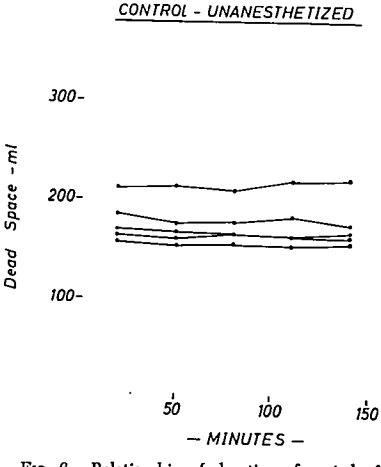

FIG. 6. Relationship of duration of period of observation (horizontal) in awake volunteer subjects lying supine to changes in dead space (vertical). Lines connect observations in the same patient.

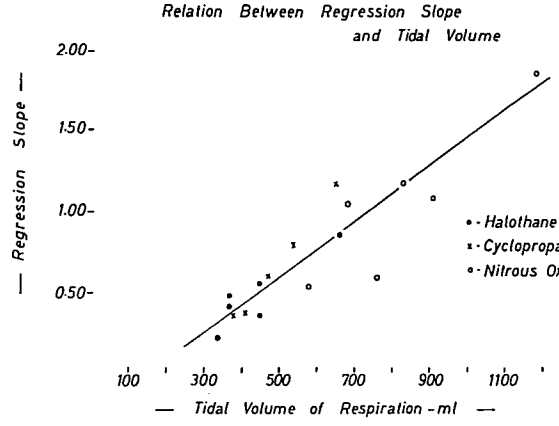

FIG. 7. Relationship between the regression slope (vertical) and tidal volume of respiration (horizontal) in the 18 anesthetized patients.

mercury found by Briscoe[14] under similar circumstances. The average arterial–end-tidal P_{CO_2} difference was 2.8 mm. of mercury in the 18 anesthetized patients.

The changes produced by the three anesthetics studied may have been due to an anesthetic effect on the pulmonary vascular bed or to differences in ventilation. High tidal volumes and constant monotonous ventilation seemed to produce greater increases in V_{D_P} than did low tidal volumes. Severinghaus[15] ventilated anesthetized dogs at the same rate and volume as they were observed to respire when awake and in these circumstances V_{D_P} did not increase. In our halothane group, patients were ventilated with tidal volumes of 330–650 ml. and in these patients we found the smallest percentile increase in V_{D_P}. The individuals given nitrous oxide had the highest tidal volumes, 570–1190 ml., and this group had the greatest percentile increase in V_{D_P}. Dead space has been shown to be related to tidal volume and to arterial CO_2 levels. The higher the tidal volume or the P_{CO_2}, the greater the dead space. Our data suggest that in general the larger the tidal volumes, the greater the dead space. However, no explanation is apparent as to why the percentile increases in dead spaces should be greatest with the larger tidal volumes.

Dead space did not always show a steady increase with anesthesia time. Some of the reasons for the lack of complete uniformity in response may relate to blood loss during the operation with or without a decrease in arterial blood pressures, different degrees of vasodilation, and changes in total lung-chest compliance dependent upon sensory stimulation by the operative procedure. All of these conditions have been shown to alter respiratory dead space.[1, 16, 17]

Our data suggest the development of uneven distribution of blood and gases in the lungs during anesthesia. This might be aggravated by constant ventilation although previously[1] similar changes have been observed with manual and variable ventilation. Others claim that intermittent deep breaths are essential to maintain arterial oxygen tension during anesthesia,[8] a conclusion with which our data do not agree. It is possible that our failure to control ventilation in the volunteer group explains the unchanging character of the respiratory dead space noted therein. This group differed from the anesthetized groups in that the subjects' tracheas were not intubated and their ventilation was not controlled. While a request was made that the subjects lie as still as possible and avoid deep breaths, there is no assurance this was done for the entire investigative period. They did, however, breathe approximately the same concentration of oxygen as breathed by the nitrous oxide

and halothane groups, and their tidal volumes ranged between 400 and 885 ml.

Our data did not permit distinguishing between the various anesthetics so far as their effect on physiologic dead space is concerned. Dead space increased with all agents, and the degree of increase appeared more related to tidal volume than to anesthetic agent. To clearly delineate individual anesthetic effects, it would be necessary to repeat the experiments in normal unoperated patients, controlling more precisely the depth of anesthesia and using similar tidal and minute exchange in all patients. To separate ventilatory and anesthetic actions, the use of curarized awake volunteers would be needed. This, however, might introduce confusion from the ganglionic blocking properties of large doses of curare. This already is a point of importance in the data presented since the nitrous oxide group received an average dose of 35 mg. *d*-tubocurarine, whereas the other groups were given much less.

Bendixen and his associates have reported that continuous automatic respiration without intermittent deep breaths is associated with a progressively falling arterial oxygen tension.[8] They have attributed this phenomenon to atelectasis and "shunting." The trend could be reversed by "sighing" for the patient. Our data fail to reveal a progressive change in P_{CO_2} with automatic and rhythmical ventilation but do show a progressive increase in physiological dead space as determined by a widening arterial–end-tidal P_{CO_2} difference. We cannot explain our lack of agreement concerning oxygen but it appears to us that both groups may be measuring different aspects of a similar phenomenon. Atelectasis possibly occurs, but this may be only part of the explanation. We prefer to look upon it as an interference with the normal ventilation/perfuson ratio with some alveolae overperfused and under-ventilated and others not perfused and over-ventilated. Our previous observations during deliberate hypotension with manual inconstant ventilation showed marked variation in both arterial–end-tidal P_{O_2} and P_{CO_2} differences. Further, under these circumstances with sympathetic blockade present, body tilting, further hypotension, or increased airway pressure might widen the discrepancies. There is some reason, therefore, to suggest that atelectasis not be considered the sole cause of the changes noted by Bendixen and co-workers and that deep inspiration not be thought of as the preventive or therapeutic panacea.

TABLE 2. Mean Tidal Volume and Mean Slopes for Each Group

Agent	Number of Subjects	Mean Slope V_D	SD	V_T
Control	5	0	—	615
Halothane	6	0.48	0.21	440
Cyclopropane	5	0.65	0.33	490
Nitrous oxide	6	1.05	0.47	824

Pending further investigation along these lines, it is well for the anesthetist to recall that anesthesia is associated with a gradual increase in that proportion of tidal volume failing to participate in gaseous exchange with blood. This leads to a slow rise in arterial P_{CO_2} unless there is adequate compensation by hyperventilation. It is not likely to cause hypoxia except in those situations where the oxygen content of inspired gas is low; this might occur where high concentrations of nitrous oxide or ethylene are being used. The rise in physiological dead space would be of greater significance in patients who have pulmonary emphysema, kyphoscoliosis, and the like.

Summary

The effect on respiratory dead space of halothane, cyclopropane and nitrous oxide anesthesia combined with controlled mechanical ventilation has been investigated in 18 patients. Five awake volunteers were investigated for comparison.

A gradual increase in physiological dead space, arterial to end-tidal P_{CO_2} difference and the ratio of physiological dead space to tidal volume was observed in each one of the anesthetized patients. It was not possible to distinguish between the effect of the different anesthetic agents. The relative increase in dead space seemed more related to tidal volume of respiration than to anesthetic agent. There was no change in similar measurements made in the volunteer group.

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POSTOPERATIVE PAIN A significant aspect of postoperative pain is psychological. The principles of "natural childbirth" were applied to surgical patients, to remove fear and promote pulmonary ventilation and early mobility. The patient is told to expect pain, and that early activity is both desirable and safe. He is taught deep breathing, coughing, and use of a positive pressure machine. Narcotics are given only on direct order of a physician, using 1 or 2 mg. of morphine intravenously. The total dose of morphine during the postoperative period has been reduced from 50 to 100 mg. to an average of 4 mg. The study group consisted of over 600 thoracotomy patients. (*Roe, B. B.: Are Postoperative Narcotics Necessary?, Arch. Surg. 87: 912 (Dec.) 1963.*)