OBSERVATIONS ON ANATOMICAL DEAD SPACE DURING GENERAL ANAESTHESIA*

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THE EFFECT of anaesthetic drugs on bronchial muscle and airway calibre is of utmost interest to anaesthesiologists. Unfortunately, because of ethical and instrumental difficulties, direct measurement of bronchomotor tone is yet hard to realize in man. So far, our knowledge of the subject derives in great measure from either studies on isolated lung structure in animals or clinical deductions. Both may fail decidedly to reach the truth. Reactions seen in animals are impressive but sometimes worthless because of species differences. Clinical inferences may also conceal truth under the cover of paradox. For instance, we know that all anaesthetic agents, when administered in specific conditions, may either relieve bronchospasm, as in status asthmaticus,¹⁻³ or induce such a spasm when a faulty technique of administration is used.

The study of anatomical dead space may be used as a quantitative, yet simple, indirect method of measuring changes in bronchomotor tone in man. At first glance, this seems as simple as the measurement of the mechanical dead space of a mask or a tube by determination of the volume of water it can hold. The difficulty stems from the highly versatile terminology used by different writers when they have to differentiate anatomical and physiological dead volumes. Even after years of controversy and research on the subject, the famous problem once confronting Haldane and Krogh has yet to be solved. There is a tendency to avoid the term anatomical dead space in the literature, because of its assumed undefined frontiers. A great deal of work has been done on physiological or respiratory dead space under experimental conditions, even during anaesthesia.^{4a, b} Most investigators agree that anaesthesia increases this volume, probably by alteration of the ventilation/perfusion ratio. Unfortunately, these studies do not take into account the anatomical dead space and seem to neglect the fact that when an investigator determines physiological dead space, he measures a functional volume which encloses a mensurable anatomical entity. An increase in physiological dead space may well be due, at least in part, to changes induced by anaesthetic drugs in airway calibre and bronchomotor tone.

Knowing the values of tidal volume, and the concentrations of carbon dioxide in inhaled, expired, and alveolar air, one then calculates anatomical dead space by simple application of the Bohr formula

$$VD_{\text{anat}} = VT(FACO_2 - FE\text{CO}_2) / FACO_2,$$

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where VD = anatomical dead space,
 VT = tidal volume,
 $FACO_2$ = fractional concentration of CO_2 in alveolar gas,
 $FECO_2$ = fractional concentration of CO_2 in expired air

The difficulty in applying this formula rests in obtaining an acceptable value for alveolar air composition. Some investigators utilize complex end-tidal samplers which, especially at small tidal volumes, may not completely avoid contamination with dead air. Others use the arterial sampling method to appreciate alveolar CO_2 or O_2 concentrations. These arterial parameters do bear some relationship to the alveolar gases, but the alveolo-arterial gradient would have to be established experimentally for every determination, and not merely ignored or assumed. Continuous analysis of a physiologic gas, CO_2 , during cyclic normal respiration, makes possible the repetitive determination of alveolar CO_2 concentration. Using an infra-red monitor, the instantaneous concentration of expired air CO_2 , when suitably recorded on graph paper, yields a curve which can be partitioned into three components:

- 1 An isoelectric base-line, indicating a complete absence of CO_2 . This fraction of expired air is identical with inspired air and represents the beginning of dead air washout.

- 2 A more or less sharply ascending line, which denotes contamination of alveolar air with dead space air,

- 3 A sustained plateau, ideally uniform and closely resembling a straight line, though very slightly ascending in practice because of the uninterrupted arrival of CO_2 from mixed venous blood to the alveoli. This plateau is indicative of the expiration of homogeneous alveolar air, after complete dead air washout.

There is yet some uncertainty in locating the point which is representative of real alveolar CO_2 on this slightly ascending plateau. Some place it at the beginning, some at the end of the plateau, most authors, however, favour a compromise in between. In individuals with normal lungs and an unobstructed airway who breathe a tidal volume just sufficient to produce complete dead air washout, such an alveolar plateau is always present on expiration, and its ascension does not rise above 0.2 per cent CO_2 . In asthma, emphysema, and other pathological conditions where the ventilation/perfusion ratio is not uniform, the plateau may be either sharply ascending, or absent, being replaced by a triangular aspect of the curve. In both cases, the sharpness of the rise bears some relationship to the severity of the disease (Fig 1).

METHOD

In the following experiments, tidal volume was measured by means of a Wright ventilometer affixed to the face mask. Ventilation was measured during a whole minute, then divided by the frequency. The tidal volume thus obtained represented the mean of steady state tidal volumes over a minute. This practice has the advantage over the single breath technique that results are uninfluenced by the dead space variations known to occur during the respiratory cycle, i.e. increase during inspiration and decrease during the following expiration. So the dead

FIGURE 1

volumes obtained in our patients are mean dead space over one minute of steady state breathing. The presence of a steady state was assessed by the clinical smoothness of anaesthesia, by the similitude between two or three consecutive minute volume determinations, and by the regularity of the expired CO₂ curve on the recorder. Another advantage of this curve was to permit a precise determination of the respiratory rate. As a minimal error in frequency may lead to gross distortion of the results, great emphasis must be laid on the graphic determination of frequency. Time as obtained from a chronometer is far from accurate in comparison with graphically recorded time.

Sampling of expired as well as of inspired air was obtained from under the mask by means of a 15 gauge needle transfixed through it at a point just in front of the patient's nostrils. A short length of polyethylene tubing aspirated the gas to be analysed from the needle into the infra red cell of the Godart capnograph. The response time of the capnograph is as rapid as 0.08 second. This apparatus is highly selective for CO and no correction is necessary for diluent gases or anaesthetic vapours. The presence of halothane, halothane-ether azeotropic mix

ture, and methoxyflurane in the analysing cell produced no deflection of the CO₂ meter, while a 50–50 nitrous oxide–oxygen mixture induced a constant error of 0.09 per cent CO₂, this minimal error being neglected afterwards. Experiments with explosive vapours were precluded by the fact that this unit is not explosion-proof.

FACO₂ was determined at a point lying one centimetre before the end of the CO₂ plateau. FECO₂ was obtained from planimetric measurement of the area under the curve of CO₂ concentration. Both measurements were made on every curve yielded during a period of one minute, so they indicate mean FACO₂ and mean FECO₂ during that time. The instrumental dead space of our valve and face mask, as measured by the amount of water they can hold, was standardized at 100 c.c. and suitably corrected from total dead space. As indicated by the steady return to the isoelectric line during inspiration, no rebreathing was produced by this head assembly because of the constant washout achieved under the mask by the suction pump of the analyser. The flow rate of this vacuum pump driving part of the respired gases through the analyser was adjusted at 2 litres per minute. All sampling procedures and determinations were performed simultaneously.

These studies were performed in the operating room on 36 patients, 19 males and 17 females, of ages ranging from 17 to 76 years. All patients were in excellent clinical condition and most of them were scheduled for extra-abdominal and extra-thoracic minor surgical procedures. As a premedication they all received a moderate dose of meperidine, along with 0.4 mg atropine intramuscularly 1 hour prior to anaesthesia. After a control dead volume determination, which served later as a point of reference for the other determinations in the same subject, induction was obtained in 8 patients with halothane by inhalation, in 9 with methoxyflurane vapour, in 10 with inhalation of halothane–ether azeotropic mixture, and in 9 with intravenous thiopentone. Oxygen and nitrous oxide were used in concentrations of 50 per cent as vaporizing agents. The pharmacological action of these two agents on bronchial calibre was demonstrated to be negligible at the concentrations used.⁵ The course of anaesthesia conformed to standard practice, although we would like to emphasize that in no instances were curare, endotracheal intubation, oral or nasopharyngeal airways, and positive pressure used, except in two cases where airway patency could not be obtained otherwise. Respiration was left unassisted throughout the whole period of anaesthesia, the patency of the airway being maintained by slight rotation and extension of the neck. We were particularly careful in holding the face mask in the same position for the same patient. About four dead space determinations were obtained in every subject during anaesthesia, followed by a last measurement in the recovery room after complete arousal.

CRITICAL ANALYSIS OF THE METHOD

Haldane⁶ called attention to the fact that dead space measured from CO₂ yields lower results than those obtained from oxygen or foreign gases. Our study confirms his conclusions.

Before we discuss the evolution of airway calibre during administration of

TABLE I
ANATOMICAL DEAD SPACE AND RELEVANT DATA IN SEVEN CONSCIOUS SUBJECTS
(three determinations at 10-minute intervals)

Subject, sex, age, weight	Pulmonary ventilation, L /min	Frequency	FACO ₂	FECO ₂	Dead volume (anat)	Standard deviation
1 Male	9200	14	4 1	3 2	144 2	
31 years	8750	14	4 08	3 0	140	
173 pounds	8225	12	4 0	3 1	146	3 1
2 Female	7788	13	5 3	4 07	109	
43 years	7120	14	5 3	4 1	115	
130 pounds	6780	13	5 3	4 2	108	3 76
3 Male	8900	20	5 3	4 1	100 6	
38 years	8150	21	5 3	4 0	95 2	
135 pounds	9315	19	5 4	4 3	101	3 15
4 Male	8150	24	5 8	3 29	145 4	
28 years	6800	18	5 7	3 45	149	
168 pounds	6090	17	6 18	3 75	140 7	3 75
5 Male	8900	21	5 59	3 92	126	
49 years	8250	20	5 9	4 12	125	
154 pounds	8800	20	5 94	4 14	131	4 3
6 Male	7800	27 2	5 02	2 49	144	
35 years	7250	26 1	5 25	2 55	143	
182 pounds	8200	28 8	4 83	2 24	154	6 5
7 Male	8000	13 3	4 53	2 61	154	
30 years	7850	14 4	4 60	2 54	144	
145 pounds	8225	14 2	4 60	2 61	151	5 1

different anaesthetic drugs, it seems necessary to evaluate the dispersion of the results of dead volume determinations in the same subject without anaesthesia, in order to appreciate the reproducibility of our technique and its percentage of error. Therefore, seven conscious subjects were submitted to three consecutive dead space measurements at 10-minute intervals. These experimental data are presented in Table I. In every case, the standard deviation between the two last determinations and the first one, considered as control value, averaged 4.23, with extremes of 3.1 and 6.5. Thus, having established both the limitation and the validity of our technique, we then proceeded to use it clinically on anaesthetized patients in the operating room.

RESULTS

Effects of Thiopentone

Table II indicates the effects of thiopentone anaesthesia in nine patients for whom this agent was the main drug administered during surgery, along with oxygen and 50 per cent nitrous oxide. After a control determination, anaesthesia was induced with a sleep dose of 2.5 per cent thiopentone, then maintained either with successive doses of the same solution, or with a drip of 1 gm of thiopentone in 250 cc of a 5 per cent dextrose solution. Most patients in this series were fit males undergoing limb surgery of about 45 minutes' duration. Mean thiopentone dosage necessitated by this method of anaesthesia was 809 mg.

TABLE II
ANATOMICAL DEAD SPACE AND RELEVANT DATA IN NINE PATIENTS DURING THIOPENTAL
ANAESTHESIA (SPONTANEOUS BREATHING)

Subject, sex, age, weight	Time, min	Pulmonary ventilation, L/min	Frequency	FACO ₂	FECO ₂	Dead volume (anat)	Dosage, mg
1 Male 20 years 150 pounds	-10	9000	25 5	3 48	2 12	138	875
	5	5400	21 4	4 44	2 77	94 8	
	10	5100	21	4 63	3 28	70	
	30	7475	25	5 21	3 42	101	
	40	8700	28 5	5 49	3 70	99	
	70	9050	26 6	5 17	3 20	128	
2 Male 45 years 150 pounds	-10	10675	23 3	5 10	3 50	146	830
	5	5655	20 7	5 31	3 53	92	
	15	7650	20	5 93	3 90	130	
	25	9050	20	6 57	4 83	127	
	45	10100	25 3	6 39	4 18	138	
	60	11065	13	4 70	3 97	152	
3 Male 32 years 124 pounds	-5	5450	21 8	4 19	2 08	130	800
	10	6490	16 3	5 13	3 45	131	
	20	7219	21 5	4 20	3 15	84	
	30	7335	24	4 03	2 55	112	
	60	7075	22 5	4 20	2 99	90	
	75	8000	19 1	5 20	3 13	166	
4 Male 50 years 190 pounds	-5	6600	12 5	5 82	4 48	127	425
	5	5050	16 2	6 32	5 07	63	
	10	6675	14 4	6 81	5 14	115	
	25	7875	14 7	7 87	5 75	144	
	60	7000	14 2	6 33	4 44	148	
5 Male 30 years 152 pounds	-5	8075	16 5	5 46	4 00	131	800
	10	6275	12 4	7 70	6 25	95	
	20	9350	17 3	6 82	5 19	129	
	45	8750	17 1	7 04	5 23	131	
	60	9425	16 2	6 42	5 00	128	
6 Female 50 years 144 pounds	-5	4500	19 5	6 15	3 28	107	500
	5	5950	23	6 32	4 05	92	
	10	5500	19 6	5 63	4 61	50+20	
	60	7210	25 7	5 26	3 27	106	
7 Male 21 years 175 pounds	-10	6800	15 9	6 25	3 91	159	950
	10	5000	18 5	7 88	5 41	85	
	20	8580	26 4	6 82	5 00	87	
	30	8250	25	6 79	4 30	121	
	45	10800	30 8	7 00	4 12	144	
	75	6620	15 7	7 10	4 72	140	
8 Male 21 years 175 pounds	-10	4620	11	6 25	4 25	134	1300
	10	3750	12 5	7 23	4 53	112	
	25	5550	13 5	7 57	5 75	98	
	35	4600	18 4	7 51	4 78	90	
	50	8220	20 5	8 52	6 25	106	
	60	8900	21 2	8 05	5 30	143	
	90	6320	16 5	6 38	4 08	138	
9 Male 40 years 170 pounds	-10	5300	13 5	6 25	3 92	146	800
	10	4350	18	7 42	4 06	108	
	30	4750	8 6	7 45	6 14	96	
	45	5950	16 6	7 00	4 53	127	
	60	5850	12 5	6 01	4 01	148	

Initially, every patient reacted by a marked decrease in anatomical dead space (from a mean of 135 before to a mean of 95 c c 10 minutes after induction, $P < 0.001$) Later on, such a decrease was sustained in most subjects, although at a somewhat higher level (mean dead volume during maintenance 107 c c, $P < 0.01$) As soon as anaesthesia was discontinued, dead space returned to the control preoperative level

There is evidence, therefore, that thiopentone markedly decreases anatomical dead space in most patients receiving it, even if they do not exhibit a clinical syndrome of overt bronchiolar obstruction with wheezing

Effects of Halothane

In this group of eight patients, undergoing anaesthesia for surgical procedures where no muscular relaxation was required, induction and maintenance were obtained with halothane vaporized through a Vernitrol vaporizer Carrier gases were oxygen and 50 per cent nitrous oxide We should like to point out that, in order to evaluate the dose/effect ratio, some of these patients enjoyed moderate levels of narcosis, while some others were carried to deep anaesthesia In every case, our results indicate very little variation in anatomical dead space during and after halothane administration The over-all mean dead space before anaesthesia was 114 c c During anaesthesia, it remained at a mean of 106 c c No significant difference among these means could be demonstrated ($P > 0.05$) So it is obvious from these results and from study of Table III that there is no large amount of variation between the halothane group and our control group without anaesthesia

Effects of Methoxyflurane

The anatomical dead space in nine patients who received a methoxyflurane induction and maintenance is listed in Table IV Every patient reacted the same way—by an increase in dead volume From a mean control of 112 c c before induction, dead space rose to 131 during anaesthesia, a result which is highly significant at the 5 per cent probability level Reviewing individual results, it will be seen that this increase did not appear very soon after induction in many patients Three subjects even showed initially a decrease in airway calibre In most patients a significant increase becomes manifest only after 30 minutes of anaesthesia This indicates implicitly that some of the pharmacological effects of methoxyflurane may be elicited only after an adequate tissue concentration is reached

Effects of Halothane-Ether Azeotrope

Table V lists the dead space values in 10 patients anaesthetized with the azeotrope Its effects on anatomical dead space are indistinguishable from those found with methoxyflurane An increase in airway calibre was present in every patient, but usually did not appear before the first half hour of anaesthesia. Seemingly, the ether fraction must also reach an adequate tissue level before having some pharmacological influence Eventually, it induced in our patients a 20 per cent increase in dead volume (from a mean of 111 c c before to 135 c c during anaesthesia, $P \leq 0.05$) At emergence, there remained some increase in dead space in many patients for an undetermined period of time

TABLE III
ANATOMICAL DEAD VOLUME AND RELEVANT DATA IN NINE PATIENTS
DURING HALOTHANE ANAESTHESIA (SPONTANEOUS BREATHING)

Subject, sex, age, weight	Time, min	Pulmonary ventilation, L /min	Frequency	FACO ₂	FECO ₂	Dead volume (anat)	Concen- tration inhaled, %
1 Female 49 years 129 pounds	-5	7100	21 8	5 11	3 54	100	
	5	5680	21 6	4 58	2 62	93	2
	15	8975	28 8	5 61	3 85	98	0 7
	30	8765	36	5 09	3 04	98	0 7
	40	5100	32	5 00	2 60	77	0 5
	55	6290	36	4 61	2 23	90	0 5
	90	6580	26 2	7 68	4 22	113	
2 Female 64 years 164 pounds	-5	5100	21 3	5 00	3 10	93	
	5	6920	38 5	5 90	4 80	93	2
	10	10070	46	5 86	3 24	98	0 75
	20	10190	40 4	6 05	3 63	101	0 75
	30	7740	41	5 30	3 01	81	1
	60	7800	29 3	5 62	3 48	101	
3 Male 40 years 198 pounds	-5	8200	23	4 65	3 34	100	
	10	11400	30 5	5 55	3 86	113	2
	25	9500	28	5 40	3 65	110	1
	45	11275	30 5	5 40	3 97	98	1
	75	10025	18	5 19	4 21	105	
4 Male 31 years 126 pounds	-5	9800	12 5	5 71	4 53	162	
	20	12800	26 6	5 81	4 00	150	1 5
	30	9000	28	6 79	3 59	152	1 2
	45	10850	28	6 41	3 99	146	1
	90	7600	19 1	5 77	3 32	169	
5 Male 82 years 138 pounds	-5	3900	14 7	4 95	2 79	116	
	5	6910	28 7	5 59	2 92	115	2
	15	6850	30 7	5 14	2 45	116	1
	35	5500	17 1	5 16	3 00	134	
6 Male 20 years 113 pounds	-5	4975	14 4	5 41	3 75	106	
	15	7410	27 3	5 34	3 57	90	1
	25	5150	24 2	5 29	3 00	92	0 5
	35	6010	23	6 35	3 90	100	0 5
	60	5355	20	5 70	3 82	89	
7 Female 46 years 107 pounds	-5	8750	15 8	5 62	4 46	113	
	10	2250	8 5	7 55	5 26	91	2 5
	20	3700	13 2	8 68	5 47	103	1 2
	35	4200	16 1	7 58	4 75	97	0 5
	45	5150	13 6	7 00	5 38	88	0 5
	75	6650	12	5 43	4 40	105	
8 Male 44 years 152 pounds	-5	5940	14 5	5 36	3 75	123	
	10	2700	10	5 74	3 00	128	2
	20	3600	6 5	6 91	5 35	124	2
	60	8150	15	4 80	3 43	154	

TABLE IV
ANATOMICAL DEAD SPACE AND RELEVANT DATA IN NINE PATIENTS
DURING METHOXYFLURANE ANAESTHESIA (SPONTANEOUS BREATHING)

Subject, sex, age, weight	Time, min	Pulmonary ventilation, L/min	Frequency	FACO ₂	FECO ₂	Dead volume (anat)	Concen- tration inhaled, %
1 Male 86 years 180 pounds	-10	7325	18	5 05	3 44	130	
	10	11250	15	5 02	3 90	167	3
	25	7425	16 2	4 64	3 21	142	3
	40	5450	13 7	5 05	3 77	101	1
	60	8100	16 8	5 18	4 00	110	
2 Female 47 years 204 pounds	-10	6100	16	6 17	4 62	95	
	15	4395	17 1	5 81	3 48	103	3
	30	12550	26 6	3 24	2 45	115	0 8
	45	9800	21 9	4 70	3 19	144	0 5
	75	6475	24	5 25	3 00	116	
3 Female 53 years 113 pounds	-5	3600	7 5	6 44	5 07	102	
	15	2620	11	8 05	5 31	80	3
	25	5270	14	6 79	4 12	147	1
	35	4400	12	6 38	4 11	130	0 6
	50	4000	12	6 72	3 83	143	0 6
	90	3100	9	6 63	4 88	90	
4 Female 24 years 165 pounds	-5	8080	16 5	5 90	4 79	92	
	15	6375	23 7	7 34	4 53	103	3
	30	7185	26 2	6 00	3 60	109	1
	50	6825	25 3	6 00	3 33	120	0 6
	90	5750	20 5	6 37	4 43	85	
5 Male 38 years 150 pounds	-5	7500	26 5	5 34	2 92	128	
	20	9700	41 7	5 74	2 64	125	3
	30	9360	40 5	5 33	2 10	140	1
	45	9225	34 7	6 31	2 94	142	1
	55	9075	31 5	6 38	3 20	143	1
	90	10000	24 2	5 40	3 25	164	
6 Female 53 years 164 pounds	-5	5125	21	5 74	3 80	82	
	15	4925	21 9	7 20	4 20	93	2 5
	20	4700	21 4	8 03	3 87	114	1
	30	4670	17 0	7 05	4 41	103	1
	35	4700	16	7 18	4 41	113	1
	90	5650	12 5	6 31	5 00	93	
7 Male 30 years 200 pounds	-5	9050	13 3	5 36	4 20	147	
	15	9510	27	4 80	2 52	185	3
	35	10900	28 4	5 43	3 00	172	3
	90	7040	10 5	6 06	4 12	214	
8 Female 53 years 205 pounds	-5	10025	19 1	5 50	4 28	117	
	15	8410	18	8 24	5 87	135	3
	25	7850	21 7	7 54	4 74	134	2
	40	5350	17 5	8 00	4 81	122	1
	50	5350	13	8 52	5 60	141	1
	60	6690	14	8 30	5 65	152	1
	100	9300	13 5	4 48	3 75	114	
9 Male 43 years 140 pounds	-5	6900	21 3	6 88	4 28	122	
	15	6250	19	5 68	3 58	121	3
	30	7380	21	5 33	3 02	152	2
	45	7880	21	5 56	3 28	154	2
	90	5700	19	6 06	2 62	170	

TABLE V
ANATOMICAL DEAD VOLUME AND RELEVANT DATA IN 10 PATIENTS
DURING AZEOTROPIC HALOTHANE-ETHER ADMINISTRATION (SPONTANEOUS BREATHING)

Subject, sex, age, weight	Time, min	Pulmonary ventilation, L/min	Fre- quency	FACO ₂	FECO ₂	Dead volume (anat)	Concen- tration inhaled, %
1 Female	-15	3700	24	6 67	2 50	96	
76 years	20	4570	21 4	6 18	3 40	96	4
119 pounds	45	5650	27 7	5 65	2 80	103	2
	60	6250	30 6	6 18	2 20	132	2 5
	105	4175	36 1	6 49	1 88	94	
2 Male	-15	13450	20	6 20	3 60	173	
35 years	25	8400	20 5	6 30	5 91	252	5
100 pounds	60	11100	17 5	5 30	3 60	203	
3 Female	-15	4646	13 7	5 62	4 00	98	
21 years	15	5130	13 1	6 51	3 23	195	5
85 pounds	30	6050	29 7	6 78	3 04	112	2 5
	60	8150	45 8	6 11	3 00	90	2 5
	90	6750	19 8	5 58	3 84	106	
4 Female	-15	6353	24 4	5 62	3 25	109	
46 years	40	6220	14	6 00	4 50	111	3
118 pounds	60	6530	16 4	6 35	4 16	133	2
	75	6700	17	6 25	4 10	135	1 25
	120	8130	26	5 95	3 00	154	
5 Female	-15	3050	22	5 20	2 31	100	
76 years	90	6300	30	6 60	2 45	132	2
122 pounds	120	6000	28	7 00	2 15	148	0 5
	150	6000	20	5 30	3 00	130	
6 Male	-15	9600	20	4 27	3 00	143	
32 years	30	7125	32	7 95	3 00	139	3 0
153 pounds	60	10180	26	5 55	3 10	172	2 5
	75	6350	20	6 40	3 45	156	2
	110	7600	18	5 17	3 50	136	
7 Female	-15	4700	13	5 51	4 14	90	
64 years	15	7240	20	4 74	3 45	98	5
201 pounds	30	8830	21	5 12	3 22	155	2 5
	90	9200	26	5 30	3 68	108	1 5
	105	8600	26	5 08	3 33	115	2
	120	9600	21	4 15	3 45	78	
8 Female	-15	6050	20	5 70	3 80	100	
23 years	15	5000	25	6 24	3 40	91	2 5
132 pounds	30	9300	40	5 82	3 20	104	2 5
	45	9350	32	6 38	2 80	161	1 2
	120	10750	30	5 55	3 33	143	
9 Female	-15	6650	21	5 02	3 65	86	
24 years	30	6100	37	5 66	3 00	77+70	2
217 pounds	60	7850	37	5 90	4 20	61+70	1 2
(endotracheal	90	5700	32	5 40	3 40	66+70	1 2
tube inserted)	120	6800	33	4 95	3 70	52+70	1
	180	8400	22	5 63	3 01	178	
10 Male	-15	5200	10 8	6 36	4 75	122	
22 years	15	11250	34 3	4 93	3 27	110	4 5
128 pounds	25	8700	36	5 85	2 86	124	2 5
	40	10650	34 5	5 49	2 53	166	2
	50	9700	27 1	6 15	4 00	168	2
	90	8700	26 8	4 65	2 91	121	

DISCUSSION

We shall now proceed to examine first the nature, then the function, of anatomical dead space as related to anaesthesia. Anatomical dead space may be defined as the inside volume of the airway down to the respiratory bronchioles. Its upper portion (nose, mouth, pharynx, larynx) is rather invariable in its physical dimensions, being fixed to a rigid osteocartilaginous frame. In contrast, its lower part, which includes trachea, bronchi, and bronchiolar divisions, has ensheathed in its wall a geodesic network of smooth muscle whose elastic properties can induce tremendous variations in airway calibre through relaxation or constriction of its lumen. In consideration of the greater flexibility of this lower part, as compared with the relatively rigid structures above, there is some reason for assuming that variations other than minimal in airway calibre take place in bronchial divisions down to the respiratory bronchioles.

The relationship between FACO_2 and FECO_2 which actually defines the Bohr formula can be disturbed by physiological or pathological alterations of alveolar CO_2 concentrations as induced by an unsteady state, rebreathing, diffusion anomalies, or lack of uniformity in the ventilation/perfusion ratio.

The steady state is a difficult problem. In the conscious patient, it involves absolute physical and mental rest, fasting, relaxation, and passivity. In the anaesthetized patient, such a basal state is easily obtained, but yet this is not a steady state. Even reflex activity must be overcome because of its resonance on ventilation. Thus, a steady state would theoretically require deep anaesthesia. However, unfortunately, at this stage, hypoventilation leads to progressive CO_2 retention and again breaks the labile equilibrium. In this study, a steady state was said to exist when ventilation changed very little over a few minutes. If extremes in ventilation of the lungs are avoided, i.e. if tidal volume remains between 250 and 700 c.c., there is almost no interrelationship between anatomical dead volume and tidal volume. Moderate degrees of hyperventilation or hypoventilation, as observed in anaesthetized patients breathing spontaneously, cause only very slight changes in anatomical dead volume. In fact, the best information available on the subject indicates that an increase of 10 c.c. is produced by each 1000 c.c. increase in tidal volume.⁷ This variation, observed during spontaneous respiration in the biological steady state, is negligible in practice. Indeed, it should become more important when positive pressure is applied to the airway during artificial ventilation because of the mechanical factors involved.

It seems very unlikely that anaesthetic agents might cause limitation of CO_2 diffusion across the alveolar-capillary membrane. Coefficients of gas exchange through this membrane were once determined by means of anaesthetic gases, nitrous oxide, ethyl iodide, and acetylene.⁸ Furthermore, so high is the CO_2 diffusing capacity that even gross alterations of diffusing membranes, as observed in alveolo-capillary block, hardly hinder its free transfer across alveolar-capillary membranes.

Information about ventilation/blood flow during anaesthesia may be provided, as stressed by Comroe *et al.*,⁹ by continuous monitoring of CO_2 in expired air and from capnographic curves. The appearance of a plateau on these curves

involves three factors (1) the contribution by the pulmonary capillaries of a uniform CO₂ output to the alveoli, (2) uniform ventilation of the alveoli, (3) synchronous emptying of every part of the lung during expiration. If expired alveolar CO₂ concentrations rise significantly during expiration, then the lung not only empties asynchronously, but also contains alveoli with no blood flow, or alveoli with a decreased blood flow and a relatively high ventilation, or, at last, alveoli adequately perfused but grossly hyperventilated. That such anomalies in the distribution and mixing of intrapulmonary gases may be eliminated from our study is evidenced by the fact that in our patients either before, during, or after anaesthesia with the aforementioned agents, a uniform plateau of CO₂ concentration occurred during expiration. This provides good evidence that experiments of this kind can be of value in obtaining reliable values of anatomical dead space, uncontaminated with physiological components.

Our data suggest that the halothane-ether azeotropic mixture and methoxyflurane both dilated the bronchial tree. Halothane anaesthesia seems to have left the bronchial lumen unaffected in size. With thiopentone, the tendency to bronchoconstriction is evident. If we assume that bronchomotor tone is controlled by a fine balance between sympatho-adrenal and cholinergic influences, then the mechanism underlying these changes becomes less obscure. Dysautonomia seems to be at work. Halothane, by virtue of its ganglioplegic properties, may isolate bronchial divisions from neurogenic control. Theoretically, they should open more widely during inspiration and narrow to a greater degree than normal during expiration, the "mean" dead volume, however, showing no significant change. With thiopentone, no such neurovegetative blockade is induced, but catecholamine outpouring from adrenergic sites is known to be very low with this barbiturate,¹⁰ so the vagi may well become predominantly active. On the contrary, adrenergic stimulation seemingly occurs during methoxyflurane and halothane-ether administration.^{11 12} On the whole, however, the pharmacodynamics of the changes induced by anaesthetic drugs on the bronchial musculature still remain enigmatical and no good reason exists to preclude a direct action of these agents on muscular fibres themselves.

In reviewing our results on anatomical dead space determinations and our conclusions on bronchomotor tone, one might speculate about the consequences in the anaesthetized patient of such changes. On the one hand, the advantages of bronchodilatation are obvious:

- 1 The resistance to breathing is decreased, so the work of breathing is kept minimal.

- 2 IPPB is achieved at a lower mean intrathoracic pressure.

- 3 A complete obstruction of bronchial divisions by mucus or foreign material with ensuing atelectasis is less likely to occur.

On the other hand, the increase in anatomical dead space encroaches upon alveolar ventilation. For the same tidal volume, the greater the dead fraction, the smaller the effective portion committed to respiratory interchanges. Thus, during anaesthesia with agents which increase the calibre of the bronchial tree, hypercapnia may occur, even if measurements of total pulmonary ventilation seem at first glance acceptable and within normal limits, because a greater portion

of each tidal volume is wasted to fill a wider conducting airway and is ineffective as far as alveolar ventilation is concerned. This leads us to a somewhat unforeseen conclusion, that, with some anaesthetic agents, even the normoventilating patient should receive respiratory assistance.

Bronchoconstriction, as observed with thiopentone likewise carries well-known difficulties. As airway resistance increases, compliance falls to a low value, a fact well illustrated in anaesthesia by increased resistance to positive pressure ventilation.

SUMMARY AND CONCLUSION

The determination of anatomical dead space is proposed as a suitable means to indirect appreciation of changes induced by anaesthetic agents on bronchomotor tone and bronchial calibre. Such determinations were performed in 36 patients prior to, during, and after anaesthesia produced with halothane, thiopentone, methoxyflurane, and with the azeotropic mixture of halothane-ether. No significant changes were observed with halothane. Thiopentone administration induced a consistent reduction in anatomical dead space. Significantly higher values, however, were found during methoxyflurane and halothane-ether anaesthesia, a finding we interpreted as bronchodilatation.

We suggest that the mechanism underlying the production of these variations in airway calibre is one of autonomic imbalance between sympathetic bronchodilator and parasympathetic bronchoconstrictor fibres, although either a direct action of anaesthetic drugs on bronchial smooth muscle itself or an indirect humoral approach may well be involved.

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