ALVEOLAR COLLAPSE INDUCED BY DENITROGENATION

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IT HAS BEEN WELL ESTABLISHED that the surgical patient undergoing general anaesthesia is prone to develop pulmonary atelectasis whenever periodic overinflations of the lungs are omitted during either spontaneous or mechanical ventilation.[13] Intensive research has thrown light on many features of this alveolar collapse: it can be detected neither by clinical nor by usual roentgenographic means; it increases venous admixture and induces a reduction in lung compliance; it may lead to arterial desaturation during the first 24 hours of the post-operative period.[4]

The implications of these recent discoveries have been of great concern to anaesthesiologists, who by tradition are more devoted to the prevention of alveolar collapse and hypoxaemia than to the induction of such disorders in patients committed to their care. However there seems to be no general application of the suggested corrective measure of reopening the collapsed alveoli by intermittent deep breaths or overinflations during surgery. Such hesitancy may be in part due to the fact that the basic studies on the subject have not yet succeeded in defining the cause underlying this alveolar collapse and have rather, by discussing a multiplicity of postulated aetiological factors, created a picture that is difficult to interpret.

The primary aim of the work reported here was to study the variations in functional residual capacity (FRC) during general anaesthesia. When we realized that this measurement could be relied upon as a useful and reproducible diagnostic test of alveolar collapse, we then engaged in an investigative program directed to elucidate the mechanism leading the alveoli to shrink and eventually to collapse during anaesthesia.

SUBJECTS AND PROCEDURES

The experiments reported in this investigation were performed in 19 normal subjects, who were divided into 4 groups. These subjects were essentially devoid of pulmonary symptomatology.

The first group included 7 adult patients, 3 males and 4 females, who were studied during general anaesthesia and surgery. In order to exclude external factors which may affect FRC values (retractors, assistants leaning on patients, position), most of the operations selected were peripheral surgery in the supine position, as indicated in Table I. The same procedure was followed in each

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TABLE I

RESPIRATORY DATA IN 7 PATIENTS (GROUP 1) DURING GENERAL ANAESTHESIA WITH HIGH OXYGEN INSPIRED MIXTURE

Subject, sex, age, weight, nature of operation	Time (minutes)	Pulmonary ventilation (L/min.)	Functional residual capacity (c.c. BTPS)	Arterial oxygen tension (mm. Hg)	Arterial CO_2 tension (mm. Hg)	Dead volume	
						anatomical	physiologica
1. Female, 34 years, 105 pounds, varicose veins	8	9150	2790	388	14.9	93	87.6
	38	8675	2033	363	14.5	86.7	83
	75	9650	2004	354	14.3	122	124
	105*	16720	2356	373	10.1	124	146
2. Male, 47 years, 125 pounds, herniotomy, enterostomy	6	6000	2307	464	32.5	79	150
	36	6210	2224	439	36.7	117	189
	66	6940	2129	420	35.7	110	207
	110*	4925	2585	459	41.2	82	153
3. Female, 36 years 162 pounds, varicose veins	5	7625	1855	412	28.3	90	188
	45	6200	1348	359	25.9	99	162
	65	6000	1459	335	26.8	99	140
	90*	6300	1697	365	24.4	65	116
4. Female, 38 years, 125 pounds, varicose veins	5	7100	1770	356	21.2	82	92
	40	7700	999	314	20.0	93	112
	75	8050	984	274	22.3	114	128
	100*	8000	1221	318	20.5	124	135
5. Male, 52 years, 135 pounds gastrectomy	15	8850	1839	354	21.3	94	100
	55	8100	1626	334	20.2	170	189
	100	6550	1665	336	20.6	158	140
	140*	6100	2015	358	24.0	107	123
6. Female, 30 years, 100 pounds, cholecystectomy	10	6220	1976	400	26.2	74	191
	50	6510	1374	374	31.6	60	211
	85	5600	1521	380	32.3	101	218
	125*	7850	2024	490	30.2	85	212
7. Male, 20 years, 135 pounds varicose veins	7	11300	2050				
	37	11000	1363				
	60*	9600	1542				
	125‡	7800	1617				

*These data were collected after overinflation of the lungs.
†In this case, ventilation was doubled without overinflation of the lungs.
‡Data obtained in the recovery room, the patient breathing air.

experiment. After a standard premedication of 75–100 mg. of meperidine along with 0.4 mg. of atropine, sleep was induced with thiopental in moderate dosage. Endotracheal intubation was facilitated with short-acting relaxants. Particular attention was paid to obtaining a strictly air-tight circuit by a slight overdistention of the endotracheal cuff. Careful auscultation of both lungs ensured proper position of the tracheal tube. Controlled ventilation was achieved throughout the procedure by means of a Bird Mark 4-Mark 8 assembly, delivering a mixture of pure oxygen with methoxyflurane or halothane-ether azeotrope at constant pressure and constant volume. A steady state of muscular paralysis was maintained by intermittent liberal doses of gallamine. In six patients of this series, a 21-gauge spinal needle was inserted into a brachial artery to provide serial determinations of blood gas parameters. Five to ten minutes after induction, an initial control FRC determination was obtained, along with a blood sampling and a measurement of anatomical and physiological dead-space volumes. Thereafter this sequence was repeated every 30 minutes. At the end of surgery, careful inflation of the lungs was achieved to overcome the changes in FRC which might have occurred previously, and then, after 5 to 10 minutes of normal ventilation, the last measurements were made.

Group 2 was studied as a control series of group 1. In an attempt to exclude from this investigation as many incidental factors as possible (premedication, anaesthetic drugs, intubation, intermittent positive pressure breathing), 7 healthy men, most of them residents in anaesthesia, volunteered to have their FRC determined in our pulmonary physiology laboratory. Resting quietly in the semi-recumbent position on a Recamier sofa, they were asked to breathe 100 per cent oxygen through an Edison or Ruben four-way valve adapted to a Godart seal mouthpiece. A control FRC determination was performed after 5 minutes of denitrogenation, and followed by two further measurements at 30 minute intervals.

In group 3 we studied the same volunteers (minus one who developed allergic cheilitis following his first use of the rubber mouthpiece); this time they inhaled a mixture of 50 per cent oxygen and 50 per cent nitrogen under the same experimental conditions as those of group 2.

The last group was made up of 5 anaesthetized patients who were studied under the same conditions as those of group 1, but who were ventilated from the beginning of anaesthesia with a mixture of 50 per cent oxygen and 50 per cent nitrogen delivered at constant pressure and volume by means of a Bird respirator. After an initial FRC control, two subsequent measurements were obtained 30 and 60 minutes later. The inspired gas mixture was then changed abruptly to 100 per cent oxygen, and again, at 75 and 90 minutes, FRC was measured. Before the end of the operation, renitrogenation was achieved by resumption of the 50 per cent oxygen-50 per cent nitrogen mixture; automatic respiration was interrupted for a few moments to permit over-inflations of the lungs by "sighs," and then the last FRC measurement was obtained. In these subjects, as in group 1, arterial blood samples were drawn and analysed for oxygen tension with an Epsco Blood Parameters analyser (model 101).

At first glance, measurement of Functional Residual Capacity in the operating

room may seem a complex procedure necessitating cumbersome instrumentation. Admittedly, plethysmographic methods become prohibitive when the subject to be studied lies on an operation table. In this instance, one must rely on open- or closed-circuit gas-dilution techniques using a spirometer and a tracer gas monitor. However these instruments are usually stationary and cannot be brought to the patient, nor can the anaesthetized patient be brought to the laboratory during surgery. We solved this problem by interposing between the patient in the operating room and the spirometer in the laboratory a movable reservoir, filled with a standard volume of gas at known helium concentration. A to-and-fro anaesthesia unit, with its canister well packed with Baralyme, its connections siliconized, and its rubber bag repeatedly tested for helium impermeability, was selected for the purpose. This method introduces a very slight technical variation to the standard helium closed-circuit technique described by Meneely;[5] in fact, instead of a lung-spirometer system, we used a lung-intermediate reservoir-spirometer system, in which the to-and-fro unit can initially be filled with a known volume of the gas-helium sampling mixture from the spirometer, then carried to the operating room where it is mixed with the alveolar air, and finally re-introduced in the spirometer for analysis of the changes induced by the pulmonary sampling. The results obtained are then used to solve the following equation, as derived from the dilution principle:

$$y = \{[(EM + V_1) \times He_1] - [(EM + V_2) \times He_2]\}/He_2$$

where: y = functional residual capacity; EM = dead volume of the spirometer circuit; V_1 = volume of gas added initially in the to-and-fro unit; He_1 = initial helium concentration; V_2 = volume of gas in the to-and-fro unit at the end of the sampling period; and He_2 = final helium concentration.

The spirometer used in this study was a Godart Pulmonet, which includes a thermal conductivity analyser designed to yield a linear response in a range from 0 to 5 per cent of helium (Fig. 1).

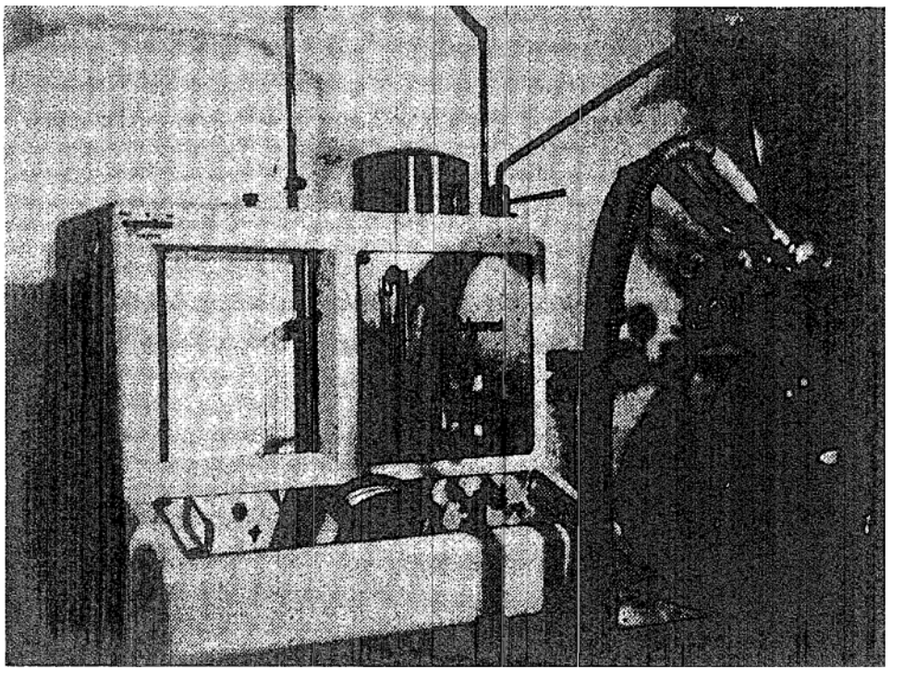

FIGURE 1. The Godart Pulmonet.

With groups 1 and 2 the sampling mixture enclosed in the movable reservoir and the spirometer circuit was pure oxygen with helium as a tracer, whereas with groups 3 and 4 the system was filled with 50 per cent oxygen and 50 per cent nitrogen, along with a known small percentage of helium. FRC determinations were started and concluded at the end-expiratory level, which was assumed ideally stable in the paralysed patient during surgery. No more than three seconds elapsed between the connection of the to-and-fro unit to the airway and the beginning of the subsequent sampling. Then the content of the sampling reservoir was intermittently ventilated by hand into the lungs at the same pressure and frequency as previously used during automatic ventilation. A standard period of three minutes was found adequate to provide a homogeneous mixture on the basis of accepted notions on nitrogen washout curves and pulmonary mixing time in normal subjects.[6] To substantiate this statement, nitrogen washout curves were obtained from some subjects of the present report and actually resulted in mixing times well below three minutes.

The oxygen content of the gas mixtures expired by the subject or used in the sampling devices was measured with a Beckman analyser. End tidal CO_2 was monitored between sampling periods with the Godart Capnograph. A Wright Ventilometer was used to determine minute-volume ventilation.

The accuracy inherent in our measurements of functional residual capacity was periodically evaluated by reproducing "in vitro" known gas volumes with the closed-circuit helium dilution technique. Our precision index averaged ± 0.74 per cent (2 S.D.), a very slight error indeed, and probably due to minimal inadequacy in the visual appreciation of helium concentrations on the catapherometer. The method requires special attention to the crossed sensitivity of the last monitoring device for nitrous oxide. This explains the exclusion of nitrous oxide from our anaesthesia technique. However halothane, methoxyflurane, and the azeotrope of halothane and ether were found to induce no deflection of the meter when used in usual clinical concentrations. Carbon dioxide and water vapor both underwent chemical absorption at the input line of the spirometer and consequently did not interfere with the reading and calibration of the helium meter.

Results

Group 1

Table I illustrates the results obtained in the subjects of group 1, who breathed 100 per cent oxygen during general anaesthesia. It can be seen that control determinations of functional residual capacity remained well within the range of accepted limits in supine subjects. After 30 minutes of anaesthesia, however, FRC invariably exhibited a considerable decrease, from a mean control value of 2121 c.c. to 1581 c.c., a 25 per cent difference which proved of statistical significance as determined by the Student's t test ($p < 0.05$). At the end of the first hour of anaesthesia, no further decrease in lung volume could be detected, as if FRC had been reset to a new low and relatively stable level (mean FRC at 60 minutes: 1627 c.c.). The last measurement, obtained within 10 minutes after

three deep breaths, indicated a definite, although incomplete, trend towards a return to control level, the mean result (1930 c.c.) falling somewhat lower than the control value. In patient number 1, no opening pressures were performed at the end of anaesthesia, but instead pulmonary ventilation was merely doubled. This procedure proved inadequate to reopen the lung completely.

From the beginning of anaesthesia, arterial oxygen tension in every case showed a moderate decrease. As expected, and as confirmed by our results, this decrease could be reversed by over-inflation of the lungs at the end of the experiment. It is of interest to point out that this fall was rather small (13%) when compared to the fall in FRC (25%); these results, however, are in agreement with those of Collier and Mead,[7] who used a compliance method to study atelectasis, and obtained a disproportionate effect on compliance as compared to venous admixture, greater changes occurring in the former than in the latter.

Dead-space studies carried out in this series of patients indicated in general a slight increase in anatomical dead volume and a parallel increase in physiological dead volume. This suggests an interrelationship between these phenomena, the increase in physiological dead space probably occurring as a consequence of the increase of its major component, the anatomical dead space. Similar increments in dead space were observed by our group in a previous study dealing with anatomical dead space during anaesthesia, and were postulated to result from pharmacological effects of anaesthetic drugs on bronchomotor tone.[8]

Group 2

The results obtained in conscious subjects breathing 100 per cent oxygen are depicted in Table II. In every case, after 30 minutes of denitrogenation, the normal initial values of functional residual capacity have declined consistently, from a mean control value of 2215 c.c. to 1716 c.c. (-22.5%, $p < 0.01$). After one hour, FRC determinations averaged the same result as after 30 minutes: 1722 c.c.; as previously suggested in the study of group 1, functional residual capacity, after a significant initial fall, has seemingly reached a steady plateau at a lower volume.

Group 3

Table II also shows FRC determinations in group 3, which was made up of the same volunteers breathing a mixture of 50 per cent oxygen and 50 per cent nitrogen. The results obtained after either 30 or 60 minutes of experiment closely duplicated initial values. In fact, so little variation occurred between these serial measurements that one can hardly refrain from using these data as indirect evidence of the precision and reproducibility of our technique.

Group 4

Data obtained in group 4 are illustrated in Table III. They pertain to 5 anaesthetized patients ventilated first with a 50 per cent oxygen-50 per cent nitrogen mixture, then shifted to 100 per cent oxygen. Figure 2 depicts the typical pattern followed by one of these subjects (no. 1). No important variations in FRC occurred as long as patients were allowed to breathe the nitrogen-enriched

TABLE II

COMPARATIVE DETERMINATIONS OF FUNCTIONAL RESIDUAL CAPACITY* IN SEVEN CONSCIOUS SUBJECTS, IN STEADY STATE

	Inspired gas: 100% oxygen			Inspired gas mixture: 50% O_2–50% N_2		
Subject, sex, age, weight	Control determination	After 30 minutes	After 60 minutes	Control determination	After 30 minutes	After 60 minutes
1. Male, 39 years, 135 pounds	2382	1738	1673	2313	2291	2219
2. Male, 33 years, 182 pounds	2048	1870	1797	2077	2110	2100
3. Male, 33 years, 175 pounds	2077	1838	1797	2093	2134	1987
4. Male, 25 years, 185 pounds	2014	1544	1546	1962	1962	1895
5. Male, 28 years, 145 pounds	2737	2037	1883	—	—	—
6. Male, 27 years, 168 pounds	2267	1678	1657	2235	2248	2247
7. Male, 28 years, 194 pounds	1985	1507	1696	1966	1985	1992

*All results were corrected BTPS.

TABLE III

EVOLUTION OF FUNCTIONAL RESIDUAL CAPACITY* AND ARTERIAL OXYGEN TENSION IN FIVE PATIENTS (GROUP 4) DURING GENERAL ANAESTHESIA WITH CONSTANT VENTILATION

Subject, sex, age, weight, nature of operation		Time in minutes from induction					
		5	30	60	75	90	120
		Inspired gas mixture: 50% O_2–50% N_2			Denitrogenation: 100% O_2		Renitrogenation + overinflations: 50% O_2–50% N_2
1. Female, 56 years, 135 pounds, cystectomy	FRC	2133	2281	2163	1881	1436	1796
	pO_2	256	264	246	442	432	189
2. Female, 39 years, 190 pounds, varicose veins	FRC	1332	1249	1268	1111	1049	1373
	pO_2	218	207	215	416	388	216
3. Male, 49 years, 160 pounds, varicose veins, herniotomy	FRC	2623	2585	2600	—	1674	2952
	pO_2	286	296	296	—	445	284
4. Male, 49 years, 142 pounds, herniotomy	FRC	1628	1520	1628	1115	—	—
	pO_2	195	215	210	375	—	—
5. Male, 45 years, 145 pounds, herniotomy	FRC	1910	1916	1925	1504	1439	1670
	pO_2	183	178	196	426	401	158

*FRC results were corrected BTPS.

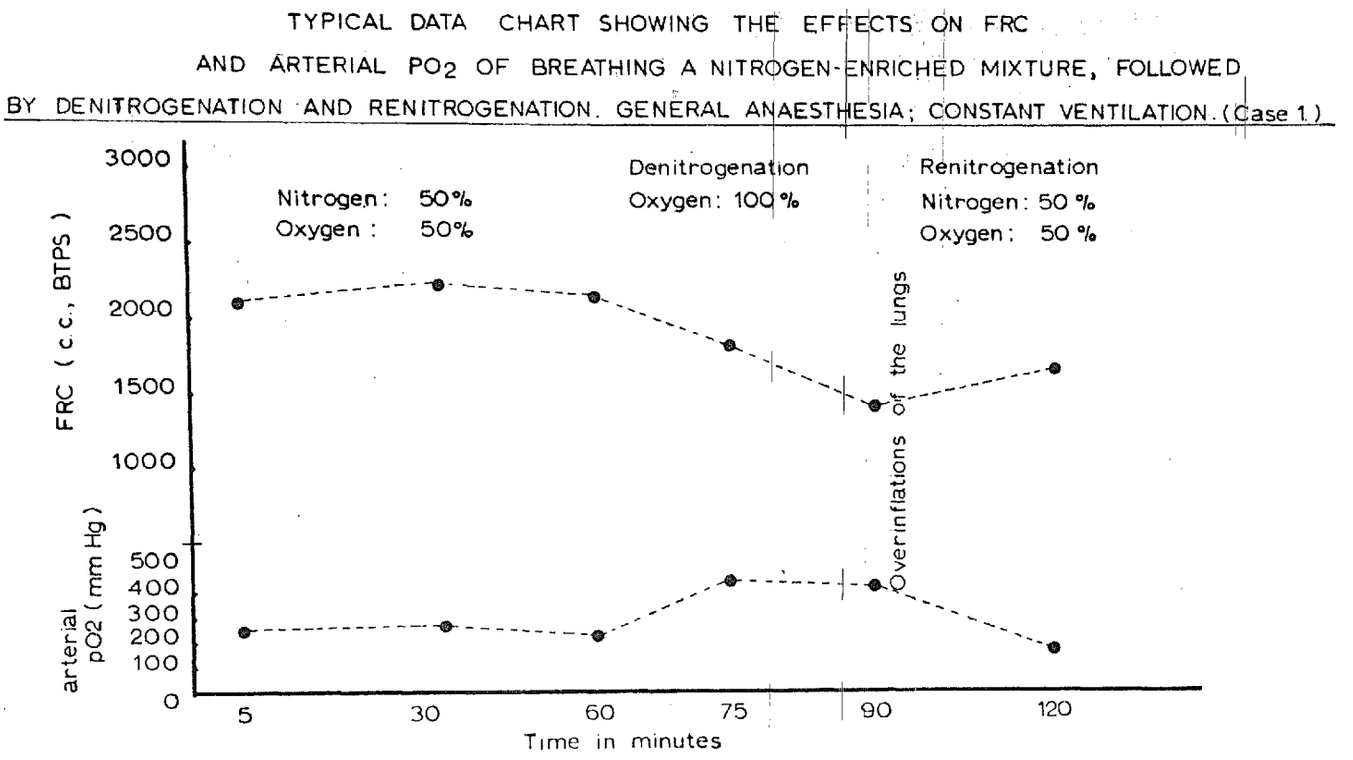

FIGURE 2. Results in Case 1.

mixture. Meanwhile, arterial oxygen tensions remained at a steady level and did not show the usual fall previously noticed during breathing of pure oxygen.

Major differences in this pattern were disclosed as soon as patients were shifted to inhalation of nitrogen-free atmosphere. They all responded by a rapid drop in FRC, from a mean control value of 2065 c.c. to 1402 c.c. after 30 minutes of denitrogenation. This decrease represented a 32 per cent smaller lung volume and was considered significant. The course of arterial oxygen tensions was also markedly affected by this sudden denitrogenation; since a higher oxygen tension was built up in the lungs, arterial pO_2 rose to high levels. From a mean stable value of 230 mm. of mercury during the nitrogen-oxygen period, pO_2 rose to 428 mm. of mercury (mean of 3 determinations after 15 minutes of denitrogenation), then started to decline as usually observed in patients breathing 100 per cent oxygen. After 30 minutes, pO_2 had dropped to 407 mm. of mercury.

It might be of interest to point out that no important distress was experienced by conscious volunteers while breathing pure oxygen. Some became drowsy, others irritable, but on the whole, individual reactions were inconstant and could not be predicted. A slight tachypnoea was more frequently observed, together with a moderate decrease in tidal volume, after 30 minutes of denitrogenation.

DISCUSSION

The analysis of these data leads us to the following statements:

1. Miliary atelectasis during anaesthesia should be considered as an unquestionable reality that every anaesthesiologist has to deal with every day. The present investigation, using a new approach to detect this disorder, strongly supports the conclusions previously reached by other investigators on its occurrence.[1–3] However, our method allows a more selective approach to lung volume

measurement than compliance determination and venous admixture calculation. Because it actually measures the volume of gas enclosed in alveoli that are specifically engaged in exchanges, FRC determination should be recognized as a useful, direct, and simple means for the quantitation of alveolar collapse.

2. The incidence of miliary atelectasis is high. In fact, it occurred in all the anaesthetized subjects included in this report, and we are prone to look on this disorder as a constant consequence of the anaesthesia techniques used today. Its rapidity of onset is surprising: in most cases, 30 to 45 minutes were long enough to allow a 25 per cent decrease in the lung volume.

3. This restriction of lung volume means real collapse—wall-to-wall agglutination of implicated alveoli—rather than some kind of partial shrinkage of the lumen of the alveolus. Had there been partial collapse, some distortion would have been induced in the alveolar gas distribution. This was not the case, as demonstrated by close monitoring of expired CO_2 on capnographic curves. The occurrence in our subjects of a stable plateau of alveolar CO_2 throughout our experiments indicated a homogeneous gas distribution to alveoli actually engaged in ventilation. Atelectatic alveoli, receiving no CO_2 from capillary blood, no longer contributed to the alveolar pattern of CO_2 distribution.

4. Nitrogen seems of paramount importance in the prophylaxis of miliary atelectasis. In fact, the role played by nitrogen in delaying the appearance of atelectasis in a lung lobule distal to an occluded bronchus is not a new discovery; it was remarkably described in 1952 by Dale and Rahn.[9] However our data confronted us with a new problem, namely the occurrence of alveolar closure in the absence of airway obstruction.

Our results from control studies in conscious subjects outside the operating room made it highly likely that this atelectasis could be related neither to anaesthesia nor to ventilation techniques. The sole similarity between our subjects in the operating room and those in the laboratory lay in the fact that the latter inhaled 100 per cent oxygen, i.e., also a nitrogen-free mixture. This postulated the thesis that over-oxygenation and its obligatory counterpart, denitrogenation, were the causative factors implicated in the alveolar collapse observed in both groups to the same degree. Indeed, evident confirmation was provided by subsequent experiments in which we demonstrated that atelectasis did not occur whenever a nitrogen-enriched mixture was inhaled under otherwise similar experimental conditions.

The mechanism whereby denitrogenation may reduce lung volume entails a closer approach to the study of alveolar volume and dynamics. Alveolar volume, or functional residual capacity, is currently defined by pulmonary physiologists[10] as the volume of gas contained in the lungs at a balanced or neutral position, the resting expiratory level. This resting position is described as the result of an equilibrium between two forces: the elastic properties of the thoracic cage, directed towards inflation; and the elastic forces of the lung, directed towards deflation. Both forces, as we see, are extrinsic ones, working from outside the alveolus to maintain its internal volume steady at the resting expiratory level. Admittedly, the interplay of these two forces explains rather poorly the massive collapse of the lungs which occurs in the paralysed laboratory animal when

tracheal occlusion follows pulmonary denitrogenation with 100 per cent oxygen. Under these conditions, the two forces are ideally equilibrated owing to curarization, hence lung volume should be kept eminently stable. The occurrence of massive collapse in the present example provides clear evidence that these two forces, thorax and lung elasticities, are but a part of a more complex mechanism that we shall now try to analyse.

We might conceive a second pair of forces, this time working from inside the alveolus to keep it open. These internal forces may be related to the absorbability of alveolar gas mixture. Oxygen, a highly absorbable gas, behaves like a constant leak in alveolar volume, creating a real tendency for this volume to shrink; it is thus easily likened to a deflation force. On the contrary, nitrogen diffuses poorly; it behaves as a stabilizer of alveolar volume, produces a cushion-like effect on alveolar walls, opposes deflation, and thus should be considered as an inflation force. Nitrogen should not be taken, of course, as a dynamic force which would actually increase alveolar volume, but rather as a static force intended to keep alveoli in a state of normal inflation. When a nitrogen-free mixture is breathed, alveolar internal equilibrium between diffusible and undiffusible fractions is disrupted, and the balance of forces is turned towards deflation and collapse.

Our data suggested that some other factor was at work to limit the extent of alveolar collapse. In none of our subjects did massive collapse of the lungs occur; after an initial 25 per cent decrease, functional residual capacity leveled to this new low volume which remained almost stable as long as experimental conditions were not changed. This finding can possibly be explained in the following way: a fraction of the lung volume must provide physical accommodation to the tidal volume which is added to FRC during inspiration. There is no doubt that in normal quiet breathing, tidal volume is not distributed evenly throughout lung lobules and alveoli. It is conceivable that some alveoli, less actually engaged in ventilating this tidal volume, are probably yet in a state of partial shrinkage, though not complete collapse owing to the presence of nitrogen. When denitrogenation occurs, these alveoli undergo further deflation till a critical point is reached where surface tension forces are brought into action and unavoidably cause the alveolar walls to fold up. Meanwhile, surrounding alveoli, which are mechanically more engaged in tidal volume ventilation, never reach the critical alveolar volume, and therefore do not undergo closure. This correlation during denitrogenation between tidal volume, collapsible alveolar volume, and uncollapsible alveolar volume, suggests a logical explanation of the fact that overventilation with large tidal volumes is prone to induce less lung collapse than hypoventilation with small tidal volumes.

It might be of interest to point out the consequences of this miliary atelectasis. During anaesthesia itself, miliary atelectasis should not be given more emphasis than perhaps is warranted. As a matter of fact, our results demonstrated that the absence of effective ventilation in as much as 25 per cent of the lung induced no trouble whatsoever in CO_2 elimination as monitored with capnographic curves and arterial CO_2 tensions. This observation stresses the adequacy and the magnitude of pulmonary reserve, as far as CO_2 homeostasis is concerned. Furthermore, miliary atelectasis resulted in no arterial desaturation during anaesthesia. In our

experiments, as well as in earlier work on the subject,[2] only a slight decrease in arterial oxygen tension was observed. This should not be misinterpreted as hypoxia. Lowering pO_2 from 400 to 300 or to 200 mm. of mercury does not mean impaired oxygenation, because the patient whose pO_2 is at 200 mm. of mercury is still in the comfortable range of hyperoxia and is in no danger. Venous admixture caused by miliary atelectasis during anaesthesia seems to be rather small and easily concealed by the oxygen-enriched mixtures currently used during surgery. The disproportion between venous physiological shunts and FRC changes can possibly be explained in two ways: first, collapse of individual alveoli may well cause a partial closure of the capillary network running in their walls, thus creating little disturbance in the ventilation/perfusion ratio; second, miliary atelectasis may especially affect physiologically hypoventilated alveoli as previously suggested. The role played by these alveoli in haematosis was probably of no great importance; thus their complete collapse would add no major disturbance in blood arterialization.

The potentially harmful effects of miliary atelectasis should be a matter of greater concern in the early recovery period when the patient is allowed to breathe room air. A high incidence of hypoxia was recently reported in recovery-room patients on returning to breathing air, even though their pulmonary ventilation was found to remain essentially within normal limits.[4, 11] It is very tempting to correlate the pO_2 decrease during anaesthesia with anoxia during emergence, and to link up both disorders with denitrogenation atelectasis. In the operating room the administration of high oxygen tensions may well overcome physiological shunts and prevent arterial desaturation, but in the recovery room an inspired oxygen concentration of 20 per cent may be insufficient to neutralize the venous admixture from the same uncorrected atelectasis. Some other factors may be at work, however, but more research is needed on ventilation/perfusion ratio during recovery from anaesthesia.

Our results postulate many applications in clinical anaesthesia as well as in other fields of medicine and sciences dealing with environmental factors. During clinical anaesthesia, miliary atelectasis may be prevented by the administration of a gas mixture enriched with nitrogen. Our data suggest that the inhalation of 50 per cent nitrogen in the inspired gas mixture may effectively prevent alveolar collapse even in the absence of deep breaths and periodic overinflations. Many anaesthetics have now been conducted in our department using this particular technique without any adverse effect. For this purpose, our operating rooms are supplied with air output lines and terminals from a centralized air compressor, and debimeters especially calibrated for air administration.

The problem of miliary atelectasis can also be faced from another point of view. It is conceivable that the anaesthesiologist may want to tolerate alveolar collapse during anaesthesia in the view that, as long as high oxygen concentrations are used, arterial gas homeostasis is very slightly affected by this pathology. This position seems acceptable. If alveolar collapse is tolerated, however, careful correction of the condition becomes mandatory at the end of anaesthesia. This can be achieved by deep breaths artificially performed through high pressures exerted in the airway. In order to prevent recurrence of atelectasis with

threatening hypoxia in the recovery room, it is then most important to renitrogenate the lung volume. If renitrogenation is understood as the opposite of denitrogenation, which is relatively complete after two minutes of normal tidal exchanges, then nitrogen wash-in at the end of anaesthesia should likewise be achieved in about two minutes of ventilation with a nitrogen-enriched gas mixture. Incidentally, renitrogenation may be carried out with an Ambu resuscitator either at the end of anaesthesia or while the patient is wheeled to the post-anaesthetic recovery room.

Some authors[11, 12] have recently advocated that all patients receive oxygen following general anaesthesia, to allow them to cope with the threats of respiratory and circulatory depression. We agree with them, if oxygen is administered by nasal catheter as commonly done, because at a gas flow of 4 to 6 litres per minute this technique cannot deliver more than 35 to 40 per cent oxygen. The balance of the inhaled mixture is made up of room air, so the patient breathes enough nitrogen (about 50%) to prevent alveolar collapse; meanwhile enough oxygen is provided for protection and security.

Whether or not pure oxygen is irritative for the alveolar epithelium and may directly induce lung damage is open to question. The harmful effects of prolonged exposure to 100 per cent oxygen have long been stressed [13–16] and described as "oxygen pneumonia." There exists some evidence, however, that this pneumonopathy may in fact be diffuse miliary atelectasis. In some patients who died following extracorporeal circulation with highly increased oxygen tensions (near one atmosphere), a peculiar alveolar collapse, totally unlike ordinary atelectasis, was noticed.[17] The histologic change was one of diffuse atelectasis, where small areas of collapse were surrounded by aerated lung. Experiments involving laboratory animals have also emphasized the pulmonary consequences of continuous exposure to high concentrations of oxygen at normal atmospheric pressure. Dogs and smaller animals die within three days of exposure to 100 per cent oxygen; post-mortem examination of their lungs have shown atelectasis, hyperaemia and oedema.[18] Our experiments in conscious and in anaesthetized subjects breathing 100 per cent oxygen have already established the occurrence of a 25 per cent decrease in the lung volume and demonstrated the role of denitrogenation in the pathogenesis of this disorder. They suggest that the lung manifestations of hyperoxia might not be entirely related to the toxicity of oxygen itself, but to the lack of adequate nitrogenation.

Summary

1. Fifty-seven determinations of functional residual capacity (FRC) were performed by the closed-circuit helium dilution technique in both conscious and anaesthetized subjects breathing 100 per cent oxygen. In all these subjects we demonstrated the occurrence of miliary atelectasis, as indicated by a decrease in FRC and arterial oxygen tension.

2. Thirty-seven determinations were repeated in subjects breathing a 50 per cent oxygen-50 per cent nitrogen mixture. In these instances, neither FRC nor arterial oxygen tension was found to undergo significant change.

3. The importance of denitrogenation and renitrogenation as related to anaesthesia is emphasized.

4. Our study suggests that the lung manifestations of hyperoxia might not be entirely related to the toxicity of oxygen itself, but to the lack of adequate nitrogenation.

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