THE PHYSIOLOGICAL BASIS OF MECHANICAL VENTILATION

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I. INTRODUCTION

Artificial ventilation of the lungs with positive-pressure devices is commonly used in two clinical circumstances - first, for support of patients with severe respiratory failure who would otherwise be incapable of sufficient ventilation to sustain life; and second, for patients with non-life-threatening degrees of respiratory disease in whom positive-pressure breathing serves as one of several "routine" therapeutic measures aimed at preventing or ameliorating complications. Because all forms of mechanical ventilation in either of these circumstances employ some method of periodically inflating the lungs by increasing the pressure of gas applied to them, "intermittent positive pressure breathing" (IPPB) is often used as a general descriptive term.

The popularity of IPPB has grown rapidly since its applicability to clinical medicine was established in the 1940's. Its use, both as a life-support method and as routine in-patient therapy in various acute and chronic lung diseases, has increased to the point that the logistic, epidemiologic, and financial consequences are considerable (Table 1)(1).

MAGNITUDE OF USAGE OF IPPB IN VARIOUS GEOGRAPHIC AREAS, JRCITE SURVEY (MONTHLY AVERAGES, 127 HOSPITALS)*

Zip Code Area (N)	IPPB/Bed	IPPB/Adm	IPPB/Chest PT	IPPB/ABG	IPPB/Spir	IPPB/Pers
0 (10)	10.4	3.2	5.6	5.6	198	356.4
1 (19)	4.8	1.9	6.0	5.5	28	149.6
2 (9)	10.0	3.9	39.3	33.9	44	189
3 (13)	4.4	1.6	3.7			
4 (18)	7.0	2.3	2.0			164
5 (7)	5.9	2.4	10.2			
6 (18)	5.3	2.0	4.1	11.4	65.4	192
7 (15)	7.9	0.9	5.4	12.1	21.7	
8 (10)	10.6	3.6	29.5			
9 (8)	6.9	1.8	10.9	26.9	45.3	
Average	7.32	2.36	11.67	15.90	67.07	210.2

TABLE I. Usage of IPPB in a group of hospitals related to number of beds (IPPB/Bed), admission rate (IPPB/Adm), chest physiotherapy treatments (IPPB/Chest PT), blood gas determinations (IPPB/ABG) spirometry measurements (IPPB/Spir), and number of personnel (IPPB/Pers). IPPB treatments per admission per month are shown in the third column; values range from 0.9 to 3.9, the higher number representing a remarkable rate of IPPB therapy. Parkland Memorial Hospital is at the upper end of this range, with approximately four IPPB treatments per monthly admission. From Baker (1).

The early popularity of IPPB was based upon a number of unscientific assumptions concerning its efficacy, supported by some rather uncritical clinical studies. Recently, many investigators and clinicians have

become more skeptical, and as increasing numbers of questions were raised about the role of IPPB, it seems to have become fashionable to profess a cynical attitude toward its use. Even some earlier advocates have editorially criticized the unnecessarily widespread application of IPPB (2, 3).

Nobody denies the importance of IPPB in support of a critically ill patient, but not so generally accepted is its usefulness in the routine management of chronic lung diseases or in the prevention of pulmonary complications of surgery and other acute insults. In either case, the rational use of IPPB and intelligent decisions concerning its indications, contraindications, and consequences require at least a basic understanding of the physiological effects of IPPB. This review will approach the subject by first examining studies on the clinical consequences of mechanical ventilation; second, published accounts of physiological measurements during IPPB will be reviewed; and third, possible bases for these physiological changes will be sought in some recent investigations and a few theoretical considerations about the functional effects of positive-pressure ventilation.

Two general points should be made at the outset. First, it should be kept in mind that the standard against which IPPB is judged and analyzed is normal respiration, for it is spontaneous breathing that IPPB is expected to replace or augment in any clinical circumstance.

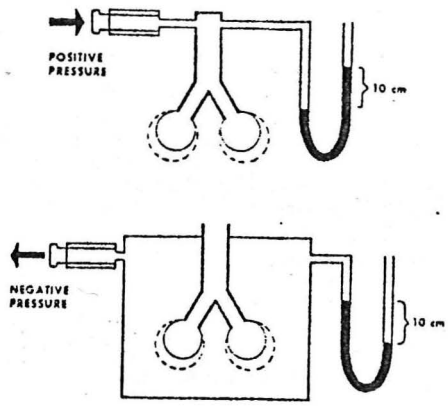

Figure 1. Comparison of positive and negative pressure breathing. Whether the pressure change is induced by positive pressure delivered to the airway or by negative pressure generated within the thorax (box), with equal amounts of pressure the effects on inflation of lung units is theoretically the same. Thus, analysis of IPPB should relate its physiological effects to those occurring during spontaneous breathing.

A true picture of the effects of IPPB can only be achieved by clinical or experimental studies which determine its ability to reproduce or improve upon the effects of spontaneous ventilation (Fig. 1). Second, it is not the purpose of this review to compare the many different devices available for delivering positive pressure to the airways, or to describe the technical and mechanical features of any IPPB machine. For the sake of brevity, certain assumptions will be made, including the generalization that virtually all the devices currently in widespread use are capable of producing the major desired effect in much the same way; i.e., the production of pressure differences down the airways which result in air flow into the lungs.

For more extensive coverage of other aspects of this subject, a number of excellent review articles are available (4-9).

II. CLINICAL EFFECTS OF IPPB

The ability of IPPB to maintain normal levels of alveolar ventilation in normal, anesthetized human subjects was established by

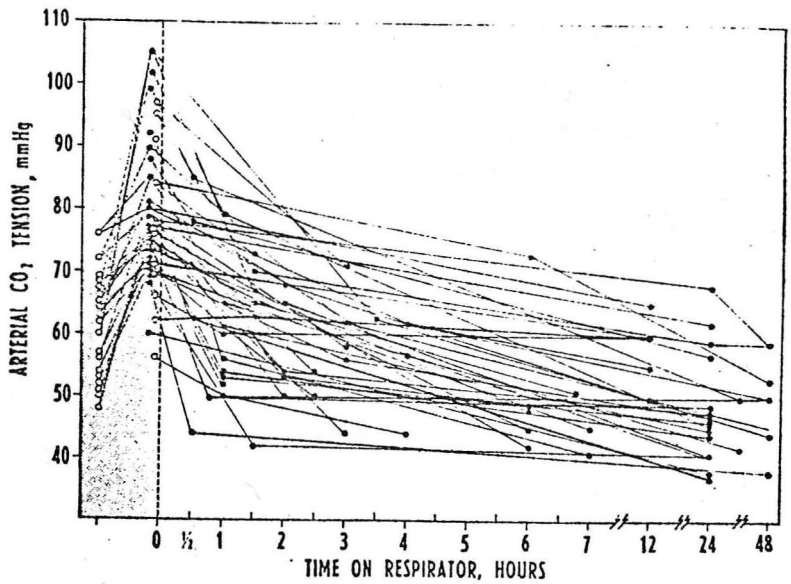

Figure 2. Effect of prolonged mechanical ventilatory support on arterial PCO_2 in patients with respiratory failure due to COPD. Elevated levels of PCO_2 were present in all patients before treatment; respirator therapy decreased PCO_2 significantly in all cases, reflecting a favorable effect on alveolar ventilation. From Billingham and Eldridge (12).

early clinical studies (10). Its effectiveness in surgery during pharmacologic paralysis and apnea presaged its applicability to other forms of respiratory failure. Subsequently, a number of descriptions appeared concerning the successful management of severe chronic obstructive pulmonary disease (COPD) with mechanical ventilatory support (Fig. 2)(11, 12). It was demonstrated that IPPB was capable of preventing CO_2 retention in patients with COPD who were treated with supplemental inspired oxygen (Fig. 3)(13). In addition to its therapeutic benefits, IPPB was said to have a prophylactic role in post-operative patients at risk for atelectasis and other pulmonary complications (14). Although such reports were poorly controlled if at all, utilized no comparisons with spontaneous breathing, and measured only a few imprecise clinical parameters, they established IPPB as a useful tool in the management of a variety of pulmonary disorders.

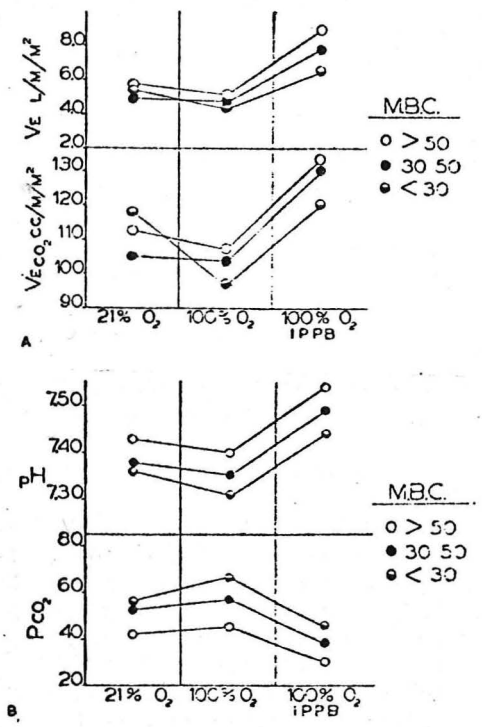

Figure 3. Changes in ventilatory parameters during oxygen therapy with and without IPPB in patients with COPD. Administration of 100% oxygen results in hypoventilation, as reflected in a fall in overall ventilation (V_E), CO_2 excretion (V_{ECO_2}), and pH; CO_2 tension (P_{CO_2}) rises concurrently. When IPPB is used to give the oxygen, however, all values indicate large increases in alveolar ventilation, with a fall in P_{CO_2}. From Fraimow et al (13).

Concurrently, however, a number of reports were appearing which failed to confirm the benefits of IPPB in some patients with COPD (15-17). Additionally, a disturbing variety of undesirable side effects were reported, including decreased alveolar ventilation and worsening CO_2 retention (16), impaired oxygenation due to atelectasis (18, 19) increased bronchospasm (20), pneumothorax and other forms of "barotrauma" (21), nosocomial infection (22), derangements of fluid, electrolyte, and acid-base status (23-27), massive intestinal distention (28), pulmonary edema in experimental animals (29), and others (30). Moreover, none of several well-controlled studies was able to show any advantage from the long-term use of IPPB in patients with COPD (Table 2) (31-33).

MEAN ± SE VALUES FOR MORBIDITY AND MORTALITY ON HOME CARE PROGRAM AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE GIVEN ONE OF 3 MODES OF THERAPY

		Morbidity				Mortality	
		No. of Hospital Admissions Per Year		No. of Days in Hospital Per Year			
Therapy	Time on Program (years)	Prior	During	Prior	During	No. Alive	No. Dead
No aid	2.6 ± 0.3	2.2 ± 0.28	0.9 ± 0.37	38.6 ± 6.0	8.5 ± 4.1	21	12
Air compressor	2.2 ± 0.3	1.6 ± 0.16	1.2 ± 0.28	34.4 ± 4.1	11.7 ± 3.0	12	31
IPPB	2.5 ± 0.3	2.3 ± 0.30	0.8 ± 0.17	40.1 ± 4.4	11.4 ± 5.1	12	33

Table 2. Comparison of long-term results of IPPB with no treatment and with air-compressor nebulization. Patients on no treatment were not as sick as the other groups, as reflected in shorter hospital admissions and lower mortality. There was no difference in these parameters between the other two groups; IPPB resulted in no improvement in morbidity or mortality. From Cherniack and Svanhill (33).

The potential for complications and the apparent lack of benefit in some patients have warranted a more critical appraisal of IPPB.

III. "INDIRECT" PHYSIOLOGICAL EFFECTS OF IPPB

A. *ALVEOLAR VENTILATION.* Most investigators have shown the greatest interest in the effects of IPPB on alveolar ventilation. This emphasis resulted from the frequency with which patients with severe COPD manifested alveolar hypoventilation, marked by arterial hypoxemia and hypercapnia. It was presumed that this abnormality resulted from the physical inability of the patients to move air in and out of their alveoli, thus impairing the clearance of CO_2 and oxygenation of the blood; it seemed logical that if ventilatory assistance could increase tidal volume (with or without a change in respiratory rate), overall alveolar ventilation would be favorably affected, and this has been the most widespread justification for the use of IPPB. Unfortunately, a number of studies have failed to confirm that this effect is a universal consequence of IPPB therapy. One group was able substantially to increase maximum inspired volumes (vital capacity) in only 53 per cent of a mixed group

of patients (Fig. 4); those with COPD increased their vital capacity in 69 per cent of cases (34). No measurements of alveolar ventilation were made in this study, so no conclusions can be drawn regarding effects on gas exchange.

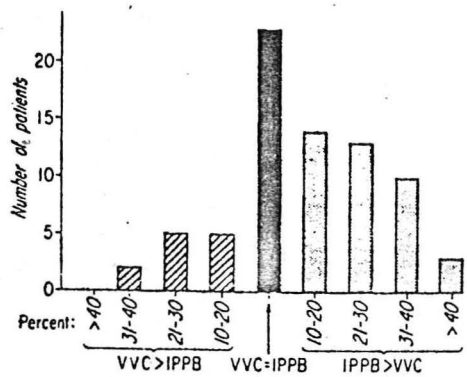

Figure 4. Ability of IPPB to increase vital capacity in patients with a variety of pulmonary diseases. Only in 53% of cases was IPPB capable of exceeding the voluntary vital capacity (V_{VC}) by more than 10%; in some patients, IPPB delivered considerably smaller volumes than V_{VC}. From Cheney et al (34).

Since the arterial CO_2 tension (P_aCO_2) is the hallmark of alveolar ventilation (elevated $PaCO_2$ = hypoventilation; low $PaCO_2$ =hyperventilation), this parameter has been monitored during IPPB in normal subjects, experimental animals, and patients with COPD by a large number of investigators. Several groups have published favorable reports, demonstrating a fall in $PaCO_2$ after IPPB in virtually every patient studied (35, 36). The effects were not great in these series, and one report (36) showed an equivalent improvement in alveolar ventilation during voluntary hyperventilation. Another study compared IPPB to spontaneous respiration and also found only slight differences (37). One series demonstrated improvement in $PaCO_2$ with IPPB in patients with moderate degrees of lung disease, but those with severe COPD failed to augment alveolar ventilation (Fig. 5)(38). Several other publications have described improvement in alveolar ventilation in only certain patients with COPD, and there is a trend that confirms the observation of the least benefit in patients with the most advanced disease (15 -17, 39). Most of these articles are difficult to compare due to major differences in study designs, patient populations, and the manners in which IPPB was delivered; only a few (36, 37) made any attempt to control their observations by comparisons with spontaneous breathing; those demonstrating the least benefit from IPPB, and even significant detrimental effects (15, 16), attempted to hyper-

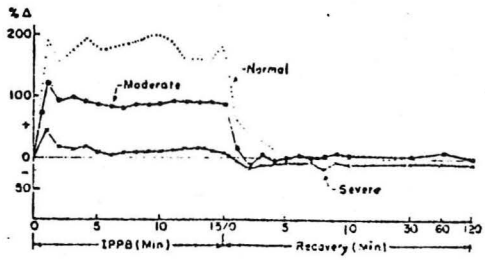

Figure 5. Effect of IPPB on alveolar ventilation in patients with varying degrees of COPD. Normal subjects and patients with moderate COPD experience a substantial increase in alveolar ventilation during IPPB. Patients with severe lung disease, however, have practically no change in ventilation. From Birnbaum et al (38).

ventilate their subjects with grossly inadequate pressures and flow rates (Table 3). Such vagaries plague much of the literature on IPPB and will continue to limit our ability to reach firm conclusions throughout this review.

		SaO_2%	pCO_2	pH
Patient No. 15	Control	90	40	7.40
5 cm. IPPB/I	5 minutes	91	47	7.34
	15 minutes	91	47	7.34
Patient No. 17	Control	90	44	7.38
10 cm. IPPB/I	5 minutes	87	35	7.47
	15 minutes	87	45	7.37
Patient No. 18	Control	72	49	7.40
10 cm. IPPB/I	5 minutes	89	41	7.43
	15 minutes	90	46	7.40

Table 3. Unfavorable response to IPPB in patients with COPD. Each of these three patients had either no change or a rise in PCO_2 after IPPB for 15 minutes, indicating no beneficial effect on alveolar ventilation. The reason may be obvious from the table, in that IPPB was administered with 5-10 cm H_2O peak inspiratory pressure, a level inadequate to hyperventilate even normal subjects. From Kamat et al (16).

B. *DISTRIBUTION OF VENTILATION AND PERFUSION.* Uneven distribution of ventilation and mismatching of ventilation and perfusion are the most important physiological derangements in patients with COPD, as well as a large number of other lung diseases. Even individuals with previously normal lungs may suffer ventilatory maldistribution during acute stresses or illnesses, such as during general anesthesia, in the postoperative period, following sedative drug overdose, and with pneumonia and other inflammatory lung conditions. Normal lungs have a slight degree of unevenness of both ventilation and perfusion, which may be accentuated in the supine position. An important potential benefit of IPPB might be an improvement in the uniformity of ventilation distribution, and this has also been extensively investigated. The most popular technique in this regard is the nitrogen wash-out curve; the evenness of ventilation distribution is reflected in the speed with which nitrogen is cleared from the alveoli during pure oxygen breathing. Because of the same inconsistencies described earlier, it is not surprising that results reported with this technique have varied widely. Some authors have shown a slight beneficial effect of IPPB on nitrogen clearance, but equivalent spontaneous breathing patterns were not compared. (Fig. 6) (35). Other investigators have also been able to improve distribution of ventilation with IPPB, but no more than was possible with voluntary hyperventilation (36, 40, 41); this finding suggests that advantages ascribed to IPPB may reflect only larger volumes, slower rates, or other differences. Using more elaborate refinements of this method, the nitrogen wash-out of each lung was measured separately in subjects

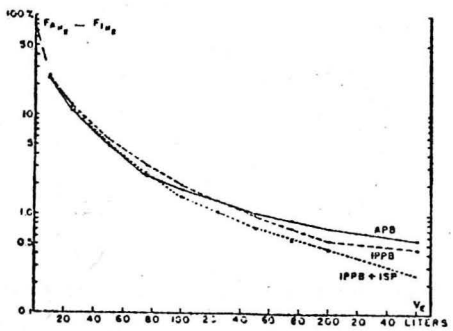

Figure 6. Effect of IPPB on nitrogen clearance in patients with COPD. There is a slight improvement in the rate of wash-out during IPPB alone and during IPPB with isoproterenol (IPPB+ISP) compared to spontaneous or "ambient-pressure" breathing (APB). Thus, IPPB resulted in greater uniformity in the distribution of ventilation, although the changes are quite small. From Cohen et al (35).

reclining in the lateral position, and ventilation was found to be more evenly distributed between dependent and non-dependent lungs during IPPB than during spontaneous breathing (42). Unfortunately, these subjects were anesthetized and paralyzed so the findings may not be universally applicable, and the observations were poorly controlled in that data on spontaneous breathing were obtained from a separate study. Several other reports show no changes in ventilation distribution, as measured by nitrogen clearance, during IPPB (43).

Another way of measuring ventilation distribution is by monitoring the distribution of an inhaled radioactive gas (^{133}Xe) with external scintillation counters. Using a technique that involves counting during breath holding, different groups of investigators have reached variable conclusions, but none has demonstrated more than slight differences in ventilation and perfusion distribution between spontaneous and positive-pressure breathing (Fig. 7) (44, 45). These authors made little or no attempt to match or compare respiratory patterns between the modes of ventilation, and any observed changes could well have been due only to differences in tidal volumes, breathing frequencies, or flow rates. Studies with ^{133}Xe during tidal breathing with careful matching of breathing

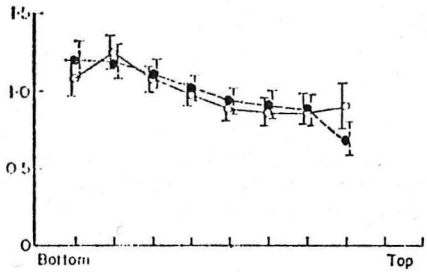

Figure 7. Distribution of ventilation measured with ^{133}Xe during spontaneous and artificial respiration in normal subjects. There is no significant difference between spontaneous breathing (open circles) and IPPB (closed circles) in the distribution of ventilation per unit lung volume (expressed in arbitrary units on the ordinate) from the bottom to the top of the lung. From Hulands et al (45).

patterns demonstrated some important differences between IPPB and spontaneous breathing (46, 47). In the supine posture in both normal subjects and those with COPD, IPPB resulted in a relative decrease in ventilation and perfusion at the lung bases, adjacent to the diaphragm

(Fig. 8); in patients with lung disease, spontaneous hyperinflation

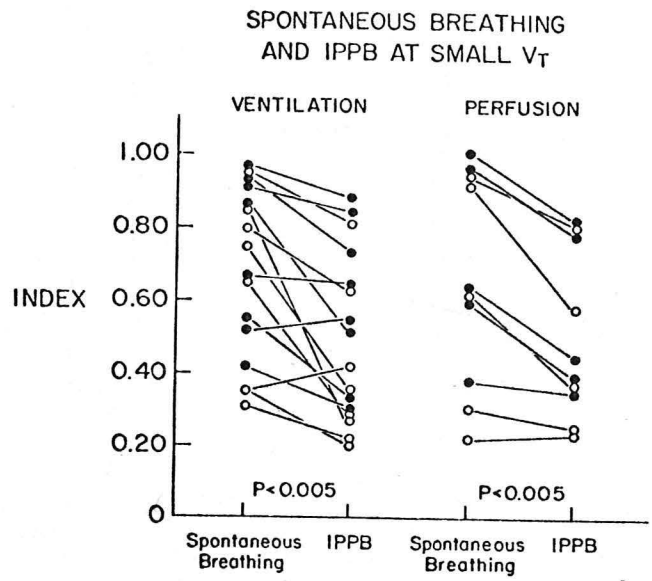

Figure 8. Ventilation and perfusion indices at the lung bases during spontaneous and positive-pressure breathing in normal supine subjects. An index is calculated to reflect ventilation or perfusion per unit lung volume. Both basilar indices are lower during IPPB than during spontaneous breathing. This suggests that, in the supine position, both ventilation and perfusion are diminished by IPPB at the bases relative to the remainder of the lungs, and that spontaneous respiration of equal magnitude results in better basilar lung function. From Bynum et al (46).

caused greater improvement in the distribution of ventilation, perfusion and ventilation-perfusion ratios than IPPB at equal volumes (Figs. 9 & 10). Thus, beneficial effects of IPPB seem to have been difficult to document, and recent evidence suggests the potential for detrimental effects on ventilation and perfusion distribution when compared to voluntary ventilation.

C. *DEAD SPACE VENTILATION.* Total ventilation (measured in liters per minute) is made up of two components: alveolar ventilation is the portion of inhaled gas that reaches functioning alveoli and participates in exchange of O_2 and CO_2; dead space ventilation is gas that never gets past conducting airways to the alveolar level, or else reaches alveoli whose perfusion is absent or low and hence cannot contribute normally

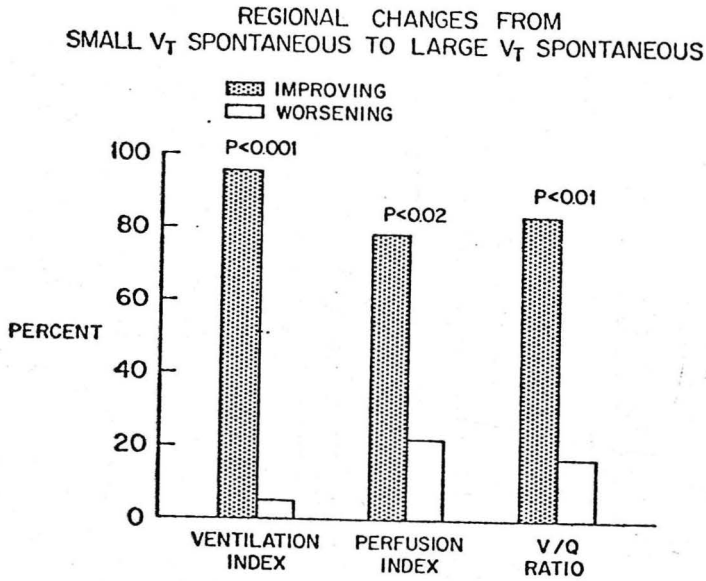

Figure 9. Changes in ventilation and perfusion indices from small to large tidal volumes (V_T) during spontaneous breathing in patients with COPD. The percentage of lung regions showing improvement toward normal values (dark bars) is significantly greater than the percentage worsening (light bars) for all three determinations. This reflects substantial increase in uniformity of distribution of ventilation, perfusion, and ventilation-perfusion (V/Q) ratios with spontaneous deep breaths. From Bynum et al (47).

to gas exchange. A reduction in dead space, or "wasted" ventilation, is a reasonable goal in any type of lung disease; unfortunately, if IPPB has any effect at all, it appears to increase dead space in some individuals. Several reports have described a higher ratio of dead space to tidal volume during IPPB in patients with COPD (17) and in normal subjects (37, 48); one of these found the increase in dead space/tidal volume ratio to be proportional to the duration of inspiration (48). Another group reported large increases in dead space ventilation in experimental animals and normal human subjects (49). A later report, however, found no changes in dead space ventilation during IPPB in patients with respiratory failure (39). Again, most of these investigators failed to control their observations of IPPB with carefully matched spontaneous respiration, so it is frequently difficult to attribute all the reported changes to IPPB alone, when differences in ventilatory patterns may have affected the results.

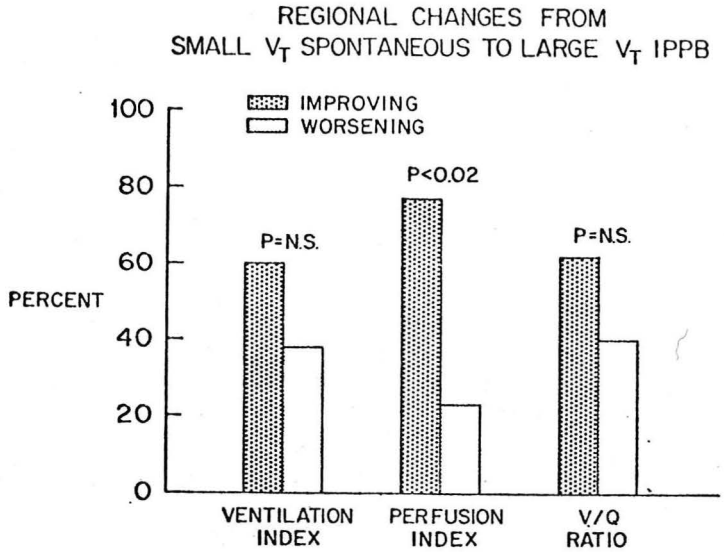

Figure 10. Changes in ventilation and perfusion indices from spontaneous small tidal volumes (V_T) to large tidal volumes delivered by IPPB in patients with COPD. The percentage of lung regions improving is not significantly different from the percentage worsening for ventilation index or ventilation-perfusion (V/Q); there is a significant trend toward improvement in perfusion index. Comparing these data to those depicted in Figure 9 reveals that IPPB is less effective than spontaneous hyperinflation of equal magnitude in amelioration of ventilatory maldistribution. From Bynum et al (47).

D. *ALVEOLAR-ARTERIAL OXYGEN TENSION DIFFERENCE.* Normally, there is little or no difference between the oxygen tension in the alveoli and that in arterial blood. An impairment of the ability of alveolar oxygen to enter the blood may result from several different derangements, such as decreased alveolar ventilation and any imbalance in the relationship between ventilation and perfusion. The difference between alveolar and arterial oxygen tensions is thus an overall indication of the effects of all these factors. Based on early clinical observations, it has become well established that prolonged mechanical ventilation may increase the alveolar-arterial oxygen tension difference, both in normal subjects undergoing general anesthesia (18, 37, 50-52) and in patients requiring ventilatory support (23, 39). The phenomenon has also been documented in experimental animals (53, 54). It has been most widely attributed to atelectasis, thought to result from constant, small tidal volume breathing without periodic hyperinflation, or "sighs" (Fig 11) (18). The abnormality in oxygenation can be corrected by hyperinflation,

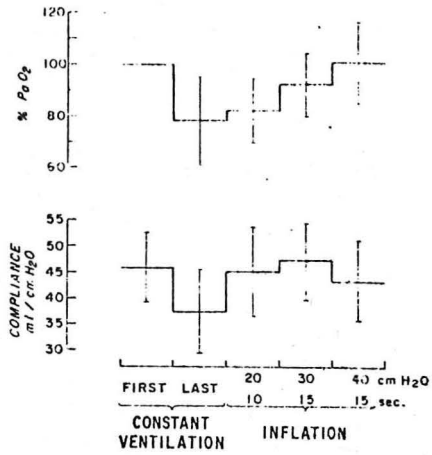

Figure 11. Effect of constant volume ventilation followed by hyperinflation. During constant ventilation, both oxygen tension (PaO_2) and compliance fall significantly. Subsequent inflation of the lungs with 20-40 cm H_2O inspiratory pressure results in a progressive increase in both values, suggesting that the underlying mechanism is atelectasis. From Bendixen et al (18).

either continuously or periodically (18, 51); however, this maneuver may not totally reverse the process and other factors may be involved (51, 54). Radiographically apparent atelectasis is a known complication of prolonged IPPB, supporting the theory that it accounts for the oxygen tension differences (30); however, one report has suggested that water retention and subclinical pulmonary edema may also be important factors (23). These concepts form the basis for some current principles of ventilator management, e.g., the use of periodic "sighs" and the administration of large tidal volumes (i.e., 12-15 ml per kg body weight) to patients requiring ventilatory support.

E. *LUNG COMPLIANCE.* The normal lung has a great deal of elasticity, or stretchiness; this property is called compliance and is measured by determining the increase in lung volume that results from a given pressure applied to stretch the lung. For instance, a normal lung will increase its volume by 2000 ml (from its resting level) when 10 cm H_2O pressure is exerted across it; the ratio of volume change to pressure change, 2000/10 or 200 ml/cm H_2O, is the lung compliance. Any factors that cause closure or fluid-filling of lung units, or that alter the parenchymal elasticity by fibrosis, edema, etc, will increase the stiffness of the lung and thus reduce its compliance.

Many of the same investigators cited in the section on alveolar-

arterial O_2 tension differences also reported decreased lung compliance after prolonged IPPB (19, 52, 54) but not in short-term studies (43). These changes were presumed to be due to the same mechanism, i.e., atelectasis, but other influences such as pulmonary edema and pneumonia are also possible (19, 23). Like the increased alveolar-arterial O_2 tension difference, the abnormal lung compliance can be improved, although not always completely normalized, by hyperinflation (Fig. 11) (54). Of interest is the finding that, acutely, compliance decreases with increasing inspiratory flow rates during IPPB but not during unassisted breathing; it was speculated that this phenomenon was due to differences in ventilatory distribution or lung distortion with IPPB (55).

F. *WORK OF BREATHING.* One of the theoretical benefits of IPPB that has been shown actually to occur is a reduction in the work of breathing. Early clinical observations suggested that increasing overall ventilation with IPPB was primarily of value in patients unable to achieve or maintain an effective level of ventilation voluntarily, due to the excessive work of breathing required (40). Subsequently, more sophisticated measurements have been made in an effort to substantiate this hypothesis. The amount of effort, or work, that an individual must expend to inflate and deflate his lungs can be assessed in several ways. Respiratory work can be estimated from pressure-volume (compliance) relationships and expressed as kilogram-meters per liter; with this technique, it was shown that the work of breathing may be zero during IPPB if the individual is able to relax completely, but may be greatly increased over spontaneous breathing if the subject "leads" or "fights" the machine (Fig. 12) (55). Other investigators have used the rate of oxygen consumption as a reflection of the work of breathing, an index that is particularly useful if related to the amount of increase in ventilation produced; IPPB has been shown to decrease the absolute level of resting oxygen consumption (39) and to cause one fourth the increase in oxygen consumption per volume of added ventilation that occurs with voluntary hyperventilation (36, 39) in patients with obstructive airways disease. Still another indicator of respiratory work is the level of CO_2 production, which has been shown to be diminished in patients on IPPB (38). Thus, the effect of IPPB on the work of breathing has been repeatedly found to be favorable. However, it is important to remember that this benefit occurs only if the machine is able to satisfy the patient's ventilatory needs and allow him to relax; the degree to which this is possible may be variable from one patient to another and difficult to assess objectively (16, 17).

IV. "DIRECT" PHYSIOLOGICAL EFFECTS OF IPPB.

In spite of the variability of results found in many studies of IPPB, most investigators remain convinced that IPPB has some unique effect on the lung. To explain differences in measured physiological parameters one must investigate not only how IPPB can cause changes in breathing patterns, but also how IPPB may directly influence the mechanical events of respiration.

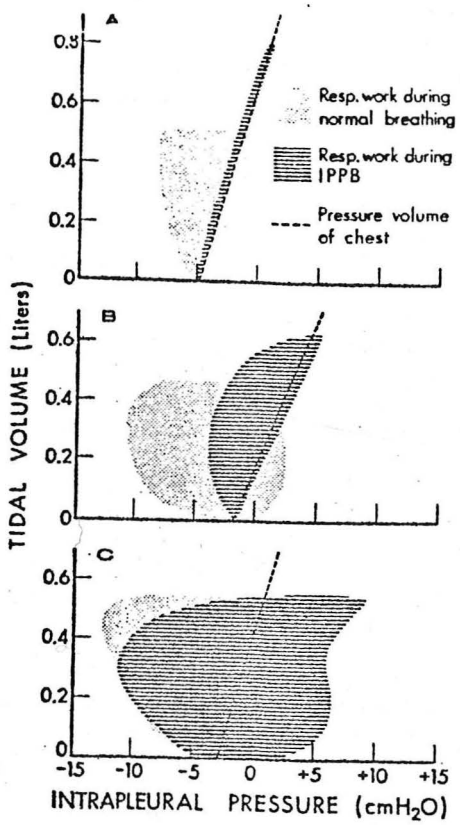

Figure 12. Effect of IPPB on the work of breathing in patients with COPD. The size of the shaded area represents the magnitude of work. Only a few patients experienced a decrease in work of breathing as in panel A. The majority had no significant change or a slight increase, as in panel B. A few patients had marked increases in the work of breathing, as in panel C. From Sukumalchantra et al (17).

A. *CHANGES IN TOTAL VENTILATION AND PATTERNS OF BREATHING.* Clinical studies described earlier (37, 40) have often concluded that the greatest advantage of IPPB is an increase in tidal volume or overall ventilation in patients incapable of such changes spontaneously. It has been demonstrated that improved ventilation distribution and gas exchange result from increases in inspired volume (56), decreases in respiratory rate (57), and changes in the character of the inspiratory phase, particularly prolongation of inspiration (58, 59). If IPPB causes such changes, it will benefit gas exchange, but since unassisted respiration of the same pattern will have the same effect, these benefits cannot be attributed to mechanical ventilation per se. If lung volumes are increased over what is voluntarily possible, other changes may occur which can be either beneficial or detrimental. Increased

airway and alveolar pressures might adversely affect airways resistance (20) and could diminish perfusion to well-ventilated alveoli (60). Changes in the rate of air flow during inspiration, a frequent consequence of IPPB, also profoundly influence ventilation; although several authors describe increased uniformity of ventilation with higher flow rates in normal subjects (61, 62), fast inspiratory flow has also been shown to worsen ventilation-perfusion relationships (63) and to decrease lung compliance during IPPB (55). A diminished pleural pressure gradient has been described during (and attributed directly to) mechanical lung inflation in experimental animals, but may have only been due to increases in lung volume or inspiratory flow, which were not controlled (64).

B. *ELASTIC PROPERTIES OF THE LUNG.* In addition to changes in breathing patterns, a number of physiological alterations have been ascribed to a direct effect of IPPB, independent of other factors. One of these concerns lung compliance; a significant fall in compliance has repeatedly been found after prolonged mechanical breathing in subjects with both normal and diseased lungs, as described earlier (18, 23). It was generally accepted that the observed lung stiffness was related to ventilation with constant, small tidal volumes in the absence of periodic hyperinflations ("sighs") with which collapse of lung units is prevented during normal breathing; this conclusion was supported by the reversal of compliance changes and alveolar-arterial O_2 differences with intermittent or sustained deep breaths (Fig. 11) (18). Some authors felt that other factors, such as pulmonary edema, might also play a role (23). Furthermore, reports appeared suggesting that hyperinflation did not completely correct the abnormalities (54, 65), and the defect in gas exchange, presumed to be directly related to the low compliance, could not be totally explained on the basis of atelectasis alone (50). It subsequently became apparent that structural lung damage, and not merely reversible alveolar collapse, might be important in the pathogenesis of these changes. One group suggested that the collapse process itself caused alterations of alveolar surface characteristics (e.g., structural or distributional changes in the surfactant molecules) which prevented restoration of normal mechanical function by hyperinflation (54). This theory was supported and expanded by the finding of increased surface forces in the lung (i.e., decreased surfactant activity) following IPPB, especially when large volumes were given for prolonged periods (66, 67). Evidence favoring anatomical damage to the lung was provided by studies demonstrating diffuse interstitial and alveolar pulmonary edema following mechanical ventilation with very high inflation pressures, but also with only moderate pressures (29). These findings seem to indicate a direct effect of IPPB on the lungs; however, the observations were not controlled by comparison with spontaneous breathing at equal volumes and pressures, and this would probably not be possible. Nonetheless, one cannot confidently conclude that the same changes would not result from voluntarily achieved ventilation at comparably large volumes and high pressures.

The breathing patterns administered during these studies are, in fact, of the type and magnitude not uncommonly employed for ventilatory support of patients, so that the danger of this type of structural lung damage, and the resulting physiological derangements, are very real.

C. *DIAPHRAGMATIC MECHANICS.* Alterations in the normal function of respiratory muscles during IPPB has been postulated for some time; the action of the diaphragm has been the most extensively investigated, during both unassisted and assisted ventilation, since it is the most accessible of the respiratory muscles to study. It might be presumed that, since IPPB is often used in apneic patients, the machine does all the work and respiratory muscle activity is minimal or absent; a further presumption might be that "pushing" air into the lungs with positive pressure could result in major differences in the distribution of ventilation as compared to "pulling" air in with negative pressure generated by normal respiratory muscle contraction. These are presumptions in need of proof, however, and a number of investigators have addressed themselves to the problem. Indirect evidence for inhibition of muscular activity during machine breathing was described earlier; i.e., the finding that oxygen consumption and the work of breathing were substantially reduced (39). More direct evidence along the same lines is available; e.g., it has been shown by electromyographic recordings from the diaphragms of cats that significant inhibition of diaphragmatic muscle potentials occurs as positive pressure is applied to the lung, in marked contrast to the increase in muscular activity that occurs with negative intra-pulmonary pressure (68). These findings are supported by measurements of chest wall and abdominal (diaphragmatic) displacement recorded by magnetometers, which demonstrated a predominance of diaphragmatic contribution to tidal volume (60%) during normal respiration, whereas diaphragmatic displacement accounted for only 28% during anesthesia and mechanical ventilation (69). Other studies on normal human subjects during anesthesia with and without muscular paralysis and IPPB, using radiographic analysis of diaphragmatic position and motion, have shown remarkable changes in diaphragmatic function related to the weight of abdominal contents; in the supine position, the posterior aspect of the diaphragm is displaced farther cranialward than the anterior half due to greater pressure from abdominal viscera (70). The result is that spontaneous breathing moves the posterior diaphragm the most, since the greatest contractile displacement is possible there, and yet positive pressure breaths will cause greater movement of the anterior diaphragm, due to a lesser degree of resistance from abdominal contents (Fig. 13). Presumably, the logical result would be greater ventilation of the posterior base of the lung during spontaneous breathing in the supine posture, but more ventilation distributed toward anterior lung regions with IPPB. These findings are only qualitative, however, and the authors made no attempt to quantitate changes in any physiological parameters.

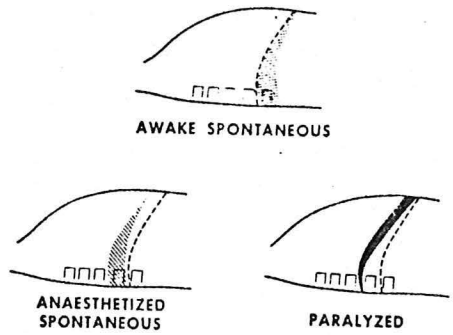

Figure 13. Changes in diaphragmatic function in supine subjects during spontaneous and mechanical respiration. The weight of abdominal contents displaces the posterior diaphragm more than anterior portions; diaphragmatic excursion is thus greater posteriorly during normal breathing. With mechanical ventilation during paralysis, however, the positive pressure causes greater excursion of the anterior diaphragm due to less resistance from abdominal contents. Therefore, the posterior lung base may be less well ventilated during IPPB. From Froese and Bryan (70).

Quantitative measurements of the ventilation of each lung of dogs in the lateral position were made during anesthesia, paralysis, and IPPB; previous findings were confirmed by these studies, in that ventilation of the dependent lung (where the weight of abdominal contents offers greater resistance to passive displacement of the diaphragm) was substantially reduced during mechanical breathing (71). Other investigators have examined the importance of varying degrees of diaphragmatic contraction on quantitative measurements of ventilatory function. Diaphragmatic paralysis in animals caused marked changes in pleural pressures, with a decrease in pressure changes near the diaphragm and lower rib cage when compared to spontaneous respiration (72). The expected effect on ventilation distribution would be a reduction in regional ventilation at the lung bases when diaphragmatic activity is diminished, as might occur during IPPB in an apneic or paralyzed individual, or possibly also in awake subjects on IPPB as other studies have indicated (46). Regional transpulmonary pressures have been studied in other experimental models, and found to be relatively diminished in the basilar parts of the lung with lesser degrees of diaphragmatic activity, further suggesting a basis for diminished basilar ventilation during IPPB (73).

The contribution of diaphragmatic function to ventilatory patterns has also been investigated in man. The homogeneity of lung emptying, measured by wash-out of helium, was found to be less during expiration with a relaxed diaphragm than during voluntary diaphragmatic contraction,

an effect that was again attributed to altered pleural pressure gradients (74). This, in turn, could help explain why maldistribution of ventilation or perfusion in COPD is improved less by IPPB than by spontaneous hyperinflation (47).

D. *INTERDEPENDENCE.* Theoretical models and animal experiments have been used to show that the function of any lung unit is in part dependent upon the function of adjacent lung units; i.e., the degree of expansion of an alveolus is influenced by traction placed upon its walls by expansion of neighboring alveoli, an effect known as interdependence (75-77). This physical property of the lung tends to maintain uniform distension throughout the lung during volume changes, a result of tissue interlinkage (75). Related to this concept is the theory that a similar mechanical and functional linkage exists between lung parenchyma and respiratory muscles through pleural apposition (78). This effect is especially important in basilar lung regions due to their proximity to the diaphragm and the most mobile intercostal muscles. Thus, uniform distension of the lung bases depends upon normal respiratory muscle action through its effect upon interdependence of neighboring lung units. Measuring interdependence of basilar segments in experimental animals, investigators have shown that mechanical ventilation causes significant reduction in interdependence as compared to spontaneous breathing, an effect they attributed to the relative lack of diaphragmatic and intercostal muscle activity during IPPB (78). These same authors subsequently verified this hypothesis by radiographic measurement of diaphragmatic excursion, demonstrating that, compared to unassisted breathing, both diaphragmatic movement and interdependence were less during IPPB and that interdependence varied directly with excursion of the diaphragm (79). These findings complement previously described reports of alterations in respiratory muscle mechanics during IPPB (68-74); moreover, they provide a rational physiological basis for the relative underventilation of the lung bases observed during IPPB (46) and the inability of IPPB to improve overall distribution of ventilation and ventilation-perfusion relationships (47). The same phenomena may also explain similar effects of IPPB on the distribution of perfusion as described in these same reports, in that interdependence also occurs between air-containing spaces and pulmonary blood vessels (80).

V. SUMMARY

In conclusion, IPPB seems not to be the clinical panacea that many had hoped for, and although it appears helpful in a number of clinical situations, indications for its use must be carefully considered if its cost and associated complications are to be justified. It has become obvious that there are many circumstances in which IPPB is not beneficial, and it may have deleterious effects in some patients. Many of the physiological consequences attributed to IPPB can be explained by nothing

more than changes in tidal volume and other parameters, and much of its benefit may be duplicated by voluntary alterations in breathing patterns if these are possible. The most important role of mechanical ventilation is, of course, in the support of the patient with respiratory failure unable to maintain a level of respiration adequate for survival; it appears also to benefit those stable patients who are unable to raise their level of ventilation, for therapeutic and prophylactic purposes, without assistance. In this regard, the ability of IPPB to alleviate the work of breathing seems to be its best established property, but the importance of patient relaxation must be emphasized (Fig. 14).

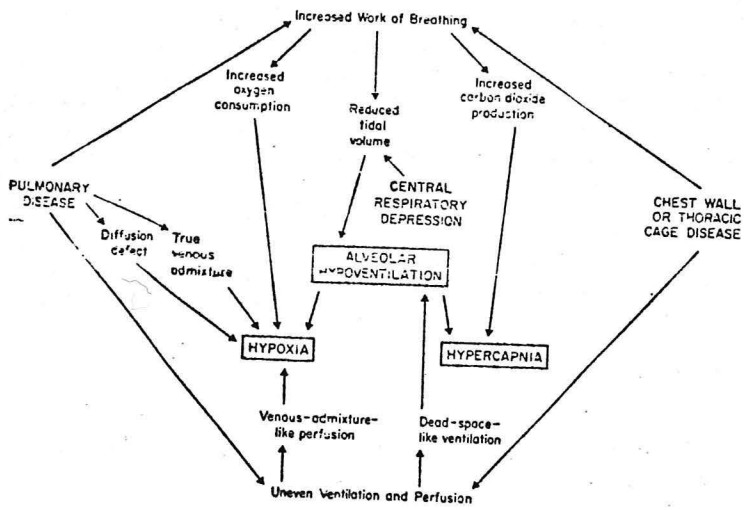

Figure 14. Summary of physiological factors that play a role in the pathogenesis of acute respiratory failure. Mechanical ventilation has been shown to have either a beneficial or an adverse effect on the work of breathing, venous admixture, and alveolar ventilation; it has been shown either to increase or not to affect dead space ventilation.

Underlying the measured physiological effects of IPPB is primarily its ability to increase tidal volume and alter patterns of air flow. However, there are certain direct effects of mechanical ventilation that cannot be attributed solely to alterations in the patterns of spontaneous breathing. These effects have been related, mostly in experimental animals, to changes in pleural pressure gradients and the mechanics of respiratory muscle function. The consequences of these changes on interdependence of lung units, especially in basilar regions, may account for the potentially important - and, for the most part, undesirable - alterations in distribution of ventilation and perfusion described in clinical studies on IPPB.

Thus it seems that the best-documented advantage of IPPB is also the basis for some of its reported disadvantages; i.e., its ability to relieve the work of breathing depends upon a relative inhibition of respiratory muscle contraction, which in turn determines some of the differences in ventilation and perfusion distribution and interdependence that exist between IPPB and spontaneous respiration. This observation is not meant as a condemnation of IPPB, nor is this review intended, in general, to be judgemental concerning the justification for ventilator therapy. It must be concluded that, although IPPB falls short of ideal physiological replacement of normal respiration, there are certain circumstances in which it serves as a valuable, indeed often absolutely essential, substitute for spontaneous respiration when lung function is deranged. Just as hemodialysis is never expected fully to duplicate normal renal function, mechanical devices will never replace or improve upon the capabilities of normal lungs; however, this by no means constitutes grounds for condemning or rejecting IPPB as a useful therapeutic modality. The primary intent of this review has been to point out that, like any treatment, IPPB must be administered with care and judgement. If this review can help to identify the clinical situations in which IPPB is most likely to be helpful, to facilitate the proper application of principles of ventilator management, and to increase awareness of the possible shortcomings and complications of mechanical ventilation, it will have served a worthwhile purpose.

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