

CLINICAL PULMONARY FUNCTION
AND THE
PHYSIOLOGICAL EFFECTS OF USING INDUSTRIAL RESPIRATORS

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Reviews of earlier work involving the physiological aspects of respirator wear were prepared from data collected in the authors capacity as a consulting physiologist to the Respirator Division (H-5) Los Alamos Scientific Laboratory, Los Alamos New Mexico.

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In our recent review (1), we identified six major areas of physiological concern, when man is required to wear an industrial respirator. These concerns dealt with the effects of the respirator on (a) maximal and submaximal work performance; (b) the resistance to inspiratory and expiratory air flow; (c) the increase in respiratory dead space; (d) the cardiovascular and metabolic adjustments; (e) the thermoregulatory responses; and finally (f) the psychological considerations. It was readily apparent that the ventilatory adaptations as a consequence of breathing against an increased inspiratory and/or expiratory resistance had received primary investigative emphasis. Undoubtedly, this concentration of effort was a result of the realization that the primary physiological load, imparted by a respirator, is placed on the human's pulmonary system. The sum total of this review resulted in us concluding, along with many others, i.e. Silverman (2), Johnson (3), Bentley (4) and Cotes (5), that when man is challenged by an inhibition to his ventilatory air flow he attempts to reduce the total respiratory workload by altering inspiratory and expiratory time relationships. As a compensation for the increased inspiratory time, man reduces the exhalation time to a minimum, with the result that lung ventilation is impaired. At the point of minimum efficient exhalation time (approx. 0.66 secs) physical exhaustion occurs (2). These findings quantifiably identify the respiratory load of critical impairment a fact which earlier has been subjectively verified by Silverman (2), Cooper (6), Johnson (7), Sennek (8) and Bentley et.al. (4). This early data related the perceptive concept of work to the actual expiratory work, Table 1.

From this beginning, it would appear that we have enough information to establish standards of respirator performance and design, especially if one accepts the modelling procedures of Silverman (2) and Johnson (3). In fact, the data of Silverman (2) published in 1951 appears to form the basis of the manufacturer compliance tests outlined in 30 CFR Part ii. However, it is apparent from my position statement made at the opening of the conference that even though a respirator may pass the certification test it in no way conforms to the demands placed on it by the working human. In fact, it was obvious that where protection was assumed (positive pressure breathing) the possibility of breakdown of the protection factor was real. As I have previously summarized my earlier work concerning self contained breathing apparatus (SCBA) it is my intention in this presentation to focus on my recent work with respect to pulmonary impairment and respirator wear. In addition, I will address the problem of standards for clinical screening tests in identifying worker capability while using a respirator.

Previously (9), we have documented the fact that weight-bearing alone was the primary cause of a 20% reduction in maximal work capacity when wearing a SCBA. This finding agrees well with Myhre et al's (10) reported 20% increase in energy expenditure at given submaximal workload when wearing a SCBA. However, the physiological efficiency of the human was unaltered during work. This suggests that the weight of the SCBA provides an increase in load to be carried (similar to carrying excess body fat). This increase in energy requirements may prove detrimental to an individual whose energy reserves are minimal as a result of cardiopulmonary and metabolic disease states, age or just low fitness levels.

The work of Myrhe et.al. (10) has identified some significant practical areas of concern which we must attend to in the future. These concerns are summarized in Table 2.

Subsequently we have verified these findings in both normal subjects and subjects with mild pulmonary impairment. A description of the procedures and the resultant findings utilized in the investigation of respirator wear and of pulmonary impaired subjects follows:

i. Clinical pulmonary function and "demand" mode respirator breathing

Both male and female subjects of this investigation were selected from a volunteer population aged 18-65 years of age. Recruitment of subjects was accomplished by television and newspaper advertising along with local physician referrals. More than 150 persons were screened by exercise stress and clinical pulmonary function testing as a means of selecting and grouping the subjects. Eighty-five subjects were selected to participate as experimental subjects. As in all investigations using human subjects, a certain number of subjects dropped out during the course of the repeat experiments. A final count of sixty subjects completed all visits. The sixty male and female volunteers selected were asked prior to participation in the investigation to sign an informed consent form (as approved by the Institutions' Human Subjects Review Committee). The subjects then underwent a preliminary pulmonary screening examination in order to group the subjects according to their pulmonary function. Group A consisted of those subjects defined as normal with respect to forced vital capacity (FVC) and forced expiratory volume in one second ($FEV_{1.0}$) expressed as a percentage of FVC ($FEV_{1.0}/FVC\%$). Normal lung function was accepted as being within 10% of the individuals age and sex predicted FVC and/or greater than 70% value of the $FEV_{1.0}/FVC\%$. Group B consisted of those subjects defined as impaired i.e. an FVC less than 90% but greater than 60% of age and sex predicted norms and/or $FEV_{1.0}/FVC\%$ less than 70% but greater than 50% of their individual FVC. In addition, groups A and B were further defined with respect to their single-breath diffusion capacity to carbon monoxide (D_LCO) (11) and their closing capacity (CC) (12). Table 3 provides a descriptive summary of the two groups of subjects. In addition, Table 4 provides a summary of the symptomology and clinical diagnosis of the impaired subjects.

a. Clinical pulmonary function testing

Each subject was evaluated on a series of standardized pulmonary function tests both with (w) and without (w/o) and industrial respirator. Certain tests were not performed with the respirator because the increase in dead space provided by the full-face mask compromised the validity and reliability of the tests. Static lung volume estimates FVC, residual volume (RV), functional residual capacity (FRC), total lung capacity (TLC), closing volume (CV), closing capacity (CC), forced inspiratory capacity (FIVC), expiratory reserve volume, diffusion capacity (D_LCO) and isoflow volume (V_{isoV}) were made using the best effort tests of duplicate tests. Similarly, the dynamic lung function tests of timed forced expiratory volumes ($FEV_{1.0}$, and $FEV_{3.0}$), flows at 50% of FVC (V_{max50}) and at 75% of FVC (V_{max25}), maximum breathing capacity for 15 seconds ($MBC_{.25}$) and one minute ($MBC_{1.0}$) along with the peak flows were performed using both room air and a 80% helium-20% oxygen (He-Ox) breathing mixture.

The order the subject performed the pulmonary tests, either w or w/o the respirator, was randomized among the subjects. The subject in the standing position was asked to connect himself to a mouthpiece which in turn was connected via minimal dead space to a dry rolling seal spirometer (Ohio Medical Series 2300-AIRCO) for volume measurements. In addition, this spirometer was equipped with a nitralizer (Model 720) for determination of CV and RC, a carbon monoxide analyzer (Ohio Model 790) and helium analyzer (Mijnhardt) for determination of D_LCO . All instrument outputs were connected to an X-Yt recorder (Hewlett-Packard). Flow measurements were obtained by computer differentiation of volume over time. Volume measurements were made according to the standardized measurement procedures outlined by Bates et.al (13), while measures of V_{isoV} and CV were made using the procedures of Hutcheon et.al (14) and Benson et.al (6) respectively. Since the modified Krogh breath-holding technique (11) was more reproducible than the steady state technique (15) D_LCO was measured using breath-hold during rest at two oxygen tensions (20% O_2 and 60% O_2). This procedure permitted use of calculations of Roughton and Forster (16) for determining the membrane constant (Dm).

Repeatability analysis was carried out on all clinical testing using ten subjects with and without the mask. All absolute data (i.e. FVC, RV, TLC, $FEV_{1.0}$, PF etc) proved to be extremely reliable having correlation coefficients (r) of greater than 0.9. However, different scores (i.e. Delta V_{max50} or Delta V_{max25}) between room air and He-O₂ breathing mixtures were less reliable (r ranged from 0.73 to 0.66). The respirator masks were mechanically modified to fit the pulmonary testing machine. However, these modifications did not interfere with the respirator's operation. The demand respirator was a full face mask (MSA-ultravue) equipped with an inhalation resistance of 85 mmH₂O at 85 l/min flow. Prior to and following the investigation the resistance pressure of the respirator was calibrated against known flows at Los Alamos Scientific Laboratories. In the one year period of the investigation the regulator showed a decrease in resistance pressure of 0.3 cm (or 0.12") H₂O at 11 liters/minute flow and a 1.5 cm (or 0.6") H₂O at 154 liters/minute flow.

b. Data analysis

The data were analyzed by factorial analysis of variance (2x2) two factor ANOVA with repeated measures across mask conditions (17). This analysis provides us with information concerning a) the difference between the impaired and the normals: b) the difference between wearing and not wearing the mask; as well as c) describing the interaction between mask wear and pulmonary impairment, see Figure 1.

c. Results and discussion

The average values of the pulmonary testing w and w/o the respirator mask of both normals and impaired are summarized in Table 5. These data along with the summary provided in Table 3 identify the major differences between the impaired and normals. The normals had significantly greater (+24%) forced vital capacities (FVC) than the impaired (p less than 0.00001) and the respirator mask significantly reduced the FVC of both groups by -3% (p less than 0.03) see Figure 2. Obviously this small difference was significant primarily as a consequence of consistency.

The interaction between impairment and mask wear was insignificant (p greater than 0.7). The normals had on average an FVC 10% greater than that predicted from their height and age (13) whereas, the impaired had on average 10% less than their predicted values, Table 3. Timed forced expiratory volumes ($FEV_{1.0,2.0,3.0}$) showed similar consistent differences to those observed for the FVC, however, when expressed as a percentage of FVC, the time $kFEVs$ were relatively unaffected by impairment and or mask wear. The average $FEV_{1.0}$ of the normals was some 10% greater than predicted while the impaired $FEV_{1.0}$ was some 9% less than predicted. Mask wear significantly reduced $FEV_{1.0}$ (p less than 0.003) by -7% for both groups, however, the interaction between impairment and mask wear was not significant (p greater than 0.8), Tables 3 and 5.

The forced inspiratory vital capacity (FIVC) was significantly decreased (-8%) by mask wear for both groups even though the normals had approximately a one liter greater FIVC than the impaired (p less than 0.0001), Figure 3. Measures of static volumes and capacities describing the two groups of subjects were not significantly different with respect to tidal volume (TV), residual volume (RV), closing volume (CV), and closing capacity (CC), p greater than 0.1. However, the normals had significantly greater total lung capacities (TLC) and functional residual capacities (FRC) than the impaired (p greater than 0.01). Also when the CV, CC, and RV are normalized to the specific lung volumes and expressed as a percentage of VC, TLC and TLC respectively, the impaired had significantly greater ratios, p less than 0.0001. This finding is indicative of obstructive small airway disease. This was confirmed by the measured diffusing capacities to carbon monoxide (DL_{CO}) of the normals and impaired. The predicted DL_{CO} for the normal group of subjects was 34.2 ml/mmHg compared to the obtained value of 33.8 ml/mmHg. The impaired, however have a (35%) reduced DL_{CO} compared to their predicted values and was on average 42% less than the normals DL_{CO} , P less than 0.0001. This reduced diffusion capacity of the lung was apparently related to a reduction in the membrane diffusing capacity and may be indicative of underlying emphysema regardless of the symptomology or diagnoses presented in Table 4.

By far the greatest differences due to mask wear and impairment are evidenced in pulmonary tests of dynamic function. These being forced expiratory volumes on both room air (RA) and helium-oxygen (He-Ox) mixtures (80:20). Peak flows (PF) on both RA (+27%) and He-Ox (+30%) were greater in the normal subjects than in the impaired (p less than 0.0001) while mask wear significantly (p less than 0.001) reduced PF for both RA and He-Ox by -19% and -18% respectively. However, in the normal's PF was greatly more affected than the impaired in both tests -2.1% reduction compared 1.1 to 1.5% reduction, (p less than 0.05), see Table 5. Obviously, the respirator mask was interfering with the effort dependent areas of the lung. This was verified by the fact that the mask reduced the $V_{\max 50}$ flow of He-Ox for both groups of subjects (p less than 0.001) yet, did not affect the lower flows of RA $V_{\max 25}$ on either RA or He-Ox (p greater than 0.05) for either groups, Figure 4. Differences in flows between RA and He-Ox at 50% (Delta $V_{\max 50}$) and 25% (Delta $V_{\max 25}$) of the 1FVC above RV are extremely sensitive to areas of small airways and laminar flows. Both these measures identify the fact that the normal group of subjects have greater flows and therefore less small airway disease than the impaired (p less than 0.05). However, only Delta $V_{\max 50}$ indicates the effect of the mask, Figure 5. The mask reduced the Delta $V_{\max 50}$ in both groups (p less than 0.001) and affected the flow of the normals greater than the impaired (p less than 0.001). In fact, it would appear that wearing the mask reduced the lung performance of the normals to approach that of the impaired subjects.

The greater reduction of the normals compared to that of the impaired in dynamic performance of the lung in response to respirator wear was patently obvious when performing a maximum breathing capacity test for 15 seconds ($MBC_{.25}$) and one minute ($MBC_{1.0}$). The average $MBC_{.25}$ of the normals is 144.6 l/min. and was greater than the impaired 115.2 l/min, p less than 0.006, yet the normal's performance of this test was more affected by the mask (-33%) than the impaired (-28%), p less than 0.05. However, both groups of subjects have significantly less performance capability with the mask than without (p less than 0.00001). $MBC_{1.0}$ is consistent with the data obtained in the $MBC_{0.25}$ test, see Figure 6.

The data presented here suggests that a "demand" type respirator with an inspiratory resistance pressure of 85 mmH₂O (3.4" H₂O) at 85 liters/min flow and expiratory resistance pressure of 25 mm H₂O (1" h₂O) at 85 liters/min flow produces significant reductions in the maximum dynamic capabilities of the lung. However, viewed from a physiologically mechanistic aspect it appears that the respirator mask does not differently affect a person with obstructive lung impairment from that observed for a person without lung impairment.

The combination of inspiratory and expiratory resistances used in this study produced a 30% reduction in MBC of the normal subjects and a 27% reduction in the moderately impaired subjects. This is in contrast to a previous report (18) that showed a greater reduction (20% compared to 10%) in persons who had severe chronic obstructive pulmonary disease (COPD). Their instrumentation resistance ranged from 0.7 to 1.3 cm H₂O/l sec⁻¹, whereas the inspiratory resistance used in the present work was 6 cm H₂O/l sec⁻¹ at 85 l/min air flow and ranged from 1.36 cm H₂O/l sec⁻¹ at 11 l/min to 11.0 cm H₂O/l sec⁻¹ at 134 l/min air flow, and the expiratory resistance was 1.76 cm H₂O/l sec⁻¹ at 85 l/min flow and ranged from 2.72 cm H₂O/l sec⁻¹ at 11 l/min air flow to 2.03 cm H₂O/l sec⁻¹ at 157 l/min air flow. This dissimilarity of results between the two investigations may be due to differences in the degree of the COPD patient listed or the greater levels of inspiratory resistance used. In summary, these findings strongly suggest that only those tests which measure dynamic capability of the lung will be useful in evaluating worker performance. Interestingly, from our data it is more easy to predict decrement in MCB due to wearing a mask in the impaired group than in the normal group. Correlations between MBC without the mask and the decrement produced by wearing the mask were $r=0.65$ for the normals and $r=0.83$ for the impaired. These correlations represent a 42% and 69% predictability of effect by the result obtained on the MBC test, see Figure 7. Apparently the people with a high lung performance capability are more variable in their response to wearing the mask.

ii. Physiological responses to "demand" mode respirator wear at three different workloads

Subsequently, the sixty subjects described and utilized in the investigation concerning clinical pulmonary function testing were invited to participate in a further study involving exercise workloads. Twenty-five of the thirty-one subjects previously designated as normal with regard to lung function (i.e. within 10% of the individuals age and sex predicted FVC and/or having a greater than 70% value of FEV_{1.0}/FVC, %) were available for exercise testing. Subjects with normal lung function were designated as group B. Lung impairment was defined as an FVC less than 90% but greater than 60% of age and sex predicted norms and/or FEV_{1.0}/FVC, % less than 70% but greater than 50% of their individual FVC.

a. Maximal exercise stress testing

Each subject was given a 12-lead resting electrocardiogram (ECG) prior to the exercise test. The Balke maximal stress test protocol (19) was utilized for all subjects. Multiple-leads from the standard limb, augmented and chest positions provided a continuous ECG trace on an oscilloscope while recording of the trace was made at 1 minute intervals during the test. Any deviation from normal in a resting or exercising ECG was analyzed by the attending physician. During the stress test on-line monitoring of expired oxygen and carbon dioxide along with minute by minute measurement of ventilatory volumes was carried out to determine maximal aerobic capacity (VO_{2max}). Ventilation volumes were determined minute by minute using a Dry Gas meter

(CD₄-Instrumentation Associates). A continuous recording of the oxygen and carbon dioxide content in the expired air was obtained using a Respiratory Gas Analyzer - Mass Spectrometer (Perkin-Elmer Corp.). All variables were

recorded on a multichannel pen recorder (Soltec Corp.) and properly manipulated to produce the necessary metabolic outputs as averages for each minute of rest, exercise and recovery. All analyzers were calibrated against known standard gases. The appearance of the subject at the termination of the test, maximum heart rate (HR_{max}), a plateauing of V_{O2} during the final stages of the test were used as criteria for determining maximum effort (20). Metabolic calculations were made according to formulae reported by Consolazio, Johnson and Pecora (24).

b. Submaximal exercise testing

Subsequent to the maximal stress test evaluation the subjects accepted to the investigation were scheduled for two sessions of submaximal exercise testing. The exercise tests were performed wearing (w) a "demand" respirator full-face mask (MSA ultravue) and without (w/o) a respirator but using a mouthpiece and nose-clip to enable collection of respiratory and metabolic data. The three sub-maximal exercise walks were performed at a constant speed of 3.4 mph and grades of 3%, 8% and 12% for normal subjects, while the grades selected for the impaired subjects were 2%, 5%, and 8%. The time of each walk was ten minutes. The order of performing the tests (i.e. w or w/o the respirator) was randomly assigned to each individual. However, both sets of exercise loads were performed on the same day and were progressive from low to high grades. Each change in grade was separated by a 5-minute seated rest, while the two tests (i.e. w or w/o respirator) were separated by fifteen minutes of seated rest. See Figure 8 for a schematic outline of the protocol.

During both rest and exercise 'w' and 'w/o' the respirator mask, metabolic, ventilatory, cardiovascular and psychophysiological assessments were made at 4-5 minutes of rest and exercise and 9-10 minutes of exercise. The respirator mask was mechanically modified such that its protection and resistance factors were maintained at its operational values, yet enabling us to make the required measurements of ventilation volume, masks pressures and flows along with expired gas concentrations of oxygen and carbon dioxide. In addition to the monitoring devices already described for maximal testing inspired flows were monitored by a heated pneumotacograph (Fleisch) interfaced with a differential pressure transducer (Validyne) in the range of + 2 cm of water and linearly calibrated from 0.5 l/sec through 8.5 l/sec while mask pressures during inspiration and expiration were monitored using a differential pressure transducer ranging between + 50 cm of water. The "demand" respirator was equipped with an inhalation resistance of 85 mm H₂O at 85 l/min flow and an exhalation resistance of 25 mm H₂O at 85 l/min flow. As reported above, the resistances of the respirator were calibrated against known flows at Los Alamos Scientific Laboratories prior to and following the investigation. No significant changes in the flow/resistance profile were noted.

c. Data analysis

Initially the data were analyzed by a three factor (2X2X9) factorial analysis of variance (ANOVA) with repeated measures across mask and workloads (17). This analysis provided us with information concerning a) differences during exercise between the impaired and the normals; b) differences due to mask wear; and c) the interaction between exercise, mask wear and lung impairment.

Individual levels of work were further probed by two factor (2X2) ANOVA which provided information concerning the responses to a specific relative workload (i.e. % of $\text{VO}_{2\text{max}}$). One workload, the 8% grade at 3.4 mph speed, provided a comparison between impaired and normals across a specific absolute load (i.e. $\text{VO}_2 = \text{LO}_2/\text{min}$) see Figure 9 for schematic outline of research design (i.e. 'F' statistic, p less than 0.05) were found a Neuman-Keuls 'Post-Hoc' test of significance was carried out (17). Unfortunately, the screening stress test identified eleven subjects as unable to perform the three submaximal loads (classified as severely impaired). Hence, only 16 moderately impaired subjects performed the three submaximal tests.

d. Results and discussion

i. Maximal exercise testing ($\text{VO}_{2\text{max}}$)

The data obtained during maximal test from the normals (N=25) moderately impaired (N=16) and severely impaired (N=11) are outlined in Table 6. As can be seen the severely impaired subjects were significantly older than the moderately impaired. The $\text{CO}_{2\text{max}}$ of the normal subjects showed they were of average fitness and were significantly greater than the moderately impaired (p less than 0.05) who were of low fitness. However, the moderately impaired were significantly more fit (p less than 0.05) than the severely impaired subjects. The severely impaired subjects stopped their tests early primarily because of pulmonary impairment. This can be seen from their attained HR_{max} compared to the predicted HR_{max} . The severely impaired were then asked to perform one ten-minute bout, (with and without the respirator) at a load of work 50% of their volitional maximum as an assessment of their submaximal performance.

ii. Submaximal exercise testing ($\%\text{VO}_{2\text{max}}$)

In Figure 8 the outlined work grades on the treadmill of 3%, 8% and 12% for the normals and 2%, 5%, and 8% for the moderately impaired were equivalent to a relative workload of 35%, 50% and 62% of the maximal capacity ($\%\text{VO}_{2\text{max}}$) of both groups. The submaximal workload (i.e. the 50% volitional maximal workload) of the severely impaired subjects was equivalent to 87% $\text{VO}_{2\text{max}}$.

Mean values of various measured and calculated physiological parameters for both normals and moderately impaired subjects during rest and 62% work are summarized in Table 7. The percentage of carbon dioxide in end-tidal air (ETCO_2) was significantly increased as a result of exercise (p less than 0.0001). During the heavier exercise loads the wearing of the mask produced a greater ETCO_2 than the mouthpiece (p less than 0.001). Inspired carbon dioxide percentage ($\text{F}_\text{I}\text{CO}_2$) was greater for the impaired than for the normals whether they were breathing on a mouthpiece or through the respirator mask (P less than 0.003). The mask produced a significant increase in $\text{F}_\text{I}\text{CO}_2$ for both groups of subjects (p less than 0.02), while exercise significantly reduced the $\text{F}_\text{I}\text{CO}_2$ of both groups (p less than 0.0001). Once exercise was begun the mask produced a greater reduction (delta) in $\text{F}_\text{I}\text{CO}_2$ than the mouthpiece (p less than 0.0001), however, this probably reflected the greater levels of $\text{F}_\text{I}\text{CO}_2$ in the mask at rest compared to the mouthpiece.

Calculated dead space (DS), using the Bohr equation and ETCO_2 as a measure of alveolar CO_2 gas concentration, of the impaired subjects (240 ml) while breathing through a mouthpiece was not significantly different from the normal subjects (270 ml) p greater than 0.05, despite their impairment. As expected, the respirator mask significantly increased the DS, which at rest was calculated regardless of impairment to be 100 ml, while during exercise an increase in DS due to the mask ranged from an average of 250 to 300 ml (p less than 0.0001). Obviously then, an interaction between exercise and the mask is occurring producing a greater effective dead space during work than during rest despite the fact that the $\text{F}_\text{I}\text{CO}_2$ is lower in exercise than in rest. Also, it appears that the impaired have greater increases in DS wearing the mask (+250 ml) than the normals (+200 ml), (p less than 0.07) while exercise itself alters DS approximately 250 ml regardless of impairment.

Cardiovascularly, the moderately impaired subjects increased their heart rates more during exercise than the normals (p less than 0.02) however, the respirator mask had a consistent yet minor effect on the subjects (p less than 0.09) in that the mask conditions produced a slightly greater heart rate during work than did the no mask condition. In addition, the systolic blood pressure (SBP) was increased by mask wear both at rest and during exercise (p less than 0.01) while diastolic blood pressure was unaffected by the mask (p greater than 0.1). The moderately impaired subjects, however, did not decrease the DBP during exercise as much as the normals (p less than 0.02).

Increases in peak inspiratory flow (P_IF) and ventilation volumes (V_I) of both the normals and moderately impaired subjects as a result of increases in workload are described in Figure 10 A & B during both mouthpiece and respirator mask wear.

Peak inspiratory flows (PF) generated at rest and during the relative workloads were not differently related to workload as a result of impairment (p greater than 0.26) however, the mask significantly reduced PF during exercises (p less than 0.003) but not at rest. Furthermore the degree of reduction in PF was greater the higher the level of exercise (p less than 0.0001), i.e. the higher peak flows the greater was the effect. The PF of the impaired subjects was less than the normal subjects during exercise (p less than 0.06) however, this was probably related to the differences in absolute workloads that were assigned to the different groups of subjects needed to obtain the same relative loads. This was readily apparent when describing alterations in ventilatory volumes, Figure 10A. Similar to the PF the peak inspiratory pressures (PP_I) showed no significantly different relationships to workload or ventilation volumes between subject groups (p greater than 0.7), however, respirator mask wear significantly increased PP_I at rest (+30%) to a 400% increase during 62% $\text{VO}_{2\text{max}}$ work see Figure 11. Average work PP_I at 62% $\text{VO}_{2\text{max}}$ were 10.42 cm H_2O (4.1" H_2O) at mean PF of 224 + 40 (SD) l/min for the normals and 9.89 cm H_2O (3.9" H_2O) at mean PF of 203 + 43 (SD) l/min for the impaired. Obviously, as workload and PF increased PP_I increased (p less than 0.00001), see Figure 12. Peak expiratory flows (PP_E) had similar significant trends with a 160% increase at rest and a 256% increase during 62% $\text{VO}_{2\text{max}}$ work. The average PP_E was 4.46 cm H_2O (1.75" H_2O) for the normal subjects and 3.86 cm H_2O (1.52" H_2O), see Figure 13.

Evaluation of the metabolic effects of mask wear suggests that the oxygen uptake (VO_2) of the submaximal work was slightly less with the mask than without (p less than 0.09) however, this is of minor physiological importance and appears to be within the error of measurement. The expected trends of increasing VO_2 with exercise differences between absolute workloads of the impaired and the normals were found (p less than 0.00001) however, the relative workloads of the two groups were not different (p greater than 0.5). Similarly, carbon dioxide production (VCO_2) and ventilation volume (V_I l/min) reflected the differences in absolute workloads was also maintained when V_I was expressed as a percentage of the individuals MBC (V_IMBC).

Further comparison between the moderately impaired and normal subjects was made at the same absolute workload and summarized in Table 8. Even though the 8% grade produced a significant difference in relative workload of the two groups (47% $\text{VO}_{2\text{max}}$ for the normals and 64% $\text{VO}_{2\text{max}}$ for the impaired), only one of the respiratory parameters measured (V_I/MBC) indicated further differences between the two groups. However, respirator mask wear significantly altered the calculated DS , PP_I and PF_I and the ratio V_I/MBC . Further comparisons of respirator mask wear failed to significantly alter the response of the wearer regardless of their level of impairment. Cardiovascular differences between groups reflected the higher relative workloads normal $\text{HR}=128$ beats/min and $\text{SBP}=155$ mmHg and impaired $\text{HR}=152$ beats/min and $\text{SBP}=173$ mmHg) and percentages of their maximal capabilities. However, the respirator mask wear significantly increased HR on average 3 beats/min in both groups and SBP 6 mmHg in the normals and 10 mmHg in the moderately impaired p less than 0.001.

Statistical comparisons of the severely impaired subjects with the two other groups was not carried out as neither their absolute nor their relative workloads provided any basis upon which to carry out a meaningful comparison. However, changes within the group of severely impaired subjects as a result of respirator mask wear are summarized in Table 9. Only seven of the eleven severely impaired subjects completed their ten minute exercise bout. The average relative workload of this group was 76-78% $\text{VO}_{2\text{max}}$ during the 9th minute of work, however, during the 5th minute of work, inclusive of the four drop-outs, the average group workload was 87% $\text{VO}_{2\text{max}}$. Respirator mask wear failed to significantly alter the subjects physiological response to their individual submaximal workloads despite a 268% average increase in expired pressure (p less than 0.09) and a 455% average increase in inspired pressure (p less than 0.01).

It was apparent from the data the the "demand" type air purifying respirator as used in these investigations produced large changes in pressure across the mouthpiece. These pressure changes ranged from 2 cm H₂O at 10 liters/min ventilation volume, or 12.0 I/sec instantaneous flow, at rest to 16 cm H₂O at ventilations volumes of 60 liters/min or 4 I/sec instantaneous flow at workloads of 60% $\text{VO}_{2\text{max}}$. This flow/pressure response was the same in both the normals and the moderately impaired subjects. In addition, the data points available for the severely impaired subjects confirmed that the pressure/flow response was not altered by degree of impairment when using a mouthpiece. However, when breathing through a respirator mask interface the pressure-swings across the mouth were severely attenuated (9.7 cm H₂O) at flows of 4.5 I/sec. This reduction in pressure flow relationships occurred on both the inspired (a reduction of 5 cm H₂O) and the expired (a reduction of 3.5 cm H₂O) sides, see Table 9. When related to ventilation volume, as in Figure 12, the severely impaired had similar pressure responses to the normals and moderately impaired. Obviously their lung impairment was both obstructive and restrictive and therefore they were unable to generate comparable peak flows for a given ventilation volume. Their impairment resulted in the subjects not challenging the respirator interface at the point of maximum inhalation. The severely impaired were working at 78% $\text{VO}_{2\text{max}}$ at the same ventilation flow relationship as the normals and impaired, who were working at 62% $\text{VO}_{2\text{max}}$. In addition, using a calculated index, termed dyspnea index (ventilatory volume/maximal breathing capacity), the lung performance of the severely impaired was 53% of maximum compared to the 32-37% of the normals and moderately impaired subjects. Astrand (22) has identified a 70% dyspnea index as being related to maximal work capacity. Hence, further increases in workload for the severely impaired would have caused them to terminate their work as a result of their individual lung impairment and not as a result of the added respiratory burden of the respirator, although it was probable that those subjects PF were maximized at this workload. Hence, we conclude that it may be the relationship between lung impairment and work capacity that is probably important with respect to respirator wear and its effect on the working individual. This would suggest that the degree of impairment and its relationship to work performance is of primary importance in evaluating a worker's capability of using a respirator. However, more importantly it would appear that knowledge of the workload of the job requiring respirator wear is a consideration in this evaluation.

From the data of the clinical pulmonary function testing we suggested that respirator wear produced an impairment of dynamic lung function which mimics the lung function of a clinically impaired subject. Especially evident was the test of maximal breathing capacity (MBC) as a prediction of impairment produced by the wearing of a respirator. However, further analysis of the present data using multiple regression techniques did not significantly single out MBC, as a predictor of respirator wear during work (9 times in 41) more than other measures of lung function, nor did it identify the individual $\text{VO}_{2\text{max}}$ as a predictor of response. However, the critical question of relating MBC to $\text{VO}_{2\text{max}}$ while wearing the respirator was unable to be answered from the present data. Previous work (9) showing a decrement in maximal work performance due to respirator wear was compounded by the factor of weight bearing (35 lbs) of the self contained breathing apparatus, while the work of Myrhe et.al. (10) showed both weight bearing and respiratory response differences at 80% $\text{VO}_{2\text{max}}$. Hence, further work on the specific relationship between changes in work performance and respirator wear needs to be carried out.

Many investigators (4, 9, 23, 24) have documented changes in the respiratory system during work, when inspiratory and expiratory resistances were increased. The changes identified were reductions in respiratory rate or tidal volume and increases in alveolar and arterial PCO_2 (24), other changes included a reduction in minute ventilation without changes in oxygen uptake, heart rate or diffusion capacity (23). These investigations have related altered physiological states to subjective responses and the degree of pressure swing across the mouth (4,23). This pressure swing has been shown by Bentley et.al (4) to subjectively affect performance when greater than 17 cm H_2O . This was later confirmed by Love et.al (23) in older subjects and agrees well with the earlier work of Silverman et.al. (25) and Cooper (6). In the present investigation the pressure swing across the mouthpiece did not exceed 15 cm H_2O and except for slight reduction in PF and slight increase in cardiovascular work significant physiological alterations were not observed for either the normals or the moderately impaired. However, both groups of subjects subjectively perceived their breathing (PB) and their workload (RPE) to be harder during respirator wear for each given workload, yet there were not differences between each group, Figure 14. Also all subjects indicated that the wearing of the respirator was tolerable to the workloads imposed. These findings confirm further the work of Bentley et.al. (4) and Love et.al.(24). Based upon these results and using the relationship between pressure swing and % $\text{VO}_{2\text{max}}$ of the present investigation one would predict that workloads equivalent to 80% $\text{VO}_{2\text{max}}$ would be intolerable during work when the respiratory resistances used in this investigation are employed.

At rest the subjects were re-inspiring greater levels of carbon dioxide (approaching 0.7% in the normals and 1% in the impaired) than during work (approaching 0.3% in the normals and 0.5% in the impaired). However, the levels of CO_2 re-inspired were less than the 3% level needed to reduce working performance with or without added resistance (25). In addition, the level of inspired CO_2 did not reach a stimulatory level for ventilation as the ventilation volume on the mask was equal to that without the mask.

Functional dead space of the respirator increased from rest to work ranging from 100 ml at rest to 300 ml at 63% $\text{VO}_{2\text{max}}$ workload and ventilation volumes of 10 liters/min and 60 liters/min in normals and 50 liters/min in the moderately impaired respectively. However, as inspired CO_2 was decreasing with the increasing ventilation and functional dead space it would appear that the face mask design adequately reduced the danger of re-inspiring significant levels of carbon dioxide.

iii. Conclusions

It was apparent that the workload required to be performed during respirator wear is an important component of the psychophysiological response of the worker. Mild pulmonary impairment was of minimal importance with respect to the workloads below 63% $\text{VO}_{2\text{max}}$. The psychophysiological responses may become disproportionate to the metabolic stress above the 80% $\text{VO}_{2\text{max}}$ workload. Severe pulmonary impairment is more likely to cause termination of work regardless of the respirator. Hence, it is probable that a simple performance test such as an exercise stress test may prove to be an adequate clinical screening test for respirator wear during various work levels. This requires the examining physician to be cognisant of the ranges of work stress of a specific industrial task than an employee will encounter.

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TABLE 1

Sennek's (8) Equation Relating
Perception to Actual Respirator Work

$$W = 0.14[M/10 + (M/10)^2 + 0.1 (M/10)^3] \text{ Kg/min.}$$

W = Total External Respiratory Work Rate
 M = Volume of Ventilation in Liters/Min.

This Curve:

- a. Divides unnoticed from noticed responses
- b. Passes through 6.0 Kg. M/Min at 50 L/min.
- c. Passes below 13.3 Kg. M/Min at 64.5 L/min and 28.0 Kg.. M/min at 90.3 L/min.

TABLE 2
SUMMARY OF THE MAJOR PRACTICAL FINDINGS IN THE
WORK OF MYRHE et. al. (10)

1. Weight-bearing of the SCBA increases the energy requirement of a task 20%.
2. The time-rating of a breathing bottle is significantly reduced during heavy work. e.g. A 30 min bottle at rest may empty within 8-10 min in heavy work
3. The NIOSH bench certification test inadequately challenges the respirator.
4. "Pressure-demand" mode will be drawn negative when workloads exceed 50% of the individuals maximal capacity.

TABLE 3

PULMONARY FUNCTION DESCRIPTION OF THE NORMAL AND IMPAIRED SUBJECTS
(Mean $\pm$ SD)

Pulmonary measures	Normal subjects (N=31) mean age = 33.7 $\pm$ 1.9 yrs)	Impaired subjects (N=29) (mean age = 42.4 $\pm$ 2.14 yrs)
FVC (L)	5.65 $\pm$ 0.87	4.32 $\pm$ 1.24
FEV _{1.0} (L)	4.54 $\pm$ 4.24	3.44 $\pm$ 3.19
FEV _{1.0} /FVC, (%)	81 $\pm$ 8	78 $\pm$ 8
D _L CO (ml. mmHg)	33.8 $\pm$ 9	19.6 $\pm$ 7
CC (l)	2.94 $\pm$ 0.9	3.26 $\pm$ 1.0
RV/TLC (%)	30.6 $\pm$ 5.6	40.45 $\pm$ 9.0
CC/TLC	39.4 $\pm$ 7.4	51.7 $\pm$ 10.0

TABLE 4*

CLINICAL SYMPTOMS AND DIAGNOSIS OF THE IMPAIRED SUBJECTS

Symptom and Diagnosis**	N
Heavy smoker	16
Bronchitis	16
Asthma (Clinical & Allergenic)	11
Pneumonia (previous history)	7
Emphysema	21
Tuberculosis	1
Cancer (lung lobe removal)	2

* The total N is greater than the total number of impaired subjects (N=29) because of the fact that some of the subjects had one or more symptoms and/or diagnosis.

** Heavy smoker was defined as those who smoked a minimum of 2 packs/day for at least ten years.

[From Raven, et al (1977), with permission]

TABLE 5

PULMONARY FUNCTION MEASURES OF NORMAL AND IMPAIRED SUBJECTS
WITH (w) AND WITHOUT (w/o) THE RESPIRATOR (means $\pm$ SD)

PULMONARY MEASURE	NORMAL SUBJECTS (N = 31) mean age = 33.7 $\pm$ 1.9 yrs		IMPAIRED SUBJECTS (N = 29) mean age = 42.4 $\pm$ 2.14 yrs	
	Without mask	with mask	without mask	with mask
FVC (L)	5.65 ($\pm$ 0.87)	5.5 ($\pm$ 0.89)	4.32 ($\pm$ 1.24)	4.21 ($\pm$ 1.14)
FEV _{1.0} (L)	4.54 ($\pm$ 0.68)	4.24 ($\pm$ 0.79)	3.44 ($\pm$ 1.2)	3.19 ($\pm$ 1.02)
FEV _{1.0} /FVC, %	80.76 ($\pm$ 7.71)	77.54 ($\pm$ 8.3)	78.47 ($\pm$ 8.25)	75.42 ($\pm$ 11.22)
FIVC (L)	4.1 ($\pm$ 0.78)	3.83 ($\pm$ 0.85)	3.19 ($\pm$ 0.92)	2.94 ($\pm$ 0.82)
MBC _{.25} (L/min)	144.63 ($\pm$ 33.48)	97.12 ($\pm$ 23.8)	115.17 ($\pm$ 43.68)	82.68 ($\pm$ 25.29)
MBC _{1.0} (L/min)	116.82 ($\pm$ 25.17)	80.21 ($\pm$ 22.39)	97.92 ($\pm$ 36.52)	71.16 ($\pm$ 25.03)
PF _{HO} (L/sec)	11.37 ($\pm$ 1.38)	9.28 ($\pm$ 1.76)	8.75 ($\pm$ 2.84)	7.29 ($\pm$ 2.27)
PF _{RM} Air (L/sec)	9.14 ($\pm$ 1.04)	7.15 ($\pm$ 1.55)	7.20 ($\pm$ 2.25)	6.11 ($\pm$ 2.04)
V _{max} 50-Ho (L/sec)	7.24 ($\pm$ 1.75)	5.94 ($\pm$ 1.77)	4.75 ($\pm$ 3.01)	4.14 ($\pm$ 2.35)
V _{max} 50-RmA (L/sec)	5.01 ($\pm$ 1.17)	4.66 ($\pm$ 1.17)	3.59 ($\pm$ 2.05)	3.41 ($\pm$ 1.71)
V _{max} 25-Ho (L/sec)	2.81 ($\pm$ 1.13)	2.42 ($\pm$ 1.03)	1.44 ($\pm$ 1.12)	1.49 ($\pm$ 1.0)
V _{max} 25-RmA (L/sec)	2.03 ($\pm$ 0.71)	2.04 ($\pm$ 0.79)	1.35 ($\pm$ 0.84)	1.33 ($\pm$ 0.85)
Visov (L)	0.78 ($\pm$ 0.11)	1.21 ($\pm$ 0.63)	0.95 ($\pm$ 0.32)	0.99 ($\pm$ 0.40)

TABLE 6

DESCRIPTIVE DATA OF SUBJECTS TESTED ON THE MAXIMAL STRESS TEST
(means = SE means)

	Normal Function (N=25)	Moderately Impaired (N=16)	Severely Impaired (N=11)
Age (yrs)	33.4 1.9	36.9 2.5	47.3 3.5
VO ₂ max (ml O ₂ /kg.min)	44.10 2.34	35.51 2.00	22.41 1.59
HR _{max} (beats/min)	185 3	184 4	160 5
predicted HR _{max} (beats/min)	187 2	183 2	173 4

TABLE 7

Cardiorespiratory parameters obtained during the final measurement period of each workload for the normal (N=25) and moderately impaired (N=16) subjects with (w) and without (w/o) the respirator (means $\pm$ standard deviation)

		REST				62% VO ₂ max			
		normal		impaired		normal		impaired	
		w/o	w	w/o	w	w/o	w	w/o	w
End Tidal CO ₂ (%)	$\bar{x}$	5.56	4.99	5.23	5.04	6.24	6.77	6.13	6.38
	SD	± 0.35	± 0.43	± 0.61	± 0.62	± 0.48	± 0.6	± 0.59	± 0.69
Inspired CO ₂ (%)	$\bar{x}$	0.56	0.66	0.66	0.98	0.24	0.20	0.29	0.33
	SD	± 0.20	± 0.36	± 0.26	± 0.31	± 0.06	± 0.10	± 0.08	± 0.20
Calculated DS (ml)	$\bar{x}$	270	370	240	350	540	790	450	720
	SD	± 70	± 110	± 120	± 90	± 130	± 210	± 190	± 160
Heart Rate (beats/min)	$\bar{x}$	77	75	88	83	151	152	152	156
	SD	± 20	± 14	± 15	± 14	± 24	± 22	± 19	± 18
Syst. BP (mmHg)	$\bar{x}$	122	125	127	130	168	179	174	186
	SD	± 7	± 11	± 17	± 16	± 21	± 21	± 17	± 16
Diast. BP (mmHg)	$\bar{x}$	78	79	79	80	74	74	80	80
	SD	± 8	± 7	± 14	± 10	± 6	± 7	± 12	± 10

TABLE 8

Comparisons of Normal and Moderately Impaired Subjects w and w/o the
Respirator Mask at the Same Workload of 8% Grade
(mean $\pm$ standard error of the means)!

		Normals (N=21)		Moderately Impaired (N=14)		Significance*
		w/o	w	w/o	w	
VO ₂ max	(%)	47.1 ($\pm$ 3.31)	47.0 ($\pm$ 3.0)	63.8 ($\pm$ 4.0)	62.7 ($\pm$ 3.8)	p less than 0.001 !
End Tidal CO ₂	(%)	6.54 ($\pm$ 0.9)	6.57 ($\pm$ 0.15)	6.13 ($\pm$ 0.17)	6.39 ($\pm$ 0.2)	NS
Inspired CO ₂	(%)	0.28 ($\pm$ 0.01)	0.23 ($\pm$ 0.01)	0.29 ($\pm$ 0.02)	0.33 ($\pm$ 0.06)	NS
Calculated DS	(mL)	510 ($\pm$ 38)	740 ($\pm$ 49)**	450 ($\pm$ 54)	720 ($\pm$ 47)**	NS
Peak Pressure Expired	(cmH ₂ O)	+1.17 ($\pm$ 0.14)	+3.48 ($\pm$ 0.47)**	+1.16 ($\pm$ 0.10)	+3.85 ($\pm$ 0.51)**	NS
Peak Pressure Inspired	(cmH ₂ O)	1.88 ($\pm$ 0.18)	-7.42 ($\pm$ 0.73)**	-2.04 ($\pm$ 0.23)	-9.90 ($\pm$ 1.80)**	NS
Peak Flow Inspired	(l/sec)	3.62 ($\pm$ 0.21)	3.14 ($\pm$ 0.13)**	3.96 ($\pm$ 0.29)	3.38 ($\pm$ 0.21)**	NS
Ventilation Volume	(l/min)	45.1 ($\pm$ 2.5)	44.1 ($\pm$ 2.0)	42.5 ($\pm$ 5.7)	49.1 ($\pm$ 3.7)	NS
V _I /MBC	(%)	31.8 ($\pm$ 2.4)	32.0 ($\pm$ 2.1)**	34.2 ($\pm$ 3.3)	37.3 ($\pm$ 3.7)**	p less than 0.05

! Numbers within the brackets are standard errors

* Difference comparison between normals and impaired

** Difference comparison between wearing and not wearing the respirator mask

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TABLE 9

Comparaisons during Exercise With and Without the Respirator Mask
for the Severely Impaired Subjects
(mean $\pm$ standard error of the mean)!

Severely Impaired

(N=7)

VO _{2max}	(%)	78.4	(<u>+9.4</u>)	76.5	(<u>+10.2</u>)	NS
End Tidal CO ₂	(%)	5.57	(<u>+0.3</u>)	5.67	(0.2)	NS
Inspired CO ₂	(%)	0.38	(<u>+0.1</u>)	0.41	(<u>+0.1</u>)	NS
Calculated DS	(ml)	429	(<u>+43</u>)	467	(<u>+80</u>)	NS
Peak Pressure Expired	(cmH ₂ O)	+0.92	(+0.12)	+2.47	(<u>+0.78</u>)	p less than 0.8
Peak Pressure Inspired	(cmH ₂ O)	-1.59	(+0.15)	-7.23	(<u>+1.55</u>)	p less than 0.01
Peak Flow Inspired	(l/sec)	4.1	(<u>+0.25</u>)	4.4	(<u>+1.11</u>)	NS
Ventilation Volume	(l/min)	43.1	(<u>+3.96</u>)	42.5	(<u>+5.17</u>)	NS
V _I /MBC	(%)	53.5	(<u>+9.39</u>)	51.9	(<u>+8.36</u>)	NS

! Numbers within the brackets are standard errors

[From Raven, et al (1979), with permission]

Figure Legends

- Figure 1 Research design of the clinical pulmonary function investigation of respirator wear
- Figure 2 A comparison of mean values of Forced Vital Capacity (FVC) in liters between the normal and impaired subjects while wearing an industrial respirator.
- Figure 3 A comparison of mean values of Forced Inspiratory vital Capacity (FIVC) in liters between the normal and impaired subjects while wearing an industrial respirator.
- Figure 4 A comparison of the mean values of air flow rate at 50% of FVC ($V_{\max 50\%}$) in liters/second of the normal and impaired subjects while wearing an industrial respirator and breathing room air (Rm Air) and 80% helium 20% oxygen mixtures (He/Ox).
- Figure 5 A comparison of the differences in flow between Rm Air and He-Ox mixture obtained at 50% FVC ($\Delta V_{\max 50}$) and at 75% VC ($\Delta V_{\max 25}$) in liters/second of normal and impaired subjects while wearing an industrial respirator.
- Figure 6 The alterations of maximum breathing capacity (MBC) expressed as liters/minute of normal and impaired subjects obtained over fifteen seconds ($MBC_{.25}$) and one minute ($MBC_{1.0}$) that occur while wearing an industrial respirator.
- Figure 7 A comparison of the relationship between the maximum breathing capacity (MBC) obtained without the respirator and the changes in MBC (Δ MBC) that occurs while wearing the respirator. The regression equation for both normal and impaired subjects are diagrammed.
- Figure 8 A schematic outline of the submaximal exercise (3.4 mph and % grade) evaluation of moderately impaired (hatched) and normal subjects with and without respirators. *denotes the time at which measurements were made.
- Figure 9 A schematic representation of the research design used to evaluate respirator wear with respect to relative and absolute workloads.
- Figure 10 The relationships between ventilation volumes (A) and peak flows (B) of both normals and moderately impaired subjects with respect to workloads with and without the respirator.
- Figure 11 Alterations that occur in inspiratory and expiratory pressure as a result of increasing workloads: a comparison between mouthpiece and respirator wear. In the test increasing inspiratory pressures denote a greater negative pressure with respect to ambient pressure (this is consistent for figures 11-13)

- Figure 12 Changes in mouthpiece and mask pressure in relation to peak flows.
- Figure 13 Changes in inspiratory and expiratory pressures of both mouthpiece and respiratorymask with respect to ventilation volume.
- Figure 14 Subjective differences between mouthpiece and respiraor mask wear as estimated in terms of perception of breathing (A) and perception of effort (RPE) in B.

FIGURE I

Research Design of Clinical Pulmonary Function

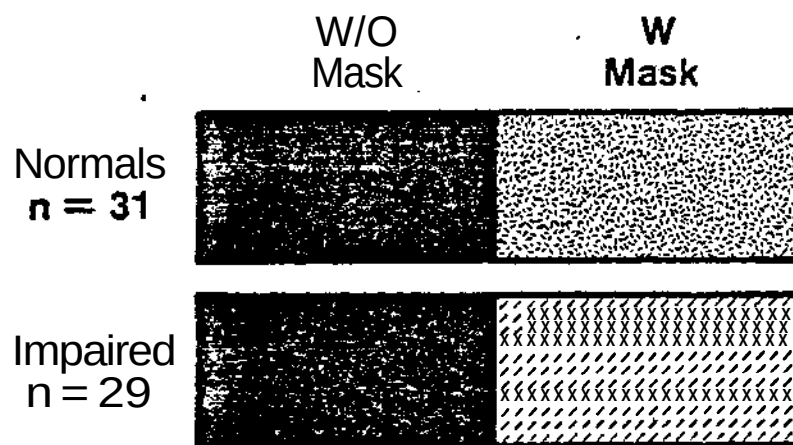


Figure 2

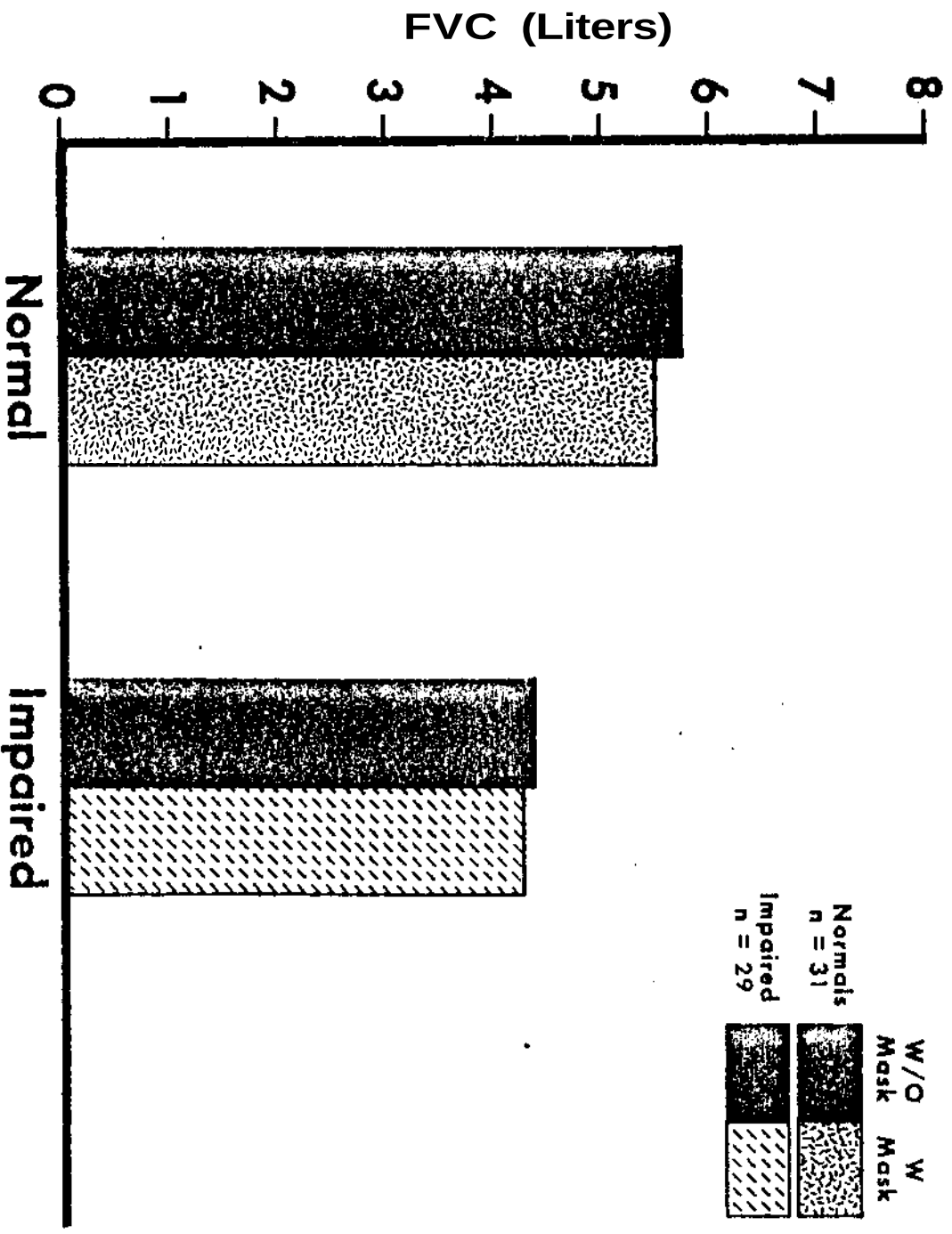


Fig 003

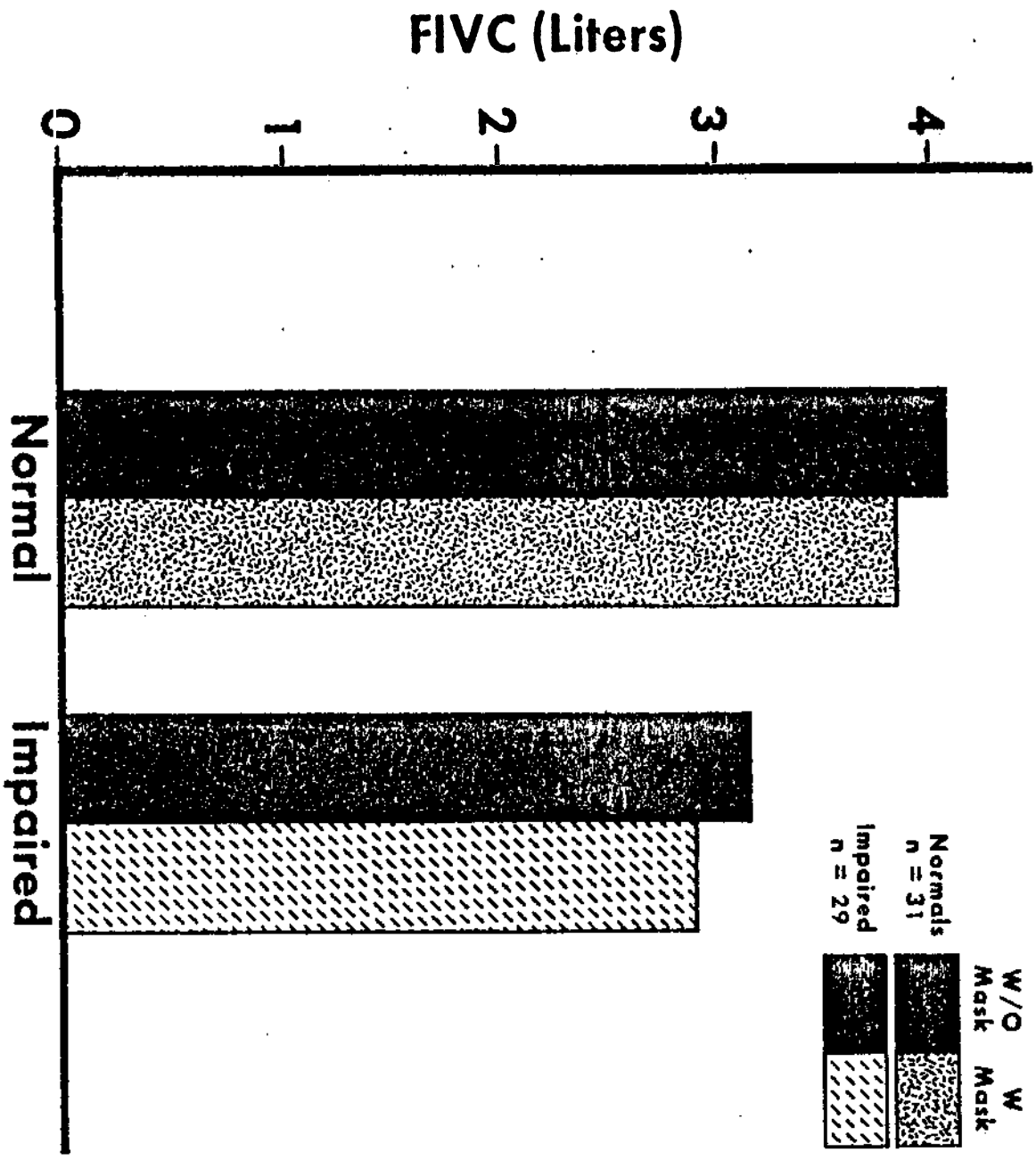


Figure 4

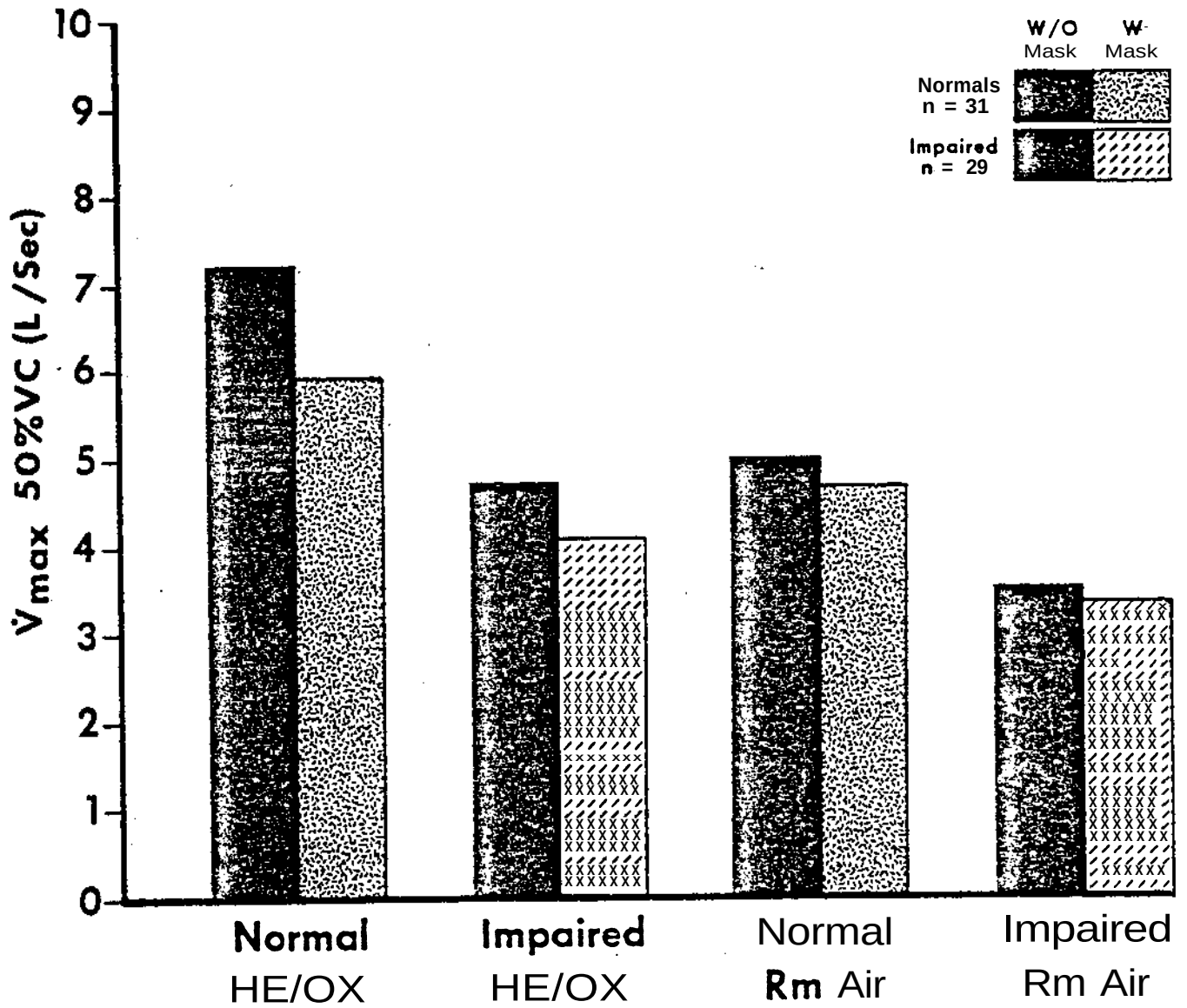


Figure 5

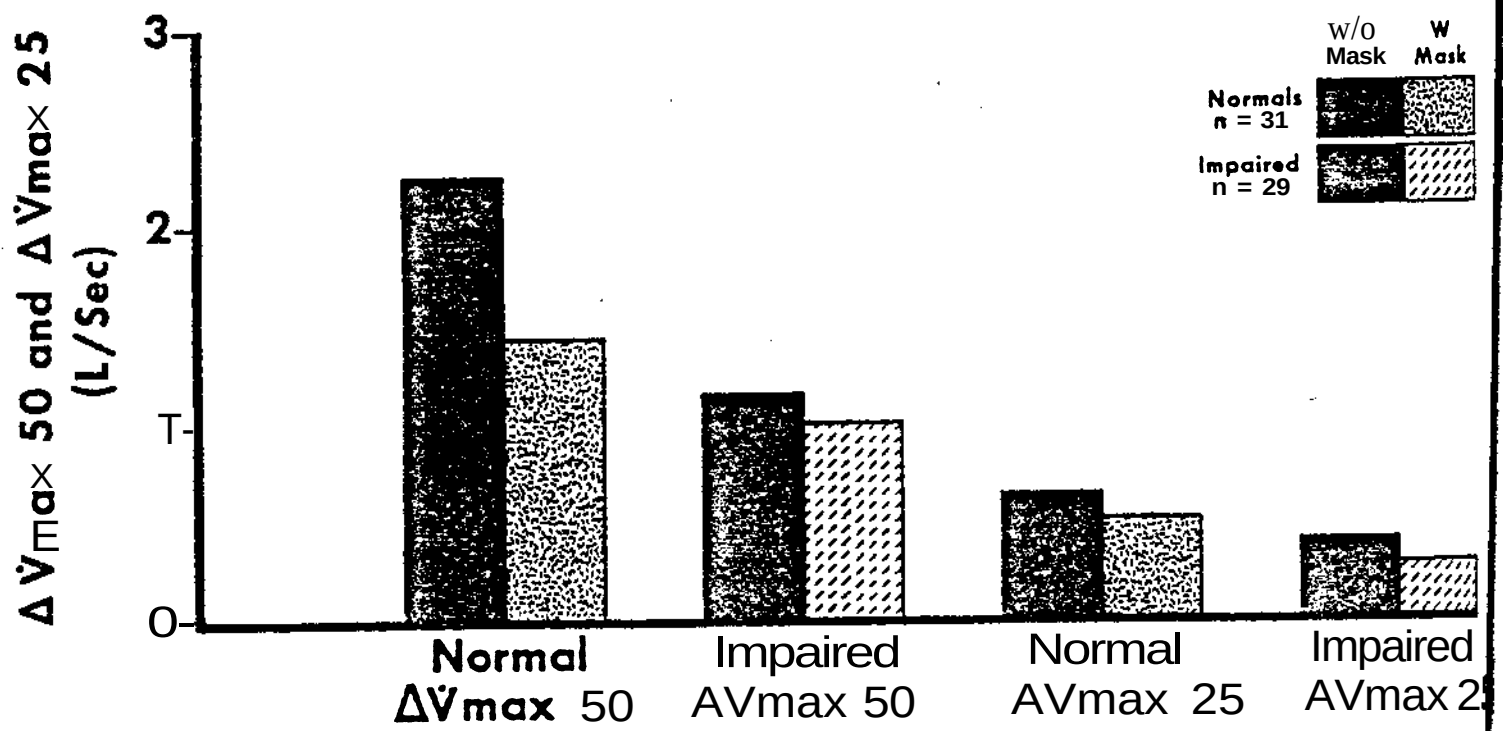


Figure 6

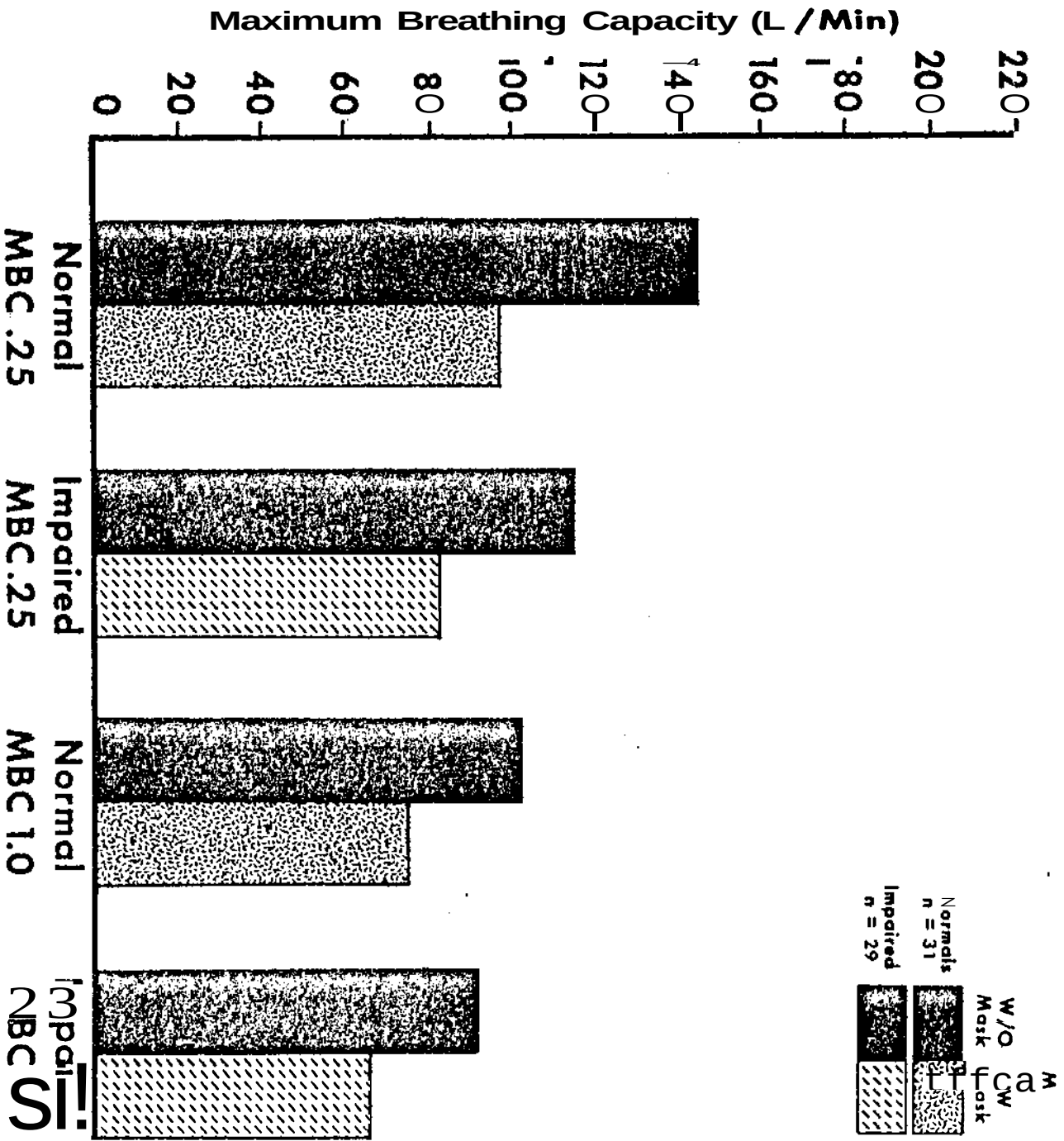
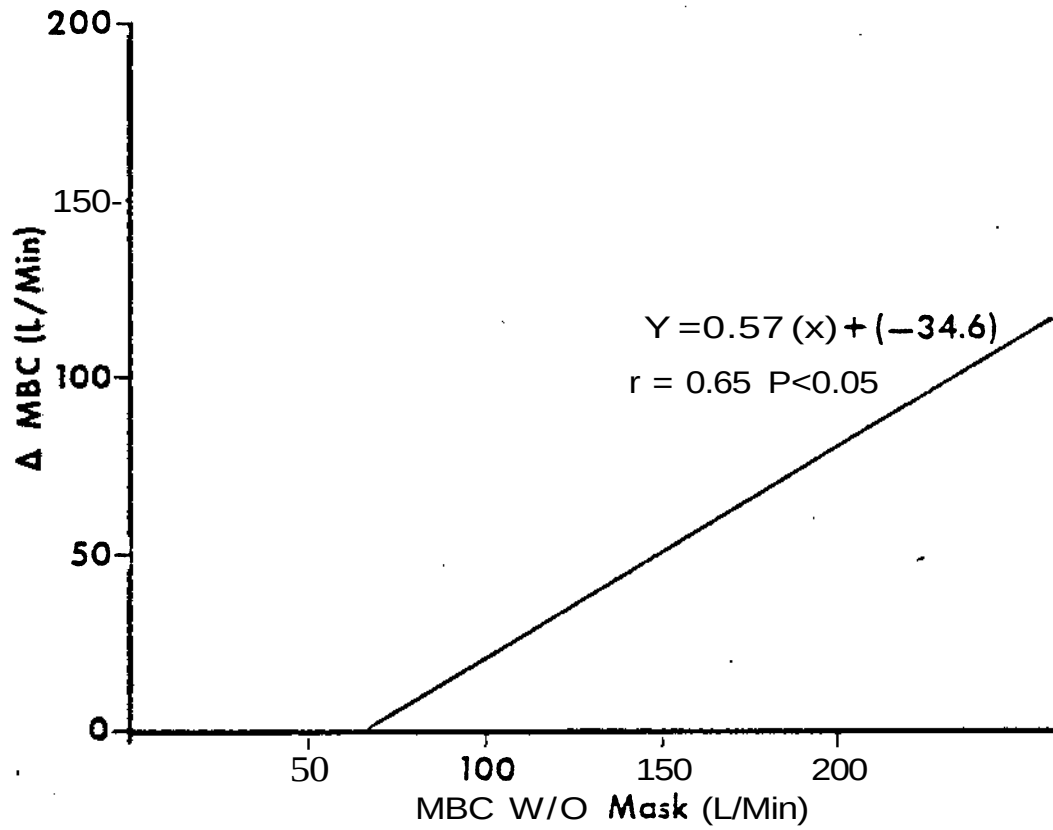


Figure 7

Normals



Impaired

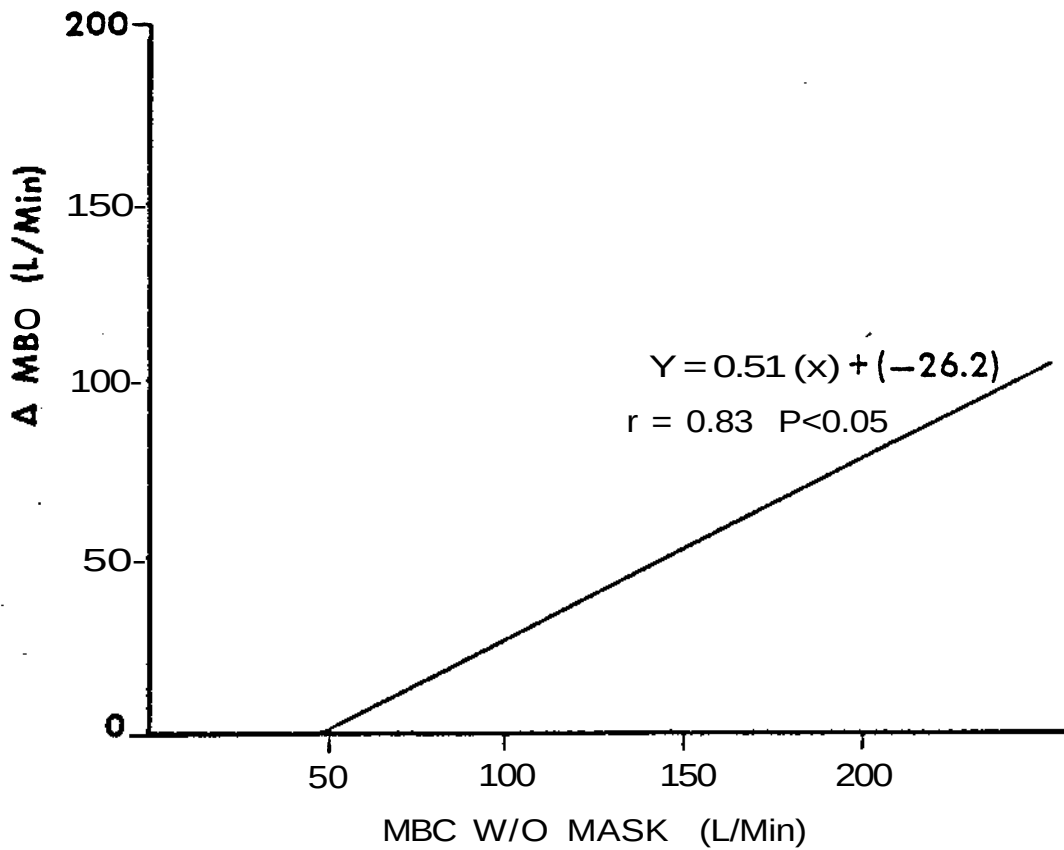


Figure 8 [From Raven, et al (1979) , with permission]

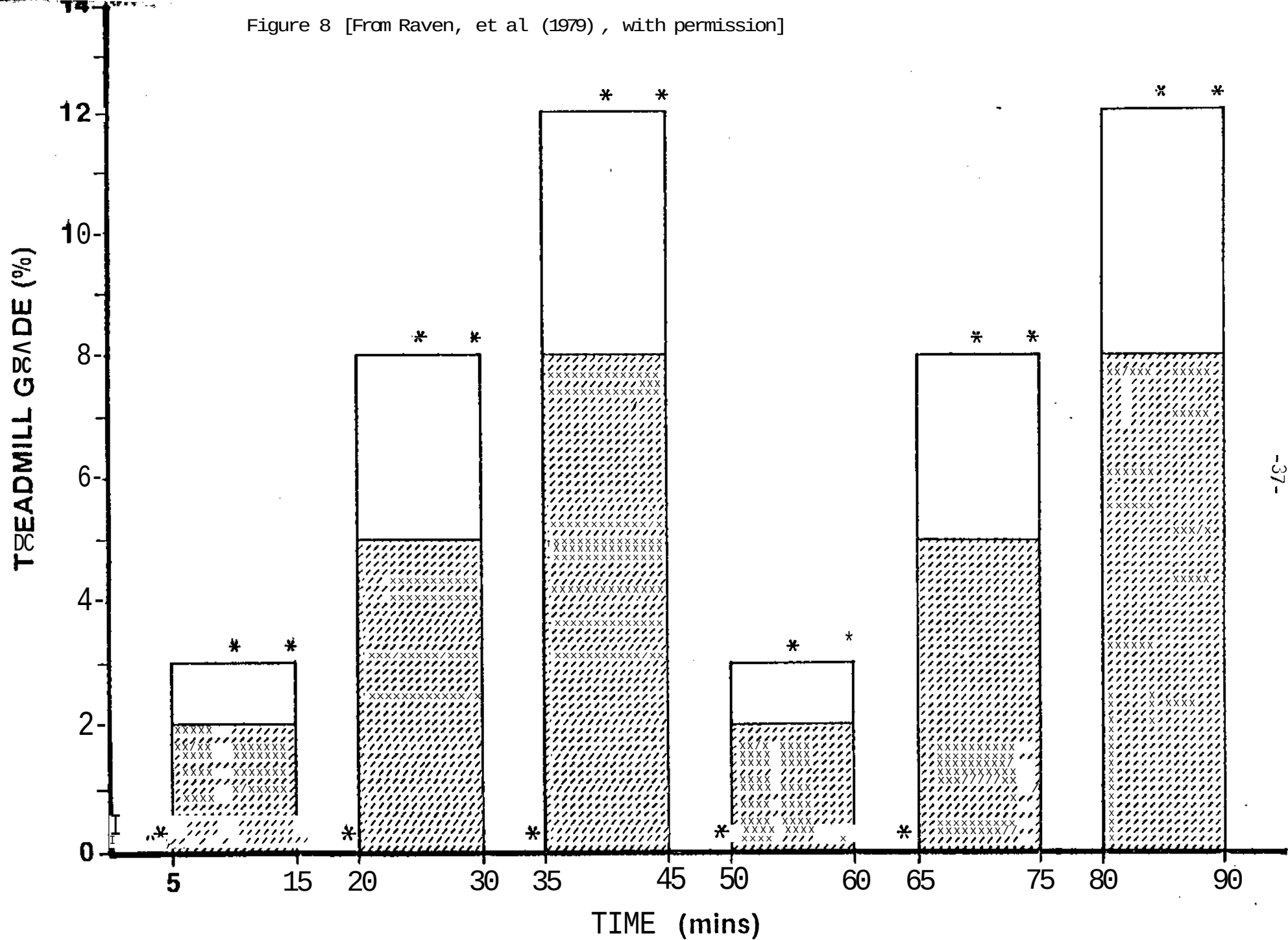
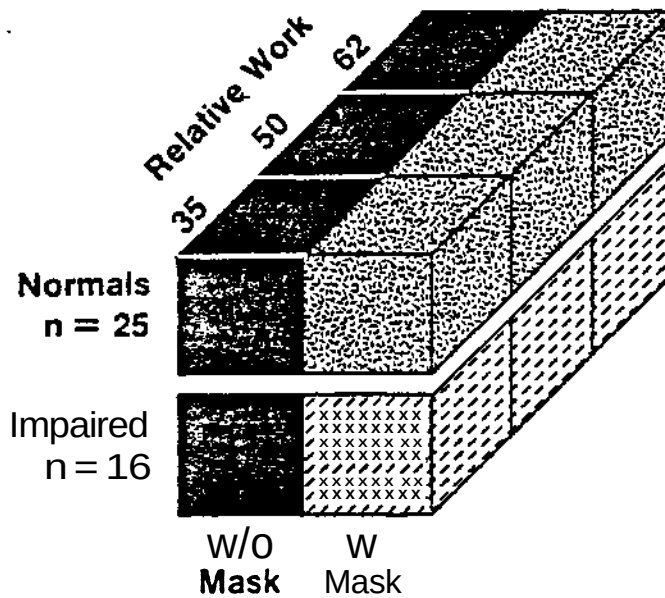


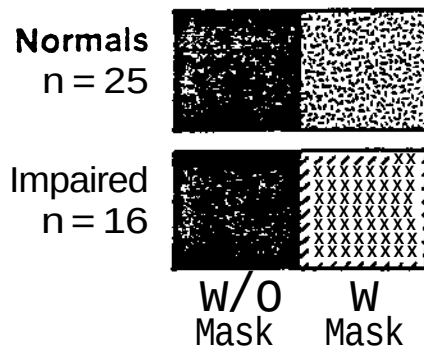
Figure 9

Research Design for Submaximal Exercise Testing

a. **Relative Workload Comparisons**



b. **Absolute Workload (8% Grade) Comparison**



[From Raven, et al (1979), with permission]

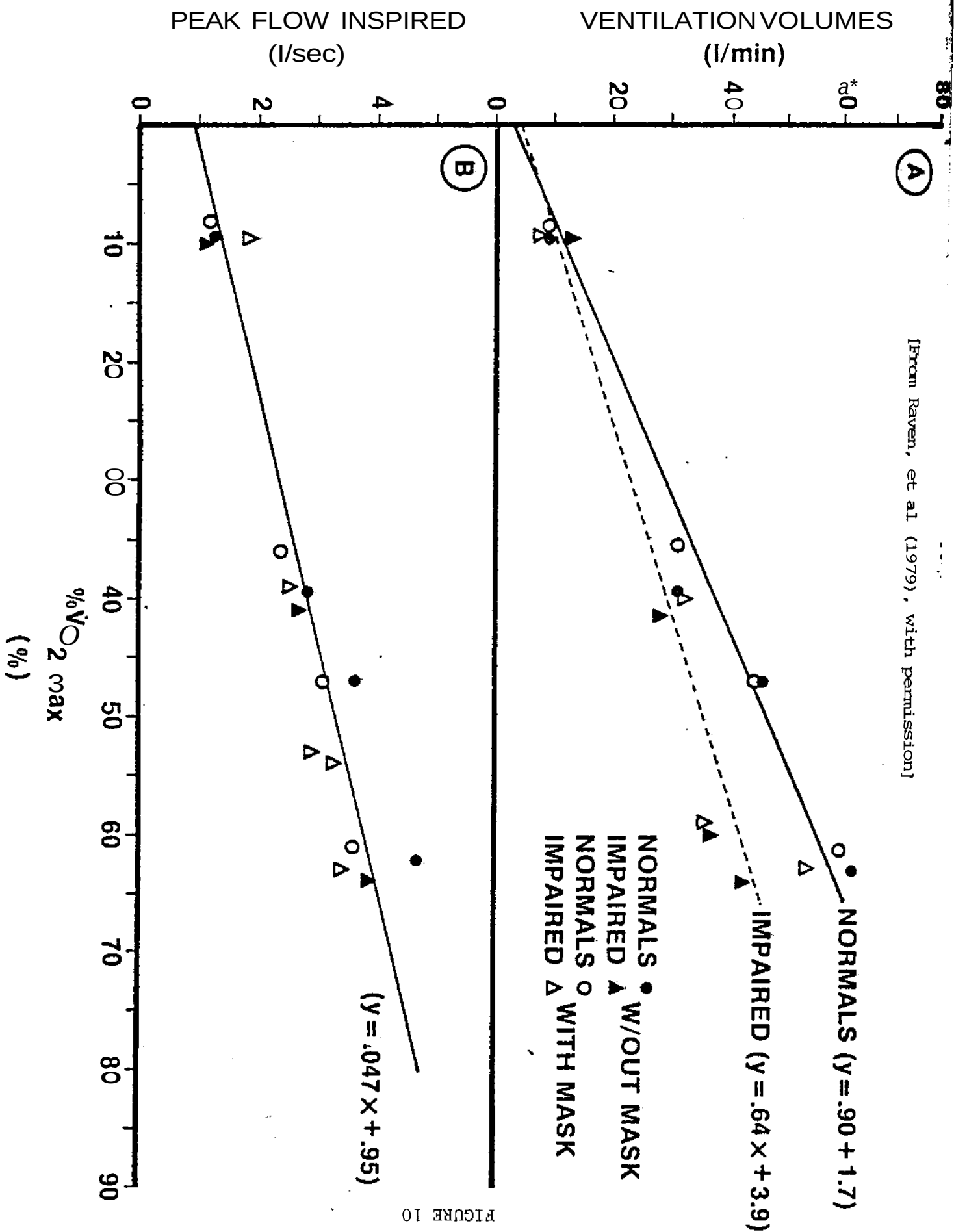


FIGURE 10

FIGURE 11

[From Raven, et al (1979), with permission]

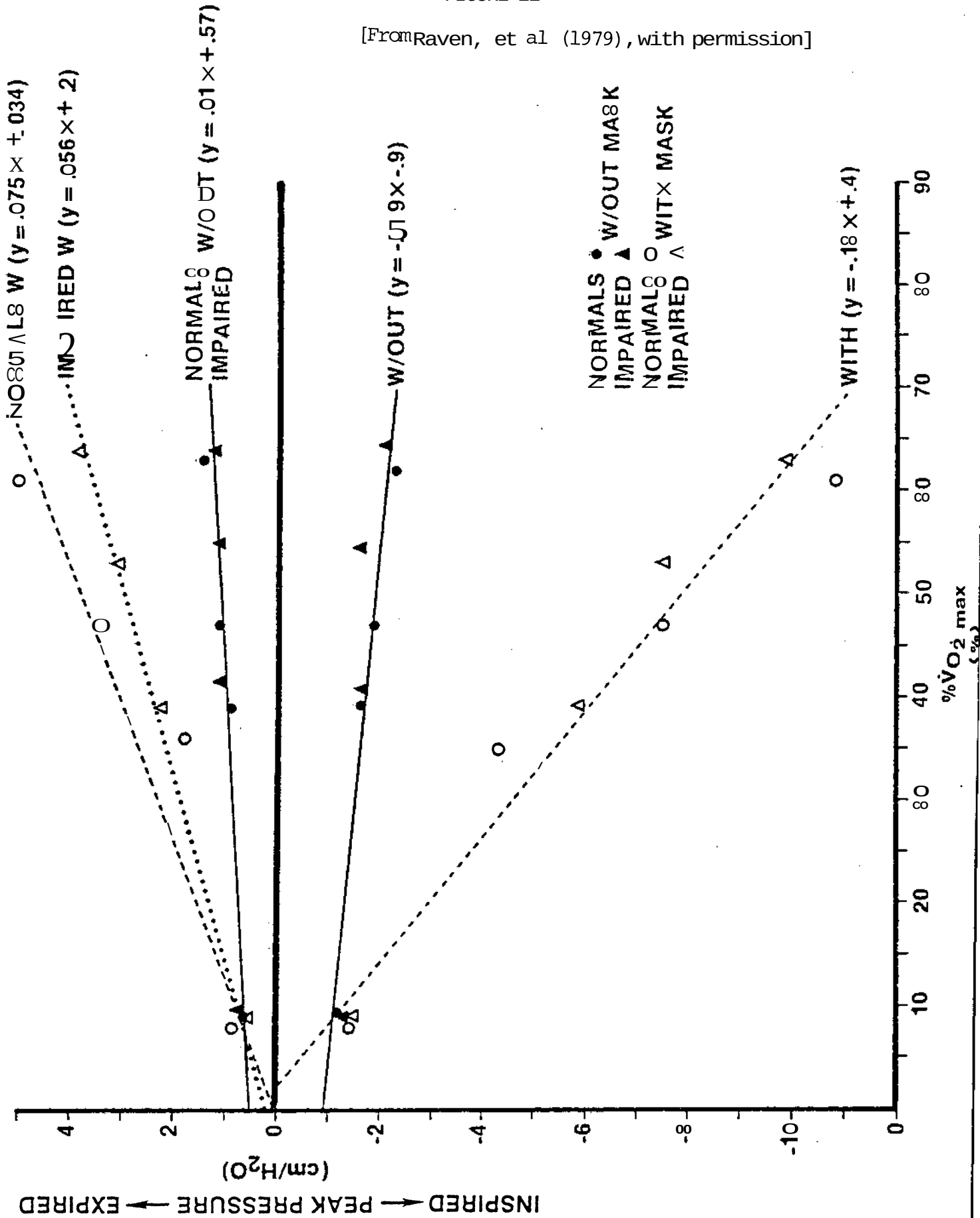


FIGURE 12

[From Raven, et al (1979), with permission]

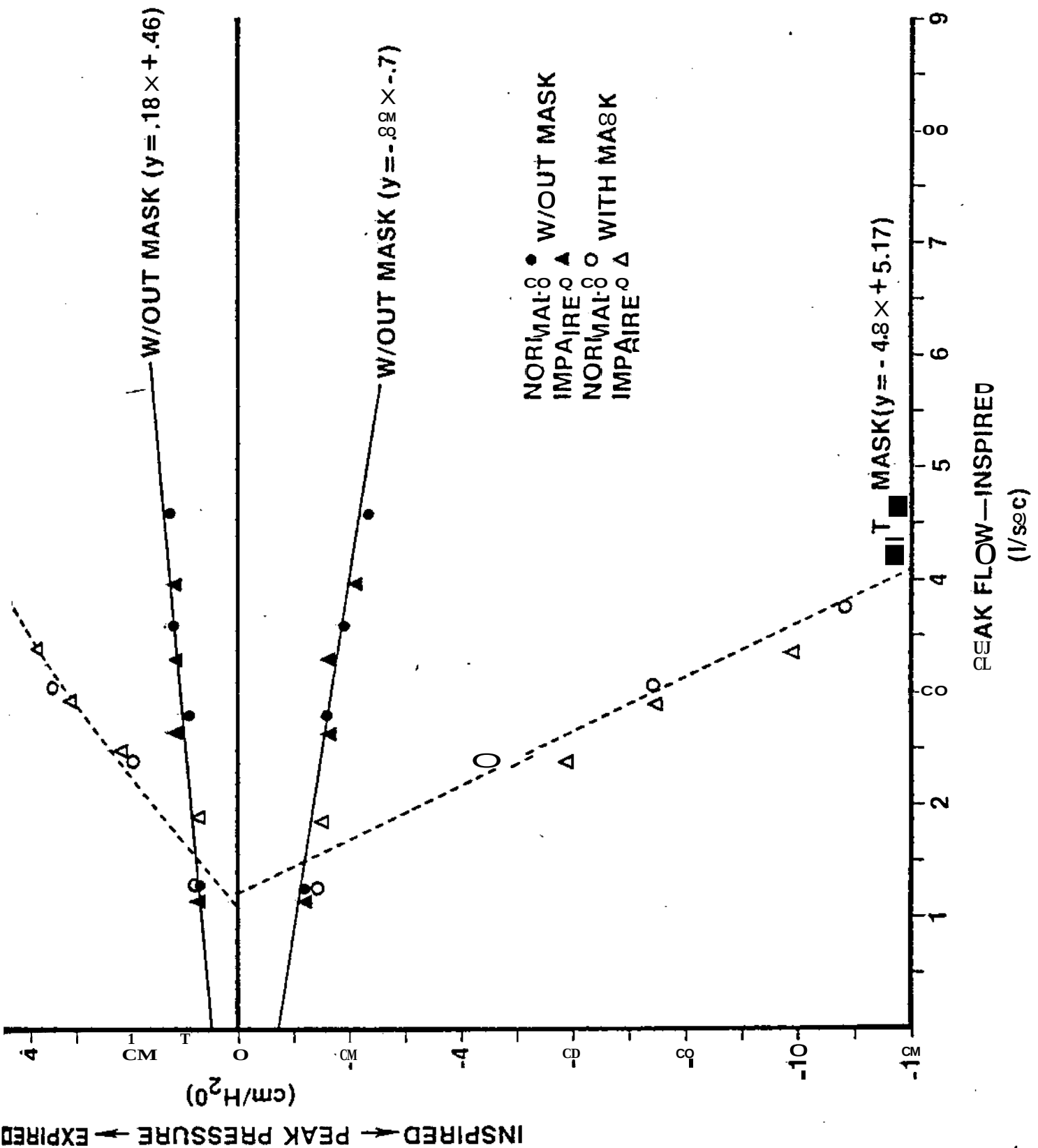


FIGURE 13

[From Raven, et al (1979), with permission]

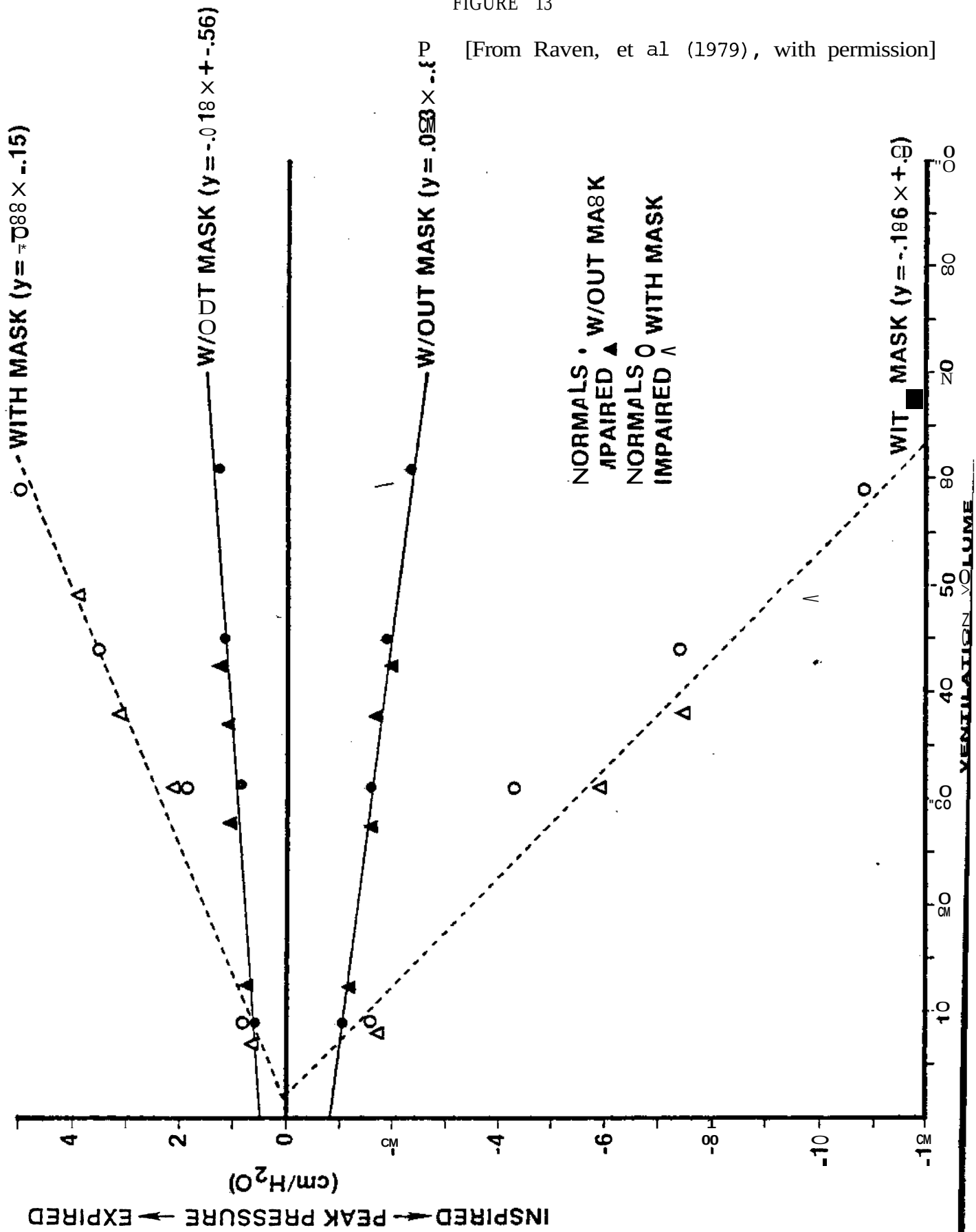


FIGURE 14

[From Raven, et al (1979), with permission]

