Prowse Prize

THE OXYGEN COST OF BREATHING IN OBESITY

Barry J. Kaufman, M.D.[1]

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[1] Medical Research Fellow, National Research Council, Canada.

Introduction

Recently, numerous reports have noted the association between marked obesity and hypoxia, hypercapnia, polycythaemia and right heart failure, in the absence of apparent intrinsic pulmonary disease. Weight loss has been followed by alleviation of the derangements in some cases (1,2,3,4), and this syndrome has been called the "Pickwickian Syndrome" by Burwell et al (5).

Fairly general agreement exists that the basic physiological defect in these cases is alveolar hypoventilation which leads to hypoxia and hypercapnia followed by polycythaemia and eventual cor pulmonale. It has been suggested that the alveolar hypoventilation in obesity is due to an increased work of breathing (2,6,7), although evidence to support this has not been advanced.

The purpose of this paper is to report measurements of the oxygen cost of breathing in obesity and to attempt to correlate these measurements with the occurrence of hypoventilation.

Methods

Twenty-five obese individuals, whose physical characteristics are shown in Table I, were studied. The mean age was 46 years, the mean weight

was 113 kg., with mean heights and body surface areas of 168 cm. and 2.18 m^2 respectively. Nine normal subjects, five males and four females, served as controls being studied in the same way as the obese subjects. Data from normals will be more fully reported elsewhere (8).

Any patient giving a history of lung disease such as chronic cough and sputum, cardiac disease or neuromuscular disease was excluded from the series.

Ventilatory function was assessed in twenty subjects while the oxygen cost of breathing was measured in all.

Ventilatory Studies

Vital capacities, timed vital capacities and maximum breathing capacities were measured, using a Collins Respirometer with the valves and CO_2 absorber removed and incorporating a high-speed rotating drum. The maximum of at least two to three trials was recorded. Predicted values were determined from the data of Baldwin et al (9).

The intrapulmonary distribution of inspired gas was checked by the measurement of the concentration of nitrogen in alveolar gas after seven minutes of oxygen breathing and by determining the washout of nitrogen from the lungs while breathing oxygen, using an instantaneously-recording nitrogen

meter (10).

Oxygen Cost of Breathing

The oxygen cost of the respiratory mechanism was determined using the method of Campbell et al (11) as modified by Cherniack (8). The oxygen consumption at rest and at increased ventilation was measured using a closed-circuit spirometer in which a carbon dioxide absorber was incorporated. A cam on the pulley of the spirometer activated a micro-switch which in turn controlled a solenoid valve, through which oxygen was delivered from a second spirometer. It was thus possible to keep a level non-sloping baseline on the records of ventilation while the second spirometer recorded the oxygen consumed.

Ventilation was increased by the interposition of dead space tubing of thick-walled rubber, 2.5 cm. internal diameter, between the subject and the spirometer circuit. Tubes of different lengths were chosen in random order and the individuals were allowed to increase their ventilation spontaneously with no control of rate or depth of breathing.

Before studies were begun the subjects, who had fasted for at least nine hours, rested in a comfortable chair for one hour in the case of out-patients and for twenty minutes in the case of hospitalized patients.

Resting oxygen consumption and ventilation were recorded at the beginning and the end of each study. Before each measurement, whether resting or at increased ventilation, the subjects breathed oxygen from a meteorological balloon for ten minutes and then into and out of the oxygen-filled spirometer circuit for five minutes in order to allow the attainment of a steady state. Recordings were taken over a five- to ten-minute period. Oxygen consumption was corrected to S.T.P.D. and ventilation to B.T.P.S. Ten to twenty minutes' rest were allowed between each measurement.

Figure 1 is an example of the type of oxygen consumption-ventilation curve obtained. It shows the curve in one obese subject, 17, on whom measurements were obtained at a year's interval, during which period his weight did not change. Also shown is the curve in a normal non-obese man. It is seen that the curve in the obese subject has an initial linear portion and at higher ventilations tends to become increasingly curved upwards.

In each subject oxygen consumption at the resting ventilation and at least two increased ventilations were obtained, one of these ventilations being around 20 L/min. From the individual curves the oxygen consumption at 20 L/min. was determined and from this was subtracted the oxygen consumption at the resting ventilation, and this value was divided by the differ-

ence in ventilations. The resultant figure has been used as the oxygen cost of increased ventilation.

In 17 of these subjects simultaneous samples of arterial blood and expired air were obtained after the individuals had been in the semi-recumbent position for 20-30 minutes. Arterial carbon dioxide and oxygen tensions were determined by the technique of Brinkman et al (12). Expired air was collected over a three-minute period in a Tissot spirometer and analyzed with the Micro-Scholander apparatus (13). From this data physiological dead space, calculated by the Bohr method, and tidal volume were obtained.

Results

1. Ventilatory Function

The results of the ventilatory function studies are listed in Table I. Timed vital capacities and maximum mid-expiratory flow rates performed before and after bronchodilator revealed no evidence of bronchiolar obstruction. As can be seen, the index of intrapulmonary mixing was normal in all subjects. The washout of N_2 from the lungs was within normal range in all the obese individuals except for subjects 18, 20, 23 and 25, in whom it was somewhat slower.

2. Oxygen Cost of Breathing

The oxygen cost of increased ventilation for each subject is given in Table I. Nine normal subjects had values ranging from 0.5 to 2.0 ml. O_2 per liter. These values agree with those obtained by Cournand et al (14) and Liljestrand (15). Thus, 18 of the 25 obese subjects had values above the normal range. This can also be seen in Figure 2 which, in addition, shows that in most obese subjects there was a disproportionate increase in the oxygen cost of breathing with further increases in ventilation.

No relationship between oxygen cost of increased ventilation and weight, height, body surface area or percent of excess weight could be found in the obese subjects.

The relationship between the oxygen cost of increased ventilation and the resting arterial oxygen and carbon dioxide tensions in the 17 obese subjects who had arterial blood estimations is shown in Figures 3 and 4. It can be seen that there was a tendency for the highest costs of increased ventilation to be associated with the lowest arterial oxygen tensions while the highest values were associated with the highest arterial carbon dioxide tensions.

In Figure 5 the tidal volumes and physiological dead spaces of the

subjects are presented. Except for one patient with hypoxia, all physiological dead spaces were within normal limits as defined by Comroe et al (16). It will be noted that there was a tendency for the tidal volumes in those patients with hypoxia to be less than those with normal gas tensions, and this more pronounced in those subjects with both hypoxia and hypercapnia.

In two of the patients with the highest carbon dioxide tensions the physical properties of the lungs were studied. The lung compliance of subject 24 was .220 while subject 25 had a compliance of .300. The viscous resistance, as expressed by the pressure required to cause a flow of 30 L/min. was 0.9 in subject 24 and 1.2 in subject 25 on expiration, with similar values for inspiration. These measurements are within normal range (17).

Discussion

The data presented indicate that the oxygen cost of breathing is increased in obese individuals. If we make the assumption that the oxygen cost of breathing obtained from measurements of small increments in ventilation can be extrapolated back to the resting level, then obese individuals have increased costs of breathing even at rest.

An increased oxygen cost of breathing could be due to increased muscular work being done on the lungs or on the thorax. The findings of es-

sentially normal distribution of inspired gas, the absence of evidence of bronchiolar obstruction and lack of clinical history of lung disease suggest that there was no intrinsic lung pathology producing an increased work of breathing. In addition, measurement of the physical properties of the lungs in two of the subjects with high costs of breathing and hypercapnia, 24 and 25, revealed normal lung compliance and non-elastic resistance. Hence it is postulated that the increased cost of breathing is due to increased mechanical work necessary to move thoracic cage, diaphragm and abdominal wall and contents -- presumably due to obesity.

The data also indicates that in the obese individual, who may already have an increased cost of breathing at rest, further small increments in ventilation could result in a disproportionate increase in metabolic work of breathing and carbon dioxide production. This would probably be even more exaggerated if an obese person developed a bronchitis or other lung disease. Conversely, in individuals with chronic lung disease and increased work of breathing the development of obesity would lead to further increase in the oxygen cost of breathing and possible alveolar hypoventilation. The therapeutic implications of obesity in chronic lung disease, thus, become apparent.

It is of interest that there appears to be a relationship between the oxygen cost of breathing, alveolar ventilation and arterial carbon dioxide tension in the obese subjects. Thus, it appears from our data that those individuals who have the highest oxygen cost of breathing also have the lowest tidal volumes and the highest arterial carbon dioxide tensions. This is in accordance with the hypothesis advanced by Otis (18) and Riley (19) to explain the occurrence of hypoventilation with an increased work of breathing.

Summary and Conclusions

1. The oxygen cost of breathing is increased in obese subjects.

2. A relationship between the metabolic cost of breathing and the arterial blood tensions of carbon dioxide and oxygen has been indicated.

Acknowledgements

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References

1. Weil, M. H. J.A.M.A. 159: 1592, 1955.

2. Lillington, G. A., M. W. Anderson and R. O. Brandenburg. Dis. of Chest 32: 1, 1957.

3. Estes, E. H., Jr., H. O. Sieker, H. D. McIntosh and G. A. Kelser. Circulation 16: 179, 1957.

4. Burwell, C. S. New England J. Med. 254: 944, 1956.

5. Burwell, C. S., E. D. Robin, R. D. Whaley and A. G. Bickelmann. Am. J. Med. 21: 811, 1956.

6. Auchincloss, J. H., Jr., E. Cook and A. D. Renzetti. J. Clin. Invest. 34: 1537, 1955.

7. Carroll, D. Am. J. Med. 21: 819, 1956.

8. Cherniack, R. M. Unpublished data.

9. Baldwin, E. de F., A. Cournand and D. W. Richards, Jr. Medicine 27: 243, 1948.

10. Cournand, A., E. de F. Baldwin, R. C. Darling and D. W. Richards, Jr. J. Clin. Invest. 20: 681, 1941.

11. Campbell, E. J. M., E. K. Westlake and R. M. Cherniack. J. Appl. Physiol. 11: 303, 1957.

12. Brinkman, G. L., C. J. Johns, H. Donoso, R. L. Riley and B. McNamara. J. Appl. Physiol. 7: 340, 1954.

13. Scholander, P. F. J. Biol. Chem. 167: 235, 1947.

14. Cournand, A., D. W. Richards, Jr., R. A. Bader, M. E. Bader and A. P. Fishman. Tr. A. Am. Physicians 67: 162, 1954.

15. Liljestrand, G. Skandinav. Arch. f. Physiol. 35: 199, 1918.

16. Comroe, J. H., Jr., R. E. Forster, II, A. B. Dubois, W. A. Briscoe and E. Carlsen. The Lung: Clinical Physiology and Pulmonary Function Tests. Chicago: The Year Book Publishers, 1955, p. 183.

17. Cherniack, R. M., T. E. Cuddy and J. B. Armstrong. Circulation 15: 859, 1957.

18. Otis, A. B. Physiol. Rev. 34: 449, 1954.

19. Riley, R. L. Ann. Int. Med. 41: 172, 1954.

Table I

CLINICAL DATA OF OBESE SUBJECTS

Subject	Sex	Age	Ht. in cm.	Wt. in Kgm.	Body Surface Area m^2	Vital Capacity		Maximum Breathing Capacity		I.I.P.M.[1] $\%N_2$	O.C.I.V.[2] ml. O_2/L.
						cc.	% Pred.	L/min.	% Pred.		
1	F	46	163	100	2.04	-	-	-	-	-	5.76
2	F	46	162	111	2.13	-	-	-	-	-	4.45
3	F	53	165	90	1.97	-	-	-	-	-	2.5
4	F	31	174	114	2.26	-	-	-	-	-	2.57
5	F	47	160	97	1.98	3420	129	93	113	0.4	9.73
6	F	53	163	99	2.03	2355	86	74	75	0.4	1.75
7	F	35	162	101	2.02	3810	131	154	174	0.4	0.82
8	M	37	180	131	2.47	4500	107	124	103	0.4	5.24
9	F	38	151	115	2.07	2095	82	69	88	0.4	1.75
10	F	69	155	101	1.94	1875	88	56	84	0.4	1.75
11	M	56	166	86	1.95	3920	114	127	140	0.4	1.86
12	F	51	170	127	2.33	3260	111	79	89	0.4	3.47
13	F	47	156	103	2.00	2650	104	71	92	0.4	2.57
14	M	43	175	123	2.44	4650	119	166	151	-	1.80
15	F	28	178	124	2.40	3670	109	110	108	0.4	2.77
16	M	36	185	135	2.55	6030	136	129	98	0.4	2.70
17	M	64	174	114	2.26	3380	98	82	90	0.4	2.01
18	M	61	182	111	2.36	4120	112	122	123	2.3	3.93
19	F	52	155	122	2.14	2930	122	101	120	0.4	2.30
20	F	44	163	98	2.02	2900	104	72	88	0.4	1.6
21	M	40	175	120	2.31	3820	93	104	90	-	2.76
22	M	45	173	121	2.31	-	-	-	-	-	3.85
23	F	49	155	88	1.87	2260	70	73	83	0.4	4.77
24	M	33	173	167	2.65	2970	75	65	55	0.7	6.46
25	F	57	153	125	2.12	1280	56	52	59	0.4	7.04

1 Index of intrapulmonary mixing.
2 Oxygen cost of increased ventilation.

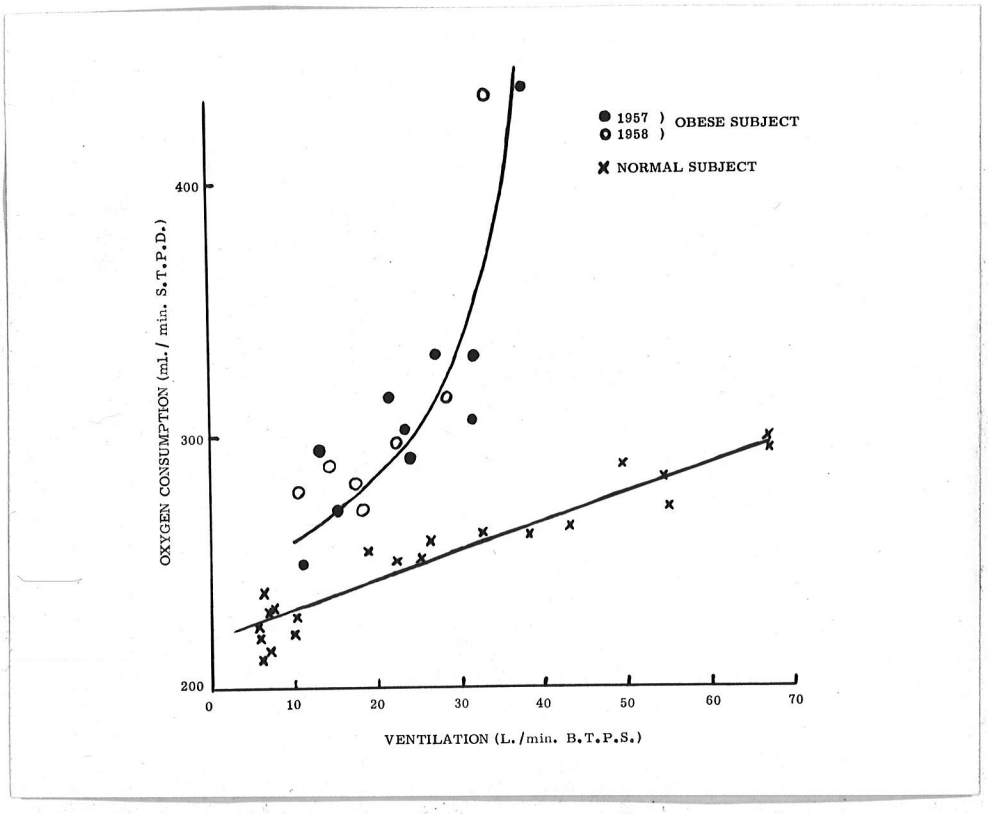

Figure 1. Oxygen consumption at different levels of ventilation in one obese and one normal subject. The obese subject was studied on two occasions at a year's interval.

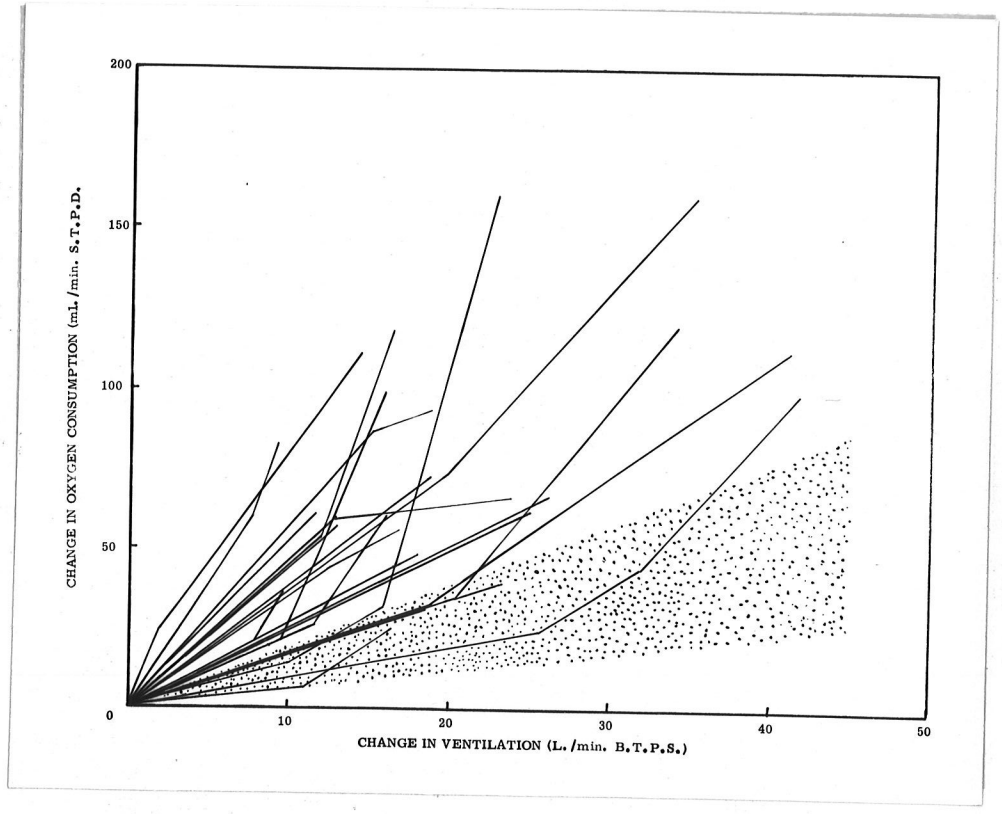

Figure 2. Increments in oxygen consumption associated with change in ventilation in 25 obese subjects. The stippled area indicates the range of normal values.

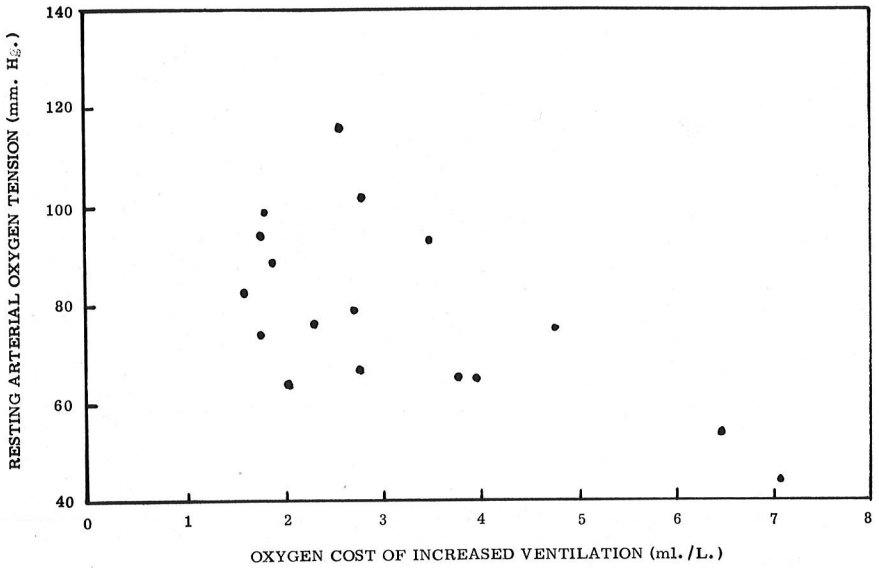

Figure 3. The relationship between the oxygen cost of increased ventilation and the resting arterial oxygen tension in 17 obese subjects.

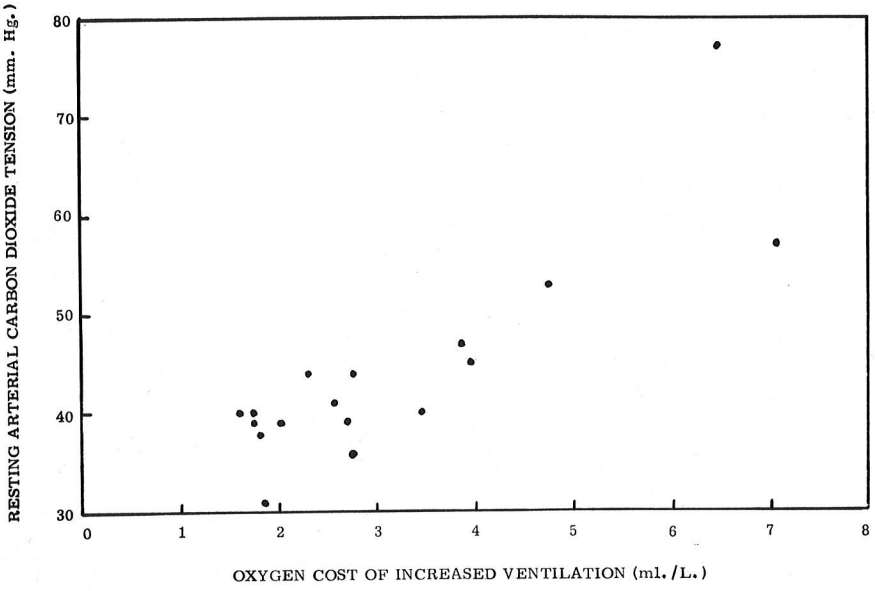

Figure 4. The relationship between the oxygen cost of increased ventilation and the resting arterial carbon dioxide tension in 17 obese subjects.

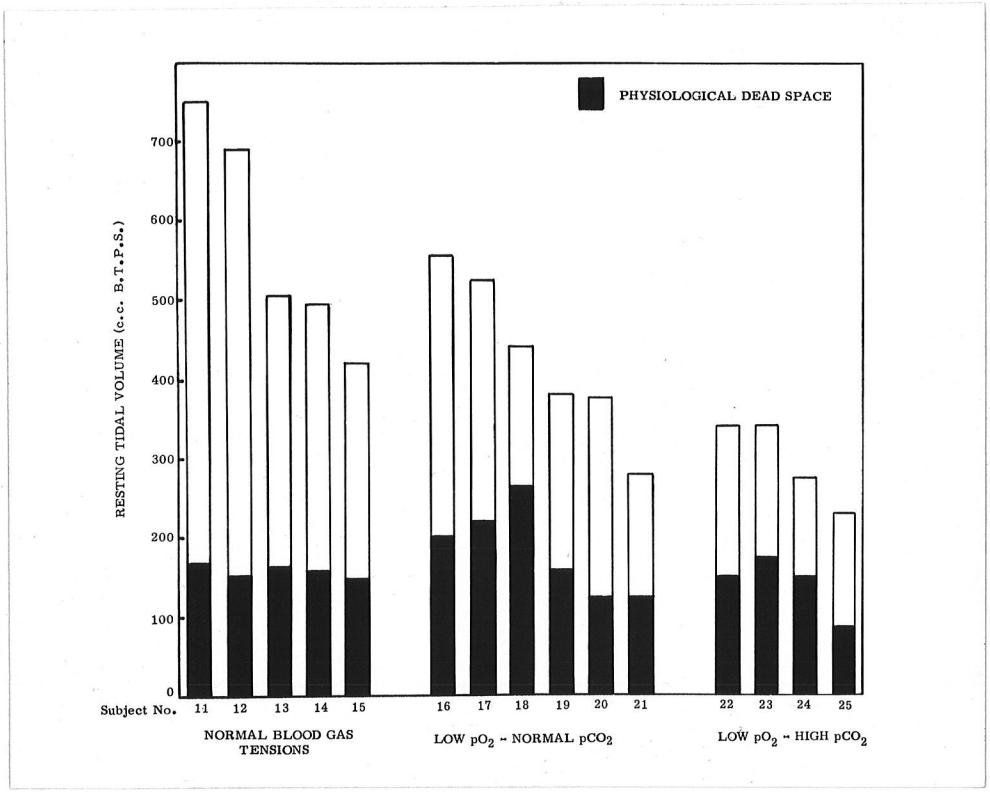

Figure 5. Tidal volume and physiological dead space in 15 obese subjects. The subjects are subdivided into three groups according to normal pO_2 being greater than 90 mm. Hg and normal pCO_2 being less than 45 mm. Hg.