PULMONARY FUNCTION IN OBESE PERSONS [1, 2]

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The purpose of this paper is to report a study of lung function in extremely obese persons. In 1936, Kerr and Lagen (2) called attention to the fact that some obese persons develop dyspnea, cyanosis, polycythemia, and cardiac failure. They thought that these signs and symptoms developed because of mechanical interference with ventilation, especially movement of the diaphragm. Sieker, Estes, Kelser and McIntosh (3) reported studies in four obese patients and postulated a cardiorespiratory syndrome peculiar to obese persons and characterized by somnolence, Cheyne-Stokes respirations, intermittent cyanosis, and polycythemia. At the same time that Sieker and his associates were working on this problem, Auchincloss, Cook and Renzetti (4) and Weil and Prasad (5) observed a peculiar type of polycythemia associated with obesity. Most of the investigators previously mentioned have reported additional patients characterized by obesity, hypoxemia, polycythemia and alveolar hypoventilation (6–9), and they have been joined by others (10–18). Burwell, Robin, Whaley and Bickelmann (12) have given the picturesque name "Pickwickian Syndrome" to this combination of signs and symptoms.

There is agreement that the cardinal characteristics of these patients are obesity, alveolar hypoventilation, and polycythemia. The basic physiologic defect is alveolar hypoventilation. This leads to arterial hypoxemia and hypercapnia. Arterial hypoxemia provokes polycythemia. Therefore, the polycythemia of these patients is no longer of a mysterious type but is secondary to hypoxemia.

No agreement exists on what initiates alveolar hypoventilation. Several theories have been advanced. One is that the amount of work necessary to keep the arterial carbon dioxide pressure (P_{CO_2}) at a normal level is too great. A compromise is made which allows the P_{CO_2} to rise rather than to employ the continuous excess effort necessary to keep the P_{CO_2} normal (13, 15). Another is that in some persons there is a critical degree of obesity at which ventilatory insufficiency appears (12). Still another is that massive obesity restricts pulmonary ventilation and leads to alveolar hypoventilation (5, 8, 9).

We decided to study a number of obese persons to determine the frequency of various abnormalities and to investigate the mechanism of alveolar hypoventilation. We are reporting studies on 28 obese persons with restudy of 16 following weight loss.

METHODS

The patients were selected from the wards and clinics of the University Hospitals and Veterans Administration Hospital, Iowa City. We required that all patients be at least 100 pounds over ideal weight based on height and size of subject's frame (19). Each patient had a complete history, physical examination, roentgenogram of the chest, and the indicated laboratory tests. Pulmonary function tests were done in the morning after the patient had eaten breakfast. The vital capacity, inspiratory capacity and expiratory reserve volume were measured separately using a Benedict Roth spirometer. The maximum of at least three trials was recorded. The functional residual capacity of the lungs was measured in duplicate by the nitrogen washout method of Darling, Cournand and Richards (20). Volumes were corrected to body temperature, ambient pressure, and saturated with water vapor, hereafter called B. T. P. S. Predicted normal values for lung volumes were calculated on the basis of the patient's height (21) rather than the body surface area. Rate, depth and minute volume of ventilation were measured while the patient was breathing air, 99.6 per cent oxygen, and 7.5 per cent carbon dioxide in air. Expired volumes were collected in a Douglas bag or a Tissot spirometer simultaneously with the drawing of samples of arterial blood. Volumes were corrected to B. T. P. S. Physiologic dead space was calculated using Bohr's equation. Measured and derived values used

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in this calculation are the volume of expired air over a three minute period, the per cent CO_2 in the expired air, and the arterial P_{CO_2}. Calculation is based on the formula given by Comroe, Forster, DuBois, Briscoe and Carlsen (22). Uniformity of intrapulmonary distribution of inspired gas was checked by the single breath nitrogen test of Comroe and Fowler (23) and the measurement of the percentage of nitrogen at the end of seven minutes breathing of oxygen as described by Cournand, Baldwin, Darling and Richards (24). To measure maximal breathing capacity (MBC), the subject breathed for 15 seconds through a mouthpiece, low resistance valve, and wide tubing into a Tissot spirometer. Predicted normal values for the MBC were based on age (25). The highest value obtained with three trials was calculated in liters per minute. Maximal inspiratory (or expiratory) flow rate was measured between 200 and 1,200 ml. of the inspiration (or expiration) according to the method of Danzig and Comroe (26). Diffusion was studied using the single breath carbon monoxide method of Ogilvie, Forster, Blakemore and Morton (27).

Arterial blood was obtained from the brachial artery while the semirecumbent subject breathed air, and again after he had breathed 99.6 per cent oxygen for at least 10 minutes. The samples were analyzed for total oxygen content, oxygen capacity, and whole blood carbon dioxide content by the manometric technique of Van Slyke and Neill (28). Blood was rotated with air in a tonometer at room temperature for 20 minutes before measuring oxygen capacity. Appropriate corrections were made for physically dissolved oxygen and for differences in total hemoglobin in the content and capacity samples. Direct measurement of dissolved oxygen was not made, but an approximate calculation was made on the samples collected during the inhalation of oxygen by subtracting the oxygen capacity from the total oxygen content of such blood. Arterial blood pH was measured in a closed Cambridge glass electrode at either 37° C. or, if done at room temperature, the pH value was corrected to 37° C. using the factor of Rosenthal (29). Plasma carbon dioxide content and P_{CO_2} were determined from pH, hematocrit, oxygen saturation and whole blood carbon dioxide content using the nomogram of Singer and Hastings (30).

Some of our patients had edema of the legs thought to be caused by congestive heart failure. When these patients decreased their activity after hospitalization and had appropriate therapy for heart failure, they promptly lost from 5 to 30 pounds which probably represented water loss. Our "initial" studies were done after this rapid loss of water in most cases. When the initial studies were completed, we placed the patients on an 800 calorie diet and later restudied those who lost a significant amount of weight. Digitalis, salt restriction, and diuretics were used only when indicated. Weight reduction was best accomplished by continuous hospitalization of these patients. When possible, patients were hospitalized until they had lost 50 to 100 pounds. In some cases this took six months.

RESULTS

The patients are divided into two groups, depending on arterial oxygen saturation at rest. Arterial hypoxemia is considered to be present when arterial saturation is below 93.2 per cent (31). Thirteen patients had normal saturation and are considered in Group I. Fifteen patients had arterial hypoxemia and constitute Group II.

A. Patients with normal arterial oxygen saturation

This group consists of 13 patients whose weight averaged 303 pounds at the time of initial study. There were 6 men and 7 women. The age range was 19 to 67 years. The results of pulmonary function studies in these patients are listed in Tables I and II. Lung volumes were normal. Mean inspiratory capacity was 92 per cent of predicted normal; mean expiratory reserve volume was 75 per cent of predicted normal; mean vital capacity was 89 per cent of predicted normal; mean residual volume was 136 per cent of predicted normal; and mean total lung capacity was 100 per cent of predicted normal. Mean minute volume of ventilation was 9.9 liters and mean minute volume of alveolar ventilation was 6.2 liters. The physiologic dead space averaged 218 ml. Distribution of inspired air was slightly uneven as measured by the single breath nitrogen test, but normal as measured by the less sensitive test based on the per cent of nitrogen at the end of seven minutes of oxygen breathing. Mechanical tests showed mild abnormalities. The maximal breathing capacity was slightly below normal, the mean value being 87 per cent of predicted normal. The maximal expiratory flow rate averaged 212 liters per minute while the maximal inspiratory flow rate averaged 156 liters per minute. Diffusion studies done in nine patients were normal.

Six patients were restudied after weight loss. These six patients averaged 304 pounds at the time of original study and 252 pounds at the time of the last study. Weight loss changed the lung volumes only slightly with the exception of the expiratory reserve volume which increased from a mean value of 63 per cent of predicted normal to a mean value of 102 per cent of predicted normal. Minute volume of ventilation was essentially unchanged: 10.0 liters before weight loss and 10.2 liters after weight loss. Mean alveolar ventilation

TABLE I

Physical characteristics and lung volumes in obese patients with normal arterial oxygen saturation

Patient	Age	Sex	Height (*inches*)	Weight (*pounds*)	Date of study	Lung volumes: Inspiratory capacity *ml.*	Inspiratory capacity %*	Expiratory reserve volume *ml.*	Expiratory reserve volume %*	Vital capacity *ml.*	Vital capacity %*	Residual volume *ml.*	Residual volume %*	Total lung capacity *ml.*	Total lung capacity %*	Residual volume/ total lung capacity ratio ×100
D. C.	19	F	71	321	15 Nov. 56	3,100	80	1,070	82	3,790	84	1,630	145	5,420	96	30
				274†	22 Jan. 57	2,790	76	1,470	113	4,370	103	1,510	134	5,770	103	26
R. W.	21	M	68	250	11 Dec. 56	3,500	108	1,590	147	5,110	119	1,750	162	6,860	127	26
D. V.	35	F	70	313	21 May 57	3,400	128	750	84	4,040	114	1,600	147	5,640	124	28
F. S.	38	M	72	314	6 Dec. 56	2,960	86	810	70	3,870	85	1,700	121	5,570	93	30
				270†	8 Feb. 57	2,580	75	1,400	122	4,030	88	2,350	206	6,380	105	37
F. P.	38	M	66	274	18 June 57	4,050	128	700	66	4,750	112	2,160	204	6,910	131	31
W. B.	39	M	70	382	26 July 56	2,960	89	570	52	3,440	78	1,170	123	5,110	89	33
M. F.	41	F	64	348	11 June 57	2,240	91	370	46	2,890	88	2,100	210	4,990	117	45
E. T.	47	F	69	305	23 May 57	2,480	94	1,370	157	3,820	109	2,130	199	5,950	131	36
F. H.	48	F	62	243	6 Dec. 56	1,880	63	480	51	2,790	71	1,040	86	3,830	74	27
N. S.	54	F	65	319	31 July 56	1,850	75	340	40	2,290	69	1,890	78	4,180	71	46
				260†	30 Apr. 57	1,920	78	940	114	2,470	75	2,260	93	4,730	83	48
J. R.	55	F	66	345	3 Sept. 57	2,200	88	480	57	2,610	78	1,290	53	3,900	68	33
				306†	5 Nov. 57	2,460	98	700	83	2,890	87	1,080	44	3,970	69	27
R. G.	61	M	68	254	3 Dec. 56	2,730	84	600	55	3,190	73	2,430	100	5,620	83	43
				175†	16 May 57	2,740	84	890	82	3,600	83	1,980	81	5,580	83	35
R. M.	67	M	68	272	9 Aug. 56	2,680	83	770	72	3,390	79					
				229†	21 Mar. 57	2,160	67	1,080	100	3,700	86	3,570	147	7,270	108	52
Mean, (initial) 13 patients				303			92		75		89		136		100	
Mean, (before weight loss) 6 patients				304			83		63		78		99‡		82‡	
Mean, (after weight loss) 6 patients				252			80		102		87		112‡		89‡	

* Per cent of predicted value based on height (21).
† Indicates weight after weight loss at the time of repeat study.
‡ Mean value represents only five patients.

TABLE II

Studies of ventilation, respiratory mechanics, and diffusion in obese patients with normal arterial oxygen saturation

Patient	Ventilation					Mechanical tests				
	Minute volume		Physiologic dead space	Alveolar gas distribution		Maximal breathing capacity		Maximal expiratory flow rate	Maximal inspiratory flow rate	Diffusion
	Total *L.*	Alveolar *L.*	*ml. %**	7 min. washout (% N_2)†	Single breath N_2 test (% N_2)‡	*L./min.*	%§	*L./min.*	*L./min.*	*ml. CO/mm. Hg/min.*
D. C.	5.9			0	1.7	100	79	171	171	
	4.5	2.4	122 (33)	1.7	2.0	117	93	158	158	31
R. W.	8.3	5.4	249 (42)	0	1.5	115	91	250	90	
D. V.	13.5	9.0	265 (33)	2.0	1.5	115	129	250	188	32
F. S.	7.9	6.2	145 (29)	0	2.3	68	62	214	300	
	14.2	9.2	469 (43)	1.0	2.3	84	77	222	300	28
F. P.	10.5	6.7	238 (36)	1.8	1.0	114	105	300	171	37
W. B.	11.0	7.2	204 (41)	1.4	0	89	81	250	151	
M. F.	10.7	6.0	170 (36)	1.5	1.0	63	71	167	146	
E. T.	10.6	7.3	254 (31)	2.2	1.7	87	98	176	167	40
F. H.	3.4	2.1	105 (44)	0	2.0	69	77	207	81	
N. S.	13.4	7.3	282 (46)	4.1	2.0	63	85	103	101	
	10.5	8.2	135 (22)	2.0	2.0	70	95	92	92	20
J. R.	9.6	5.3	250 (51)	0.2	2.1	70	96	250	176	27
	9.0	4.1	258 (55)	0.7		86	118	260	174	24
R. G.	10.4	5.6	199 (54)	0	7.5	74	81	200	98	
	14.3	6.8	270 (53)	5.0	2.7	108	119	300	230	14
R. M.	12.6	6.9	253 (45)	0.6	1.9	64	71	214	179	
	8.7	5.5	188 (47)	0.3	2.0	64	71	222	188	43
Mean, (initial) 13 patients	9.9	6.2	218 (41)	1.0	2.0		87	212	156	
Mean, (before weight loss) 6 patients	10.0	6.3‖	226 (45)‖	0.8	3.1‖		79	192	171	
Mean, (after weight loss) 6 patients	10.2	6.8‖	264 (44)‖	1.8	2.2‖		96	209	190	

* Per cent of tidal volume.
† Normal values for seven minute nitrogen washout are less than 2.5 per cent N_2.
‡ Normal values for single breath nitrogen test are less than 1.5 per cent N_2.
§ Per cent of predicted value based on age (25).
‖ Mean value represents only five patients.

increased from 6.3 liters to 6.8 liters in five patients. Alveolar gas distribution was practically unchanged (the per cent nitrogen after seven minutes of oxygen breathing averaged 0.8 per cent before weight loss and 1.8 per cent after; the single breath nitrogen test averaged 3.1 per cent before weight loss and 2.2 per cent after weight loss). Weight loss increased the mean maximal breathing capacity from 79 per cent of predicted normal to 96 per cent of predicted normal. Maximal flow rates were also increased; the mean expiratory rate increased from 192 liters per minute to 209 liters per minute and the mean inspiratory rate increased from 171 liters per minute to 190 liters per minute.

The results of arterial blood studies in these patients are listed in Table III. Mean arterial oxygen saturation at rest was 96.0 per cent, mean P_{CO_2} was 39 mm. Hg, mean pH was 7.40, and the mean hematocrit was 46 per cent. Weight loss in six patients made no change except that the hematocrit decreased from a mean value of 46 per cent to 41 per cent.

B. Patients with arterial hypoxemia

This group is composed of 15 patients whose mean weight was 315 pounds and who had arterial hypoxemia. There were 12 women and 3 men. Their ages ranged from 39 to 67 years. Ten of the 15 patients had clinical or laboratory evidence of lung disease. Two women had bronchial asthma; two men had pulmonary emphysema; one man had multiple pulmonary infarcts; two women had pulmonary edema secondary to heart disease; three women had no clinical evidence of lung disease but laboratory evidence suggested it. Two women had myxedema, and three women had hypoxemia without evidence of lung disease. The initials, clinical diagnoses, physical characteristics, and results of pulmonary function tests in these patients are listed in Tables IV and V. The results of arterial blood studies are listed in Table VI. Ten patients were restudied after weight reduction. The average initial weight in these 10 patients was 323 pounds and at the time of last study it was 251 pounds, a mean loss of 72 pounds.

TABLE III

Arterial blood studies in obese patients with normal arterial oxygen saturation

Patient	Date of study	O_2 content (rest) *vol. %*	O_2 capacity *vol. %*	O_2 saturation (Rest) %	O_2 saturation 100% O_2* %	P_{CO_2} (rest) *mm. Hg*	pH (rest)	Hematocrit %
D. C.	15 Nov. 56	15.30	15.43	99.2	100 + 2.27	34	7.44	39
	22 Jan. 57	13.69	14.25	96.1	100 + 1.91	39	7.39	34
R. W.	11 Dec. 56	18.14	18.82	96.4	100 + 2.11	33	7.46	53
D. V.	21 May 57	15.95	16.47	96.8	100 + 2.03	42	7.35	41
F. S.	6 Dec. 56	19.70	20.89	94.3	100 + 1.35	36	7.46	51
	8 Feb. 57	17.99	17.66	100 + 0.33	100 + 2.70	35	7.41	45
F. P.	18 June 57	19.56	20.52	95.3	100 + 0.87	38	7.39	48
W. B.	26 July 56	18.66	19.07	97.9	100 + 2.56	42	7.39	52
M. F.	11 June 57	18.71	19.39	96.5	100 + 1.56	40	7.34	47
E. T.	23 May 57	15.51	16.18	95.9	100 + 1.83	46	7.34	39
F. H.	6 Dec. 56	17.71	18.92	93.6	100 + 1.20	38	7.44	56
N. S.	31 July 56	20.61	23.03	93.6		33	7.41	52
	30 Apr. 57	16.93	17.60	96.2	100 + 1.78	31	7.48	43
J. R.	3 Sept. 57	16.82	17.95	93.7	100 + 1.54	46	7.36	42
	5 Nov. 57	17.11	18.41	93.0	100 + 1.73	46	7.35	42
R. G.	3 Dec. 56	18.46	18.71	98.7	100 + 2.34	35	7.41	50
	16 May 57	15.05	16.14	93.3	100 + 1.62	37	7.40	41
R. M.	9 Aug. 56	16.78	17.48	96.0	100 + 2.11	37	7.35	40
	21 Mar. 57	17.00	17.41	97.7	100 + 1.46	37	7.39	43
Mean, (initial) 13 patients				96.0		39	7.40	46
Mean, (before weight loss) 6 patients				95.9		37	7.41	46
Mean, (after weight loss) 6 patients				96.1		38	7.40	41

* Values following + sign refer to ml. O_2 per 100 ml. blood in excess of that required to saturate hemoglobin (*i.e.*, dissolved O_2). Normal value for dissolved O_2 is 2.00 ml.

TABLE IV

Physical characteristics and lung volumes in obese persons with hypoxemia

Patient	Clinical diagnosis	Age	Sex	Height (*inches*)	Weight (*pounds*)	Date of study	Lung volumes										
							Inspiratory capacity		Expiratory reserve volume		Vital capacity		Residual volume		Total lung capacity		Residual volume/ total lung capacity ratio ×100
							ml.	%*	*ml.*	%*	*ml.*	%*	*ml.*	%*	*ml.*	%*	
A. H.	Bronchial asthma	39	F	64	317	14 June 56	1,660	68	390	48	1,950	60	2,390	240	4,340	102	55
					208	21 Feb. 57	1,345	55	510	63	1,880	58	1,650	166	3,530	82	47
I. K.	Bronchial asthma	51	F	61	349	18 Sept. 56	1,030	44	670	87	1,590	51	2,020	83	3,610	65	56
					285	7 Jan. 57	1,110	48	950	122	1,890	61	2,210	91	4,100	74	54
					254	18 Mar. 57	1,300	56	1,130	146	2,170	70	2,610	107	4,780	86	55
					233	28 May 57	1,520	65	1,230	159	2,310	74	2,280	94	4,590	83	50
					200	11 Nov. 57	1,750	75	1,240	160	2,710	87	1,890	78	4,600	83	41
W. C.	Pulmonary emphysema	48	M	69	237	21 Sept. 56	1,725	53	740	66	2,350	54	2,800	210	5,150	90	53
					211	25 Oct. 56	2,120	65	870	77	2,730	62	2,750	206	5,480	95	48
W. B.	Pulmonary emphysema	44	M	71	289	26 Nov. 56	2,650	79	1,190	106	3,190	71	3,270	247	6,460	110	51
					232	23 Apr. 57	2,545	75	1,180	104	3,720	83	3,480	262	7,200	122	48
H. B.	Pulmonary infarcts	45	M	65	268	13 Dec. 56	840	27	130	13	980	24	2,750	218	3,730	69	74
F. W.	Aortic stenosis—pulmonary edema	62	F	62	243	24 June 57	1,670	71	510	65	2,130	67	2,450	101	4,630	83	53
I. F. K.	Arteriosclerotic heart disease—pulmonary edema	52	F	64	322	24 Jan. 57	1,730	71	220	27	1,920	59	1,510	62	3,430	60	44
					250	6 Aug. 57	2,340	99	430	55	2,890	91	2,280	94	5,170	92	44
L. R.	Myxedema	67	F	69	388	14 Mar. 57	1,240	47	410	45	1,550	44	1,390	57	2,940	50	50
					245	21 Nov. 57	1,760	72	1,360	167	2,990	92	940	39	3,930	69	24
K. P.	Myxedema	41	F	65	318	3 Sept. 57	2,340	94	430	52	2,750	83	910	36	3,660	62	25
E. B.	Essential hypertension—pulmonary disease, type not determined	54	F	64	366	8 Dec. 55	1,330	55	440	54	1,750	54	2,060	85	3,810	67	54
					335	19 Apr. 56	1,720	70	530	65	1,730	53	2,010	83	3,740	66	54
A. L.	Pulmonary disease, type not determined	39	F	64	280	16 Feb. 56	1,330	55	270	33	1,460	45	1,850	187	3,310	78	56
					234	6 Mar. 56	1,550	64	590	73	2,090	65	2,910	294	5,000	119	57
O. R.	Pulmonary disease, type not determined	42	F	62	342	15 Aug. 57	1,060	45	740	94	1,456	46	1,980	204	3,430	83	58
					300	15 Oct. 57	2,025	85	810	102	2,610	82	2,010	207	4,620	117	41
H. H.	No lung disease	51	F	65	337	7 Mar. 57	2,075	80	550	66	2,570	78	2,100	86	4,670	82	44
					296	15 July 57	1,995	77	1,270	148	3,280	95	1,850	76	5,130	86	36
A. D.	No lung disease	52	F	65	414	27 Aug. 57	2,870	116	270	33	3,120	95	1,390	57	4,530	77	34
M. F.	No lung disease	62	F	67	255	27 June 57	2,860	87	300	27	3,260	73	2,190	90	5,340	78	41
Mean (initial) 15 patients					315												
Mean (before weight loss) 10 patients					323												
Mean (after weight loss) 10 patients					251												

* Per cent of predicted value based on height (21).

TABLE V

Studies of ventilation, respiratory mechanics, and diffusion in obese patients with hypoxemia

Patient	Ventilation					Mechanical tests				
	Minute volume			Alveolar gas distribution		Maximal breathing capacity		Maximal expiratory flow rate	Maximal inspiratory flow rate	Diffusion
	Total L.	Alveolar L.	Physiologic dead space ml. (%)*	7 min. washout % N_2†	Single breath N_2 test % N_2‡	L./min.	%§	L./min.	L./min.	ml. CO/ mm. Hg/ min.
A. H.	10.2	7.5	161 (32)	3.8	7.0	41	46	55	82	
	6.8	3.5	143 (49)	2.3	1.5	41	46	63	109	
I. K.	9.3	3.6	242 (68)	5.0	1.8	33	45	34	63	
	7.5	3.2	204 (69)	4.0	2.5	42	57	26	146	25
	6.8	3.3	135 (52)	1.5	2.8	37	50	22	162	27
	10.3	5.9	165 (44)	2.2	2.4	42	57	45	182	
	8.4	4.1	183 (44)	1.8	4.5	45	61	53	154	26
W. C.	7.4	4.0	153 (52)	13.2	6.5	32	36	34	111	
	7.6	4.1	209 (55)	2.1	5.3	46	51	97	140	
W. B.	7.6	3.3	272 (65)	0.7	8.5	51	47	72	109	
	11.7	5.9	363 (50)	0.3	3.3	66	61	105	143	18
H. B.	6.4	1.9	150 (78)			25	23	35	83	
F. W.	7.3	4.4	223 (40)	2.5	1.5	75	101	122	167	12
I. F. K.	6.2	5.0	97 (31)	1.9	0.5	48	65	158	75	12
	8.0	5.2	153 (35)	1.8	0.9	84	113	214	188	35
L. R.	8.5	2.6	126 (70)	1.3	1.3	70	95	46	64	10
	10.6	4.4	295 (59)	0.4	0.8	111	135	286	125	15
K. P.	7.7	3.7	200 (42)	1.7	2.2	57	64	207	136	20
E. B.	10.0			1.8	2.5	57	78	47	88	
	9.0	4.1	221 (54)	1.5	6.0	40	54	43	61	
A. L.	7.0	3.2	165 (59)	7.0		27	30	31	86	
	9.0	6.3	121 (30)	6.3	6.3	43	37	59	128	
O. R.	7.3	4.0	145 (40)	1.4	6.5	40	45	110	154	15
	9.0	6.0	300 (33)	0.2	3.9	79	89	188	115	16
H. H.	7.1	3.9	128 (45)	0.2	0.5	45	61	250	188	34
	10.6	5.4	208 (49)	0.4	1.6	97	131	285	220	27
A. D.	10.5	4.8	329 (54)	0.4	1.5	83	113	231	160	20
M. F.	8.0	5.0	214 (48)	1.0	0.9	105	142	250	97	19

* Per cent of vital capacity.
† Normal values for seven minute nitrogen washout are less than 2.5 per cent N_2.
‡ Normal values for single breath nitrogen test are less than 1.5 per cent N_2.
§ Per cent of predicted value based on age (25).

The asthmatic patients had reduced vital capacities, normal or increased residual volumes, uneven distribution of inspired air, diminished maximal breathing capacities and maximal flow rates, arterial hypoxemia, and carbon dioxide retention. Following weight loss of 109 pounds, Patient A. H. was unimproved as measured by pulmonary function studies and arterial blood studies. Patient I. K. lost 149 pounds. She had the following evidence of improvement: Vital capacity changed from 51 per cent to 87 per cent of predicted normal, arterial oxygen saturation increased from 90 per cent to 98 per cent and P_{CO_2} changed from 66 to 44 mm. Hg. This patient has been studied five times over a period of 14 months; the studies demonstrate gradual progressive improvement with continued weight loss (see Tables IV, V, and VI).

The two patients with pulmonary emphysema had reduced vital capacities, increased residual volumes, uneven distribution of inspired air, reduced maximal breathing capacities, and maximal expiratory flow rates, hypoxemia, and carbon dioxide retention. Following weight loss of 26 pounds, Patient W. C. had improvement in arterial oxygen saturation, decrease in carbon diox-

ide retention, more even distribution of inspired air, and improvement in the measurements of mechanical function. This man was probably benefited in part also by phlebotomy, salt restriction, and mercurial diuretics. Patient W. B. lost 57 pounds in weight and improved similarly. His arterial oxygen saturation and P_{CO_2} returned to normal.

The patient with multiple pulmonary infarcts had severe hypoxemia and carbon dioxide retention. On breathing 99.6 per cent oxygen for 10 minutes, his arterial blood did not become fully saturated indicating that a sizable amount of blood was not coming into contact with ventilated alveoli before entering the left heart. His vital capacity was 24 per cent of predicted normal, his alveolar ventilation was 1.9 liters per minute, and the results of tests of mechanical function were abnormally low. The diagnosis of multiple pulmonary infarcts was proved at necropsy.

Patients I. F. K. and F. W. who had pulmonary edema and L. R. and K. P. who had myxedema had similar results. They had reduced vital capacities, normal or reduced residual volumes, and reduced total lung capacties. All four had normal distribution of inspired air but low diffusing capacities. Tests of mechanical function were normal or only slightly impaired. All four patients had arterial hypoxemia and three patients had carbon dioxide retention. Following weight loss of 72 pounds, I. F. K. had normal arterial oxygen saturation, increased vital capacity

TABLE VI

Arterial blood studies in obese patients with hypoxemia

Patient	Date of study	O_2 content (rest) *vol. %*	O_2 capacity *vol. %*	O_2 saturation (Rest) %	O_2 saturation 100% O_2* %	P_{CO_2} (rest) *mm. Hg*	pH (rest)	Hematocrit %
A. H.	14 June 56	14.39	17.96	80.1	100 + 0.45	52	7.36	49
	21 Feb. 57	15.21	21.38	71.1	96.5	59	7.30	62
I. K.	18 Sept. 56	16.65	18.45	90.2	100 + 1.22	66	7.26	58
	7 Jan. 57	18.44	19.98	92.3	100 + 1.56	50	7.37	48
	18 Mar. 57	17.80	18.44	96.5	100 + 1.81	48	7.35	46
	28 May 57	17.30	17.27	100 + 0.03	100 + 2.15	39	7.42	43
	12 Nov. 57	15.97	16.25	98.3	100 + 2.33	44	7.38	41
W. C.	21 Sept. 56	20.29	24.86	81.6	100 + 2.56	63	7.31	72
	25 Oct. 56	19.16	20.21	94.8	100 + 1.77	50	7.34	52
W. B.	28 Nov. 56	20.16	23.41	79.3	100 + 0.06	51	7.38	65
	23 Apr. 57	16.57	16.66	99.5	100 + 2.50	42	7.37	45
H. B.	13 Dec. 56	6.68	17.88	37.4	89.4	98	6.99	50
F. W.	24 June 57	14.85	17.44	85.2	100 + 0.91	47	7.38	47
I. F. K.	24 Jan. 57	17.56	19.54	89.9	100 + 1.77	32	7.53	50
	6 Aug. 57	16.48	17.40	94.7	100 + 1.10	40	7.39	40
L. R.	14 Mar. 57	12.34	15.01	82.2	100 + 1.70	54	7.31	41
	21 Nov. 57	13.96	14.64	95.4		42	7.36	37
K. P.	3 Sept. 57	12.99	14.33	90.6	100 + 0.75	49	7.34	37
E. B.	8 Dec. 55							
	19 Apr. 56	12.55	13.98	89.8	100 + 1.32	45	7.37	36
A. L.	16 Feb. 56	9.25	17.78	52.0	100 + 1.49	70	7.37	53
	6 Mar. 56	18.23	22.08	87.3		46	7.39	60
O. R.	15 Aug. 57	13.97	18.30	76.3	100 + 1.60	48	7.36	50
	15 Oct. 57	16.27	18.83	86.4	100 + 1.00	48	7.36	51
H. H.	7 Mar. 57	14.99	16.54	90.6	100 + 0.71	45	7.36	41
	15 July 57	15.45	15.46	99.9	100 + 1.90	44	7.36	39
A. D.	27 Aug. 57	15.56	16.80	91.4	100 + 0.96	45	7.39	40
M. F.	27 June 57	17.19	18.60	92.4	100 + 1.49	40	7.38	43

* Values following + sign refer to ml. O_2 per 100 ml. blood in excess of that required to saturate hemoglobin (*i.e.*, dissolved O_2). Normal value for dissolved O_2 is 2.00 ml.

and residual volume, and improvement of maximal breathing capacity and maximal flow rates. Diffusion returned to normal. Patient L. R. lost 143 pounds and in addition received dessicated thyroid for myxedema. Repeat studies demonstrated normal arterial oxygen saturation, normal P_{CO_2}, only minor changes in lung volumes, increased alveolar ventilation, and improvement in the maximal breathing capacity and maximal flow rates. Diffusion returned toward normal. Patients F. W. and K. P. have not been restudied.

Three patients (E. B., A. L. and O. R.) had laboratory evidence of lung disease of unclassified type resembling pulmonary emphysema. They had reduced vital capacities, normal or increased residual volumes, uneven distribution of inspired air, reduced maximal breathing capacities, and severely reduced maximal flow rates with the expiratory flow rates being reduced out of proportion to the reduction in inspiratory flow rates. Diffusion was low in the one patient in whom it was measured. Study of the patients' arterial blood revealed hypoxemia and carbon dioxide retention. All three patients have been restudied after weight loss. Weight loss varied from 31 pounds in Patient E. B. to 46 pounds in Patient A. L. In two patients the vital capacity increased. The residual volume was unchanged in two patients but increased in one patient. Alveolar ventilation increased in all three patients. All three patients still have evidence of uneven distribution of inspired air. After weight loss, two patients were improved as measured by the maximal breathing capacity test; the other patient did worse on retesting. Maximal flow rates continue to be abnormal in all three patients. The diffusing capacity has not changed in the one patient in whom this was studied. Study of the arterial blood in two patients before and after weight loss demonstrated improved oxygen saturation in both, and a fall in P_{CO_2} toward normal in one.

Three patients (H. H., A. D. and M. F.) had arterial hypoxemia without evidence of lung disease. Patient H. H. lost 41 pounds in weight. This was associated with a return of arterial oxygen saturation to normal.

DISCUSSION

We sought to determine the frequency and nature of alveolar hypoventilation in obese persons. In 28 we found 10 who had alveolar hypoventilation as manifested by increased arterial P_{CO_2}. Five other obese persons had hypoxemia not associated with alveolar hypoventilation. Alveolar hypoventilation was associated with myxedema or lung abnormalities including bronchial asthma, emphysema, infarction, edema, and lung disease of unclassified type. Others (32, 33) have reported alveolar hypoventilation in obese patients who had normal lungs but who were thought to have a lesion of the medullary respiratory center. Disorders of the muscles of respiration such as poliomyelitis could produce an abnormal ventilatory response in obese persons and be associated with alveolar hypoventilation. We have no such cases but no doubt they exist.

The existence of alveolar hypoventilation in any patient must be caused by lung disease, malfunction of the chest bellows, inadequate neuro-muscular coordination, or a central nervous system lesion. The physiologic problem in the obese patient with hypoventilation is to identify in which of these four areas lies the derangement of function. Others have advanced the following theory to explain alveolar hypoventilation in obese people who have normal lungs. In the obese individual the work of breathing is increased (16, 34). Some increased work of breathing can be tolerated, but when obesity reaches a certain point the work of breathing becomes excessive and the patient adjusts to suboptimal ventilation by development of a refractory medullary state, thereby permitting alveolar hypoventilation. When weight is reduced, the work of breathing is reduced, normal medullary activity reappears, and the alveoli are properly ventilated. No one has demonstrated the point at which the work of breathing becomes so excessive that alveolar hypoventilation is preferable to a further increase in the work of breathing. Our group of obese patients with normal lungs consists of people between the ages of 19 and 67 years and weighing as much as 382 pounds. None of these persons had alveolar hypoventilation. Our obese persons with normal lungs tolerated the increased work load satisfactorily. We believe that the obese patient with normal lungs and a normal respiratory center may be able to move his chest enough to provide adequate ventilation. However, we still must deal with the mechanism of production of alveolar hypoventila-

tion in obese patients without disease of the lungs. Is it possible that obesity alone, by putting a severe load on the respiratory bellows, leads to a derangement of the respiratory center? Whether obesity alone is enough to produce such a lesion we cannot say. We have no evidence to support the theory that it does. Nor can we say categorically that it doesn't. If such patients exist we have not studied one, although we have searched diligently for one.

We suspect that the increased work of breathing when associated with even mild lung disease, malfunction of the muscles of respiration, or a central nervous system lesion is enough to produce alveolar hypoventilation and the events which follow. Others have shown that weight loss reduces the work of breathing (16) and improves alveolar ventilation. We believe that this mechanism is responsible for the improvement in lung function in our obese patients who lost weight. However, weight reduction alone does not correct underlying lung disease. One of our asthmatic patients (A. H.) lost weight but discontinued her cortisone. At this point pulmonary function tests showed that she was worse than before weight reduction.

Three of our patients had laboratory evidence of lung disease of unclassified type. This lung disease was characterized by reduced vital capacity, normal or increased residual volume, uneven distribution of inspired air, reduced maximal breathing capacity, reduced maximal flow rates with the expiratory flow rate being reduced out of proportion to the reduction in the inspiratory flow rate, and diminished diffusing capacity. Following weight loss, all three patients continued to have uneven distribution of inspired air and abnormal mechanical tests. These persistent abnormalities are consistent with a structural defect similar to that seen in local and diffuse pulmonary emphysema, although clinical evidence of either condition was not present. In these patients the pulmonary abnormalities were mild in degree but they were associated with hypoxemia and carbon dioxide retention. Pulmonary insufficiency could be reversed by weight reduction but evidence of lung disease persisted.

A possibility exists that the obese patient may have a lesion in one of the four areas previously mentioned which is transient, which results in temporary hypoventilation, and which eventually clears up regardless of whether or not the patient loses weight. This mechanism, a transient lesion in one of these four areas, for example a pulmonary infarct or edema of the medullary respiratory center, could explain some of the cases reported by others. Then, too, some of the patients reported by others were studied incompletely and thus the possibility of lung disease was not excluded. Other patients had "complete" studies, but this implies only that all available tests were done. Lung disease can exist in the presence of normal "complete" pulmonary studies.

Necropsies have been done on several patients. One patient had mild emphysema (17), one patient had bronchopneumonia (13), one patient had extensive thrombi in the pulmonary trunk and pulmonary arteries with infarction of the lower lobe of the right lung (15), and one patient had pulmonary artery atherosclerosis, focal areas of atelectasis, and recent pulmonary infarction (35). The patient studied by us (H. B.) who died had extensive pulmonary infarction.

Two of our patients with alveolar hypoventilation had myxedema. These patients may have had pulmonary edema to explain reduced vital capacity, reduced diffusing capacity, and hypoxemia. The mechanism of production of hypercapnia is unknown; however, we can postulate a myxedematous lesion involving the muscles of respiration or the central nervous system to produce alveolar hypoventilation.

Three patients had hypoxemia without evidence of lung disease. The most reasonable explanation for hypoxemia in these persons is that they had a disturbance in ventilation perfusion ratios, either mixed venous blood perfusion of underventilated lung areas or overperfusion of normally ventilated lung areas. Some support for this comes from the fact that two of the three failed to come to full values for oxygen saturation after breathing 99.6 per cent oxygen for 10 minutes. The third patient has an arterial saturation of 92.4 per cent while breathing room air. This is just below the normal range. These patients did not develop the "Pickwickian Syndrome" as alveolar hypoventilation was not present.

Several of our patients clinically resembled the

"Pickwickian" patient. One example was F. S. who was somnolent, plethoric and obese. While waiting his turn to be seen in the medical clinic he was found sleeping soundly and was promptly called to our attention as an example of this syndrome. Lung function studies were normal. His somnolence had some other cause than hypoxemia or hypercapnia.

SUMMARY AND CONCLUSIONS

We have studied 28 persons who weighed at least 100 pounds more than their ideal weight. Of this group 13 had normal arterial oxygen saturation. Fifteen had hypoxemia and 10 of the 15 had alveolar hypoventilation as manifested by increased arterial P_{CO_2}. Alveolar hypoventilation was associated with myxedema or lung disease.

Obese persons who had normal arterial oxygen saturation had reduced expiratory reserve volumes, reduced maximal breathing capacities, and reduced maximal flow rates. When these patients lost weight, their lung function returned toward normal.

Some obese persons who did not have lung disease did have arterial hypoxemia without hypercapnia. We believe this is caused by a disturbance in ventilation perfusion ratios in the lungs. However, when alveolar hypoventilation is present (arterial hypoxemia and hypercapnia), one should suspect intrinsic lung disease, a disturbance of the respiratory musculature, or a central nervous system lesion. In our experience obese persons with normal lungs, normal respiratory muscles, and an apparently normal respiratory center did not have alveolar hypoventilation. Most obese persons with pulmonary insufficiency are benefitted by weight loss. Presumably the improvement is caused by reduction in the work of breathing. Obese persons who have lung disease need therapy which is directed toward correcting or alleviating the basic lung disease.

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