The Cardiorespiratory Syndrome of Obesity

GLEN A. LILLINGTON, M.D.,* MILTON W. ANDERSON, M.D., F.C.C.P.**
and ROBERT O. BRANDENBURG, M.D.**

Rochester, Minnesota

The association between obesity, impaired respiratory function and polycythemia has recently aroused considerable speculation and investigation. While it has long been known that the hypoxemia present in certain pulmonary and cardio-vascular diseases may lead to secondary polycythemia, it is now postulated that marked obesity per se, in the absence of intrinsic pulmonary disease, may compromise respiratory function to such an extent that secondary polycythemia ensues.

The reduced vital capacity in obesity has been described by many workers.1-3 In 1936, Kerr and Lagen4 reported a series of patients with obesity, plethoric facies and cyanosis, reduced vital capacity, polycythemia and, in some cases, the development of congestive heart failure. They postulated that obesity gave rise to "postural emphysema" which led to alveolar hypoventilation, arterial hypoxemia and secondary polycythemia, and stated that loss of weight was accompanied by reversal of the syndrome. A high incidence of polycythemia in obese persons was reported by Báez Villaseñor and associates5 in 1951 and more recently by Weil,6 who ascribed the polycythemic state in his cases to ventilatory impairment secondary to obesity. In Lawrence and Berlin's7 study of the "polycythemia of stress," obesity was present in eight of 18 cases. Boyer and Bailey8 noted an elevated carbon dioxide tension in expired gas of obese persons. The triad of obesity, alveolar hypoventilation with hypoxemia and secondary polycythemia, in the absence of intrinsic pulmonary disease, has been further described in several recent reports.9-15

Although it is generally agreed that arterial oxygen saturation is normal in polycythemia vera,16, 17 this has been questioned in two recent papers. Newman and co-workers18 performed detailed studies of pulmonary function in five patients whose condition had been diagnosed as polycythemia vera. Two of these patients, both very obese, exhibited hypoxemia, hypercapnia and considerable impairment in ventilatory function. It would appear likely that the polycythemia in these two cases is secondary rather than primary. Ratto and associates19 reported the presence of alveolar

---

* Fellow in Medicine, Mayo Foundation.
** Section of Medicine, Mayo Clinic and Mayo Foundation.

The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

Copyright, 1957, by the American College of Chest Physicians
### TABLE I

RESULTS OF TESTS OF PULMONARY FUNCTION IN SEVEN OBESE PATIENTS*

<table>
<thead>
<tr>
<th>Date of test</th>
<th>Vital capacity (liters)</th>
<th>Residual volume (liters)</th>
<th>Total capacity (liters)</th>
<th>Residual volume (liters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1 (M, 44 yr., 238 lb., 71 in.)</td>
<td>3.54 (68)</td>
<td>4.24 (88)</td>
<td>3.98 (128)</td>
<td>0.96 (80)</td>
</tr>
<tr>
<td>Case 2 (M, 46 yr., 238 lb., 69 in.)</td>
<td>3.43 (65)</td>
<td>4.24 (88)</td>
<td>3.98 (128)</td>
<td>0.96 (80)</td>
</tr>
<tr>
<td>Case 3 (P, 28 yr., 64 lb., July 26, 1955)</td>
<td>2.71 (59)</td>
<td>2.04 (43)</td>
<td>2.71 (59)</td>
<td>2.04 (43)</td>
</tr>
<tr>
<td>Case 4 (M, 40 yr., 164 lb., 70 in.)</td>
<td>4.93 (115)</td>
<td>5.24 (86)</td>
<td>5.24 (86)</td>
<td>5.24 (86)</td>
</tr>
<tr>
<td>Case 5 (M, 48 yr., 250 lb., 69 in.)</td>
<td>2.54 (169)</td>
<td>2.49 (156)</td>
<td>2.54 (169)</td>
<td>2.49 (156)</td>
</tr>
<tr>
<td>Case 6 (M, 49 yr., 260 lb., 70 in.)</td>
<td>2.09 (63)</td>
<td>2.09 (63)</td>
<td>2.09 (63)</td>
<td>2.09 (63)</td>
</tr>
<tr>
<td>Case 7 (M, 46 yr., 276 lb., 67 in.)</td>
<td>3.65 (113)</td>
<td>3.65 (113)</td>
<td>3.65 (113)</td>
<td>3.65 (113)</td>
</tr>
<tr>
<td>Case 8 (M, 50 yr., 276 lb., 67 in.)</td>
<td>2.87 (64)</td>
<td>2.87 (64)</td>
<td>2.87 (64)</td>
<td>2.87 (64)</td>
</tr>
</tbody>
</table>

- **Total volume X 100 (per cent)**: 19, 48, 55, 46
- **Functional residual capacity (liters)**: 2.13 (112), 3.37 (125), 2.88 (99), 3.06 (113)
- **Inspiratory capacity (liters)**: 3.5 (92), 3.1 (89), 2.87 (120), 3.03 (78)
- **Expiratory reserve (liters)**: 0.08 (6), 1.14 (87), 1.18 (169), 0.40 (29)
- **Maximal breathing capacity (liters per minute)**: 98 (81), 45 (36), 35 (24), 49 (40)
- **Expiratory slowing† (grade)**: 0, 2, 3, 0-1
- **Nitrogen washout index‡ (per cent)**: 5.9, 5.5, 5.5, 0.9
- **Arterial oxygen saturation (per cent); breathing room air§**: Rest: 87-94, 96-96, 70-90, 95-98, 97-98, 84-87, 85-90, 96-97, Exercise: 91, 93, 98, 95, 80, 81, 93
- **Duration of exercise**: 5 min, 1.5 min, 2.5 min, 2 min, 1.7 min, 1.7 min, 3.5 min

*All volumes are expressed as liters or liters per minute BTPS.

Figures in parentheses indicate percentage of predicted normal values derived from the formulae of Bateman.†

†Measured by the maximal midexpiratory flow method of Leuallen and Fowler and graded 0 to 4.

‡Normal value is < 2.5 per cent.

§Normal value is 95 to 98 per cent.
hypoventilation, hypoxemia and polycythemia in a "large man" with normal lung volumes and normal maximal breathing capacity. They attributed the alveolar hypoventilation to depressed sensitivity of the respiratory center, the cause of which was undetermined.

From these studies has arisen the concept of a clinical syndrome characterized by extreme obesity, cyanosis, breathing irregularities, congestive heart failure and a tendency toward excessive lethargy and somnolence. Laboratory studies reveal absolute polycythemia, pulmonary hypertension, arterial hypoxemia and hypercapnia, compensated respiratory acidosis, alveolar hypoventilation and certain abnormalities in the ventilatory tests of pulmonary function. Definitive evidence of primary pulmonary disease or a right-to-left cardiovascular shunt is lacking. Appropriate reduction in weight appears to reverse the clinical and laboratory signs of the syndrome.

Although obesity is now considered to be the primary factor in the development of this syndrome, the exact mechanism by which the excessive weight leads to hypoxemia and hypercapnia is not entirely clear. In an effort to clarify this problem and to document further the occasional occurrence of this interesting disease entity, the clinical records of a series of extremely obese patients seen at the Mayo Clinic were reviewed. Only patients on whom arterial oxygen saturation studies had been made were included in the series.

Eight cases were selected for presentation: Four obese patients had polycythemia and were free from evidence of intrinsic pulmonary or cardiac disease; three obese patients with secondary polycythemia had definite bronchopulmonary disease of some form, but obesity was considered to play a significant role in the genesis of the arterial hypoxemia; one patient had obesity without polycythemia but displayed arterial oxygen desaturation on exercise.

Report of Cases

Case 1: A 44 year old man came to the clinic in November, 1951, complaining of moderately severe exertional dyspnea, without orthopnea, of several years' duration and of cyanosis of the face and lips for the previous year. The cyanosis was said to be more marked when he was asleep. He had noticed excessive drowsiness and some edema of the ankles for 6 months. He had been told in 1949 that his blood pressure was elevated, and he had weighed more than 300 pounds for several years.

His height was 71 inches and his weight was 370 pounds. He had ruddy cyanosis which was more marked on recumbency. There was minimal edema of the legs but abnormalities of the heart or lungs were not noted. Funduscopic examination revealed congestive retinal veins. Blood pressure was 185 mm. of mercury systolic and 120 mm. diastolic. It was noted that his breathing was very shallow.

A roentgenogram of the thorax showed minimal linear fibrosis in the lower left lung. Tests showed the presence of albuminuria, grade 2, and casts in the urine sediment. The concentration of hemoglobin was 16.4 gm. per 100 cc. of blood; the hematocrit reading was 60 per cent; erythrocytes numbered 5,790,000 and leukocytes 5,600 per cubic millimeter of blood, and the differential blood count was normal. Carbon dioxide combining power measured 29 mEq. and serum chlorides 88.3 mEq. per liter. The value for urea was 21 mg. and for fasting blood sugar, 115 mg. per 100 cc. of blood. The values for serum calcium, cholesterol, proteins, potassium and sodium were normal, and measurements of urinary excretion of 17-ketosteroids and corticoid gave normal results. The electrocardiogram (Fig. 1) disclosed an R-R' configuration in lead V1, prominent S waves in leads I, aVL, and V4, a late R deflection in lead aVF, prominent P waves in leads I and II, a normal electric axis and
inverted T waves from leads V1 to V4. The interpretation was that of right ventricular overload.

Treatment consisted of reduction of weight (600 calorie diet) and removal of 1,000 cc. of blood by phlebotomies. Studies of pulmonary function were carried out 2 weeks after his admission, at which time he weighed 336 pounds (Table 1). The vital capacity and expiratory reserve volumes were significantly reduced.* There was no spirometric evidence of expiratory obstruction, but the tidal volumes were low (less than 200 cc.) and the tracing showed apneic periods. Arterial oxygen saturation (determined by ear oximetry with the double scale oximeter11) with the patient breathing room air was 87 to 94 per cent when he was at rest and 91 per cent on exercise (stepping up and down from a 9-inch step 15 times per minute for 5 minutes), but increased to 100 per cent when he breathed pure oxygen.

*All values for lung volumes, minute ventilation, and maximal breathing capacity are expressed as liters or liters per minute BTPS.

FIGURE 1: Electrocardiograms for a 44 year old man (Case 1). Note the changed electric axis, decreased height of P waves in the standard leads, elevation of T waves in the right precordial leads and the decreased amplitude of the S wave in V1 after a loss of 70 pounds.
Arterial blood samples, obtained in all cases by needle puncture of the radial artery, were studied 2 days later (Table II). On breathing air, arterial desaturation and an elevated Pco2 (partial pressure of carbon dioxide in arterial blood expressed in millimeters of mercury) were noted. On breathing pure oxygen, the saturation increased to 100 per cent but the Pco2 increased from 55 to 70 mm. and the pH decreased from 7.36 to 7.25. This was interpreted as partially compensated respiratory acidosis which was aggravated by a further decrease in ventilation on breathing oxygen. Arterial dye-dilution curves, measured by continuous ear oximetry after injection of Evans blue dye into a peripheral or central vein, did not show evidence of shunts but the circulation time was somewhat prolonged. Continuous oximetry while the patient breathed room air showed remarkable changes in oxygen saturation of arterial blood with each respiration; saturation decreased when the breath was held in expiration and increased to normal range on voluntary hyperventilation. These fluctuations were abolished by breathing 100 per cent oxygen.

At the time of his dismissal a week later, the patient weighed 329 pounds. Final diagnosis was arterial hypoxemia with secondary polycythemia due to mechanical restriction of ventilation by obesity.

He returned to the clinic in August, 1952, weighing 300 pounds. He stated that he stayed awake more easily and had less dyspnea and no pedal edema. On examination, his blood pressure was 140/90 and cyanosis was absent. The urine did not contain albumin, the concentration of hemoglobin was 15.4 gm. per 100 cc. of blood, and erythrocytes numbered 4,630,000 and leukocytes 6,300 per cubic millimeter of blood. The hematocrit reading was 52 per cent and serum chlorides measured 99.4 mEq. per liter. The electrocardiogram (Fig. 1) showed smaller P waves and some left axis deviation. The R' in lead V4 and the S in leads I and V6 were smaller.

Case 2: A 46 year old farmer was brought to the clinic in a semicomatose condition in December, 1951. He had been grossly overweight for many years "due to an uncontrollable appetite" and had recently weighed 273 pounds. Pilethra and excessive drowsiness had been present for 9 years, and his condition had been diagnosed as nacrolepsy. Dyspnea occurred on minimal exertion and he became cyanotic on coughing or lying down.

On the patient's admission, the oral temperature was 101° F. He was restless, somewhat disoriented and confused, and fell asleep repeatedly. He was plethoric and deeply cyanotic. His respirations were irregular, shallow and rapid, with recurrent episodes of apnea resembling Cheyne-Stokes breathing. He had a dry nonproductive cough. Peripheral venous distension and edema were not noted; the heart tones were normal, but coarse rales were heard over the right lung. Blood pressure was 160/90 and funduscopic examination showed dark, dilated retinal veins.

The concentration of hemoglobin was 19.0 gm. per 100 cc. of blood; the hematocrit reading was 72 per cent. Erythrocytes numbered 7,120,000 per cubic millimeter of blood, but the platelet, leukocyte and differential counts were normal. Albuminuria, grade 3, was present as well as microscopic hematuria, the latter being attributed to the indwelling catheter. The carbon dioxide combining power was 39.4 mEq and the value for chlorides was 93.6 mEq. per liter. The values for blood sugar, blood urea, serum sodium and potassium were within normal limits. A roentgenogram of the thorax showed a questionable density in the left costophrenic angle. The electrocardiogram (Fig. 2) showed right axis deviation, high peaked P waves in leads II and III, a W-shaped QRS in V4, a deep S wave in V6, and shallow inverted T waves in V4 and V6.

Penicillin was given intramuscularly and the patient was placed in an oxygen tent, which relieved his cyanosis but seemed to make him sleepier. Daily for 6 consecutive days 500 ml. of blood was removed by phlebotomy. His temperature became normal; he appeared more alert the day after admission, and was taken from the oxygen tent 2 days subsequently. A roentgenogram of the thorax on the fourth day of hospitalization showed clear lung fields and slight enlargement of the cardiac silhouette. An electro-encephalogram and a determination of 17-ketosteroids excreted in the urine were within normal limits.

Studies of pulmonary function were made on the tenth hospital day, at which time he was alert and greatly improved clinically with a relatively normal breathing pattern. He weighed 222 pounds and his height was 69 inches. Ventilatory studies gave essentially normal results (Table I). Although the arterial oxygen saturation when the patient was at rest was 86 per cent initially, it later increased to 96 per cent but decreased to 93 per cent after 1.5 minutes of exercise. The saturation increased to 100 per cent when pure oxygen was breathed. Arterial blood studies 3 days later showed a radial pressure of 122/88 and an oxygen saturation of 96 per cent when room air was breathed and 100 per cent when oxygen was breathed. Arterial dye-dilution studies showed a normal circulation time and no evidence of shunts.

Before his dismissal from the hospital, the patient was given 6.5 mc. of radioactive phosphorus. He weighed 220 pounds on dismissal and the hematocrit reading was 50
per cent. The diagnosis was considered to be polycythemia vera at that time.

He returned to the clinic in November, 1962, complaining of dyspnea and excessive somnolence as before. He weighed 226 pounds; blood pressure was 140/80 and musical rales could be heard over both lungs. Albuminuria, grade 2, was noted; the concentration of hemoglobin measured 17.6 gm. per 100 cc. of blood; erythrocytes numbered 5,800,000 and the hematocrit reading was 62 per cent. Platelets and leukocytes were normal in all respects. The total blood volume* was 8,358 cc. and the plasma volume was 3,176 cc. A roentgenogram of the thorax did not show evidence of abnormality. Phlebotomy of 500 ml. of blood was performed, another 4 mc. of radiophosphorus was administered, and he was advised to lose weight.

He returned to the clinic in June, 1954, complaining of increased dyspnea and sleepiness. He had had repeated phlebotomies by his home physician. His weight had increased to 242 pounds and moist rales and wheezes were heard over both lungs. Albuminuria, grade 2, was present. The concentration of hemoglobin was 12.6 gm. per 100 cc. of blood; erythrocytes numbered 5,890,000 and the hematocrit reading was 52 per cent. Leukocyte and platelet counts were normal and the sternal bone marrow was reported to be “moderately hypocellular.” The electrocardiogram appeared

*All blood volumes were determined by the Congo red dye-dilution technic.

FIGURE 2: Electrocardiograms for a 46 year old man (Case 2) before and after a loss of 80 pounds.
unchanged from the one made in 1951, but a roentgenogram of the thorax revealed some cloudiness at the base of the right lung and slight cardiac enlargement. A similar roentgenogram made a week later showed considerable clearing. Two specimens of sputum showed acid-fast bacilli on bacteriologic examination or abnormal cells on cytologic examination. He was again advised to lose weight.

The patient returned to the clinic in December, 1954, with complaints of dyspnea and orthopnea of sufficient severity to incapacitate him completely. He had had 12 phlebotomies in the previous 6 months and had been given digitals. His weight was 250 pounds and the blood pressure was 140/78. He was plethoric and cyanotic. Congestive heart failure was not evident, but rales were heard at the bases of both lungs on inspiration and expiration. Urinary and hematologic findings were essentially unchanged, and a roentgenogram of the thorax showed slight cardiac enlargement with pulmonary congestion, mostly at the base of the right lung. The patient was given a rigid reduction diet of 800 calories.

He followed the diet faithfully and by August, 1955, had reduced to 166 pounds. He reported that he felt very well and was able to perform full-time farm labor. Somnolence, cyanosis and dyspnea had disappeared; phlebitis had not been required and he had not had to take digitals.

He reported to the clinic again in June, 1956. Although his weight was up to 190 pounds, he had no symptoms except for some cough and expectoration which he attributed to smoking. Blood pressure was 120/80 and the lungs were normal on physical examination. The concentration of hemoglobin was 15.4 g. per 100 cc. of blood; erythrocytes numbered 5,390,000 per 100 cc. of blood, and the hematocrit reading was 53 per cent. Albumin was not present in the urine and the blood urea measured 26 mg. per 100 cc. The electrocardiogram (Fig. 2) showed striking improvement with a normal electric axis, normal P and T waves and a normal QRS in lead V. The roentgenogram of the thorax revealed a normal cardiac silhouette, but because of persistent opacity at the base of the right lung, bronchoscopy was performed. All bronchi were patent. The bronchial tree contained some mucoid secretions and it was noted that the bronchi appeared unusually pliable and tended to collapse during expiration. Examination of aspirated secretions for acid-fast bacilli and neoplastic cells gave negative results. The patient was advised to reduce to 180 pounds and to stop smoking.

Case 3: A 28 year old single woman came to the clinic in March, 1955, complaining of dyspnea and cyanosis of recent onset. She had weighed more than 350 pounds for several years. Her parents had noted excessive somnolence at times, and her home physician recently had discovered that she had hypertension and polycythemia. Her height was 62 inches and her weight was 427 pounds. She was cyanotic, dyspneic at rest, lethargic and somewhat incoherent. Physical examination revealed tachycardia, a blood pressure of 220 mm. of mercury systolic and 150 mm. diastolic, fine rales at the bases of both lungs and normal cardiac tones. There was no pitting edema of the legs. Respirations were rapid, shallow and irregular, with frequent short periods of complete apnea, particularly when she was asleep. Funduscopic examination showed "the neuroretinopathy of acute polycythemia."

Laboratory examinations and tests showed the following results: albuminuria, grade 4; 64 mg. per 100 cc. of blood; carbon dioxide combining power of 22 mEq. per liter; concentration of hemoglobin of 20.5 gm. per 100 cc. of blood; 7,120,000 erythrocytes and 7,800 leukocytes per cubic millimeter of blood; hematocrit reading of 76 per cent; total blood volume of 12,892 cc., and plasma volume of 3,046 cc. A roentgenogram of the thorax showed cardiac enlargement with engorgement of hilar vessels and the electrocardiogram (Fig. 3) showed sinus tachycardia, right axis deviation, high peaked P wave in lead II, a qRventricular complex in lead V, reduced amplitude of QRS complex, and a late R wave in lead aVR. The arterial oxygen saturation when the patient breathed room air varied periodically from 70 to 90 per cent, but it was constant at 100 per cent when oxygen was breathed (Tables I and II). The central venous pressure was increased (31/15 to 28/15) and the radial arterial blood pressure by direct measurement was 170/74. Arterial dye-dilution curves did not show evidence of shunts, but the circulation time was somewhat prolonged.

Treatment included removal of 2,870 cc. of blood by phlebotomy, use of mercurial diuretics, and anticoagulants, and reduction of weight to 391 pounds. On dismissal she was much improved symptomatically and the concentration of hemoglobin was 16.8 gm. per 100 cc. of blood with a hematocrit reading of 64 per cent.

On return to the clinic in October, 1956, she was asymptomatic and weighed 251 pounds. She was not cyanotic, and physical examination gave negative results except for the blood pressure which measured 190/130. A roentgenogram of the thorax and an electrocardiogram (Fig. 3) did not show any abnormality. She did not have albuminuria; the blood urea was normal and the results of hematologic studies and pulmonary-function studies (Table I) were entirely normal.
She reported in August, 1956, that she had reduced to 135 pounds and felt completely well.

In each of these three cases, a significant degree of arterial hypoxemia was demonstrated. In each instance, this was attributed to the alveolar hypoventilation which was strikingly apparent clinically. Unfortunately, satisfactory quantitative determinations of minute ventilation were not performed. Although the reduced vital capacity characteristic of obesity was noted in the first case, the ventilatory studies were normal in the other two patients. However, the ventilatory studies in Case 3 were performed after a loss of approximately 175 pounds. In each case, loss of weight was accompanied by disappearance of polycythemia and cyanosis, reduction in cardiac size and blood pressure, clearing of adventitious sounds from the thorax, disappearance of albuminuria, return of an elevated blood urea to normal, disappearance of the tendency toward excessive somnolence and reversal of the electrocardiographic evidences of right ventricular overload.

Case 4: A 40 year old man came to the clinic in July, 1951, with the complaints of increasing exertional dyspnea for many years and intermittent edema of the legs during the past year. He had never been orthopneic. He had been obese all his life and had weighed more than 400 pounds for several years.

His height was 70 inches and his weight was 430 pounds. He was plethoric and cyanotic and there was marked pitting edema of the legs. No abnormality of the

### Table II

<table>
<thead>
<tr>
<th>Number of Case and Date of Test</th>
<th>1 (Dec. 7, 1951)</th>
<th>3 (Mar. 25, 1955)</th>
<th>5 (Jan. 17, 1956)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor measured</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Content (volume per 100 cc.)</td>
<td>20.4</td>
<td>17.7</td>
<td>14.5</td>
</tr>
<tr>
<td>Capacity (volume per 100 cc.)</td>
<td>23.4</td>
<td>24.6</td>
<td>21.4</td>
</tr>
<tr>
<td>Saturation (per cent)</td>
<td>87</td>
<td>72</td>
<td>68</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Content (volume per 100 cc.)</td>
<td>56</td>
<td>57</td>
<td>84</td>
</tr>
<tr>
<td>Partial pressure in arterial blood (mm. of mercury)</td>
<td>55</td>
<td>70</td>
<td>61</td>
</tr>
<tr>
<td>pH</td>
<td>7.36</td>
<td>7.25</td>
<td>7.46</td>
</tr>
<tr>
<td>Ventilation (liters per minute)</td>
<td>13.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tidal volume (milliliters)</td>
<td>600</td>
<td>600</td>
<td></td>
</tr>
</tbody>
</table>
heart or lungs was noted on physical examination and the blood pressure was 128 mm.
of mercury systolic and 100 mm. diastolic. Funduscopic examination gave negative
results. No comment on the ventilatory pattern was recorded.

A roentgenogram of the thorax showed cardiac enlargement and clear lung fields.
The electrocardiogram revealed a normal electric axis, a high peaked P wave in lead II
and a prominent S in leads I and V5. Microscopic hematuria and albuminuria,
grade 3, were present. The concentration of hemoglobin was 17.8 gm. per 100 cc.
of blood on his admission, but this increased to 19.4 gm. after the onset of mercurial
diuresis. Erythrocytes numbered 6,010,000 and leukocytes 5,800 per cubic millimeter
of blood with a normal differential count and platelet count. The hematocrit reading
was 69 per cent. The values for blood urea and serum proteins and the sedimentation
rate of erythrocytes were within normal limits. The total blood volume was 12,085
cc., and the plasma volume was 4,100 cc.

On a low-sodium, 800-calorie diet, he lost 22 pounds in 3 days. The use of
mercurial diuretics and ammonium chloride caused further loss of weight and resolution
of edema. Two weeks after his admission, when his weight had dropped to 364
pounds and he was much improved clinically, studies of pulmonary function were
performed (Table 1). The vital capacity and expiratory reserve volumes were
significantly enlarged, but there was no spirometric evidence of expiratory obstruction.
Arterial oxygen saturations on breathing room air varied from 98 per cent at rest
to 95 per cent during exercise, and the arterial saturation increased to 100 per cent
on breathing pure oxygen.

Digitalis was administered and 3,000 cc. of blood was removed by phlebotomy.
When he was dismissed 6 weeks after admission, he weighed 387 pounds. The con-
centration of hemoglobin was 14.6 gm. per 100 cc. of blood; erythrocytes numbered
4,790,000 per cubic millimeter of blood and the hematocrit reading was 54 per cent.
Roentgenograms of the thorax showed a marked decrease in cardiac size and the
blood pressure was 136/86.

By January, 1952, he had reduced to about 300 pounds, and reported that he was
feeling very well. He began to regain weight subsequently, and when he returned
to the clinic in August, 1953, he weighed 440 pounds and complained of edema of the
legs and severe dyspnea on exertion. The blood pressure measured 165/125 and fine
rales were heard at the bases of both lungs. Albuminuria and cylindruria were
present; the concentration of hemoglobin was 18.1 gm. (after diuresis) and the
hematocrit reading was 56 per cent. The value for blood urea was normal. The
thoracic roentgenogram showed an increase in cardiac size. He was treated for 3
weeks with mercurial diuretics and a low-sodium, 800-calorie diet. On dismissal, he
weighed 385 pounds and was much improved symptomatically. No further follow-up
was obtained.

Although hypoxemia was not demonstrated in this case, the studies of pulmonary function were not performed until the patient had had 2
weeks of rest in bed, had been on a reducing diet and had received mer-
curial diuretics, all of which had resulted in a loss of 66 pounds and
decided clinical improvement. The reduced vital capacity and expiratory
reserve, and the clinical resemblance of this patient to the patients in
Cases 1, 2 and 3 suggest that hypoxemia had been present earlier.

Case 5: A 58 year old man came to the clinic in January, 1966. He had been obese
all his life; in 1946 he had weighed 250 pounds and had gained 100 pounds since
then. In 1950 he had been treated for mental depression. For years he had had a
chronic cough with production of some mucoid and occasionally purulent sputum. He
had been troubled with increasing exertional dyspnea for 15 years, had noticed inter-
mittent cyanosis for 7 years, and had had intermittent edema of the legs for 5 years.
He had been treated for pneumonia by his home physician in November, 1956, at which
time cyanosis was noted. Results of studies of pulmonary function had been
reported to be normal. His family had noted excessive lethargy and somnolence in
the past few years.

His height was 68 inches and he weighed 335 pounds. He was awake and rational
but was dyspneic at rest and had a wheezy cough. Cyanosis was marked. The thorax
expanded poorly with maximal inspiratory effort and expiratory rales were heard
over both lungs. Cardiac sounds were distant and there was marked pitting edema
of the feet and legs. Blood pressure was 226 mm. of mercury systolic and 130 mm.
diastolic; respirations were 28 per minute and shallow, and the pulse rate was 120
per minute. Funduscopic examination showed cyanosis of the retinas due to polythemia or to right-sided cardiac failure, plus minimal hypertensive changes.
Albuminuria, grade 2, was present and the value for blood urea was 24 mg. per 100 cc. The concentration of hemoglobin was 15.6 gm. per 100 cc. of blood and the erythrocytes numbered 6,150,000 and the leukocytes 7,200 per cubic millimeter of blood. The hematocrit reading was 65 per cent and the sedimentation rate of erythrocytes was 7 mm. in the first hour (Westergren method). Total proteins measured 6.6 gm. per 100 cc. of serum. The value per liter of serum for sodium was 133 mEq.; for potassium, 4.9 mEq.; for carbon dioxide combining power, 25 mEq., and for chlorides, 88.5 mEq. The pH of venous blood was 7.36. A roentgenogram of the thorax showed pulmonary congestion and slight cardiac enlargement, and an electrocardiogram showed normal axis deviation with tall peaked P waves in leads II and III.

The day after his admission to the hospital, fever developed (102° F.) and his condition deteriorated seriously. Respirations became wheezy and irregular and he began to cough up varying amounts of thick tenacious purulent sputum. He became semicomatose, disoriented and confused, and the cyanosis increased. Crepitant rales could be heard over both lung fields.

He was treated with digitalis, antibiotics, mercurial diuretics, aminophyllin given intravenously, oxygen by nasal catheter at a rate of 1 to 4 liters per minute and intermittent positive pressure breathing with oxygen and isuprel aerosol for 10

FIGURE 3: Electrocardiograms for a 28 year old woman (Case 3) before and after a loss of 176 pounds.
CARDIORESPIRATORY SYNDROME OF OBESITY

minutes every hour. Sputum was raised with the aid of a Barach coffiater and, on one occasion, by direct aspiration of the tracheobronchial tree by means of a laryngoscope. Caloric intake was minimal and a total of 1,500 cc. of blood was removed in four phlebotomies, after which the concentration of hemoglobin was still 15.4 gm. and the hematocrit reading, 61 per cent. The patient was semicomatose for 3 weeks, during which his respirations were irregular and sometimes Cheyne-Stokes in type. The administration of oxygen greatly decreased the cyanosis. Whenever the use of oxygen was discontinued, his respirations would become deeper for a period, but after about an hour he seemed to tire and the cyanosis would become more marked. The carbon dioxide combining power measured as high as 39.5 mEq. per liter, and the value for urea was 72 mg. per 100 cc. of blood on one occasion.

One week after his admission, respiratory minute volumes and arterial blood samples were studied (Table II). On breathing room air, the total ventilation was 13.8 liters per minute, there was marked arterial hypoxemia and hypercapnia and the pH was 7.46. On breathing pure oxygen, the respiratory minute volume decreased to 8.3 liters, the arterial oxygen saturation rose to 94 per cent, $P_{\text{a}}\text{CO}_2$ increased and the pH fell to 7.42.

By the fourth week of hospitalization, the patient had shown considerable improvement clinically, manifested by loss of edema, loss of 45 pounds, marked reduction in dyspnea and cyanosis, almost complete clearance of auscultatory abnormalities from the thorax, subsidence of fever and diminished disorientation and somnolence. The blood pressure was frequently within the normal range. He was out of bed for short periods and the use of oxygen was discontinued. The concentration of hemoglobin was 13.5 gm. with a hematocrit reading of 48 per cent; the value for urea decreased to 30 mg. per 100 cc. of blood and the carbon dioxide combining power decreased to 29 mEq. per liter. At this time, the total blood volume was 8,428 cc. and the plasma volume was 3,877 cc.

Four weeks after admission, severe thoracic pain, dyspnea and shock developed while the patient was walking about his room. An electrocardiogram showed the pattern of partial right bundle branch block and nodal tachycardia with atrioventricular dissociation. Death occurred 2 hours later.

At necropsy, a large embolus was found which filled the pulmonary trunk and extended into both pulmonary arteries. There were small recently formed emboli in the lower lobe of the right lung with areas of fresh infarction. The heart weighed 970 gm. and both ventricles showed some hypertrophy. Coronary sclerosis was slight to moderate. Some purulent bronchitis throughout both lungs and minimal bronchiectasis in the right lower lobe were observed, but the pulmonary parenchyma was normal except for congestive changes and some scattered areas of emphysema. The large muscular branches of the pulmonary arteries showed medial hypertrophy (Fig. 4). Sections of the intercostal muscles did not reveal abnormalities.

Although this patient undoubtedly had chronic bronchitis with bronchiectatic changes, it seems likely that obesity was an important factor in the genesis of his ventilatory dysfunction. When he first presented at the clinic, he appeared to be hypoventilating. The exacerbation of his chronic endobronchial infection, manifested by fever, production of purulent sputum and marked clinical deterioration, critically compromised his already impaired ventilatory function, probably by plugging certain bronchi to produce regional alterations of the ventilation-perfusion ratio and “functional shunts” in the lungs. The presence of functional shunts would explain the following: (1) his inability to overcome the hypoxemia and hypercapnia on breathing room air with a ventilatory minute volume of 13.8 liters (tidal volume, 600 ml.), and (2) the failure of his arterial oxygen saturation to rise above 94 per cent when he breathed pure oxygen at 8.3 liters per minute. Necropsy did not show evidence of alveolar-capillary block, and the pulmonary emboli appeared to be merely a terminal phenomenon on clinical, electrocardiographic and pathologic grounds. It is suggested that the mechanical effects of his obesity on respiration prevented him from making a more adequate ventilatory response to the arterial hypoxemia and hypercapnia. The arterial pH values were interpreted as follows: Prior to the arterial blood studies,
the patient had breathed an oxygen mixture for 6 days and presumably had compensated his respiratory acidosis by the usual renal mechanisms. On breathing room air, the consequent relative hyperventilation lowered the \( \text{PaCO}_2 \) sufficiently that the respiratory acidosis was temporarily overcompensated, and the arterial \( \text{pH} \) was actually in the alkaline range (7.46). When he then breathed pure oxygen, the total ventilation was divided almost in half, and the arterial \( \text{pH} \) decreased toward the normal range again.

Case 6: A 48 year old man first came to the clinic in July, 1955, complaining of increasingly severe exertional dyspnea since 1950. He was a heavy smoker and had had a chronic cough for 15 years. He had weighed more than 200 pounds for 15 years or more. He had been hospitalized in 1951 because of congestive heart failure, at which time he weighed 250 pounds, was cyanotic and drowsy, and apparently had become very disoriented and confused while in an oxygen tent. Roentgenograms of the thorax did not show evidence of abnormality. He was given mercurial diuretics and lost 30 pounds. In 1954, he was again hospitalized and treated for congestive cardiac failure.

His height was 68 inches and he weighed 240 pounds. He was plethoric, drowsy and moderately cyanotic, and his respirations were rapid, shallow and grunting. The pulse rate was 100 beats per minute and the blood pressure was 130 mm. of mercury systolic and 80 mm. diastolic. Cardiac murmurs were not heard, but the second sound at the pulmonic area was louder than at the aortic area. Inspiratory rales and expiratory rhonchi were heard over both lungs. He had some ascites and moderate pitting edema of the legs. The thorax expanded poorly on inspiration. Funduscopic examination showed "cyanosis retinae."

Urinalysis gave normal results, but the value for blood urea was 72 mg. per 100 cc. The concentration of hemoglobin was 15.4 gm. per 100 cc. and leukocytes numbered 4,100 with a normal differential count. The carbon dioxide combining power was 24 mEq. per liter. A roentgenogram of the thorax showed pulmonary vascular congestion and cardiac enlargement. An electrocardiogram showed right axis deviation, tall peaked \( P \) waves in leads II and III, prominent \( S \) deflections in leads I, \( V_1 \) and \( V_6 \), and inversion of \( T \) waves with depression of \( ST \) segments from leads \( V_1 \) and \( V_6 \). The pattern seen was consistent with that of right ventricular overload.

The patient was put in an oxygen tent and it was noted that he became more lethargic and confused. He gradually improved on digitalis, mercurial diuretics, aminophyllin and a reducing diet. Ten days after his admission, the concentration

![FIGURE 4: View of tissue from the right lung of a 58 year old man (Case 5), showing medial hypertrophy in a large muscular artery (stained with Verhoeff's elastic tissue stain and counterstained with van Gieson's connective tissue stain; X1000).](http://journal.publications.chestnet.org/pdfaccess.ashx?url=data/journals/chest/21295/ on 06/21/2017)
of hemoglobin was 17.9 gm. and the value for urea was 48 mg. per 100 cc. of blood; the carbon dioxide combining power was 30 mEq per liter. Three phlebotomies totaling 1,500 cc. of blood were performed, after which the hematocrit reading was 64 per cent.

Studies of pulmonary function (Table I) 2 weeks after admission showed reduced vital, total and maximal breathing capacities but the residual volume was increased and the nitrogen washout index was abnormal. Arterial oxygen saturation was 84 per cent at rest and decreased to 80 per cent on exercise while breathing room air, but increased to 100 per cent on breathing oxygen. There was moderate expiratory slowing but no air trapping. The minute ventilation on oxygen was 12 liters, with a tidal volume of 660 ml.

On dismissal a week later, he weighed 191 pounds and felt greatly improved.

Studies of pulmonary function of this patient suggest that he had intrinsic pulmonary disease, but the abnormalities demonstrated are not definitively diagnostic. The striking reduction in maximal breathing capacity is somewhat out of proportion to the degree of airway obstruction demonstrated, and suggests a mechanical restriction of ventilation. The achievement of 100 per cent saturation on breathing pure oxygen rules out significant cardiovascular shunts. It was considered that this patient's obesity played a significant, if not the major role, in his respiratory dysfunction.

Case 7: A 46 year old dairyman came to the clinic in August, 1953, because of exertional dyspnea and easy fatigability. For many years he had had chronic asthmatic bronchitis with production of thick sputum on coughing. In the 10 years prior to registration at the clinic his weight had risen from 190 to 276 pounds, but he had recently lost 30 pounds by dieting.

His height was 69 inches and his weight was 246 pounds. The blood pressure was 140 mm. of mercury systolic and 104 mm. diastolic; he was plethoric; many rhonchi, dry ra les and wheezes were heard over the chest and cardiac sounds were distant. The retinal veins appeared congested on fundoscopic examination.

The concentration of hemoglobin was 16.6 gm. per 100 cc., with an erythrocyte count of 4,830,000, a leukocyte count of 8,600 and a hematocrit reading of 64 per cent. The total blood volume was 9,517 cc. and the plasma volume was 3,426 cc. A roentgenogram of the thorax showed cardiac enlargement with some passive congestion of the lungs, and an electrocardiogram showed slight left axis deviation with a prominent P wave in lead II.

Vital capacity, total lung capacity, expiratory reserve volume and maximal breathing capacity were reduced and the residual volume and the nitrogen washout index were elevated (Table I). Spirographic evidence of severe expiratory obstruction was observed. Arterial desaturation occurred when the patient was at rest and increased during exercise, but the saturation rose to 100 per cent when pure oxygen was breathed. The minute ventilation on oxygen was 6 liters, with a tidal volume of 390 cc.

The patient was advised to reduce weight, and measures to control his asthmatic bronchitis were prescribed.

He was examined again in August, 1954, at which time he complained that the dyspnea had increased in severity. He weighed 260 pounds, the concentration of hemoglobin was 19.1 gm. and the hematocrit reading was 74 per cent. The leukocyte and platelet counts were normal, but the total blood volume was 11,373 cc. A total of 2,500 cc. of blood was removed in five phlebotomies, which lowered the hematocrit reading to 63 per cent and caused some symptomatic improvement. He was given 4 mc. of radiophosphorus, and urged to reduce weight and stop smoking.

He reduced his weight to 215 pounds by January, 1955, and stayed at that weight for the subsequent year. Repeated hematologic examinations by his home physician showed normal results. He felt well, had minimal dyspnea and was able to carry on his usual occupation. In the spring of 1956 he gained 10 pounds in weight and noted increased dyspnea, cough and expectoration. The concentration of hemoglobin increased to 16.8 gm.

In June, 1956, he weighed 230 pounds and inspiratory and expiratory rhonchi were heard over the chest. The roentgenogram of the thorax was without abnormality, but the hematocrit reading was 63 per cent. Plasma clearance of radioiron was indicative of absolute polycythemia. Two phlebotomies were performed, radiophosphorus was administered, and he was again urged to lose weight.

The results of studies of pulmonary function, while not diagnostic, are consistent with the findings in asthmatic bronchitis plus early emphysema
and fibrosis. The clinical improvement associated with the loss of weight and the recurrence of symptoms with gain suggest that obesity may have been a considerable factor in aggravating the effects of this patient's chronic pulmonary disease.

Case 8: A 66 year old attorney came to the clinic in July, 1956, for further orthopedic treatment of a fracture-dislocation of the left humerus incurred in 1948. He had been obese for many years, and had weighed more than 300 pounds on several occasions. He had had exertional dyspnea for years. In 1954, he was treated for “chest congestion” with antibiotics. A roentgenogram of the thorax did not show evidence of any abnormality, but an electrocardiogram showed inverted T waves from leads V5 to V6. In May, 1956, he again had an episode of “chest congestion” and was given digitalis, with some improvement in his dyspnea.

His height was 67 inches and he weighed 300 pounds. He had dyspnea on mild exertion but no plethora or cyanosis. The lungs and heart appeared normal on physical examination and the blood pressure was 150 mm. of mercury systolic and 70 mm. diastolic. There were muscular atrophy and stiffness of the joints in the left hand and shoulder.

The hemoglobin measured 13.6 gm. per 100 cc. of blood and the erythrocyte sedimentation rate was 66 mm. in the first hour (Westergren method). The values for blood urea and serum proteins were normal. Albuminuris, grade 2, was present. A roentgenogram of the thorax appeared normal. The electrocardiographic findings of left axis deviation and inverted T waves in leads II, III, V5, V6 and V7, were interpreted as indicating left ventricular hypertrophy.

The patient was placed on a reduction diet of 800 calories and the use of digitalis was continued. A loss of 25 pounds occurred in a month, at which time tests for pulmonary function were performed (Table I). The vital capacity, expiratory reserve volume and maximal breathing capacity were greatly reduced, and the residual volume was slightly increased. Air trapping was not present and expiratory slowing was minimal. The arterial oxygen saturation was 97 per cent at rest, decreased to 93 per cent after 3.5 minutes of exercise on breathing room air and increased to 100 per cent on breathing pure oxygen. The minute ventilation on air was 13 to 14 liters at rest and this increased to 40 liters per minute after 3 minutes of exercise.

FIGURE 5: Graphic relationship of total blood volumes in five obese persons to normal blood volume-weight regression line (derived from the data of Funkhouser and associates."

Extrapolated portions of regression line are indicated by dots. The numeral beside each plotted total blood volume indicates the case number. In Case 5, the plotted value does not include 1,500 ml. of blood removed previously by phlebotomies.
The lung volumes in this case are compatible with those found in cases of extreme obesity. The marked reduction in maximal breathing capacity in the absence of obstruction in the airway and the inability of the patient to ventilate sufficiently during exercise to maintain a normal arterial saturation is strong evidence in favor of a mechanical restriction of ventilatory capacity. The normal nitrogen washout index and the absence of significant expiratory slowing rule out chronic obstructive emphysema. Although the history suggests that pulmonary congestion of cardiac origin might have been present in this patient, it has been shown that exertional dyspnea of cardiac origin is not accompanied by significant reductions in vital capacity or maximal breathing capacity in the absence of signs of congestive failure.

Comment

The mechanism by which obesity produces respiratory insufficiency is of great theoretical interest. The immediate cause of the arterial hypoxemia appears to be alveolar hypoventilation, which has been a prominent feature of those reported cases with complete studies of pulmonary function. In the Cases 1, 2 and 3 of this report, hypoventilation was diagnosed on clinical grounds, but adequate studies of minute ventilation were not performed. Sieker and associates suggested that the reduced functional residual capacity which has been recorded in some cases may be a contributory factor in that the lung volume "may be inadequate to prevent marked swings in arterial oxygenation with shallow breathing."

A reduced vital capacity, which has been attributed to diaphragmatic elevation and mediastinal deposition of fat has been an almost constant finding in the reported cases of obesity with polycythemia, but it is not clear how a reduction in vital capacity, per se, can cause alveolar hypoventilation and hypoxemia. It is well known that patients with certain neuromuscular diseases may exhibit large decreases in vital capacity and yet maintain a normal arterial oxygen saturation at rest. In a large series of patients studied at the Mayo Clinic at varying intervals after pneumonectomy, arterial oxygen saturations were invariably normal when the patient was at rest despite striking reductions in vital capacities and functional residual capacities. Even during the standard exercise test, a significant decrease in arterial oxygen saturation was infrequent in these patients.

Kerr and Lagen postulated that obesity causes lumbar lordosis and thoracic kyphosis which lead to postural emphysema. It has never been shown that the ill-defined condition known as postural emphysema can lead, in itself, to arterial hypoxemia. Mack and Snider stated that thoracic kyphoscoliosis never leads to chronic cor pulmonale in the absence of recurrent bronchial infections with the development of chronic obstructive emphysema. Spirographic evidence of obstruction of the airway
has not been a conspicuous feature in the reported cases of obesity with polycythemia.

Other authors\textsuperscript{10, 13, 14} have suggested that alveolar hypoventilation in extreme obesity is a result of impaired ventilatory mechanics. Although there are no reported studies on the work of breathing in obese persons, it is reasonable to assume that deposits of fat on the thoracic wall and in the abdomen could significantly increase the mechanical work of breathing, and hence the consumption of oxygen. The almost universal presence of dyspnea in the obese would support this concept.

It can be postulated that the mechanical effects of extreme obesity upon ventilation may, in some instances, be accompanied by such an increase in the work of breathing that the respiratory centers maintain alveolar ventilation at a suboptimal level in order to decrease the work load. This suboptimal level permits alveolar and other bodily carbon dioxide tensions to increase, and may represent a compromise between the abnormally large amount of work required to accomplish ventilation and the tendency of the respiratory center to prevent accumulation of carbon dioxide by increasing alveolar ventilation. That a normal respiratory center will permit elevated arterial levels of carbon dioxide to persist when the work of breathing is abnormally increased has been demonstrated by Cherniack and Snidal\textsuperscript{26} who found that artificial increases of airway resistance in normal persons greatly reduced the ventilatory response to inhaled carbon dioxide.

In extreme obesity, the mechanical restriction of ventilation might be manifested by failure of ventilation to increase adequately during exercise (as in Case 8) and later by alveolar hypoventilation at rest. The consequent hypercapnia would eventually diminish further the sensitivity of the respiratory centers and thus tend to perpetuate the hypoventilation. The functional nature of the entire process is shown by (1) the ability of one patient (Case 1) to achieve normal arterial oxygen saturation on voluntary hyperventilation and (2) the repeated reports of complete recovery after adequate loss of weight (as in Case 3).

In Cases 5, 6 and 7 the minute ventilation, though of sufficient magnitude to maintain oxygenation in normal persons, was not adequate to prevent arterial oxygen desaturation in these three patients who had diseased lungs. It is postulated that the increased work of breathing due to obesity prevented these patients from achieving a more adequate ventilatory response to hypoxemia and hypercapnia caused by intrinsic pulmonary disease.

The cardiovascular manifestations of the syndrome are of interest. Clinical signs of congestive failure have been noted in several reported cases. Cardiac catheterization in three cases\textsuperscript{10, 12} revealed pulmonary hypertension which was attributed to chronic arterial hypoxemia. Electrocardiographic evidence of right ventricular hypertrophy or strain has been noted commonly, and right ventricular dilatation and hypertrophy was demonstrated at necropsy in one instance.\textsuperscript{27} For these reasons, the
signs of congestive failure have been attributed to right heart failure. Although cardiac catheterization was not performed on any patients in the present series, the repeated electrocardiographic findings of right ventricular overload which improved with loss of weight and the pathologic demonstration of hypertrophy of the pulmonary arterioles in Case 4 are confirmatory evidence that pulmonary hypertension is commonly present. However, the possible presence and importance of left cardiac failure cannot be summarily dismissed. In Cases 2, 3 and 4, the findings on physical examination were suggestive of pulmonary congestion, and dye curves in Cases 1 and 3 showed prolonged circulation time. The deleterious effect of obesity on cardiac disease is well documented, and in a pathologic study of the hearts of 139 obese patients, Smith and Willius reported four cases in which frank congestive failure had occurred in the absence of organic heart disease, necropsy demonstrating only fatty deposits in the subepicardium with some fatty infiltration between the muscle bundles. Pulmonary congestion and edema may lower the vital capacity and maximal breathing capacity and increase the work of breathing. Thus pulmonary congestion, whether due to left ventricular failure or to polycythemia, would tend to decrease alveolar ventilation even further. In several cases of the present series, phlebotomy and control of cardiac failure with the use of digitalis and mercurials appeared to bring about considerable clinical improvement before any great reduction in weight had been achieved.

Arterial hypertension which diminished with loss of weight was found in Cases 1, 3 and 5. Although a high incidence of hypertension has been reported among obese persons, it has been shown that indirect recordings of arterial pressure with the standard 13 cm. cuff often give erroneously high values in these persons. In Case 3, the blood pressure measured directly with an intra-arterial needle was strikingly lower than the indirect measurements.

Polycythemia noted in patients in the present series and in series previously reported appears to be secondary rather than primary. This concept is supported by (1) the absence of leukocytosis, thrombocytosis, myeloid immaturity and splenomegaly, (2) the presence of arterial hypoxemia and (3) the tendency of the polycythemia to correct itself after weight is reduced and arterial oxygen saturations return to the normal range. The values for total blood volume in the present series, when calculated on the basis of actual weight, are within the accepted range. However, it has been shown recently that the regression line relating total blood volume to body weight, while linear, does not pass through the intersection of the co-ordinates. Therefore, the volume of blood per kilogram of body weight is not constant at different weight values; the blood volume per kilogram body weight for thin people is higher than the "normal" value and that of obese people is lower. The graphic plots of total blood volume against weight were significantly above the true regression line in each of the five cases in this series in which blood volume was studied, indicating absolute polycythemia (Fig. 5).
SUMMARY

Marked obesity may be associated with alveolar hypoventilation, arterial hypoxemia, hypercapnia and secondary polycythemia in the absence of primary pulmonary or cardiac disease. Pulmonary hypertension and right cardiac failure may develop secondarily. Appropriate loss of weight is accompanied by reversal of these complications. In patients with primary pulmonary or cardiac disease, obesity aggravates the dysfunction and loss of weight may produce considerable clinical improvement.

The cases of eight obese patients studied at the Mayo Clinic are reported. In four patients, obesity and secondary polycythemia were present without intrinsic pulmonary disease. In three patients with primary pulmonary disease, obesity was thought to have played a significant role in the development of hypoxemia and secondary polycythemia. One patient did not have polycythemia but tests of pulmonary function suggested that he manifested the early stages of ventilatory impairment of obesity.

It is suggested that the mechanical effect of obesity in increasing the work of breathing is the primary factor in the genesis of the alveolar hypoventilation which appears to be the significant abnormality.

RESUMEN

La obesidad marcada puede asociarse con hipoventilación alveolar, hipoxemia, hipercapnia y policitemia secundaria en ausencia de enfermedad primaria respiratoria o cardíaca. La hipertensión pulmonar y la insuficiencia cardíaca derecha pueden desarrollarse más tarde. La pérdida de peso adecuadamente obtenida se acompaña de mejoría de estas complicaciones. En los enfermos con enfermedad primaria pulmonar o cardíaca la obesidad agrava la disfunción y la pérdida de peso produce mejoría considerable.

Se relatan los casos de ocho enfermos obesos estudiados en la Clínica Mayo. En cuatro enfermos la obesidad y la policitemia secundaria se encontraron sin enfermedad pulmonar intrínseca. En tres enfermos con enfermedad pulmonar primaria se pensó que la obesidad desempeñó un papel de significación en el desarrollo de hipoxemia y policitemia secundaria.

Un enfermo no tuvo policitemia pero las pruebas de función pulmonar sugirieron que manifestaba los inicios de una insuficiencia ventilatoria de la obesidad.

Se sugiere que el efecto mecánico de la obesidad al aumentar el trabajo de la respiración es el factor primario en la génesis de la hipoventilación alveolar que parece ser la anormalidad significante.

RESUME

Une obésité accentuée peut être associée à une hypoventilation alvéolaire, à l’hypoxémie artérielle, à l’hypercapnée et à la polycythémie en l’absence d’affection initiale pulmonaire ou cardiaque. Une hypertension pulmonaire et une atteinte cardiaque droite peuvent survenir secondairement. Une perte de poids proportionnée suit la régression de ces compli
cations. Chez les malades atteints d'affection initiale pulmonaire ou cardiaque, l'obésité aggrave le dysfonctionnement et la perte de poids peut amener une amélioration clinique considérable.

Les auteurs rapportent les cas de huit malades obèses étudiés à la Clinique Mayo. Chez quatre malades, l'obésité et la polycythémie existaient sans affection pulmonaire initiale. Chez trois malades atteints d'affection pulmonaire primitive l'obésité fut considérée avoir joué un rôle indiscutable dans l'apparition de l'hypoxémie et de la polycythémie secondaire. Un seul malade n'était pas atteint de polycythémie mais les tests de la fonction pulmonaire montrèrent qu'il présentait les premiers symptômes d'un trouble ventilatoire dû à l'obésité.

Les auteurs pensent que l'effet mécanique de l'obésité, en augmentant le travail respiratoire, est le premier facteur dans la génèse de l'hypoventilation alvéolaire qui paraît à première vue être l'anomalie essentielle.

**ZUSAMMENFASSUNG**


Es wird die Vermutung ausgesprochen, dass die mechanische Wirkung der Fettsucht mit ihrem Anstieg der Atemtätigkeit der primäre Faktor bei der Genese der alveolären Hypoventilation ist, die die bezeichnende Abweichung von der Norm zu sein scheint.

**REFERENCES**