Reversible Cardiopulmonary Syndrome with Extreme Obesity

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A syndrome consisting of obesity, somnolence, cyanosis, periodic breathing, and polycythemia, with congestive heart failure has been observed in 6 patients. The effect of weight reduction and the mechanisms responsible for the symptoms and signs are discussed.

Six obese patients have been observed during the past 3 years, with remarkably similar symptoms and findings. These consisted of somnolence, cyanosis, periodic breathing, polycythemia, rightward electric axis by electrocardiogram, and the clinical picture of congestive heart failure. The syndrome appears to be related to obesity and may be reversed by weight reduction. The present report outlines the features of the syndrome and offers a tentative explanation of its production.

Case Reports

Case 1 (E. F.)

A 50-year-old white housewife was admitted to Duke Hospital in May 1951, with dyspnea, orthopnea, and ankle edema, of 1 year's duration. She had been obese all of her life. At age 13 she weighed 193 pounds; at age 22 she reached 258 pounds. This weight was maintained until about age 37, when she was told she had hypertension, and was treated with diet, bed rest, and "thyroid tablets." She lost 50 pounds and her blood pressure was said to have become normal. However, she again began to gain weight, and 1 year before admission, when her symptoms began, she weighed 325 pounds. About 11 months prior to admission the patient was placed on a low-salt diet by her local physician with relief of dyspnea, orthopnea, and ankle edema. This improvement continued until about 3 months before admission, when symptoms recurred. At that time she also noted a blue tinge to her lips and nails. Marked somnolence had developed, and the patient's daughter described periods of alternate apnea and deep noisy respirations during sleep.

On admission the patient was in respiratory distress. Her weight was 364 pounds; her height was 64\(\frac{1}{4}\) inches. Blood pressure as measured by a standard cuff, was 150/90 mm. Hg; the respiratory rate was 28 per minute. There was cyanosis of the lips and nails. Rales at both lung bases, cardiomegaly, ascites, and moderate pitting edema of both legs were observed.

The red blood count was 6.75 million, the hemoglobin 19.0 Gm., and the hematocrit 61 volumes per cent. The white blood count was 8,800 with a normal differential count. The number of platelets on a stained smear was not increased. Urine examination revealed a specific gravity of 1.013, a trace of protein, and no sugar. A fasting blood sugar was 109 mg. and the blood cholesterol was 110 mg. per 100 ml. The basal metabolic rate was plus 36 per cent by the usual weight-height standards. An electrocardiogram revealed right axis deviation and T-wave abnormalities that were of uncertain significance (fig. 1).

The patient received digoxin, mercurial diuretics, and a low-salt 800-calorie diet. Improvement in symptoms was prompt. Blood pressure fell to normotensive levels on the second hospital day, and remained there during the entire hospitalization. Inhalations of 100 per cent oxygen produced a reversal of her cyanosis to a normal pink color. As the patient lost edema fluid and weight, the red blood count, hemoglobin level, and hematocrit level gradually rose. One liter of blood was withdrawn during the latter part of her hospital stay. She lost 66 pounds of weight in 20 days and was remarkably improved symptomatically.

After discharge the patient was occasionally seen in the outpatient department. Her weight gradually fell to 208 pounds in March 1952. At this time her hemoglobin level was 13.5 Gm. and the hematocrit value was 46 volumes per cent. She was symptom free, and digitalis was discontinued. During the next 1\(\frac{1}{2}\) years she again began to gain weight and was readmitted to Duke Hospital on August 21, 1953, at her own request for more intensive dietary restriction. At this time she weighed 234 pounds. There were no symptoms of congestive heart failure. Blood pressure was 120/85 mm. Hg. The lungs were normal, and there was no cardiomegaly. Hemoglobin level was 14.0 Gm., red blood count was 4.6 million, and the hematocrit reading was 45 volumes per cent. White blood count was 6,600. Urine examination revealed a specific gravity of 1.025, with no protein or sugar. An electrocardio-
after exertional dyspnea was noted, he was seen by his physician, who administered mercurial diuretics with moderate relief of symptoms. The past history was unremarkable except for an episode of arthritis involving both feet and knees, 8 years previously. He recovered from this episode in 2 weeks, and had been symptom free until the onset of the above symptoms. He denied previous chest pain, hypertension, or renal disease.

On admission the patient was dyspneic and orthopneic. His weight was 257 pounds and his height was 63 1/2 inches. The blood pressure was 140/120 mm. Hg, and the pulse was regular at 150 per minute. The fundi were normal. Bilateral basilar rales, cardiomegaly, a grade I apical systolic murmur, hepatomegaly, ascites, and marked lower extremity edema were present on admission.

The hemoglobin was 14.8 Gm., and the hematocrit value was 43 volumes per cent. The white blood count was 5,500, with a normal differential count. Urinalysis showed a specific gravity of 1.006, a faint trace of protein, and no sugar. The fasting blood sugar was 108 mg. and the nonprotein nitrogen was 38 mg. per cent. An electrocardiogram revealed a vertical electric axis, atrial flutter with 2:1 A-V block, and a ventricular rate of 150 per minute. Films of the chest showed marked cardiac enlargement that was thought to be chiefly left ventricular. Fluoroscopy revealed no atrial enlargement. Skull films were normal. Basal metabolic rate was plus 32 per cent.

On admission the patient was placed on a 1000-calorie, 200-mg. sodium diet, and a mercurial diuretic was administered. The patient lost 7 pounds during the first 24 hours. Symptomatic improvement was striking. The atrial flutter with 2:1 block remained unchanged for the first 4 hospital days; digitalization then increased the block to 4:1. Quinidine failed to abolish the atrial flutter.

With improvement in dyspnea and orthopnea in the first few days of hospitalization, the patient was noted to be extremely somnolent, falling asleep whenever left quiet for a few minutes. During these periods Cheyne-Stokes respirations were noted. On the third day of hospitalization, during cardiac catheterization, arterial oxygen saturation ranged from 51 to 78 per cent during the periodic breathing. Inhalations of 100 per cent oxygen for 15 minutes raised the arterial oxygen saturation from 78 to 99 per cent.

After 3 weeks of hospitalization the patient was allowed to return home for a 2-week leave of absence. During this period he stopped all medications and relaxed his dietary sodium restriction without change in his symptoms. Atrial flutter continued with a regular 4:1 block. He was then discharged on April 28, 1954, on a 1200-calorie low-salt diet, but with no digitalis or diuretics. He had lost 65 pounds during his hospitalization.

On a return visit his weight was 187 pounds.
He had noted no return of his original symptoms of congestive heart failure. Blood pressure was 140/100 mm Hg, and the pulse rate varied between 60 and 100 per minute. The rhythm was irregular as the degree of A-V block shifted from 2:1 to 4:1. There were no signs of congestive heart failure.

The hemoglobin was 14.4 Gm., the hematocrit value 48 volumes per cent, and the white blood count 6,100. Urine analysis was negative except for a slight trace of protein. Arterial oxygen saturation was 93.5 per cent. Because of the arrhythmia he was digitalized and a regular 4:1 block resulted. He was discharged on June 7, 1954, having further reduced his weight to 177 pounds.

The patient was readmitted on April 11, 1955, for reevaluation of the cardiac status. His weight had increased to 206 pounds. He had continued to take digitals, but had not followed his salt-free reduction diet. In spite of the weight gain and the dietary indiscretions, the patient felt well, with no recurrence of the original signs and symptoms of congestive heart failure. Blood pressure on admission was 160/120 mm Hg. There was no somnolence or cyanosis. Cheyne-Stokes respirations again appeared when the patient slept. Mild cardiomegaly was seen on chest film. The hemoglobin was 15.2 Gm. with a hematocrit reading of 48 volumes per cent. Fasting blood sugar was 108 mg. per 100 ml. Glucose tolerance test was normal. Visual fields were normal. An electrocardiogram revealed normal sinus rhythm and a shift in electric position from a vertical position to a normal intermediate position. Arterial oxygen saturation ranged from 90 per cent to 93 per cent, rising to 100 per cent with inhalations of 100 per cent oxygen.

He was again placed on a low-sodium, 1000-calorie diet at the time of discharge. Since then he has remained free of symptoms, but has been unable to follow his diet. His weight had increased to 214 pounds on his last outpatient visit on November 10, 1955.

Though the onset of congestive failure in this patient may have been immediately precipitated by the development of the atrial flutter, this abnormality did not explain the arterial oxygen unsaturation, the somnolence, and other features. For this reason the case was regarded as a true example of the syndrome.

Case 3 (R. P.)

A 34-year-old white farmer was admitted to the Veterans Administration Hospital, Fayetteville, North Carolina, on October 18, 1954. He had been referred to that hospital because of signs and symptoms of congestive heart failure. The patient weighed 147 pounds in 1945 at the time of discharge from the Army. He had gradually gained weight up to a maximum of 300 pounds at the time of admission. Progressive exertional dyspnea had been present for 4 years, and ankle edema and orthopnea for 1 year.

During that time he had received weekly mercurial diuretics from his local physician. On admission he was acutely dyspneic and plethoric. There was cyanosis of the lips and nail beds. Blood pressure was 104/70 mm Hg. Moist rales were heard over both lung bases, and there was pitting edema of both feet and ankles.

Admission laboratory work was as follows: hemoglobin 18 Gm., hematocrit 63 volumes per cent, white blood count 10,600, with a normal differential count. Urine analysis was negative except for a trace of protein and 6 to 8 white blood cells per high-power field. Nonprotein nitrogen was 38 mg. per 100 ml. A chest film revealed cardiomegaly and prominence of the pulmonary arteries. An electrocardiogram showed a Q wave in lead III, and in V1 to V4. The QRS vector was extremely posteriorly directed, the QRS being predominantly down in all the V leads. These findings were of uncertain significance.

The patient was placed on an 800-calorie low-sodium diet and digitalized with digoxin. He was maintained on 0.15 mg. of digoxin daily and was given mercurial diuretics every 2 to 3 days. He lost 25 pounds in the first 3 weeks. His improvement in symptoms was dramatic.

To obtain more specialized studies the patient was transferred on November 19, 1954, to the Veterans Administration Hospital, Durham, North Carolina. At that time he was much improved symptomatically as compared to his state 3 weeks earlier. He complained only of dyspnea on unusual exertion; however, cyanosis was still present. His weight was 269 pounds. Blood pressure was 130/85 mm Hg. Cheyne-Stokes respiration was noted during sleep. There were no signs of congestive heart failure except for a 1 plus pitting edema of the ankles. Heart size was difficult to evaluate because of the patient’s obesity. There was no hepatomegaly or splenomegaly.

Laboratory studies were as follows: hemoglobin 19.3 Gm., hematocrit 60 volumes per cent. The cells were normochromic and normocytic. White blood count was 11,550, with a normal differential count. Platelet count was normal. Urine analysis revealed no abnormalities. Nonprotein nitrogen was 18 mg. and blood cholesterol was 210 mg. per 100 ml. Serum uric acid was elevated to 7.7 mg. per 100 ml. A bone marrow smear and iron turnover studies were normal. Visual fields and skull films were normal. Fluoroscopy of the chest revealed a transversely placed heart with no specific chamber enlargement. An electrocardiogram revealed a vertical electric axis. The T waves were inverted in V1, V2, and V3, and were compatible with anterior wall ischemia.

Pulmonary function studies showed a reduced functional residual capacity and expiratory reserve. Cardiac catheterization studies revealed moderate elevation of pulmonary arterial pressure (mean =
25 mm. Hg) with a normal pulmonary wedge pressure (3 mm. Hg). Cardiac output was normal. Resting arterial oxygen saturation was 90 per cent. During periodic breathing his arterial oxygen saturation fell to 75 per cent.

The patient remained hospitalized for 6 weeks, during which period he was given an 800-calorie low-sodium diet. His weight declined to 243 pounds, with a steady improvement in dyspnea and somnolence. He was discharged on the same diet and digitoxin, 0.15 mg. daily.

The patient returned 6 months later for further study. He had lost weight to 233 pounds and still complained of mild dyspnea on exertion. There were no other signs or symptoms of congestive heart failure, but digitoxin was continued.

**Case 4 (N. S.)*

A 41-year-old white man was admitted to Duke Hospital in November 1954 for evaluation of lifelong obesity. Between the age of 16 and 26 years the patient weighed from 240 to 250 pounds. On occasions, with dieting, his weight decreased to 200 pounds. One year before admission he weighed 380 pounds. He continued to gain weight rapidly to the time of admission. With the rapid weight gain the patient had noted marked somnolence and would fall asleep when seated. Exertional dyspnea, orthopnea, and ankle edema had been present for 6 months.

On admission the patient was markedly obese, somnolent, dyspneic, and cyanotic with Cheyne-Stokes respiration. His weight was 462 pounds, his height 69 inches. Blood pressure was 170/110 mm. Hg, pulse rate 110 and respiratory rate 20 per minute. The remainder of the physical examination was remarkable only in the marked obesity and the presence of brawny edema of the lower abdomen and legs.

The hemoglobin level was not determined but the hematocrit value was 60 volumes per cent. The white blood count was 9,500, with a normal differential count. Urinalysis revealed a specific gravity of 1.018, no sugar, and a trace of protein. The fasting blood sugar was 111 mg., the blood cholesterol was 154 mg. per 100 ml., carbon dioxide combining power was 22.3 mEq. per L. Chest x-ray showed cardiac enlargement and increased lung markings. Skull films were negative. Right axis deviation was present on the electrocardiogram. Urine gonadotropin and 17-ketosteroid excretions were within normal limits.

The patient was placed on a reduction diet and 2 months later his weight was 342 pounds, representing a loss of 120 pounds. Digitalis and mercurial diuretics were not used, though salt intake was restricted as part of the reduction diet. He was less somnolent and less dyspneic on exertion. He had no orthopnea, and Cheyne-Stokes breathing occurred only intermittently with deep sleep. The hemoglobin was 16 Gm. per 100 ml.

The diet was followed closely and 1 year later the patient weighed 286 pounds and no longer had exertional dyspnea, ankle edema, somnolence, or Cheyne-Stokes breathing. At this time the hemoglobin was 15.7 Gm. per 100 ml.

**Case 5 (R. G.)**

A 44-year-old white farmer was admitted to Duke Hospital in May 1955 because of substernal pain that had been present for 1 day. The patient first began to gain weight about 15 years before admission and reached a maximum of 268 pounds 2 to 3 years before admission. At that time he noted exertional dyspnea, orthopnea, occasional episodes of paroxysmal nocturnal dyspnea, and ankle edema. The patient had somnolence during this period and his family commented on his irregular breathing during sleep. The somnolence and irregular breathing were so severe that the patient's family and friends often urged that he seek medical aid. The past history was otherwise negative except for bouts of epigastric pain occurring before meals and relieved by food and antacids.

On physical examination the patient was obese and somnolent, weighed 230 pounds, and was 70 inches in height. The blood pressure was 140/100 mm. Hg, the pulse rate was 80 per minute, the respiratory rate was 12 per minute with Cheyne-Stokes breathing during sleep (fig. 2). The optic fundi were normal. There were scattered rhonchi throughout the chest. Cardiomegaly and abdominal obesity were present, but there was no peripheral edema.

Pertinent admission laboratory data included a hemoglobin of 20 Gm., a hematocrit of 61 volumes per cent, and a white blood count of 8,950. Urinalysis showed a specific gravity of 1.013 and a 1 plus protein. Fasting blood sugar initially was 145 mg. per 100 ml.; when repeated later it was found to be 110 mg. fasting and 145 mg. per 100 ml. 2 hours after a meal. The blood cholesterol was 401 mg. per 100 ml. The electrocardiogram showed slight right axis deviation. Chest x-ray revealed cardiomegaly, and skull films were negative. A gallbladder series

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* Courtesy of Dr. Walter Kempner.

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**Fig. 2.** Variation in arterial oxygen saturation (ordinate, per cent) with various phases of Cheyne-Stokes breathing, case 5 (R. G.). Arterial oxygen values were read from an ear oximeter.
Case 6 (S. W.)

A 28-year-old unemployed Negro man was admitted to Duke Hospital in April 1954 for investigation of marked obesity. At age 10 years, the patient weighed 125 pounds and continued to gain in association with excessive intake of food. The patient weighed 355 pounds at age 20 and 550 pounds at the time of admission. The estimated food intake during this period was 11,000 calories per day. Somnolence had been noted for several years, more marked in the year before admission. During the previous year the patient had also noted ankle edema, orthopnea, and exertional dyspnea. Cheyne-Stokes breathing during sleep was described by the family. Polyuria, polydipsia, and nocturia had also been observed for a period of 6 to 8 months before admission.

On physical examination the patient weighed 555 pounds and was 74½ inches tall (fig. 3). The blood pressure was 210/160 mm. Hg., pulse rate was 140 per minute, and the respiratory rate was 23 per minute. Prominent physical findings were striae over the shoulders and buttocks, massive obesity, and 4-plus pretibial edema. Neurologic examination was negative. Rectal examination revealed thrombosed and bleeding hemorrhoids.

The accessory laboratory findings included a hemoglobin of 12.1 Gm., a white blood count of 7,900, a urine specific gravity of 1,022, with 1 plus proteinuria and 1 plus sugar. Repeat urine analysis did not show glycosuria. The fasting blood glucose was 111 mg. and 113 mg. per 100 ml. 2 hours after eating. The carbon dioxide combining power was 35.7 mEq. per L., and the cholesterol was 135 mg. per 100 ml. Urinary excretion of gonadotropins and 17-ketosteroids was slightly low. Skull films were negative. Chest x-ray was impossible because of the marked obesity. Electrocardiogram showed no axis deviation, T waves were inverted in leads I and aV_{5}, and flat in V_{2} and V_{6}; they were thought to be compatible with left ventricular ischemia.

After these studies it was believed that the patient's excessive obesity was solely the result of his tremendous food intake, and he was discharged on a reduction diet.

The patient did not follow his diet and was readmitted to the hospital in June 1955. He had gained weight to 598 pounds and was more dyspneic.

Physical examination was essentially unchanged except that the patient was obviously more obese.

The admission hemoglobin was 12.0 Gm. per 100 ml., and urinalysis showed 1- to 2-plus proteinuria and no sugar. The fasting blood sugar was 108 mg., and the blood cholesterol 85 mg. per 100 ml. Other laboratory values were a blood carbon dioxide combining power of 32 mEq., a serum sodium of 148 mEq., and a serum potassium of 4.5 mEq. per L. Radioactive iodine uptake was 18 per cent. Skull x-rays were again negative and chest x-ray was not possible. The electrocardiogram showed no axis deviation, atrial flutter, and nonspecific T-wave changes. An initial stool specimen was guaiac positive, which was thought to be related to bleeding hemorrhoids. A later stool revealed no occult blood.

The patient was placed on an 800-calorie low-sodium diet and after 1 week was digitalized with
1.2 mg of digitoxin and maintained on 0.1 mg of digitoxin daily. In 2 weeks the patient had lost 44 pounds and showed moderate symptomatic improvement, but continued to be somnolent with marked periodic breathing during sleep. At this time the patient was given 10 mg of dextroamphetamine (Dexedrine) daily to decrease his somnolence, and started on active program of exercise by the physiotherapy department. Four weeks later he had lost 94 pounds, was no longer drowsy or orthopneic, and had less exertional dyspnea. Ten weeks after the above program was instituted the patient had lost 143 pounds, weighing 455 pounds. After discharge the patient did not follow the diet, and the progressive decline in weight observed in the hospital did not continue. He remained markedly improved, however, and found employment as a ditch digger and plasterer. During this time he complained of moderate ankle edema, but no exertional dyspnea, orthopnea, or somnolence.

**Review of Literature**

The authors are not the first to recognize such a syndrome associated with extreme obesity. Grant has studied several such cases, one of which came to postmortem examination and was found to have marked right ventricular hypertrophy and advanced pulmonary siderosis, with no hemosiderin in other areas. He postulated that this was related to a combination of unusual oxygen requirements and a mechanical ventilatory impairment, both secondary to obesity. The existence of such a syndrome was first suggested to the authors by Dr. Robert P. Grant, who reviewed the electrocardiograms of case no. 1.

Previous published reports have described one or more features of the syndrome in extremely obese patients. Spitz reported 3 obese patients with narcolepsy, periodic breathing, and somnolence. At autopsy, 2 of these patients had findings compatible with Cushing’s syndrome. The third improved with weight reduction, with disappearance of the polycythemia and narcolepsy. One of the 2 autopsied cases had hypertrophy of both ventricles with marked left ventricular dilatation. During life this patient had had left axis deviation on the electrocardiogram. The other autopsied case had marked hypertrophy of the right ventricle. During life this patient had a normal electrocardiogram. The third patient, who improved on weight reduction, had hypertrophy and dilatation of the left ventricle on chest film, but marked right axis deviation by electrocardiogram. Though all of Spitz’s cases show certain features of the syndrome, the third case seems to fit all the criteria, including improvement with weight reduction.

Olsen and Wilius reported a male patient with extreme obesity, congestive failure, marked dyspnea, cyanosis, and polycythemia. The electrocardiogram revealed marked right axis deviation. With weight reduction from 302 to 277 pounds, diuresis, and 3 venesections, he was greatly improved symptomatically. The illness was thought to be related to pulmonary arteriolar sclerosis (Ayerza’s disease) and hypertensive vascular disease, though the blood pressure ranged from 94/74 to 145/92 during the period of observation.

Cutting has emphasized the frequent coexistence of obesity and narcolepsy suggesting that both might be of hypothalamic origin. Polycythemia is also pointed out as a frequent finding in narcolepsy. Three cases were cited.

Auchincloss, Cook, and Renzetti have reported a markedly obese patient with cyanosis, polycythemia, and heart failure in whom detailed pulmonary function studies and cardiac catheterization were carried out. The markedly reduced arterial oxygen saturation (30 percent) and the carbon dioxide retention seen in this patient were thought to be caused by alveolar hypoventilation. The pulmonary arterial pressure was elevated (95/50).

Weil and Prasad have reported 5 markedly obese patients with marked polycythemia, in 3 of whom the polycythemia was reversed by weight reduction alone. These patients were found to have a decreased vital capacity, a decreased arterial oxygen saturation, and an elevated serum carbon dioxide content. Polycythemia was thought to be a result of hypoxia resulting from poor ventilation.

Johnson, Lillehei, and Miller have studied 2 patients with extreme obesity, arterial oxygen unsaturation, and carbon dioxide retention. These patients demonstrated profound alterations in pulmonary ventilation and blood flow, particularly in the supine position. In this position there was a rise in intrathoracic pressure and a decrease in total lung volume and fune-
tional residual capacity. The effective diffusing capacity of the lung was decreased, and the work of breathing greatly increased in the supine position. Other studies suggested the appearance of a true right-to-left shunt in the supine position. All these alterations were thought to be entirely related to obesity.

Benaim and Worster-Drought\(^9\) have reported an individual with dystrophia myotonica of the diaphragm, with pulmonary hypoventilation and secondary polycythemia. This individual was also obese. Other cases fitting the syndrome have been reported by Burwell\(^11\) and Counihan.\(^12\)

**Discussion**

The similarity of the 6 patients reported here and those cited suggests that the occurrence of somnolence, cyanosis, polycythemia, and congestive heart failure in conjunction with severe obesity is not a mere chance relationship but a true syndrome (fig. 4). The degree of obesity necessary for the development of the syndrome is not well defined. Several patients were obviously obese but at least 2 of the group were only obese when considered in relation to their height. Case 5, though complicated by possible arteriosclerotic heart disease, illustrates this point. In these individuals the excess weight was mainly confined to a large protuberant abdomen. It should be noted that most of the patients had gained large amounts of weight in the 6 to 12 months prior to onset of symptoms.

All were somnolent, and during sleep had a type of Cheyne-Stokes breathing. This type of breathing differed from the usual Cheyne-Stokes breathing seen in heart failure in that the periods of apnea and hyperpnea were shorter than usual, being 10 to 20 seconds in duration. All had evidence of hypoventilation during sleep, and in those patients in whom measurements were made, there was arterial oxygen unsaturation and elevation of carbon dioxide tension. In cases 2 through 6, the degree of arterial oxygen unsaturation was remarkably variable, usually in relation to the cycles of Cheyne-Stokes breathing. In case 1 the level of arterial oxygen saturation was not measured. In all in whom the observation was made, the cyanosis could be quickly reversed by several deep breaths or by inhalation of 100 per cent oxygen. Detailed data from cardiac and pulmonary function studies on these and other obese patients will be presented elsewhere.\(^13\)

Polycythemia occurred frequently, but was not always pronounced. One patient (S. W.) was anemic, which may have been the result of hemorrhoidal bleeding. A rightward electric axis was common but not always observed. On the other hand, none of the patients had left axis deviation or horizontal electric axis as would be expected in an obese patient. Not all of the patients had clinical evidence of congestive heart failure. The presence or absence of failure may be related to the stage of the illness and the presence of other unknown factors. Furthermore, the clinical impression of congestive heart failure was difficult to evaluate because dyspnea, orthopnea, and ankle edema could be related to the obesity.

Additional laboratory studies indicated that the syndrome observed was not related to a recognizable endocrinopathy such as Cushing’s syndrome. It is of interest that the patients had a high oxygen consumption and a low blood cholesterol.

The correction of the findings with weight reduction in 5 of the 6 patients suggests that obesity is the primary etiologic factor. The dietary restriction used in these patients caused a rapid decrease in weight except for case 5, who failed to lose significant weight during the period of observation. In 5 of the 6 patients, digitalization was carried out and mercurial diuretics were used at the same time that weight reduction was begun. In case 4, the symptoms were reversed by weight reduction.

![Fig. 4. Summary of findings in the 6 cases reported.](http://circ.ahajournals.org/lookup/fig/4)
alone, and in case 1 and 2, the symptoms have failed to recur after omission of digitalis and diuretics. For this reason weight reduction is considered to be the most important factor in treatment. The reversibility of the signs and symptoms of heart failure with weight loss is believed to be of significance in that it adds another to the list of reversible disorders causing congestive heart failure.

The signs and symptoms of congestive failure, when present, responded quickly to digitalis, diuretics, and salt restriction. Somnolence, Cheyne-Stokes respirations, and intermittent hypoxia persisted, however, disappearing only as weight loss progressed. In an attempt to reverse these latter findings more quickly, amphetamine was used in conjunction with diet in case 6, and was found to be effective in markedly reducing the degree of somnolence, the occurrence of Cheyne-Stokes breathing, and the hypoxia.

The exact relationship between obesity and the various features of the syndrome remains largely speculative. The somnolence and the Cheyne-Stokes respirations are presumed to be of central origin, yet the mechanism of their production remains unknown. They have been observed to disappear with weight reduction; therefore they are assumed to be related to the obesity. The question may be raised of the role of cerebral anoxia or hypercapnia in their production, yet other patients, i.e., those with congenital heart disease and chronic lung disease, have similar changes in blood gases without such symptoms.

The somnolence and Cheyne-Stokes respirations result in periodic hypoventilation, which is especially marked in sleep. Associated with these periods of hypoventilation there are remarkable drops in arterial oxygen saturation. The mechanism of the rapid fall in arterial oxygen saturation seems reasonably well established from studies of pulmonary function in these and other obese subjects. They have been found to have a striking reduction in expiratory reserve, especially with recumbency. Thus there is a smaller "reserve" of oxygen at the end of a normal expiration. At the same time the total consumption of oxygen in such obese subjects is very large. These features combine to produce a rapid fall in arterial oxygen saturation with breath holding or with the apneic phase of Cheyne-Stokes respiration.

The polycythemia seen in 4 of the 6 patients in this group is thought to be related to prolonged arterial oxygen unsaturation. The chief feature distinguishing it from polycythemia vera is its reversibility with weight reduction.

The mechanism of the heart failure and indeed its nature are obscure. Borderline hypertension has been seen in several subjects, but is thought to be due largely to the error of indirect blood pressure measurement in the obese individual. The roentgenograms of the chest were most often described as showing left ventricular enlargement or generalized cardiac enlargement. The electrocardiograms, though showing right axis deviation on standard and unipolar limb leads, show a posterior orientation of the QRS vector in space, rather than the anterior orientation usually seen in right ventricular hypertrophy. The electrocardiographic findings and the manner of their reversal are suggestive of the verticalization of the electric field seen with pulmonary emphysema, which is perhaps a distortion of the electric field as a result of the presence of poorly conducting, overdistended lungs. Obesity could conceivably produce similar changes as a result of the presence of epicardial fat, yet it is difficult to see why the change to a right axis is not seen more commonly in obese subjects if this is the case. At the present time, the electrocardiographic changes are considered to be secondary to changes in the heart, not to a recording artifact secondary to obesity. It seems more likely that the changes are a result of increased pressure on the right side of the heart or an increased relative size of the right side of the heart.

Cardiac catheterization is carried out with great difficulty in such patients because of their huge size and the resultant difficulty in visualization of the catheter during the procedure. In those that have been done, pulmonary arterial pressures have been moderately elevated. These patients show considerable variability of pulmonary arterial pressure during a single study. This has not been correlated with changes in arterial oxygen saturation, but is perhaps related to periodic anoxia. The authors
have had no opportunities for postmortem study of such cases. As previously stated, in the only known case in which the heart has been examined post mortem, right ventricular hypertrophy was present.

On the basis of present information it is postulated that the hypoventilation associated with periodic breathing especially during sleep, leads to hypercapnia and hypoxia, and that these in turn contribute to the development of polycythemia, pulmonary hypertension, right-sided cardiac enlargement, and ultimately to heart failure. Additional studies are needed to prove many of the steps in the above postulation.

**Summary**

A syndrome consisting of somnolence, cyanosis, periodic breathing, polycythemia, right axis deviation, and the clinical picture of congestive heart failure has been seen in a group of markedly obese patients. The symptoms and findings appear to be related to obesity and were, in most instances, reversed by weight reduction. It is postulated that hypoventilation leads to hypercapnia and hypoxia, and that these contribute to the development of polycythemia, pulmonary hypertension, right-sided cardiac enlargement, and ultimately to heart failure.

**Summario in Interlingua**

Un syndrome consistente de somnolentia, cyanosis, respiration periodic, polycythemia, e le tableau clinic de congestive disfallimento cardiac esseva notate in un grupo de marcatemente obese patiente. Le symptomas e le constatationes clinic esseva apparentemente connectite con le obesitate. In le majoritate del casos illos esseva revertite per reduction de peso. Es postulare que hypoventilation produce hypercapnia e hypoxia e que istos contribue al disveloppamento de polycythemia, hypertension pulmonar, allargamento dextero-cardiac, e ultimemente disfallimento cardiac.

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