# Massive Obesity Treated by Intermittent Fasting*

## *A Metabolic and Clinical Study*

WILLIAM K. STEWART, M.B., LAURA W. FLEMING, B.SC. *and* PETER C. ROBERTSON, M.B.
*Dundee, Scotland*

*"He that eats till he is sick must fast till he is well."*
T. FULLER
Gnomologia; Adagies and Proverbs, 1732.

RECENT therapy for obesity has included a variety of dietary regimens involving various combinations of fat, carbohydrate and protein; nevertheless, a successful outcome has been infrequent [*1*]. Even among those few who desire weight reduction sufficiently to endure a strict regimen, success has depended more on simple calorie restriction than on the detailed dietary composition [*2–6*]. It is surprising that complete starvation was not advocated as a specific therapy until six years ago [*7*] since it is presently recognised as both effective and relatively easily tolerated [*8–10*]. As starvation treatment is now likely to become widespread, it is important to study possible hazards. Ill effects, if they exist, will probably be most obvious in massively obese patients treated over long periods.

The arbitrary weight above which a patient can be regarded as massively obese is not established. We suggest that massive obesity exists when an adult weighs more than twice the normal predicted for his height at twenty-five years of age. Relatively few metabolic studies have been reported on the reduction of massive obesity [*11–14*]. Recently cases have been recorded as examples of the "Pickwickian syndrome" [*15*], the cardiorespiratory syndrome of obesity [*16*], the hypoventilation syndrome [*17*] and the cardiopulmonary syndrome [*18*] by investigators who emphasized the respiratory and cardiac consequences.

We have measured some of the metabolic consequences of prolonged starvation in a male patient who initially weighed over 200 kg.

### CASE REPORT

W.D. was born in 1901; his birth weight is unknown and during childhood he was tall but thin. Both parents, but only one of his grandparents, were obese. At fifteen years of age he became a deep sea fisherman and his weight began to increase until at the age of eighteen he weighed 86.4 kg. In his early thirties his weight was 114.5 kg. and remained steady until he was fifty-three years old, when he changed his occupation from deep sea fishing to river dredging. His weight then increased over the following eighteen months to 146.4 kg. Because he had dyspnoea on exertion he left the dredger and became a night watchman. His weight immediately increased, reaching 209.4 kg. at the age of fifty-six. Breathlessness became a severe handicap, and concurrently his legs began to swell.

In May 1957 the patient entered hospital elsewhere for treatment of his obesity. At that time there was no evidence of cardiac failure. Steroid assays did not reveal any abnormalities but glucose tolerance tests especially after cortisone administration demonstrated mild diabetes. On a 1,000 kcal. diet his weight decreased steadily from 209.4 to 169.2 kg. in nine months.

The patient returned to work but without supervision his weight again increased and he was admitted to our hospital in December 1962. He complained of breathlessness on minimal exertion and severe swelling of his feet and ankles. He was subject to "dizzy turns," pain in his back and pain in his legs on walking. He smoked about 30 cigarettes daily and had a frequent raucous cough which made him deeply cyanosed and was productive of mucoid sputum. He was not unduly somnolent and did not complain of attacks of angina pectoris or abdominal pain. Previous history otherwise was not relevant.

On examination (December 1962) his height was

* From the Department of Medicine, University of St. Andrews, Queen's College, Dundee, Scotland. Manuscript received October 18, 1965.

TABLE I
AVERAGE DAILY INTAKES

| Phase | No. of Days | Duration of Phase (days) | Type of Phase | Location | Treatment | Kcal. | Carbohydrate (gm.) | Fat (gm.) | Nitrogen† (gm.) | Sodium† (mEq.) | Potassium† (mEq.) | Calcium† (mg.) | Phosphorus (mg.) | Magnesium (mg.) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1–150* | 210 | Balance | Hospital | Eight 10 day periods of fasting alternating with seven 10 day periods of diet | 40 | 9 | 0 | 0 | 0 | 4 | 40 | 30 | 12 |
| | | | | | | 300 | 14 | 12 | 5 | 5 | 23 | 60 | 380 | 58 |
| | 151–210* | | | | Three 10 day periods of fasting alternating with three 10 day periods of diet | 80 | 11 | 1 | 1 | 3 | 5 | 250 | 210 | 30 |
| | | | | | | 380 | 25 | 13 | 6 | 9 | 25 | 310 | 590 | 87 |
| 2 | 211–280 | 70 | | Home | Home diet I | 760 | .. | .. | 8 | 66 | 33 | 425 | 810 | ... |
| 3 | 281–350* | 70 | Balance | Hospital | Four 10 day periods of fasting alternating with three 10 day periods of diet | 70 | 10 | 1 | 1 | 3 | 5 | 245 | 200 | 29 |
| | | | | | | 400 | 27 | 14 | 7 | 16 | 29 | 310 | 610 | 86 |
| 4 | 351–420 | 70 | | Home | Home diet II | 1,210 | 104 | 53 | 13 | 123 | 67 | 660 | 1,220 | 240 |
| 5A | 421–430 | 20 | Balance | Hospital | Same as in phase 4 | 1,210 | 104 | 53 | 13 | 123 | 67 | 660 | 1,220 | 240 |
| 5B | 431–440 | | | | Fasting | 70 | 10 | 1 | 1 | 5 | 26 | 260 | 240 | 70 |
| 6 | 441–456 | 16 | Equilibration | Home | Home diet II + calcium‡ supplements: 4 tablets/day | 1,210 | 110 | 50 | 13 | 149 | 87 | 2,180 | 1,240 | 240 |
| 7 | 457–466 | 10 | Balance | Hospital | Same as in phase 6 | 1,210 | 110 | 50 | 13 | 149 | 87 | 2,180 | 1,240 | 240 |
| 8 | 467–528 | 62 | Equilibration | Home | Home diet II + calcium‡ supplements: 2 tablets/day | 1,050 | 99 | 45 | 10 | . | . | 1,340 | 950 | ... |
| 9 | 529–540 | 12 | Balance | Home | Same as in phase 8 | 1,050 | 99 | 45 | 10 | . | . | 1,340 | 950 | ... |

* Intakes are expressed as the over-all averages for the ten day fasting periods and ten day diet periods, respectively.
† Confirmed by diet analysis
‡ Effervescent Calcium-Sandoz® tablets, each containing 380 mg. calcium as the glucogalacto-gluconate salt.

184 cm. and weight 200.4 kg. Obesity was generalized, affecting equally the trunk, face, neck and limbs. (Fig. 1.) The abdomen was pendulous, reaching to his knees. He was plethoric, cyanosed and breathless at rest. There was edema of the ankles, legs and sacrum but the jugular veins were obscured. He was in sinus rhythm with a blood pressure of 140/92 mm. Hg. The apex beat was not palpable and no cardiac murmurs were heard. Chest expansion was poor and sonorous rhonchi were heard. Abdominal organs were not palpable and there was no tenderness. Hernias, varicose veins and papilledema were absent.

During treatment (July 1963) there was an episode of severe epigastric pain associated with nausea and pyrexia. The gallbladder became palpably distended but roentgenograms did not reveal gallstones. With antibiotic therapy the cholecystitis subsided and the episode did not recur.

We estimated that during the patient's thirty-eight years as a fisherman his average daily intake while at sea was approximately 3,800 kcal., 16 per cent of which was provided by protein and 51 per cent by carbohydrate. His daily caloric intake doubled for two days every fortnight, due mainly to the consumption of beer while on shore; this 8,000 kcal. intake for two days every two weeks raised his over-all average daily intake to 4,400 kcal. Throughout this period the daily calcium intake, mainly from evaporated milk, was 1,900 mg.; vitamin intake was adequate.

The increase in weight, which occurred on changing to the less strenuous work on a dredger, coincided with a change in dietary intake. Caloric intake was decreased to between 3,000 and 3,200 kcal. daily, 12 to 14 per cent being provided by protein and about 40 per cent by fat. Calcium intake was between 800 and 900 mg. daily, but the patient's diet was probably inadequate in vitamins due to a complete lack of fruit and vegetables. There was no change in this diet when he became a night watchman.

## METHODS

The nineteen months of treatment have been divided into nine consecutive phases according to diet and location. (Fig. 2.) Details of the mean dietary constitution during the various phases are given in Table I. Diet analysis confirmed the intake data as calculated from standard tables [*19*] for every element measured except phosphorus, for which analysis gave results considerably lower than found in the tables. The latter were used for balance calculations. Calorie-free fluids (tea without milk) were allowed *ad libitum* throughout the periods of treatment. Vitamin supplements* were given, except during phases 4 and 5A. After 147 days 200 ml. milk was allowed daily at the request of the patient.

Twenty-four hour collections of urine were ana-

* Total daily: vitamin A, 5,000 units; aneurine hydrochloride, 1.0 mg.; ascorbic acid, 125 mg.; calciferol, 500 I.U. (12.5 μg.).

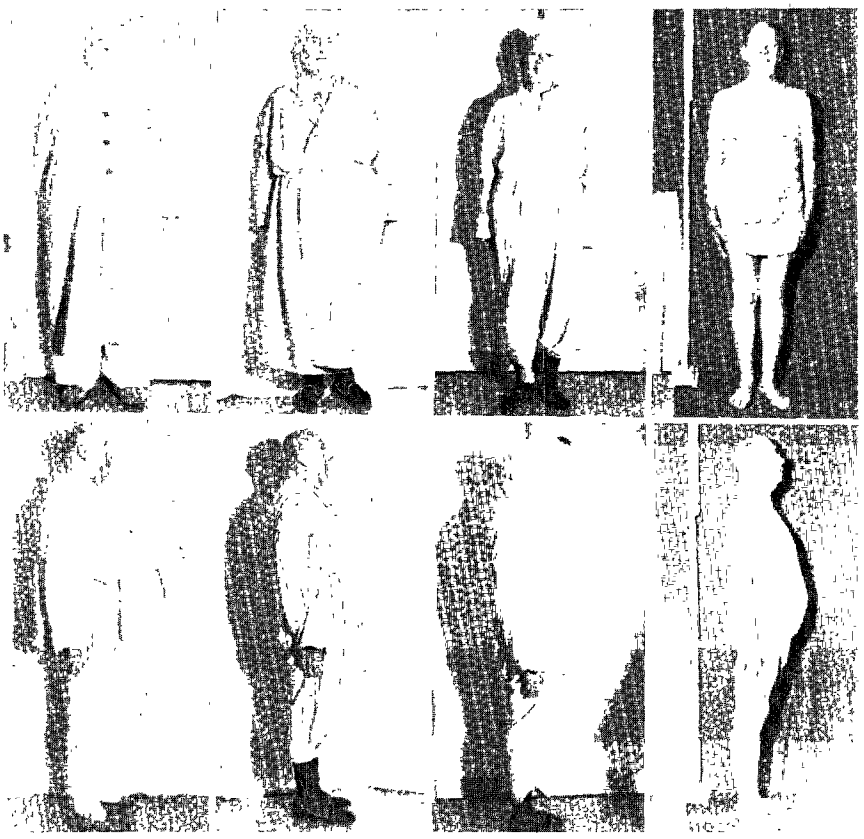


FIG. 1. Effect of treatment. First panel, February 2, 1963. Second panel, July 5, 1963. Third panel, November 27, 1963. Fourth panel, April 14, 1964.

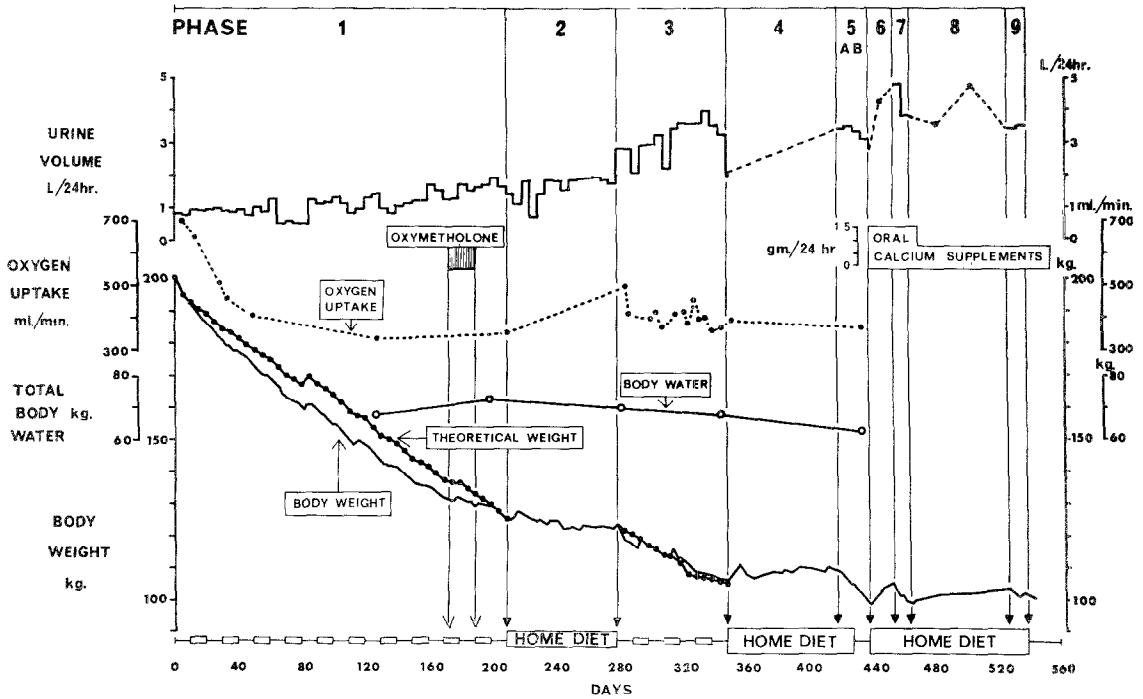
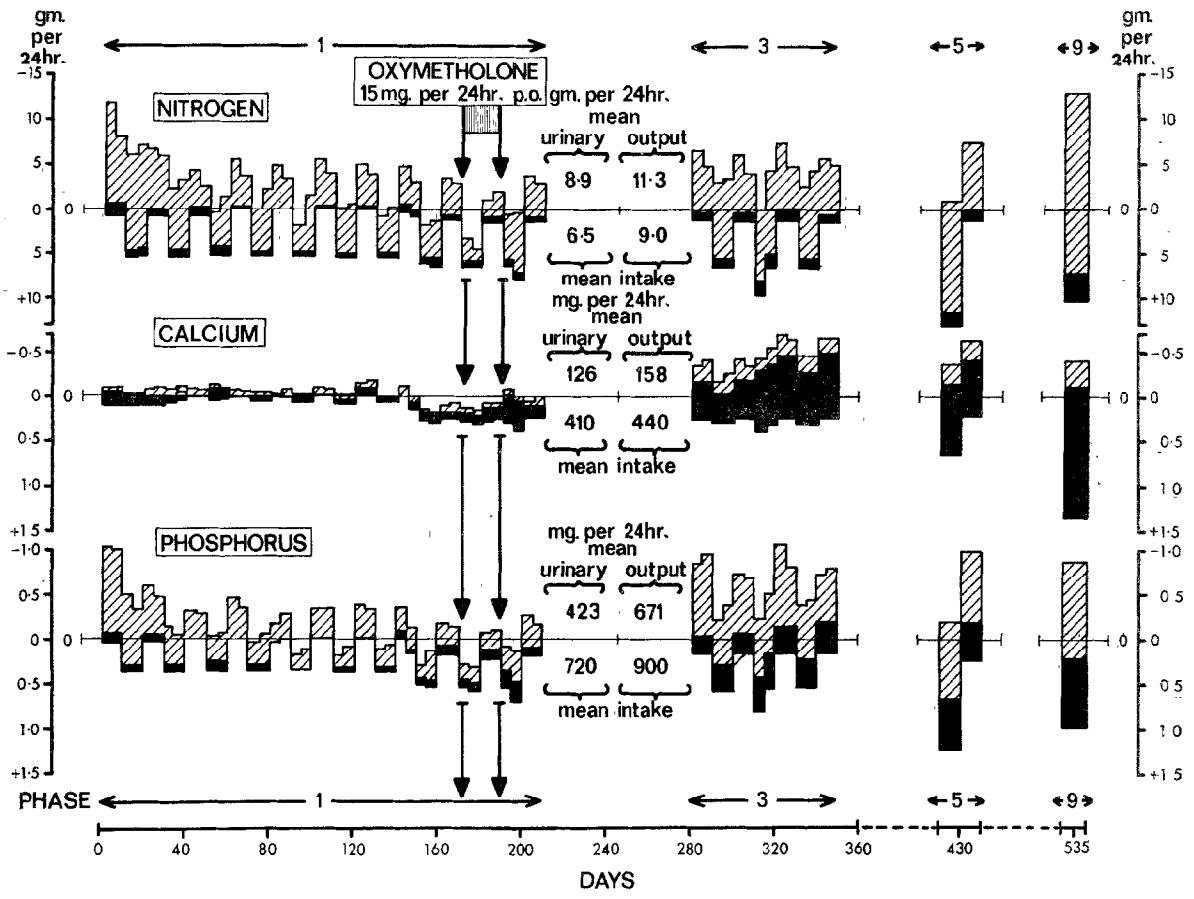



FIG. 2. Actual and theoretical weights, total body water, oxygen uptake and urine volume.



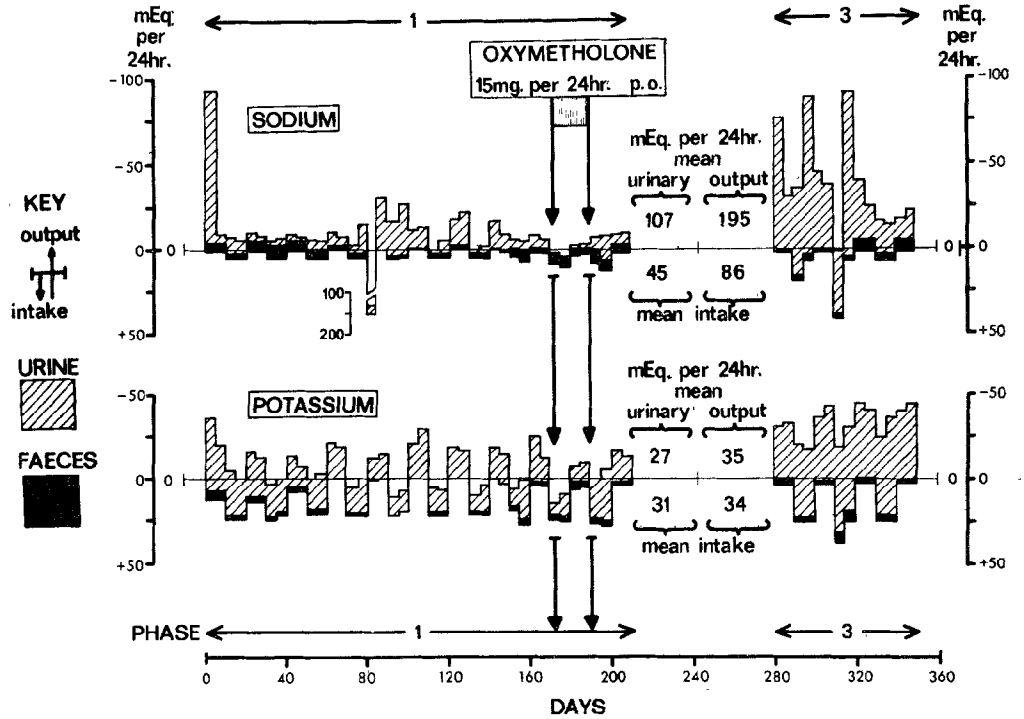




FIG. 3. Balance studies.

TABLE II
AVERAGE RATES OF WEIGHT LOSS

| Phase | Period | Duration | Weight Loss (gm./day) |
|---|---|---|---|
| 1 | Both diet and starvation periods | Twenty-one 10 day periods | 380 |
| | Both diet and starvation periods | Nineteen 10 day periods (excluding days on anabolic steroid therapy) | 420 |
| | Both diet and starvation periods | 205 days (excluding first 5 days) | 360 |
| | Both diet and starvation periods | 185 days (excluding first 5 days and days on anabolic steroid therapy) | 400 |
| | Starvation periods only | Eleven 10 day periods | 520 |
| | Starvation periods only | Ten 10 day periods (excluding days on anabolic steroid therapy) | 560 |
| | Starvation periods only | 95 days (excluding first 5 days and days on anabolic steroid therapy) | 520 |
| | First 5 days | 5 days | 1,180 |
| | Diet periods only | Ten 10 day periods | 220 |
| | Diet periods only | Nine 10 day periods (excluding days on anabolic steroid therapy) | 260 |
| 3 | Both diet and starvation periods | Seven 10 day periods over-all | 280 |
| | Both diet and starvation periods | 55 days (excluding two periods of dietary lapse) | 380 |
| | Starvation periods only | Four 10 day periods | 440 |
| | First day | 1 day | 2,040 |
| | Diet periods only | Three 10 day periods | 40 |
| | Diet periods only | 15 days (excluding two periods of dietary lapse) | 240 |
| 5A | On home diet in hospital | 10 days | 450 |
| 5B | Starvation period | 10 days | 560 |
| | First day of starvation period | 1 day | 1,100 |
| 9 | On home diet at home (balance) | 12 days | 160 |

lyzed either individually or in 48 or 72 hour pooled specimens. Stools were collected in ten day periods corresponding to the changes in dietary intake; markers were not used. The fecal collections were homogenized in a Waring blendor and diluted with distilled water. For electrolyte studies 10 ml. aliquots were evaporated to dryness on a sandbath and dry-ashed in a muffle furnace for 16 to 18 hours at 520°c. The white ash was dissolved in 3 by 1 ml. 10 per cent hydrochloric acid and made up to the original volume (10 ml.) with deionized water.

Routine methods of estimation were employed (details available on request). Total body water, red cell mass and plasma volume were measured by isotope dilution. Body density was calculated from total body volume, estimated by immersion in water [*20*]. Percentage fat content and changes therein were calculated using the formulas of Siri [*21*] and Edelman et al. [*22*], respectively.

Lung volumes, oxygen uptake and minute ventilation were measured with a Benedict-Roth spirometer, and helium was used to obtain the residual volume. Maximum expiratory flow rate was measured with the Wright Peak-Flow Meter.

## RESULTS

*Weight Loss.* The progressive change in body weight is shown in Figure 2 and rates of weight loss are given in Table II. At the beginning of phases 1, 3 and 5B the rate exceeded 1 kg. per day. Thereafter the rates during periods of deprivation remained similar, allowing for dietary lapses and excluding the effect of oxymetholone. The rate of loss during starvation periods was double that of dietary periods. At home during phase 4 the patient's weight remained steady, yet with nominally the same diet in hospital during phase 5A the rate of weight loss approached that of the starvation regimen. In phase 9, when he was at home subsisting on the same nominal diet with calcium supplements, rate of loss was 160 gm. per day. During this time he was coming to the hospital every two days to be weighed and specimens for balance study were being collected.

From the chemical balances of sodium, potassium and nitrogen (Figs. 3 and 4) it is possible to calculate the theoretical weight loss [*23*]. It can be seen (Fig. 2) that the theoretical weight curve in phases 1 and 3 agrees fairly closely with the actual weight loss, confirming that gross discrepancies in the estimations did not occur.

*Anthropometry.* Weight reduction was accompanied by a 38 per cent change in girth (Table

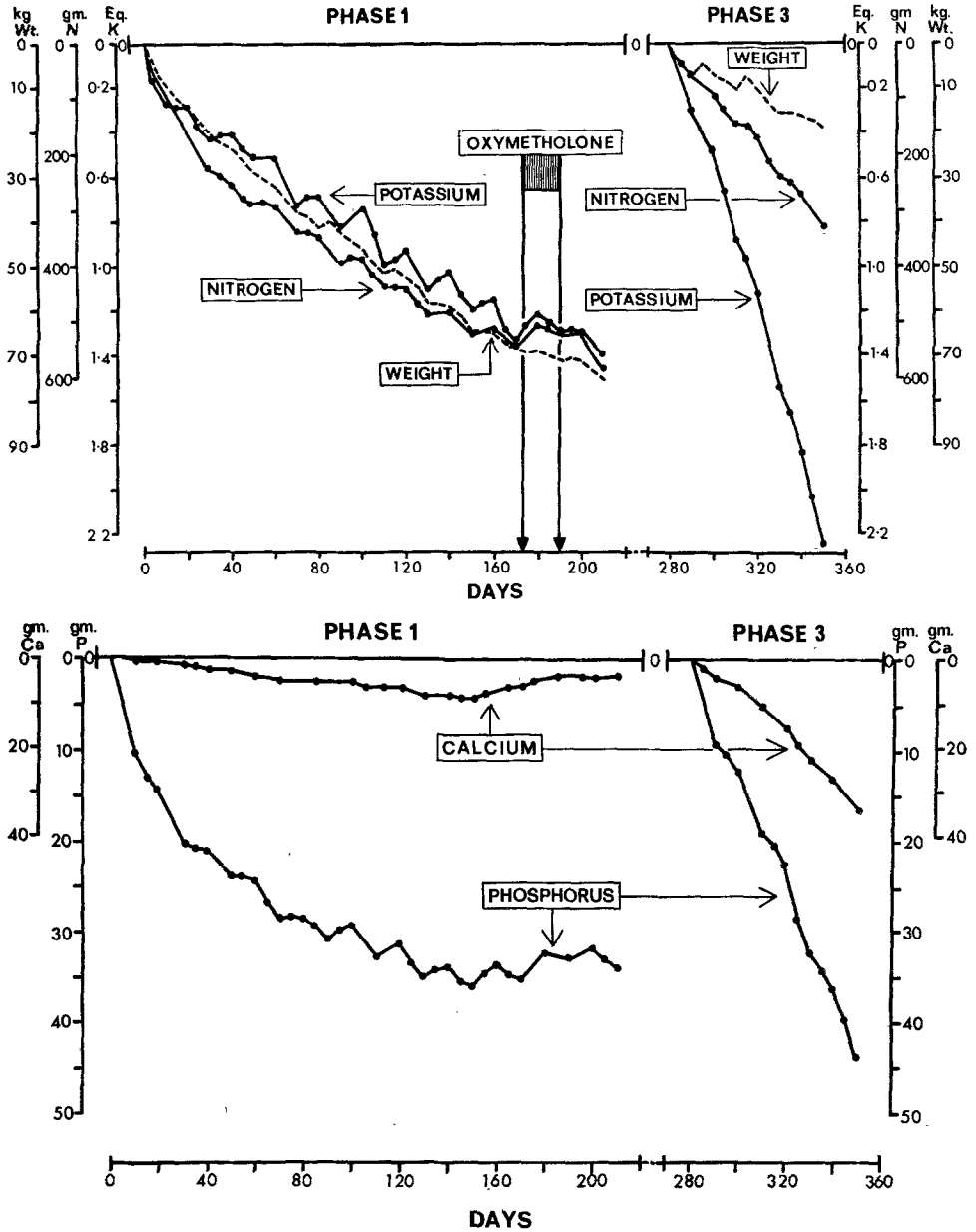



FIG. 4. Cumulative balances of potassium, nitrogen, calcium and phosphorus, compared with weight loss. Scales are such that 40 gm. nitrogen is made equivalent to 100 mEq. potassium and to 2.72 gm. phosphorus (ratio in protoplasm, from breakdown of 1 kg. cell tissue). Also 2.08 gm. calcium is made equivalent to 1 gm. phosphorus (ratio in bone). The body weight is plotted as one fifth of the equivalent scale.

III) causing loose skinfolds on the limbs and abdomen. The face did not become drawn, no changes in the colour or texture of the skin occurred and edema did not develop. Abdominal muscle tone was poor and the patient had to wear a surgical belt. There was no significant change in height.

*Compartment and Fluid Changes.* The estimated change in body fat content during the latter half of phase 1 was 19.5 kg., indicating a mean rate of fat loss of 267 gm. per day whereas the concurrent rate of protein loss was less than 7 gm. per day. Thus at this time the fat loss accounted for practically 100 per cent of the weight loss. Dur-

TABLE III
ANTHROPOMETRIC MEASUREMENTS

| Day | Weight (kg.) | Height (cm.) | Span (cm.) | Stem (cm.) | Circumference Waist (cm.) | Chest (cm.) | Neck (cm.) |
|---|---|---|---|---|---|---|---|
| 3 | 198.2 | ... | ... | ... | 183 | 183 | 56 |
| 221 | 126.0 | 184 | 189 | 100 | 138 | 131 | 47 |
| 352 | 106.6 | ... | ... | ... | 119 | 117 | 45 |
| 440 | 98.7 | 183 | 192 | ... | 116 | 114 | 43 |
| 600 | 103.8 | 184 | 191 | 97 | 118 | 117 | 44 |

ing phase 3 the rate of fat loss was lower, 183 gm. per day, and comprised 75 per cent of the weight loss whereas the protein loss accounted for 12 per cent. Near the end of phase 3 (day 329) total body fat content estimated by densitometer [*20*] was 19.5 per cent, which still was high.

Total body water did not change significantly after 120 days but the red cell volume continued to decrease throughout the remainder of phase 1, reaching 2.8 L., a volume almost half that found at the beginning of the phase. Plasma volume also decreased but not to the same extent. By the end of phase 1 the blood volume had fallen by 39 per cent and red cell volume no longer exceeded the plasma volume, although the peripheral venous hematocrit remained above 50 per cent. Neither volume changed significantly during phases 2 and 3. Plasma volume exceeded red cell volume throughout phase 3, and no change was found subsequently.

Urine output increased progressively over the whole period of study. The daily volume was as low as 300 to 400 ml. during the early stages of phase 1, but averaged over 5 L. during phase 6. A water deprivation test carried out at the beginning of phase 8 indicated that the kidneys were capable of an appropriate response, although the concentration achieved was not maximal. The rate of urine formation decreased to 0.4 ml. per minute after 12 hours of deprivation, but the maximum specific gravity obtained was only 1.022. Urinary specific gravity before the test ranged from 1.004 to 1.008. The maximum urine osmolality after 13 hours of water deprivation was 800 mOsm. per kg., with a serum level of 271 mOsm. per kg.

*Blood Levels.* Some of the results obtained from plasma estimations are presented in Table IV and Figure 5. No significant changes were observed in the levels of sodium, chloride and bicarbonate (as estimated by carbon dioxide combining power) or in the levels of calcium, phosphorus, cholesterol, beta lipoprotein and creatinine.

A slight fall in plasma total protein was ob-

TABLE IV
PLASMA LEVELS

| Constituent | Phase 1 Mean ± S.D. | Phase 1 No. of Estimations | Phase 3 Mean ± S.D. | Phase 3 No. of Estimations | Other Phases Comments |
|---|---|---|---|---|---|
| Sodium (mEq./L.) | 138 ± 3 | 71 | 136 ± 2 | 11 | No change |
| Potassium (mEq./L.) | 3.8 ± 0.4 | 71 | 4.5 ± 0.3 | 11 | Same as in phase 3 |
| Chloride (mEq./L.) | 96 ± 3 | 69 | 100 ± 3 | 11 | >100 on days after anabolic steroid therapy ~ 109 during phase 2 |
| $CO_2$ combining power (mEq./L.) | 28 ± 2 | 65 | 26 ± 2 | 11 | No change |
| Calcium (mg./100 ml.) | 9.4 ± 0.4 | 43 | 9.6 ± 0.4 | 10 | No change |
| Phosphorus (mg./100 ml.) | 3.2 ± 0.5 | 53 | 3.8 ± 0.6 | 11 | No change |
| Cholesterol (mg./100 ml.) | 190 ± 30 | 18 | 190 | 1 | No change |
| β-lipoprotein (mm.) | 2.9 | 1 | 3.0 ± 0.2 | 7 | ... |
| Creatinine (mg./100 ml.) | 1.1 ± 0.2 | 5 | 1.1 ± 0.5 | 6 | No change |
| Total protein (gm./100 ml.) | 6.6 ± 0.4 | 13 | 6.6 ± 0.4 | 10 | No change |

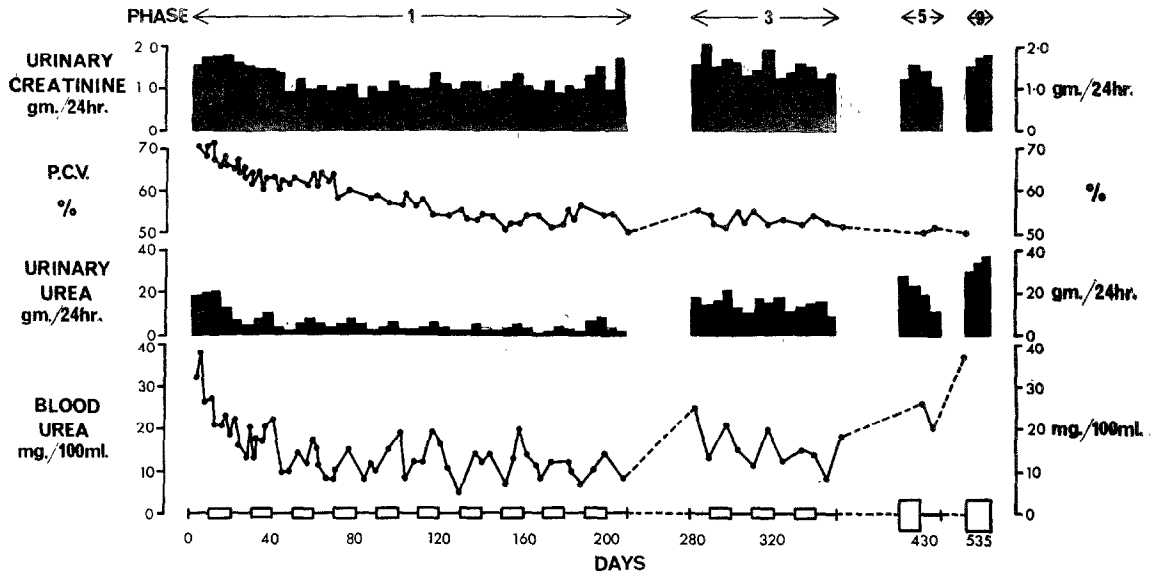



FIG. 5. Nonprotein nitrogen and hematocrit changes.

served during phase 1, the average of three consecutive estimations decreasing from 7.1 through 6.6 to 6.2 gm. per 100 ml. by the end of the phase. No such fall was noted in phase 3. During the first twenty days of phase 1 the plasma potassium level averaged 4.2 mEq. perL., thereafter falling slightly to give an over-all average of 3.8 mEq. per L. during phase 1. During phase 3 there was no tendency for potassium levels to decrease, and the average was higher (4.5 mEq. per L.) than in phase 1, despite a striking increase in rate of potassium loss during this time. (Fig. 4.)

By the sixth day of phase 1 ketones had appeared in the blood; they persisted throughout the remainder of the phase during both fasting and dietary periods. The ketones disappeared at the beginning of phase 2, and appeared only intermittently in traces throughout phase 3. Blood sugar levels estimated during the first starvation period of phase 1 were greater than 100 mg. per 100 ml., which is probably above normal in a fasting subject. During phase 3 the values were consistently lower than 85 mg. per 100 ml., indicating the disappearance of any diabetic tendency.

Uric acid, estimated late in the study, was within the normal range (1.9 to 6.5 mg. per 100 ml.). Blood urea (Fig. 5) showed a periodic variation between dietary and starvation periods, in addition to a significant downward trend to very low levels, over the course of phase 1. The pattern was repeated in phase 3.

*Balance Studies* (*Fig. 3*). Except for the initial few days, during phase 1 the patient was virtually in balance for sodium; potassium balance was negative during starvation periods although positive during dietary periods. Subsequently, both sodium and potassium balances were negative, except during the later phases of the 1,200 kcal. diet when potassium balance was again positive.

With the very low intake during the early stages of phase 1, calcium excretion decreased within four days to low levels in both feces, and urine (18 mg. per day). Although the balance was negative during starvation periods to the extent of 50 to 100 mg. per day, equilibrium was achieved during the intervening dietary periods when the intake was of the order of 61 mg. per day. After 150 days calcium intake was increased to 250 mg. per day. Adaptation occurred over the remaining sixty days of phase 1, positive balance being achieved immediately and then lessening, until during the last twenty days of the phase balance was achieved in both dietary and fasting periods. Administration of an anabolic steroid had no appreciable effect on calcium balance. It is not known whether or not our patient remained in balance over the two summer months of phase 2 when he was at home. On an approximate intake of 420 mg. per day, urinary

excretion of calcium gradually increased from 64 to 210 mg. per day, the averages for the first and last ten days being 90 and 162 mg. per day, respectively.

In phase 3 a remarkably negative balance resulted from a striking increase in calcium excretion in both feces and urine. Net absorption became negative, i.e., fecal calcium excretion greatly exceeded intake, but the percentage of total calcium excreted in the feces (73 per cent) was still normal. Urinary calcium excretion remained in the 150 to 200 mg. per day range. This failure to adapt to the low intake occurred in the autumn and continued throughout the phase. During the latter part of phase 3 total calcium excretion exceeded 900 mg. per day. Calcium balance remained negative during phase 5. Calcium supplements which increased daily calcium intake to 2,400 mg. did not produce a positive balance (phase 7). Since the time allowed for equilibration at the new intake level may not have been sufficient, the balance study was repeated after a further sixty days of calcium supplementation giving a total daily intake of 1,350 mg. calcium. The balance still remained negative (400 mg. per day).

Phosphorus balance during the first thirty days of phase 1 was negative, progressively lessening until a fairly regular pattern developed in which a negative balance during starvation periods alternated with a balanced state during dietary periods. The balance gradually became more positive in character towards the end of phase 1. Oxymetholone did not alter the pattern significantly. As with the other balances, the phosphorus balance became more negative in character during phase 3; the pattern during this phase resembled that of the concurrent calcium balance although the losses were predominantly urinary. Calculation of the theoretical phosphorus balance showed that within the limits of experimental error phosphorus excretion could be accounted for by the accompanying calcium and nitrogen excretion. While the patient was being maintained on diets at home, phosphorus balance remained slightly negative. The high calcium intake exerted no appreciable effect on the phosphorus balance.

Nitrogen balance during the first thirty days of phase 1 became progressively less negative in character. Thereafter a consistent pattern developed in which a negative balance during the starvation periods alternated with a more or less balanced state during the dietary periods. The balance consistently became less negative in the second five days of each starvation period, and more negative in the second five days of each dietary period. By the end of phase 1 the negative balance during the second five days of the starvation periods had decreased to the order of 3 gm. nitrogen per day, never becoming lower than 2.5 gm. per day except in the brief period during which anabolic steroid was administered. The nitrogen balance showed a different pattern during phase 3. It was more negative over the whole period and did not approach balance during dietary periods. During the first part of phase 5 nitrogen balance was only slightly negative, and it is assumed that the patient had been in equilibrium or in slightly negative balance on his home diet (phase 4). As expected, during the starvation period of phase 5 the balance was of the same negative degree as that noted at the beginning of phases 1 and 3. During phases 7 and 9, when the patient was given calcium supplements with an unchanged nitrogen intake, the balance became strikingly negative, exceeding 15 gm. per day towards the end of phase 9. At this time a furuncle on the leg developed which subsided after treatment with penicillin.

*Nonprotein Nitrogen Changes.* Creatinine excretion diminished gradually during the first eighty days of phase 1 and thereafter reached a steady state in which average excretion during the dietary periods was slightly higher than during the starvation periods. (Fig. 5.) In contrast, during the first thirty days of phase 3 creatinine excretion tended to increase, diminishing again towards the end of the phase and showing the same difference between dietary and starvation periods. Output during the later phases remained at the level determined during the first few days of phase 1. Blood urea and urinary urea excretion followed essentially the same pattern (Fig. 5), decreasing most rapidly during the first eighty days and then gradually decreasing to values lower than 8 mg. per 100 ml. and 4 gm. per day, respectively, despite small increases during dietary periods. Both excretions returned to the initial prestarvation levels promptly on commencement of a normal intake (phases 4, 6, 7, 8 and 9). Creatine output was unchanged throughout the period of study.

*Subsidiary Studies. Fecal fat excretion:* The average fecal fat content throughout phase 3 was 2.4 (S.D. ± 0.8) gm. per day (normal range 1.5 to 6.4 gm. per day). There was no difference between starvation and dietary periods. The

average output with the home diet was 3.6 gm. per day compared with 2.0 gm. per day in phase 5B (starvation).

*Steroid excretion:* The results of the urinary steroid estimations were variable. Initially 17-oxosteroid excretion rates were normal, but these later increased to 30 mg. per 24 hours. Urinary 17-hydroxycorticosteroid excretion rates were increased at first, and after a transient decrease increased again to over 25 mg. per 24 hours.

*Hematology:* At the beginning of phase 1 the patient showed a marked polycythemia (hemoglobin 23.4 gm. per 100 ml., red blood cells 6.8 per cu. mm., hematocrit 70.5 per cent). There was no increase in white cell or platelet counts; blood film was normal. By the end of phase 1 the hematocrit was 52 per cent with a hemoglobin of 16.6 gm. per 100 ml. The hematocrit did not change significantly during phase 3. Subsequently there was little alteration and the hemoglobin remained slightly increased at 15.8 gm. per 100 ml., with a hematocrit of 50 per cent and a normal red cell count. The only other hematologic abnormality was a relative lymphocytosis.

*Pulmonary function:* Marked improvement in lung function accompanying weight loss was shown by the progressive increase in lung volumes and the decrease in airways resistance. (Fig. 6.) The vital capacity almost doubled during phase 1 and increased by a further 33 per cent in phase 3. At first this was achieved largely by an expansion of 71 per cent in the inspiratory reserve volume but in phase 3 the expiratory reserve volume considerably increased, partly at the expense of a small reduction in the inspiratory reserve. During phase 1 the tidal volume increased slightly but returned to the previous level in phase 3. During the first thirty days respiratory rate, minute ventilation and oxygen uptake decreased, the latter by 300 ml. per minute, and thereafter there were no consistent changes. Maximum expiratory flow rate, initially fairly low, practically doubled in phase 1 after which there was no change. Air-trapping after a deep inspiration was conspicuous on the spirograms and did not improve during the study.

The arterial blood carbon dioxide pressure on admission was 61 mm. Hg and fell steadily over the next ten days to 46 mm. Hg. Initially arterial oxygen saturation at rest was 80 per cent but it increased to 95 per cent by the end of phase 1.

*Emotional changes:* Our patient showed definite changes in mood. On admission he was ill and anxious, but fasting in phase 1 was tolerated well and a good-humoured, jovial personality was revealed. The alternating regimen was readily accepted but after 100 days the ten day periods on low calorie diet were eagerly anticipated. Phase 1 was ended largely because the patient did not wish to continue it longer. He ruefully shook his head and requested a spell at home. The later phases of treatment were broadly similar. Infrequently, minor quarrels with the nursing staff over the provision of tea and such small matters did occur but the emotional heat so engendered subsided within a few hours. As time advanced the patient took increasing pride in his own therapeutic response, a feature which greatly helped the management of the case.

## COMMENTS

*Weight Loss.* There is controversy in the literature over the rate of weight loss to be expected during fasting [*14*]. Bloom [7] and Duncan et al. [*8,9*] have reported average rates greater than 1 kg. per day, whereas the majority of investigators, including us, found average rates in the 300 to 600 gm. per day range, with losses approaching the high rates only in the initial few days if at all. Relatively few patients have been studied so far, and as wide individual variation in response to fasting certainly is recognised [*9,10*] it may be that the two groups of rates merely represent the extremes of the range of variation. Further, average rates calculated for short periods of time and including the initial rates will tend to be higher than the values reported for longer periods. Generally, the heavier the patient is initially, the greater the rate of weight loss [*10*].

It is interesting that with a diet of 800 kcal. McCance's patient [*12*], originally 265 kg., should lose almost 300 gm. per day, a rate approaching fasting rates. Our patient during phase 5A lost 450 gm. per day on an intake of 1,200 kcal., although his weight remained steady with nominally the same diet while at home. During phase 5A he was in hospital and we would suspect that the diet at home had been supplemented, but this still does not explain the high rate of loss equalling that of the starvation periods while the patient was subsisting on a normal caloric intake. Also the effect of any decrease in physical activity while in hospital must have been more than balanced by the factors

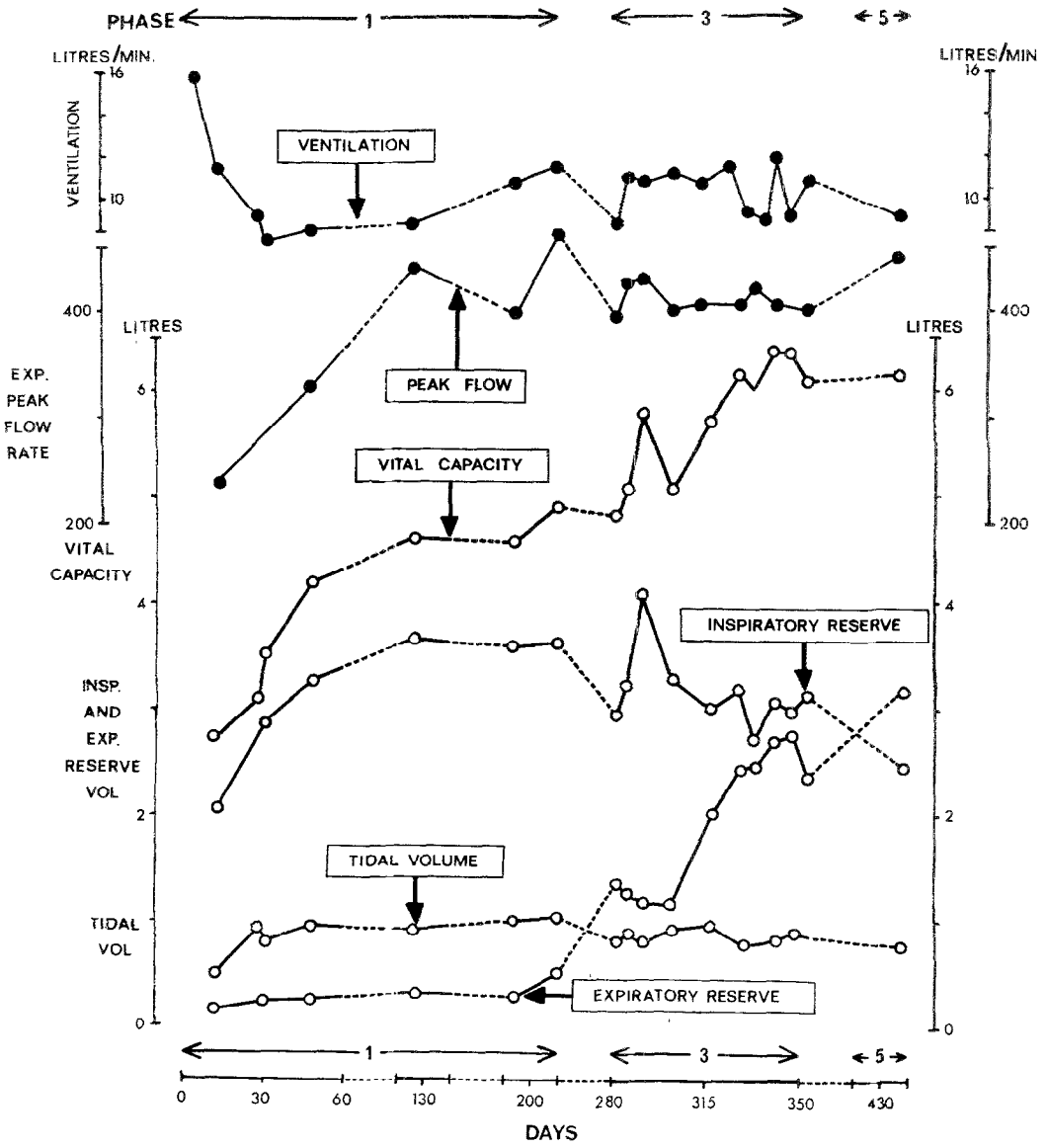



FIG. 6. Respiratory function.

causing the weight loss. We are tempted to conclude that under certain circumstances, at present still obscure, the actual change in intake may have a greater effect than actual calories consumed. Since rapid weight loss is associated with sodium and fluid changes [*24*], a decrease in salt intake may have been contributory. Blondheim et al. [*25*], in a carefully documented study, have shown that in their patients intermittent fasting did not increase the amount of weight lost eventually, mainly because of the temporary increase in weight which occurred on changing from starvation to diet periods, although the actual rate of loss was higher during the ten day starvation period.

The comparative uniformity of rate of weight loss in our obese subject during minimum caloric intake can be contrasted with the progressive decrease in rate noted in fasting normal volunteer subjects [*26*]. Diminution in body mass might be expected to decrease the rate of weight loss even in obese subjects [*24,27*] but it is also possible that increasing physical activity might have an opposing influence. A balance between these factors would result in a constant rate of weight loss. Recently it has been found

that obese patients on continuous starvation [*10*] stabilize at a fairly constant rate of weight loss after the initial twenty days or more.

In phase 3 the average rate of loss, excluding the two lapses of diet, was unchanged. During the first seventy days of phase 1 the total nitrogen lost (328 gm.) did not differ significantly from that lost during phase 3 (338 gm.), although the weight loss was twice as great (38 kg. as opposed to 19 kg.). This could be accounted for by the fourteen days of phase 3 which were taken up re-losing the 6 kg. gain in weight which occurred due to the two lapses in diet. These two gains in weight during phase 3 were due mainly to an increased intake of salt and probably carbohydrate over a few days. Protein intake remained the same and therefore the nitrogen balance was not affected.

*Compartmental and Fluid Changes.* The total body water measurement obtained at the beginning of the study was high (111.5 kg.), and this estimation was discarded as erroneous for the following reasons. If it and the subsequent measurement were correct, 89 per cent of the 49 kg. weight loss during the first 120 days would have been due to water loss, leaving only 2.5 kg. accounted for by loss of fat, with 3.0 kg. of protein loss (calculated from the nitrogen balance). More fat must have been metabolized in order to supply the daily energy requirements during starvation, and this is further borne out by the relatively high oxygen uptake. (Fig. 2.)

It is possible that the extreme obesity present initially prevented complete equilibration during estimation of water content. Kyle et al. [*28*] have cited an example in which compartmental analysis of body content was not accurate in an extremely obese subject whose specific gravity was less than 1.000. Our patient's specific gravity was only 1.018 by the end of phase 3, and must have been much lower initially. Kyle and co-workers have pointed out that compartmental methods of analysis utilizing the formula of Edelman et al. would tend to underestimate fat loss, and our experience agrees with this. The underestimation of fat loss may be due to overestimation of water content in the massively obese subject. As the patient loses weight, or fat, the error would progressively decrease.

The reason for the striking increase in urine volume is obscure. Rapoport et al. [*24*] have stated that urine volume appears to parallel weight loss and that both are greater earlier in starvation, whereas we found a gradual increase which had no correlation at all with weight loss. (Fig. 2.) Presumably the lower limit of urine volume is reached long before the lower limit of weight loss, and thereafter no parallelism would be found. It is assumed that the increase in urine output in our case coincided with a gradual increase in fluid intake, although this is impossible to verify since it was not measured. Fluid intake during phase 1 was reported as approximately 20 cups (4 L.) daily. It is known that during the later phases at home the patient was consuming over 30 large cups of tea per day. It is probable that in our patient psychogenic polydypsia developed during the starvation regimen, although it should be noted that even before his admission to hospital his fluid intake was high—composed then of beer, when available, rather than tea. Primary renal disease appears unlikely although we cannot exclude an element of kalopenic nephropathy consequent upon the observed excessive potassium losses. In contrast, thirst abatement and decrease in fluid consumption have been reported [*10*], with urine output diminishing to oliguric levels after thirty days of starvation. It is interesting to note the different effects found, leading to opposing conclusions, depending on whether fasting occurs periodically over several hundred days or continuously over ten to twenty days.

*Blood Levels.* Plasma analysis revealed little of interest. The lack of significant changes reflects the capacity of the homeostatic mechanism to withstand gross deprivation. The lowering of plasma potassium levels during phase 1 was insufficient to constitute clinically significant hypokalemia. Drenick et al. [*10*] also found a decrease in serum potassium to low-normal limits. The continuous presence of plasma ketones in our patient is in contrast to their finding that ketosis tended to disappear with extended fasting. Paradoxically, it is possible that the intermittent periods of diet in our case, although not sufficient to eliminate the ketosis, actually prevented it from disappearing as it did in the patients of Drenick and co-workers. Alternatively, it has been suggested that unless ketonuria is continually present, the fast has been incomplete [*29*]. The only other significant changes in our case were in the packed cell volume and blood urea. (Fig. 5.)

*Calcium Metabolism.* The striking feature apparent from the metabolic studies was the unexpectedly negative character of the calcium balance in phase 3 and subsequently, especially

when contrasted with the virtually negligible losses during phase 1.

In his classic work on long-term calcium balances Malm [*30*] described three types of response to a low calcium intake. A few subjects (category A) are capable of immediate adjustment and rapidly achieve positive or insignificantly negative balance. The majority of subjects (category B) go into marked negative balance, and then gradually "improve" and approach balance. Those in the third category (C) show a continuous negative balance with no signs of adaptation. Malm subdivides category B into (1) those who demonstrate "compensatory adaptation," with restoration of initial loss before establishing equilibrium again; (2) those who finally establish a new equilibrium level either in balance or in slightly negative balance without restoration of initial loss; and (3) those who merely show a progressively lessening negative balance as time goes on.

It is interesting that in our patient there appeared, in turn, the features of each of the three categories during the course of one year. In the first 150 days of phase 1 the pattern was that of category A, i.e., immediate adaptation to the very low intake of 60 mg. calcium per day. The low intake used by Malm was 460 mg. per day. Unlike the majority of Malm's subjects, adaptation in our patient was due to a marked decrease in urinary as well as fecal output. When milk was added to his diet the patient appeared to respond according to the pattern of category B, with a markedly positive balance initially, gradually diminishing thereafter until balance was attained. Although the cumulative loss of calcium was 8.7 gm. after 150 days, by the end of phase 1 the total loss was only 4.1 gm. Thus 53 per cent of the calcium lost in the first 150 days was restored by day 210, on a calcium intake of less than 300 mg. daily, which is very low in comparison to the normal recommended intake of 800 mg. daily [*31*]. A more recent recommendation [*32*] for a lower "suggested practical allowance" of 400 to 500 mg. daily has been severely criticized as inadequate [*33*].

During phase 3 the complete failure of adaptation to the 250 mg. intake became a subject of concern. Although urinary excretion increased, the principal calcium loss was via the feces, causing negative net absorption; fecal excretion exceeded intake to the extent of 480 mg. per day in the last two starvation periods of phase 3. Cases of similar negative absorption have been reported in the literature [*34–36*]. By the end of phase 3 the cumulative calcium loss (excluding phases 1 and 2) had amounted to 34 gm. When compared with the cumulative loss of 4.1 gm. on day 210, the ninefold increase in calcium loss which occurred during phase 3 is striking.

Although it has been shown [*30,37,38*] that some subjects fail to show urinary adaptation to low calcium intakes, it is apparent that there are subjects, including our patient, capable of considerable adaptation in urinary as well as fecal excretion [*39,40*]. Our patient's urinary excretion ranged from the very low value of 18 mg. daily during a starvation period to 492 mg. daily while taking calcium supplements at home.

It is noteworthy that although the increased negative balances of calcium and potassium were the most striking aspects of phase 3, the negative character of the nitrogen, phosphorus and sodium balances was also increased. Since more than half the phosphorus loss could be accounted for by accompanying cell loss, as reflected in the nitrogen balance, the phosphorus loss due to bone resorption was masked.

Mutually compatible explanations for both the effective initial adaptation to low calcium intake and the negative calcium balance in the later stages of the study are difficult to find. Despite the extensive calcium loss in the later stages, which possibly continued even with calcium supplements, osteoporosis as such did not appear to be present. Further evidence is that complaints of backache and significant diminution in height did not occur either during or after the year of negative calcium balance. Two explanations are possible.

1. Acquired failure of intestinal calcium absorption. The negative balance became apparent after nine months of treatment. Was the striking intestinal loss due to the development of an intestinal fault caused by the prolonged starvation to which the patient submitted? If the high calcium losses found during the later stages were a direct consequence of his treatment, which aspect of his therapeutic diet produced the change? Malm related the negative net intestinal absorption of his patient [*34*] to increased emotional stress, but this factor was not operative in our patient. The negative balance might have resulted from the prolonged cumulative effect of low caloric, protein or calcium intake, separately or in any combination.

Failure of intestinal calcium absorption can develop as a consequence of avitaminosis D, but

in our case this appears unlikely because calciferol supplements were given (500 I.U. per day). Furthermore the calcium losses began in the autumn when vitamin D must have been available from ultraviolet synthesis induced during the summer. Intermittent relative resistance to vitamin D has been postulated [*41*] and might have occurred in our case but this cannot be positively identified from the data. We know that the over-all vitamin intake was adequate by ordinary criteria throughout the whole period of study and that the intake ratios of calcium : phosphorus and calcium : magnesium were within favorable limits [*42*] when the "fault" developed. The absence of excessive fecal fat excludes the possibility of calcium malabsorption due to steatorrhoea but absorption failure, affecting both dietary calcium and the calcium component of intestinal secretions, has been known to occur in some cases without steatorrhoea [*43*]. It is possible that our diet was not ideal and lacked some essential amino acid [*44*] or essential fatty acid necessary for intestinal absorption, so that eventually the absorption mechanism failed.

The negative balance might have been the direct result of prolonged calcium deprivation. It has been suggested that there are no pure calcium deficiency diseases [*45,46*] but opinions are divided on this point [*47,48*]. It is conceivable that the alteration in calcium balance could have happened even without the starvation regimen. Some degree of negative balance is not uncommon in men of our patient's age, but the fact of the negative net absorption remains to be explained. The possibility that dietary restriction in the present circumstances may injure the calcium secretory or absorptive capacity of the gut cannot be discounted.

2. Calcium excretion by the gut. The intestine, to a greater extent than the kidney, is the regulator of calcium balance [*49*]. Accordingly, negative net absorption of calcium might represent a purposive response to the successful treatment of massive obesity.

In our patient the calcium deficit during phase 3 alone was 34 gm. Losses of this magnitude have been described. Petersen's patient [*36*], who was suffering from malabsorption syndrome, lost 35 gm. calcium in sixty days on a normal intake. These quantities could only have come from osseous stores, since the "metabolic pool" of calcium usually amounts to no more than 5 gm. [*37*]. During his thirty-eight years as a fisherman our patient's intake of calcium was more than twice the recommended value, and quite possibly during that period of his life he laid down an unusually large amount of bone salt to provide a strong skeletal system in response to the demands of excessive body weight. Malm originally pointed out that subjects consistently in positive balance must deposit bone continually, whether or not it is structurally useful, and that "degenerative bone deposition" could amount to an accumulated storage of around 200 gm. after twenty-five years [*30*]. More recently Malm has discussed the development of trabecular "storage" bone in people who exercise constantly [*49*]. Thus it would appear that the notion of surplus skeletal mass is not new. It is possible that the fairly rigorous life involved in fishing at sea, coupled with the demands of excess weight, caused the development of "extra" bone in our patient. Reduction in body weight might reverse this physiologic demand on skeletal function and lead to the elimination of surplus calcium by the intestine, possibly by the kidney also. The hypothesis of skeletal surplus is compatible with the complete failure of adaptation (category C) shown in phase 3. Bone dissolution did not become apparent until about 38 per cent of the original weight had been lost. Nevertheless, if one assumes that resorption of calcium and phosphorus from bone would occur only after the excessive load was substantially reduced, the hypothesis is not incompatible with the immediate type A response during most of phase 1.

It is more difficult to explain the transient positive balance during the last sixty days of phase 1, for it must be noted that on day 150, when 33 per cent of the patient's original weight had been lost, an increase in calcium intake from 60 to 250 mg. daily brought about an immediate positive balance. This could mean that the previous relatively low calcium losses were being restored as a priority, or it could merely reflect a slow adaptation to the new intake in contrast to the immediate response at the beginning of the regimen.

Our patient failed to show positive balance when subsequently given a great amount of calcium (phases 7 and 9). By phase 9 he had been taking calcium supplements for two months. This could also be interpreted as an indication that his skeleton was not depleted and that previous calcium losses originated from "expendable" bone stores, although it has been shown [*49*] that

a "skeletal need" for calcium is not necessarily reflected by consistent changes in intestinal absorption or urinary excretion when dietary calcium is increased. Heaney [*50*] has postulated a correlation between net intestinal absorption and bone accretion or resorption, but it is always difficult to differentiate between cause and effect. Even knowing the bone accretion rates, we could not tell whether it was the intestinal mechanism which reacted in response to bone demand or vice versa. The increase in alimentary calcium excretion could be taken as indicative of an increased resorption from bone, or decreased accretion, or both.

Immobility plays a significant role in the occurrence of negative calcium balance [*51*]. Just as prolonged exercise can cause the accretion of extra trabecular or "storage" bone [*49*], prolonged immobility can effectively bring about substantial calcium losses [*30*]. However, in our patient the increase in calcium output coincided, not with a period of immobility, but with the occurrence of increased exercise as his size diminished. Our patient was only immobile at the beginning of phase 1, when calcium losses were minimal. Thus in our case the effect of immobility can be ruled out as a significant factor in the calcium balance.

In summary, we suggest that our patient was losing calcium from surplus bone but we recognize the possibility that as a result of our starvation regimen a fault may have developed in his intestinal absorption mechanism which prevented his taking advantage of the subsequent high intake. Immediate and complete adaptation, in both urinary and fecal excretion, occurred throughout phase 1 and yet was succeeded by a markedly negative calcium balance involving negative net intestinal absorption. The development of an intestinal fault might be one of the risks inherent in starvation regimens undertaken over long periods of time. If such a fault is present, is it reversible? Our period of study has not been sufficiently prolonged to provide an answer.

*Nitrogen Metabolism.* The question arises whether or not the protein loss during a prolonged starvation regimen is detrimental to health. It should be noted that possible overestimation of intake and underestimation of output produces nitrogen balance calculations erring on the positive side, so that actual nitrogen loss is often greater than presented [*52*].

During phase 1 the trend towards a negative nitrogen balance lessened until the daily loss was of the order of 2 to 5 gm. per day. This may represent obligatory nitrogen loss [*44,53*]. Our patient's nitrogen intake in the dietary periods was of the order of 5 gm. per day from lean meat protein which would be expected to contain the essential amino acids. It has been shown [*44*] that if all essential amino acids are present, the minimum intake of nitrogen necessary to maintain balance lies between 3 and 3.5 gm. per day.

Protein loss in our patient, during the first 127 days of phase 1, amounted to 3.0 kg., which is only 13 per cent of the assumed total lean tissue solids content, assuming that the original content was within the normally accepted limits for a man of his height. Any possible increase in total body protein content to support his massive size would reduce this percentage further. It has been shown that up to 50 per cent of body protein can be lost during starvation, but loss of more than 30 per cent produces a marked sensation of weakness [*53*]. During the remaining seventy days of phase 1, only a further 0.5 kg. protein was catabolized, reflecting a substantial decrease in rate of protein loss and suggesting that the protein remaining might be the essential portion of the labile "protein pool" mentioned by Whipple [*54*].

Protein loss eventually reflects depletion of muscle. It is apparent that even after the presumably nonessential cellular protein has been lost obligatory nitrogen loss continues, and that this is a drain on essential body protein. However, van Reit et al. [*14*] have pointed out that only a small proportion of body energy requirements are met by protein catabolism during starvation in the obese subject. In our case, during the later half of phase 1, and to a slightly lesser extent in phase 3, the fat loss accounted for the major portion of the weight loss, protein and water levels remaining relatively unchanged. It should be noted that during the periods of low caloric intake when limited protein intake was permitted and nitrogen was thus available, the patient did not go into positive nitrogen balance but was on average in balance. This finding suggests that the protein loss during the starvation periods was not seriously depleting the essential body content and this possibility is further borne out by the fact that during the second five days of the ten day diet periods the nitrogen balance was always tending towards the more negative side of equilibrium. In the literature on the therapy of gross obesity there are no studies re-

ported so far which indicate that negative nitrogen balance is a practical hazard of extreme caloric and dietary protein restriction. Indeed, a case of gross weight reduction prior to and during pregnancy has been reported [*55*] in which nitrogen balance remained positive and protein gain exceeded fetal requirements, indicating that net nitrogen loss is not necessarily concomitant with prolonged weight reduction.

It is possible that in long-term obesity an increased proportion of total body protein would be involved in the formation of a matrix to support the excess fat, and that this supporting protein could be lost without harm to the patient as weight decreased. Body lean tissue solid content consists of skeletal and soft tissue masses, but our data are insufficient to enable us to assess the relative content and it is possible that in our patient the ratio of muscle to skeleton was altered.

Unfortunately we cannot tell whether the protein loss at the end of phase 1 was restored on an average daily intake of 8 gm. nitrogen during phase 2, and therefore it is difficult to interpret the change of pattern during phase 3 when the rate of nitrogen loss was increased relative to the total weight loss with a concurrent increase in the rate of calcium, phosphorus and potassium losses. The further increase in nitrogen loss towards the end of the period of study, and in phase 9 in particular, is not considered to be a direct consequence, detrimental or otherwise, of the starvation treatment but a reflection of intake in excess of the patient's needs. The development of the furuncle may also have contributed to the protein catabolism in phase 9.

The Minnesota experiment [*56*] showed that basal oxygen consumption decreased by 40 per cent during the time when approximately 25 per cent of body weight was lost, and the nitrogen excretion data suggested that protein depletion during this time paralleled the decrease in body weight. The total weight loss in the Minnesota group was approximately 25 per cent, whereas in our case the 25 per cent weight loss was only part of the total weight loss and occurred during the first 120 days of phase 1. Effects of starvation in normal subjects and in massively obese persons are not necessarily comparable but it is worth mentioning that oxygen consumption decreased by 40 per cent in our patient during this time. Also, the rate of nitrogen excretion was decreasing, although weight loss continued at the same rate.

Since most urinary nitrogen is derived from urea, creatinine, ammonia and uric acid, systematic decrease in the excretion of urea and creatinine (Fig. 5) during starvation is to be expected. Ashley and Whyte [*13*] found similar decreases in both over-all nitrogen loss and plasma nonprotein nitrogen concentrations in their three patients. In contrast, van Reit et al. [*14*] found no decrease in serum urea or creatinine, but their periods of investigation included only three ten day starvation periods which were probably not long enough to cause any significant change. In our patient the decrease in the average daily creatinine excretion during phase 1 was approximately 800 mg., whereas if all the nitrogen loss had been from muscle the hypothetical decrease would have been in the region of 1,540 mg.* Ashley and Whyte [*13*] have assumed in a similar patient (subject C) that this means muscle protein supplied only about 50 to 55 per cent of the total nitrogen loss, leaving a normal content in the remaining muscle tissue.

*Potassium Metabolism.* During phase 1 the potassium and nitrogen balances closely paralleled each other (Fig. 4), although the potassium balance consistently became positive in dietary periods. Drenick et al. found a significant potassium deficit in three of their four patients [*10*] and pointed out that since the ratio between total body potassium and body weight remained constant throughout and because relatively potassium-free fatty tissue and water were being eliminated, the proportional loss of potassium from the nonfatty tissue was greater than that accounted for by the actual weight loss. In contrast with the first phase the pattern during phase 3 is striking. The scales of Figure 4 show nitrogen and potassium losses in the ratio present in cellular tissue. During phase 3 the potassium loss was greatly increased and quite out of proportion to the nitrogen loss. The occurrence of a total body potassium deficit during phase 3, although likely, cannot be proved since repeated total body potassium estimations were not feasible due to radiation hazards.

In seeking an explanation for the striking potassium loss we cannot ignore the possibility that a systematic error in the record of potassium intake could account for the cumulative effect. Careful checks have been made on the intake

* Associating 1 gm. noncollagenous nitrogen with 0.138 gm. creatine [*57*].

over this period and although our patient might have had some extra source of potassium such as salt substitutes, which he could have taken unknown to us, there seems to be no adequate reason for doubting his word. Therefore we have to assume that the intake records during phase 3 are as accurate as those of the other phases. The effect of a small daily error in balance studies can cause gross discrepancies when cumulated over long periods of time [*58*] and it may be that this factor contributed to the increased potassium loss as recorded. If the potassium intake was underestimated by 25 mEq. daily during phase 3, this would account for the increased rate of potassium loss over the rate in phase 1.

The problem remains: what was the source of the potassium loss? Slightly less than half of it can be accounted for by breakdown of cellular tissue, as reflected in the nitrogen balance. Total body water content did not change significantly during this phase (Fig. 2) and plasma potassium levels did not decrease as in phase 1. In normal adults total body potassium amounts to some 3,000 to 3,500 mEq. [*59*], possibly more than this in overweight persons. The net loss of potassium in our patient during phases 1 and 3, over 3,700 mEq., constitutes an extraordinary depletion even allowing for an originally increased total body content due to obesity. Adipose tissue is known to contain only negligible amounts of potassium, in the region of 4 mEq. per kg. fat tissue [*60*]. There appears to be what might be called an "obligatory potassium loss." With one exception, the patients studied by Drenick et al. [*10*] lost on the average about 13 mEq. potassium daily after the first month of starvation. After 200 days this would have amounted to 2,600 mEq. cumulative loss, a figure approaching ours. Losses of this magnitude are thus not impossible.

*Pulmonary Function.* On admission our patient's condition satisfied the diagnostic criteria of the Pickwickian syndrome. Paradoxically, he was cyanosed although he had an increased oxygen uptake at rest, but cyanosis disappeared after the first month despite a concurrent decrease in oxygen consumption. During the initial fortnight when carbon dioxide pressure became normal, minute ventilation decreased. There was no evidence of resolving chest infection at this time to explain the rapid improvement in the blood gas concentrations. Sputum, although mucoid, was not purulent and pulmonary congestion was not detected clinically or roentgenologically. The readings on the Wright Peak-Flow Meter indicated only moderately severe airways obstruction.

Alveolar hypoventilation due to obesity alone has been reported [*61*] but our patient almost certainly suffered from chronic lung disease as well. Air-trapping, indicative of increased airways resistance, was always demonstrable, and the peak flow rate never reached that expected for his age. Other investigators [*61*] have also found impaired ventilatory capacity but have attributed it to fatigue and the inertia of the large abdominal mass when performing a maximum breathing capacity test. It is unlikely that the inertia of the chest wall and obese abdomen remained major factors during the later phases in our patient. Calculations of his physiologic dead space showed it to be significantly increased and it did not decrease with weight loss. His residual lung volume was increased by one third whereas Hackney et al. [*61*] reported normal values in the pure obesity-hypoventilation syndrome.

The great weight of the chest wall and the raised intra-abdominal pressure of the obese abdomen would impose a greater mechanical load for each breath. This increased work of ventilation was probably responsible for the very high oxygen uptake (Fig. 2) found initially in our patient, despite which hypoxemia occurred. The marked decrease in oxygen uptake in the first month suggests he had the ability to reset his ventilatory mechanism at a more optimum work level after even a modest loss of weight. This was achieved partly by a decrease in the respiratory rate and consequently an increase in tidal volume. It is reasonable to expect an increase in alveolar ventilation following weight reduction, but there was no such increase in our patient. Indeed, blood gases improved despite a decrease in minute ventilation. As the respiratory dead space was elevated, tachypnoea would increase energy expenditure without improving alveolar ventilation. The slight increase in tidal volume in phase 1 would increase alveolar ventilation but expansion of the lung volumes alone at this time would not increase ventilatory efficiency unless accompanied by a simultaneous improvement in ventilation: perfusion ratio. Hackney et al. [*61*] also found decreased lung volumes, similar to those observed initially in our patient, in which the expiratory reserve volume was reduced to less than one third of predicted normal values.

We conclude that the compression effect of

the fat in our patient, who already had chronic obstructive airways disease, led to such a decrease in the lung volumes and ventilatory: perfusion ratios that ventilatory insufficiency resulted. A compensatory increase in ventilation was attempted largely by an increased respiratory rate which disproportionately added to the work of breathing without relieving the respiratory failure. Weight reduction improved lung function and reduced the energy cost of ventilation, but air-trapping remained.

*Emotional Changes.* Natural famine and experimental semistarvation are characteristically accompanied by depression, apathy and occasional paradoxical irritability [*62*]. Such a "neurosis of inanition" did not develop during the prolonged period of dietary restriction in the present case. Admittedly outbursts of disagreement did take place during the latter portion of the study, usually over trivial matters of ward routine, but emotional difficulties were inconspicuous. On the whole the degree of good humour and cooperation throughout the long study were outstanding. Our experience indicates that gross obesity is not necessarily more difficult to treat than obesity of lesser degrees, and also that emotional hazards need not be great.

*General Remarks.* There is no doubt that our patient derived material benefit from weight reduction. Lung function, hematocrit and exercise tolerance were obviously improved. Excluding potassium, the negative balances were not necessarily indicative of detrimental processes; all negative balances might have resulted from the dispersal of bone and muscle which was a structural necessity only when the body weight to be supported was itself excessive. Such external balances fail to indicate the amount of tissue calcium, potassium and nitrogen present initially or finally. Although the total known calcium and phosphorus losses over the nineteen months would represent a substantial proportion of the total bone salt in an average adult man, we have not established that the skeleton of the patient when he attained a weight of 100 kg. was osteoporotic. The relative immobility involved in the prolonged hospital stay necessitated by starvation regimens for the treatment of massive obesity did not appear to be detrimental in our case.

Nevertheless, caution is warranted on the present evidence. Adaptation to continuous fasting can be good [*10*] and perhaps the only advantage of fasting with intermittent periods of low caloric intake is that the regimen can be tolerated for longer periods. The development of more negative nitrogen, calcium and phosphorus balances in phase 3, the predominant fecal route of calcium loss and the increase in the rate of urinary calcium and potassium losses could signify a derangement of homeostatic mechanisms, perhaps located partly in the intestinal mucosa. Studies of accretion rates in a comparable fasting situation would be of value.

The most disquieting feature was the delayed occurrence of a markedly negative potassium balance. This cannot be explained in terms less significant than the assumed presence of an underlying intracellular potassium deficiency. That there were no clinical signs of such a deficit is encouraging.

SUMMARY

The effect of ten day periods of starvation, alternating with ten day periods of low caloric intake, has been studied in a male patient who originally weighed over 200 kg. Metabolic balance and clinical studies extended over a period of nineteen months, during which time 290 days were spent fasting. Weight loss has been assessed in the light of the concurrent losses of nitrogen, calcium, phosphorus and potassium. The rates of loss of calcium and potassium increased later in the study and reasons for this have been discussed. We suggest that the calcium losses may have been due to the resorption of bone unnecessary once the demands of excessive weight were removed. Potassium losses may have indicated an intracellular potassium deficit.

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