Special Contribution

A New Concept in the Treatment of Obesity

A 48-hour total fast followed by six meals a day and later by stepwise increases in food and calorie intake has permitted patients to lose weight that they show no tendency to regain for periods of up to 6 months. It also promoted spontaneous evolution of good dietary habits.

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OBESITY is a problem of affluent society and occurs only in those geographical areas and during those periods of human history that are characterized by an abundance of food available to great masses of people. Conversely, during war, famine, and economic catastrophe, when food becomes scarce, obesity and related diseases rapidly disappear. At mid-20th century Americans have been made acutely aware that, over many huge, underdeveloped areas of the earth representing more than one half of the world's population, a base subsistence level of food supply or actual famine and starvation are still the "normal" ways of life. Among these people obesity is unknown. In other countries, such as the US and those of western Europe, a superabundance of food has led to a high and continuously rising incidence of obesity. There could be no more eloquent testimony to overeating as the basic cause of this problem.

Within any society which is provided with an abundant food supply, however, certain individuals will become overweight and many will not. Furthermore, among the obese group, therapeutic weight reduction is a relatively easy procedure for some and exceedingly difficult for many others. Excluding those numerous individuals who are deceiving themselves (and their doctors) into believing that they eat little but fail to lose weight, there remains a significant group which can be demonstrated under metabolic ward conditions to lose weight very slowly and with great difficulty when simple caloric restriction is imposed upon them. It seems only logical that this phenomenon must have a reasonable explanation that is physiologically and biochemically acceptable. The very existence of the individuals who manifest this resistance to weight loss suggests that there must be factors other than simple caloric balance that complicate this baffling problem.

Accordingly, about 3 years ago, detailed studies of obese subjects were undertaken with the basic objective of ascertaining if their patterns of energy metabolism are significantly different from those of normal control subjects. These efforts were facilitated by an impressive and growing fund of basic information in this field that has accumulated especially during the last 10 years, and by the availability of numerous elegant new biochemical research techniques that had never been applied to the investigation of this clinical problem. It became apparent very early in these studies that a number of metabolic anomalies could be demonstrated, each one representing a biochemical or physiological measurement in which the obese subjects behaved entirely differently from normal control subjects. The magnitudes of these differences

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have been found to vary widely from one subject to another, so that the abnormalities that characterize this condition may not be regarded as all or none, black or white, but constitute, instead, a continuum of varying shades of gray extending from extreme abnormality to completely normal.

A list of these abnormal findings is presented in this report. It should be emphasized that marked variation may be seen from one individual to another, so that many of these anomalies may be present in only a limited number of patients. Of particular interest is the group designated as "resistant obese," which we formerly labeled "metabolic obese." These people always have presented a difficult and perplexing problem of management to physicians.

Since these findings represent the contributions of many laboratories, documentation is provided in the references as designated.

1. Failure to lose weight, even when maintained for prolonged periods on severe caloric restriction.
2. Hypometabolism, as indicated by basal metabolic rate, Achilles tendon reflex, and direct measurement of oxidation rates of glucose, fatty acids, and ketone compounds.[1,2]
3. Low normal or subnormal blood PBI and iodine 131 uptake by the thyroid gland.
4. Low blood cholesterol.[1]
5. Mildly elevated blood triglycerides (TG).[1]
6. Elevated fasting blood free fatty acids (FFA).[3-5]
7. No significant change in blood FFA concentration with fasting.[4,5]
8. Subnormal response of blood FFA and of blood glucose to l-epinephrine injection.[6,7]
9. Resistance to development of ketosis.[8]
10. Resistance to development of negative nitrogen balance on low protein intake.[8]
11. Low rate of oxidation of glucose, palmitate, and beta hydroxybutyrate.[1,2]
12. Increased rate of palmitate oxidation after human growth hormone administration.[9]
13. Increased rate of glucose oxidation after glucagon administration.[2]
14. Failure of rise of glucose oxidation following insulin injection.[2]
15. Low respiratory quotient.
16. Return of patterns of oxidation to normal after triiodothyronine administration.[1,2]
17. Increased tolerance to high pCO_2.[1,23]
18. Low glomerular filtration rate.[10]
19. Decreased renal clearance of water.[10]
20. Impaired ability to excrete a salt load.[11]
21. Exaggerated postural effect on renal clearance of water.
22. Failure of pituitary growth hormone release in response to hypoglycemia, fasting, and exercise.[12]
23. Elevated excretion of 17 ketosteroids and 17 hydroxysteroids.[13]
24. The presence of a "latent" diabetic state.[14,15]
25. High blood insulin concentrations.[16]

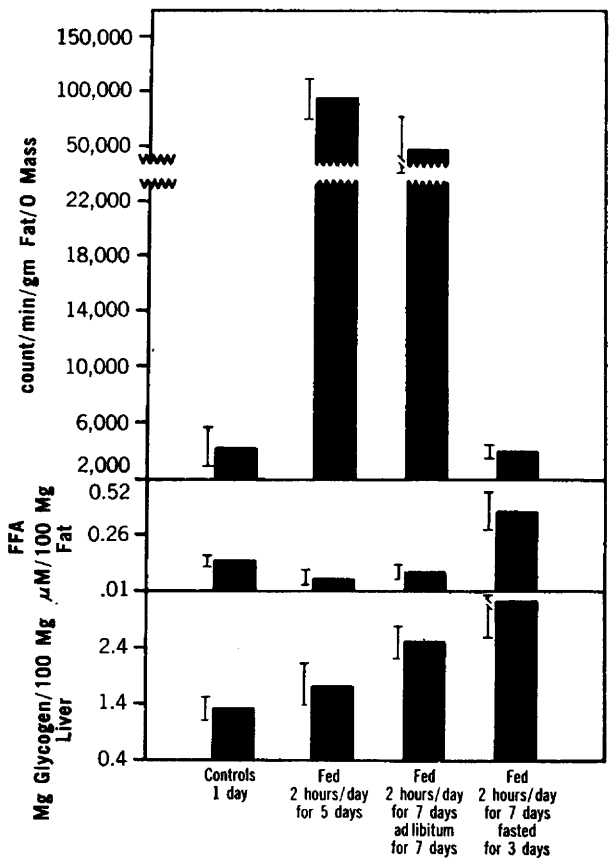


Fig 1.—Augmentation of lipogenesis in four groups of rats taught to eat their daily ration in 2 hours.[20]

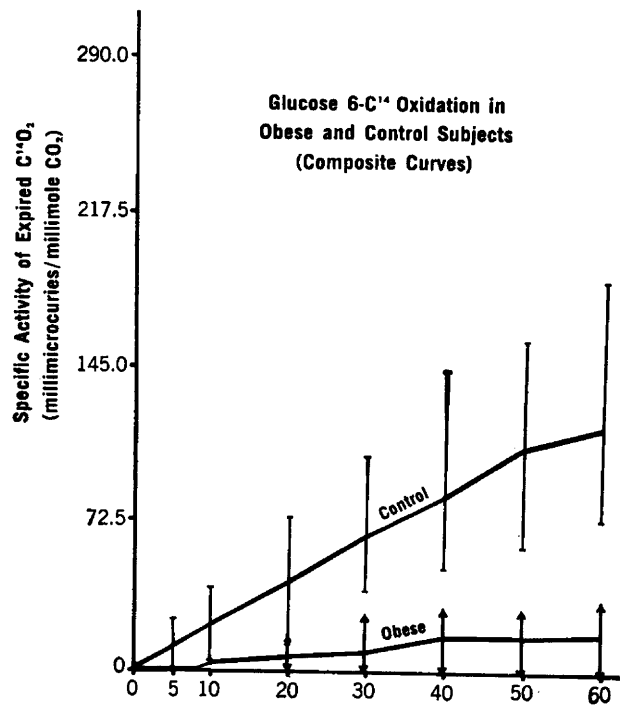


Fig 2.—Radioactivity of C^{14} in expired air is plotted against time. Intravenous injection of radioactive glucose was given at zero time and magnitudes of rise above base line indicate concentration of radioactivity from minute to minute as a result of total oxidation of the glucose.[1]

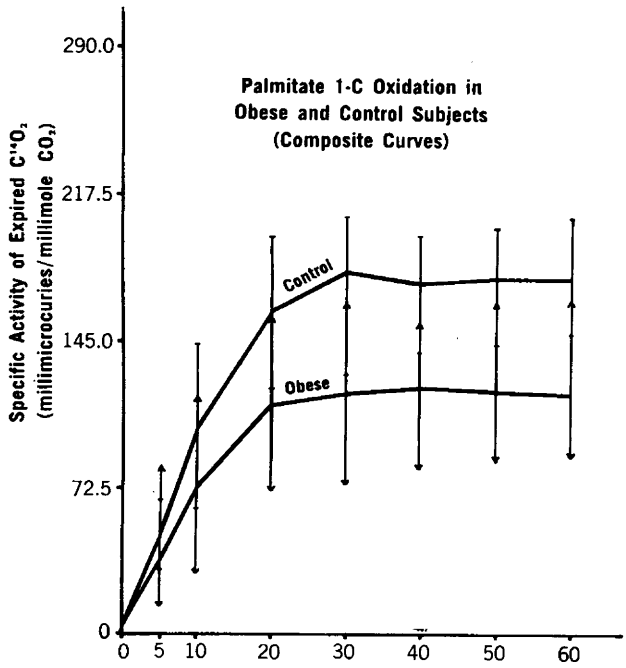


Fig 3.—Data from human obese and control subjects plotted as C^{14} radioactivity in expired air following injection of radioactive palmitate at zero time. Note mild depression in obese subjects.

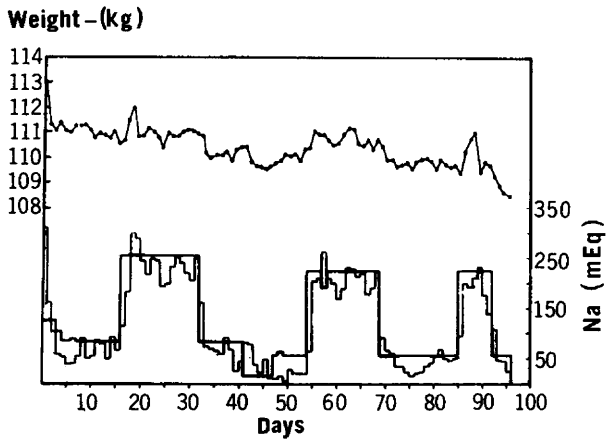


Fig 4.—Rapid adjustment of sodium and water excretion to salt load when obese subject is on maintenance calorie intake. There are no weight changes.[11]

26. High fasting blood pyruvate, lactate, and citrate concentrations.[17]

27. Failure of FFA concentrations to fall normally after glucose administration.[17]

It is not within the scope of this report to discuss each of these findings in detail, since they will appear as research reports in separate publications. Furthermore, some of these findings are not yet well enough documented by clinical studies to be accepted as established fact, and such abnormalities therefore must still be regarded as tentative. Discussion, therefore, will be concentrated on those items which are relevant for an understanding of the therapeutic regimen which has been formulated with the specific intent of correcting, if possible, as many abnormalities of metabolism as possible.

Observations dating back to 1943 have demonstrated an increased rate of lipogenesis (conversion of carbohydrate into fat) in rats fed an adequate caloric diet when feeding was limited to 1 hour a day. The phenomenon has been well documented since that time by the Teppermans,[18,19] by Hollifield and Parson,[20] and by Cohn and Joseph.[21,22] The latter group has found a remarkable increase in carcass fat with a fall in protein and water content in pair-fed rats as compared with normal control animals. It seems very apparent that the experimental animals had sacrificed body protein to synthesize and store fat to produce a state that has been called "nonobese obesity." Accordingly, Cohn and Joseph have concluded that a real increase in efficiency of food utilization occurs when food is eaten in larger amounts at frequent intervals. The experimental data do not adequately bear out this conclusion, but the observation, nevertheless, cannot be doubted. Hollifield and Parson, in extending these studies, confirmed a 25-fold increase in lipogenesis (Fig 1) and have demonstrated, in addition, a marked increase in synthesis of enzymes in liver and adipose tissue, of all those pathways involved in lipogenesis, by concentrated "meal" eating in rats which normally "nibble" most of the time. Such changes are designated technically as adaptive enzyme synthesis. They further showed that this metabolic pattern could most easily be broken by imposing a 48-hour fast on the animals, after which continuous availability of food leads to a restoration of a normal eating pattern, return to normal low level of lipogenesis, and atrophy of the previously hypertrophied enzyme systems.

Since there appear to be justifiable reasons to believe, on the basis of animal experiments, that one or two large meals eaten daily tend to promote storage of fat (obesity), the eating habits of the vast majority of obese human subjects seem almost certainly to be more than a coincidence. For *most* obese patients describe spontaneously their own efforts at weight control through dietary privation during most of the day, with food intake concentrated at one period, most often in the evening. The "night eating syndrome" is an exaggerated form of this same pattern. Accordingly, it became a matter of great interest to study human metabolism in obesity by appropriate methods to determine if the same physiological principles first demonstrated in animals applied to clinical problems. Isotope studies using carbon-14-labeled glucose very quickly showed that obese subjects do not burn glucose normally, but dispose of it, instead, through increased lipogenesis (Fig 2). In this regard, as well as in many others, obese patients behave metabolically exactly like mild diabetics.

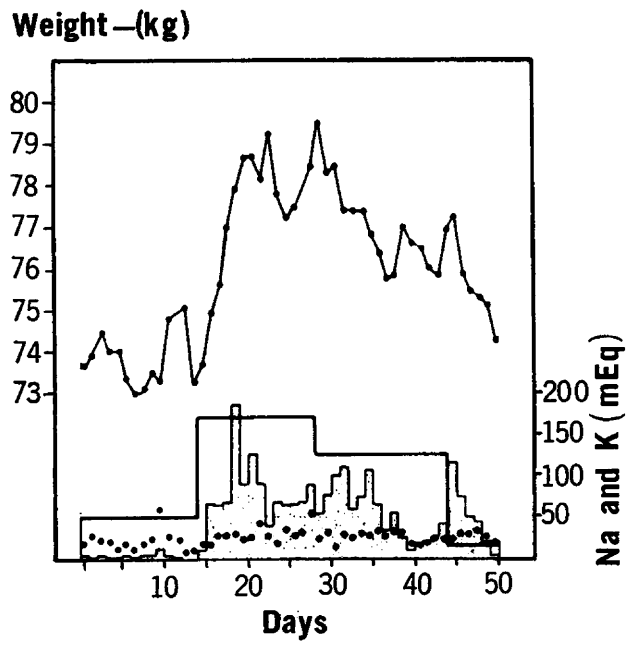


Fig 5.—Poor adjustment to salt load in obese subject on diet of caloric restriction. There is marked gain in weight [12] which persists for the duration of the salt load.

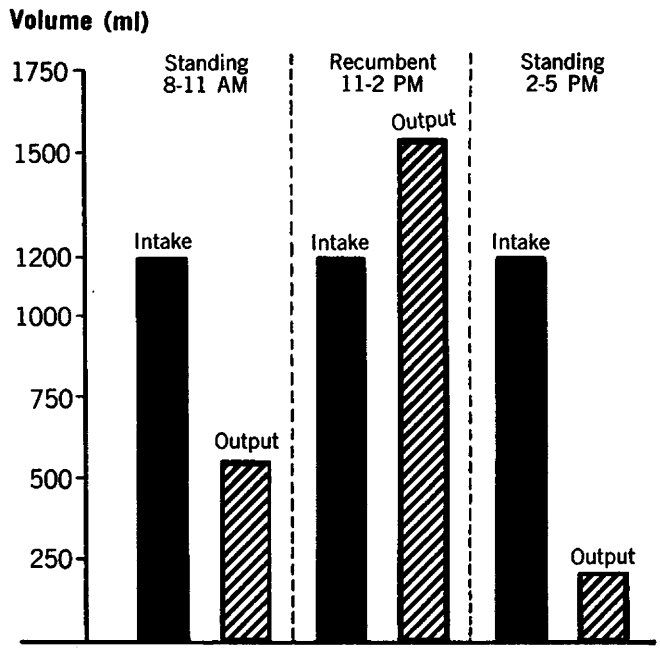


Fig 6.—Response in standing and recumbent positions of female patient given continuous water load. Note marked diuresis when patient is recumbent.

It also was possible to demonstrate that a brief fasting period changed this toward a normal pattern of glucose oxidation to carbon dioxide and water.

The hypometabolism that accompanies obesity has been a perplexing problem. Many or most overweight subjects manifest one or more abnormalities indicative of this hypometabolic state. The iodine 131 uptake by the thyroid gland is usually in the range of 8% to 17% and the PBI of blood, although it often is as high as 6μg%, often falls below 3.5μg%. The photomotogram recording of the Achilles reflex often shows a half-relaxation time of more than 360 milliseconds, which is indicative of a hypometabolic state at the tissue level. Often these tests are not in agreement and in other instances they may all be uniformly abnormal. Direct measurement by carbon 14 methods often, or usually, demonstrates rates of oxidation of palmitate and beta hydroxybutyrate as well as glucose that are below the levels observed in normal subjects (Fig 3). Correction of this abnormality would seem to be best brought about through use of thyroid medication. However, in studying the effects of various thyroid analogs on several parameters of lipid metabolism, the major correction of defective FFA mobilization by l-epinephrine (see abnormality No. 8 on list) occurred in response to triiodothyronine and triiodothyroacetic acid and did not respond to thyroxine, triiodothyropropionic acid, or desiccated thyroid. Triiodothyronine (Cytomel) also was found to increase directly and promptly the oxidation of glucose, as measured by isotope methods, in those individuals who had previously manifested a depressed rate of oxidation.

The close relationship between the metabolism of carbohydrate (glucose) and the synthesis of both fatty acids and triglyceride or neutral fat has been abundantly documented in the literature during the last few years. In brief review, this link is known to be mediated through three main pathways as follows: (1) Glycolysis (chemical degradation of glucose) is the main source of pyruvic acid and, in sequence, the most important of all intermediate compounds, acetyl CoA from which fatty acids are synthesized. (2) Oxidation of glucose by the pentose pathway or the hexose monophosphate shunt generates the essential cofactor, reduced triphosphopyridine nucleotide (TPNH), required for certain steps in the enzymatic combination of acetyl CoA units to form fatty acids. It is generally believed that there is no other quantitatively significant source of this reduced coenzyme. (3) Conversion of fatty acids into triglyceride (the normal storage form of fat) requires the presence of alpha glycerophosphate which can be derived *only* from glucose.

For these reasons, and perhaps especially the last, it may be stated categorically that the storage of fat, and therefore the production and maintenance of obesity, cannot take place unless glucose is being metabolized. Since glucose cannot be used by most tissues without the presence of insulin, it also may be stated categorically that obesity is impossible in the absence of adequate tissue concentrations of insulin. This statement is equally true for obese diabetics who are known to have too much, rather than too little, insulin.[16] Thus an

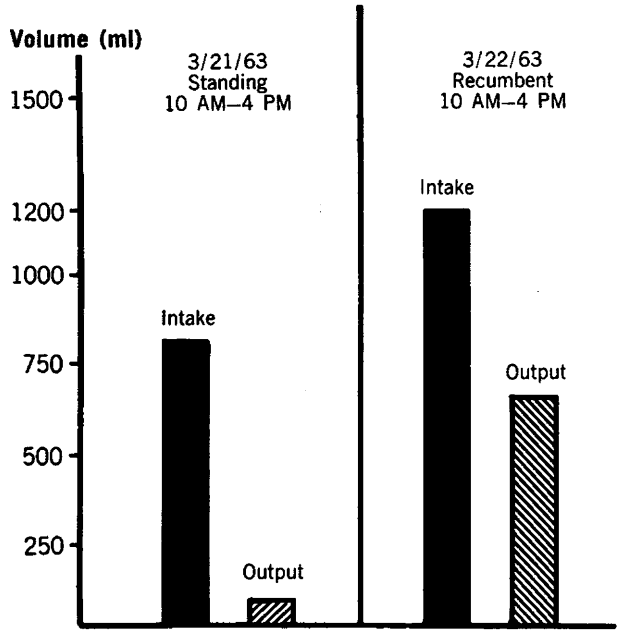


Fig 7.—Marked antidiuresis following water load in a female patient in standing position and relatively poor response even when patient is recumbent.

abundant supply of carbohydrate food exerts a powerful influence in directing the stream of glucose metabolism into lipogenesis, whereas a relatively low carbohydrate intake tends to minimize the storage of fat.

Incorporation of a supplement of polyunsaturated fatty acid in the diet of human subjects has been found to accelerate the rate of oxidation of saturated or body fat. The actual clinical studies were performed with carbon-14-labeled palmitic acid, during which the rate of oxidation was measured by the quantitation of carbon 14 dioxide in expired air. In several obese subjects, after baseline measurements had been made, the substitution of 40% of dietary fat by a linoleic acid concentrate (corn oil) for 1 week led to an augmentation of palmitate oxidation by 20% to 25%. The exact mechanism of this effect remains unknown.

It has always appeared to be a paradox of thermodynamics for any human or other higher living animal to subsist for a prolonged period on a severe caloric restriction and still manifest no weight loss. This phenomenon, however, is well known in the medical literature and is a familiar experience to every clinician who has studied obese subjects even under carefully controlled conditions. Obviously, it must have some reasonable explanation which, in all probability, is the remarkable defect in renal excretion of water that accompanies the obese state. The magnitude of this problem in the practical management of obese patients is often not fully appreciated. In the explanation of the physiological background, it should first be pointed out that the oxidation of 100 gm of fatty acid yields, as a by-product, 112 gm of metabolic water. This water, therefore, weighs more than the adipose tissue that was oxidized in its formation and, if not excreted promptly, can completely cancel the loss of body weight that would otherwise have occurred from metabolism of storage fat.

It has been demonstrated recently that obese human subjects have a diminished glomerular filtration rate, an elevated titer in blood, of posterior pituitary antidiuretic hormone (ADH), and a markedly reduced renal clearance of water.[10] In addition, they manifest a defect in renal clearance of sodium and dispose of a sodium load very slowly while storing simultaneously an added increment of water, presumably in the extracellular compartment[11] (Fig 4 and 5). One remarkable aspect of this phenomenon is the normal excretion of a salt load when the caloric intake is adequate for maintenance of body weight, but a powerful antidiuretic and antinaturetic effect occurs when a caloric restriction is imposed. The edema which results often is visible as pretibial pitting, but, even when it is not noticeable, fluid accumulation regularly takes place during weight reduction.

An additional feature of the water reduction problem in obese individuals is exaggeration of the normal postural effect on renal clearance of water. Diminution of water excretion by the kidney in the standing position, and acceleration in the recumbent position, has been known for many years. In obese subjects, however, this influence is considerably greater and fluctuates in importance from one patient to another (Fig 6 and 7). Almost complete cessation of urine formation in the erect position is seen in some individuals.

The actual program of therapy that has been instituted in connection with these studies is as follows:

1. Forty-eight-hour total fast.
2. Diet:

Protein	100 gm	400 calories
Fat	80 gm	720 calories
Carbohydrate	50 gm	200 calories
	Total	1,320 calories

This diet is given in six feedings daily corresponding to breakfast, midmorning, lunch, midafternoon, supper, and bedtime. Every feeding is a substantial amount of food rather than a "snack." Ideally, all feedings should be approximately the same size. The salt content of the diet is low (between 2 and 3 gm daily). A supplement of polyunsaturated fatty acid is added, the caloric content of which is calculated as part of the fat content.

3. Triiodothyronine is used in most patients, beginning with 25μg three times daily (morning, noon, and night) and increasing the dose by 25μg-increments every 3 to 5 days until tolerance is reached, as indicated by signs of toxicity such as tachycardia, nervousness, and sweating.

4. A diuretic is used about every 10 to 14 days. On the basis of experience, mercurials are most effective (meralluride [Mercuhydrin] sodium, for

example, 2 ml injected at bedtime). Because of the practical difficulties of an injected medication, oral agents may be used, such as chlorothiazide (Diuril) 500 to 1,000 mg or hydrochlorothiazide (Hydro-Diuril) 50 to 100 mg, also administered at bedtime. Methyclothiazide (Enduron), chlormerodrin (Neohydrin), and others also have been used successfully. Ammonium chloride in daily doses of 4 to 6 gm may be used before each dose for potentiation of diuretic action, but usually is not necessary. It is not necessary for any voluntary restriction of fluid intake to be imposed on the patient.

In commenting on this regimen of therapy, it is worth emphasizing again that it contains, so far as we are aware, no philosophical ideas about weight control. It is formulated, instead, on the basis of measured, documented abnormalities in the metabolic functions of obese patients in the hope of achieving a plan of therapy for weight reduction by correcting each one, if possible.

The 48-hour fast initiates the treatment; derived from rat experiments, it is designed not to produce a spectacular loss of weight, but rather to break a metabolic pattern of augmented lipogenesis. During the fast, patients may have as much water, black tea, or black coffee as they wish. They may drink non-nutritious beverages sweetened with saccharin if they wish, and they also may be as active as they wish.

The diet has been planned around the basic concept that its carbohydrate content should be low. This measure seems justified because of the stimulating effect of glucose on lipogenesis and also because of the poor utilization of glucose for energy purposes by obese subjects. The protein content is moderately high for two specific reasons: (1) its high satiety value and (2) its high specific dynamic action. Both criteria seem reasonable on the basis of experience thus far. The fat content is moderate and cannot be considered either high or low. Between 15% and 20% of this fat is polyunsaturated fatty acid supplement. The total caloric value is quite high in terms of reducing diets, but its success provides excellent evidence that severe caloric restriction is not necessary for successful and even rapid weight reduction. Careful study has indicated that the diet is adequate in every respect for adults and would also seem especially satisfactory for children and pregnant women because of its high protein content, even though no clinical application has been made in either pediatrics or obstetrics. When used for children and pregnant women, a supplement of calcium, riboflavin, and ascorbic acid is recommended.

The multiple feedings are designed to emulate the "nibbling" pattern of rats and ruminant animals; this has been shown to minimize lipogenesis and *possibly* decrease the efficiency of food utilization. Six feedings daily has proven to be highly acceptable to all patients and none, to date, has

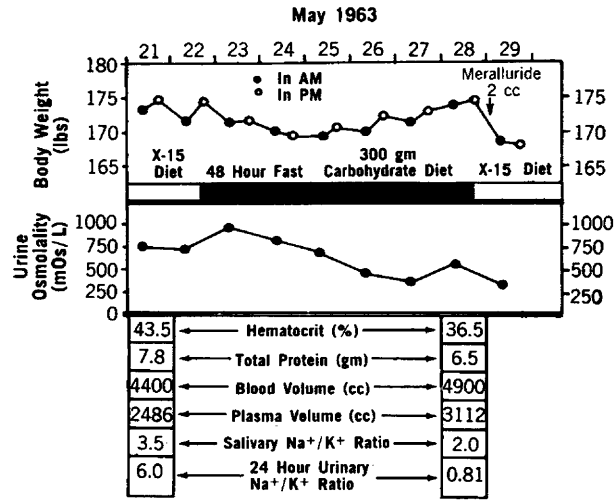
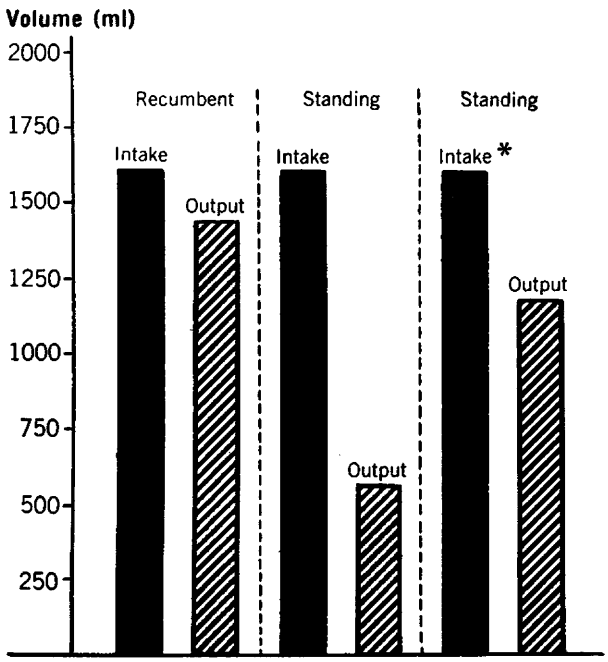


Fig 8.—Fluid and sodium retention incident to a high carbohydrate diet. Note fall in hematocrit level and rise in plasma and blood volume throughout the diet period. The fall in urine osmolality and the sodium:potassium ratio also indicate sodium retention. Body weight rose by 5 lb until carbohydrate intake was reduced.

complained of hunger at any time. Indeed, a common complaint from most is their inability to eat so much food. Eight or ten feedings daily would be equally satisfactory or possibly even better, if some conscientious patients wish to try such a program. The mild salt restriction is not severe enough to make the food unpalatable, but it does tend to minimize the sodium and fluid retention problem. The polyunsaturated fat supplements are a difficult obstacle for some patients. When it becomes unpalatable or poorly tolerated, it is often satisfactory to suggest that salad dressings be made of corn or safflower oil in addition to the use of one of the special margarines as a substitute for butter. In rare instances the supplement has been discontinued altogether.

The use of triiodothyronine was designed originally as a therapeutic requirement for those individuals who manifested significant true evidences of hypometabolism, but it was tested successfully in more and more subjects with equivocal or no indications of this problem. Tolerance varies very widely from those who do not seem to be able to use even a single 25μg-tablet to those who can tolerate up to 250μg daily with no unpleasant reactions of toxicity. It is important to emphasize that the indications of toxicity (tachycardia, nervousness, etc) always should be corrected by a reduction in dosage of 25μg followed by further stepwise reduction until the signs disappear. Tolerance for large doses does not appear to be correlated directly with excessive obesity, but reduction of dosage is usually necessary in all patients as weight declines. Symptoms of toxicity often appear after 50 lb (22.7 kg) of weight reduction on a dose that formerly was tolerated without difficulty. Patients with coronary artery disease probably should not



*Includes 30 cc ethanol.

Fig 9.—Two pairs of columns at left demonstrate marked postural effect on water excretion and columns at right depict diuresis expected when ethanol inhibits release of ADH.

be given this thyroidal compound at all, or, if they are, then only with the greatest of care. It is, however, one of the most effective preparations known to reduce circulating lipid concentrations, including cholesterol.

The problem of fluid retention in obesity, for reasons that are unknown, is almost invariably more severe in female patients. This sex difference appears not to depend on the presence of estrogen, since it is as troublesome in postmenopausal women as it is in younger women. It involves the accumulation of true edema fluid, the release of which, through the action of a diuretic, often is not associated with the development of thirst and a tendency for the patient to regain the lost weight. Without some assistance from medication, some female patients have been observed to continue fluid retention for many weeks with no weight loss and often some weight gain. In young women the problem always is aggravated during the premenstrual week and usually is slightly relieved after the flow begins.

A spectacular demonstration of the effect of posture on renal clearance of water occurs in the course of a standard water diuresis test. Under fasting conditions, a steady diuresis is produced over a 9-hour period by administration to the patient of 200 ml of water orally every 30 min. Urine output is measured once each hour. During the first 3-hour period the patient is required to be standing or walking, the second 3 hours is passed in recumbency, and during the final 3 hours the patient is again standing or walking. The marked diuresis during the second period is always surprising even to the patient, and the antidiuresis during periods one and three sometimes amounts almost to a cessation of urine flow. Because of this postural effect, many obese patients notice puffiness or even pitting edema of the ankles in the evening and often comment spontaneously about their low urine output during the day, only to be troubled after retiring with nocturia, which substantially reduces the edema by the time of arising in the morning. This same observation is helpful in augmenting the therapeutic effect of diuretic medication which, when taken in the morning on arising, often produces little or no response. The same dose taken at bedtime usually will result in a remarkable diuresis. Bedtime hardly seems like the logical time to use a diuretic, but the mild disturbance of sleep it causes is more than compensated for by the excellent response.

Administration of diuretic medication should not be oftener than about once in 10 days or even longer. It seems wise to allow an accumulation of metabolic water before causing its release and, of perhaps even greater importance, when used only infrequently, the danger of all long-term electrolyte disturbances is avoided. Otherwise, hyponatremia and hypokalemia might become real problems. Brief electrolyte depletion does occur, however, very frequently. This usually takes the form of giddiness and mild anorexia upon arising and, occasionally, muscle cramps. Blood chemical studies at these times demonstrate hyponatremia and occasionally mild postural hypotension can be detected. All of these reactions disappear, however, within an hour or so, even without any remedial therapy. In many patients, the diuretic episodes may cause the loss of slightly more than the excess edema fluid. When this happens, the normal homeostatic mechanism results in enough thirst to correct, very promptly, the water deficiency and the patient's weight will "rebound" to a certain extent. None of these minor matters requires any attention, but it has been found desirable to forewarn the patients so that there will be no uneasiness if mild symptoms develop for an hour or so.

One further observation should be noted. The intake of an appreciable quantity of concentrated carbohydrate food (for example, a rich dessert) regularly leads to the "binding" of a large amount of water, probably through an antidiuretic effect that is not understood. In a typical experimental demonstration, a severely obese man who had been losing weight very successfully on a therapeutic regimen was deliberately given an 800-gm carbohydrate, 4,000-calorie-per-day-diet for 2 days, during which he gained 18 lb (8.2 kg). Three weeks subsequently was required for his weight to return to its "precarbohydrate" level, during which time fluid balance measurements indicated marked and sustained retention. The experimental data illus-

Values Used for Protein, Fat, and Carbohydrate in the Diet

One egg	6.0	6.0	.....	.....
11 oz meat*				
{6 oz group A	42.0	26.4	3.9	.....
{5 oz group B	35.0	15.5	.....	.....
7 servings fat				
{4 teaspoons corn oil	.....	20.0	10.0	.....
{3 teaspoons margarine	.....	12.0	3.3	.....
2 cups skim milk	16.0	.....	.....	24
2 servings fruit	.....	.....	.....	20
½-slice bread or ½-cup B vegetable	2.0	.....	.....	7
2 to 4 cups A vegetable	.....	.....	.....	.....
Totals	**101.0**	**79.9**	**17.2**	**51**

Per cent of fat that is polyunsaturated, 21.5.
* Averages of values given in Nutritive Value of Foods, Home and Garden Bulletin No. 72, US Department of Agriculture.

trated in Fig 8 demonstrate the effects produced by change to a high carbohydrate diet in the course of weight reduction. Observations of this kind, which have been repeated many times, have led to the belief that some physiological link must exist between posterior pituitary ADH and carbohydrate metabolism. A comparable link between aldosterone production and release by the adrenal cortex and carbohydrate metabolism has been noted in primary aldosteronism,[24] so that the homeostasis of both water and electrolytes may be influenced by fluctuations in the patterns of energy metabolism (Fig 9).

Details of the Diet Plan

Following the principles outlined above, the diet plan is high in protein, moderate in fat, and low in carbohydrate and salt. Six feedings daily, each containing protein, are required. The patient who so desires may eat more often than the six times a day outlined, but a minimum of six feedings is essential and should be well spaced throughout the patient's waking hours. The diet will be outlined in detail. Foods considered "free" and foods especially contraindicated are listed first, followed by the specific foods to be eaten. Explanations are given to clarify food selections. A suggested meal pattern is given and possible changes are suggested.

"Free" Foods.—As in other reducing diets, a number of foods which are calorie-free or exceedingly low in calories are allowed in unlimited quantities. These are: noncaloric sweeteners, clear fat-free broth (Use of boullion cubes is discouraged because of their high sodium content. Instead, patients are encouraged to make their own broth, refrigerate it, and then remove the fat which hardens at the top.), unsweetened plain gelatin, artificially-sweetened gelatin products, lemon, vinegar, spices and herbs, and carbonated beverages prepared with noncaloric sweeteners.

Contraindicated Foods.—Although it should be obvious that foods not listed on the diet are not to be eaten, experience has shown it wise to specify foods especially contraindicated because of their high carbohydrate or saturated fatty acid content. These are: butter; carbonated beverages, unless prepared with a noncaloric sweetener; nuts, except for California (English) walnuts; potato chips, pretzels, crackers; sugar, syrups, molasses, honey, and candy; sweetened pickles; all desserts; gelatin products sweetened with sugar; gravy and meat drippings; and alcoholic beverages.

The Daily Food Plan

1. One egg
2. Eleven oz (cooked weight) lean meat (see meat list)
3. Seven servings fat (see fat list)
4. Two cups skim milk
5. Two servings fruit (see fruit list)
6. Two to four cups vegetables from the A list (see "Vegetable A" list)
7. One-half slice bread (see bread and "Vegetable B" list)

(See Table for protein, fat, and carbohydrate values.)

Meat List: Group A.—Chicken, turkey, pork (includes chops, roast, and steak).

Group B.—Fish (any kind—canned fish should be "water packed" instead of "oil packed"), lamb (all cuts), veal (all cuts), beef (all cuts, including liver).

The meats are divided into two groups, A and B, according to their content of polyunsaturated fatty acids and total fat. Six ounces of meat or more should come from group A and 5 oz or less should come from group B. The group A meats contribute small amounts of polyunsaturated fatty acids to the diet. Although it seems more logical to place pork in the B group of meats because of its relatively high total fat content, it was placed in the A group instead for the following reasons:

1. In the amount eaten on the diet, pork will contribute measureable amounts of polyunsaturated fatty acids, and the 80-gm fat allowance of the diet easily will allow liberal use of this high-fat meat.
2. Over-all cost of this diet has previously been mentioned as a disadvantage when compared with isocaloric diets higher in carbohydrate. Pork, a lower-cost meat than beef, lamb, and veal, can make the diet a reality for people in the lower income brackets.
3. Liberal use of pork allows the diet to meet National Research Council recommended allowances for thiamine.

There are good reasons for placing fish in either group A or group B. Fish was placed in group B because, in the small amounts usually eaten in the American diet, as compared with meat, it would not contribute markedly to the polyunsaturated fatty acid content of the diet.

Possible substitutions are suggested for some of the meat. Any of these substitutions alter the constituents of the diet, but are included to make the diet more realistic to follow. Substitutions suggested are:

1. For 1 oz of meat in group A, one tablespoon of peanut butter. (This substitution should not be made more than twice a week, because it raises the carbohydrate content and lowers the protein content of the diet.)
2. For 1 oz of meat in group B, one fourth of a cup of cream-style cottage cheese.
3. For 2 oz of meat in group B, 1 oz of cheddar, American, or Swiss cheese. (This substitution lowers the protein content and slightly elevates the fat content of the diet, so not more than 1 oz should be substituted daily.)
4. For 2 oz of meat in group B, one egg. (This substitution keeps the fat almost the same, but lowers the protein content of the diet so not more than one egg should be substituted daily.)

The question of possible use of frankfurters and luncheon meats frequently arises. In general, their use is discouraged. Their relative fat content is usually higher than plain cuts of meat and the sodium content is high as well. Cereal "fillers" and dried skim milk powder frequently are added to luncheon meats. Either of these additions would increase the carbohydrate content of the diet.

Fat List

Fat	Amount in One Serving
Corn oil, cottonseed oil, safflower oil*	1 teaspoon
Mayonnaise (not more than 4 teaspoons should be used per day because of a slightly lower polyunsaturated fatty acid content and a small carbohydrate content not found in the recommended oils.)	2 teaspoons
California (English) walnuts (not more than 2 tablespoons or 10 halves should be used per day because of carbohydrate content.)	1 tablespoon chopped or 4 to 5 halves
Margarine made with corn oil or safflower oil (not more than 3 teaspoons should be used per day because of lower polyunsaturated fatty acid content than the recommended oils.)	1 teaspoon

*The oil should not be heated to high temperatures, such as those reached in frying, because oxidation occurs. In calculating values for the fat list in the diet, the seven servings allowed were broken down into 4 teaspoons of corn oil and 3 teaspoons of margarine.

Fruit List

Fruits may be fresh, dried, cooked, or canned, so long as no sugar is added to them. One of the two servings of fruit allowed daily should be a good source of ascorbic acid and are designated by an asterisk (*).

Fruit	Amount in One Serving
Apple (2-in. diameter)	1 small
Apple sauce	½ cup
Apricots, fresh	2 medium
Apricots, dried	4 halves
Banana	½ small
Blackberries	1 cup
Raspberries	1 cup
*Strawberries	1 cup
Blueberries	⅔ cup
*Cantaloupe (6-in. diameter)	¼
Cherries	10 large
Dates	2
Figs, fresh	2 large
Figs, dried	1 small
*Grapefruit	½ small
*Grapefruit juice	½ cup
Grapes	12 large
Grape juice	¼ cup
Honeydew melon, medium	⅛
Mango	½ small
*Orange	1 small
*Orange juice	½ cup
Papaya	⅓ medium
Peach	1 medium
Pineapple	½ cup
Pineapple juice	⅓ cup
Plums	2 medium
Prunes, dried	2 medium
Raisins	2 tablespoons
Rhubarb	1 cup
*Tangerine	1 cup
Watermelon	1 cup

Vegetable List

These vegetables are allowed either raw or cooked. A green or yellow vegetable is recommended daily for its vitamin A content. These vegetables, all very low in protein, fat, and carbohydrate, are considered "free" in calculating their values. However, since they actually do contain small amounts of carbohydrate, an upper limit of 4 cups daily is made. A lower limit is indicated so that recommended nutritional allowances can be met.

	Greens	
Asparagus	Beet greens	Lettuce
Broccoli	Chard	Mushrooms
Brussel sprouts	Collard	Pepper
Cabbage	Dandelion	Radishes
Celery	Kale	String beans
Chicory	Mustard	Summer squash
Cucumbers	Spinach	Tomatoes
Escarole	Turnip greens	Tomato juice
Eggplant		Watercress
Cauliflower		

Vegetable B and Bread List

Either one-half slice of bread *or* one-half cup of any of the vegetables listed below can be eaten, since their protein, fat, and carbohydrate values are so nearly the same.

Beets	Carrots	Onions
Peas	Squash	Turnips
Pumpkin	Rutabagas	

Suggested Daily Meal Plan

Breakfast
½-cup vitamin C fruit or juice
1 egg
1 oz meat
1 teaspoon margarine
½-slice bread
Coffee or tea

Midmorning
1 cup skim milk
1 oz meat

Lunch
3 oz meat
Vegetable A
1 teaspoon margarine
2 teaspoons corn oil
Coffee or tea

Midafternoon
2 oz meat
½ cup skim milk

Dinner
3 oz meat
Vegetable A
1 teaspoon margarine
2 teaspoons corn oil
1 serving fruit
Coffee or tea

Evening
½-cup skim milk
1 oz meat

Ideally, the protein in the diet would be divided equally in each of the six feedings. However, a larger amount is given at the luncheon and dinner meals to more nearly resemble the American meal pattern. The fruit, which could be eaten at any time during the day, was placed at breakfast, which is the usual meal for having a fruit high in ascorbic acid, and at dinner, so that a "dessert" can be eaten when the entire family is usually together. Margarine is allowed at each meal, to be used on toast at breakfast and on cooked vegetables at the other two meals. The remaining fat allowance is used as oil which can be put on salads in combination with vinegar, lemon, and spices and herbs. Other combinations of fats from the fat list also could be made. Some individuals prefer to drink the oil straight, as they would a medication.

Skim milk is suggested as the beverage between meals, since coffee or tea usually is available at meal time either at home or in a restaurant.

Women who spend their day at home have found the diet quite easy to handle. Those people working away from home must be more ingenious. Cold meat, such as leftover chicken or roast beef, can be wrapped in waxed paper and taken to work. The substitution of cheese or hard-cooked eggs can be made and may be easily slipped into a bag or

purse. A meat prepared without fat or carbohydrate can be obtained in the humblest of restaurants, for if no roasted, boiled, or broiled meats are available, beef patties usually are. Skim milk can be carried in a thermos bottle. Celery sticks, radishes, and raw tomatoes are good for packed lunches and are usually available in restaurants. Lettuce, vinegar, and oil are universally available, even if not listed on restaurant menus.

If skim milk cannot be made available in any way during the day between meals, the following changes may be made in the diet plan:

1. Drink the cup of skim milk listed for the midmorning feeding at breakfast instead of at midmorning, and eat the ounce of meat listed for breakfast at midmorning. This means that no meat is eaten at breakfast and 2 oz are eaten at midmorning.

2. Eat 2 oz of meat at midafternoon and instead of drinking the one-half cup of milk listed at that time, drink it at the evening feeding. This means that the midafternoon feeding consists of 2 oz of meat and the evening feeding is one cup of skim milk and 1 oz of meat.

Four eggs should be eaten each week. If a person does not want an egg every day as outlined on the diet, an ounce of meat from either group A or group B may be substituted for the egg.

For those people who find the quantity of food too large, the most advisable action to take is proportionate reduction of the amount eaten of all of the food groups. A single food or food group should not be eliminated from the diet and feedings should not be eaten less often than six times a day.

The diet as outlined meets 1958 recommended daily allowances of the National Research Council for adults. To retain the protein, fat, and carbohydrate values, as well as the National Research Council's recommended allowances, the only suggested change in food selection would be to reduce the fruit to one serving daily and to increase the bread to one slice daily. Other changes in food selection cannot be made which will meet the protein, fat, and carbohydrate values and still meet these recommended allowances. If a patient has known allergies or if a patient, after sincere attempts, finds the food as outlined in the diet impossible to eat, a different diet, retaining the protein, fat, and carbohydrate values, would have to be planned with nutritional supplements given to meet recommended allowances.

Comment

Clinical results that have followed the use of this plan of therapy have been remarkably encouraging and surprising (Fig 10). No patient to date has complained of hunger at any time; some who have been especially addicted to high-carbohydrate food, particularly rich desserts, have had some "withdrawal unhappiness" for a short time, but it is not

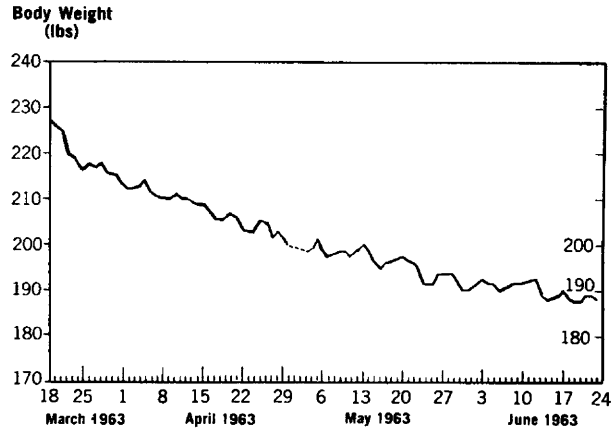


Fig 10.—Typical weight loss curve over 3-month period during which 45 lb (20.4 kg) were lost. During this period the patient (female) felt no hunger.

attended by hunger. Several patients have returned to normal weight after losses of 50 to 100 lb (22.7 to 45.4 kg) and this circumstance has necessitated changes of management to maintain their improvement. The first modification has been to broaden the use of fruits and vegetables to include some which previously had not been included. These changes are additions rather than isocaloric substitutions. Patients are asked to do this carefully, allowing at least 2 weeks after each change before proceeding to further additions. They are next allowed increased bread, up to one slice per meal, included as additions rather than substitutions. Throughout all these stepwise increases in food and calorie intake, they are asked to continue to divide their daily food allotment into six feedings and are again admonished that desserts should be the last additions for experimentation. Under these circumstances all patients who have evolved through this procedure have maintained their weight loss despite increased caloric intake and have manifested no tendency to regain weight over periods of up to 6 months. Much more experience is necessary regarding this transition period before any significant conclusions can be drawn.

One of the most surprising features of this therapeutic program has been the autonomous manner in which it has operated. At the time of discharge of patients from the hospital, careful instruction is given concerning all details of treatment and they are asked merely to communicate by mail after 1 month, during which time no physician sees them. In contrast to our previous experience, very few patients thus far have failed to continue the weight loss which began in the hospital. Losses have varied from 9 to 28 lb (4.1 to 12.7 kg) during that month and have continued thereafter until the first progress visit, approximately 2 months after discharge.

In surveying this vast spectrum of metabolic changes associated with the obese state, it is mani-

festly difficult or impossible to establish which abnormalities are causes and which are the effects of obesity. Likewise, we are unable to throw very much light on the baffling question of the relative importance of genetic and environmental or adaptive factors in the etiology of this condition, although the former influences are being studied [25, 26] and the latter are self-evident.

We have an intuitive feeling that fasting is not the correct way to manage obesity, since it provides no opportunity for readjustment and re-education of the patient's dietary and eating habits. One unexpected dividend that has emerged from the institution of this therapeutic program has been the spontaneous evolution of new and more beneficial dietary habits in a great many patients who have commented with great surprise about the apparent loss of old compulsions to eat and modification of cravings for certain high-carbohydrate foods.

Finally, it is pertinent to ask: Is there such a clinical condition as "metabolic obesity?" The striking deviations from normal in most of the metabolic findings that have been described led originally to the impression that these subjects represented a separate clinical entity. With further experience, however, the magnitude of these changes, as they are studied in patient after patient, is now seen to cover a continuous spectrum and we are more inclined to believe that "metabolic obesity" may be a stage of the obese state rather than a separate and distinct form of the condition. It appears to be more closely related to the duration than to the degree of obesity. Only increased experience can provide the perspective necessary for a final, correct interpretation.

In conclusion, the authors wish to reiterate that the original investigations on which this therapeutic program is based were initiated as an unbiased effort to study the perplexing and controversial problem of energy metabolism in human obesity. It is still a research project and this tentative plan of management is offered for broad trial by physicians with hope that the resulting extensive experience and further modification as new information becomes available will help to establish a final judgment of its validity.

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Generic and Trade Names of Drugs

Meralluride sodium—*Mercuhydrin Sodium.*
Chlorothiazide—*Diuril.*
Hydrochlorothiazide—*Esidrix, HydroDiuril, Oretic.*
Chlormerodrin—*Neohydrin.*

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