Prolonged Starvation as Treatment for Severe Obesity

Ernst J. Drenick, MD, Marion E. Swendseid, PhD, William H. Blahd, MD, and Stewart G. Tuttle, MD, Los Angeles

Eleven obese, ambulatory patients were starved for periods of 12 to 117 days. Only water and vitamins were consumed. Weight losses averaged 0.91 pounds (0.41 kg) daily. Hunger was virtually absent. Complications which developed during starvation were severe orthostatic hypotension in three cases; severe normochytic, normochromic anemia in one case; and gouty arthritis in two cases. With refeeding all ill effects were promptly reversed. Serum electrolytes, lipids, proteins, and amino acids remained unchanged during starvation. Serum uric acid increased; blood glucose levels fell in some cases. Considerable amounts of body protein and potassium were lost. Prolonged starvation is not advised for obese patients with a history of ischemic cardiovascular or cerebral disease, with history of gout, or with hepatic disease.

A steadily increasing number of obese patients have been asking physicians to help them to lose weight. Diets have been prescribed, but in many instances, sustained and adequate weight reduction is not accomplished.1 The greatest difficulties are faced by extremely obese individuals. For these patients efforts should be directed toward accelerating weight loss to a maximum so that normal weight can be re-established in a reasonable period of time. Complete abstinence from caloric consumption would appear to be the best approach, since most seriously overweight patients are no longer capable of performing the physical exercises which would result in a significant expenditure of calories.

Various weight reducing routines employing starvation have been used for many years.2-3 Recently it has been recommended that weight loss be brought about by repeated periods of ten-day or two-week fasts.4 Other methods with starvation or semistarvation up to a month or longer have been described.5 All reports have emphasized that prolonged fasts are easily tolerated, little discomfort is experienced, and no serious adverse side effects are observed.

For editorial comment, see page 144.

However, the limit of the starvation period in obese subjects which is compatible with good health has not been well established. The purpose of the present investigation was to study the factors which limit the duration of starvation in obesity and to study other clinical and metabolic changes which might occur during the treatment.

Methods and Material

Eleven obese patients were hospitalized on a metabolic-balance ward. All but one of the individuals were male. Ages ranged from 32 to 71 years, and the weights, from 240 to 450 pounds (108 to 204.1 kg). A variety of clinical conditions was represented among the patients (Table 1). The period of total starvation ranged from 12 days to a maximum of 117 days. The patients were permitted to drink tap water ad libitum. Multivitamins were given orally each day. These contained 5,000 units of vitamin A, 400 units of vitamin D, 2 mg of thiamin hydrochloride, 3 mg of riboflavin, 75 mg of ascorbic acid, and 20 mg of nicotinamide. No mineral supplements were administered. Activity was not restricted.

The patients were weighed each morning. The blood pressure was measured with the subject in the prone and in the upright position every morning. Urine was collected for 24-hour periods and measured. Aliquots were analyzed for the content of total nitrogen, using the micro Kjeldahl method. Uric acid,6 sodium, and potassium7 were determined in selected patients. Semiquantitative determinations of acetone8 were done. Blood was examined at intervals for the following components: total lipids,9 cholesterol,10 glucose,11 uric acid, electrolytes12 albumin and globulin fractions,13 and

From the medical and radiisotope services, Veterans Administration Center, Department of Medicine, and School of Public Health, University of California.
Table 1.—Clinical Data on 11 Obese Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, Yr</th>
<th>Sex</th>
<th>Height Ft, In (Cm)</th>
<th>Weight, Lb (Kg)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33</td>
<td>M</td>
<td>5, 10 (177.8)</td>
<td>284 (128.8)</td>
<td>Bilateral above-knee Amputation</td>
</tr>
<tr>
<td>2</td>
<td>37</td>
<td>M</td>
<td>6, 7 (200.7)</td>
<td>550 (158.8)</td>
<td>Hypertension; Pickwickian syndrome</td>
</tr>
<tr>
<td>3</td>
<td>38</td>
<td>M</td>
<td>6, 1 1/2 (186.7)</td>
<td>344 (156.1)</td>
<td>Hypertension</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>F</td>
<td>5, 6 (167.6)</td>
<td>315 (142.9)</td>
<td>Hypertension</td>
</tr>
<tr>
<td>5</td>
<td>46</td>
<td>M</td>
<td>6, 1 (185.4)</td>
<td>301 (136.6)</td>
<td>Arteriosclerotic heart disease; osteoarthritis</td>
</tr>
<tr>
<td>6</td>
<td>41</td>
<td>M</td>
<td>6, 2 1/2 (189.3)</td>
<td>268 (121.5)</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>7</td>
<td>43</td>
<td>M</td>
<td>5, 10 (177.8)</td>
<td>285 (129.3)</td>
<td>Aseptic necrosis of femoral heads; diabetes mellitus</td>
</tr>
<tr>
<td>8</td>
<td>51</td>
<td>M</td>
<td>5, 8 (175.7)</td>
<td>284 (128.8)</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>9</td>
<td>63</td>
<td>M</td>
<td>5, 10 (177.8)</td>
<td>315 (142.9)</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>10</td>
<td>64</td>
<td>M</td>
<td>6, 1 1/2 (184.2)</td>
<td>243 (110.2)</td>
<td>Leukemiec's cirrhosis</td>
</tr>
<tr>
<td>11</td>
<td>71</td>
<td>M</td>
<td>5, 10 (177.8)</td>
<td>236 (107)</td>
<td>Arteriosclerotic heart disease</td>
</tr>
</tbody>
</table>

Results

The attitudes of individual patients toward the proposed plan of weight reduction varied. Some patients treated early in the course of this study did not seem particularly disturbed about their overweight; among these cooperation was not satisfactory. In general, patients who spontaneously requested inclusion in this study and who had much to gain by attaining a normal weight tended to tolerate the fast better and longer without serious subjective complaints. Hunger sensation was experienced for 2 to 4 days after the last meal; but, in some cases, it never became noticeable. The severity of the hunger was surprisingly mild in all cases and never constituted a reason for abandoning the fast. Oral medications in the form of pills or solutions for intercurrent illnesses were taken reluctantly, and occasionally nausea followed. Some patients stated that the vitamins also caused unpleasant digestive symptoms; in one case the vitamins had to be administered parenterally.

No attempt was made to encourage a high fluid intake. Accurate records of the intake were not maintained, but it was observed that thirst abated and water consumption decreased drastically. Urinary output actually diminished to oliguric levels in some patients who continued fasting into the second month. In one patient, during a five-day period, an average daily urine output of 120 cc was observed, while renal function remained normal. Patients who fasted up to two months frequently stated that water, also, seemed unappetizing and that they preferred to drink as little as possible.

Elimination of fecal matter ceased after three to four days; and, after that, only small amounts of mucus material were evacuated at two- or three-week intervals. After resumption of eating, bowel activity proceeded normally.

The only female in this study had a normal menstrual cycle prior to starvation. She missed one menstruation and had two periods of somewhat increased flow during the fast.

Physical endurance and energy decreased slowly. Severe weakness was uncommon. Younger patients up to about 45 years of age actually seemed to remain fairly vigorous, and some were able to do physical work. Older patients were content to walk moderate distances but felt tired soon and required frequent short rests on their beds during the day. Sleep patterns did not seem to be different during starvation, but prolonged siestas were common. Sensitivity to cold was noted by one third of the subjects.

Four patients in this group had significant hypertension on routine determinations. At the end of starvation, the blood pressure was normal. It was realized that the obesity of the arm may cause false inaccurate readings. Therefore, in two patients, intra-arterial pressures were obtained. One man showed 220/120 mm Hg by cuff and 165/95 mm Hg by intra-arterial catheter. The female had a pressure of 240/140 mm Hg and an intra-arterial pressure of 150/90 mm Hg; after three months of fasting, the cuff readings were 110/80 mm Hg and the intra-arterial pressure 110/70 mm Hg. In most subjects who initially were found to be normotensive, a moderate decrease of blood pressure was noted, which tended to rise slightly upon refeeding but not to prestarvation levels. Pulse rates

Table 2.—Weight Loss, Side Effects, and Duration of Starvation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Period of Continuous Starvation, Days</th>
<th>Weight Loss, Lb (Kg)</th>
<th>Serious Side Effects</th>
<th>Cause of Termination of Starvation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75</td>
<td>41 (18.6)</td>
<td>None</td>
<td>Personal reasons</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>91 (41.3)</td>
<td>Gout</td>
<td>Postural hypotension</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>41 (18.6)</td>
<td>None</td>
<td>Personal reasons</td>
</tr>
<tr>
<td>4</td>
<td>117</td>
<td>116 (52.6)</td>
<td>Gout, anemia</td>
<td>Postural hypotension</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>28 (12.7)</td>
<td>None</td>
<td>Personal reasons</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>23 (10.4)</td>
<td>None</td>
<td>Noncooperative</td>
</tr>
<tr>
<td>7</td>
<td>12</td>
<td>18 (8.2)</td>
<td>None</td>
<td>Noncooperative</td>
</tr>
<tr>
<td>8</td>
<td>52</td>
<td>63 (28.6)</td>
<td>Postural hypotension</td>
<td>Personal reasons</td>
</tr>
<tr>
<td>9</td>
<td>20</td>
<td>32 (14.5)</td>
<td>Postural hypotension</td>
<td>Noncooperative</td>
</tr>
<tr>
<td>10</td>
<td>43</td>
<td>35 (15.9)</td>
<td>Weight</td>
<td>Postural hypotension</td>
</tr>
<tr>
<td>11</td>
<td>25</td>
<td>29 (13.2)</td>
<td>Postural hypotension</td>
<td>Postural hypotension</td>
</tr>
</tbody>
</table>

Routine blood cell counts. In selected patients, plasma amino acids were measured. These were determined in picric acid extracts of plasma by ion exchange chromatography, using an automatic instrument. In several patients, total body potassium was determined by K measurements in a body-radiation counting chamber.

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and sleeping respiratory rates declined very slightly during the fast.

Weight Loss.—Weight loss was the expected and most obvious result of starvation. Table 2 shows the number of days each patient starved and the weight lost. The greatest net loss in a single continuous period of starvation was observed in the only female included in this group. She lost 116 pounds (52.6 kg) in 117 days of fasting. Only one patient was able to attain a near-normal weight as the result of one single continuous period of fasting. Another five subjects required repeated fasts before they were thought to have acceptable weight levels. Two patients were considered failures because the actual weight loss failed to approach the desired goal. Initially, weights decreased very rapidly, and the loss seemed greater the heavier the patient. One subject who weighed 450 pounds (204.1 kg) lost 9 pounds (4.1 kg) in one day. Most individuals lost two to three pounds (0.9 to 1.3 kg) daily for the first ten days, unless they had been on a reducing diet prior to the fast. After the second ten-day period, the rate of daily weight reduction decreased progressively until it reached about 0.7 pounds (0.31 kg) daily at the end of the second month. From then on, the losses per day tended to remain fairly constant (Table 3). There were considerable differences in the rates of loss; but, in the group under observation, there was no evidence of inability to lose weight. Occasional temporary weight gains were observed. Significant gains occurred in the female during menstrual periods.

Protein Metabolism.—In starvation, with the exhaustion of carbohydrate stores, amino acids are used for glyconeogenesis and substantial numbers of cells, in addition to fat tissue, are metabolized to provide the protein for this need. A measure of protein metabolism is the amount of nitrogen excreted in the urine.

From several studies of starvation it has been reported that urinary nitrogen from initial high values tended to decrease during the course of the fast. With four subjects of the present study, the initial values of approximately 9 gm of total urinary nitrogen per day decreased until, after one month of fasting, the amounts excreted remained relatively constant at approximately 4 gm per day. This represents a protein loss of approximately 25 gm per day. In one individual (patient 1), nitrogen excretion was reduced to 2.4 gm per day after 70 days of starvation.

It has been reported that individuals who consumed a diet containing 3.5 gm of nitrogen per day for four to six weeks showed, in postabsorption plasma, a decrease in essential amino acids and an increase in nonessential amino acids, with a resultant decrease in the ratio (EN ratio) from 0.45 to values as low as 0.21. In the present study, plasma amino acids were measured in subjects at the beginning and at intervals during the starvation period. The results for five subjects are shown in Table 4.

It has been found that many, but not all, obese subjects have high plasma EN ratios due to increased amounts of the three branched-chain amino acids—valine, isoleucine, and leucine. The significance of this finding is not known at the present time. The five subjects shown in Table 3 had concentrations of branched-chain amino acids ranging from 10% to 20% of the total amino acids. These values can be compared with a range of 13% to 18% found in 18 healthy nonobese subjects. The amounts of essential and nonessential amino acids were not greatly altered for any of the four subjects after 20 to 30 days of fasting; the EN ratio and the branched-chain amino acids remained high. Prolongation of the fast to 50 or 60 days tended to decrease the branched-chain amino acids and the EN ratio in most individuals; patient 4, after 90 days of starvation, had values for these parameters within the normal range. These results with starving subjects are, therefore, different from
results obtained with subjects maintained on low-protein diets. In starving subjects, despite continuous loss of nitrogen from the body, plasma amino acids tended to remain at their prefast concentration; and one individual, after 90 days of starvation, had essentially normal plasma amino acid values.

Similarly, no significant changes occurred in the serum albumin and globulin fractions in any of the subjects during the starvation period.

**Serum Cholesterol, Glucose, and Electrolytes.**—In the present series, serum cholesterol levels were surprisingly low in the majority of these patients, with values ranging from 125 mg/100 cc to 275 mg/100 cc. There seemed to be no consistent trend toward a lower cholesterol with progressive weight loss in the entire group or even in most individuals. Considerable variation occurred in most subjects throughout the fast. No significant rise was observed in the early period, following initiation of starvation. Total serum lipids remained largely unchanged.

Mild ketosis appeared in all subjects within one week of fasting, and serum or urine occasionally showed a strongly positive reaction for acetone. With extended fasting, many specimens were negative or contained only traces. Hunger sensation had often disappeared before ketosis became clinically manifest, and it did not reappear during periods when serum and urine were free of acetone.

Fasting blood sugar levels were normal in nine of the 11 patients, ranging from 56 mg/100 cc to 102 mg/100 cc before starvation. Two diabetic patients had moderately elevated levels. In six of the 11 subjects, including the two diabetic patients, there was a moderate to severe fall in fasting blood sugar, with the levels becoming progressively lower as the fast continued. In three of these patients, glucose levels of 36 mg or less were recorded, but these were not associated with any manifestations of a hypoglycemic syndrome. In five patients, glucose levels remained stable. Blood sugar levels in the diabetic patients remained essentially normal, and glycosuria subsided during the period of starvation. No medication to control the diabetes had to be administered during the fast.

Serum electrolytes remained essentially unchanged throughout the period of starvation. Sodium, calcium, and chloride values were within normal limits before and during starvation. Potassium levels tended to decrease to low normal levels. The elements from catabolized cells apparently sufficed to maintain normal serum electrolyte concentrations. In four patients, urine was collected quantitatively for various five-day periods; and sodium and potassium excretion was measured. Within 25 days after beginning starvation, daily excretion of sodium fell to an average of 7 to 10 mEq, demonstrating the ability of the kidney to preserve electrolytes when the intake was low. On some days, the urine of two patients contained no measurable amounts of sodium. Potassium excretion also diminished, but this varied from one subject to the next and averaged from 10 to 15 mEq in 24 hours. In one patient, potassium excretion was considerably lower than in all others. During one five-day period, he lost less than 1 mEq of potassium per day. After a month of starvation, potassium losses tended to remain constant.

**Body Potassium.**—Quantitative determination in the body radiation counting chamber showed that, during the first month, about 0.75 gm of potassium was lost daily. After that, the loss amounted to approximately 0.5 gm a day. The ratio of potassium to body weight fell very slightly or remained stable throughout the fast. Since the bulk of the overall weight loss consisted of potassium-poor obesity tissue and water, the proportional loss of potassium was considerably higher. Thus, a substantial potassium deficit developed in three out of four patients (Table 5). Patient 1 had the lowest urinary potassium content (0.8 mEq per day). He was the only one who escaped a potassium deficit. The original body potassium was restored by feeding a low-calorie, protein diet without any potassium supplements.

**Side Effects of Starvation.**—Common early side effects consisted of mild headaches, occasional nausea, and some nervousness and tension. The difficulties seemed to abate readily and rarely required medication for relief. There was no clear correlation of any of these symptoms with chemical changes observed in blood or urine.

In one patient for whom vitamins were omitted purposely for two months, there developed gingival bleeding, glossitis, fissures at the corners of the mouth, dryness of the skin, and a pruritic, macular, erythematous eruption; the prothrombin time decreased to 50% The abnormalities were promptly reversed by administration of therapeutic doses of vitamins.

One of the most striking and potentially serious complications was the development of orthostatic hypotension. In one patient it occurred after only 12 days of starvation, but usually it did not become noticeable until the third or fourth week of fasting. The drop in blood pressure was accompanied by an increase in pulse rate. Sometimes the patients remained asymptomatic; but, in several instances, there were extreme weakness, faintness, and syncope upon arising from the bed.
Blood-pressure levels of 180 mm Hg systolic and 120 mm Hg diastolic fell to 70 mm Hg systolic and 40 mm Hg diastolic. A number of measures to relieve postural hypotension proved ineffective. These consisted of intravenous infusion of glucose, potassium chloride, sodium chloride, and oral administration of ephedrine sulfate. With refeeding, the postural fall of blood pressure was promptly reversed to a normal pattern. In two patients who underwent successive periods of fasting, the postural hypotension recurred each time and the period of fasting prior to onset of symptoms became progressively shorter.

Hyperuricemia developed in all patients within two weeks of fasting. Serum concentrations ranged from 11 mg/100 cc to 18 mg/100 cc. The female patient (4), who had a normal prestarvation uric-acid level (6.4 mg/100 cc), showed a gradual rise to 17.7 mg/100 cc. After three months of starvation, acute arthritis of the left ankle developed. The joint appeared swollen and red, and it was painful to touch and on motion. Fluid was aspirated, but no uric acid crystals could be identified. No medication was given; the joint improved with rest and warm, moist compresses. Two weeks later, a flare-up occurred in the same joint and also in the first metatarsophalangeal joint. Acute gouty arthritis was thought to be the cause of these symptoms, and the patient was re-fed. The arthritis slowly subsided, and uric acid levels decreased. Another patient (2), with an initial normal serum uric acid, was starved for 40 days; the uric-acid level increased to 17.1 mg/100 cc. At that point, the right ankle joint became painful, hot, and red. Fluid was aspirated, but no uric acid crystals were found. Treatment with colchicine resulted in improvement within hours. The patient was maintained on colchicine and continued to fast without recurrence of the arthritis.

In four of the 11 patients an anemia developed during the second month of starvation. In three patients, the anemia was mild with a drop of the hematocrit of less than 14%. In the female patient who starved for a total of 117 days, there was a progressive, slow fall of the hematocrit from 41% to 26% after 110 days. In all patients, the red blood cells remained normochromic and normocytic. Reticulocyte level ranged from 0.6% to 3.1%. Two bone-marrow aspirations in the female patient revealed only a scarcity of blood-forming elements, but no other abnormalities. This anemia was refractory to iron, orally and parenterally to folic acid, and to vitamin B-12. With refeeding, reticulocytes increased to 10%, and the anemia gradually improved.

Comment

The most astonishing aspect of this study, to the patient and to the physician, was the ease with which prolonged starvation was tolerated. This experience contrasted most dramatically with the hunger and suffering described by individuals who, over a prolonged period, consume a calorically inadequate diet. It is remarkable that the fast seemed easier for the patient the longer it lasted. To our knowledge, the 117-day starvation of one of the patients in this group has not been exceeded in other similar experiments.

It appears that the length of starvation which the individual patient will be able to tolerate is unpredictable, but most subjects will be able to continue long enough to reach the point where appetite or hunger is no longer felt. From then on, the fast can be safely continued, provided close clinical supervision is maintained. It is not clear why the sensation of hunger subsides, but the disappearance is apparently not related to ketosis. It is also interesting that severe, prolonged hypoglycemia does not produce the hunger sensation or other symptoms associated with abnormally low blood-sugar levels.

The rapidity of the weight loss has not been noted to cause any deleterious side effects. In patients with serious respiratory or cardiovascular embarrassment, the rapid and extensive loss of weight resulted in prompt improvement of their condition. This, together with the objective decrease in body size, served to encourage these patients in their determination to continue fasting. Those who attained a normal body weight were enthusiastic and delighted to resume living as normal-weight human beings. The eating habits and appetite of these individuals seemed to have undergone a decisive change; and, during a limited follow-up period, these patients seemed to have little difficulty in maintaining their weight. They continue to eat a substantially smaller amount of food than prior to starvation. We recognize that the number of patients and the follow-up periods are inadequate for making valid statements concerning long-range results.

This study has shown that hyperuricemia is a normal sequel of prolonged starvation. At this time, we are unable to decide if such a state, lasting several months, constitutes a danger to the kidney. It might be possible to improve uric acid clearance with the aid of uricosuric agents and to extend the limits of safe starvation. It seems unlikely that lasting damage would result from temporary hyperuricemia, because normal uric-acid levels returned as soon as a positive protein balance was re-established. In two cases of acute gouty arthritis in this group, specific treatment or ingestion of protein in adequate amounts resulted in prompt alleviation of clinical symptoms. The hyperuricemia seems to be a result of catabolism of cells, coupled with a decrease in renal excretion of uric acid. These experiences would suggest that obese patients who are known to have gout should avoid total starvation and also reducing diets.
leading to a negative protein balance.

The postural hypotension is an interesting phenomenon, which needs further clarification as to cause. It may constitute a potentially serious hazard. Obese patients with a history of cerebral ischaemic disease and patients with coronary insufficiency or recent myocardial infarctions would appear to be in danger if starvation were prolonged to the point when orthostatic hypotension develops. A number of factors may contribute in the development of this complication. Among them might be alterations in total blood volume or splanchnic vascular filling, or depletion of electrolyte, protein, or pantothenic acid. All patients manifesting this complication were still quite obese, and malnutrition with exhaustion or lack of available calories certainly did not play a part in the development of hypotension.

The anemia which developed in one patient after three months of starvation caused no clinical symptoms. The peripheral blood picture seemed to be normal, except for a reduction in the number of red cells and hemoglobin. In the course of the therapeutic regimen, most of the usual antianemic factors were offered no improvement. There seems to be a possibility that, in some patients, the body's demand for protein was fulfilled in part by catabolism of marrow and blood cells, as well as from other sources such as muscle, bone, and inner organs. As long as the protein balance remained negative, no amelioration occurred. With protein refeeding and without any antianemic medication, there was a slow increase in reticuloocyte and hematocrit levels. This improvement occurred even though the patient remained in a negative total-energy balance and continued to lose weight.

Veterans Administration Center, Wilshire and Sawtelle Blvds, Los Angeles 90073 (Dr. Drenick).

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References


**HISTORY OF GIN.**—Gin . . . was created, quite intentionally, to fulfill a specific purpose. Credit for the creation goes to Francisca de la Boe, also known as Dr. Sylvius, a seventeenth-century physician and professor of medicine at Holland's famed University of Leyden.

The good Dr. Sylvius was not thinking of a beverage, let alone a dry Martini. His objective was medicinal in the purest sense. He knew that the oil of the juniper berry had diuretic properties. . . He felt by putting juniper berries into pure alcohol and redistilling it, he could obtain its therapeutic oil in a form that would provide an inexpensive medicine. He succeeded. Within a few years, all Holland found itself suffering from ills that could be cured only by Dr. Sylvius' medicine.

The juniper berry is the principal and all-important flavoring in all true gins. In the seventeenth century, this berry was better known by its French name—genievre. Thus, Dr. Sylvius called his medicine "genever," as it still is known in Holland. The English shortened it to "gin."—History of Gin, Consumer Reports, vol. 25, November, 1960.