SOME HAZARDS OF TOTAL FASTS IN THE CONTROL OF OBESITY AND DIABETES AND THEIR PREVENTION

By GARFIELD G. DUNCAN, M.D.* and (*by invitation*) THEODORE G. DUNCAN, M.D.†, GUY LACY SCHLESS, M.D.‡, and FRED C. CRISTOFORI, M.D.§

PHILADELPHIA

In employing intermittent total caloric fasts in the treatment for intractable obesity in approximately 875 patients in the past three years, we have encountered several unfavorable but preventable side effects. This report deals with potential hazards when the fast periods have not, except in unusual instances, exceeded two weeks. No nourishment is given during the period of fasting unless specific indications for an interruption of the program arise. Water, artificially flavored beverages, a variety of teas and coffee are allowed as desired and supplementary vitamins are prescribed. Minimal physical activity was prescribed in every instance.

Cardiac Disorders—atrial flutter: Three adult male patients developed atrial flutter during the fast. In each instance this abnormality followed a breach of the rule that physical exercise be kept at a minimum.

W.K., a male aged 62 years, had a history of having had attacks of supraventricular arrythmias for 25 years. An attack occurred on the fourth day of the fast and followed a six mile walk—part of a daily routine advised by his cardiologist prior to the fast during which this exercise was continued surreptitiously. A prompt return to normal rhythm following resumption of a 1500 calorie diet, the administration of quinidine and the temporary elimination of extra physical exercise.

T.S., a male aged 57 years, (weight 259½ lbs. and height, 6′4″), with a 32-year history of arteriosclerotic heart disease, diabetes of seven years, and grade three hypertension of recent development and intractable obesity of many years with cholelithiasis, when permitted a daily leave from the hospital for a two-hour visit to his office—a few city squares from the hospital—incorporated in this privilege a circuitous 2-mile walk going and again on returning. The attack of atrial flutter

* Director of the Divisions of Medicine, Pennsylvania Hospital and Benjamin Franklin Clinic, Philadelphia; Professor of Medicine, University of Pennsylvania, Philadelphia.

† Assistant Physician to the Pennsylvania Hospital; Associate in Medicine, University of Pennsylvania, Philadelphia.

‡ Assistant Physician to the Pennsylvania Hospital; Associate in Medicine, University of Pennsylvania, Philadelphia.

§ Senior Research Fellow, Pennsylvania Hospital; Assistant Instructor in Medicine, University of Pennsylvania, Philadelphia.

occurred on the eighth day of the fast. Prompt restoration of a normal cardiac rate and rhythm ensued with the resumption of a 1500 calorie diet and with strict curtailment of exercise.

The third patient, R.L., gave a history of rheumatic disease. He developed atrial flutter on the fifth day of the fast following excessive exercise. Physical rest, digitalis and resumption of food, 1500 calories, restored a normal cardiac rhythm and rate. He has had prior to and subsequent to the fast, attacks of atrial fibrillation. These had no causative relationship to the fast.

Though there seems to be a direct connection between the attacks of atrial flutter and excessive exercise in these cases, the mechanism is not clear. A cellular potassium deficit may have played a part but, if so, it was without a co-existing hypokalemia.

Many patients with arteriosclerotic and hypertensive vascular disease tolerated the fast regimen well and derived benefit from it but, with exceptions already mentioned, close adherence to the rule pertaining to minimal exercise was observed.

Labile Diabetes: Obesity, though not common in patients with labile diabetes, does occur as the result of excessive caloric intake plus insulin therapy. Total fasting is particularly hazardous in these cases unless a "tight control" of the diabetes is maintained throughout the process. Such control is illustrated in the case of S.S., a 14-year-old girl whose pre-fast daily insulin need was 56 units. On the first day of the fast, regular insulin was given every six hours, the initial dose being one-fourth of the previous total. Subsequent doses were cautiously reduced when no glycosuria ensued. This policy was pursued until a base line of four units every six hours was reached. Glycosuria occurred at no time. A prompt ketonuria due to fasting developed, but the CO_2 combining power remained within normal limits.

The case of M.W., aged 59 years, height 64 inches, weight 180 lbs., who had been under our care for long standing and well documented labile diabetes, illustrates the hazard of precipitating diabetic ketosis when the insulin is omitted in such a case. The pre-fasting daily need for insulin was 32 units. The dose was reduced to 20 units on the first day of the fast but this amount when repeated on the following day provoked a hypoglycemia. The omission of the insulin on the third day was followed by the appearance and progression of diabetic ketosis. On the fourth day without insulin, there was 4+ glycosuria, 4+ hyperketonemia, blood sugar 300 mg./100 ml. and a CO_2 combining power of 13 mEq.—the chemical criteria upon which the diagnosis of diabetic coma is based. Despite these values, the only symptoms complained of were fatigue and anorexia. Resumption of the pre-fast diet and insulin

promptly corrected the ketosis. After 36 months during which one fast day per week was observed at varying intervals, her body weight is 133 lbs.

Had the same caution been exercised as in the foregoing case, (S.S.), the diabetic ketosis would surely have been prevented. Furthermore, we concede that the wisdom of employing the total fast regimen for a woman weighing only 180 pounds (height 64″) might be questioned. Nevertheless, the result serves to illustrate the very real hazard to which the fast regimen exposes the patients with uncontrolled labile diabetes.

Attacks of profound exhaustion: The occasional patient complains, usually in the second week of fasting, of profound weakness. In the case of A.W., a male, aged 43 and weight 320 pounds, this was associated with cramps in the voluntary muscles, nausea, headache, restlessness, and light headedness. Despite the absence of hyponatremia these symptoms are attributed to depletion of body sodium as suggested by the naturesis which occurred in the early phases of the fast and the prompt relief—within a few minutes—which followed the administration of two grams of sodium chloride. In such cases a break in the fast regimen is not necessary. Once corrected the foregoing symptoms rarely recur before the fast period is concluded. The administration of one gram of NaCl daily prevents these attacks but it also prevents the detection of those patients who are retaining large quantities of water. If salt is witheld entirely, the occasional patient loses as much as ten pounds in the first 24 hours of the fast. Almost without exception patients who lose in excess of six pounds in the first 24 hours of fasting have a benign hypertension which is readily controlled during the first two or three days of the fast. For these subjects restriction of salt intake is recommended for an indefinite period.

Hyperuricemia and Gout: Hyperuricemia develops in all patients during the fast periods.[1] This has been attributed to decreases in clearance of uric acid, reduced glomerular filtration, alteration of tubular transport of uric acid, and increased catabolism. Greater degrees of hyperuricemia occur in patients with gout unless measures are taken to prevent them. Of 18 obese patients who had gout, only one developed a mild attack of gout which responded to colchicine therapy without interruption of the fast. Another patient had an attack of arthritis typical of gout with the serum uric acid reaching 17 mg.% and yet this patient had no personal or family history of gout. Good response to colchicine therapy occurred within a few hours and without interruption of the fast. Unlike the patients known to have gout previously, a dramatic decrease in the serum uric acid occurred in the first 24 hours of resumption of a 1300 calorie diet and after two days the value had decreased from 16 to 8.5 mg.%. The administration of probenicid 0.5

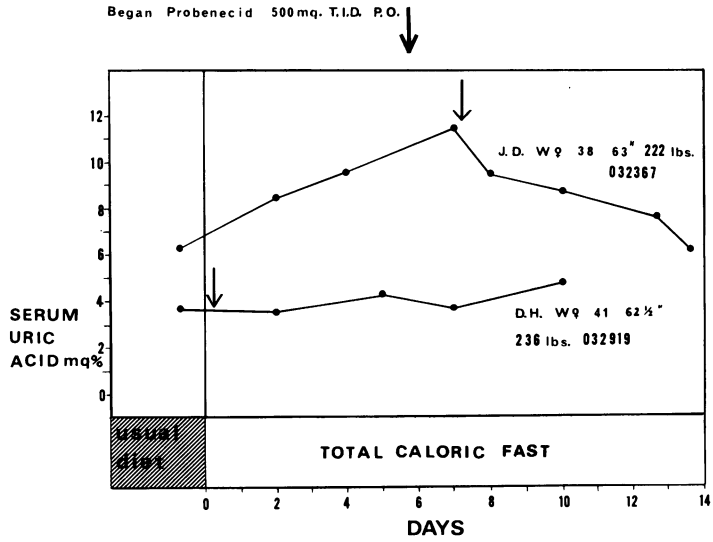

FIG. 1. Illustrated in Fig. 1 are: the hyperuricemia that occurs regularly during the total fast (top curve); the restoration of normal serum uric acid values by probinecid therapy and without interrupting the fast; and the prevention of hyperuricemia by administering probenecid throughout the "fast" period.

gram t.i.d. during the fast prevents increases in the serum uric acid content in non-gouty and gouty patients. The former is illustrated in Figure 1.

Renal Complications: No renal complications attributable to total fasting were detected in our series. However, we have had personal communications from two physicians regarding two patients, one in this country and one in South Africa, who developed oliguria and anuria during the total fasts. One responded well to the resumption of food but the hematuria subsided slowly. The other patient died of uremia and at autopsy acute and chronic abnormalities were found in both kidneys.

Hyperuricemic nephritis must be considered a possible complication of total fasts even though its occurrence in patients subjected to two-week fasts must be exceedingly rare if, indeed, they ever occur. Barry and his associates[2] alleviated renal failure secondary to hyperuricemia in two patients—one by provoking a diuresis by the intravenous infusion of mannitol and in the other by the additional use of peritoneal dialysis. The nephropathy in each of these instances was attributed to hyperuricemia provoked by cytotoxic therapy for lymphoblastic leukemia. It is highly improbable that these promising therapeutic devices will be

necessary in fasting patients if the daily urine output of the fasting patient is adequate. We aim to maintain a urinary output of at least 1500 ml./24 hours. We anticipate that if an oliguria develops and is not easily corrected and especially if RBC's appear in the urine, the fast will be terminated at once.

Anemia: We have not encountered anemia as a complication of the two-week fast regimen nor has orthostatic hypotension been more than an extremely minor problem. Both of these complications were encountered by Renick and his group,[3] the anemia being first detected during the second month of starvation. Oliguria was also noted by these authors when the fast was continued into the second month and that an acute gouty arthritis occurred after three months of starvation in one case and 40 days in another. These findings were the basis for the suggestion that gouty patients should not be subjected to total starvation. Our experience with 18 gouty and intractably obese subjects indicates that shorter periods of total fasting, 10 days to two weeks and repeated later if necessary, are well tolerated and highly desirable and effective in this refractory group. Sixteen of the 18 patients with gout also had diabetes. The benefit that accrues from therapeutic reduction in weight and the effectiveness of probenicid as an anti-hyperuricemic agent makes the "fast" regimen a doubly effective remedial measure for these individuals. Our experience indicates that the gouty patient need not be deprived of the advantages of intermittent periods of total fasting when this means of reducing is indicated.

In conclusion, the following safeguards against complications during a ten to fourteen day total caloric fast are pertinent:

Total fasts are to be prescribed only in cases of severe grades of obesity which have been refractory to conventional methods of reduction and in whom no contraindications to this therapy are detected.

Physical activity is restricted to a minimum during the fast period in all cases but especially in those who have or who are suspected of having chronic cardiovascular disease.

When total fasts are prescribed for obese patients with labile diabetes, the insulin therapy should not be discontinued, but rather it is adjusted by giving reduced amounts of crystalline (regular) insulin at six-hour intervals, the aim being to prevent glycosuria and yet avoid hypoglycemic reactions. This precaution will prevent the addition of diabetic ketosis to that due to fasting.

Gout is not a contraindication to short periods of total fasting. These patients tolerate the fast equally as well as the non-gouty subjects, and the fact that 16 of 18 had diabetes, they stand to gain greatly from it.

Efforts should be made, especially in this group, to keep the hyperuricemia in hand by means of a uricosuric agent and by maintaining an adequate urinary output.

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DISCUSSION

Dr. Stewart Wolf (Oklahoma City): I was very much interested in Dr. Duncan's account of the appearance of hyperuricemia and gout in presumably non-gouty individuals during fast.

Dr. Frank Tyler of Utah observed typical podagra in a young girl with anorexia nervosa who also had hypochloremia probably due to clandestine vomiting. She had no family history and no other reason for gout.

Dr. Edgar S. Gordon (Madison, Wisconsin): Inasmuch as lipogenesis depends on the presence of an adequate amount of insulin, it seems to me that the presence of obesity in a diabetic suggests very strongly that he has enough functioning insulin at the time. This is one of the criteria that we use. I was wondering therefore, in these patients that are obese and also are getting insulin, what happens to them if insulin is completely eliminated? I realize that these people will get ketosis eventually but in our experience, they get it much more slowly than normal people do. I would like to ask Dr. Duncan if any of his patients with ketosis have developed acidosis as a result of the ketosis?

Dr. Robert H. Furman (Oklahoma City): We, too, have been interested in the problem of total starvation and have recently completed the study of a 400-pound man in his mid-fifties who has no demonstrable abnormality of carbohydrate utilization or fasting plasma free fatty acid level. There are a number of points on which I am tempted to comment, but I will speak only to the matter of the serum uric acid level. This man gave a strong family history of gout, although he himself never had experienced clinically evident gout. His serum uric acid level was usually between 8.1 and 9.3 mg % and we were apprehensive regarding the levels which might be reached during total starvation in this subject. Therefore, before the starvation program was initiated he was placed on benemid which reduced the serum uric acid level to the range of 4.5 to 5.3 mg %. We then went ahead with the starvation study. Curiously, there was no increase in his serum uric acid level above that noted before starvation prior to benemid administration, even after six weeks of starvation. We fasted this man for a total of 124 days and there was no further increase in the serum uric acid. After six weeks of starvation benemid was discontinued and there was no rise in the subject's serum uric acid level nor any change in his urinary uric acid excretion. I wonder if you have encountered this phenomenon in any of your obese subjects whom you have subjected to starvation.

Dr. Duncan: The decrease in serum chloride during total fast periods mentioned by Dr. Wolf has been encountered by us and by others but in none of our cases did the value go below normal.

In answer to Dr. Furman's remarks, it is of interest that the uric acid values remained low without probenecid in the case mentioned. The effect of the course of probenecid therapy on the "uric acid pool" may be such that a considerable period of time may elapse before the hyperuricemia is again detectable. The follow-up should be interesting. We have not discontinued probenecid in our gouty patients after the fast period was concluded and so have had no opportunity to note what happened to the serum uric acid values if this were done.

In answer to Dr. Gordon's remarks, it is true that obese patients with "adult-acquired" diabetes do produce insulin in large amounts and that these patients, barring acute complications, are very resistant to diabetic ketosis even though they are not resistant to starvation ketosis. However, the patients I referred to were those with juvenile type (labile) diabetes who occasionally become obese by virtue of exogenous insulin and excessive calories. In such cases there is great danger of precipitating diabetic keto-acidosis by total fasting unless the diabetes is kept under "tight control" throughout the fast periods. These patients produce negligible amounts, if any, insulin and their obese state, in contradistinction to that of adult acquired diabetes in obese subjects, is not an indication of mild diabetes nor is it an indication of increased resistance to ketosis. Indeed, if insulin is abruptly withdrawn from such patients they are prone to develop diabetic ketosis with great rapidity and this hazard is intensified in speed and degree if they are on a fasting regimen which completely deprives them of exogenous carbohydrate. This is not what occurs in the obese patient acquiring diabetes in adult life. In such cases there is no such danger of diabetic ketosis, in the absence of acute complications, and the ketosis that results from fasting in such cases is a benign innocent affair. These patients are relatively resistant to insulin and the abrupt withdrawal of large amounts of insulin in such cases involves no hazard when the intermittent fast regimen is instituted.

Except in three cases of labile diabetes, we have not encountered acidosis during the intermittent fast regimen. This was true even when the ketosis due to fasting was of moderate degree. I should say that acidosis did not occur in the first, approximately 120, patients.

Ketosis has accounted for 4-plus ketonuria and 2-, 3- and occasionally 4-plus hyperketonemia without reducing appreciably the CO_2 combining power or the pH of the blood. Keto-acidosis only occurred when, in the three cases of labile diabetes, we failed to maintain "tight control" of the diabetes. This danger has been by-passed in subsequent cases, as I have indicated, by adopting an "every six-hour administration" of regular insulin the dosage of which was manipulated to maintain "tight control" of the diabetes.

Patients with juvenile type diabetes must have insulin in amounts adequate to prevent all but minimal glycosuria during total fasts.