Anorexia Nervosa

Treatment Efficacy of Cyproheptadine and Amitriptyline

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• **Patients with anorexia nervosa have concurrent problems of emaciation and depression. Therefore, treatment with medications affecting both weight gain and depression seemed reasonable. Seventy-two anorectic patients were randomly assigned in a double-blind study to receive cyproheptadine hydrochloride, a weight-inducing drug, amitriptyline hydrochloride, a tricyclic antidepressant, or placebo. Overall, cyproheptadine had a marginal effect on decreasing the number of days necessary to achieve a normal weight. There was a differential drug effect present in the bulimic subgroups of the anorectic patients: cyproheptadine significantly increased treatment efficiency for the nonbulimic patients and significantly impaired treatment efficiency for the bulimic patients when compared with the amitriptyline- and placebo-treated groups. The differential cyproheptadine effect on the anorectic bulimic subgroups is the first pharmacologic evidence of the validity of these subgroups. Cyproheptadine had an antidepressant effect demonstrated by a significant decrease in the Hamilton depression ratings.**

(*Arch Gen Psychiatry* 1986;43:177-181)

A cogent reason for testing the efficacy of an antidepressant in the treatment of anorexia nervosa is that anorectic patients have symptoms of depression, such as sleep disturbance, irritability, and crying spells, and they rate themselves as depressed on depression rating scales.[1] In addition, anorectic patients have some biologic signs of depression, such as dexamethasone resistance, decreased 3-methoxy-4-hydroxy-phenylglycol urinary excretion, and impaired growth hormone response to levodopa.[2]

A special interest in the use of amitriptyline hydrochloride to treat anorexia is that this drug induces weight gain in depressed patients receiving maintenance drug treatment,[3] and two open trial studies suggested that this drug may be effective in treating anorexia nervosa.[4,5]

Several outpatient studies[6-8] have suggested that cyproheptadine hydrochloride is effective in stimulating weight gain in anorectic patients. Weight gain and the associated medical rehabilitation produce beneficial psychological changes in anorectic patients.[9] One controlled inpatient study established the safety of cyproheptadine hydrochloride used in high doses of 32 mg/day and suggested that cyproheptadine may be more effective in treating a subgroup of anorectics with a worse prognosis.[10] Since cyproheptadine has few of the complicating side effects associated with the antidepressants (eg, hypotension and tachycardia), it appeared to be an especially attractive drug to assess in emaciated anorectics. Therefore, it seemed worthwhile to design and conduct a study of amitriptyline and cyproheptadine for the treatment of anorexia nervosa.

SUBJECTS AND METHODS

Seventy-two patients meeting *DSM-III* criteria for anorexia nervosa and the additional criterion of amenorrhea were randomly assigned to receive cyproheptadine, amitriptyline, or placebo. The study was conducted in two centers: the University of Minnesota Hospitals, Minneapolis, and the New York Hospital–Cornell Medical Center, Westchester Division, White Plains. Diagnosis was established with independent interviews by two psychiatrists. Agreement on the diagnosis of anorexia nervosa was necessary for the patient to be admitted to the study. During the seven-day pretreatment period, baseline assessments were obtained on days 2 and 5. These evaluations were then conducted weekly during treatment until the patients reached within 5% of a normal weight for age and height. Normal weights were determined by the Iowa Growth Chart and the 1959 Metropolitan Height-Weight Charts.[11,12] The patients also had extensive medical evaluations during the pretreatment period.

In this double-blind study, the drug dosage was increased at a rate according to the discretion of the investigator to obtain maximal drug dosage at the end of the second week of treatment. The maximal daily dose for each drug was 32 mg for cyproheptadine hydrochloride and 160 mg for amitriptyline hydrochloride. The patients were maintained on the highest tolerated dosage regimen.

Body weight was measured daily at 7 AM in the same hospital gown, after urination, and before breakfast. A structured social and psychiatric history was obtained by a social worker from the patient and family informants. The Side Effects Inventory,[13] the Hamilton Depression Scale,[14] and the Anorectic Behavior Scale[15] were administered by two nurses twice during the pretreatment period and weekly throughout treatment. The self-rating scales (Hopkins Symptom Checklist [HSCL-90],[16] Anorectic Attitude Scale,[17] Beck Depression Inventory [BDI],[18] a situational discomfort scale [derived from a previous study],[19] and a self-description

Accepted for publication Oct 24, 1984.

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Table 1.—Treatment Efficiency in Drug- and Placebo-Treated Groups

Drug Treatment	No. of Patients	Treatment Efficiency*
Amitriptyline hydrochloride	23	3.21±2.85
Cyproheptadine hydrochloride	24	3.07±2.95
Placebo	25	2.30±3.45

*Treatment efficiency equals the reciprocal of days to target weight times 90 (mean±SD). One hundred twenty was substituted for patients who did not reach target weight.

Table 2.—Pretreatment Weight Change

	%*	
	Day 1	Day 7
Amitriptyline hydrochloride	79.0±7.0	82.4±7.8
Cyproheptadine hydrochloride	77.0±6.2	80.5±6.6
Placebo	75.0±8.7	77.8±8.3

*Mean percentage of target weight plus or minus SD.

questionnaire [derived from a previous study][19]) were given to the patients twice during the pretreatment period and weekly throughout treatment. Caloric intake was measured daily.

All patients received a medical evaluation by an internist who was not part of the study team. The internist completed a medical rating form, assessed any medical complications, and determined if the more seriously ill patients were to continue in the study. In addition to being removed from the study by the internist for medical complications, patients were regarded as treatment failures if they had not gained at least 2 kg after six weeks of drug treatment, the minimal weight gain to justify continuing a patient in the protocol.

During the seven-day pretreatment period, the patients were allowed to choose their own food. When the drug treatment began on day 8, patients received a special nutritious liquid product (Sustacal) diluted to 1 kcal/mL. It was given in six equal feedings and was the only source of nutrient for the first 15 days of treatment. The patients were allowed to take as much of the nutritious mixture as they wished. After 15 days the patients received three meals of a regular diet and an evening snack. Again, they were allowed to eat as much food as they pleased.

RESULTS

Description of Patients

All 72 patients were female. Age at the time of hospitalization ranged from 13 to 36 years, with a mean (±SD) age of 20.56±5.1 years. The age at onset of anorexia nervosa ranged from 12 to 30 years, with a mean age at onset of 17.44±4.6 years. The duration of illness was from four months to ten years, with a mean duration of 2.9±2.3 years. Sixty-five of the patients were never married, three were divorced or separated, and four were married at the time of the study. The mean Hollingshead social level score was 2.0±1.2, which corresponds to an education level predominantly that of high-school graduates and an employment level between that of white-collar workers and administrative personnel.[20] This result is similar to a previous large demographic study of anorectic patients in the United States.[19] The patient population included 33 patients with bulimia, defined as recurrent episodes of binge eating or a rapid consumption of a large amount of food in a discrete period of time. Thirty-nine of the patients had no history of binge eating.

Nineteen of the 72 patients entering the study were treatment failures. There were 15 failures in the 46 patients treated at the University of Minnesota Hospitals and four treatment failures in the 26 patients treated at the Cornell Medical Center. It is of interest that twice as many patients (nine) taking placebo failed to achieve target weight compared with those patients (four) who failed and were taking cyproheptadine. Six patients who were receiving amitriptyline failed to achieve target weight.

Table 3.—Weight Gain in Patients Achieving Target Weight

Drug Treatment	No. of Patients Achieving Target Weight	Mean±SD	
		Days to Target Weight*	Average Weight Gain, kg/Day†
Amitriptyline hydrochloride	17	32.24±17.37‡	0.31±0.17
Cyproheptadine hydrochloride	20	36.50±19.53§	0.30±0.19‖
Placebo	16	45.00±18.34	0.23±0.12

*Overall drug effect, $P<.076$.
†Overall drug effect, $P<.07$.
‡Amitriptyline vs placebo, $P<.051$.
§Cyproheptadine vs placebo, $P<.05$.
‖Interaction of cyproheptadine and weight on day 7 of treatment vs placebo, $P<.03$.

Of the 24 patients receiving cyproheptadine, 19 were maintained on the maximum dosage regimen. The χ^2 statistics showed no significant relationship between achieving target weight and maximum drug dose with cyproheptadine ($\chi^2=0.05$, $df=1$, $P<.82$). Sixteen of the 19 patients receiving the maximum dose achieved their target weight, and four of the five patients receiving a less than maximum dose achieved their target weight. Of the 23 patients receiving amitriptyline, 16 were maintained on the maximum dosage regimen. Fourteen of those 16 patients achieved target weight, whereas only three of the seven patients receiving less than a maximum dose reached their target weight. For those patients taking amitriptyline, there was a significant relationship between achieving target weight and maximum drug dose ($\chi^2=5.03$, $df=1$, $P<.02$). Thus, the maximum dose of 160 mg of amitriptyline hydrochloride was effective for these patients.

Drug Effect on Weight

The drug effect on weight was assessed by three analyses, which included a treatment efficiency equation, the rate of weight gain, and the number of days required for patients to attain target weight. In the first analysis, a treatment efficiency variable was created so that all the patients in the treatment study could be included in the analysis. As the treatment progressed, patients reached 95% of target weight at varying times, some patients were withdrawn from the study because of clinical deterioration, and some patients had to leave the study because they were not meeting the minimal weight gain requirement. The treatment efficiency equation (Table 1) was a means by which all of these patients could be included in an analysis of drug effect on weight. Its expression is the reciprocal of the number of days to target times the constant 90, which is the maximal length of treatment. To designate lack of target achievement, the patients not reaching their target weights were given the arbitrary value of 120 as their days to target weight. (The use of any other large value would not materially affect the result.) The greater this variable is, the more efficient the treatment is. There was a significant difference between hospitals on treatment efficacy ($F[1,70]=4.73$; $P<.033$). A hierarchical multiple regression analysis[21] was used to determine drug effect on the treatment efficiency. Five sets of variables were entered into this analysis. The hospital differences accounted for 6% of the variance ($F[1,70]=4.73$; $P<.04$), the pretreatment weights on day 1 accounted for 14% of the variance ($F[1,69]=12.32$; $P<.001$), and the pretreatment weights on day 7 accounted for 12% of the variance ($F[1,68]=12.87$; $P<.001$). The drug treatment variables did not result in a significant increase in the variance. Although drug treatment did not have a significant impact on the treatment efficiency, two factors, the hospital at which the treatment was given and the patient's pretreatment weight, did have an effect on the treatment efficiency. (See Table 2 for pretreatment weight status.)

Table 4.—Drug Treatment Efficiency in Anorectic Subgroups

Drug Treatment	Treatment Efficiency (Mean ± SD)* Bulimic Patients (n=33)	Nonbulimic Patients (n=39)
Amitriptyline hydrochloride	4.99 ± 3.55 (n=9)	2.06 ± 1.51 (n=14)
Cyproheptadine hydrochloride	2.37 ± 1.78 (n=15)	4.23 ± 4.12 (n=9)
Placebo	3.65 ± 5.45 (n=9)	1.54 ± 1.21 (n=16)

*Treatment efficiency equals the reciprocal of days to target weight times 90. One hundred twenty was substituted for patients who did not reach target weight.

Table 5.—Caloric Intake in Drug- and Placebo-Treated Groups

Drug Treatment	No. of Patients	Average Daily Caloric Intake, kcal (Mean ± SD)*
Amitriptyline hydrochloride		
Pretreatment week	23	1,802 ± 746
Treatment week	21	2,450 ± 1,094
Cyproheptadine hydrochloride		
Pretreatment week	24	1,934 ± 940
Treatment week	23	3,023 ± 1,103†
Placebo		
Pretreatment week	25	1,746 ± 542
Treatment week	24	2,390 ± 844

*Overall group differences, $P<.07$.
†Cyproheptadine vs placebo, $P<.04$; cyproheptadine vs amitriptyline, $P<.06$.

For those patients who did achieve their target weights, we assessed the drug effect on weight in two analyses. First, we determined the drug effect on the average weight gain per day (in kilograms). Second, we measured drug effect on the number of days required to obtain the target weight. The results are shown in Table 3. The rate of weight gain was the amount of weight required to attain target weight divided by the number of days to target weight. Again, there was a significant hospital difference ($F[1,51]=4.27$; $P<.05$). A hierarchical regression analysis with five sets of variables (hospital, two pretreatment weights, the two drugs, and drug-pretreatment weight interaction) showed that the interaction of drug treatment with weight on day 7 of pretreatment resulted in a 5% increase in the r^2 value ($F[2,45]=2.73$; $P<.08$). The source of this increase was the cyproheptadine-placebo contrast interacting with the patient's weight at day 7 ($t=2.30$, $df=45$, $P<.03$), ie, those patients who were taking cyproheptadine and who had a greater weight on day 7 were the ones with a greater rate of weight gain than the patients taking placebo.

The variable "days to target weight" is simply the number of days from the day of hospitalization to the day of achieving target weight. Again, the hospital difference is present ($F[1,51]=5.51$; $P<.02$). In a hierarchical regression analysis with the variables hospital, two pretreatment weights, the drugs, and the drug by pretreatment weight interactions, a 7% increase in the r^2 value occurred for the drug treatment ($F[2,47]=2.73$; $P<.08$). Both the cyproheptadine-placebo contrast and the amitriptyline-placebo contrast were significant (Table 3). Thus, patients who were taking cyproheptadine and amitriptyline attained their target weights an average of 10.5 days earlier than patients taking placebo.

Both drugs had a marginal impact on days to target, and cyproheptadine had a weak interactional effect on the rate of weight gain. However, the greater proportion of explained variance for both days to target and rate of weight gain was in the patients' pretreatment weights on days 1 and 7.

Table 6.—Effect of Drug Treatment on Hamilton Depression Ratings

Treatment Period	Hamilton Depression Score* (Mean ± SD) Amitriptyline Hydrochloride (n=23)	Cyproheptadine Hydrochloride (n=24)	Placebo (n=25)
Pretreatment			
Day 2	17.3 ± 10.0	19.6 ± 9.5	20.4 ± 7.8
Day 7	15.7 ± 6.9	17.1 ± 6.8	17.8 ± 6.9
Treatment			
Day 14	14.6 ± 6.8 (n=23)	13.4 ± 7.9† (n=21)	18.1 ± 7.8 (n=25)
Day 28	14.1 ± 6.9 (n=16)	13.2 ± 6.5 (n=18)	17.7 ± 8.5 (n=20)

*Overall drug effect, $P<.005$.
†Cyproheptadine vs placebo, $P<.001$.

Table 7.—Effect of Drug Treatment on Self-rated Depression

Treatment Period	Beck Depression Scores Mean ± SD Amitriptyline Hydrochloride (n=23)	Cyproheptadine Hydrochloride (n=24)	Placebo (n=25)
	Beck Depression Scores		
Pretreatment			
Day 2	26.0 ± 9.2	21.7 ± 12.7	22.0 ± 10.8
Day 7	19.7 ± 11.9	15.7 ± 9.4	14.4 ± 8.6
Treatment			
Day 14	17.9 ± 10.4	12.9 ± 9.5	14.5 ± 9.3
Day 28	13.1 ± 12.1	11.5 ± 9.4	13.6 ± 9.8
	Composite Depression Scores*		
Pretreatment			
Day 2	5.1 ± 1.0	4.7 ± 1.5	4.3 ± 1.2
Day 7	4.3 ± 1.3	3.8 ± 1.2	3.6 ± 1.0
Treatment			
Day 14	4.0 ± 1.1	3.6 ± 1.1	3.6 ± 1.0
Day 28†	3.6 ± 1.1	3.5 ± 1.2‡	3.5 ± 1.0

*This score consists of the sum of the mean response to the depression subscale of the Hopkins Symptom Checklist and the Beck Depression Scale.
†Overall drug effect on day 28, $P<.03$.
‡Interactive effect between cyproheptadine and weight change vs placebo, $P<.01$.

Earlier studies repeatedly confirmed the presence of two distinct subgroups, ie, the bulimic and nonbulimic, within the population with anorexia nervosa.[22-24] It seemed reasonable to determine if a differential drug effect was present in those subgroups. Table 4 shows the surprising results. The overall analysis of variance was significant ($F[5,66]=2.41$; $P<.05$). No main effects were present ($F[3,66]=1.18$), but the two-way interaction was significant ($F[2,66]=4.27$; $P<.02$). Significant differences were present for treatment efficacy when the effects of cyproheptadine were contrasted with those of amitriptyline across the bulimia diagnosis ($t=-5.58$, $df=66$, $P<.01$). Contrast of cyproheptadine and placebo across the bulimia diagnosis showed a significant differential effect ($t=-4.63$, $df=66$, $P<.01$). Thus, cyproheptadine significantly increased treatment efficiency in the nonbulimic patients and significantly decreased treatment efficiency in the bulimic patients.

Table 8.—Treatment Failures (n=19)

Drug Treatment	Discharged AMA*	Clinical Course Deterioration	Other Illness	Failure to Gain Minimal Weight†	Total Treatment Failures
Amitriptyline hydrochloride	1	2	0	3	6
Cyproheptadine hydrochloride	1	1	0	2	4
Placebo	1	2	1	5	9
Total	3	5	1	10	19

*AMA indicates against medical advice.
†Minimal weight gain indicates failure to gain 2 kg by treatment day 42.

Table 9.—Mean Number of Physical Symptoms During Treatment

Day of Treatment	Amitriptyline Hydrochloride (n=21)		Cyproheptadine Hydrochloride (n=23)		Placebo (n=25)	
	Moderate*	Severe†	Moderate*	Severe†	Moderate*	Severe†
7	1.80	0.29	1.83	0.13	2.48	0.36
21	1.95	0.14	0.91	0	1.80	0.28

*Moderate rating by two nurses on Side Effects Inventory.
†Severe rating by two nurses on Side Effects Inventory.

As we expected, the increase in caloric intake reflected the increase in weight gain during treatment. Table 5 shows the average daily caloric intake during pretreatment and during the third week of drug treatment, at which time cyproheptadine had a modest effect over placebo for a greater caloric intake ($t=2.13$, $df=65$, $P<.04$).

Drug Effect on Depression

The patients with anorexia nervosa were moderately depressed at the time they entered the hospital for treatment (Table 6). An antidepressant effect of cyproheptadine was present on the 14th day of treatment. A multiple regression analysis taking into consideration prior Hamilton ratings, hospital, and weight showed a significant drug effect ($F[2,65]=5.84$; $P<.005$). This effect was found to be attributable to the contrast of cyproheptadine and placebo. At day 28 of drug treatment, posttreatment Hamilton ratings accounted for 57% of the variance ($F[1,56]=103.87$; $P<.0001$). Weight change added a small but significant increase to the accounted-for variance ($F[1,54]=6.81$; $P<.02$). At this time, the greater the increase in weight, the greater the decrease in depression rating.

For self-evaluation of depression, the anorectic patients were given the BDI and the depression subscale of the HSCL-90. To obtain a more reliable and robust measure of self-evaluated depression, we created a composite depression scale score composed of the BDI and the HSCL-90 depression factor. This score was created from the sum of the mean responses to the HSCL-90 depression factor and to the BDI (Table 7). During the treatment prior to day 28, there was no significant drug or weight gain effect on self-reported depression. On the 28th treatment day, a regression analysis showed that the greater the weight gain, the less the depression score ($B=-.191$, $t=-2.99$, $df=52$, $P<.004$). Thus, on average, for every increase in kilogram of a patient's weight, there was a corresponding decrease of 0.191 in the self-reported depression scale score. There was a significant interaction between drug treatment and weight change on the depression scale score on day 28 of treatment ($F[2,46]=3.69$; $P<.03$). Thus, in comparing the cyproheptadine treatment with the placebo treatment, those patients receiving cyproheptadine who had a greater weight gain were less depressed (Table 7). More simply, cyproheptadine and weight gain resulted in less depression when compared with placebo.

In contrast to the differential drug effect on weight in the anorectic subgroups of bulimic and nonbulimic patients, there was no differential drug effect on depression. There was, however, a significant difference in the self-report of depression between the bulimic and nonbulimic subgroups, with the former being more depressed during the pretreatment period ($F[1,66]=4.69$; $P<.03$).

In general, there were surprisingly few side effects observed in the study. In the Side Effects Inventory, we rated 33 signs and symptoms on a scale from 1 (absent) to 4 (severe) (Table 8). Since few patients complained of any particular side effect, we combined all of the side effects recorded for all 33 items and all patients under the moderate and severe ratings. Table 9 shows the mean number of side effects per patient in the moderate and severe categories. On day 7 of treatment, the greatest number of physical symptoms recorded was from the placebo-treated group. By day 21 of treatment, considerably fewer physical symptoms were recorded in the cyproheptadine-treated group, and the placebo-treated group continued to exceed the amitriptyline-treated group in number of physical symptoms. None of the patients had to be withdrawn from the study because of drug side effects. For those patients taking amitriptyline, the most common physical complaints were drowsiness, excitement, confusional state, increased motor activity, tachycardia, dry mouth, and constipation. In those patients taking cyproheptadine, there was no particular pattern of moderately or severely rated physical symptoms. In those patients taking placebo, the most common physical complaints were drowsiness, excitement, and increased motor activity.

No drug effect was present on the factors of the scales measuring typical anorectic attitudes and behaviors.

COMMENT

Mere hospitalization of a patient with anorexia nervosa can have an impact on that patient's weight gain. Table 2 shows that all treatment groups had an increase in weight during the pretreatment period. This increase was actually an average of 1.96 kg, which was significant for all patients ($t=6.38$, $df=71$, $P<.0009$). The weight gain of the patients during this period had an impact on all three of the dependent variables relevant to weight gain efficiency: treatment efficiency, days to target, and average weight gain per day. Drug treatment effects, specifically the cyproheptadine treatment, did account for some variance when the patients who did achieve target weight were

considered. A main effect was observed marginally for the number of days to target, while an interaction with drug treatment and weight at day 7 was present for the average daily weight gain.

An unexpected finding in this study was that a differential drug effect was present in the bulimic subgroups of the anorectic patients. Cyproheptadine significantly increased treatment efficiency for the nonbulimic patients and significantly impaired treatment efficiency for the bulimic patients when compared with amitriptyline- and placebo-treated groups. Although no obvious explanation for this drug effect is apparent, we know from a previous study[22] that anorectic bulimic patients can be differentiated from anorectic nonbulimic patients on their ratings of appetite. In an earlier study of asthmatic children, treatment with cyproheptadine increased appetite.[24] One could postulate that there is a difference in appetite and satiety mechanisms in bulimic and nonbulimic anorectic patients and that cyproheptadine is affecting these appetitive mechanisms.

The differential cyproheptadine effect on the bulimic anorectic subgroups is the first pharmacologic evidence of the validity of these subgroups. Previous studies have shown clinical differences in the bulimic and nonbulimic subgroups.[22-24] These findings warrant further investigations into the biologic mechanisms underlying the bulimic and nonbulimic anorectic subgroups.

There are few systematic randomized controlled treatment studies of anorexia nervosa. No single treatment modality can be regarded as a "cure" for this disorder. Controlled pharmacotherapeutic studies have investigated clomipramine hydrochloride,[25] lithium carbonate,[26] pimozide,[27] and cyproheptadine.[28] One multicenter study evaluated the efficacy of cyproheptadine and behavioral therapy.[10] In all of these studies, the drugs had a mild effect on weight gain or weight maintenance.

Depression ratings decreased during the pretreatment week, with the self-report depression ratings decreasing more than the observer ratings. Cyproheptadine had a significant effect on the observer Hamilton depression ratings, when compared with placebo on day 14 of treatment, and had an interactive effect with weight gain on day 28 of treatment. On the latter date, weight gain alone contributed to lowering the Hamilton ratings when prior Hamilton scores were considered. It is of special interest that there was no significant drug or weight gain effect on self-reported depression until the 28th treatment day. At that time, a greater weight gain indicated decreased depression, and there was also a significant interaction between cyproheptadine treatment and weight change on depression ratings, ie, patients receiving cyproheptadine who had gained more weight had lower depression ratings.

What can the clinician find useful from the present study? Cyproheptadine, a drug relatively free of serious side effects, can be useful for increasing the rate of weight gain and reducing depressed mood in nonbulimic anorectics. Cyproheptadine should not be given to bulimic anorectics, since it is likely to reduce the rate of weight gain in these patients. It should be emphasized that this study investigated short-term treatment and that the long-term effects of cyproheptadine or amitriptyline on weight maintenance are unknown. Amitriptyline may also increase rate of weight gain in anorectics, but this drug has more complicating side effects that make monitoring the patient more difficult. Cyproheptadine should be considered a useful therapeutic adjunct to a structured milieu and psychotherapy treatment program for hospitalized anorectic patients.

This study was supported by grants 5R01 MH26409 and 2R01 MH34105 from the National Institute of Mental Health, Bethesda, Md.

The authors gratefully acknowledge the assistance of their eating disorder research nurses: Leah LaBeck, RN, and Noelle Strauss, RN.

References

1. Eckert ED, Goldberg SC, Halmi KA, Casper R, Davis JM: Depression in anorexia nervosa. *Psychol Med* 1982;12:115-122.

2. Halmi KA, Sherman BM: Prediction of treatment response in anorexia nervosa, in Obiols J, Ballus C, Gonzalez M, Pujol J (eds): *Biological Psychiatry Today.* New York, Elsevier North Holland Inc, 1979, pp 609-614.

3. Paykel ES, Mueller PS, DeLavergne PM: Amitriptyline weight gain in carbohydrate craving: A side effect. *Br J Psychiatry* 1973;123:501-507.

4. Needleman HL, Waber D: Use of amitriptyline in anorexia nervosa, in Vigersky R (ed): *Anorexia Nervosa.* New York, Raven Press, 1977, pp 357-362.

5. Mills IV: Amitriptyline therapy in anorexia nervosa. *Lancet* 1976;2: 687.

6. Benady DR: Cyproheptadine hydrochloride (Periactin) and anorexia nervosa: A case report. *Br J Psychiatry* 1970;117:681-682.

7. Silverstone T, Schuyler D: The effects of cyproheptadine on hunger, calorie intake and body weight, abstract 1279. Program and abstracts of the Fifth International Congress on Pharmacology, San Francisco, July 23-28, 1972.

8. Zubiate T: Treatment of anorexia nervosa with a combination of cyproheptadine and vitamins. *Rev Med Caga Mac Ceguro Soc* 1970;19: 147-153.

9. Morgan HG, Russell GFM: Value of a family background and clinical features as predictors of long-term outcome in anorexia nervosa: Four-year follow-up study of 41 patients. *Psychol Med* 1975;5:355-371.

10. Goldberg SC, Halmi KA, Eckert ED, Casper R, Davis JM: Cyproheptadine in anorexia nervosa. *Br J Psychiatry* 1979;134:67-70.

11. Hamill P: *NCHS Growth Curves for Children,* US Dept of Health, Education, and Welfare publication 165. National Council of Health Care Services, November 1977.

12. *Metropolitan Insurance Co Height-Weight Charts.* New York, Metropolitan Insurance Co, 1959.

13. Levine J, Schooler N: *Systematic Assessment for Emergent Event (SAFTEE).* Rockville, Md, Pharmacologic and Somatic Treatments Research Branch, National Institute of Mental Health, 1983.

14. Hamilton M: A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1963;23:56-61.

15. Slade PD: A short anorexic behavior scale. *Br J Psychiatry* 1973;122: 83-85.

16. Derogatis LR, Lipman R, Rickels S, Uhlenhuth EH, Covi L: The Hopkins Symptom Checklist (HSCL): A measure of primary symptom dimensions, in Pischot P (ed): *Psychological Measurements in Psychopharmacology.* New York, S Karger AG, 1974, pp 79-110.

17. Goldberg SC, Halmi KA, Eckert ED, Casper R, Davis JM: Attitudinal dimensions in anorexia nervosa. *J Psychiatry Res* 1980;15:239-251.

18. Beck AT, Ward CH, Mendelson H, Mock J, Erbough J: An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:53-61.

19. Halmi KA, Goldberg SC, Casper RC, Eckert E, Davis JM: Pretreatment predictors of outcome in anorexia nervosa. *Br J Psychiatry* 1979;134: 71-78.

20. Redlich FC, Hollingshead AV, Roberts BH, Robinson HA, Freedman LZ, Myers JK: Social structure and psychiatric disorders. *Am J Psychiatry* 1953;109:729-734.

21. Cohen J, Cohen P: *Applied Multiple Regression/Correlation Analysis for the Behavioral Sciences,* ed 2. Hillsdale, NJ, Lawrence Erlbaum Associates, 1983, pp 120-123, 360-366, 508-512.

22. Casper RC, Eckert ED, Halmi KA, Goldberg SC, Davis JM: Bulimia: Its incidence and clinical importance in patients with anorexia nervosa. *Arch Gen Psychiatry* 1980;37:1030-1035.

23. Garfinkel PE, Moldofsky H, Garner DM: The heterogeneity of anorexia nervosa: Bulimia as a distinct subgroup. *Arch Gen Psychiatry* 1980;37:1036-1040.

24. Strober M: The significance of bulimia in juvenile anorexia nervosa: An exploration of possible etiologic factors. *Int J Eating Disord* 1981;1: 28-43.

25. Lacey JH, Crisp AH: Hunger, food intake and weight: The impact of clomipramine on a refeeding anorexia nervosa population. *Postgrad Med J* 1980;56:79-85.

26. Gross HA, Ebert MH, Faden VB, Goldberg SC, Nee LE, Kaye WH: A double-blind controlled trial of lithium carbonate in primary anorexia nervosa. *J Clin Psychopharmacol* 1981;1:376-381.

27. Vandereycken S, Pierloot R: Pimozide combined with behavior therapy in the short-term treatment of anorexia nervosa. *Acta Psychiatr Scand* 1982;66:440-450.

28. Vigersky RA, Loriaux DL: The effect of cyproheptadine in anorexia nervosa: A Double-Blind Trial, in Vigersky R (ed): *Anorexia Nervosa.* New York, Raven Press, 1977.