CLINICAL AND RESEARCH REPORTS

This section contains 1) new research findings, including preliminary data from pilot studies, either clinical or laboratory; 2) worthwhile replication studies; 3) case reports that describe a truly new syndrome or cast new light on established ones; and 4) case reports that indicate a new therapeutic procedure of potential value or call attention to adverse effects of drugs or previously unreported complications of therapeutic interventions. Program descriptions and literature reviews cannot be printed in this section. Criteria for format are listed in "Information for Contributors" in each issue; papers that do not adhere to these criteria will be returned to the author.

Maintenance Therapy with Amitriptyline: A Controlled Trial

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The continued administration of tricyclic antidepressants after the acute treatment of depressive symptomatology has gained increasing support. Reduced relapse rates in patients given medication as compared with placebo have been noted in patients treated acutely with either ECT (1–4) or antidepressants (4–8).

Almost all of the studies on maintenance tricyclic therapy used populations that were totally or predominantly composed of inpatients. Paykel and associates (7), in the only study that used outpatients exclusively, found amitriptyline superior to placebo in preventing relapse in an outpatient clinic population. Covi and associates (9) reported similar findings, but their study lasted only 16 weeks, an interval intermediate between an acute trial and a continuation study. Because both of these studies used clinic populations, we thought it would be important to examine outpatients treated in private psychiatric practice.

Method

Subjects. The sample consisted of 55 nonpsychotic depressed psychiatric outpatients treated in private psychiatric practice. All patients had completed an acute treatment trial of amitriptyline (o.d. versus t.i.d.) lasting 6 weeks and were judged to be at least moderately improved. The larger sample from which these subjects were drawn and other aspects of methodology have been described in detail in Weise and associates (10).

Most patients who participated in the maintenance phase of the study were white (96%), married (67%), and female (65%). Seventy-eight percent of the patients had at least a high school education, and the majority (82%) belonged to social class IV or above. Their mean age was 42.3 years (SD=12.8).

All patients fulfilled the Feighner and associates criteria for major depressive disorder, which overlap with those of *DSM-III*. The diagnoses were depressive reaction (44%) and depression with significant anxiety (56%). Many of the patients were chronically ill, the majority having been depressed for more than 6 months (64%). More than half (56%) had had at least one prior depressive episode.

Procedure. The treatment program was divided into three phases: 1) a 6-week acute trial, 2) a 2-week "open-therapy" phase, and 3) a 6-month maintenance phase. Patients who participated in the acute treatment phase were eligible for maintenance treatment if both the patient and physician rated the patient as at least moderately improved and the Raskin Depression Scale total was reduced by at least 50%.

Patients who met these criteria and who agreed to participate in the maintenance trial entered the 2-week open-therapy phase. During this period, the patients received 100 mg of amitriptyline in 50-mg tablets at

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ime. If any deterioration in the patient's condition rred, the physician could increase the dosage to a imum of 150 mg/day. The patient then had to re- to his or her clinical status at the beginning of the -therapy phase in order to enter the maintenance e. As in the acute phase, written informed consent obtained after participation in the trial had been ained.

the end of the 2-week period, patients were ran- ly assigned under double-blind conditions to ei- amitriptyline or placebo. They were seen at thly intervals for 6 months. They continued with optimum dosage established in the open therapy od, i.e., either two or three tablets h.s. If the pa- reported a worsening of symptomatology, the ician could increase the dosage to a maximum of tablets h.s. If the deterioration continued over next 1-2 weeks, the patient's participation in the y was terminated.

tings. The Hamilton Depression Scale, a measure he physician's overall judgment of psycho- ology, and the Raskin scale were used to assess ptomatology. Ratings of global improvement or ening, as well as reasons for study termination, reported on the treatment exit disposition form.

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significantly greater proportion of amitriptyline nts than placebo patients completed more than 2 ths of maintenance treatment (69% versus 38%, .99, $p<.05$). Of the amitriptyline patients who ped out during the first 2 months, 6 had become e, and 3 had continued to maintain their improve- ; all 16 placebo patients who dropped out had re- d ($\chi^2=3.32$, $p<.10$).

er the 6-month period, 28% of the amitriptyline nts versus 69% of the placebo patients relapsed 7.94, $p<.01$). Of the placebo patients who re- d, 72% did so within the first month, and 89% re- d within 2 months.

alyses of covariance were conducted at each time d for the Raskin and Hamilton scale scores and he physician's overall rating. At 1 month, ami- line patients scored significantly lower on all mea- than placebo patients. For example, the total ad- d means on the Hamilton scale at 1 month were r patients receiving amitriptyline and .67 for pla- patients ($F=18.8$, $p<.005$). These differences no longer found for subsequent time periods. most relapses occurred within the first months, patients who remained in the study after this time maintaining their improvement.

In addition, we examined several variables that might have been related to treatment outcome, including illness history, family history of mental illness, previous psychiatric treatment, presenting symptoms, and response to acute treatment. None of these variables was significantly associated with maintenance treatment outcome.

Discussion

The results of this study indicate that continued treatment with tricyclic antidepressant medication following acute symptomatic improvement is appropriate for depressed outpatients seen in private psychiatric practice. The rapid clinical deterioration that occurred in most of the patients who relapsed suggests that the medication was controlling the depressive symptoms of an episode that had not yet run its course. Thus continued treatment would offer a distinct advantage for these patients. However, this is clearly not necessary for all patients, as shown by the fact that almost one-third of the patients who received placebo maintained their therapeutic gains. We believe that continued treatment for 6–8 months would benefit most patients. However, should the physician decide to discontinue medication, the patient should be alerted to the possibility of a return of symptoms and told to call the doctor at the first sign of symptoms.

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