and it is seldom found in patients without chronic gastritis. Although 40% to 60% of patients with nonulcerative dyspepsia have chronic C *pyloris*-associated gastritis, the relationship between the organism and gastritis, as well as other gastroduodenal disease, is not clear. The most effective treatments likewise are not clearly established; eradication is difficult, and probably requires a multi-drug approach.

However, identification of the organism and eradication may be important. It is known that nearly all patients with duodenal ulcer also have C *pyloris*-associated gastritis, and that C *pyloris* is found in the duodenal bulb in duodenal ulcer patients only on foci of gastric metaplasia. C *pyloris* is not found on duodenal mucosa. It is unknown whether these relationships point toward an etiologic role of C *pyloris* in duodenal ulcer disease.

Although the 7- to 10-day acute phase of C *pyloris* gastritis produces characteristic symptoms (gnawing hunger sensation, occasional vomiting, bloating, and borborygmi), the chronic phase is frequently asymptomatic and may remain so for years. Because endoscopic findings correlate poorly with the presence of histologic gastritis, antral biopsies must be performed for the diagnosis of C *pyloris*-associated gastritis. Furthermore, histologic identification of the organism requires special staining techniques. Testing for urease activity in biopsy specimens, however, is very helpful in making a rapid preliminary diagnosis.

Treatment of patients with dyspepsia and C *pyloris*-associated gastritis is best attempted in the context of a research protocol. Single-agent therapy with drugs possessing in vitro activity against C *pyloris* has not been effective. A regimen of bismuth subsalicylate (30 mL or 2 tablets qid for 3 weeks) and amoxicillin (500 mg tid during the last 2 weeks) is associated with an eradication rate of 50% to 70%. Regimens that use two antibiotics along with the bismuth preparation reportedly have eradication rates of up to 90%.

JAMES S. BARTHEL, MD
Department of Gastroenterology

BIBLIOGRAPHY

Barthel JS, Westblom TU, Havey AD, Gonzalez F, Everett ED. Gastritis and *Campylobacter pylori* in healthy asymptomatic volunteers. Arch Intern Med 1988; 148:1149-1151.

Rauws EAJ, Langenberg W, Houthoff HJ, Zanen HC, Tytgat GNJ. *Campylobacter pyloridis*-associated chronic active antral gastritis: a prospective study of its prevalence and the effects of antibacterial and antiulcer treatment. Gastroenterology 1988: **94**;33-40.

## MANAGEMENT OF DEPRESSION: BOTH DRUGS AND PSYCHOTHERAPY ARE NEEDED

A combination of pharmacologic intervention and psychotherapy is needed for adequate management of bipolar affective disorders, which are relatively common. Newer therapeutic agents may be useful in the management of the patient with lithium-resistant disease.

The incidence of manic depression is high and the mortality and morbidity are significant. The incidence of manic depression is comparable to diabetes mellitus: 20% of the worldwide population is now being treated, in some form, for depression.

Manic depression has three phases: mania, depression, and a mixed phase. The mixed phase, characterized by high and low episodes within a 24- to 48-hour period, is difficult to diagnose and tends to resist treatment. Approximately half of these patients deny the existence of manic-depressive symptoms because, to themselves, they seem normal. Consequently, taking a history is a labor-intensive chore that must involve the family.

Because manic depression is a biological and psychological disorder, pharmacologic intervention must be complemented by psychotherapy. If a patient has had a mood disorder since adolescence, his self-esteem and confidence are "atrophied," and require rehabilitation in addition to drug therapy. The phenomenon can be compared to the need for cardiac rehabilitation in a heart surgery patient in whom rehabilitation is employed in conjunction with drug therapy. The patient whose mood disorder did not begin until adulthood is more likely to respond to drug therapy alone.

DRUG THERAPY

### Lithium

Lithium carbonate is the gold standard for treatment of manic depression. It has potent anti-manic properties in both acute and prophylactic settings. Lithium has some antidepressant effect as well. The upper limits of the therapeutic range are 1.0 to 1.2 mEq/L; serum measurements will identify noncompliance, the most likely reason for poor response or relapse.

Most of the 20% to 30% of patients who are truly resistant to lithium therapy have rapid-cycling manic depression. Rapid cycling is a variant of bipolar mood disorder, characterized by at least four major mood swings annually. The mood swing may last for several weeks, and initially the highs and lows are relatively mild. They

will increase with amplitude over time, and they will become more frequent, so it is important that diagnosis and treatment not be delayed. People in this subgroup tend to function relatively well because they take advantage of the high swings, during which their productivity increases.

About half of patients with intractable rapid-cycling manic depression have a history of overt thyroid failure caused by surgery or thyroiditis. Elevated TSH is present in 90% of these patients, and some have subclinical hypothyroidism. Thyroid hormones, particularly T4, are now being used to enhance the effect of psychotropic drugs in the treatment-resistant patient.

**Carbamazepine, valproic acid, and clonazepam**

Patients with rapid-cycling manic depression benefit from the addition of an anticonvulsant to the lithium regimen. The anticonvulsants being used in this setting are carbamazepine, valproic acid, and clonazepam. The response rate among patients with intractable disease is 60% to 65%.

Carbamazepine has been studied in thousands of patients, and has a therapeutic spectrum similar to that of lithium. Valproic acid is less well studied, but data indicate a therapeutic profile similar to lithium and carbamazepine.

Clonazepam, a newer agent, is a benzodiazepine with antimanic and antipanic properties. Compared to alprazolam, which is rapid-acting and associated with rebound anxiety, clonazepam is probably preferable for treatment of biologic anxiety. Although potent, its action has a gradual onset and discontinuation of the drug is better tolerated. It is best used in patients with bipolar affective disorder type 2, which is characterized by depression with mild highs. Clonazepam has no antidepressant properties.

JOSEPH R. CALABRESE, MD
Department of Psychiatry

**BIBLIOGRAPHY**

Kupfer DJ, Carpenter LL, Frank E. Possible role of antidepressants in precipitating mania and hypomania in recurrent depression. Am J Psychiatry 1988; 145:804-808.

McElroy SL, Pope HG, eds. [In] Use of Anticonvulsants in Psychiatry: Recent Advances. Clifton, NJ: Oxford Health Care, 1988.