Thus, adverse effects on blood pressure, pulse, and cardiac rhythm are not typically seen. The development of these side effects depends on dosage used (concomitant use of other medications, especially CNS depressants, and alcohol) and the sensitivity of the individual being treated. With repeated dosing, most patients develop tolerance to sedation. The suggestion that automobile accidents are more likely to occur among benzodiazepine users (assuming tolerance to the early sedative effects) is complicated by the possibility that the condition being treated (e.g., anxiety, insomnia) may be a contributing factor. The interpretation of laboratory studies of attention, cognitive control, and driving ability are difficult to generalize to real-life situations.

Acute dosages of benzodiazepines may produce transient anterograde amnesia. This effect appears to be independent of sedation; acquisition of new information is specifically impaired. The risk of anterograde amnesia appears to be worsened by concomitant ingestion of alcohol.

Uncommon side effects include dysarthria, confusion, abnormal coordination, ataxia, depression or worsening of mood (see below), dry mouth, constipation, nausea, slurred speech, dizziness, and tremor. Side effects due to rapid decrease or abrupt withdrawal from benzodiazepines may include agitation, heightened sensory perception, paresthesias, muscle cramps, muscle twitching, diarrhea, reduced concentration, worsening of mood, anxiety, nervousness, restlessness, sleeping difficulties, insomnia, tremors, and, in rare cases, seizures and hallucinations.

Benzodiazepine-Induced Disinhibition. Reports of paradoxical reactions to benzodiazepines (disinhibition), in particular describing rage outbursts or aggression in patients on chlordiazepoxide, diazepam, alprazolam, or clonazepam, have been published. Disinhibition can probably occur with any benzodiazepine, but the lower potency, slowly absorbed oxazepam may be less likely to trigger this effect. Many clinicians feel that the highest incidence of disinhibition occurs in personality disorder patients with prior histories of dyscontrol. When paradoxical excitement occurs in a patient given a benzodiazepine in an emergency department or inpatient ward, the administration of an antipsychotic drug is often effective in reversing the state.

Benzodiazepine-Induced Depression. All benzodiazepines have been associated with the emergence or worsening of depression; whether they were causative or only failed to prevent the depression is unknown. If the depression occurs during the course of treatment, the benzodiazepine can be combined with or replaced by an antidepressant.

Benzodiazepine Overdose. With respect to lethality, benzodiazepines have proved to be relatively safe in overdose in that benzodiazepines alone have only rarely been implicated in fatal overdoses. However, when combined with other CNS depressants, such as alcohol, barbiturates, or narcotics, benzodiazepines may contribute to the lethality of the overdose.

The treatment of benzodiazepine overdose includes induction of emesis or gastric lavage, when appropriate, and supportive care for patients who are stuporous or comatose. The benzodiazepine antagonist flumazenil is available for the treatment of benzodiazepine overdose. In benzodiazepine-dependent patients, this drug may precipitate withdrawal symptoms in analogy with the actions of naloxone in opiate-dependent individuals.

Benzodiazepine Interactions with Alcohol and Other Drugs. Serious pharmacokinetic drug interactions are rare with benzodiazepines but may occur (Table 5.3). Benzodiazepines can cause a mild to moderate increase in CNS depression caused by