**TABLE 466-10 ANTIPSYCHOTIC AGENTS**

| Name | Usual PO Daily Dose, mg | Side Effects | Sedation | Comments |
|---|---|---|---|---|
| **First-Generation Antipsychotics** | | | | |
| Low potency | | | | |
| Chlorpromazine (Thorazine) | 100–1000 | Anticholinergic effects; orthostasis; photosensitivity; cholestasis; QT prolongation | +++ | EPSEs usually not prominent; can cause anticholinergic delirium in elderly patients |
| Thioridazine (Mellaril) | 100–600 | | | |
| Midpotency | | | | |
| Trifluoperazine (Stelazine) | 2–50 | Fewer anticholinergic side effects | ++ | Well tolerated by most patients |
| Perphenazine (Trilafon) | 4–64 | Fewer EPSEs than with higher potency agents | ++ | |
| Loxapine (Loxitane) | 30–100 | Frequent EPSEs | ++ | |
| Molindone (Moban) | 30–100 | Frequent EPSEs | 0 | Little weight gain |
| High potency | | | | |
| Haloperidol (Haldol) | 5–20 | No anticholinergic side effects; EPSEs often prominent | 0/+ | Often prescribed in doses that are too high; long-acting injectable forms of haloperidol and fluphenazine available |
| Fluphenazine (Prolixin) | 1–20 | Frequent EPSEs | 0/+ | |
| Thiothixene (Navane) | 2–50 | Frequent EPSEs | 0/+ | |
| **Second-Generation Antipsychotics** | | | | |
| Clozapine (Clozaril) | 150–600 | Agranulocytosis (1%); weight gain; seizures; drooling; hyperthermia | + + | Requires weekly WBC count for first 6 months, then biweekly if stable |
| Risperidone (Risperdal) | 2–8 | Orthostasis | + | Requires slow titration; EPSEs observed with doses >6 mg qd |
| Olanzapine (Zyprexa) | 10–30 | Weight gain | ++ | Mild prolactin elevation |
| Quetiapine (Seroquel) | 350–800 | Sedation; weight gain; anxiety | +++ | Bid dosing |
| Ziprasidone (Geodon) | 120–200 | Orthostatic hypotension | +/++ | Minimal weight gain; increases QT interval |
| Aripiprazole (Abilify) | 10–30 | Nausea, anxiety, insomnia | 0/+ | Mixed agonist/antagonist |
| Paliperidone (Invega) | 3–12 | Restlessness, EPSEs, increased prolactin, headache | + | Active metabolite of risperidone |
| Iloperidone (Fanapt) | 12–24 | Dizziness, hypotension | 0/+ | Requires dose titration; long acting injectable available |
| Asenapine (Saphris) | 10–20 | Dizziness, anxiety, EPSEs, minimal weight gain | ++ | Sublingual tablets; bid dosing |
| Lurasidone (Latuda) | 40–80 | Nausea, EPSEs | ++ | Uses CYP3A4 |

***Abbreviations:*** EPSEs, extrapyramidal side effects; WBC, white blood cell.

addressed. Anticholinergic and parkinsonian symptoms respond well to trihexyphenidyl, 2 mg bid, or benztropine mesylate, 1–2 mg bid. Akathisia may respond to beta blockers. In rare cases, more serious and occasionally life-threatening side effects may emerge, including hyperprolactinemia, ventricular arrhythmias, gastrointestinal obstruction, retinal pigmentation, obstructive jaundice, and neuroleptic malignant syndrome (characterized by hyperthermia, autonomic dysfunction, muscular rigidity, and elevated creatine phosphokinase levels). The most serious adverse effects of clozapine are agranulocytosis, which has an incidence of 1%, and induction of seizures, which has an incidence of 10%. Weekly white blood cell counts are required, particularly during the first 3 months of treatment.

The risk of type 2 diabetes mellitus appears to be increased in schizophrenia, and second-generation agents as a group produce greater adverse effects on glucose regulation, independent of effects on obesity, than traditional agents. Clozapine, olanzapine, and quetiapine seem more likely to cause hyperglycemia, weight gain, and hypertriglyceridemia than other atypical antipsychotic drugs. Close monitoring of plasma glucose and lipid levels are indicated with the use of these agents.

A serious side effect of long-term use of first-generation antipsychotic agents is *tardive dyskinesia*, characterized by repetitive, involuntary, and potentially irreversible movements of the tongue and lips (bucco-linguo-masticatory triad) and, in approximately half of cases, choreoathetosis. Tardive dyskinesia has an incidence of 2–4% per year of exposure and a prevalence of 20% in chronically treated patients. The prevalence increases with age, total dose, and duration of drug administration. The risk associated with second-generation agents appears to be much lower. The cause may involve formation of free radicals and perhaps mitochondrial energy failure. Vitamin E may reduce abnormal involuntary movements if given early in the syndrome.

The CATIE study, a large-scale investigation of the effectiveness of antipsychotic agents in "real-world" patients, revealed a high rate of discontinuation of treatment over 18 months. Olanzapine showed greater effectiveness than quetiapine, risperidone, perphenazine, or ziprasidone but also a higher discontinuation rate due to weight gain and metabolic effects. Surprisingly, perphenazine, a first-generation agent, showed little evidence of inferiority to newer drugs.

Drug treatment of schizophrenia is by itself insufficient. Educational efforts directed toward families and relevant community resources have proved to be necessary to maintain stability and optimize outcome. A treatment model involving a multidisciplinary case-management team that seeks out and closely follows the patient in the community has proved particularly effective.

## ASSESSMENT AND EVALUATION OF VIOLENCE

Primary care physicians may encounter situations in which family, domestic, or societal violence is discovered or suspected. Such an awareness can carry legal and moral obligations; many state laws mandate reporting of child, spousal, and elder abuse. Physicians are frequently the first point of contact for both victim and abuser. Approximately 2 million older Americans and 1.5 million U.S. children are thought to experience some form of physical maltreatment