

# Obsessive-Compulsive Disorder: Diagnosis and Treatment

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Obsessive-compulsive disorder (OCD) is a chronic, disabling anxiety disorder that is characterized by recurrent obsessions and uncontrolled compulsions such as repetitive behavioral or mental acts that are performed in response to an obsession. OCD often occurs comorbidly with a number of depressive and anxiety disorders. In addition, patients with OCD suffer significant personal and social morbidity and may have difficulty maintaining a job, finishing school, and developing relationships. The backbone of pharmacologic treatment for OCD is a 10- to 12-week trial with a selective serotonin reuptake inhibitor (SSRI) in adequate doses. In most cases, treatment should be initiated with an SSRI because of the superior safety, tolerability, and equivalent efficacy of this class of drugs compared with clomipramine. When dealing with patients who do not respond to one SSRI, effective alternatives include switching to a different SSRI, combining another medication or behavioral therapy with SSRI therapy, considering novel or experimental drug treatments, or employing nonpharmacologic biological approaches, such as electroconvulsive therapy, neurosurgery, or repetitive transcranial magnetic stimulation. This article provides an update on the diagnosis and medical management of OCD and will discuss guidelines for the use of SSRIs and novel approaches for managing treatment-refractory patients.

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Obsessive-compulsive disorder (OCD) is a chronic and often disabling anxiety disorder. Typical symptoms of OCD include obsessions, characterized by recurrent or persistent thoughts, impulses, or images that are experienced as intrusive or inappropriate, and compulsions, which manifest as repetitive behaviors or mental acts often performed in response to an obsession.<sup>1</sup> Some of the more common obsessions include fear of contamination, need for order or symmetry, pathologic doubt, and recurrent aggressive or horrific images. The most common compulsive behaviors include washing, checking, counting, ordering, and repeating words or actions. For example, a patient with OCD who has a contamination obsession may spend hours washing until the skin becomes raw in order to neutralize certain obsessive thoughts. Not surprisingly, obsessions and compulsions are time consuming and can significantly interfere with normal daily routine and occupational functioning.

Data from the Epidemiologic Catchment Area (ECA) survey and other epidemiologic studies suggest that the lifetime prevalence of OCD is between 2% and 3% in the general population,<sup>2-4</sup> and between 4 and 6 million people in the United States are affected with this disorder.<sup>5</sup> Obsessive-compulsive disorder is the fourth most common psychiatric diagnosis in the United States, following phobias, substance abuse, and major depression.<sup>6</sup> Rates of OCD may be even higher than expected because many patients do not seek treatment and often are able to hide obsessions and compulsions for long periods before detection.<sup>4,6</sup> The incidence of OCD is slightly higher in women, and approximately 50% of patients have onset of symptoms during adolescence and usually before 25 years of age.<sup>7-9</sup>

Obsessive-compulsive disorder has a chronic course, and few patients achieve true remission.<sup>10</sup> Although symptoms may fluctuate over time, the disorder rarely resolves spontaneously without appropriate treatment.<sup>11,12</sup> Patients with OCD often are impaired socially and suffer from lowered quality of life. One survey reported that patients with OCD were less able to develop and maintain interpersonal relationships and had significant interference in academic or occupational functioning.<sup>13</sup> The ECA database of more than 13,000 subjects noted that 36% of patients with OCD experienced job troubles, 23% had marital or relationship problems, and 19% were violent.<sup>14</sup> It is estimated that patients with OCD lose up to 3 years of wages during their lifetime.<sup>15</sup> Thus, OCD clearly is associated with significant functional disability.

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## DIAGNOSIS

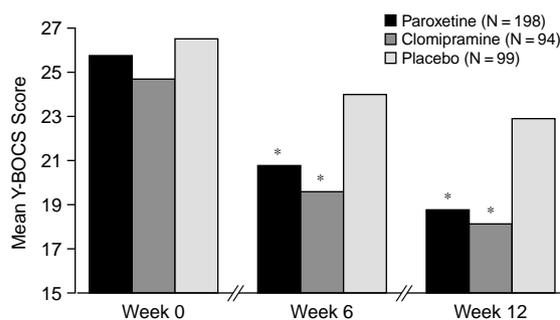
Based on the diagnostic criteria outlined in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), obsessions and compulsions are time consuming, taking more than 1 hour each day, and cause marked distress and significantly impair the patient's ability to function normally.<sup>1</sup> Although most adult patients with OCD recognize that their obsessions and compulsions are unreasonable, children may be unable to make the distinction. However, the clinical presentation of OCD is similar in children and adults.<sup>12</sup> Some patients may attempt to resist the obsessive and compulsive thoughts or behaviors. However, the urge to perform compulsive actions often is irresistible and may cause the person significant distress if the actions are not performed.

It is important to note that 60% of patients with OCD do not seek psychiatric care, and some individuals initially may consult primary care physicians or religious leaders.<sup>6</sup> In addition, patients with OCD may present with actual physical symptoms, such as seeking dermatologic care for dry, chapped skin mediated by excessive washing. Unless the physician is attuned to the condition and asks specific questions, the diagnosis of OCD may be missed. Some simple screening questions may be useful for eliciting symptoms in 85% of patients with OCD: Do you have to wash your hands repeatedly? Do you have to check things several times? Do you have recurrent thoughts that distress you? Do you have to complete actions again and again or in a certain way?<sup>11</sup> The 10-item Yale-Brown Obsessive Compulsive Scale (Y-BOCS) is another useful tool for identifying OCD and monitoring severity of illness.<sup>16,17</sup>

## TREATMENT

OCD was traditionally thought to have poor prognosis, and many patients were refractory to conventional pharmacotherapy. However, the treatment of OCD has significantly advanced in the past 10 years, and both pharmacologic and behavioral approaches are effective and important components in the management of OCD. Medications that exhibit potent serotonergic properties have consistently been effective in improving OCD symptoms, and it is hypothesized that the pathophysiology of OCD is associated, at least in part, with abnormal serotonergic regulation.<sup>18,19</sup> Clomipramine, a tricyclic antidepressant (TCA) with specificity for serotonin, has well-demonstrated efficacy and was considered the standard of therapy for OCD for years.<sup>20</sup> Clomipramine is thought to be more effective than other TCAs because of its preferential actions on serotonin reuptake. Although clomipramine may be more effective than the selective serotonin reuptake inhibitors (SSRIs), anticholinergic and antiadrenergic adverse effects may limit its utility in clinical practice.<sup>21</sup> In addition, because clomipramine is toxic in overdose, it should not be used in patients

Figure 1. Efficacy of Paroxetine and Clomipramine in Acute Treatment of Obsessive-Compulsive Disorder<sup>a</sup>



<sup>a</sup>Data from reference 23. Abbreviation: Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

\* $p < .05$  vs. placebo.

who are at risk for suicide. Currently, the SSRIs are the mainstays of therapy for patients with OCD.

### Selective Serotonin Reuptake Inhibitors

The SSRIs are effective for the treatment of OCD and are safe and well tolerated.<sup>19,22,23</sup> Selective serotonin reuptake inhibitors have fewer anticholinergic adverse effects compared with clomipramine and are safe when taken in overdose. Paroxetine, fluoxetine, fluvoxamine, and sertraline have proven efficacy in the treatment of OCD, and all 4 agents have been approved by the U.S. Food and Drug Administration for use in patients with OCD.<sup>23-27</sup> Although there are no data to suggest that one agent is more effective than another,<sup>28</sup> some patients may respond specifically to one agent.<sup>11,21</sup>

There have been relatively few comparative studies between the SSRIs in the treatment of OCD.<sup>28,29</sup> Studies comparing SSRIs and clomipramine have shown that clomipramine may be slightly more effective than the SSRIs, but it also is associated with an increased incidence of adverse effects.<sup>23,30-32</sup> In a flexible-dose trial of paroxetine compared with clomipramine in 406 patients with OCD,<sup>23</sup> paroxetine and clomipramine were more effective than placebo ( $p < .05$ ). In terms of efficacy, no significant differences between paroxetine (mean dose = 37.5 mg/day) and clomipramine (mean dose = 113.1 mg/day) were noted beginning at week 6, and the response was nearly equivalent at week 12 (Figure 1). However, significantly more patients treated with clomipramine withdrew from the study because of adverse effects.

A large, systematic meta-analysis compared data from multicenter, placebo-controlled trials of sertraline, fluvoxamine, fluoxetine, and clomipramine.<sup>26</sup> This analysis found that the 3 SSRIs were comparable to each other in efficacy and that clomipramine was more effective than the SSRIs. Several studies comparing fluoxetine or fluvoxamine with clomipramine showed similar results.<sup>30-32</sup> Although clomipramine and the SSRI were similarly effi-

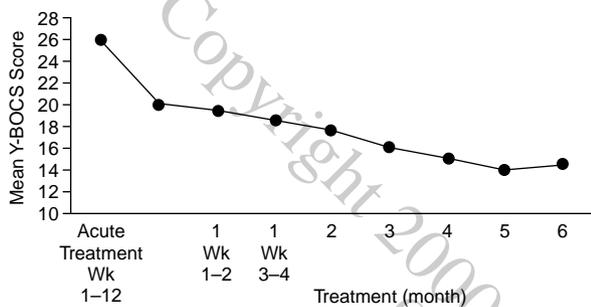
**Table 1. Targeted Daily Dose of Medication for the Treatment of Obsessive-Compulsive Disorder (OCD)**

Medication	Daily Dose (mg)
Paroxetine	40–60
Fluoxetine	20–80
Fluvoxamine	150–300
Sertraline	100–200
Clomipramine	150–250

**Table 2. Management Strategies for Treatment-Refractory OCD Patients<sup>a</sup>**

Switching to another SSRI
Combining SSRI with another medication
Combining SSRI with behavioral therapy
Novel and experimental drug treatments
Nonpharmacologic approaches

<sup>a</sup>Abbreviation: SSRI = selective serotonin reuptake inhibitor.

**Figure 2. Efficacy of Long-Term Paroxetine Treatment of Obsessive-Compulsive Disorder<sup>a</sup>**

<sup>a</sup>Modified from reference 40, with permission.

caxious in the management of OCD, clomipramine typically was associated with higher rates of adverse effects, particularly anticholinergic effects.

### Pindolol Augmentation

The combination of pindolol with an SSRI is being studied as a possible technique for hastening response to SSRI therapy. Pindolol is a  $\beta$ -blocker that inhibits serotonin-1A (5-HT<sub>1A</sub>) receptors. Acute administration of SSRIs decreases the firing rate of serotonin neurons. It is hypothesized that pindolol blocks somatodendritic 5-HT<sub>1A</sub> receptors and prevents suppression of firing rate and synthesis by serotonin. The actions of serotonin at the terminal end of the receptor are unimpeded by inhibition at the cell body, which results in a more rapid and robust increase in serotonin availability.<sup>33</sup> Although studies evaluating pindolol augmentation in depression showed mixed results, pindolol has been used to potentiate antidepressant medications and may be useful in treatment-refractory depressed patients.<sup>33-37</sup> On the basis of beneficial results in depressed patients, several researchers have begun to evaluate the use of adjunctive pindolol to initiate a more rapid onset of SSRI effects in patients with OCD. However, preliminary data suggest that adjunctive pindolol is ineffective in treatment-resistant OCD.

### Course of Therapy

When initiating SSRI therapy, medications should be initiated gradually. The standard pharmacologic regimen is a 10- to 12-week trial with an SSRI in adequate doses before

initiating alternative therapy.<sup>11</sup> In many cases, the adequate dose is the maximum tolerated amount because doses needed for the treatment of OCD may be higher than those for other anxiety disorders or depression (Table 1). Even with maximum pharmacotherapy, some patients do not experience complete relief of symptoms.<sup>38</sup> Full remission is rare, and as many as 25% of patients fail initial therapy.<sup>39</sup>

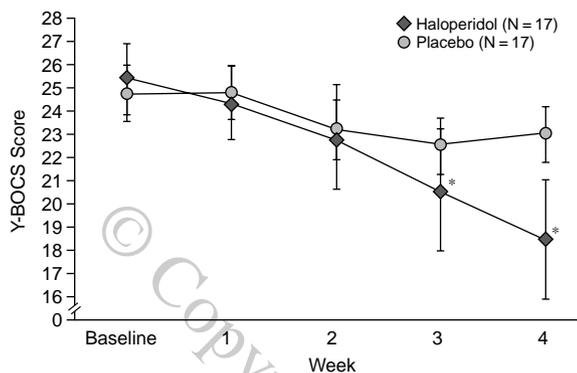
Initial response to medications in OCD can take 4 to 8 weeks, and maximal response may take as long as 20 weeks. Therapy should be continued for at least 6 months to 1 year once a therapeutic response is achieved<sup>11</sup> (Figure 2). Medications should be tapered slowly during discontinuation and should be restarted if symptoms reappear.<sup>21</sup> In one study, the risk of relapse was 2.7 times greater in patients who discontinued therapy compared with patients who remained on therapy.<sup>40</sup>

### TREATMENT-REFRACTORY PATIENTS

Unfortunately, between 40% and 60% of patients with OCD do not respond to SSRI therapy, and some patients who respond do not experience complete remission of symptoms.<sup>41</sup> There is evidence that patients who exhibit hoarding obsessions are relatively treatment resistant.<sup>42</sup> Patients who fail an adequate 10- to 12-week trial with 2 different SSRIs or clomipramine, using appropriate doses, may be considered medication resistant (Table 2). Strategies for the management of SSRI-resistant OCD patients include switching to a different SSRI or combining another medication or behavioral therapy with the SSRI. Patients who do not respond to one SSRI often have favorable response to another SSRI.<sup>21</sup> Additionally, cognitive-behavioral therapies, with an emphasis on exposure, may be beneficial when administered concomitantly with pharmacotherapy to patients with OCD, particularly in patients who have had a partial response to SSRI therapy. Other options for treatment-refractory patients include considering novel or experimental drug treatments or employing nonpharmacologic biological approaches, such as electroconvulsive therapy, neurosurgery, or repetitive transcranial magnetic stimulation.<sup>41</sup> However, neurosurgical techniques should be reserved as a last option for severely ill patients who have not responded to other reasonable therapies.

Most of the combination treatments, such as addition of fenfluramine or buspirone to SSRI therapy, have not been

Figure 3. Change in Severity of Obsessive-Compulsive Symptoms in Patients Treated With Fluvoxamine Plus Haloperidol or Placebo<sup>a</sup>



<sup>a</sup>Reproduced from reference 52, with permission.

\* $p < .05$  vs. placebo.

adequately investigated in treatment-resistant cases.<sup>38,41,43,44</sup> The addition of buspirone, a 5-HT<sub>1A</sub> agonist, to SSRI maintenance therapy may improve obsessive-compulsive symptoms in a small number of patients with comorbid anxiety or panic disorder.<sup>11</sup> However, several studies have suggested that the addition of buspirone does not significantly improve response to SSRI therapy and may produce a worsening of symptoms in some patients.<sup>44-46</sup> Patients with OCD who have comorbid depression may respond to SSRI therapy combined with lithium,<sup>47</sup> although some studies have demonstrated that this combination offers no significant improvement for either OCD or depressive symptoms.<sup>48,49</sup>

Patients with OCD who have comorbid tic disorder may benefit from pharmacologic augmentation with neuroleptics, such as haloperidol.<sup>44</sup> Risperidone also may be useful for adjunctive therapy in treatment-refractory OCD patients.<sup>50,51</sup> In a study conducted by McDougle and colleagues,<sup>52</sup> 34 patients with OCD who were refractory to fluvoxamine therapy were randomly assigned to receive either haloperidol or placebo in addition to fluvoxamine. Sixty-five percent of patients who received haloperidol augmentation demonstrated improved OCD symptoms compared with 0% of placebo-treated patients (Figure 3). Although the study by McDougle and colleagues<sup>52</sup> showed that OCD patients with tics had the best response to haloperidol augmentation, Saxena and associates<sup>53</sup> found that OCD patients with comorbid tic disorders had the lowest rate of response to augmentation. Additional studies are needed to better define the utility of concomitant neuroleptic therapy in patients with OCD.

Intravenous clomipramine may be an option in the management of treatment-resistant OCD. Several small open-label trials have evaluated the efficacy of intravenous clomipramine in patients with OCD.<sup>54-56</sup> In a randomized, double-blind study evaluating intravenous ver-

sus oral clomipramine in 15 patients with OCD, Koran and associates<sup>56</sup> found that 4.5 days after initiating therapy, 86% of patients treated with intravenous clomipramine responded to therapy compared with 13% of patients treated with oral clomipramine. In a recent study, Fallon and associates<sup>57</sup> randomly assigned 54 patients who were nonresponsive to oral clomipramine to receive intravenous clomipramine (25–250 mg/day) or placebo. After 14 infusions, 21% of patients receiving intravenous clomipramine responded to therapy compared with none of the placebo-treated patients. Although the exact mechanism of action is unknown, intravenously administered clomipramine may cause a rapid down-regulation of serotonergic receptors. However, intravenously administered clomipramine for the treatment of OCD is considered experimental and should be reserved for patients who have not responded to other approved therapies.

## RELATED CONDITIONS

A number of disorders are included in the OCD spectrum of disorders, such as obsessive-compulsive personality disorder, hypochondriasis, trichotillomania, eating disorders, and Tourette's syndrome.<sup>58,59</sup> Patients with obsessive-compulsive personality disorder have onset, clinical course, and response to therapy similar to those of patients with OCD. It has been hypothesized that these disorders may be considered across a continuum with risk aversion at the compulsive end and risk seeking at the other end.<sup>58</sup>

Patients with Tourette's syndrome and Sydenham's chorea frequently exhibit childhood-onset OCD.<sup>60</sup> A pediatric subtype of OCD is identified by the relationship between childhood OCD and Tourette's syndrome. Approximately 50% of patients with Tourette's syndrome present with symptoms of OCD.<sup>61,62</sup> Antipsychotics, such as haloperidol, are effective in combination with SSRIs for OCD patients with comorbid Tourette's syndrome or multiple motor tics.<sup>61</sup>

Sydenham's chorea, the neurologic variant of rheumatic fever, is characterized by abnormal movements and behavioral changes and may serve as a medical model for a subtype of OCD.<sup>63</sup> Although rheumatic fever is rarely diagnosed and is considered a preventable illness, there have been several outbreaks in the United States during the past decade.<sup>64</sup> It is noteworthy that not all patients who are exposed to streptococcal infections develop rheumatic fever complications, such as carditis, arthritis, and central nervous system effects. Approximately 2% to 3% of children who are infected develop rheumatic fever,<sup>64</sup> and about 10% to 30% of patients with rheumatic fever subsequently develop Sydenham's chorea.<sup>65</sup> There is evidence that vulnerability to complications may depend on the streptococcal strain. However, Sydenham's chorea is difficult to diagnose because the onset of symptoms may occur 1 to

6 months after the initial pharyngitis, and serologic evidence often is not detectable.<sup>65</sup> Several studies have described children who developed OCD symptoms with the onset of Sydenham's chorea and who recovered following treatment for the chorea.<sup>65-67</sup> A variety of treatments are being evaluated for this putative form of OCD, including penicillin prophylaxis.<sup>21,60</sup> Immunomodulatory treatments, such as plasmapheresis and intravenous immunoglobulin, are still considered experimental but may be useful in some patients.<sup>65,66</sup>

## SUMMARY

Obsessive-compulsive disorder is a chronic, disabling condition characterized by recurrent obsessions and compulsions that are time consuming and that significantly disrupt the patient's ability to function normally. Notably, OCD affects a relatively large portion of the general population, and patients with the disorder suffer significant functional disability. Fortunately, once OCD is diagnosed, viable treatment options are available. Because of well-proven efficacy and safety profiles, the SSRIs are first-line therapy for the management of patients with OCD. Patients who initially do not respond to SSRI therapy may benefit from switching to another SSRI or combining another medication or behavioral therapy with the SSRI. There is evidence that addition of a neuroleptic may improve response to SSRI therapy in some patients. Other experimental approaches, including intravenous clomipramine or neurosurgery, may be considered in patients who are severely ill and who have not responded to proven methods. Appropriate diagnosis and treatment of OCD will enable most patients to resist obsessions and compulsions and will improve overall quality of life.

*Drug names:* buspirone (BuSpar), clomipramine (Anafranil and others), fluoxetine (Prozac), fluvoxamine (Luvox), haloperidol (Haldol and others), paroxetine (Paxil), risperidone (Risperdal), sertraline (Zoloft).

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