OCD and OCRDs. Strategies for the clinical evaluation (including use of laboratory tests) and treatment of the illnesses are then discussed.

DEFINITIONS

OCD is listed as an anxiety disorder by the Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition (DSM-IV). It is characterized by repetitive thoughts, images, impulses, or actions that are distressing, that are time-consuming, or that affect function. The condition is often kept a secret because of the shame associated with its peculiar symptoms. Symptoms experienced by OCD sufferers are diverse. Obsessions can focus on aggressive or sexually intrusive thoughts, religious scrupulosity, concerns about symmetry, hoarding, pathological doubt, or thoughts of contamination. Compulsions are also varied; they include washing, counting, checking, repeating, hoarding, and the conduct of mental rituals. More often than not, patients with OCD experience more than one type of symptom at any given time, and the symptoms change over the course of the illness.

OCRDs are characterized by the presence of repetitive or excessively compulsive behaviors, some of which are preceded by increased tension and followed by a sense of relief. What constitutes an “OCD spectrum” or “OCD-related” disorder remains controversial. At present, prominent researchers cannot agree on how broad the OCD spectrum should be. Thus, OCRDs discussed in this chapter are those that are most often considered in this category.

Body dysmorphic disorder (BDD) and hypochondriasis are classified by the DSM-IV as somatoform disorders, and are characterized by repetitive worries and behaviors related to a slight or imagined physical defect or illness. Trichotillomania and pathological skin picking are classified by the DSM-IV as impulse control disorders; in both conditions, affected individuals are unable to resist the urge to recurrently pull their hair or to pick their skin. Trichotillomania is the prototypical impulse control disorder that will be discussed in this chapter. Tic disorders (such as Tourette’s disorder) are characterized by recurrent stereotyped motor or phonic tics that are resisted on occasion in the short term, but not in the long term. All of these OCRDs are debilitating and distressing; they adversely affect the quality of a person’s life.

KEY POINTS

- Obsessive-compulsive disorder (OCD) is a common and underdiagnosed disorder.
- OCD has underlying genetic causes and associated neuroimaging findings.
- OCD-related disorders are also characterized by repetitive behaviors.
- OCD and OCRD-related disorders tend to be chronic.
- OCD and OCRD-related disorders are treatable with medications and cognitive-behavioral therapy (CBT).

OVERVIEW

Obsessive-compulsive disorder (OCD) is a common disorder that affects individuals throughout the life span. This disorder has been listed as one of the ten most disabling illnesses by the World Health Organization, and the National Comorbidity Survey Replication indicated that OCD is the anxiety disorder with the highest percentage (50.6%) of serious cases. Putative OCD-related disorders (OCRDs) include somatoform disorders (e.g., body dysmorphic disorder [BDD] and hypochondriasis), tic disorders (e.g., Tourette’s disorder), and impulse control disorders (e.g., trichotillomania [TTM] [Figure 33-1] and pathological skin picking).

Approximately 2% to 3% of the world’s population will suffer from OCD at some point in their lives, and higher rates will suffer from OCRDs. Most individuals with OCD spend an average of 17 years before they receive an appropriate diagnosis and treatment for this illness. Although these disorders have a waxing and waning course, they frequently increase in severity when left untreated, which causes unnecessary pain to those afflicted and to their families. Hence, an understanding of OCD and OCRDs by clinicians is imperative to reduce the gap between the onset of symptoms and the eventual diagnosis, and to promote implementation of appropriate strategies for long-term symptomatic relief. This chapter provides a general description of these conditions, followed by characterization of the epidemiology (including its risk factors), the genetics, and the clinical features for OCD and OCRDs. Strategies for the clinical evaluation (including use of laboratory tests) and treatment of the illnesses are then discussed.
EPIDEMIOLOGY AND RISK FACTORS

Prevalence
Symptoms of OCD are common. Approximately 50% of the general population engage in some ritualized behaviors,6 and up to 80% experience intrusive, unpleasant, or unwanted thoughts.7 However, for most individuals these behaviors do not cause excessive distress, occupy significant amounts of time, or impair function; thus, they do not represent OCD. Regarding a clinical diagnosis of OCD in adults, the 1-month prevalence rate is 0.6%,8 and the reported 12-month prevalence ranges from 0.6% to 1.0% for DSM-IV–defined OCD9,10 and from 0.8% to 2.3% for DSM-III-R–defined OCD.11

Measured lifetime prevalence rates for OCD appear to depend on the version of the DSM used to determine diagnoses. The estimated lifetime prevalence is 1.6% using the DSM-IV2. Using the DSM-III, the lifetime rate was 2.5% in the U.S. Epidemiologic Catchment Area Survey,11 and the prevalence ranged between 0.7% (in Taiwan) and 2.5% (in Puerto Rico and in seven other countries surveyed).12 These differences may be due to the fact that the DSM-IV better defines obsessions and compulsions and requires significant clinical distress or impairment to confirm a diagnosis.9

The prevalence rates of the OCRDs vary. Many of these disorders co-occur with each other and with OCD. Regarding somatoform disorders, the estimated prevalence rate of hypochondriasis is 1% to 5% in the general population and 2% to 7% among primary care outpatients. Unfortunately, the prevalence rate of BDD is difficult to estimate accurately (given the secrecy of the disorder), but estimates range from 0.7% to 2.3% in the general population, and from 6% to 15% in cosmetic surgery settings.13 For the other OCRDs, the prevalence of Tourette’s disorder is 0.1%. The exact lifetime prevalence of TTM is unknown, but rates from 1% to 2% have been reported for cases that satisfy the full diagnostic criteria.14 The prevalence is even higher for subclinical hair-pulling, regardless of preceding tension and subsequent gratification.14-17 In patients with OCD, the prevalence of broadly defined OCRDs exceeds that for the general population, with reported rates of over 55%.18

Age of Onset
There appears to be a bimodal age of onset for OCD. Approximately one third to one half of adults with OCD develop the disorder in childhood.12,19 The National Comorbidity Survey Replication reported that the median age of onset was 19 years; 21% of cases emerged by age 10.10 The mean onset for OCD in adults occurs between 22 and 35 years of age.20 Some studies report another incidence peak in middle to late adulthood,21 but others report that onset of OCD after age 50 is relatively unusual.22

The age of onset for individuals with OCD appears to be an important clinical variable. Early-onset OCD may have a unique etiology and outcome, and it may represent a developmental subtype of the disorder.23,24 Childhood-onset OCD is also associated with greater severity,23,25 and with higher rates of compulsions without obsessions.23,24 An earlier age of onset was associated with higher persistence rates in a meta-analysis of long-term outcomes for childhood-onset OCD.26 Co-morbid rates of tic disorders,27 attention-deficit/hyperactivity disorder (ADHD), and anxiety disorders28 are also higher than in adult-onset OCD.

For the somatoform-based OCRDs, hypochondriasis is thought to develop most frequently in early adulthood,29 whereas BDD tends to occur during adolescence. However, many individuals with BDD have had life-long sensitivities regarding their appearance. Tic disorders are much more common in children and adolescents than they are in adults, because these disorders tend to remit over time. The average age of onset of Tourette’s disorder symptoms is approximately 7 years, ranging from 3 to 8 years.30 The age of onset for TTM in adults is approximately 13 years.31 However, among children with chronic hair-pulling, the average age of onset is as low as 18 months.32

Gender
The gender profile of OCD differs between age-groups and populations. In clinical samples of those with early-onset OCD, this disorder appears to be more common in males.24,25,33 However, epidemiological studies of children and adolescents report equal rates in boys and girls.34,35 In contrast, a slight female predominance is reported in epidemiological studies for adults.12,19,21,36

There is no clear gender predominance across the OCRDs. Men and women are equally affected by both hypochondriasis57 and BDD.13 Whereas tics are four times more common in men than women,36 in contrast TTM is more common in females. However, the younger the sample is for TTM, the more even is the gender distribution.39

Race and Cultural Factors
The prevalence for OCD tends to be fairly consistent across countries, which suggests that race and culture are not central causal factors for OCD. However, these factors may influence the content of obsessions and compulsions. The disorder...
is evenly distributed across socioeconomic strata in most studies, although there tends to be a paucity of minority subjects in epidemiological and clinical studies in the United States. 11

**Risk Factors**

There are no clearly established environmental risk factors for OCD. However, some patients describe the onset of symptoms after a biologically or emotionally stressful event (such as a pregnancy or the death of a loved one). 44 Streptococcal infection may be associated with an abrupt, exacerbating-rermitting early-onset form of OCD, which is termed pediatric autoimmune disorders associated with streptococcus (PANDAS). 40,42

Little is known regarding the etiology of BDD, although genetic predisposition, serotonin system deficits, and family biases (e.g., that appearance is prized) and specific events (such as teasing) may play a role. Exacerbating factors include brightly lit rooms, locations with mirrors or reflective surfaces, and social situations with many people. 13 Hypochondriasis is likely to arise during periods of increased stress, following the diagnosis of illness or the death of a loved one, and following media exposure to illness-related stories. 43 Regarding TTM, certain factors (such as cognitions, negative affective states, and particular settings) are known to trigger hair-pulling episodes, although these are not necessarily risk factors. Our understanding of the pathogenesis of TTM remains limited. 46

**CLINICALLY RELEVANT GENETICS**

Numerous lines of evidence support the genetic basis for OCD and OCRDs. Twin and family aggregation studies of OCD report higher than expected rates of OCD in relatives. 47,50 This was confirmed in a meta-analysis of five OCD family studies that included 1,209 first-degree relatives, 51 which calculated a significantly increased risk of OCD among relatives of probands (8.2%) versus controls (2.0%) (OR = 4.0). However, in studies ascertained through children or adolescents, familial risk appears to be even higher (9.5% to 17%) than that for those with later-onset OCD. 52-58 Despite studies by Nestadt, Pauls, and others, approximately half of the OCD cases have not been familial. 59,61

Although twin studies can provide compelling evidence for the role of genetic factors in complex neuropsychiatric disorders, no large systematic twin studies have focused exclusively on OCD. Further, twin studies cannot provide conclusive evidence that unique genes are important for the manifestation of OCD. A recent review of OCD twin studies dating back to 1929 concluded that obsessive-compulsive symptoms are heritable, with genetic influences ranging from 45% to 65% in children and from 27% to 47% in adults. 62

Molecular genetic studies have begun to provide evidence that specific genes play a role in the manifestation of OCD. Segregation analyses have examined familial patterns of OCD transmission and noted the best fit for a dominant model in some studies. 63,64 However, results of combined regression analyses suggest that OCD’s familial transmission is difficult to model. The most parsimonious solution suggests that there are at least some genes of major effect 45; it is highly likely that OCD is an oligogenic disorder with several genes that are important for the expression of the syndrome. At the present time, none of the four linkage studies for OCD or OCD symptoms reported genome-wide significance. 66-68 The following regions have been suggestive for susceptibility loci: 1q, 6q, 9p, 19q, 7p, and 15q.

OCD candidate genes have been studied based on their function and also their position in the genome. Serotonin-related genes considered in OCD include those coding for the serotonin transporter (5-HTT) 69-71 and receptors 5-HT2A, 72 5-HT2B, 73 5-HT2C, 74 and 5-HT3A, 70 as well as the serotonin enzyme tryptophan hydroxylase. 75 Dopamine (DA)-related genes studied in OCD include DA transporter genes 76,77; D2, D3, and D4 receptors; 78 COMT; 79 and MAO-A enzymes. 80,81 Glutamate-related genes associated with OCD include GRIK 82,83 GRIN2B, 84,85 and SLC-1A1. 86,87 Other genes that are associated with OCD include the white-matter genes OLIG 288 and MOG. 89 Given the complexity of the OCD phenotype, it is unlikely that any candidate genes have a major impact on the disorder, and few if any genes have been consistently replicated in large samples.

With respect to family studies of OCRDs, Bienvenu and colleagues 80 explored these illnesses among the relatives of OCD probands and found significantly higher than expected rates of BDD (OR = 5.4), somatoform disorders (OR = 3.9), grooming disorders (OR = 1.8), and all spectrum disorders combined (OR = 2.7). Relatives of OCD probands have elevated rates of Tourette’s disorder and chronic tics (4.6%) versus relatives of controls (1%), regardless of a diagnosis of Tourette’s disorder in the probands. 49,91 This is especially true in families with earlier-onset OCD. Moreover, relatives of Tourette’s disorder probands have elevated rates of OCD as compared with controls. 92,93 It has also been suggested that TTM has an underlying genetic basis. 46,94,95 In the only twin study exploring the genetic basis for TTM, a significantly greater concordance rate was present among monozygotic (31.9%) than dizygotic (0%) twins for “clinically significant hair-pulling.” 96

**PATHOPHYSIOLOGY**

The pathophysiology of OCD is incompletely understood, although neurobiological models implicate dysfunction in several corticostriatal pathways. 97,98 OCD is considered to be a neuropsychiatric disorder that is associated with neurobiological conditions and movement disorders. In fact, OCD may develop following birth injury, 99 temporal lobe epilepsy, 100 or head injury. 101 Neuroimaging findings indicate that OCD involves subtle structural and functional abnormalities of the orbitofrontal cortex, the anterior cingulate cortex, the caudate, the amygdala, and the thalamus. 97,98,102,104 The nodes of the implicated frontal cortical-basal ganglia-thalamocortical circuit are inter-
connected via two principal white-matter tracts—the cingulum bundle and the anterior limb of the internal capsule.

The basal ganglia are likely associated with abnormal compulsions of OCD. Damage to this region in both humans and animal models results in behaviors that resemble compulsions. Furthermore, diseases in humans that result from deterioration of basal ganglia (such as Huntington’s chorea and Parkinson’s disease) have increased rates of OCD. Prefrontal and orbitofrontal regions are responsible for filtering information received by the brain and for suppressing unnecessary responses to external stimuli; these may be more associated with the obsessive symptoms of OCD.

There is also evidence of brain white-matter involvement in OCD. Patients with OCD have significantly more gray matter, less white matter, and abnormalities of white matter than do normal controls, which suggests a possible developmental etiological process (Figure 33-2). Neurochemically, serotonergic systems have been implicated in OCD. Other medical pathophysiological factors may be involved in the etiology of OCD. In rare cases, a brain insult (such as encephalitis, a striatal lesion [congenital or acquired], or head injury) directly precedes the development of OCD. Research suggests that autoimmune processes, precipitated in some childhood-onset cases by beta-hemolytic streptococcal infection, may cause damage to striatal neurons in childhood-onset cases of OCD.

CLINICAL FEATURES AND DIAGNOSIS

The DSM-IV is currently used for the diagnosis of OCD and OCDs (Table 33-1). The diagnosis of OCD requires the presence of either obsessions or compulsions. These must be significantly distressing, time-consuming, or interfering with the person’s normal routine, occupational function, social activities, or relationships with others. Figure 33-3 illustrates the living quarters of a patient with OCD and hoarding behavior.

Revisions from the DSM-III-R to the DSM-IV for OCD include the addition of mental compulsions, and exclusion, if the content of the obsessions or compulsions is restricted to another Axis I disorder (e.g., concern with appearance in the presence of BDD, or repeated hair-pulling with TTM) or if the obsessions or compulsions are due to the direct effects of a substance or general medical condition. A "poor insight
OCD and OCD-Related Disorders

Table 33-1 Diagnostic Criteria for Obsessive-Compulsive Disorder (DSM-IV)

<table>
<thead>
<tr>
<th>Either Obsessions or Compulsions</th>
</tr>
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<tbody>
<tr>
<td><strong>Obsessions</strong> are defined by the following:</td>
</tr>
<tr>
<td>• Recurrent and persistent thoughts, impulses, or images that are experienced, at some time during the disturbance, as intrusive and inappropriate and that cause marked anxiety or distress</td>
</tr>
<tr>
<td>• Thoughts, impulses, or images that are not simply excessive worries about real-life problems</td>
</tr>
<tr>
<td>• The effort by the affected person to ignore or suppress such thoughts, impulses, or images, or to neutralize them with some other thought or action</td>
</tr>
<tr>
<td>• Recognition by the affected person that the obsessional thoughts, impulses, or images are a product of his or her own mind rather than imposed from without</td>
</tr>
<tr>
<td><strong>Compulsions</strong> are defined by the following:</td>
</tr>
<tr>
<td>• Repetitive activities (e.g., handwashing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the person feels driven to perform in response to an obsession or according to rigid rules that must be applied rigidly</td>
</tr>
<tr>
<td>• Behavior or mental acts aimed at preventing or reducing distress or preventing some dreaded event or situation but either clearly excessive or not connected in a realistic way with what they are designed to neutralize or prevent</td>
</tr>
<tr>
<td>• Recognition, by the affected person (unless he or she is a child), at some point during the course of the disorder, that the obsessions or compulsions are excessive or unreasonable</td>
</tr>
<tr>
<td>• Obsessions or compulsions that cause marked distress, are time-consuming (take more than 1 hr/day), or interfere substantially with the person’s normal routine, occupational or academic functioning, or usual social activities or relationships</td>
</tr>
<tr>
<td>• Content of the obsessions or compulsions not restricted to any other Axis I disorder, such as an obsession with food in the context of an eating disorder, that is present</td>
</tr>
<tr>
<td>• Disturbance not due to the direct physiological effects of a substance or a general medical condition</td>
</tr>
<tr>
<td>Specified as OCD with poor insight if, for most of the time during the current episode, the person does not recognize that the obsessions and compulsions are excessive or unreasonable</td>
</tr>
</tbody>
</table>

DSM-IV, Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition. 3

Figure 33-3 OCD patient demonstrating a typical compulsive behavior of handwashing. Some patients may wash their hands hundreds of times daily, leading to inflamed, erythematous, and cracking skin.

Figure 33-4 Cluttered and overcrowded home of an OCD patient suffering with hoarding obsessions and compulsions.

"type" may be specified if the person does not recognize the excessive or unreasonable nature of the obsessions and compulsions most of the time during the current episode.

Figure 33-4 provides an image of a classic OCD symptom, handwashing.

It has been proposed that clinical features of the OCRDs may be categorized into three symptom clusters. These are a "somatic" cluster for BDD and hypochondriasis; a "reward deficiency" cluster for TTM and other impulse control disorders (such as Tourette’s disorder); and an "impulsivity"
cluster for compulsive shopping, kleptomania, and intermittent explosive disorder. However, as previously noted, whether all of these disorders (especially the latter cluster) constitute OCRDs is an issue of ongoing debate.

BDD is a disorder in which individuals suffer from a pre-occupation with a slight or imagined defect in appearance that causes significant distress or impairment that is not strictly a manifestation of another disorder. Hypochondriasis involves a preoccupation with the inaccurate belief that one has, or is in danger of developing, a serious illness. This fear persists despite extensive evaluation and subsequent reassurance of good health by a medical professional. Tourette’s disorder is characterized by the presence of chronic motor and vocal tics, with symptoms manifesting before 18 years of age. These symptoms should persist for at least a year, with no 3-month symptom-free intervals. TTM involves repetitive hair-pulling that results in significant hair loss that is preceded by increasing tension, followed by relief or pleasure, and results in impaired function or significant distress.

**EVALUATION, TESTS, AND LABORATORY FINDINGS**

To assess an individual with a suspected OCD or OCRD, a systematic approach should be applied. Elements of a standard psychiatric assessment are included in the evaluation of an individual with suspected OCD or a suspected OCRD. This includes the assessment of the history of present illness, co-morbid symptoms, past psychiatric history, family psychiatric history, social and developmental history, review of systems, medical and substance history, medications and drug allergies, and the mental status examination.

Regarding the history of present illness, the duration and severity of symptoms and their precipitating, exacerbating, and ameliorating factors should be elucidated. Functional consequences of these symptoms in home, work, and social environments and the level of insight, resistance, and control over symptoms should also be assessed. Family insight and accommodation of symptoms (which permits their perpetuation) are other important factors to be determined. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and checklist should be used to record the severity and lifetime presence of specific symptoms. There is also a children’s version of this scale, the Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS). Alternatively, the Obsessive-Compulsive Inventory or the Obsessive-Compulsive Checklist may be used.

Following the initial assessment, co-morbid illnesses or other more responsible disorders should be ruled out. (Figure 33-5 shows an algorithm for creation of a differential diagnosis.) For individuals with OCD, co-morbid OCRDs should be assessed, and vice versa. Tics and eating disorders may be more common in individuals with OCD. Clinical measures used to record OCRDs include the Yale Global Tic Severity Scale (YGTSS) for tics and Tourette’s disorder, the Massachusetts General Hospital (MGH) Hairpulling Scale for TTM, and the Body Dysmorphic Disorder Questionnaire for BDD. Other co-morbidities that should be assessed include depression and the risk of suicide. Other co-morbidities that occur at higher than expected rates include bipolar disorder, personality disorders, and anxiety disorders (such as panic disorder, social phobia, or generalized anxiety disorder). Further diagnoses (including ADHD and substance use disorders) should also be screened for.

In the assessment of past psychiatric history, the duration of time at the maximum dosage of every past medication trial should be recorded. The length and success of past behavior or cognitive therapies and other psychotherapies also needs to be established. Careful attention should be paid to determine whether actual exposure and response prevention or cognitive therapy forms of cognitive-behavioral therapy (CBT) were received or if, alternatively, this was a form of supportive therapy that has not been reported as efficacious for OCD. Other factors that may affect the treatment include a history of substance abuse, which may impede compliance. Past mood instability may indicate the risk for a switch toward mania with administration of serotonergic agents. Panic attacks should stimulate use of caution with dosage increases, because these may trigger further attacks.

Since OCD and related disorders may have a genetic component, a thorough family psychiatric history should be elicited for the presence of OCD and OCRDs. Furthermore, since medication response may also have an inherited component, information regarding family history of effective treatment trials and negative medication reactions should be gathered.

A review of systems should be conducted to establish a baseline of symptoms. The medical history is an important component of assessment; it includes currently prescribed, over-the-counter, and birth control medications, as well as drug allergies. Physical and neurological illnesses should be listed, in addition to possible symptoms that may overlap with medication side effects (e.g., insomnia or anergia). A history of thyroid problems, head injuries, or seizures should be noted, and pregnancy should be ruled out. If the patient is a child with an abrupt onset of OCD, a history of streptococcal infections should be obtained and throat cultures should be collected. This will assist in providing a diagnosis of PANDAS, in which OCD may be due to autoimmune mechanisms.

The final component of any psychiatric assessment is the mental status examination. A general description of the patient and his or her behavior should include any external signs of OCD or OCRDs (e.g., red, chapped hands, repeated behaviors, or bald spots). Abnormal movements (such as tics or choreiform movements) should be noted, in addition to abnormalities of speech, the degree of eye contact, and cooperation. Mood and affect should denote the levels of potential anxiety, depression, or anger. Thought form should be assessed with respect to circumstantiality and detail focus and thought content with respect to overvalued ideation, delusions, and thoughts of suicide and homicide. The level of insight and degree of judgment exhibited by the patient are also important to note.
Unfortunately, there are no laboratory findings that are diagnostic of OCD or OCRDs. However, for clinicians who are considering a diagnosis of PANDAS, a positive throat culture for *Streptococcus A* is required, in addition to determination of other diagnostic criteria. Although characteristic neuroimaging findings have been reported for groups of individuals with OCD, there are no pathognomonic findings that may be used to diagnose an individual with the disorder.

**TREATMENT**

Treatment of OCD typically involves use of medication in combination with other modalities (such as CBT, psychoeducation, and support groups). First-line treatment options for OCD include both serotonin reuptake inhibitor (SRI) medication and CBT. SRIs include selective serotonin reuptake inhibitors (SSRIs) and the tricyclic antidepressant (TCA) clomipramine. Other TCAs with less serotonergic activity do not tend to be as effective in the treatment of OCD. Details of large OCD controlled monotherapy SRI trials are outlined in Table 33-2. CBT includes exposure and response prevention (ERP), which has been well studied in OCD, and also cognitive therapy, which is a promising OCD treatment. ERP works by anxiety habituation following prolonged exposure to a feared OCD stimulus without compulsion performance, whereas cognitive therapy works to directly modify distorted OCD beliefs.129

The decision to initiate an SSRI alone, CBT alone, or a combination depends on individual patient variables. All three of these approaches, in addition to cognitive therapy alone,

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Figure 33-5 Algorithmic approach to establishing DSM-IV diagnoses of OCD and OCD-related disorders.

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145,146 have been demonstrated as effective for OCD when compared with treatments such as supportive therapy. For those uninterested in taking medications, or for those who are very young, pregnant, nursing, or medically ill, and for those with mild illness in which potential medication side effects outweigh benefits, an initial trial of CBT alone may be preferable. For those without access to a CBT-trained clinician or with poor motivation or insight, an initial trial with an SSRI alone may be optimal. Furthermore, co-morbid depression, psychosis, or other anxiety disorders that may interfere with CBT are factors that suggest that medication should be included in the initial management approach.

A suggested management approach in the treatment of OCD is outlined in Figure 33-6. It is advisable to initiate SRI treatment with an SSRI rather than clomipramine, given the side effects associated with TCAs. If the initial SSRI is not effective, one to two other SSRI trials should be attempted before use of clomipramine. The selection of a specific SSRI...
is open to clinical judgment, because head-to-head trials and meta-analyses of SSRIs in children and adults with OCD have not found significant differences. Factors that may be helpful in making this selection include a family history of a positive response or an adverse reaction to a specific SSRI, potential interactions with other medications, and side effect profiles.

To determine the effectiveness of a medication, a 10- to 12-week trial at the highest tolerated dose within the advised dose range is required. For treatment of OCD, doses are typically higher than are those required for depression (Table 33-3). Further, a reduction of symptoms is a more common outcome than is remission. In clinical trials, “response” is typically defined by a ≥25% or ≥35% decrease in Y-BOCS–defined OCD severity. Approximately 40% to 60% of patients respond to SSRIs with a 20% to 40% reduction of OCD symptoms.112,147

Before initiating a medication trial, it is at times necessary to conduct laboratory baseline investigations (such as blood work and an electrocardiogram [ECG]), depending on the specific agent to be used. It is also necessary to rule out a previous allergic/negative reaction to the agent and to consider potential interactions with other medications in the current regimen. Between each step in the treatment plan (see Figure 33-6), assessment of adherence/compliance and adverse effects with the medication regimen should be conducted.

Second-line medication strategies include SRI augmentation or replacement monotherapy. Details of moderate-sized controlled trials supporting these approaches are given in Table 33-4. Effective SRI augmenting agents include typical and atypical antipsychotics, clonazepam, buspirone, and lithium. Buspirone and atypical agents should be attempted before typical antipsychotics given the lower risk for irreversible tardive dyskinesia. Suggested dosages and common and rare, but serious, adverse effects of the best-studied second-line agents are found in Table 33-3. However, it should be noted that distinct adverse effect profiles also exist for certain medications within classes (e.g., ziprasidone and potential QT prolongation on the ECG).

Clonazepam, buspirone, and venlafaxine are used as replacement monotherapy medications for SSRIs, in addition to acting as augmenting agents in the OCD treatment. There is also some evidence that monoamine oxidase inhibitors (MAOIs) may be effective as SRI replacements. However, the risk of a life-threatening hypertensive crisis and a serotonergic syndrome mandate caution and a proper washout period if MAOIs are to be used. For severe refractory cases, intensive residential treatment155-156 or somatic approaches (such as deep brain stimulation,157-159 transcranial magnetic stimulation,160-162 and neurosurgery163-169) could be considered.
OCD and OCD-Related Disorders

Diagnostic assessment, psychoeducation of patient and family ± CBT

Mild OCD: no medication

OR

Moderate/severe OCD: SSRI (at maximum tolerated dose × 10–12 weeks)

Second SSRI trial

Clomipramine or third SSRI followed by clomipramine trial

SRI augmentation with clonazepam/buspirone (× 4–6 weeks)

OR

SRI replacement with SNRI (× 12 weeks)

SRI augmentation with atypical antipsychotic (× 4–6 weeks)

SRI augmentation with typical antipsychotic/lithium (× 4–6 weeks)

Other approaches:
- SRI washout and replacement with MAOI
- Combination/novel agents
- Somatic approaches (DBS, TMS, neurosurgery)

With co-morbid disorders:
1. Major depressive disorder
   → CBT → SSRI/clomipramine
   → SRI + bupropion → SRI + ritalin/lithium

2. Other anxiety disorders
   → CBT → SSRI/clomipramine → SRI + clonazepam

3. Tic disorders
   → CBT → SSRI + clonidine/guanfacine → ± bzd → clomipramine
   → SRI + atypical → SSRI + typical/atamoxetene

4. Bipolar disorder
   → CBT → SSRI + mood stabilizer and/or atypical → ± bzd

5. Psychosis
   → SRI + atypical ± bzd → SRI + second atypical
   → SRI + third atypical/typical

Step 1
Step 2
Step 3
Step 4
Step 5
Step 6
Step 7
Step 8

Figure 33-6 Algorithmic approach to the management of a patient with OCD with or without co-morbidities.
Once an effective medication and dose are identified in the treatment of OCD, this treatment should be continued for at least 1 year before its discontinuation. Unfortunately, the subsequent relapse rate following medication discontinuation is very high. In discontinuation studies of responders, these rates range from 24% to 89% at 6-month follow-up.\textsuperscript{140,143,170,171} For the individuals who have also received previous CBT, however, relapse rates are lower (12% versus 45% for clomipramine responders at 12 weeks after discontinuation).\textsuperscript{172}

Regarding treatment of OCRDs, the presence of large placebo-controlled studies in individuals without multiple co-morbidities is lacking. Thus, it is difficult to draw conclusions on medication use and psychotherapy in OCRDs. However, from preliminary data to date the SSRIs, naltrexone,\textsuperscript{173} and CBT appear to be the best medication treatment options overall for these disorders.

Both pharmacological agents and psychotherapeutic approaches have been reported to be successful in BDD. In a recent meta-analysis of BDD treatment trials, both CBT and medication were effective, although CBT was most useful.\textsuperscript{174} Components of CBT for BDD include graded exposure, cognitive therapy, social skills training, and a relapse-

| Table 33-3 Obsessive-Compulsive Disorder Medications, Dosages, and Side Effects |
|-------------------------------|-----------------|-----------------|-----------------|-----------------|
| **Drug (Generic Name)**     | **Drug (Trade Name)** | **Starting Dose (mg/d)** | **Target Dose (mg/d)** | **Adverse Effects** |
| **First-line Agents**        |                  |                  |                  |                  |
| **Selective Serotonin Reuptake Inhibitors** |                  |                  |                  |                  |
| Citalopram (Celexa)          |                  | 20               | 60               | Common: insomnia, anxiety, GI upset, sexual side effects, dizziness, sedation |
| Escitalopram (Lexapro)       |                  | 10               | 7 (probably 30)  | Rare: rash, headache |
| Fluoxetine (Prozac)          |                  | 20               | 80               |                  |
| Fluvoxamine (Luvox)          |                  | 50               | 300              |                  |
| Paroxetine (Paxil)           |                  | 20               | 60               |                  |
| Sertraline (Zoloft)          |                  | 50               | 200              |                  |
| **Tricyclics**               |                  |                  |                  |                  |
| Clomipramine (Anafranil)     |                  | 25               | 250              | Common: anticholinergic side effects, dizziness, sexual side effects, weight gain, tremor |
| **Adjunctive/Second-line Agents** |                  |                  |                  |                  |
| Buspirone (BuSpar)           |                  | 10 (divided bid) | 10-45 (divided bid) | Common: dizziness, headache, nausea |
| Lorazepam (Ativan)           |                  | 0.5 (divided bid-tid) | 0.5-4 (divided bid-tid) | Rare: sedation, rash |
| **Benzodiazepines**          |                  |                  |                  |                  |
| Clonazepam (Klonopin)        |                  | 0.25-0.5 (or divided bid) | 0.5-3 (or divided bid) | Common: sedation, tolerance |
| Lorazepam (Ativan)           |                  | 0.5 (divided bid-tid) | 0.5-4 (divided bid-tid) | Rare: impaired cognition, disinhibition, ataxia |
| **Atypical Antipsychotics**  |                  |                  |                  |                  |
| Risperidone (Risperdal)      |                  | 1 (or divided bid) | 0.5-6            | Common: weight gain, dizziness, sedation, constipation, sexual side effects |
| Olanzapine (Zyprexa)         |                  | 5                | 5-20 (or divided bid) | Rare: hyperglycemia, elevated prolactin, extrapyramidal symptoms |
| Quetiapine (Seroquel)        |                  | 50 (or divided bid) | 500 (or divided bid) |                  |
| Aripiprazole (Abilify)       |                  | 10               | 10-30            |                  |
| Ziprasidone (Geodon)         |                  | 40 (or divided bid) | 40-160 (or divided bid) |                  |
| **Typical Antipsychotics**   |                  |                  |                  |                  |
| Haloperidol (Haldol)         |                  | 0.5              | 0.5-10           | Common: sedation, extrapyramidal symptoms, sexual side effects, anticholinergic side effects |
| Pimozide (Orap)              |                  | 1                | 1-3              | Rare: ECG changes, tardive dyskinesia, neuroleptic malignant syndrome |

\textsuperscript{11} bid, Twice a day; ECG, electrocardiogram; GI, gastrointestinal; od, once daily; tid, three times daily.
The opioid-blocking agent naltrexone was reportedly superior to placebo and to fluoxetine in several studies. Similar to the experience with OCD, higher doses of SSRIs are often required. There is little evidence for the effectiveness of antipsychotic medications in BDD, although these agents are often used in clinical practice.

Antidepressants have been used to treat hypochondriasis, based on the belief that it may be an alternate manifestation due to their less favorable side effect profile. Less commonly used medications in Tourette’s disorder include anticonvulsants, tetrabenazine, pergolide, and botulinum toxin.

Treatment studies of TTM are limited. Randomized controlled trials of pharmacotherapy found clomipramine to be superior to placebo in a small study, but only approaching significance in another study. None of the three controlled studies of fluoxetine found this medication to be superior to placebo, although it was effective in an early small, open trial. Further, a recent open study reported that a combination of sertraline and CBT was more efficacious in the treatment of TTM than either approach alone. The opioid-blocking agent naltrexone was reportedly superior to placebo in one study. Behavioral therapy was superior to placebo and to fluoxetine in several studies. Habit-reversal appears to be more effective than other CBT approaches in TTM.

PROGNOSIS

OCD usually has a gradual onset, although acute onset occurs in some cases (e.g., PANDAS). The long-term course of OCD has been studied in both children and adults and in clinical and population samples. In a landmark follow-up study, 144 adult inpatients with OCD, ages 19 to 52 years, were reevaluated after a mean of 47 years. Nearly half (48%) reported clinical recovery (no clinically relevant symptoms for ≥5 years), but only 20% reported full remission (no symptoms for ≥5 years). At follow-up, 80% had clinical (52%) or subclinical (obvious symptoms without distress or interference) (28%) symptoms, 9% had no improvement, and 8% reported a deteriorating course. Forty-six percent of those in remission at the first evaluation remained in remission for at least 30 years. In an Italian 10-year follow-up study, 27% had an episodic course (26 months of full symptom remission), and 73% had a chronic course (with stable or fluctuating symptoms or with deterioration). Finally, in a U.S. study of 200 outpatients with OCD, 85% had a waxing and waning course, 10% had a deteriorating course, and 2% had an episodic course with full remissions of ≥6 months. In the single long-term outcome study of a community sample of 22 adults with OCD, a mean 13-year follow-up period was used. At follow-up only 5% met DSM-IV diagnostic criteria, 86% had no symptoms, and 9% had symptoms and moderate distress. Furthermore, only one third had received treatment.

A meta-analysis by Stewart and co-workers was conducted on 22 long-term outcome studies for childhood OCD (N = 521 subjects), with follow-up periods ranging from

### Table 33-4 Moderate-sized (N ≥ 30) Augmentation/Refractory Sample Trials in Obsessive-Compulsive Disorder

<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Baseline Medication (mg/d)</th>
<th>Augmenting Agent (mg/d)</th>
<th>Comparison Agent (mg/d)</th>
<th>Sample</th>
<th>Effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjunctive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McDougla148</td>
<td>1993</td>
<td>Fluvoxamine (300)</td>
<td>Haloperidol (10)</td>
<td>PBO</td>
<td>34</td>
<td>Yes</td>
</tr>
<tr>
<td>SRI—Refractory Cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McDougla148</td>
<td>1993</td>
<td>Fluvoxamine (300)</td>
<td>Buspirone (60)</td>
<td>PBO</td>
<td>33</td>
<td>No</td>
</tr>
<tr>
<td>McDougla150</td>
<td>2000</td>
<td>SRI with co-morbid tic disorder</td>
<td>Haloperidol (10)</td>
<td>PBO</td>
<td>34</td>
<td>Yes</td>
</tr>
<tr>
<td>McDougla151</td>
<td>2000</td>
<td>SRI</td>
<td>Risperidone (2.2)</td>
<td>PBO</td>
<td>70</td>
<td>Yes</td>
</tr>
<tr>
<td>Shapira152</td>
<td>2004</td>
<td>SRI</td>
<td>Quetiapine (300)</td>
<td>PBO</td>
<td>40</td>
<td>Yes</td>
</tr>
<tr>
<td>Erzegovesi153</td>
<td>2005</td>
<td>Fluvoxamine (300)</td>
<td>Olanzapine (6.1)</td>
<td>PBO</td>
<td>42</td>
<td>Yes, both</td>
</tr>
<tr>
<td>Carey154</td>
<td>2005</td>
<td>SRI</td>
<td>Quetiapine (169)</td>
<td>PBO</td>
<td>41</td>
<td>Yes, both</td>
</tr>
</tbody>
</table>

PB0, Placebo; SRI, serotonin reuptake inhibitor.
1 to 15.6 years. Pooled mean persistence rates were 41% for full OCD and 60% for full or subthreshold OCD. Earlier age of OCD onset, increased OCD duration, and inpatient versus outpatient status predicted greater persistence at follow-up. Hence, in general it appears that OCD is a chronic illness that exhibits a waxing and waning course, even with treatment. However, most individuals with OCD experience at least mild to moderate improvement throughout their illness course, with proper treatment.

The course of hypochondriasis tends to be episodic, alternating with relatively symptom-free periods. Episodes are often associated with psychosocial stressors, and approximately one third to one half of individuals with this disorder improve significantly. BDD is a life-long illness when left untreated, although the symptoms may wax and wane over time. However, for those receiving medication or psychotherapy, 4-year remission rates have been as high as 60%. However, of those who remitted, nearly 30% subsequently relapsed, which was associated with severity and co-morbid depression and social phobia. For those who obtain cosmetic interventions in an attempt to alleviate body-related concerns, 83% had either a worsening or no change of their symptoms. Those with BDD were found to be more disabled than those with depression, diabetes, or a recent myocardial infarction.

Limited research has been done regarding the prognosis of TTM, although both chronic and remitting forms occur. There is some evidence that self-esteem worsens over the course of the illness. Cases with onset in early childhood have a better prognosis and are more likely to respond to treatment. The majority of these individuals have co-morbid psychiatric diagnoses in addition to low self-esteem, depression, and irritability. However, the long-term course differs and tends to be associated with improvement of symptoms until 20 years of age.

CURRENT CONTROVERSIES, UNANSWERED QUESTIONS, AND FUTURE CHALLENGES

- Identifying symptom dimensions or OCD subtypes with preferential response to specific treatments
- Understanding the role of nonserotonergic factors, such as glutamate modulation, in the pathogenesis of OCD
- Understanding the role of autoimmunity in OCD (e.g., pediatric autoimmune neuropsychiatric disorders associated with streptococcus)
- Identifying genetic markers that indicate risk for OCD onset and association with response to specific treatments
- Establishing the relative efficacy of somatic treatments for OCD (e.g., transcranial magnetic stimulation, deep brain stimulation, and neurosurgery)

CLINICIAN AND CONSUMER RESOURCES

OC Foundation
676 State Street
New Haven, CT 06511

Tel: 203-401-2070
Fax: 203-401-2076
www.ocfoundation.org

Scrupulous Anonymous (for those with religious/morality-focused OCD)
http://mission.liguori.org/newsletters/scrupanon.htm

San Francisco Bay Area Resource and Internet Guide for Extreme Hoarding Behavior
www.hoarders.org

Resources for Tic Disorders
Tourette Syndrome Association, Inc.
42-40 Bell Boulevard
Bayside, NY 11361
Tel: 718-224-2999
www.tsa-usa.org/

American Academy of Child and Adolescent Psychiatry
3615 Wisconsin Ave., NW
Washington, DC 20016-3007
Tel: 202-966-7300
www.aacap.org/
www.aacap.org/publications/factsfam/index.htm

Anxiety Disorders Association of America
Tel: 301-231-9350
www.adaa.org
http://socialanxietysupport.com

Trichotillomania Learning Center
Tel: 831-457-1004
www.trich.org

Information on the Use of Medication During Pregnancy and Breast-Feeding
California Teratogen Information Service and Clinical Research
Tel: 1-800-532-3749 (CA only) or 610-543-2131
www.otispregnancy.org/ctis.html

MGH Women’s Mental Health Program
www.womensmentalhealth.com

Resources for General Information on Mental Disorders and Medications
National Institute of Mental Health (NIMH)
Public Information and Communications Branch
6001 Executive Boulevard, Room 8184, MSC 9663
Bethesda, MD 20892-9663
Tel: 1-866-615-6464
Fax: 301-443-4279

National Alliance on Mental Illness
Tel: 1-800-950-6264; or, 703-524-7600
http://www.nami.org

National Mental Health Association
1021 Prince St.
Alexandria, VA 22314-2971
Tel: 1-800-969-6642 or 703-684-7722
Fax: 703-684-5968
www.nmha.org
REFERENCES


96. Nowak C: Personal communication, 2006.


SUGGESTED READINGS

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Many thanks for your assistance.

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| 3.                | AU: Figure 33-4 description correct? Please check Figures 33-3 and 33-4. |                                                               |
| 4.                | AU: Should this be Streptococcus aureus?                             |                                                               |
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| 6.                | AU: Please update reference 83.                                      |                                                               |
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| 10.               | AU: “a prior hypothesis” correct? If not, please clarify/correct sentence. |                                                               |
| 11.               | AU: “once daily” correct?                                             |                                                               |