CLINICAL PRACTICE

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Obsessive–Compulsive Disorder

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

A 19-year-old man is brought to his primary physician by his father, who explains that his son washes his hands a hundred times a day, will not touch anything that has been touched by someone else without scrubbing it first, and has a fear of germs that has left him isolated in his bedroom, unable to eat, and wishing he were dead. Although the father reports that his son has always been finicky, this problem started approximately 2 years ago and has gradually become completely disabling. How should this patient be evaluated and treated?

THE CLINICAL PROBLEM

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N Engl J Med 2014;371:646-53.
DOI: 10.1056/NEJMcp1402176

An audio version of this article is available at NEJM.org

Obsessive–compulsive disorder (OCD) is a neuropsychiatric disorder characterized by obsessions or compulsions (or both) that are distressing, time-consuming, or substantially impairing. OCD is the fourth most common psychiatric illness, with a lifetime prevalence of 1 to 3%.[1,2] The World Health Organization has identified OCD as a leading global cause of nonfatal illness.[3]

The hallmark of OCD is the presence of obsessions, compulsions, or both (Table 1).[4] Obsessions are repetitive and persistent thoughts (e.g., of contamination), images (e.g., of violent scenes), or urges (e.g., to stab someone). Obsessions are intrusive, unwanted thoughts that cause distress or anxiety. The person attempts to ignore or suppress these obsessions with another thought or action (i.e., a compulsion). Compulsions (or rituals) are repetitive behaviors (e.g., washing) or mental acts (e.g., counting) that the person feels driven to perform in response to an obsession. Compulsions are meant to neutralize or reduce the person's discomfort or to prevent a dreaded event.

Everyone obsesses about some event occasionally. The diagnosis of OCD, however, generally requires that obsessive thoughts occur for more than 1 hour each day. In addition, obsessions related to OCD do not suddenly start and stop with a specific event. Although many people know about obsessions regarding contamination, there are many variations of OCD (Table 2), and patients often do not realize that certain thoughts they have are consistent with OCD. Most persons with OCD have multiple obsessions and compulsions. Although the themes underlying OCD (e.g., abnormal risk assessment such that the most improbable outcome is considered almost certain) appear to be similar across cultures,[5] cultural factors may influence the content of obsessions (e.g., a predominance of aggressive and religious obsessions has been reported in studies conducted in Brazil and Middle Eastern countries).[6] In addition, subtypes of OCD appear to vary according to age or developmental stage of the patient (e.g., rates of harm obsessions, such as fears of death or illness regarding oneself or loved ones, are higher among children and adolescents than among adults).[7]

Among adults with OCD, the sex ratio is approximately 1:1.[2] The age at the

KEY CLINICAL POINTS

OBSESSIVE–COMPULSIVE DISORDER

- Obsessive–compulsive disorder (OCD) is a common, disabling psychiatric disorder characterized by intrusive and unwanted thoughts, images, or urges that cause distress or anxiety and repetitive thoughts or actions that the person feels driven to perform.
- OCD is commonly misdiagnosed as anxiety or depression, and an accurate diagnosis is important for appropriate therapy.
- Only approximately one third of patients with OCD receive appropriate pharmacotherapy, and fewer than 10% receive evidence-based psychotherapy.
- First-line therapies for OCD include exposure and response prevention, which uses repeated and prolonged exposures to fear-eliciting stimuli, combined with strict abstinence from compulsive behaviors, and selective serotonin-reuptake inhibitors, which are often used at higher doses in OCD than in depression or anxiety.

onset of OCD appears to be bimodal, with onset either during childhood (mean age at onset, approximately 10 years) or during adolescence or young adulthood (mean age at onset, approximately 21 years).[8] Onset is earlier in boys than in girls,[9] and onset after 30 years of age is unusual.[10] In childhood-onset OCD, boys are more commonly affected than girls (male:female ratio, 2:1 to 3:1), whereas the sex ratio shifts among persons with onset during or after puberty (male:female ratio, 1:1.4).[11]

The cause of OCD remains poorly understood. Childhood-onset OCD is estimated to be 45 to 65% heritable, and OCD with an onset during adolescence or adulthood 27 to 47% heritable.[12] Although genomewide association studies have suggested candidate genes, findings have been inconsistent and many have not been replicated or withstood rigid statistical analysis.[13,14]

Several brain structures and functions have been implicated in OCD. Studies have consistently shown hyperactivity in the orbitofrontal cortex and caudate.[15,16] Other key implicated regions (suggesting abnormalities in functional or structural connections) include the anterior cingulate cortex, thalamus, amygdala, and parietal cortex.[17-19] Neuropsychological studies involving patients with OCD have shown deficits in cognitive abilities that are linked to the functioning of the frontal lobe and its related frontosubcortical structures, such as executive functioning, impulsivity in motor function, and cognitive inflexibility (i.e., not changing behavior on the basis of new information).[20,21]

If OCD is untreated, the course is usually chronic, often with waxing and waning symptoms. Without treatment, remission rates among adults are low (approximately 20%).[22] With appropriate treatment, patients report substantially higher rates of symptom response and remission.[23] Higher rates of symptom remission among treated patients, as compared with untreated patients, have been associated with a shorter duration of illness,[24] suggesting that early diagnosis and treatment may lead to improved outcomes. However, only approximately one third of patients with OCD receive appropriate pharmacotherapy, and fewer than 10% receive evidence-based psychotherapy.[25]

STRATEGIES AND EVIDENCE

DIAGNOSIS

The diagnostic criteria for OCD are reviewed in Table 1. OCD is often misdiagnosed as anxiety or depression, and these and other conditions may also be misdiagnosed as OCD (Table 3). Patients who meet the criteria for OCD should be assessed with regard to their conviction that their obsessive beliefs are accurate. Poor insight, to varying degrees, occurs in 14 to 31% of persons with OCD and has been associated with worse treatment outcomes.[26] In addition, up to 30% of persons with OCD have a tic disorder, the presence of which has been associated with a poor response to pharmacotherapy for OCD in children and adolescents.[27]

MANAGEMENT

Psychotherapy

Multiple types of psychotherapy have been examined in the treatment of OCD. Evidence from ran-

Table 1. Criteria for the Diagnosis of Obsessive–Compulsive Disorder (OCD).*

Obsessions
Obsessions are recurrent thoughts, urges, or images that are experienced, at some time, as intrusive and unwanted.
The person attempts to ignore or suppress such thoughts, urges, or images, or to neutralize them with some other thought or action (i.e., by performing a compulsion).
Compulsions
Compulsions are repetitive behaviors (e.g., hand washing, ordering, and checking) or mental acts (e.g., praying and counting) that the person feels driven to perform in response to an obsession.
The goal of the compulsive behavior is to prevent or reduce anxiety or distress or prevent some feared outcome.
Symptoms causing impairment
Obsessions or compulsions are time consuming (>1 hr/day).
There is clear evidence that the symptoms cause the person distress or interfere with or reduce the quality of social, academic, or occupational functioning.
Symptoms are not better accounted for by another mental disorder (e.g., depression or anxiety disorder) and are not solely attributable to the effects of a substance (e.g., a drug of abuse or medication).
Specifiers†
Insight specifier: Persons with OCD have varying levels of insight (i.e., ability to recognize that their beliefs are definitely or probably not true); poorer insight (when the person is mostly convinced that their beliefs and behaviors are not problematic, despite evidence to the contrary) has been associated with poor long-term outcome.
Tic-related specifier: When a person has a tic disorder or history of a tic disorder, this specifier reflects possible different patterns of coexisting conditions, course of illness, and familial transmission.

* The diagnosis of OCD requires that a person have obsessions, compulsions, or both. Adapted from the American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition.[4]
† Specifiers clarify features of the disorder but are not required for a diagnosis.

domized trials, however, strongly supports the use of exposure-and-response-prevention therapy or cognitive therapy for OCD.

Exposure-and-response-prevention therapy

Exposure and response prevention consists of repeated and prolonged exposures to fear-eliciting stimuli or situations, combined with instructions for strict abstinence from compulsive behaviors. Fear-eliciting stimuli or situations are presented in a hierarchical manner, beginning with moderately distressing ones and progressing to more distressing cues. The therapist then instructs the patient to abstain from the compulsive behavior that the patient believes will prevent the feared outcome or reduce the distress (e.g., washing hands after touching the toilet handle). The purpose of these exercises is to allow the patient to experience a reduction of the fear response, to recognize that these situations are not high risk, and to learn that anxiety will subside naturally if the patient does not make efforts to avoid it.

Patients are instructed to focus directly on aspects of the feared situation that increase anxiety and obsessive thoughts, and they may need to be reminded to do so during the exposure because many will engage in subtle avoidance or distraction. For exposures to be maximally effective, patients must persist with them until they learn that anxiety will reduce naturally. Patients are typically instructed to complete the exposure daily and to keep a record of their anxiety and discomfort ratings and the frequency and duration of exposure completion. Randomized trials assessing adherence to therapy have shown that complete response prevention during exposure therapy yields outcomes superior to those associated with partial or no response prevention.[28,29]

Analyses of more than two dozen randomized, controlled trials have shown that approximately 60 to 85% of patients report a considerable reduction in symptoms with the use of exposure and response prevention, and improvement is maintained for up to 5 years after the discontinuation of treatment in a majority of the patients who have a response to therapy.[30,31] Exposure-and-response-prevention therapy can be delivered in multiple formats, including by telephone[32] or by computer or Internet with minimal therapist support,[33,34] with similar efficacy. In addition, data

Table 2. Common Symptoms in OCD.

Obsession	Examples	Associated Compulsive Behaviors
Contamination	Fear of being contaminated or contaminating others; fear of contamination by germs, infections, or environmental factors; fear of being contaminated by bad or immoral people	Washing or cleaning rituals
Sexual	Recurrent thoughts about being a pedophile or sexually deviant; recurrent thoughts about acting sexually inappropriately toward others	Avoiding situations
Religious	Thoughts about being immoral and eternal damnation	Asking forgiveness, praying
Aggressive	Fear of harming others, recurrent violent images	Monitoring the news for reports of violent crimes, asking for reassurance about being a good person
Control-related	Fear of making inappropriate comments in public	Avoiding being around others
Pathologic doubt and completeness	Recurrent worries about doing things incorrectly or incompletely that thereby may negatively affect others or the patient	Checking excessively, performing actions in a particular order
Superstition-related	Fears of certain "bad" numbers or colors	Counting excessively
Symmetry and exactness	Recurrent thoughts of needing to do things in a balanced or exact fashion	Ordering and arranging

from a randomized trial indicated that self-guided exposure for OCD, with the use of standardized materials, has a level of effectiveness that is similar to therapist-supervised exposure.[35]

On the basis of data from randomized trials, exposure therapy should be delivered weekly or twice weekly, for approximately 20 to 30 total hours of therapy. After the short-term treatment, exposure therapy should be delivered as monthly "booster" sessions for 3 to 6 months to maintain gains.

Cognitive therapy

Unwanted, intrusive thoughts are a common experience in the general population.[36] Distressing and time-consuming obsessions arise when these otherwise normal, intrusive thoughts are appraised as highly meaningful and as posing a threat for which the patient is personally responsible. The person then becomes preoccupied with the unwanted thought and with trying to control it. Cognitive therapy for OCD focuses on teaching patients to identify and correct their dysfunctional belief about feared situations. Cognitive therapy assists patients in reducing anxiety and compulsions by identifying these automatic unrealistic thoughts and changing their interpretations. When undergoing cognitive therapy, the patient keeps a daily diary of obsessions and interpretations associated with the obsessions. Using Socratic questioning, the therapist challenges the unrealistic belief and helps the patient identify the cognitive distortion.

The therapist implements behavioral experiments (e.g., a patient is asked to touch a range of dirty objects without washing the hands and to keep a log of how often illness follows after doing so) to disprove errors in thinking about cause and effect. Behavioral experiments used in cognitive therapy differ from the exercises used in exposure-and-response-prevention therapy in that, while engaging in the feared behavior, patients are not focusing on anxiety reduction (as with exposure and response prevention) but instead are challenging the belief that they could ultimately become ill by not washing. Patients thereby learn to identify and reevaluate beliefs about the potential consequences of engaging in or refraining from compulsive behaviors.

In randomized, controlled trials, cognitive therapy has shown improvement in 60 to 80% of patients, with effect sizes almost as large as those with exposure and response prevention. As with exposure and response prevention, however, dropping out of cognitive therapy prematurely is common (20 to 30% of patients).[28] Although cognitive therapy may be a viable alternative for patients who are reluctant to participate in expo-

Table 3. Conditions That May Be Misdiagnosed as OCD.

Misdiagnosis	Reasons for and Prevention of Misdiagnosis
Depression	Depressed people often ruminate, which may look like obsession; however, depressive ruminations are of a depressed theme (e.g., guilt due to inadequacies or negative self-assessment).
Anxiety disorder	Anxiety is characterized by worry, which often looks like obsessive thinking; anxiety usually focuses on real-life problems (e.g., finances, health, and loved ones) without the irrational quality of OCD.
Psychotic disorder	Psychosis is often characterized by delusional beliefs, whereas OCD may appear to have no contact with reality (e.g., fearing human immunodeficiency virus contamination from doorknobs); the difference is that persons with OCD can usually recognize that their thoughts are very irrational, but they cannot control them.
ADHD*	Young people with ADHD may procrastinate and have problems with attention and focus; persons with OCD may have a need to get things done "just right" or in a "complete" fashion and therefore may be unable to complete tasks and may appear to have ADHD; it is important to determine whether mental rituals or obsessive thoughts interfere with focus and attention.

* ADHD denotes attention deficit–hyperactivity disorder.

sure and response prevention, exposure therapy is supported by a larger body of empirical data and is therefore recommended as the first-line psychotherapy treatment for OCD.[37,38]

Pharmacotherapy

In addition to exposure and response prevention, pharmacotherapy with the tricyclic antidepressant clomipramine or a selective serotonin-reuptake inhibitor (SSRI; paroxetine, fluvoxamine, fluoxetine, citalopram, escitalopram, and sertraline) has shown efficacy in OCD.[39] (Table 4). A meta-analysis of 17 randomized, double-blind, placebo-controlled trials (generally short-term; i.e., 8 to 12 weeks) that studied various SSRIs showed that all were superior to placebo and that patients were approximately twice as likely to have a response to an SSRI than to placebo.[40] A meta-analysis of 7 controlled trials of clomipramine also showed that this medication was superior to placebo.[41] Although data are limited, comparisons between different SSRIs or between an SSRI and clomipramine have shown no significant differences in efficacy. The SSRIs are recommended as first-line pharmacologic treatment for OCD (over clomipramine) owing to their better adverse-event profile.[42] When used for OCD, as compared with other disorders such as depression or generalized anxiety, SSRIs tend to take longer to be effective (between 4 and 12 weeks), and higher doses are often required.[42]

Approximately 40 to 65% of patients with OCD have a response to an SSRI or clomipramine, with a mean improvement in the severity of symptoms of approximately 20 to 40%.[23,43] The probability of full remission of OCD with the use of pharmacotherapy alone is low (11% of patients in one study).[43] An early age at OCD onset, more severe OCD, coexisting tics, and hoarding symptoms have all been associated with a poor response to clomipramine and SSRIs.[42]

For patients who have a response to pharmacotherapy, treatment is generally continued for 1 to 2 years, followed by gradual tapering of the medication. Although limited data support the 2-year recommended period of medication, 25 to 40% of patients have a relapse if they discontinue medication after 2 years, whereas treatment with medication for shorter periods of time has resulted in relapse rates of up to 80% after the discontinuation of medication.[44] When relapse occurs, medications are generally restarted and continued indefinitely.

Comparison of Treatments and Combination Therapies

A meta-analysis of nine short-term trials (generally 8 to 12 weeks) comparing exposure and response prevention with pharmacotherapy showed a greater benefit overall with exposure therapy. In stratified analyses, the differences were significant in trials involving children but not in those involving adults.[45] The use of exposure therapy in combination with medication has resulted in outcomes superior to those with medication alone but not to outcomes with exposure therapy alone.[45]

Results from a limited number of small and short-term (4 to 12 weeks), double-blind, placebo-controlled trials support a benefit to adding other medications (some second-generation antipsychotic agents, stimulants, or glutamate modulators) when there is a partial initial response to SSRIs.[46,47] However, none of these augmentation medications have been approved by the Food and Drug Administration (FDA) for this purpose, and more data are needed.

Table 4. Medications Approved by the Food and Drug Administration (FDA) for the Treatment of OCD.*

Drug	Starting Dose†	Usual Effective Dose	Adverse Events	
			Common	Serious
	mg/day			
SSRI			Anxiety, diarrhea, dizziness, dry mouth, drowsiness, tremor, bruxism, sexual dysfunction, increased sweating, insomnia	Children, teenagers and young adults <25 yr of age may have an increase in suicidal thoughts or behaviors when taking the antidepressant, especially in the first few weeks after starting therapy or when the dose is changed
Fluoxetine	20	40–80		
Sertraline	50	100–200		
Fluvoxamine	50	200–300		
Paroxetine	20	40–60		
Clomipramine	50‡	150–250	Dizziness, dry mouth, weight gain, hypotension, constipation, sexual dysfunction, tremor, difficulty urinating, yawning	Cardiac toxicity and arrhythmias; children, teenagers, and young adults <25 yr of age may have an increase in suicidal thoughts or behavior when taking the antidepressant, especially in the first few weeks after starting therapy or when the dose is changed

* The selective serotonin-reuptake inhibitors (SSRIs) listed here have been approved by the FDA for use in adults with OCD. Fluoxetine, fluvoxamine, sertraline, and clomipramine have been approved by the FDA for use in children with OCD. All SSRIs appear to be similarly effective in treating OCD. Two drugs (citalopram and escitalopram) are not FDA-approved for OCD but are used for OCD off-label.

† The initial dose may be increased after 1 week if the patient reports no bothersome side effects. The need for subsequent dose adjustments is commonly assessed after 4 weeks of taking a particular dose.

‡ The dose can be increased by 50 mg per day every week. Blood levels should be assessed when the dose is 150 mg per day or higher or at a lower dose if the drug is combined with a medication that may raise blood levels of clomipramine (e.g., an SSRI).

Choice of Initial Therapy

Guidelines from the American Psychiatric Association recommend exposure and response prevention as monotherapy for persons who are motivated to cooperate with the demands of the therapy, who do not have severe depressive symptoms, or who prefer not to take medication.[42] In the case of patients who find exposure therapy too frightening, an SSRI should be started first, and then exposure therapy initiated after the medication has reduced the OCD symptoms, if the patient is then agreeable to this therapy.

Use of an SSRI as monotherapy is recommended for persons who are not able to engage in exposure therapy, who report a previous response to an SSRI, or who prefer medication over psychotherapy. A combination of an SSRI and exposure therapy is recommended for persons who have other coexisting conditions that could benefit from medication treatment (e.g., major depression) or who have an unsatisfactory response to either monotherapeutic approach. Combined treatment is also recommended for persons who prefer to take medication for the shortest possible time, because data from uncontrolled follow-up studies suggest that exposure therapy may help to prevent or delay relapse when the SSRI is discontinued.[48]

Deep-Brain Stimulation

Deep-brain stimulation or ablative neurosurgery (e.g., capsulotomy and cingulotomy) may be considered in patients with severe, incapacitating OCD that has not had a response to an adequate number of sessions of exposure therapy, two or more adequate trials of SSRIs, a trial of clomipramine, and at least three trials of an augmentation therapy. Only a very small minority of patients with OCD qualify for such treatment. Although several centers worldwide offer ablative surgery as a last-resort option for severe OCD, only deep-brain stimulation (specifically, of the ventral capsule or ventral striatum) has been approved by the FDA for the treatment of OCD. In double-blind trials comparing stimulation with sham stimulation, response rates have been approximately 50 to 60% with stimulation, as compared with approximately 10% in the off or sham condition.[49] The data for deep-brain stimulation, however, derive from a small number of studies involving few patients. The literature on deep-brain stimulation for OCD gener-

ally reports a low rate of serious adverse events related to surgery or device malfunction. Intracerebral brain hemorrhage, postoperative confusion, which is usually transient but may persist, and device-related infection, however, are all risks associated with the surgery.[49]

AREAS OF UNCERTAINTY

Trials of medication for OCD have been largely short-term and have involved predominantly young or middle-aged adults. Data are lacking to inform long-term benefit and risks and to inform use in children and elderly persons with OCD. More research is also needed to identify the predictors of poor outcomes.

Although exposure therapy has shown a benefit in the treatment of OCD, little is known about how well the therapy is performed in the community. The genetic factors predisposing persons to OCD remain incompletely understood. A better understanding is needed with regard to childhood risk factors for OCD and how these variables interact with genetic factors. Such information may allow for the identification of children at risk for OCD and the development of early-intervention strategies. Clinical trials have largely focused on treatment of the core symptoms of OCD, but effective treatments are also needed for associated social dysfunction.

GUIDELINES

The American Psychiatric Association (United States) and the National Institute for Health and Care Excellence (United Kingdom) have published guidelines regarding the diagnosis and management of OCD.[42,50] The recommendations in this article are consistent with these guidelines.

CONCLUSIONS AND RECOMMENDATIONS

The man described in the vignette has a classic case of contamination OCD. He should be questioned regarding other possible obsessions and compulsive behaviors. Assessments regarding his level of insight and the presence of a tic disorder are relevant to assessing prognosis and the choice of therapy.

Once the diagnosis is made, the clinician should educate the patient about the nature of the illness, including the low frequency of spontaneous improvement but the high likelihood of responsiveness to therapy. The patient should be informed that exposure-and-response-prevention therapy and pharmacotherapy with an SSRI are considered to be first-line treatments that improve OCD symptoms in a majority of patients. To help the patient choose his treatment, he should be educated regarding the process of exposure therapy and the probable length of treatment (weekly sessions for approximately 16 weeks, followed by some monthly sessions). Similarly, he should be educated regarding medication side effects and told that medication ought to be continued for at least 1 year.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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