CLINICAL PRACTICE

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 33-year-old woman presents with a seven-year history of hand washing for two to six hours a day, as well as urges to check doors and stoves extensively before leaving her home. Her life is restricted, and her family members are upset about her behavior. How should she be evaluated and treated?

THE CLINICAL PROBLEM

This vignette describes a typical patient with an anxiety disorder called obsessive–compulsive disorder (OCD) (Table 1), which affects 2 to 3 percent of the world's population.[1] The patient has a general sense that something terrible may occur if a particular ritual is not performed, and the failure to perform a ritual may lead immediately to severe anxiety or a very uncomfortable, nagging feeling of incompleteness. In addition to checking and washing rituals, patients with OCD often present with persistent intrusive thoughts, extreme slowness or thoroughness, or doubts that lead to reassurance-seeking rituals. Patients with OCD commonly seek care from physicians other than psychiatrists. For example, in one study, 20 percent of patients who visited a dermatology clinic had OCD, which had been previously diagnosed in only 3 percent.[2]

The mean age at the onset of OCD ranges from 22 to 36 years, with the disorder developing in only 15 percent of patients older than 35 years.[3] Men tend to have an earlier age at onset than women, but women eventually catch up, and roughly 50 percent of adults with OCD are women.[3] OCD is typically a chronic disorder with a waxing and waning course.[3] With effective treatment, the severity of symptoms can be reduced, but typically some symptoms remain.[3] On average, people with OCD see three to four doctors and spend more than nine years seeking treatment before they receive a correct diagnosis. It takes an average of 17 years from the onset of OCD to obtain appropriate treatment.

OCD tends to be underdiagnosed and undertreated. Patients may be secretive or lack insight about their illness. Many health care providers are not familiar with the symptoms or are not trained in providing treatment. Some people may not have access to treatment, and sometimes insurance plans do not cover behavioral therapy, although the situation is improving. This lack of access or coverage is unfortunate, since earlier diagnosis and proper treatment can help patients to avoid the suffering associated with OCD and lessen the risks of related problems, such as depression, marital difficulties, and problems related to employment.[4]

OCD may have a genetic basis.[5] Concordance for OCD is greater among pairs of monozygotic twins (80 to 87 percent) than among pairs of dizygotic twins (47 to 50 percent).[6] The prevalence of OCD is increased among the first-degree relatives of patients with OCD, as compared with the relatives of control subjects, and the age at onset in the proband is inversely related to the risk of OCD among the relatives.[5,7,8] There is evidence of a dominant or codominant mode of transmission of OCD.[9-12]

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N Engl J Med 2004;350:259-65.

Table 1. DSM-IV Diagnostic Criteria for OCD.*

Either obsessions or compulsions
Obsessions are defined by the following:
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
Thoughts, impulses, or images that are not simply excessive worries about real-life problems
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
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
Compulsions are defined by the following:
Repetitive activities (e.g., hand washing, 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 rules that must be applied rigidly
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
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
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
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
Disturbance not due to the direct physiological effects of a substance or a general medical condition
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

* DSM-IV denotes *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, and OCD obsessive–compulsive disorder.

In rare cases, a brain insult such as encephalitis, a streptococcal infection (in children), striatal lesions (congenital or acquired), or head injury directly precedes the development of OCD.[13] There is some evidence of a neurologic basis for OCD. For example, patients with OCD have significantly more gray matter and less white matter than normal controls, suggesting a possible developmental abnormality.[13] Neuroimaging studies have documented consistent differences in regional brain activity between patients with OCD and control subjects, and the abnormal activity in patients with OCD shifts toward normal after either successful treatment with serotonin-reuptake inhibitors or effective behavioral therapy.[13]

STRATEGIES AND EVIDENCE

DIAGNOSIS

The diagnosis of OCD is based on the clinical picture. Unlike patients with psychotic illnesses, patients with OCD usually exhibit insight and realize that their behavior is extreme or illogical. Often embarrassed by the symptoms, patients may go to extreme lengths to hide them. In severe cases, insight can become tenuous, and patients may truly believe that their obsessional concerns are justified; such cases are designated as "OCD with poor insight" according to the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV).[1]

Since patients are often reluctant to volunteer the information that they have symptoms of OCD, three routine screening questions can greatly increase the likelihood of diagnosis: "Do you have repetitive thoughts that make you anxious and that you cannot get rid of regardless of how hard you try?" "Do you keep things extremely clean or wash your hands frequently?" And "Do you check things to excess?" An affirmative answer to any of these questions strongly suggests a diagnosis of OCD, indicating the need for further investigation to determine whether the diagnostic criteria are met.

TREATMENT

Approaches to treatment that help patients with OCD include behavioral therapy (involving exposure to feared situations and the prevention of compulsive behavior), cognitive therapy (in which maladaptive thoughts — such as an exaggerated sense of risk, an enhanced sense of personal responsibility for events, or excessive doubt — are challenged), and specific medications.[13] For most patients, combining cognitive–behavioral therapy with the use of medication is the most effective approach.[14,15] Used alone, serotonin-reuptake inhibitors (Table 2) have a generally moderate, but occasionally dramatic, effect.[15-17] When first-line medications fail, the augmentation of serotonin-reuptake–inhibitor therapy with an additional drug[13,18] and trials of alternative medications[19] are indicated. Neurosurgery should be reserved as the treatment of last resort.[13]

Table 2. Recommended Treatments for OCD.*

Treatment	Initial Daily Dose	Target Daily Dose	Common Side Effects
	mg		
Selective serotonin-reuptake inhibitors†			Anxiety, decreased libido, sexual dysfunction, diarrhea, sedation, headache, insomnia, dizziness, nausea
Fluoxetine (Prozac)	20	80	
Fluvoxamine (Luvox)	50	300	
Sertraline (Zoloft)	50	200	
Paroxetine (Paxil)	20	60	
Citalopram (Celexa)	20	60	
Escitalopram (Lexapro)	10	Unknown	
Clomipramine (Anafranil, tricyclic antidepressant)	25–50	250	Dizziness, sedation, dry mouth, weight gain, sexual dysfunction
Venlafaxine (Effexor)	75	375	Accommodation disorder, blurred vision, headache, sexual dysfunction, paresthesias, nausea, weight loss, withdrawal syndrome (dizziness, nausea, weakness)

* OCD denotes obsessive–compulsive disorder.
† All selective serotonin-reuptake inhibitors except escitalopram have been formally studied in patients with OCD. Side-effect profiles may vary among these agents; an alternative agent in this class should be tried if one agent proves to be ineffective or is associated with substantial side effects.

Cognitive–Behavioral Therapy

The gold standard for behavioral therapy for OCD involves exposure and the prevention of rituals; in such therapy, the patient repeatedly exposes himself or herself to provocative stimuli (e.g., touching a "contaminated" object) and refrains from compulsions (e.g., hand washing).[14,20] Most therapists now combine cognitive therapy, in which faulty beliefs are challenged, with the standard therapy known as exposure and response prevention to help reduce the feeling of impending catastrophe and the exaggerated sense of responsibility often seen in patients with OCD. Behavioral therapy begins with the patient's making a complete list of obsessions, compulsions, and things that he or she avoids. This list is then arranged in a hierarchy from least anxiety-provoking to most anxiety-provoking. The patient then starts with a moderately anxiety-provoking stimulus and repeatedly exposes himself or herself to it until the situation produces minimal anxiety (i.e., habituation). The next (more anxiety-provoking) stimulus in the hierarchy is then tackled, and then the next, until the most feared situation generates little or no anxiety.

Relaxation techniques alone are not helpful in the treatment of OCD and are often used as a control form of therapy in studies. Patients who have only obsessive thoughts and no compulsions are taught not to resist the thoughts but just to let them pass naturally. Doing so requires considerable practice. For patients who report repulsive, sacrilegious, or intrusive sexual thoughts that are repugnant to them, audio-loop tapes are often made of the patient voicing the thoughts; then, the patient listens to the tape for extended periods until the thoughts lose their power to be upsetting.

More than 30 open and controlled trials have consistently shown that behaviorial therapy is very effective in controlling obsessions,[14,15,21-24] with some studies demonstrating that the approach of exposure and response prevention is more effective than medication.[15,24-26] In numerous studies involving 10 to 20 treatment sessions, symptoms of OCD were at least "improved" in 85 percent of patients immediately after treatment, and in about 55 percent, target symptoms were "much improved" or "very much improved" — that is, improved by more than 50 percent.[24] At follow-up, the rates of improvement remained high, averaging about 75 percent for "much improved" and 50 percent for "very much improved," although some patients required additional therapy.[24,27]

A combined analysis of multiple randomized studies comparing treatments (medications, psychodynamic psychotherapy, behavioral therapy consisting of exposure and response prevention, or cog-

nitive therapy) with one another and comparing intervention groups with a control group found both cognitive therapy and exposure and response prevention to be highly effective in reducing the symptoms of OCD.[28] A greater number of hours spent undergoing therapist-guided exposure was associated with greater efficacy of treatment.[24] Once-weekly sessions of cognitive–behavioral therapy may suffice for patients who comply with a regimen of homework (consisting of therapist-prescribed, self-directed exposure and ritual prevention) and whose symptoms of OCD are mild.[29] Continuous exposure to anxiety-provoking stimuli of approximately 90 minutes' duration is superior to short, interrupted exposures for the reduction of anxiety.[29] If patients do not feel some relief, sessions lasting longer than 90 minutes are required. Long periods of exposure permit the anxiety to dissipate, so that feared situations provoke less reaction, thus altering a person's attitudes toward the situation and the expected outcome.[14] The number of exposure sessions varies, but often between 13 and 20 sessions are required for meaningful relief of symptoms.[4,29]

Since the availability and cost of individual sessions of cognitive–behavioral therapy can pose practical problems, group cognitive–behavioral therapy has been developed, and early results support the efficacy of this approach.[14,29] About 25 percent of patients decline behavioral treatment. Estimates of the percentage of patients who complete exposure-and-response-prevention therapy and are helped by it range from 67 to 90 percent, with dropout rates ranging from 20 to 25 percent.[25] Patients with severe symptoms or those who do not comply with assigned homework may benefit from a more intensive in-office regimen.[29]

INITIAL DRUG TREATMENT

Multiple randomized, double-blind, placebo-controlled studies support the use of serotonin-reuptake inhibitors in adults and children.[13,15,30] Although tricyclic antidepressants have also been used for OCD, the efficacy of serotonin-reuptake inhibitors has appeared to be greater in placebo-controlled as well as non–placebo-controlled studies.[30,31]

Approximately 40 to 60 percent of patients have a response to a serotonin-reuptake inhibitor, with a mean improvement in symptoms of 20 to 40 percent.[13,31] All serotonin-reuptake inhibitors that have been studied have similar efficacy according to data from groups of patients, but a single patient may have a response to only one or two of these agents; thus, serial trials are required to determine which agent helps the most while causing the fewest side effects.[13] An adequate trial of medication requires at least 10 to 12 weeks, and the optimal doses of serotonin-reuptake inhibitors for OCD may exceed those that are typically used for major depression (Table 2).[13]

In contrast to cognitive–behavioral therapy, after which less than 25 percent of patients have a relapse, the discontinuation of serotonin-reuptake inhibitors results in a high rate of relapse.[32-38] In one study, almost 90 percent of patients who received drug therapy without cognitive–behavioral therapy had a relapse after the double-blind discontinuation of medical therapy.[32] Among patients who had a response to medication, the mean time to relapse during the use of a substitute placebo was 63 days.[39]

Ongoing cognitive–behavioral therapy may decrease the risk of relapse.[14] In one study involving the discontinuation of therapy with open-label medication, only 23 percent of the patients had a relapse within one year.[33] The continuation of medical therapy at a lower maintenance dose has also been proposed, but the optimal doses remain uncertain.

Augmentation of Serotonin-Reuptake–Inhibitor Therapy and Trials of Alternative Drugs

Numerous agents have been tried in combination with serotonin-reuptake inhibitors,[13,18,40] but only a few controlled trials of such strategies have been conducted.[13,41] The most impressive data on augmentation document the benefits of adding low doses of dopamine antagonists to therapy with a serotonin-reuptake inhibitor.[41,42]

In a single placebo-controlled study, clonazepam had significant antiobsessional efficacy when used in combination with clomipramine or fluoxetine.[43] Despite case reports suggesting that lithium might be an effective medication for augmenting the effects of serotonin-reuptake inhibitors, two controlled trials had negative results.[44,45] Similarly, encouraging results from uncontrolled trials of buspirone augmentation were followed by only marginal success in controlled trials.[46] Numerous other agents have been tried in combination with serotonin-reuptake inhibitors, including clonidine,[43] tryptophan,[13] pindolol,[47] trazodone,[18] and tramadol,[48,49] as well as other antidepressants.[13] Although a few patients apparently have a response, no conclusions can be drawn, given the small number of subjects studied, the lack of sufficient controls, and

the mixed results. The results of controlled studies provide some support for trials of monotherapy with clonazepam,[43] buspirone,[50] and monoamine oxidase inhibitors[51] in patients who have no response to serotonin-reuptake inhibitors.

Neurosurgery

Despite the lack of data from controlled trials, several types of operations for severe, treatment-refractory OCD are performed around the world: anterior cingulotomy, anterior capsulotomy, subcaudate tractotomy, and limbic leucotomy. These operations all have the common objective of severing connections between dorsolateral and the orbitomedial areas of the frontal lobes and limbic and thalamic structures. In observational, prospective trials of cingulotomy and capsulotomy, approximately 45 percent of patients had a reduction of at least 35 percent in the severity of symptoms.[52] Adverse effects included seizure, weight gain, and transient headache. Negative effects on cognition or personality were rare.[52]

Deep brain stimulation, which involves surgically implanted electrodes that can be turned on and off to stimulate or inhibit activity in surrounding brain tissue, has been used for the treatment of Parkinson's disease and intractable pain; preliminary data from uncontrolled trials suggest that it also has efficacy in OCD.[53] In addition, transcranial magnetic stimulation, whereby pulses of magnetic energy are intermittently administered to surface regions of the brain through the skull, appeared to be effective in one preliminary study.[54]

AREAS OF UNCERTAINTY

A small number of patients fail to become habituated to anxiety-provoking stimuli, despite repeated exposure. There are limited data with which to predict responsiveness to cognitive–behavioral therapy or medication, but the expression of negative emotions — for example, by family members who are overtly highly critical of the patient — can have a negative effect on the outcome of treatment.[13]

Further research is warranted regarding the role of autoimmunity induced by streptococcal infection in the pathogenesis of OCD. Small, uncontrolled, preliminary studies in selected patients have shown encouraging results with the use of plasmapheresis to clear autoantibodies, as well as with the use of prophylactic antibiotic treatment for the prevention of subsequent infections and further damage,[13] but more data are needed for the accurate evaluation of the efficacy of such therapies.

Although published outcome data are not available, three residential facilities for the treatment of OCD in patients with very severe symptoms that have proved to be unresponsive to outpatient treatment are now operating in the United States (further information is available at http://www.ocfoundation.org/1003/index.html).

There have been no studies directly comparing the relative efficacy and safety of the different neurosurgical procedures. With the advent of innovative surgical devices that permit neurosurgery without requiring craniotomy (e.g., the gamma knife), it is now feasible to conduct ethical double-blind, sham-surgery–controlled trials.

GUIDELINES

Expert consensus guidelines issued in 1997[4] (http://www.psychguides.com/gl-treatment_of_obsessive-compulsive_disorder.html) ranked the effectiveness of all treatment options on the basis of published data and expert opinion. According to the guidelines, cognitive–behavioral therapy should be the first-line treatment. For severely ill patients (those who are unable to function in a job or socially because of the symptoms of OCD), it is recommended that medication be introduced first, before the addition of cognitive–behavioral therapy. The guidelines recommend that cognitive–behavioral therapy begin with weekly sessions, with homework assignments or therapist-assisted, out-of-office therapy. For most patients, 13 to 20 sessions of cognitive–behavioral therapy are adequate, although some patients require more, and some fewer. The guidelines indicate that serotonin-reuptake inhibitors are the most effective medications for OCD and recommend beginning with selective serotonin-reuptake inhibitors, with a trial of clomipramine if two or three selective serotonin-reuptake inhibitors have failed.

CONCLUSIONS AND RECOMMENDATIONS

If OCD is not adequately treated, most patients have clinically significant disability, with symptoms that wax and wane over time. Even with effective treatment, OCD rarely remits, but symptoms do diminish so that patients can work, raise a family, and have an active social life. For a patient such as the

one in the vignette, I would start with a serotonin-reuptake inhibitor and, if it is available, behavioral therapy at the same time. (The Obsessive Compulsive Foundation [http://www.ocfoundation.org] is a national nonprofit organization that provides information for patients and family members. Information on cognitive–behavioral therapists is available through this foundation, as well as through the Association for Advancement of Behavior Therapy, whose website [http://www.aabt.org] lists licensed behavioral therapists according to state.) If the patient would prefer to try behavioral therapy without medication, that would also be a reasonable approach. I would begin with a low dose of antiobsessional medication (Table 2) and increase the dose to the upper limit within a few weeks, as tolerated. For the most part, medication has only moderate effectiveness and should be combined with cognitive–behavioral therapy in order to maximize improvement. Family members should be educated regarding productive ways to help the patient; these include keeping the level of expressed negative emotions to a minimum and refraining from giving reassurance to the patient, which tends to perpetuate the disorder.[55]

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