Anxiety Disorders

Focus on obsessive-compulsive disorder

LORNE WARNEKE, MD

SUMMARY

Obsessive-compulsive disorder was once thought to be rare. Recent epidemiologic surveys reveal the lifetime prevalence rate to be as high as 3%. We now have greater understanding of the neurophysiologic and neurochemical basis of this very crippling disorder. Although obsessive-compulsive disorder often starts in adolescence or early adulthood and can last a lifetime, effective treatment enables most patients to lead relatively normal lives.

RÉSUMÉ

On croyait autrefois que le trouble obsessionnel-compulsif était une névrose rare. Des enquêtes épidémiologiques récentes révèlent que le taux de prévalence à vie pourrait atteindre 3%. Nous possédons maintenant une meilleure compréhension de la base neurophysiologique et neurochimique de cette maladie très invalidante. Même si le trouble obsessionnel-compulsif débute souvent au cours de l'adolescence ou au début de l'âge adulte et persiste toute la vie durant, il existe des traitements efficaces qui permettront à la plupart des patients à mener une vie relativement normale.

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THE *DIAGNOSTIC AND STATISTICAL Manual*[1] OF the American Psychiatric Association (DSM 3-R) classifies obsessive-compulsive disorder (OCD) with other anxiety disorders, such as generalized anxiety, panic disorder, simple phobia, and social phobia. Although anxiety is a disabling feature of OCD, the course of the illness, symptom complex, etiologic factors, and response to treatment all suggest that it is unique and should be classified separately.

Obsessive-compulsive disorder is a disabling illness characterized by intrusive, repetitive thoughts (obsessions) and stereotypical or repetitive volitional behaviours (compulsions) that can markedly disrupt day-to-day functioning.

The German neurologist Carl Westphal formally described the disorder in the late 1800s, although reference had been made to the illness for centuries. The famous English essayist Samuel Johnson suffered from the illness; Howard Hughes, industrialist and billionaire, paradoxically died in squalor because of obsessional fears of contamination and elaborate rituals to avoid it.

Dr Warneke *is Clinical Professor of Psychiatry at the University of Alberta and is Clinical Head of the Department of Psychiatry at Grey Nuns Hospital (Caritas Health Group) in Edmonton.*

Epidemiologic data

Once thought to be rare, OCD's prevalence rates were estimated to be as low as 0.05%. However, recent extensive epidemiologic surveys[2,3] have revealed the startling fact that the illness has a lifetime prevalence rate as high as 2% to 3% and a 6-month prevalence rate of 1.6%. This means about one in 50 persons in Canada might be suffering from OCD, and the total number might be as high as 600 000.

Studies of child and adolescent populations confirm that OCD is common in that age group and has the same high prevalence rate.[4] It is the fourth most common psychiatric disorder after substance abuse, phobias, and affective disorders. It has a higher prevalence rate than panic disorder or schizophrenia, and more people are affected by OCD than epilepsy or multiple sclerosis (*Table 1*[2,3]).

Earlier prevalence rates were inaccurate for several reasons. Many studies were retrospective case reviews based on hospital records. Patients with OCD, although dysfunctional, are seldom hospitalized and are often afraid to describe their symptoms for fear of being labeled "crazy." Physicians failed to recognize the illness because it was deemed so rare. Many patients, in spite of being very ill, could hide their symptoms and maintain a facade of normalcy.

Obsessive-compulsive disorder often begins at an early age with a third or more cases starting at puberty. It can also begin in childhood; cases in children as young as 3 or 4 years have been reported.[5] Male patients outnumber female patients in these very early onset cases and also seem to be more subject to motor tics. Overall, the illness affects both sexes about equally, with a slight preponderance of women. The disorder rarely begins after age 40.

Karno et al,[6] reporting from the large United States' epidemiologic catchment study, state, "Although not conclusive, the evidence is strong that OCD is a common mental disorder that, like other stigmatized and hidden disorders in the past, may be ready for discovery and demands for treatment on a large scale."[6] Jenike,[7] in an editorial in a recent issue of the *New England Journal of Medicine*, referred to OCD as "a hidden epidemic."

Etiology

As Rapoport,[8] author of the popular book *The Boy who Couldn't Stop Washing*, recently commented, OCD has moved in the last 5 years from an illness with the strongest psychodynamic explanation to an illness with the greatest evidence for a biologic origin.

Many lines of evidence suggest that OCD has a biologic basis. For years OCD was observed to be more common among patients who suffered from birth trauma, epilepsy, or other organic brain syndromes. The great encephalitis epidemic of von Economo's disease during World War I produced many cases of OCD and OCDlike syndromes as well as parkinsonism. Research in the last few years has focused on the role of the prefrontal cortex and the striatal system, in particular the caudate nuclei.

Anecdotal case reports have suggested that OCD can be a rapid sequela of necrotic lesions in the caudate that have developed following bee stings or carbon monoxide poisoning.[9] Observers have noted other associations that link OCD to the basal ganglia. Obsessive-compulsive disorder symptoms are prevalent in patients with Sydenham's chorea[10] but not in patients who have just had rheumatic fever. An earlier study[11] reported that antibodies to the cytoplasm of the subthalamic and caudate nuclei were found in a high percentage of patients with chorea as compared with patients who had only carditis and with normal control subjects. A strong association also exists between Tourette's syndrome and OCD. Up to two thirds of Tourette's sufferers have OCD symptoms and about a third of OCD patients have choreiform movements or tics.[12,13] Researchers have suggested that Tourette's syndrome and OCD might result from the same genetic factor, which has variable penetrance.[14]

Table 1. **Lifetime prevalence rates**

DISORDER	PREVALENCE (%)
Any psychiatric disorder	28.8-38.0
Substance abuse	15.0-20.6
Anxiety (phobias)	10.4-25.1
Affective disorder	6.1-10.2
Obsessive- compulsive disorder	1.9-3.0
Schizophrenia or schizophreniform	0.6-2.0

Adapted from Rasmussen and Eisen[2] and Bland et al.[3]

Other disorders that involve the caudate nuclei, such as Meige's disease and Huntington's disease, also have a high incidence of OCD symptoms. Brain imaging studies have demonstrated abnormalities of the caudate region. Computed tomographic scanning has demonstrated that OCD patients have a smaller caudate volume than normal control subjects.[15]

Positron emission tomography has demonstrated significantly elevated metabolic rates in the caudate nuclei and in frontal areas,[16] whereas single photon emission tomography has shown decreased perfusion of blood in the same regions.[17] These abnormalities seem to return to normal with treatment.[18,19]

This evidence has led to a biologic theory for OCD.[20,21] The striatal system is seen as a repository for a number of fixed action patterns of behaviour (similar to the hard wiring programs that come with a computer). These patterns are phylogenetically important for survival and involve grooming, courtship, and domestic behaviours. The striatum is thought to act as a filtering mechanism, receiving

Table 2. **Screening questions for OCD**

- Do you have thoughts that are repetitive and distressing?
- Are you overly concerned with cleanliness or fearful of contamination?
- Do you fear doing something impulsively that might cause embarrassment or harm?
- Do you have to wash your hands repeatedly?
- Do you have a need to check locks, switches, or calculations repeatedly?
- Do you have a need to do things in a ritualized way, or need to have things exact or symmetrical?

Adapted from Ciba-Geigy.[26]

CASE 1

Ms C.S. was 16 years old when she first came for help after a suicide attempt. Her OCD began a couple of years earlier when she developed the obsessive thought that she might become pregnant by touching a man or touching where a man had been. The thought was repetitive, created considerable anxiety, and led to elaborate compulsions to avoid contact with men.

She developed complicated cleaning rituals that compelled her father and brother to change their clothes at the door and to shower before putting on "clean clothes." If they did not comply, she would become hysterical. Her own cleaning rituals took several hours every night, including 2 hours in the shower. Attempts by the family to change her actions were unsuccessful.

She paradoxically then developed a fear of contamination with soap, washing her hands 30 to 40 times a day and often using corrosives like bleach, and developed severe dermatitis. Demoralization and continuous anxiety led to the suicide attempt.

Treatment with medications and behavioural therapy were successful and she was able to complete a university program with honours, was chosen winner of a Miss Teen competition, and is now married and in charge of a bank department.

sensory input from the environment that, in turn, can activate specific responses. In OCD, the function of the striatal system is altered so that triggered behaviours are not extinguished once executed, as would happen normally, leading to repetitive thinking and behaviour.

A much greater understanding of the neurochemistry of OCD has evolved also. The response of the illness to serotonin reuptake blocking drugs has led to the "serotonin hypothesis"[22] for OCD. This hypothesis is reinforced by the fact that 5-hydroxytryptamine receptors are found in high concentrations in the caudate nuclei and that drugs acting as serotonin antagonists can worsen the symptoms of the disorder.

An animal model for OCD has been described. The acral lick syndrome, which occurs in some species of large dogs, is characterized by compulsive licking of paws until tissue is eroded to the bone, which can become infected. Drugs useful for OCD in humans also have a beneficial effect on the acral lick syndrome.[23,24] Some children with OCD who compulsively wash their hands also lick their hands in a ritualistic manner.

Diagnostic criteria

The essential feature of OCD is the presence of obsessions or compulsions or, in most cases, both. The DSM 3-R[1] suggests the following diagnostic criteria.

Obsessions are marked by the following characteristics.

- Recurrent and persistent ideas, thoughts, impulses, or images that are experienced, at least initially, as intrusive and senseless.
- The person attempts to ignore or suppress such thoughts or impulses, or to neutralize them with some other thought or action.
- The person recognizes that the obsessions are a product of the mind and not imposed from without.
- If another axis I disorder is present, the content of the obsession is unrelated (eg, guilty thoughts in the presence of a major depression).

The characteristics of compulsions are as follows.

- Repetitive, purposeful, and intentional behaviours are performed in response to an obsession, according to certain rules, or in a stereotypical fashion.
- The behaviour is designed to neutralize or to prevent discomfort or some dreaded event or situation; however, either the activity is not connected in a realistic way with whatever it is designed to neutralize or prevent, or it is clearly excessive.
- The person recognizes that the behaviour is excessive and unreasonable (not usually true for children or for people whose obsessions have evolved into overvalued ideas).

The obsessions or compulsions cause marked distress, are time-consuming (more than 1 hour a day), or significantly interfere with a person's normal routine, occupational functioning, or usual activities or relationships.

Diagnosing OCD is usually not difficult. A family physician must be aware that OCD is prevalent and that patients seldom come for help specifically for this problem. A set of basic screening questions asked by a family physician (or nurse) can be very useful and takes little time. Most patients are relieved to talk about their symptoms once the illness has been discovered.

Diagnosis is based on clinical features. No specific diagnostic tests are available for OCD even though rating scales can be helpful.[25,26] *Table 2* lists useful screening questions.[26]

Clinical characteristics

Obsessive-compulsive disorder often begins in early adolescence and can also begin in childhood. The first stage is characterized by "microepisodes,"[4] which are the sudden appearance of obsessions and compulsions that last a few days or weeks then disappear for a time. Gradually, the symptoms become more frequent and intense until they are continuous, although they might wax and wane. Initially, the patient is able to conceal the symptoms or gradually draw the family into accommodating the abnormal behaviour. Families can become highly dysfunctional in accommodating the rituals of a family member who has OCD.

Most patients have OCD for about 7.5 years before receiving treatment, as it is often overlooked by physicians.

At first OCD seems to be a phenomenologically diverse syndrome. However, there are a few core features: pathologic doubting, a need for completeness, and an inability to assess risk.[2]

These core features manifest in different ways and to different extents (*Table 3*[2]). Obsessions might be repetitive thoughts to do with worry about dirt or contamination, fear that something terrible will happen, fear of harming oneself or others (horrific temptations), fear that something has been left undone or incomplete, religious thoughts (scruples), concern over symmetry or exactness, forbidden thoughts of a perverse sexual or aggressive nature, or nonsense sounds, words, or music.

Compulsions can take the form of excessive ritualized grooming; repeated rituals before a normal act (opening a door); repeated checking, counting, ordering, or arranging; hoarding or collecting; touching; taking measures to prevent harm; or rituals to remove dirt or contamination. Compulsions are usually a response to an obsession and can be a mental or motor phenomenon. A compulsion can be yielding or counteracting (ie, an obsession to do with dirt might lead to a yielding motor compulsion to wash hands). An intrusive perverse sexual image might lead to a counteracting mental compulsion to make a ritualized prayer.

Obsessions and compulsions can also occur alone. The compulsive need for exactness or completeness might lead to ritualized grooming that can take hours and is referred to as primary obsessional slowness. Touching rituals might mimic motor tics and seem reminiscent of Tourette's syndrome.

As the OCD worsens, the patient becomes locked into an endless cycle of repetitive behaviours or mentations that relieve inner tension or anxiety only for short periods. Some individuals become so handicapped that they spend most of their waking day engaged in compulsive behaviours to the point of becoming "frozen," ie, unable to complete a task, such as walking through a door, because of endless rituals. Many sufferers become so dysfunctional that they are unable to work. They develop behaviour patterns to avoid activity that will trigger the need to ritualize.

With time, patients with severe OCD become isolated, demoralized, and depressed. Relationships falter. Some patients appear relatively normal, but have to spend significant time engaging in rituals and compulsions.

Family physicians should be aware that patients could seek treatment for a number of physical symptoms without actually revealing the underlying cause (*Table 4*). For example, a compulsive handwasher might seek treatment for severe dermatitis or a compulsive face picker might present with facial lesions or scarring.

Comorbidity and differential diagnosis

Several conditions commonly associated with OCD (comorbidity), can confuse the clinical picture and lead to misdiagnosis:

- major depression,
- generalized anxiety disorder,
- panic disorder,
- phobias,
- hypochondriasis,
- delusional disorder,
- Tourette's syndrome, and
- compulsive personality.

An associated mood disorder is common, with two thirds of OCD patients having a lifetime history of depression. In most cases, the mood disorder is secondary to the OCD. About 15% of patients have coexisting primary major depression. There is also an important overlap with anxiety disorders. Up to 60% of OCD patients will experience panic attacks.

Compulsive personality is often confused with OCD. Although there might be features in common, such as the need for cleanliness or order, these symptoms are ego-syntonic in the compulsive personality and ego-dystonic in the patient with OCD. Only about 20% to 30% of OCD patients have compulsive personalities.

Related syndromes

Several syndromes seem similar to OCD in that repetitive, excessive, often senseless

CASE 2

Mr B.K. is employed as a teacher. His OCD began in adolescence when he started to have intrusive doubts about whether he had harmed anyone. This led to compulsive checking. He finished high school with difficulty because he was unable to concentrate well.

He began working in a grocery store where he was plagued with intrusive thoughts that he had handled glass jars, which had "broken" and that glass was left about and someone had been harmed. This led to endless checking for "glass" and endless phone calls to ensure that people were "okay." He then developed the fear that he had caused an accident while driving. This led to repetitive retracing of his route to work. Sometimes repeating a prayer would help temporarily. As he became more dysfunctional, he was unable to work and became very depressed. He was successfully treated to the point of an 80% reduction of symptoms. He is now married, has two children, and is teaching. He is completing a university program without difficulty.

CASE 3

Ms R.D. is a 48-year-old woman with OCD since midadolescence. She pursued a career successfully for several years. Following a surgical procedure, her OCD symptoms intensified so much that she had to quit her work. Over the years she became progressively housebound because of incapacitating rituals to do with grooming and routine household chores.

Various serotonergic drugs were either ineffective or not tolerated. She would spend most days in bed to avoid stimuli that triggered rituals, and hospitalization was delayed for months and took place with difficulty because of her inability to leave her home. Psychosurgery was only minimally effective, and she remains almost totally incapacitated, looked after and supported by a very caring husband.

behaviours are involved.[27] These syndromes might represent subtypes or variants of OCD, a hypothesis that is reinforced by the fact that treatments for OCD are often effective for these syndromes as well. These disorders are beyond the scope of this review. The more common of these syndromes are:

- trichotillomania,
- onychophagia,
- compulsive face picking,
- Tourette's syndrome,
- bulimia, and
- canine acral lick.

Treatment

Treating OCD was once thought to be difficult and unsatisfactory. However, this has changed and several treatments are now available for the disorder. Treatment can be divided into four areas:

- psychopharmacology,
- behavioural therapy,
- psychotherapy, and
- psychosurgery.

Psychopharmacology. Psychopharmacologic approaches are the mainstay of treatment, at least in the more severe cases, particularly as newer and more potent serotonergic drugs become available.

Four drugs have been proven useful in treating OCD, all potent serotonin reuptake inhibitors (*Table 5*). Clomipramine, a tricyclic antidepressant that is relatively specific for serotonin reuptake blocking, is the best studied to date and has been shown to have clear antiobsessional properties in double-blind crossover studies of both adults and children.[28,29] The drug is usually well tolerated, but can produce troublesome side effects. The other three drugs belong to the new class of selective serotonin reuptake inhibitors (SSRIs) and include fluoxetine, fluvoxamine, and sertraline. They have been less thoroughly studied for OCD. Although quite comparable in their therapeutic effects, clomipramine seems to be slightly more efficacious.[30] The advantage of the SSRIs is that they are usually better tolerated and not as dangerous if taken as an overdose.

Physicians should keep several points in mind when using any of these serotonergic agents for OCD.

- About 60% to 70% of patients receive benefit with about 30% to 40% reduction of symptoms.
- Some patients enjoy dramatic relief while others experience only a modest reduction of symptoms. Nonetheless, even a modest reduction can make a meaningful difference to a patient's life.
- Higher doses than are normally used for depression are often necessary (eg, 300 mg of clomipramine or 80 mg of fluoxetine daily).
- Response could take 8 to 12 weeks.
- Unlike other psychiatric disorders, the placebo response rate for OCD is extremely low.
- A patient's symptoms might worsen temporarily because of increased serotonin in the synaptic cleft acting on a hypersensitive postsynaptic receptor before desensitization occurs (down-regulation).
- Once improvement is achieved, medications should be taken for very long periods, or indefinitely. A high percentage of patients relapse when medication is discontinued.[31]

If a single antiobsessional drug is ineffective or only partially effective, then strategies to enhance the effectiveness of the drug can be used, such as[32-36]:

- two SRIs together, or adding
- buspirone,
- lithium,
- neuroleptics, or
- fenfluramine.

Intravenous clomipramine infusions can be considered for treatment-resistant OCD or for those patients who are unable to tolerate the side effects of oral drugs.[37] About two thirds of patients treated this way will experience moderate to marked relief of symptoms. The effectiveness of intravenous clomipramine is probably based on avoiding the "first pass" effect in the liver (less clomipramine is metabolized into desmethylclomipramine, which has a strong noradrenergic but weak serotonergic effect). Studies have shown[38] that serum levels of clomipramine correlate with a positive response in OCD whereas serum levels of desmethylclomipramine mostly do not.

Anecdotal reports have indicated other drugs effective for OCD, including dex-

troamphetamine, high potency benzodiazepines, and antiandrogens. Monoamine oxidase inhibitors or other serotonergic tricyclics can also be effective in some cases.

Behaviour therapy. Behaviour therapy is essential for treating OCD.[39] In cases where symptoms are less severe and not "overvalued," that is, on the verge of being delusions or false beliefs, and the patient has the ego strength to engage in behavioural techniques, behaviour therapy can be very effective. In most instances, behaviour therapy becomes an adjunct to pharmacotherapy, used after medication has reduced symptoms.

Behavioural techniques are relatively simple, but time and consistency are essential for the approach to be effective.

The most common technique is exposure to an evoking stimulus and response prevention, basically a form of systematic desensitization. This can be done only after a careful behavioural analysis of the patient's symptoms and after educating the patient about the behavioural techniques involved. Once a program has been initiated, most patients can do "homework" assignments, keep a record of activities, and report to a therapist weekly. Family members might have to be involved if symptoms occur only at home.

Other behavioural techniques include thought stopping, modeling, and pacing.

In the hands of an experienced behavioural therapist, the results of behaviour therapy can be impressive. Most studies report 50% or more patients achieving up to a 70% reduction of symptoms.[40] Because of the time and energy involved, and the need to endure considerable periods of psychic distress, only a few patients are willing to undergo this type of treatment.

Psychotherapy. Many psychologic theories on the origin of OCD have been advanced. Noted authors in this area have concluded that psychotherapy alone is ineffective for treating OCD and that the search for psychologic causes should be discontinued.[41,42] However, psychotherapy is useful as an adjunctive therapy. It is necessary to develop rapport, to ensure compliance, and to understand personality and any complicating psychologic conflicts. Stress and conflict can accentuate OCD symptoms. Coping with OCD and the treatment process requires support and reassurance. Family members might also have to be seen for support as well.

If symptoms are successfully reduced with medication or behaviour therapy, then psychotherapy can help a patient restructure life in terms of work, leisure time, and relationships. The average patient has been ill for 7.5 years before coming for treatment, a period of coping with a severe illness that can have a profoundly negative effect on personality and lifestyle.

Education is also very important. Many excellent self-help books are available for both patients and families.[8,43,44] Some of these books have self-rating scales that can be very useful.

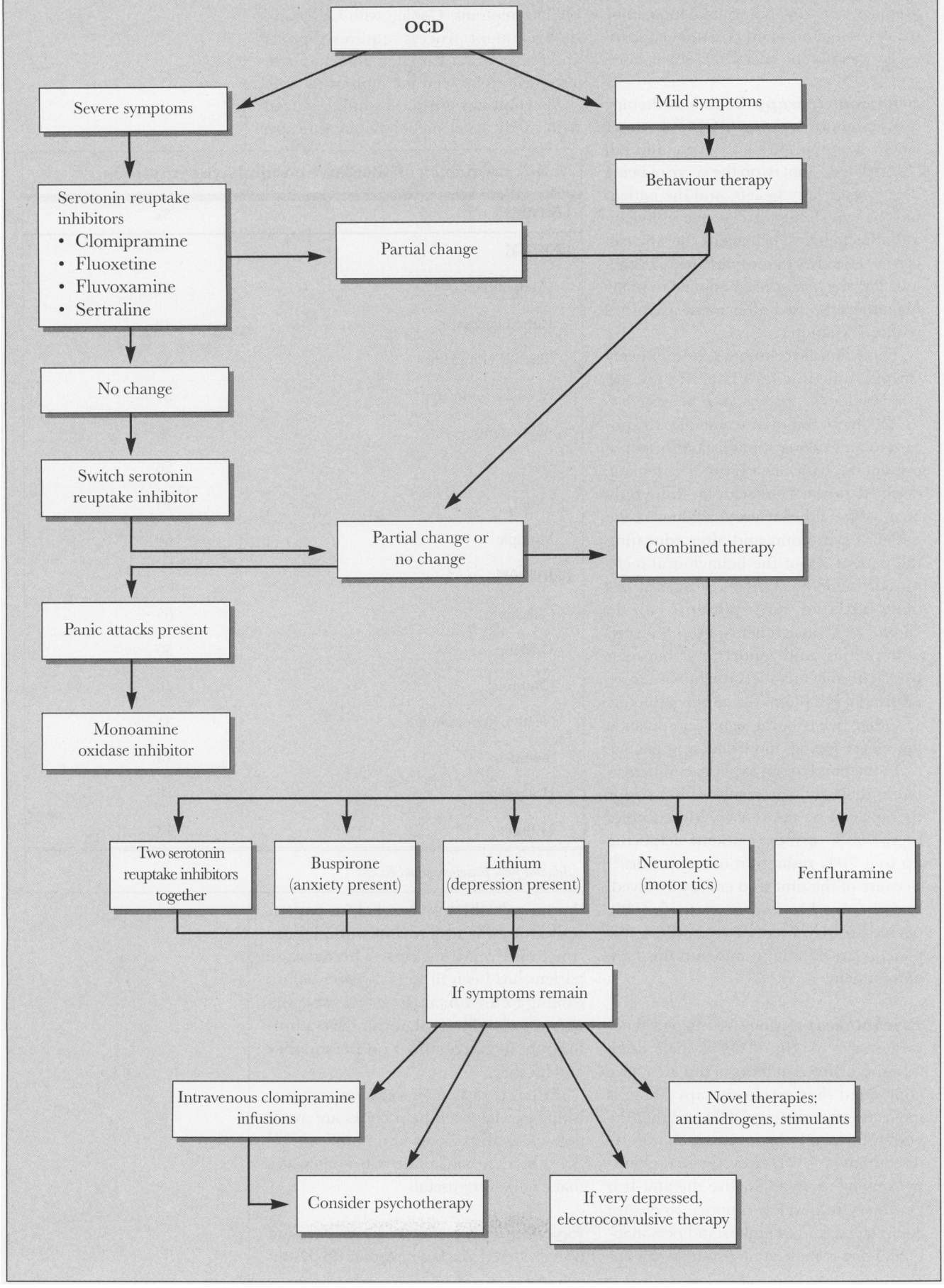
Psychosurgery. Psychosurgery should be considered as a last resort for OCD, but

Table 3. **Frequency of obsessive compulsive symptoms**

SYMPTOMS	%
OBSESSIONS	
Contamination	45
Pathologic doubt	42
Somatic complaints	36
Need for symmetry	31
Aggression	28
Sex	26
Other	13
Multiple	60
COMPULSIONS	
Checking	63
Washing	50
Counting	36
Need to ask or confess	31
Symmetry	28
Hoarding	18
Multiple	48

Adapted from Rasmussen and Eisen[2]

Figure 1. **Flow chart for treatment of OCD**



it should not be withheld indefinitely. Psychosurgery can offer dramatic relief without undue risk in most cases. The terrible long-term consequences of untreated OCD on personality, relationships, role functioning, and personal suffering should not be minimized.

Bilateral anterior cingulotomy and bilateral anterior capsulotomy are two procedures used for OCD.[45-47] Both are effective; favourable outcomes are reported in up to 80% of patients, a meaningful figure considering that only treatment-resistant cases receive psychosurgery.

There are few complications from psychosurgery and no evidence of neurocognitive deficits. Performance on intelligence tests actually increases after surgery.

Patients who have had adequate trials with two or three serotonin reuptake inhibitors, along with augmentation strategies, a course of intravenous clomipramine infusions, and a trial of behavioural therapy, have been consistently ill for more than 5 years, and remain very dysfunctional are candidates for psychosurgery.[48] Treatment for OCD is summarized in *Figure 1*.

What is the role of the family physician?

Most patients with psychiatric disorders are treated by professionals not specializing in the area of mental health. The role of the family physician is extremely important for many reasons.

- A family physician, by routinely asking screening questions when reviewing the mental health status of a patient, can easily detect most cases of OCD.
- Cases can be detected by remembering that OCD can present as physical problems, such as dermatitis and facial sores or deformed nails.
- Adequate trials of one of the serotonin reuptake inhibitors can often be quickly and dramatically effective.
- A family physician can facilitate referral to a specialist if necessary.
- If specialized care is required, a family physician can continue to support both the patient and family, ensure compliance, and supervise long-term effective drug therapy.

Conclusion

Obsessive-compulsive neurosis is a surprisingly prevalent psychiatric disorder with up to 3% of the population suffering from the illness over a lifetime. Recent research has led to a much better understanding of the neuroanatomic and neurochemical basis for the illness. Effective treatments are available, and most patients with OCD can be given at least some relief from symptoms and thus be able to lead relatively normal lives.

Although easily diagnosed, the disorder is frequently overlooked by family physicians. This might be because patients are reluctant to talk about their symptoms or because they present with other complaints, such as dermatitis. The condition might be misdiagnosed because of comorbid symptoms of such conditions as depression or anxiety. Being aware of the prevalence of OCD and routinely asking a few screening questions will usually allow family practitioners to identify cases of OCD and either initiate treatment or refer the patient to a psychiatrist. ■

Table 4. **Physical presentations of OCD**

CONDITION	CAUSE
Dermatitis	Compulsive hand washing
Badly bitten nails	Compulsive nail biting
Facial lesions	Compulsive face picking
Patchy baldness	Compulsive hair pulling
Gum lesions, worn enamel	Compulsive tooth brushing
Repeated visits to physician	Compulsive worry about illness
Visits to plastic surgeon	Preoccupation with body parts

Table 5. **Serotonin reuptake inhibitors for OCD**

GENERIC NAME	TRADE NAME	DOSE RANGE (MG)
Clomipramine	Anafranil	150-300
Fluoxetine	Prozac	40-80
Fluvoxamine	Luvox	150-300
Sertraline	Zoloft	100-200

***Requests for reprints to**: Dr L. Warneke, 217, 3017 66th St, Edmonton, AB T6K 4B2*

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3rd ed, revised. Washington, DC: American Psychiatric Association, 1987.
2. Rasmussen S, Eisen J. The epidemiology and differential diagnosis of obsessive compulsive disorder. *J Clin Psychiatry* 1992;53(Suppl 4):4-10.
3. Bland R, Newman S, Orn H. Lifetime prevalence of psychiatric disorders in Edmonton. *Acta Psychiatr Scand Suppl* 1988;77(Suppl 338):24-32.
4. Flament M, Whitaker A, Rapoport J, Davies M, Berg C, Kolikow K, et al. Obsessive compulsive disorder in adolescence: an epidemiologic study. *J Am Acad Child Adolesc Psychiatry* 1988;27:764-71.
5. Rapoport J, Swedo S, Leonard H. Childhood obsessive compulsive disorder. *J Clin Psychiatry* 1992;53(Suppl 4):11-6.
6. Karno M, Golding J, Sorenson S. The epidemiology of obsessive compulsive disorders in five U.S. communities. *Arch Gen Psychiatry* 1988;45:1094-9.
7. Jenike M. Obsessive compulsive and related disorders: a hidden epidemic [editorial]. *N Engl J Med* 1989;321:539-41.
8. Rapoport J. *The boy who couldn't stop washing.* New York: Dutton, 1989.
9. LaPlane D, Baulac M, Wedlocker D, Dubois B. Pure psychic akinesia with bilateral lesions of basal ganglia. *J Neurol Neurosurg Psychiatry* 1984;47:377-85.
10. Swedo S, Rapoport J, Cheslow D, Leonard H, Ayoub E, Hosier D, et al. High prevalence of obsessive compulsive symptoms in patients with Sydenham's chorea. *Am J Psychiatry* 1989;146:246-9.
11. Husby G, van de Rijn I, Zabriskie J, Abdin Z, William R. Antibodies reacting with cytoplasm of subthalamic and caudate nuclei neurons in chorea and rheumatic fever. *J Exp Med* 1976;144:1094-110.
12. Pitman R, Green R, Jenike M, Mesulam M. Clinical comparison of Tourette's disorder and obsessive compulsive disorder. *Am J Psychiatry* 1987;144:1166-71.
13. Denckla MB. The neurological examination. In: Rapoport J, editor. *Obsessive compulsive disorder in children and adolescents.* Washington, DC: American Psychiatric Association Press, 1989: 107-18.
14. Pauls DL, Leckman JF. The inheritance of Gilles de la Tourette's syndrome and associated behaviours: evidence for autosomal dominant transmission. *N Engl J Med* 1986;315:993-7.
15. Luxenberg J, Swedo S, Flament M, Friedland R, Rapaport J, Rapoport S, et al. Neuroanatomical abnormalities in obsessive compulsive disorder detected with quantitative x-ray computed tomography. *Am J Psychiatry* 1988;145:1089-93.
16. Baxter L. Brain imaging as a tool in establishing a theory of brain pathology in obsessive compulsive disorder. *J Clin Psychiatry* 1990;51(Suppl 2):22-5.
17. Adams B, Warneke L, McEwan A, Fraser B. Single photon emission computerized tomography in obsessive compulsive disorder. *J Psychiatry Neurosci* 1993;18(3):109-12.
18. Baxter L, Schwartz J, Bergman K, Szuba M, Guze B, Mazziotta J, et al. Caudate glucose metabolic rate changes with both drug and behavior therapy for obsessive compulsive disorder. *Arch Gen Psychiatry* 1992;49:681-9.
19. Swedo S, Pietrini P, Leonard H, Schapiro M, Rettew D, Goldberger E, et al. Cerebral glucose metabolism in childhood onset obsessive compulsive disorder. *Arch Gen Psychiatry* 1992; 49:690-4.
20. Rapoport J. The biology of obsessions and compulsions. *Sci Am* 1989;260(3):82-9.
21. Insel T. Toward a neuroanatomy of obsessive compulsive disorder. *Arch Gen Psychiatry* 1992; 49:739-74.
22. Barr L, Goodman W, Price L, McDougle C, Charney D. The serotonin hypothesis of obsessive compulsive disorder: implications of pharmacologic challenge studies. *J Clin Psychiatry* 1992; 53(Suppl 4):17-28.
23. Rapoport JL, Ryland DH, Kriete M. Drug treatment of canine acral lick. An animal model of obsessive compulsive disorder. *Arch Gen Psychiatry* 1992;49:517-21.
24. Stein D, Shoulberg N, Helton K, Hollander E. The neuroethological approach to obsessive compulsive disorder. *Compr Psychiatry* 1992; 33(4):274-81.
25. Goodman W, Price L, Rasmussen S, Mazure C, Delgado P, Heninger G, et al. The Yale-Brown obsessive compulsive scale (Y-BOCS). Part I: development, use and reliability. *Arch Gen Psychiatry* 1989;46:1006-11.
26. Ciba-Geigy. *OCD: when a habit isn't just a habit. A guide to obsessive-compulsive disorder.* Pine Brock, NJ: Pharm Ethics Inc, 1991:22.
27. Christenson G, Mackenzie T, Mitchell J. Characteristics of 60 adult chronic hair pullers. *Am J Psychiatry* 1991;148:365-70.
28. The Clomipramine Collaborative Study Group. Clomipramine in the treatment of patients with obsessive compulsive disorder. *Arch Gen Psychiatry* 1991;48:730-8.
29. Leonard HL, Swedo S, Lenane M, Rettew D, Cheslow D, Hamberger S, et al. A double blind desipramine substitution during long term

clomipramine treatment in children and adolescents with obsessive compulsive disorder. *Arch Gen Psychiatry* 1991;48:922-7.
30. Goodman W, McDougle C, Price L. Pharmacotherapy of obsessive compulsive disorder. *J Clin Psychiatry* 1992;53(Suppl 4):29-37.
31. Pato M, Zohar-Kadouch R, Zohar J, Murphy D. Return of symptoms after discontinuation of clomipramine in patients with obsessive compulsive disorder. *Am J Psychiatry* 1988;145:1521-5.
32. Simeon J, Thatte S, Wiggans D. Treatment of adolescent obsessive compulsive disorder with a clomipramine-fluoxetine combination. *Psychopharmacol Bull* 1990;26:285-90.
33. Jenike M, Baer L, Buttolph L. Buspirone augmentation of fluoxetine in patients with obsessive compulsive disorder. *J Clin Psychiatry* 1991;52:13-4.
34. Golden R, Morris J, Sack D. Combined lithium tricyclic treatment of obsessive compulsive disorder. *Biol Psychiatry* 1988; 23:181-5.
35. Hollander E, De Caria C, Schneier F, Schneier H, Liebowitz M, Klein D, et al. Fenfluramine augmentation of serotonin reuptake blockade anti-obsessional treatment. *J Clin Psychiatry* 1990;51:119-23.
36. McDougle C, Goodman W, Price L, Delgado P, Krystal J, Charney D, et al. Neuroleptic addition in fluvoxamine refractory obsessive compulsive disorder. *Am J Psychiatry* 1990;147:652-4.
37. Warneke L. Intravenous clomipramine therapy in obsessive compulsive disorder. *Can J Psychiatry* 1989;34:853-9.
38. Mavissakalian M, Jones B, Olson S, Perel J. The relationship of plasma clomipramine and N-desmethyl clomipramine to response in obsessive compulsive disorder. *Psychopharmacol Bull* 1990;26:119-22.
39. Griest J. Treatment of obsessive compulsive disorder: psychotherapies, drugs and other somatic treatment. *J Clin Psychiatry* 1990;51(Suppl 8):44-50.
40. Foa E, Steketee G, Ozarow B. Behavior therapy with obsessive compulsives: from theory to treatment. In: Mavissakalian M, Turner SM, Michelson L, editors. *Obsessive compulsive disorder: psychological and pharmacological treatment.* New York: Plenum Press, 1985:49-129.
41. Malan D. *Individual psychotherapy and the science of psychodynamics.* London: Butterworths, 1979: 218-9.
42. Salzman L. *Treatment of the obsessive personality.* New York: Aronson, 1980.
43. Baer L. *Getting control: overcoming your obsessions and compulsions.* Toronto: Little, Brown and Co, 1991.
44. Steketee G, White K. *When once is not enough – help for obsessive compulsives.* Oakland, Calif: New Harbinger Pub, 1990.
45. Chiocca E, Martuza R. Neurosurgical therapy of obsessive compulsive disorder. In: Jenike M, Baer L, Minichello W, editors. *Obsessive compulsive disorders: theory and management.* 2nd ed. Chicago: Year Book Publishers, 1990:238-94.
46. Mindus P, Jenike M. Neurosurgical treatment of malignant obsessive compulsive disorder in the psychiatric clinics of North America. *Psychiatr Clin North Am* 1992;15: 921-38.
47. Ballantine HT Jr, Bouchoms A, Thomas EK, Giriunas I. Treatment of psychiatric illness by stereotactic cingulotomy. *Biol Psychiatry* 1987;22:807-19.

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