

# Obsessive-compulsive disorder

Abdulsamad Aljeshi, MBBS, FRCPC.

## ABSTRACT

يستعرض المقال اضطراب الوسواس القهري من منظور المعلومات السريرية ذات الصلة والتي يحتاجها الأطباء الممارسين، وأطباء الأسرة، والمجتمع، وغيرهم من المتخصصين في مجال الرعاية الصحية. يركز المقال على مدى انتشار المرض، ومسبباته، ومعايير التشخيص، ومصاحبة أعراض المرض لأمراض أخرى. كما يلخص المقال أيضا الطرق المتاحة المعترف بها لعلاج هذه الحالة.

This review article addresses obsessive-compulsive disorder from the prospective of information that is relevant to general practitioners, family physicians, and other medical health specialists, focusing on epidemiology, etiology, diagnostic criteria, comorbidity, and a summary of well recognized treatment modalities and approaches that are available to treat this condition.

*Neurosciences 2011; Vol. 16 (4): 313-319*

*From the Department of Medical Specialties, Psychiatric Services Unit, Saudi Aramco Medical Services Organization, Dhahran, Kingdom of Saudi Arabia.*

*Address correspondence and reprint request to: Dr. Abdulsamad Aljeshi, Child and Adult Psychiatrist, PO Box 5888, Saudi Aramco, Dhahran 31311, Eastern Province, Kingdom of Saudi Arabia. Tel. +966 (3) 8778310. Fax. +966 (3) 8778414. E-mail: aljeshi@hotmail.com*

Obsessive-compulsive disorder (OCD) is a common and incapacitating neuropsychiatric disorder that occurs across the whole life span. It is characterized by recurrent obsession, compulsions, or both.<sup>1</sup> Obsessions are frequent and troubling thoughts, feelings, ideas, or sensations, while compulsions are conscious, steady, and constant pattern of actions, for example counting, checking, or avoiding. Obsessions increase the anxiety, and compulsions usually reduce it. Anxiety is usually worsened in patients who try to oppose executing their compulsions.<sup>2</sup> Obsessive-compulsive related disorders (OCRD) are a group of disorders with overlapping symptoms and compulsive qualities that are otherwise, distinct disorders from OCD.<sup>3</sup> Regrettably, OCD and related disorders are frequently under-diagnosed and under treated. A recent study indicated that 59.5% of OCD patients worldwide receive no treatment for their

disorder.<sup>1</sup> The financial costs of OCD are enormous. In the USA, the projected direct cost of treatment of OCD is estimated to be within \$5 billion a year.<sup>4</sup>

**Epidemiology.** There is a lack of data estimating either the prevalence or the incidence of this disorder within the Kingdom of Saudi Arabia. It is estimated that 2-4% of individuals in the general population will develop OCD before the age of 18 years,<sup>5,6</sup> and epidemiologic research studies have revealed that OCD has a lifetime prevalence of 2-3%.<sup>7</sup> Some researchers have projected that the disorder is found in as many as 10% of outpatients in psychiatric clinics. The peak ages of onset appear to be from 10-19 years, closely followed by the ages of 20 and 29.<sup>8</sup> Studies have shown a prevalence of approximately 1% in children and adolescents.<sup>7</sup> Throughout adulthood, OCD symptoms follow a chronic course, with exacerbations accompanying periods of life stress. In adults, pronounced functional impairment has been observed in all areas of daily functions such as education, employment, marital status, life satisfaction, and general health. Retrospective studies suggest that most children with OCD will continue to have significant symptoms through adolescence and adulthood.<sup>9,10</sup> It is estimated that 90% of OCD patients describe low self-esteem, and around 75% of them have impaired family relations. In addition, around 66% of them complain of difficulties maintaining friendships, poor school performance, and low vocation ambitions. Also, around 40% of patients are incapable of working for a period of 2 years; and unfortunately, 15% eventually commit suicide.<sup>11</sup> Also, data showed that late adolescence is the period of increased vulnerability for the development of OCD; OCD affects predominantly female adults and male children and adolescents; and that those who are unmarried or abusing drugs are more likely to present with OCD.<sup>12</sup>

The OCD is considerably more common in children and adolescents than expected. It is estimated that OCD has a 6-month prevalence of one in 200 children and adolescents,<sup>13,14</sup> and it is linked with a significant functional impairment in a wide range of domains.<sup>15</sup> It is believed that one third to one half of adult OCD patients develops the disorder during the childhood period but unfortunately, the disorder often goes unrecognized until adulthood.<sup>16</sup> The most common obsessive symptoms

relate to aggression, contamination, symmetry, saving/collecting, sexual impulses, or religious matters. The most common compulsive rituals include checking, cleaning, counting, ordering, and hoarding rituals.<sup>8,16,17</sup> In Saudi Arabia, religious themes predominate in both the obsessions (66%) and compulsions (78%).<sup>18</sup>

**Etiology.** Several etiological theories have been proposed for OCD, which include neurobiological, immunologic, genetics, and psychosocial theories.

**Neurobiology.** Evidence from neurochemistry and neuroimaging studies offer substantial support for neurobiological causes of OCD.<sup>19</sup> Serotonin dysregulation is implicated in the mediation of idiopathic OCD symptoms. The data show that serotonergic agents that block the presynaptic uptake of serotonin are effective, but the sites of activity of these agents are unknown.<sup>20</sup> Various neuroimaging studies including positron emission tomography (PET) have indicated differences in radiotracer uptake between patients with OCD and healthy controls, mainly in the orbital gyrus and the head of the caudate nucleus.<sup>21</sup> Also, there is an increase in the cortical and basal ganglia metabolism and blood flow of patients with OCD compared with controls.<sup>22</sup> A recent meta-analysis study<sup>23</sup> of brain volume in OCD points toward volumetric variations in the cortical and thalamic regions in OCD patients and control subjects, suggesting that structural change of the thalamocortical pathways may contribute to the functional disruptions of front subcortical circuits in OCD. Also, MRI and CT studies have revealed a mild reduction in caudate nuclei volume,<sup>24</sup> and white matter abnormalities in the frontal lobe region.<sup>25</sup>

**Immunology.** A group of researchers at the National Institute of Mental Health described a subgroup of OCD in children, which was triggered or exacerbated by group A beta-hemolytic streptococcal (GABHS) infection.<sup>26,27</sup> It is theorized that the obsessive and compulsive symptoms are related to caudate nucleus enlargement caused by an autoimmune reaction between caudate tissue and anti-neuronal antibodies formed against GABHS.<sup>28</sup> The acronym PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections) is used to identify a subgroup of pediatric patients who meet the following 5 criteria: presence of OCD and/or tic disorder, pre-pubertal symptom onset, sudden onset or episodic course of symptoms, temporal association between streptococcal infections and neuropsychiatric symptom exacerbations, and associated neurological abnormalities.<sup>29,30</sup>

**Genetics.** Although some cases of OCD appear to have a sporadic form, twin, family, segregation, and linkage studies have demonstrated that OCD is familial and that the familiarity is due in part to genetic factors, and there are regions of the genome that very likely harbor susceptibility loci for OCD.<sup>31,32</sup> Studies in twins

found a higher concordance rate among monozygotic twins, 53% and 87%, compared with 22% and 47% in dizygotic twins.<sup>32,33</sup> Also, the rate of OCD among first-degree relatives is 5-6 folds higher than in the general population.<sup>34,35</sup>

There are certain regions in the genome that are expected to retain OCD susceptibility loci.<sup>32</sup> There are more than 60 studies focusing on genes in the serotonergic and dopaminergic pathways, but unfortunately, with the exception of the glutamate transporter gene, none have accomplished genome-wide significance or are constantly replicated.<sup>36</sup>

**Psychosocial.** An earlier psychodynamic conceptualizations model of obsession did not hold up for long because of poor response of OCD patients to psychoanalytic and equivalent forms of treatment. However, most behavioral conceptualizations of OCD are based on Mowrer's 2-factor conditioning theory,<sup>37</sup> which states that a neutral event or object may become aversive (namely, a conditioned stimulus) when it is associated with an unrelated fear-inducing event. Any act such as compulsion could lead to a decline in the level of fear or of some other negative affect, which is then reinforced through principles of higher-order conditioning. According to this theory, compulsions build up as a result of their anxiety-reducing properties. Unfortunately, conditioning theories do not explain why the OCD develops as most patients cannot remember specific fear-eliciting events associated with the beginning of their OCD symptoms. More recent behavioral conceptualizations have included other mechanisms, which include modeling, observation, and informational learning, as required precursors to the development of the disorder.<sup>38</sup>

**Diagnostic criteria and clinical features.** The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) classification categorizes OCD as an anxiety disorder jointly with agoraphobia, panic disorder, generalized anxiety disorder (GAD), and posttraumatic stress disorder (PTSD).<sup>1</sup> The essential criteria for OCD according to the DSM-IV-TR are intrusive thoughts or images (obsessions), which increase anxiety, and by repetitive or ritualistic actions (compulsions), which decrease anxiety.<sup>1</sup> The most recent revision of the diagnostic criteria for OCD in DSM-IV emphasizes that compulsions can be observable behaviors or mental rituals.<sup>1</sup> Obsessive-compulsive disorder symptoms can vary little by time or place and similar symptoms are seen across many cultures.<sup>39</sup> Although the major symptoms can vary with time in any patient with OCD, the symptoms are similar in both children and adults.<sup>39</sup> The DSM-IV-TR criteria specify that, the obsessions or compulsions must cause marked distress, consume more than one hour a day, or interfere considerably with routine, professional or academic function, social

activities or relationships of OCD patients. Also, DSM-IV-TR states that symptoms must not be caused by a general medical condition or a substance.<sup>1</sup>

Four clinical dimensions were identified in OCD. The first is obsessions/checking, which is characterized by obsessions related to aggression, gender, religion, own body, and various checking behaviors. The second is engagement and preoccupations with rituals such as order, symmetry, or exactness, and/or involvement with various compulsions for instance counting, rearranging, or ritualistic repetitions. The third is obsessions concerning contamination and compulsive washing and cleaning. The final dimension is hoarding obsessions and compulsions.<sup>40</sup>

**Comorbidity.** Coexistence of mood disorders, other anxiety disorders, tic disorders, attention deficit hyperactivity disorder (ADHD), eating disorders and psychotic symptoms with obsessive-compulsive symptoms were reported in the early psychiatric literature. The Epidemiology Catchment Area study found that two-thirds of OCD patients had a lifetime comorbid psychiatric disorder.<sup>41,42</sup> Comorbidity in childhood OCD is common; as many as 80% of children with OCD meet diagnostic criteria for an additional Axis I disorder, and as many as 50% experience multiple comorbid conditions.<sup>15</sup>

**Mood disorder.** Patients with OCD frequently have complicated depression. It may be difficult to distinguish them from depressed patients with obsessive symptoms. In studies, 53% of adult OCD patients,<sup>43</sup> and 25% of children had a diagnosis of affective disorder.<sup>44</sup>

**Other anxiety disorders.** Although anxiety is not a requisite manifestation of OCD, OCD is formally categorized among the anxiety disorders. Patients with OCD who experience a high level of anxiety may describe panic-like episodes. Several studies have assessed the occurrence of OCD in patients in treatment for other anxiety disorders. Seventeen percent of panic disorder patients suffered from OCD,<sup>45</sup> and 23% of adults, and 13% of children with OCD had comorbid anxiety disorders.<sup>43</sup> Another study of 100 subjects with primary OCD reported estimated lifetime rates of social phobia (18%), panic disorder (12%), and specific phobia (22%).<sup>46</sup>

**Tic disorders.** At least 50% of children and adolescents with Tourette's disorder expand to develop OC symptoms or disorder by adulthood.<sup>47</sup> The necessity to touch or rub, the blinking and staring rituals, the anxiety over symmetry and exactness, the sense of incompleteness, and the intrusive aggressive thoughts and images are notably more common in OCD patients specially with comorbid tics.<sup>48,49</sup> In contrast, contamination doubts and cleaning compulsions are more frequent in patients with non-tic-related OCD.<sup>50</sup>

**Trichotillomania.** It is well known that trichotillomania resembles OCD, but also has some differences, and that leads to the assumption that the repetitive hair pulling behavior is an obsessive-compulsive spectrum disorder.<sup>51</sup> Studies of OCD and trichotillomania (compulsive hair-pulling) have shown that both share common co-morbidity, phenomenology, and familial transmission. However, the extent to which these 2 disorders share a similar cognitive phenotype has yet to be elucidated.<sup>52</sup> In a recent study, Chamberlain et al<sup>53</sup> found out that OCD and trichotillomania share spatial working memory problems, while the neuropsychological dysfunction, which is present in OCD was intact in trichotillomania. Although the frequency of OCD is elevated among children and adolescents with trichotillomania and their first-degree relatives, most patients with this condition do not have other obsessive or compulsive symptoms.<sup>54</sup>

The disruptive behavior disorders are usually reported in children and adolescents with OCD with an estimation of 51% and 36% for ADHD; and 51% and 47% for oppositional defiant disorder. It was also found that 53% of boys are likely to have comorbid ADHD compared with 24% in girls.<sup>55,56</sup> Also, it was noted that unusually high rates of both specific and pervasive developmental disorders are identified in some OCD referred samples, but it is unclear whether this increase reflects referral bias (Berkson's bias) or is a correlate of associated comorbidity rather than being a correlate specific to childhood-onset OCD.<sup>57</sup>

**Other psychiatric conditions.** Obsessive compulsive symptoms and disorders are common in patients with anorexia nervosa (AN) or bulimia nervosa. It is estimated that the lifetime obsessions and compulsions occurred in 68% of the AN restricting type, and in 79.1% of the AN binge/purge type.<sup>58</sup> Body dysmorphic disorder (BDD) also can present with obsessive preoccupation with an imagined or slight defect in appearance. It can either exist alone or be accompanied by compulsive behaviors such as excessive mirror-checking and grooming.<sup>59</sup> Some patients with OCD can act in bizarre ways, show near-delusional tenacity in their conviction of potential unrealistic dangers or the necessity of performing rituals, and have a dramatic deterioration in adaptive functioning that may raise the question of psychotic or schizophrenic worsening. The absence of thought disorder or hallucinations and the preservation of reality testing outside the area of obsessional concern can help to differentiate OCD symptoms from those of psychosis. In a recent study, the co-occurrence of OCD with schizophrenia in adolescent patients was estimated at 26%.<sup>38</sup> For this reason, OCD must be considered as part of the differential diagnosis in older children and adolescents with psychotic features.<sup>60</sup>

**Other medical conditions.** Obsessive compulsive disorder has been reported to arise as a result of a variety of neurological conditions, following carbon monoxide poisoning, tumors, allergic reactions to wasp sting, postviral encephalitis, brain injury, Sydenham's chorea (SC), and other basal ganglia pathologies.<sup>61</sup> Compulsive eating and preoccupation with food also has been found in at least 50% of children with Prader-Willi syndrome, a genetic condition resulting from deletion of a portion of chromosome 15.<sup>62</sup>

**Psychiatric assessment of OCD.** Symptoms of OCD vary between mild and moderate severity, wax and wane over time, become prominent in one setting and not another. Sometimes, symptoms are kept secret from others - including families - for years before they acquire medical attention. Factors that point out the need to screen and treat individuals for OCD include: time engaged by OC symptoms, level of subjective stress on the individual, and severity of functional impairment. These factors are best and reliably assessed using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS),<sup>63</sup> and the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS).<sup>64</sup> Due to the inconsistency of phenotype of OCD, clinicians may pursue heterogeneous symptoms occurring in OCD and assess their presence, consistency, and severity. A complete psychiatric evaluation should include a full psychiatric history, assessment of other comorbid psychiatric disorders, and current mental state exam. Also, it is important to perform a full family, medical, school, and developmental history as a part of standard assessment of all patients with OCD.

**Treatment modalities.** The main central immediate therapeutic intervention in OCD is education and destigmatization. On average, an OCD patient may remain 7 years after their first symptoms before seeking help.<sup>65</sup> Patience and persistence in treatment and intervention with those individuals are the keys for a successful outcome. It is likely that treatment may take a full 6 weeks for benefit to occur. On average, treatment is generally continued for 6-12 months following stabilization and then slowly withdrawn. To optimally treat patients suffering from OCD, the clinician needs to integrate various approaches with the patient. Two treatment modalities, cognitive behavioral therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs), have been studied systematically and have empirically shown specific efficacy for the core symptoms of OCD.

**Cognitive behavioral therapy (CBT).** The best development in the last decade for the treatment of OCD pertains to well-conducted systemic trials of CBT applied to OCD patients. Numerous studies have shown its consistency, acceptability, and efficacy.<sup>66</sup> It is now considered the first line of treatment for mild to moderate cases of OCD. In 1966, Meyer<sup>67</sup> was the

first to expose 2 patients with OCD to anxiety-evoking stimuli, and with constant staff supervision prevented them from engaging in compulsions. Both patients remained improved at the end of 2-year follow-up.

Recent research studies have shown that CBT is a recognized treatment for OCD, equal or maybe superior to pharmacotherapy.<sup>68</sup> The CBT is effective in reducing compulsive rituals and obsessive thoughts by exposure to the feared situation or object, and response prevention in which the patient resists the urge to perform the compulsion after exposure.<sup>69</sup> Hierarchy-based exposure and response prevention (E/RP) are the central part in the treatment, which relies on the fact that anxiety is usually reduced after adequate length of contact with a feared stimulus. Outcome research studies of E/RP have found that around 60-70% of OCD patients significantly improved, and approximately all patients have continued their improvement after 2 years of follow-up following behavioral treatment.<sup>70</sup> Unlike the adults, children with OCD are found to be "embedded" within their families. Because these children are very reliant on their caregivers, they are susceptible to many influences over which they have little control. Behavioral family intervention is of great importance and has influenced the course of treatment of children with OCD.<sup>71</sup> Cognitive behavioral family treatment (CBFT) has been found to be highly efficient in the treatment of these children.<sup>72,73</sup> Records have shown that when applied to adults with OCD, CBT has caused an obvious reduction in the number of symptoms and associated functional impairments - and so has great potential. However, the experimental findings' base value resulting from the application of CBT to youths has many restrictions. It is primarily related to the treatment of OCD in very young children.<sup>74</sup>

**Pharmacotherapy.** While CBT is the first line treatment for mild to moderate OC symptoms, more severe symptoms are an indication for medication trials. Pharmacotherapy is an essential component of the multimodal treatment of adults, children, and adolescents with OCD. Severe impairment based on time spent in rituals, subjective distress, and functional limitations provide a reasonable consideration for drug intervention. Also, the presence of any situation that impedes successful CBT treatment may lead to an earlier consideration of medication treatment. The presence of additional psychopathology such as comorbid anxiety disorders, major mood disorder, and disruptive behavioral disorder may reduce acceptance of or compliance with CBT and may require medication.

The past decade has seen rapid advances in our understanding of pharmacotherapy for OCD. The SSRIs have emerged as a main therapeutic progress in psychopharmacology. Large systemic multi-site randomized controlled trials of SSRIs (including

sertraline,<sup>75</sup> fluoxetine,<sup>76</sup> paroxetine,<sup>77</sup> fluvoxamine,<sup>78</sup> and escitalopram<sup>79</sup>) have demonstrated significant efficacy compared with placebo. The current literature recommends that pharmacotherapy should be continued in responders. The SSRIs have to be continued in the same doses (if possible) for a minimum of 1-2 years and may be lifetime in those with persistent symptoms and in those with multiple relapses after satisfactory acute treatment response.<sup>80</sup>

Generally, the SSRI medications are well tolerated and much safer than tricyclic antidepressants (TCA) especially if there is misuse or overdose. Adjusting the dose and finding the therapeutic window that provides the best clinical response can minimize side effects. The most common described side effects in various SSRIs include nausea, headache, gastrointestinal complaints, drowsiness, or insomnia.<sup>81</sup>

## References

- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Text Revision (DSM-IV-TR). Washington (DC): American Psychiatric Association; 2000.
- Hollander E. Obsessive-Compulsive Related Disorders. Washington (DC): American Psychiatric Press; 1993.
- Swedo S, Rapoport J. Phenomenology and differential diagnosis of obsessive-compulsive disorder in children and adolescents. In: Rapoport JL, editors. Obsessive-Compulsive Disorder in Children and Adolescents. Washington (DC) American Psychiatric Press; 1989. p. 13.
- Hollander E, Wong C. Psychosocial functions and economic costs of obsessive-compulsive disorder. *CNS Spectr* 1998; 3 (S1): 48-58.
- Geller DA, Biederman J, Jones J, Shapiro S, Schwartz S, Park K. Obsessive-compulsive disorder in children and adolescents: a review. *Harv Rev Psychiatry* 1998; 5: 260-273.
- Grabill K, Merlo L, Duke D, Harford KL, Keeley ML, Geffken GR, et al. Assessment of obsessive-compulsive disorder: a review. *J Anxiety Disord* 2008; 22: 1-17.
- Zohar AH. The epidemiology of obsessive-compulsive disorder in children and adolescents. *Child Adolesc Psychiatr Clin N Am* 1999; 8: 445-460.
- Kolada JL, Bland RC, Newman SC. Epidemiology of psychiatric disorders in Edmonton. Obsessive-compulsive disorder. *Acta Psychiatr Scand Suppl* 1994; 376: 24-35.
- Practice parameters for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. AACAP. *J Am Acad Child Adolesc Psychiatry* 1998; 37 (10 Suppl): 27S-45S. Review.
- Hanna GL. Demographic and clinical features of obsessive-compulsive disorder in children and adolescents. *J Am Acad Child Adolesc Psychiatry* 1995; 34: 19-27.
- Hollander E, Kwon JH, Stein DJ, Broatch J, Rowland CT, Himelein CA. Obsessive-compulsive and spectrum disorders: overview and quality of life issues. *J Clin Psychiatry* 1996; 57 Suppl 8: 3-6.
- Fontenelle LF, Hasler G. The analytical epidemiology of obsessive-compulsive disorder: risk factors and correlates. *Prog Neuropsychopharmacol Biol Psychiatry* 2008; 32: 1-15.
- Flament MF, Whitaker A, Rapoport JL, Davies M, Berg CZ, Kalikow K, et al. Obsessive-compulsive disorder in adolescence: an epidemiological study. *J Am Acad Child Adolesc Psychiatry* 1988; 27: 764-771.
- Rasmussen SA, Eisen J. Epidemiology of obsessive-compulsive disorder. *J Clin Psychiatry* 1990; 53 (Suppl): 10-14. Review.
- Piacentini J, Bergman RL. Obsessive-compulsive disorder in children. *Psychiatr Clin North Am* 2000; 23: 519-533.
- Baer L. Factor analysis of symptom subtypes of obsessive-compulsive disorder and their relation to personality and tic disorders. *J Clin Psychiatry* 1994; 55 Suppl: 18-23.
- Rasmussen SA, Eisen JL. The epidemiology and clinical features of obsessive-compulsive disorder. *Psychiatr Clin North Am* 1992; 15: 743-758.
- Mahgoub OM, Abdel-Hafeiz HB. Pattern of obsessive-compulsive disorder in eastern Saudi Arabia. *Br J Psychiatry* 1991; 158: 840-842.
- Westenberg HG, Fineberg NA, Denys D. Neurobiology of obsessive-compulsive disorder: serotonin and beyond. *CNS Spectr* 2007; 12 (2 Suppl 3): 14-27.
- Swerdlow NR. Obsessive-compulsive disorder and tic syndromes. *Med Clin North Am* 2001; 85: 735-755.
- Whiteside SP, Port JD, Abramowitz JS. A meta-analysis of functional neuroimaging in obsessive-compulsive disorder. *Psychiatry Res* 2004; 132: 69-79.
- Hansen ES, Hesselbalch S, Law I, Bolwig TG. The caudate nucleus in obsessive-compulsive disorder. Reduced metabolism following treatment with paroxetine: a PET study. *Int J Neuropsychopharmacol* 2002; 5: 1-10.
- Rotge JY, Guehl D, Dilharreguy B, Tignol J, Bioulac B, Allard M, et al. Meta-analysis of brain volume changes in obsessive-compulsive disorder. *Biol Psychiatry* 2009; 65: 75-83.
- Rauch SL. Neuroimaging and neurocircuitry models pertaining to the neurosurgical treatment of psychiatric disorders. *Neurosurg Clin N Am* 2003; 14: 213-223, vii-viii.
- Garber HJ, Ananth JV, Chiu LC, Griswold VJ, Oldendorf WH. Nuclear magnetic resonance study of obsessive-compulsive disorder. *Am J Psychiatry* 1989; 146: 1001-1005.
- Murphy TK, Sajid MW, Goodman WK. Immunology of obsessive-compulsive disorder. *Psychiatr Clin North Am* 2006; 29: 445-469. Review.
- Snider LA, Swedo SE. Childhood-onset obsessive-compulsive disorder and tic disorders: case report and literature review. *J Child Adolesc Psychopharmacol* 2003; 13 Suppl 1: S81-S88.
- Snider LA, Swedo SE. PANDAS: current status and directions for research. *Mol Psychiatry* 2004; 9: 900-907. Review.
- Swedo SE, Schrag A, Gilbert R, Giovannoni G, Robertson MM, Metcalfe C, et al. Streptococcal infection, Tourette syndrome, and OCD: is there a connection? PANDAS: horse or zebra? *Neurology* 2010; 74: 1397-1398; author reply 1398-1399.
- Leonard HL, Swedo SE. Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS). *Int J Neuropsychopharmacol* 2001; 4: 191-198.
- Pato MT, Pato CN, Pauls DL. Recent findings in the genetics of OCD. *Clin Psychiatry* 2002; 63 Suppl 6: 30-33.
- Pauls DL. The genetics of obsessive-compulsive disorder: a review of the evidence. *Am J Med Genet C Semin Med Genet* 2008; 148: 133-139. Review.
- van Grootheste DS, Cath DC, Beekman AT, Boomsma DI. Twin studies on obsessive-compulsive disorder: a review. *Twin Res Hum Genet* 2005; 8: 450-458.
- Nestadt G, Samuels J, Riddle M, Bienvenu OJ 3rd, Liang KY, LaBuda M, et al. A family study of obsessive-compulsive disorder. *Arch Gen Psychiatry* 2000; 57: 358-363.
- Grabe HJ, Ruhrmann S, Ettelt S, Huht F, Hochrein A, Schulze-Rauschenbach S et al. Familiality of obsessive-compulsive disorder in nonclinical and clinical subjects. *Am J Psychiatry* 2006; 163: 1986-1992.

36. Hemmings SM, Stein DJ. The current status of association studies in obsessive-compulsive disorder. *Psychiatr Clin North Am* 2006; 29: 411-44. Review.
37. Mowrer OH. On the dual nature of learning: a reinterpretation of "conditioning" and "problem solving." *Harv Educ Rev* 1947; 17: 102-148.
38. Neziroglu F, Henricksen J, Yaryura-Tobias JA. Psychotherapy of obsessive-compulsive disorder and spectrum: established facts and advances, 1995-2005. *Psychiatr Clin North Am* 2006; 29: 585-604. Review.
39. Stein DJ. Obsessive-compulsive disorder. *Lancet* 2002; 360: 397-405. Review.
40. Leckman JF, Zhang H, Alsobrook JP, Pauls DL. Symptom dimensions in obsessive-compulsive disorder: toward quantitative phenotypes. *Am J Med Gen* 2001; 105: 28-30.
41. Attiullah N, Eisen JL, Rasmussen SA. Clinical features of obsessive-compulsive disorder. *Psychiatr Clin North Am* 2000; 23: 469-491.
42. Geller DA, Biederman J, Stewart SE, Mullin B, Farrell C, Wagner KD, et al. Impact of comorbidity on treatment response to paroxetine in pediatric obsessive-compulsive disorder: is the use of exclusion criteria empirically supported in randomized clinical trials? *J Child Adolesc Psychopharmacol* 2003; 13 Suppl 1: S19-S29.
43. Fireman B, Koran LM, Leventhal JL, Jacobson A. The prevalence of clinically recognized obsessive-compulsive disorder in a large health maintenance organization. *Am J Psychiatry* 2001; 158: 1904-1910.
44. Ivarsson T, Melin K, Wallin L. Categorical and dimensional aspects of co-morbidity in obsessive-compulsive disorder (OCD). *Eur Child Adolesc Psychiatry* 2008; 17: 20-31.
45. Breier A, Charney DS, Heninger GR. Agoraphobia with panic attacks. Development, diagnostic stability, and course of illness. *Arch Gen Psychiatry* 1986; 43: 1029-1036.
46. Rasmussen SA, Eisen JL. The epidemiology and clinical features of obsessive-compulsive disorder. In: Jenike MA, Baer L, Minichiello WE, editors. *Obsessive-Compulsive Disorders: Practical Management*. 3rd ed. St. Louis (MO): Mosby; 1998. p. 12-43.
47. Como PG, LaMarsh J, O'Brien KA. Obsessive-compulsive disorder in Tourette's syndrome. *Adv Neurol* 2005; 96: 249-261.
48. Leckman JF, Bloch MH, King RA. Symptom dimensions and subtypes of obsessive-compulsive disorder: a developmental perspective. *Dialogues Clin Neurosci* 2009; 11: 21-33.
49. Bloch MH, Landeros-Weisenberger A, Rosario MC, Pittenger C, Leckman JF. Meta-analysis of the symptom structure of obsessive-compulsive disorder. *Am J Psychiatry* 2008; 165: 1532-1542.
50. Storch EA, Abramowitz J, Goodman WK. Where does obsessive-compulsive disorder belong in DSM-V? *Depress Anxiety* 2008; 25: 336-347.
51. O'Sullivan RL, Mansueto CS, Lerner EA, Miguel EC. Characterization of trichotillomania. A phenomenological model with clinical relevance to obsessive-compulsive spectrum disorders. *Psychiatr Clin North Am* 2000; 23: 587-604.
52. Dell'Osso B, Altamura AC, Allen A, Marazziti D, Hollander E. Epidemiologic and clinical updates on impulse control disorders: a critical review. *Eur Arch Psychiatry Clin Neurosci* 2006; 256: 464-475. Review.
53. Chamberlain SR, Fineberg NA, Blackwell AD, Clark L, Robbins TW, Sahakian BJ. A neuropsychological comparison of obsessive-compulsive disorder and trichotillomania. *Neuropsychologia* 2007; 45: 654-662.
54. Tukul R, Keser V, Karali NT, Olgun TO, Calikusu C. Comparison of clinical characteristics in trichotillomania and obsessive-compulsive disorder. *J Anxiety Disord* 2001; 15: 433-441.
55. Geller DA, Biederman J, Faraone SV, Craddock K, Hagermoser L, Zaman N, et al. Attention deficit/hyperactivity disorder in children and adolescents with obsessive-compulsive disorder: fact or artifact? *J Am Acad Child Adolesc Psychiatry* 2002; 41: 52-58.
56. Geller DA, Coffey B, Faraone S, Hagermoser L, Zaman NK, Farrell CL, et al. Does comorbid attention-deficit/hyperactivity disorder impact the clinical expression of pediatric obsessive-compulsive disorder? *CNS Spectr* 2003; 8: 259-264.
57. Geller DA. Obsessive-compulsive and spectrum disorders in children and adolescents. *Psychiatr Clin North Am* 2006; 29: 353-370 Review.
58. Halmi KA, Sunday SR, Klump KL, Strober M, Leckman JF, Fichter M, et al. Obsessions and compulsions in anorexia nervosa subtypes. *Int J Eat Disord* 2003; 33: 308-319.
59. Eisen JL, Phillips KA, Coles ME, Rasmussen SA. Insight in obsessive-compulsive disorder and body dysmorphic disorder. *Compr Psychiatry* 2004; 45: 10-15.
60. Nechmad A, Ratzoni G, Poyurovsky M, Meged S, Avidan G, Fuchs C, et al. Obsessive-compulsive disorder in adolescent schizophrenia patients. *Am J Psychiatry* 2003; 160: 1002-1004.
61. Dell'Osso B, Altamura AC, Mundo E, Marazziti D, Hollander E. Diagnosis and treatment of obsessive-compulsive disorder and related disorders. *Int J Clin Pract* 2007; 61: 98-104. Review.
62. Young J, Zarcone J, Holsen L, Anderson MC, Hall S, Richman D, et al. A measure of food seeking in individuals with Prader-Willi syndrome. *J Intellect Disabil Res* 2006; 50: 18-24.
63. Garnaat SL, Norton PJ. Factor structure and measurement invariance of the Yale-Brown Obsessive Compulsive Scale across four racial/ethnic groups. *J Anxiety Disord* 2010; 24: 729-733.
64. Freeman J, Flessner CA, Garcia A. The Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity for use among 5 to 8 year olds with obsessive-compulsive disorder. *J Abnorm Child Psychol* 2011; 39: 877-883.
65. El-Sayegh S, Bea S, Agelopoulos A. Obsessive-compulsive disorder: unearthing a hidden problem. *Cleve Clin J Med* 2003; 70: 824-825, 829-830, 832-833.
66. Watson HJ, Rees CS. Meta-analysis of randomized, controlled treatment trials for pediatric obsessive-compulsive disorder. *J Child Psychol Psychiatry* 2008; 49: 489-498.
67. Meyer V. Modification of expectations in cases with obsessional rituals. *Behav Res Ther* 1966; 4: 273-280.
68. Foa EB, Liebowitz MR, Kozak MJ, Davies S, Campeas R, Franklin ME, et al. Randomized, placebo controlled trial of exposure and ritual prevention, clomipramine and their combination in the treatment of obsessive-compulsive disorder. *Am J Psychiatry* 2005; 162: 151-161.
69. Riddle M. Obsessive-compulsive disorder in children and adolescents. *Br J Psychiatry Suppl* 1998; (35): 91-96.
70. Miguel EC, Rauch SL, Jenike MA. Obsessive-compulsive disorder. *Psychiatr Clin North Am* 1997; 20: 863-883.
71. Freeman JB, Garcia AM, Fucci C, Karitani M, Miller L, Leonard HL. Family-based treatment of early-onset obsessive-compulsive disorder. *J Child Adolesc Psychopharmacol* 2003; 13 Suppl 1: S71-S80.
72. Barrett P, Healy-Farrell L, March JS. Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: a controlled trial. *J Am Acad Child Adolesc Psychiatry* 2004; 43: 46-62.

73. Waters TL, Barrett PM, March JS. Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: preliminary findings. *Am J Psychother* 2001; 55: 372-387.
74. Freeman JB, Choate-Summers ML, Moore PS, Garcia AM, Sapyta JJ, Leonard HL, et al. Cognitive behavioral treatment for young children with obsessive-compulsive disorder. *Biol Psychiatry* 2007; 61: 337-343. Review.
75. March JS, Biederman J, Wolkow R, Safferman A, Mardekian J, Cook EH, et al. Sertraline in children and adolescents with obsessive-compulsive disorder: a multicenter randomized controlled trial. *JAMA* 1998; 280: 1752-1756.
76. Geller DA, Hoog SL, Heiligenstein JH, Ricardi RK, Tamura R, Kluszynski S, et al. Fluoxetine treatment for obsessive-compulsive disorder in children and adolescents: a placebo-controlled clinical trial. *J Am Acad Child Adolesc Psychiatry* 2001; 40: 773-779.
77. Geller DA, Wagner KD, Emslie G, Murphy T, Carpenter DJ, Wetherhold E, et al. Paroxetine treatment in children and adolescents with obsessive-compulsive disorder: a randomized, multicenter, double-blind, placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry* 2004; 43: 1387-1396.
78. Riddle MA, Reeve EA, Yaryura-Tobias JA, Yang HM, Claghorn JL, Gaffney G, et al. Fluvoxamine for children and adolescents with obsessive-compulsive disorder: a randomized, controlled, multicenter trial. *J Am Acad Child Adolesc Psychiatry* 2001; 40: 222-229.
79. Stein DJ, Andersen EW, Tonnoir B, Fineberg N. Escitalopram in obsessive-compulsive disorder: a randomized, placebo-controlled, paroxetine-referenced, fixed-dose, 24-week study. *Curr Med Res Opin* 2007; 23: 701-711.
80. Math SB, Janardhan Reddy YC. Issues in the pharmacological treatment of obsessive-compulsive disorder. *Int J Clin Pract* 2007; 61: 1188-1197.
81. Kaplan A, Hollander E. A review of pharmacologic treatments for obsessive-compulsive disorder. *Psychiatr Serv* 2003; 54: 1111-1118.

#### Related topics

Gad EM. Socio-demographic study of obsessive compulsive disorder in Qatar. *Neurosciences (Riyadh)* 2004; 9: 295-298.

Al-Sughayir MA. In-patient treatment for resistant obsessive-compulsive disorder. *Neurosciences (Riyadh)* 2000; 5: 128-130.