In a preliminary study, home-based bibliotherapy reduced nighttime fears and avoidant behaviors in young children. The treatment, which involves reading to the child at bedtime and conducting simple exposure exercises, may come to be considered a first-line approach for mild-to-moderate nighttime fears.

**Background:** The treatment is based on a book called *Uncle Lightfoot, Flip That Switch: Overcoming Fear of the Dark.* The book, designed to be read to the child by an adult at bedtime, tells the story of a young boy who overcomes his fear of the dark by playing exposure games with a supportive character (Uncle Lightfoot). The volume includes a parent guidebook and encourages exercises such as looking for a toy in the dark and identifying sounds.

**Methods:** Study participants were 9 children, aged 5–7 years, with a primary or secondary diagnosis of specific phobia. Children and their mothers visited the study clinic for initial evaluation. Following a randomly selected 1, 2, or 3 week baseline, they returned to receive the book and instructions. Response was evaluated at completion (4 weeks) and again 1 month post treatment. Mothers were instructed to read chapters from the book to the child each evening and to play as many of the exposure games as the child was willing. The primary study outcome was change from baseline in the Anxiety Disorders Interview Schedule for Children, Parent Version (ADIS-P).

**Results:** All families completed the treatment, and 6 of the parents read through the book at least twice, as recommended. Mothers read to the child an average of nearly 6 nights during the first week and about 4 nights per week afterward. Children showed significant change in ADIS-P symptoms from baseline to 4 weeks (p=0.011) and to 1-month post treatment (p=0.011), with improvement remaining stable during the follow-up month. Estimates of reliable change showed that 8 of the 9 children exceeded clinical cutoffs for reliable change in specific phobia, and 3 reached the non-clinical range post treatment.
Children also showed reduction in avoidant behaviors, which was operationally defined as inability to sleep in their own bed. They slept alone a mean of 2 nights per week before treatment and 5 nights afterward. The children also showed significant improvement on several standardized measures of fear of the dark, nighttime fears, separation anxiety, and fear-related behavior. One parent reported only slight improvement in their child’s fear of the dark, 5 indicated moderate improvement, 2 reported major improvement, and 1 said the child was entirely free of their fear. Parents reported a high level of satisfaction with the treatment (mean score, 4.2 on a 5-point scale).

Discussion: Nighttime fears are extremely common in children and are not a separate diagnostic entity, but some children are affected seriously enough to qualify for a diagnosis of specific phobia. Cognitive behavioral therapy (CBT) is the accepted first-line treatment for childhood fear and anxiety. The present study provides initial support for bibliotherapy, an approach that may have superior efficacy to CBT for other anxiety disorders and in somewhat older children.

References:
1 Lewis K, Amatya K, Coffman M, Ollendick T: Treating nighttime fears in young children with bibliotherapy: evaluating anxiety symptoms and monitoring behavior change. *Journal of Anxiety Disorders* 2015;30 (March):103–112. From the University of Illinois at Chicago; and other institutions. Source of funding not stated. The authors did not include disclosure of potential conflicts of interest.

**Family-Based Therapy for Preadolescent Depression**

In a randomized trial, family-based interpersonal psychotherapy (FB-IPT) was effective in the treatment of depression in preadolescents.

Background: There have been few controlled studies of effective treatments for preadolescent depression. Cognitive behavioral therapy is promising, but there is a need for treatment that involves the parents and that addresses interpersonal impairment. FB-IPT is an adaptation of interpersonal psychotherapy that actively involves parents in weekly sessions and directly addresses parent–child conflicts and interpersonal impairment.

Methods: FB-IPT was compared with child-centered therapy (CCT) in 38 patients, aged 7–12 years, who sought treatment at a specialty clinic for youth depression. Patients were allowed to use medication during the trial; 2 met criteria for depression at enrollment despite continuing stable SSRI therapy and another 6 began SSRIs during the initial weeks of psychotherapy, with the investigators’ consent. Patients were randomly assigned in a 2:1 ratio to FB-IPT or CCT, the latter an effective supportive treatment that closely approximates usual depression treatment in community mental health. Both treatments were provided in 14 weekly sessions. For FB-IPT, the patient and 1 or both parents were seen either jointly or sequentially, depending on the phase of the intervention. Parents of children receiving CCT could attend the first 10 minutes of their child’s session but were not otherwise involved. The primary outcome measure was the Children’s Depression Rating Scale, Revised (CDRS-R), with a score <28 indicating remission.

Results: Children who received FB-IPT were more likely than those who received CCT to achieve remission post-treatment (66% vs. 31%; p=0.04). The FB-IPT group had lower CDRS-R scores (27 vs. 35; p=0.002) and superior outcomes on the child and parent versions of the Mood and Feelings Questionnaire.

A path analysis was conducted to determine whether the change in depression was the result of changes in various intermediate treatment outcomes. There were no indirect effects of changes in parent–child conflict on depression, and the mediating effect of reduced anxiety, while greater in FB-IPT, was not statistically significant. FB-IPT-related changes in social
impairment were larger than with CCT (p=0.001) and were linked with improvement in depression, thus partially accounting for the association of FB-IPT with relief of depressive symptoms.

**Discussion:** The results of this study support the advantage of FB-IPT over supportive therapy; its effects on mediating risk factors of anxiety and social impairment suggest that FB-IPT may act by addressing these mechanisms.

**Study Rating:**—15 (88%): This study met most criteria for a randomized controlled trial; however, only 60% of post-treatment assessments were conducted by blinded raters.

Dietz L, Weinberg R, Brent D, Mufson L: Family-based interpersonal psychotherapy for depressed preadolescents: examining efficacy and potential treatment mechanisms. *Journal of the American Academy of Child and Adolescent Psychiatry* 2015;54 (March):191–199. From the University of Pittsburgh School of Medicine, PA; and the Columbia University College of Physicians and Surgeons/New York State Psychiatric Institute. **Funded by the NIMH. Three authors disclosed potentially relevant financial relationships; the fourth author declared no conflicts of interest.**

**Safety Signals with Antipsychotics**

Analysis of data from the FDA Adverse Event Reporting System (FAERS) suggests that antipsychotics are among the top 5 suspect therapeutic drug classes in young patients. Because antipsychotics are being prescribed with increasing regularity for children and adolescents, a data mining study was undertaken to assess the association between these drugs and serious, potentially fatal adverse events.

**Methods:** More than 4.5 million FAERS reports spanning late 1997 through mid-2011 were screened to identify cases of neuroleptic malignant syndrome (NMS), QT prolongation, leukopenia, and suicide attempts in children aged <12 years who were treated with haloperidol or a second-generation antipsychotic. Four different data mining algorithms, in use by various national regulatory bodies and the World Health Organization, were used to identify signals—events reported at a higher frequency of association than expected. An adverse event was considered drug related when ≥1 of the algorithms detected a signal.

**Results:** The number of reported cases of each adverse event was small (<15 each); nevertheless, many safety signals were detected. (See table.) Signals for NMS were identified for all drugs except clozapine and ziprasidone, but were larger for haloperidol and aripiprazole than for the other drugs. For QT prolongation, signals were detected only for risperidone and, more strongly, ziprasidone. Leukopenia was associated with quetiapine, risperidone, and especially clozapine. Suicide attempts were associated with haloperidol, olanzapine, quetiapine, risperidone, and aripiprazole.

**Discussion:** Recent studies suggest antipsychotics are not homogeneous with regard to efficacy or safety. The present analysis extends this conclusion to rare, potentially fatal adverse events. Research should be continued in order to obtain a large quantity and variety of data.


**Drug Trade Names:** aripiprazole—Abilify; clozapine—Clozaril; haloperidol—Haldol; olanzapine—Zyprexa; quetiapine—Seroquel; risperidone—Risperdal; ziprasidone—Geodon
Mazindol for ADHD: Pilot Study

Treatment with the catecholaminergic agonist mazindol reduced ADHD symptoms in an open-label pilot study in children who had experienced poor response with stimulants.

**Background:** Mazindol works by blocking norepinephrine and dopamine reuptake, as do stimulants, but has a lower potential for abuse. It is available in Canada and Europe for the short-term treatment of obesity. Mazindol is available in the U.S. as an orphan drug for the treatment of Duchenne muscular dystrophy. It has been studied in sleep disorders such as narcolepsy.

**Methods:** Study participants were 21 children, aged 9–12 years, with impairing symptoms of ADHD that required a change from their current medication. All had been poor responders to methylphenidate for ≥6 months. After a 10-day washout of all ADHD medications, the children received 1 mg/day mazindol for 7 days. Pharmacokinetic studies were performed starting after the first dose. The primary outcome measure was change from baseline in mean ADHD Rating Scale-IV (ADHD-RS-IV) total score.

**Results:** ADHD-RS-IV total scores decreased from a mean of 43 before treatment to 18.9 on the last day (p<0.0001). Scores returned to baseline levels a week after mazindol discontinuation. A similar pattern was observed for the Conners Parent Rating Scale–Revised: Long (p<0.0001). The mean Clinical Global Impression–Severity score decreased from 5.6 to 3.1. Only 2 children had an illness severity score of ≥5 (markedly ill) while on treatment, and 12 had a score of ≤3 (mildly ill). Twelve patients had a CGI–Improvement rating of much or very much improved.

A total of 19 patients experienced adverse events, but none was severe enough to discontinue treatment. One-third had decreased appetite, which was severe but transient in 4 patients. There were no reports of insomnia or changes in blood pressure, heart rate, or ECG parameters.


**PANDAS/PANS**

In the late 1990s, researchers at the NIH described a syndrome of acute-onset tics and/or OCD symptoms associated with a streptococcal infection. Controversy about the validity of this syndrome—termed Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS)—continues to exist in spite of supporting biological models and effective treatment studies. More recently it was found that children without a documented streptococcal infection experienced a similar array of acute-onset neuropsychiatric symptoms, and the PANDAS concept was expanded to include nonstreptococcal infection and re-termed Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS). The *Journal of Child and Adolescent Psychopharmacology* recently published a theme issue on PANDAS/PANS, which includes information on the clinical presentation and recommendations for clinical evaluation of suspected PANDAS/PANS. In addition, the issue includes open and controlled treatment results, which are summarized in the following stories in this issue of *Child & Adolescent Psychiatry Alerts*.

Chang K, Koplewicz H, Steingard R: Special issue on pediatric acute-onset neuropsychiatric syndrome. *Journal of Child and Adolescent Psychopharmacology* 2015;25 (1):1–2. From Stanford University School of Medicine, CA; and the Child Mind Institute, New York, NY. The authors did not include disclosure of potential conflicts of interest.

**Cefdinir for Tics/OCD**

Results of a preliminary, randomized, controlled trial suggest that the cephalosporin antibiotic cefdinir may reduce symptoms of OCD and tics in young patients with recent-onset symptoms.
Methods: Study subjects were 20 children, aged 4–13 years (mean age, 7.5 years; 75% male), with new onset tics or OCD symptoms with (n=14) or without (n=6) evidence of an infectious trigger within the previous 6 months. Participants were randomized to receive double-blind treatment with either 14 mg/kg/day cefdinir or placebo for 30 days. OCD symptoms were evaluated using the Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS) and then analyzed by symptom group (i.e., OCD or tics). Phonic and motor tics were measured with the Yale Global Tic Severity Scale (YGTSS).

Results: In the group of children who presented with OCD symptoms, mean CY-BOCS scores decreased from 22.7 at baseline to 14.8 at 30 days in the cefdinir group and from 18.6 to 13.9 in the placebo group. Although the difference between the groups was not statistically significant, within-group effect sizes* were 1.22 for active treatment, compared with 0.51 for placebo. In the children who presented with tics, YGTSS scores decreased from a mean of 20.4 to 10.9 in the cefdinir group and from 13.5 to 13.4 in the placebo group. Within-group effect sizes were 0.97 and 0.01 in the groups, respectively, but again the between-group difference was not significant.

Four patients (2 in each treatment group) experienced a >50% decrease in OCD symptoms, and 2 patients receiving cefdinir experienced dramatic improvements in tic severity (YGTSS decrease of 20 points). All of the patients with large symptom reductions entered the study with both OCD symptoms and tics.

Discussion: Although the etiology of OCD and tics remains unclear, infectious or immune-based etiology has been implicated for some patients. While preliminary and not statistically significant, the results of this study suggest that antibiotic treatment may be effective for these patients. The large within-group treatment effects appear to warrant further study in fully-powered samples.

Study Rating*—17 (100%): This study met all criteria for a randomized controlled trial.

Murphy T, Parker-Athill C, Lewin A, Storch E, et al: Cefdinir for recent-onset pediatric neuropsychiatric disorders: a pilot randomized trial. Journal of Child and Adolescent Psychopharmacology 2015; 25 (1):57–64. From The University of South Florida, Tampa. Funded by the National Alliance for Research on Schizophrenia and Affective Disorders (NARSAD). Four study authors disclosed relationships with commercial sources; the remaining 2 authors declared no conflicts of interest.

*See Reference Guide.

IV Immunoglobulin for PANDAS

Children with PANDAS have been shown to improve with intravenous immunoglobulin (IVIG) therapy, but long-term outcomes have not previously been reported. To address the issue of long-term efficacy, case files from a clinical practice specializing in the treatment of PANDAS were reviewed.

A total of 12 youths with a confirmed PANDAS diagnosis received IVIG and had sufficient follow-up data for inclusion in the case series. The patients, aged 7–16 years, all underwent IVIG after other treatments—e.g., antibiotics, antidepressants, cognitive behavioral therapy, and steroid bursts—failed to control their neuropsychiatric symptoms. IVIG therapy was completed in a single day. Most patients (9 of 12; 75%) experienced rapid and dramatic resolution of their symptoms after IVIG. One patient experienced remission of symptoms at a slower pace (approximately 12 months), and 2 patients required a second IVIG infusion to achieve complete recovery. As PANDAS is an episodic disorder, recurrence of symptoms is expected. Five patients required a second course of IVIG therapy for recurrence of tics/OCD during follow-up. Long-term follow-up data were available for 11 of the 12 patients, all of whom were reportedly in remission or symptom free at last contact after a range of 12 months to 7 years.
In these 12 patients, IVIG was used as part of a multimodal treatment plan that included ongoing antibiotic prophylaxis and/or other therapies. However, all patients had undergone unsuccessful treatment with other therapies before IVIG, suggesting that the immunomodulatory treatment produced the beneficial effects.

Kovacevic M, Grant P, Swedo S: Use of intravenous immunoglobulin in the treatment of twelve youths with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections. *Journal of Child and Adolescent Psychopharmacology* 2015;25 (1):65–69. From Loyola University School of Medicine, Maywood, IL; and the NIMH, Bethesda, MD. The authors declared no conflicts of interest.

**Plasma Apheresis for PANDAS**

The neuropsychiatric symptoms characteristic of PANDAS have been hypothesized to stem from post-infection autoimmunity, mediated through cross-reactive antibodies. Theoretically, removing the offending autoantibodies should produce symptomatic improvements.

**Methods:** Between 2009 and 2013, 40 young patients received therapeutic plasma apheresis (TPA) for severe PANDAS at a single university hospital. Follow-up information was available for 35 patients (mean age at TPA, 11.5 years; 23 boys). All patients had received antibiotic therapy without symptom relief, and most had not experienced response with previous steroids (n=5) or IVIG (n=17). Antibiotic prophylaxis was continued throughout the TPA protocol, which involved insertion of a central line and administration of three 1.5 volume therapeutic exchanges over 3–5 days. Long-term follow-up ranged from 6 months to >5 years.

**Results:** At baseline, 34 of the 35 children were experiencing OCD symptoms. In the 6 months following TPA, 8 patients continued to experience OCD. Tic symptoms were present in 22 patients at baseline, but at 6 months only 6 patients continued to experience them. At the 6-month evaluation, parents reported their children’s symptoms had decreased by an average of 65%. At longer term follow-up, parents reported a 78% decrease in symptoms. All other evaluated symptoms (e.g., anxiety, anorexia, behavioral regression, depressed mood) also showed substantial improvement, with some of the most worrisome decreasing to negligible levels. There was no correlation between symptom duration and TPA response. Transient adverse effects ranged from tingling lips to vasovagal reactions, but none were severe. Two subjects experienced bleeding at the central line site.

**Discussion:** Results of the present study support TPA as a safe and effective treatment for PANDAS in young patients. However, because TPA is an invasive procedure, it should be reserved for severely affected patients.

Latimer M, L’Etoile N, Seidlitz J, Swedo S: Therapeutic plasma apheresis as a treatment for 35 severely ill children and adolescents with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections. *Journal of Child and Adolescent Psychopharmacology* 2015;25 (1):70–75. From Georgetown University School of Medicine, Washington, DC; and other institutions. The authors declared no conflicts of interest.

**Reference Guide**

**Effect Size:** The effect size represents the amount of change in outcome that can be attributed to treatment, where 0.2 indicates a small effect, 0.5 a medium effect, and 0.8 a large effect. It is relatively independent of clinical significance and large effect sizes do not ensure treatment efficacy.

**Study Rating:** A measure of how well a study conforms to quality standards. The study rating uses a checklist system based on the comprehensive Strength of Evidence Report from the Evidence-based Practice Center Program of the Agency for Healthcare Research and Quality (AHRQ). The rating checklists have been posted at www.alertpubs.com.