Sertraline in Children and Adolescents With Obsessive-Compulsive Disorder
A Multicenter Randomized Controlled Trial

John S. March, MD, MPH; Joseph Biederman, MD; Robert Wolkow, MD; Allan Saferman, MD; Jack Mardekian, PhD; Edwin H. Cook, MD; Neal R. Cutler, MD; Roberto Dominguez, MD; James Ferguson, MD; Betty Muller, MD; Robert Riesenberg, MD; Murray Rosenthal, DO; Floyd R. Sallee, MD, PhD; Hans Steiner, MD; Karen D. Wagner, MD, PhD

Context.—The serotonin reuptake inhibitors are the treatment of choice for patients with obsessive-compulsive disorder; however, empirical support for this assertion has been weaker for children and adolescents than for adults.

Objective.—To evaluate the safety and efficacy of the selective serotonin reuptake inhibitor sertraline hydrochloride in children and adolescents with obsessive-compulsive disorder.

Design.—Randomized, double-blind, placebo-controlled trial.

Patients.—One hundred eighty-seven patients: 107 children aged 6 to 12 years and 80 adolescents aged 13 to 17 years randomized to receive either sertraline (53 children, 39 adolescents) or placebo (54 children, 41 adolescents).

Setting.—Twelve US academic and community clinics with experience conducting randomized controlled trials.

Intervention.—Sertraline hydrochloride was titrated to a maximum of 200 mg/d during the first 4 weeks of double-blind therapy, after which patients continued to receive this dosage of medication for 8 more weeks. Control patients received placebo.

Main Outcome Measures.—The Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS), the National Institute of Mental Health Global Obsessive Compulsive Scale (NIMH GOCS), and the NIMH Clinical Global Impressions of Severity of Illness (CGI-S) and Improvement (CGI-I) rating scales.

Results.—In intent-to-treat analyses, patients treated with sertraline showed significantly greater improvement than did placebo-treated patients on the CY-BOCS (adjusted mean, −6.8 vs −3.4, respectively; P = .005), the NIMH GOCS (−2.2 vs −1.3, respectively; P = .02), and the CGI-I (2.7 vs 3.3, respectively; P = .002) scales. Significant differences in efficacy between sertraline and placebo emerged at week 3 and persisted for the duration of the study. Based on CGI-I ratings at end point, 42% of patients receiving sertraline and 26% of patients receiving placebo were very much or much improved. Neither age nor sex predicted response to treatment. The incidence of insomnia, nausea, agitation, and tremor were significantly greater in patients receiving sertraline; 12 (13%) of 92 sertraline-treated patients and 3 (3.2%) of 95 placebo-treated patients discontinued prematurely because of adverse medical events (P = .02). No clinically meaningful abnormalities were apparent on vital determinations, laboratory findings, or electrocardiographic measurements.

Conclusion.—Sertraline appears to be a safe and effective short-term treatment for children and adolescents with obsessive-compulsive disorder.

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Common obsessions are generally accompanied by distressing negative affects, such as fear, disgust, doubt, or a feeling of incompleteness, and include contamination fears, scrupulosity, fear of harm to self or others, symmetry urges, or hoarding urges. Not surprisingly, persons with OCD typically attempt to ignore, suppress, or neutralize obsessive thoughts and associated feelings by performing compulsions, which are repetitive, purposeful behaviors that are usually performed according to certain rules or in a stereotyped fashion to temporarily neutralize or alleviate obsessions and their accompanying dysphoric affects. Compulsions can be observable behaviors (eg, hand washing) or covert mental acts (eg, counting). Among children and adolescents with OCD, few receive a correct diagnosis and even fewer receive appropriate treatment. An extensive empirical literature demonstrates that the potent serotonin reuptake inhibitors (SRIs) clomipramine hydrochloride, fluoxetine, fluvoxamine, paroxetine, and sertraline hydrochloride are effective treatments for adults with OCD. Although empirical support is more limited, pharmacotherapy for children and adolescents with OCD also relies on SRIs. The earliest pediatric studies were conducted with the tricyclic compound clomipramine. In the mid 1980s, Flament et al reported that clomipramine was statistically superior to...
placebo in a placebo-controlled, double-blind, crossover study. Leonard et al. then showed that clomipramine was superior to the predominantly noradrenergic reuptake inhibitor desipramine hydrochloride. Subsequently, an 8-week multicenter, double-blind, parallel comparison of clomipramine vs placebo led to US Food and Drug Administration approval of clomipramine for the treatment of OCD in children and adolescents aged 10 years and older.6

Unfortunately, clomipramine causes a wide spectrum of anticholinergic, antihistaminergic, and antiadrenergic adverse effects, including excessive sedation, weight gain, adverse cardiovascular effects, and an increased risk for drug-induced seizures.14 These difficulties encouraged the search for more effective and better-tolerated treatments for young persons with OCD.15 One such agent is the selective serotonin reuptake inhibitor (SSRI) sertraline, a naphthyloplamino compound that specifically blocks neuronal reuptake of serotonin via competitive inhibition at the presynaptic serotonin transporter.16 Controlled trials of sertraline in adults with OCD demonstrate that sertraline is more effective than placebo at doses ranging from 50 to 200 mg and that benefits are maintained with continued drug treatment.17 Controlled studies of fluoxetine and fluvoxamine in pediatric OCD suggest benefits comparable with those seen with clomipramine.18 As yet, to our knowledge there have been no published studies regarding the safety and efficacy of sertraline in pediatric OCD. We report the results of a 12-week, multicenter, double-blind, placebo-controlled, randomized, parallel-group trial of sertraline vs placebo in children and adolescents aged 6 to 17 years with OCD. The primary hypothesis was that sertraline would prove to be a well-tolerated and effective short-term treatment for pediatric OCD.

**METHODS**

**Experimental Design**

The trial began with a 1-week single-blind placebo lead-in to eliminate placebo responders even though placebo responses in pediatric OCD appear minimal.20 Following the placebo lead-in, patients were randomized within site to 12 weeks of double-blind flexible-dose treatment using a computer-generated randomization algorithm. To ensure that the age distribution was similar for each treatment condition, patients were stratified into 2 age groups: children (aged 6-12 years) and adolescents (aged 13-17 years). Twelve sites representing all major geographic regions in the United States participated in the study, which passed human subjects review at each of the participating institutions. All investigators obtained assent of the child or adolescent and written informed consent from parents or legal guardians.

**Inclusion and Exclusion Criteria**

Patients were male and female outpatients aged 6 to 17 years who met full Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R) diagnostic criteria for OCD on clinical interview. At the baseline visit, patients were required to have a score of at least 7 on the National Institute of Mental Health Global Obsessive Compulsive Rating Scale (NIMH GOCS), indicating at least moderate impairment in global functioning from OCD, and a score of 17 or less plus a score of 0 (none) or 1 (minimal) on item 1 (depressed mood) of the 24-item Hamilton Depression Scale, indicating the absence of significant depression. Baseline electrocardiographic and laboratory results were required to be normal or not clinically significant if outside the normal range.

Patients having a primary psychiatric disorder other than OCD on clinical interview were excluded, as were those with medical contraindications to treatment with sertraline or who had participated in a previous sertraline study or been treated with sertraline. Treatment with a neuroleptic, anxiolytic, or antidepressant medication within 2 weeks (or fluoxetine within 5 weeks) prior to the initiation of double-blind treatment or concomitant therapy with any other psychotropic medication was prohibited. Adolescent females of childbearing potential were required to have a negative result for a serum gonadotropin pregnancy test on day 1 of the placebo lead-in phase. Patients were not permitted to receive behavior therapy or any other form of psychotherapy during the course of the study.

**Medication Procedures**

Sertraline hydrochloride and pill placebo were packaged in identical blister packs of 25-mg sertraline hydrochloride tablets or identical placebo tablets. The starting dosage for both active treatment and placebo was 25 mg/d for children and 50 mg/d for adolescents. To maximize efficacy, although perhaps at the cost of more adverse effects in those treated with sertraline, doses were titrated upward in a forced titration procedure by 50 mg/wk to a maximum dosage of 200 mg/d or their maximum tolerated dose during the first 4 weeks of double-blind treatment following a predefined dosing schedule. Further dosage adjustment was permitted only in the event of dose-limiting adverse experiences.

**Measures**

The primary efficacy measures were the Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS), the NIMH GOCS, and the NIMH Clinical Global Impression of Severity of Illness (CGI-S) and Improvement (CGI-I) scales. The CY-BOCS is identical in form and scoring to the widely used adult Yale-Brown Obsessive Compulsive Scale, but the questions are slightly modified for age appropriateness.21 The CY-BOCS scale ranges from 0 to 40, with a score of 20 indicating moderate severity of obsessive and compulsive symptoms and a score of 10 or below indicating subclinical OCD. The NIMH GOCS has been extensively used in both adult22 and pediatric23 OCD trials. It assesses severity of OCD symptoms in relation to their functional impact.24 Scores of 1 to 3 indicate minimal impairment, scores of 7 or more indicate clinically meaningful OCD symptoms, and scores of 13 to 15 indicate very severe obsessive and compulsive behaviors. The NIMH CGI scales provided clinician-rated overall summary: the CGI-S scale ranges from 1 (normal, not at all ill) to 7 (extremely ill) and the CGI-I scale ranges from 1 (very much improved judgments) to 7 (very much worse judgments).

Efficacy measures were obtained on day 1 of the placebo lead-in phase, 1 week later at the end of the placebo lead-in phase (baseline), and at the end of weeks 1, 2, 4, 6, 8, 10, and 12 of double-blind treatment (or at the time of early termination). Vital signs (eg, blood pressure, pulse) and body weight were recorded at every study visit as were all adverse experiences volunteered by the patient or observed by the investigator. Blood samples for routine hematology and serum chemistry studies and urine samples for routine urinalysis were obtained on day 1 of the placebo lead-in phase and at the end of weeks 1, 2, 4, 6, 8, 10, and 12 of double-blind treatment. A 12-lead electrocardiogram was obtained on day 1 of the placebo lead-in phase and at the end of weeks 1, 4, and 12 of double-blind treatment.

**Statistical Analyses**

For the efficacy parameters, analysis of covariance models were used, including baseline and any additional postbaseline efficacy data. Except for the CGI-I score, the baseline value was added to the model as a covariate so that the full statistical model included terms for treatment, site, interaction-by-site, age group (6-12 years and 13-17 years), sex, and the interactions of age group and treatment, sex and age group, sex and treatment, and sex, age group, and treatment. Age, weight, Hamilton Depression Scale score, and duration of illness were compared at baseline between the treatment groups using analyses of variance with terms for site and treatment group. Sex, race, and socioeconomic status were compared us-
between treatment groups using the Wil- point in body weight was compared be- test. Mean change from baseline to end treatment groups were compared using ratory and vital sign parameters between treatment groups. Ninety-two patients (53 chil- and all received at least 1 dose of study medication. Forty-two patients (57%) of 53 children and 81 (82%) of 39 adolescents were treated and 180 mg/d, respectively. Among those treated with sertraline hydrochloride, 30 (57%) of 53 children and 32 (82%) of 39 ado- lescents were receiving a dosage of 200 mg/d at end point. Trough plasma levels of sertraline and its primary active metabo- lites, desmethylsertraline, normalized for body weight, were not significantly corre- lated with age or sex and did not predict clinical response in those treated with ser- traline.

Efficacy

The effects of sertraline and placebo on the CY-BOCS and NIMH GOCS, CGI-S, and CGI-I ratings at end point are summarized in Table 2. On the most conservative efficacy analyses, sertra- line-treated patients exhibited signifi- cantly greater improvement than those taking placebo on the CY-BOCS (P = .005) and NIMH GOCS (P = .02) and CGI-I scale (P = .002). There was a trend favoring sertraline over placebo at end point on the NIMH CGI-S scale that failed to reach the threshold for statis- tical significance (P = .09). Similar but slightly more robust outcomes favoring sertraline were seen in patients who completed all 12 weeks of the study.

Table 2.—Baseline Comorbidity

<table>
<thead>
<tr>
<th>Comorbid Disorders</th>
<th>Sertraline Hydrochloride</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
<td>13 (14%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Depression</td>
<td>22 (24%)</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>10 (11%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Depressive�</td>
<td>14 (15%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Attention-deficit/</td>
<td>12 (13%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Hyperactivity disorder</td>
<td>7 (8%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Tic disorder</td>
<td>5 (5%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>13 (14%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

**Table 1.—Baseline Comorbidity**

<table>
<thead>
<tr>
<th>No. (%) of Subjects</th>
<th>Sertraline Hydrochloride</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any comorbid disorder at baseline</td>
<td>19 (21)</td>
<td>17 (18)</td>
</tr>
<tr>
<td>Attention-deficit/</td>
<td>6 (7)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Hyperactivity disorder</td>
<td>2 (2)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Tic disorder</td>
<td>5 (5)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2 (2)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Depression</td>
<td>7 (8)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

RESULTS

Sample Characteristics

Figure 1 shows patient flow through all phases of the study. Two patients random- ized to receive sertraline were excluded from the data analyses reported herein. One received active medication and an- other withdrew consent during the pla- cebo lead-in phase. Full intent-to-treat ef- ficiency analyses including these 2 patients did not appreciably change the results on the main dependent measures. There were no placebo lead-in responders.

One hundred eighty-seven patients en- tered the double-blind phase of the study and all received at least 1 dose of study medication. Ninety-two patients (53 chil- dren and 41 adolescents) were random- ized to receive sertraline and 95 (54 chil- dren and 39 adolescents) were random- ized to receive placebo. The pooled mean age for sertraline and placebo treatment groups was 12.6 years (10.4 years in chil- dren and 15.5 years in adolescents). Among the children, the average duration of OCD was 3.4 years and 4.2 years for the sertraline and placebo groups, respec- tively. Among the adolescents, the average duration of OCD was 6.1 years and 5.5 years for the sertraline and pla- cebo groups, respectively. Mean baseline scores by treatment group for each of the efficacy measures reveal a patient sample with moderate to severe OCD. The mean CYBOCS score at baseline was 23.4 for patients randomized to sertraline and 22.2 for patients randomized to placebo. The mean NIMH-GOCS score at baseline was 9.2 for patients randomized to sertraline and 9.1 for patients randomized to pla- cebo. The mean CGI-S score was 4.7 for patients randomized to sertraline and 4.6 for patients randomized to placebo.

Age, race, sex, body weight, baseline OCD score, baseline depression score, comorbidity, socioeconomic status, and plasma sertraline and desmethylsertra- line levels did not predict the outcome of treatment.

Safety

The average length of treatment for the sertraline group was 74.8 days and for the placebo group it was 75.9 days of 94 pos- sible double-blind treatment days. Seventy-four (80%) of the 92 patients treated with sertraline and 82 (86%) of the 95 indi- viduals treated with placebo completed the 12 weeks of double-blind treatment. Of the 31 patients (18 in the sertraline group and 13 in the placebo group) who dis- continued treatment during the double- blind treatment period, only 3 sertraline- treated and 2 placebo-treated individuals discontinued the study because of insufficient clinical response.

As shown in Figure 1, 12 (13%) of 92 patients treated with sertraline and 3 (3.2%) of 95 placebo-treated patients discontinued treatment because of an adverse medical event (P = .02). Time to discontinuation did not differ between groups. Table 4 summarizes the inci- dence of adverse events that were statis- tically associated with sertraline in con- trast with placebo treatment. A pa- tient reporting more than 1 episode of the same complaint, even of differing se- verity, was counted once using the high- est level of severity. Among all adverse
Table 2.—Mean Change From Baseline to End Point in Efficacy Measures: Intent-to-Treat Analysis

<table>
<thead>
<tr>
<th>Efficacy Measure*</th>
<th>Adjusted Mean (SEM)</th>
<th>95% Confidence Interval (Sertraline vs Placebo)</th>
<th>P Value</th>
<th>Adjusted Mean (SEM)</th>
<th>95% Confidence Interval (Sertraline vs Placebo)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CY-BOCS Hydrochloride</td>
<td>-4.8 (0.87)</td>
<td>-7.4 to -2.2</td>
<td>.005</td>
<td>-4.0 (0.95)</td>
<td>-6.3 to -1.8</td>
<td>.004</td>
</tr>
<tr>
<td>Placebo</td>
<td>-3.4 (0.62)</td>
<td>-5.7 to -1.1</td>
<td>.005</td>
<td>-5.2 (0.83)</td>
<td>-7.5 to -2.9</td>
<td>.001</td>
</tr>
<tr>
<td>NIMH Global Obsessive Compulsive Scale</td>
<td>-2.2 (0.29)</td>
<td>-3.5 to -0.9</td>
<td>.03</td>
<td>-2.5 (0.32)</td>
<td>-3.6 to -1.4</td>
<td>.001</td>
</tr>
<tr>
<td>Placebo</td>
<td>-1.3 (0.27)</td>
<td>-2.6 to -0.1</td>
<td>.05</td>
<td>-1.5 (0.30)</td>
<td>-2.8 to -1.1</td>
<td>.001</td>
</tr>
<tr>
<td>NIMH CGI Improvement Scale</td>
<td>2.7 (0.14)</td>
<td>1.6 to 3.8</td>
<td>.002</td>
<td>2.6 (0.14)</td>
<td>1.5 to 3.7</td>
<td>.002</td>
</tr>
<tr>
<td>Placebo</td>
<td>3.3 (0.13)</td>
<td>2.3 to 4.3</td>
<td>.002</td>
<td>3.2 (0.13)</td>
<td>2.2 to 4.3</td>
<td>.002</td>
</tr>
<tr>
<td>NIMH CGI Severity of Illness Scale</td>
<td>-1.0 (0.14)</td>
<td>-2.0 to 0.0</td>
<td>.09</td>
<td>-1.2 (0.16)</td>
<td>-2.2 to 0.0</td>
<td>.01</td>
</tr>
<tr>
<td>Placebo</td>
<td>-0.7 (0.13)</td>
<td>-1.6 to 0.2</td>
<td>.09</td>
<td>-0.8 (0.14)</td>
<td>-1.8 to 0.2</td>
<td>.09</td>
</tr>
</tbody>
</table>

*CY-BOCS indicates the Children’s Yale-Brown Obsessive Compulsive Scale; NIMH, National Institute of Mental Health; and CGI, Clinical Global Impressions.

In what is, to our knowledge, the largest placebo-controlled trial of pharmacotherapy for pediatric OCD conducted to date, children and adolescents treated with sertraline fared better than those receiving placebo on 3 of the 4 main dependent measures. Statistically and clinically significant group mean differences emerged at week 3 and persisted for the duration of the study. Eighty percent of sertraline-treated patients and 86% of placebo-treated patients completed treatment. Insomnia, nausea, agitation, and tremor were more common in those receiving sertraline, and more sertraline-treated patients than placebo-treated patients discontinued treatment prematurely because of adverse events. No adverse effects attributable to sertraline use were apparent on vital sign measurement or laboratory or electrocardiographic studies. Thus, we conclude that sertraline appears to be a safe and effective short-term treatment for pediatric OCD.

Because this study used a forced upward titration procedure, no firm statement regarding the relationship between dose and overall efficacy, speed of improvement, or adverse effects can be made. However, experts generally agree that the SSRIs as a group are better tolerated than the nonselective SRI clomipramine. In a study of sertraline in adults with OCD, the most frequently occurring adverse events were nausea, insomnia, somnolence, diarrhea, and decreased libido. A similar adverse effect profile was noted in this study, with the extent of adverse effects in the sertraline group at least in part a function of rapid upward titration to maximum doses. Importantly, the present study failed to reveal significant differences in sertraline’s adverse effect profile for children (aged 6-12 years) or adolescents (aged 13-17 years). Thus, the same dosage regimen used in adults appears appropriate for children and adolescents, with dosage tailored to the individual patient as a function of benefits and adverse effects.

COMMENT

In this regard, a previous fixed-dose study of sertraline in adults with OCD demonstrated that 50-, 100-, and 200-mg dosage conditions were, on average, equal in efficacy. Similar conclusions were seen in a fixed-dose study of fluoxetine, also in adults with OCD. In both studies, adverse effects appeared to increase with higher doses. The magnitude of improvement seen in this study is comparable with that seen in other flexible-dose clinical trials of SSRIs for OCD in adults and youth. Hence,
to remain consistent with expert recommendations regarding SRI dosing in OCD, clinicians would be well advised to begin with 50 mg of sertraline hydrochloride, moving to maximum dosages by 6 to 8 weeks in nonresponders or partial responders for an adequate acute trial duration of 10 to 12 weeks.

In contrast with tricyclic antidepressants, including clomipramine, which have been reported to cause quinidine-like cardio toxicity in children and adolescents, the SSRIs show negligible cardiovascular effects. In this context, the absence in this study of significant electrocardiographic changes associated with sertraline is reassuring, and, absent specific indications for doing so, no generic requirement for monitoring cardiovascular or electrocardiographic parameters during sertraline treatment is apparent.

Consistent with findings from other pediatric OCD studies, age, sex, and other measured baseline parameters, including extent of comorbidity, did not predict response to treatment. However, 2 patients who discontinued the study prematurely despite receiving active drug previously were taking medication for attention-deficit/hyperactivity disorder. Although concomitant pharmacotherapy was an exclusion criterion in this study, expert clinical recommendations favor concomitant treatment with a psychostimulant and an SSRI for youth with both attention-deficit/hyperactivity disorder and OCD. Although treatment with sertraline provided clinically meaningful benefits, as in other studies of SSRIs in OCD, the average sertraline-treated patient remained in the mildly ill range on the CY-BOCS at the end of treatment. Accordingly, most experts agree that the probability of clinical normalization is enhanced by combining pharmacotherapy with OCD-specific cognitive-behavioral psychotherapy. Although current treatments are not generally curative, given a correct diagnosis and skilful treatment most children and adolescents with OCD will improve considerably.

This study was funded by Pfizer Inc, New York, NY.

References
Pott Puffy Tumor Associated With Intranasal Methamphetamine

To the Editor: Pott puffy tumor (PPT) is an anterior extension of a frontal sinus infection that results in frontal bone osteomyelitis and subperiosteal abscess. Since the advent of antibiotics, PPT has been rarely reported and most cases have been described in children and adolescents. We report a case of PPT associated with use of intranasal methamphetamine hydrochloride.

Report of a Case. A 34-year-old woman presented with fever, chills, photophobia, and neck pain for 9 days. Nine months previously, she had developed swelling on her forehead that gradually enlarged over 5 days and then spontaneously drained purulent material. Over several weeks, a fistula developed at the site of the forehead swelling, and was accompanied by intermittent bloody, purulent drainage for approximately 9 months. The patient had no other contributory medical illnesses. However, she had used intranasal and inhaled methamphetamine weekly for 15 years and reported continued intranasal use immediately prior to the development of the forehead lesion. She reported no history of intravenous or other drug use.

Physical examination revealed a sinocutaneous fistula in the midline of the forehead with seropurulent drainage but no local erythema or tenderness. The patient had nuchal rigidity, but findings of the neurologic examination were within normal limits. The remainder of the physical examination was noncontributory. The white blood cell count was 15.3 × 10⁹/L (77 neutrophils and 9 bands). Examination of cerebrospinal fluid, obtained by lumbar puncture, revealed a white blood cell count of 0.5 × 10⁹/L (91% neutrophils, 2% lymphocytes), glucose level of 63 mg/dL (3.5 mmol/L), and a total protein level of 81 mg/dL. A Gram stain showed no organisms and the cerebrospinal fluid cultures and blood cultures were sterile. Computed tomographic scan of the head showed complete opacification of all sinuses with a 1-cm connection between the anterior frontal sinus and the skin. There were no epidural fluid collections or underlying brain parenchymal lesions.

The patient was treated with intravenous cefadiazinam and ceftriaxone sodium, and oral ciprofloxacin for osteomyelitis with presumed bacterial meningitis secondary to a contiguous focus of infection. On day 5 of her hospital stay, she underwent endoscopic sinus surgery. A second surgical procedure for debridement of the infected frontal bone, ablation of the frontal sinus, and repair of the frontal sinocutaneous fistula was also performed. Aerobic and anaerobic cultures of the purulent drainage from the maxillary sinuses grew Streptococcus milleri and Candida albicans. At the end of 2 weeks, antibiotics were changed to intravenous ceftazolin and oral metronidazole and this therapy was continued for 4 additional weeks at home. No further complications occurred at 2 months. The patient was then lost to follow-up.

Comment. Osteomyelitis of the frontal bone is most commonly caused by trauma and frontal sinusitis. We propose that the use of intranasal methamphetamine by this patient contributed to chronic sinus inflammation, which led to the frontal bone osteomyelitis and subperiosteal abscess. Noskin and Kalish have implicated the use of intranasal cocaine as a cause of chronic sinusitis associated with PPT in a 34-year-old man. The sympathomimetic effects of methamphetamine cause vasoconstriction of the mucosal vessels that may result in ischemic injury to the sinus mucosa, and thereby could provide an environment conducive to bacterial growth. We propose that PPT is a potential complication of methamphetamine use.

Peyman Banooni, MD
Leland S. Rickman, MD
David M. Ward, MD
University of California, San Diego


CORRECTIONS

Incorrect Value and Wording: In the Caring for the Critically Ill Patient article entitled “Pharmacist Participation on Physician Rounds and Adverse Drug Events in the Intensive Care Unit” published in the July 21, 1999, issue of The Journal (1999;282:267-270), there was an incorrect value in a table. On page 269, in Table 2, the number of total patients days for Phase 1 in the Study Unit should be 1061 and not 787 as listed. In the “Results” section on the same page, the statement that 300 mg 3 times per day is the correct oral dose of phenytoin is erroneous. It should read “Examples were a recommendation to reduce an excessive dose of intravenous phenytoin from 300 mg 3 times per day to 100 mg 3 times per day. . . .”

Omissions: In the Original Contribution entitled “Sertraline in Children and Adolescents With Obsessive-Compulsive Disorder: A Multicenter Randomized Controlled Trial” published in the November 25, 1998, issue of The Journal (1998;280:1752-1756), Hans Steiner, MD, of the Department of Psychiatry, Stanford University, Stanford, Calif, was omitted from the list of authors. Additionally, on page 1754, at the end of the second paragraph under the heading “Sample Characteristics,” the following sentences were omitted: “The mean CY-BOCS score at baseline was 23.4 for patients randomized to sertraline and 22.2 for patients randomized to placebo. The mean NIMH GOCs score at baseline was 9.2 for patients randomized to sertraline and 9.1 for patients randomized to placebo. The mean CGI-s score was 4.7 for patients randomized to sertraline and 4.6 for patients randomized to placebo.”