The Underrecognized Toll of Prescription Opioid Abuse on Young Children

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**Study objective:** The impact of prescription opioid abuse on young children is underrecognized and poorly documented. We hypothesize that poisoning of young children from prescription opioids occurs regularly in the United States and is associated with serious health events, including death.

**Methods:** Using data from poison centers participating in the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) System, exposures in children younger than 6 years, involving buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, and oxycodone (January 2003 to June 2006), were quantified and described.

**Results:** We identified 9,179 children exposed to a prescription opioid. The median age was 2.0 years (range newborn to 5.5 years), and 54% were boys. Nearly all exposures involved ingestion (99%) and occurred in the home (92%). Exposures to any opioid were associated with 8 deaths, 43 major effects, and 214 moderate effects. Of 51 patients who experienced a major effect or death, 35 were treated with naloxone: a beneficial response was documented in 34 patients. All 5 exposures to buprenorphine associated with a major effect were treated with naloxone, and a beneficial response was recorded in all 5. Nearly all exposures were to medications prescribed for adults in the household. The number of prescriptions filled for an opioid in an area correlated well with exposures in young children in the same area; children have access to household members’ prescription drugs.

**Conclusion:** Young children are exposed to prescription opioids, typically prescribed for other patients, resulting in major health effects and death. [Ann Emerg Med. 2009;53:419-424.]

INTRODUCTION

An estimated 32.7 million people in the United States aged 12 years and older have used a prescription opioid nonmedically at least once in their lifetime.1 Prescription opioid abuse consequences are similar to heroin abuse, including loss of employment, incarceration, and medical complications such as respiratory arrest and death. In addition, the number of opioid analgesic poisonings as documented on death certificates increased 91% between 1999 and 2002.2

Although extensive research on the adverse effects of opioid drugs on adults is available, the adverse effects of prescription opioids on young children have not been well documented. Most new parents are young adults; because the primary prescription drug abusers are also young adults,3 concern is raised that their children may be exposed to these drugs.3

*All members are listed in the Appendix.

The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) System is composed of multiple signal detection systems that monitor prescription opioid abuse and diversion, one of which collects data from most US poison centers and captures detailed information about exposures in young children.4 We hypothesized that prescription opioid poisoning of young children occurs regularly and is associated with serious health events, including death.

MATERIALS AND METHODS

Poison centers employ nurses, pharmacists, physician assistants, and physicians, who collect data on a computerized standard data collection form. Staff are trained and nationally certified to medically manage calls. Poison center data fields have standard definitions found in the Toxic Exposure Surveillance System’s manual.5
Poison centers participating in the RADARS System are geographically dispersed and increased in number from 11 of 61 US centers in the first quarter of 2003 to 40 in the second quarter of 2006, serving 59,612,144 (first quarter 2003) to 176,286,593 persons (second quarter 2006) (US Census Bureau, Census 2000 Data). Each poison center obtained institutional review board approval to participate in the RADARS System.

Participating poison centers submit data weekly to the RADARS System on the opioids of interest (buprenorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, and oxycodone). Data submitted to the RADARS System include more complete information than data submitted to the national centralized poison center database, such as detailed case notes, and undergo a rigorous quality control process. In addition, training was provided to participating poison centers about accurate coding of opioid drugs.6–8

Exposures involving children younger than 6 years and a RADARS System opioid were selected for analysis from first quarter 2003 through second quarter 2006 (3.5 years). Exposures and associated medical outcomes were characterized with an opioid mention as the unit of analysis. Each mention represents a prescription opioid that a child was exposed to and for which information was gathered through a call to a participating poison center. A case may include multiple mentions if the exposed individual was exposed to more than 1 prescription opioid of interest.

Associated medical outcomes are assigned by trained poison center staff at the time of the call, using standard definitions5:

- Minor effect: The patient exhibited some symptoms as a result of the exposure, but they were minimally bothersome to the patient.
- Moderate effect: The patient exhibited symptoms as a result of the exposure, which are more pronounced, more prolonged, or more of a systemic nature than minor symptoms. Usually, some form of treatment is or would have been indicated.
- Major effect: The patient has exhibited symptoms as a result of the exposure, which were life-threatening or resulted in significant residual disability or disfigurement.
- Death: The patient died as a result of the exposure or as a direct complication of the exposure when the complication was unlikely to have occurred had the toxic exposure not preceded the complication.

All mentions associated with a major effect or death outcome were abstracted with a standard abstraction form.

To test the hypothesis that childhood exposures are associated with drug availability in a region, Spearman’s rank-order correlation was computed between the number of childhood exposures and raw number of persons who received a dispensed opioid analgesic from retail pharmacies (unique recipients of dispensed drug [URDD]) by 3-digit ZIP code (Verispan LLC, Yardley, PA). One URDD represents a unique individual who received a dispensed prescription for the opioid of interest during a given quarter, eliminating refills and repeated prescriptions to the individual. Because drug diversion and appropriate medication storage are dependent on the individual’s actions, this method represents drug availability through the medical system. For URDD analyses at the 3-digit ZIP code level, ZIP codes with fewer than 25 URDD were excluded because the standard errors of rates calculated are greater than 10%, placing their accuracy into question. The number of excluded 3-digit ZIP codes varied by opioid and ranged from 2 (0.3%) for oxycodone and fentanyl to 191 (29%) for buprenorphine.

RESULTS

A total of 9,240 exposure mentions involving 9,179 children younger than 6 years were identified (Table 1), most involving hydrocodone or oxycodone. The median age was 2 years (range newborn to 5.5 years). Nearly all exposures involved ingestion (99%) and were unintentional (>99%), and more than half (54%) occurred in boys. Nearly all exposures occurred in the child’s home (92%) or other residence (6%), suggesting that opioids were discovered during toddlers’ exploration of their environment.

Seven thousand seven hundred six (83%) mentions originated from the public, of which 2,872 (37%) were referred to a health care facility. Contact with a poison center was initiated by a health care facility in 1,534 (17%) mentions. In total, 4,358 (47%) mentions were en route to or referred to a health care facility.
Table 1. Characteristics and outcomes of childhood (<6 years of age) exposures by opioid analgesic.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Buprenorphine (n=176)</th>
<th>Fentanyl (n=123)</th>
<th>Hydrocodone (n=6,003)</th>
<th>Hydromorphone (n=68)</th>
<th>Methadone (n=415)</th>
<th>Morphine (n=419)</th>
<th>Oxycodone (n=2,036)</th>
<th>Total (n=9,240)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>2.0 (0.8–5.0)</td>
<td>2.0 (0.2–5.0)</td>
<td>2.0 (0.8–5.0)</td>
<td>2.0 (0.1–5.0)</td>
<td>2.0 (0.1–5.0)</td>
<td>2.0 (0.1–5.0)</td>
<td>2.0 (0.1–5.0)</td>
<td>2.0 (0.1–5.0)</td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>99 (56.3)</td>
<td>64 (52.5)</td>
<td>3,232 (53.9)</td>
<td>33 (48.5)</td>
<td>232 (56.7)</td>
<td>224 (53.5)</td>
<td>1,081 (53.5)</td>
<td>4,965 (53.9)</td>
</tr>
<tr>
<td>Exposure site No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Own home</td>
<td>169 (96.0)</td>
<td>111 (90.2)</td>
<td>5,581 (93.0)</td>
<td>59 (86.8)</td>
<td>372 (89.6)</td>
<td>363 (86.6)</td>
<td>1,821 (89.4)</td>
<td>8,476 (91.7)</td>
</tr>
<tr>
<td>Other home</td>
<td>3 (1.7)</td>
<td>4 (3.3)</td>
<td>335 (5.6)</td>
<td>7 (10.3)</td>
<td>27 (6.5)</td>
<td>45 (10.7)</td>
<td>195 (7.6)</td>
<td>576 (6.2)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (2.3)</td>
<td>8 (6.5)</td>
<td>87 (1.4)</td>
<td>2 (2.9)</td>
<td>16 (3.9)</td>
<td>11 (2.6)</td>
<td>60 (2.9)</td>
<td>188 (2.0)</td>
</tr>
<tr>
<td>Route, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ingestion</td>
<td>175 (99.4)</td>
<td>77 (62.6)</td>
<td>5,993 (99.8)</td>
<td>65 (94.2)</td>
<td>408 (98.1)</td>
<td>412 (97.6)</td>
<td>2,020 (99.1)</td>
<td>9,150 (99.0)</td>
</tr>
<tr>
<td>Ocular</td>
<td>1 (0.6)</td>
<td>0</td>
<td>1 (0.02)</td>
<td>1 (1.4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3 (0.03)</td>
</tr>
<tr>
<td>Dermal</td>
<td>0</td>
<td>30 (24.4)</td>
<td>1 (0.02)</td>
<td>1 (1.4)</td>
<td>1 (0.2)</td>
<td>0</td>
<td>0</td>
<td>6 (0.3)</td>
</tr>
<tr>
<td>Injection</td>
<td>0</td>
<td>3 (2.4)</td>
<td>0</td>
<td>1 (1.4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (0.1)</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
<td>5 (0.08)</td>
<td>0</td>
<td>4 (1.0)</td>
<td>1 (0.2)</td>
<td>7 (0.3)</td>
<td>17 (0.2)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>13 (10.6)</td>
<td>3 (0.05)</td>
<td>1 (1.4)</td>
<td>3 (0.7)</td>
<td>3 (0.7)</td>
<td>3 (0.1)</td>
<td>26 (0.3)</td>
</tr>
<tr>
<td>Outcome, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No effect</td>
<td>40 (32.0)</td>
<td>51 (46.4)</td>
<td>2,673 (77.3)</td>
<td>32 (74.4)</td>
<td>173 (62.2)</td>
<td>171 (64.8)</td>
<td>916 (78.4)</td>
<td>4,056 (74.9)</td>
</tr>
<tr>
<td>Minor effect</td>
<td>55 (44.0)</td>
<td>17 (21.5)</td>
<td>708 (20.5)</td>
<td>11 (25.6)</td>
<td>55 (19.8)</td>
<td>64 (24.2)</td>
<td>186 (15.8)</td>
<td>1,096 (20.2)</td>
</tr>
<tr>
<td>Moderate effect</td>
<td>25 (20.0)</td>
<td>8 (10.1)</td>
<td>71 (2.1)</td>
<td>0</td>
<td>34 (12.2)</td>
<td>24 (9.1)</td>
<td>52 (4.4)</td>
<td>214 (4.0)</td>
</tr>
<tr>
<td>Major effect</td>
<td>5 (4.0)</td>
<td>3 (3.8)</td>
<td>6 (0.2)</td>
<td>0</td>
<td>14 (5.0)</td>
<td>5 (1.9)</td>
<td>10 (0.8)</td>
<td>43 (0.8)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>2 (0.1)</td>
<td>0</td>
<td>2 (0.7)</td>
<td>0</td>
<td>4 (0.3)</td>
<td>8 (0.1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>47</td>
<td>44</td>
<td>2,985</td>
<td>22</td>
<td>127</td>
<td>136</td>
<td>779</td>
<td>3,540</td>
</tr>
<tr>
<td>Confirmed</td>
<td>4</td>
<td>0</td>
<td>158</td>
<td>3</td>
<td>10</td>
<td>19</td>
<td>89</td>
<td>283</td>
</tr>
</tbody>
</table>

Childhood exposures may be either intentional or unintentional. Unintentional exposures typically result from a child gaining inappropriate access to a drug. Intentional exposures in children are primarily the result of an adult’s unintentional actions resulting in exposure in a child.

*Proportion of 9,209 mentions. The sex was unknown in 31 mentions.
†More than 1 exposure route may be involved in a mention.
‡Percentage calculated on total mentions followed to a known outcome (no effect; minor, moderate, or major effects; and death).
§Includes the categories of “not followed—judged as nontoxic exposure,” “not followed—minimal clinical effects possible,” “unable to follow—judged as a potentially toxic exposure,” “unrelated effect,” and “data missing.”

Associated medical outcomes included 8 deaths, 43 major effects, and 214 moderate effects (Table 1). The proportion of mentions associated with any effect followed to a known outcome was significantly greater for buprenorphine (proportion; 95% confidence intervals [CIs]: buprenorphine [0.68; 0.60 to 0.76]; fentanyl [0.35; 0.25 to 0.46]; hydrocodone [0.23; 0.21 to 0.24]; hydromorphone [0.26; 0.13 to 0.39]; methadone [0.38; 0.32 to 0.43]; morphine [0.35; 0.29 to 0.41]; oxycodone [0.22; 0.19 to 0.24]). All mentions associated with major effects or death involved ingestion, except 2 nonfatal cases of inappropriate fentanyl patch application. Of 51 patients who experienced a major effect or death, 35 were treated with naloxone: a beneficial response was recorded in 34 and no record of the response was noted in one case. Although the package labeling for buprenorphine indicates that opioid effects may not be reversed by naloxone, all 5 buprenorphine exposures associated with a major effect were treated with naloxone, and a beneficial response was recorded in all 5.

All deaths associated with the exposures involved children younger than 3 years and involved oxycodone in 4 mentions, hydrocodone in 2 mentions and methadone in 2 mentions (Table 2).

The medication source was assessed for each of the 51 mentions associated with major effects or death; the source could be determined from the case notes in 39 mentions. Of these, only 2 documented the medication was the child’s, one of which was a therapeutic error and the other an adverse reaction. In 37 mentions, the medication was intended for an adult, most commonly the child’s mother. The child’s father, grandparents, and friends of the parents were also sources.

Because a significantly higher proportion of buprenorphine mentions were associated with any medical effect, these exposures were examined in detail. Nine Subutex and 136 Suboxone (buprenorphine and naloxone combination) mentions were reported during the study period, consistent with the fact that 86% of buprenorphine patients in 2006 received Suboxone (Verispan LLC). Most exposures to buprenorphine (n=95) were associated with no effect or minor effect (Subutex 57%; Suboxone 78%). Buprenorphine exposures were associated with zero deaths, 5 major effects, and 25 moderate effects. For those mentions with a known outcome, 29% of Subutex mentions and 2% of Suboxone mentions were associated with a major effect (P=.034).

A positive association was found between exposure mentions and URDD by 3-digit ZIP code for all opioid analgesics (correlation coefficient; 95% CIs: all opioids combined [0.67; 0.65 to 0.68]; buprenorphine [0.31; 0.23 to 0.39]; fentanyl [0.35; 0.28 to 0.41]; hydrocodone [0.81; 0.78 to 0.83]; hydromorphone [0.28; 0.20 to 0.35]; methadone [0.48; 0.42 to 0.54]; morphine [0.52; 0.46 to 0.57]; oxycodone [0.69; 0.65 to 0.73]). Therefore, as drug availability through outpatient pharmacies increases in a region, so do calls to poison centers for
pediatric exposures to that drug. The analysis was repeated including the 3-digit ZIP codes originally excluded, and similar results were yielded.

LIMITATIONS
Several limitations exist for this study. First, not all exposures were captured because not all poison centers participate in the RADARS System and because the number of participating poison centers varied during the study period. Additionally, poison center data are collected through a passive data collection system, relying on individuals with access to telephones and emergency department (ED) staff and physicians to report cases. Finally, poison centers rely on verbal report of the caller for their data; there is no comparison to medical records to confirm the data collected.

DISCUSSION
Our results indicate that young children are endangered by prescription opioids. Typical victims of prescription opioid abuse include families and friends, who may be subjected to theft, loss of income, incarceration, and other adverse effects associated with abuse and dependence. Unlike most drugs, for which both the beneficial and adverse effects occur primarily in the intended recipient (ie, a pain patient), major health consequences, including death, are often found in unintended populations such as children.

Prescription opioids pose a difficult risk-benefit analysis because they are valuable in pain treatment but may be misused or abused. Because outpatient use of prescription opioids is not common in young children, little medical exposure should occur in this group. Nevertheless, we documented 9,179 exposures and 8 deaths in young children, most of which involved the drug of an adult in the child’s household. Many cases were treated by the health care system, typically the ED. Only a portion of US poison centers participated during the study period; therefore, the true number of exposures and poor outcomes is likely higher.

Our results have implications for future research. These cases occur mainly by ingestion of medications present in the home. A common cause of exposure is a toddler discovering the medication during exploration of their environment. The problem of inadvertent exposure of young children has been addressed for medications other than opioids by caregiver education and the use of mechanical and engineering barriers to access. However, the effectiveness of mechanical controls such as blister packaging or childproof closures, methods that mainly serve to slow down a child’s access to the medication, is questionable when a single dose may be fatal. These controls are useful, but most of our reports indicated that the child found a lost or discarded tablet, an open container, or a partially filled cup of medication. Prevention of this type of exposure is particularly difficult because an adult has already opened the container.

Education of caregivers is an imperfect solution but has been reasonably effective for many medications. Although medications are often labeled “keep away from children,” no products to our knowledge note extreme danger, such as warning that 1 pill can kill a young child. The potential role of education in eliminating access to potent opioids is unclear because some portion of the population may exhibit greater risk-taking behaviors than other caregivers.

Finally, it has been proposed according to the pharmacology of buprenorphine that its toxicity is resistant to naloxone treatment. However, all cases in our study in which the effect of

<table>
<thead>
<tr>
<th>Age, mo</th>
<th>Sex</th>
<th>Route</th>
<th>Opioid Analgesic</th>
<th>Other Drugs</th>
<th>Presentation Consistent With Opioid Analgesic Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Male</td>
<td>Ingestion</td>
<td>Methadone tablet</td>
<td>None</td>
<td>Yes. Patient found “not breathing.” Mother was being treated with methadone. Mother described “white powder” around the baby’s mouth. Indeterminate. Patient with respiratory arrest on ED arrival but seizures prominent.</td>
</tr>
<tr>
<td>11</td>
<td>Female</td>
<td>Ingestion</td>
<td>Hydrocodone</td>
<td>Amitriptyline Muscle relaxant Anticonvulsant Tramadol Diphenhydramine Tramadol Naproxen Cimetidine Amitriptyline Anticonvulsant Benzodiazepine</td>
<td>Yes. Patient seen by parent playing with medications, which were removed, but no action taken until found in respiratory arrest.</td>
</tr>
<tr>
<td>16</td>
<td>Male</td>
<td>Ingestion</td>
<td>Oxycodone</td>
<td>None</td>
<td>Indeterminate. Patient arrived with normal vital signs. ECG without tricyclic antidepressant effect. Urine screen positive for opiates. Bilateral cerebellar infarcts and hemorrhages found. Proximate cause of death was sepsis.</td>
</tr>
<tr>
<td>24</td>
<td>Male</td>
<td>Ingestion</td>
<td>Hydrocodone</td>
<td>None</td>
<td>Yes. Found unresponsive.</td>
</tr>
<tr>
<td>30</td>
<td>Male</td>
<td>Ingestion</td>
<td>Oxycodone</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>36</td>
<td>Female</td>
<td>Ingestion</td>
<td>Oxycodone</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>24</td>
<td>Male</td>
<td>Ingestion</td>
<td>Oxycodone</td>
<td>None</td>
<td>Yes. Found unresponsive.</td>
</tr>
</tbody>
</table>
naloxone after ingestion of buprenorphine was documented a beneficial response. Therefore, it is reasonable to use naloxone if it is needed for medical management of buprenorphine overdose. As for other opioids, the effect of rapid opioid reversal must be balanced with the risks of opioid withdrawal.

Young children are exposed frequently to prescription opioids, resulting in major health effects and death. Because 1 tablet of an opioid analgesic may be lethal to a young child, interventions are needed to prevent exposure and reduce deaths.

Supervising editor: Steven M. Green, MD

Dr. Green was the supervising editor on this article. Dr. Dart did not participate in the editorial review or decision to publish this article.

Author contributions: JEB and RCD conceived and designed the study and obtained funding through an unrestricted educational grant. The RADARS System Poison Center Investigators were responsible for collecting the data, performing quality control checks on the data, and commenting on the article. EC analyzed the data. Each author was responsible for drafting different sections of the article and contributed substantially to the revisions of the article as a whole. JEB takes responsibility for the paper as a whole.

Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article, that might create any potential conflict of interest. See the Manuscript Submission Agreement in this issue for examples of specific conflicts covered by this statement. Reckitt Benckiser Pharmaceuticals Inc., Richmond, VA, supported these analyses through an unrestricted educational grant but did not participate in the data collection, analysis, or preparation of the article. Denver Health—Rocky Mountain Poison & Drug Center (RMPDC) is a nonprofit public hospital that operates the RADARS® System Poison Center Signal Detection System: Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®). Data presented are from poison centers participating in this system. RADARS® System is supported by several subscribers from the pharmaceutical industry.


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REFERENCES


APPENDIX.

In addition to the authors, the following individuals and institutions participated in the RADARS System Poison Center Signal Detection System:

- Banner Poison Control Center, Phoenix, AZ: Pamela Orletsky, RN, CSPI
- Blue Ridge Poison Center, Charlottesville, VA: Stephen G. Dobmeier, BSN, CSPI
- CA Poison Control System (Fresno/Madera, San Diego, Sacramento, San Francisco Divisions), San Francisco, CA: Judith A. Alsop, PharmD, DABAT
- Central Ohio Poison Center, Columbus, OH: S. David Baker, PharmD, DABAT
- Central Texas Poison Center, Temple, TX: Douglas J. Borys, PharmD, DABAT
- Children’s Hospital of Michigan, Detroit, MI: Susan Smolinske, PharmD, DABAT
- Cincinnati Drug and Poison Information Center, Cincinnati, OH: G. Randall Bond, MD, ABMT
- DeVos Children’s Hospital, Grand Rapids, MI: Susan Smolinske, PharmD, DABAT
- Florida Poison Information Center–Jacksonville, Jacksonville, FL: Dawn R. Sollee, PharmD
- Florida Poison Information Center–Miami, Miami, FL: Richard S. Weisman, PharmD
- Florida Poison Information Center–Tampa, Tampa, FL: Twyla Kimball, RN, BSN, CSPI
- Hennepin Regional Poison Center, Minneapolis, MN: Christian Lintner, RPh, CSPI

APPENDIX.
Diagnosis: Guttate psoriasis. The patient was diagnosed with guttate psoriasis, which is most commonly observed in children and young adults. It is strongly associated with antecedent or concomitant streptococcal infection and often occurs 1 to 2 weeks after streptococcal pharyngitis or a viral upper respiratory infection. Typically, this rash manifests as scaly, droplike pink papules appearing primarily on the trunk and the extremities, sparing the palms and soles. Guttate psoriasis can be mistaken for a drug rash if the patient is evaluated before the development of scale, particularly in individuals who have been treated with antibiotics for the streptococcal infection. Throat cultures to evaluate for streptococcal infection should be obtained, and increased antistreptolysin O titer levels are common. Guttate psoriasis may resolve spontaneously in a few weeks or may require phototherapy to expedite resolution. The patient’s rash spontaneously resolved within 6 weeks of onset.

References