

## CLINICAL PRACTICE

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## Acute Sinusitis in Adults

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*This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

**A 28-year-old woman presents with an acute onset of nasal discharge, a frontal headache, and a temperature of 39.5°C. Her temperature normalizes within 2 days, but after 12 days she has bothersome nasal congestion and purulent postnasal drip that does not improve. Does this pattern of illness suggest acute bacterial sinusitis or a persistent viral upper respiratory infection? How should this case be managed?**

## THE CLINICAL PROBLEM

SINUSITIS, WHICH IS DEFINED AS SYMPTOMATIC INFLAMMATION OF THE paranasal sinuses and nasal cavity, is reported by nearly 30 million adults annually in the United States.<sup>1</sup> Sinusitis is classified according to duration as acute (lasting up to 4 weeks), chronic (lasting more than 3 months), or subacute (lasting between 4 weeks and 3 months). Although most episodes of acute sinusitis are caused by viral upper respiratory tract infections, they are also associated with asthma, allergic rhinitis, smoking, and exposure to secondhand smoke.<sup>2-5</sup> Sinusitis is often called rhinosinusitis because the inflammation involves the paranasal sinuses and nasal mucosa.<sup>6</sup>

Acute sinusitis is further classified according to presumed cause as either acute bacterial sinusitis or acute viral sinusitis. Although up to 90% of patients with viral upper respiratory tract infections have concurrent acute viral sinusitis, only 0.5 to 2.0% have sinusitis that progresses to acute bacterial sinusitis.<sup>7,8</sup> The most common pathogens in adults with acute bacterial sinusitis are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Staphylococcus aureus*.<sup>9,10</sup>

The natural history of acute sinusitis in adults is very favorable; approximately 85% of persons have a reduction or resolution of symptoms within 7 to 15 days without antibiotic therapy.<sup>11</sup> Nonetheless, antibiotics are prescribed for 84 to 91% of patients with acute sinusitis that is diagnosed in emergency departments and outpatient settings.<sup>12-14</sup> This discrepancy relates, in part, to patient expectations regarding antibiotic therapy<sup>15</sup> and to an inconsistency between clinical guidelines and antibiotic-prescribing patterns.<sup>16</sup>

## STRATEGIES AND EVIDENCE

## DIAGNOSIS

An accurate diagnosis of acute bacterial sinusitis involves first distinguishing acute sinusitis from a viral upper respiratory tract infection on the basis of signs and symptoms and then distinguishing bacterial infection from viral infection on

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## KEY CLINICAL POINTS

## ACUTE SINUSITIS IN ADULTS

- The diagnosis of acute bacterial sinusitis is based on the presence of purulent nasal discharge accompanied by nasal obstruction; facial pain, pressure, or fullness; or both that persists for at least 10 days without improvement or worsens within 10 days after initial improvement.
- Analgesics, nasal irrigation with saline, and topical intranasal glucocorticoids or decongestants may be used to relieve symptoms.
- Randomized trials that primarily involve otherwise healthy nonpregnant adults seen in primary care settings have compared watchful waiting (without antibiotics) with initial antibiotic therapy. These trials have shown small clinical benefits of antibiotics over placebo (number needed to treat to reduce symptoms, 7 to 18). Both of these approaches are valid initial management options.
- Watchful waiting is offered only if the clinician is sure that the patient will return for follow-up if the symptoms do not decrease. Antibiotic therapy is initiated if the patient's condition has not improved by 7 days after diagnosis or if it worsens at any time. If antibiotics are used, amoxicillin or amoxicillin-clavulanate are recommended as first-line therapy.

the basis of the temporal pattern of the illness (Fig. 1). Patients with acute sinusitis typically have more prominent and focused sinonasal symptoms than patients with a viral upper respiratory tract infection. Acute sinusitis manifests with up to 4 weeks of purulent anterior or posterior nasal drainage accompanied by nasal obstruction; facial pain, pressure, or fullness; or both.<sup>6</sup> A diagnosis based on the presence of purulent nasal drainage is most accurate,<sup>6,17</sup> even though some guidelines permit diagnosis without the presence of nasal drainage.<sup>18-20</sup>

The temporal pattern of a typical upper respiratory tract infection can be used as a proxy for acute viral sinusitis because nearly 90% of patients with colds have inflammation that extends to the mucous membranes in the paranasal sinuses.<sup>7</sup> Viral upper respiratory symptoms generally peak rapidly, decline by the third day of illness, and end after 1 week, although in 25% of patients the symptoms last longer but decrease.<sup>21</sup> In contrast, acute bacterial sinusitis persists for 10 days or longer without improvement or, less often, manifests with worsening of symptoms in the first 10 days after initial improvement, in a double-worsening pattern.<sup>6</sup>

Purulent nasal discharge is associated with an increased likelihood of bacteria in the maxillary sinus and of radiographic evidence of acute sinusitis.<sup>17,22,23</sup> However, neither this finding nor other individual signs or symptoms (e.g., fever or facial pain) can be used to accurately distinguish between bacterial and viral infection.<sup>24,25</sup> Similarly, findings on plain radiographs and computed tomography cannot be used to distinguish between these two types of infection. Imaging

studies are reserved for patients with suspected orbital or intracranial complications.<sup>26</sup>

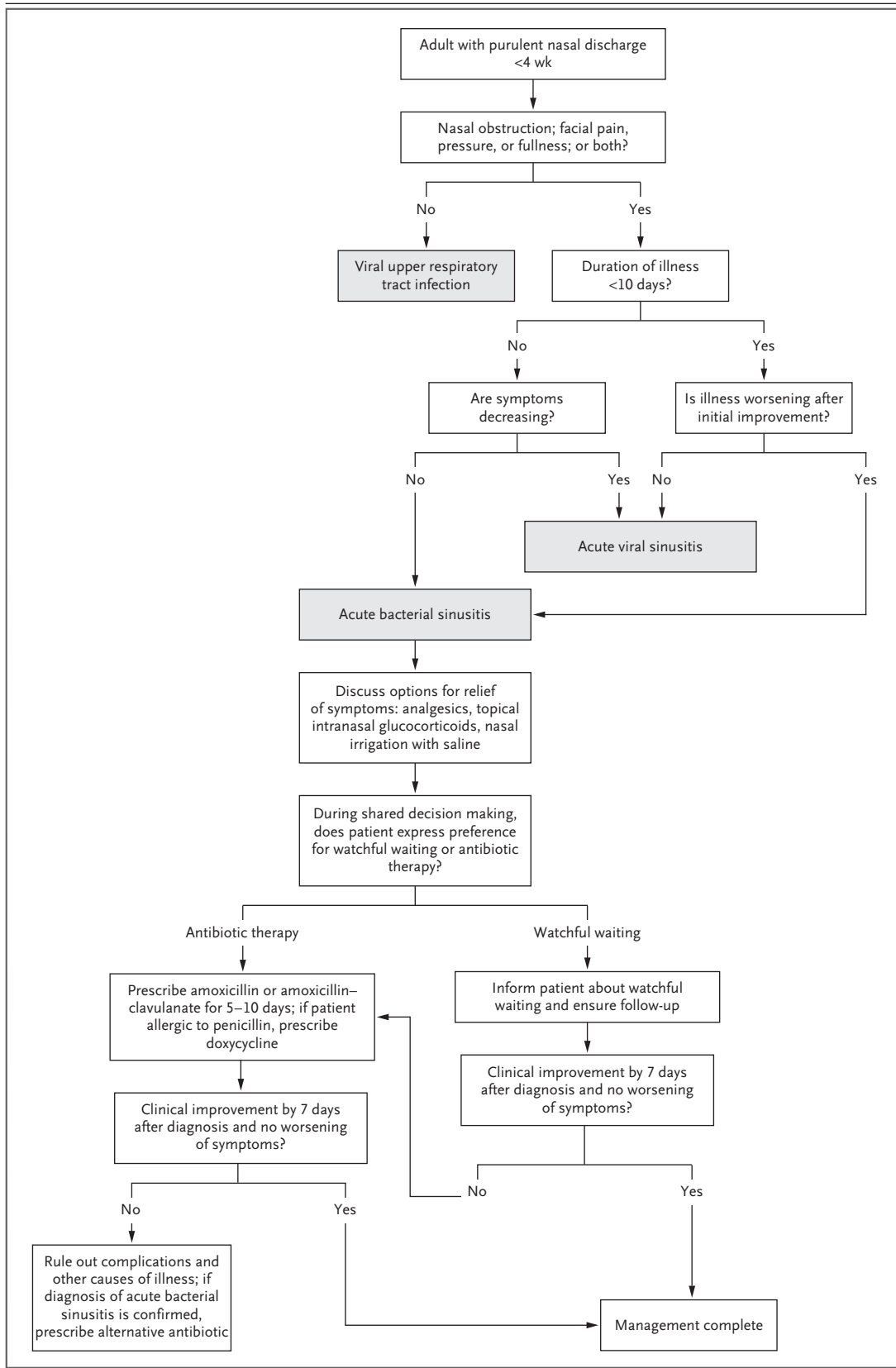
## MANAGEMENT

*Antibiotic Therapy versus Watchful Waiting*

Trials of the efficacy of antibiotics for acute sinusitis have included adult patients who were generally healthy before the onset of illness and who received treatment in primary care settings.<sup>11,27-30</sup> Most trials have excluded patients who are pregnant, are lactating, or have recently received antibiotics, and some have excluded patients with severe illness, long-lasting symptoms, coexisting conditions (e.g., diabetes, pulmonary disease, or congestive heart failure), immunodeficiency, previous sinus surgery, or any type of sinusitis other than maxillary sinusitis.<sup>27,30</sup>

Amoxicillin is the most commonly assessed antibiotic in placebo-controlled trials. Trials of the comparative efficacy of antibiotics have evaluated cefuroxime axetil, amoxicillin-clavulanate, levofloxacin, moxifloxacin, and clarithromycin.<sup>31</sup> Current guidelines, however, caution against the use of clarithromycin or azithromycin because of macrolide-resistant *S. pneumoniae*.<sup>20</sup>

Most individual randomized, placebo-controlled trials do not show any effect of antibiotic therapy on the median duration of pain or illness in patients with acute sinusitis.<sup>30,32</sup> Systematic reviews of placebo-controlled trials generally show a significantly higher rate of clinical improvement at 7 to 15 days (the primary outcome in most trials) with antibiotic therapy than with placebo, but they show small differences between groups. Success rates range from 77 to 88% with antibiotic therapy and from 73 to 85%



**Figure 1 (facing page).** Algorithm for the Diagnosis and Initial Management of Acute Sinusitis in Adults.

with placebo.<sup>11,29,30</sup> The numbers needed to treat with antibiotics (vs. placebo) for 1 patient to have clinical improvement are high (7 to 18) (see Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org).<sup>11,27-30</sup> One systematic review<sup>27</sup> involving eight trials showed that antibiotics shortened the time to cure (an outcome not reported by other reviews), but 18 patients (95% confidence interval [CI], 10 to 115) would need to receive antibiotics rather than placebo for 1 additional patient to be cured at any time point between 7 and 14 days.

The generalizability of these findings to adults with acute bacterial sinusitis (as defined above) is limited because of varying inclusion criteria such as acute rhinorrhea that lasts only a few days, purulent rhinitis, and nonspecific sinusitis-like symptoms.<sup>30</sup> However, one systematic review of six trials<sup>11</sup> that restricted inclusion to patients with illness lasting 7 days or longer showed no significant benefit of antibiotic therapy over placebo with respect to the rate of clinical improvement after 10 days (88% vs. 85%). In subgroup analyses, patients who had had symptoms lasting 10 days or more when the study drug (or placebo) was initiated were no more likely to benefit from antibiotic therapy than were patients who had had symptoms lasting for a shorter duration.<sup>28</sup>

The potential benefits of antibiotic therapy must be balanced against adverse effects, which may include allergic reactions and the emergence of drug-resistant bacteria. The numbers needed to harm (i.e., the numbers of patients who would have to receive antibiotics for one adverse effect to occur) range from 8 to 12 (Table S1 in the Supplementary Appendix); this indicates that adverse effects from antibiotics are as likely as, or more likely than, benefits. Common adverse effects of antibiotics include nausea, vomiting, diarrhea, and abdominal pain. These effects occur, on average, in 27% (range, 3 to 59) of patients who receive antibiotics, as compared with 15% (range, 0 to 40) of patients who receive placebo.<sup>27</sup> In May 2016, a Food and Drug Administration advisory recommended that fluoroquinolone antibiotics (levofloxacin and moxifloxacin) be reserved for patients who do not have

alternative treatment options (Table 1). The potential serious side effects of these drugs can involve the tendons, muscles, joints, nerves, and central nervous system.<sup>34</sup>

Suppurative complications of acute sinusitis (e.g., cellulitis, meningitis, and orbital or intracranial abscess) are rare, and the incidence of these complications is similar among patients who receive antibiotics and those who receive placebo.<sup>11,30,31</sup> A systematic review<sup>27</sup> of 10 placebo-controlled trials showed that one serious disease-related complication occurred among 1211 adults in the placebo group (0.08%) and none occurred among 1239 adults in the antibiotic group. The one serious event was a brain abscess that occurred after treatment of symptoms without antibiotics for 14 days followed by treatment with amoxicillin–clavulanate for 7 days.<sup>33</sup> No other serious infectious complications were reported in the systematic review<sup>27</sup> or in a subsequent trial.<sup>32</sup>

No differences in the comparative efficacy of antibiotics in the treatment of acute bacterial sinusitis have been reported, probably because of the high rate of spontaneous improvement and the noninferiority design of most trials.<sup>20</sup> A systematic review of five trials showed no difference between quinolones and amoxicillin–clavulanate with respect to rates of clinical success.<sup>35</sup> Comparative trials of amoxicillin versus amoxicillin–clavulanate are lacking; the argument for the use of amoxicillin–clavulanate is based on patterns of bacterial resistance.<sup>20</sup>

In most trials of antibiotics for acute bacterial sinusitis, these drugs are prescribed for 7 to 10 days. A systematic review<sup>36</sup> of 12 trials showed no difference in rates of clinical success or adverse events between patients who received antibiotics for 3 to 7 days and those who received antibiotics for 6 to 10 days. A sensitivity analysis comparing treatment for 5 days with treatment for 10 days also showed equivalent rates of clinical success, but the odds of adverse events were 21% (95% CI, 2 to 37) lower among patients who received the shorter course of treatment.

#### *Adjuvant Therapy*

Two systematic reviews (one including four trials<sup>37</sup> and the other including six trials<sup>38</sup>) showed small but significant benefits of topical intranasal glucocorticoids with respect to a decrease in symptoms, especially pain and nasal congestion, after 14 to 21 days (number needed to treat, 13).

**Table 1. Recommended Antibiotics for the Treatment of Acute Bacterial Sinusitis in Adults.\***

Clinical Scenario and Antibiotic Options	Comment
Initial therapy in a patient who is not allergic to $\beta$ -lactam penicillin Amoxicillin (1000 mg orally three times a day for 5–10 days)	
Amoxicillin–clavulanate (500 mg of amoxicillin and 125 mg of clavulanate orally three times a day for 5–10 days, or 875 mg of amoxicillin and 125 mg of clavulanate orally twice a day for 5–10 days)	Amoxicillin–clavulanate is recommended when bacterial resistance is likely (in smokers, patients who have recently received antibiotics, health care providers, and areas where there is a high rate of community resistance), if the patient's infection is severe or protracted, if the patient is older than 65 yr, or if he or she has a co-existing condition (diabetes, an immunocompromised state, or chronic cardiac, hepatic, or renal disease) <sup>6</sup>
Initial therapy in a patient who is allergic to $\beta$ -lactam penicillin	Macrolide antibiotics and trimethoprim–sulfamethoxazole are not recommended because of high rates of resistance (40–50%) by <i>Streptococcus pneumoniae</i> <sup>20</sup>
Doxycycline (100 mg orally twice a day or 200 mg once a day for 5–10 days) <sup>†</sup>	
Clindamycin (300 mg orally three times a day for 10 days) plus cefixime (400 mg orally once a day for 10 days) or cefpodoxime (200 mg orally two times a day for 10 days)	
Levofloxacin (500 mg orally once a day for 5–10 days) <sup>‡</sup>	
Moxifloxacin (400 mg orally once a day for 5–10 days) <sup>‡</sup>	
Therapy in patient who had initial treatment failure with antibiotics	
Amoxicillin–clavulanate (2000 mg of amoxicillin and 125 mg of clavulanate orally twice a day for 10 days) if the patient is not allergic to penicillin	The antibiotic used in a patient who has had treatment failure should be different from the antibiotic used as initial therapy
Doxycycline (100 mg orally twice daily or 200 mg once a day for 10 days) <sup>†</sup>	
Levofloxacin (500 mg orally once a day for 10 days) <sup>‡</sup>	
Moxifloxacin (400 mg orally once a day for 10 days) <sup>‡</sup>	

\* Adapted from Chow et al.<sup>20</sup> and Rosenfeld et al.<sup>6</sup>

<sup>†</sup> Doxycycline is contraindicated in pregnant women.

<sup>‡</sup> The Food and Drug Administration has advised that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with sinusitis. Fluoroquinolones should be reserved for patients with sinusitis who do not have alternative treatment options.<sup>33</sup>

Although no serious adverse events were reported, the generalizability is limited by the inclusion of children in some trials and by the fact that some trials assessed glucocorticoids alone, whereas others assessed glucocorticoids as an adjunct to antibiotics. The minor adverse events reported in these trials included epistaxis, headache, and nasal itching.

A meta-analysis of four trials of oral glucocorticoids used as an adjunct to oral antibiotic therapy showed a slightly higher rate of improvement in symptoms at 3 to 7 days or at 4 to 12 days among patients who received glucocorticoids than

among patients who received placebo.<sup>39</sup> However, methodologic limitations, including substantial loss to follow-up in the individual trials, raise questions about the estimates of benefit. One trial showed that oral glucocorticoids used as monotherapy had no significant benefit over placebo.<sup>40</sup> No additional adverse effects were shown in these trials, but the well-documented risks associated with oral glucocorticoids argue against their use in patients with acute bacterial sinusitis.

Limited data from randomized trials involving adults with acute sinusitis suggest that nasal

irrigation with saline reduces symptoms and improves quality of life and mucociliary clearance.<sup>41,42</sup> A systematic review of nasal irrigation with saline for acute upper respiratory tract infections, including sinusitis, in adults and children showed inconsistent benefits in five small, randomized, controlled trials that were judged to have a high risk of bias.<sup>43</sup> Side effects were uncommon but included nasal discomfort and irritation. Worsening or progression of infection was not reported.

Randomized trials of the efficacy of decongestants (topical or systemic), antihistamines, or guaifenesin (a mucolytic agent) specifically for the treatment of acute bacterial sinusitis in adults are lacking.<sup>6</sup> One trial, which was limited to patients with acute sinusitis who had also had allergic rhinitis, showed that loratadine, as compared with placebo, significantly reduced the incidence of sneezing and nasal obstruction.<sup>44</sup>

#### *Special Circumstances*

Pregnant women may have nasal vascular engorgement (rhinitis of pregnancy) that can mimic acute sinusitis<sup>45</sup>; this makes accurate diagnosis (Fig. 1) important. Acceptable antibiotics for the treatment of sinusitis in pregnant women include amoxicillin, amoxicillin–clavulanate, and, in patients who are allergic to penicillin (if the hypersensitivity to penicillin is not immediate [type I]), clindamycin plus cefixime or cefpodoxime.<sup>46</sup>

Patients with diabetes or other conditions that compromise the immune system are more likely than patients without these conditions to harbor resistant bacteria, and they should receive amoxicillin–clavulanate. If the symptoms do not decrease within 72 hours, a nasal culture for atypical or resistant organisms should be performed.<sup>47</sup> A high temperature (>39°C), nasal crusting, or severe facial pain should arouse suspicion for invasive fungal sinusitis, a medical emergency that is more common in patients with diabetes and immunocompromised patients than in other patients.<sup>48</sup>

Referral to an otolaryngologist is appropriate for patients with refractory illness or recurrent acute bacterial sinusitis (three or more episodes in 6 months) or if other causes of sinonasal symptoms (e.g., tumors and structural abnormalities) are suspected. Urgent referral and evaluation are indicated in patients in whom there is

suspicion for a developing orbital or intracranial complication (e.g., because of periorbital edema, restricted extraocular movements, or severe headache).

#### AREAS OF UNCERTAINTY

Additional research to validate or improve on current criteria for distinguishing acute viral sinusitis from acute bacterial sinusitis with the use of signs, symptoms, and the temporal pattern is lacking. The current criteria primarily identify patterns of illness that are inconsistent with viral infection, but the true prevalence of bacterial infection among these patients, as determined by means of sinus sampling or culture, remains unknown.

Since some randomized trials include patients who have been ill for less than 10 days and who are likely to have viral sinusitis, there remains substantial uncertainty about which patients might benefit most from initial antibiotic therapy rather than watchful waiting. This uncertainty is compounded by restrictive inclusion criteria in many trials that exclude patients who are pregnant and those with diabetes and other coexisting conditions. There is also uncertainty about the course and relative incidence of suppurative complications among patients with acute bacterial sinusitis who do not receive antibiotic therapy as compared with those who do receive antibiotic therapy, since many trials include patients with viral sinusitis and exclude patients with severe illness, prolonged symptoms, or disease beyond the maxillary sinuses.

#### GUIDELINES

Table 2 reviews clinical practice guidelines<sup>6,18,20</sup> and a position statement addressing the diagnosis and management of acute sinusitis.<sup>19</sup> The guideline from the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) differs from the others in that it includes consumer representatives and a nurse in the guideline development group and it offers a plain-language summary for patients.<sup>49</sup> The guidelines consistently state that acute sinusitis should be diagnosed on the basis of signs and symptoms plus a distinct temporal pattern, but there is less consistency regarding the specific criteria used.



**Table 2. Clinical Guidelines for the Management of Acute Sinusitis in Adults.\***

Variable	AAO-HNS Clinical Practice Guideline for Adult Sinusitis <sup>6</sup>	Canadian Clinical Practice Guideline for Acute and Chronic Rhinosinusitis <sup>18</sup>	European Position Statement on Rhinosinusitis <sup>19</sup>	IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis <sup>20</sup>
Signs and symptoms of acute sinusitis	Up to 4 wk of purulent nasal drainage accompanied by facial pain, pressure, or fullness; nasal obstruction; or both	Up to 4 wk of at least two major symptoms: nasal obstruction; facial pain, pressure, or fullness; purulent nasal discharge; or hyposmia or anosmia	Up to 12 wk of two or more symptoms, one of which is nasal discharge or nasal obstruction, with or without facial pain, pressure, or fullness or hyposmia or anosmia	Up to 4 wk of at least two major symptoms† or one major symptom† and at least two minor symptoms‡
Criteria for acute bacterial sinusitis	Condition persists for >10 days without improvement or worsening within 10 days after initial improvement	Condition persists for >7 days without improvement, worsening after 5–7 days (biphasic illness), or severe symptoms with purulence and fever for 3 or 4 days	Condition persists for >10 days, worsening after 5 days, or severe symptoms with three or more of the following: discolored nasal discharge, severe local pain, temperature >38°C, elevated erythrocyte sedimentation rate and C-reactive protein level, or increase in symptoms after an initial milder phase	Condition persists for >10 days without improvement, worsening after 5 or 6 days after initial improvement, or severe symptoms with purulence and fever for 3 or 4 consecutive days at beginning of illness
Initial therapy	Choice of watchful waiting or antibiotic therapy, regardless of severity of illness	Watchful waiting for mild illness; antibiotic therapy for severe illness or if coexisting conditions present	Watchful waiting for mild symptoms; antibiotic therapy for severe illness	Antibiotic therapy for all patients with presumed bacterial sinusitis
First-line antibiotic	Amoxicillin with or without clavulanate	Amoxicillin	Not specified	Amoxicillin with clavulanate
Antibiotic if patient allergic to penicillin	Doxycycline or quinolone (levofloxacin, moxifloxacin)	Macrolide or trimethoprim–sulfamethoxazole	Not specified	Doxycycline or quinolone
Topical glucocorticoids	Optional	Recommended	Recommended	Recommended
Oral glucocorticoids	Not recommended	Not discussed	Optional for severe illness	Not discussed
Nasal irrigation with saline	Optional	Optional	Limited effect	Recommended
Definition of initial failure of treatment (either watchful waiting or antibiotic therapy)	Symptoms do not decrease within 7 days after diagnosis or worsen at any time	Symptoms do not decrease within 72 hr after therapy	Symptoms do not decrease within 48 hr in a patient with severe illness or within 14 days in a patient with mild-to-moderate illness	Symptoms do not decrease despite 3–5 days of therapy or worsen after 48–72 hr of therapy

\* AAO-HNS denotes American Academy of Otolaryngology–Head and Neck Surgery, and IDSA Infectious Diseases Society of America.

† Major symptoms are purulent anterior or posterior nasal discharge, nasal congestion or obstruction, facial congestion or fullness, facial pain or pressure, hyposmia or anosmia, and fever.

‡ Minor symptoms are headache; ear pain, pressure, or fullness; halitosis; dental pain; cough; and fatigue.

The guidelines differ regarding watchful waiting in patients with acute bacterial sinusitis. Whereas the AAO-HNS guideline states that watchful waiting is similar to antibiotic therapy as an initial management strategy,<sup>6</sup> the Infectious Diseases Society of America (IDSA) guidelines<sup>20</sup> recommend that all patients receive antibiotics as initial treatment. The IDSA guidelines note that although symptoms decreased after 7 days in 70% of patients with acute sinusitis who received placebo in clinical trials,<sup>30</sup> the benefit of antibiotics would presumably be greater if more stringent diagnostic criteria for bacterial sinusitis were applied.

The guidelines also differ with respect to recommendations for adjuvant therapy and in the definition of initial treatment failure, which in the AAO-HNS guideline<sup>6</sup> is failure to reduce symptoms by 7 days and in other guidelines<sup>18-20</sup> is failure to reduce symptoms by 2 to 5 days. The cutoff point of 7 days was selected to avoid an inappropriately high percentage of treatment failures, because only approximately 30 to 40% of patients in randomized trials have reduced symptoms by 3 to 5 days.<sup>30</sup>

#### CONCLUSIONS AND RECOMMENDATIONS

Initial management of acute bacterial sinusitis should be based on shared decision making with the patient, which can be facilitated by a decision grid (Table S2 in the Supplementary Appendix). If watchful waiting is chosen, the patient in the

vignette may be given a “safety-net” or “wait-and-see” prescription for an antibiotic to use if the illness worsens at any time or if the symptoms do not decrease within 7 days. She should be advised to contact her physician if the symptoms have not decreased by that time or if she begins to have worsening symptoms at any point.

If antibiotic therapy is chosen as the initial treatment, I would prescribe amoxicillin at a dose of 1000 mg orally three times a day for 5 days, unless the patient had coexisting conditions (Table 1) that would warrant the use of amoxicillin-clavulanate. If the patient is allergic to penicillin, I would prescribe doxycycline at a daily dose of 200 mg for 5 days.

I would recommend the use of analgesics or nasal glucocorticoids as needed for facial pain, pressure, or fullness. Nasal congestion is also relieved by topical glucocorticoids, and (on the basis of clinical experience) the patient may benefit from the use of nasal decongestant spray such as oxymetazoline for no more than 5 days to limit the risk of rebound congestion.<sup>50</sup> The use of a nasal rinse with saline may be helpful if the patient has purulent nasal drainage, especially if the drainage is difficult for her to expel. Antihistamines should be reserved for patients with known allergies to inhalants or prominent allergic symptoms. Oral glucocorticoids are not recommended.

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Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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