INTRODUCTION

Chronic rhinosinusitis (CRS) is defined as a complex inflammatory condition involving the paranasal sinuses and linings of the nasal passages that lasts 12 weeks or longer, despite attempts at medical management.

CRS can be divided into three distinct clinical syndromes, since the underlying causes and contributing factors as well as the response to medical or surgical management are different:

- CRS without nasal polyposis
- CRS with nasal polyposis
- Allergic fungal rhinosinusitis

GOALS OF THERAPY

Chronic rhinosinusitis (CRS) cannot be "cured" in most patients, and therapy is intended to reduce symptoms and improve quality of life. Thus, the goals of CRS therapy include the following:

- Control of mucosal inflammation and edema.
- Maintenance of adequate sinus ventilation and drainage.
- Treatment of colonizing or infecting microorganisms, if present.
- Reduction in the number of acute exacerbations.
TREATMENT OF CRS WITHOUT NASAL POLYPOSIS

Medical management:

Intensive medical management is appropriate for patients with symptoms and computed tomography (CT) findings suggestive of CRS without NP who have not received treatment in the immediate past.

For such patients, two potential initial treatment options are presented.

Option 1: Intensive treatment with oral glucocorticoids combined with antibiotics:

This option is "intensive medical management" consisting of a brief course of oral glucocorticoids, combined with a prolonged course of oral antibiotics and one or more adjunctive therapies.

<table>
<thead>
<tr>
<th>A typical regimen involves:</th>
<th>Dose: 20 mg prednisone twice daily for five days, followed by 20 mg daily for five days (i.e., total of 10 days of treatment) PLUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral prednisone (in adults)</td>
<td>Three to four weeks of oral antibiotics may be extended for up to six weeks (or for seven days after symptoms have cleared) in patients with colored secretions that are improving gradually but have not cleared.</td>
</tr>
<tr>
<td>PLUS oral antibiotics.</td>
<td></td>
</tr>
</tbody>
</table>

Antibiotic selection

Empiric regimens: Antibiotic regimens for CRS are generally oral since this is primarily an outpatient disease.

Antibiotic selection is depends upon several factors:

1- History of drug allergies.  
2- Cost of therapy.  
3- Incidence of and/or risk factors for beta-lactamase–producing organisms and methicillin-resistant S. aureus (MRSA).  
4- If antibiotics have been given over the past three months, a different class of antibiotics should be used.
These three regimens cover aerobic and anaerobic organisms with a single preparation:

- **Amoxicillin-clavulanate** (in children: 45 mg/kg per day divided every 12 hours; in adults: 500 mg three times daily or 875 mg twice daily or two 1000 mg extended-release tablets twice daily)
- **Clindamycin** (in children: 20 to 40 mg/kg per day orally divided every 6 to 8 hours; in adults: 300 mg four times daily or 450 mg three times daily)
- **Moxifloxacin** (400 mg once daily) generally in adults only

These regimens are more cumbersome and are usually reserved for refractory cases, in which the patient has been evaluated by an otolaryngologist and cultures have been obtained to guide therapy.

If there is concerns of MRSA add:

- **Clindamycin** (see previous section for dosing) is usually the preferred initial therapy because it is also effective against anaerobes.
- Alternatives (in patients older than seven years include:
  - **TMP-SMX**, **doxycycline** or **minocycline** and **linezolid** which should be added to one of the above regimens that covers anaerobes.

**Antibiotics Duration of therapy:**

Therapy is typically given for at least 3 weeks and may be extended for up to 10 weeks in refractory cases.

Patients who might benefit from the longer duration of 10 weeks include:

1. Those who have severe symptoms,
2. Long duration of illness,
3. Failure of prior courses of antibiotics,
4. Extensive surgery.
Parenteral therapy

Is indicated for patients:

1. Seriously ill.
2. Undergoing surgery.
3. In whom compliance is questionable.

- Sinus cultures should be obtained from patients requiring parenteral therapy.
- **Parenteral antibiotics effective against both anaerobes and aerobes include:** ampicillin-sulbactam, ticarcillin-clavulanate, piperacillin-tazobactam, clindamycin, moxifloxacin, the carbapenems (imipenem, meropenem, ertapenem), and the second-generation cephalosporins (cefoxitin and cefotetan).

- If *Pseudomonas aeruginosa* is suspected, the preferred antibiotics:
  1. fluoroquinolone (eg, moxifloxacin or levofloxacin);
  2. a third- or fourth-generation cephalosporin with antipseudomonal activity (ceftazidime or cefepime);
  3. aminoglycoside
  4. carbapenems, imipenem or meropenem (but not ertapenem, which lacks activity against *Pseudomonas*).

- **Metronidazole** may also be given parenterally to cover anaerobes in combination with an agent with aerobic activity. The absorption of oral metronidazole and the fluoroquinolones (eg, moxifloxacin) are excellent, so these should only be given parenterally if the patient is unable to take oral medications.

- If MRSA: we give vancomycin, linezolid, and daptomycin

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**Initial treatment failure:**

- A culture should be obtained in patients who fail to have significant improvement or who demonstrate signs of deterioration despite therapy, preferably directly from the sinus cavity. We use the culture results to ensure that coverage is adequate for organisms resistant to the empiric regimen.

- We generally suggest **not** narrowing the regimen to cover only the organisms cultured because certain bacteria, such as anaerobes, may be difficult to isolate.
**Nebulized antimicrobials:**
Nebulized antibacterial and antifungal agents are being used with increasing frequency in patients with rhinosinusitis, although they are not licensed for this indication and there are few published data to support this practice. The use of nebulized antimicrobials is most often applied to postsurgical patients, in whom there are wider than usual openings into the sinus cavities.

**Nebulized medications include:** ciprofloxacin, tobramycin, betadine, and mixed agents used for other sites such as ophthalmic solutions and preparations for genitourinary irrigation.

**Adjunctive treatment**

In addition to antibiotics and oral glucocorticoids, we administer one or more of the following adjunctive treatments, which are continued indefinitely after the oral antibiotics and glucocorticoids are completed:

- **Intranasal saline** irrigations or saline nasal spray. Saline washes can be used immediately prior to administration of other intranasal medications so that the mucosa is freshly cleansed when the medications are introduced.

- **Intranasal glucocorticoids:** Topical glucocorticoids are the cornerstone of maintenance treatment for many types of rhinitis and have been shown in randomized trials to be helpful as a maintenance therapy for CRS. These agents can be administered either as nasal sprays (tabl1) or as solutions for instillation. We typically begin therapy with nasal sprays. For patients with persistent nasal congestion or blockage despite consistent use of glucocorticoid nasal sprays, we suggest changing to nasal glucocorticoid instillation.

To optimize effectiveness and patient compliance with nasal sprays, we suggest the following:

- Preparations with once daily dosing are convenient and can help optimize compliance: triamcinolone acetonide, budesonide, fluticasone propionate, mometasone furoate, or fluticasone furoate.

  - Most intranasal glucocorticoids are used at a dose of 1 to 2 sprays in each nostril once or twice a day.

  - If obvious mucus or crusting is present, patients can clean the nose with saline nasal sprays or irrigation before the nasal glucocorticoid is applied.

  - Patients should be instructed to keep their head pointed slightly downward during spraying and avoid tilting the head back, as this can cause drainage of the medicine from the nose to the throat. In addition, they should avoid pointing the tip of the bottle at the septum to minimize septum irritation and bleeding.
## Table 1

**Glucocorticoid nasal sprays**

<table>
<thead>
<tr>
<th>Name</th>
<th>United States trade name</th>
<th>Generic available in United States</th>
<th>Available without a prescription in United States</th>
<th>Usual adult dose (per nostril)</th>
<th>Usual pediatric dose (per nostril)</th>
<th>Type of preparation (alcohol content*)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second-generation (systemic bioavailability &lt;1% or undetectable)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>Omnaris</td>
<td>No</td>
<td>No</td>
<td>Two sprays once daily</td>
<td>Two sprays once daily</td>
<td>Aqueous suspension pump spray</td>
</tr>
<tr>
<td>Zetonia</td>
<td></td>
<td>No</td>
<td>No</td>
<td>One spray once daily</td>
<td>One spray once daily for children ≥12 years</td>
<td>Pressurized aerosol spray (3.4% alcohol)</td>
</tr>
<tr>
<td>Fluticasone furoate</td>
<td>Flonase Sensimist (OTC), Veramyst</td>
<td>No</td>
<td>Yes</td>
<td>Two sprays once daily</td>
<td>One spray once daily</td>
<td>Aqueous suspension pump spray</td>
</tr>
<tr>
<td>Fluticasone propionate</td>
<td>Flonase, Flonase Allergy Relief (OTC), Ticspray</td>
<td>Yes</td>
<td>Yes</td>
<td>Two sprays once daily or one spray twice daily</td>
<td>One spray once daily</td>
<td>Aqueous suspension pump spray (0.25% alcohol)</td>
</tr>
<tr>
<td>Mometasone</td>
<td>Nasonex</td>
<td>No</td>
<td>No</td>
<td>Two sprays once daily</td>
<td>One spray once daily</td>
<td>Aqueous suspension pump spray</td>
</tr>
<tr>
<td><strong>First-generation (systemic bioavailability 10 to 50%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Budesonide</td>
<td>Beconase AQ</td>
<td>No</td>
<td>No</td>
<td>One or two sprays twice daily</td>
<td>One spray twice daily</td>
<td>Aqueous suspension pump spray (0.25% alcohol)</td>
</tr>
<tr>
<td>Qnasil</td>
<td></td>
<td>No</td>
<td>No</td>
<td>Two sprays once daily</td>
<td>One spray once daily for children ≥12 years</td>
<td>Pressurized aerosol spray (8% alcohol)</td>
</tr>
<tr>
<td>Budesonide</td>
<td>Rhinocort.Aqua, Rhinocort Allergy (OTC)</td>
<td>Yes</td>
<td>Yes</td>
<td>One spray once daily</td>
<td>One spray once daily</td>
<td>Aqueous suspension pump spray</td>
</tr>
<tr>
<td>Flunisolde</td>
<td>Nasarel (brand version no longer available in United States)</td>
<td>Yes</td>
<td>No</td>
<td>Two sprays twice daily</td>
<td>One spray three times per day or two sprays twice daily</td>
<td>Aqueous suspension pump spray (contains propylene glycol, a possible irritant)</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>Nasonate AQ, Nasacon Allergy 24 Hr (OTC)</td>
<td>Yes</td>
<td>Yes</td>
<td>Two sprays once daily</td>
<td>One spray once daily (age 2 to 5 years) One to two sprays once daily (age 6 to 11 years)</td>
<td>Aqueous suspension pump spray</td>
</tr>
</tbody>
</table>
Incomplete response

In patients in whom intensive medical treatment appears to help but does not result in sufficient improvement in symptoms or resolution of CT findings, the next logical step after failure of intensive medical treatment is **sinus surgery**.

However, a **second course** of empiric intensive treatment can be undertaken provided the following conditions are true:

1. There is no **clear indication** for surgical intervention.

**Indications for surgical intervention include the following:**

- Restoration of sinus ventilation (i.e., restoration of sinus ostial patency and removal of material from opacified sinuses)
- Debulking of severe polyposis
- Failure of intensive medical treatment
- Bony erosion or extension of disease beyond the sinus cavities

2. The patient does not have any signs or symptoms concerning for other conditions and does not appear toxic.
3. The patient prefers to continue medical treatment in order to avoid surgery.

**Option 2: Long-term macrolide antibiotic treatment which is not yet proven to be effective and the role of macrolides in medical management has not been adequately demonstrated.**

**Maintenance treatment**

Maintenance treatment for CRS without NP is guided by the patient's symptoms and by the presence or absence of underlying allergic rhinitis:

1. **Topical glucocorticoids**: We usually initiate a maintenance regimen of a glucocorticoid nasal spray and saline irrigation in all patients.
2. **Treatment of underlying allergic rhinitis** — In patients with CRS and concomitant allergic rhinitis, other therapies, including remediation of allergen exposure, allergen immunotherapy, and oral and topical antihistamines, may be helpful. Newer, minimally-sedating oral antihistamines (such as cetirizine, fexofenadine, or loratadine) are preferred over older agents.
3. **Adjunctive therapies**: An leukotriene agents **montelukast** or **zafirlukast** may be useful in patients with refractory nasal congestion and postnasal drainage.

Chronic use of oral decongestants such as **pseudoephedrine** is generally avoided for maintenance treatment.
TREATMENT OF CRS WITH NASAL POLYPOSIS

Medical management:

1. **Initial interventions**: Initial treatment is primarily intended to reduce the size and extent of nasal polyps and control mucosal inflammation with glucocorticoids. It is the author's approach to administer a course of antibiotics in previously untreated patients at the same time, because it is usually difficult to determine if a concomitant bacterial infection is present. (See 'Option 1: Intensive treatment with oral glucocorticoids combined with antibiotics')

2. **Oral glucocorticoids** — A brief course of oral glucocorticoids may be administered if the patient is very uncomfortable with nasal blockage or impaired sense of smell.

   The improvement achieved with oral glucocorticoids is usually temporary (several weeks to months), although reducing polyp size is an important first step for patients who are sufficiently obstructed that topical therapies cannot penetrate into the nasal cavities.

3. **Specific regimens**:

   A 10- to 15-day course of oral glucocorticoids will temporarily reduce nasal blockage in most patients with CRS with NP.

   ● We typically administer oral **prednisone** (in adults) 20 mg twice daily for 5 days, followed by 10 mg twice daily for 5 days, then 10 mg once daily for 5 days (i.e., total of 15 days of treatment).
   
   ● British guidelines suggests **prednisolone** (0.5 mg per kilogram each morning for 5 to 10 days), accompanied by instillations of **betamethasone** nasal drops.

**Surgery for glucocorticoid failure**: Sinus surgery should be considered if oral glucocorticoids do not reduce polyp tissue sufficiently and the patient has persistent blockage or anosmia.
Maintenance therapies for CRS with NP include topical glucocorticoids, antileukotriene agents, and antihistamines.

- **Topical glucocorticoids**: The mainstay of maintenance treatment is topical glucocorticoids. Several different topical glucocorticoids have been shown either to reduce the size or prevent the regrowth of NP following surgical removal, including beclomethasone dipropionate, budesonide, ciclesonide, flunisolide, fluticasone furoate, fluticasone propionate, mometasone furoate, and triamcinolone acetonide.

- **Antileukotrienes**: Antileukotriene agents may be used as an adjunct to topical glucocorticoids in the treatment of CRS with NP. Small, randomized trials demonstrated modest benefit after one to two months of montelukast, either as monotherapy or as adjunctive therapy to oral prednisolone and budesonide nasal spray. We usually administer a three-month trial of montelukast and continue it indefinitely in patients who experience clinical benefit.

- **Biologic agents for refractory disease**: Biologic agents that have been studied for the treatment of CRS with NP include omalizumab, mepolizumab, and dupilumab. The effect size of each agent appears to be similar and less than that of oral glucocorticoids, based on indirect comparisons.

**REFERENCES:**


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