1. Asthma education and health maintenance
   - Educational action plan
   - Self-management plan
   - Vaccination
   - Smoking cessation
   - Healthy lifestyle (diet, exercise, sleep)
2. Identify patient-related factors
   - Disabilities, age, poor general health
   - Poor health literacy
   - Lack of access to health care
   - Inability to afford medication

3. Diagnose and manage comorbidities
   - Rhinosinusitis/nasal polyps
   - Gastroesophageal reflux
   - Obstructive sleep apnea
   - Vocal cord dysfunction
   - Allergic bronchopulmonary aspergillosis
   - Eosinophilic granulomatosis with polyangiitis (previously known as Churg-Strauss syndrome)
   - Obesity
   - Psychological factors (personality, depression, anxiety)
   - Drug side effects: aspirin, NSAIDs, beta-blockers, ACE inhibitors
   - Aspiration

4. Close follow-up.
   - Reduce treatment intensity after at least 3–6 months of stable, good control, per GINA/NAEPP guidelines

5. Consider adding a non-biologic therapy
   - Tiotropium
   - Leukotriene modifier
   - Thalidomide
   - Macrolide antibiotic
   - Oral glucocorticoid (short course)

6. Address environmental factors
   - Allergen exposures (indoor, outdoor, pets)
   - Occupational exposures
   - Respiratory infections (e.g., viruses)
   - Second-hand cigarette smoke
   - Traffic-related pollution
   - Respiratory irritants

7. Optimize inhaled therapy
   - Choose best device for patient
   - Check inhaler technique frequently
   - Correct patient’s inhaler technique

8. Maximize adherence and minimize side effects
   - Assess knowledge and attitudes about medication
   - Assess barriers to proper medication use
   - Acknowledge patient beliefs about medications
   - Teach ways to improve adherence
   - Ask and educate about possible side effects
   - Use strategies to reduce side effects (e.g., spacers for MDIs)

9. IS ASTHMA STILL UNCONTROLLED, DESPITE TREATMENT WITH HIGH-DOSE ICS + LABA AND A NON-BILOGIC ADD-ON THERAPY?
   - YES
   - NO

10. Refer patient to an asthma specialist

SEVERE ASTHMA: INFLAMMATORY PHENOTYPES AND TREATMENT APPROACHES

<table>
<thead>
<tr>
<th>Inflammatory Phenotype</th>
<th>Common Clinical Features</th>
<th>Biomarkers in Patients Receiving High-Dose ICS</th>
<th>Add-on Pharmacologic Maintenance Therapies</th>
<th>Additional Strategies in Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 (Th2) inflammation</td>
<td>IL-4, IL-5, IL-13 elevated inflammation with high eosinophilic or neutrophilic inflammation</td>
<td>Blood eosinophil count &gt; 300 µL</td>
<td>Anti-IL-4, Anti-IL-5, Omalizumab</td>
<td>Maximum treatment of concomitant conditions associated with Th2 inflammation (e.g., rhinosinusitis, AERD, APBA)</td>
</tr>
<tr>
<td>Non-Type 2 inflammation</td>
<td>Neutrophilic inflammation with high eosinophilic or neutrophilic infiltration</td>
<td>Sputum PMNs &gt; 40–60%</td>
<td>No phenotype-specific treatment currently available</td>
<td>Address exposures (smoke, irritants, pollutants) and altered nutrition</td>
</tr>
<tr>
<td></td>
<td>Paucigranulocytic (noninflammatory) asthma</td>
<td></td>
<td></td>
<td>Maximize clearance strategies</td>
</tr>
<tr>
<td></td>
<td>Mixed eosinophilic and neutrophilic inflammation</td>
<td></td>
<td></td>
<td>Consider Bronchial Thermoplasty</td>
</tr>
</tbody>
</table>

Assumes that alternative diagnoses have been excluded, comorbidities have been identified and managed, patient-related factors and environmental exposures have been addressed, inhaled therapy and adherence have been optimized, and non-biologic therapy has been considered or tried (see Roadmap for details).

**References**

© 2018 National Jewish Health