Addressing the Unmet Needs of Refractory Chronic Cough



RAPID RECAP

Improving RCC Diagnosis in Accordance With Evidence-Based Guidelines

Chronic cough is a cough lasting > 8 weeks in duration[1,2]

In a patient with **chronic cough and no abnormalities**, who[1-3]

- Is a **nonsmoker**
- Is **not receiving ACE inhibitors**
- Has a **normal or stable CXR** identified on initial assessment

Assess for these 3 most common underlying causes of chronic cough[1,2]



Upper Airway Cough Syndrome (UACS)

- Allergy evaluation and empiric treatment
- Sinus imaging
- Nasopharyngoscopy



Asthma/Non-Asthmatic Eosinophilic Bronchitis (NAEB)

- Spirometry
- Bronchodilator reversibility
- Bronchoprovocation challenge
- Sputum eosinophilia
- Peripheral eosinophilia
- FeNO



GERD

- Trial of PPI and withdrawal
- Endoscopy
- Barium esophagram
- Prolonged esophageal acid monitoring
- Impedance monitoring

- Refractory chronic cough (RCC) is a cough that persists despite proper evaluation and treatment of underlying etiologies[1,2]

Abbreviations: ACE = angiotensin-converting enzyme; CXR = chest X-ray; FeNO = fractional exhaled nitric oxide; GERD = gastroesophageal reflux disease; PPI = proton pump inhibitor

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The Underlying Pathophysiology of RCC

Driven by cough hypersensitivity syndrome[4,5]

- Cough reflex becomes overstimulated and hyperreactive
- Both the peripheral and central pathways can become sensitized
- Central cough hypersensitivity results from central sensitization of higher brain centers and reduced cortical inhibition, lowering the threshold for cough in response to minimal stimuli

Hypersensitivity may be driven by[4]:

- Airway inflammation
- Neuroinflammation
- Neural plasticity and remodeling

Molecular pathways:

- TRPV/TRPA1 irritant-sensing pathways
- P2X3-mediated ATP signaling

Abbreviations: P2X3 = P2X purinoceptor 3; TRPA1 = transient receptor potential ankyrin; TRPV = transient receptor potential vanilloid

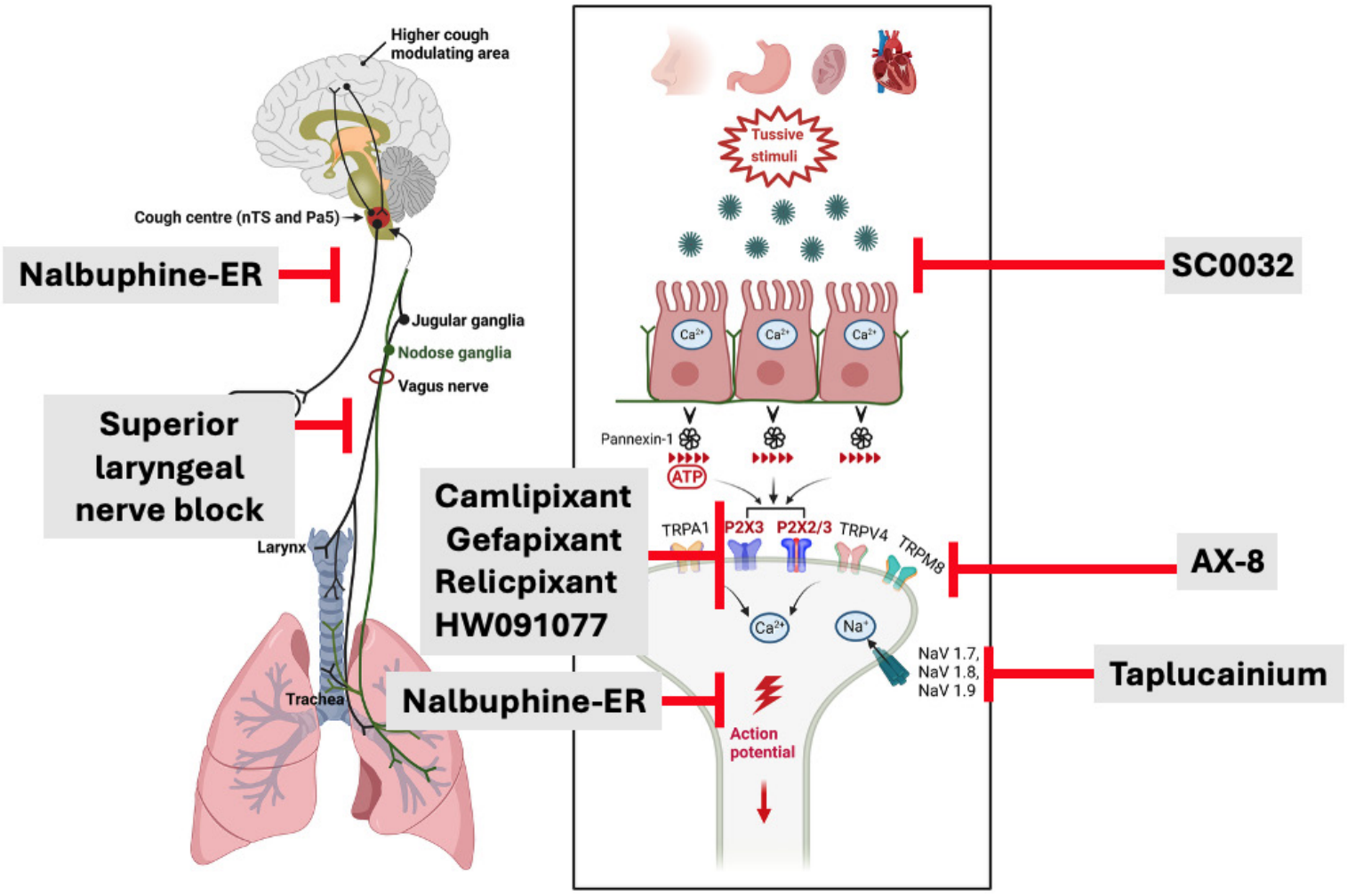
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Emerging Approaches for Addressing RCC Disease Burden and Improving Patient Outcomes

Targets for Novel Therapies[6,7]



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Key Takeaways

- RCC is a diagnosis made after appropriate evaluation and treatment of identifiable causes of chronic cough
- RCC is increasingly understood as a disorder of cough hypersensitivity
- Multiple peripheral and central mechanisms contribute to cough hypersensitivity and provide potential therapeutic targets
  - These include ATP (adenosine triphosphate)–P2X3 and TRP signaling, sensory nerve remodeling, vagal afferent signaling, and impaired central inhibition of cough
- Management is shifting toward individualized, mechanism-based cough suppression
  - Current approaches include behavioral cough suppression and off-label pharmacotherapy
  - Emerging therapies target different components of the cough pathway
- Multidisciplinary care and shared decision making remain important given variable treatment responses

References

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