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Chronic Sinusitis: A Comprehensive Review of Etiology, Diagnosis, and Modern Management

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Abstract:

Background: Chronic rhinosinusitis (CRS) is a prevalent inflammatory condition affecting the paranasal sinuses, persisting for over 12 weeks and impacting millions globally. It arises from a multifactorial etiology, including anatomical obstruction, microbial infections, allergies, and an exaggerated immune response. Recent studies have emphasized the role of biofilms, genetic predispositions, and microbiome imbalances in its pathogenesis. **Aim:** This review aims to elucidate the multifactorial causes of CRS, explore advancements in diagnostic techniques, and evaluate emerging treatment modalities to enhance patient outcomes. **Methods:** A comprehensive review of recent literature was conducted, focusing on the etiology of CRS, including anatomical, infectious, allergic, and immunological factors. The role of biofilms, genetics, and microbiome imbalances was also analyzed. Diagnostic criteria and therapeutic approaches, including medical treatments (intranasal corticosteroids, antibiotics, biologics) and surgical interventions (functional endoscopic sinus surgery and airway reconstruction), were evaluated. **Results:** The review highlights that CRS is driven by a complex interplay of anatomical, infectious, allergic, and immunological factors, with biofilms, genetics, and microbiome imbalances emerging as significant contributors. Diagnostic advancements include refined criteria and next-generation sequencing for microbiome analysis. Treatment options encompass medical therapies (intranasal corticosteroids, antibiotics, biologics) and surgical approaches, with functional endoscopic sinus surgery gaining prominence. **Conclusion:** This review underscores the complex etiology of CRS and the importance of advanced diagnostics and innovative therapies. By addressing current challenges and exploring new research directions, clinicians and researchers can optimize treatment strategies to improve outcomes for patients with CRS.

Keywords: Chronic rhinosinusitis, sinusitis, biologics, microbiome, diagnosis.

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Introduction

Chronic rhinosinusitis (CRS) is a debilitating inflammatory condition of the paranasal sinuses and is defined by symptoms of nasal congestion, facial pain or pressure, nasal discharge (either anterior nasal or posterior nasal drainage), and loss of smell lasting greater than 12 weeks. CRS symptoms negatively affect the quality of life for millions of patients worldwide. CRS is highly prevalent, with estimates indicating a population prevalence of 5-12%, leading to both direct and indirect costs in billions (Fokkens et al., 2020; Rudmik, 2015). CRS presents in two primary phenotypes, namely: CRS with nasal polyps (CRSwNP), characterized by soft, benign masses, and CRS without nasal polyps (CRSsNP), which is often described as having different inflammatory mechanisms.

Although its various phenotypes share similarities in their clinical presentations, CRS phenotypes can differ considerably in their pathophysiology, clinical presentations, and responses to treatments. Future approaches should look to target therapy (Shaker, 2023). This systematic review will detail the complexity of the etiology of CRS. We will look to identify and outline existing and novel diagnostic techniques and examine standard and novel approaches to treatment. This review serves to be an evidence-based resource for clinicians and researchers and seeks to identify knowledge gaps in order to help drive future research toward tailoring and optimizing the management of CRS in individual patients.

Causes of Chronic Sinusitis

Chronic rhinosinusitis occurs due to an interaction of many causes, including anatomical anomalies, microbial infections, allergies and environmental triggers, immunologic dysfunction, and genetic predisposition. Understanding these causative factors is critical in providing adequate assessments and treatment plans to successfully target the primary causes of the disease.

Anatomical Considerations

Anatomical factors are one of the predominant causes of CRS, as they adversely affect normal sinus drainage and ventilation, creating a chronic inflammatory environment. Examples of obstructive anatomical issues (e.g, nasal septal deviation - misalignment of the nasal septum) result in disruption of airflow and lead to mucus stasis, increasing the risk for secondary infections (Hamilos, 2016). *Concha bullosa* (bilateral pneumatization of the middle turbinate) and narrowed osteomeatal complexes impair mucociliary clearance capacity, further worsening the condition by allowing pathogens and inflammatory mediators to collect in the sinuses (Shaker, 2023). Thus, these anatomical variations can create a cycle of obstruction and inflammation, then form a constellation of additional CRS symptoms. Imaging studies, most importantly computed tomography (CT), are vital in identifying anatomical factors, as noninvasive imaging techniques allow visualization of the relevant sinus anatomy if surgical intervention may be necessary (Norwood et al., 2023). Critically for patients experiencing refractory disease requiring surgery, correcting anatomical factors is often decisive to successful treatment of CRS.

Infectious Agents

Inflammation is caused by infectious agents, as the development of CRS is caused by a plethora of bacteria, viruses, and occasionally fungal pathogens that contribute to the pathogenesis and disease process

of CRS. *Staphylococcus aureus* and *Pseudomonas aeruginosa* are the primary bacterial pathogens underwriting the majority of cases of CRS, as they cause CRS when presented with infecting biofilms—structured assemblages of microorganisms in a multi-species community formed within a protective environment called extracellular polysaccharide matrix. Biofilms increase antibiotic resistance, which makes infections difficult to eradicate and sustain chronic inflammation (Huang et al., 2022). Fungal infections (primarily from *Aspergillus* species) are common in patients with allergic fungal rhinosinusitis (AFRS) or immunocompromised states and can exacerbate mucosal inflammation and polyps (Deutsch et al., 2019). Viral infections, like those associated with rhinoviruses or coronaviruses, can also lead to acute exacerbations in CRS patients, which make the patient's deterioration of symptoms worse and complicate the management of the disease (Cho et al., 2024). Ultimately, the dynamic between microbial pathogens and the host immune response highlights the importance of targeted antimicrobial therapies and the interruption of biofilm.

Allergic and Environmental Triggers

Allergic and environmental triggers are known to be contributors to CRS, with attention to allergic factors in patients with CRSwNP, who are thought to have a predominantly type 2 inflammatory response. Allergic rhinitis is triggered by allergens, such as pollen, dust mites, pet dander, and mold. Allergic rhinitis is known to induce eosinophilic inflammation and mast cell activation, resulting in mucosal edema and the development of polyps (Stevens et al., 2019). Prolonged environmental exposures to irritants such as air pollution, tobacco smoke, and other occupational exposures to chemicals increase CRS in patients with CRS by mediating oxidative stress and impairing ciliary function and mucociliary clearance (Fokkens et al., 2020). Modern studies have shown a potential increase in the burden of urban pollutants, including particulate matter and nitrogen dioxide, on scores of CRS, especially in highly populated and industrialized areas (Leland et al, 2021). These external modifiers intensify the inflammatory cascade, so the environment and its allergens are paramount in CRS management.

Immunologic / Genetic factors

Immunologic dysregulation of chronic rhinosinusitis is obvious when comparing different inflammatory profiles to differentiate between CRSwNP and CRSsNP. In CRSwNP type 2 inflammation is primarily driven by IL-4, IL-5, and IL-13 cytokines, which all drive eosinophilic infiltration and elevated IgE levels (Bachert et al, 2018). alternatively, the type of inflammation depicted in CRS is neutrophilic inflammation and type 1 or type 3 immune defense (Xie et al, 2023). Genetic susceptibilities further contribute to CRS, with possible mutations in the CFTR gene being a relevant apprehension. This would change mucus viscosity to impair forms of an innate immune response, predisposing to chronic infection and inflammation (Wang et al, 2014). Since then, dysbiosis of the microbiome or imbalance of microbial communities of the sinuses has become a major consideration in the etiology of CRS, regardless of phenotype. Less diversity of microbial species, most commonly induced by antibiotic overuse or chronic inflammation, has been shown to reflect disease that persists and is unresponsive to treatment, indicating another factor of alienation in the disease process (Fischer & Lee, 2024). These immunological and genetic factors underscore the necessity for individualized models of care in CRS, which aim at specific inflammatory pathways and microbial imbalances (Table 1). Figure 1 illustrates a schematic

representation of the pathophysiology of chronic rhinosinusitis (CRS). This schematic is a comprehensive representation of the interaction between anatomical obstruction, microbial biofilms, allergic triggers, and immune dysregulation.

Table 1. Key Causes of Chronic Sinusitis

Cause Category	Examples	Impact on CRS	References
Anatomical	Nasal septal deviation, concha bullosa	Obstructs sinus drainage, promotes inflammation	Shaker, 2023; Hamilos, 2016
Infectious	*S. aureus*, *P. aeruginosa*, *Aspergillus*	Forms biofilms, resists antibiotics	Huang et al., 2022; Deutsch et al., 2019
Allergic/Environmental	Pollen, pollutants, tobacco smoke	Triggers type 2 inflammation, ciliary dysfunction	Stevens et al., 2019; Leland et al., 2021
Immunological/Genetic	Type 2 inflammation, CFTR mutations	Drives eosinophilia, microbiome dysbiosis	Bachert et al., 2018; Fischer & Lee, 2024

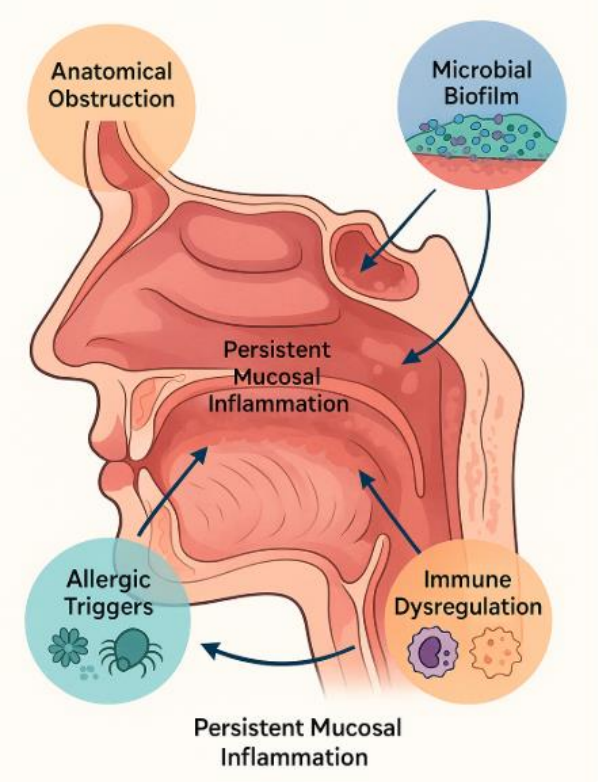

Figure 1: Pathophysiological Mechanisms of Chronic Rhinosinusitis.

Diagnosis of Chronic Sinusitis

The accurate diagnosis of chronic rhinosinusitis (CRS) is an important foundation for effective management and requires a multifaceted clinical, endoscopic, imaging, and biomarker-based approach. These methods work in an augmentation manner, permitting identification of CRS, differentiation of it from other sinonasal diseases, and phenotyping and endotyping for targeted treatments. By combining subjective and patient-reported observations with objective diagnostic assessments, the clinician learns various aspects of disease degree, underlying causative mechanisms, and the most appropriate therapeutic mechanisms.

Clinical Criteria

The diagnosis of CRS starts with and includes a comprehensive clinical evaluation based on the standardized criteria in the EPOS 2020 guidelines (Fokkens et al. 2020). According to these guidelines, CRS is diagnosed when 2 or more cardinal symptoms occur for at least 12 weeks and include nasal obstruction, nasal discharge (anterior rhinorrhea or posterior post-nasal drip), facial pain or pressure, and smell loss or reduction (Fokkens et al., 2020). In order to meet diagnostic criteria, at least one of the symptoms has to be nasal obstruction (blocked nasal passage) or nasal discharge (runny nose). The diagnostic workup varies, but a detailed history of the patient is vital to ensure that it is CRS and rule out other possible causes of similar symptoms, such as acute rhinosinusitis, allergic rhinitis, and non-sinonasal disorders such as migraine or temporomandibular joint dysfunction (Dhar et al., 2024).

Clinicians look at the chronicity of the symptoms, triggers, and contributory factors (allergies, work exposures) to provide context to the condition. Clinicians also use validated tools such as the Sino-Nasal Outcome Test (SNOT-22) to quantify the severity of their symptoms and burden to their quality of life; and provide a standardised measure to monitor disease progression and response to treatment (Hopkins, 2019). The SNOT-22 measures patients' physical symptoms, a functional (health-related quality of life) measure, and an emotional measure to offer a rounded perspective of the patient's experience. Pound for pound, using a clinical assessment is very subjective and with the potential for diagnostic confusion due to the overlap of symptoms with other conditions. Thus, there is a need for further objective diagnostic tests.

Nasal endoscopy

Nasal endoscopy is an important diagnostic tool for CRS. It enables first-hand visualisation of the nasal and sinus mucosa, which can confirm the presence of inflammation, nasal polyps, and/or purulent nasal discharge. This is very effective for diagnosing CRS with nasal polyps (CRSwNP) because nasal polyps are a major component of the condition, and for assessing disease severity (Bachert et al., 2021) - endoscopy allows the clinician to evaluate mucosal edema, erythema, and anatomical factors, such as septal deviation or ostial obstruction, which may be contributing to a persistent state of disease (Hopkins, 2019). This procedure can also aid in determining the appropriate treatment, since if one sees extensive polyposis or purulent discharge, it might mean that surgery is required or more targeted medical therapy is necessary; for example, polyps may prompt the clinician to consider biologics for CRSwNP. It is worth noting that nasal endoscopy requires expertise and special equipment, so its availability may be limited in primary care or resource-poor settings. Moreover, given the discomfort to the patient, the procedure pushes the limits of the patient's tolerability, and this need for skill is essential for maximizing diagnostic yield.

Imaging Studies

High-quality imaging, like computed tomography (CT) studies, is recognised as a gold standard for examination of sinus anatomy and extent of CRS disease. CT provides high-definition images of the paranasal sinuses, allowing the clinician to visualize mucosal thickening, sinus opacification, and anatomical abnormalities such as a narrowed osteomeatal complex or the presence of a concha bullosa (Lund et al., 2018). Severity of disease can be measured with the Lund-Mackay scoring system, where scores depend on the degree of opacification of each sinus, with increased disease extent indicated by

increased scores. This quantitative evaluation helps in treatment planning and response to therapy monitoring (Norwood et al., 2023). MRI is reserved for particular cases, such as suspected fungal rhinosinusitis, soft tissue complications, or orbital and intracranial extension, due to its superior soft tissue contrast (Ni Mhurchu et al., 2017; Meng et al., 2019). New technology advances in low-dose CT scans have reduced radiation dose while maintaining diagnostic quality, and they render imaging safer and more accessible (Norwood et al., 2023). However, the cost of imaging and unnecessary radiation exposure issues among younger patients or those requiring repeated studies highlight the need for judicious use and supplementation by other methods of diagnosis.

Emerging Biomarkers

The progression of biomarker research has transformed CRS diagnosis as it enables endotype-directed approaches that identify specific inflammatory pathways in the condition. Such biomarkers as ECP, IL-5, and periostin are closely associated with type 2 inflammation, which is common in CRSwNP, and guide the selection of biologic therapy like dupilumab or mepolizumab (Xie et al., 2023). Nasal cytology involves the examination of nasal secretions for inflammatory cells, eosinophils, or neutrophils, which not only provides further detail to the inflammatory profile but also distinguishes between CRSwNP and CRSsNP (Kumar et al., 2023). Microbiome profiling is a new method that examines the microbial communities in the sinuses and their patterns of dysbiosis related to chronic inflammation. Having low diversity among the microbes is related to greater severity of disease with reduced efficacy of treatment (Fischer & Lee, 2024). These biomarker-directed strategies permit individualized diagnosis and treatment but are limited by their current unavailability and lack of standardization within clinical practice. Further investigation aims to authenticate these biomarkers and incorporate them into routine diagnostic algorithms, potentially revolutionizing the management of CRS by enabling precision medicine (Table 2). Figure 2 provides an overview of the pathway for diagnosing chronic rhinosinusitis and includes the clinical criteria, nasal endoscopy, imaging (CT or MRI), and biomarker assessment. This is represented as a stepwise flowchart that can guide accurate classification and patient-centered management.

Table 2. Diagnostic Modalities for CRS.

Modality	Description	Advantages	Limitations	References
Clinical Criteria	EPOS guidelines: ≥2 symptoms for ≥12 weeks	Non-invasive, cost-effective	Subjective, overlaps with other conditions	Fokkens et al., 2020; Dhar et al., 2024
Nasal Endoscopy	Visualizes mucosal changes, polyps	High specificity guides treatment	Requires expertise, invasive	Bachert et al., 2021; Hopkins, 2019
CT Imaging	Assesses sinus anatomy, Lund-Mackay score	Gold standard, quantifiable	Radiation exposure, cost	Lund et al., 2018; Norwood et al., 2023
Biomarkers	ECP, IL-5, microbiome profiling	Personalized diagnosis, endotyping	Limited availability, research stage	Xie et al., 2023; Kumar et al., 2023

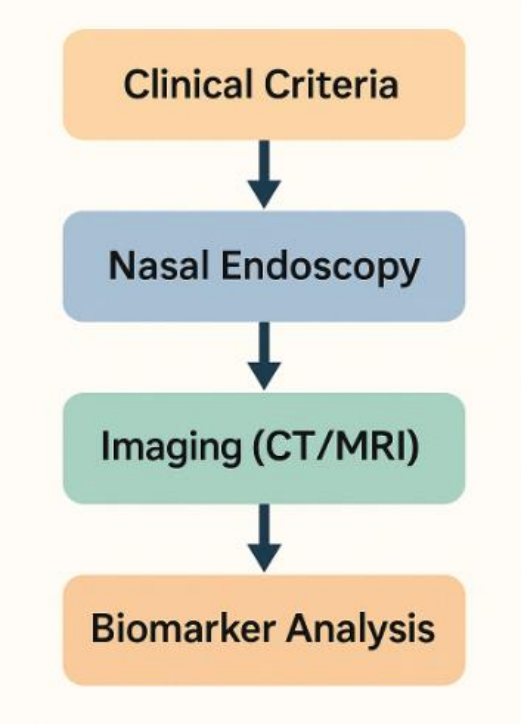

Figure 2. Stepwise Diagnostics in CRS

Contemporary Approaches to Chronic Sinusitis

The treatment for chronic rhinosinusitis (CRS) is to manage symptoms of CRS, decrease mucosal inflammation, and address underlying etiological reasons in a step-wise manner, so that it includes medical, surgical, and newer treatment options. Treatments are guided by the patient's CRS phenotype, either CRS with nasal polyps (CRSwNP) or CRS without nasal polyps (CRSsNP) at acute/chronic severity. For most patients, medical management is the main approach, while surgery is considered when other, less invasive methods fail. Advances in treatment, specifically in biologics and other therapy options, are adding a new dimension to treatment and targeting patients with complex disease processes. This section reviews treatment measures, including classifications, mechanisms of action, indications, limitations, evidence, standards, and novel treatment options.

Medical management

Medical therapies will be the first line of treatment for CRS; their purpose is to treat patients with CRS and provide control of inflammation, infection, and, therefore, the patient's symptom burden without a surgical procedure. Medical treatment generally starts based on clinical practice guidelines and is modified based on the response of the patient and implementation of medical therapy based on the individual patient's disease phenotype.

Corticosteroids

Corticosteroids are the mainstay of treatment for CRS because of their powerful anti-inflammatory action, reducing mucosal edema and polyp size, especially in CRSwNP. Intranasal corticosteroids (budesonide, fluticasone propionate, mometasone furoate) can be delivered directly to the nasal mucosa and tend to have far fewer systemic side effects while successfully reducing nasal obstruction, nasal discharge, and facial pain (Macias-Valle & Psaltis, 2021). Corticosteroids are effective at preventing the production of pro-inflammatory cytokines and limiting eosinophilic inflammation. In particular, they are useful in treating type 2 inflammatory conditions such as CRSwNP. However, for severe and refractory patients, systemic corticosteroids (e.g., oral prednisone) can be safely initiated for short courses or intermittent use to provide rapid symptom control. However, adverse reactions are significant in magnitude, including but not limited to osteoporosis, adrenal suppression, and metabolic complications (Poetker, 2015). Recently, there have been innovations in corticosteroid delivery through corticosteroid-eluting sinus implants (containing mometasone, for example), which allow and maintain localized administration after surgery, generating clarity between patients where surgical and medical treatment impact positively in maintaining sinus patency and reducing inflammation weeks to months (Norwood et

al., 2023). The use of corticosteroid-eluting sinus implants may limit the recurrence of polyps in the long term and reduce the use of systemic steroids, thereby providing a safer alternative for long-term management. While intranasal corticosteroids can work, they may be less effective in cases of severe CRSwNP or if clinically significant anatomical obstruction is present, and additional treatments may be warranted.

Antibiotics

Antibiotics are used in CRS for the treatment of acute bacterial exacerbations or for biofilm-related infections that are common with CRSsNP and CRSwNP. Antibiotics are important in CRS, and use is most common with macrolides such as azithromycin and clarithromycin. Macrolides affect both the bacterial infection and neutrophilic inflammation by having both antibacterial and anti-inflammatory effects (Niekrash, 2023). First, the macrolides interact directly with the immune system to decrease neutrophilic inflammation and decrease bacterial load, especially in CRSsNP (Niekrash, 2023). Statistically, there are hundreds of molecules and thousands of drug target combinations, so identifying suitable drugs is limited only to the dosage and habits of most physicians regarding potential adverse effects on patients. The use of antibiotics among medical professionals is usually deliberate; it raises concerns about antimicrobial resistance by broadening the number of bacterial spp., especially in biofilm-driven acute or chronic CRS, which presents with bacterial insertion into a protective matrix resulting in decreased drug action/outcomes.

Biofilms make treatment resistant and advance disease to persistent disease by offering organisms both protection and an advanced weapon; both decrease drug action and efficacy of the standard regimen (Huang et al., 2022). Overall, research suggests it is important to develop strategies that differentiate infection-induced treatment-resistant biofilms in CRS by developing strategies that either offering combination therapies/or developing agents to disrupt biofilms. There are other potential concerns regarding the duration of antibiotic treatment that include antibiotic adverse effects, such as effects on the gut (viability and build up plus complement activity) and effects on the sinus microbiome. Since Macrolides have other antimicrobial functions in inflammatory conditions that are such as their ability to inhibit pro-inflammatory cytokines, such as IL-8, antibiotics are a treatment option in CRSwNP and CRSsNP (Cervin & Wallwork, 2014).

Biologics

Biologics have changed the management of severe, refractory CRSwNP by targeting particular inflammatory pathways, specifically type 2 inflammation with eosinophilia and high IgE. Dupilumab is a monoclonal antibody that targets the IL-4 receptor alpha subunit (IL-4Rα), inhibiting IL-4 and IL-13 signaling pathways, and is proven to reduce polyp size, nasal congestion, and severity of symptoms while improving quality of life (Bachert et al., 2021). Clinical trials have demonstrated that dupilumab produces sustained reductions in polyp score and SNOT-22 score, effectively changing the treatment course for patients who do not respond to corticosteroids or surgery. Omalizumab (anti-IgE) and mepolizumab (anti-IL-5) can be effective alternatives, particularly in patients with comorbid asthma or high IgE levels (Cavaliere et al., 2024; Vanderhaegen et al., 2022). These biologics target specific endotypes as well, and both have the potential to be billed as precision medicine because they treat the underlying

inflammatory processes of CRSwNP. Although biologics are transformative, they are also prohibitive because of their cost and have limitations related primarily to cost and the lack of long-term safety data and durability of response. Another concern is the potential side effects, which may include injection-site reactions, hypersensitivity (rare), and require the use of clinical judgement. Therefore, additional work is taking place within research to determine dosing regimens, dosing, and possible combinations with other therapies.

Surgical Procedures

Surgical procedures are reserved for patients with Chronic Rhinosinusitis (CRS) related to failure of medical management, to restore sinus ventilation, drainage, and alleviate symptoms. The surgical procedures are dependent on the extent of disease and anatomy available; however, the expected procedures may vary in terms of invasiveness.

Functional endoscopic sinus surgery (FESS) has become the procedure of choice for the surgical treatment of CRS, and is especially beneficial in those patients with refractory CRSsNP or CRSwNP. FESS surgery utilizes endoscopes to remove obstructing tissue, enlarge sinus ostia, and re-establish mucociliary clearance, and provides 80-90% symptom improvement in patients (Norwood et al., 2023). FESS is exceptionally valuable for correcting anatomical issues such as nasal polyps or osteomeatal complex obstruction, and in these cases is most effective when performed with supplemental postoperative medical therapy to minimize future recurrence. FESS can include a variety of procedures to treat the cause of CRSsNP and CRSwNP, depending on the disease pattern, from limited procedures like maxillary antrostomy to extensive clearance of the sinuses in patients with severe disease. While FESS is effective for treating CRS, it is not without risk, including bleeding, infection, and possibly cerebrospinal fluid leaks, and until further studies are published reporting on recurrence in CRSwNP patients (20-40% recurrence rate), it demonstrates the operational need for continued medical management (Shaker, 2023).

Balloon sinuplasty is a less invasive technique that can achieve similar dilatation of sinus ostia without violating any tissue and may be beneficial in selected patients with limited disease or who are not interested in traditional surgery (Koskinen et al., 2016). This outpatient procedure has the potential for quicker recovery and lower complication rates, but will likely be less effective in patients with extensive polyposis or considerably more complex anatomical obstructions. Both FESS and balloon therapy reiterate the importance of postoperative care, including intranasal corticosteroids and saline irrigations to promote sinus patency and to minimize the chances of disease recurrence.

Emerging Therapies

Innovative therapies are emerging to fulfill unmet needs in the therapy needs of CRS patients, especially for patients with refractory disease, or all CRS patients seeking alternatives to surgery and biologics. Microbiome-based therapies (i.e., topical probiotics, microbial transplant) would aim to restore the microbial burden in the sinuses, to combat an imbalance called dysbiosis commonly associated with chronic inflammation (Cope et al., 2023). Although this is still an emerging therapy, there is early evidence to suggest that probiotics, especially *Lactobacillus* species, in CRS patients may reduce inflammatory markers in addition to symptomatic improvement due to restoring a healthy microbial burden. Photodynamic therapy (PDT) employs light-activated photosensitizers to directly target biofilms (and decrease density of the biofilms if they are vascularized), and at least early studies suggest PDT

can impact antibiotic-resistant bacterial communities, important especially in the recalcitrant CRS population (Biel et al, 2014).

Nitric oxide-based therapies, which utilize the antimicrobial and anti-inflammatory effects of nitric oxide, are being studied for their potential to abolish biofilms as well as their mucosal healing properties (Zajda et al., 2018). Additionally, nanoparticle-based drug delivery systems have been studied to allow for direct delivery of anti-inflammatory or anti-microbial agents to the sinus mucosa, which increases the drug's ability to penetrate the mucosa but also decreases systemic side effects (Pramanik et al., 2021). The research focused on these therapies is still in the experimental phase, and there are further clinical trials to be conducted to ensure efficacy, safety, and delivery are established (Table 3).

Table 3. Treatment Modalities for CRS.

Treatment	Mechanism	Indications	Limitations	References
Intranasal Corticosteroids	Reduces mucosal inflammation	CRSsNP, CRSwNP	Limited efficacy in severe cases	Macias-Valle & Psaltis, 2021; Poetker, 2015
Antibiotics	Targets infections, anti-inflammatory	Acute exacerbations, biofilms	Antibiotic resistance, side effects	Niekrash, 2023; Cervin & Wallwork, 2014
Biologics	Targets type 2 inflammation	Severe CRSwNP	High cost, limited long-term data	Bachert et al., 2021; Cavaliere et al., 2024
FESS	Improves sinus drainage	Refractory CRS	Invasive, recurrence risk	Norwood et al., 2023; Koskinen et al., 2016
Emerging Therapies	Restores microbiome, eradicates biofilms	Research stage	Limited clinical evidence	Cope et al., 2023; Biel et al., 2014

Future Directions

Despite progress in many avenues, there are still challenges to the management of CRS, including treatment resistance, the cost of biologics, and variability in operative outcomes. Personalized medicine, utilizing endotyping and biomarker

identification in the patient population, can help customize therapies to individual inflammatory patterns (Bachert et al., 2021). Longitudinal biologic trials must ascertain durability and safety (Fokkens et al., 2023). Therapeutic effectiveness would be enhanced by advances in drug delivery, e.g., nanoparticle systems, by affecting specific sinus regions (Pramanik et al., 2021). Exploring the sinus microbiome as a cause of disease progression could also unleash novel probiotic or prebiotic therapies (Fischer & Lee, 2024). Multidisciplinary research integrating otolaryngology, immunology, and microbiology will be crucial to advancing the treatment of CRS.

Conclusion

Chronic rhinosinusitis is a complex, multifactorial disease that requires an integrated diagnosis and treatment approach. Advances in diagnostic technology, including biomarkers and low-dose imaging, have increased accuracy, while biologics and minimally invasive procedures have increased therapeutic success. But cost, accessibility, and recurrence of the disease are challenges that require continued investigation. By integrating the latest literature, this review highlights the changing CRS management landscape and the promise of personal, microbiome-targeted treatments to revolutionize patient care.

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