

The Role of Infection and Antibiotics in Chronic Rhinosinusitis.

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Objective: To review the current understanding of the role of infection and antibiotics in chronic rhinosinusitis.

Review methods: PubMed literature search

Results: Chronic rhinosinusitis (CRS) in adults is an inflammatory condition and the role of infection is unclear. Biofilms are present in both CRS and normal patients so their role in CRS is unknown. Sinus cultures in CRS demonstrate a mixture of aerobic and anaerobic bacteria but may be hard to interpret due to contaminating nasal flora. *Staphylococcus aureus* is common in CRS patients but also present in 20-30% of nasal cultures in the normal population; eradicating this organism did not lead to symptom improvement versus placebo in a randomized controlled trial (RCT). In CRS patients who develop an episode of acute rhinosinusitis (ARS), bacteria typical of ARS can generally be cultured and require short-course treatment. For CRS, topical antibacterial or antifungal agents have shown no benefit over placebo in RCTs, although RCTs of topical antibacterial agents have been small. Oral macrolides and doxycycline, antibiotics with anti-inflammatory properties, are the only systemic antibiotics that have been evaluated in RCTs. One RCT found 3 weeks of doxycycline beneficial in patients with polyps but follow up was short (<3 months); RCTs of prolonged macrolide therapy have produced mixed results, and most show no benefit after cessation of therapy. Long-term antibiotic therapy may produce side effects and select increasingly resistant flora. The American Academy of Otolaryngology—Head and Neck Surgery guidelines recommend against treatment of CRS with antifungal agents but do not comment on the role of antibacterial treatment.

Conclusion: The role of infection in CRS is unknown, and the only well-defined role for antibiotics is for treatment of ARS episodes or their infectious complications.

Key Words: chronic sinusitis, rhinosinusitis, antibiotics, sinus infection.

Level of Evidence: N/A.

INTRODUCTION

Sinusitis is common. The 2012 National Health Interview Survey found that 12% of adults in the United States had been diagnosed with sinusitis over a 12-month period.¹ Chronic sinusitis, more accurately termed chronic rhinosinusitis (CRS), is diagnosed more often than acute rhinosinusitis (ARS). Survey studies in the U.S., Brazil, China, Korea, and Europe report CRS prevalence rates of 5% to 11%²⁻⁶.

Antibiotics are commonly prescribed for CRS. One U.S. study found that sinusitis accounted for 11% of primary care visits for which an antibiotic was prescribed, with CRS accounting for 7% and ARS 4%.² Although a number of antibiotics have an indication from the Food and Drug Administration (FDA) for treating ARS, no antibiotic has FDA approval for treating CRS. This is largely because the role of antibiotics in the treatment of CRS

remains unclear. This review summarizes the pertinent literature on the role of infection and antibiotics in CRS.

Definition

In order to determine the role of infection and antibiotics in CRS, a standard definition for CRS must be used. A clear definition has been available only since 2003.⁷ Clinical practice guidelines from the American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS) were published in 2007 and updated in 2015.⁸ The 2015 AAO-HNS definitions of CRS, ARS, and recurrent ARS are listed in Table 1; CRS requires at least two symptoms for 12 weeks plus objective findings of inflammation by examination or radiologic studies. Patients who had acute exacerbations of CRS (AECRS) were not considered separately by the AAO-HNS, but have been in other guidelines.

Identifying CRS cases by use of office diagnoses by non-otolaryngologists or billing data is frequently inaccurate.^{9,10} For example, in a series of 114 cases billed as CRS by primary care or emergency medicine providers, only one patient actually met CRS criteria.¹¹ Fewer than 10% of patients in this study met the 12-week criteria for symptom duration, no patient had evidence of inflammation on physical examination, nearly 70% of patients who had computed tomography (CT) scans performed had no or only mild CT evidence of sinusitis, and only 7% of narrative assessments described patients as having CRS. Ideally, the AAO-HNS definition of CRS should be used for studies of antibiotic efficacy.

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TABLE 1.
Definitions of Sinusitis Categories.

Term	Definition
Rhinosinusitis (RS)*	Symptomatic inflammation of the paranasal sinuses and nasal cavity
Acute rhinosinusitis (ARS)*	≤ 4 weeks of purulent nasal drainage (anterior, posterior or both) accompanied by nasal obstruction (congestion, blockage, stuffiness), facial pain-pressure-fullness, or both
Chronic rhinosinusitis (CRS)*	≥12 weeks' of at least 2 of the following: <ul style="list-style-type: none"> ■ Mucopurulent drainage ■ Nasal obstruction (congestion) ■ Facial pain, pressure, or fullness ■ Decreased sense of smell PLUS inflammation as documented by one of the following: <ul style="list-style-type: none"> ■ Purulent mucus or edema in the middle meatus or anterior ethmoid ■ Polyps in the nasal cavity or middle meatus ■ Radiographic imaging showing sinus inflammation
Recurrent acute rhinosinusitis (RARS)	≥ 4 episodes of acute rhinosinusitis over preceding 12 months, without symptoms between episodes
Acute exacerbation of chronic rhinosinusitis (AECRS) [†]	Sudden worsening of symptoms in a patient with a previous diagnosis of CRS, with return to baseline following treatment

*From reference 8.

[†]From Reference 13. Many authors use "AECRS" to mean an ARS episode in a CRS patient.

Chronic rhinosinusitis is often further divided into CRS with and without nasal polyps, CRSwNP and CRSsNP, respectively. Approximately 20% of CRS cases have nasal polyposis, and CRSwNP is one of the most common indications for sinus surgery.¹² Orlandi and colleagues recently published a 180-page "international consensus statement" on rhinosinusitis (RS), which included over 100 authors from around the world and included a review of the literature on CRS.¹³ The authors considered CRSwNP and CRSsNP separately when possible.¹³ In some cases, as in the use of topical or intravenous antibiotics in CRS, the two categories were combined due to insufficient data. Orlandi et al. in the International Consensus Statement considered AECRS as a separate category but noted that "there is a paucity of data on the diagnostic criteria of AECRS";¹³ their definition of AECRS is included in Table 1, but many authors use "AECRS" to mean an ARS episode in a CRS patient.

Pathogenesis

The pathophysiology of CRS is multifactorial. As Rudmik and Soler note, CRS was once thought to be infectious in etiology "but now is recognized as an inflammatory disease of the upper airways analogous to asthma in the lower airways."¹⁴ It is possible that infection by viruses or bacteria play a role in the pathogenesis of some cases, but this is difficult to determine. Because the nose is not sterile, a culture of the sinus obtained via the nose will always grow microbes, and causality in CRS is not established by a positive culture. Trying to determine the role of infection based on a response to antibiotic treatment is also difficult. Acute exacerbations of CRS may be caused by bacterial infection and respond to treatment, but CRS alone usually does not. As discussed further below, macrolides or doxycycline may produce transient benefits in CRS patients,

but these antibiotics have anti-inflammatory properties so the benefits may be due to the anti-inflammatory rather than the anti-bacterial properties.

Microbiology

Studies of the microbiology of CRS have demonstrated a variety of bacteria and fungi. The microbiology may vary by location (which sinus was cultured), prior surgery, and recent antibiotic use. The technique used for culturing may influence results. In general, cultures of CRS patients reveal a mixture of aerobic and anaerobic bacteria, with a shift towards more resistant bacteria with time likely reflecting selective pressure from frequent antibiotic use.

Bacteria

Brook reported a range for bacteria recovered in studies of CRS in various sinuses, including *Staphylococcus aureus* (14-24%), Enterobacteriaceae (6-47%), *Pseudomonas* (3-14%), acute sinusitis pathogens (5-15%) such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*, and anaerobes.¹⁵ The frequency of anaerobes in CRS varies widely but depends on specimen collection and culture techniques; in studies using careful techniques, anaerobes are recovered in two-thirds of CRS cases.¹⁵ The microbiology of CRSwNP does not differ significantly from CRSsNP.¹⁵ A recent report pooled microbiology results from 43 studies published 1975–2010 and involving 3,500 CRS patients; 77% of cultures were obtained intraoperatively.¹⁶ Results were similar to those reported by Brook except that anaerobes were reported in fewer patients (likely reflecting inadequate culture techniques) and coagulase-negative staphylococci were the most common organisms isolated (25% of cases). Coagulase-negative staphylococci

are part of the normal nasal flora, and infectious disease specialists do not consider them to be respiratory tract pathogens.

Fungi

Fungi have been cultured from nasal secretions of 96% of CRS patients but also 100% of normal controls.¹⁷ This is not surprising since nasal mucus is effective at trapping the fungal spores that are ubiquitous in the air. Fungi are associated with an allergic response in some patients but antifungal medications have proven ineffective in CRS, as discussed below.

Colonizer or pathogen?

It can be difficult to interpret cultures in an individual CRS patient who has no evidence of acute infection. Some bacteria such as staphylococci grow robustly on culture media so may be overrepresented, and bacteria such as anaerobes that require special collection and culture techniques may be underrepresented. In addition, cultures will reflect colonizing bacteria that may or may not be pathogens. It is nearly impossible to obtain a sinus culture via the nose without contamination by resident nasal flora. Given the microscopic size of bacteria (1-2 microns), contamination is frequently unrecognized yet even a few colonizing bacteria, doubling every 20 minutes, may result in a positive culture. Distinguishing pathogens from colonizing bacteria can be especially difficult in cultures from CRS patients. *Staphylococcus aureus* is present in the nasal flora of 20-30% of the normal adult population, and methicillin-resistant *S. aureus* (MRSA) in 3-6%, so growth of either of these organisms from a sinus culture may signify colonization rather than infection. Many CRS patients are convinced that they have a "chronic staph infection" in the sinuses because cultures repeatedly grow *S. aureus*, but these may represent normal colonizers and not pathogens. A recent trial of mupirocin nasal irrigations for patients with *S. aureus*-positive cultures trial found no symptomatic benefit over saline nasal irrigations even though *S. aureus* was eliminated in 89% of the mupirocin but none of the saline group.¹⁸

Gram-negative bacilli are often cultured from patients with CRS, but the colonizing flora in these patients is often altered by sinus surgery, repeated courses of antibiotics, and irrigations with tap water or distilled water. Tap water contains many gram-negative bacilli including *Pseudomonas*, and CRS patients who use non-sterile water for nasal irrigations may be introducing these bacteria into their sinuses. Repeated courses of first-line antibiotics such as beta-lactams may alter the colonizing flora so that resistant bacteria are selectively enhanced.

Biofilms

A biofilm is a community of bacteria or fungi that surrounds itself with a protective extracellular matrix. Using quorum-sensing molecules, bacteria communicate density and form a biofilm once sufficient bacterial

concentration has been reached.¹⁹ The biofilm provides resistance to host defenses, and the organisms in the biofilm undergo a change to require less oxygen and nutrients, increasing their resistance to antibiotics. Antibiotic treatment against susceptible bacteria may induce resistant bacteria to produce biofilms. Kaplan's group has found that low doses of amoxicillin, for example, stimulate biofilm formation in MRSA.²⁰

The role of biofilms in CRS has received increasing attention since biofilms were first described on sinonasal mucosal surfaces of patients with CRS in 2004.²¹ However, the role of biofilms in CRS pathogenesis is not yet certain. Approximately 20% of CRS patients and 50% of CRS surgical candidates are biofilm-positive, but biofilms can also be found in control patients without CRS.²²⁻²⁴ Bezzara and colleagues evaluated mucosal biopsies by electron microscopy and found biofilms present in more CRS than control patients (73% vs 48%, respectively), but this difference was not significant.²⁴ Treatment of biofilms is an area of active research. In vitro studies have shown that corticosteroids have some effect against *S. aureus* biofilms,²⁵ and macrolides inhibit quorum sensing in *Pseudomonas*.¹³ A combination of a macrolide plus quinolone was effective in eliminating a *Pseudomonas* biofilm in one experimental model.²⁶

Microbiology of AECRS

Patients with CRS who develop ARS may have pathogens typical of both. Brook and colleagues performed multiple endoscopically directed sinus cultures in 7 CRS patients during at least three acute exacerbations over a period of 4-8 months; each acute episode was treated with antibiotics.²⁷ Typical of CRS, anaerobes were present in all cultures of all 7 patients, and *S. aureus* was present in all cultures of one patient. Acute sinusitis pathogens (*H. influenzae*, *S. pneumoniae*, *M. catarrhalis*) were present in many of the episodes, but the same patient would often have a different isolate with each episode. An increase in antibiotic resistance with time was noted in nearly all patients.

Treatment with Topical Antibiotics

The concept of topical antibiotics for treatment of chronic sinusitis is very appealing in that one might expect topical administration to deliver high concentrations of antibiotics to the sinus surfaces where they may penetrate a bacterial biofilm, without the downsides of causing side effects such as deep organ toxicity, diarrhea, or alterations of the systemic microbiome. Topical antibiotics are especially appealing in the current era of increasing antibiotic resistance. Topical antifungals hold appeal for treatment of chronic sinusitis for similar reasons, and also because of the thought by some authors that chronic sinusitis may result from an exaggerated allergic response to fungi in nasal mucus.

However, distribution of topical treatments to unoperated sinuses is limited, with less than 2-3% of the total irrigation volume or nebulized solution attaining sinus penetration in the setting of CRS with mucosal edema.²⁸

TABLE 2.
Topical Antibiotics for Chronic Rhinosinusitis; Results of Randomized Controlled Trials.

Study	Year	N	Study group (N)	Control group (N)	Endpoints	Benefit of topical antibiotic?
Sykes ²⁹	1986	50	Neomycin + tramazoline + dexamethasone by nasal spray (20)	(1) Tramazoline + dexamethasone by nasal spray (20) (2) Placebo (10)	Culture, endoscopy, manometry, x-ray, mucociliary clearance	No
Desrosiers ³⁰	2001	19	Tobramycin by nasal nebulizer (9)	Saline by nasal nebulizer (10)	Symptoms, histology	No
Videler ³¹	2008	14	Bacitracin-colimycin by nasal nebulizer + oral levofloxacin (7)	Saline plus oral levofloxacin (7)	Symptoms, endoscopy	No
Jervis-Bardy ¹⁸	2012	22	Mupirocin rinse plus oral placebo (9)	Saline rinse plus oral amoxicillin-clavulanate (13)	Culture, symptoms, endoscopy	No for symptoms

In postoperative sinuses, topical distribution is much more effective, but the results of trials evaluating the benefit of topical antibiotics in patients with chronic sinusitis have been disappointing.

Topical antibacterial agents

Four randomized controlled trials (RCTs) of topical antibiotics in adults with CRS have been performed (Table 2).^{18,29-31} Studies were small, with study arm subjects totaling 20 patients in the largest trial and only 7-9 in the other three trials. Three of these trials—using topical neomycin spray, nebulized tobramycin, and nebulized bacitracin—showed no benefit of topical antibiotics over saline.²⁹⁻³¹ One trial included oral levofloxacin in both study and placebo arms.³¹ One reason that has been cited for lack of efficacy in these trials is inadequate sinus penetration with the delivery methods used, as none of these trials used large volume irrigation. The fourth trial, by Jervis-Bardy and colleagues, evaluated four weeks of topical mupirocin irrigations versus saline irrigations (plus two weeks of oral amoxicillin-clavulanate) in post-surgical patients with positive cultures for *S. aureus*.¹⁸ The study was small (9 study, 13 control patients). At the end of four weeks, mupirocin was highly effective (89%) in eliminating *S. aureus* and endoscopy scores were significantly improved, but symptoms were similar in both groups. Gains in endoscopy were not sustained in the mupirocin group, and 2-6 months later both symptoms and endoscopic findings had worsened to pre-treatment baselines.

Toxicity from topical antibiotics is rare but a potential concern, especially for topical aminoglycosides. Whalley et al. measured serum gentamicin levels in 12 patients who had received nasal irrigations twice daily for 3-15 weeks and found that 83% had detectable post-treatment levels ranging from 0.3-0.7 µg/ml, including four patients whose levels were 0.5 or higher, so in therapeutic trough ranges.³² Prolonged exposure could potentially have adverse effects on hearing or renal function.

The idea of using topical antibiotics to impact biofilms in vitro is an area of ongoing interest and active investigation, but there is little evidence so far in vivo that impacting biofilms improves symptoms or quality of life in the short or long term.

Topical anti-fungal agents

Regarding topical antifungals, an early RCT found topical amphotericin to be beneficial in reducing mucosal thickening on CT.³³ However, subsequent RCTs failed to demonstrate any benefit for topical antifungal agents (Table 3).³⁴⁻³⁷ Most studies were larger than RCTs for topical antibacterial agents; the Ebbens study involved over 110 patients.³⁵ Nearly all have evaluated topical amphotericin, but one recent RCT used topical fluconazole and also found no benefit.³⁷ Multiple meta-analyses looking at topical antifungal treatment with amphotericin B included several RCTs that met inclusion criteria.^{38,39} Results indicated no differences between treatment and placebo groups for quality of life, nasal endoscopy, or symptom scores. In a meta-analysis pooling five studies investigating topical and one study investigating systemic antifungal agents, symptom scores statistically favored placebo, and adverse event reporting was higher in the antifungal group.⁴⁰

Summary of topical antibiotics

In summary, there is no evidence to date that topical antibiotics are effective for treating CRS, although studies using antibacterial agents have been small. Nasal irrigations with aminoglycosides should be avoided due to potential systemic absorption and toxicity. Multiple RCTs have found no benefit with topical antifungal agents. The recent International Consensus Statement recommends against using topical antibacterial or antifungal treatment for CRS.¹³ The AAO-HNS Guidelines recommend against using topical or oral antifungal agents for CRS.⁸

Treatment with Systemic Antibiotics

Oral antibiotics. Oral antibiotics are frequently prescribed for CRS despite a lack of good data regarding efficacy. There are very few studies that have examined antibiotic use in CRS patients by RCTs using a placebo arm, and all have used macrolides or doxycycline—antibiotics known for their anti-inflammatory properties. Six major RCTs in adults are summarized in Table 4; all were small and had different inclusion criteria regarding

TABLE 3.
Topical Antifungal Agents for Treatment of Chronic Rhinosinusitis; Results of Randomized Controlled Trials.

Study	Year	N	Study group (N)	Control group (N)	Endpoints	Benefit of topical antifungal?
Weschta ³⁴	2004	60	Amphotericin spray x 8 weeks (28)	Saline spray (32)	CT, endoscopy, QoL, symptoms	No (symptoms worse with amphotericin)
Ponikau ³³	2005	24	Amphotericin lavage x 6 months (10)	Placebo (14)	CT, endoscopy, symptoms, inflammatory markers	Not for symptoms; less mucosal thickening on CT
Ebbens ³⁵	2006	116	Amphotericin lavage x 3 months (59)	Placebo (57)	Visual analog score, symptoms, QoL	No
Gerlinger ³⁶	2009	30	Amphotericin spray (14)	Placebo (16)	CT, symptoms, QoL	No
Hashemian ³⁷	2016	48	Fluconazole drops x 8 weeks (24)	Placebo (24)	CT, symptoms, endoscopy	No

CT = computed tomography, QoL = quality of life

polyps and recent surgery.^{41–46} The control arm was a placebo in four studies but nasal corticosteroids in two. All 5 studies of macrolides evaluated long-term therapy (three months or more). Results were mixed, with studies involving patients with polyps showing some benefit. The study of short course doxycycline was small (47 patients divided into three arms) but concluded that three weeks of doxycycline was moderately effective in decreasing polyp size at 12 weeks compared with placebo.⁴⁶ A three-week oral corticosteroid taper also decreased polyp size but the effect did not persist beyond 8 weeks.

Systematic reviews have been published that rely primarily on these RCTs. Rudmik and Solar reviewed 29 publications, including 12 meta-analyses (>60 RCTs), four additional RCTs, and 13 systematic reviews, and concluded that a short course of doxycycline (three weeks) may be considered as an alternative to a short course of systemic steroids or a leukotriene antagonist in patients with nasal polyps, while a prolonged course

(three months) of macrolide antibiotic may be considered for patients without polyps.¹⁴ A 2016 Cochrane review by Head and colleagues included RCTs with a follow-up period of at least three months and compared systemic or topical antibiotic treatment to placebo, no treatment, or other pharmacologic interventions.⁴⁷ The analysis included four of the 6 RCTs or oral antibiotics listed in Table 4; no RCTs of topical antibiotics met the inclusion criteria. The authors concluded that there was very little evidence that systemic antibiotics are effective in patients with CRS. They found moderate quality evidence of a modest improvement in disease-specific quality of life in adults with CRS without polyps receiving three months of an oral macrolide, with a moderate improvement size (0.5 points on a 5-point scale) seen only at the end of the three-month treatment course; by three months later, no difference was found. The authors conclude that more research is needed, especially regarding longer-term outcomes and adverse effects.

TABLE 4.
Systemic Antibiotics for Chronic Rhinosinusitis in Adults.

Study	Year	Study location	Inclusion criteria	N	Study group	Control or comparison group	Benefit of antibiotics?
Wallwork ⁴¹	2006	Australia	No polyps	64	roxithromycin daily x 3 months	placebo	Yes at end of therapy but no clear benefit 3 months later
Videler ⁴²	2011	Europe	With or without polyps	60	azithromycin daily x 3 days during week 1, then once weeks 2-12	placebo	No
Zeng ⁴³	2011	China	No polyps	43	clarithromycin daily x 12 weeks	nasal corticosteroids	Similar benefit to nasal corticosteroids
Varvyanskaya ⁴⁴	2014	Russia	After surgery (CRS with polyps)	66	clarithromycin plus nasal corticosteroids daily for 12 or 24 weeks	nasal corticosteroids	Yes, decreased polyps, improved symptoms at 24 weeks vs. nasal corticosteroids alone
Haxel ⁴⁵	2015	Germany	After surgery (CRS with or without polyps)	58	erythromycin daily x 3 months postoperatively	placebo	No improvement in symptoms; endoscopy scores better
Van Zele ⁴⁶	2010	Europe	polyps	47	doxycycline daily x 20 days	(1) placebo (2) oral corticosteroid taper x 20 days	Either doxycycline or steroids decreased polyp size at week 12 vs placebo

CRS = chronic rhinosinusitis

The use of long-term antibiotics raises great concern for promoting antimicrobial resistance. Other concerns include potential adverse effects of systemic antibiotics such as *Clostridium difficile* colitis, antibiotic-associated diarrhea, alteration of the microbiome, tendon disease, etc. Antibiotics are a major cause of adverse drug events in general. In one study, antibiotics accounted for 19% of emergency room visits for adverse drug events, and the risks of adverse effects with some antibiotics were comparable to those of insulin, warfarin, and digoxin.⁴⁸

In this setting, it seems reasonable to continue to try to address the question of antibiotic efficacy in CRS by performing studies in more uniform populations—e.g., patients who either do or do not have nasal polyps, who have or have not had endoscopic sinus surgery, who have or have not failed more standard therapies (e.g., saline irrigations, topical corticosteroids), who have or have not achieved sinus aeration and adequate mucociliary clearance—and in trials in which patients receive antibiotics that target the appropriate spectrum of flora from carefully-collected cultures and are followed up for an adequate duration of time after the course of antibiotics is prescribed.

In the meantime, the 2015 AAO-HNS clinical practice guideline recommends treatment of CRS with saline nasal irrigation, topical intranasal corticosteroids, or both for symptomatic relief.⁸ It does not directly address the question of topical or systemic antibacterial antibiotics. It makes an explicit recommendation that clinicians should not prescribe topical or systemic antifungal therapy for patients with CRS.

Antibiotics for AECRS

Patients with AECRS usually require short courses of antibiotics to treat the pathogens of ARS (e.g. *H. influenzae*, *S. pneumoniae*, *M. catarrhalis*). Antibiotic choice may also need to include activity against recent CRS colonizers in a given patient so culture-directed therapy may be helpful, although studies of optimal treatment of AECRS are lacking. The International Consensus Statement notes that “There are no trials to endorse an evidence-based treatment of AECRS, though there is a tendency to treat AECRS like an episode of ARS or RARS.”¹³ Empiric antibiotic options for ARS are discussed in the AAO-HNS guidelines and in a recent clinical practice review in the *New England Journal of Medicine*.^{8,49} Antibiotic recommendations in the latter reference take into account the 2016 FDA advisory against use of fluoroquinolones for ARS unless there are no other treatment options for a given patient, since fluoroquinolones have potential serious musculoskeletal and neurological side effects that can be permanent.⁵⁰

Intravenous antibiotics

No RCTs have been performed for intravenous (IV) antibiotics in CRS. The few observational or retrospective studies that have been reported have demonstrated a high rate of complications without evidence of

sustained benefit. Fowler and colleagues, for example, performed a retrospective review of 31 CRS patients who had failed three courses of oral antibiotics and were treated with several weeks of culture-directed IV antibiotics.⁵¹ Only 29% of patients had resolution by endoscopy or CT, and of these patients, 89% relapsed at an average of 11.5 weeks after antibiotics ended. Complications occurred in 26% including thrombophlebitis, catheter-related infection, diarrhea, and neutropenia. The International Consensus Statement group concluded that IV antibiotics should not be used for routine cases of CRS, and should be reserved “for patients with complications or extrasinus manifestations of CRS.”¹³ The authors of this statement explain that by “extrasinus manifestations” they mean “the orbital, intracranial, and osseous complications related to AECRS.” An orbital complication, for example, may occur from an acute superinfection of a chronic mucocele in a CRS patient.

Summary of systemic antibiotics

In summary, the data supporting use of systemic antibiotics in CRS is very limited. Short course doxycycline may be indicated in patients with nasal polyps, but evidence for use of long-term macrolide therapy is not convincing for CRS patients with or without polyps. Data are lacking for other types of antibiotics. Acute bacterial sinusitis episodes and their complications (e.g., extra-sinus extension of infection), should be treated with antibiotics. Initial empiric antibiotics should be tailored based on culture results in cases of extra-sinus extension of infection.

CONCLUSION

Chronic rhinosinusitis in adults is an inflammatory rather than an infectious condition. Cultures in CRS demonstrate a mixture of aerobes and anaerobes but whether they are colonizers or play a role in symptoms is unknown. In CRS patients who develop an episode of ARS, bacteria typical of ARS can generally be cultured. Aside from treating these ARS episodes or extra-sinus complications of ARS in a CRS patient, the role of antibiotics in CRS remains unclear. Randomized controlled trials evaluating topical antibacterial agents have been small but have not demonstrated efficacy, and even large trials have shown no benefit for topical antifungal agents. The only RCTs for systemic antibiotics have evaluated doxycycline or macrolides, antibiotics with anti-inflammatory properties. Short-course doxycycline appears to have some benefit in patients with polyps, although study follow up was <3 months. Studies of long-term macrolides have had mixed results, with no clear lasting benefit following cessation of therapy.

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