

# Crohn's Disease of the Voice

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CROHN'S DISEASE IS AN INFLAMMATORY BOWEL disease (IBD) with increasing presence in the Western world. IBD primarily affects the gastrointestinal tract, but due to widespread inflammation, extraintestinal manifestations (EIMs) of the disease are common.

More specialists need to be included in the diagnosis and treatment of IBD due to these EIMs. Individuals with IBD frequently seek treatment for what is ultimately determined to be a symptom of underlying disease processes. It is important for physicians to be aware of these EIMs in IBD. Commonly overlooked EIMs in Crohn's disease are laryngeal and other otolaryngologic manifestations, which tend to be subtle and nonspecific, leading to confusion of their etiology. The recognition of EIMs is particularly important in professional voice users, especially singers, who are very sensitive to changes in the voice. It may be possible that subtle changes of the voice and laryngeal regions due to inflammatory conditions, such as Crohn's disease, may go unnoticed, and hence undiagnosed, in the general population.

Crohn's disease was first published as "Regional ileitis," in the *Journal of the American Medical Association* in October 1932.<sup>1</sup> At the time, it was described as a disease of the terminal ileum that affected mainly young adults and marked by inflammation of the small bowel. The description of the disease has expanded with time and is now described as a panenteric disease that can affect any part of the gastrointestinal tract.<sup>2</sup> The disease is named after Burrill B. Crohn, a physician from Mount Sinai Hospital in New York who authored the first published article on the condition. The typical clinical scenario is a young person presenting with abdominal pain, chronic diarrhea, rectal bleeding, weight loss, and fatigue.<sup>3</sup> Although the disease is incurable, current treatment strategies aim for long lasting clinical remission, with the goal of avoiding surgery and halting the natural disease progression. The cause for IBD is unknown, but is believed to be related to the interplay between genetics that make a person susceptible, environmental factors, and intestinal microflora, resulting in an abnormal immune response within the mucosa and weakened epithelial barrier function. Currently, researchers have identified more than 200 alleles associated with IBD, making genetics a far from perfect predictor of the disease. Cigarette smoking is the most studied environmental factor and is associated with a two-times increased risk.<sup>4</sup> Regardless of the causative factors in Crohn's disease, overactivation of the immune response leads to transmutable inflammation. The natural history of Crohn's disease is one of relapsing symptoms that may require dietary, surgical, pharmacologic, and disruptive lifestyle intervention.

Although IBD is known to manifest in the GI tract, its manifestation in extraintestinal organs can significantly alter a patient's quality of life. Extraintestinal manifestations (EIMs) are defined as "an inflammatory pathology in a patient with IBD that is located outside of the gut and for which the [pathology is an extension] of immune responses from the intestine, or is an independent inflammatory event perpetuated by IBD."<sup>5</sup> EIMs may present in up to 50% of patients and in up to 26% of patients before the onset of intestinal symptoms.<sup>6</sup> Often, EIMs require specific treatments outside the gastroenterology office and need to be considered when treatments are discussed. EIMs may occur concurrently with an IBD flare but may also occur independently of IBD activity. EIMs most commonly involve the musculoskeletal system (arthritis, etc.), skin (pyoderma gangrenosum, erythema nodosum, etc.), hepatobiliary tract (primary sclerosing cholangitis [PSC], etc.), and eyes (uveitis, episcleritis, etc.); however, almost any organ can be affected, and these EIMs may not be readily detectable by the patient and their treating physician.

Although sometimes indistinct, many clinical presentations of Crohn's disease, both specific and nonspecific, have been documented in the oral cavity, nose, larynx, and lungs. Lesions in the oral cavity, on the gums, tongue, cheeks, etc. are common and liable to be underestimated when not expressly sought.<sup>7</sup> As a general rule, the oral ulcers associated with Crohn's disease seem to be more widespread and severe than those seen in other conditions. Frequently reported laryngeal pathologies associated with general autoimmune disease include nodules, vocal fold edema and erythema, viscous secretions, a "lump in the throat," difficulty breathing, painful swallowing, and cough.<sup>8</sup> Though laryngeal involvement is noted as uncommon in Crohn's disease, nonspecific edema of the epiglottis and arytenoid area would noticeably affect more sensitive professional voice users, most specifically, singers.

Inflammatory conditions, such as Crohn's disease, are relevant to singers because singers have a heightened awareness of their own vocal production and its capabilities. They may detect vocal troubles from minute pathology. Crohn's disease symptoms affect parts of the body that are outside the GI tract through pathways that can trigger inflammation in any body system. A weakened immune system and heightened expression of inflam-

matory factors in the body can lead to enlargement of lymph nodes, which in the neck and laryngeal areas may affect vocal production. The intestinal epithelium produces mucus and antimicrobial factors, establishing a barrier between the contents of the intestine and itself.<sup>9</sup> Disruption of this buffer zone might promote bacterial translocation associated with IBD. In turn, bacterial translocation may dampen effects of the immune system to prevent dissemination of invasive bacterial species in IBD patients, creating a vicious cycle. Furthermore, dendritic cells, which are key antigen-presenting cells within the immune system, secrete proinflammatory factors into the blood in inflammatory conditions. Their secretion has the potential to affect any part of the body, including the voice.

The subtleties of the voice are vulnerable to many different aspects of body health. Singing places intense demands on muscles in the head and neck. Laryngologist L. Arick Forrest has noted that because of the extreme range, fine motor control, and stamina that classically trained singing demands, the laryngeal anatomy often will appear healthier overall with the addition of highly elastic vocal folds that can elongate easily.<sup>10</sup> Singers can be considered small-muscle athletes with a hyperawareness of factors affecting their performance. Getting a proper amount of sleep, eating foods that aim to maintain low blood sugar, exercising to maintain lung function, and abundant hydration are imperative to keeping the voice in top shape. Substances that may not noticeably affect the nonprofessional voice user may cause immediate threat to the livelihood of a singer. Caffeine, alcohol, high dosage of vitamin C, and salt intake can dehydrate the vocal fold epithelium with negative effect on singing, as dry unprotected folds are susceptible to injury. Additionally, many prescription and over the counter medications have the potential to pose a threat to the voice as well. Furthermore, the physical demands and stressful aspects of performance can decrease the ability of the immune system to fight infection. The effects of such stress on immunity would likely be exacerbated by the inflammatory conditions of an IBD.

Singing with swollen vocal folds can be particularly straining and may be unavoidable in a patient with IBD. Swollen vocal folds are thicker and stiffer, making them harder to control during phonation. More effort

is needed to produce sound, often resulting in excessive tension. Swollen, dehydrated, or fatigued folds are vulnerable and may lead to vocal compensatory behaviors and strain while singing, increasing the risk of vocal fold lesions and other complications. Swelling along any aspect of the vocal tract will produce perceptible alterations to vocal production such as dampened resonance or difficulties reaching higher registers.<sup>11</sup>

Many ambiguous transgressors affect the vocal folds, as there are many indirect inflammatory conditions that affect IBD patients. Asthma is caused by inflammation of the smooth muscles of the bronchi and alveoli in the lungs and may result in stenosis of these areas due to longstanding inflammation. The lungs are the driving force for the voice, and with decreased airflow comes a decrease in vocal stamina. This impairment in respiratory support can lead not only to faulty phonation, but also to compensatory hyperfunction that may cause vocal fatigue and/or structural pathology on its own. Inflammation factors in the blood and throughout the body of an IBD patient may cause issues such as asthma and/or the mucosa of the entire resonating tract to become edematous and erythematic and may be severe enough to mimic laryngitis. Additionally, the classic GI symptoms of Crohn's disease may also play a role in vocal quality. The discomfort of GI tract inflammation could intensify with pressure of diaphragmatic distention on inhalation, limiting one's ability to take the deep breaths required for singing. Intestinal discomfort may also disrupt a singer's ability to engage abdominal muscles while singing, interfering with the ability to support sustained tones.

A very common EIM of IBD is arthritis. The tiny joints of the larynx are like those of other areas in the body. Injury to or inflammation of any joint structure within the laryngeal areas can limit the joint's range of motion or cause pain. The movement of the vocal folds required for singing requires fine motor control and resistance free motion. Any small hindrances to this motion can result in vocal change. The first aspects affected by this reduction in fine motor control are typically easy vocal access to higher pitches and a decrease in vocal agility, which are often accompanied with breathiness. Aspects of vocal production may be compromised until inflammation can be controlled. Because many of the EIMs of IBD are related to system wide inflammation, it may

be posited that a Crohn's disease patient who also happens to be a professional voice user may encounter any number of these vocal issues and should be aware of their prevalence.

As explored, the larynx, vocal tract, and resonators are incredibly sensitive to many influences, and singers, in particular, take notice of issues within the vocal tract that the everyday voice user may not notice. Laryngeal and respiratory manifestations of Crohn's disease are considered to be rare, but it could be that vocal health issues in most IBD patients are simply overlooked, as vocal production is not imperative to their livelihood. The larynx has few pain receptors and the vocal folds have none, which may cause a disregard for symptoms.<sup>12</sup> Case studies of more serious complications within the larynx and respiratory system suggest many patients may experience these complications of disease to a lesser extent, complications that would greatly affect a singer.

One of the main issues with the presence of these symptoms is that the spectrum of IBD related changes in the chest and larynx is broad and may mimic many other conditions. The lungs, the masters of powerful singing, are one of these organ systems that may experience change. The most prevalent pattern of respiratory involvement in IBD is large airway inflammation, followed by lung alterations. In a review published in 2018 by Cozzi et al. in the journal of *Gastroenterology Research and Practice*, it is said that, "Current estimates for the prevalence of respiratory abnormality in patients with IBD are around 40% . . . Furthermore, in up to 10% of patients with IBD, respiratory involvement may be underdiagnosed because their manifestations may precede presentation of bowel disease by months or years."<sup>13</sup> It is thought that the inflammatory process from the bowel to the lung is often possible because of the common ancestry of the bowel and bronchial tissue from the primitive gut. Both play critical roles in host mucosal defense within the autoimmune system. In a clinical setting, patients may present with nonspecific symptoms, such as cough and shortness of breath.

Respiratory tract involvement can be traced back some years, with a case study by Lemann et al. published in 1987.<sup>14</sup> A previously healthy 24 year old French woman first presented with diarrhea and fever. Upon admission to the hospital, physical examination was nonspecific except for abdominal tenderness. Lab

studies showed abnormality in white blood cell counts. X-ray of the chest and abdomen, stool cultures, and parasitic research were normal. Colonoscopy revealed abnormalities confined to the ascending and sigmoid colon. After initial improvement with antibiotics, on the tenth hospital day, the patient became voiceless and experienced cough and difficulties swallowing and breathing. There was mild exacerbation of the digestive symptoms. Upper airway examination revealed edema of the nasopharynx, epiglottis, arytenoids, and true vocal folds. Biopsy of present granulomas showed white blood cell infiltrate. The patient was treated with 40 mg of oral steroid daily. She responded dramatically, with complete symptom relief in a few days and a tapering off of the steroid medication. Colonoscopy two months later showed marked improvement of intestinal lining of the colon.

Aside from cases affecting the lungs, there are case studies exhibiting inflammatory vocal fold lesions in patients as an extraintestinal symptom of their IBD, something that would very directly affect a professional voice user. A 2009 case study published in *Annals of Otolaryngology, Rhinology & Laryngology* describes a Crohn's disease patient who experienced recurrent hoarseness due to these inflammatory vocal fold lesions.<sup>15</sup> A 31 year old woman was admitted to the hospital in December 2005 with a one month history of hoarseness, sore throat, and painful swallowing. The patient had endured lower abdominal pains and diarrhea since April 2004. Imaging revealed small bowel obstruction and narrowing, and a scope led to diagnosis of Crohn's disease due to visible inflammatory lesions of the small bowel. The patient was treated with an oral anti-inflammatory drug (5-aminosalicylic acid derivative) from July 2005. The patient's abdominal symptoms improved, but the patient had not received this medication for two months before the hoarseness was noted. Flexible-fiber endoscope identified ulceration of the left vocal fold, extending from the vocal fold to the false vocal fold. Biopsy of the ulceration indicated a chronic inflammatory process in line with the patient's Crohn's disease. The patient was treated with antibiotics and 30 mg of oral steroid daily for five days. The symptoms resolved and the patient received no further treatment. The laryngeal symptoms recurred after six months, with ulceration in the same area. The patient was treated with the same oral protocol and

steroid spray twice daily. The symptoms again resolved and results were maintained by daily use of steroidal throat sprays.

Cases like these are not old news and are by no means a problem of the past. A most recent and severe case published in 2021 explores the "Laryngeal Manifestations of Crohn's Disease in a Toddler with Very Early Onset-IBD," and also provides a full scale literature study, chronicling all of the cases of Crohn's disease with laryngeal involvement found in the literature to date.<sup>16</sup> There were 15 cases found across the literature since 1940.

A 20 month old female presented to the emergency room for evaluation of inspiratory stridor and sternal retractions.<sup>17</sup> Her past medical history showed symptoms of very early onset IBD (Crohn's disease), diagnosed at six months of age. Her treatment was escalated when she developed a rectovaginal fistula, fevers, and oropharyngeal ulcers. Her management included high dose steroids and biologics. Upon admission to the hospital for respiratory symptoms, flexible scope laryngoscopy showed supraglottic narrowing with thickened and erythematous epiglottis and edema of the mucosa overlying the arytenoid cartilages, obstructing the view of the glottis. She was treated with more intensive steroid use, both orally and by inhalation. Despite IBD treatment with four different biologics, the patient was admitted to the hospital three additional times in the next three months for similar airway symptoms, usually coincided by the return of large oral ulcers, fever, bloody bowel movements, decreased eating, and elevated inflammatory factors in the blood. Airway exacerbations appeared 7–10 days before biologic administration monthly and continued to be treated with inhaled steroids. Time intervals between hospital trips gradually decreased, until finally fiberoptic revealed marked thickening of the supraglottic structures and a new mass on the arytenoid cartilage. The mass was removed with a CO2 laser. Pathology showed nonspecific inflammation. Improvement was short lived. Despite maximal medical therapy she was readmitted to the hospital for airway obstruction. Due to the chronic and severe nature of her symptoms, the patient underwent tracheotomy tube placement at 27 months old. Four months later her airway obstruction resolved along with her gastrointestinal involvement. She was weaned from all medication

except for one biologic and her tracheotomy tube was removed at 41 months.

Cases such as these are rare, but mild or related symptoms and experiences may not be as few and far between as it would appear. For a singer, even small amounts of inflammation in the vocal tract, chest, and abdominal regions could hinder dynamics and vocal production, limit vocal range, and decrease breath support. Even minute effects could be incredibly frustrating, as a professional voice user relies on their voice in ways that the general population does not. One thing seems to be common when it comes to treatment of these inflammatory issues: the use of steroids. In the more severe cases presented, steroid use is almost ubiquitous when it comes to treatment of this chronic inflammation. Long-term use of corticosteroids may lead to side effects such as fluid retention, high blood pressure, mood swings, and weight gain. Furthermore, steroid usage has particular consequences for singers. Although steroids can be a miracle drug and a performance saver when used in the right setting, long-term use may have deleterious effects. Many singers describe a rebound effect after completing use of steroids, as the medication tends to cause the voice to feel falsely invincible.<sup>18</sup> Specifically *inhaled* steroids, as mentioned above in the toddler's case, may even exacerbate laryngeal symptoms. Any medication that is inhaled can result in vocal fold irritation, as they need to pass between the vocal folds to enter the lungs.

One thing is clear and significant in all of the cases presented: treatment of IBD symptoms was a successful strategy to relieve laryngeal involvement of the disease. Furthermore, treatment of the initial laryngeal symptoms marginally improved gastrointestinal disease states. This suggests that relief from the physiologic stressors of EIMs may directly impact and improve IBD outcome at its core. IBD and EIMs are not isolated diseases but have common disease pathways. As treatments for IBD continue to develop, the days of patients being on and off steroids may soon be behind us. Biologics have maintained a relatively safe profile over the years since their introduction into the treatment of IBD.<sup>19</sup> It therefore seems imperative to introduce biologics earlier in treatment, as opposed to long-term use of steroids. Recent studies of biologics have linked their use to increased mucosal healing, and the medicine surely poses less risk to singers. Typically a biologic drug is an antibody to an

inflammatory factor (cytokine) in the blood, administered by injection or infusion. With remission without steroids being possible in a much larger population of patients, extraintestinal manifestations, including those in the laryngeal regions, may become much less prevalent.

As more aspects of inflammatory diseases are studied and treated, physicians of all specialties will be included in the treatment of these conditions. Crohn's disease may be rare, but inflammation is not. Singers should be aware of the presence and effects of inflammation, to any degree, whether due to an underlying health condition or otherwise. Professional voice users, singers specifically, who experience these kinds of issues should not be afraid to take a multidisciplinary approach to their vocal health and to fight for their instincts when it comes to the subtleties of the voice. In terms of patients with Crohn's disease, it is important to be aware of the features of laryngeal manifestation, so that, when they do present, appropriate care can be administered in a timely manner.

## NOTES

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