AN UPDATE ON THE
DIAGNOSIS AND TREATMENT OF
Hidradenitis Suppurativa
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Hidradenitis suppurativa (HS) is a chronic, inflammatory, scarring disease that occurs most frequently along the milk lines of the body from axillae to groin, is most common in the second and third decades of life, and is rarely observed before puberty. It disproportionately affects women and is associated with a host of comorbidities and dramatically reduced quality of life. The delay from HS symptom onset to diagnosis is approximately 7 years, with drastic consequences for patient well being. Early diagnosis and treatment are of paramount importance. While several nonpharmacologic, pharmacologic, and surgical treatment modalities exist for HS, only one agent, adalimumab, has been approved by the US Food and Drug Administration for this indication. Lifestyle modifications, dietary changes, patient education, and psychosocial support are important components of HS therapy.

Hidradenitis suppurativa (HS) is a chronic, inflammatory, scarring condition of follicular occlusion involving the follicular portion of the pilosebaceous unit. Similar to acne, HS begins with follicular occlusion and is followed by cyst formation and eventual cyst rupture, which results in inflammation of the surrounding dermis. Hidradenitis suppurativa typically manifests along the so-called milk lines of the body, including the intertriginous skin of the axillary, inframammary, inguinal, genital, and perineal areas, and is characterized by recurrent, inflamed, deep-seated acneiform nodules. These nodules gradually become abscesses associated with chronic draining sinus tract formation, resulting in scarring, disfigurement, and life-altering disability. As part of what is referred to as the follicular occlusion tetrad, dissecting cellulitis of the scalp, acne conglobata, and pilonidal sinus are thought to share a similar pathophysiology and often coexist with HS.

Prevalence
The estimated prevalence of HS ranges from less than 1% to 4% and varies according to the age and demographics of the population studied, the background rates of diagnosis/misdiagnosis, and the spectrum of disease. Hidradenitis suppurativa is most common in the second and third decades of life and is rarely observed before puberty. The female-to-male ratio is approximately 3.3:1, and the population with highest incidence is women ages 20 to 29 years. However, severe and atypical presentations are more common in men.

Pathogenesis
The pathogenesis of HS remains uncertain; however, many factors appear to play a role. Certain behavioral risk factors (eg, smoking, obesity, and mechanical friction), are modifiable. Although HS is not an infectious disease, bacteria may play an important role by creating an occlusive biofilm or by promoting an inflammatory response. A role for hormone imbalance, particularly hyperandrogenism, is suspected but unproven. Some patients may have a heritable form of HS, and as many as one-third of patients have first-degree relatives with the disease. Host defenses, including enhanced expression of toll-like receptors, release of proinflammatory cytokines, increased tumor necrosis factor (TNF) α expression, activation of the interleukin (IL) 23/T helper 17 pathway, and overproduction of IL 1β, have also been implicated in HS pathogenesis. One hypothesis regarding the pathogenesis of HS posits a combination of environmental factors in genetically susceptible individuals.

Diagnosis
The average delay from symptom onset to HS diagnosis is approximately 7 years. Patients may be ashamed to seek medical attention until forced to
do so by severe symptoms. When patients do present, they and their providers may fail to appreciate the disease for what it is.\textsuperscript{2} Those with HS may visit primary care providers or the emergency department repeatedly for incision and drainage of recurrent “boils.” During this time, the disease may worsen without proper treatment. Even mild disease, which can be messy, smelly, and painful, has a substantial negative impact on quality of life (QOL). Thus, accurate and timely diagnosis of HS is critical.

Without therapeutic intervention, HS typically progresses and becomes increasingly debilitating. A missed diagnosis is a missed opportunity. The QOL impact of HS is greater than that of chronic urticaria, psoriasis, and atopic dermatitis, among the worst conditions systematically studied in dermatology.\textsuperscript{15,16} Patients often experience feelings of shame, isolation, and stigmatization\textsuperscript{16} and substantially diminished sexual health.\textsuperscript{17} Because HS is also associated with a number of comorbidities (eg, arthropathies, dyslipidemia, polycystic ovarian syndrome, psychiatric disorders, obesity, drug dependence, hypertension, diabetes, thyroid disease, alcohol dependence, and lymphoma), accurate diagnosis presents an important opportunity to address these comorbid factors.\textsuperscript{18}

The diagnosis of HS must be made clinically. Biopsies may rule out alternate diagnoses but are otherwise nonspecific, and there are no confirmatory tests.\textsuperscript{2} The diagnostic criteria for HS can be expressed succinctly as characteristic lesions in characteristic locations with cyclical recurrence and chronicity.\textsuperscript{2,19} Lesions should be multiple and bilateral over time. Typical findings are open comedones, particularly double-headed comedones; inflammatory, tender, eroded or draining nodules; draining abscesses; fibrous scarring; and subcutaneous sinus tract formation.\textsuperscript{2} Examples of mild, moderate, and severe presentations of HS are shown in Figures 1 to 3.

Roughly 66\% of patients with HS can be classified as having Hurley stage I disease, with single or multiple abscesses but no sinus tracts or scarring.\textsuperscript{6} Twenty-seven percent have Hurley stage II disease, which is characterized by single or multiple separate, recurrent abscesses with sinus tract formation and scarring. Hurley stage III disease accounts for 7\% of patients and involves multiple interconnected tracts and abscesses effacing an entire anatomic area.\textsuperscript{6} The Sartorius score, commonly used in HS clinical trials, is a more complex scoring system that allows for more detailed assessment.\textsuperscript{20} Such designations can be a useful way to conceptualize disease severity and plan treatment. Accurate and early diagnosis as well as treatment commensurate with disease severity is essential to reduce disease burden and progression and resulting disability.

## Treatment

There is no definitive cure for HS and no therapy universally effective for all patients. In most cases, Hurley stage I disease can be slowed or arrested with effective treatment options. However, control of Hurley stage II and III disease can be elusive, and progressive suppuration, fibrosis, scarring, and contracture may result in permanent disability. Effective management frequently requires a trial of more than one agent or a combination of agents over time.

Lifestyle and Supportive Measures—Lifestyle modifications, including smoking cessation and weight loss, can be an important part of HS therapy. Wearing loose-fitting clothing and avoiding topical irritants, such as shaving creams or antiperspirants, may diminish symptoms. Dietary modification, such as avoiding brewer’s yeast,\textsuperscript{21} dairy products, and high glycemic diets,\textsuperscript{1} is a frequent subject of interest among patients but is of unproven benefit.

Supportive measures include coordination of care with mental health services and connecting patients to others with HS through local or national support groups. Patients may benefit from simple discussion and education regarding the pathophysiology of HS and its exacerbating factors in order to reduce
fear of stigma, acknowledge and address the psychosocial burden and QOL issues, and restore some sense of control over the disease and its treatment. Support groups, such as the Hidradenitis Suppurativa Foundation, have been formed for these reasons.

While no studies specifically address the issue of wound care in HS, counseling regarding options for nonstick wound care, absorbent dressings, and the use of tubular net or mesh dressings instead of tape to anchor bandages, can be useful. Physical therapy consultation may help preserve or improve range of motion through stretching and exercises and decrease uncomfortable dependent lymphedema by using slings, wraps, and compression devices.

**Pharmacotherapy**—Topical therapies may be of some utility, particularly for mild, Hurley stage I disease. Many providers recommend daily use of soaps, detergents, or washes such as chlorhexidine or benzoyl peroxide, for which some evidence of effectiveness exists. Some topical antibiotics may treat the odor and pain associated with HS and decrease lesion count. The efficacy of topical clindamycin (solution or gel) was established in one study and replicated in another. Anecdotally, dapsone gel has been helpful, but its utility has not been established and its use may be limited by cost. A study using resorcinol 15% for the treatment of flares showed that it reduced the average duration of painful abscesses. Triamcinolone acetonide is commonly injected into painful, flaring lesions to provide quick relief of pain and inflammation, but no relevant clinical trial has been conducted.

Oral doxycycline and minocycline are generally well tolerated, and prescribers are comfortable with their use. Anecdotally, these agents are helpful for mild or moderate, Hurley stage I or II disease, though in the only controlled study of this class of drug, tetracycline failed to show superiority to topical clindamycin alone. Conversely, the combination of oral clindamycin with rifampin, each taken twice daily, was associated with dramatic improvement in Sartorius score in a cohort of 116 patients, 56% of whom had Hurley stage II or III disease. These medications were well tolerated, with only 8 stopping treatment due to adverse effects. Dapsone has been used as a therapeutic agent in a few small, uncontrolled case series, with improvement reported in 38% to 100% of patients. As with most treatments, disease tends to recur when maintenance therapy is stopped. In one small retrospective study, the combination of oral metronidazole with rifampin and moxifloxacin resulted in remission in 57% of patients, though dose-limiting side effects occurred in the majority of those treated. Other combination oral and intravenous antibiotic regimens have shown promise for treating HS in case series.

Retinoids such as acitretin and isotretinoin may improve symptoms in some patients, but their usefulness is generally limited by monitoring parameters and side effects at doses necessary to induce a response. Hormonal therapies aimed at modulating the contribution of androgens to disease pathogenesis may be useful in some cases. These agents probably work best as an add-on component of a combination regimen and are best suited for those with obesity, irregular menses, or metabolic syndrome, and for those whose HS seems to flare with menses.

Biologic agents, particularly tumor necrosis factor α inhibitors, are an option for severe, inflammatory, Hurley stage II or III disease. Controlled trials have demonstrated the efficacy of infliximab and adalimumab for HS, while etanercept is not recommended based on current evidence. A double-blind, prospective study of 38 patients with moderate-to-severe HS showed moderate (25%-50% HS Severity Index score) improvement in 60% of those receiving infliximab 5 mg/kg (at weeks 0, 2, 6, and every 8 weeks after that) versus 6% receiving placebo. A phase II randomized, placebo-controlled trial of adalimumab in 154 patients with moderate-to-severe HS showed meaningful improvement (HS Physician Global Assessment score of clear, minimal, or mild with at least a 2-grade improvement relative to baseline) in 17.6% of those receiving adalimumab 40 mg weekly versus 9.6% of those receiving 40 mg every other week and 3.9% of those receiving placebo. Two subsequent phase III studies of adalimumab at higher doses similar to those used for Crohn disease have shown more impressive results, leading to the recent approval of adalimumab by the US Food and Drug Administration as the first and only medication approved for the treatment of HS.
approved for the treatment of moderate-to-severe HS.\textsuperscript{46} These 2 unpublished, randomized, double-blind, placebo-controlled studies (PIONEER I and PIONEER II) evaluated the safety and efficacy of adalimumab in 633 adult participants with moderate-to-severe HS (Hurley stage II or III disease). In both studies, participants received placebo or adalimumab at an initial dose of 160 mg at week 0, 80 mg at week 2, and 40 mg weekly starting at week 4 and continuing through week 11, with clinical response evaluated at week 12. Hidradenitis suppurativa clinical response was defined as at least 50\% reduction in total abscess and inflammatory nodule count with no increase in abscess or draining fistula count relative to baseline. In PIONEER I, response was 42\% for high-dose adalimumab versus 26\% for placebo; in PIONEER II, response was 59\% versus 28\%, respectively. No study has compared the effectiveness of infliximab and adalimumab at optimal dosing using identical response criteria.\textsuperscript{47} A few small studies have reported results both mixed and promising for other biologics in HS, with targets including the IL-23/T helper 17 (ustekinumab) and IL-1\(\beta\) (anakinra) pathways.\textsuperscript{48-50} These and similar drugs are the subject of active and ongoing investigations. Other agents, such as methotrexate, cyclosporine, prednisone, and zinc, may provide temporary relief in some patients but are limited by adverse effects and incomplete efficacy.\textsuperscript{25,51,52}

Surgical Therapy—A variety of laser and surgical treatment modalities are available to those with HS. The 1064-nm Nd:YAG laser, a device used primarily for hair removal, has been applied successfully in HS patients, supporting the hypothesis of a primary follicular pathogenesis of the condition.\textsuperscript{53} In a prospective randomized controlled trial split body study of 22 patients with Hurley stage II or III HS, use of the 1064-nm Nd:YAG laser on individual lesions monthly for 3 months produced on average a 65\% decrease in severity for treated sites.\textsuperscript{53} In a second prospective randomized controlled trial split body study, also in 22 patients, monthly Nd:YAG treatments for 4 months decreased average severity by 73\% for treated sites compared to controls (23\%).\textsuperscript{22} In surgical deroofing, a blunt probe is used to explore the extent of each lesion prior to surgically removing the roof with a scalpel or loop electrocautery. A curette is used to scrape away the floor of the exposed lesion, which is then allowed to heal by secondary intention. In an open study of 88 deroofed lesions in 44 consecutive patients with HS, no recurrence was detected in 83\% of lesions after a median follow-up of 34 months.\textsuperscript{54} Median patient satisfaction was rated 8 on a scale of 0 to 10, and 90\% of patients reported they would recommend the deroofing procedure to other patients.\textsuperscript{54}

Surgical excision of involved areas using the carbon dioxide laser is an additional option. In a study of 61 patients and 185 treated areas, use of the carbon dioxide laser excision and marsupialization technique with healing by secondary intention resulted in only 2 recurrences after a follow-up of 1 to 19 years.\textsuperscript{55} Radical excision with complete lesion resection and wide margins involving the entire anatomic unit may be another effective means of achieving long-term remission. However, such surgeries may be highly morbid, and the risk of recurrence (2.5\%–33\%) is related to the natural course of the disease and the width of the excision.\textsuperscript{56,57} Based on the accumulated data regarding the treatment of HS, evidence-based treatment approaches to HS Hurley stages I to III are shown in the Table.
Conclusion
Hidradenitis suppurativa is a chronic, relapsing disorder of the pilosebaceous unit that leads to recurrent inflammation and scarring of the dermis and subcutaneous tissue. The pathogenesis of HS, which is complex and poorly understood, appears to be a combination of environmental factors in genetically susceptible individuals. Some behavioral risk factors, such as smoking and obesity, are modifiable, while the role of bacteria and the host inflammatory response may be modulated by pharmacologic and surgical therapies.

Even in its milder forms, HS can negatively impact QOL in a substantial way. The disease is frequently painful, messy, and stigmatizing, problems made worse by long periods of diagnostic delay. Because of the serious and chronic nature of HS, its sequelae, and comorbidities, a thoughtful and multimodal approach to treatment, including medical and surgical modalities but also patient education, lifestyle modification, pain control, and emotional support, is necessary. The recent US Food and Drug Administration approval of adalimumab offers a promising new option and dosing regimen for patients with severe disease.

REFERENCES
Hidradenitis Suppurativa: Diagnosis and Treatment

COVER: Morphologic features of early, moderate, and severe hidradenitis suppurativa (HS) in the axilla. 

*Early HS (left):* Inflammatory, tender, eroded, and draining papules or nodules resemble furuncles or “boils.”

*Moderate HS (center):* Multiple ulcerated draining abscesses; fibrous scarring; and sinus tract formation are present, with subcutaneous cordlike induration. 

*Severe HS (right):* Multiple inflammatory nodules, sinus tracts, and fibrous scars cover the entire axilla.