Hidradenitis Suppurativa: An Update

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EDITORIAL COMMENT

When hidradenitis suppurativa is severe, it may produce disabling pain, repulsive odor, and scarring that ruins the quality of life. Therapy has, for decades, depended upon antibiotics and intrallesional steroids for mild disease and surgery for severe involvement. The advent of immunomodulatory medications and the use of antiandrogens are expanding our options. Drs. Kist and Lee staff a clinic that is dedicated to the care of patients who have hidradenitis suppurativa (HS). They share their therapeutic experience along with the published evidence supporting their recommendations. The algorithm summarizing management is invaluable.

William D. James, MD

Hidradenitis suppurativa (HS), was first described in 1833 by French physician Alfred Verneuil for its characteristic intertriginous distribution [1,2]. It is a common inflammatory dermatosis characterized by painful, recurrent abscesses and nodules primarily in intertriginous areas, such as the axilla, groin, gluteal cleft, and inframammary folds. Chronic inflammation can lead to sinus tract formation, scarring, and malodorous discharge, leading to pain, discomfort, and a decreased quality of life. Current treatments are often unsatisfactory. Medical interventions generally provide only temporary, if any, relief of symptoms and are not curative. The success of surgical approaches varies greatly, depending on the location and severity of the affected areas. Patients presenting with advanced disease in functionally sensitive areas often develop either recurrent disease with insufficiently wide excisions or suffer extensive scarring from surgery. This review will summarize the current literature for the treatment of HS with emphasis on recent therapeutic advances in medical therapies.

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CLINICAL FEATURES
Patients typically present with painful, firm nodules in the axilla, perineum and/or groin (Fig. 1). Patients may experience discomfort or pruritus in the affected region before the nodules form. The nodules may regress, but recurrence is common. Often they expand and merge together to form abscesses (Figs. 2–4). These lesions may spontaneously rupture and release a purulent discharge. Prominent open comedones are often found (Fig. 5). The inflammatory lesions heal but fibrosis, dermal contractures, disfiguring scars, and sinus tracts may develop. This cycle repeats and can extend into neighboring areas (Fig. 6). Early lesions can be mistaken for folliculitis, furuncles, or other diseases presenting in intertriginous areas (Box 1). Nonintertriginous areas are only rarely affected (Fig. 7) [3].

The most comprehensive epidemiologic study to date demonstrates that HS has a point prevalence of 4.1% in the general population. It is found more commonly in women than men (odds ratio 2.9; 95% CI, 1.1-7.7) [4]. The mean age of onset for men is 31.7 years (SD 9.8). The mean age of onset for women is 26.4 years (SD 8.0). Genitofemoral lesions are more commonly found in women (odds ratio 5.4; 95% CI, 1.5-19.3). The prevalence of axillary lesions does not differ significantly with sex [4]. There is no racial predilection.

Obesity tends to be more prevalent in patients with HS [5], although it is not been universally demonstrated in all studies [6]. It has been reported that the body mass index for women and men with HS is elevated at 28.5 (±5) and 27.8 (±3), respectively [7]. However, it is generally believed that obesity, rather

Fig. 1. Mild HS with distinct inflammatory nodules.
than being a primary cause, acts as a secondary factor, aggravating disease through mechanical trauma at skin folds.

A high incidence of smoking occurs amongst hidradenitis patients. Of HS patients, 89% are active smokers compared with 46% of controls [8,9]. While HS is not typically thought to be related to medications, it has been reported to be exacerbated by lithium [10,11] and sirolimus [12].

In women, HS occurs almost exclusively after menarche. Premenstrual flares are common in about 50% of all cases. HS tends to improve with pregnancy and rebounds after parturition. Signs of virilization can been seen in HS but...
most case series indicate no significant change in serum hormone levels in HS patients [13]. The relationship between HS and hyperandrogenism is largely based on the finding that the free androgen index is increased because of a low level of sex-hormone-binding globulin, which is influenced by body weight. This argues that hormonal effects are likely localized in the skin.
However, no significant difference in androgen metabolism was noted in apocrine glands isolated from HS patients compared with matched controls [14]. Thus, the roles of androgens in the pathogenesis of HS remain unclear, and may prove to be secondary rather than primary.

Familial forms of HS have been described, although no specific gene has been identified [15]. A recent genome-wide scan in a Chinese family showed that a disease gene of acne inversa is located on chromosome 1p21.1-1q25.3 [16]. Further molecular characterization is in progress.

HS has been associated with various dermatologic syndromes (Box 2) [17–37], including keratitis-ichthyosis-deafness [38,39], synovitis-acne-pustulosis-hyperostosis-osteitis syndrome [40], and Crohn’s syndrome [41–44], in addition to

**Box 1: Differential diagnosis**

- Furuncle/carbuncle
- Lymphadenopathy/lymphadenitis
- Cutaneous Langerhans cell histiocytosis
- Actinomycosis
- Granuloma inguinale
- Lymphogranuloma venereum
- Apocrine nevus
- Inflamed epidermal inclusion cyst
- Crohn’s disease
- Cutaneous tuberculosis

**Fig. 6.** Severe HS with deep sinus tracts and scarring.
the follicular triad of acne vulgaris, dissecting cellulitis, and hidradenitis [45]. Arthritis is also commonly associated with HS and can worsen with a flare of HS. Arthropathy typically involves the large joints in the extremities, particularly the knee joints. Anemia, hypoproteinemia, and amyloidosis were reported in a patient who died of infection after surgical excision of extensive anogenital lesions [46].

Chronic HS lesions also have a higher risk of developing malignancy. A large cohort study of 2119 patients showed an elevated relative risk of 1.5 for all cancers and of 4.6 for nonmelanoma skin cancers [47–49]. Hypercalcemia with an elevated parathyroid hormone-related protein has been reported in an HS patient who developed a squamous cell carcinoma [50].

It is not surprising that HS has a significant impact on the quality of life of affected individuals. Multiple studies have demonstrated that HS has a significant negative impact upon quality of life that correlates with disease severity and with a more detrimental effect than other dermatologic conditions previously reported [51,52].

Multiple classification schemes have been developed for HS [53,54]. The best known was developed by Hurley and separates HS into three stages based on severity: Stage I is limited to the presence of abscesses without evidence of sinus tracts or scarring (see Fig. 1). Stage II demonstrates sinus tracts and scarring with discrete recurrent abscesses (see Fig. 2). Stage III represents diffuse involvement of interconnected sinus tracts, scars, and abscesses (see Fig. 3). Prominent open comedones, often with multiple orifices are seen (see Fig. 4). The more severe the disease, the more refractory it is to medical treatment and the more likely it is to recur after surgical intervention.

HISTOPATHOLOGY
HS lesions are concentrated where apocrine hair follicles are typically found. Thus, the most commonly affected sites are the axilla, the areas under the

![Image](image-url)
breasts, and the perianal and perigenital regions, though other locations may be affected. However, the role of the apocrine gland is controversial.

The mechanism of disease for HS is not completely understood and has evolved from being a process centered on apocrine glands [55] to a process centered on hair follicles. While inflammation of the apocrine glands can be seen, the pathophysiology of HS is thought to be similar to acne vulgaris, with hair follicle occlusion being the initiating event. The disease begins with spongiosis of the infrainfundibular region, follicular hyperkeratosis, and dilatation of follicular infundibula, leading to comedone formation and follicular rupture [56–58]. Follicular rupture induces the recruitment first of neutrophils, followed by a granulomatous infiltrate with foreign body giant cells [56,59]. The dermal abscess then extends into the subcutaneous fat to involve the adnexal structures. Thus, the inflammation of the apocrine glands, or hidradenitis, is thought to be a secondary event [60]. The subsequent fibrosis and formation of sinus tracts are likely a result of tissue repair response to chronic inflammation, bacterial

Box 2: Diseases associated with hidradenitis suppurativa

- Squamous cell carcinoma [49]
- Dowling-Degos disease [17–19]
- Synovitis-acne-pustulosis-hyperostosis-osteitis syndrome [40]
- Pyoderma gangrenosum [20]
- Keratitis-ichthyosis-deafness [38]
- Bazex-Dupre-Christol syndrome [21]
- Follicular occlusion triad [22]
- Myotonic dystrophy [23]
- Lumbosacral epidural abscess [24]
- Crohn’s disease [43]
- Reflex sympathetic dystrophy [25]
- Spondyloarthropathy [26,27]
- Verrucous carcinoma [28]
- Arthritis [29]
- Scrotal elephantiasis [30]
- Multiple keratoacanthomas [31]
- Pachyonychia congenita [32]
- Ankylosing spondylitis [33]
- Natal teeth and steatocystoma multiplex [34]
- Acanthosis nigricans [35]
- Anemia [36]
- Fox-Fordyce disease [37]
superinfection, and necrotic debris [61]. Unlike acne, excessive sebum production is not observed in HS [62].

**MICROBIOLOGY**

With multiple species of bacteria isolated from HS lesions, the role of infection is not clearly understood. While organisms can be isolated from HS lesions, many cultures are routinely negative. Thus, bacterial infection is likely secondary to chronic sinus tracts and moisture rather than of primary etiologic importance. When present, bacterial cultures are often polymicrobial. *Staphylococcus aureus*, *S epidermidis*, *Streptococcus milleri*, and *S hominis* have all been described from aspiration of deep lesions about 49% of the time [63]. Cultures taken from carbon dioxide laser ablation studies show coagulase-negative staphylococci are the most common aerobic organisms isolated from HS lesions (21 of 25 patients). *S aureus* was second (14 of 25 patients). *Peptostreptococcus* was the most common anaerobic organism (9/25). *Enterococcus*, *Enterobacteriaceae*, diphtheroids, *Bacillus cereus*, *Propionibacterium acnes*, *Lactobacillus*, and *Bacteroides* have also been described [64].

**THERAPY**

Treatment of HS is challenging and response depends on the clinical severity of the disease. While its pathophysiology remains unclear, HS shares many similar features with acne vulgaris and is approached therapeutically in a similar manner. Medical treatments can reduce inflammation and associated tenderness and drainage, but usually do not halt disease progression. Antibiotics can be helpful, particularly if specific organisms can be demonstrated. However, antibiotics require fairly long courses of therapy.

Medical therapy can be divided into topical and systemic. Clindamycin is the only topical medication that has been extensively studied. A randomized control trial with 27 patients showing improvement of abscesses and pustules, but not of inflammatory nodules, at 12 weeks with clindamycin 1% solution twice daily [65].

Systemic medications can be further divided into antibiotics, retinoids, hormonal modulators, and immunosuppressants. Systemic antibiotics are often prescribed for HS. In a randomized control comparing topical clindamycin 1% twice a day to tetracycline 500 mg twice daily, patients using tetracycline showed significant improvement over baseline for at least 3 months. However, there was no statistical difference in improvement between the two treatment arms [66]. All patients were on at least 3 months of treatment. Pustules and abscesses appeared to improve within the first 3 months but inflammatory nodules were more refractory to treatment, requiring longer treatment duration to see any effect. A recent case series of 14 patients receiving oral clindamycin 300 mg twice a day and rifampicin 300 mg twice a day for 10 weeks achieved remission in 8 of the 14 patients. Remission was induced in 2 additional patients when minocycline was substituted for clindamycin, and 4 patients were unable to tolerate the treatment because of diarrhea [67].
Results from systemic retinoids, particularly isotretinoin, have proven to be disappointing in the treatment of HS, unlike the results in treating acne vulgaris. Despite some promising case reports, a prospective trial with long-term follow-up showed that only 23% of HS patients benefit from isotretinoin 0.5 to 1 mg/kg. Only 16% of patients showed any durable remission after treatment withdrawal [68]. These clinical results may reflect the minor role sebum production appears to play in HS.

Antiandrogen therapy is also used in acne vulgaris and has been studied in HS. A randomized controlled trial comparing cyproterone acetate and norgestrel using a reverse sequential regimen with a crossover at 6 months. Patients were followed for 12 months. Seven patients cleared, five improved, four remained unchanged, and two worsened. There was no significant difference between the two treatment groups [69]. A case series of four patients treated with cyproterone acetate 100 mg per day showed improvement by 2 months, but symptoms tended to flare once the dose was lowered to 50 mg per day [70]. Finasteride, a 5-alpha reductase inhibitor, has also been reported to improve HS symptoms. A case series of six patients on finasteride 5 mg once a day showed improvement by 8 weeks and remissions from 8 to 18 months. Main side effects were generalized pruritus and breast tenderness [71]. Spironolactone has been used successfully in the treatment of acne [72, 73]. While its use in acne is not universally accepted [74], its antiandrogen properties merit further investigation for its effectiveness in treating HS.

Immunosuppressive therapy has been used to address the acute inflammatory stages of the disease with varying degrees of success. An interesting case of a renal transplant patient with severe HS and chronic granulomatous disease showed remission of his HS lesions with his posttransplantation immunosuppression regimen of prednisone 5 mg per day, mycophenolate mofetil 1000 mg twice a day, and tacrolimus 1 mg twice a day [75]. Cyclosporine A (3-4 mg/kg) has been reported in multiple case reports to work in about 8 weeks [76]. Relapse of milder disease has been noted when the drug is withdrawn [77]. A single case report of a combination of azathioprine, methylprednisolone, and isotretinoin was effective in a patient with both Crohn’s disease and HS [78]. In a small case series of three patients, methotrexate was not shown to be effective in HS [79]. Patients administered dapsone (50-150 mg per day) demonstrated significant improvement of their disease by 4 to 12 weeks but would relapse when the medicine was stopped. Short courses of systemic and intrallesiional steroids have been reported but have not been studied systematically [80].

Tumor necrosis factor α (TNF-α) is a proinflammatory cytokine that can be produced by multiple cells of the body, including activated T cells, keratinocytes, and Langerhans cells. TNF-α has numerous effects at the cellular level, and these effects may be relevant to the pathophysiology of HS. Initially, patients with Crohn’s disease with concomitant HS showed improvement of their HS lesions when treated with the anti-TNF-α agent infliximab [81]. Further reports of other agents followed.
Infliximab is a human-mouse monoclonal chimeric antibody against the TNF-\(\alpha\) molecules. Multiple case series with a follow-up period of up to 6 months showed significant improvement [81–86]. More recently, a patient was reported to have a sustained, excellent response (including an 80% improvement in his quality-of-life score) to infliximab 5 mg/kg every 8 weeks in combination with methotrexate 7.5 mg/wk for 104 weeks [87]. Less impressive efficacy was observed in seven patients with severe HS who were treated with multiple infusions of infliximab 5 mg/kg. While five of the seven patients demonstrated improvement at week 6, only two patients were substantially improved by week 10. Moreover, significant adverse events were noted, including the development of colon cancer, a multifocal motor neuropathy, and a severe allergic reaction [88]. Thus, enthusiasm generated through success in observational reports and small studies must be tempered with a cautious respect for the recalcitrance of HS and for the potential of medication-associated adverse events.

Etanercept is a recombinant soluble fusion protein consisting of two identical chains of the TNF-\(\alpha\) receptor fused with the Fc portion of human IgG1. Etanercept functions as a competitive inhibitor for binding of TNF-\(\alpha\) at its receptor. In a case series, six female patients treated with etanercept with 17 to 40 weeks of follow up showed significant improvement. Most patients did have at least one flare [89]. Adalimumab is a humanized monoclonal antibody against the TNF-\(\alpha\) molecules. Both etanercept and adalimumab bind to soluble and membrane-bound TNF leading to cell lysis. Two case reports on adalimumab for the treatment of hidradenitis showed it was effective in one patient who became refractory to infliximab [90,91]. While no long-term safety data is available for TNF-\(\alpha\) inhibitors, a meta-analysis of rheumatoid arthritis patients using infliximab and adalimumab suggests an increase in serious infections and malignancies [92].

Nonsurgical local modalities have been reported, none of which have proved satisfactory. Cryotherapy has been tried but involves significant comorbidity. A case series of 10 patients reports improvement in 8 patients. However, there was a significant rate of complications, with 6 patients developing infections and 5 developing ulcers [93].

Carbon dioxide laser [94] appeared to be promising alternative to surgery. A case series of 34 patients who were treated with a scanner-assisted carbon dioxide laser and who had an average follow-up of 34 months showed a low recurrence rate at treated sites (4 of 34 patients). However, this treatment did not prevent further disease flares [95].

Photodynamic therapy with topical aminolevulinic acid has been attempted. One case series reported no effect of photodynamic therapy using 20% topical aminolevulinic acid and either a 633-nm diode laser or a broad-spectrum red light source. Four patients enrolled with only two patients completing the study. One demonstrated modest improvement but the other patient worsened [96]. Another case series reports four patients with a response to topical aminolevulinic acid using a blue light source [94].
There is a single patient with concomitant hyperhidrosis who benefited from injection of botulinum toxin for axillary HS [97].

Radiotherapy with x-rays has been reported to be useful in control of the disease [98]. Destruction of the hair follicles is thought to play a role in sustained remissions. No randomized controlled studies have been performed with this technique.

Surgical excision is the treatment of choice for early disease. Surgical techniques for excision and repair vary, depending on extent of disease, location of lesions, existing comorbidities, and chronicity of disease [99]. Hair follicle and apocrine gland areas should be excised to fascia to ensure adequate removal of appendageal structures [100]. While a detailed discussion of surgical techniques employed is beyond the scope of this review, there are certain recurring themes impacting recurrence rates [2]: location of lesions, extent of excision, method of closure, and age of patient. The extent of excision is probably the most important modifiable factor. Exteriorization of lesions is thought to be important for proper reepithelialization and closure. Incisional techniques uniformly lead to disease recurrence (Fig. 8) and should be avoided. Thus, wide local excision correlates with decreased recurrence [101]. Healing by secondary intention is thought to offer the lowest rate of recurrence, but is associated with a prolonged postoperative recovery [102]. Closures with flaps and grafts have a significantly lower recurrence rate than do primary closures [103]. Later age of onset appears to have a favorable prognosis in recurrence rates [104]. Other factors to consider include operative risk, likelihood of infection, postoperative recovery time, scarring and associated wound contracture, skin irritation, and cutaneous sensory changes.

Fig. 8. Moderate HS with linear scars after multiple incision and drainage procedures.
SUMMARY

HS is a chronic, debilitating inflammatory dermatosis that is often refractory to treatment. Many medical therapies have been tried and some show efficacy. The introduction of new immunosuppressive medications has revolutionized the treatment of psoriasis in dermatology. These therapies have the potential to powerfully abort the molecular signals driving inflammation in HS and perhaps even induce a remission. This may offer patients an alternative to radical excisional surgery. However, more studies are needed to evaluate the long-term effects of these medications, particularly in light of their association with an increased risk of malignancy and infection.

Evaluation of treatment efficacy has been hindered by a lack of uniform standards to track treatment response. The classic clinical classification system has

### Box 3: Laboratory studies

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<td>Culture swab (aerobic) of HS lesions</td>
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<td>Skin aspirate (aerobic and anaerobic) of HS lesions</td>
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Consider these additional studies at baseline, depending on elected treatment:

- Complete blood cell count with differential
- Basic metabolic panel plus magnesium
- Liver function tests
- Glucose-6-phosphate dehydrogenase level
- Fasting lipids
- Purified protein derivative

Additional studies if patient is female and has hirsutism

- Dihydroepiandrosterone sulfate
- Testosterone total and free
- Sex-hormone-binding globulin
- Progesterone

Additional studies if patient refractory to antibiotics

- Nasal swab
- Anaerobic culture (skin aspirate)

Additional studies if patient has complaint of diarrhea

- Consider colonoscopy with possible biopsy

Additional studies if patient has complaint of arthritis

- Rheumatoid factor
- Erythrocyte sedimentation rate
- Antinuclear antibody

Additional study if lesion has features of malignancy

- Biopsy
limitations but is a useful scheme to guide selection of treatments. Further laboratory studies may be warranted, depending on the clinical presentation (Box 3). While there are many approaches to treating HS, the authors offer an algorithm based on disease severity (Fig. 9).

It is important to address many patient-oriented concerns, such as the pain, dampness, and smell associated with draining sinuses. Communication with the patient about expectations is important to direct treatment. Often a multidisciplinary approach involving dermatology, plastic surgery, gynecology, and

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<th>MALE DISEASE SEVERITY</th>
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**TREATMENTS TO BE CONSIDERED REGARDLESS OF SEVERITY**
- Adjunctive therapy (weight loss, smoking cessation, Sitz bath, warm compresses)
- Intralesional steroids
- Pain management (non-steroidal anti-inflammatories, opiates)
- Surgical Excision

**Fig. 9.** Treatment algorithm. BID, twice a day; DS, double strength (trimethoprim 160 mg and sulfamethoxazole 800 mg); QD, every day.
urology may be necessary to diagnose and treat the disease. Both medical and surgical options should be explored before embarking on therapy.

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