A practical guide to hidradenitis suppurativa

Early diagnosis and treatment of hidradenitis suppurativa is key to avoiding severe disease and minimizing its negative psychological impact.

Hidradenitis suppurativa (HS), also known as acne inversa or Verneuil disease, is a chronic, recurrent, inflammatory occlusive disease affecting the terminal follicular epithelium in apocrine gland-bearing skin areas. HS manifests as painful nodules, abscesses, fistulas, and scarring and often has a severe psychological impact on the affected patient.

When HS was first identified in the 1800s, it was believed to result from a dysfunction of the sweat glands. In 1939, scientists identified the true cause: follicular occlusion.

Due to its chronic nature, heterogeneity in presentation, and apparent low prevalence, HS is considered an orphan disease. Over the past 10 years, there has been a surge in HS research—particularly in medical management—which has provided a better understanding of this condition.

In this review, we discuss the most updated evidence regarding the diagnosis and treatment of HS to guide the family physician (FP)’s approach to managing this debilitating disease. But first, we offer a word about the etiology and pathophysiology of the condition.

3 events set the stage for hidradenitis suppurativa

Although the exact cause of HS is still unknown, some researchers have hypothesized that HS results from a combination of genetic predisposition and environmental and lifestyle factors. The primary mechanism of HS is the obstruction of the terminal follicular epithelium by a keratin plug. A systematic review of molecular inflammatory pathways involved in HS divides the pathogenesis of HS into 3 events: follicular occlusion followed by dilation, follicular rupture and inflammatory response, and chronic inflammatory state with sinus tracts.

An underreported condition

HS is often underreported and misdiagnosed. Globally, the prevalence of HS varies from < 1% to 4%. A systematic review...
A family history of hidradenitis suppurativa is associated with earlier onset, longer disease duration, and severe disease.

With meta-analysis showed a higher prevalence of HS in females compared to males in American and European populations. In the United States, the overall frequency of HS is 0.1%, or 98 per 100,000 persons. The prevalence of HS is highest among patients ages 30 to 39 years; there is decreased prevalence in patients ages 55 years and older.

**Who is at heightened risk?**

Recent research has shown a relationship between ethnicity and HS. African American and biracial groups (defined as African American and White) have a 3-fold and 2-fold greater prevalence of HS, respectively, compared to White patients. However, the prevalence of HS in non-White ethnic groups may be underestimated in clinical trials due to a lack of representation and subgroup analyses based on ethnicity, which may affect generalizability in HS recommendations.

**Genetic predisposition.** As many as 40% of patients with HS report having at least 1 affected family member. A positive family history of HS is associated with earlier onset, longer disease duration, and severe disease. HS is genetically heterogeneous, and several mutations (eg, gamma secretase, PSTPIP1, PSEN1 genes) have been identified in patients and in vitro as the cause of dysregulation of epidermal proliferation and differentiation, immune dysregulation, and promotion of amyloid formation.

**Obesity and metabolic risk factors.** There is a strong relationship between HS and obesity. As many as 70% of patients with HS are obese, and 9% to 40% have metabolic syndrome. Obesity is associated with maceration and mechanical stress, increased fragility of the dermo-epidermal junction, changes in cutaneous blood flow, and subdermal fat inflammation—all of which favor the pathophysiology of HS.

**Smoking.** Tobacco smoking is associated with severe HS and a lower chance of remission. Population-based studies have shown that as many as 90% of patients with HS have a history of smoking ≥ 20 packs of cigarettes per year. The nicotine and thousands of other chemicals present in cigarettes trigger keratinocytes and fibroblasts, resulting in epidermal hyperplasia, infundibular hyperkeratosis, excessive cornification, and dysbiosis.

**Hormones.** The exact role sex hormones play in the pathogenesis of HS remains unclear. Most information is based primarily on small studies looking at antiandrogen treatments, HS activity during the menstrual cycle and pregnancy, HS exacerbation related to androgenic effects of hormonal contraception, and the association of HS with metabolic-endocrine disorders (eg, polycystic ovary syndrome [PCOS]).

Androgens induce hyperkeratosis that may lead to follicular occlusion—the hallmark of HS pathology. A systematic review looking at the role of androgen and estrogen in HS found that while some patients with HS have elevated androgen levels, most have androgen and estrogen levels within normal range. Therefore, increased peripheral androgen receptor sensitivity has been hypothesized as the mechanism of action contributing to HS manifestation.

**Host-defense defects.** HS shares a similar cytokine profile with other well-established immune-mediated inflammatory diseases, including pyoderma gangrenosum (PG) and Crohn disease. HS is characterized by the expression of several immune mediators, including tumor necrosis factor-alpha (TNF-alpha), interleukin-1 alpha (IL-1 alpha), IL-1 beta, IL-8, IL-17, and the IL-23/T helper 17 pathway, all of which are upregulated in other inflammatory diseases and also result in an abnormal innate immune response. The recently described clinical triad of PG, acne, and HS (PASH) and the tetrad of pyogenic arthritis, PG, acne, and HS (PAPASH) further support the role of immune dysregulation in the pathogenesis of HS. Nonetheless, further studies are needed to determine the exact pathways of cytokine effect in HS.

**Use these criteria to make the diagnosis**

The US and Canadian Hidradenitis Suppurativa Foundations (HSF) guidelines base the clinical diagnosis of HS on the following criteria:

- Typical HS lesions: Erythematous skin lesions; inflamed, deep-seated...
painful nodules; “tombstone” double-ended comedones; sinus tracts; scarring; deformity. **FIGURES 1A-1E** show typical lesions seen in patients with HS.

- Typical locations: Intertriginous regions—apocrine gland-containing areas in axilla, groin, perineal region,
buttocks, gluteal cleft, and mammary folds; beltline and waistband areas; areas of skin compression and friction.

- Recurrence and chronicity: Recurrent painful or suppurating lesions that appear more than twice in a 6-month period.2,41-43

Patients with HS usually present with painful recurrent abscesses and scarring and often report multiple visits to the emergency department for drainage or failed antibiotic treatment for abscesses.15,44

**Ask patients these 2 questions.** Vinding et al45 developed a survey for the diagnosis of HS using 2 simple questions based on the 3 criteria established by the HSF:

1. “Have you had an outbreak of boils during the last 6 months?” and
2. “Where and how many boils have you had?” (This question includes a list of the typical HS locations—eg, axilla, groin, genitals, area under breast.)

In their questionnaire, Vinding et al45 found that an affirmative answer to Question 1 and reports of > 2 boils in response to Question 2 correlated to a sensitivity of 90%, specificity of 97%, positive predictive value of 96%, and negative predictive value of 92% for the diagnosis of HS. The differential diagnosis of HS is summarized in **TABLE 1**.42,45-52

These tools can help you to stage hidradenitis suppurativa

Multiple tools are available to assess the severity of HS.53 We will describe the Hurley staging system and the International Hidradenitis Suppurativa Severity Score System (IHS4). Other diagnostic tools, such as the Sartorius score and the Hidradenitis Suppurativa Physician’s Global Assessment Scale (HS-PGA), can be time-consuming and challenging to interpret, limiting their use in the clinical setting.2,54

**Hurley staging system** (available at www.hsdiseasesource.com/hs-disease-staging) considers the presence of nodules, abscesses, sinus tracts, and scarring affecting an entire anatomical area.13,55 This system is most useful as a rapid classification tool for patients with HS in the clinical setting but should not be used to assess clinical response.2,13,56

**The IHS4** (available at https://online library.wiley.com/doi/10.1111/bjd.15748) is a validated and easy-to-use tool for assess-
As many as 90% of patients with hidradenitis suppurativa have a history of smoking ≥ 20 packs of cigarettes per year.

No diagnostic tests, but ultrasound may be helpful
There are currently no established biological markers or specific tests for diagnosing HS. Ultrasound is emerging as a tool to assess dermal thickness, hair follicle morphology, and number and extent of fluid collections. Two recent studies showed that pairing clinical assessment with ultrasound findings improves accuracy of scoring in 84% of cases. For patients with severe HS, skin biopsy can be considered to rule out squamous cell carcinoma. Cultures, however, have limited utility except for suspected superimposed bacterial infection.

Screening for comorbidities
HSF recommends clinicians screen patients for comorbidities associated with HS (TABLE 2). Overall, screening patients for active and past history of smoking is strongly recommended, as is screening for metabolic syndrome, hyperlipidemia, type 2 diabetes (1.5- to 3-fold greater risk of type 2 diabetes in HS patients), and PCOS (3-fold greater risk). Screening patients for depression and anxiety is also routinely recommended. However, the authors of this article strongly recommend screening all patients with HS for psychiatric comorbidities, as research has shown a 2-fold greater risk of depression and anxiety, social isolation, and low self-esteem that severely limits quality of life (QOL) in this patient population.

Management
Treat existing lesions, reduce formation of new ones
The main goals of treatment for patients with HS are to treat existing lesions and reduce associated symptoms, reduce the formation of new lesions, and minimize associated psychological morbidity. FPs play an important role in the early diagnosis, treatment, and comprehensive care of patients with HS. This includes monitoring patients, managing comorbidities, making appropriate referrals to dermatologists, and coordinating the multidisciplinary care that patients with HS require.

A systematic review identified more than 50 interventions used to treat HS, most based on small observational studies and randomized controlled trials (RCTs) with a high risk of bias. FIGURE 2 provides an evidence-based treatment algorithm for HS, and TABLE 3 summarizes the most commonly used treatments.

<table>
<thead>
<tr>
<th>TABLE 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen patients for comorbidities associated with hidradenitis suppurativa&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
</tr>
<tr>
<td>Follicular occlusion tetrad&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Acne</td>
</tr>
<tr>
<td>Depression/anxiety</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Polycystic ovary syndrome</td>
</tr>
<tr>
<td>Impaired sexual health</td>
</tr>
<tr>
<td>Pyoderma gangrenosum and autoimmune syndromes&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Arthropathies&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Squamous cell carcinoma&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> The strength of recommendation to screen for these conditions is A, with 3 exceptions: pyoderma and arthropathies B and squamous cell carcinoma C. See page E1 for SOR definitions.

<sup>b</sup> Hidradenitis suppurativa, acne conglobata, dissecting cellulitis of the scalp, and pilonidal sinus.

<sup>c</sup> Only if suggested by review of systems.

<sup>d</sup> Of the hidradenitis suppurativa–affected skin.
ity, and induces apoptosis of TNF-expressing mononuclear cells. It is the only medication approved by the US Food and Drug Administration for active refractory moderate and severe HS. Several double-blinded RCTs, including PIONEER I and PIONEER II, studied the effectiveness of ADA for HS and found significant clinical responses at Week 12, 50% reduction in abscess and nodule counts, no increase in abscesses or draining fistulas at Week 12, and sustained improvement in lesion counts, pain, and QOL.

[IL-1 and IL-23 inhibitors. The efficacy of etanercept and golimumab (anti-TNF), as well as anakinra (IL-1 inhibitor) and ustekinumab (IL-1/IL-23 inhibitor), continue to be investigated with variable results; they are considered second-line treatment for active refractory moderate and severe HS after ADA. Infliximab (IL-1 beta inhibitor) has shown no effect on reducing disease severity.]

Compared to other treatments, biologic therapy is associated with higher costs (TABLE 3), an increased risk for reactivation of latent infections (eg, tuberculosis, herpes simplex, and hepatitis C virus [HCV], and B [HBV]), and an attenuated response to vaccines. Prior to starting biologic therapy, FPs should screen patients with HS for tuberculosis and HBV; consider HIV and HCV screening in

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**Figure 2: Management of hidradenitis suppurativa**

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line: Topical clindamycin 1% lotion bid for 12 wk</td>
<td>Clindamycin 300 mg po bid + rifampicin 300 mg po bid for 10 wk</td>
<td>Improved: Treat the flares</td>
</tr>
<tr>
<td>Second-line: Tetracycline 500 mg po bid for 4 mo</td>
<td></td>
<td>Failed: Combine topical clindamycin + tetracycline 500 mg bid for 4 mo</td>
</tr>
<tr>
<td>Failed: Consider local excision</td>
<td>Improved: Treat the flares</td>
<td>Yes</td>
</tr>
<tr>
<td>De-roofing, laser, local, and wide excision</td>
<td>Failed: Consider local excision</td>
<td>No</td>
</tr>
</tbody>
</table>

*a This stepwise approach was developed by the authors, based on their practice and cited sources.
*b For all patients: (1) provide education and support, (2) treat wounds and recommend proper skin care, (3) provide pain management, (4) encourage smoking cessation and weight loss, and (5) assess and manage comorbidities.
TABLE 3
Commonly used treatments for hidradenitis and their cost2,63,64,70-75

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Strength of recommendation</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>B</td>
<td>$41-$80 per bottle of topical solution</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>C</td>
<td>$13-$15 per 118-mL bottle</td>
</tr>
<tr>
<td>Triamcinolone (intrallesional)</td>
<td>C</td>
<td>$19 (40 mg/mL injectable suspension)</td>
</tr>
<tr>
<td>Benzoyl peroxide</td>
<td>C</td>
<td>$24-$30 per 60 g of generic gel tube</td>
</tr>
<tr>
<td><strong>Systemic antibiotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>B</td>
<td>$610-$1000 for 30-day supply</td>
</tr>
<tr>
<td>Rifampicin + clindamycin</td>
<td>B</td>
<td>$83-$520 for 30-day supply</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>C</td>
<td>$700-$1400 per 10 vials of 1 g</td>
</tr>
<tr>
<td><strong>Hormonal therapies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiandrogen contraceptives</td>
<td>C</td>
<td>Varies from $20-$170 according to brand</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>C</td>
<td>$12-$23 for 30-day supply (25 mg tablet)</td>
</tr>
<tr>
<td>Metformin</td>
<td>C</td>
<td>$15 for 30-day supply (500 mg tablet)</td>
</tr>
<tr>
<td>Finasteride</td>
<td>C</td>
<td>$11-$84 for 30-day supply (1 mg tablet)</td>
</tr>
<tr>
<td><strong>Biologics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>A</td>
<td>$7000-$13,000 for 2 pens of 40 mg/0.4 mL</td>
</tr>
<tr>
<td>Infliximab</td>
<td>C</td>
<td>$1239 for 100 mg intravenous powder injection</td>
</tr>
<tr>
<td>Anakinra</td>
<td>B</td>
<td>$1265 for a supply of 4.69 mL (100 mg/0.67 mL)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>C</td>
<td>$1700 to &gt; $10,000, depending on dosing and presentation</td>
</tr>
<tr>
<td><strong>Retinoids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isotretinoin, acitretin, alitretinoin</td>
<td>B</td>
<td>From $147 to &gt; $6000 per month, depending on retinoid</td>
</tr>
<tr>
<td><strong>Systemic immunomodulators</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic corticosteroids</td>
<td>C</td>
<td>$10-$20</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>C</td>
<td>Price varies greatly as dose is estimated by weight</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td><strong>Surgical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wide excision</td>
<td>B</td>
<td>Variable</td>
</tr>
<tr>
<td>Unroofing/deroofing</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Abscess drainage</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

a See page E1 for SOR definitions.

at-risk patients, and optimize the immunization status of the patient.82,83 While inactivated vaccines can be administered without discontinuing biologic treatment, patients should avoid live-attenuated vaccines while taking biologics.81

**Antibiotic therapy**

■ **Topical antibiotics** are considered first-line treatment for mild and moderate uncomplicated HS.63,64 Clindamycin 1%, the only topical antibiotic studied in a small double-blind RCT of patients with Hurley stage I and stage II HS, demonstrated significant clinical improvement after 12 weeks of treatment (twice-daily application), compared to placebo.64 Topical clindamycin is also recommended to treat flares in patients with mild disease.2,64

■ **Oral antibiotics.** Tetracycline (500 mg twice daily for 4 months) is considered a
All patients with hidradenitis suppurativa should be screened for depression, anxiety, social isolation, and low self-esteem.

Corticosteroids and systemic immunomodulators

Intralesional triamcinolone (2-20 mg) may be beneficial in the early stages of HS, although its use is based on a small prospective open study of 33 patients. A recent double-blind placebo-controlled RCT comparing varying concentrations of intralesional triamcinolone (10 mg/mL and 40 mg/mL) vs normal saline showed no statistically significant difference in inflammatory clearance, pain reduction, or patient satisfaction.

Short-term systemic corticosteroids (eg, prednisone, starting at 0.5-1 mg/kg) are recommended to treat flares. Long-term corticosteroids and cyclosporine are reserved for patients with severe refractory disease; however, due to safety concerns, their regular use is strongly discouraged. There is limited evidence to support the use of methotrexate for severe refractory disease, and its use is not recommended.

Hormonal therapy

The use of hormonal therapy for HS is limited by the low-quality evidence (eg, anecdotal evidence, small retrospective analyses, uncontrolled trials). The only exception is a small double-blind controlled crossover trial from 1986 showing that the antiandrogen effects of combination oral contraceptives (ethinylestradiol 50 mcg/cyproterone acetate in a reverse sequential regimen and ethinylestradiol 50 mcg/norgestrel 500 mcg) improved HS lesions.

Spironolactone, an antiandrogen diuretic, has been studied in small case report series with a high risk for bias. It is used mainly in female patients with mild or moderate disease, or in combination with other agents in patients with severe HS. Further research is needed to determine its utility in the treatment of HS.

Metformin, alone or in combination with other therapies (dapsone, finasteride, liraglutide), has been analyzed in small prospective studies of primarily female patients with different severities of HS, obesity, and PCOS. These studies have shown improvement in lesions, QOL, and reduction of workdays lost.

Finasteride. Studies have shown finasteride (1.25-5 mg/d) alone or in combination with other treatments (metformin, liraglutide, levonorgestrel-ethinyl estradiol, and dapsone) provided varying degrees of resolution or improvement in patients with severe and advanced HS. Finasteride has been used for 4 to 16 weeks with a good safety profile.

Retinoids

Acitretin, alitretinoin, and isotretinoin have been studied in small retrospective studies to manage HS, with variable results. Robust prospective studies are needed. Retinoids, in general, should be considered as a second- or third-line treatment for moderate to severe HS.

Surgical intervention

Surgical interventions, which should be considered in patients with widespread mild, moderate, or severe disease, are associated with improved daily activity and work productivity. Incision and drainage should be avoided in patients with HS, as this technique does not remove the affected follicles and is associated with 100% recurrence.

Wide excision is the preferred surgical technique for patients with Hurley stage II and stage III HS; it is associated with lower recurrence rates (13%) compared to local excision (22%) and deroofing (27%). Second-
ary intention healing is the most commonly chosen method, based on lower recurrence rates than primary closure.102

STEP and laser techniques. The skin-tissue-sparing excision with electrosurgical peeling (STEP) procedure involves successive tangential excision of affected tissue until the epithelialized bottom of the sinus tracts has been reached. This allows for the removal of fibrotic tissue and the sparing of the deep subcutaneous fat. STEP is associated with 30% of relapses after 43 months.71

Laser surgery has also been studied in patients with Hurley stage II and stage III HS. The most commonly used lasers for HS are the 1064-nm neodymium-doped yttrium aluminum garnet (Nd: YAG) and the carbon dioxide laser; they have been shown to reduce disease severity in inguinal, axillary, and inflammatory sites.72-74

Pain management: Start with lidocaine, NSAIDs

There are few studies about HS-associated pain management.103 For acute episodes, short-acting nonopioid local treatment with lidocaine, topical or oral nonsteroidal anti-inflammatory drugs, and acetaminophen are preferred. Opioids should be reserved for moderate-to-severe pain that has not responded to other analgesics. Adjunct therapy with pregabalin, gabapentin, selective serotonin reuptake inhibitors, or serotonin-norepinephrine reuptake inhibitors can also be considered for the comanagement of pain and depression.62,104

Consider this tool to measure treatment response

The HS clinical response (HiSCR) tool is an outcome measure used to evaluate treatment outcomes. The tool uses an HS-specific binary score with the following criteria:

1. ≥ 50% reduction in the number of inflammatory nodules;
2. no increase in the number of abscesses; and
3. no increase in the number of draining fistulas.105

The HiSCR was developed for the PIONEER studies105,106 to assess the response to ADA treatment. It is the only HS scoring system to undergo an extensive validation process with a meaningful clinical endpoint for HS treatment evaluation that is easy to use. Compared to the HS-PGA score (clear, minimal, mild), HiSCR was more responsive to change in patients with HS.105,106

References

13. von Laaff M, Helmbold P, Wohlrab J, et al. Hidradenitis suppurativa for age-appropriate biologic therapy, considering imum garnet (Nd: YAG) and the carbon dioxide laser; they have been shown to reduce disease severity in inguinal, axillary, and inflammatory sites.72-74

When considering biologic therapy, screen all patients with hidradenitis suppurativa for tuberculosis and hepatitis B, and confirm they are current with age-appropriate immunizations.


