REVIEW ARTICLE

Flashes on Hidradenitis Suppurativa

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ABSTRACT

Hidradenitis suppurativa (HS) is a chronic, none contagious, inflammatory and scarring skin disorder affecting mainly axillae, groin, anogenital and the inframammary regions. It affects quality of life in most of patients. Its prevalence is up to 4% worldwide. Follicular apocrine occlusion is the main pathogenetic factor for the occurrence of HS. The two main predisposing factors for the development of HS are smoking and obesity. There is no single effective therapy for HS, and choice of the treatment should be based upon Hurley's staging classification system.

KEYWORDS: Hidradenitis suppurativa (HS)

INTRODUCTION

Hidradenitis suppurativa is a chronic, cutaneous disorder characterized by recurrent, painful nodules, abscesses, and draining sinuses, with resultant scarring. It affects the intertriginous body areas including the axillae, the inguinal folds, the anogenital, the perineum, the inframammary regions, and the nape of neck.[1]

Hidradenitis suppurativa (HS) was described in 1854 by French surgeon Verneuil who linked the disease to apocrine sweat glands. Apocrine sweat glands empty their contents into the follicular canal, just above the sebaceous gland duct, in contrast to eccrine sweat glands that empty their ducts directly into the skin surface.[2]

The term acne inversa was suggested by Plewig and Steger in 1989 as another name for HS.[3] The term acne inversa is based on the infundibular hyperkeratosis seen in terminal follicles in HS that parallels the infundibular hyperkeratosis of the pilosebaceous unit in acne vulgaris;[3] however, HS is not a type of acne. In HS, there are no closed comedones, as it is deeper and not the superficial part of the follicle that is affected.[4] Also, hyperseborrhea and/or sebum lipid changes are not noted in HS, whereas they have prominent roles in the pathogenesis of acne. A similar frequency, density, and pattern of active sebaceous glands were found in HS patients and controls, and there was no significant facial, axillary, or genital seborrhea.[6]

DEFINITION

According to the"Hidradenitis Suppurativa Foundation 2009". HS was defined as a chronic, inflammatory, recurrent, debilitating, skin follicular disease that usually presents after puberty with painful deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly, the axillary, inguinal, and anogenital regions.[7]

Prevalence and epidemiology

The global prevalence of HS ranges between 1%

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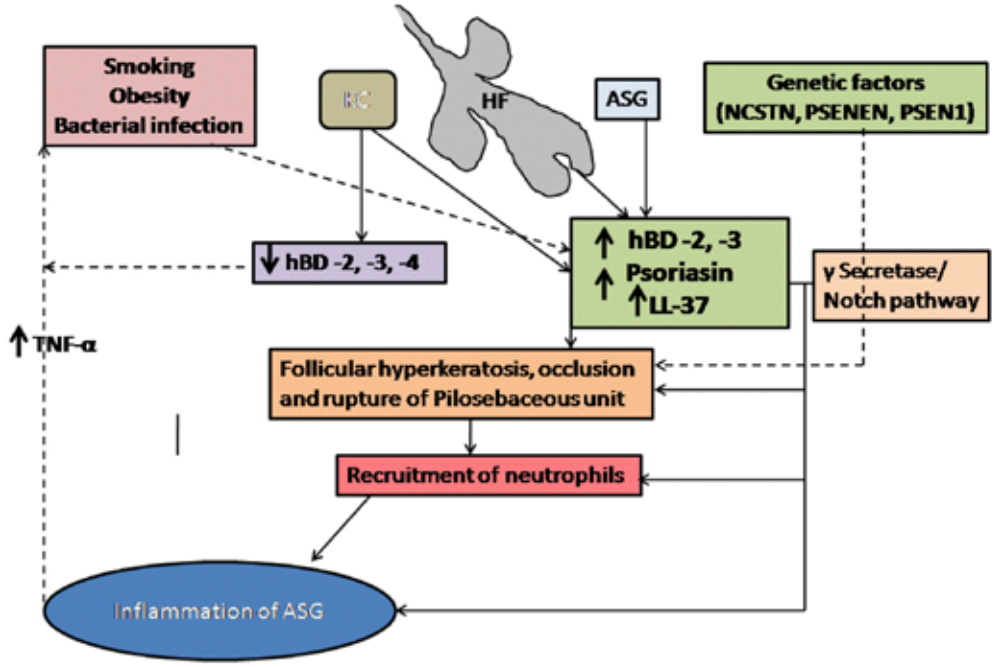

Fig. 1 Summarized diagram for pathogenies of HS.
KC, Keratinocyte; HF,Hair follicle; ASG, Apocrine sweat gland; hBD, Human b-defensin; LL-37, cathelicidin.

and 4%. There are no racial differences, but the female to male ratio is 3.3:1. Women are affected under the breasts (22%) and in the groin (93%); men are affected on the buttocks (40%) and perianal area (51%).[8] Patients are usually affected in the second and third decades. The onset of the disease occurs earlier to those with a family history, and is unusual after menopause. In men, it can continue into old age.[9]

Predisposing factors

Obesity and nicotine smoking have been identified in HS as the two major exacerbating factors.[8,10] Although sweating, shaving, depilation, deodorant use, and friction have also been implicated.[11,12]
In the past several years, a different trigger has been identified: diet. In 2010, Melnik[13] proposed a link between high glycemic foods and worsening acne. He noted that many of the proposed triggers for acne and HS (high carbohydrate diet, milk consumption, stress, and nicotine use) converge into one pathway, the phosphoinositol-3 kinase/ Akt/Fox01 pathway, which may play a role in the disease.[13] However, correlation between diet and HS exacerbation is not well established, further studies are needed to explore the role of diet in HS.
HS can be initiated or exacerbated by lithium. The proposed underlying mechanism is lithium's ability to enhance neutrophil migration and phagocytic ability, increase epithelial cell proliferation, or its ability to cause follicular plugging through its direct effect on follicular keratinocytes (as in acne).[13,14]

Pathogenesis of HS

Multiple factors have been implicated in the pathogenesis of HS including genetic factors, hormones, smoking, obesity, bacterial infection, and alteration of antimicrobial peptides (AMPs) that regulate cutaneous innate immunity (Fig. 1).[15-17]
The main mechanism for development of HS is

increased outer root sheath (ORS) keratinocyte proliferation with subsequent follicular occlusion and occlusion of the apocrine sweat gland.[4] This is followed by rupture of the follicular canal and extrusion of contents, including corneocytes, bacteria, sebum, and hair follicles, into the surrounding connective tissue, and the development of an inflammatory infiltrate.[15,16] In a study of 94 operative specimens from 60 patients with HS, hyperkeratosis of the terminal follicles was found in 82% (77⁄94) of the cases. Hyperplasia of follicular epithelium was evident in 77% (72⁄94), and pronounced perifolliculitis was observed in 68% (64⁄94) of the cases. Follicle ruptures, in contrast, were only found in 28% (26⁄94) of the tissue samples.[4]

Loss of function mutations in the γ-secretase component genes have been identified as the culprit for a subset of familial HS, which implicate the γ-secretase-Notch pathway in the molecular pathogenesis of this disease subset.[17] Nicastrin is a 150 - 160 kDa protein. It is a component of the aspartyl protease γ-secretase complex and serves to stabilize and direct γ-secretase components to proper positions in the plasma membrane. It contains a 636 aa extracellular domain (aa 34 - 669) that shows a 58 aa sequence (aa 312-369), which interacts with γ-secretase substrates. Nicastrin itself has no catalytic activity. Nicastrin mutations have been detected in Chinese[17-19] and French families with HS.[19] Mutations of the sonic hedgehog pathway could not be identified in HS patients.[20,21]

The severity of HS is strongly associated with smoking; smokers are generally known to suffer from severe disease than nonsmokers. The effect of nicotine on the skin of HS patients compared to controls showed a significantly thicker epidermis and follicular plugging in the presence of nicotine. This finding correlated with the production of non-neuronal acetylcholine in the skin, as suggested by an increased expression of acetylcholine receptors found around the follicular infundibulum in the epidermis of HS patients.[22,23]

Obesity may aggravate HS in several ways: through sweat retention and maceration, shearing of follicular or ductal outlets, and abnormal hormonal metabolism. In obese patients, the axilla is nestled between the enlarged lateral thoracic wall and the upper arm, resulting in overlapping skin folds and subsequent friction, maceration, and occlusion of the skin. Shearing associated with increased skin-to-skin contact may trigger both follicular hyperkeratosis and follicular plugging via epidermal desquamation.[24] Furthermore; the juxtaposition of skin surfaces may promote keratin hydration within sweat glands. This potentially reduces the diameter of the follicular orifice, further predisposing to poral occlusion. In addition, obesity has been associated with changes in the production, metabolism, and biologic activity of sex hormone binding globulin, androgens, and estrogens, causing a state of relative androgen excess. This androgen excess may result in coarsening of the hair shaft with subsequent follicular plugging.[25]

There is a direct and strong relationship between sex hormones and HS. The female preponderance suggests a greater sensitivity of females to androgens. There are no elevations in serum androgens in the vast majority of HS patients. End-organ sensitivity is likely responsible. Increased access to the androgen receptor is mediated by insulin and insulin-like growth factor-1 (IGF-1), both chronically raised by dietary factors.[26]

In Females, the onset of HS starts at around

menarche, flares premenstrually and following exposure to androgenic progestins like medroxy progesterone acetate (MPA) or levonorgestrel.[27] But, it improves with pregnancy and fades after menopause. Anti androgen therapy helps HS patients of both sexes. Finasteride, a selective inhibitor of the type II isomer of 5α-reductase, reduces the levels of 5αr DHT. It was used to improve six of seven adults with HS and three children, one with premature adrenarche and one with polycystic ovarian syndrome.[28]

Bacteria have no direct role in the pathogenesis of HS, but as secondary invaders, may share in the pathogenesis of the chronic relapsing lesions. Septicemia and systemic illness are rare in HS. The observation of many bacterial species, including Streptococcus viridans, Staphylococcus aureus, S milleri, anaerobes (Peptostreptococcus species, Bacteroides melaninogenicus, and B corrodens), coryneform bacteria, and Gram-negative bacteria, such as Escherichia coli, Klebsiella, and Proteus, and no dominant single species, suggests that bacteria found on the surface of HS lesions are secondary colonizers rather than etiologic agents.[29] A study involving an aspiration technique to sample deeper parts of early HS lesions clearly showed negative cultures in 51% of the cases, suggesting that HS is primarily a disease of the follicular epithelium that is secondarily colonized and infected by bacteria; however, the persistence of bacteria frequently found in chronic and relapsing HS may contribute to flares of the disease.[30,31]

Biofilms are densely packed communities of microbial cells that grow on living or inert surfaces and surround themselves with secreted polymers (Fig. 2).

Many bacterial species form biofilms, and their

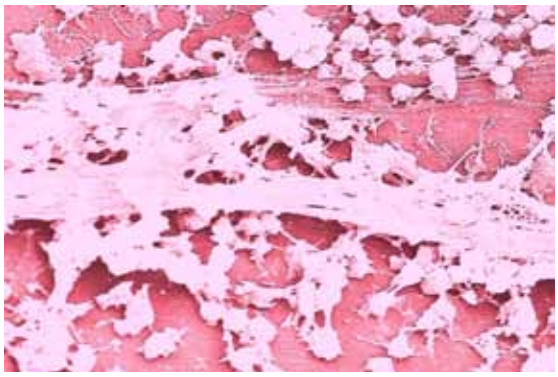

Fig. 2 Biofilms: Microorganism connecting to each other forming polymer.

study has revealed them to be complex and diverse in nature. The structural and physiological complexity of biofilms has led to the idea that they are coordinated and cooperative groups, analogous to multicellular organisms.[31] Biofilms are a relatively new topic in dermatology but have been studied for many years in other disciplines, in both medicine and industry. Perhaps the most common clinical examples of biofilms are dental plaques. Dentists have been studying the biofilms that constitute dental plaques for many years and have discovered that the artificial sweetener, xylitol, can help degrade the biofilm, resulting in fewer dental caries.[32,33] A biofilm is first formed by the reversible binding of bacteria to a substrate.[34] Then, irreversible binding occurs when the bacteria secrete a sticky, polysaccharide matrix that surrounds and protects the community from outside insults, including antibiotics.[35] Microcolonies form and varying phenotypes within the biofilm allow the community of bacteria to quickly adapt to stressors, increasing its overall chances of survival.[36,37] As the biofilm expands, the central bacteria lose some access to nutrients and oxygen, which are more abundant in the periphery of the biofilm. The net result is a slower metabolism and thus lower efficacy of antibiotics, which work on rapidly dividing cells.[38] Because

the skin lesions in HS are chronic and recurring and require long courses of antibiotics for treatment, it seems likely that HS is a biofilm disease. Two studies have reported biofilms adherent to sinus tract epithelium[39,40] and hair follicles[40] in HS. These two studies confirm the hypothesis that biofilms may play a secondary role in the pathogenesis of HS. In addition, the treatment of the bacteria that is forming the biofilms will be difficult. However, further studies are needed to explain role of biofilm in pathogenesis of HS.

An alteration of the cutaneous innate immune system plays a role in the follicular occlusion and the inflammation of HS. Innate immunity is the first line of defense against foreign microorganisms. AMPs exhibit antimicrobial and immunomodulatory functions, and they promote keratinocyte differentiation and/or proliferation.[41] The majority of AMPs is expressed by epithelial cells, such as keratinocytes (human β–defensin [HBD]-3, ribonuclease [RNase], and psoriasin) or by epithelial appendages, such as eccrine sweat glands (dermcidin). Whereas, α–defensins, human neutrophil peptides 1 to 3, and human cathelicidin LL-37 are contained within or secreted by circulating leukocytes. Innate immune markers were studied with immunohistochemistry in biopsies from 12 patients with HS, from both normal (uninvolved) skin and from inflammatory nodules. Skin biopsies from non-HS individuals were used as controls. The expression of TLR-2, -3, -4, -7, and -9, IL-6,TGF-β, α-MSH, β-defensin 2, β-defensin 4, and IGF-1, was suppressed in involved and uninvolved skin of HS patients compared to the controls. Also, compared to the control skin, TNF-α was suppressed in non lesional HS skin ($P < .001$), while there was no difference in lesional HS skin ($P = .08$). Defensins also have anti infectious properties, and a decrease in defensins may enable the development of bacteria. Similarly, defective immune response was found in the blood of HS patients in another study. Monocytes isolated from healthy controls ($n = 6$) were more active for the secretion of TNF-α compared to those isolated from HS patients ($n = 53$).[42] In contrast, some studies had reported significantly increased IL-1β, TNF-α, and IL-10 levels in lesional and perilesional HS skin compared with healthy control skin and psoriatic skin, suggesting that the inflammation is strong in HS skin and providing a rationale for anti-TNF therapy in HS patients.[43] The in situ expression of proinflammatory cytokines TNF-α, IL-8, as well as, α-MSH, a potent antinflammatory neuropeptide, and antimicrobial peptides, such as psoriasin, lysozyme, cathelicidin (LL-37), and hBD-3, was studied with immunohistochemistry in biopsies from lesional skin from 18 HS patients compared to 12 controls. There was increased immunoreactivity for LL-37 in the apocrine sweat gland and distal ORS epithelium of inflammatory HS skin ($P \leq .01$), psoriasin was increased in the epidermis and distal outer root sheath in inflammatory HS skin, hBD-3 was increased in the epidermis and the distal ORS in HS skin and α-MSH was significantly increased in the epidermis of inflammatory HS skin ($P \leq .01$). Compared to the controls, TNF-α was increased in the epidermis and the dermis of inflamed HS skin but decreased in the proximal ORS. IL-8 was increased in the epidermis and the ORS of inflamed HS skin. It is unclear if the up regulation of AMPs is a primary or a secondary event due to bacterial superinfection.[44,45] The epidermis of HS patients shows signs of hyperplasia[44] which is well in line with the concept that excessive LL-37 secretion

can lead to epithelial hyperproliferation. The observed up regulation of psoriasin and hBD-3 in HS epidermis may also be of relevance to stimulate keratinocyte proliferation and/or differentiation and induce follicular hyperkeratinization and subsequent follicular occlusion. Psoriasin stimulates α-defensin and TNF α transcription.[44] Up regulation of IL-8 expression in HS skin may lead to a vicious circle that promotes neutrophil, mast- and T-cell chemotaxis, activation of NF-κB in neutrophils. The macrophages, and neutrophils, are induced by IL-8 to produce more LL-37. Elevated levels of tumor necrosis factor (TNF-α) have been found in HS skin.[44,45] The expression of AMPs, hBD-3, ribonuclease 7 (RNase 7), psoriasin, and dermcidin, were studied in skin biopsies in 33 patients with HS and in axillary or inguinal biopsy specimens from normal-appearing skin of 6 patients with melanoma undergoing lymphadenectomy. Immunohistochemistry showed increased immunoreactivity of HBD-3 in the HS lesions compared to controls. Real time reverse transcription-polymerase chain reaction (RTPCR) showed HBD-3 mRNA levels were increased in HS of lower severity (grades I and II) compared with controls (P = .046). Interestingly, lesional skin of patients with severe HS (Hurley grade III) clearly showed no significant induction of HBD-3 mRNA expression compared with healthy skin. In addition, compared to controls, RNase 7 mRNA levels were significantly lower in HS skin, while there was no difference for psoriasin expression. The authors proposed that reduced HBD-3 inducibility may represent a predisposing factor for severe HS and, therefore, be present in these patients independent of the duration of the disease, or be the result of a secondary inhibition of AMP production due to longstanding disease.[46] Another study also recently reported increased HBD-2 and HBD-3 in patients with HS (n = 7) compared with healthy control subjects (n = 8) (P =.0001 and P = .004, respectively); however, there were reports of an over expression of psoriasin in lesional HS skin compared with normal-appearing skin of different locations, as in submammary region and trunk.[45,46] These discordant results may be explained in part by the fact that psoriasin secretion is dependent on the body location with highest levels secreted in head, hands, and axillae. Deficiency of IL-22 in HS may explain the low psoriasin expression, because IL-22 strongly induces expression of cutaneous AMPs, including psoriasin in vivo.[45]

Clinical features

Typical areas affected in HS include axillae, groins, and anal fold (Fig. 3, 4, 5). The sub-mammary region and skin folds due to obesity can also be involved, but affection of these areas without axillary or groin involvement is rare.[6] The disease starts with inflammatory painful nodules and sterile abscesses followed by tissue fibrosis. Over time, sinus tracts and fistulas develop. Hypertrophic scarring can often be seen. This can be accompanied by malodorous putrid discharge.[3] Pain is the main symptom of HS. The type of pain described by patients is hot, burning, pressure, cutting, sharp, taut, splitting, gnawing, sore, throbbing, and aching to sometime during their disease or as a chronic symptom in others. Pilonidal sinus is seen by some authors as a unilocalized type of HS. The involvement of the head and neck region is a rare event. There can be overlapping with acne keloidalis nuchae and dissecting folliculitis seen in some cases.[4]

HS is a chronic, inflammatory skin disorder

notorious for its tendency for recurrence that affects the quality of life, with pain as just one of contributing factors. Stigmatization, depression, and anxiety are highest in patients with severe anogenital HS.[4]

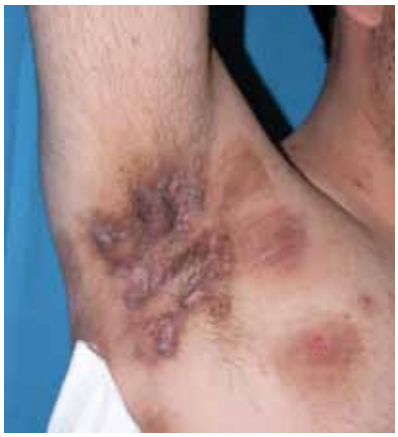

Fig. 3 Multiple nodules/abscesses with sinus tracts and cicatrization in right axillae.

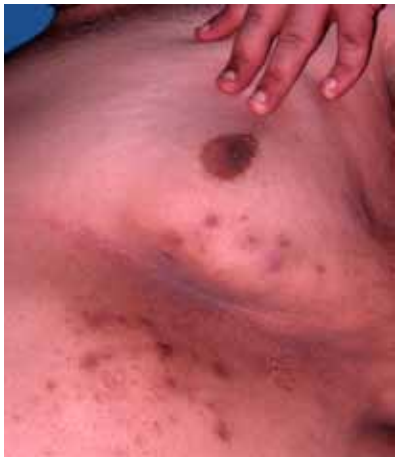

Fig. 4 Multiple nodules and pigmentation in inframammary region.

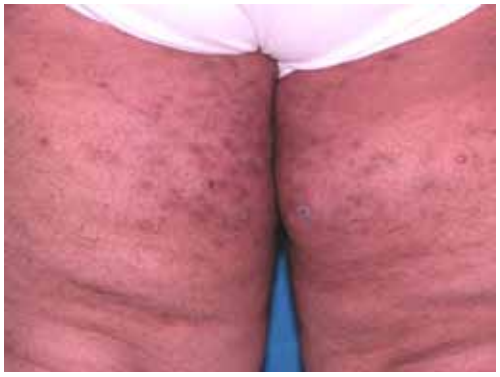

Fig. 5 Multiple nodules and pigmentation in thighs.

Clinical staging

In 1989, Hurley proposed the first staging systems for HS (Table I).[47] Hurley categorized the patients into three groups based largely on the presence and extent of cicatrization and sinuses.[47] It has been used as a basis for clinical trials in the past, and is a useful basis to approach therapy for patients. Its advantage is its simplicity.[47,48] However, Sartorius et al have suggested that the Hurley system is not sophisticated enough to assess treatment effects in clinical studies. They suggested a system that incorporates the involved anatomic regions, number and types of lesions, distance between lesions, and the presence of normal skin in between lesions.[49] Points are accumulated in each of the mentioned categories and added to give both a regional and total score. In addition, the authors suggest adding a visual analog scale for pain or using the dermatology life quality index (DLQI) when assessing HS.[49] This classification staging system will be the basis of further clinical studies.

Table 1 Hurley's staging system for HS

Hurley›s stages	Extent of disease in tissue
Stage: I	Abscess formation (single or multiple) without sinus tracts and cicatrization
Stage: II	One or more widely separated recurrent abscesses with tract formation and scars
Stage: III	Multiple interconnected tracts and abscesses throughout an entire area

Differential diagnosis

There are numerous diseases that cannot be easily differentiated from HS (Table 2).

HS can be differentiated from other diseases by the appearance of the lesions, postpubertal age of onset, characteristic locations, resistance to antibiotics, recovery of multiple species(rather than a single species) of bacteria on culture, absence of fever,

and the lack of significant laboratory findings. An important feature distinguishing almost all of these other diseases from HS is the specific histology (often with special stains for organisms) in the non-HS diseases.[50,51]

Table 2 Differential diagnosis of hidradenitis suppurativa

New lesion	Acne, furuncles, carbuncles, cellulitis, cutaneous blastomycosis, dermoid cyst, erysipelas, inflamed epidermoid cysts, lymphadenopathy, pilonidal cyst, perirectal abscess.
Old lesion	Anal fistula, actinomycosis, crohn disease, cat scratch disease, granuloma inguinale, ischiorectal abscess, lymphogranuloma venereum, nocardia infection, noduloulcerative syphilis, pilonidal disease, tuberculous abscess, tularemia.

COMPLICATIONS

Complications of HS are mainly local, such as scarring and infection. Systemic complications can develop like anemia, hypoproteinemia, nephritic syndrome, arthropathies, dactylitis, polyarthritis, secondary lymphedema (scrotal or vulvar), fistulae to rectum, vagina, urethra, peritoneum or bladder.[51-55] Lymphangioma circumscriptum of the vulva is a possible complication of HS.[56] Synovitis, acne pustulosis, hyperostosis, and osteitis (SAPHO)-syndrome has been described in HS patients.[57] Pyoderma gangrenosum is another complication in HS patients unresponsive to various treatments.[58] Secondary amyloidosis has been observed occasionally with multisystemic manifestations including renal and heart affection.[59] Squamous cell carcinoma developing on HS is a rare with fatal complication since these tumors are aggressive with early metastatic spread with a higher mortality rate of 50%.[60-67]

TREATMENT

The major problem in treatment of HS is that, there is no single effective therapy or cure from the disease. But the only permanent cure can be achieved with wide surgical technique for severe cases of HS (Hurley's III).

Prophylactic care is recommended without evidence-based trials: Gentle local hygiene. Wash with a mild non-soap cleansing bar. Where there is odor, an antiseptic cleanser with triclosan could be used. Wash by hands only, no washcloths or washrags. Avoid friction and irritation. Reduce trauma, heat, humidity, sweating, and friction. Wear loose ventilated clothing. Avoid tight or synthetic garments. Do not pinch or squeeze the lesions. Patients are advised to diet to achieve ideal body weight, stop smoking and avoid all tobacco and nicotine-replacement products.[68]

Various therapeutic options are used for treatment of HS such as medical, surgical, laser and photodynamic therapy.

MEDICAL TREATMENTS

The aim of medical treatments is to decrease the bacterial load, reducing follicular occlusion, decreasing the immune response, altering the hormonal balance, improving wound healing, reducing pain, and improving the patient's quality of life. Clindamycin-rifampicin, or rifampicin-moxifloxacin-metronidazole combinations are effective in treatment of HS by targeting the biofilm formation.[69-71] Traditional medical treatments for HS had included antibacterial washes, benzoyl peroxide wash, topical clindamycin with or without adjuvant azelaic acid and intralesional steroid injections (usually as an adjuvant to antibiotics). Most of these topical treatments have been shown to be effective in preventing or treating flares of HS. The use of topical preparations twice daily is also difficult for patients to use consistently for the prevention of flares. In addition, the use of antibiotic

monotherapy is not recommended as it leads to drug resistance.[70]

Acitretin, a systemic retinoid, has been effective in some cases suffering from HS.[72-74] Theoretically, it should be beneficial since follicular occlusion is a contributing factor in the pathogenesis of HS and acitretin's mechanism of action includes normalization of epithelial cell proliferation and differentiation.[75] However, its common adverse effects and high rate of relapse after discontinuation of therapy limit its long term use. Acitretin should be avoided in women of childbearing age because of its teratogenic effects, which can last for up to 3 years after discontinuation. Isotretinoin, another systemic retinoid, appears to be ineffective for HS, likely because this agent primarily decreases the size and sebum output of the sebaceous glands, which appear to already have significantly reduced volume in clinically uninvolved skin in HS patients compared with healthy controls.[75-78] Those patients who do respond are likely benefitting from isotretinoin's immunomodulatory effect.[79]

Anti-androgen as cyproterone acetate (CypA) combined with ethinyl estradiol 50 mg for 6 months cleared seven out of 24 for 19 months.[80] Finasteride 5-10 mg/day, usually used for prostate cancer, has been successfully used in HS.[81] Off label use of dutasteride has also helped clear both males and females in anecdotal personal cases. Both must be used with caution, as they are teratogenic. If oral contraceptives are considered, those containing ethinyl estradiol and drospirenone are preferred, combined with the antiandrogen spironolactone 50-100 mg when possible.[82]

Metformin has been reported to be useful in treatment of HS in combination with medical or another options of therapies.[83,84] Its mechanism of action through improvement of the sensitivity of peripheral cells to insulin, enhances the passage of glucose into individual cells, and lowers plasma glucose levels, reducing the level of circulating insulin. And also, it decreases the sensitization of the androgen receptors.[84] Zinc has anti-inflammatory and antiandrogenic, it inhibits both isoenzymes of 5a-reductase.[85] A study done on 22 patients using zinc gluconate 90 mg/day, yielded eight complete and 14 partial remissions.[85]

Infliximab is one of TNF inhibitors which has shown its efficacy in treatment of HS.[86] The dosage for HS is 5 mg/kg intravenously at 0, 2, and 6 weeks, followed by infusions every 8 weeks.[87-92] A study of Moriarty and colleagues observed that many patients experience flares between infusions. When, the drug was given every 4 weeks, 9 out of 11 patients had sustained improvement in their quality-of-life scores, physician assessments, and visual analog scores with a median of 49.1 months of treatment.[93] The main adverse effects noted with Infliximab, were secondary infections such as upper respiratory infections, and tonsillitis, which were treated with oral antibiotics. One patient developed Hodgkin's lymphoma, currently responding to chemotherapy, 36 months after infliximab treatment, and was shifted to adalimumab.[93]

In comparison with infliximab, adalimumab 40 mg every other week appears to be less impressive and large trials have yielded very modest results. A randomized trial in which 154 adults with Hurley stage III HS were treated with loading and increased doses of adalimumab, showed that 18% of weekly adalimumab recipients versus 4% of placebo recipients achieved a clinical response.[94]

A few reported studies are available for anakinra (an IL-1 receptor antagonist)[95-97] and ustekinumab (an inhibitor of the IL-12/IL-23 pathway), [98,99]

but further studies are needed to explore any meaningful conclusions. Regarding etanercept, there is no convincing evidence of its therapeutic benefit in the treatment of HS. The randomized controlled trials for etanercept failed to show a statistically significant difference between placebo and treatment groups.[100] Further studies, with long term are needed to clarify efficacy and safety of biologics therapy in HS.

Laser and photodynamic therapy

Laser and photodynamic therapy have been used for treatment of HS in few of the reported studies.[101-105] In 2011, Highton et al, used intense pulsed light (IPL) twice-weekly for four weeks. In their prospective trial, 18 patients were enrolled with lesions on both sides of the body. One side was treated, and the other side served as control. A significant improvement was noted but no cure. Therefore, the authors concluded that IPL could be added to other HS treatments in particular for patients keen on avoiding surgery.[101] Long-pulsed Nd:YAG laser (1064 nm) was used in Hurley grade II patients (n = 19) twice a months. Improvement was seen for axillary and groin lesions followed by fibrosis and scarring, noted one and two months after treatment.[103] Two other prospective, randomized trials with long-pulsed Nd:YAG laser achieved a significant improvement over a 3 or 4 months period of treatment.[105,106] Carbon dioxide laser excision and marsupialization was successful in a series of 61 patients with long-standing HS. Recurrences were noted in only two of 185 sites treated.[106] Photodynamic therapy (PDT) with 20% 5-aminolevulinic acid was applied weekly for four weeks (n = 12) with either IPL or blue light. Blue light therapy was more comfortable for patients. Complete remission was obtained in 25% of patients,[102] while earlier reports were unsuccessful.[104] Although laser and photodynamic therapy seem to be attractive in controlling HS, the cure rate is low and the time needed to improvement is longer, i.e., several weeks to several months. Laser and light therapies may be used in patients with limited disease to achieve temporary improvement, but we still do not have enough data about long-term effects. It seems to work better in the axillary region, than in the anogenital area. At present, there is a combination of relative lack of data and relative abundance of treatment schedules and techniques. It is also not clear, if laser/light therapy reduces the risk of fibrosis, lymphedema, or scarring.[107] So, further studies are needed to explain role of laser and photodynamic therapy in treatment of HS.

SURGICAL TREATMENT

The most effective options for treatment of severe HS are the surgical de-roofing or wide excision procedures. But, there is no guarantee that HS will not recur in the previously excised areas. An alternative to the traditional surgical procedures was described by Blok and colleagues.[108] This technique, known as the skin tissue-sparing excision with electrosurgical peeling (STEEP), involves probing and electrosurgically incising the sinus roof with a wire loop tip, similar to the deroofing technique. Affected tissue is then removed in successive tangential electrosurgical transections until the whole area is clear of lesions and fibrotic tissue. The epithelialized sinus floors and subcutaneous fat are spared, and wounds are left to heal by secondary intention. This novel technique spares healthy tissue in severe HS, resulting in shorter healing times and fewer contractures after surgery, which are known

complications of traditional surgical techniques.[108] Assessment the extent of HS lesions by the use of imaging with ultrasound is useful prior to surgical treatment. Ultrasound has been used in a series of 34 patients with HS to provide key anatomic information that is often clinically unavailable. Direct visualization of the sinus tracts in HS could allow the surgeon to calculate the extent of area that would need to be excised.[109]

In cases of contraindication for medical or surgical treatments, cryo insufflation, a modified spray cryotherapy performed by injecting liquid nitrogen through a needle directly into HS tracts, might be of value. This technique has been tried in two patients as monotherapy with successful symptom control and scarring of sinus tracts. Both patients experienced pain and a vagal reaction with nausea, sweating, and weakness. Cryo insufflation can be used as a monotherapy in pregnant women.[110]

APPROACH TO TREATMENT

Selection of therapy in HS should be based upon Hurley's stage (Table 3).[6]

Table 3 Treatment of hidradenitis suppurativa based upon Hurley's stages

Hurley›s stages	Therapy
Stage I	-Clindamycin 1% lotion AM&PM Short courses of antibiotics from 7to10 days: tetracyclines, doxycycline, minocycline, amoxicillin, clavulanic acid, clindamycin. -Zinc gluconate -Intralesional triamcinolone -Mini-unroofing
Stage II	-Medical therapy: Clindamycin+ rifampicin for 3 months, or dapsone Intralesional triamcinolone -Maintenance: tetracyclines or dapsone -Zinc -Scarring/sinus tracts: Surgical therapy; Early mini-unroofing of new lesions Wide unroofing of all active lesions - staged
Stage III	**Medical therapy** Anti-inflammatory Antibiotics - clindamycin rifampin Steroids - prednisone, triamcinolone cyclosporine Biologics - TNFa inhibitors and others infliximab, adalimumab, etanercept, ustekinumab. **Surgical therapy** Aggressive total clearance using unroofing. If above is inadequate, extensive plastic and reconstructive surgery with special nursing and wound care.

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