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Review Article

Hidradenitis suppurativa alias acne inversa- A review

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Abstract Hidradenitis suppurativa (HS), also known as acne inversus, is a challenging, long-term inflammation of the skin that leads to sinuses, thickened scars, and deep-seated nodules and abscesses. These lesions appear most frequently in the intertriginous regions that are laden with apocrine glands. The quality of life of the patients gets adversely impacted due to the persistent nature, accompanying pain, involvement of sensitive areas, malodorous drainage, and scarring. The precise pathogenic pathways are still not well understood, which makes it difficult to develop effective management strategies. This manuscript revisits the epidemiology, aetiopathogenesis, clinical presentation, and current treatment modalities of HS.

Key words
Hidradenitis Suppurativa; Acne Inversa; Scar; Abscess; Pseudocomedones; Sinus Tract; Biologics; Microbiome; Staging.

Introduction

Hidradenitis suppurativa (HS) is a chronic, inflammatory, debilitating skin disorder that typically affects the apocrine gland-rich anatomical areas of the body areas such as axillae, groin, perineum, submammary folds, and other intertriginous areas.[1-2] The condition is multifactorial and causes the hair follicle to occlude, rupture, and eventually leading to the development of deep-seated inflammatory nodules that can further progress to abscesses, sinus tracts, and irreversible thick fibrotic scars.[3] HS remains widely unrecognized with inconsistent treatment protocols, and there is generally a significant diagnostic delay.[4-5] The chronic nature of HS and its recurrent relapses have adverse impact on the patient's quality of life, negatively affecting the social, occupational, emotional and psychological facets.[6-7]

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Methods and Materials

A comprehensive literature review was carried out using the keywords "hidradenitis suppurativa," "Verneuil's disease," and "acne inversa" in electronic databases like PubMed, SciSpace, ResearchGate, SEMANTIC SCHOLAR, and Scopus. Individual keywords were used in the search together with a Boolean logic (AND) combination. Studies that were published in the English language and that were carried out between the years 2000 and 2023 were selected. References from earlier states were only used if they had substantial historical value.

Brief historical background

A surgeon with a practice in Paris, Velpeau, identified and described HS for the first time in his publications between 1833 and 1839. In 1854, one of his contemporaries, named Verneuil, described HS as 'hidrosadénite phlegmoneuse'. This is how the term "Verneuil's

disease" came into being to identify HS.[8] Schiefferdecker proposed a pathogenic connection between HS and apocrine sweat glands in 1922. The phrase "follicular occlusion triad" was first used by Pillsbury *et al*. in 1956 to group HS with perifolliculitis capitis abscendens et suffodiens ("dissecting cellulitis of the scalp") and acne conglobata. In 1975, a pilonidal cyst was added as an additional entity to this triad by Plewig and Kligman, forming the follicular occlusion tetrad.[8] In 1989, Plewig and Steger changed the name of HS to "acne inversa", indicating that the disease shares histopathological and clinical characteristics with acne vulgaris, but with the difference that it affects intertriginous localizations (inverse areas) rather than the typical acne-affected areas. Numerous recent studies have concurred with this conclusion, and it has been proposed that the term "hidradenitis suppurativa" for this condition be replaced with "acne inversa".[9–11] However, in 2017, Chen and Plewig proposed renaming the condition "dissecting terminal hair folliculitis" in light of the developments in clinical, histological, and pathophysiological findings.[12]

Epidemiology

There is a dearth of information from developing and underdeveloped nations, despite the fact that the epidemiology of HS has been widely researched in the western population. The prevalence of HS varies significantly depending on demographics, data collection techniques, and data sources.[4] The estimated global prevalence is 0.00033–4.1%, with the western nations like the USA, UK, Denmark, and Norway having a significantly greater prevalence of 0.7–1.2%, with a surge in recent years, than the non-western nations like Japan (0.03–0.40%)[13] and Korea (0.06%).[14] This disparity could be caused by racial or ethnic differences. However, it could also be a result of underreporting of minor illnesses, incorrect classification, or under diagnosis. According to US data, African Americans (0.3%) have a higher prevalence of HS than the white population (0.09%), though biracial people have an intermediate prevalence rate of 0.22%.[15] Studies have found an incidence of HS of more than 2.0–3.8 times in women. The age of onset is typically after puberty, peaking between the ages of 30 and 39, and HS before puberty is uncommon.[16-18]

Etiopathogenesis

The precise etiopathogenesis of HS is still not clearly known. As illustrated in **Figure 1**, multiple research projects in recent years have proposed that the disease is complex and is caused by a variety of endogenous and external variables.[19]

Genetic factors

Although various genetic loci have been found that may be connected to HS, no causal genes have been identified with certainty to date. There is evidence that 34% of the cases of HS have the disease in first-degree relatives, and that in both genders, vertical transmission across several generations is recorded, pointing towards autosomal dominant inheritance.[11] A genome-wide scan was conducted by Gao *et al*.[21] on a family of Chinese origin in an effort to identify

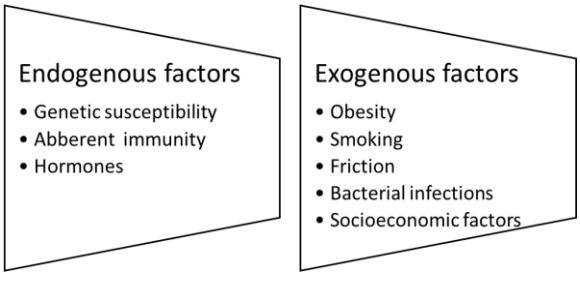

Figure 1 Factors linked to the pathogenesis of hidradenitis suppurativa.

the responsible gene's chromosomal position, and a 76 Mb locus was detected at chromosomes 1p21.1–1q25.3 flanked by D1S248 and D1S2711. Mutations have been identified in the genes of the gamma-secretase enzyme, and when gamma-secretase function is impaired in mice, features similar to those of HS have been found to occur, including keratinization or atrophy of follicles, deficiency of sebaceous glands, hyperplastic changes, and cystic degeneration in the epidermis.[22–23]

Aberrant immune response

The chronicity of HS and its association with disorders like sterile arthritis and Crohn's disease have led to probes into the role of aberrant immunity **(Figure 2)**, and the levels of multiple cytokines have been found to be elevated in HS lesions, including interleukin (IL)-1, tumor necrosis factor (TNF)-alpha, interleukin (IL)-10, CXCL9, an interferon-induced monokine, interleukin (IL)-11, a chemoattractant of B lymphocytes, and interleukin (IL)-17A.[24] The notion of auto-inflammation, which can be explained by improper regulation of the gamma-secretase/ Notch pathway-25, was first put forth by Melnik and Plewig in 2013.[25] Appropriate Notch signaling plays a pivotal role in the maintenance of the inner and outer root sheaths of the hair follicle and skin appendages, and defects in this pathway can change hair follicles into keratin-filled epidermal cysts with disturbed apocrine gland function. Additionally, innate immunity that is mediated by toll-like receptors (TLR) is stimulated, promoting and maintaining an ongoing inflammatory response.[26] This hypothesis has found support in the reports of elevated levels of several pro-inflammatory cytokines, most notably TNF-alpha, IL-1, and IL-17, in HS lesions.[24] The most prevalent cells in HS lesions are macrophages and dendritic cells (DCs), and altered TLR signalling on these cells results in increased levels of these

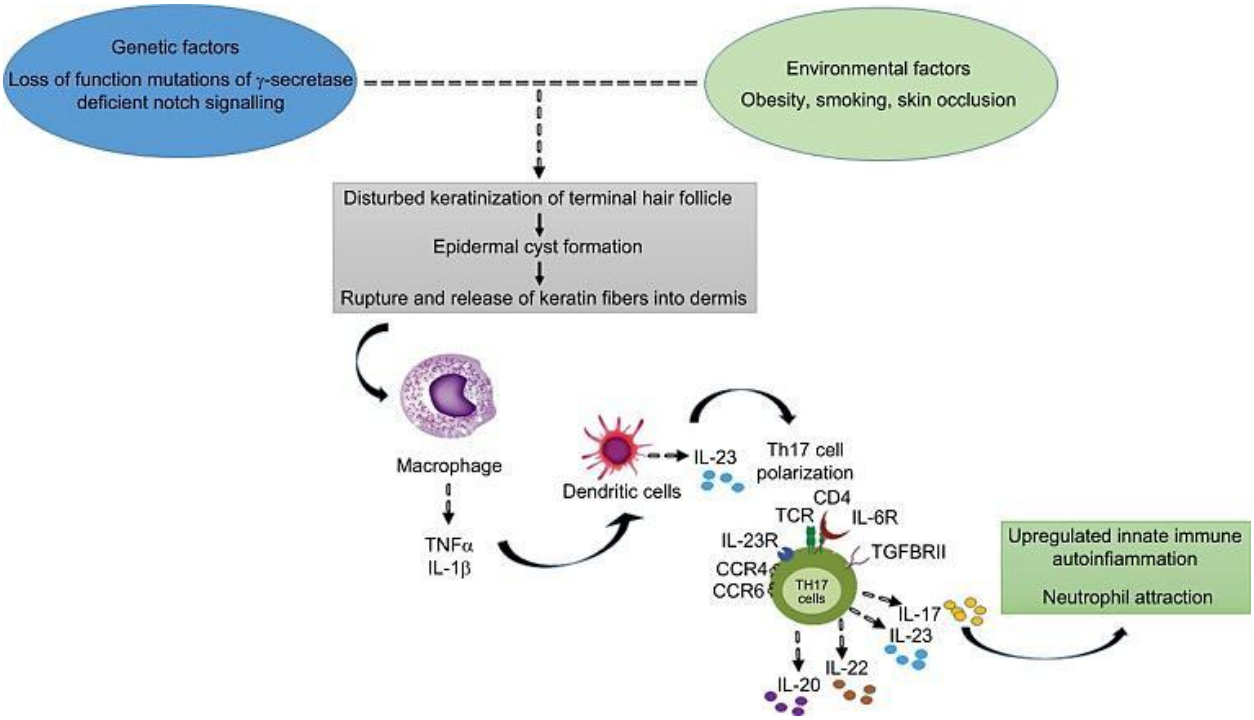

Figure 2 A schematic overview of pathophysiology of Hidradenitis suppurativa:
Source: 'Clinical, Cosmetic and Investigational Dermatology 2017:10 ;105-115' Originally published by and used with permission from Dove Medical Press Ltd. DOI: https://doi.org/10.2147/CCID.S111019

cytokines, activating DCs, which then secrete IL-23, promoting the polarization of Th17 cells, and interleukin-17-producing T helper cells have been shown to spread through the dermis in chronic HS lesions.[27] Also, it has been discovered that the activity of TNF-alpha has a positive association with the severity of the disease and overexpression of TNF- has been reported in the skin affected by HS.[28]

Hormonal Influences

A link between hormones and HS appears conceivable, since the disease generally manifests after puberty and tends to decrease in prevalence after menopause. When androgens are dominant yet similar to acne vulgaris during precocious puberty, which is common in paediatric cases of HS, the effect is thought to be mediated by end-organ sensitivity rather than an increase in the quantity of serum androgens.[23]

Smoking

According to studies, smokers make up between 70 and 89 percent of HS patients, and their clinical conditions are typically more severe than those of non-smokers, thereby indicating that tobacco may be a possible trigger.[29–30] Nicotine has been demonstrated to promote various steps in inflammation, including degranulation of mast cells and improvement in the survival and chemotaxis of neutrophils. Apart from that, nicotine has been demonstrated to cause follicular plugging and hyperplasia of the epidermis in experimental setups.[19]

Obesity

About 45–80% of HS patients are overweight or obese (BMI> 30 kg/m^2), and this set of patients has been found to exhibit a more severe clinical manifestation of disease than the normal-weight cohort.[2] The following are some of the theories that have been advanced on a potential mechanism by which obesity could play a role in the development of HS,[2,31] among others:

1. greater mechanical friction via skin-to-skin contact creates microtears in hair follicles and keratin hydration in sweat glands. As a result, the follicular opening's diameter decreases, which obstructs pores.
2. retention of sweat because of overlapping skin folds, which causes maceration and irritation.
3. the warm, humid environment that exists in the skin folds has a favourable effect on bacterial growth.
4. elevated blood levels of pro-inflammatory cytokines

altered hormonal metabolism, which results in an excess of androgens that may cause follicular clogging and a coarsening of the hair shaft.

Bacterial infection

Bacterial involvement in HS is still a matter of dispute. There is a possibility that bacteria may have some role in the maintenance of the chronic inflammatory process, but HS lesions typically produce sterile bacterial cultures, indicating thereby that the bacterial colonization may only be a secondary phenomenon.[32–33]

External factors

Several external causes, such as shaving, chemical depilatories, deodorants, and talc, have the potential to cause chemical irritation that closes pores or changes the normal flora of the skin. Moreover, the use of razors may facilitate bacterial entry by transection of the follicular infundibulum. Nevertheless, shaving, applying deodorant, and using talcum powder did not reveal any appreciable changes in the matched case-control study by Morgan and Leicester.[34]

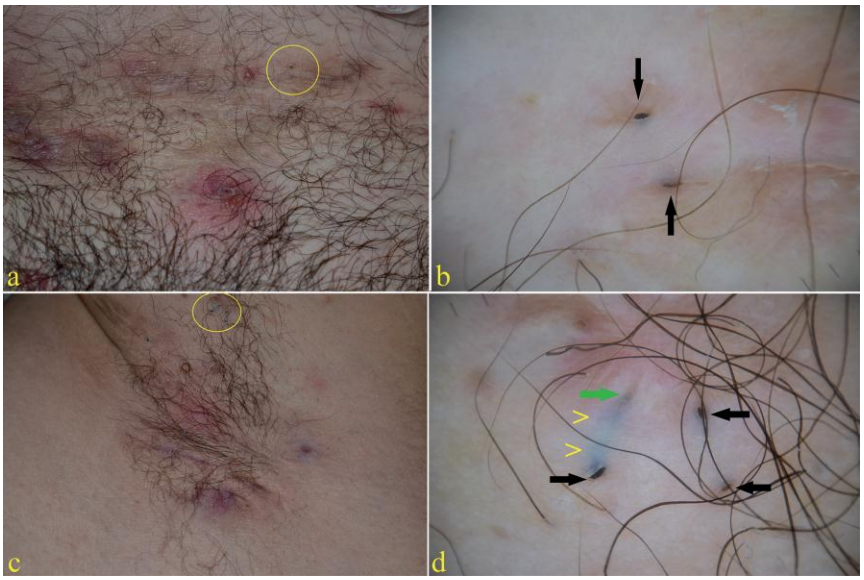

Figure 3 Hidradenitis suppurativa: Clinical and dermoscopic findings. Pseudocomedones (yellow circles) are seen in (a & c). Dermoscopy under polarized light (b and d), display superficial (black arrows) or deep (green arrow) keratin accumulations, and embedded in pale cicatrix or connected via a bluish tunnel (arrowheads).

Source: Acta Derm Venereol. 2017 Jun 9;97(6):763-764." Originally published by and used with permission from Acta Dermato-Venereologica ". DOI: 10.2340/00015555-2601.

Even though shaving was regarded as harmful by 75% of participating HS cases in a recent survey of deodorant and antiperspirant use and hair removal habits by Cutler *et al.*;[35] laser hair removal was rated as helpful by roughly 86% of respondents. Wearing tight clothing has been found to induce mechanical friction and thereby increase the frequency of inflammatory lesions; conversely, wearing loose clothing alleviates the symptoms of HS.[19]

Socioeconomic status

There isn't enough data to prove that people from lower socioeconomic strata are more likely to get HS, despite the widespread impression that this is the case. Socioeconomic status (SES) is a significant factor in determining health outcomes, and numerous studies have attempted to assess SES in HS patients. In Dutch cohort research by Deckers *et al*. that included roughly 1018 HS patients, lower SES was found to be considerably more common in the HS patients than in an age- and sex-matched reference group. However, significant confounders, including obesity, smoking habits, and race, were not taken into consideration in this study, which may have an impact both on the outcome of low SES and HS.[36] In their analysis, Wertenteil *et al.* were unable to determine a directionality between HS and SES; however, they hypothesized that the moderate link between HS and low SES may be caused by the quality-of-life impacts of HS (namely, symptoms like pain and foul-smelling discharge) and that low SES might not actually play a role in the development of HS.[37]

Clinical features

HS has an insidious onset, and up to 50% of HS patients describe a prodromal syndrome, which manifests itself 12 to 48 hours before a lesion appears and includes minor discomfort, erythema, burning, stinging, itching, and hyperhidrosis in the affected area. Unless there is a secondary infection or the condition is advanced, individuals usually appear healthy and afebrile at the time of presentation.[1,7] Painful, deep-seated nodules that are typically 0.5 to 2 cm in size and that last for days or even months are characterized as primary lesions. These lesions are frequently mistaken for boils or furuncles, but unlike furuncles, which typically respond quickly to antibiotics or drainage, HS lesions are deeply rooted, expand,

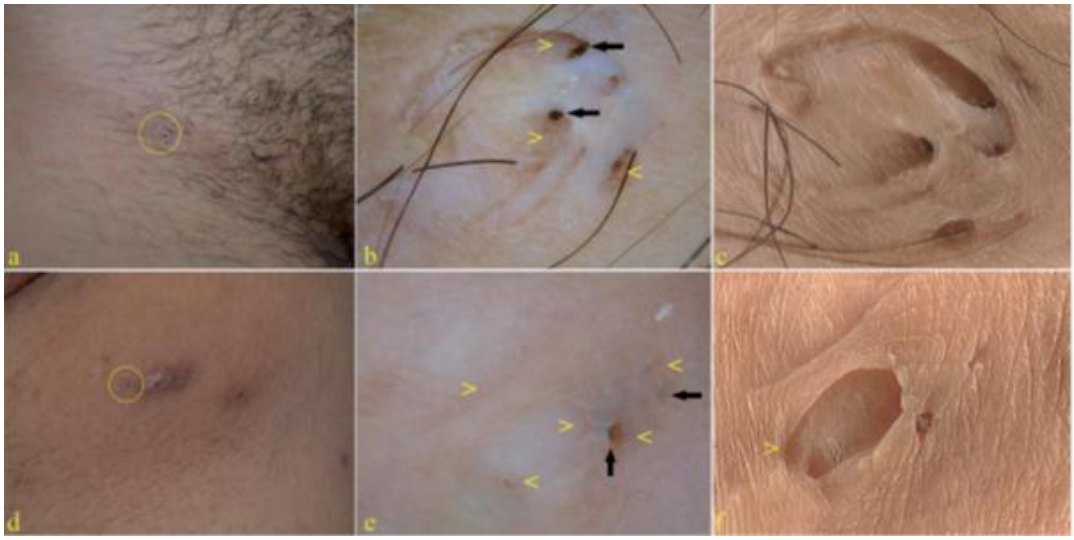

Figure 4 Dermoscopic view of hidradenitis suppurativa (a, d) Double-ended pseudocomedones on naked eye examination. Polarized light dermoscopy revealing openings/hollows of different shapes and dimensions (arrowheads) and keratin accumulations (black arrows) embedded in a cicatricial tissue (b, e). Incident light dermoscopy (c, f) reveals circinate (c) & bridging scars (f).
Source: Acta Derm Venereol. 2017 Jun 9;97(6):763-764." Originally published by and used with permission from Acta Dermato-Venereologica ". DOI: 10.2340/00015555-2601.

and coalesce to form sizable, painful abscesses that may ulcerate or rupture, releasing foul-smelling pus. Recurrent or persistent HS leads to the creation of double-ended comedones **(Figures 3,4)**, intercommunicating sinus tracts, and scarring **(Figures 5,6)**.

The intertriginous skin is largely affected, typically with a bilateral distribution, and includes the axillae, perineum, inframammary folds, and inguinal areas **(Figures 5,6)**. If the condition progresses, the waist, the nape of the neck, the retro-auricular region, the trunk, and other places vulnerable to repetitive mechanical stress may also be affected.

Since no conclusive biological or pathological tests are available for this purpose, diagnosis is typically reached through extensive clinical evaluation. Unless there is a suspicion of malignant transformation or the diagnosis is ambiguous, a histopathological analysis is not necessary. Imaging is not usually done, but if surgical options are being considered, ultrasound or even MRI may be a useful tool, especially in severe perianal disease, to assess the extent of the sinus tracts. Furthermore, unless a secondary infection or a separate diagnosis is suspected as the cause, bacterial cultures are not very helpful.[1,7]

Differential diagnosis

Many skin conditions can mimic HS,[38–39] and

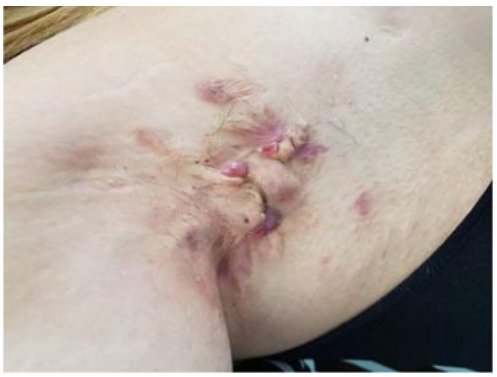

Figure 5 Hidradenitis suppurativa (axilla): clinical aspects.
Source: 'Clinical, Cosmetic and Investigational Dermatology 2017:10 ;105-115' Originally published by and used with permission from Dove Medical Press Ltd. DOI: https://doi.org/10.2147/CCID.S111019.

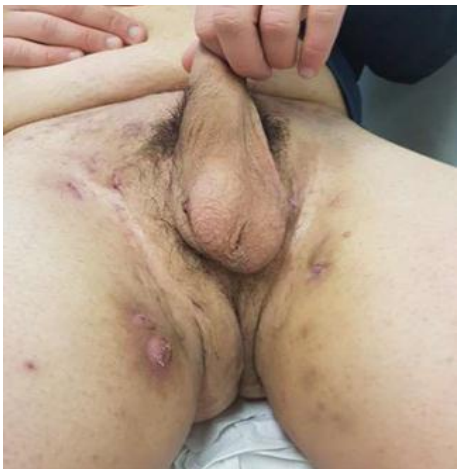

Figure 6 Hidradenitis suppurativa (perineum): clinical aspects.
Source: 'Clinical, Cosmetic and Investigational Dermatology 2017:10 ;105-115' Originally published by and used with permission from Dove Medical Press Ltd.
DOI: https://doi.org/10.2147/CCID.S111019

Differential Diagnosis	Follicular pyoderma
	Granuloma inguinale
	Nodulo-ulcerative syphilis
	Lymphogranuloma venereum
	Actinomycosis
	Granuloma inguinale
	Lymphogranuloma venereum
	Erysipelas
	Tuberculosis
	Acne vulgaris
	Epidermoid / dermoid cyst
	Pilonidal disease
	Bartholin cysts
	Crohn's disease of the perineum

Figure 7 Differential diagnoses of HS.

the following differential diagnoses are some of them.

Diagnostic Delays

The majority of patients experience years of delayed or incorrect diagnosis because HS mimics several disorders , and primary healthcare practitioners are generally not aware of it.[40] When HS symptoms first appear, it takes roughly 2.3 years before a patient contacts a physician, and it took approximately 7.2 years for the condition to be correctly diagnosed.[41] Until a final diagnosis is reached, the majority of patients consult four to five physicians over the course of more than 17 clinic appointments.[42] Zimman *et al.* did a retrospective investigation in Buenos Aires, Argentina's University Teaching Hospital. The interval until diagnosis was quite variable, sometimes occurring at the first visit and stretching as long as 142 months and 21 visits.[43] The negative effects of delayed and incorrect diagnoses include:

i. Disease progression including pain, aesthetic deformity, and reduced quality of life;
ii. Inappropriate utilization of healthcare facilities.

Classification and severity assessment

The severity of the HS disease has been assessed using a variety of rating systems. When used in clinical practice, each of them has advantages and drawbacks, but none has yet been acknowledged as the gold standard.[44]

Hurley staging system

This categorization divides HS into three stages[45] and is by far the most popular and straightforward one as shown in **Figure 8**.

The classification lacks quantitative information, which is a drawback because it makes it difficult to track the effectiveness of therapeutic interventions in clinical trials.

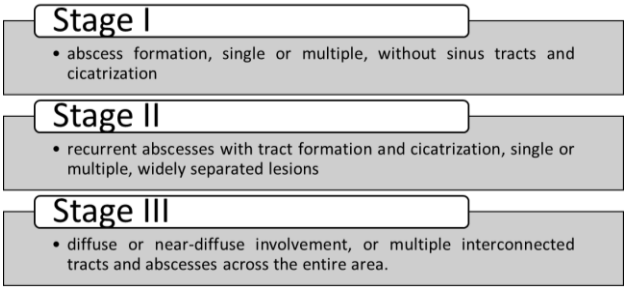

Figure 8 Hurley staging system for HS.

Modified Sartorius score (MSS)

Based on the number of distinct nodules and fistulas across all of the seven anatomical regions, this more thorough and dynamic classification approach can be used. This is the first disease-specific tool for dynamic monitoring of the clinical severity of the disease and was created by Sartorius *et al.* in 2003[46] and later improved in 2009.[47] Within each anatomical region, the longest distance between two lesions of the same type is measured using this technique, and after that, specified weights are assigned to specific kinds of lesion features. The approach, however, has not been judged ideal for evaluating inflammatory symptoms in clinical practice or trials because it is time-consuming and at times difficult to interpret.[48]

Hidradenitis Suppurativa -Physician's Global Assessment (HS-PGA)

The HS-PGA is a frequently used tool to evaluate clinical progress in clinical trials of pharmacological therapy because of its simplicity and simple interface.[49] This tool determines the number of abscesses, fistulas, and nodules in all the skin regions and then, as per the severity, assigns six stages from 1 to 6 (from stage 1: clear with no nodular lesions to stage 6: high severity with greater than five abscesses or draining fistulas).

The main drawback of the measure is that patients may experience clinically significant improvement without a corresponding drop in their HS-PGA score since those in the most severe category may display notable heterogeneity.[49]

Hidradenitis Suppurativa Severity Index (HSSI)

HSSI incorporates categorical objective parameters with categorical subjective parameters: body surface area (BSA) involved, the total number of skin lesions, the severity of pain as determined through a visual analogue scale (VAS), and drainage as quantified by the number of dressing changes. Scores of 13 or higher indicate severe disease, whereas values between 0 and 7 indicate mild disease. Scores between 8 and 12 indicate intermediate disease.[3] This tool's inter-rater reliability is subpar, and Goldfarb in 2020 has proposed a revised system termed Hidradenitis Suppurativa Area and Severity Index Revised (HASI-R).[50]

Severity and Area Score for Hidradenitis (SASH)

Kirby *et al.* established the Severity and Area Score for Hidradenitis (SASH) in 2020 as a valid and reliable HS outcome measure that may encompass a variety of patients by analysing body surface area.[51] In their study, 10 healthcare professionals contributed to the concept elicitation, and the results showed great intra-rater reliability of 0.98 and high inter-rater reliability of 0.75 and 0.76 when body surface was graded on an ordinal scale. The SASH score additionally displayed convergence validity using the available techniques.

Refinement Hurley classification: the 3-step algorithm

The Hurley staging was improved upon in 2017 by the Netherlands HS expert group, which is a component of the European Hidradenitis Suppurativa Foundation.[52] They proposed a three-step methodology that involved determining whether sinus tracts were present, gauging the extent of the inflammation, and gauging the severity of the various HS phenotypes before suggesting an ideal course of action, as illustrated in **Figure 9**. This classification subdivides the Hurley I and II

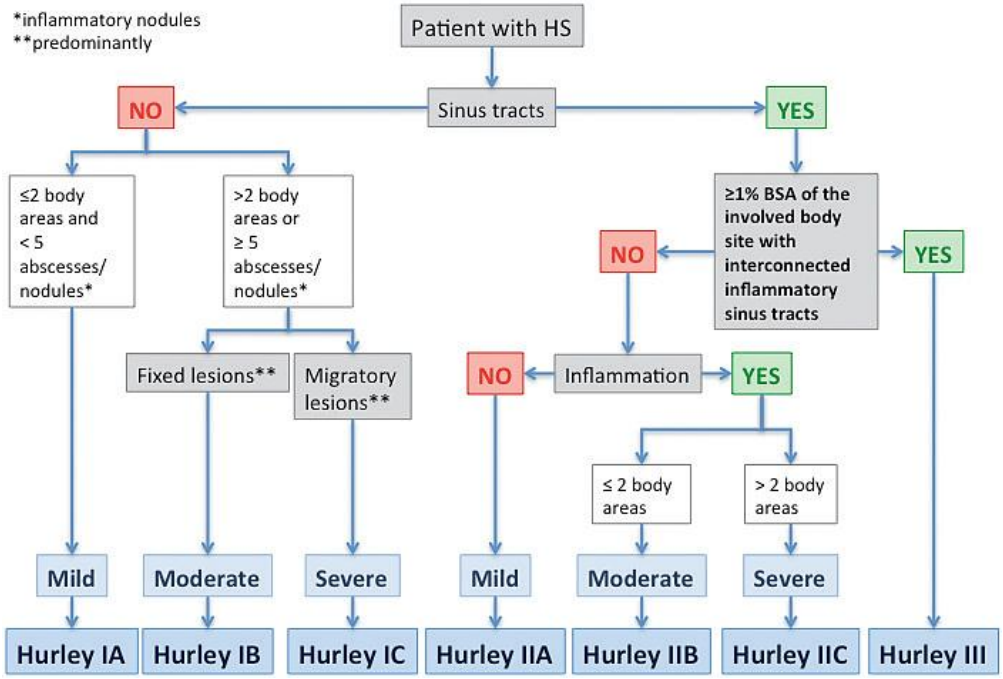

Figure. 9 Refined Hurley classification with a the 3-step algorithm.
Source: Acta Derm Venereol. 2017 Mar 10;97(3):412-413. Originally published by and used with permission from Acta Dermato-Venereologica". DOI: 10.2340/00015555-2513.

stages.

In 2019, Rondags *et al*. looked at the reliability of a patient self-assessment questionnaire that corresponded to the items covered in the updated Hurley classification, and they discovered that it was reliable with the potential for extended clinical application.[53]

Co morbidities/ Systemic associations

Recent studies have revealed that HS is a systemic condition with a heavy burden of comorbidities.[54–56] The most frequently seen comorbidities[57–59] include inflammatory bowel disease (IBD), cardiovascular disease, mental illnesses, obesity, and metabolic syndrome (MetS) . Overweight/ obesity affects 45–80% of HS patients, and obesity has been linked to a worsening of the condition.[2] It has been postulated that macrophages in visceral fat may release larger quantities of pro-inflammatory cytokines, such as TNF- alpha and IL-1, which could therefore worsen HS disease activity. Some recent investigations have demonstrated that obese patients with HS show dysregulated adipokine levels.[39,60]

Metabolic syndrome

Metabolic syndrome and its components have been discovered to be more common in HS patients. A hospital-based case-control study with 80 HS patients and 100 controls with matched age and gender was conducted by Sabat *et al.*[61] It was discovered that HS patients had significantly higher rates of central obesity (odds ratio 5.88), hypertriglyceridemia (odds ratio 2.24), hypo-HDL-cholesterolemia (odds ratio 4.56), and hyperglycaemia (odds ratio 4.09) than did controls. In a retrospective assessment, Gold *et al.*[58] discovered that patients with HS had a metabolic syndrome prevalence of 50.6%, which was substantially higher than the control group's prevalence of 30.2% (P=0.001).

Cardiovascular disorders

The risk of unfavourable cardiovascular (CV) outcomes such as myocardial infarction (MI), stroke, CV-associated death, major adverse CV events (MACEs), and all-cause mortality has been reported to be significantly elevated in individuals with hidradenitis suppurativa. Patients with HS had a greater probability of dying from a CV-related cause than did controls and people with severe psoriasis.[62] According to Reddy *et al*.;[63] patients with HS have an elevated risk of developing MI and cerebrovascular accidents (CVA), and this raises the possibility that early management of their modifiable cardiovascular risk factors may be necessary. However, a recent study by Kridin *et al.*[64] indicated that patients with HS have an elevated risk of MI but not CVA or peripheral vascular disease (PVD). They stressed that awareness of these epidemiological findings is important for clinicians managing patients with HS.

Psychiatric Disorders

It has been found that HS significantly affects patients' mental well-being. They are more prone to mental comorbidities, lower levels of self-esteem, and higher levels of emotional brittleness and rage.[65–67] In a cross-sectional study comprising 9,619 patients, Shavit *et al.*[68] discovered that HS patients had greater rates of anxiety (3.9%) and depression (5.9%) than controls. In a different study by Kurek *et al*.;[69] 38.6% of HS patients and 2.4% of the control subjects experienced depression. According to Tzur Bitan *et al*.;[70] schizophrenia is ten times more common among HS patients. The same researchers' later analysis[71] found HS to be separately and significantly associated with bipolar disorders (OR 2.12, 95% CI 1.21-3.27, p 0.01). It was hence emphasized that screening for severe mental illness be carried out during the assessment of patients with HS, as the outcomes of treatment may be affected.

Gastrointestinal disorders

It has been observed that gastrointestinal conditions affect HS patients more frequently. Deckers *et al*.[59] discovered that although there is no correlation with any specific HS subtype, inflammatory bowel disease (IBD) is 4–8 times more common in HS patients when compared to the general population. According to Yadav *et al*.;[72] patients with IBD have an incidence rate ratio of 8.9, implying that they have a nine-times higher chance of developing HS than the general population. The most typical symptom of both HS and Crohn disease is perianal disease, and according to a study by Kamal *et al*.;[73] most ulcerative colitis sufferers who also got HS did so after having a colectomy, in the context of pouchitis. Pyoderma gangrenosum (PG), which is usually linked to IBD, and HS have also been correlated.[74] In a recently released two-sample bidirectional Mendelian randomization study, Bao *et al*.[75] demonstrated that whereas IBD and its subtypes have a causal relationship with HS, HS does not affect IBD. To better understand the pathophysiology of the causal connection between IBD and HS, further research was suggested, and it has been proposed that gut-skin axis interactions may aid in understanding this connection.

Rheumatological disorders

HS patients have a significant prevalence of musculoskeletal symptoms (28.8%), evidence of arthritis, enthesitis, or inflammatory back pain (6.9%), and 3.7% have the diagnosis of spondyloarthropathy, according to an observational study by Richette *et al*.[76] Joint discomfort was discovered to typically begin 3.6 years (on average) before HS in 90% of instances. There are significant clinical and

pathophysiological similarities between HS and spondyloarthritis (SpA), a chronic inflammatory rheumatic illness, including the relationship with inflammatory bowel disease and higher cytokine (IL-17 and TNF-alpha) levels.[77] Rheumatologic joint diseases, specifically spondyloarthropathies, synovitis, arthritis, hyperostosis, and osteitis have been linked, according to Miller *et al*.[57]

Malignant Transformation

The management of HS-related lesions might be challenging since they occasionally (1% to 3.1%) develop into squamous cell carcinoma (Marjolin's).[78-81] Due to a combination of ongoing HS inflammation, impaired cellular immunity, and the presence of the human papillomavirus, the risk seems to be greater in the gluteal, perianal, and perineal regions. As a result, when ulcerative lesions, persistent wounds, nodules, or ulcerative nodules appear and do not respond to standard immunosuppressive or antibiotic treatments used in HS patients, healthcare providers should increase their index of suspicion for this malignancy and drop their biopsy threshold.[82-83]

Impact on Quality of Life

Patients usually have unpleasant symptoms such as discomfort, pruritus, malodor, and suppuration, which can have a serious detrimental effect on their quality of life (QOL).[84–87] The unpleasant discharge encountered by patients with HS has a significant psychosocial impact and is usually cited as a source of humiliation, low self-esteem, social stigma, and interpersonal interaction difficulties, according to Alavi *et al*.[88] who evaluated QOL using the Dermatology Life Quality Index (DLQI) and the Skindex-29 instruments. They further emphasized that Skindex, rather than DLQI, has the potential to capture that effect. In another study, Kontzias *et al*.[89] hypothesized that marriage might increase social support and quality of life (QOL). Kurek *et al*., however, have demonstrated that HS patients, particularly females, suffer from sexual dysfunction and distress.[61]

Role of Microbiome

The gut-brain-skin axis has garnered a lot of attention in recent years as evidence of a potential involvement of the microbiome in the pathophysiology of HS.[90–92] Most investigations have shown that HS lesions contain lower levels of skin commensal species such as Cutibacterium and higher levels of Porphyromonas, Peptoniphilus, and Prevotella spp. Although the precise role of the blood and gut microbiomes in HS is still not entirely understood, it has been postulated that the main connection with the intestine is based on the enhanced probability of acquiring Crohn's disease and ulcerative colitis.[93] Since probiotics, dietary changes, and ways of life all seem to affect the microbiome, this sector may offer a promising method as adjuvant therapy. However, more study is needed in this field.

Management

Treatment choices are implemented for HS based on the severity of the condition and each individual's subjective impact, which makes managing HS frequently challenging. In clinical practice, which is based on the Hurley staging system, topical treatments are utilized as first-line therapy for less invasive disease, whereas systemic antibiotics, biologics, surgery, and light therapy are used for more severe disease.[60, 94–95]

Medical management

The medical treatment options for HS are depicted in **Figure 10**, and the modalities are

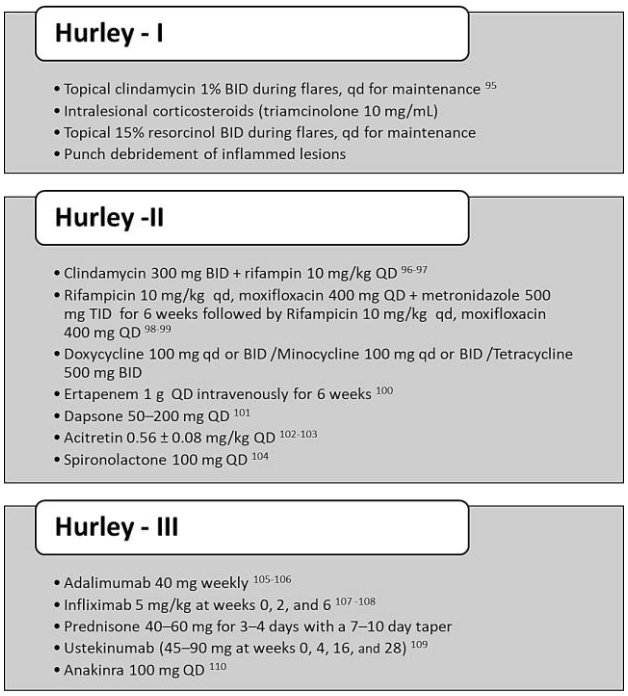

Figure 10 Medical management modalities of HS.

adopted as per the severity determined by staging systems.

Emerging medical therapies

Recently, additional therapies for HS lesions have included laser and pulsed light treatment.[111–112] These procedures aim to eradicate the large, persistent lesions and minimize the frequency of uncomfortable flare-ups by reducing the number of sebaceous glands, hair follicles, and microbes in the affected areas.[113] According to Hamzavi *et al.*;[113] the sort of laser or pulse light that should be used varies depending on the severity of the lesions. In contrast to patients with advanced Hurley stage II or III, who display better response to carbon dioxide laser vaporization and surgical excision of sinus tracts, patients with Hurley stage I and stage II benefited from decrease in hair follicles and bacterial load with Nd: YAG laser and photodynamic therapy.[113] Mikkelsen *et al*. showed that 91% of the treated patients would suggest laser surgery to other HS patients, and they also reported considerable improvement.[114] After medical care for intramammary HS, residual cribriform scarring was effectively removed by Krakowski *et al*.[115] with a fractionated 10,600-nm carbon dioxide laser.

Metformin has been tried in some recent studies and has emerged as a potential adjuvant therapy for HS. Although the precise mode of action is unknown, it has been suggested that metformin might be working in HS through an antiandrogenic mechanism. In a 2013 pilot study, Verdolini *et al*.[116] showed that metformin is an effective substitute for high-dose, long-term antibiotics. In a study by Jennings *et al*;[117] promising clinical responses were seen in 68% cases subjectively. Moussa *et al*.[118] found that for some paediatric patients, metformin as an additional medication may enhance control of HS with few adverse effects.

Since zinc salts are anti-inflammatory and antioxidant, they may be able to slow the progression of HS and minimize the frequency of flare-ups. According to Brocard *et al*;[119] oral therapy of 90 mg of zinc gluconate per day caused a significant improvement in the majority of patients with Hurley stage I or II HS and a full remission in about a quarter. After the doses were decreased to fewer than 60 mg per day, patients did, however, have a tendency to relapse.

Surgical management

A final, effective therapeutic option for patients with extensive and recurrent HS lesions (Stage II or III disease) is surgery. The literature mentions a variety of surgical techniques, each with advantages and disadvantages, and the strategy should be customized for the specific patient.[94,120-124] The options include:

i. Incision of abscesses to drain pus and temporarily attain relief from discomfort.

ii. Localized annihilation using photodynamic treatment, electrosurgery, cryosurgery, and cryoinfusion.
iii. Extensive unroofing, debridement and laying open of the sinus tracts to allow healing by secondary intention.[122]
iv. Complete surgical excision past all clinically visible margins followed by primary closure, skin grafts, or local flaps for repair. Although this method is a successful, permanent treatment, it might not be favourable cosmetically.

Menderes *et al*.[123] after a prospective study, found that less invasive surgical approaches had little or no effect, especially in the axillary region and perineum, and the only viable surgical option for HS is wide surgical excision with reconstruction. Stumpfe *et al*.[125] in 2022 reported the successful treatment of fifteen cases with vacuum-assisted wound therapy in combination with radical excision and reconstruction with skin grafts or fasciocutaneous flaps as a multi-stage procedure. If there are no perifocal manifestations of infection after debridement, Elboraey *et al*.[126] recommend using propeller flaps for either immediate or delayed reconstruction following radical excision of axillary hidradenitis suppurativa. Rieger *et al*.[127] propose the medial thigh lift, an otherwise aesthetic surgical procedure, for immediate reconstruction after radical excision of limited inguinal HS if there are no clinical features of infection. In a recent study published in 2023, Gierek *et al*.[128] proposed that split-thickness skin grafts, co-grafted ADM, and platelet-rich plasma (PRP) injection into skin flaps are all feasible surgical alternatives for treating hidradenitis suppurativa.

Conclusion

Hidradenitis suppurativa (HS) is a persistent, progressive inflammatory condition of follicular occlusion with onset during puberty that causes inflammatory lumps, sinus tracts, and tunneling in apocrine-gland-rich inverse regions of the body. The disease's progression has a negative impact on quality of life and can cause keloids, contractures, scars, and potentially malignant transformations. A multidisciplinary approach is essential for achieving the best possible illness control because management can be difficult. The early stages can be controlled with a variety of medicinal treatments, but surgical intervention is almost certainly needed for the severe stages. Delayed diagnosis is frequently encountered, and hence there is a need to raise awareness of the disease.

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References

1. Goldburg SR, Strober BE, Payette MJ. Hidradenitis suppurativa: Epidemiology, clinical presentation, and pathogenesis. J Am Acad Dermatol. 2020 May;82(5):1045-1058.
2. Anduquia-Garay F, Rodríguez-Gutiérrez MM, Poveda-Castillo IT, Valdes-Moreno PL, Agudelo-Rios DA, Benavides-Moreno JS, Lozada-Martínez ID, Bolaño-Romero MP, Borraez-Segura B, Rahman S. Hidradenitis suppurativa: Basic considerations for its approach: A narrative review. Ann Med Surg (Lond). 2021 Aug 5;68:102679.
3. Napolitano M, Megna M, Timoshchuk EA, Patruno C, Balato N, Fabbrocini G, Monfrecola G. Hidradenitis suppurativa: from pathogenesis to diagnosis and treatment. Clin Cosmet Investig Dermatol. 2017 Apr 19;10:105-115.
4. Jemec GB, Kimball AB. Hidradenitis suppurativa: Epidemiology and scope of the

problem. J Am Acad Dermatol. 2015 Nov;73(5 Suppl 1):S4-7.
5. Dufour DN, Emtestam L, Jemec GB: Hidradenitis suppurativa: a common and burdensome, yet under-recognised, inflammatory skin disease. Post Grad Med J 2014;90:216-221.
6. Włodarek K, Głowaczewska A, Matusiak Ł, Szepietowski JC. Psychosocial burden of Hidradenitis Suppurativa patients' partners. J Eur Acad Dermatol Venereol. 2020 Aug;34(8):1822-1827.
7. Preda-Naumescu A, Ahmed HN, Mayo TT, Yusuf N. Hidradenitis suppurativa: pathogenesis, clinical presentation, epidemiology, and comorbid associations. Int J Dermatol. 2021 Nov;60(11):e449-e458.
8. Fimmel S, Zouboulis CC. Comorbidities of hidradenitis suppurativa (acne inversa). Dermatoendocrinol. 2010 Jan;2(1):9-16.
9. Bazex J, Bayle P, San B. Hidradenitis suppurativa is acne inversa. Int J Dermatol. 2007 Mar;46(3):330.
10. Sellheyer K, Krahl D. "Hidradenitis suppurativa" is acne inversa! An appeal to (finally) abandon a misnomer. Int J Dermatol. 2005 Jul;44(7):535-40.
11. von Laffert M, Stadie V, Wohlrab J, Marsch WC. Hidradenitis suppurativa/acne inversa: bilocated epithelial hyperplasia with very different sequelae. Br J Dermatol. 2011 Feb;164(2):367-71.
12. Chen W, Plewig G. Should hidradenitis suppurativa/acne inversa best be renamed as "dissecting terminal hair folliculitis"? Exp Dermatol. 2017 Jun;26(6):544-547.
13. Kurokawa I, Hayashi N; Japan Acne Research Society. Questionnaire surveillance of hidradenitis suppurativa in Japan. J Dermatol. 2015 Jul;42(7):747-9.
14. Lee JH, Kwon HS, Jung HM, Kim GM, Bae JM. Prevalence and comorbidities associated with hidradenitis suppurativa in Korea: a nationwide population-based study. J Eur Acad Dermatol Venereol. 2018 Oct;32(10):1784-1790.
15. Garg A, Kirby JS, Lavian J, Lin G, Strunk A. Sex- and Age-Adjusted Population Analysis of Prevalence Estimates for Hidradenitis Suppurativa in the United States. JAMA Dermatol. 2017 Aug 1;153(8):760-764.
16. Garg A, Lavian J, Lin G, Strunk A, Alloo A. Incidence of hidradenitis suppurativa in the United States: A sex- and age-adjusted population analysis. J Am Acad Dermatol. 2017 Jul;77(1):118-122.
17. Garg A, Wertenteil S, Baltz R, Strunk A, Finelt N. Prevalence Estimates for Hidradenitis Suppurativa among Children and Adolescents in the United States: A Gender- and Age-Adjusted Population Analysis. J Invest Dermatol. 2018 Oct;138(10):2152-2156.
18. Vuong CL, Park HH, Zhang S, Conic RRZ, Hightower GK. Neighborhood-based analysis of adolescent hidradenitis suppurativa prevalence in a large metropolitan area. JAAD Int. 2022 Aug 30;9:80-81.
19. Deckers I.E., van der Zee H.H., Prens E.P. Epidemiology of hidradenitis suppurativa: prevalence, pathogenesis, and factors associated with the development of HS. Curr. Derm. Rep. 2013; 3:54–60.
20. Von Der Werth JM, Williams HC, Raeburn JA. The clinical genetics of hidradenitis suppurativa revisited. Br J Dermatol. 2000; 142:947–953.
21. Gao M, Wang PG, Cui Y, Yang S, Zhang YH, Lin D, Zhang KY, Liang YH, Sun LD, Yan KL, Xiao FL, Huang W, Zhang XJ. Inversa acne (hidradenitis suppurativa): a case report and identification of the locus at chromosome 1p21.1-1q25.3. J Invest Dermatol. 2006 Jun;126(6):1302-6.
22. Li X, Jiang L, Huang Y, Ren Z, Liang X, Wang P. A gene dysfunction module reveals the underlying pathogenesis of hidradenitis suppurativa: An update. Australas J Dermatol. 2020 Feb;61(1):e10-e14.
23. Lee E.Y., Alhusayen R., Lansang P., Shear N., Yeung J. What is hidradenitis suppurativa? Can. Fam. Physician. 2017;63(2):114–120.
24. van der Zee HH, Laman JD, de Ruiter L, Dik WA, Prens EP. Adalimumab (antitumour necrosis factor-α) treatment of hidradenitis suppurativa ameliorates skin inflammation: an in situ and ex vivo study. Br J Dermatol. 2012;166:298–305.
25. Melnik BC, Plewig G. Impaired Notch-MKP-1 signalling in hidradenitis suppurativa: an approach to pathogenesis by evidence from translational biology. Exp Dermatol. 2013; 22:172–177.
26. Pan Y, Lin MH, Tian X, *et al*. Gamma-secretase functions through Notch signaling to maintain skin appendages but is not required for their patterning or initial morphogenesis. Dev Cell. 2004; 7:731–743.

27. Schlapbach C, Hänni T, Yawalkar N, Hunger RE. Expression of the IL-23/Th17 pathway in lesions of hidradenitis suppurativa. J Am Acad Dermatol. 2011; 65:790–798.
28. Mozeika E, Pilmane M, Nürnberg BM, Jemec GB. Tumour necrosis factor-alpha and matrix metalloproteinase-2 are expressed strongly in hidradenitis suppurativa. Acta Derm Venereol. 2013;93:301–304.
29. Freiman A, Bird G, Metelitsa AI, Barankin B, Lauzon G. Cutaneous effects of smoking. Surgery. 2004;8:415–423.
30. Revuz JE, Canoui-Poitrine F, Wolkenstein P, Viallette C, Gabison G, Pouget F, Poli F, Faye O, Roujeau JC, Bonnelye G, Grob JJ, Bastuji-Garin S. Prevalence and factors associated with hidradenitis suppurativa: results from two case-control studies. J Am Acad Dermatol. 2008 Oct;59(4):596-601.
31. Wiseman MC. Hidradenitis suppurativa: a review. Dermatol Ther. 2004;17:50–54.
32. Benzecry V, Grancini A, Guanziroli E, *et al*. Hidradenitis suppurativa/acne inversa: a prospective bacteriological study and review of the literature. G Ital Dermatol Venereol. 2020;155(4):459–463.
33. Danby F.W., Margesson L.J. Hidradenitis suppurativa. Dermatol. Clin. 2010;28(4):779–793.
34. Morgan WP, Leicester G. The role of depilation and deodorants in hidradenitis suppurativa. Arch Dermatol 1982;118:101–102.
35. Cutler B, Hagstrom E, Greiling TM. Deodorant/antiperspirant use and hair removal practices for hidradenitis suppurativa: recommendations from a single-center survey. Int J Womens Dermatol. 2023 Jan 10;9(1):e028.
36. Deckers IE, Janse IC, van der Zee HH, Nijsten T, Boer J, Horváth B, Prens EP. Hidradenitis suppurativa (HS) is associated with low socioeconomic status (SES): A cross-sectional reference study. J Am Acad Dermatol. 2016 Oct;75(4):755-759.e1.
37. Wertenteil S, Strunk A, Garg A. Association of Low Socioeconomic Status With Hidradenitis Suppurativa in the United States. JAMA Dermatol. 2018 Sep 1;154(9):1086-1088.
38. Kromann CB, Deckers IE, Esmann S, Boer J, Prens EP, Jemec GB. Risk factors, clinical course and long-termprognosis in hidradenitis suppurativa: a cross-sectional study. Br J Dermatol. 2014 Oct;171(4):819-24.
39. Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. J Am Acad Dermatol 2009;60(4):539-61.
40. Chiricozzi A, Micali G, Veraldi S. The patient journey: a voyage from diagnosis to hidradenitis suppurativa multidisciplinary unit. J Eur Acad Dermatol Venereol. 2019 Oct;33 Suppl 6:15-20.
41. Saunte DM, Boer J, Stratigos A, Szepietowski JC, Hamzavi I, Kim KH, Zarchi K, Antoniou C, *et al*. Diagnostic delay in hidradenitis suppurativa is a global problem. Br J Dermatol. 2015 Dec;173(6):1546-9.
42. Kokolakis G, Wolk K, Schneider-Burrus S, Kalus S, Barbus S, Gomis-Kleindienst S, Sabat R. Delayed Diagnosis of Hidradenitis Suppurativa and Its Effect on Patients and Healthcare System. Dermatology. 2020;236(5):421-430.
43. Zimman S, Comparatore MV, Vulcano AF, Absi ML, Mazzuoccolo LD. Hidradenitis Suppurativa: Estimated Prevalence, Clinical Features, Concomitant Conditions, and Diagnostic Delay in a University Teaching Hospital in Buenos Aires, Argentina. Actas Dermosifiliogr (Engl Ed). 2019 May;110(4):297-302.
44. van Straalen KR, Ingram JR, Augustin M, Zouboulis CC. New treatments and new assessment instruments for Hidradenitis suppurativa. Exp Dermatol. 2022 Sep;31 Suppl 1(Suppl 1):33-39.
45. Hurley HJ. Axillary hyperhidrosis, apocrine bromhidrosis, hidradenitis suppurativa, and familial benign pemphigus: surgical approach. In: Roenigk RK, Roenigk HH, editors. Dermatologic Surgery. New York: Marcel Dekker; 1996. pp. 623–645.
46. Sartorius K, Lapins J, Emtestam L, Jemec GB. Suggestions for uniform outcome variables when reporting treatment effects in hidradenitis suppurativa. Br J Dermatol. 2003;149:211–213.
47. Sartorius K, Emtestam L, Jemec GB, Lapins J. Objective scoring of hidradenitis suppurativa reflecting the role of tobacco smoking and obesity. Br J Dermatol. 2009;161:831–839.
48. van der Zee HH, Laman JD, Boer J, Prens EP. Hidradenitis suppurativa: viewpoint on clinical phenotyping, pathogenesis and

novel treatments. Exp Dermatol. 2012;21:735–739.
49. Shaver RL, Jemec GBE, Freese R, Alavi A, Lowes MA, Goldfarb N. A survey of clinicians regarding preferred severity assessment tools for hidradenitis suppurativa. Int J Dermatol. 2021 Jun;60(6):e248-e251.
50. Goldfarb N, Lowes MA, Butt M, King T, Alavi A, Kirby JS. Hidradenitis Suppurativa Area and Severity Index Revised (HASI-R): psychometric property assessment. Br J Dermatol. 2021 May;184(5):905-912.
51. Kirby JS, Butt M, King T. Severity and Area Score for Hidradenitis (SASH): a novel outcome measurement for hidradenitis suppurativa. Br J Dermatol. 2020 Apr;182(4):940-948.
52. Horváth B, Janse IC, Blok JL, Driessen RJ, Boer J, Mekkes JR, Prens EP, van der Zee HH. Hurley Staging Refined: A Proposal by the Dutch Hidradenitis Suppurativa Expert Group. Acta Derm Venereol. 2017 Mar 10;97(3):412-413.
53. Rondags A, Volkering RJ, Turcan I, Zuidema YS, Janse IC, Horvath B. The Refined Hurley Patient Questionnaire: An Accurate Self-assessment Instrument for Deriving the Correct Refined Hurley Stage in Hidradenitis Suppurativa. Acta Derm Venereol. 2019 Jun 1;99(7):703-704.
54. Dessinioti C, Katsambas A, Antoniou C. Hidradenitis suppurrativa (acne inversa) as a systemic disease. Clin Dermatol. 2014 May-Jun;32(3):397-408.
55. Shlyankevich J, Chen AJ, Kim GE, Kimball AB. Hidradenitis suppurativa is a systemic disease with substantial comorbidity burden: a chart-verified case-control analysis. J Am Acad Dermatol. 2014;71(6):1144–1150.
56. Kohorst JJ, Kimball AB, Davis MD. Systemic associations of hidradenitis suppurativa. J Am Acad Dermatol. 2015 Nov;73(5 Suppl 1):S27-35.
57. Miller IM, Ellervik C, Vinding GR, *et al*. Association of metabolic syndrome and hidradenitis suppurativa. JAMA Dermatol. 2014; 150:1273–1280.
58. Gold DA, Reeder VJ, Mahan MG, Hamzavi IH. The prevalence of metabolic syndrome in patients with hidradenitis suppurativa. J Am Acad Dermatol. 2014; 70:699–703.
59. Deckers IE, Benhadou F, Koldijk MJ, Del Marmol V, Horváth B, Boer J, van der Zee HH, Prens EP. Inflammatory bowel disease is associated with hidradenitis suppurativa: Results from a multicenter cross-sectional study. J Am Acad Dermatol. 2017 Jan;76(1):49-53.
60. Scheinfeld N. Hidradenitis suppurativa: a practical review of possible medical treatments based on over 350 hidradenitis patients. Dermatol Online J. 2013;19:1.
61. Sabat R, Chanwangpong A, Schneider-Burrus S, *et al*. Increased prevalence of metabolic syndrome in patients with acne inversa. PLoS One. 2012;7:e31810.
62. Egeberg A, Gislason GH, Hansen PR. Risk of major adverse cardiovascular events and all-cause mortality in patients with hidradenitis suppurativa. JAMA Dermatol. 2016;152(4):429–434.
63. Reddy S, Strunk A, Jemec GBE, Garg A. Incidence of Myocardial Infarction and Cerebrovascular Accident in Patients With Hidradenitis Suppurativa. JAMA Dermatol. 2020 Jan 1;156(1):65-71.
64. Kridin K, Valido K, Cohen JM, Cohen AD. Hidradenitis suppurativa and the risk of myocardial infarction, cerebrovascular accident, and peripheral vascular disease: a population-based study. Arch Dermatol Res. 2023 Apr;315(3):429-435.
65. Tugnoli S, Agnoli C, Silvestri A, Giari S, Bettoli V, Caracciolo S. Anger, Emotional Fragility, Self-esteem, and Psychiatric Comorbidity in Patients with Hidradenitis Suppurativa/Acne Inversa. J Clin Psychol Med Settings. 2020 Sep;27(3):527-540.
66. Ooi XT, Choi E, Han H, Ahmad H, Patwardhan KR, Chandran NS. The psychosocial burden of hidradenitis suppurativa in Singapore. JAAD Int. 2022 Dec 7;10:89-94.
67. Frings VG, Bauer B, Glöditzsch M, Goebeler M, Presser D. Assessing the psychological burden of patients with hidradenitis suppurativa. Eur J Dermatol. 2019 Jun 1;29(3):294-301.
68. Shavit E, Dreiher J, Freud T, Halevy S, Vinker S, Cohen AD. Psychiatric comorbidities in 3207 patients with hidradenitis suppurativa. J Eur Acad Dermatol Venereol. 2015 Feb;29(2):371-376.
69. Kurek A, Johanne Peters EM, Sabat R, Sterry W, Schneider-Burrus S. Depression is a frequent co-morbidity in patients with acne inversa. J Dtsch Dermatol Ges. 2013 Aug;11(8):743-9, 743-50.
70. Tzur Bitan D, Berzin D, Cohen AD. Hidradenitis suppurativa and schizophrenia:

a nationwide cohort study. J Eur Acad Dermatol Venereol. 2020 Mar;34(3):574-579.
71. Tzur Bitan D, Berzin D, Cohen A. Hidradenitis Suppurativa and Bipolar Disorders: A Population-Based Study. Dermatology. 2020;236(4):298-304.
72. Yadav S, Singh S, Edakkanambeth Varayil J, Harmsen WS, Zinsmeister AR, Tremaine WJ, Davis MD, Wetter DA, Colombel JF, Loftus EV Jr. Hidradenitis Suppurativa in Patients With Inflammatory Bowel Disease: A Population-Based Cohort Study in Olmsted County, Minnesota. Clin Gastroenterol Hepatol. 2016 Jan;14(1):65-70.
73. Kamal N, Cohen BL, Buche S, Delaporte E, Colombel JF. Features of patients with Crohn's disease and hidradenitis suppurativa. Clin Gastroenterol Hepatol. 2016;14(1):71–79.
74. Hsiao JL, Antaya RJ, Berger T, Maurer T, Shinkai K, Leslie KS. Hidradenitis suppurativa and concomitant pyoderma gangrenosum: a case series and literature review. Arch Dermatol. 2010;146(11):1265–1270.
75. Bao B, Zhu C, Shi J, Lu C. Causal association between inflammatory bowel disease and hidradenitis suppurativa: A two-sample bidirectional Mendelian randomization study. Front Immunol. 2023 Jan 26;14:1071616.
76. Richette P, Molto A, Viguier M, Dawidowicz K, Hayem G, Nassif A, Wendling D, Aubin F, Lioté F, Bachelez H. Hidradenitis suppurativa associated with spondyloarthritis -- results from a multicenter national prospective study. J Rheumatol. 2014 Mar;41(3):490-4.
77. Rondags A, Arends S, Wink FR, Horváth B, Spoorenberg A. High prevalence of hidradenitis suppurativa symptoms in axial spondyloarthritis patients: A possible new extra-articular manifestation. Semin Arthritis Rheum. 2019 Feb;48(4):611-617.
78. Constantinou C, Widom K, Desantis J, Obmann M. Hidradenitis suppurativa complicated by squamous cell carcinoma. Am Surg. 2008;74(12):1177–1181.
79. Ben AJ, Bouasker I, Najah H, Zribi H, Bedoui R, Guesmi F, Hani MA, Nouira R, Zoghlami A, Najah N. Squamous cell carcinoma arising in Verneuil's disease. Tunis Med. 2008 Feb;86(2):169-70.
80. Atri S, Ben Mahmoud A, Zehani A, Chammakhi A, Rebai W, Kacem MJ. The management of hidradenitis suppurativa degenerating into squamous cell carcinoma: About three case reports. Ann Med Surg (Lond). 2021 Mar 24;64:102239.
81. Juviler PG, Patel AP, Qi Y. Infiltrative squamous cell carcinoma in hidradenitis suppurativa: A case report for early surgical intervention. Int J Surg Case Rep. 2019;55:50-53.
82. Yon JR, Son JD, Fredericks C, Morton M, Kingsley S, Gupta S, Poulakidas S, Bokhari F. Marjolin's Ulcer in Chronic Hidradenitis Suppurativa: A Rare Complication of an Often Neglected Disease. J Burn Care Res. 2017 Mar/Apr;38(2):121-124.
83. Racanelli E, Jfri A, Gefri A, O'Brien E, Litvinov IV, Zubarev A, Savin E, Netchiporouk E. Cutaneous Squamous Cell Carcinoma in Patients with Hidradenitis Suppurativa. Cancers (Basel). 2021 Mar 8;13(5):1153.
84. Matusiak L, Bieniek A, Szepietowski JC. Hidradenitis suppurativa markedly decreases quality of life and professional activity. J Am Acad Dermatol 2010;62(4):706-8, 708.e1.
85. Nguyen TV, Damiani G, Orenstein LAV, Hamzavi I, Jemec GB. Hidradenitis suppurativa: an update on epidemiology, phenotypes, diagnosis, pathogenesis, comorbidities and quality of life. J Eur Acad Dermatol Venereol. 2021 Jan;35(1):50-61.
86. Montero-Vilchez T, Diaz-Calvillo P, Rodriguez-Pozo JA, Cuenca-Barrales C, Martinez-Lopez A, Arias-Santiago S, Molina-Leyva A. The Burden of Hidradenitis Suppurativa Signs and Symptoms in Quality of Life: Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2021 Jun 22;18(13):6709.
87. Molina-Leyva A, Cuenca-Barrales C. Pruritus and Malodour in Patients with Hidradenitis Suppurativa: Impact on Quality of Life and Clinical Features Associated with Symptom Severity. Dermatology. 2020;236(1):59-65.
88. Alavi A, Farzanfar D, Lee RK, Almutairi D. The Contribution of Malodour in Quality of Life of Patients With Hidradenitis Suppurativa. J Cutan Med Surg. 2018 Mar/Apr;22(2):166-174.
89. Kontzias CL, Pixley JN, Feldman SR, Pichardo RO. Marriage Is Associated With

Improved Social Support and Quality-of-Life in Hidradenitis Suppurativa. J Cutan Med Surg. 2023 Mar-Apr;27(2):178-179.
90. Wark KJL, Cains GD. The Microbiome in Hidradenitis Suppurativa: A Review. Dermatol Ther (Heidelb). 2021 Feb;11(1):39-52.
91. Williams SC, Frew JW, Krueger JG. A systematic review and critical appraisal of metagenomic and culture studies in hidradenitis suppurativa. Exp Dermatol. 2021 Oct;30(10):1388-1397.
92. Świerczewska Z, Lewandowski M, Surowiecka A, Barańska-Rybak W. Microbiome in Hidradenitis Suppurativa-What We Know and Where We Are Heading. Int J Mol Sci. 2022 Sep 24;23(19):11280.
93. Luck ME, Tao J, Lake EP. The Skin and Gut Microbiome in Hidradenitis Suppurativa: Current Understanding and Future Considerations for Research and Treatment. Am J Clin Dermatol. 2022 Nov;23(6):841-852.
94. Nesbitt E, Clements S, Driscoll M. A concise clinician's guide to therapy for hidradenitis suppurativa. Int J Womens Dermatol. 2019 Dec 27;6(2):80-84.
95. Zouboulis CC, Desai N, Emtestam L, Hunger RE, Ioannides D, Juhász I, Lapins J, Matusiak L, Prens EP, Revuz J, Schneider-Burrus S, Szepietowski JC, van der Zee HH, Jemec GB. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. J Eur Acad Dermatol Venereol. 2015 Apr;29(4):619-44.
96. Gener G, Canoui-Poitrine F, Revuz JE, Faye O, Poli F, Gabison G, Pouget F, Viallette C, Wolkenstein P, Bastuji-Garin S. Combination therapy with clindamycin and rifampicin for hidradenitis suppurativa: a series of 116 consecutive patients. Dermatology. 2009;219(2):148-54.
97. Dessinioti C, Zisimou C, Tzanetakou V, Stratigos A, Antoniou C. Oral clindamycin and rifampicin combination therapy for hidradenitis suppurativa: a prospective study and 1-year follow-up. Clin Exp Dermatol. 2016;41(8):852–857.
98. Join-Lambert O, Coignard H, Jais JP, Guet-Revillet H, Poirée S, Fraitag S, Jullien V, Ribadeau-Dumas F, Thèze J, Le Guern AS, Behillil S, Leflèche A, Berche P, Consigny PH, Lortholary O, Nassif X, Nassif A. Efficacy of rifampin-moxifloxacin-metronidazole combination therapy in hidradenitis suppurativa. Dermatology. 2011 Feb;222(1):49-58.
99. Delage M, Jais JP, Lam T, Guet-Revillet H, Ungeheuer MN, Consigny PH, Nassif A, Join-Lambert O. Rifampin-moxifloxacin-metronidazole combination therapy for severe Hurley stage 1 hidradenitis suppurativa: prospective short-term trial and 1-year follow-up in 28 consecutive patients. J Am Acad Dermatol. 2023 Jan;88(1):94-100.
100. Join-Lambert O, Coignard-Biehler H, Jais JP, Delage M, Guet-Revillet H, Poirée S, Duchatelet S, Jullien V, Hovnanian A, Lortholary O, Nassif X, Nassif A. Efficacy of ertapenem in severe hidradenitis suppurativa: a pilot study in a cohort of 30 consecutive patients. J Antimicrob Chemother. 2016 Feb;71(2):513-20.
101. Yazdanyar S, Boer J, Ingvarsson G, Szepietowski JC, Jemec GB. Dapsone therapy for hidradenitis suppurativa: a series of 24 patients. Dermatology. 2011;222:342–346.
102. Boer J, Nazary M. Long-term results of acitretin therapy for hidradenitis suppurativa. Is acne inversa also a misnomer? Br J Dermatol. 2011;164:170–175.
103. Matusiak L, Bieniek A, Szepietowski JC. Acitretin in hidradenitis suppurativa treatment – own experiences. Przegl Dermatol. 2012;99:356–357.
104. Golbari N.M., Porter M.L., Kimball A.B. Antiandrogen therapy with spironolactone for the treatment of hidradenitis suppurativa. J Am Acad Dermatol. 2019;80(1):114–119.
105. Arenbergerova M, Gkalpakiotis S, Arenberger P. Effective long-term control of refractory hidradenitis suppurativa with adalimumab after failure of conventional therapy. Int J Dermatol. 2010;49:1445–1449 .
106. Sotiriou E, Apalla Z, Vakirlis E, Ioannides D. Efficacy of adalimumab in recalcitrant hidradenitis suppurativa. Eur J Dermatol. 2009;19:180–181.
107. Paradela S, Rodriguez-Lojo R, Fernandez-Torres R, Arévalo P, Fonseca E. Long-term efficacy of infliximab in hidradenitis suppurativa. J Dermatolog Treat. 2012;23:278–283.
108. Lasocki A, Sinclair R, Foley P, Saunders H. Hidradenitis suppurativa responding to treatment with infliximab. Australas J Dermatol. 2010;51:186–190.

109. Takeda K, Kikuchi K, Kanazawa Y, Yamasaki K, Aiba S. Ustekinumab treatment for hidradenitis suppurativa. J Dermatol. 2019 Dec;46(12):1215-1218.
110. Tzanetakou V, Kanni T, Giatrakou S, Katoulis A, Papadavid E, Netea MG, Dinarello CA, van der Meer JWM, Rigopoulos D, Giamarellos-Bourboulis EJ. Safety and Efficacy of Anakinra in Severe Hidradenitis Suppurativa: A Randomized Clinical Trial. JAMA Dermatol. 2016 Jan;152(1):52-59.
111. Gracia Cazaña T, Berdel Díaz LV, Martín Sánchez JI, Querol Nasarre I, Gilaberte Y. Systematic Review of Light-Based Treatments for Hidradenitis Suppurativa. Actas Dermosifiliogr (Engl Ed). 2020 Mar;111(2):89-106.
112. Saunte DM, Lapins J. Lasers and Intense Pulsed Light Hidradenitis Suppurativa. Dermatol Clin. 2016 Jan;34(1):111-9.
113. Hamzavi I.H., Griffith J.L., Riyaz F., Hessam S., Bechara F.G. Laser and light-based treatment options for hidradenitis suppurativa. J Am Acad Dermatol. 2015;73(5 Suppl 1):S78–S81.
114. Mikkelsen P.R., Dufour D.N., Zarchi K., Jemec G.B. Recurrence rate and patient satisfaction of CO2 laser evaporation of lesions in patients with hidradenitis suppurativa: a retrospective study. Dermatol Surg. 2015;41(2):255–260.
115. Krakowski AC, Admani S, Uebelhoer NS, Eichenfield LF, Shumaker PR. Residual scarring from hidradenitis suppurativa: fractionated CO2 laser as a novel and noninvasive approach. Pediatrics. 2014 Jan;133(1):e248-51.
116. Verdolini R, Clayton N, Smith A, Alwash N, Mannello B. Metformin for the treatment of hidradenitis suppurativa: a little help along the way. J Eur Acad Dermatol Venereol. 2013 Sep;27(9):1101-8.
117. Jennings L, Hambly R, Hughes R, Moriarty B, Kirby B. Metformin use in hidradenitis suppurativa. J Dermatolog Treat. 2020 May;31(3):261-263.
118. Moussa C, Wadowski L, Price H, Mirea L, O'Haver J. Metformin as Adjunctive Therapy for Pediatric Patients With Hidradenitis Suppurativa. J Drugs Dermatol. 2020 Dec 1;19(12):1231-1234.
119. Brocard A., Knol A.C., Khammari A., Dréno B. Hidradenitis suppurativa and zinc: a new therapeutic approach. A pilot study. Dermatology. 2007;214(4):325–327.
120. Scuderi N, Monfrecola A, Dessy LA, Fabbrocini G, Megna M, Monfrecola G. Medical and Surgical Treatment of Hidradenitis Suppurativa: A Review. Skin Appendage Disord. 2017 May;3(2):95-110.
121. Shukla R, Karagaiah P, Patil A, Farnbach K, Ortega-Loayza AG, Tzellos T, Szepietowski JC, Giulini M, Schepler H, Grabbe S, Goldust M. Surgical Treatment in Hidradenitis Suppurativa. J Clin Med. 2022 Apr 21;11(9):2311.
122. van Hattem S, Spoo JR, Horváth B, Jonkman MF, Leeman FW. Surgical treatment of sinuses by deroofing in hidradenitis suppurativa. Dermatol Surg. 2012 Mar;38(3):494-7.
123. Menderes A., Sunay O., Vayvada H., Yilmaz M. Surgical management of hidradenitis suppurativa. Int J Med Sci. 2010;7(4):240–247.
124. Gierek M, Łabuś W, Słaboń A, Ziółkowska K, Ochała-Gierek G, Kitala D, Szyluk K, Niemiec P. Co-Graft of Acellular Dermal Matrix and Split Thickness Skin Graft-A New Reconstructive Surgical Method in the Treatment of Hidradenitis Suppurativa. Bioengineering (Basel). 2022 Aug 14;9(8):389
125. Stumpfe MC, Horch RE, Arkudas A, Cai A, Müller-Seubert W, Hauck T, Ludolph I. The Value of Negative-Pressure Wound Therapy and Flap Surgery in Hidradenitis Suppurativa - A Single Center Analysis of Different Treatment Options. Front Surg. 2022 Jun 28;9:867487.
126. Elboraey MA, Alali AB, Alkandari QA. Immediate and Delayed Reconstruction after Excision of Axillary Hidradenitis Suppurativa Using a Propeller Flap. Plast Reconstr Surg Glob Open. 2019 Aug 12;7(8):e2387.
127. Rieger UM, Erba P, Pierer G, Kalbermatten DF. Hidradenitis suppurativa of the groin treated by radical excision and defect closure by medial thigh lift: aesthetic surgery meets reconstructive surgery. J Plast Reconstr Aesthet Surg. 2009 Oct;62(10):1355-60.
128. Gierek M, Klama-Baryła A, Łabuś W, Bergler-Czop B, Pietrauszka K, Niemiec P. Platelet-Rich Plasma and Acellular Dermal Matrix in the Surgical Treatment of Hidradenitis Suppurativa: A Comparative Retrospective Study. J Clin Med. 2023 Mar 8;12(6):2112.