Hidradenitis Suppurativa (HS) is a clinical entity based on a clinical definition. The diagnostic criteria are wide and usually include scarring, the recurrent nature of the disease, and the characteristic multifocal location restricted to axillae, inframammary region, and groin. Inflamed pilonidal cysts and staphylodococcus are the most common differential diagnoses, but rarer differential diagnoses such as multiple trichoepitheliomas, steacystoma multiplex, and apocrine nevus exist.2-4 A staging classification of hidradenitis has been proposed by Hurley.5 The Hurley classification describes the evolution of the disease from early localized inflammation to fulminant disease (Fig. 1).

No pathognomonic signs exist, but clues to the diagnosis are provided by the distribution of the lesions and their clinical appearance. Early studies stressed the shape of the lesions, describing them as characteristically rounded rather than pointed as seen in furunculosis, the lack of central necrosis, and the "deep" location.6,7

Definition
Hidradenitis suppurativa is a recurrent disease, restricted to inverse areas, and characterized by a progression from noninflamed nodules to painful, rounded, deep-seated, inflamed lesions and subsequent scarring and chronic suppuration (Fig. 1). Nodules are restricted to the skin and may persist for years with occasional episodes of inflammation. Inflamed nodules progress into scarred lesions when spontaneously draining dermal sinus tracts appear. Sinus tracts persist and cause periodic flares of inflammation. The end stage is characterized by widespread scarring in the region.

Nosology
Classification of diseases or nosology is important for our understanding of the pathological processes and subsequent clinical management of disease. HS was first described by Velpeau in 1839 (quoted in ref 8) based on the characteristic distribution of the lesions, i.e., the...
"anatomical predisposition" of the affected regions. Later, Verneuil described the clinical course and suggested an association with the sweat glands which were particularly "well developed" and "voluminous" in the affected areas. He identified HS as a subcutaneous process and distinguished it from furunculosis.

This idea was perpetuated until Pillsbury coined the term "follicular occlusion," suggesting that acne vulgaris, perifolliculitis capitis, pilonidal cysts, and hidradenitis are closely related diseases involving the hair follicle. Clinical manifestations and response to treatment, however, remain very different, e.g., acne prominently involves the sebaceous apparatus while HS does not. The continued publication of case reports of the follicular occlusion triad also suggest that co-occurrence is rare. Even if the diseases are not identical, they may share pathogenic steps involving the hair follicle. Human experiments by Shelly and Cahn reproduced HS-like lesions in healthy volunteers after occlusion of the hair follicles, and the concept is further supported by recent histological studies. Some authors are now proposing that the term hidradenitis be abolished in favor of a new term "acne inversa." The distinction between the new acne inversa and the old follicular occlusion triad is unclear, and thus both theoretical and practical problems remain associated with this new concept.

**Epidemiology**

Studies have estimated the prevalence at 1/3000 without specifying a time frame or specific diagnostic criteria. In a study of the "hidden" or unrecognized dermatological diseases in patients attending a dermatological clinic, a physical examination of general dermatological patients found a point prevalence of hidradenitis at a rate of 1/1000. From interviews among healthy women (mean age 31 years), a lifetime prevalence rate of 4% was found. The women interviewed were all hospital employees (nurses and students) and therefore may have overreported events in comparison to the general population.

Later studies of a population sample in Denmark, using the proposed combined clinical definition of positive signs and symptoms and exclusion criteria, found that hidradenitis was more common than previously estimated, with a point prevalence of 4.1% (5.0-6.0%) in a younger adult population. A one-year prevalence of 1% (0.4-2.2%) in the general population was based on the subjects' recollection only and is similar to that of other major dermatoses, e.g., psoriasis.

Active hidradenitis is generally more prevalent in women with an odds ratio of 2.9. Active genital genitalum lesions occur significantly more often in female patients, while no sex difference is seen in the rarer axillary lesions. Noninflamed quiescent nodules are also more prevalent in women and in genitofemoral lesions. Conditions have been suggested as precursor lesions for HS, but, in contrast to the manifested disease, they appear to be equally distributed in both sexes and sites.

**Etiology and Pathogenic Factors**

A limited number of investigations into the etiology of hidradenitis have been made. Hidradenitis has been described in dogs, but no experimental studies are available using a canine model of the disease.

**Genetic Factors**

HS patients report cases among their relatives more frequently than controls, and families in which hidradenitis, acne, and other poral occlusion diseases occur have been reported. However, specific genetic studies have yielded conflicting results. One study has suggested that inherited factors may be important in hidradenitis following HLA-typing in 27 patients, although the results did not reach statistical significance due to the small number of patients used. A later and larger study of HLA in Swedish patients compared with a population sample did not find any HLA-A, HLA-B, HLA-DW association. One study describing an autosomal dominant pattern of inheritance has also been reported, but the penetrance appeared variable, indicating that other non-
genetic factors are involved. A later review of the data has renewed the suspicion of a dominant pattern of inheritance in this group of patients using a better clinical definition of the cases.

Co-occurrence of phenotypes may support a genetic linking. In case reports or series of case reports, hidradenitis suppurativa has been associated with a number of diseases. Most frequently, association with Crohn's disease (n = 34) and Dowling-Degos's disease (n = 8) has been reported. However, it is unclear to what extent these reports truly reflect hidradenitis lesions as defined in the above, and even if these observations represent causal relationships or merely the coincidental findings of a comparatively common disease such as hidradenitis.

**Immunological Host Factors**

An immunological etiology of HS has been considered a possible predisposing factor to bacterial infection. One study failed to identify immune deficiency in HS patients, although individual patients may be found in whom correctable bacterial effects can be identified. It should be noted that disease definition in this case was poor. Immunology may also play a role in the development of infections. A pilot study suggested that excessive free oxygen radical generation by neutrophils from HS patients may be an etiological factor, although the data are preliminary and require additional verification. Similar mechanisms have previously been implicated in parodontitis and inflammatory bowel disease which share histological features with HS.

**Hormonal Factors**

Hypertroandrogenic syndromes are clinically expressed in women. A clear female preponderance exists in HS. Although some cases have been attributed to the presence of adrenarche (n = 5) or with acne in acromegaly (n = 1),

Premenstrual flareup is reported in several studies by approximately 50% of women with hidradenitis, while improvement is reported by only a minority.

Flareups may be absent in anovulatory cycles. Pregnancy and childbirth are also reported to influence the intensity of the disease favorably, with subsequent postpartum flareup. Reduced fecundity in some patients may be causally related to the changes in circulating sex hormones, but correlation with clinical markers of hyperandrogenism is poor.

Careful studies of cutaneous signs of virilism, including shrunk excretion rate, have failed to show any significant abnormalities in hidradenitis patients, further supporting a localized androgen effect. However, it should be noted that the variation in hirsutism and acne scores in hidradenitis patients was larger than in healthy controls, which may suggest that a subpopulation of patients exist in whom signs of cutaneous virilism are more pronounced and where androgens may play a pathogenic role. Antianadrogenic treatment has been found to be effective in some cases and in one randomized controlled trial. The mechanism behind this effect is not clear. In a published measurement of circulating androgens, a considerable overlap to normal values was found, suggesting that androgen sensitivity may be involved, and it has been suggested that in patients with hidradenitis, an increased capacity for androgen metabolism which may play a role in follicular hyperkeratinization.

There have also been studies that failed to show any abnormalities of circulating androgens in hidradenitis.

The main weaknesses of the articles dealing with possible androgen involvement are the possible confusion of acne conglobata with HS and the wide range in the level of circulating androgen which shows a large number of patients with normal or low androgen levels. A number of patients diagnosed in these studies also had extensive acne lesions, leading to the speculation that what was interpreted as hidradenitis was in fact acne, an acknowledged androgen-sensitive disorder. Finally, the possible pathogenic role of androgens is further confounded by early reports suggesting that testosterone can be used in the treatment of hidradenitis. The exact role of androgens in HS therefore remains to be established.

The use of oral contraceptives may also affect potential androgen-dependent diseases. The pattern of use among patients was not different from that of the general population. Finally, the female preponderance may also be explained by other sex-specific factors such as the oestrogenic influence on inflammation.

**Obesity**

Obesity has often been suggested as an etiological factor. Previous studies have shown conflicting results: one study found HS patients to be more obese (n = 11), another study was unable to reproduce the findings (n = 76). It is suggested that while obesity may not be a primary pathogenetic factor, it may aggravate preexisting hidradenitis through mechanical irritation, occlusion, and maceration.

**Infection**

Bacteria have traditionally been implicated in hidradenitis. Early histological studies suggested staphylococci to be causally involved, and, although later studies have separated staphylococcosis and hidradenitis as two different clinical entities, topical and systemic antibiotics are still used in the treatment of hidradenitis.

Routine microbiological culture of lesions is frequently negative, although more extensive investigations have managed to identify a number of different bacteria in lesions diagnosed as hidradenitis: staphylococci, S. aureus, S. epidermidis, S. pyogenes, and S. saprophyticus. The species have been isolated from a wide range of lesions at many different stages and definitions of hidradenitis. Frequently, the different species of bacteria have also been found in only a few cases as a
part of more general investigations of the flora of skin infections.84-86

Sampling problems may have influenced the results of these studies. Needle aspiration of early lesions has yielded recognized pathogens in a minority of the examined lesions (9/41; S. aureus in 8/41 lesions and S. albus in 1/41).86 Patients seek medical help sooner if their lesions contain S. aureus than if their lesions contain other bacteria or are sterile. A more recent study has attempted to overcome the sampling problems by using laser ablation to expose the HS lesions before sampling.86 Using this technique, the involved structures can be visualized before sampling and thus the sampling error is abolished. In the study,86 positive cultures were found in all the examined patients, with Staph. aureus and coagulase-negative staphylococci found most frequently. Therefore, it is speculated that coagulase-negative staphylococci play a pathogenic role. These bacteria are known to produce clinically significant infections in association with nonvital tissue and artificial implants or implants.87,88 In HS an analogous situation may exist in conjunction with the spillover of follicular material from ruptured hair follicles. IgG precipitins have been studied as an indirect measure of bacterial involvement in HS.89 No association between precipitins and bacteria was found, nor did the precipitins clearly differ from normal values. The highest number of precipitins was found against S. aureus.

Infections may co-occur with HS. A possible causal association between genital-femoral hidradenitis and Chlamydia trachomatis has been suggested, but the organism was not found in the pus of any lesion.88 A study of patients attending an STD clinic failed to identify any association between Chlamydia infection and HS but suggested that human papilloma virus (HPV) infection was common in HS patients.90 It has also been suggested that HPV infection is a cofactor in complications such as malignant degeneration of HS lesions.91 The possible causal relationship of HPV infection and the primary hidradenitis lesion is obscure, although the virus has been associated with parakeratotic change in the serrated eccrine duct.89

Drugs
Hidradenitis is rarely a side effect of drug use, but oral contraceptives (n = 7) and lithium (n = 1) have been associated with its development.88,90,91

Cosmetics
Early reference suggested a causative role for cosmetics, especially in women shaving their axillae on the assumption that shaving may provide an entry point for bacterial infection.99 Self-reported skin irritation due to cosmetics is significantly more common in HS patients.90 Two studies have been unable to identify differences in the pattern of use of cosmetics, shaving, or use of talcum in HS.92,93 Histological data which could substantiate an irritant component of early HS provide mixed results. One study found inframammary spongiosis in early lesions, while another study found no signs of irritant reactions (spongiosis or parakeratosis).91,97 The study by Shelley and Cahn98 has been interpreted to imply a role for cosmetics in HS. They epilated the axillae of 12 healthy volunteers and applied occlusive tape for one week to produce "hidradenitis-like" lesions, which is obviously different from customary use of cosmetics.

Tobacco
Two independent epidemiological studies have suggested that the use of tobacco by HS patients is more common than among healthy controls, although no specific mechanism has been identified to link the use of tobacco with HS.94,95 Lung and buccal cancers are more common among HS patients than in the general population as would be expected with increased tobacco smoking or chewing.96

Morphology of Hidradenitis Suppurativa

Histology
Hidradenitis is a follicular disease that may secondarily involve other structures such as apocrine or eccrine glands (Fig. 2).94 Occlusion of the hair follicle produces hidradenitis-like lesions,96 while destruction of the apocrine gland duct orifices produces distended apocrine glands.97 Fove apocrine gland affection is found in 5% of the cases, predominantly occurring in the axilla, and is clinically indistinguishable from HS.91 The follicular nature of the disease seen is highlighted by the description of spongiform inflammatory changes of the inframammary of early lesions.93 The HS lesions present a consistent histological image as shown in a study of multiple biopsies from individual patients.98 Sinus tracts have been heralded as the hallmark of hidradenitis and used to further underline the similarities between hidradenitis and acne.94,95 It is not clear whether sinus tract formation is a host-specific response pattern of or a specific tract connected to the diagnosis of hidradenitis. Sinus tracts have been experimentally produced in the rhino-mouse by inserting a transferal stent from one distended follicle to another, suggesting that it is related to the host rather than to the stimulus.100

Based on published histological studies, it is suggested that HS is an inflammatory disease originating from the hair follicle and subsequently spreading inflammation to the surrounding tissues where characteristic secondary changes develop.91,101 Sinus tract formation is speculated to represent reparative mechanisms that encapsulate necrotic debris, and, with abnormal hair follicles, sinus tracts may create the morphological prerequisites for the subsequent chronic, recurrent course of the disease.
FIGURE 2: Histology of hidradenitis suppurativa. Lesions show inflammatory infiltrate surrounding hair follicles (top), while apocrine glands are unaffected (bottom).

High-Frequency Ultrasound
Normal hair follicles appear as elongated, parallel, low echogenic structures occurring at regular intervals within the dermis and oriented at an angle of approximately 45°–60° to the surface of the skin as seen in normal histology specimens. In HS, changes have been found in the clinically uninvolved axillary and genitofemoral hair follicles. The follicles appear to be of a larger diameter and a distorted shape with a wider deep follicular diameter, in agreement with the clinical impression that the primary event in HS is deep-seated rather than superficial.

Consequences and Complications
HS causes significant morbidity. The general self-reported level of health is poorer among HS patients, the average Danish patient lost 2.7 days of work per year (stages I and II) due to flares of HS. Similarly, the quality of life is lower than in any other dermatological disease studied using the DLQI for assessment of life quality. The data strongly support the clinical impression that HS is a "heart sink" condition for patients.

The soreness, discharge, and appearance of lesions are described as problems in both work and leisure activities by 51% of all patients. For grades I and II, the main problem is soreness, which can be used to assess the efficacy of treatment.

A number of case reports exist describing rare but serious complications. Death due to HS has occurred (n = 2). Nonlethal complications range from anemia to increased white blood cells. HS-associated arthritis, axial spondyloarthropathy, and sterile osteomyelitis-like lesions also occur but do not appear to be associated with HLA B27. Rare complications include benign and malignant ulcers arising from chronic hidradenitis (n = 17)

Squamous cell carcinomas originating from HS lesions may be associated with hypercalcemia. A general association between HS and cancer was confirmed in a nationwide case-control study involving all Swedish HS patients admitted to hospital between 1987 and 94. It was shown that HS patients have a higher overall incidence of cancer (1.5; 1.1–1.8) than the general population. The incidence of nonmelanoma skin cancer standard incidence rate (SIR) = 4.6; 1.5–10.7), buccal (SIR = 5.5; 1.8–12.5), and hepatic cancer (SIR = 10.0; 2.1–29.1) was increased.

Finally, there are complications caused by the chronic inflammation of hidradenitis extending to surrounding tissues, e.g., edema of the scrotum or breast, fascial, anorectal abscesses, and polyloid outgrowths.

Treatment
Physical or Adjuvant Treatment
Early studies stressed the usefulness of wet warm compresses, unspecified ointments, and sulfur. As an indication of the clinical difficulties of treating hidradenitis, it may be noted that some of these treatments are still used today. The avoidance of mechanical stress on the surface of the skin, i.e., shear forces, is also commonly recommended, although no experimental evidence exists to support the advice. It has been speculated that the abnormally thick skin and dystrophic hair follicles are more susceptible to mechanical stresses, but no experiment has yet been designed to test this hypothesis.

Radiotherapy
A body of early literature supports the use of X rays in depilatory doses and a total dose of 1.5–18 GY. A dosage giving temporary epilation has been suggested as optimal by Zeligman. The dosage given in a single-session treatment schedule was 4–5 GY (100 kV, 100 mA, 0.8- mm Al filter), reportedly with good effect and without subsequent irradiation dermatitis or scarring. This suggests that improved drainage of the follicle may be of importance to the clinical effect; although the locally immunosuppressive effect may also play a role. No randomised controlled trials (RCTs) have been con-
ducted in this field. The possible beneficial effects of laser epilation do, however, suggest that hair removal may be of independent importance (personal observation, G.B.E. James).

**Antibiotics**

It has been pointed out that the standard length of antibiotic treatment closely resembles the duration of untreated flares in HS. However, antibiotics continue to be widely used in the treatment of hidradenitis. They are used both as monotherapy and in conjunction with surgery. While they are of crucial importance in the treatment of concomitant bacterial infection, antibiotics role vis-à-vis HS is currently as unclear as the role of bacteria in the disease.

Topical clindamycin has been shown to have an effect in a double-blind placebo-controlled study (n = 30). A significant reduction of symptoms was seen within one month of treatment (p < 0.01). A subsequent 3-month double-blind double-dummy study comparing topical clindamycin with systemic tetracycline (n = 34) failed to show significant differences between the two treatments.

**Hormonal Therapy**

The possible beneficial effects of testosterone is a curiosity to the results of a double-blind crossover trial which found cyproterone acetate useful. Cyproterone acetate in combination with ethinyloestradiol is the only other treatment, apart from topical clindamycin, that has been shown to have an effect in a controlled trial. A dose of 50 μg ethinyloestradiol/50 mg cyproterone acetate was compared with 50 μg ethinyloestradiol/500 μg norgestrel and found to be superior, with 29% of the patients (7/24) clearing completely and 21% (5/24) improving within an 18-month followup period.

Finasteride may have also an effect as may more aggressive manipulation of the sex hormones, e.g., the use of gonadotropin-releasing agonists in combination with oophorecto-salpingectomy-hysterectomy. Combination therapy with antiandrogens and antibiotics has also reportedly been successful.

**Immunosuppressive Treatment**

Since the disease is not a classic infectious disease universally caused by known pathogens, simple antiinflammatory treatment offers great relief for many patients. ACTH, hydrocortisone, azathioprine, and cyclosporin have all been used with good effect. Prednisolone may be used as adjuvant treatment, for periodic systemic therapy to treat flares (personal communication, Dr. J. von der Werth) or intravascularly. More specific, targeted therapy using infliximab has been reported in a case, and it may hold more promise for future therapy. Appropriate bacteriological sampling must be obtained if antiinflammatory therapy is instituted.

Recently, the successful outcome of dapson treatment has been reported.

**Retinoids**

Retinoids have been tested in a number of case reports. No double-blinded design studies have been published. The predominant number of publications deal with the use of isotretinoin in a dosage similar to acne treatment, but reports have also been published on the use of etretinate and acitretin. Etretinate and acitretin may have an effect in patients who are unresponsive to isotretinoin. The biggest case series (n = 68) suggests that less than 25% of HS patients derive benefit from isotretinoin therapy, although it has been suggested that a longer treatment period may be necessary than in acne. One review has suggested that patients in which hidradenitis occurred in conjunction with acne lesions on convex areas of the body, i.e., acne conglobata with lesions in inverse regions, were more responsive than patients in whom lesions were confined to the inverse regions.

**Surgery**

Removal of the lesions through surgery is strongly recommended at an early stage of the disease. The published data on the efficacy of different methods are neither uniform nor extensive; a more uniform reporting would therefore improve the usefulness of future reports.

Simple lancing is ineffectual and should actively be discouraged. An improved technique involves exterminatization of the lesion. Proper exterminatization involves removal of the "roots" of sinus tracts, removal of all granulation tissue by curetage, and healing by secondary intention. A similar result can be achieved by CO2 laser evaporation of the tissue. This method allows visualization of the lesions during the procedure and therefore may be less invasive than cold steel surgery. Good results have been reported with low recurrence rates and healing times of 3–5 weeks.

Specific factors appear to influence the risk of recurrence:

**The Extent of the Excision**

Single-lesion treatment offers lower immediate morbidity, while larger excisions may offer a better prognosis. Long-term followup of simple excision has shown a wide range of recurrence rates (see Table I). This reflects two aspects of surgical treatment: First, when single or adjacent elements are excised, recurrences do occur locally even after surgery; second, patients may develop new foci of hidradenitis in another region. Local recurrences may appear either rapidly and in direct association with the scar, suggesting that diseased tissue had been left at the time of operation, or over a longer period suggesting de novo occurrence of disease. The appearance of new foci strongly suggests the disease is intrinsically multifocal.
### TABLE I

<table>
<thead>
<tr>
<th>Method of closure</th>
<th>Region</th>
<th>Followup (months) (range)</th>
<th>Recurrence rate</th>
<th>Year (ref)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary closure</td>
<td>Mixed</td>
<td>38 (7–2)</td>
<td>21% (6/24)</td>
<td>1968 (121)</td>
</tr>
<tr>
<td>SSG</td>
<td>Mixed</td>
<td>38 (7–2)</td>
<td>4% (2/32)</td>
<td>—</td>
</tr>
<tr>
<td>Flap</td>
<td>Mixed</td>
<td>38 (7–2)</td>
<td>22% (3/25)</td>
<td>—</td>
</tr>
<tr>
<td>Primary closure</td>
<td>Mixed</td>
<td>120</td>
<td>42% (10/48)</td>
<td>1981 (153)</td>
</tr>
<tr>
<td>SSG or Flap</td>
<td>Mixed</td>
<td>120</td>
<td>0% (0/42)</td>
<td>—</td>
</tr>
<tr>
<td>Incision</td>
<td>Mixed</td>
<td>n.a.</td>
<td>81% (11/14)</td>
<td>1983 (153)</td>
</tr>
<tr>
<td>Primary closure</td>
<td>Mixed</td>
<td>n.a.</td>
<td>30% (9/30)</td>
<td>—</td>
</tr>
<tr>
<td>SSG</td>
<td>Mixed</td>
<td>n.a.</td>
<td>13% (5/38)</td>
<td>—</td>
</tr>
<tr>
<td>Secondary healing</td>
<td>Mixed</td>
<td>47 (6–89)</td>
<td>74% (19/26)</td>
<td>1982 (150)</td>
</tr>
<tr>
<td>Primary closure</td>
<td>Mixed</td>
<td>54 (12–112)</td>
<td>78% (24/31)</td>
<td>1988 (153)</td>
</tr>
<tr>
<td>Secondary healing</td>
<td>Mixed</td>
<td>27 (15–47)</td>
<td>25% (6/24)</td>
<td>1991 (144)</td>
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<tr>
<td>Incision</td>
<td>Mixed</td>
<td>72 (7–10)</td>
<td>50% (11/22)</td>
<td>1990 (145)</td>
</tr>
<tr>
<td>Primary closure</td>
<td>Mixed</td>
<td>72 (7–10)</td>
<td>51% (11/22)</td>
<td>1990 (145)</td>
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<tr>
<td>SSG or Secondary healing</td>
<td>Mixed</td>
<td>72 (7–10)</td>
<td>27% (2/7)</td>
<td>—</td>
</tr>
<tr>
<td>Mixed</td>
<td>Axillary</td>
<td>36 (6–2)</td>
<td>2.5% (1/4)</td>
<td>2000 (95)</td>
</tr>
<tr>
<td>Local excision (primary, flaps or SSG)</td>
<td>Axillary</td>
<td>n.a.</td>
<td>21% (2/20)</td>
<td>2000 (154)</td>
</tr>
<tr>
<td>Hair-bearing skin (primary, flaps or SSG)</td>
<td>Axillary</td>
<td>n.a.</td>
<td>7% (1/14)</td>
<td>—</td>
</tr>
<tr>
<td>Hair-bearing skin + 2 cm (flaps or SSG)</td>
<td>Axillary</td>
<td>n.a.</td>
<td>0% (0/0)</td>
<td>—</td>
</tr>
<tr>
<td>Lesion + 2 cm to fascia</td>
<td>Axillary/green</td>
<td>96 (0-252)</td>
<td>13% (20/20)</td>
<td>2001 (155)</td>
</tr>
</tbody>
</table>

* SSG = split-skin graft, n.a. = not available.

### The Method of Closure

It has been argued that better results can be obtained by leaving wounds to secondary healing rather than direct closure by apposition, flaps, or grafts. In studies of secondary healing, scarring has not been reported. For large lesions this method is slow, and, even though modern bandaging provides good clinical results and improved ease of management, morbidity can still be considerable for a protracted period. Healing periods of several months can be expected following large excisions.

### Location

In addition to the extent of excision, the location may be of importance to the outcome of surgery, with perianal and axillary surgery having a lower recurrence rate than inguinalperineal or submammary excision. It remains to be seen if the regional differences are merely a secondary factor to the size of the primary excision.

### Patient Age

This may also play a role, with older patients having lower recurrence rates irrespective of the preparative duration.

### For chronic recurrent diseases, patient satisfaction with any given therapeutic modality is particularly important. No data are available on patient satisfaction with medical treatment, but it is generally found to be high following any kind of surgical treatment. Early and aggressive treatment is therefore recommended as are additional RCTs in this disheartening disease.

### References


Background: Hidradenitis Suppurativa is a clinically defined disease that causes considerable morbidity for patients. The results of recent studies, which have increased the understanding of this disease are reviewed.

Objective: The epidemiology, risk factors, pathogenesis and treatment of this disease are summarized to help clinicians with practical patient management.

Conclusion: Hidradenitis Suppurativa remains a clinical challenge to patients and physicians alike. Physicians should be familiar with the impact this disease has on the patient and with the range of treatments available. Use of simple incisions as treatment is strongly discouraged. Additional pathogenic as well as therapeutic studies are necessary.

Sommaire

Antecedent: L’hidrosadenite supparante est une entite clinique bien definie qui est une cause important de morbidite. Les resultats d’etudes recentes qui ont accru la comprehension de cette maladie sont revus dans cette etude.

Objectifs: L’épidemiologie, les facteurs de risque, la pathogenicite, et la traitement de cette maladie sont resumés dans le but d’aider la gestion pratique de ces patients.

Conclusion: L’hidrosadenite suppurante reste un defi clinique a la fois pour les patients et pour les medecins. Les praticiens devraient de plus se familiariser avec l’impacte de cette maladie sur le patient et avec les traitements disponibles. Les lecteurs sont dissuades d’utiliser de simples incisions comme traitement. Des etudes pathogeniques et therapeutiques supplementaires sont necessaires.

Definition

Hidradenitis Suppurativa is a recurrent disease, restricted to inverse areas, and is characterized by a progression from noninflamed nodules to painful, rounded, deep-seated inflamed lesions and subsequent scarring and chronic suppuration (Fig. 1). Nodules are restricted to the skin and may persist for years with occasional episodes of inflammation. Inflamed nodules progress into scarred lesions when spontaneously draining dermal sinus tracts appear. Sinus tracts persist and cause periodic flares of inflammation. The end stage is characterized by widespread scarring in the region.

FIGURE 1 (Photo omitted)

Photo caption: Typical hidradenitis suppurative. Recurrent abscesses with tract formation and cicatrization. Single or multiple, widely separated lesions.
Nosology

Classification of diseases or nosology is important for our understanding of the pathological processes and subsequent clinical management of disease. HS was first described by Velpeau in 1839 (quoted in ref. 8) based on the characteristic distribution of the lesions, i.e., the “anatomical predisposition” of the affected regions. Later, Verneuil described the clinical course and suggested an association with the sweat glands which were particularly “well developed” and “voluminous” in the affected areas. He identified HS as a subcutaneous process and distinguished it from furunculosis.

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Epidemiology

Studies have estimated the prevalence at 1/3000 without specifying a time frame or specific diagnostic criteria. In a study of the “hidden” or “unrecognized” dermatological diseases in patients attending a dermatological clinic, a physical examination of general dermatological patients found a point prevalence of hidradenitis at a rate of 1/1000. From interviews among healthy women (mean age 31 years), a lifetime prevalence rate of 4% was found. The women interviewed were all hospital employees (nurses and students) and therefore may have overreported events in comparison to the general population.

Later studies of a population sample in Denmark, using the proposed combined clinical definition of positive signs and symptoms and exclusion criteria, found that hidradenitis was more common than previously estimated, with a point prevalence of 4.1% (3.0-6.0%) in a younger adult population. A one-year prevalence of 1% (0.4-2.2%) in the general population was based on the subjects’ recollection only and is similar to that of other major dermatoses, e.g., psoriasis.

Active hidradenitis is generally more prevalent in women with an odds ratio of 2.9. Active genitofemoral lesions occur significantly more often in female patients, while no sex difference is seen in the rarer axillary lesions. Noninflamed quiescent nodules are also more prevalent in women and in genitofemoral lesions. Comedones have been suggested as precursor lesions for HS, but, in contrast to the manifested disease, they appear to be equally distributed in both sexes and sites.

Etiology and Pathogenic Factors

A limited number of investigations into the etiology of hidradenitis have been made. Hidradenitis has been described in dogs, but no experimental studies are available using a canine model of the disease.

Genetic Factors

HS patients report cases among their relatives more frequently than controls, and families in which hidradenitis, acne, and other poral occlusion diseases occur have been reported. However specific genetic studies have yielded conflicting results. One study has suggested that inherited factors may be important in hidradenitis following HLA-typing in 27 patients, although the results did not reach statistical significance due to the small number of patients used. A later and larger study of HLA in Swedish patients compared with a population sample did not find any HLA-A, HLA-B, HLA-DR association. One study describing an autosomal dominant pattern of inheritance has also been reported but the penetrance appeared variable, indicating that other non-genetic factors are involved.

A later review of the data has renewed the suspicion of a dominant pattern of inheritance in this group of patients using a better clinical definition of the cases. Co-occurrence of phenotypes may support a genetic linking. In case reports or series of case reports, hidradenitis has been associated with a number of diseases. Most frequently, association with Crohn’s disease (n=34) and Dowling-Dego’s disease (n=8) has been reported. However, it is unclear to what extent these reports truly reflect hidradenitis lesions as defined in the above, and even if these observations represent causal relationships or merely the coincidental findings of a comparatively common disease such as hidradenitis.

Immunological Host Factors

An immunological etiology of HS has been considered a possible predisposing factor to bacterial infection. One study found that other non-genetic factors are involved.
although individual patients may be found in whom correctable bactericidal effects can be identified. It should be noted that disease definition in this case was poor. Immunology may also play a role independent of bacteria. A pilot study suggested that excessive free oxygen radical generation by neutrophils from HS patients may be an etiologic factor, although the data are preliminary and require additional verification. Similar mechanisms have previously been implied in paradentosis and inflammatory bowel disease which share histological features with HS.

**Hormonal Factors**

Hyperandrogenic syndromes are clinically expressed in women. A clear female proponderance exists in HS. It appears to occur exclusively in adults, but it may occur as the presenting feature of adrenarche (n=5) or with acne in acromegaly (n=1).

Premenstrual flareup is reported in several studies by approximately 50% of women with hidradenitis, while improvement is reported by only a minority. Flareups may be absent in anovulatory cycles. Pregnancy and childbirth are also reported to influence the intensity of disease favorably with subsequent postpartum flareup. Reduced fecundity in some patients may be causally related to the changes in circulating sex hormones, but correlation with clinical markers of hyperandrogenism is poor.

Careful studies of cutaneous signs of virilism, including sebum secretion rate, have failed to show any significant abnormalities in hidradenitis patients, further supporting a localized androgen effect. However it should be noted that the variation in hirsutism and acne scores in hidradenitis patients was larger than in healthy controls, which may suggest that a subpopulation of patients exists in whom signs of cutaneous virilism are more pronounced and where androgens may play a pathogenic role. Antiandrogenic treatment has been found to be effective in some cases and in one randomized controlled trial. The mechanism behind this effect is not clear. In a published measurement of circulating androgens, a considerable overlap to normal values was found, suggesting that end-organ sensitivity may be involved and it has been suggested that infrainfundibular keratinocytes have an increased capacity for androgen metabolism which may play a role in follicular hyperkeratinization. There have also been studies which failed to show any abnormalities of circulating androgens in hidradenitis.

The main weaknesses with the articles relating to androgen involvement are the possible confusion with acne conglobata with HS and the wide range in the level of circulating androgen which shows a large number of patients with normal or low androgen levels. A number of patients diagnosed in these studies also had extensive acne lesions, leading to the speculation that what was interpreted as hidradenitis was in fact acne, an acknowledged androgen sensitive disorder. Finally, the possible pathogenic role of androgens is further confounded by early reports suggesting that testosterone can be used in the treatment of hidradenitis. The exact role of androgens in HS therefore remains to be established.

The use of oral contraceptives may also affect potential androgen-dependent disease. Obesity has often been suggested as an etiological factor. Previous studies have shown conflicting results: one study found HS patients to be more obese (n=11), another study was unable to reproduce the findings (n=76). It is suggested that while obesity may not be a primary pathogenic factor, it may aggravate preexisting hidradenitis through mechanical irritation, occlusion, and maceration.

**Infection**

Bacteria have traditionally been implicated in hidradenitis. Early histological studies suggested staphylococci to be causally involved, and, although later studies have separated staphylococcosis and hidradenitis as two different clinical entities, topical and systemic antibiotics are still used in the treatment of hidradenitis.

Routine microbiological culture of lesions is frequently negative, although more extensive investigations have managed to identify a number of different bacteria in lesions diagnosed as hidradenitis: staphylococci, *S. lugdeniensis*, *Strep Milleri*, *Bilophila wadsworthia*, and *anaerobes*. The species have been isolated from a wide range of lesions at many different stages and definitions of hidradenitis. Frequently, the different species of bacteria have also been found in only a few cases as a part of more general investigations of the flora of skin infections.

Sampling problems may have influenced the results of these studies. Needle aspiration of early lesions has yielded recognized pathogens in a minority of examined lesions (9/41; *S. Aureus* in 8/41 lesions and *S. Milleri* in 1/41). Patients seek medical help sooner if their lesions contain *S. aureus* than if their lesions contain other bacteria or are sterile. A more recent study has attempted to overcome the sampling problems by using laser ablation to expose the HS lesions before sampling. Using this technique, the involved structures can be visualized before sampling and thus the sampling error is abolished. In the study, positive cultures were found in all the examined patients, with *Staph. aureus* and coagulase-negative staphylococci found most frequently. Therefore it is speculated that coagulase-
negative staphylococci play a pathogenic role. These bacteria are known to produce clinically significant infections in association with nonvital tissue and artificial implants or allografts. In HS an analogous situation may exist in conjunction with the spillover of follicular material from ruptured hair follicles. IgG precipitins have been studied as an indirect measure of bacterial involvement in HS. No association between precipitins and bacteria was found, nor did the precipitins clearly differ from normal values. The highest number of precipitins was found against *S. aureus*.

Infections may co-occur with HS. A possible causal association between genitofemoral hidradenitis and *Chlamydia trachomatis* has been suggested but the organism was not found in the pus of any lesion. A study of patients attending an STD clinic failed to identify any association between *Chlamydia* infection and HS but suggested that human papilloma virus (HPV) infection was more common in HS patients. It has also been suggested that HPV infection is a cofactor in complications such as malignant degeneration of HS lesions. The possible causal relationship of HPV infection and the primary hidradenitis lesion is obscure, although the virus has been associated with palmar cysts through infection of the distal eccrine duct.

**Drugs**

Hidradenitis is rarely a side effect of drug use, but oral contraceptives (n=7) and lithium (n=1) have been associated with its development.

**Cosmetics**

Early reference suggested a causative role for cosmetics, especially in women shaving their axillae on the assumption that shaving may provide an entry point for bacterial infection. Self-reported skin irritation due to cosmetics is significantly more common in HS patients. Two studies have been unable to identify differences in the pattern of use of cosmetics, shaving, or the use of talcum in HS. Histological data which could substantiate an irritant component of early HS provide mixed results. One study found infrainfundibular spongiosis in early lesions, while another study found no signs of irritant reactions. The study by Shelley and Cahn has been interpreted to imply a role for cosmetics in HS. They epilated the axillae of 12 healthy volunteers and applied occlusive tape for one week to produce “hidradenitis-like” lesions, which is obviously different from customary use of cosmetics.

**Tobacco**

Two independent epidemiological studies have suggested that the use of tobacco by HS patients is more common than among healthy controls, although no specific mechanism has been identified to link the use of tobacco with HS. Lung and buccal cancers are more common among HS patients than in the general population as would be expected with increased tobacco smoking or chewing.

**Morphology of Hidradenitis Suppurativa**

**Histology**

Hidradenitis is a follicular disease that may secondarily involve other structures such as apocrine or eccrine glands (Fig.2). Occlusion of the hair follicle produces hidradenitis-like lesions, while destruction of the apocrine gland duct orifices produces distended apocrine glands. Pure apocrine gland affection is found in 5% of the cases, predominantly occurring in the axilla, and is clinically indistinguishable from HS. The follicular nature of the disease seen is highlighted by the description of spongiform inflammatory changes of the infrainfundibulum of early lesions. The HS lesions present a consistent histological image as shown in a study of multiple biopsies from individual patients.

Sinus tracts have been heralded as the hallmark of hidradenitis and used to further underline the similarities between hidradenitis and acne. It is not clear whether sinus tract formation is a host-specific response pattern of or a specific trait connected to the diagnosis of hidradenitis. Sinus tracts have been experimentally produced in the rhino-mouse by inserting a trans-dermal suture from one distended follicle to another, suggesting that it is related to the host rather than to the stimulus.

Based on published histological studies, it is suggested that HS is an inflammatory disease originating from the hair follicle and subsequently spreading inflammation to the surrounding tissues where characteristic secondary changes develop. Sinus tract formation is speculated to represent reparative mechanisms that encapsulate necrotic debris, and, with abnormal hair follicles, sinus tracts may create the morphological prerequisites for the subsequent chronic, recurrent course of the disease.

**FIGURE 2 (photo omitted)**

Caption: Histology of hidradenitis suppurativa. Lesions show inflammatory infiltrate surrounding hair follicles (top), while apocrine glands are unaffected (bottom).

**High-Frequency Ultrasound**

Normal hair follicles appear as elongated, parallel, low echogenic structures occurring at regular intervals within the dermis and oriented at an angle of approximately 45°-60° to the surface of the skin as seen in normal histological
specimens. In HS, changes have been found in the clinically uninvolved axillary and genitofemoral hair follicles. The follicles appear to be of a larger diameter and a distorted shape with a wider deep follicular diameter, in agreement with the clinical impression that the primary event in HS is deep-seated rather than superficial.102

Consequences and Complications

HS causes significant morbidity. The general self-reported level of health is poorer among HS patients; the average Danish patient lost 2.7 days of work per year (stages I and II) due to flareups of HS.74 Similarly, the quality of life is lower than any other dermatological disease studied using the DLQI for assessment of life quality.103 The data strongly support the clinical impression that HS is a “heart sink” condition for patients.

The soreness, discharge, and appearance of lesions are described as problems in both work and leisure activities by 51% of all patients. For grades I and II, the main problem is soreness, which can be used to assess the efficacy of treatment.74,104

A number of case reports exist describing rare but serious complications. Death due to HS has occurred (n=2).105,106 Non-lethal complications range from anemia to increased white blood cells.107 HS-associated arthritis, axial spondyloarthropathy, and sterile osteomyelitis-like lesions also occur but do not appear to be associated with HLA B27.108-110

Rare complications include benign and malignant ulcers arising from chronic hidradenitis (n=37).88,111 Squamous cell carcinomas originating from HS lesions may be associated with hypercalcemia.112 A general association between HS and cancer was confirmed in a nationwide case-control study involving all Swedish HS patients admitted to hospital between 1987 and 94.96 It was shown that HS patients have a higher overall incidence of cancer (1.5; 1.1-1.8) than the general population. The incidence of nonmelanoma skin cancer standard incidence rate (SIR) =4.6; 1.5-10.70, buccal (SIR= 5.5; 1.8-12.9), and hepatic cancer (SIR= 10.0; 2.1-29.1) was increased.

Finally, there are complications caused by the chronic inflammation of hidradenitis extending to surrounding tissues e.g., edema of the scrotum or breast, fistulas, anorectal abscesses, and polypoid outgrowths.67,113-115

Treatment

Physical or Adjuvant Treatment

Early studies stressed the usefulness of wet warm compresses, unspecified ointments, and sulphur. As an indication of the clinical difficulties of treating hidradenitis, it may be noted that some of these treatments are still used today.1 The avoidance of mechanical stress on the surface of the skin, i.e., shear forces, is also commonly recommended, although no experimental evidence exists to support the advice. It has been speculated that the abnormally thick skin and dystrophic hair follicles are more susceptible to mechanical stresses, but no experiment has yet been designed to test this hypothesis.

Radiotherapy

A body of early literature supports the use of X rays in depilatory doses and a total dose of 1.5-18 Gy. A dosage giving temporary epilation has been suggested as optimal by Zeligman.116 The dosage given in a single-session treatment schedule was 4-5 Gy (100kV, 100 mA, 0.8-mm A1 filter), reportedly with good effect and without subsequent irradiation dermatitis or scarring. This suggests that improved drainage of the follicle may be of importance to the clinical effect, although the locally immunosuppressive effect may also play a role.117-119 No randomized controlled trials (RCTs) have been conducted in this field. The possible beneficial effects of laser epilation do, however suggest that hair removal may be of independent importance (personal observation, G.B.E. Jemec).

Antibiotics

It has been pointed out that the standard length of antibiotic treatment closely resembles the duration of untreated flares in HS.38 However, antibiotics continue to be widely used in the treatment of hidradenitis. They are used as both monotherapy and in conjunction with surgery. While they are of crucial importance in the treatment of concomitant bacterial infection, antibiotics role vis-a-vis HS is currently as unclear as the role of bacteria in the disease.35

Topical clindamycin has been shown to have an effect in a double-blinded placebo-controlled study (n=30). A significant reduction of symptoms was seen within one month of treatment (p < 0.01). A subsequent 3-month double-blinded double-dummy study comparing topical clindamycin with systemic tetracyclin (n=34) failed to show significant differences between the two treatments.104,120

Hormonal Therapy

The possible beneficial effects of testosterone is a curious contrast to the results of a double-blinded crossover trial which found cyproterone acetate useful.9,63,64,121
Cyproterone acetate in combination with ethinyloestradiol is the only other treatment, apart from topical clindamycin that has been shown to have an effect in a controlled trial. A dose of 50 ug ethinyloestradiol/50 mg cyproterone acetate was compared with 50 ug ethinyloestradiol/500 ug norgestrel and found to be superior, with 29% of patients (7/24) clearing completely and 21% (5/24) improving within a 18-month followup period.129

Finasteride may also have an effect as may more aggressive manipulation of the sex hormones, e.g., the use of gonadotropin-releasing agonists in combination with oophorecto-salpingecto-hysterectomy.132,133 Combination therapy with antiandrogens and antibiotics has also been reportedly successful.134

**Immunosuppressive Treatment**

Since the disease is not a classic infectious disease universally caused by known pathogens, simple antiinflammatory treatment offers great relief for many patients. ACTH, hydrocortisone, azathioprine, and cyclosporin have all been used with good effect.35, 90, 125, 126 Prednisolone may be used as adjuvant treatment, for periodic sytemic therapy to treat flareups (personal communication, Dr. J. von der Werth) or intratessionally.127 More specific, targeted therapy using infliximab has been reported in a case, and it may hold more promise for future therapy.128 Appropriate bacteriological sampling must be obtained if antiinflammatory therapy is instituted.

Recently the successful outcome of dapson treatment has been reported.139

**Retinoids**

Retinoids have been tested in a number of case reports. No double-blinded design studies have been published. The predominant number of publications deal with the use of isotretinoin in a dosage similar to acne treatment, but reports have also been published on the use of etretinate and acitretin.25, 45, 121, 130-140 Etretinate and acitretin may have an effect in patients who are unresponsive to isotretinoin.138

The biggest case series (n=68) suggests that less than 25% of HS patients derive benefit from isotretinoin therapy, although it has been suggested that a longer treatment period may be necessary than in acne.130, 141 One review has suggested that patients in which hidradenitis occurred in conjunction with acne lesions on convex areas of the body, i.e., acne conglobata with lesions in inverse regions, were more responsive than patients in whom lesions were confined to the inverse regions.131

**Surgery**

Removal of the lesions through surgery is strongly recommended at an early stage of the disease. The published data on the efficacy of different methods are neither uniform nor extensive; a more uniform reporting would therefore improve the usefulness of future reports.

Simple lancing is ineffectual and should actively be discouraged.1, 142, 143 An improved technique involves exteriorization of the lesion.3 Proper exteriorization involves removal of the “roofs” of sinus tracts, removal of all granulation tissue by curettage, and healing by secondary intention. A similar result can be achieved by CO2 laser evaporation of the tissue. This method allows visualization of the lesions during the procedure and therefore may be less invasive that cold steel surgery. Good results have been reported with low recurrence rates and healing times of 3-5 weeks.144, 145

Specific factors appear to influence the risk of recurrence:

**The Extent of the Excision**

Single-lesion treatment offers lower immediate morbidity, while larger excisions may offer a better prognosis. Long-term followup of simple excision has shown a wide range of recurrence rates (see Table 1). This reflects two aspects of surgical treatment: First, when single or adjacent elements are excised, recurrences do occur locally even after surgery; second, patients may develop new foci of hidradenitis in another region. Local recurrences may appear either rapidly and in direct association with the scar, suggesting that diseased tissue had been left at the time of operation, or over a longer period suggesting de novo occurrence of disease. The appearance of new foci strongly suggest the disease is intrinsically multifocal.135

**The Method of Closure**

It has been argued that better results can be obtained by leaving wounds to secondary healing rather than direct closure by apposition, flaps, or grafts. In studies of secondary healing, scarring has not been reported.146,148 For large lesions this method is slow, and even though modern bandaging provides good clinical results and improved ease of management, morbidity can still be considerable for a protracted period. Healing periods of several months can be expected following large excisions.

**Location**

In addition to the extent of excision, the location may be of importance to the outcome of surgery, with perianal and axillary surgery having a lower recurrence rate than inguinoperineal or submammary excision.149, 150 It remains to be seen if the regional differences are merely a secondary factor to the size of the primary excision.

**Patient Age**

This may also play a role, with older patients having lower recurrence rates irrespective of the preoperative duration.149, 150
For chronic recurrent diseases, patient satisfaction with any given therapeutic modality is particularly important. No data are available on patient satisfaction with medical treatment, but it is generally found to be high following any kind of surgical treatment. Early and aggressive treatment is therefore recommended as are additional RCTs in this disheartening disease.

References


<table>
<thead>
<tr>
<th>Method of closure</th>
<th>Region</th>
<th>Followup Months (range)</th>
<th>Recurrence Rates</th>
<th>Year (ref.)</th>
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</thead>
<tbody>
<tr>
<td>Primary closure</td>
<td>Mixed</td>
<td>38 (? - ?)</td>
<td>21% (5/24)</td>
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<td>SSG</td>
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<td>38 (? - ?)</td>
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<td>2001 (155)</td>
</tr>
</tbody>
</table>

* SSG = split-skin graft, n.a. = not available


66. Thiboutot DM, Knaggs H, Gilliland K et al Activity of 5a reductase is greater in the follicular infrainfundibulum compared with the epidermis. Br J Dermatol 1997; 136:166-171


