REVIEW ARTICLE

Acne inversa (alias hidradenitis suppurativa)

T Jansen,†* P Altmeyer,† G Plewig‡

*Departments of Dermatology and Allergology, †Ruhr-University Bochum and ‡Ludwig-Maximilians-University, Munich, Germany. *Corresponding author: Department of Dermatology and Allergology, Ruhr-University Bochum, Gudrunstrasse 56, D-44791 Bochum, Germany, tel. + 49 0234 509 3411; fax + 49 0234 509 3409*

ABSTRACT

Acne inversa is a recurrent, suppurative disease manifested by abscesses, fistulas, and scarring. Once considered to be a disease of the apocrine glands, it is actually a defect of follicular epithelium. Thus, the term hidradenitis suppurativa is a misnomer and should be abandoned. In cases of familial acne inversa, the pattern of transmission and number of affected individuals are consistent with autosomal dominant inheritance. Aetiological factors such as hyperandrogenism, obesity, smoking and chemical irritants are not consistently associated with the affection. Bacterial involvement is not a primary event in acne inversa, but is secondary to the disease process. Potential complications include dermal contraction, local or systemic infection due to the spread of microorganisms, systemic amyloidosis, arthropathy, and squamous cell carcinoma. As spontaneous resolution is rare and progressive disability is the rule, early definitive surgical intervention is advisable. The surgical procedure of choice in most cases is wide local excision and healing by secondary intention. Pharmacotherapeutic drugs, including synthetic retinoids and antiandrogens, do not prevent progression of the disease.
Key words: acne inversa, arthropathy, hidradenitis suppurativa, hyperandrogenism, squamous cell carcinoma

Introduction

Acne inversa (alias hidradenitis suppurativa) is a chronically relapsing inflammatory skin disease characterized by recurrent draining sinuses and abscesses, predominantly in skin folds that carry terminal hairs and apocrine glands.[1] The main localizations are the axillae, groins, and perineum, but the mammary folds, genitalia, anal fold, buttocks, nape of the neck, and even the scalp may also be affected (figs 1–3). Healing occurs with substantial scarring. Polyporous comedones are a characteristic feature of previous acne inversa. The disease is probably more common than has been thought, but the diagnosis is frequently ignored or missed, leading to both patient and physician frustration. Although the exact prevalence of the disease is not known, it has been estimated at 1 : 100,[2] 1 : 300[3] or 1 : 600.[4] Jemec *et al.*[2] reported a point prevalence of 4.1%, based on objective findings in a younger adult population, although this may be falsely elevated given the select age range. Some authors believe that acne inversa is more frequent in black people,[5] yet others report no racial predilection.[6] Both men and women may be affected, but men have anogenital lesions more frequently, whereas women are more predisposed to axillary lesions.[7] The female/male ratio in most published series is 2–5 : 1.

Historical background

The disease was first described in 1839 by Velpeau[8] who reported a peculiar inflammatory process with superficial abscess formation, affecting the axillary, mammary, and perianal regions. The disease has traditionally been considered a disorder of the apocrine glands, a concept based on a series of articles by Verneuil[9,10] who named the condition hidrosadénite phlegmoneuse and suggested its association with sweat glands. Kierland[11] wrote an influential comprehensive paper on this entity in 1951. Unfortunately, he also concluded that the target of the disease was the apocrine glands. In 1955, Shelley and Cahn[12] presented an experimental model with poral occlusion induced by manual skin depilation and application of atropine impregnated tape. The resultant changes included initial keratinous obstruction with subsequent dilatation, inflammation, and bacterial invasion of the apocrine duct. However, the authors were able to achieve occlusion in only 25% of the experimental lesions, and these occlusive lesions did not

fig. 1 Axillary lesions of acne inversa, late stage with dermal contracture.

fig. 2 Submammary lesions of acne inversa.

progress to the characteristically chronic condition of acne inversa.

In 1956, Pillsbury et al.[13] coined the term follicular occlusion triad to encompass acne conglobata, hidradenitis suppurativa, and dissecting cellulitis of the scalp (perifolliculitis capitis abscedens et suffodiens). The latter picture was originally described by Hoffmann in 1907.[14] The authors argued that the central pathogenetic event, as in acne vulgaris, was follicular hyperkeratinization, distension of the infundibulum leading to rupture, and colonization by a variety of pathogenic bacteria. They viewed retention hyperkeratosis as the primary event but again they thought that the vast destruction of tissue was a consequence of the involvement of the apocrine glands. Plewig and Kligman[15] in their textbook on acne added to the original triad another feature, pilonidal sinus (pilonidal cyst), thus creating

fig. 3 Severe involvement of the buttocks in acne inversa.

the acne tetrad as retrospectively all four could be associated with acne. In 1989, Plewig and Steger[16] introduced the term acne inversa based on the follicular origin of the disease. It is now time to flush out all outdated synonyms for this disease, including hidradenitis suppurativa and pyodermia fistulans sinifica,[17] which we now call acne inversa.

Acne inversa is a disease of the follicular epithelium

More recent studies have identified acne inversa as a disorder of follicular rather than apocrine occlusion. For example, Yu and Cook[18] compared skin samples from acne inversa with controls and found no significant morphological abnormalities of the apocrine glands. The one-third of cases presenting inflammatory changes involving the apocrine glands presented extensive inflammation that also involved other structures such as the eccrine glands and hair follicles. Attanoos et al.[19] also studied the skin biopsies of acne inversa and reported a consistent finding of follicular occlusion in all specimens compared with controls and regardless of disease duration. Jemec et al.[20] examined a total of 51 specimens from 11 patients with acne inversa; of these 30 were from synchronous biopsies and 21 from consecutive biopsies. The majority of specimens (44 of 51) contained poral occlusion, sinus tracts or cysts. This pattern was present in 50–85% of the specimens from each individual subject with acne inversa. No primary apocrine involvement was seen. The authors suggested that the homogeneous histopathology of acne inversa supports its classification as a follicular disease. From a series of 27 consecutive patients, Boer and Welterveden[21] collected clinical data and examined the histopathological pattern in biopsies of newly formed nodules. Histopathological findings showed an occluding spongiform infundibulofolliculitis with secondary involvement of apocrine glands. The results of this prospective study confirmed former histopathological studies, indicating that acne inversa is a disease of the follicular epithelium. Thus, apocrine gland involvement is only incidental or secondary to the primary developments that involve the terminal hair follicle. As a

consequence, there is no significant difference in the size or density of the apocrine glands in patients with acne inversa compared with controls, but the apocrine glands of individuals with axillary hyperhidrosis are significantly larger than those of subjects with acne inversa or controls.[22]

Acne inversa has been reported to coexist with other skin diseases that show poral occlusion, e.g., Fox–Fordyce disease,[23] pityriasis rubra pilaris,[24] acanthosis nigricans,[25] steatocystoma multiplex[26] and Dowling–Degos disease.[27,28] It is therefore possible that the genetic abnormalities of the follicle are shared by these conditions, thus predisposing to follicular occlusion.

Different from acne vulgaris, acne inversa is localized in non-facial regions, where there are terminal, pigmented, coarse hairs, as in the axillae, groins, anal fold, mons pubis, and scalp. This is the reason why the sebum excretion rate is not increased in acne inversa.[29] The regions affected by acne inversa tend to be rich in apocrine glands, which are part of the apocrine–pilosebaceous unit. Thus, it is understandable that the apocrine glands would be engulfed in the inflammatory process.

However, apocrine involvement, serious as it might be, is a secondary event, as demonstrated by our histopathological studies on many subjects with acne inversa. Control specimens were obtained from individuals undergoing surgical excision of axillary skin for the treatment of hyperhidrosis. The sections were cut stepwise, and the histological pictures were examined with particular attention to early histopathological changes. The results of our studies can be summarized as follows. The earliest inflammatory event in acne inversa is a segmental rupture of the follicular epithelium, followed by spilling of foreign body material, such as corneocytes, bacteria, sebum products, and hairs, into the dermis. The dumping of foreign products initiates an inflammatory response provoking foreign body granuloma, and epithelial strands try to encapsulate the necrotic tissue. The apocrine glands are not involved in the earliest stage of follicular hyperkeratosis. Once rupture of the follicular epithelium has occurred, the disease spreads rapidly.

The draining sinus is a late complication of acne inversa, leading to extensive, periodically inflamed lesions that are undermined by a system of fistulas. Kurzen *et al.*[30] identified three phenotypes of stratified squamous epithelia covering the draining sinuses: type 1 epithelium was cornified with epidermis-type characteristics; type 2 was non-cornified with different characteristics; and type 3 was non-cornified and prominently inflamed. The three phenotypes have been characterized as pathological stratified squamous epithelia reflecting the dynamic process of inflammation, proliferation, and stratification that occur in acne inversa.

Aetiology and pathogenesis

Acne inversa is a highly chronic disorder, but the pathogenesis of the affection is still not well understood. Some studies have shown an incidence of metabolic disorders, including diabetes

mellitus, or an abnormal glucose tolerance test of 10–33% in acne inversa subjects,[31–34] but other studies did not confirm these observations. No primary abnormalities of the cellular or humoral immune system can be held to be causal in every case. In 1977, a study of seven subjects with acne inversa found cell-mediated immunity and neutrophil function to be normal.[35] A later study of 27 cases showed that seven of the most severely affected subjects had a marked reduction in T-lymphocyte counts.[33] An increase in circulating suppressor T cells corrected by tolmetin sodium has been demonstrated.[36] A subject with a defect in polymorphonuclear leucocyte killing of bacteria associated with low levels of intracellular cyclic guanosine monophosphate has also been described.[37] The occurrence of pyoderma gangrenosum as a complication of acne inversa indicates a possible immunity disorder underlying the chronic suppurative process,[38] and in these cases the favourable response of both pyoderma gangrenosum and acne inversa to cyclosporin A supports this theory. Congenital α1-antitrypsin deficiency has been anecdotally reported,[39] but could not be confirmed in a large case series. Abnormal laboratory values associated with acne inversa may include increased erythrocyte sedimentation rate, leucocytosis, decreased serum iron and changes in serum electrophoresis pattern; such changes can be considered due to the chronic inflammatory process.[1,16]

Lithium therapy has also been implicated in the pathogenesis of acne inversa.[40,41] It has been suggested that lithium may cause lysosomal enzyme release and enhanced polymorphonuclear cell chemotaxis, thereby contributing to the inflammation in acne inversa.

There is evidence that the transmission of acne inversa in some families is consistent with single gene dominant inheritance, and thus it is probable that genetic predisposition is important in this disorder, but to date not enough is known in this regard. In 1984, Fitzsimmons *et al.*[42] studied three families with a total of 21 affected members. They reported that the pattern of transmission and number of affected individuals were consistent with autosomal dominant inheritance. Later, they studied the families of 26 subjects with acne inversa,[3,43] comprising a total of 62 affected individuals, 34% of whom were first-degree relatives in 11 families. This fell short of the 50% expected of an autosomal dominant condition. In the same study, there was a negative family history in nine families and familial occurrence only in a further three families. However, both psychosocial issues and problems of ascertainment may have been responsible for false negative family histories.

Recently, von der Werth *et al.*[44] tested the reproducibility of an autosomal dominant inheritance for acne inversa in the original study group and the original probands of previously unaffected family members. In the group where a positive family history had been noted previously, 27% of first-degree relatives were definitely affected by the disease. The concept of autosomal dominant inheritance in families from this group was further strengthened by the detection of nine new acne inversa

cases, in seven of whom the disease developed after the previous study. It is difficult to reconcile the female predominance evidenced in most studies with the proposed autosomal dominant inheritance. If acne inversa were a largely genetically determined disease, then one would have to consider the possibility of hormonal influences on gene expression or even the possibility of an X-chromosomal disease. HLA-A1 and HLA-B8 may predispose the affected subject to more severe disease,[33] but further investigations are necessary to confirm this.

Acne inversa has been reported to be associated with overt endocrine disorders, such as Cushing's syndrome[45] and acromegaly,[46] indicating that hormonal factors play an aetiological part in the development of the disease. In addition, acne inversa has been regarded as an androgen-dependent disorder.[47] There is a female predominance, and the disease usually does not occur before puberty. In women, it may persist into the climacteric, but onset after menopause is rare.[48] Acne inversa is rarely a presenting feature of premature adrenarche, leading support to the view that it is an androgen-dependent disorder.[49]

It has been suggested that enhanced peripheral conversion of androgens by apocrine glands play a critical part in the pathogenesis of acne inversa. However, Barth and Kealey[50] found equivalent activity of three peripheral androgen-converting enzymes in axillary apocrine glands of subjects with acne inversa compared with those of controls.

A relationship between acne inversa and hyperandrogenism is largely based on the finding of an increased free androgen index [testosterone/sex hormone binding globulin (SHBG)] due to a low sex SHBG, but the subjects were not controlled for body mass index (BMI).[51] This finding is compromised, as many subjects are significantly overweight,[52] and SHBG is negatively correlated with BMI.[53] Another study could only demonstrate hyperandrogenism in a subgroup of women who did not experience a premenstrual flare in their disease.[52] Recently, no supporting evidence for hyperandrogenism or suppression of SHBG has been found in women with acne inversa compared with age-, weight-, and hirsutes-matched controls.[48]

Chemical irritants such as deodorants, mechanical irritation, depilation, and shaving have been considered as aetiological factors by some investigators. However, Morgan and Leicester[54] retrospectively compared 40 subjects who had acne inversa with 40 age-matched controls and found no significant difference in the use of these items. Friction in intertriginous locations may be a contributory factor but cannot explain acne inversa on the nape of the neck and the scalp. Jemec and Gniadecka[55] studied the *in vivo* echostructure, hair follicle shape, and dermal thickness in acne inversa by high-frequency (20-MHz) B-mode ultrasound examination of lesional and paralesional skin. The results indicated that an increased skin thickness and resulting differences in the mechanical properties of the skin could be an important aetiological factor in the development of acne inversa. It was unclear, however, whether the skin thickening in acne inversa is a primary or secondary manifestation. Obesity is

another commonly cited aetiological factor. A study by Jemec[56] compared the weight of patients who had acne inversa with the corresponding ideal body weight and found no significant differences from controls. Thus, obesity may not be an aetiological factor, although the increased skin-to-skin contact may promote follicular hyperkeratosis.

The significance of bacterial findings in acne inversa is controversial. We believe with many others that bacterial involvement is not a primary pathogenic event in acne inversa, but that it is secondary to the disease process. It is likely that secondary bacterial colonization can intensify chronic inflammation. In most studies of acne inversa, samples for bacteriological culture have been collected from the surface of the lesions. With this technique, however, contamination from resident skin bacteria obscured the interpretation of the culture result. Recently, Jemec *et al.*[57] circumvented the problem by introducing a method for bacteriological sampling from the deeper parts of acne inversa by an aspiration technique. The cultures were negative in half of the cases. Thus, bacteriological analysis of aspirates from deeper parts of acne inversa may show low sensitivity. Lapins *et al.*[58] used a carbon dioxide laser method to evaporate diseased tissue level by level from the surface downwards, allowing concurrent sampling of bacteriological cultures from each level and thereby minimizing contamination with bacteria from the level above. They found that *Staphylococcus aureus* and coagulase-negative staphylococci were the most common bacteria in cultures from the deep portions of acne inversa lesions.

Brook and Frazier[59] studied the aerobic and anaerobic microbiology of this condition in a retrospective review of the microbiological and clinical data of 17 specimens obtained from axillary acne inversa over a period of 6 years. A total of 42 bacterial isolates were obtained, 12 aerobic or facultative and 30 anaerobic or microaerophilic. Aerobic and facultative bacteria were isolated in six cases, anaerobic bacteria in seven, and mixed aerobic and anaerobic bacteria in four. The predominant aerobic bacteria were *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Pseudomonas aeruginosa*. The most frequently isolated anaerobic strains were *Peptostreptococcus* spp., *Prevotella* spp., microaerophilic streptococci, *Fusobacterium* spp., and *Bacterioides* spp. *sensu stricto*. In conclusion, the flora of microorganisms found in acne inversa lesions is not constant and may change unpredictably.

Various bacteria can be isolated from the sinuses, particularly staphylococci, streptococci and Gram-negative rods. With perianal disease, there is an increased incidence of *Escherichia coli*, *Klebsiella* and *Proteus* as well as anaerobic bacteria. Several investigators have found that *Streptococcus milleri* is a major pathogen in perianal acne inversa. *Streptococcus milleri* is an organism that frequently colonizes the gastrointestinal and female genital tracts. Highet *et al.*[60] reported that the presence of *Streptococcus milleri* significantly correlated with disease activity. However, *Streptococcus milleri* was subsequently sought

in another study of 32 cases but was not found in any of the specimens.[33] *Chlamydia trachomatis* has been implicated in perineal acne inversa. Bendahan *et al.*[61] showed that six of seven subjects in the acne inversa group demonstrated IgA antibodies to *Chlamydia trachomatis*, compared with none in the control group. These findings, however, have not been confirmed.

The high percentage of active smokers among subjects with this disease has been interpreted to suggest that cigarette smoking is a major triggering factor of acne inversa. In a matched-pair case–control study, 88.9% of 63 subjects with acne inversa were active smokers, whereas the rate of smokers in the matched-pair control group was only 46% ($P < 0.001$).[62] These findings were similar to those of a previous retrospective study by Breitkopf *et al.*[63] who reported that 85% of the men and 84% of the women in a total 149 cases of acne inversa were smokers. It remains unclear precisely what pathogenetic mechanisms would be responsible for the effect of smoking on the manifestation of acne inversa, but an altered chemotaxis of polymorphic neutrophils could play a part. However, large multicentre studies are necessary to identify definitely the role of smoking in the pathogenesis of acne inversa. It is questionable whether or not stopping smoking leads to improvement of the disease.

Complications

The chronic inflammatory process may lead to scars and dermal contractures. Swellings of elephantiasis nostras following streptococcal complications may be superimposed on acne inversa lesions leading to monstrous enlargement and distortion of external genitalia.[64,65] Urethral fistula and sinus formation is another uncommon complication of the disease.[66] The most serious but rare long-term complication is development of squamous cell carcinoma, occasionally with metastases, on the background of the chronic inflammation, mostly occurring in men in the anogenital area.[67–72] The time interval between the diagnosis of acne inversa and appearance of squamous cell carcinoma is, on average, 19 years. Bacterial meningitis,[73] bronchitis, pneumonia[74] and systemic amyloidosis[75] are other serious and sometimes fatal complications.

A spectrum of articular manifestations has been reported in subjects with acne inversa. The combination of arthritis and acne inversa is rare,[76] previous reviews having mostly described arthritis occurring in combination with both acne conglobata and acne inversa rather than acne inversa alone.[77] The arthritis described is seronegative, typically asymmetrical, and affects the knee, ankle, and elbow joints most often, and occurs in subjects between the ages of 22 and 46 years with equal sex incidence. Axial involvement, typically sacroiliitis, also occurs. There have been reports describing the arthritis as occurring before the skin condition,[78] but in most cases onset of the arthritis follows the skin lesions by 2–25 years. In most cases the arthritis is episodic, oligoarticular, and non-deforming, but a

few patients have progressive disease with joint erosions and ankylosis and require aggressive immunosuppressive therapy to control the disease. Rosner *et al.*[77] found no significant HLA association in their study, although there was a suggestion of B27 association with more severe sacroiliitis. The presence of HLA-DR or D antigens was not evaluated. Vasey *et al.*[79] reported finding DR4 in all six of their cases with arthropathy. However, there has been no further confirmation of this observation. Analysis of circulating immune complexes when present to find any bacterial antigens may be useful in evaluating the role of bacteria in the pathogenesis of the arthropathy-associated acne inversa. Arthritis associated with acne conglobata and acne inversa is a condition that may fall within the spectrum of SAPHO syndrome (synovitis, acne, palmoplantar pustulosis, hyperostosis, and osteitis) and other HLA-B27-negative spondyloarthropathies.

Differential diagnosis

Acne inversa is often a diagnostic challenge, particularly when it presents with odd variants, in which case one has to search for other signs of the disease from the history and by total-body examination. Acne inversa should be differentiated from foruncles, carbuncles, vegetating pyoderma, tuberculosis subcutanea et fistulosa, actinomycosis, and lymphogranuloma inguinale. The differentiation of acne inversa and Crohn's disease merits special attention. Perianal lesions are the initial presentation in 5% of all cases of Crohn's disease and, at times, these two diseases may be clinically indistinguishable. Evaluation of perianal lesions includes proctoscopy to access any involvement of the anus or rectum. Several investigators have reported the comorbidity of acne inversa and Crohn's disease.[80–83] Church *et al.*[81] retrospectively reviewed 61 cases of acne inversa and found that 38% had a concomitant diagnosis of Crohn's disease, the latter typically preceding the development of acne inversa. Tsianos *et al.*[83] speculated that acne inversa appears to be another cutaneous manifestation of Crohn's disease. However, this remains to be verified.

Treatment

When properly diagnosed and adequately treated, the early stages of the disease can be controlled with medical measures. However, in established acne inversa there is no evidence that treatment other than surgery has any effect on the natural course of the condition.

Topical treatments, including antiseptics, antibiotics, and corticosteroids, are usually only of limited benefit. Clindamycin, in particular, has been favoured in the literature. Clemmensen[84] treated 30 subjects with either clindamycin or placebo in a double-blind trial and reported significant improvement without side-effects. Acne inversa shows a much less favourable response to systemic antibiotics than acne vulgaris. In a clinical

study, therapy with systemic tetracycline did not show better results than topical therapy with clindamycin.[85] In general, after withdrawal of antibiotic treatment, relapse of acne inversa is almost inevitable. Although antibiotics are not curative, they may diminish odour and discharge, and reduce pain. Systemic[86] or intralesional[87] corticosteroids have been used with variable results, but may be of transient benefit in some patients.

The concept of acne inversa as an androgen-dependent disease has led to attempts at hormonal therapy. One report details seven women with acne inversa after starting oral contraceptive use, which improved after stopping or changing the oral contraceptive to a higher oestrogen/progesterone ratio.[88] Sawers *et al.*[89] reported on four women with acne inversa who responded within 2 months to treatment with cyproterone acetate and ethinyl oestradiol. When the cyproterone acetate was reduced to half the original dosage, three of the four subjects showed worsening. After discontinuing therapy, two of the four subjects maintained the same level of improvement for several months. Mortimer *et al.*[90] carried out a double-blind, controlled, cross-over trial comparing ethinyl oestradiol/cyproterone acetate with ethinyl oestradiol/norgestrel treatments in 24 women with acne inversa. Both regimens produced significant improvement, including seven subjects free of disease at 18 months, five improved, four unchanged, and two worsened. The remaining six subjects withdrew because of side-effects or disease exacerbation. Farrell *et al.*[91] reported the beneficial use of finasteride, a competitive inhibitor of the 5-α reductase type II enzyme, in two cases of severe, long-standing acne inversa. In our experience, antiandrogen therapy has been effective for a few subjects, while remaining ineffective for most others. Treatment using gonadotrophin-releasing hormone agonists in combination with dexamethasone[92] or total abdominal hysterectomy and bilateral salpingo-oophorectomy[93] have been shown to eradicate persistent acne inversa in individual cases. In conclusion, hormonal influence remains controversial. However, the theoretical basis for hormonal treatments makes this an interesting future field of investigation.

Because isotretinoin (13-*cis*-retinoic acid) is effective in acne vulgaris it seems reasonable to suppose that isotretinoin might also be effective in acne inversa, as shown in a few reports in the literature.[94] However, isotretinoin is, with rare exceptions, insufficient to stop the disease.[95–97] The experience of Boer and van Gemert,[98] who administered low-dose isotretinoin monotherapy in 68 cases over a period of almost 9 years, has confirmed our impression and previous reports that isotretinoin is only of limited value in treating acne inversa. However, we recommend the use of oral isotretinoin because of its anti-inflammatory activity during the weeks or months before surgery and even postoperatively.

Chow and Mortimer[99] have reported that etretinate and acitretin are more effective than isotretinoin. There have been reports of successful treatment with etretinate[99] and acitretin[100] in cases previously unresponsive to isotretinoin.

Radiotherapy has been used in some series but often fails to eradicate the lesions completely; troublesome sinuses and scarring may follow.[101]

Although incision and drainage and exteriorization of individual lesions may be useful in some instances, radical surgical excision at the earliest recognized stage remains a mainstay of therapy. Various surgical techniques have been employed for treating acne inversa.[6,102] The complete excision of all involved skin and tissues is necessary to ensure eradication of the condition. A comparison of techniques is difficult because of the various methods of excision and reconstruction used. Split-thickness skin grafts, fasciocutaneous flaps, and primary closure have been advocated for repairing the surgical defects.

Available data indicate that inadequate excision is the main reason for recurrence and that radical excision with healing by secondary intention is the treatment of choice in most cases. Ritz *et al.*[103] examined the extent of surgery in terms of the clinical course of acne inversa. The operative procedures were divided into drainage procedures, limited regional, and radical wide excisions. At a mean follow up of 72 months, they found developed locoregional recurrence of acne inversa in 45% of cases. There was 100% recurrence after drainage, 42.8% after limited, and 27% after radical excision. Acne inversa recurred after a median interval of 3 months for drainage, 11 months for limited excision, and 20 months for radical excision. The disease-free interval continued up to 35 months. A study by Harrison *et al.*[104] reported the following rates of recurrence in 82 subjects treated with 118 radical excisions: axillary, 3%; perianal, 0%; inguinoperineal, 37%; and submammary, 50%. In this study, recurrence appeared 3–72 months after surgery, with a median of 24 months. Poor success rates in cases of submammary disease have led some investigators to avoid recommending formal surgical excision for this region.

Carbon dioxide laser excision is another treatment option for acne inversa.[105,106] Finley and Ratz[105] treated seven subjects with carbon dioxide laser excision and reported a healing time of 4–8 weeks. They considered the advantage of laser treatment to be improved haemostasis, which affords better visualization and therefore more complete removal of affected tissue. Carbon dioxide laser treatment is a rapid, efficient, and economical treatment of acne inversa that gives good results especially when done by an experienced technician.

Therapeutic interventions in the articular manifestations of acne inversa have centred mainly on anti-inflammatory medications with the presumption that the underlying pathogenesis was immunological. Treatments employed have included non-steroidal anti-inflammatory drugs, corticosteroids, methotrexate, and D-penicillamine.

Prognosis

With rare exceptions, surgical intervention is sufficient to stop the disease. Too often precious time is lost with inadequate

treatment, with the consequence that many affected individuals drift away from society, and many subjects develop new lesions at a site not affected at the time of their initial surgery. Although spontaneous resolution may occur, this is rare. This reinforces the need for early recognition and treatment of this potentially disabling disease.

References

1 Jansen T, Plewig G. Acne inversa. *Int J Dermatol* 1998; **37**: 96–100.

2 Jemec GBE, Heidenheim M, Nielsen NH. The prevalence of hidradenitis suppurativa and its potential precursor lesions. *J Am Acad Dermatol* 1996; **35**: 191–194.

3 Fitzsimmons JS, Guilbert PR, Fitzsimmons EM. Evidence of genetic factors in hidradenitis suppurativa. *Br J Dermatol* 1985; **113**: 1–8.

4 Harrison BJ, Mudge M, Hughes LE. The prevalence of hidradenitis suppurativa in South Wales. In: Marks R, Plewig G, editors. *Acne and Related Disorders*. Martin Dunitz, London, 1989: 365–366.

5 Paletta C, Jurkiewicz MJ. Hidradenitis suppurativa. *Clin Plast Surg* 1987; **14**: 383–390.

6 Banerjee AK. Surgical treatment of hidradenitis suppurativa. *Br J Surg* 1992; **79**: 863–866.

7 Jemec GBE. The symptomatology of hidradenitis suppurativa in women. *Br J Dermatol* 1988; **119**: 345–350.

8 Velpeau A. In: *Dictionnaire de Médecine, un Répertoire Général des Sciences Médicales sous la Rapport Théorique et Practique* 2nd edn, Vol. 2. Bechet Jeune, Paris, 1839: 91.

9 Verneuil A. Études sur les tumeurs de la peau et quelques maladies des glandes sudoripares. *Arch Gén Méd* 1854; **94**: 447–468, 693–705.

10 Verneuil A. De l'hidrosadénite phlegmoneuse et des abcés sudoripares. *Arch Gén Méd* 1864; **114**: 537–557, 1865; **115**: 327–337, 437–453.

11 Kierland RR. Unusual pyodermas (hidrosadenitis suppurativa, acne conglobata, dissecting cellulitis of the scalp). A review. *Minn Med* 1951; **34**: 319–341.

12 Shelley WB, Cahn MM. The pathogenesis of hidradenitis suppurativa in man: experimental and histologic observations. *Arch Dermatol* 1955; **72**: 562–565.

13 Pillsbury DM, Shelley WB, Kligman AM. Dermatology. 1st edn.Saunders, Philadelphia, 1956: 482–484, 489.

14 Hoffmann E. Perifolliculitis capitis abscedens et suffodiens. Berliner Dermatologische Gesellschaft. Sitzung am 12 November 1907. *Dermatol Z* 1908; **15**: 120–135.

15 Plewig G, Kligman AM. Acne. *Morphogenesis and Treatment*. Springer, Berlin, 1975: 192–193.

16 Plewig G, Steger M. Acne inversa (alias acne triad, acne tetrad or hidradenitis suppurativa). In: Marks R, Plewig G, editors. *Acne and Related Disorders*. Martin Dunitz, London, 1989: 345–357.

17 Krauspe C, Stelzner F. Die Pyodermia fistulans sinifica. *Chirurg* 1962; **33**: 534–538.

18 Yu CCW, Cook MG. Hidradenitis suppurativa: a disease of follicular epithelium, rather than apocrine glands. *Br J Dermatol* 1990; **122**: 763–769.

19 Attanoos RL, Appleton MA, Douglas-Jones AG. The pathogenesis of hidradenitis suppurativa: a closer look at apocrine and apoeccrine glands. *Br J Dermatol* 1995; **133**: 254–258.

20 Jemec GBE, Thomsen BM, Hansen U. The homogeneity of hidradenitis suppurativa lesions. A histological study of intra-individual variation. *APMIS* 1997; **105**: 378–383.

21 Boer J, Weltevreden EF. Hidradenitis suppurativa or acne inversa. A clinicopathological study of early lesions. *Br J Dermatol* 1996; **135**: 721–725.

22 Morgan WP, Hughes LE. The distribution, size and density of the apocrine glands in hidradenitis suppurativa. *Br J Surg* 1979; **66**: 853–856.

23 Spiller JF, Knox J. Fox-Fordyce disease with hidradenitis suppurativa. *J Invest Dermatol* 1958; **31**: 127–135.

24 Bergeron JR, Stone OJ. Follicular occlusion triad in a follicular blocking disease (pityriasis rubra pilaris). *Dermatologica* 1968; **136**: 362–367.

25 Stone OJ. Hidradenitis suppurativa following acanthosis nigricans. Report of two cases. *Arch Dermatol* 1976; **112**: 1142.

26 McDonald RM, Reed WB. Natal teeth and steatocystoma multiplex complicated by hidradenitis suppurativa. A new syndrome. *Arch Dermatol* 1976; **112**: 1132–1134.

27 Bedlow AJ, Mortimer PS. Dowling-Degos disease associated with hidradenitis suppurativa. *Clin Exp Dermatol* 1996; **21**: 305–306.

28 Weber LA, Kantor GR, Bergfeld WF. Reticulate pigmented anomaly of the flexures (Dowling-Degos disease): a report associated with hidradenitis suppurativa and squamous cell carcinoma. *Cutis* 1990; **45**: 446–450.

29 Jemec GBE, Gniadecka M. Sebum excretion in hidradenitis suppurativa. *Dermatology* 1997; **194**: 325–328.

30 Kurzen H, Jung EG, Hartschuh W *et al.* Forms of epithelial differentiation of draining sinus in acne inversa (hidradenitis suppurativa). *Br J Dermatol* 1999; **141**: 231–239.

31 Chapman J. The surgical treatment of hidradenitis suppurativa. *J Natl Med Assoc* 1972; **64**: 328–330.

32 Endo Y, Tamura A, Ishikawa O, Miyachi Y. Perianal hidradenitis suppurativa: early surgical treatment gives good results in chronic or recurrent cases. *Br J Dermatol* 1998; **139**: 906–910.

33 O'Loughlin S, Woods R, Kirke PN *et al.* Hidradenitis suppurativa. Glucose tolerance, clinical, microbiologic, and immunologic features and HLA frequencies in 27 patients. *Arch Dermatol* 1988; **124**: 1043–1046.

34 Wiltz O, Schoetz DJ Jr, Murray JJ *et al.* Perianal hidradenitis suppurativa. The Lahey Clinic experience. *Dis Colon Rectum* 1990; **33**: 731–734.

35 Dvorak VC, Root RK, MacGregor RR. Host-defense mechanisms in hidradenitis suppurativa. *Arch Dermatol* 1977; **113**: 450–453.

36 McDaniel DH, Welton WA. Furunculosis and hidradenitis suppurativa response. *Arch Dermatol* 1984; **120**: 437.

37 Ginder PA, Ousley M, Hinthorn D *et al*. Hidradenitis suppurativa: evidence for a bactericidal defect correctable by cholinergic agonist *in vitro* and *in vivo*. *J Clin Immunol* 1982; **2**: 237–241.

38 Buckley DA, Rogers S. Cyclosporin-responsive hidradenitis suppurativa. *J R Soc Med* 1995; **88**: 289–290.

39 Eberle F, Adler G, Roth SL. Pyodermia fistulans sinifica und kongenitaler Alpha-1-Antitrypsinmangel. *Hautarzt* 1980; **31**: 100–104.

40 Gupta AK, Knowles SR, Gupta MA *et al*. Lithium therapy associated with hidradenitis suppurativa: case report and a review of the dermatologic side effects of lithium. *J Am Acad Dermatol* 1995; **32**: 382–386.

41 Marinella MA. Lithium therapy associated with hidradenitis suppurativa. *Acta Derm Venereol (Stockh)* 1997; **77**: 483.

42 Fitzsimmons JS, Fitzsimmons EM, Gilbert G. Familial hidradenitis suppurativa: evidence in favour of single gene transmission. *J Med Genet* 1984; **21**: 281–285.

43 Fitzsimmons JS, Guilbert PR. A family study of hidradenitis suppurativa. *J Med Genet* 1985; **22**: 367–373.

44 Von der Werth JM, Williams HC, Raeburn JA. The clinical genetics of hidradenitis suppurativa revisited. *Br J Dermatol* 2000; **142**: 947–953.

45 Curtis AC. Cushing's syndrome and hidradenitis suppurativa. *Arch Dermatol Syphilol* 1950; **62**: 329–330.

46 Chalmers RJG, Ead RD, Beck MH *et al*. Acne vulgaris and hidradenitis suppurativa as presenting features of acromegaly. *Br Med J* 1983; **287**: 1346–1347.

47 Ebling FJG. Hidradenitis suppurativa: an androgen-dependent disorder. *Br J Dermatol* 1986; **115**: 259–262.

48 Barth JH, Layton AM, Cunliffe WJ. Endocrine factors in pre- and postmenopausal women with hidradenitis suppurativa. *Br J Dermatol* 1996; **134**: 1057–1059.

49 Lewis F, Messenger AG, Wales JKH. Hidradenitis suppurativa as a presenting feature of premature adrenarche. *Br J Dermatol* 1993; **129**: 447–448.

50 Barth JH, Kealey T. Androgen metabolism by isolated human axillary apocrine glands in hidradenitis suppurativa. *Br J Dermatol* 1991; **125**: 304–308.

51 Mortimer PS, Dawber RPR, Gales MA, Moore RA. Mediation of hidradenitis suppurativa by androgens. *Br Med J* 1986; **292**: 245–248.

52 Harrison BJ, Read GF, Hughes LE. Endocrine basis for the clinical presentation of hidradenitis suppurativa. *Br J Surg* 1988; **75**: 972–975.

53 Franks S, Kiddy DS, Hamilton-Fairley D *et al*. The role of nutrition and insulin in the regulation of sex hormone binding globulin. *J Steroid Biochem Mol Biol* 1991; **39**: 835–838.

54 Morgan WP, Leicester G. The role of depilation and deodorants in hidradenitis suppurativa. *Arch Dermatol* 1982; **118**: 101–102.

55 Jemec GBE, Gniadecka M. Ultrasound examination of hair follicles in hidradenitis suppurativa. *Arch Dermatol* 1997; **133**: 967–970.

56 Jemec GBE. Body weight in hidradenitis suppurativa. In: Marks R, Plewig G, editors. *Acne and Related Disorders*. Martin Dunitz, London, 1989: 375–376.

57 Jemec GBE, Faber M, Gutschik E, Wendelboe P. The bacteriology of hidradenitis suppurativa. *Dermatology* 1996; **193**: 203–206.

58 Lapins J, Jarstrand C, Emtestam L. Coagulase-negative staphylococci are the most common bacteria found in cultures from the deep portions of hidradenitis suppurativa lesions, as obtained by carbon dioxide laser surgery. *Br J Dermatol* 1999; **140**: 90–95.

59 Brook I, Frazier EH. Aerobic and anaerobic microbiology of axillary hidradenitis suppurativa. *J Med Microbiol* 1999; **48**: 103–105.

60 Highet AS, Warren RE, Staughton RC, Roberts SO. *Streptococcus milleri* causing treatable infection in perineal hidradenitis suppuratia. *Br J Dermatol* 1980; **103**: 375–381.

61 Bendahan J, Paran H, Kolman S *et al*. The possible role of *Chlamydia trachomatis* in perineal suppurative hidradenitis. *Eur J Surg* 1992; **158**: 213–215.

62 König A, Lehmann C, Rompel R, Happle R. Cigarette smoking as a triggering factor of hidradenitis suppurativa. *Dermatology* 1999; **198**: 261–264.

63 Breitkopf C, Bockhorst J, Lippold A *et al*. Pyodermia fistulans sinifica (Akne inversa) und Rauchgewohnheiten. *Z Hautkr* 1995; **70**: 332–334.

64 Grösser A. Surgical treatment of chronic axillary and genito-crural acne conglobata by split-thickness skin grafting. *J Dermatol Surg Oncol* 1982; **8**: 391–398.

65 Konety BR, Cooper T, Flood HD, Futrell JW. Scrotal elephantiasis associated with hidradenitis suppurativa. *Plast Reconstr Surg* 1996; **97**: 1243–1245.

66 Buckley C, Sarkany I. Urethral fistula and sinus formation in hidradenitis suppurativa. *Clin Exp Dermatol* 1989; **14**: 158–160.

67 Anstey AV, Wilkinson JD, Lord P. Squamous cell carcinoma complicating hidradenitis suppurativa. *Br J Dermatol* 1990; **123**: 527–531.

68 Dufresne RG Jr, Ratz JL, Bergfeld WF. Squamous cell carcinoma arising from the follicular occlusion triad. *J Am Acad Dermatol* 1996; **35**: 475–477.

69 Manolitsas T, Biankin S, Jaworski R, Wain G. Vulval squamous cell carcinoma arising in chronic hidradenitis suppurativa. *Gynecol Oncol* 1999; **75**: 285–288.

70 Mendonca H, Rebelo C, Fernandes A *et al*. Squamous cell carcinoma arising in hidradenitis suppurativa. *J Dermatol Surg Oncol* 1991; **17**: 830–832.

71 Shukla VK, Hughes LE. A case of squamous cell carcinoma complicating hidradenitis suppurativa. *Eur J Surg Oncol* 1995; **21**: 106–109.

72 Zachary LS, Robson MC, Rachmaninoff N. Squamous cell carcinoma occurring in hidradenitis suppurativa. *Ann Plast Surg* 1987; **18**: 71–73.

73 Nobl G. Follikularprozeß der Kopfhaut. *Arch Dermatol Syphilol* 1905; **74**: 80.

74 Wöbling RH, Milbradt R. Akne conglobata et sinifica sive Pyodermia fistulans sinifica. *Akt Dermatol* 1985; **11**: 198–199.

75 Duperrat B, Meunier P, Pringuet R. Acné conglobata fessière: discussion d'une amylose secondaire. *Bull Soc Fr Dermatol Syphiligr* 1957; **64**: 264–266.

76 Bhalla R, Sequeira W. Arthritis associated with hidradenitis suppurativa. *Ann Rheum Dis* 1994; **53**: 64–66.

77 Rosner IA, Burg CG, Wisnieski JJ *et al.* The clinical spectrum of the arthropathy associated with hidradenitis suppurativa and acne conglobata. *J Rheumatol* 1993; **20**: 684–687.

78 Bennett RE, Wilke WS, Murphy DP. Spondyloarthropathy and hidradenitis suppurativa. *Ann Intern Med* 1983; **98**: 112.

79 Vasey FB, Fenske NA, Clement GB *et al.* Immunological studies of the arthritis of acne conglobata and hidradenitis suppurativa. *Clin Exp Rheumatol* 1984; **2**: 309–311.

80 Burrows NP, Jones RR. Crohn's disease in association with hidradenitis suppurativa. *Br J Dermatol* 1992; **126**: 523.

81 Church JM, Fazio VW, Lavery IC *et al.* The differential diagnosis and comorbidity of hidradenitis suppurativa and perianal Crohn's disease. *Int J Colorectal Dis* 1993; **8**: 117–119.

82 Ostlere LS, Langtry JA, Mortimer PS, Staughton RC. Hidradenitis suppurativa in Crohn's disease. *Br J Dermatol* 1991; **125**: 384–386.

83 Tsianos EV, Dalekos GN, Tzermias C *et al.* Hidradenitis suppurativa in Crohn's disease. A further support to this association. *J Clin Gastroenterol* 1995; **20**: 151–153.

84 Clemmensen OJ. Topical treatment of hidradenitis suppurativa with clindamycin. *Int J Dermatol* 1983; **22**: 325–328.

85 Jemec GBE, Wendelboe P. Topical clindamycin versus systemic tetracycline in the treatment of hidradenitis suppurativa. *J Am Acad Dermatol* 1998; **39**: 971–974.

86 Norris JFB, Cunliffe WJ. Hidradenitis suppurativa and response to oral steroids. *Br J Dermatol* 1987; **117** (Suppl. 32): 96.

87 Newell GB. Treatment of hidradenitis suppurativa. *JAMA* 1973; **223**: 556–557.

88 Stellon AJ, Wakeling M. Hidradenitis suppurativa associated with the use of oral contraceptives. *Br Med J* 1989; **298**: 28–29.

89 Sawers RS, Randall VA, Ebling FJ. Control of hidradenitis suppurativa in women using combined antiandrogen (cyproterone acetate) and oestrogen therapy. *Br J Dermatol* 1986; **115**: 269–274.

90 Mortimer PS, Dawber RP, Gales MA, Moore RA. A double-blind controlled cross-over trial of cyproterone acetate in females with hidradenitis suppurativa. *Br J Dermatol* 1986; **115**: 263–268.

91 Farrell AM, Randall VA, Vafaee T, Dawber RPR. Finasteride as a therapy for hidradenitis suppurativa. *Br J Dermatol* 1999; **141**: 1138–1139.

92 Camisa C, Sexton C, Friedman C. Treatment of hidradenitis suppurativa with combination hypothalamic-pituitary-ovarian and adrenal suppression. A case report. *J Reprod Med* 1989; **34**: 543–546.

93 Bogers JW, Minderhoud-Bassie W, Huikeshoven FJM. A case of hidradenitis suppurativa treated with gonadotropin-releasing hormone agonist and by total abdominal hysterectomy with bilateral salpingo-oophorectomy. *Am J Obstet Gynecol* 1992; **167**: 517–518.

94 Brown CF, Gallup DG, Brown VM. Hidradenitis suppurativa of the anogenital region: response to isotretinoin. *Am J Obstet Gynecol* 1988; **159**: 12–15.

95 Dicken CH, Powell ST, Spear KL. Evaluation of isotretinoin treatment of hidradenitis suppurativa. *J Am Acad Dermatol* 1984; **11**: 500–502.

96 Jones DH, Cunliffe WJ, King K. Hidradenitis suppurativa–lack of success with 13-*cis*-retinoic acid. *Br J Dermatol* 1982; **107**: 252.

97 Norris JFB, Cunliffe WJ. Failure of treatment of familial widespread hidradenitis suppurativa with isotretinoin. *Clin Exp Dermatol* 1986; **11**: 579–583.

98 Boer J, van Gemert MJ. Long-term results of isotretinoin in the treatment of 68 patients with hidradenitis suppurativa. *J Am Acad Dermatol* 1999; **40**: 73–76.

99 Chow ET, Mortimer PS. Successful treatment of hidradenitis suppurativa and retroauricular acne with etretinate. *Br J Dermatol* 1992; **126**: 415.

100 Hogan DJ, Light MJ. Successful treatment of hidradenitis suppurativa with acitretin. *J Am Acad Dermatol* 1988; **19**: 355–356.

101 Zeligman I. Temporary X-ray epilation therapy of chronic axillary hidradenitis suppurativa. *Arch Dermatol* 1965; **92**: 690–694.

102 Hughes LE, Harrison BJ, Mudge M. Surgical management of hidradenitis–principles and results. In: Marks R, Plewig G, editors. *Acne and Related Disorders*. Martin Dunitz, London, 1989: 367–370.

103 Ritz JP, Runkel N, Haier J, Buhr HJ. Extent of surgery and recurrence rate of hidradenitis suppurativa. *Int J Colorectal Dis* 1998; **13**: 164–168.

104 Harrison BJ, Mudge M, Hughes LE. Recurrence after surgical treatment of hidradenitis suppurativa. *Br Med J* 1987; **294**: 487–489.

105 Finley EM, Ratz JL. Treatment of hidradenitis suppurativa with carbon dioxide laser excision and second-intention healing. *J Am Acad Dermatol* 1996; **34**: 465–469.

106 Lapins J, Marcusson JA, Emtestam L. Surgical treatment of chronic hidradenitis suppurativa: CO_2 laser stripping-secondary intention technique. *Br J Dermatol* 1994; **131**: 551–556.