Into the (gluteal) fold: pilonidal disease and hidradenitis suppurativa – association or continuum?

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Linked Article: Benhadou *et al.* Br J Dermatol 2019; **181**:1198–1206.

Diseases of follicular occlusion syndrome [hidradenitis suppurativa (HS), acne conglobata (AC), dissecting cellulitis of the scalp (DCS) and pilonidal sinus disease (PSD)] occur in association with one another. This observation has been established for more than 60 years through the work of Pillsbery *et al.*[1] and explained through follicular occlusion as the inciting event leading to follicular rupture, dermal inflammation and (occasionally) fibrosis and fistulae formation. With the current paradigm shift in HS as a disease where follicular occlusion may be secondary rather than a primary phenomenon,[2] the role of inflammation as a primary driver in other follicular occlusion disorders merits consideration.

In this issue, Benhadou *et al.*[3] provide the initial epidemiological evidence required to reconsider PSD as within the spectrum of inflammatory dermatoses related to HS. Interestingly, the pathogenesis of PSD mirrors previous pathological paradigms in HS. Both diseases were considered infectious and the result of perspiration and poor hygiene, both consider occlusion to be major contributing factors and epidemiological associations with smoking, obesity and metabolic syndrome are well established.[4] The most tantalizing possibility is that PSD may be an extension of the latent classification (LC)2/LC3/gluteal continuum of male-predominant/smoking-predominant HS.[5] This would open up the potential for nonsurgical therapies for those with complex, recurrent disease.

The clinical and histological diagnosis of PSD/HS, as Benhadou *et al.* have discussed, is inherently prone to diagnostic and confirmation bias.[3] The same intergluteal lesion, in the hands of a surgeon or a dermatologist may be called PSD or HS, respectively. A general surgeon excising a PSD where extensive genital and inguinal lesions exist may be more inclined to document the lesion as HS, whereas axillary lesions may go unnoticed. A pathological diagnosis may be swayed by clinical notes indicating a history of HS, or a pathologists' knowledge of HS, given that no reproducible pathological criteria are widely used. Such biases, inherent in a retrospective observational study may explain some of the associations in clinical diagnosis, such as the negative association of axillary lesions with intergluteal HS.

The next stage is comparative histology,[4] lesional inflammatory mediators and prospective clinical studies in order to validate the work of Benhadou *et al.*[3] Such work should be encouraged not just in PSD, but also in DCS and AC, where the possibility of common inflammatory and mechanistic pathways may lead to increasing nonsurgical treatment options for patients and a better understanding of these debilitating inflammatory dermatoses.

Conflicts of interest

None declared.

Laboratory of Investigative Dermatology, Rockefeller University, New York, U.S.A.
E-mail: *jfrew@rockefeller.edu*
J.W. Frew
K. Navrazhina

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Appearance in acne: an often-overlooked concept

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Acne is one of the most common skin conditions affecting all age groups, especially adolescents and young adults.[1] The transition into adulthood is a crucial period of development including many changes and challenges, such as professional progress, making and strengthening relationships and forming one's personal identity.[2] Having visible acne impedes these developmental tasks and, in the absence of a cure, affected people must learn to live with their skin condition. Effective treatments are therefore essential. In order to measure efficacy of different treatments, well-developed and validated patient-reported outcome measures should be available and capture improvements from the patient's perspective.[3] Being an important outcome of acne treatments, appearance should be measured in every clinical trial. What is more important for an affected patient, especially for adolescents and young

adults, than how their skin, acne and acne scars look and improve? Because appearance is in the eye of the beholder, a self-report is needed to capture this concept. There are some acne-specific measures available, but they often overlook this subjective concept. In this issue of the *BJD*, Klassen *et al.* dared to develop a new instrument filling this gap, the ACNE-Q.[4] Addressing the concept *appearance* comprehensively, this measure is novel. An important criterion to ensure good quality of the development of a measure is a patient-oriented approach. Patients as well as different healthcare providers were involved in the whole development process. Three top-level domains with several major and minor themes emerged. Feedback of clinical experts was obtained and cognitive interviews with affected patients were conducted to assess content validity of the scales according to the COSMIN criteria.[5] Modern psychometric analyses using the Rasch Measurement Theory were performed to identify items with poor fit and different measurement properties of the ACNE-Q, such as structural validity, internal consistency, test–retest reliability and construct validity, were assessed. The study is limited to the North American population. However, a large sample size (n = 256) recruited from two countries and different settings, i.e. hospital and community dermatology clinics, was involved in the validation study. Although the ACNE-Q is quite long, with 73 items in seven scales, it is a comprehensive and promising measure that can be used in clinical practice and research to measure appearance and appearance-related distress and symptoms. This study lays the ground for future studies on the validation and feasibility of the ACNE-Q.

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M. Gabes

Department of Medical Sociology, Institute of Epidemiology and Preventive Medicine, University of Regensburg, Regensburg, Germany
E-mail: *michaela.gabes@klinik.uni-regensburg.de*

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Oxytosin as a novel antidegenerative?

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Cellular senescence, the transition of many different mitotic cell types to a permanently nondividing state accompanied by a profound change in phenotype, is now recognized as a primary cause of ageing and ill health in mammals. Multiple lines of evidence have led to this conclusion, including the observations that normal human fibroblasts have a limited capacity to divide *in vitro*, that this capacity is dependent on the age and health status of donors, that diseases such as Werner syndrome and Hutchinson–Gilford progeria syndrome combine premature fibroblast senescence *in vitro* with a host of clinical changes resembling ageing *in vivo* and the demonstration that experimental deletion of senescent cells in transgenic mice extends lifespan and improves health.[1,2] The entry of human fibroblasts into senescence triggers a phenotypic shift marked by reduced production of collagen and overproduction of collagenase coupled with the release of a range of antiproliferative and proinflammatory cytokines collectively termed the senescence-associated secretory phenotype (SASP).[1] Exposure to SASP components induces senescence in a paracrine fashion, consistent with the evolutionary role of senescence as a tumour-suppression mechanism.

In light of these findings there is growing clinical interest in the development of senolytics, compounds that can selectively destroy senescent cells, with the first open-label clinical trial conducted earlier this year.[3] However, an alternative route to clinical benefit is the reversion of senescent cells to a growth-competent phenotype through the development of antidegenerative compounds. Perhaps the first demonstration of the utility of this approach was the work of Latorre and colleagues who showed that treatment of multiple strains of senescent human fibroblasts with resveralogues allowed the cells to escape senescence and reinitiate division.[4] This occurred via a resetting of the pattern of RNA splicing factors, probably via the extracellular signal-regulated kinase (ERK) and AKT pathways.[5]