Dermatologic Disease in IBD: What the Gastroenterologist Needs to Know

Alan Menter, MD

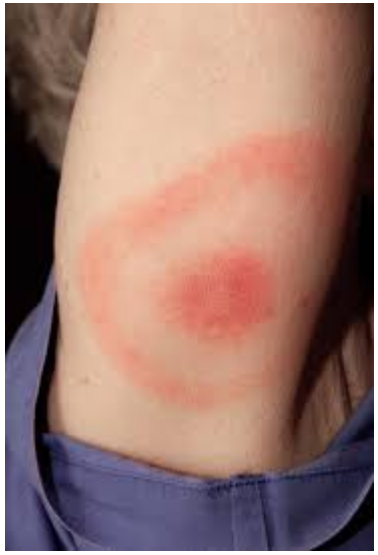
Baylor Scott & White, Dallas, TX

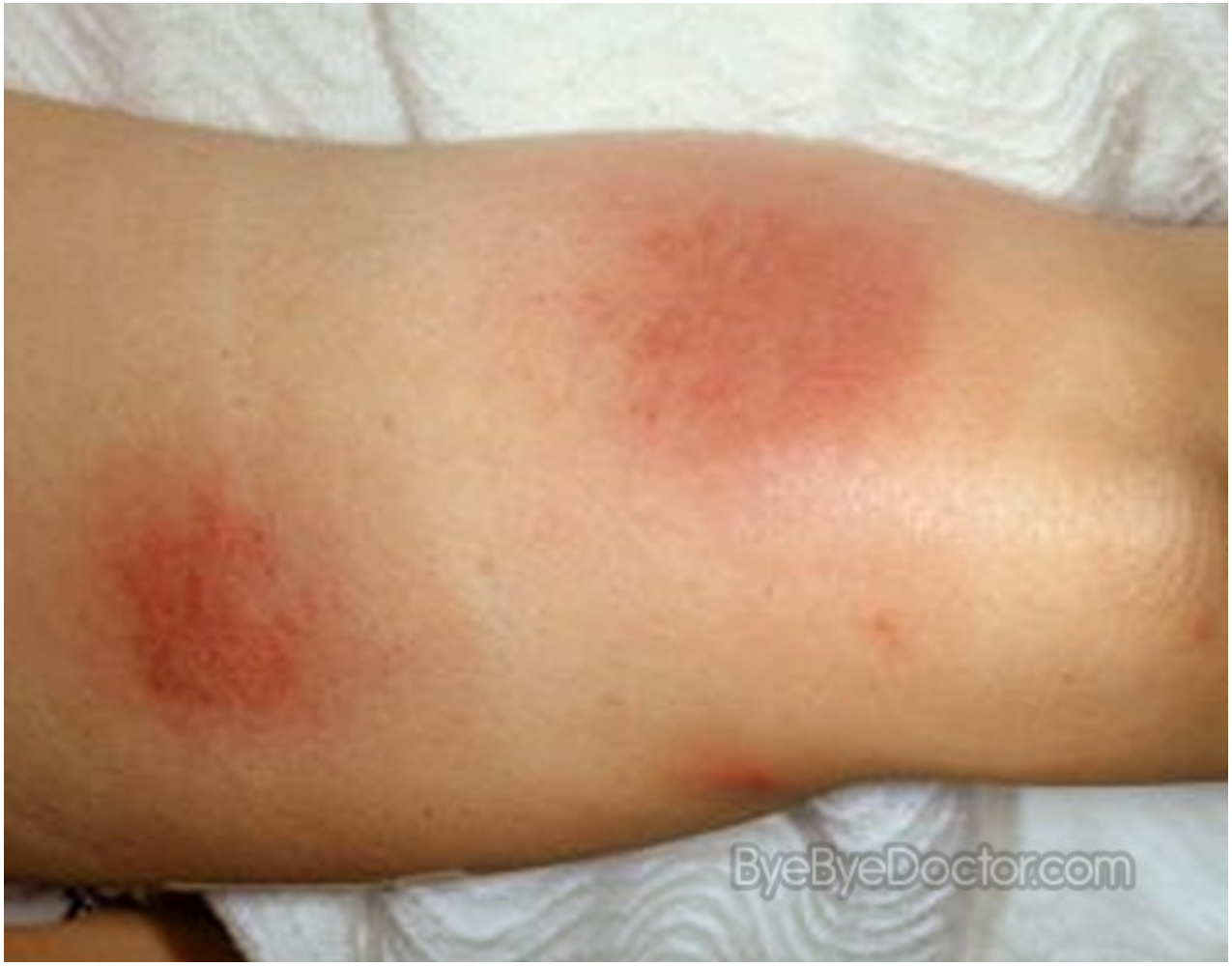
IBD Symposium
14, April 2018

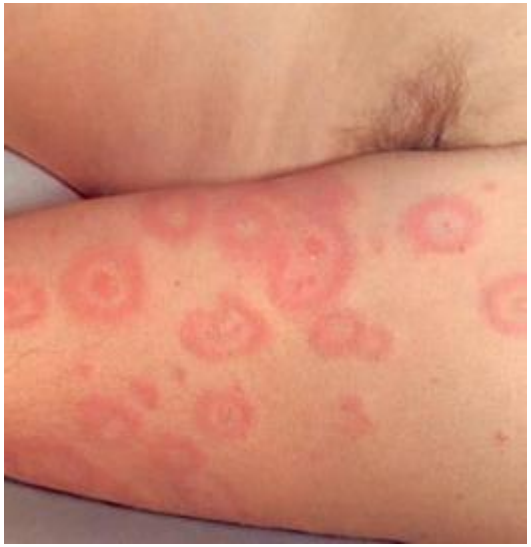
Dermatologic Diseases in IBD

- Erytherma Nodosum
  - Most common
  - Up to 15% of patients
- Pyoderma Gangrenosum (up to 3%)
- Psoriasis
- Hidradenitis Suppurative resembling (Crohn's disease-17% incidence)
- Leucocytoclastic Vasculitis

Erytherma Nodosum







Common Conditions Associated with Erythema Nodosum (1)

- Streptococcus B haemolyticus infection
- Primary Tuberculosis
- Yersinia, salmonella, coccidiodomycosis, and heliobacter infections

Systemic Disease

- Sarcoidosis
- Inflammatory bowel disease (Crohn's disease and ulcerative colitis)
- Behcet's diease
- Connective tissue diease
- Sweet's syndrome

Common Conditions Associated with Erythema Nodosum (2)

Malignancy

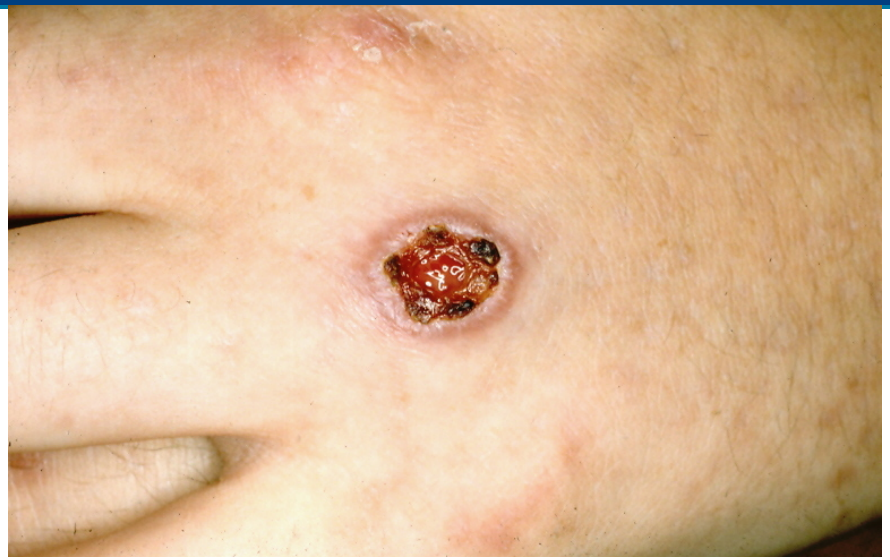
- Haematological neoplasms (lymphoma)

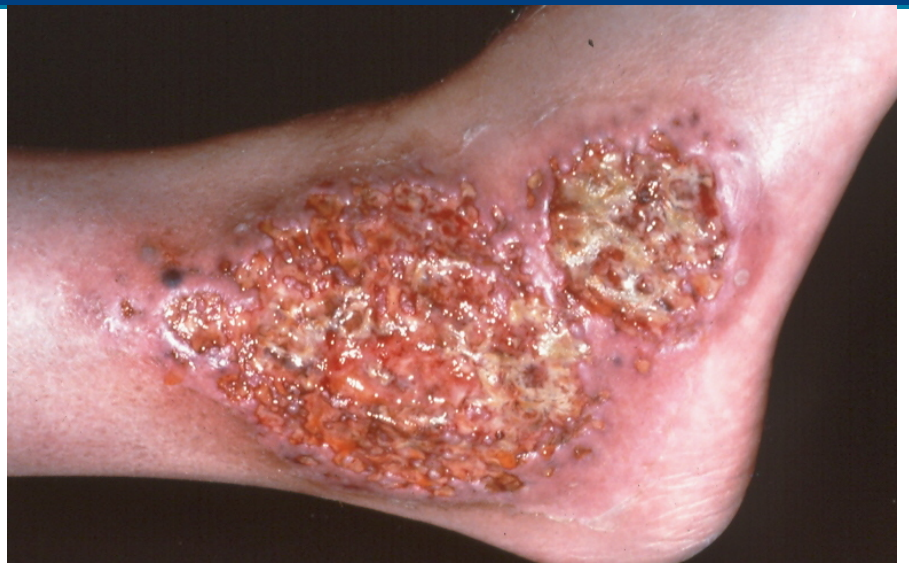
Drugs

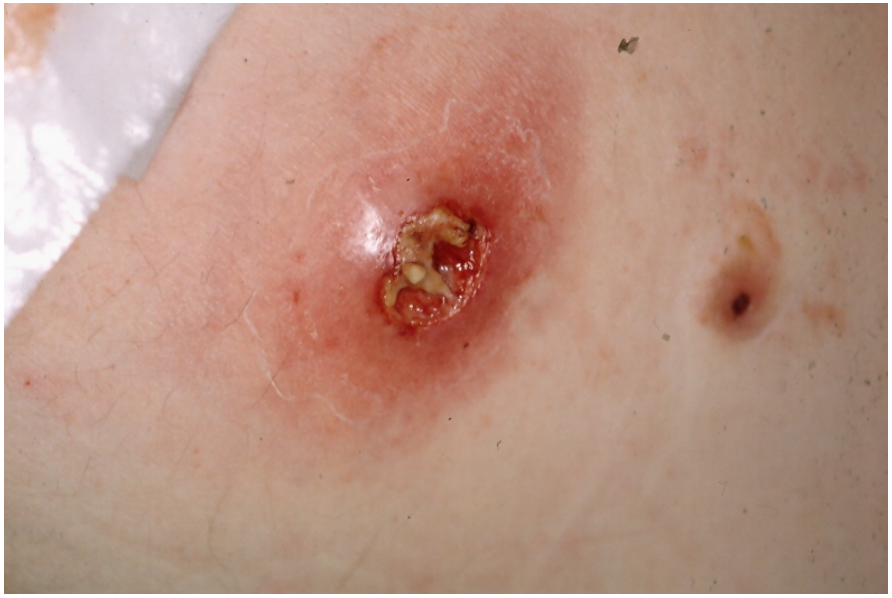
- Oral contraceptives
- Penicillins
- Sulfonamides
- Bromides
- Iodides
- Analgesics

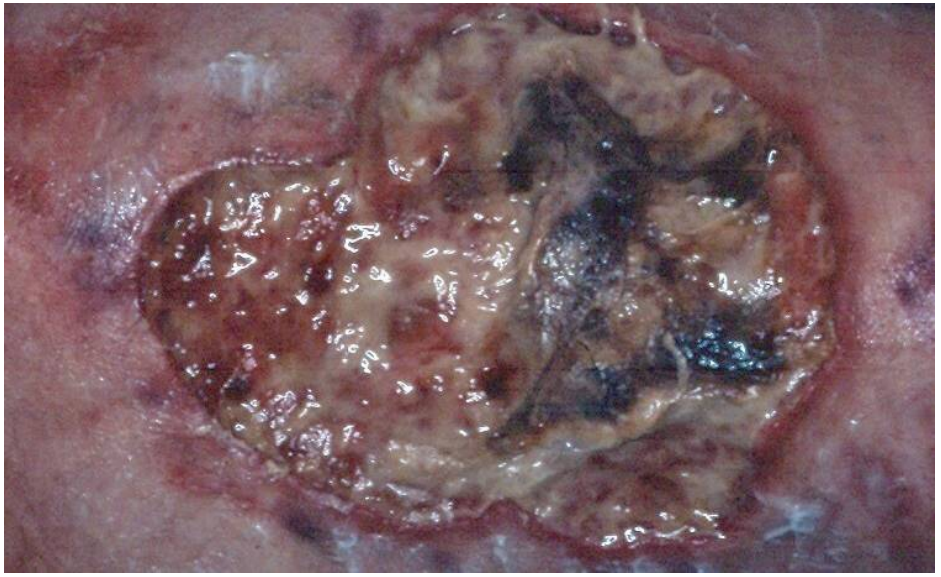
Pregnancy

Pyoderma Gangrenosum









Differential Diagnosis of Pyoderma Gangrenosum (1)

- Bacterial infection
- Mycobacterial infection
- Fungal infection
- Parasitic infection
- Viral infection

Differential Diagnosis of Pyoderma Gangrenosum (2)

- Sweet's syndrome
- Spider bite
  - Brown recluse spider
- Malignancy
  - Squamous cell carcinoma
  - Basal cell carcinoma
  - Cutaneous T cell lymphoma

Differential Diagnosis of Pyoderma Gangrenosum (3)

- Factitial ulceration
- Vascular disease
- Antiphospholipid antiobody associated occlusive disease
- Thrombophlebitis with gangrene
- Systemic disease
  - Sytemic lupus erythematosus
  - Rheumatoid arthritis
  - Behcet's disease
  - Wegener's granulomatosis

Orofacial Manifestations in IBD

Aplthous Up to 20% incidence

- Stomatitis
- Pyostomatitis Vegetans
- Angular Cheilitis (Candidiasis-common)
- Cobblestoning of the buccal mucosa
- Nodules on the gingival and alveolar mucosa

Secondary Cutaneous Manifestations due to complications of IBD or its Therapies

- Acquired Acrodermatitis Enteropathica
- Pellagra (Niacin deficiency)
- Scurvy (Vitamin C deficiency)
- Purpura (Vitamin C & K)
- Hair & Nail Abnormalities (malabsorption of amino acids)
- Nodules on the gingival and alveolar mucosa

IBD and Psoriasis

- The most frequently associated cutaneous disease is psoriasis which occurs in 7-11% of the IBD population compared to the 2% of general population.
- In one study, psoriasis was found to be more prevalent in Crohn's (11.2%) than Ulcerative Colitis (5.7%)
- The association of IBD with psoriasis is believed to be both genetically and immunologically related
- In a recent study of 146 patients with both IBD and psoriasis compared to a control of 146 patients with only psoriasis, it was found that patients with both IBD and psoriasis had significantly
  - higher rates of autoimmune thyroiditis (6.8 vs 2.1%)
  - hepatitis (6.2 vs 0.7%),
  - diabetes (26.7 vs 11.0%)

PATIENTS WITH PSORIASIS HAVE HIGHER RATES OF IBD

~3.5x INCREASED PREVALENCE

of IBD in US patients with psoriasis (n=5492) vs matched controls (n=5492)[1]

~4x INCREASED RISK

of CD in US women (N=174,476) with confirmed psoriasis, according to 2 studies[2]

GENETICS[3]

- Psoriasis and IBD may be genetically linked

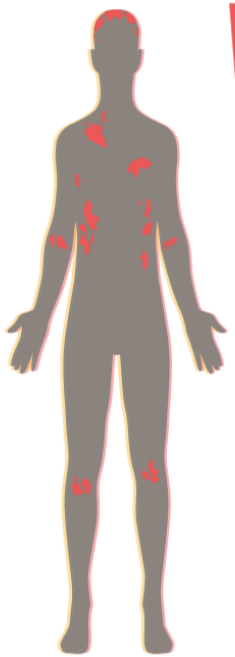
DISEASE COURSE[4]

- The onset of psoriasis usually precedes IBD
- The course of psoriasis is independent of IBD disease activity

1. Feldman SR, et al. *J Manag Care Spec Pharm.* 2015;21(10):874-888. 2. Li WQ, et al. *Ann Rheum Dis.* 2013;72(7):1200-1205. 3. Skroza N, et al. *Biomed Res. Int.* 2013;2013:1-8. 4. Peppercorn MA, Cheifetz AS. UpToDate. https://www.uptodate.com/contents/dermatologic-and-ocular-manifestations-of-inflammatory-bowel-disease. Accessed August 23, 2017.

PLAQUE PSORIASIS AND HS LOOK DIFFERENT ON THE SURFACE

Plaque Psoriasis[2]

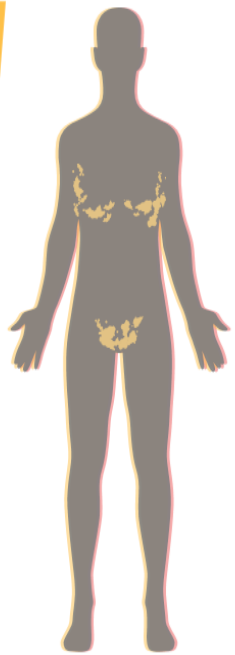


- Raised, reddish patches
- Silvery-white scales
- Itch
- Nail problems

Common Locations[1]

HS[3,4]

- Painful nodules or abscesses
- Double open comedones
- Draining sinus tracts
- Bridged scarring



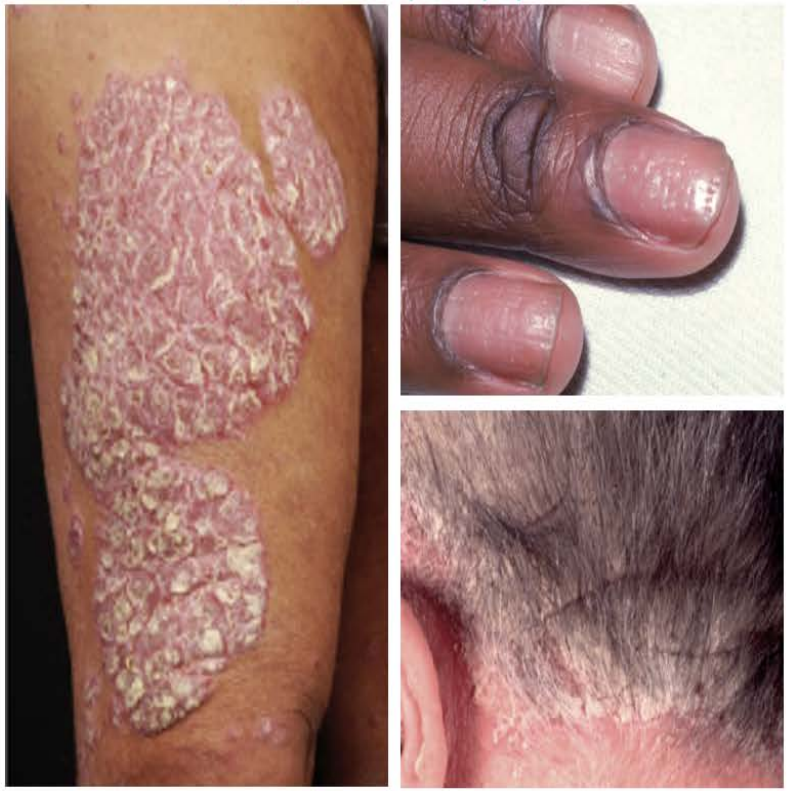
Common Locations[3]

1. Menter A, et al. *J Am Acad Dermatol.* 2008;58(5):826-850. 2. AAD. https://www.aad.org/media/stats/conditions/psoriasis. Accessed August 18, 2017. 3. Alikhan A, et al. *J Am Acad Dermatol.* 2009;60(4):539-561.
4. Margesson LJ, Danby FW. *Best Pract Res Clin Obstet Gynaecol.* 2014;28(7):1013-1027.

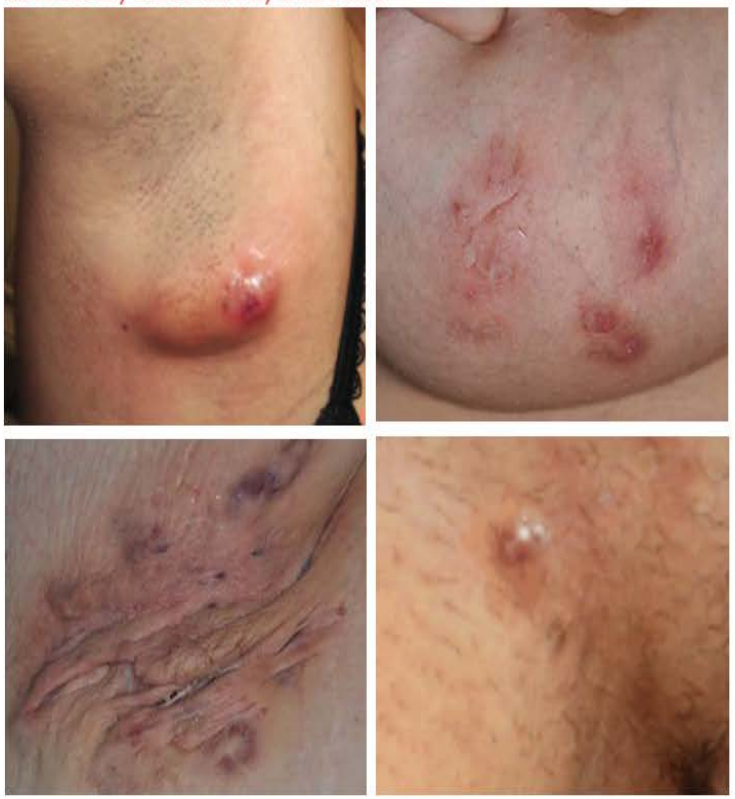
DIAGNOSING PLAQUE PSORIASIS AND HS

BOTH RELY ON A PHYSICAL EXAM[1,2]

Plaque psoriasis:
Examination of skin, nails, and scalp for symptoms[3-5]



HS: Examination of common locations for nodules, abscesses, sinus tracts, and scars[2,6-8]



1. NPF. https://www.psoriasis.org/sites/default/files/diagnosing_psoriasis_fact_sheet.pdf. Accessed August 22, 2017. 2. Micheletti RG, *Semin Cutan Med Surg.* 2014;33(3 Suppl):S51-53. 3. Baliwag J, et al. *Cytokine.* 2015;73(2):342-350. 4. Weigle N, McBane S. *Am Fam Physician.* 2013;87(9):626-633. 5. Wozel G, *Clin Dermatol.* 2008;26(5):448-459. 6. Revuz J, *J Eur Acad Dermatol Venereol.* 2009;23(9):985-998. 7. Ingram JR, UpToDate. https://www.uptodate.com/contents/hidradenitis-suppurativa-acne-inversa-pathogenesis-clinical-features-and-diagnosis. Accessed August 22, 2017. 8. Gill L, et al. *F1000Prime Rep.* 2014;6:112.

DIFFERENT PRESENTATION, BUT SEVERAL SHARED COMORBIDITIES

The list of comorbidities associated with psoriasis and HS is extensive, and there are several that are similar between these 2 conditions

Comorbidities of Plaque Psoriasis[1]

- Psoriatic arthritis
- Cardiovascular disease
- Metabolic syndrome
- Depression
- Crohn's disease (CD)
- Ulcerative colitis (UC)

Comorbidities of HS[2-6]

- Spondyloarthritis*
- Cardiovascular disease
- Metabolic syndrome
- Depression
- Crohn's disease (CD)
- Ulcerative colitis (UC)

*Includes ankylosing spondylitis and psoriatic arthritis.

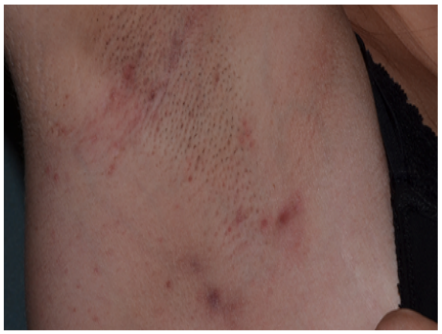
1. Menter A, et al. *J Am Acad Dermatol.* 2008;58(5):826-850. 2. Richette P, et al. *J Rheumatol.* 2014;41(3):490-494. 3. Arthritis Foundation. http://www.arthritis.org/about-arthritis/types/spondyloarthritis/. Accessed August 21, 2017. 4. Egeberg A, et al. *JAMA Dermatol.* 2016;152(4):429-434. 5. Miller IM, et al. *JAMA Dermatol.* 2014;150(12):1273-1280. 6. Miller IM, et al. *Dermatol Clin.* 2016;34(1):7-16.

CONSEQUENCES OF HS PROGRESSION[1]

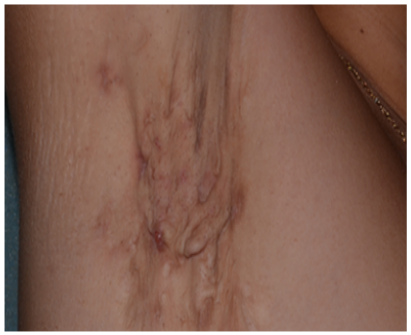
- Lymphatic obstruction
- Squamous cell carcinoma
- Anemia
- Malaise
- Arthropathy
- Infections
- Contractures and limb mobility limitation

Complications can affect the skin alone or may have broader impact[2]

As HS progresses, small lesions can develop into deep-seated nodules and abscesses and rupture, leading to scars that can thicken over time and impair movement[3-5]



Patient with a small nodule in the armpit[6]

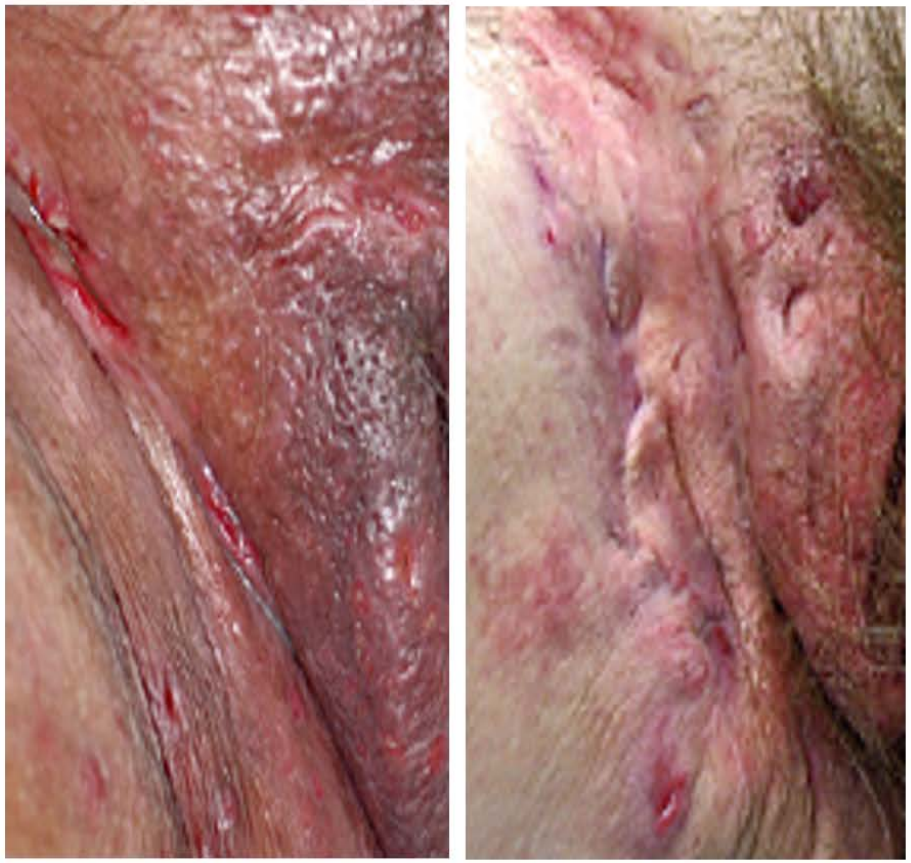


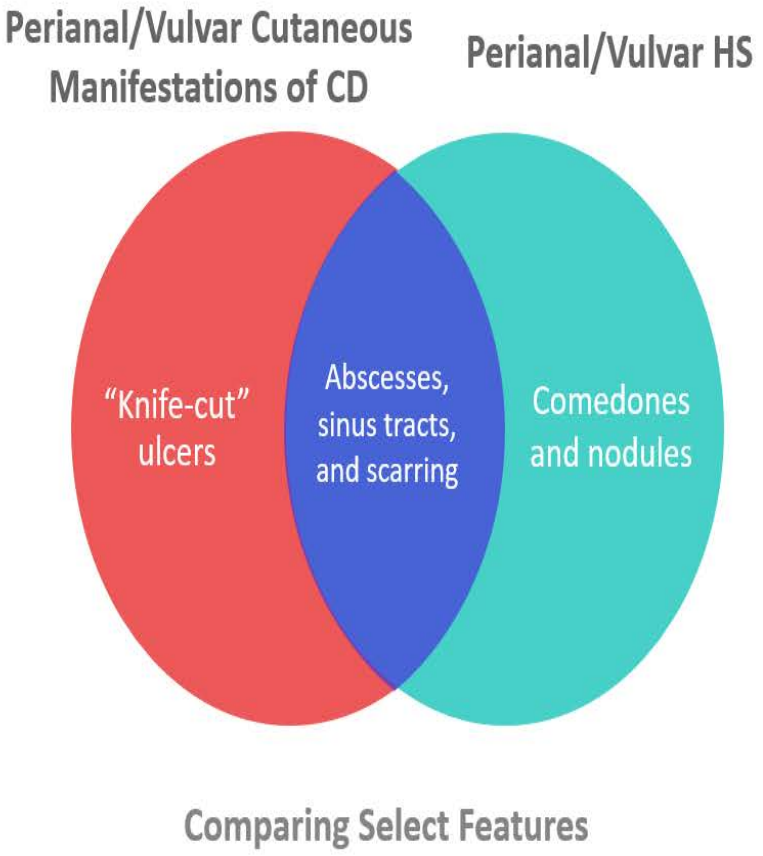
Patient with scarring and fistulae in the armpit[6]

1. Margesson LJ, Danby FW. *Best Pract Res Clin Obstet Gynaecol.* 2014;28(7):1013-1027. 2. Yuan JT, Naik HB. *Semin Cutan Med Surg.* 2017;36(2):79-85. 3. AAD. https://www.aad.org/public/diseases/painful-skin-joints/hidradenitis-suppurativa. Accessed August 21, 2017. 4. Ingram JR. UpToDate. https://www.uptodate.com/contents/hidradenitis-suppurativa-acne-inversa-pathogenesis-clinical-features-and-diagnosis Accessed August 22, 2017. 5. Alikhan A, et al. *J Am Acad Dermatol.* 2009;60(4):539-561. 6. No BS About HS. https://www.nobsabouths.com/what-is-hidradenitis-suppurativa/symptoms. Accessed August 21, 2017.

CUTANEOUS MANIFESTATIONS OF CD MAY BE DIFFICULT TO DIFFERENTIATE FROM HS[1]

What Is the Diagnosis?

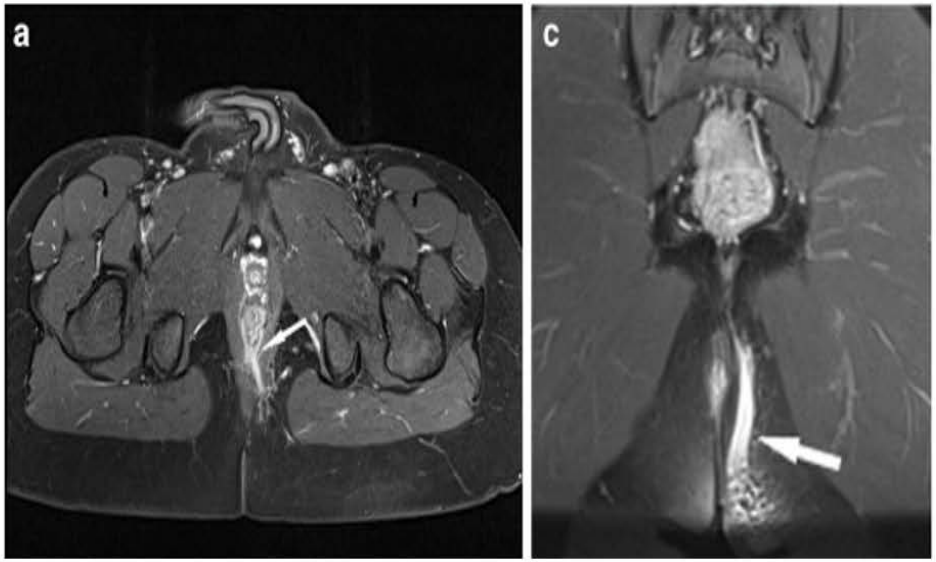




1. Ingram JR. UpToDate. https://www.uptodate.com/contents/hidradenitis-suppurativa-acne-inversa-pathogenesis-clinical-features-and-diagnosis. Accessed August 22, 2017.

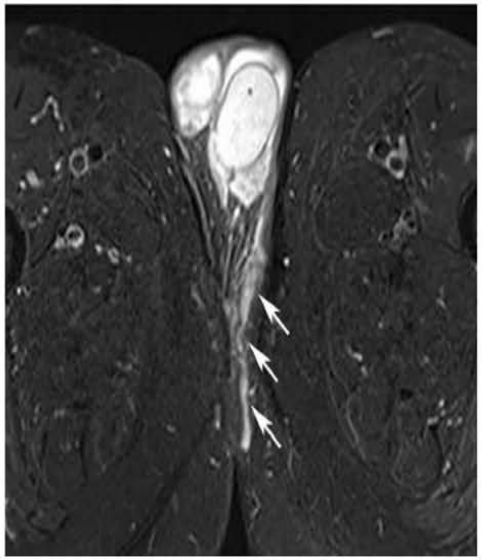
MRI DISTINCTION OF PERIANAL HS FROM CD[1]*

Fistulae also communicate more often with the anal sphincters in patients with CD than those with HS



MR image of patient with CD:

Fistula communicates with the sphincter mechanism, involving the perianal area and ischioanal fossa



MR image of patient with HS:

Fistula does not extend to the sphincter complex

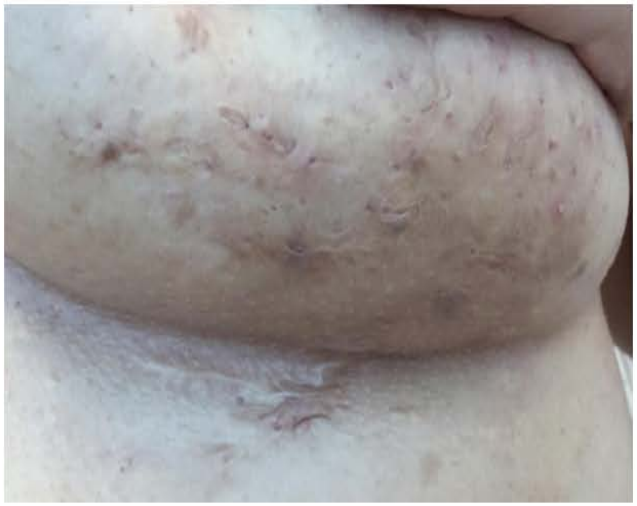
MRI signs of HS-related perianal disease include

- Bilaterality of abnormalities
- Absence of rectal wall thickening
- Either posterior localization of lesions or absence of predominance of lesions in the perianal area

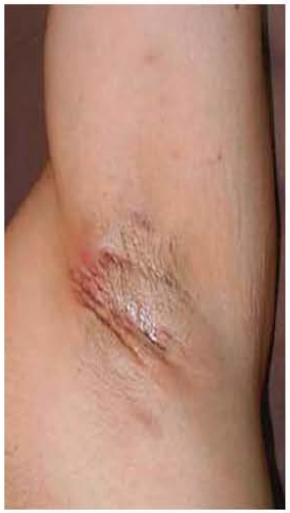
*Retrospective French study of adults with HS (n=23) and CD (n=46) that underwent pelvic MRI for suspicion or evaluation of anoperineal disease.
MRI=magnetic resonance imaging.

1. Monnier L, et al. *Eur Radiol.* 2017;27(10):4100-4109.

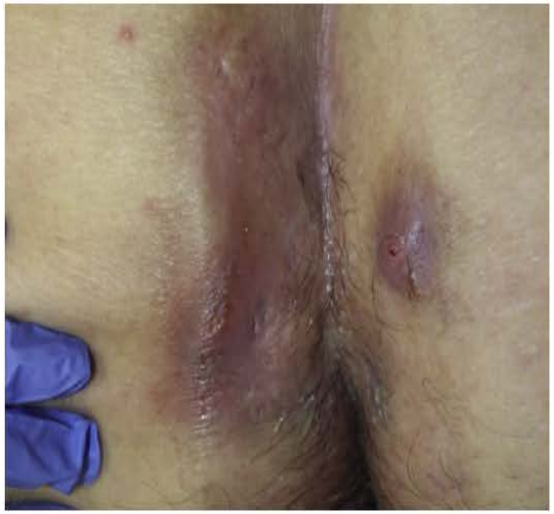
HS IN OTHER COMMON LOCATIONS



Inframammary[1]



Axilla[2]



Buttocks[3]

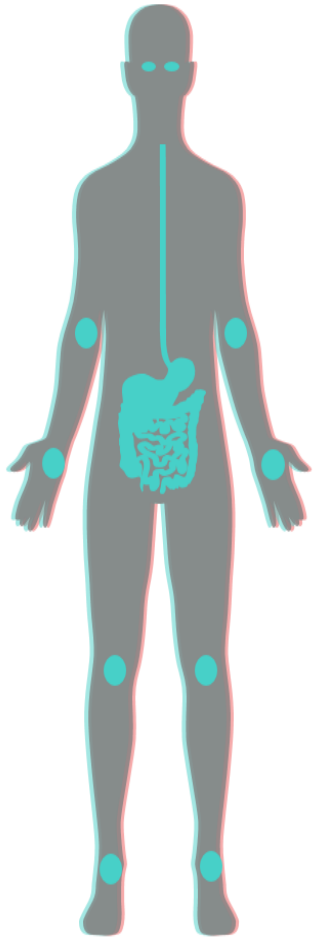
1. Yuan JT, Naik HB. *Semin Cutan Med Surg.* 2017;36(2):79-85. 2. Zouboulis CC, et al. *Dermatology.* 2015;231(2):184-190. 3. Martorell A, et al. *Actas Dermosifiliogr.* 2015;106(9):703-715.

IBD MAY AFFECT MORE THAN JUST THE GUT

In a large cohort study, extraintestinal manifestations (EIMs) were identified in[1]

43% (n=580) of patients with CD

31% (n=370) of patients with UC



Multiple organ systems can be affected by IBD[1,2]

- Skin
- Eyes
- Joints
- Liver

Musculoskeletal manifestations[2]

- Ankylosing spondylitis
- Psoriatic arthritis

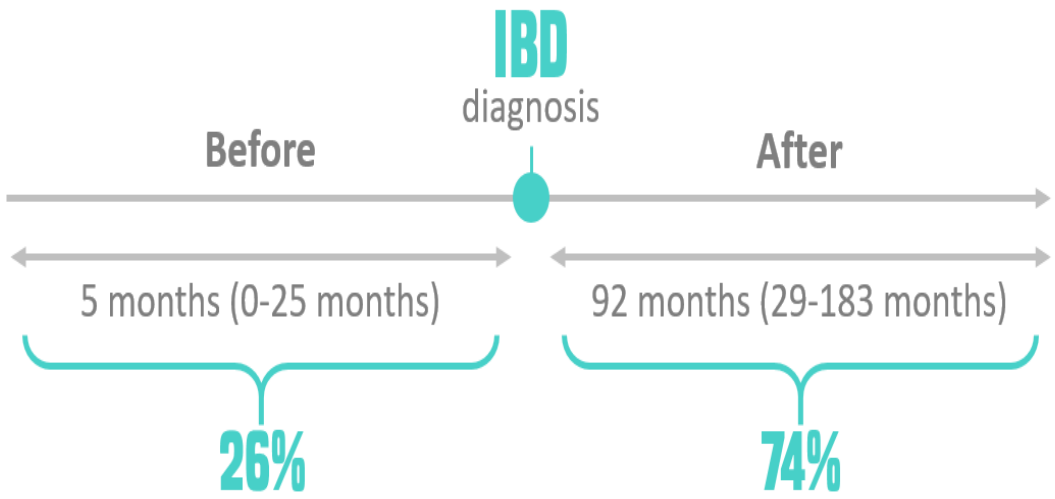
Cutaneous manifestations or associations[1]

- Perianal lesions
- Erythema nodosum
- Pyoderma gangrenosum
- Psoriasis

1. Huang BL, et al. *Front Physiol*. 2012;3:13. 2. Levine JS, Burakoff R. *Gastroenterol Hepatol (N Y)*. 2011;7(4):235-241.

EXTRAINTESTINAL MANIFESTATIONS (EIMs) MAY OCCUR BEFORE OR AFTER AN IBD DIAGNOSIS[1]

Chronology of EIM Occurrences[1,2]



IN YOUR PATIENTS WITH PSORIATIC DISEASE, BE AWARE OF THE POTENTIAL FOR IBD

1. Vavricka SR, et al. *Inflamm Bowel Dis.* 2015;21(8):1982-1992. 2. Vavricka SR, et al. *Inflamm Bowel Dis.* 2015;21(8):1794-1800.

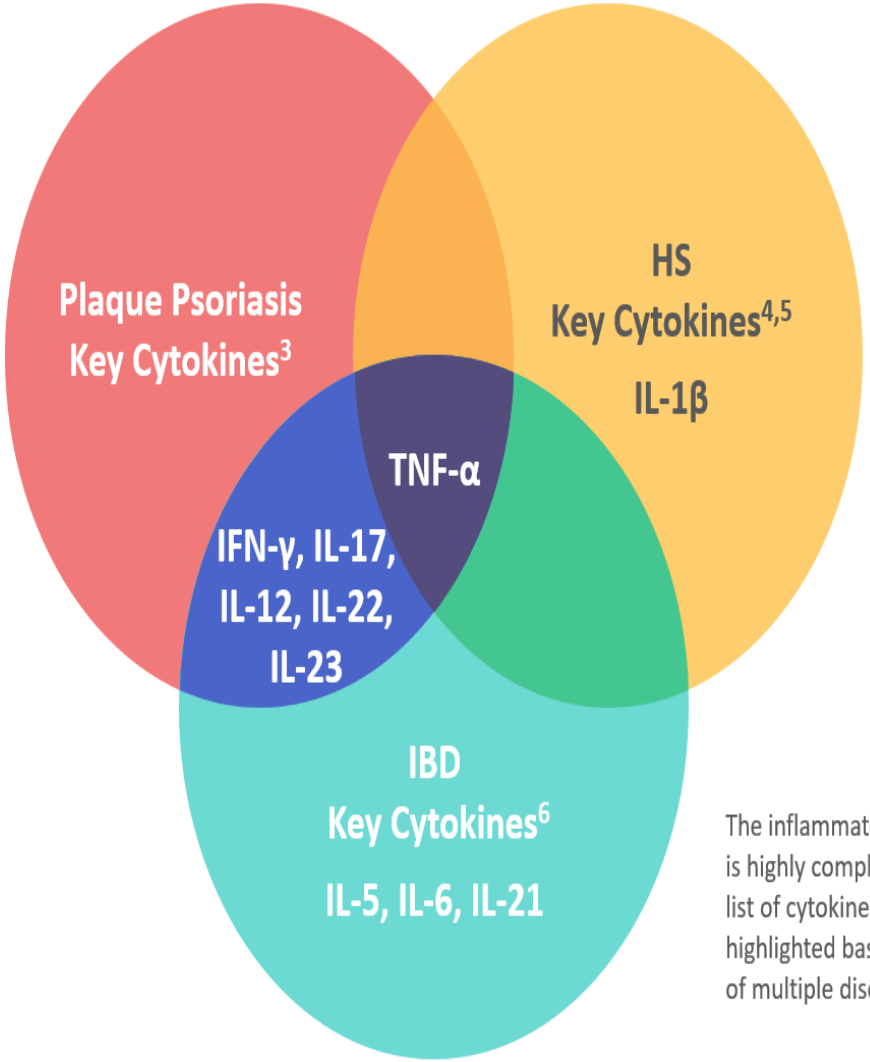
IMMUNE DYSREGULATION: A SHARED CONNECTION

Plaque Psoriasis[1-3]

Proinflammatory cytokines contribute to cyclic inflammation and keratinocyte proliferation

IBD[6]

Proinflammatory cytokines contribute to the development and potential perpetuation of mucosal inflammation



HS[4,5]

The production of proinflammatory cytokines initiates the pathogenic process

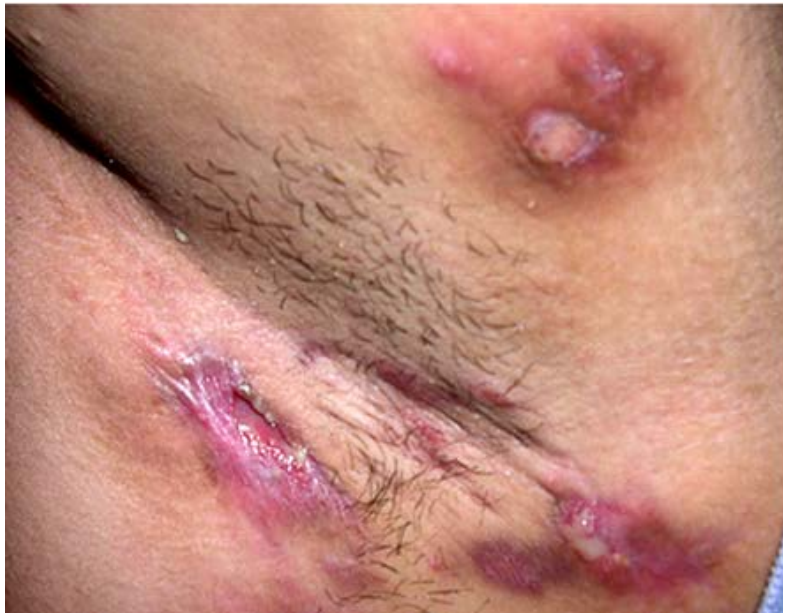
The inflammatory response in immune-mediated diseases is highly complex. This example does not reflect a complete list of cytokines involved. Select cytokines have been highlighted based on their involvement in the pathogenesis of multiple disease states.

IFN=interferon. IL=interleukin. TNF=tumor necrosis factor.

1. Nickoloff BJ. *Nat Med*. 2007;13(3):242-244. 2. Nestle FO, et al. *N Engl J Med*. 2009;361(5):496-509. 3. Lowes MA, et al. *Annu Rev Immunol*. 2014;32:227-255. 4. van der Zee HH, et al. *Exp Dermatol*. 2012;21(10):735-739. 5. van der Zee HH, et al. *Br J Dermatol*. 2011;164(6):1292-1298. 6. Neurath MF. *Nat Rev Immunol*. 2014;14(5):329-342.

Pathology: Hidradenitis Suppurative

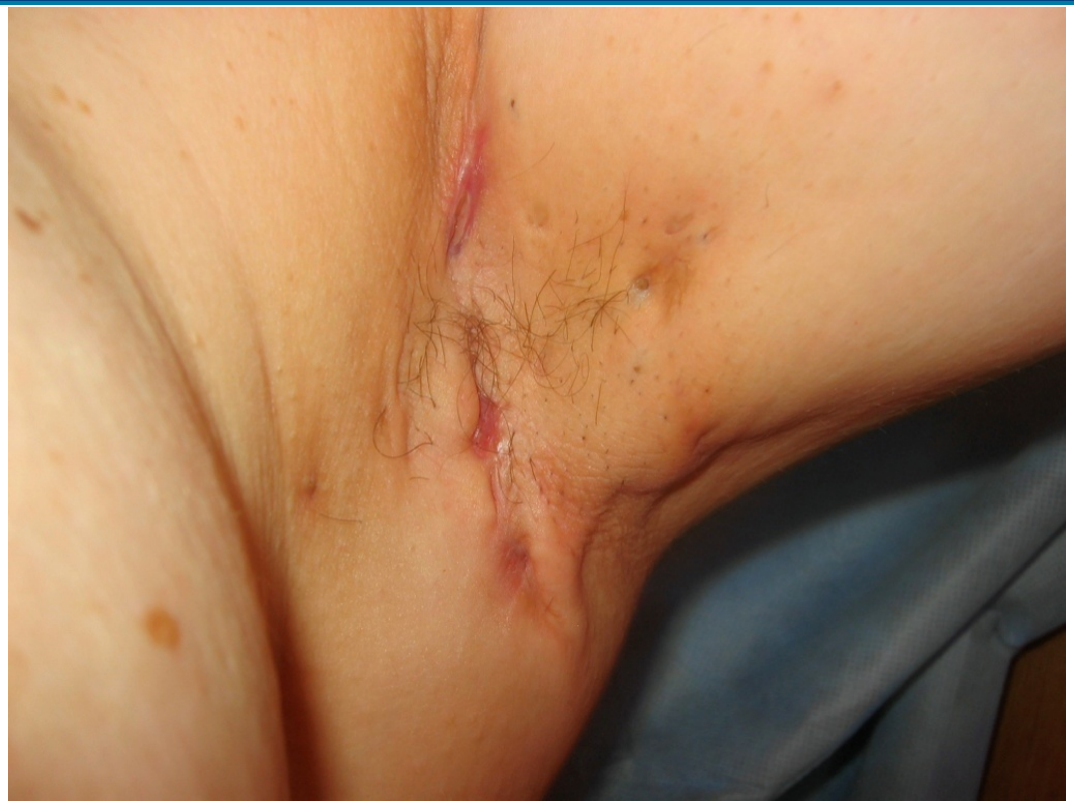
- Active
- Primary lesions:
  - Acute form: recurrent, painful, deep-seated, inflamed nodules
  - Symptoms: burning, itch, pain, local warmth, hyperhidrosis
- Abscesses form sinus tracts that re-epithelize and contain inflammatory material
  - May drain to skin surface
  - Multiple tracts may coalesce to form subcutaneous honeycomb



Alikhan A. et al. JAAD 2009;60:539–561
Photo courtesy of J Crowley, Bakersfield Dermatology

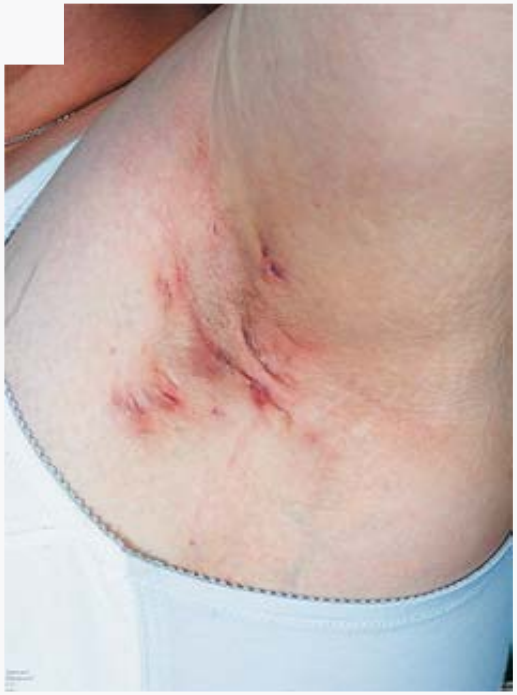
Hidradenitis Suppurative Clinical presentation: Chronic form

- Multiple abscesses
- Double comedones
- Foul-smelling discharge
- Secondary lesions
  - Scarring
  - Ulceration
  - Sinus tracts
- May be more than one phenotype (comedonal versus other)



Jemec GB. NEJM 2012;366:158–164

Hidradenitis Suppurative Hurley staging system



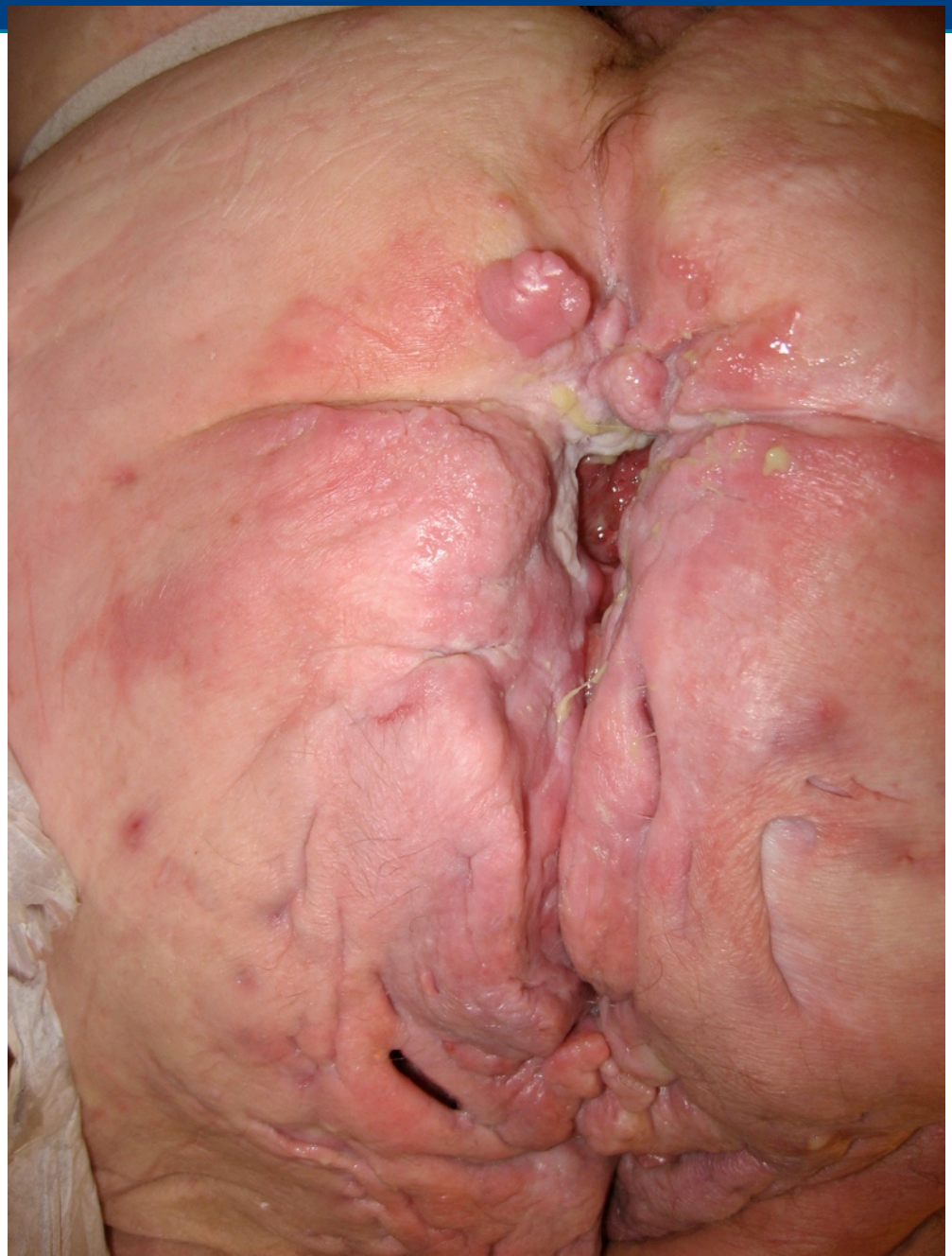
Stage I
Single or multiple abscesses

Stage II
Recurrent abscesses, sinus tract formation

Stage III
Diffuse involvement of area, multiple interconnected tracts and abscesses

Jemec GB. NEJM 2012;366:158–164

Hidradenitis Suppurative



Hidradenitis Suppurative Microbiology

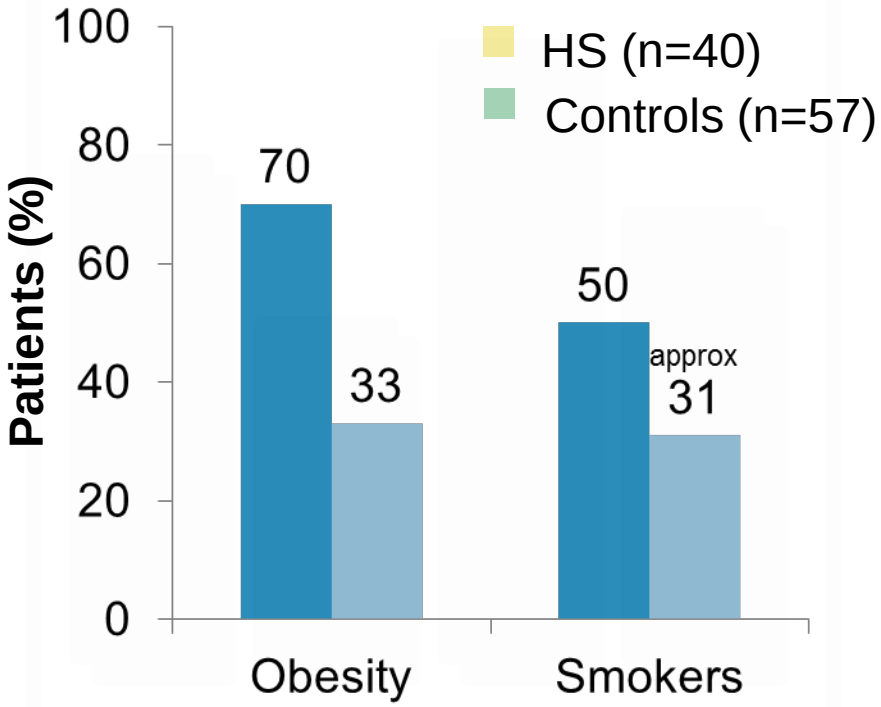
- HS is a sterile inflammation
  - Aerobic: Staphylococcus – coag neg
  - Anaerobic: Peptostreptococcus
  - Cornyebacterium
  - No substantial role for staph aureus
- Immune-mediated mechanisms of inflammation
  - Dysregulated immune response in the hair follicles
  - Antibiotics for antimicrobial but also anti-inflammatory effects
- Biofilm and microbiome may be relevant

Sartorius.BJD 2012, Apr;166:879-83

Hidradenitis Suppurative Risk factors

- Smoking
  - Increases severity
  - HS vs matched controls: odds ratio = 12.55
- Obesity
  - Correlation with severity
  - HS vs matched controls: odds ratio = 4.42

- Johns Hopkins Questionnaire

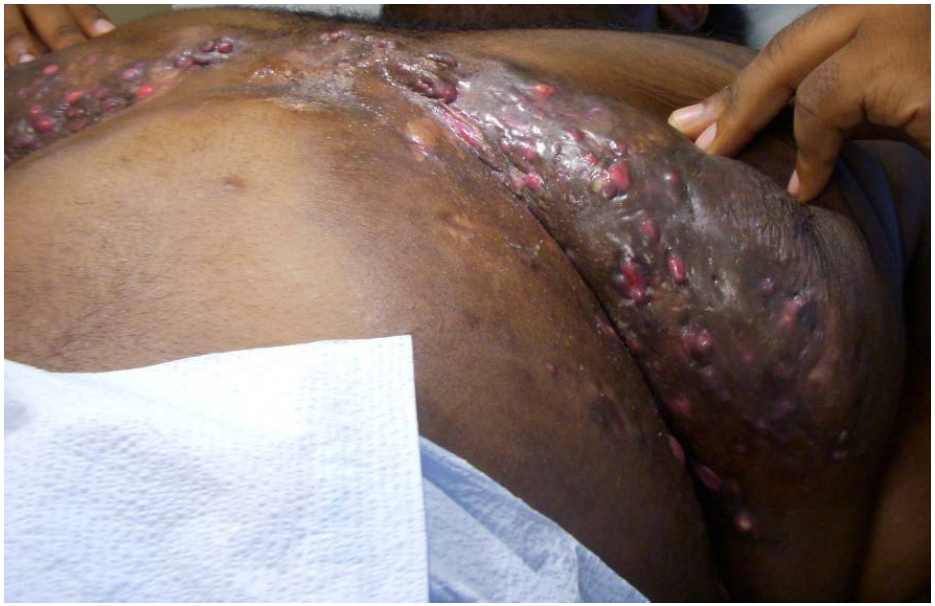


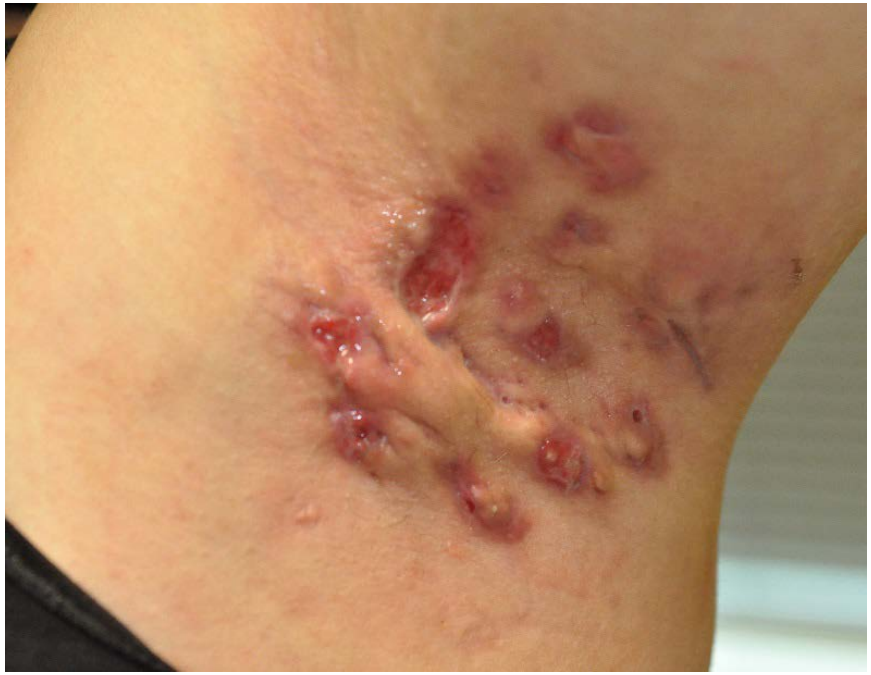
- Role of smoking and obesity not known to be causal, but high incidence suggests that modifying these factors is reasonable as an adjuvant therapy.

Revuz JE, et al. JAAD 2008;59:596–601
Vlassiva N, et al. AAD 2012: P4822

Complications of Hidradenitis Suppurative

- Scars
- Restricted movement
- Obstructed lymph drainage
- Psychosocial issues





Depression in Patients with Hidradenitis Suppurative

- 211 HS patients and 233 dermatological control patients
- DLQI was significantly higher for HS patients than for the control patients, 8.4 ± 7.5 vs. 4.3 ± 5.6 ($P<0.0001$) correlated with Hurley stage severity scores
- Mean MDI scores were significantly higher for HS patients, 11.0 vs. 7.2 ($P<0.0001$)
- Clinically defined depression rates (ICD-10) criteria were not significantly higher in HS patients compared with controls (9% vs. 6%)

Onderdijk AJ et al. JEADV 2013;27:473–478.

DLQI, dermatology life quality index ; HS, hidradenitis suppurativa; ICD, international classification of diseases; MDI, major depression inventory.

Hidradenitis Suppurative Sexual health

- Questionnaire given to 45 women (24 HS, 21 control) and 40 men (20 HS, 20 control). DLQI used for QoL. The Female Sexual Function Index, the International Index of Erectile Dysfunction, and the Frankfurt Self-Concept Scale for Sexuality were used to assess sexual health
- HS subjects exhibited sexual distress compared with control group ($P<0.01$)
- Distress was higher in female patients with HS ($P=0.02$ compared with male HS patients)
- Greater sexual dysfunction and distress correlated with lower QoL in female patients with HS

DLQI, dermatology life quality index ; HS, hidradenitis suppurativa; QoL, quality of life.

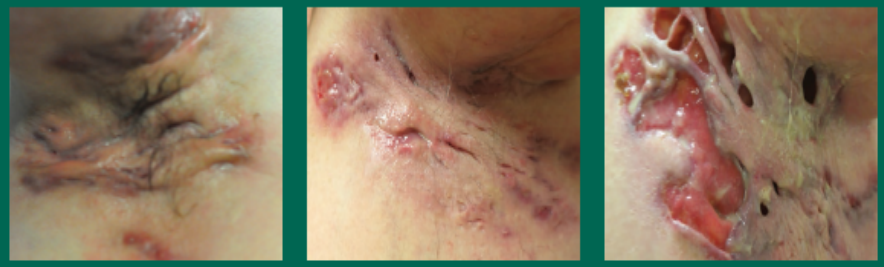
Kurek A et al. J Am Acad Dermatol. 2011;67:422-8.

TABLE Diseases Commonly Associated With Hidradenitis Suppurativa

Diseases of follicular occlusion (follicular occlusion triad) • Acne Vulgaris • Acne conglobata • Dissecting cellulitis of the scalp
Pilonidal cyst
Crohn’s disease
Obesity/metabolic syndrome

A CME-CERTIFIED SUPPLEMENT TO
Skin & Allergy News®

Hidradenitis Suppurativa: Update on Diagnosis and Treatment



Original Release Date: June 2014
Most Recent Review Date: June 2014
Expiration Date: July 31, 2016
Estimated Time to Complete Activity: 3.0 hours
Medium or Combination of Media Used: Written Supplement
Method of Physician Participation: Journal Supplement

Faculty

Francisco A. Kerdel, BSc, MBBS
Director of Inpatient Dermatology
University of Miami Hospital
Professor of Dermatology and Vice Chairman
Florida International University
Miami, Florida

Alan Menter, MD
Chief, Division of Dermatology
Baylor University Medical Center
Clinical Professor of Dermatology
University of Texas, Southwestern Medical School
Director, Fellowship Program
Baylor Psoriasis Center
Chair, Psoriasis Guidelines Committee,
American Academy of Dermatology
Dallas, Texas

Robert G. Micheletti, MD
Assistant Professor of Dermatology and Medicine
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, Pennsylvania

A CME-CERTIFIED SUPPLEMENT TO
Skin & Allergy News®

Hidradenitis Suppurativa: Update on Diagnosis and Treatment

Faculty

Francisco A. Kerdel, BSc, MBBS
Director of Inpatient Dermatology
University of Miami Hospital
Professor of Dermatology and Vice Chairman
Florida International University
Miami, Florida

Alan Menter, MD
Chief, Division of Dermatology
Baylor University Medical Center
Clinical Professor of Dermatology
University of Texas, Southwestern Medical School
Director, Fellowship Program
Baylor Psoriasis Center
Chair, Psoriasis Guidelines Committee
American Academy of Dermatology
Dallas, Texas

Robert G. Micheletti, MD
Assistant Professor of Dermatology and Medicine
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, Pennsylvania

Reprinted from
Seminars in Cutaneous Medicine and Surgery

The manuscript was originally published as a supplement to *Seminars in Cutaneous Medicine and Surgery*, Vol. 33, No. 3S, June 2014. It has been reviewed and approved by the faculty as well as the Editors of *Seminars in Cutaneous Medicine and Surgery*.

The Guest Editors acknowledge the editorial assistance of Global Academy for Medical Education, LLC, and Joanne Still, medical writer, in the development of this supplement.

This continuing medical education (CME) supplement was developed from interviews with the faculty. Neither the editors of *Skin & Allergy News* nor the Editorial Advisory Board nor the reporting staff contributed to its content. The opinions expressed are those of the faculty and do not necessarily reflect the views of the supporter or of the Publisher.

Global Academy for Medical Education

Dermatologic Disease in IBD: What the Gastroenterologist Needs to Know

Alan Menter, MD

Baylor Scott & White, Dallas, TX

IBD Symposium
14, April 2018