# Acne and Acne related disorders

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### Acne vulgaris

-Acne vulgaris is a chronic disease originating within the pilosebaceous follicles.

-Four interrelated processes are involved:

sebum overproduction, abnormal shedding of follicular epithelium, follicular colonization by Cutibacterium acnes (previously called Propionibacterium acnes), and inflammation

### Pathogenesis

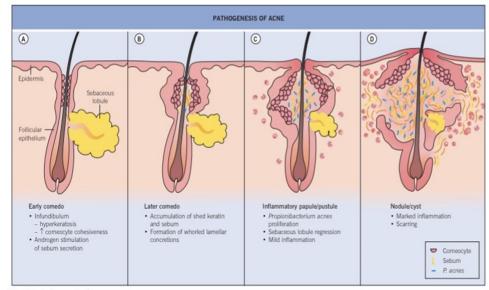


Fig. 36.1 Pathogenesis of acne.

### Clinical types (Comedonal acne) open (blackheads) and closed (whiteheads) comedones





#### COMEDONAL ACNE



Blackhead (Open comedome)



Whitehead (Closed comedome)

#### INFLAMMATORY ACNE



Papules

Pustules





Nodule

Cysts

### Moderate Acne



## Moderate to severe acne vulgaris. Multiple coalescing papules, pustules, and small nodules



### Post-inflammatory hyperpigmentation secondary to acne. Such pigmentary changes are most common in patients with darker skin colors





### scarring secondary to acne



Rolling Scar

Boxcar Scar

Ice Pick Scar

Keloid (Hyperthropic)



#### • Acne fulminans :

- Is the most severe form of acne and is characterized by the abrupt development of nodular and suppurative acne lesions in association with systemic manifestations (Fever , arthritis , leukocytosis

Synovitis , acne , pustulosis, hyperostosis, and osteitis (SAPHO) syndrome

- Recommended treatment of acne fulminans : prednisone 0.5–1 mg/kg/day as monotherapy for at least 2–4 weeks, followed by initiation of low-dose isotretinoin (e.g. 0.1 mg/kg/day) after the acute inflammation subsides

#### Acne conglobata :

- Acne conglobata is a severe form of nodulocystic acne that may have an eruptive onset but without systemic manifestations

- This recalcitrant acne variant is part of the follicular occlusion tetrad ; dissecting cellulitis of the scalp, hidradenitis suppurativa, and pilonidal sinus

- The association of sterile pyogenic arthritis, pyoderma gangrenosum, and acne conglobata can occur in the context of an autosomal dominant autoinflammatory disorder referred to as PAPA syndrome



#### Solid facial edema





• Neonatal acne (neonatal cephalic pustulosis) :

- The pathogenesis of neonatal acne has been the subject of debate.

-An inflammatory response to Malassezia has been proposed as the etiology by some investigators, leading to a renaming of the disorder as "neonatal cephalic pustulosis".

- Treatment : topical antifungal (e.g. ketoconazole 2% cream)

# Other acne variants

-Acne excoriée

-Acne associated with endocrinologic abnormalities (PCOS, cushing syndrome)

-Drug-induced acne: lithium , hydantoin , isoniazid, glucocorticoids, OCP, iodides , bromides, androgens, high dose vit b complex

-Occupational acne (tar, chloracne, oils)

-Acne cosmetica

-Tropical acne

-Radiation acne

# Drug induced (Steroid induced ) acne

- No comedones
- Monomorphous
- Predilection to chest and back



### Treatment

COMMON THERAPIES FOR	ACNE VULGARIS
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Topical therapy	Systemic therapy	
Benzoyl peroxide (1) Antibiotics – Clindamycin (1) – Erythromycin (1) – Sodium sulfacetamide/sulfur (1) Retinoids (1) Salicylic acid (2) Azelaic acid (1) Dapsone (1)	Oral minocycline (1) Oral doxycycline (1) Oral tetracycline (1) Oral erythromycin (1) Oral azithromycin (1) Oral contraceptives (1) Oral spironolactone (1) Oral isotretinoin (1)	

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**Table 36.5** Common therapies for acne vulgaris. Key to evidence-based support: (1) prospective controlled trial; (2) retrospective study or large case series; (3) small case series or individual case reports.

### Treatment

TREATMENT OF ACNE VULGARIS								
	Mild		Moderate		Severe			
	Comedonal	Papular/pustular	Papular/pustular	Nodular	Conglobata/fulminans			
First line	Topical retinoid	Topical retinoid + topical antimicrobial*	Oral antibiotic <sup>†</sup> + topical retinoid $\pm$ BPO	Oral antibiotic <sup>†</sup> + topical retinoid $\pm$ BPO	Oral isotretinoin (may require concurrent oral corticosteroid, esp. for acne fulminans)			
Second line	Alternative topical retinoid Azelaic acid Salicylic acid	Alternative topical retinoid + alt. topical antimicrobial Azelaic acid Salicylic acid Topical dapsone	Alternative oral antibiotic <sup>‡</sup> + alt. topical retinoid $\pm$ BPO/azelaic acid	Oral isotretinoin Alternative oral antibiotic <sup>†</sup> + alt. topical retinoid $\pm$ BPO/azelaic acid	Dapsone High-dose oral antibiotic + topical retinoid + BPO			
Options for female patients			Oral contraceptive/ antiandrogen	Oral contraceptive/ antiandrogen	Oral contraceptive/ antiandrogen			
Surgical options	Comedo extraction		Comedo extraction	Comedo extraction Intralesional corticosteroid	Intralesional corticosteroid			
Refractory to treatment		Exclude Gram-negative folliculitis	Exclude Gram-negative folliculitis					
			Female patient: exclude adrenal or ovarian dysfunction Exclude use of anabolic steroid or other acne-exacerbating medications					
Maintenance			Topical retinoid $\pm$ BPO	Topical retinoid $\pm$ BPO	Topical retinoid $\pm$ BPO			
*Antibiotic (e.g. clindamycin, erythromycin or sodium sulfacetamide) and/or BPO. <sup>†</sup> Tetracycline derivatives. <sup>‡</sup> e.g. azithromycin or trimethoprim–sulfamethoxazole.								

**Table 36.4** Treatment of acne vulgaris. Lack of response should also lead the clinician to consider non-compliance with treatment or another diagnosis. In general, monotherapy with a topical or oral antibiotic should be avoided. alt, alternative; BPO, benzoyl peroxide. Adapted from Gollnick H, Cunliffe W, Berson D, et al. J Am Acad Dermatol. 2003;49(1 Suppl):S1–37.

### Tetracyclines

### <u>S/E:</u>

-GI upset

- -Photosensitivity : more with doxycycline
- -Dyspigmentation , Skin , teeth, scar site mainly with minocycline
- -Drug induced Lupus mainly minocycline
- -Pseudotumor cerebri
- -Use in pregnancy: CI in 2<sup>nd</sup> & 3<sup>rd</sup> trimester AE on fetal teeth and bones
- -CI in children less than 9 yrs old d.t yellow discoloration of teeth , affects the bone development

#### • BOX 9.5 Drug Risks Profile—Tetracyclines

#### Contraindications

Hypersensitivity to tetracyclines or components of formulations

#### **Boxed Warnings**

None listed

#### Warnings & Precautions<sup>a</sup> Hypersensitivity Reactions

SJS/TEN, anaphylaxis rarely reported aMinocycline only—DRESS, serumsickness like reaction, drug-induced LE, vasculitis (autoimmune hepatitis)

#### Miscellaneous

Nephrogenic diabetes insipidus (demeclocycline only) aTissue hyperpigmentation (minocycline) aPseudotumor cerebri (alone or with isotretinoin)

#### **Pregnancy Prescribing Status**

Traditional US Food and Drug Administration rating—Category D *Newer rating*<sup>b</sup>—Moderate-high risk

<sup>a</sup>Under "Warnings & Precautions" these adverse effects can be considered relatively high risk or important clinical scenarios to avoid.

<sup>b</sup>See Chapter 65, Dermatologic Drugs During Pregnancy and Lactation, for detailed explanations of terms for "Newer rating" based on 2015 US Food and Drug Administration rulings. *DRESS*, Drug reaction eosinophils systemic symptoms; *LE*, lupus erythematosus; *SJS/TEN*, Stevens–Johnson syndrome/toxic epidermal necrolysis. Data from Facts & Comparisons eAnswers (online database). St. Louis: Wolters Kluwer. (https:// www.wolterskluwerodi.com/facts-comparisons-online/).

### Macrolides

#### • BOX 9.3 Drug Risks Profile—Macrolides

#### Contraindications

*Erythromycin*—dihydroergotamine, ergotamine, pimozide<sup>a</sup> *Azithromycin*—(a) hypersensitivity telithromycin, (b) cholestatic jaundice or hepatic dysfunction with prior azithromycin

#### **Boxed Warnings**

None listed

#### Warnings & Precautions<sup>a</sup> Cardiovascular

<sup>a</sup>Altered cardiac conduction, QTc prolongation, Hx torsades de pointes (uncorrected hypomagnesemia, hypokalemia) Clarithromycin possibly a risk in patients with CAD

#### Hypersensitivity Reactions

Urticaria, angioedema, SJS/TEN, DRESS, vasculitis (HSP)

#### **Pregnancy Prescribing Status**

*Traditional US Food and Drug Administration rating*—category B (Clarithromycin C) Clarithromycin—(a) cholestatic jaundice with prior clarithromycin, (b) hx QTc prolongation, torsades, (c) dihydroergotamine, ergotamine, pimozide

#### GI

 <sup>a</sup>Elevated LFT/hepatitis (esp. clarithromycin), usually reversible upon discontinuation
<sup>a</sup>Caution azithromycin patients significant liver impairment
<sup>a</sup>CDAD (has been reported to occur 2 months after d/c rx)

#### Neurologic

May aggravate weakness in patients with myasthenia gravis

Newer rating b-compatible

<sup>a</sup>Under "Warnings & Precautions" these adverse effects can be considered relatively high risk or important clinical scenarios to avoid.

<sup>b</sup>See Chapter 65, Dermatologic Drugs During Pregnancy and Lactation, for detailed explanations of terms for "Newer rating" based on 2015 US Food and Drug Administration rulings.

CAD, Coronary artery disease; CDAD, clostridium difficile-associated disease; DRESS, drug reaction eosinophils systemic symptoms; GI, gastrointestinal; HSP, Henoch-Schonlein purpura; LFT, liver function tests; SJS/TEN, Stevens–Johnson syndrome/toxic epidermal necrolysis.

Data from Facts & Comparisons eAnswers (online database). St. Louis: Wolters Kluwer. (https://www.wolterskluwercdi.com/facts-comparisons-online/).

### Isotretinoin

#### BOX 22.2 Drug Risks Profile—Isotretinoin

#### Contraindications

Hypersensitivity to acitretin, other retinoids, components of formulation (retinoid cross-reactivity data limited)

#### Boxed Warnings

Women of childbearing potential must follow all elements of iPLEDGE program (see text)

#### Warnings & Precautions<sup>a</sup>

Teratogenicity <sup>a</sup>Avoid blood donation during rx and  $\geq$  1 month after rx

#### Metabolic

\*Lipid effects—1 triglycerides/cholesterol, 1 HDL levels Glucose control may be impaired

#### Hepatic

Liver effects-as with acitretin, but much less likely

#### Musculoskeletal

\*Musculoskeletal—myopathy, arthralgia \*Extreme exertion—rhabdomyolysis reported (\*renal) \*Growth effects—DISH, premature epiphyseal closure Bone mineral density loss (caution concurrent corticosteroids)

Hematologic Neutropenia, rare agranulocytosis

#### Pregnancy Prescribing Status

Traditional US Food and Drug Administration rating-Category X

Sensitivity to parabens (Zenatane only) Pregnant or potentially pregnant women

Major risk of retinoic acid embryopathy in early pregnancy (see text)

Neurologic Pseudotumor cerebri (especially concurrent tetracyclines)

Psychiatric <sup>a</sup>Depression, suicide, psychosis

Visual & Hearing "Visual effects—1 night vision, dryness, 1 tolerance contacts Tinnitus and impaired hearing reported

Gastrointestinal Pancreatitis (especially with severe hypertriglyceridemia) Inflammatory bowel disease (largely disproven)

*Cutaneous* Avoid skin resurfacing procedures at least 6 months post rx

Hypersensitivity Reactions EM, SJS/TEN rarely reported

Newer rating ----CONTRAINDICATED

"Under "Warnings & Procautions" these adverse effects can be considered relatively high risk or important clinical scenarios to axoid. \*See Chapter 65, Dermatologic Drugs During Pregnancy and Lactation, for detailed explanations of terms for "Never raing" standard on 2015 US Food and Drug Administration rulings. DISH, Diffuse interstitial skeletal hyperostosis; EM entythemer multiformer; HDL, high density lipoprotein; SIS/TEM, Stevens-Johnson Syndrome/Toxic epidemal Anerolysis. Data from Facts & Comparisons enforces ionline diabasei. St. Louis: Wolters Klawer, Brites Jewww.veltersklaver.odi.comfacts.comparisons-online/.

### Isotretinoin

#### • BOX 22.7

**Relatively Common Minor Adverse Effects Caused by Systemic Retinoids** 

#### Cutaneous

#### Xerosis Palmoplantar, digital desquamation 'Retinoid dermatitis' Photosensitivity Pyogenic granulomas Stickiness sensationpalms, soles Staphylococcus aureus infections

#### Hair

Telogen effluvium Abnormal hair texture. drvness

#### Nails

Fragility with nail softening Paronvchia Onycholysis

#### Ocular

Dry eyes with visual blurring Blepharoconiunctivitis Photophobia

#### Oral

Cheilitis-especially lower lip Dry mouth Sore mouth and tongue

#### Nasal

Nasal mucosa drvness Decreased mucus secretion Epistaxis

#### Musculoskeletal

Arthralgias **Mvalgias** Fatique, muscle weakness Tendinitis

Neurologic Headache Mild depression

#### Gastrointestinal

Nausea Diarrhea Abdominal pain

#### • BOX 22.4 **Potentially Serious Adverse Effects Caused By Systemic Retinoids**

#### Teratogenicity

Retinoic acid embryopathy Spontaneous abortions

#### **Ocular**

Reduced night vision Persistent dry eyes Staphylococcus aureus infections

#### Bone

Diffuse skeletal hyperostosis Osteophyte formation Premature epiphyseal closure

#### Lipids Hypercholesterolemia<sup>a</sup> Hypertriglyceridemia

#### Gastrointestinal

Inflammatory bowel disease flare Pancreatitis<sup>b</sup> (because of 1 trialvcerides)

#### Hepatic

Transaminase elevations Toxic hepatitis (rarely)

#### Other Endocrine Effects

Hypothyroidism (central)b **Diabetes mellitus** (controversial)

#### Hematologic

Leukopenia<sup>b</sup> Agranulocytosis<sup>b</sup>

#### Neurologic

Pseudotumor cerebri Depression—suicidal ideation

#### Muscle

Myopathy

<sup>a</sup>Theoretically increased coronary artery disease risk with long-term therapy, <sup>b</sup>Primarily a risk with bexarotene (Targretin); pancreatitis also rarely reported with isotretinoin.

#### • BOX 22.5 Guidelines for Pregnancy Monitoring

#### **General Requirements**

- Must have had two negative urine or serum pregnancy tests with a sensitivity of at least 25 mlU/mL before receiving the initial isotretinoin prescription.
- The second pregnancy test should be done during the first 5 days of the menstrual period immediately preceding the beginning of isotretinoin therapy.
- For patients with amenorrhea, the second test should be done at least 11 days after the last act of unprotected sexual intercourse (without using two effective forms of contraception).
- Each month of therapy, the patient must have a negative result from a urine or serum pregnancy test.
- Must commit to two forms of contraception (at least one primary) for at least 1 month before initiation of isotretinoin therapy, during isotretinoin therapy, and for 1 month after discontinuing isotretinoin therapy.

#### **Additional Guidelines**

- Effective forms of contraception include both primary and secondary forms of contraception.
- Primary forms of contraception include: tubal ligation, partner's vasectomy, intrauterine devices, birth control pills, and injectable/implantable/ insertable hormonal birth control products.
- Secondary forms of contraception include diaphragms, latex condoms, and cervical caps; each must be used with a spermicide.
- Patients do not need to commit to two forms of contraception if they are abstinent or have undergone hysterectomy

### Rosacea

-A chronic skin rash involving the central face

-Starts between the age of 30 and 60 years.

-It is a common skin condition in those with fair skin



### Pathogenesis

-There are several theories regarding the cause of rosacea, including genetic, environmental, vascular, and inflammatory factors. Skin damage due to chronic exposure to UV light plays a role

-Hair follicle mites (Demodex folliculorum) are sometimes observed within rosacea papules

-Steroid induced rosacea

-An increased incidence of rosacea has been reported in those who carry Helicobacter pylori

### Triggering factors :

- -UVR
- -Extreme heat or cold
- -Spices
- -Hot beverages
- -Alcohol

### **Clinical picture :**

-Stage 1: persistent erythema and telangectasia

-Stage 2: persistent erythema and telangectasia, papules and pustules

-Stage 3: Solid edema and rhinophyma

-Ocular Rosacea : blepharitis , conjunctivitis , episcleritis







### **Perioral dermatitis**



### Treatment

### **General measure**

-Reduce exposure to triggers ( UV , Heat , steroid , hot spicy food, alcohol )

### Treatment

-Topical Rx:

Abx : Metronidazole , Erythromycin , Clindamycin Anti-mite : Ivermectin Alpha-2 agonist : brimonidine, oxymetazoline hcl Azelaic acid Calcineurin inhibitors (eg, tacrolimus and pimecrolimus)

-Oral Abx: Tetracyclines , Macrolides

-Oral Ivermectin

-Oral Isotretinoin

-Vascular Lasers

### Hidradenitis suppurativa (HS)

-Also called acne inversa, is a chronic inflammatory skin condition that affects apocrine gland-bearing skin in the axillae, groin, and under the breasts.

-It is characterized by persistent or recurrent boil-like nodules and abscesses that culminate in a purulent discharge, sinuses, and scarring.

-Hidradenitis suppurativa often starts at puberty, is most active between the ages of 20 and 40 years, and in women can resolve at menopause.

-It is three times more common in females than in males.

-HS can have a significant psychological impact, and many patients suffer from anxiety, depression.

### **Risk Factors**

-Family history of HS; 30-40% report at least one other family member affected

-Obesity and insulin resistance (metabolic syndrome)

-Cigarette smoking

-African ethnicity

-Follicular occlusion syndrome tetrad : acne conglobata, dissecting cellulitis of scalp, pilonidal sinus and HS

-Inflammatory bowel disease, particularly Crohn disease

-Other skin disorders: psoriasis, acne, hirsutism

-Comorbidities: hypertension, diabetes mellitus, dyslipidaemia, thyroid disorders, arthropathies, polycystic ovary syndrome, adverse cardiovascular outcomes

-Drugs: lithium

-Syndromes: PAPA syndrome PASH syndrome (pyoderma gangrenosum, acne, suppurative hidradenitis) PAPASH syndrome (pyogenic arthritis, pyoderma gangrenosum, acne, suppurative hidradenitis

#### Causes

HS is an autoinflammatory syndrome. The exact pathogenesis is not yet understood. Factors involved in the development of acne inversa include:

- -Follicular occlusion
- -An abnormal cutaneous or follicular microbiome
- -Release of pro-inflammatory cytokines
- -Inflammation causing rupture of the follicular wall, destroying sebaceous and apocrine glands and ducts.

## **Clinical picture**

Acne inversa can affect single or multiple areas in the axillae, neck, inframammary fold, and inner upper thighs. Anogenital involvement most commonly affects the groin, mons pubis, vulva, scrotum, perineum, buttocks, and perianal folds.

### **Clinical features**

It is characterized clinically by:

-Open double-headed comedones

-Painful firm papules and nodules ,Pustules, fluctuant pseudocysts, and abscesses

-Draining sinuses linking inflammatory lesions

-Hypertrophic and atrophic scars.



### **Double headed comedones**



# Draining sinuses and scars









The diagnosis of acne inversa requires all three components of the triad to be met:

- -Characteristic lesions
- -Typical distribution
- -Presence and recurrence of lesions.

# Assessment of disease severity :

The Hurley system, the most widely used assessment tool, describes three clinical stages.

Stage I: solitary or multiple isolated abscess formation without sinus tracts or scarring.

Stage II: Recurrent abscesses, single or multiple widely spaced lesions, with sinus tract formation.

Stage III: Diffuse involvement of an area with multiple interconnected sinus tracts and abscesses.



Figure 1. Typical Hidradenitis Suppuration (Hurley Stage I, II, and III)

# **Complication :**

-Secondary infection

-Psychological effects and negative impact on quality of life

-Lymphoedema of genitalia

-Squamous cell carcinoma

-Anemia of chronic disease

**General measures:** 

General measures for treating patients with hidradenitis suppurativa include:

Weight loss

Smoking cessation

Loose fitting clothing

Absorbent dressings

Analgesics

Management of anxiety and depression

**Topical treatments :** 

Antibacterial wash

Topical clindamycin

Other topical antibiotics: fusidic acid, dapsone, metronidazole.

**Intralesional steroid** 

**Systemic treatments:** 

-Antibiotics : Tertracyclines , clindamycin , Rifampin ,Short oral course for acute staphylococcal abscess

-Tetracyclines can be given as a single agent

-Prolonged courses of at least three months of combination antibiotics: clindamycin plus rifampicin; tetracyclines plus rifampicin

**Other systemic treatments** 

-Hormonal therapies: estrogens, anti-androgen therapy

-Biologics: Anti-TNF-alpha adalimumis , Infliximab

-Other systemic medical treatments used off-label: metformin, acitretin, dapsone, colchicine, and zinc gluconate

**Surgical and other procedural measures** 

- -Incision and drainage of acute abscesses
- -Local excision of persistent nodules, abscesses, and sinuses
- -Deroofing and curettage of persistent abscesses and sinuses
- -Radical excisional surgery of an entire affected area
- -Laser ablation (CO2) of nodules, abscesses, and sinuses
- -Laser/light hair removal.

Time for Q & A