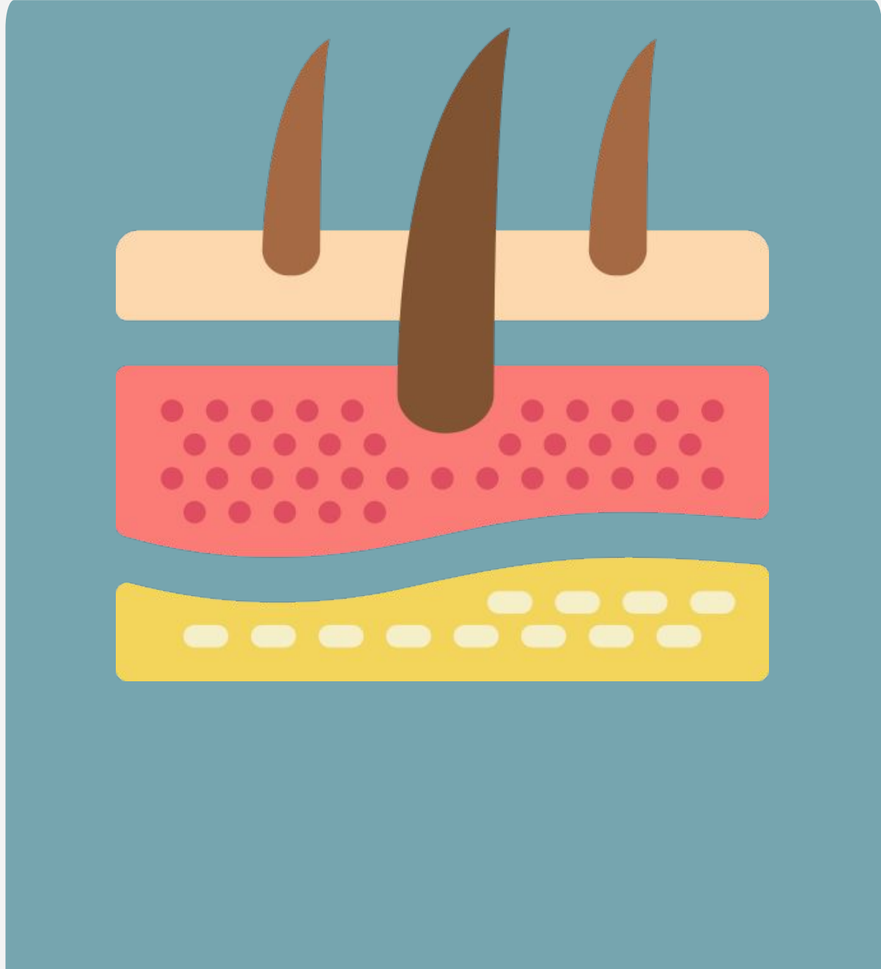


8-Acne Vulgaris & Acne Related Disorders

Objectives:

1. To know the multiple pathogenetic mechanisms causing acne
2. To recognize the clinical features of acne.
3. To differentiate acne from other acniform eruptions such as rosacea.
4. To prevent acne scars and treat acne efficiently.
5. To recognize the clinical features of rosacea, its variable types. differential diagnosis and treatment.
6. To recognize the features of perioral dermatititis, differential diagnosis and treatment.
7. To recognize the features of hidradenitis suppurativa and treatment.

Done by: AlHanouf AlJaloud, AlAnoud AlMansour, Ghada AlQarni
Revised by: Rotana Khateeb

References: Doctors slides + Notes

Color Index:

- Important
- Doctor's Notes
- Extra

Editing File

Acne Vulgaris

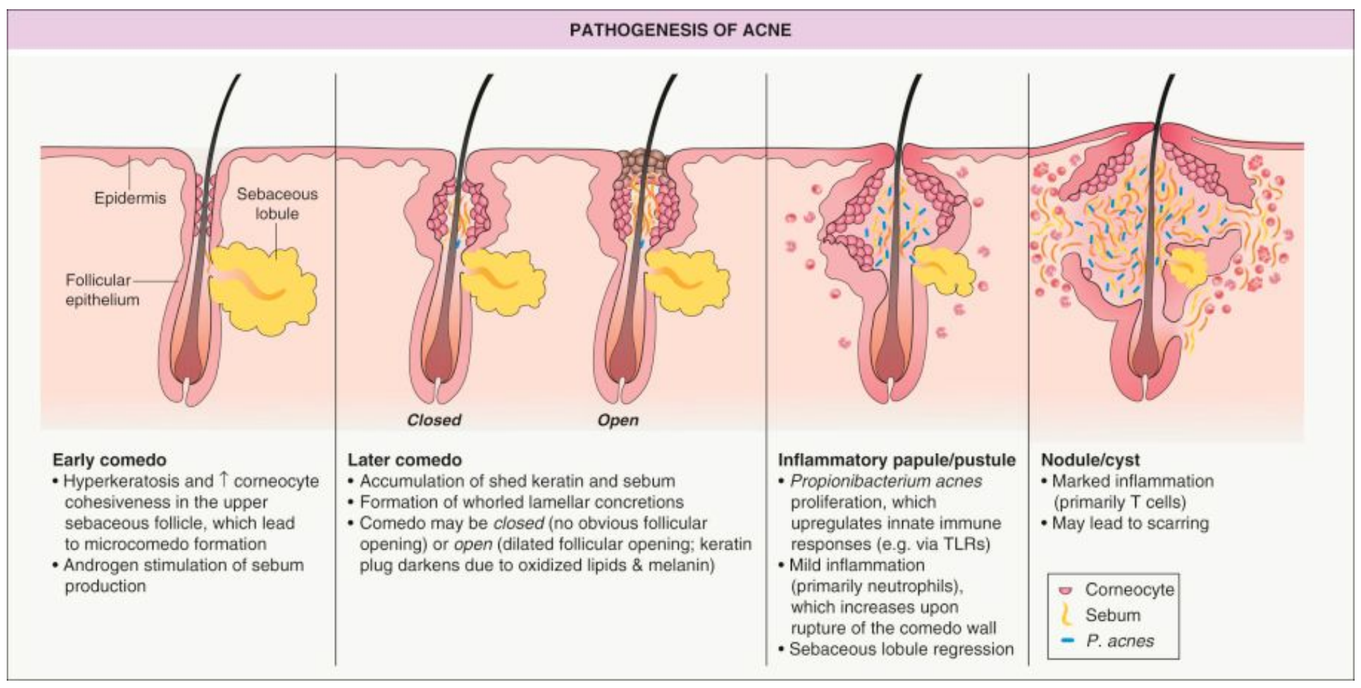
- Is a chronic inflammatory skin disease affecting the <u>pilosebaceous unit:</u>
  - (hair follicle + sebaceous gland + arrector pili muscle.)
- Affect the approximately 85% of the population at some point of their lives
- Occurs mostly during adolescence

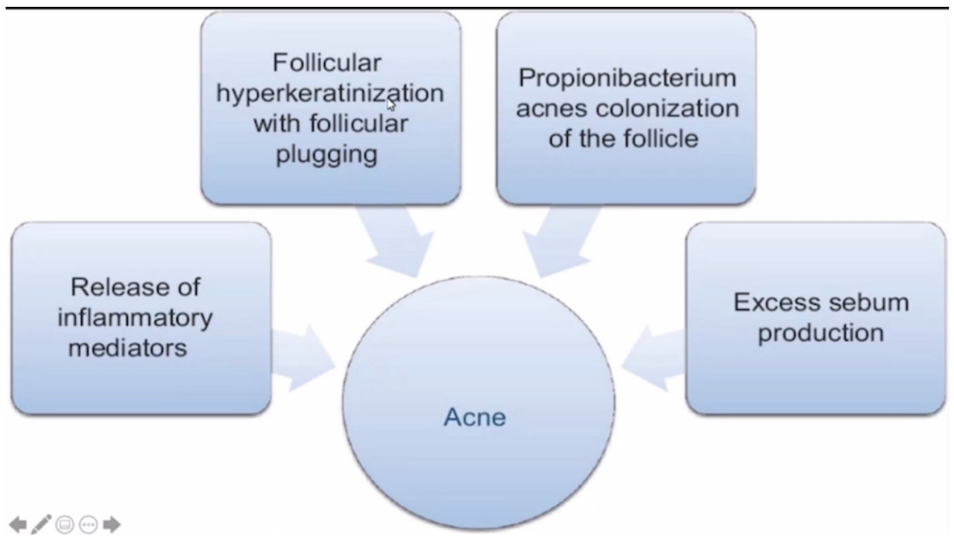
Pathogenesis

Four key pathogenic processes lead to the formation of acne lesions: know them in order

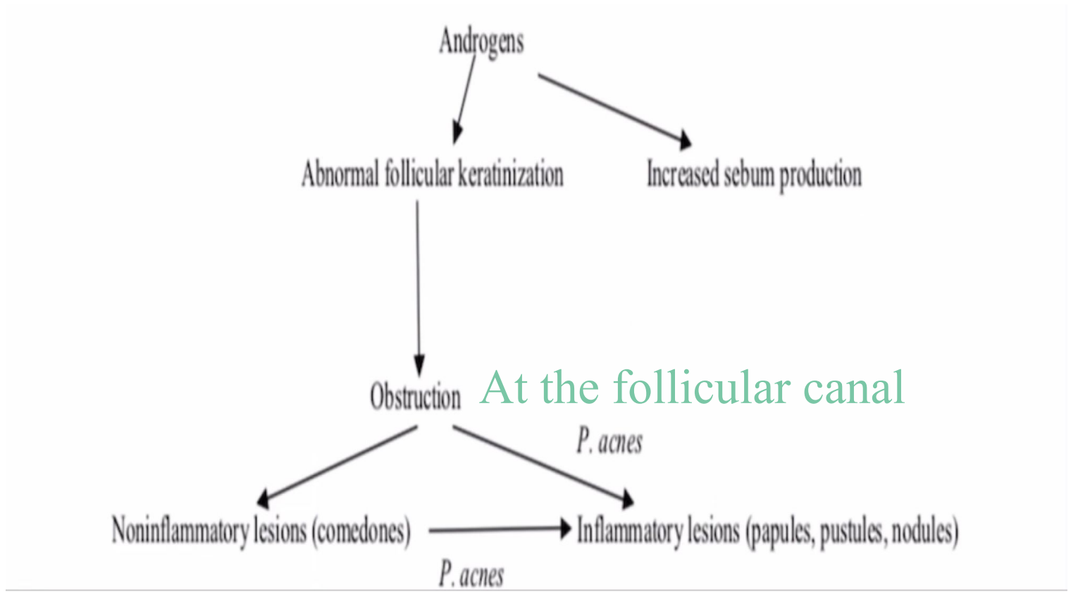
1. Alteration of follicular keratinization that leads to microcomedones (precursor for acne lesions, which are **hyperkeratotic plugs** made of **keratin** and **sebum** usually in the upper part of the follicular canal.
2. Increased and altered sebum production under androgen control
3. Follicular colonization by Propionibacterium acnes (bacteria)
4. Inflammatory mechanisms

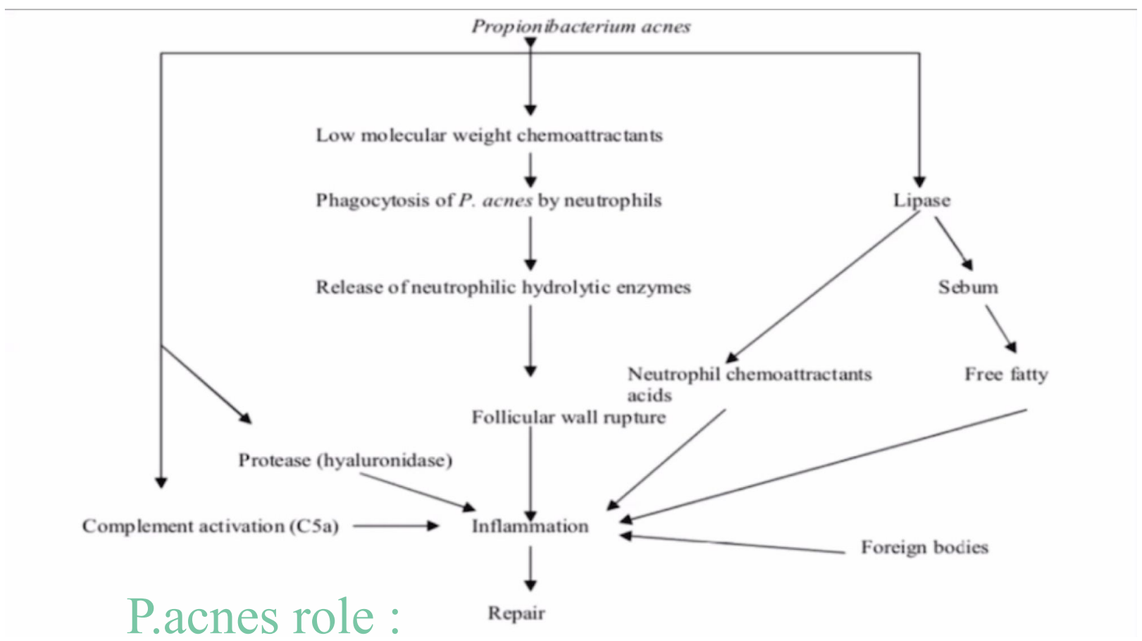
- Other factors which can contribute to the pathogenesis of acne:
  - Family history of severe acne (early disease onset and a severe clinical course)
  - Diet: controversial, hyperglycemic diet (other foods and supplements that have been reported to possibly exacerbate or trigger acne include skim milk, whey protein supplements, vit B12)
  - Environmental factors (smoking)
  - Occlusive cosmetics (hair products, hats)





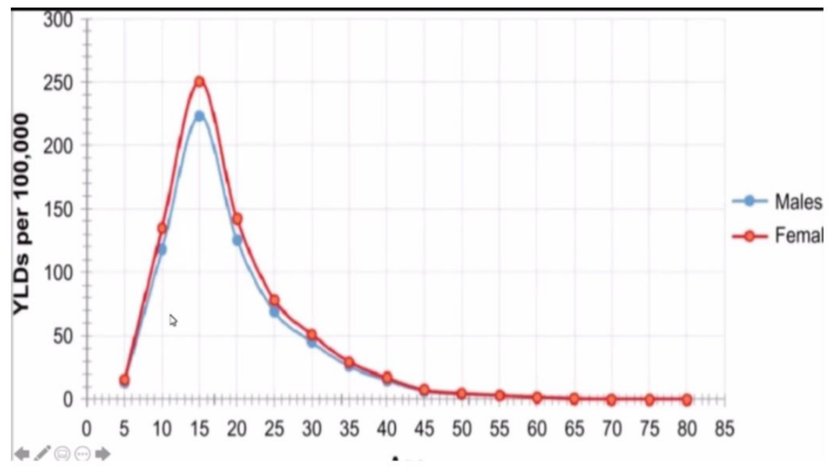
Androgen role:





P.acnes role :

Acne Vulgaris



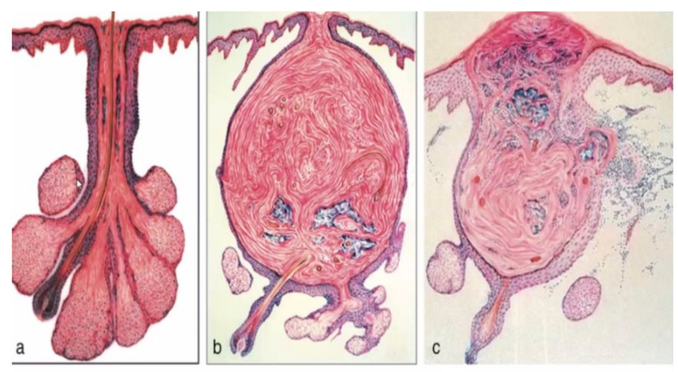
Shows the peak age of developing acne

Epidemiology:

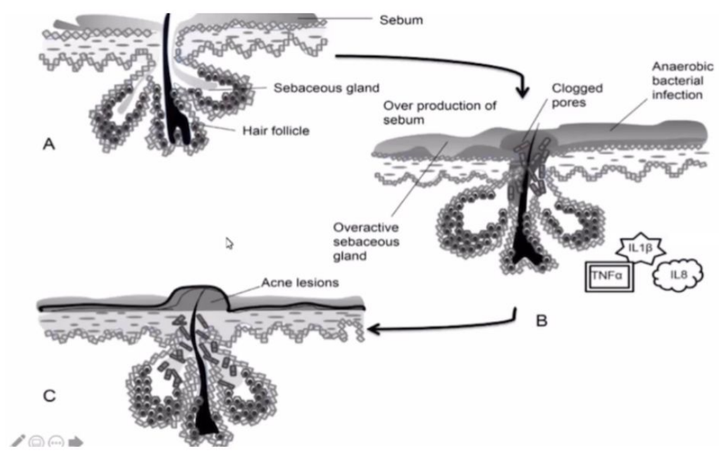
- 85% prevalence rates in those aged 12-24 years
- Has a peak incidence in 14-17-year-old girls and in 16-19-year-old boys
- Women have a high prevalence and incidence when compared with men, especially after 25 years of age (adult acne)
- Acne often persists into adulthood, with 26% of women and 12% of men reporting acne in their 40s (late-onset acne)
- About 20% of the affected individuals develop severe acne which results in scarring.
- Asians and Africans tend to develop severe acne

Clinical Features:

- Acne commonly affects: face, shoulders, upper part of the chest and back
- Has a pleomorphic appearance: Primary skin lesions & secondary skin lesions
  - **Primary Acne Lesions:**
    1. Non-inflammatory lesions:
       - **Comedones**
         - Pathognomonic for acne
         - Hyperkeratotic plug made of sebum and keratin in follicular canal
         - **Closed comedones (whiteheads)**
           - Are generally small (1 mm), skin-colored papules with no apparent follicular opening or associated erythema
         - **Open comedones (blackheads)**
           - Have a conspicuous dilated follicular opening (open follicular canal) that is filled with an inspissated core of shed keratin (melanin and oxidized lipids responsible for the black color)
    2. Inflammatory lesion p.acnes plays important role
       - Papules and pustules
       - Nodules
  - Secondary Acne Lesions:
    - Abscesses
    - Cyst
    - Post-inflammatory hyperpigmentation (mostly) or hypopigmentation
    - Excoriations
    - Scars

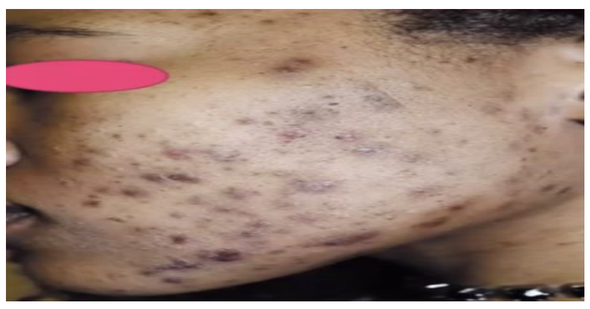


Normal sebaceous follicle (a), closed comedo (b), and ruptured follicle (c). From [1] with permission.



Acne Vulgaris

Pictures from the slides:














Scoring System:

Grading versus lesion counting

- Simple grading system:
  - **Grade 1:** Comedones, occasional papules
  - **Grade 2:** Papules, comedones, few pustules
  - **Grade 3:** Predominant pustules, nodules, abscesses
  - **Grade 4:** Mainly cysts, abscesses, widespread scarring
- **Mild, Moderate, Severe:**

General Classification	AAD[a]	Global Alliance	EDF	AAP
Mild	–	Comedonal or mixed and papular/ pustular	Comedonal or mild to moderate papulopustular	Comedonal or inflammatory/mixed lesions
Moderate	–	Mixed and papular/ pustular or nodular	Mild to moderate papulopustular	Comedonal or inflammatory/mixed lesions
Severe	–	Nodular or conglobate	Severe papulopustular/ moderate nodular or severe nodular/ conglobate	Inflammatory/mixed and/or nodular lesions

Acne Subtypes

1. Neonatal Acne (Neonatal Cephalic Pustulosis):

- Onset between 0-6 w of age (usually at 2 weeks of age)
  - Androgens comes from the mother through the placenta, so they develop acne in the 1st few weeks of life.
- Affect up to 20% of newborn
- Presents as small papulopustules on:
  - the cheeks, forehead, eyelids and chin
- A possible etiology is an inflammatory response to:
  - Malassezia spp. (e.g. sympodialis, furfur) normal microbiota
- Usually resolves by 3 months of age
- Due to the transient and benign nature of neonatal acne, reassurance of parents alone is usually adequate not a precursor to other lesions/types.
- No relation with later development of acne
- Can treat with topical imidazoles such as ketoconazole 2% cream but usually self limiting.

2. Infantile Acne:

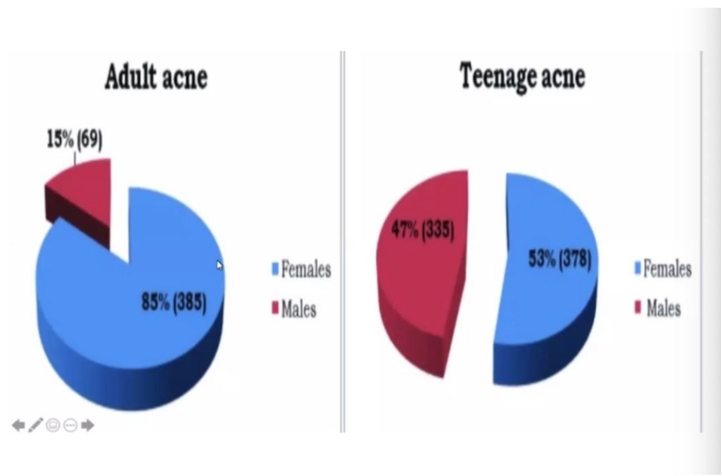
- Affects less than 2% of infants
- Between 2-12 months of age
- Male predominance
- **Pathogenesis:**
  - Here the androgens are produced by the baby, and you need to look for the source.
  - Androgen production intrinsic to this stage of development, including elevated levels of LH stimulating testicular production of testosterone in boys during the first 6-12 months of life and elevated levels of DHEA produced by the infantile adrenal gland in both boys and girls
  - These androgen levels normally decrease substantially by 12 months of age and remain so until adrenarche
- Patients should be assessed for signs of hyperandrogenism, precocious puberty secondary to brain **hamartoma** and **astrocytoma**, or abnormal growth;
  - If these findings are present, endocrinologic evaluation including:
    - Hand/wrist X-ray to determine **bone age**
    - Laboratory testing of **hormone levels** should be performed especially LH
- Presents as closed and open comedones, papules, pustules, nodules, and cysts
- Commonly over face
- Usually resolves within 6 to 18 months
- At higher risk of severe acne during adolescence
- **1st line treatment:**
  - Topical retinoid or benzoyl peroxide
  - Severe inflammatory lesions
    - Oral antibiotics such as erythromycin or azithromycin
  - In recalcitrant or severe nodulocystic type Isotretinoin avoid tetracycline

3. Mid-Childhood Acne:

- Same as infantile acne
- Between the ages of 1 and 8 years
- More in boys
- Uncommon time for acne development
- Consider the possibility of an underlying hyperandrogenic condition such as:
  - Premature adrenarche
  - Congenital adrenal hyperplasia
  - Androgen-secreting tumor
- Assess for signs and symptoms of hyperandrogenism and precocious puberty,
  - The child's growth curve should be carefully reviewed
  - Hand/wrist bone age X-ray performed if there are signs of accelerated growth
- If abnormalities are present on exam, labs or imaging, complete endocrine evaluation
- Treatment is similar the infantile acne depending on severity (topical benzyl peroxide ,..)

4. Adult Acne:

- More in female
- Above 25 y/o
- Present with mixture of inflammatory and comedonal acne over face and trunk
- Mandibular region most commonly affected
- Associated with smoking
- If associated with **hirsutism**, **irregular periods** evaluate for hyper secretion of ovarian androgens
  - (e.g. Polycystic ovary syndrome); female above 25 with acne
- Approximately 1/2 of the patients report persistence of acne lesions from adolescence, and 1/4 report periods of remission then recurrence
- The classical presentation of adult acne consist of inflammatory papulopustular in the lower half of the face specially jaw line.



5. Acne Conglobata:

- A rare but severe form of acne, **men** > women
- Maybe eruptive, no systemic symptoms
- **Second and third decade of life**
- Believed that **Propionibacterium acnes** may play an important role in the disease by changing its reactivity as an antigen.
  The hypersensitivity to this antigen induces an intense immunological reaction that presents with a chronic inflammatory state.
- Paired or aggregates of blackheads on the trunk, neck, upper arms, and buttocks
- Highly inflammatory lesions: nodules, **abscesses draining sinuses**, over the back and chest
- Heals with scars (Depressed or Keloidal)

6. Acne Fulminans:

- Most severe form of acne
- Abrupt development of nodular and **suppurative** (oozing) **acne lesions**
- Associated with systemic features such as:
  - **Fever**, **arthralgias**, **hepatosplenomegaly**
- Lab abnormalities include:
  - **Leukocytosis, high ESR, anemia**
- More common in boys 13-16 years
- Typically patients have mild to moderate acne before, then numerous microcomedones suddenly erupt and become inflamed
- Evolve into painful **oozing** friable plaques, can ulcerate, scar significantly
- Face, trunk, arms commonly affected
- Recommended treatment:
  - Prednisone (1st line)
    - To decrease the inflammation
    - 0.5-1 mg/kg/day as monotherapy **for at least 2-4 weeks.**
  - followed by initiation of low-dose isotretinoin
    - **After the acute inflammation subsides**
    - (e.g. 0.1 mg/kg/day)

7. Drug Induced Acne:

- Mostly caused by steroids
- The characteristic feature:
  - Absence of comedones
  - Monomorphic lesions composed of small pustules and papules
    Same color and same size

monomorphic lesions

CAUSES OF DRUG-INDUCED ACNE	
Common	Uncommon
Anabolic steroids (e.g. danazol, testosterone)	Azathioprine
Bromides *	Cyclosporine
Corticosteroids (see Fig. 36.13)	Disulfiram
Corticotropin	Ethosuximide
EGFR inhibitors (see Fig. 36.15 and Ch. 21)	Phenobarbital
Iodides †	Propylthiouracil
Isoniazid (see Fig. 36.14)	Psoralen + ultraviolet A
Lithium	Quinidine
MEK inhibitors (e.g. trametinib)	Quetiapine
Phenytoin	TNF inhibitors
Progestins (see text)	Vitamins B 6 and B 12

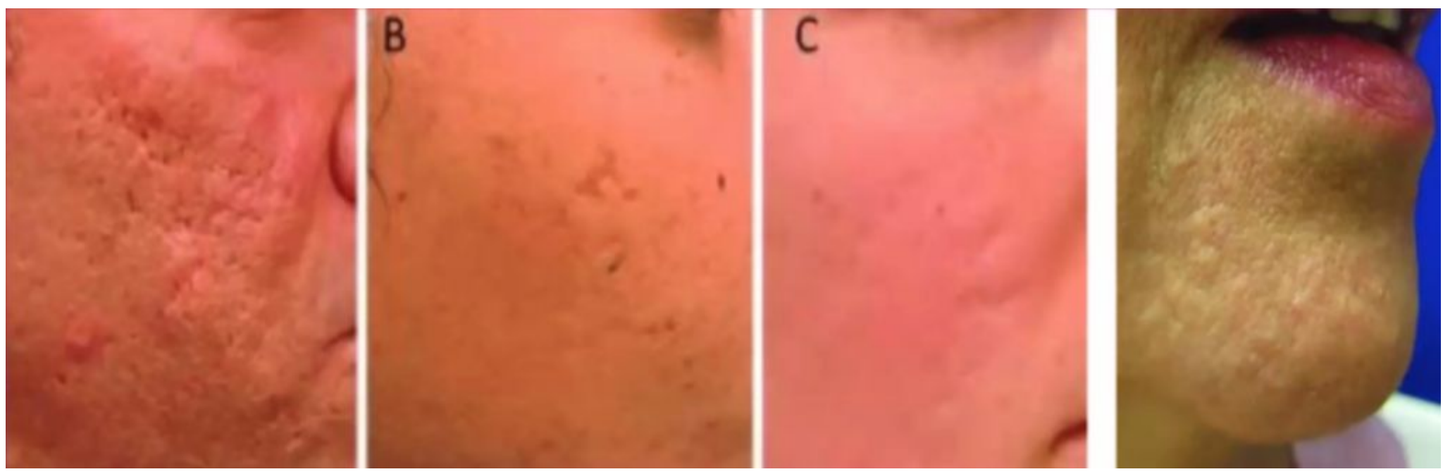
* Found in sedatives, analgesics and cold remedies.
† Found in contrast dyes, cold/asthma remedies, kelp, and combined vitamin–mineral supplements.

8. Other Rare Acne Subtypes:

- Chloracne
  - Occupational acne with severe systemic effects (CNS symptoms, liver damage, decrease lung vital capacity)
- SAPHO (Synovitis, acne, pustulosis In pustular psoriasis, hyperostosis and osteitis)
- Occupational acne
- Acne excoriée
- Acne cosmetica face/hair products
- Pomade acne (forehead, temples)
- Tropical acne excessive heat exposure
- Acne mechanica violinist : they rest the violin on the chin leading to ”occlusion” and acne only on the chin area.

Acne Complications

- **Quality of life:** Significant association between severity of acne and QQL (the most important)
- Post inflammatory hyperpigmentation
- **Scars:** types of acne scars
  - Atrophic acne scars (4 types)
    A. Icepick scar
    B. Box scar
    C. Rolling scar
    D. Papular scar
      - (cobblestone-like papules)
  - Hypertrophic or keloid scars



Icepick scar Box scar Rolling scar Papular scar

Management of Acne

1. Education:

- About: course, diet and smoking.

2. Cleansing:

- Washing frequency
- Soaps bars (Benzoyl Peroxide, Salicylic Acids, Alpha Hydroxy Acids)
- Gentle liquid cleansers

3. Topicals:

- **Retinoid** (Adapalene, tretinoin, tazarotene) (comedolytic)
- **Benzoyl Peroxide** (antibacterial) - doesn't lead to resistance
- **Azelaic Acid** (antibacterial, bleaching) The only topical that is safe during pregnancy
- **Salicylic Acids** (comedolytic) less potent than retinoic acid
- **Resorcinol/ sulfur** (keratolytic)
- **Topical Antibiotics:**
  - Erythromycin
  - Clindamycin (more chance of developing resistance)
  - Sodium sulfacetamide
  - Dapsone Gel 7.5%

Summary of recommendations for topical therapies

Topical antibiotic monotherapy is highly discouraged. *Level 1+, Grade A*

Combination topical therapy is preferable and more effective than topical antibiotic alone. *Level 1+, Grade A*

Consider alternative antibacterial agents, such as benzoyl peroxide, salicylic acid, or dermocosmetics. *Level 4, Grade D, GPP*

Addition of BPO to adapalene is significantly more effective than adapalene monotherapy or BPO monotherapy. *Level 1+, Grade A*

Topical retinoids are effective first line therapy against both comedonal and inflammatory acne. *Level 1++, Grade A*

Fixed-combination therapy of BPO and adapalene provides significantly greater efficacy for the treatment of acne vulgaris as early as week one relative to monotherapies, with a comparable safety profile to adapalene. *Level 1+, Grade A*

Topical retinoids are recommended for maintenance in acne after successful treatment of acne. *Level 1+, Grade A*

Antibiotics do not prevent the development of microcomedones and should be discouraged as maintenance. *Level 4, Grade D, GPP*

TIPS FOR TOPICAL ACNE THERAPY	
Improve adherence – often compromised due to patients having busy schedules or quitting when the response is not rapid	• Simplify the regimen: once daily when possible; consider combination products (e.g. benzoyl peroxide + adapalene or clindamycin; tretinoin + clindamycin), especially in less motivated adolescents • Inform patients that it will take 6–8 weeks of treatment for substantial improvement • Ask specifically about adherence: "Out of 7 nights, how many times do you apply the medication?"
Educate on proper use	• In general, topical medications (especially retinoids) should be used to the entire acne-prone region rather than as "spot treatment" of individual lesions • Provide instructions on where to apply the medication and how much to use
Minimize irritation – most common in adolescents with atopic dermatitis and adults	• Note that using too much medication or applying it too frequently can increase irritation • Devise a gradual initial approach to improve tolerance in patients with sensitive skin; for example, a single agent may be used for the first 2–3 weeks (starting every other day for retinoids), followed by slow introduction of a second medication (e.g. transitioning from alternate days to daily) • Advise to avoid harsh scrubs and other irritating agents (e.g. toners, acne products that are not part of the regimen) • Suggest use of a non-comedogenic sensitive skin moisturizer if dryness occurs
Avoid exacerbation	• Review all skin care products and cosmetics; having patients bring everything that they apply to their face to a visit may help to determine the source of problems • Advise non-comedogenic products (e.g. moisturizers, sunscreens, make-up) and to avoid having oily hair or using pomades that may contribute to acne. • Instruct patients not to pick or manipulate lesions

TREATMENT OF ACNE VULGARIS

	Mild		Moderate		Severe
	Comedonal	Papular/pustular	Papular/pustular	Nodular	Conglobata/fulminans
First line	Topical retinoid	BPO ± topical antibiotic Topical retinoid + topical antimicrobial(s)*	Oral antibiotic† + topical retinoid ± BPO Topical retinoid + BPO ± topical antibiotic	Oral antibiotic† + topical retinoid ± BPO	Oral isotretinoin (may require concurrent oral corticosteroid, esp. for acne fulminans)
Second line	Alternative topical retinoid Azelaic acid Salicylic acid	Alternative topical retinoid and/or topical antimicrobial Azelaic acid Salicylic acid Topical dapsone	Alternative oral antibiotic‡ + alt. topical retinoid ± BPO/ azelaic acid	Oral isotretinoin Alternative oral antibiotic‡ + alt. topical retinoid ± BPO/azelaic acid	Oral antibiotic (± high dose)+ topical retinoid + BPO Oral dapsone
Options for female patients			Oral contraceptive/ antiandrogen	Oral contraceptive/ antiandrogen	Oral contraceptive/ antiandrogen
Procedural 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 ± BPO	Topical retinoid ± BPO	Topical retinoid ± BPO

*Antibiotic (e.g. clindamycin (preferred), erythromycin, or sodium sulfacetamide [level 1 evidence for all 3]) and/or BPO (level 1 evidence).
†Tetracycline derivatives: tetracycline, doxycycline, minocycline (level 1 evidence for all 3).
‡e.g. azithromycin (level 1 evidence) or trimethoprim–sulfamethoxazole.

Summary of recommendations for the management of pediatric patients

Topical treatment with benzoyl peroxide is safe and effective and can be used as monotherapy or in topical combination products for mild acne or in regimens of care for acne of all types and severities. *Level 4, Grade A*

Fixed-dose combination topical therapies might be useful in regimens of care for all types and severities of acne *Level 1−, Grade A for adolescents, Grade B for preadolescents and younger*

Oral isotretinoin is recommended for severe, scarring, and/or refractory acne in adolescents and can be used in younger patients *Level 1+, Grade A for adolescents, Grade B for preadolescents and younger*

A low starting concentration (i.e., 2.5% BPO) is recommended as children are more prone to irritation. It might minimize development of antibiotic-resistant *P. acnes* when used with topical or systemic antibiotics *Level 4, Grade D*

4. Systemic treatment

A. Oral antibiotics: (will not work much in cases of comedonal acne)

- For <u>moderate to severe inflammatory acne</u>, Usually used for 3-6 months
- **Tetracycline** group:
  - Doxycycline (1st line) more preferable
  - Minocycline (2nd line) more rare sever side effects (induces SLE)
- **Macrolides**:
  - Erythromycin, azithromycin (1st line)
- **Trimethoprim-sulfamethoxazole**
  - In resistant cases.
- **Clindamycin**

Summary of recommendations for systemic antibiotics

Doxycycline, tetracycline and erythromycin are recommended as first line oral antibiotics. The absorption of tetracycline is restricted by food and dairy products. Erythromycin can be used to treat acne in pregnancy. *Level 1+, Grade A*

Minocycline is considered as a second-line antibiotic for acne due to evidence of more severe adverse events in comparison to doxycycline. *Level 1+, Grade A*

Cotrimoxazole is recommended only as a third-line antibiotic, when other treatments have failed. *Level 2++, Grade B*

Systemic antimicrobials should not be used together with topical antibiotics or as monotherapy. *Level 4, Grade D, GPP*

B. Hormonal Therapy:

- Considered as second-line treatment for female patients with acne and can be effective whether or not the serum androgen levels are abnormal (Acne with irregular menstrual cycle)
- Suitable for long-term therapy:
  - Represent an alternative to systemic antibiotics, no potential to induce bacterial resistance.
- Recommended in the following situations:
  - Presence of severe seborrhea;
  - Worsening in the premenstrual period
  - Presence of endocrine changes
  - Persistent recalcitrant inflammatory acne in which standard treatments have failed
- Combined oral contraceptives (COCS)
  - Effective in the treatment of both non inflammatory mostly and inflammatory acne
- Antiandrogens include:
  - Cyproterone acetate, spironolactone, and flutamide.

Systemic treatment

C. Isotretinoin

- Works to normalize all four key pathogenic features of acne vulgaris
- Very severe acne
- Scarring acne
- Significant acne that has not responded to therapy within 3-4 months
- Standard dose:
  - 0.5-1 mg/kg with a total cumulative dose between 120 mg-150 mg/kg
- Better taken with fatty meals to enhance absorption
- Start with a small dose for the first months to avoid initial acne flare and allow adjustment to dose dependent side effects like dryness
- Patients who are less likely to respond to isotretinoin or require multiple or longer courses include:
  - Adolescents under 16 years of age who have nodulocystic acne
  - Individuals with endocrine abnormalities PCOS
  - Women with less severe acne

- **Side effects:**

  - **Skin and mucous membranes** are the most common and dose-dependent:
    - Cheilitis inflammation of the lips due dryness
    - Dryness of the oral and nasal mucosa
    - Generalized xerosis
    - Skin fragility.
    - Others include induction of an acne fulminans-like flare, formation of excessive granulation tissue, paronychias, and cutaneous infections (Staphylococcus aureus)
  - **Teratogenicity**
    - Is a serious potential complication; Female patients of childbearing potential must have at least one negative pregnancy test before starting treatment and must practice effective contraception for 1 month prior to, during, and for 1 month after completing therapy
  - **Elevated serum triglyceride and/or cholesterol levels** in 20-50% of patients, however, severe elevations are uncommon and develop within the first two months of therapy dose dependent
  - **Musculoskeletal system**
    - (e.g. myalgias, elevation of serum creatine kinase levels),
  - **Eyes:**
  - **Liver**
    - Elevated transaminases x2 or x3 the level is worrisome either lower the dose or stop med
  - **Intestines**
    - (controversial, no link with inflammatory bowel disease found in a recent meta-analysis)
  - **Central nervous system**
    - Headache
    - Pseudotumor cerebri rare, Should not be given with tetracycline it increases its risk.
    - No firmly established causal association with depression or suicide has been demonstrated
    - A recent meta-analysis did not show an association between isotretinoin treatment and increased risk of depression; instead, 12 acne therapy led to a decreased prevalence of depression

Management of Acne

Summary of recommendations for systemic isotretinoin

Oral isotretinoin is recommended for the treatment of severe acne that has not responded to conventional therapy. *Level 1++, Grade A*

Referral to a dermatologist is recommended in cases of severe nodulocystic acne or conglobate acne. *Level 4, Grade D, GPP*

An acceptable high-dose isotretinoin therapy of nodulocystic acne is 120 to 150mg/kg cumulative dose. *Level 1+, Grade A*

For non-nodulocystic or moderate acne, a 0.3 to 0.5mg/kg dose for six months might be sufficient. *Level 1+, Grade A*

Low-dose maintenance for adult persistent acne can be considered, but with caution due to potential adverse events. *Level 2+, Grade C*

Pregnancy is an absolute contraindication to systemic isotretinoin. Sexually active female patients should be made aware of the risk of teratogenicity and must be screened for pregnancy. *Level 4, Grade D, GPP*

Contraception should be discussed with the patient. The patient must be routinely reminded to avoid pregnancy. *Level 4, Grade D, GPP*

Screen for symptoms of depression before and during treatment and inform the patient of possible risk of depression and suicidal behaviors. *Level 4, Grade D, GPP*

For long-term therapy, monitoring of laboratory parameters (e.g., serum cholesterol, triglycerides, liver function tests) every six months is recommended. *Level 4, Grade D, GPP*

Maintenance with topical retinoids is recommended for at least several months after treatment cessation with oral isotretinoin. Addition of BPO might be required for

Summary recommendation for treatment of acne scars.

Fractional resurfacing is recommended to treat acne scars. *Level 1+, Grade B*

For ice pick scars, it might be necessary to excise or punch out the lesion or perform chemical reconstruction. For box car scar, an excision, punch elevation/excision, or subcision can be performed. For rolling scars, subcision can be performed. *Level 2+, Grade C*

Summary recommendation for treatment of acne scars.

Fractional resurfacing is recommended to treat acne scars. *Level 1+, Grade B*

For ice pick scars, it might be necessary to excise or punch out the lesion or perform chemical reconstruction. For box car scar, an excision, punch elevation/excision, or subcision can be performed. For rolling scars, subcision can be performed. *Level 2+, Grade C*

Treatment choices for pregnant and lactating women

TREATMENT		EVIDENCE LEVEL
First-line	1. Antibiotics (erythromycin, clindamycin) 2. Benzoyl peroxide 3. Azelaic acid 4. Salicylic acid	Level 2– to 3, Grades C to D
Second-line	1. Oral macrolides (azithromycin) 2. Cephalexin	Level 3, Grade D
Third-line	1. Chemical peel (glycolic acid) 2. Light-based therapy (intense pulsed light, blue or red light phototherapy) in addition to topical and/or oral therapies	Level 3, Grade D

Rosacea (Acne Rosacea)

- A common chronic inflammatory skin disease of the central facial skin and is of unknown origin, more common in females with fair skin. The disease presents with:
- The hallmark is:
  - Episodes of flushing and central facial erythema in butterfly distribution. SLE is one of the Ddx.
  - Telangiectasias
  - Papules/pustules.
  - In contrast to acne, comedones are not present.
- In severe cases, the nose develops a large, bulbous shape (rhinophyma).

Epidemiology:

- Affecting approximately 10% of the population
- More in Fitzpatrick skin type I and II and from northern European or Celtic ancestry
- Females = males

Pathogenesis:

- The pathogenesis of rosacea is a complex interplay of:
  - Genetic
    - Genetic predisposition (up to 20% have family history)
    - Both environmental factors and genetic predisposition play a role
  - Immunologic
  - Neurovascular factors.
    - The major abnormalities that play a role are aberrant innate immune response and neurovascular dysregulation
- Constitutional predisposition to flushing and blushing
- UV radiation
- Skin barrier dysfunction
- Demodex mites (folliculorum brevis)
- Current evidence suggest that it is unlikely that H.pylori infection plays an etiological factor in rosacea

Triggers: Anything that causes flushing and blushing of the skin.

- Hot or cold temperature or wind
- Hot drink
- Spicy food
- Alcohol
- Heavy exercise
- Emotional stress
- Topical products that irritate the skin and decrease the barrier
- Medications that cause flushing and photosensitivity (amiodarone, nicotinamide)

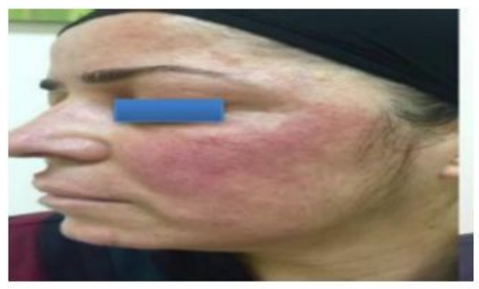
Clinical presentation:

1. **Patient History:**
   - Does the patient describe experiencing a warm sensation over the face, or flushing?
   - Does the patient recognize his or her own redness, or erythema?
   - Burning or stinging in association with skin care products. Sensitive skin
   - History of acne diagnosis and failed acne treatments
   - Triggers, such as heat, spicy foods, and stress.
   - Family history
   - Recognition of signs and symptoms of rosacea
2. **Examination**

Classification of Rosacea

1. Erythemato-telangiectatic Rosacea

- Flushing
- Persistent redness (erythema) of the central face
- Telangiectasias
- Very sensitive skin, and may feel as if their skin stings or burning sensation


Persistent erythema (checks,nose,forehead,chin)

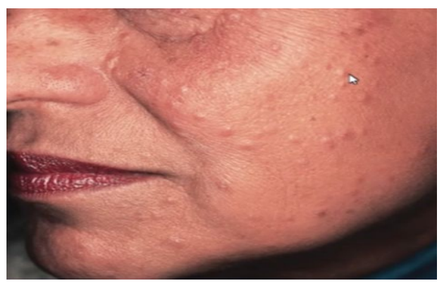
2. Papulopustular Rosacea

- May occur along with the facial redness and flushing of rosacea subtype
- Papules and/or pustules that come and go, combined with transient or persistent facial redness
- On the central face: burning and stinging; small visible blood vessels (telangiectasia); raised, scaly red patches known as plaques




3. Granulomatous Rosacea

- Rare
- **Characterized by:**
  - Monomorphous, persistent skin colored to dull red-brown 1-3 mm facial papules.
  - Favoring central face
- Histological examination shows granulomatous dermatitis

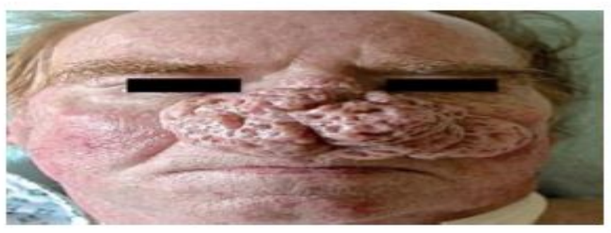


Classification of Rosacea

4. Phymatous Rosacea

- Sebaceous glands hypertrophy and fibrosis
- Phymatous rosacea can affect **nose (rhinophyma**, most common), **chin (gnathophyma)**, **forehead (metophyma)**, **ears (otophyma)** and **eyelids (blepharophyma).**
- Earliest clinical sign of rhinophyma is **dilated pores** over the distal portion of the nose
- Shows marked skin thickenings and irregular surface nodularities
- Telangiectasia

rhinophyma



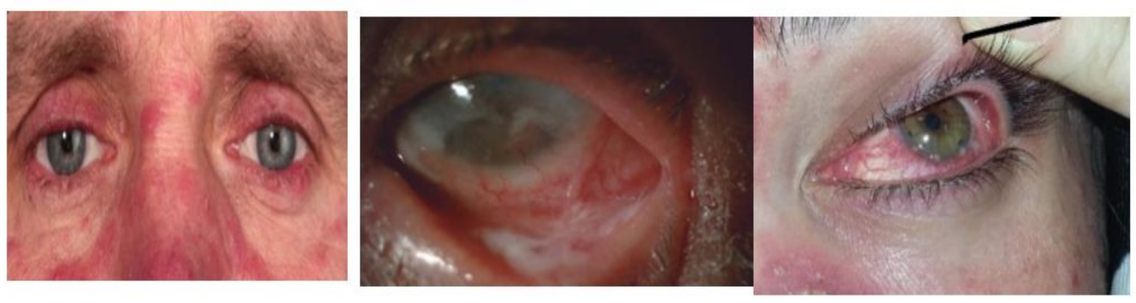
Severe rhinophyma

metophyma

gnathophyma

5. Ocular Rosacea Common , sometimes not diagnosed due to the absence of cutaneous lesions

- May or may not be associated with cutaneous lesions
- Ocular rosacea range from minor irritation to sever inflammatory keratitis
  - Conjunctival hyperemia (most common)
  - Blepharitis
  - Dry eyes
- **Symptoms**:
  - Dryness, gritty sensation
  - Tearing crusting at the corneal margins
  - Pruritus, frequent styes
- **Signs**:
  - Conical dandruff
  - Mild scaling at the eyelid margin
  - More active disease, signs of blepharitis → eyelid swelling conjunctival injection
- Severe ocular disease is rare
  - e.g. keratitis, corneal neovascularization, uveitis, scleritis, and iritis



Management of Rosacea

1. General Measures

- Chronic relapsing nature
- **Avoid recognized triggers**
- Change work (e.g. sailars)
- **Gentle skin care regimen t**o maintain skin hydration and barrier function
- Gentle, PH-na;anced, fragrance-free, soap-free cleanser once per day in the evening
- Light, water-based cosmetics (but powders are preferable to creams)
- **Photoprotection** SPF 30 or above

Management of Rosacea

2. Topical Therapies

- **Metronidazole** 0.75% (gel, cream, and lotion; twice-daily application), metronidazole 1% (gel and cream; once-daily application). Topical antibiotics
- Azelaic acid 15% gel (twice-daily)
- Ivermectin 1% cream (once-daily application)
- **Brimonidine tartrate** 0.33% gel (MIRVASO Gel): Temporary Tx of erythema (someone going to event)
  - Topical treatment of persistent facial erythema associated with rosacea
  - Brimonidine gel is a selective α2-adrenergic receptor agonist with **vasoconstrictive activity.**
- Permethrin cream
- Topical calcineurin inhibitors: Pimecrolimus 1% cream or Tacrolimus 0.03 or 0.1% ointment

3. Systemic Therapies

- **Doxycycline:**
  - 40 mg daily usually for 4-8 weeks
- Oral **isotretinoin** therapy:
  - First-line for phymatous rosacea
  - (0.3 mg/kg daily), can also be an option for rhinophyma
- Minocycline, tetracycline, erythromycin, azithromycin and metronidazole

4. Physical Modalities

Pulsed dye laser (PDL 585–595 nm) for telangiectasia

Rhinophyma:

CO2 laser

Surgical excision

Electrosurgery

Trigger	Therapeutic regimen
Sun exposure, wind, heavy exercise, alcohol consumption, emotional stress, skin care products and cosmetics (formaldehyde), medication, and microorganisms	Avoidance, anti-inflammatory therapy, and antibiotics
Sun exposure, emotional stress, alcohol, exercise, microorganisms/gut microbiome, topicals, and medication	Avoidance, 30+ SPF sunscreen, and brimonidine
Emotional stress, heat/hot weather/hot steam, exercise, alcohol, and spicy food (capsaicin)	Avoidance and brimonidine

GENERAL RECOMMENDATIONS FOR FACIAL SKIN CARE AND EDUCATION IN PATIENTS WITH ROSACEA

Facial skin care

- Wash with lukewarm water and use soap-free cleansers that are pH balanced
- Cleansers are applied gently with fingertips
- Use sunscreens with both UVA and UVB protection and an SPF ≥30
- Sunscreens containing the inorganic filters titanium dioxide and/or zinc oxide are usually well tolerated
- Use cosmetics and sunscreens that contain protective silicones
- Water-soluble facial powder containing inert green pigment helps to neutralize the perception of erythema
- Moisturizers containing humectants (e.g. glycerin) and occlusives (e.g. petrolatum) help to repair the epidermal barrier
- Avoid astringents, toners, and abrasive exfoliators
- Avoid cosmetics that contain alcohol, menthols, camphor, witch hazel, fragrance, peppermint, and eucalyptus oil
- Avoid waterproof cosmetics and heavy foundations that are difficult to remove without irritating solvents or physical scrubbing
- Avoid procedures such as glycolic peels or dermabrasion

Patient education

- Reassure the patient about the benign nature of the disorder and the rarity of rhinophyma, particularly in women
- Emphasize the chronicity of the disease and the likelihood of exacerbations
- Direct patients to information websites such as those of the National Rosacea Society (www.rosacea.org) or the American Academy of Dermatology (www.aad.org)
- Advise to avoid recognized triggers
- Explain the importance of compliance with topical regimens
- Educate on the importance of sun avoidance

Hidradenitis Suppurativa (HS)
(Acne Inversus)

Chronic inflammatory follicular occlusive disease predominantly involving the intertriginous areas
Targets apocrine gland bearing skin sites especially axilla and anogenital region can involve other areas as well

Epidemiology

- Prevalence rates for HS range from 0.03 to 4.1
- These numbers are likely underestimated because of under-reporting and misdiagnosis
- **Female predominan**ce with a 3:1
- Onset is commonly at or soon after puberty
- People of African descent have a higher prevalence

Pathophysiology

- Inflammatory disorder **originating from the hair follicle:**
  - Follicular occlusion:
    - Terminal follicular hyperkeratosis, hyperplasia of the follicular epithelium
  - Cyst formation, followed by rupture of the hair follicle
  - Induces an inflammatory response and subsequent formation of abscess, sinus tracts, fibrosis and scars.
- Bacteria:
  - Role controversial, postulated that an overzealous immune response to commensal flora within hair follicles triggers the initial follicular inflammation (worsened by secondary infections)
- Immune dysregulation:
  - Mediated by tumor necrosis factor (TNF)-α, IL-1B, IL-23/T-helper (Th) 17 and IL-12/Th1 pathways
- Genetics:
  - One-third of patients with HS report a positive family history
- Smoking:
  - More than 70 percent of patient with HS are smokers and a strong association between smoking and HS has been demonstrated
- Obesity:
  - Risk factor for HS

PIC 1

Clinical Features

- The diagnosis of HS relies on the clinical features
- Typically:
  - **Recurrent**, painful, inflamed nodules, most commonly in the axillae and/or inguinal areas
- To diagnosed HS: **requires the following <u>three criteria</u>:**
  1. Typical morphology (nodules, abscesses, sinus tracts, scars)
     - Double headed comedones [characteristic lesion] **PIC 1.**
  2. Characteristic distribution or typography of lesions (intertriginous areas, axillae, inframammary folds, groins, buttocks, <u>perianal and perineal areas</u> occurs more in males. With crohn's disease)
  3. A relapsing, chronic disease course.

Staging

HIDRADENITIS SUPPURATIVA – GRADING SYSTEMS AND THERAPEUTIC LADDER
Hurley staging system
Stage I – one or more abscesses with no sinus tract or scar formation Stage II – one or more widely separated recurrent abscesses, with sinus tract and scar formation Stage III – multiple interconnected sinus tracts and abscesses throughout an affected region; more extensive scarring
Sartorius grading system[79]
• Anatomical regions involved: axilla (left +/or right), groin (left +/or right), gluteal (left +/or right) or other region (e.g. inframammary): 3 points per region involved • Number and scores of lesions for each region: nodules = 1; fistulae = 6 • The longest distance between two relevant lesions*, i.e. nodules and fistulae, in each region: <5 cm = 1; 5–10 cm = 3; >10 cm = 9 • Are all lesions clearly separated by normal skin? In each region – yes 0/no (Hurley III) 9

Comorbidities

- Frequently associated with other diseases of follicular occlusion
  - **Follicular occlusion tetrad:**
    - Acne conglobata.
    - Hidradenitis Suppurativa.
    - Dissecting cellulitis of the scalp.
    - Pilonidal cyst.
- Autoinflammatory disorders such as **PASH**:
  - Pyoderma gangrenosum
  - Acne
  - Hidradenitis Suppurativa
- Higher odds of metabolic syndrome, DM, obesity, and HTN
- **IBD:**
  - Crohn's disease (26%)
  - Ulcerative colitis (18%)
- Seronegative spondyloarthropathies
- Depression

Complications

- **Secondarily infections:**
  - Erysipelas and sepsis
- Extensive fibrosis and scarring
- Lymphedema
- Squamous cell carcinoma (any chronic inflammatory disease can lead SCC)
- Anemia
- Secondary amyloidosis
- Fistulae (e.g. to the urethra or bladder)

Treatment

- **General measures:** 1st we do this
  - Weight reduction
  - Smoking cessation
  - Management of pruritus
  - Local antiseptic
  - Reduce friction
    - e.g. loose garments, absorbent powders, topical aluminum chloride
- **Topical treatments**:
  - Clindamycin
  - Fusidic acid
  - Benzoyl peroxide
- **Intralesional steroids**
- **Systemic treatments**:
  - Antibiotics (minocycline, doxycycline and rifampicin)
  - Isotretinoin or acitretin
  - Dapsone
  - Antiandrogen such as finasteride
  - Biologic treatment (infliximab, adalimumab)
- **Surgical treatment:**
  - Incision and drainage of abscess **better avoided**
  - Excision of sinus tracts and chronic nodules
  - Complete excision (last measure) of the area with or without grafting
  - Co2 laser

Wide surgical excision of the lesions

Therapeutic ladder	
Indication	*Therapeutic interventions*
General measures	• If obese or overweight, weight reduction • Reduce friction and moisture via loose undergarments, absorbent powders, and topical aluminum chloride • Antiseptic soaps • Smoking cessation
Hurley Stage I	• Intralesional triamcinolone (5 mg/ml) injections into early inflammatory lesions • Topical clindamycin • Eradication of *S. aureus* carriage with topical mupirocin in nose, axillae, umbilicus, and perianal regions • Oral antibiotics tailored to results of bacterial cultures from pustular discharge or abscess contents • Oral antibiotic therapy (alone or in combination) for its anti-inflammatory effect (rifampin + clindamycin[80], tetracycline, doxycycline, minocycline, dapsone, trimethoprim–sulfamethoxazole) • Oral anti-androgen therapy (e.g. finasteride)
Hurley Stage II (see Fig. 38.15A)	• Oral antibiotic therapy (see Stage I) • Acitretin[81] • Systemic immunosuppressive agents including adalimumab[82,^], infliximab[52], and cyclosporine[83] Surgical treatments† • Limited local excisions with second intention healing • CO_2 laser ablation with second intention healing • Nd:YAG laser treatments, at least 3–4 monthly sessions
Hurley Stage III (see Fig. 38.15B)	Medical treatments outlined for Stages I and II Surgical treatments† • Early wide surgical excision of involved areas • CO_2 laser ablation with second intention healing

*Or size if only one lesion.
^FDA-approved dosing regimen: 160 mg (four 40 mg injections) on Day 1 -*or*- 80 mg daily on Days 1 and 2 followed by 80 mg on Day 15 then 40 mg on Day 29 and weekly thereafter.
†Incision and drainage is discouraged given high rate of recurrence.

Questions:

1) a patient has acne and with a resistant acne on topical antibiotic what would you give with antibiotic to enhance antibiotics role also f treat his condition

A. tretinoin
B. benzoyl peroxidase
C. azelaic acid

2) Which of following makes diagnosis of acne vulgaris more likely over rose acne?

A. Mostly comedones
B. Mostly papules
C. Mostly pustules
D. Mostly plaques

3) Which of these findings favors a diagnosis of acne instead of rosacea?

A- Scarring
B- Papules
C- Pustules
D- Erythema

4) Which of the following dermatological disorders cause hypertrophy of sebaceous glands?

A. Rosacea
B. Acne
C. Atopic dermatitis

5) A 30-year-old lady who has recently exposed to the sun and taking vitamin B6 supplements for over a year. She presented with episodic flushing, telangiectasia, few papules and pustules over both cheeks and forehead. The clinical picture is characteristic of which of the following diseases?

A. Rosacea
B. Drug induced lupus
C. Drug induced acne
D. Folliculitis

1	2	3	4	5
B	A	A	A	A