

In the Name of God

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IUMS



ACNE AND IT'S TREATMENT

INTRODUCTION

- Acne vulgaris is the most common cutaneous disorder affecting adolescents and young adults
- Primarily an inherited disorder with environmental factors playing a secondary role
- Patients with acne can experience significant psychological morbidity and, rarely, mortality due to suicide

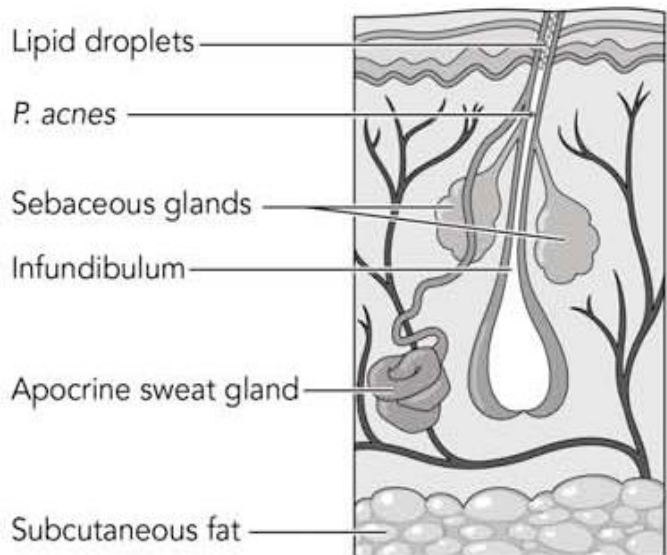
PATHOGENESIS

- **Pilosebaceous follicles**
- Acne vulgaris is a disease of pilosebaceous follicles
- Four factors are involved :
- Follicular hyperkeratinization
- Increased sebum production
- Propionibacterium acnes within the follicle
- Inflammation

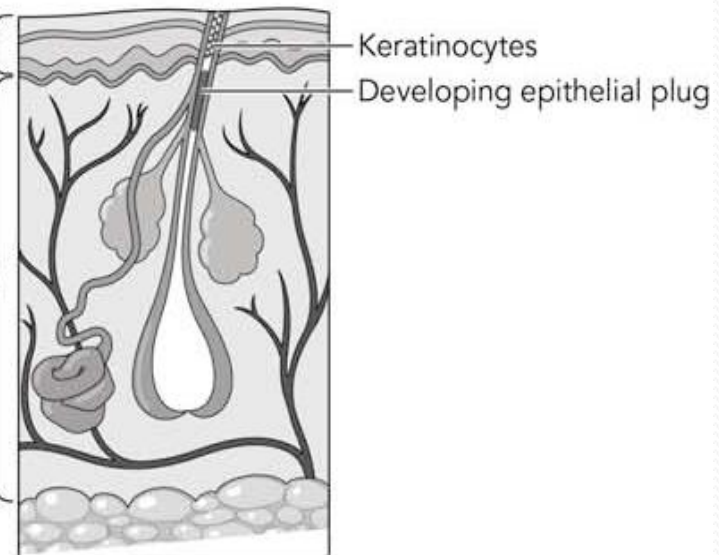
Pathogenesis

- The increased amount of keratin leads to blockages of the follicles and the formation of microcomedones
- A microcomedone can develop into a non-inflammatory lesion (comedone), or into an inflammatory lesion

A. Normal follicle (pilosebaceous unit)



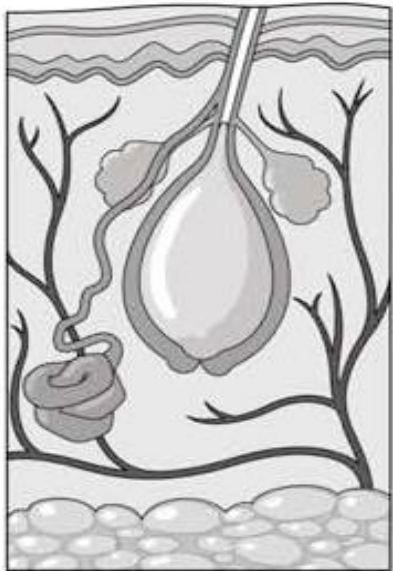
B. Microcomedo



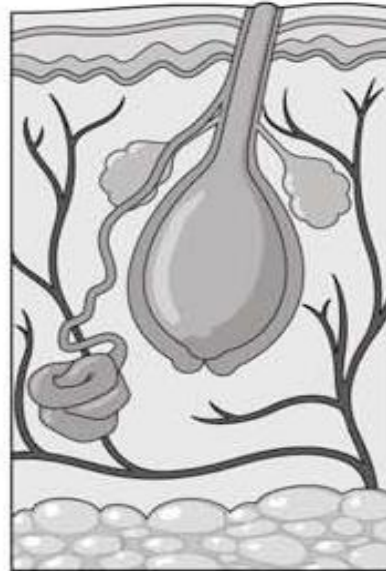
Noninflammatory lesions

- The sebum in closed comedones cannot reach the surface of the skin. The plug of keratin, which is at the entrance to the follicle in a comedone, is initially white (a whitehead), later becoming darker-coloured because of the accumulation of melanin (a blackhead).

C. Closed comedo (whitehead)

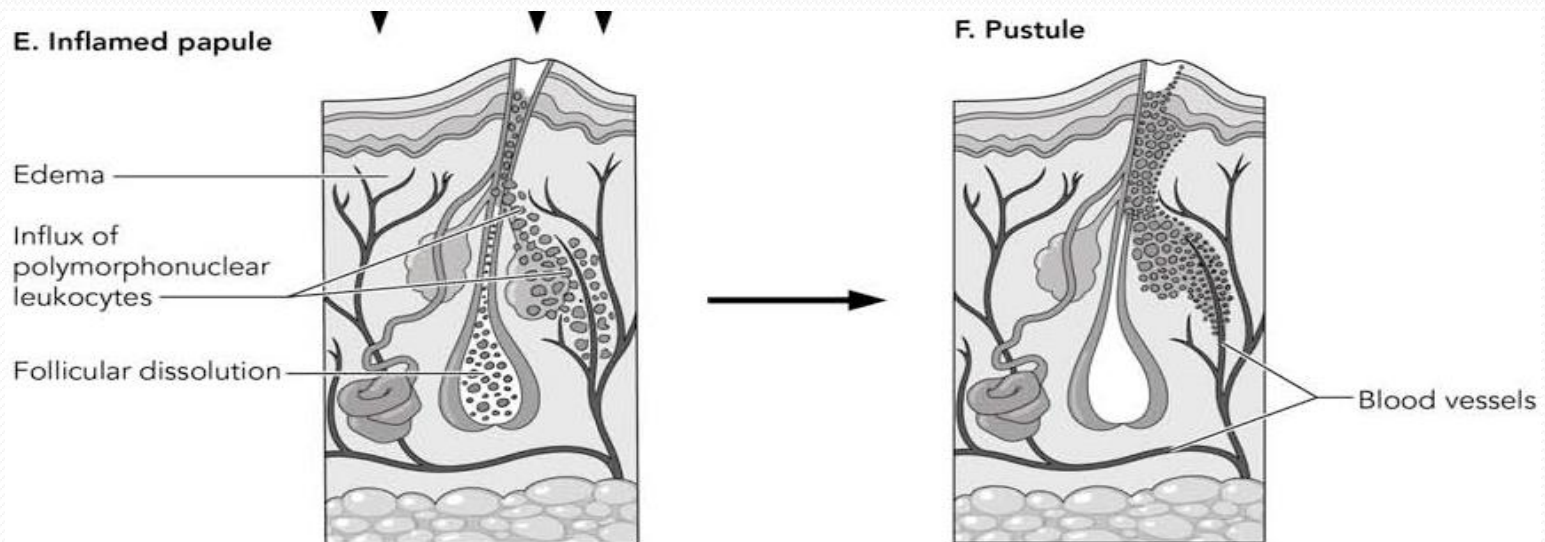


D. Open comedo (blackhead)



Inflammatory lesions

- Sebum is still produced, swelling occurs & comedone ruptures, discharging its contents under the skin's surface
- Excess sebum → growth of P.acnes → development of inflammatory lesions
- The released sebum → inflammatory response → papules (or in more severe acne, red pustules)



Inflammatory lesions

- Differences in **the host inflammatory response to P. acnes or the pathogenicity of specific strains of P. acnes** that colonize skin may contribute to the variation in the prevalence and severity of acne

Type of lesions

- **Noninflammatory lesions:**

Comedon: whiteheads or blackheads



- **Inflammatory lesions (erythematous):**

Pustules (raised, superficial, pus-filled lesions)

Papules (raised, solid lesions up to several millimeters)

Nodules (like papules but larger and deeper in the skin)



❖ **Scars:** as a result of inflammatory acne lesions



❖ **Residual Hyperpigmentation:** can persist weeks to months after resolution of lesion

Role of androgens

- Testosterone is metabolized in the skin by 5- α -reductase to DHT => stimulates sebum biosynthesis=> hyperkeratinization & comedogenesis
- Increased sebum production=> lipid-rich environment=> growth of *P.acnes* => inflammatory response
- However, most acne patients do not have an endocrine abnormality.
- Acne-affected pilosebaceous units apparently have a hyperresponsiveness to androgens

External factors

- Soaps, detergents, and astringents remove sebum from the skin surface but do not alter sebum production.
- Repetitive mechanical trauma caused by scrubbing with these agents may worsen the disorder by rupturing comedos, promoting the development of inflammatory lesions

Diet

- A potential role for diet in acne **is controversial**
- Association between acne and **intake of milk**
- A 12-week randomized trial that compared low and **high glycemic load diets** in 43 male patients with acne found a greater reduction in lesion counts with the **low glycemic load diet**

Diet

- There is no reliable evidence that **ingestion of chocolate** is associated with an increased prevalence or severity of acne
- **Data on favorable effects of dietary factors** such as zinc, omega-3 fatty acids, antioxidants, vitamin A, and dietary fiber on acne vulgaris are limited

OTHER FACTORS

- **Family history**
- Individuals with close family members with acne are at increased risk for the disorder
- **Stress**
- Patients and clinicians commonly believe that psychological stress can exacerbate acne
- **Receptors for corticotropin releasing hormone (CRH)**, a hormone involved in the stress response, are present in human sebaceous glands
- **Body mass index**
- A correlation between low BMI and a reduced risk for acne

CLINICAL MANIFESTATIONS AND CLASSIFICATION

- Acne vulgaris typically affects those areas of the body that have the largest, hormonally-responsive sebaceous glands, including the face, neck, chest, upper back, and upper arms
- In addition to the typical lesions of acne vulgaris (eg, open comedones, closed comedones, and inflammatory lesions), scarring and postinflammatory hyperpigmentation can occur

CLINICAL MANIFESTATIONS AND CLASSIFICATION

- **Adult women** may present with acne involving the lower face and neck that is often associated with **premenstrual flares**
- These women, in particular, seem to benefit from **hormonal therapies for acne**

Postadolescent acne



Characteristic location of acne along the jaw line in a woman. Multiple papules have been excoriated.

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Classification

- A description of the actual lesions encountered will be most useful when considering management of acne
- Young adolescents often have primarily comedonal acne consisting of noninflammatory lesions (closed and/or open comedones) involving the forehead, nose and chin

Classification

- As the acne progresses, patients develop **inflammatory lesions** (papules, pustules, and nodules)
- **Nodules** are tender inflammatory acne lesions that are larger than **5 mm in diameter**
- Nodular acne is sometimes inaccurately referred to as "cystic" or "nodulocystic" acne
- **In reality, true cysts are rare**

Acne nodules



Severe nodular acne on the forehead.

Nodular acne



Erythematous papules, pustules, and nodules are present on the face. This patient also has postinflammatory hyperpigmentation and scarring.

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Severity classification

- **Mild:** few lesions, little or **no inflammation** (open & closed **comedones**)
- **Moderate:** many lesions, significant **inflammation**
- **Severe:** numerous lesions, extreme inflammation and/or **nodules**, significant **scarring**



DIAGNOSTIC EVALUATION

- **Hyperandrogenism**
- In women, polycystic ovary syndrome (PCOS) is the most common cause of hyperandrogenism.
- The rapid appearance of acne in conjunction with virilization suggests an underlying adrenal or ovarian tumor

DIAGNOSTIC EVALUATION

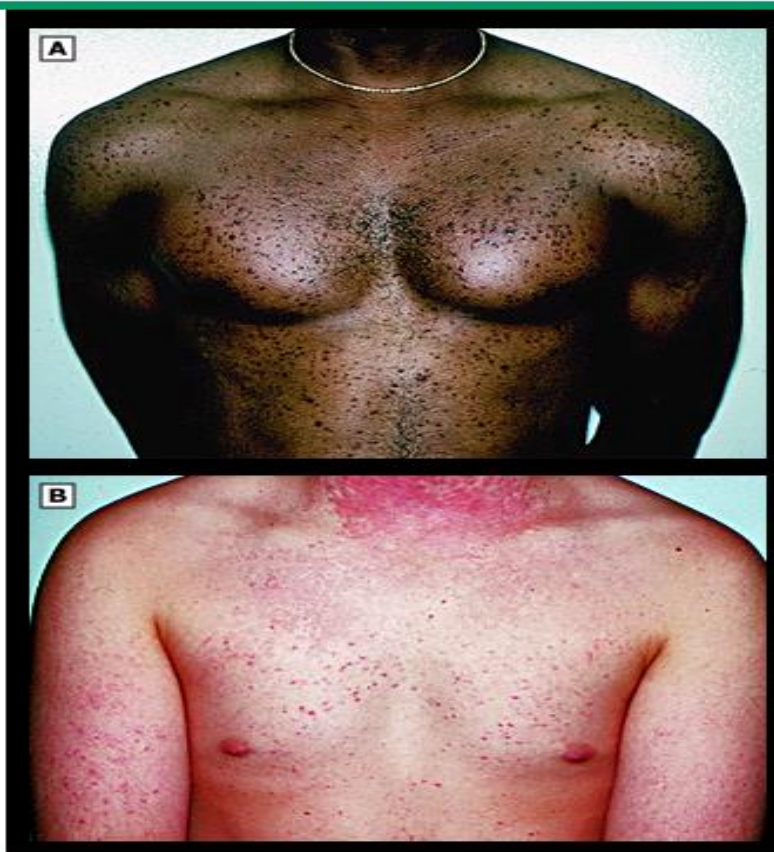
- Patients with Cushing's disease or syndrome and late-onset congenital adrenal hyperplasia may also experience acne vulgaris.
- Dehydroepiandrosterone sulfate (**DHEAS**), total testosterone, and free testosterone levels are reasonable initial tests.

Medications

Major causes of drug-induced acne

Glucocorticoids
Phenytoin
Lithium
Isoniazid
Epidermal growth factor receptor inhibitors
Iodides
Bromides
Androgens
Corticotropin
Cyclosporine
Disulfiram
Psoralens
Thiourea
Vitamins B2, B6, and B12
Azathioprine

Systemic glucocorticoid-induced acneiform eruption



A) Drug-induced acneiform eruption. This patient was taking prednisone for sarcoidosis. B) This patient is taking systemic glucocorticoids for severe asthma.

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DIAGNOSTIC EVALUATION

- **Acne mechanica**
- **Acne cosmetica**
- Cosmetic products that contain comedogenic ingredients can induce the formation of acne lesions.
- Heavy, oil-based hair products
- **Occupational acne**
- **Radiation acne**



Treatment of acne vulgaris

Goals of treatment

The goals of treatment are:

- To **prevent** the formation of new acne lesions
- Heal existing lesions
- Prevent or **minimize scarring**
- Decrease morbidity associated with the **psychological implication** of acne
- ❖ Treatment regimens are targeted to **types of lesions** and acne **severity**



Nondrug Therapy

- Plays a **minimal role**
- Twice-daily **washing** with warm water and a mild facial cleanser
- **Manipulation** (e.g., squeezing, picking) of acne lesions should be discouraged (risk of scarring)
- **Drugs** known to cause acne & **oil-based cosmetics** should be avoided
- Oil-free, **noncomedogenic moisturizers** improve penetration and tolerability of topical acne drugs by improving the skin's hydration (**esp. in sensitive skin**)



HOME SKIN CARE RECOMMENDATIONS

- Patients should apply a gentle synthetic detergent cleanser (ie, syndet) with their fingers, and rinse with warm (not hot) water twice daily.
- Synthetic detergent cleansers possess a pH of 5.5 to 7, which is close to normal skin pH, while soap has a pH of 9 to 10.
- The lower pH of synthetic detergents, such as Cetaphil, minimizes skin irritation and dryness

HOME SKIN CARE RECOMMENDATIONS

- After four weeks, the patients washing with the synthetic detergent bar exhibited less skin peeling, dryness, and irritation than those using soap.

HOME SKIN CARE RECOMMENDATIONS

- Patients should not aggressively scrub the skin;
- **Gentle massage** with the fingertips is sufficient for cleansing.
- **Repetitive mechanical trauma** can aggravate inflammatory acne and promote the development of new acne lesions

HOME SKIN CARE RECOMMENDATIONS

- Several reports have suggested that antibacterial soaps such as triclosan, povidone-iodine, and chlorhexidine can improve acne vulgaris.
- However, data supporting their use are limited, and these agents have not been proven superior to conventional therapy.
- We do not recommend these soaps for the management of acne vulgaris.

HOME SKIN CARE RECOMMENDATIONS

- **Water-based** lotions, cosmetics, and hair products are less comedogenic than oil-based products.
- **Patients should be encouraged to seek out** noncomedogenic skin care and cosmetic products.
- **Patients should be advised not to pick** their acne lesions, as this may exacerbate scarring.


Drug Therapy

Based on treating one or more of the primary pathogenic factors:

- Normalizing follicular keratinization (e.g., **retinoids**, **benzoyl peroxide**, **azelaic acid**);
- Decreasing sebum production (e.g., **isotretinoin**, **hormonal therapies**);
- Suppressing *P. acnes* (e.g., **antibiotics**, **benzoyl peroxide**, **azelaic acid**, **systemic isotretinoin**);
- Reducing inflammation (e.g., **antibiotics**, **retinoids**).



Acne treatment algorithm

					
	Mild		Moderate		Severe
	Comedonal	Mixed and papular/pustular	Mixed and papular/pustular	Nodular*	Nodular/conglobate
1st choice	Topical retinoid	Topical retinoid + Topical antimicrobial*	Oral antibiotic + Topical retinoid +/- BPO*	Oral antibiotic + Topical retinoid + BPO	Oral isotretinoin ^Δ
Alternatives [◇]	Alternative topical retinoid or Azelaic acid [§] or Salicylic acid	Alternative topical antimicrobial* + Alternative topical retinoid or Azelaic acid [§]	Alternative oral antibiotic + Alternative topical retinoid +/- BPO*	Oral isotretinoin versus Alternative oral antibiotic + Alternative topical retinoid +/- BPO*/Azelaic acid [§]	High-dose oral antibiotic + Topical retinoid + BPO
Alternatives for females [◇] [¥]	See 1st choice	See 1st choice	Hormonal therapy + Topical retinoid/ Azelaic acid [§] +/- Topical antimicrobial*	Hormonal therapy + Topical retinoid +/- Topical or oral antimicrobials*	Hormonal therapy + Topical retinoid +/- Topical or oral antimicrobials*
Maintenance therapy:	Topical retinoid		Topical retinoid +/- BPO		

BPO: benzoyl peroxide; topical antimicrobials: benzoyl peroxide, topical antibiotics.

* With small nodules (>0.5 to 1 cm).

• Prescribing benzoyl peroxide concomitantly with topical or oral antibiotics will minimize the emergence of antibiotic resistance.

Δ Second course in case of relapse.

◇ Consider physical removal of comedones.

§ There was not consensus on this alternative recommendation, however, in some countries Azelaic acid prescribing is appropriate practice.

¥ For females who are not pregnant.

Reproduced with permission from: Gollnick H, Cunliffe W, Berson D, et al. Management of acne: A report from a Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol* 2003; 49:S1.

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PATIENT ASSESSMENT

- Clinical type of acne (eg, comedonal, inflammatory, nodular)
- Severity of acne
- Skin type (dry, oily)
- Presence of acne scarring or postinflammatory hyperpigmentation
- Menstrual history and history of signs of hyperandrogenism in women
- History of prior successful and failed treatments
- History of acne-promoting medications
- Psychological impact of acne on the patient

PATIENT ASSESSMENT

- Women with irregular menses or signs of hyperandrogenism may warrant laboratory work-up and anti-androgenic therapies

General approach to treatment

- Patients should be given realistic expectations regarding timelines for improvement.
- It takes approximately eight weeks for a microcomedo to mature.
- Thus, therapy must be continued beyond this duration in order to assess efficacy.

Drug Therapy

- **Comedonal (noninflammatory) acne**
- Topical retinoid (alternatives include azelaic acid and salicylic acid)

Drug Therapy

- **Mild papulopustular and mixed (comedonal and papulopustular) acne**
- Topical retinoid **AND**
- Topical antimicrobial (eg, benzoyl peroxide alone or benzoyl peroxide +/- topical antibiotic)

Drug Therapy

- **Moderate papulopustular and mixed acne**
- Topical retinoid **AND**
- Oral antibiotic **AND**
- Topical benzoyl peroxide

Drug Therapy

- **Moderate nodular acne (small nodules 0.5 to 1 cm)**
- Topical retinoid **AND**
- Oral antibiotic **AND**
- Topical benzoyl peroxide

Drug Therapy

- Severe nodular/conglobate acne
- Oral isotretinoin

General approach to treatment

- Topical retinoids are effective in the treatment of comedonal acne due to their ability to normalize follicular hyperkeratosis and prevent formation of the microcomedon
- Topical retinoids also improve inflammatory acne
- Intrinsic anti-inflammatory properties of topical retinoids and their ability to prevent the formation of microcomedones

General approach to treatment

- Topical retinoids can be used as monotherapy in individuals with exclusively comedonal acne
- However, patients with an inflammatory component often benefit from the addition of concomitant antimicrobial therapies (eg, benzoyl peroxide or topical antibiotics) that reduce the number of proinflammatory *P. acnes* colonizing the skin

General approach to treatment

- Patients with moderate to severe inflammatory acne often warrant more aggressive treatment with oral antibiotics
- Antibiotics in the tetracycline class are most frequently used, and appear to have both antibacterial and anti-inflammatory properties.
- The use of benzoyl peroxide with topical or oral antibiotics decreases the emergence of antibiotic resistant bacteria

General approach to treatment

- Acne typically recurs over years and **maintenance therapy** is an important component of acne management.
- The preventive effect of topical retinoids and the concern for antibiotic resistance **make topical retinoids ideal candidates.**
- If clinical improvement cannot be maintained with topical retinoid monotherapy, an antimicrobial agent containing benzoyl peroxide **can be added**

General approach to treatment

- **Hormonal therapy** may benefit women with moderate to severe acne, **even in the absence of a hyperandrogenic state**

General approach to treatment

- Oral isotretinoin decreases sebum production, reduces *P. acnes* colonization, and normalizes follicular keratinization.
- It is an option for patients with severe acne that essentially cures or significantly improves acne in the majority of patients who complete a full course of treatment

General approach to treatment

- Oral isotretinoin is used as monotherapy; a typical treatment course is approximately 20 weeks

General approach to treatment

- **Adjunctive therapies**, such as light-based and laser therapies, chemical peels, comedo extraction, and intralesional glucocorticoids have also been used for acne management

Choice of vehicles for topical treatments

- The choice of delivery system for topical acne medications depends upon the patient's skin type (dry versus oily) and preference
- Choice of vehicle: Gels and solutions for oily skin, creams in dry and/or sensitive skin.
- Ointments are generally too comedogenic to be useful in acne

Choice of vehicles for topical treatments

- **Solutions are drying** but they cover large areas more easily than other preparations, and foams are easy to apply to hair-bearing areas
- **Microsphere formulation of tretinoin**
- This formulation is associated with improved drug stability and decreased irritation

Truncal acne

- **Truncal acne**
- Although the treatment of both facial and truncal acne can be approached similarly, a challenge for the treatment of truncal acne is the **difficulty associated with applying topical treatments** to the entire affected area.

Truncal acne

- Given the difficulty that patients may have applying medications to areas such as the back compared with the face and the large quantity of topical medication required for use on large areas, we have a lower threshold for incorporating oral antibiotic or oral hormonal therapies into the treatment regimen.

Children

- Children
- The medical therapies used for the treatment of acne in children are similar to the management of acne in adolescents and adults.
- A significant exception is the need to avoid the use of tetracyclines in children under the age of nine years

Children

- An additional important consideration for acne therapy in children and adolescents is the implementation of measures **to optimize adherence to therapy.**
- Careful efforts should be made to recognize when the **complexity of the regimen,** the child or adolescent's dislike of the vehicle prescribed (eg, cream, lotion, gel), or drug side effects inhibit consistent use of acne medication

TOPICAL RETINOIDS

- The first topical retinoid for the treatment of acne, all-trans retinoic acid (**tretinoin**), is still extensively used.
- Adapalene and tazarotene are other effective topical retinoids
- Salicylic acid and azelaic acid are alternative comedolytic therapies for patients who are unable to tolerate topical retinoids, **but may be less effective.**

Instructions for application

- Comedolytic therapies initiated at **low concentrations** and **frequencies** and titrated up in strength, frequency, and drying effect as tolerated
- The topical retinoids are applied **once daily** and traditionally **at night** due to photolability reported with tretinoin
- Adapalene is more light-stable

Instructions for application

- Newer formulations of tretinoin, tretinoin gel microsphere (Retin-A Micro) and micronized tretinoin 0.05% in a hydrogel vehicle (Atralin), are less affected by light exposure than their precursors
- Tretinoin should **not** be applied at the same time as benzoyl peroxide.
- Tretinoin is less stable when exposed to benzoyl peroxide due to oxidation, an effect magnified during light exposure

Instructions for application

- Adapalene, tretinoin gel microsphere, and micronized tretinoin gel **remain more stable than tretinoin in the presence of benzoyl peroxide**
- **A combination product**, containing adapalene and benzoyl peroxide (Epiduo) is available

Instructions for application

- A pea-sized amount of medication is usually sufficient to cover the face
- Due to the preventive effect of topical retinoids on acne, the medication should be applied to the entire affected area, not as spot treatment of individual lesions.
- Skin should be dry at the time of application.

Instructions for application

- **Morning:** Wash face with a gentle facial cleanser. Apply a thin layer of a fixed-dose combination benzoyl peroxide/clindamycin gel to the entire face. (An alternative regimen could require the patient to wash the face with a benzoyl peroxide cleanser followed by application of a thin layer of topical clindamycin to the entire face.)
- **Night:** Wash face with a gentle facial cleanser. Apply a thin layer of the topical retinoid to the entire face.

Adverse effects

- Topical retinoids cause irritation, dryness, and flaking of the skin, an effect most notable during the first month of therapy
- To minimize irritation, patients **should avoid the concomitant use of over-the-counter irritating products, such as harsh soaps, toners, astringents, and alpha hydroxy acid or salicylic acid products**

Adverse effects

- If irritation is a problem, a decrease in the frequency of application to every other or every third night can be considered, and the frequency of application can be increased as tolerance improves

Adverse effects

- A microencapsulated (microsphere) form of tretinoin gel (Retin-A Micro) is less irritating
- A non-comedogenic facial moisturizer can be applied on top of the retinoid if needed.
- Some patients may notice a transient worsening of acne during the first few weeks of topical retinoid therapy .
- These flares spontaneously resolve with continued treatment

Adverse effects

- The use of sun-protective clothing and/or sunscreen is recommended
- The use of topical retinoids is not recommended in pregnancy. In particular, tazarotene is a pregnancy category X drug

Adapalene

- Have equivalent efficacy and greater tolerability
- Adapalene is the best tolerated.
- Tazarotene may be more effective but is the most irritating
- Irritation from topical tretinoin can **darken skin** in **dark-skinned** patients, but adapalene may **reduce hyperpigmentation** in such patients

Tazarotene

- Tazarotene can be prescribed as a 0.05 or 0.1% cream or gel.
- Tazarotene is used for the treatment of psoriasis as well as acne.
- Only the 0.1% strength is approved by the US FDA for the treatment of acne

Tazarotene

- In general, tazarotene has been considered **the most effective**, but also **most irritating** topical retinoid, when compared with adapalene and tretinoin
- **A short-contact regimen** with tazarotene is another treatment option, and can decrease irritation.
- Patients apply tazarotene for up to **five minutes** daily, then wash off the medication

TOPICAL ANTIMICROBIALS

- **Topical antimicrobials** are used to decrease the number of *P. acnes* colonizing the skin, with the goal of reducing the inflammatory response that occurs in acne.
- Benzoylperoxide, clindamycin, erythromycin , Sulfacetamide and dapsone

TOPICAL ANTIMICROBIALS

- Combination therapy with a topical antimicrobial plus a topical retinoid appears to be more effective than either agent alone, and is recommended for the treatment of patients with inflammatory acne

Benzoyl peroxide

- In addition to its antibacterial properties, benzoyl peroxide is also comedolytic
- It releases oxygen free radicals that damage bacterial cell walls, resistance cannot develop
- It is often paired with oral antibiotics to prevent the development of antibiotic resistance

Benzoyl peroxide

- It improves both **inflammatory** and noninflammatory lesions
- Concentrations of benzoyl peroxide that are **higher than 2.5%** may not contribute to increased benefit
- **Increased concentrations** of benzoyl peroxide can lead to increased skin irritation.

Benzoyl peroxide

- Antibiotics may promote the appearance of **resistant strains of *P. acnes*** when used alone.
- Resistance is diminished by combination use with benzoyl peroxide.
- ***P. acnes* resistance to benzoyl peroxide has not been identified**

Benzoyl peroxide

- Tretinoin and benzoyl peroxide should not be applied simultaneously to the skin due to the oxidizing effect of benzoyl peroxide on tretinoin.
- If both agents are prescribed, benzoyl peroxide should be applied in the morning, and tretinoin in the evening

Benzoyl peroxide

- It is usually applied to the **affected area** once or twice daily
- Patients should be instructed to **use sunscreen** while using it because the skin is more prone to burn
- Patients must be advised that benzoyl peroxide **can bleach or discolor towels, pillowcases**

Benzoyl peroxide

- **Application frequency:** Apply the product every other day for the first 1-2 W, then to daily and twice a day as tolerated, no more than BD
- It should be applied **to cool, clean and dry skin** at bedtime, half an hour after washing the face with a mild cleanser

Topical antibiotics

- **Erythromycin and clindamycin**
- Topical erythromycin and clindamycin should not be used as monotherapy for acne, as evidence shows better treatment efficacy when these drugs are combined with retinoids or benzoyl peroxide
- **Sulfacetamide**
- Data regarding the effectiveness of sulfacetamide in the treatment of acne are limited

Topical antibiotics

- Offers an option in patients who have failed first-line agents.
- Topical antibiotics are usually applied **once or twice daily** for 3 months.

Dapsone

- Dapsone 5% gel is a newer effective treatment for acne vulgaris
- Both inflammatory and noninflammatory acne lesions improve with treatment, with the greatest improvement occurring in inflammatory lesions
- Temporary yellow to orange discoloration of the skin and hair may occur when dapsone gel and topical benzoyl peroxide are applied concomitantly

AZELAIC ACID

- Azelaic acid is a naturally occurring dicarboxylic acid with antimicrobial, comedolytic, and mild anti-inflammatory properties.
- Azelaic acid also has an inhibitory effect on tyrosinase, and can improve acne-induced **postinflammatory hyperpigmentation**

AZELAIC ACID

- Azelaic acid 20% cream is effective for the treatment of both inflammatory and non-inflammatory acne
- Azelaic acid causes **less skin irritation** than other topical therapies (except for antibiotics), but may not be as effective.
- It is usually reserved for **patients who cannot tolerate benzoyl peroxide or topical retinoids.**

AZELAIC ACID

- It is also useful for postinflammatory hyperpigmentation because it has skin-lightening properties
- Usually applied twice daily on clean, dry skin.
- Patients should protect their skin with sunscreen.

ORAL ANTIBIOTICS

- Multiple studies, including randomized trials, have shown **oral antibiotics** effective for the management of **inflammatory acne**
- Should be paired with topical retinoids and/or benzoyl peroxide in patients with **moderate to severe acne**, especially if lesions are in **widespread** or difficult-to-reach areas.

ORAL ANTIBIOTICS

- Utilization of these drugs is primarily indicated for patients with moderate to severe inflammatory acne
- Oral antibiotics may also be used for patients who have milder truncal acne, for whom the application of topical antibiotics is difficult

ORAL ANTIBIOTICS

- Oral antibiotics improve inflammatory acne by inhibiting the growth of *P. acnes* within the pilosebaceous unit.
- Tetracyclines and macrolides can reduce neutrophil chemotaxis and inhibit cytokines, even at subminimal inhibitory concentration

ORAL ANTIBIOTICS

- Systemic antibiotics produce **more rapid clinical improvement** than topical preparations, but may induce side effects such as **vaginal candidiasis or gastrointestinal distress**

ORAL ANTIBIOTICS

- Oral antibiotics should be prescribed for a **limited course** to limit the emergence of antibiotic resistance
- Optimally, they are prescribed **for daily use for less than six months** with subsequent discontinuation as acne improves

ORAL ANTIBIOTICS

- No consensus exists regarding whether oral antibiotics **should be tapered or abruptly stopped**
- Oral antibiotics used in the treatment of acne include tetracycline, doxycycline, minocycline, erythromycin, trimethoprim-sulfamethoxazole, clindamycin, and azithromycin

TABLE 40-6
Frequently Used Oral Antibiotics

Drug	Dose
Doxycycline	100 mg orally twice daily
Tetracycline	500 mg orally twice daily
Minocycline	50–100 mg orally twice daily (or 1 mg/kg/d)
Erythromycin	250–500 mg orally twice daily
Trimethoprim/ sulfamethoxazole	160/800 mg orally twice daily

Source: Tan HH. Antibacterial therapy for acne: a guide to selection and use of systemic agents. *Am J Clin Dermatol*. 2003;4:307.

Macrolides

- Erythromycin may be administered for acne in doses of 500 mg twice daily.
- However, it has less anti-inflammatory activity than the tetracyclines.
- In addition, *P. acnes* often develops resistance to this drug, resulting in treatment failure
- The use of erythromycin is now recommended only for patients in whom tetracycline derivatives are contraindicated

Macrolides

- Azithromycin, another oral macrolide antibiotic, has shown efficacy for the treatment of acne
- Its long half-life permits intermittent dosing three times a week
- The risk of increasing the prevalence of antibiotic resistance makes azithromycin a less favorable choice for routine acne therapy

Tetracyclines

- In the past, tetracycline was the preferred oral antibiotic due to its low cost and studies showing high efficacy.
- However, **newer generation tetracycline** derivatives are now used more commonly

Tetracyclines

- Doxycycline and minocycline are newer generation tetracycline derivatives.
- These two drugs have replaced erythromycin and tetracycline as the most frequently used oral antibiotics for acne therapy

Tetracyclines

- Unlike tetracycline, doxycycline and minocycline can be taken with meals since absorption is not inhibited by food.
- In clinical practice, minocycline is widely considered the most effective tetracycline derivative for the treatment of acne
- Some tetracycline-resistant strains of *P. acnes* show cross-resistance to doxycycline, but not to minocycline

Tetracyclines

- Minocycline is not used as first-line therapy due to its high cost and lack of clear benefit compared with tetracycline and doxycycline, as well as concerns about more severe toxicities than other tetracyclines
- Some patients who have failed therapy with doxycycline or tetracycline may respond to minocycline.

Tetracyclines

- Tetracycline, doxycycline, and minocycline should not be administered to children **under the age of nine or to pregnant women** due to the potential for discoloration of developing permanent teeth and reduced bone growth
- **Gastrointestinal distress**, idiopathic intracranial hypertension (pseudotumor cerebri),
Photosensitivity

Tetracyclines

- Doxycycline as the most photosensitizing drug
- Minocycline is the least photosensitizing of the three drugs, but can cause vertigo, skin discoloration , serum sickness, and a lupus-like syndrome

Dosing for tetracyclines

- Tetracycline is initiated at a dose of 500 mg twice daily, although 250 mg twice daily may also be effective
- Typical doses of doxycycline are 50 to 100 mg twice daily or 150 mg once daily.
- Minocycline is usually prescribed as 50 to 100 mg twice daily.

Dosing for tetracyclines

- **Subantimicrobial dose doxycycline**
- Are doses for which the antiinflammatory properties are maintained, but antibacterial action is absent
- In this manner, the potential for inducing antibacterial resistance is diminished.
- Doxycycline 20 mg twice daily

Other antibiotics

- **Trimethoprim-sulfamethoxazole** — Trimethoprim-sulfamethoxazole is effective in the treatment of severe acne
- **Clindamycin** — The use of oral clindamycin is limited because of the potential to induce pseudomembranous colitis.
- **Cephalexin** — While some clinicians use cephalexin to treat acne, the data to support its use are sparse

HORMONAL THERAPY

- **Androgens** play an important role in the pathogenesis of acne vulgaris.
- **Thus, hormonal interventions** that reduce androgen activity can be effective treatments.

HORMONAL THERAPY

- Although endogenous or exogenous factors that cause hyperandrogenism can induce or exacerbate acne, most patients with acne have serum androgen levels that are within normal limits
- Increased sensitivity of sebaceous glands to androgens is a proposed mechanism for the development of acne in these patients.

HORMONAL THERAPY

- **Estrogens**
- The goal of hormonal therapy for acne **is** to minimize acne via the reduction of androgen action on cutaneous pilosebaceous units

HORMONAL THERAPY

- Estrogen-mediated opposition of androgens within the sebaceous gland, inhibition of gonadal androgen production through a negative feedback loop on gonadotrophin release, increases in sex-hormone binding globulin (which reduces the bioavailability of androgens), and effects on regulation of genes involved in sebaceous gland growth or lipid production

OVERVIEW OF HORMONAL THERAPY

- Antiandrogens are **avoided in males** because **gynecomastia** is likely to develop
- Oral contraceptives and spironolactone.
- **Additional therapies with antiandrogenic properties** may improve acne, but are not typically used for this indication due to specific indications or concern for adverse effects.

OVERVIEW OF HORMONAL THERAPY

- Flutamide – Flutamide is an androgen receptor blocker that is not typically used for the treatment of acne because of the potential for flutamide-induced fatal hepatitis

OVERVIEW OF HORMONAL THERAPY

- The role of 5-alpha reductase inhibitors, which inhibit conversion of testosterone to the more potent androgen dihydrotestosterone (DHT), in the treatment of acne is unclear
- There are insufficient data to support 5-alpha reductase inhibitor therapy

Indications

- **Women without hyperandrogenism** – Among women with normal androgen levels, hormonal therapy is typically used for postmenarchal adolescent and adult females with moderate to severe acne who are not trying to become pregnant and who cannot be effectively managed with topical therapy.
- **In adult women who present with inflammatory acne** involving the lower face and neck and premenstrual acne flares

Indications

- Women with milder acne who choose oral contraceptives for the purpose of pregnancy prevention can also experience the ancillary benefit of improvement in their acne.
- However, these patients often can be managed successfully with topical therapy.

Indications

- **Women with hyperandrogenism**
- Hormonal therapy is useful for the management of acne in women with hyperandrogenism because treatment reduces the excessive hormonal stimulus for acne in these patients



Thank you