



Acne Vulgaris

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Introduction

- Acne is a chronic inflammatory skin disease that is estimated to affect approximately 85% of the population at some point in their lives.
- It has a variable presentation with a constellation of lesions, including open and closed comedones, papules, pustules, nodules and cysts.
- The pathogenesis is multifactorial and involves excess sebum production, disturbed keratinization, inflammation, and stimulation of the innate immune system, such as hypercolonization by *Propionibacterium acnes*.

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Factoids

- Only 33 U.S. medical schools have undergraduate dermatology programs.
- Over half of American schools teach less than 10 hours of dermatology.
- In Europe, teaching hours vary between 18 to 60 hours during undergraduate training.

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Pathogenesis Multifactorial

- The blackhead or comedone is the sine qua non of most cases and represents increased cohesion and adhesion of follicular lining cells within the infundibulum portion of the hair follicle.
- The process is driven in almost all cases by the influence of hormones, mostly androgens, which increase follicular oil production.
- With the increased population of bacteria and their by-products and the increased sebum production, there is stimulation of the innate immune system to bring polymorphonucleated cells into the follicle, which creates the papule/pustule.

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Who gets acne?

- Acne affects males and females of all races and ethnicities. It is prevalent in adolescents and young adults, with 85% of 16 to 18-year-olds affected. However, it may sometimes occur in children and adults of all ages. Prevalence of acne in adult women is about 12%.
- Acne usually improves by age 25 but may persist, especially in females.
- Neuroendocrine, diet, and genetic androgenetic factors may contribute to this multifactorial process.

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Clinical Features of Acne

- The face is involved in most cases.
- The trunk is affected in up to 61% of patients.
- Lesions can progress to post-inflammatory hyperpigmentation or scars or both.
- It is characterized by:
 - Open and closed, uninfamed comedones
 - Inflamed papules and pustules
 - In severe acne, nodules and inflamed pseudocysts
 - Post-inflammatory, erythematous or pigmented macules and scars
- Adverse social and psychological effects

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Classification of Acne

Such classification can help to determine appropriate treatment options:

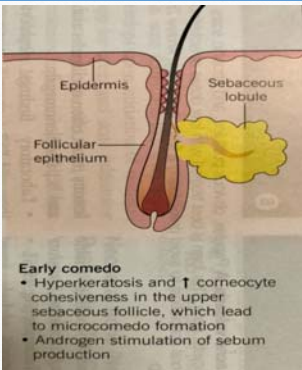
- Comedones
- Papules
- Pustules
- Nodules
- Cysts
- Scars
- Post-inflammatory Hyperpigmentation

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Early Comedo

- Closed Comedones
 - Skin colored papules without obvious follicular opening
 - First to appear, can dilate then become open

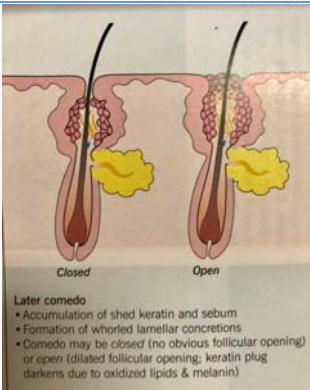


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Later Comedo

- Open Comedones (blackheads)
 - Dilated follicular opening filled with a keratin plug, black color is due to oxidized lipids and melanin Grey, orange, brown or black papules. The keratinous contents can be expressed or extracted.
 - Dilated follicular opening filled with a keratin plug, black color is due to oxidized lipids and melanin

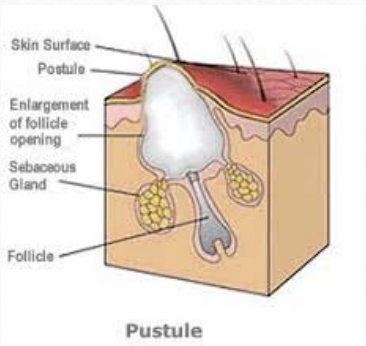


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Pustule

- Papular/pustular acne

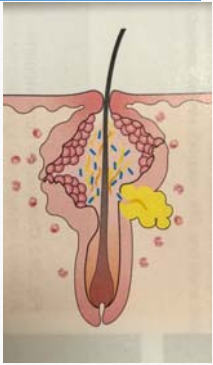


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Inflammatory Papule/Pustule

- Severe papulopustular acne
- Often results in post-inflammatory hyperpigmentation, especially in patients with darker skin, which fades slowly over time.

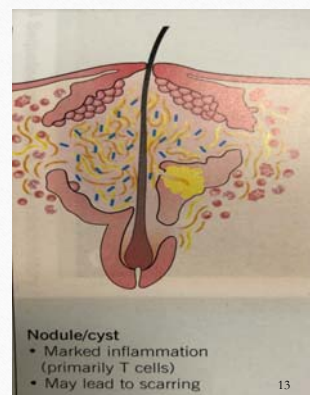


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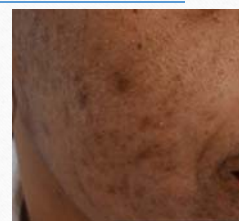
Nodulocystic

- Nodulocystic acne often leads to pitted or hypertrophic scars



Post-inflammatory Hyperpigmentation (PIH)

- Half or more of dark skin-toned patients have PIH
- Around 65% of Asian patients have hyperpigmentation
- PIH tends to be of long duration



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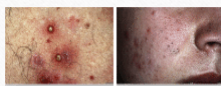
There is no universally agreed upon grading system.

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Grading of Acne

- We use a combined approach with general assessment of severity and actual lesion counts.
- We make rough numerical assessments of comedones, papules, pustules, cysts, residual erythema, and scarring. It is the divisions of these numbers that guide our treatment.
- I have found that over time we have had an internally consistent score within our office.



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Global Assessment

Grading :

- 0 : Clear
- Scattered: 1-5 lesions
- 1+ : about 6-10
- 2+ : about 11-15
- 3+ : about 16-20 lesions
- 4+ or Acne conglobate

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Severity of Acne

- Acne may be classified as mild, moderate or severe. Comedones and inflammatory lesions are usually considered separately.

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Mild Acne

- <20 comedones
- <15 inflammatory lesions
- Or, total lesion count <30

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Moderate Acne

- 20–100 comedones
- 15–50 inflammatory lesions
- Or, total lesion count 30–125



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Severe Acne

- >5 pseudocysts
- Total comedo count >100
- Total inflammatory count >50
- Or total lesion count >125



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Why do We Treat?

There is no mortality with acne, but there is significant physical and psychological morbidity such as permanent scarring, poor self-image, depression, and anxiety. The direct cost of the disease is estimated to exceed \$3 billion per year.

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Acne Treatment

- I do not use topical antibiotic therapy!
- For patients with severe acne, topical therapy may indeed be more valuable than often assumed in patients with severe acne vulgaris.
- In one study, a combination of A/BPO 0.1% plus Doxycycline 200 mg was a non-inferior alternative to oral Isotretinoin. The combination regimen compared with Isotretinoin had a significantly earlier onset of action in reducing acne lesions at week two. However, overall, Isotretinoin was superior to A/BPO 0.1% plus Doxycycline in reducing nodules, inflammatory lesions, and total lesions at week two.

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Acne Treatment: Oral Antibiotics

- Systemic antibiotics are useful for moderate to moderately severe acne, but efforts should be made to limit the duration of therapy to 3 to 4 months.
- Three factors to consider:
 - Severity of acne
 - Potential for bacterial resistance
 - Response to treatment

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Antibiotic Treatment

- Controversial for singular treatment
- Adapalene/BPO 0.3% agent was developed for first-time, topical severe inflammatory acne. Well tolerated and efficacious across the population of moderately severe inflammatory acne. These products work because they target the comedo and the bacterial process that is occurring in the follicle.
- Monotherapy with a topical antibiotic is not advised. The role of antibiotics in acne therapy has changed. Neither topical nor systemic antibiotics should be used as monotherapy of comedonal and severe inflammatory acne treatment.
- Antibiotic resistance is a worldwide problem and should be an essential consideration when selecting therapy for acne. Resistant microbial organisms are increasing throughout the world's populations, and worldwide health authorities have called upon the medical community to limit antibiotic use in situations where other management approaches might be used.

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Acne Treatment- Household Contacts

- Use of antibiotics affects a large number of people, as resistance can occur in both treated individuals and household contacts.
- Antibiotics are often prescribed for a much longer duration in acne than for typical infections.
- This exerts considerable selective pressure on microbes.
- Benzoyl Peroxide (BPO) is the preferred topical antimicrobial agent in this current management environment.
- BPO combined with topical retinoids is the most efficacious, evidence-based treatment option to prevent the development of antibiotic resistance in patients with acne.
- **A topical retinoid plus BPO is first-line therapy. This works to normalize keratinization, reduce inflammation, and kill *P. acnes*.**

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Strategies for Reducing Systemic Antibiotic Use

- First-line therapy is topical retinoids and BPO—treatment of choice
- At present, laser intense pulsed light and photodynamic therapy should not be considered first-line treatment.
- All strains of *P. acnes* are sensitive to BPO.
- Antibiotics should be avoided when effective alternatives are available.

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Strategies for Reducing Systemic Antibiotic Use(2)

- Oral antibiotics are only indicated when inflammatory acne is not responding well to topical treatments and acne involves the trunk or multiple body areas.
- Target duration of therapy less than 3 to 4 months.
- Avoid systemic antibiotic monotherapy if possible.
- Sub-antimicrobial dose antibiotics can help minimize potential for resistance.
- Isotretinoin should be first-line therapy for very inflammatory lesions and total lesions. However, treatment-related, medically relevant adverse events were less frequent in the combination treatment arm versus Isotretinoin in reducing nodulocystic acne. Overall, Isotretinoin was superior to A/BPO 0.1% plus Doxycycline.
- A/BPO 0.1% plus Doxycycline is an acceptable alternative to Isotretinoin for treatment of acne in patients who are unable or unwilling to have Isotretinoin prescribed.

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Isotretinoin

- Proven to be highly efficacious acne treatment and proven to clear acne lesions, including nodules and cysts, and achieve a prolonged remission period.
- Dosage 0.5 to 1.0 mg/kg administered over a period of 3 to 4 months.
- Accumulative dose of 120-150 mg/kg (period of 4 to 6 months).
- Systemic corticoids may be used at initiation of therapy to help speed lesion clearing.
- Proceed to full clearance plus one month.
- Oral Isotretinoin should be first-line therapy for very severe (cystic and conglobate) acne.
- Oral therapy should proceed until full clearance of acne even if that requires more than 6 months.
- Acne may flare initially. This can be minimized by initial low-dose treatment.
- Most patients should receive maintenance therapy with topical retinoids after Isotretinoin treatment.

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The pathogenesis of acne is multifactorial, involving the hormonal influence of androgens, along with excess sebum production as a consequence of that, disturbed keratinization, and inflammation and stimulation of the innate immune system by several pathways, including hypercolonization by *Propionibacterium acnes*.

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Microbiologic Testing

- *Propionobacterium acnes* is the primary bacterium implicated. Requires some non-standard culture requirements so not usually performed.
- Gram negative folliculitis: uncommon, uniform eruptive pustules—usually peri-oral and peri-nasal; usually in a setting of prolonged Tetracycline use. Caused by *Klebsiella* and *Serratia*. Usually treated by Isotretinoin or antibiotic sensitivities tested on culture

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Endocrinology Testing

- While the role of androgens in acne pathogenesis is well known, endocrinological evaluation is rarely warranted, because most acne patients will have normal hormone levels. Testing is primarily indicated for patients with clinical features suggesting hyperandrogenism.
- The most common cause of hyperandrogenism is polycystic ovarian syndrome (PCOS).
- Hormonal testing is complex. A typical hormone-screening panel includes free and total testosterone, DHEA-S, Androstenedione, LH, and FSH.

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Acne Treatment Options



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Topical Therapy

- Topical therapy includes prescription and over-the-counter drugs. Influenced by age of patient, site of involvement extent and severity of disease, sex, and patient preference. May be used as monotherapy or in conjunction with oral agents for control and maintenance.
- Typical therapies include BPO (Benzoyl Peroxide), Salicylic Acid, and antibiotics in combination with BPO.
- I do not use any topical antibiotics. I do use OTC Benzoyl Peroxides and Dapsone products.

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Mild Acne

- Mild acne characterized with just comedones
- Topical retinoid or Benzoyl Peroxide
- Tretinoin is first-line therapy. Benzoyl Peroxide and Adapalene can also be used.
- Low-dose combined oral contraceptive therapy for girls. Depends on the type of acne she is having.
- Cephalexin is my primary antibiotic, 500 mg b.i.d.
- Antiseptic or keratolytic acne washes contain Salicylic Acid.
- Be careful of severe drying.

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Moderate Acne- Papular/Pustular

- If necessary, use fixed combination or hormonal therapy and or antibiotics.
- Spironolactone or Trimethoprim
- Tetracycline derivatives such as Doxycycline, 50 to 200 mg q.d.
- Anti-androgen therapy in women not responding to low-dose combined or all contraceptive therapy, particularly women with PCOS
- Isotretinoin for persistent or prolonged

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Severe to Moderately Severe Acne

- Fixed combination plus oral antibiotic preferred.
 - Oral antibiotics are often used in higher doses than normal

OR

- Isotretinoin is usually recommended in suitable patients.
 - Oral Isotretinoin plus oral hormonal therapy
- Referral to a dermatologist

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Managing Very Severe Acne Nodular and/or Conglobate Acne

- Males—oral Isotretinoin or fixed combination plus oral antibiotics
- Females—oral Isotretinoin plus androgenic hormonal therapy
- Oral isotretinoin plus anti-androgenic hormonal therapy

OR

- Fixed Combination plus oral antibiotics and or anti-androgenic hormonal therapy

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If Response is Poor

- Check non-drug related reasons (seborrhea, stress, and diet, *Malassezia furfur*, Gram-negative bacteria. Comedogenic skin care produces endocrine profile and exclude hidradenitis suppurativa/acne inversa.
- Check drug-related reasons (type/doses of antibiotic, microbial resistance, spot treatment, consider adding Prednisone for females and check use of anti-androgenic agents.
- Consider intralesional injections of steroids and mechanical removal of macrocomedones.
Probe patients adherence (application technique, missed doses, tolerability).
- Ask about adverse events.

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Flares of Acne Can be Provoked By:

- Polycystic ovarian syndrome
- Drugs: steroids, hormones, anticonvulsants, epidermal growth factor receptor inhibitors, and other occlusive cosmetics
- High environmental humidity
- Diet high in dairy products and high glycemic foods
- Adolescence

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Acne Treatment Depends on Severity

Severity is classified as mild, moderate, or severe.

- Mild acne: total lesion count <30
- Moderate acne: total lesion count 30–125
- Severe acne: total lesion count over 125

We estimate comedones, papules, pustules, and cysts for a grading of 1+ to 4+
Normal acne is 1-2+. Serious acne is 3+. All acne above 3+ we treat with Accutane or generic equivalent - 1 mg/kg for first 4 weeks, then consider 2 mg/kg for second treatment. Insurance companies now will only approve 3mg/kg for 6 weeks.

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Dietary Restrictions

- Paleolithic diet
- Whale blubber is hard to get
- Recent article that skim milk was a problem
- Hershey story about use of chocolate



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My Approach to Treatment

In the adult female, acne is a chronic condition with a substantial negative psychological, social and emotional impact. Adult acne is mainly mild-to-moderate in severity and may be refractory to treatment. A holistic approach to acne therapy should be taken in adult females, which combines standard treatments with adjunctive therapy and cosmetic use.

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How I Treat Acne

Males:

- Begin Tretinoin 0.025%. As they tolerate it, since it is irritating, I gradually increase to 0.05% and then 0.1%. Apply sparingly, a simple dab that barely covers the face. The back and chest are easier to do.
- I sometimes use Tazorac and Adapalene, but rarely. I do not see that much use for it. Retin-A is still the gold standard.
- Antibiotics –systemic only. Usually Cephalexin. I used to use a lot of Bactrim and Minocycline but I have switched because of the increased resistance of MRSA and its ongoing sensitivity to Bactrim and Minocycline.

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How I Treat Acne in Females

Females:

- Similar treatment to boys, but I can frequently omit the use of antibiotics and substitute oral contraceptive pills (OCP).
- Some BCPs can be given for 3 months without inducing a period. This is helpful because it keeps the estrogen and progesterone at a relatively steady state for 3 months at a time. And the girls have only four periods a year.
- Try Spironolactone 100 mg (50 mg if below 130 lbs.). We are trying to avoid creating resistant bacteria
- Females usually worse just before menstrual cycle. Consider PCOS (females, overweight, hirsutism, and acne
- Hormonal (estrogens/progesterone)—usually females. Related to rise in progesterone prior to ovulation. Spironolactone

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How I Treat Acne in Females (2)

- Acne conglobate: treat with “Accutane” I have treated a 7-year-old female with Accutane. I just started to use lower dose Accutane as I discontinue antibiotics in young adults who are doing well.
- New and improved treatments are continuously being developed, and the role of various agents is changing. In the era of antimicrobial resistance, there should be diminished use of antibiotics. Because of their preventative action in acne by targeting microcomedones, retinoids should form the cornerstone of therapy. The variety of formulations and concentrations of available agents provides great flexibility for clinicians to individualize therapeutic regimens for patients while achieving good results.

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