

acne: a clear approach to clear(er) skin

Richard J. Antaya, M.D.

Professor, Dermatology and Pediatrics

Director, Pediatric Dermatology

Yale University School of Medicine

acne sufferer turned acne gladiator

“There is no single disease which causes more psychic trauma, more maladjustment between parent and children, more general insecurity and feelings of inferiority and greater sums of psychic suffering than does acne vulgaris.”

Sulzberger MB, Zaidems SH. Med Clin North Am 1948;32:669

psychosocial impact of acne

- impaired self-image
- altered body image
- decreased self-esteem
- embarrassment, shame, social impairment
- preoccupation
- anger
- depression

unemployment and acne

- 625 clinic “acne” patients (18-30 years)
- 625 general practitioner records
(age-, sex-matched)
- unemployment levels

	<u>males</u>	<u>females</u>
Acne	16.2%	14.3%
Control	9.2%	8.7%

suicidal ideation, mental health problems, and social impairment increased in adolescents with acne: a population-based study

- 3,775 Scandinavian adolescents (18-19 yrs)
- 14% with substantial acne (“a lot” and “very much”)

<i>suicidal ideation</i>	<i>“very much acne”</i>	<i>“no/little acne”</i>
girls	25.5 %	11.9 %
boys	22.6 %	6.3 %

- suicidal ideation significantly associated with substantial acne
 - odds ratio 1.80
 - adjusted for symptoms of depression, ethnicity, family income

ACNE differential diagnosis

- drugs
 - lithium
 - steroids
- milia
- papular scars
- keratosis pilaris
- halogenoderma
- syringomas
- angiofibromas of tuberous sclerosis
- eosinophilic folliculitis
- folliculitis-like - steroid acne, perioral dermatitis
- Demodicidosis

steroid acne (rosacea)

- no comedones
- diffuse pustules
- acute onset
- systemic steroids

periorificial dermatitis (perioral dermatitis)

- no comedones
- periorificial
- exacerbated by topical steroids
- treat with topical/
oral antibiotics

demodicidosis

Demodex (follicle mite) dermatitis

- no comedones
- mid facial
- papules (98%)
- erythema (96%)
- pustules (56%)
- peeling (29%)

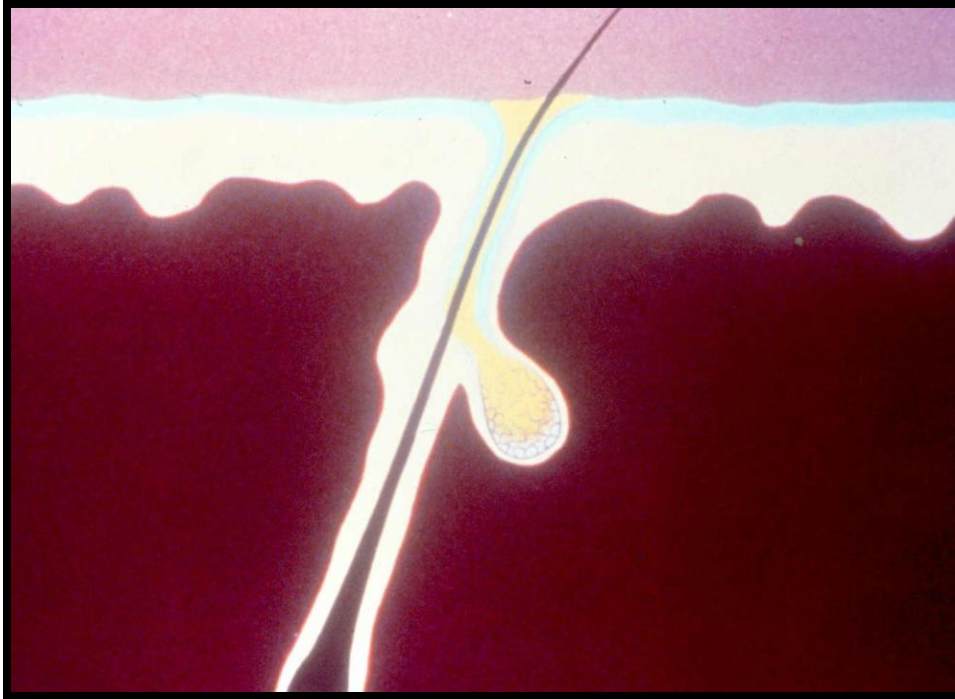
also

- styes (11%)
- conjunctivitis (4%)
- +/- immunosuppression, rosacea
- treat with topical/ oral ivermectin or antibiotics

Schroder C, Gárate M, Orlandi D et al. Clinical and epidemiological characterization of demodicosis cases in the pediatric population at the Hospital Clinic of the University of Chile (2013–2020). *An Bras Dermatol*. 2025;100(1):145-147.

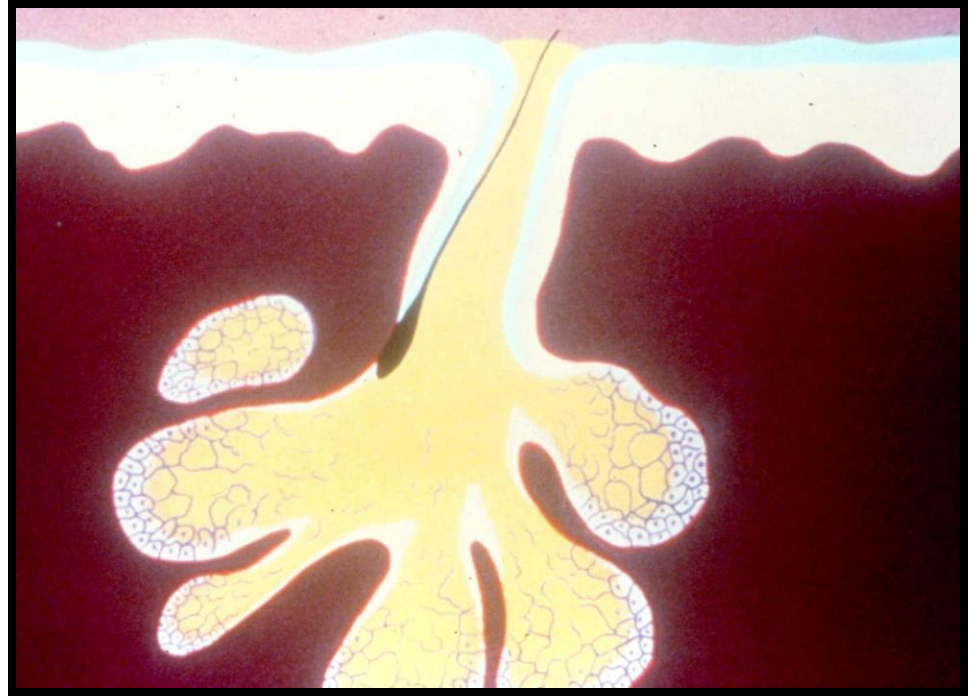
ACNE pathophysiology

- follicular keratinization defect
- sebum
- bacteria - *Cutibacterium acnes* (formerly *Propionibacterium acnes*)
slow-growing, aerotolerant anaerobic, Gram-pos rod



hair follicle

scalp
arms
legs

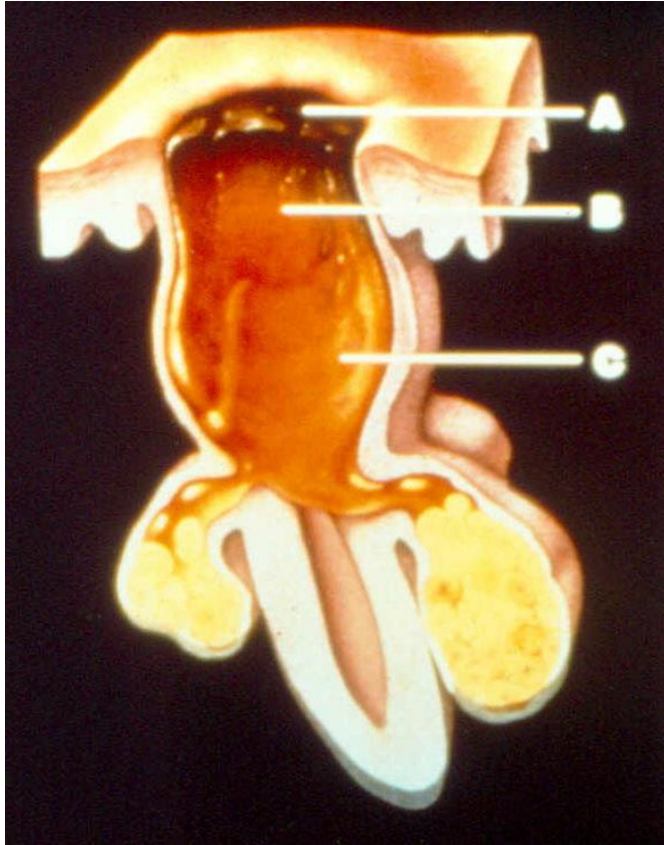


sebaceous "hair" follicle

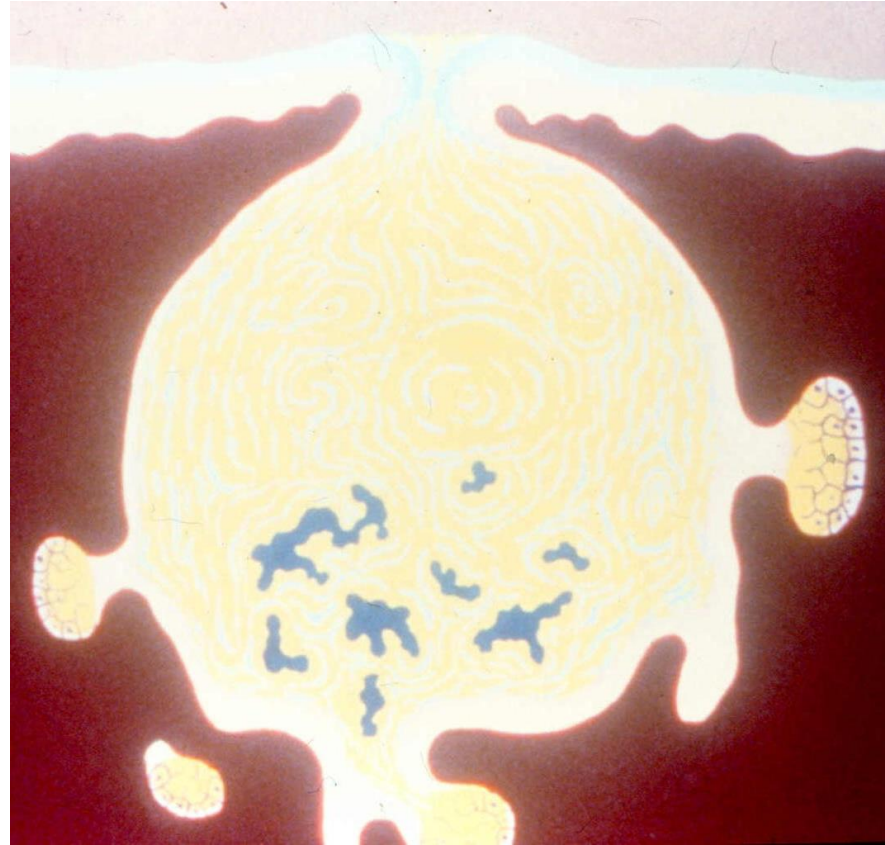
face
neck
chest
back

comedones

open



closed



pustule/
papule

nodule/cyst



acne pathogenesis

- sebum
 - triglycerides (60%), wax esters (25%), squalene (15%)
- acne patients
 - decreased linoleic acid in sebum
 - +/- higher sebum secretion rates
 - unknown influence on follicular epithelium
- androgen control
 - testosterone, dihydrotestosterone, DHEA-S

ACNE pathogenesis: inflammation

- *Cutibacterium acnes*
 - acne patients > age-matched controls
 - ingested, but not killed, by neutrophils
 - releases hydrolytic proteases
 - activates complement system → C5a
- immune response in acne patients
 - severity proportional to *C acnes* antibody titers
 - ↑ lymphocyte transformation to *C acnes* antigens

ACNE pathogenesis: summary

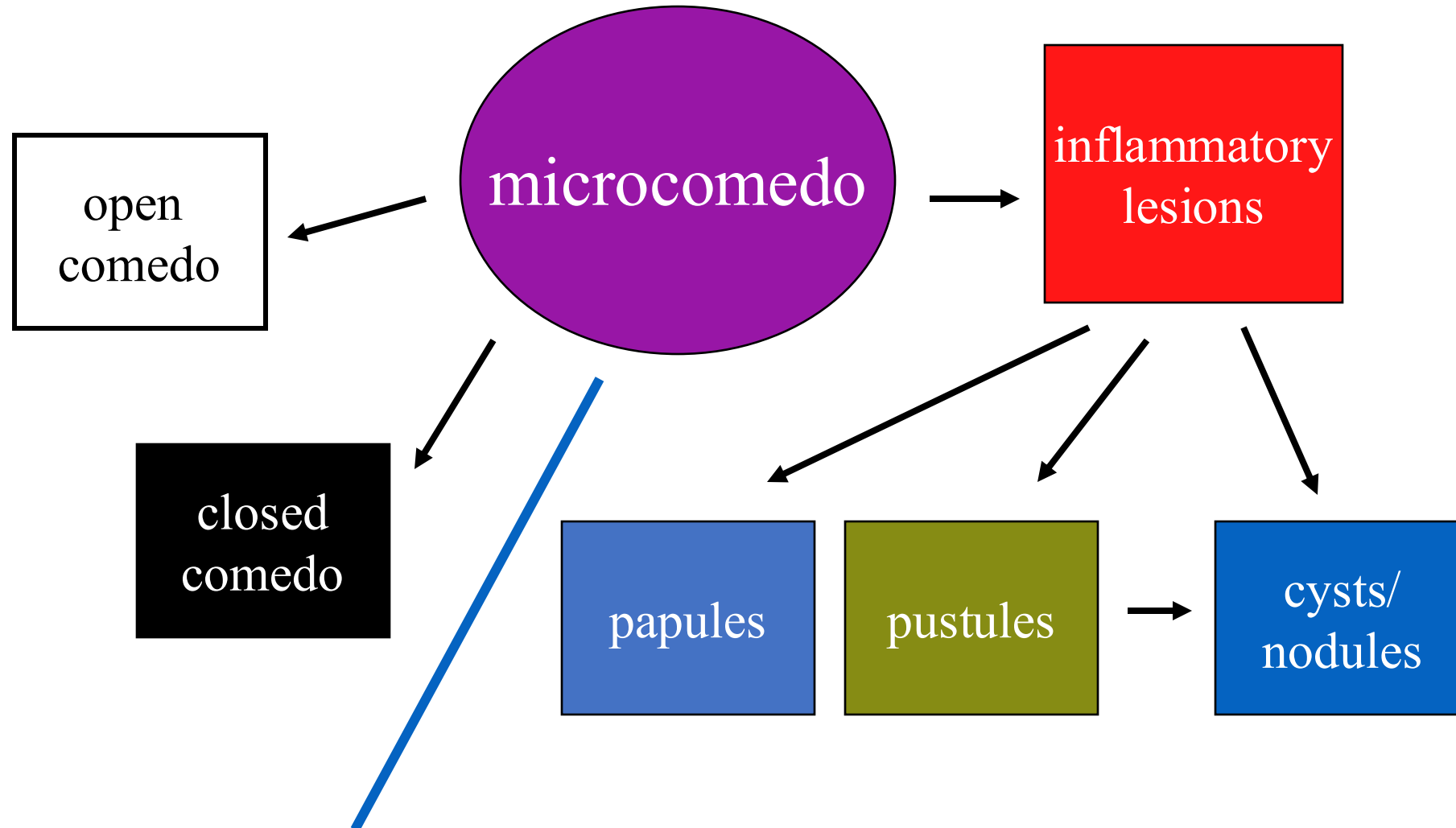
- We know

- follicular keratinization defect
- sebum plays a role
- *C acnes* → inflammation

- We don't know

- role for androgen/hormone receptors
- comedo formation at molecular level
- why some scar and some do not
- why patients go into remission

acne lesion progression



acne grading

- I comedonal
- II pustular
- III papular
- IV nodulocystic

- mild
- moderate
- severe
- call a code

acne grading

- mild
 - few localized comedones, papules, pustules
- moderate
 - many comedones, papules, pustules
 - +/- violaceous scars/post inflammatory erythema
 - mild scars
- severe
 - numerous or extensive superficial lesions
 - + nodules / cysts
 - + scars

ACNE: treatment modalities

- comedolytic
 - topical keratolytics (salicylic acid)
 - topical retinoids
- anti-inflammatory
 - topical antibacterials (benzoyl peroxide)
 - topical antibiotics
 - oral antibiotics/ anti-inflammatory
- oral retinoids (isotretinoin)
- antiandrogen hormonal therapies: COC/OCP, spironolactone (women), clascoterone cream 1% (Winlevi®)
- ablative (lasers), phototherapy (blue light), photodynamic therapy

Over-the-Counter Acne Medications

salicylic acid

benzoyl peroxide

adapalene (Differin® Gel 0.1%)



ACNE treatment

benzoyl peroxide

- antibacterial >>> comedolytic
- 2.5-10% concentration
- Rx and OTC preparations
- apply qd or bid
- side effects - erythema, scaling, bleaching fabrics, allergies
- personal favorites – Panoxyl Creamy Wash 4%[®] or CeraVe Acne Foaming Cream Cleanser 4%
 - liposomal, 30 sec – 2 min

ACNE treatment

topical retinoids: tretinoin, adapalene, tazarotene, trifarotene

topical tretinoin (Retin-A®)

- comedolytic - decreases “stickiness” of skin cells shed into follicular lumen
- preparations (in order of increasing potency)
 - 0.025%*, 0.05%* and 0.1% cream
 - 0.01% and 0.025% gel
- tretinoin slow release
 - microspheres (Retin A Micro®) gel - 0.1%, 0.06%, 0.04%, and 0.08%
 - Atralin® gel 0.05%

* Begin with lower concentrations

ACNE treatment

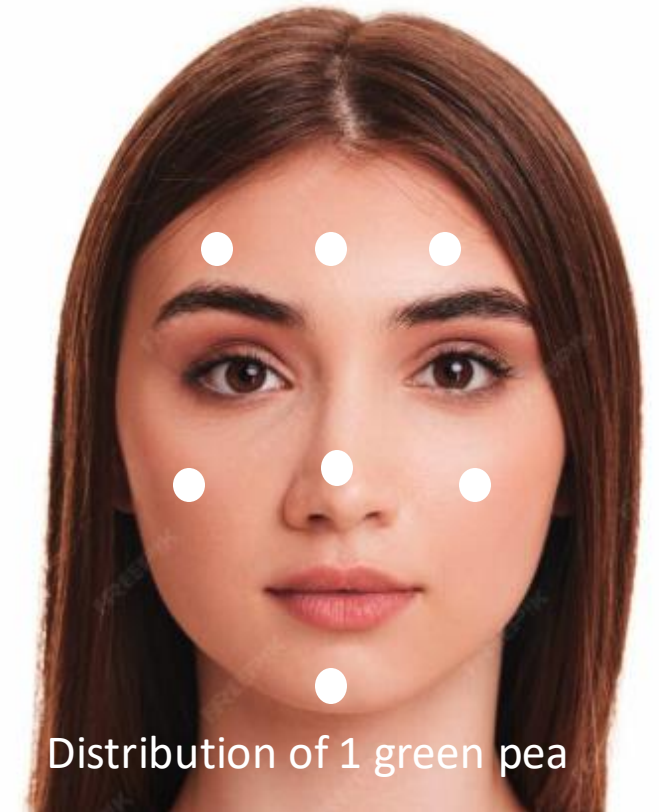
topical retinoids: tretinoin, adapalene, tazarotene, trifarotene

- adapalene (Differin gel[®] or cream) 0.1% and 0.3%
 - Differin gel[®] 0.1% is OTC
- trifarotene (Aklief[®]) 0.005%
- tazarotene (Tazorac[®] cream, gel) 0.05% & 0.1% (Arazlo[®] lotion)
 - potent
 - S.C.T (short contact therapy)
 - irritating
 - pregnancy/breastfeeding “X”

ACNE treatment

retinoid pitfalls

- irritation
 - introduce slowly – qohs x 2 weeks
 - only at bedtime
 - only on dry skin
 - only small amount (one pea-sized amount for entire face)
- transient worsening (purging) of acne at ~ 1 month
- photosensitivity
- fragility (waxing)
- tretinoin inactivated by BP (except microspheres) and sunlight



Distribution of 1 green pea

ACNE treatment

azelaic acid cream 20% (Azelex®)

- dicarboxylic acid
- produced by wheat, rye, and barley, *Pityrosporum ovale*
- mildly comedolytic and anti-inflammatory
- inhibits tyrosinase - *ideal for post-inflammatory hyperpigmentation*
- apply bid

ACNE treatment

topical antibiotics

- decrease *C. acnes*, anti-inflammatory
- preparations
 - erythromycin solution, gel, ointment
 - clindamycin solution, gel, lotion, wipes
 - dapsone gel 5%, 7.5% (don't apply with BP → orange-brown color)
 - minocycline foam
- apply qd or bid
- use with BP
- side effects: drying, erythema, peeling

ACNE treatment

BP-Antibiotic Combos

BP 5% & erythromycin 3% (Benzamycin® Gel)

BP 5% & clindamycin 1% (Benzacilin®, Duac Gel®)

BP 2.5% & clindamycin 1.2% (Acanya Gel®)

- synergistic
- antibacterial, anti-inflammatory
- help limit resistance of *P acnes*
- apply qd or bid
- use sequentially with retinoid qhs
- +/- irritating
- unstable at room temperature when mixed (BZM)
- shorter shelf life of 8-13 weeks

ACNE treatment

retinoid combos

- formulations
 - BP 2.5% & adapalene 0.1% (EpiDuo Gel[®])
 - BP 2.5% & adapalene 0.3% (EpiDuo Forte Gel[®])
 - BP 3% & tretinoin 0.1% (Twynéo Cream[®])
 - BP 3.1%, adapalene 0.15%, & clindamycin 1.2% (Cabtreo gel[®])
- synergistic
- active against comedones **AND** *C. acnes*
- stable at room temperature
- no resistance to the BP

ACNE MANAGEMENT oral antibiotics

- tetracycline 500 mg bid empty stomach
- doxycycline 50-100 mg bid
 - sub-antimicrobial dose doxy 20-40 mg
- minocycline 50-100 mg bid
 - sub-antimicrobial mino (various doses)
- sarecycline (Saysera) qd weight-based dosing
 - narrow spectrum to *C acnes*, *less resistance*, *saves gut and skin bacteria*
- erythromycin 500 mg bid or 333 mg tid
- azithromycin 250 mg tiw or Z-Pak dosing 5day/mo
- TMP/SMX DS 1 tab bid
- administer with topical retinoid or BP or both *always*
- 4-month limit x 1 then off; must continue topicals

ACNE MANAGEMENT Side Effects of Oral Antibiotics

- GI upset
- allergic reactions
- vaginal candidiasis
- esophageal ulceration (cyclines)
- hyperpigmentation (minocycline)
- dizziness (minocycline)
- photosensitivity (doxy > tetra > mino)
- decreased GI absorption with free Ca^{++} or Fe^{++}
- microbiome disruption, ? IBD signal, resistance, autoimmune d/o's

minocycline-related lupus

- females > males
- doses: 100 - 200 mg/day
- 1- 2 years of therapy
- sx: arthralgias, arthritis (hands, feet), fever, rash, malaise
- positive: ANA, anti-histone, p-ANCA
- negative: ds-DNA, RF
- most have full recovery 1 - 2 weeks after d/c of drug
- **25% persistent disease**

Pediatr 1998;101:926-8

J Rheumatol 1996;23:2160-1

J Pediatr 2008;153:314-9

minocycline-related autoimmune hepatitis

- minocycline prior to onset: 1- 25 mo
- fever, rash, arthralgias, malaise, GI symptoms, LA
- ↑ ALT/AST, ↑ serum Ig' s, + ANA, ASMA
- Rx: steroids, azathioprine
- most complete resolution
- **fulminant hepatic failure in a few**

Arch Pediatr Adolesc Med. 1998;152:1132-1136.
Pediatr Gastroenterol Hepatol Nutr. 2018;21(4):347-350.

nodulocystic / scarring
acne

ACNE treatment

isotretinoin

- indications
 - severe nodulocystic acne
 - scarring acne
 - recalcitrant disease
- actions
 - sebum suppression
 - decreases comedones
 - alters inflammatory response

ACNE treatment

isotretinoin side effects

- *SEVERE TERATOGEN....FDA's iPLEDGE registry*

common

- dry skin, lips, mucous membranes, and eyes
- musculoskeletal aches
- paronychia

rare

- ↑ TG's >> chol → pancreatitis
- ↓ night vision
- pseudotumor cerebri → H/A
- hepatotoxicity
- hyperostosis
- inflammatory bowel disease disproved*

*Am Acad Dermatol website. Position statement on isotretinoin.
<https://www.aad.org/Forms/Policies/Uploads/PS/PS-Isotretinoin.pdf>.

ACNE treatment

isotretinoin and depression

- 12 suicides while taking isotretinoin 1989-1998*
- no studies suggest a link between isotretinoin and depression, anxiety, mood changes or suicidal ideation
- population-based studies reveal no evidence of depression
- studies show improvement in mood

*JAMA, April 8, 1998; 279(14),1057

Rehn LM, J Eur Acad Dermatol Venereol. 2009;23:1294-1297

Marqueling AL, Semin Cutan Med Surg. 2005;24:92-102

ACNE treatment

combined oral contraceptives

- 4 COC's FDA-approved for acne and BC
- estrogen: all ethinyl estradiol
- progestin: norgestimate, norethindrone, or drospirenone
- decrease ovarian androgens, increase of SHBG
- significant improvement by end of 3rd cycle – inflammatory and comedonal
- R-DB-PC study 160 subjects - 6 cycles
 - total lesion count dec 53% vs 27% ($p = 0.0001$)
 - 94% vs 65% rated as improved

Obstet Gynecol 1997;89:615-22

Koltun W, *Eur J Obstet Gynecol Reprod Biol.* 2011;155:171-175

Shaw JC. *J Am Acad Dermatol.* 2000;43:498-502

ACNE treatment

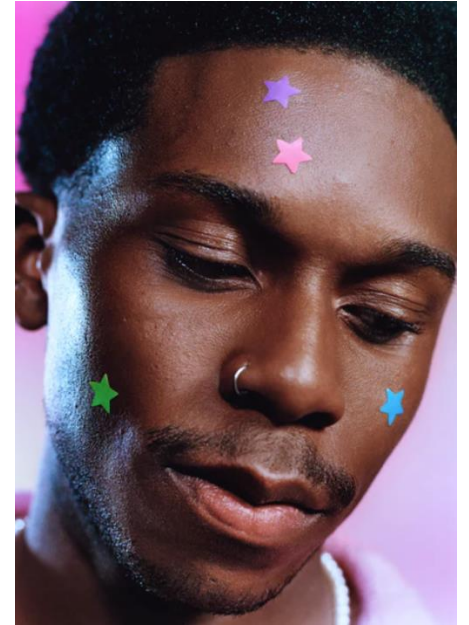
spironolactone

- potassium-sparing diuretic, off label
- androgen receptor antagonist in sebaceous glands > decreases testosterone prod
- *women only*
- both face and trunk
- dosage: 50-200 mg daily, start at 100 mg/day
- adverse effects: menstrual irregularities, PMS sx > lightheadedness, headache
- teratogen (genitalia in male offspring)
- potassium monitoring not useful in healthy young patients

ACNE treatment

hydrocolloid gels **pimple patches**

- absorbs pus and oil from pustules
- protects from picking
- NOT effective for cysts or comedones
- few controlled studies show improvement
 - redness
 - oiliness
 - hyperpigmentation
- not preventative



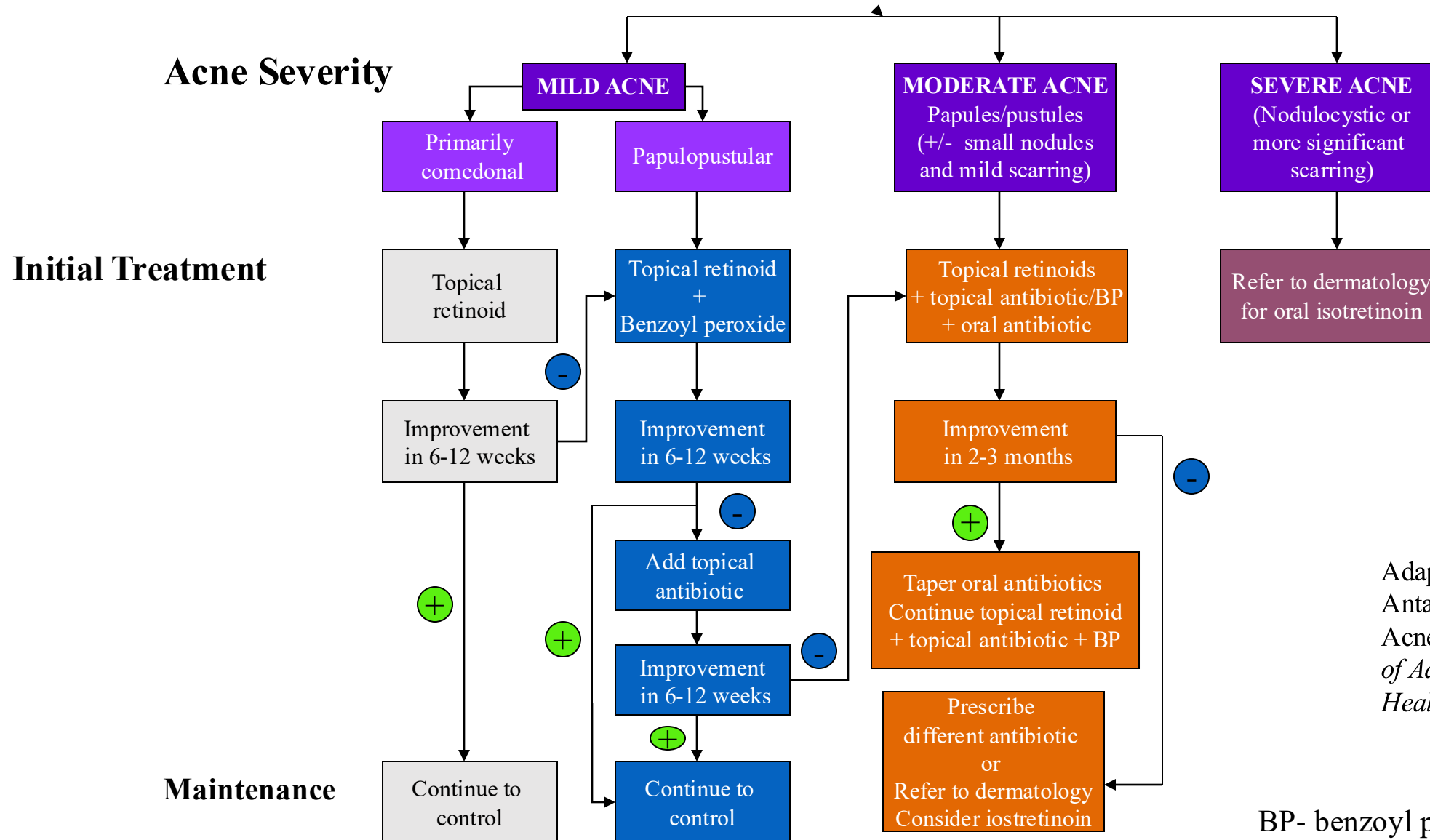
1726 nm laser

AviClear™

- targets and reduces sebaceous glands
- less oil production
- regimen: 3 sessions, 4 wks apart
- minimal / no downtime
- \$2,400 -\$3,900 !!!
- not covered by insurance 😞



acne treatment algorithm



Adapted from
Antaya, Chavel;
Acne. In *Textbook
of Adolescent
Health Care*, AAP

BP- benzoyl peroxide

practical acne management

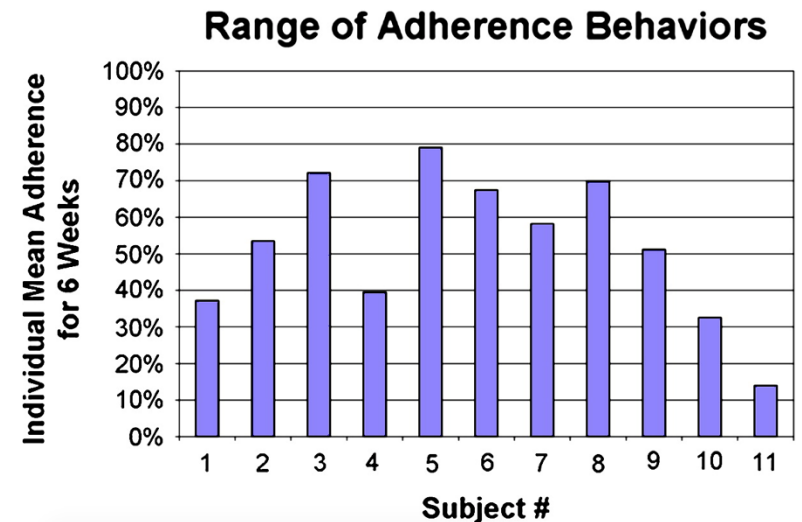
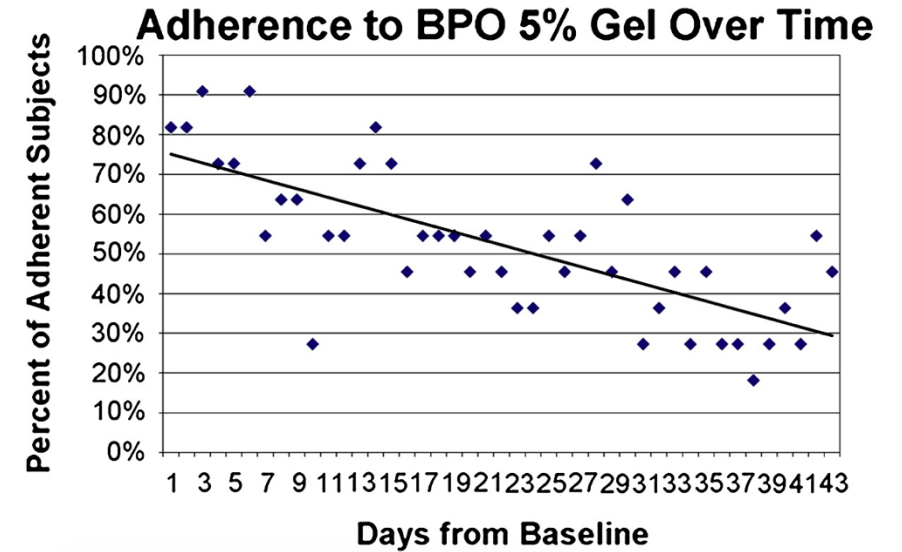
3 facts every patient must know

1. “it takes 3 months to see maximum effect of topical meds”
2. “you must use medication every day for it to work. you are conditioning your skin to prevent new acne”
3. “most topical acne meds are ~60-80% effective when used regularly”

practical acne management

adherence is everything!

- overall, 27% of patients did not fill all their acne prescriptions
- of patients given 1, 2, or 3 or more treatments, 9%, 40%, and 31%, respectively, did not fill all their prescriptions
- in one study using a hidden microchip in the cap of the medicine tube measured adherence to BP for 6 weeks ranging from 14% -79%



Anderson KL, *JAMA Dermatol.* 2015 Jun;151(6):623-6
Yentzer, Brad A. et al. *J Amer Acad Dermatol.* 2009;60(5):879-80

practical acne management

- address cutaneous side effects
- *gentle skin care*
 - cleanse gently - b.i.d. appears best
 - mild cleansers
 - moisturizers as needed
- don't pick or squeeze lesions

practical acne management

- Don't bother if the patient doesn't care
i.e. don't treat the parent
- dispel myths



diet and acne

- several published studies
- low fat and skim milk *may* worsen acne
 - higher glycemic load
 - higher androgens
 - less healthy fats
- high glycemic load diets may worsen acne
- AAD doesn't endorse any dietary restrictions

Glycemic Load and Acne

- prospective, randomized, controlled, partially blinded
- 43 males, 15-25 yrs, 12 weeks
- 23 dietary intervention group – lower carbs
- 20 control group – usual intake of carbs
- Measured: acne severity, IGF-1, insulin sensitivity, SHBG, androgen hormones, sebum outflow and composition

Smith RN, *et al.*. *Am J Clin Nutr* 2007; 86:107–115.

glycemic load and acne

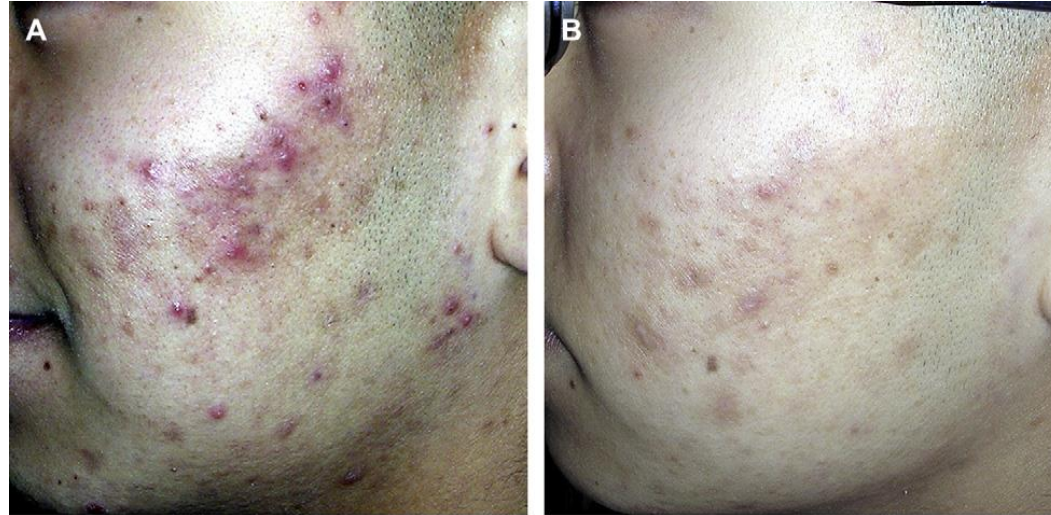
CHANGE	LOW GLYCEMIC LOAD	CONTROL
ACNE LESIONS WEEK 12	- 51%	-31% p= .003
FASTING INSULIN U/mL	0.90 (2.59, 0.79)	1.96 (0.15, 3.77) p= .03
Log (IGFBP-1) ng/mL	0.14 (0.05, 0.22)	0.09 (0.18, 0.03) p = .001
Δ SHBG, nmol/L	0.27 (1.56, 2.09)	-2.71 (-4.67, -0.74) p= .03
SEBUM*	↑sat/mono-unsaturated fatty acids	No Δ p = 0.007

Smith RN, *et al.*. *Am J Clin Nutr* 2007; 86:107–115.

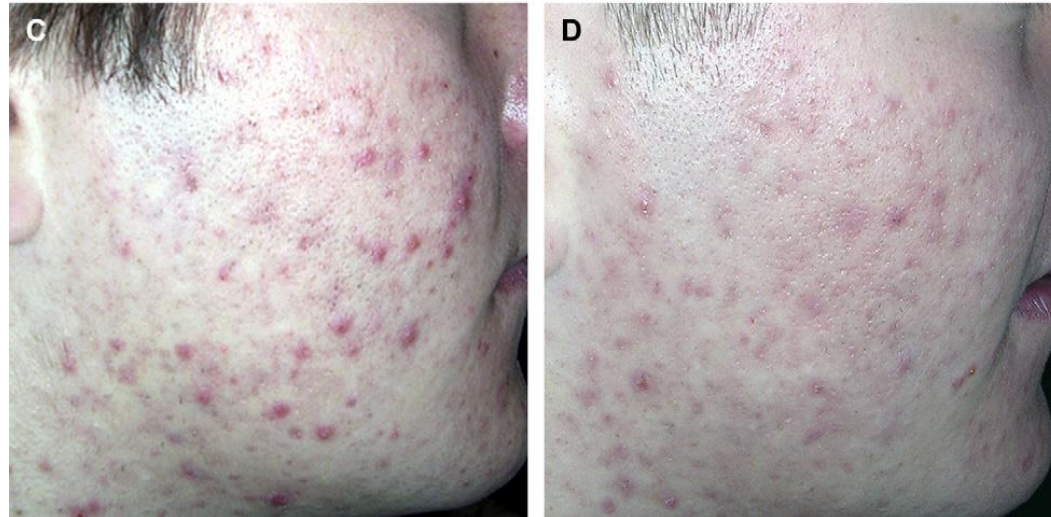
*Smith RN,. *J Dermatol Sci* 2008; 50: 41–52.

photographs of acne improvement in low glycemic load group

Patient A at
Baseline (A)
and 12 weeks (B)



Patient B at
Baseline (C)
and 12 weeks (D)



THANK YOU

cure sometimes

relieve often

comfort always