

Acne and Follicular Disorders

Joyce B. Farah, MD MS FAAD

Farah Dermatology and Cosmetic Center

Assistant Professor of Medicine, ENT and Family Medicine

Upstate Medical University

No conflict of interest

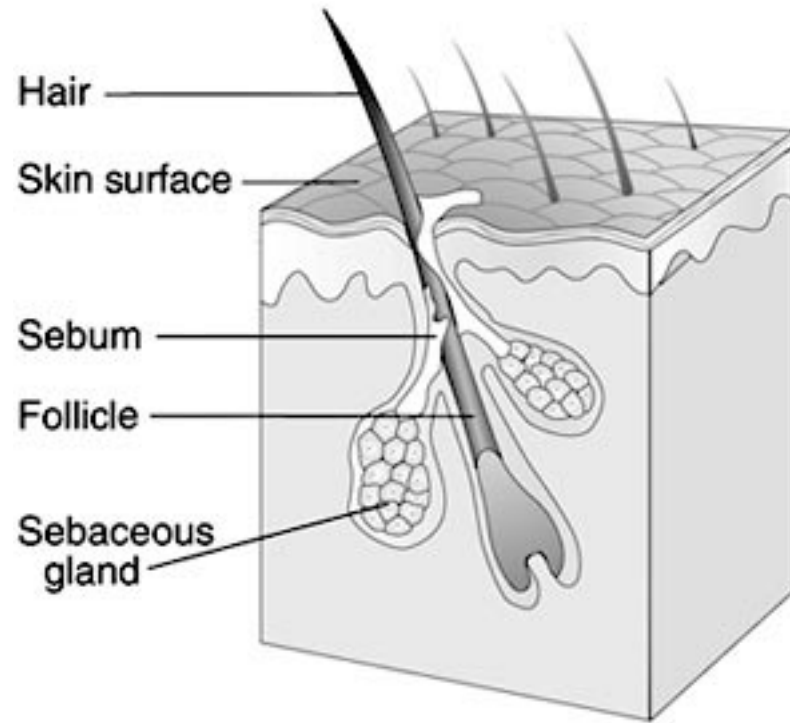


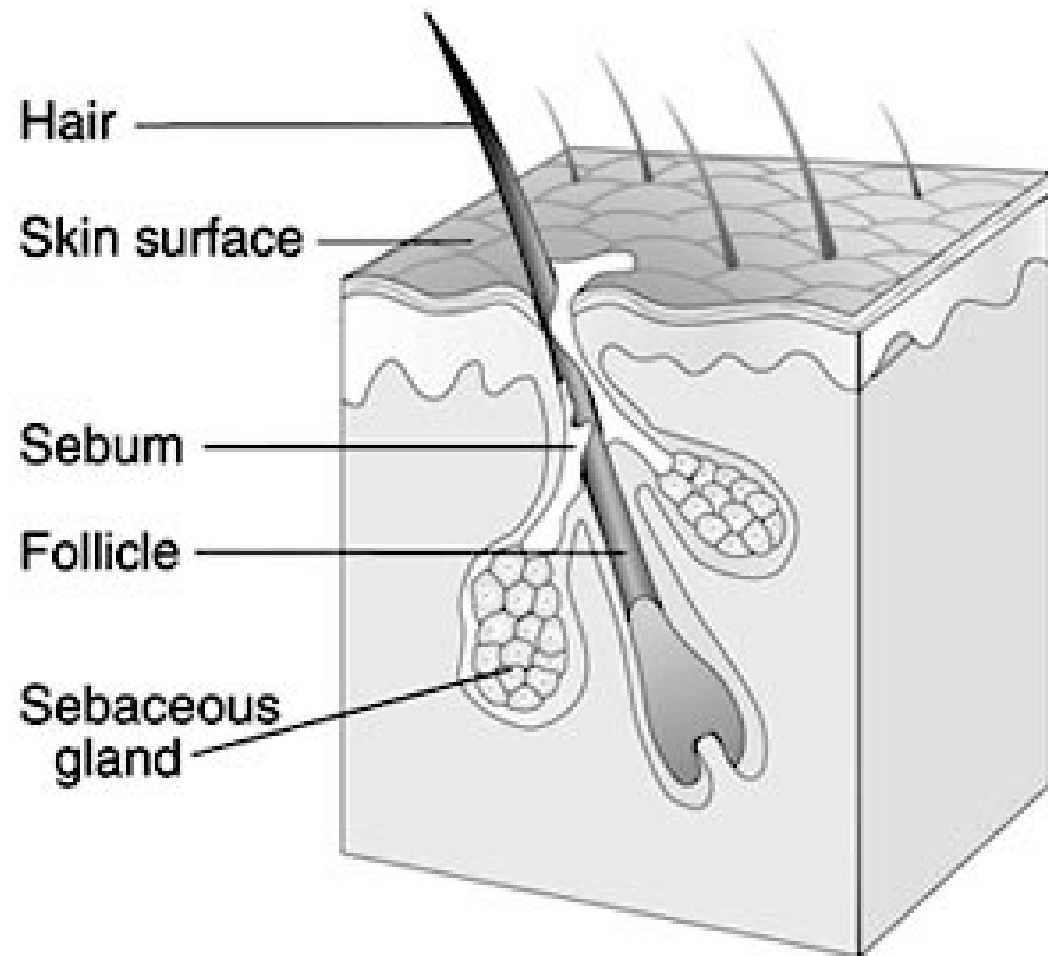


Acne Vulgaris

- ▶ Acne is the most common dermatologic disease
- ▶ 20% will have severe acne that results in scarring
- ▶ Multi-factorial
- ▶ Key factor : genetics and skin microbiome

Pilosebaceous Unit





Acne Vulgaris

- ▶ Interplay of the following 4 factors:
 - ▶ Follicular epidermal hyper-proliferation and plugging of hair follicle
 - ▶ Excess sebum production
 - ▶ Presence and activity of commensal bacteria *Cutibacterium acnes* and skin biofilm
 - ▶ Follicular and peri-follicular inflammation

Retention hyperkeratosis

Initial event

Exact underlying cause is not known

Theories:

Androgen hormones as initial trigger

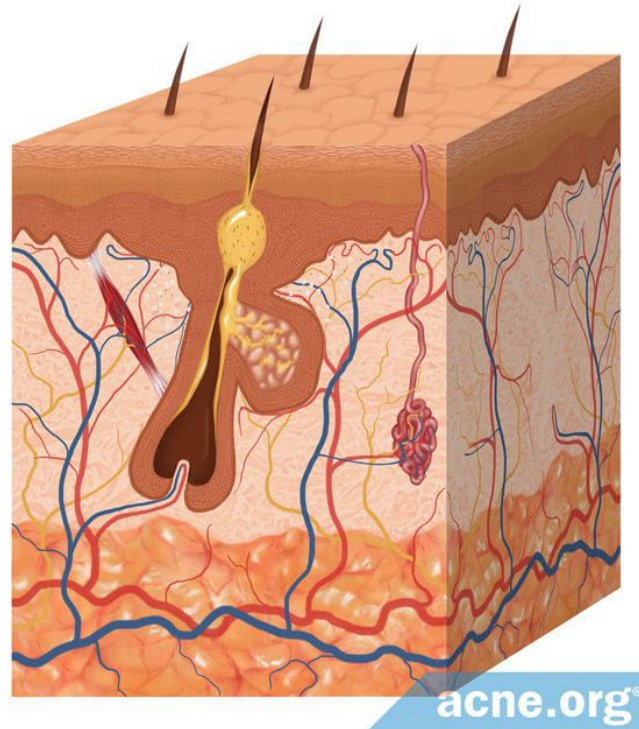
Comedones appear around puberty

Degree of comedonal acne in pre-pubertal girls correlates with levels of DHEA-S

Androgen receptors are present in sebaceous glands

Individuals with defective androgen receptors do not develop acne

**Early Stages of
Clogged Pore
Development
Microcomedone**



Retention Hyperkeratosis
Micro-comedone



ACNE VULGARIS

Role of micro-biome dysbiosis in acne disease is predominantly mediated by microbial as well as non-microbial factors such as diet, hormones and genetic predisposition

Host Microbiome Interactions and Recent Progress into Understanding the Biology of Acne Vulgaris:

O'Neil AM, Gallo RL Host Microbiome Interactions and Recent Progress into Understanding the Biology of Acne Vulgaris. *Microbiome* 2021. <https://doi.org/10.1186/s40168-018-0558-5>

Mitchel et al, Genome Wide Associated Meta-analysis Identifies 29 New Acne Susceptibility Loci. *Nature* Feb 2022

Zhan et al, The Influence of Benzoyl Peroxide on the Skin Microbiota and the Epidermal Barrier for Can Vulgaris. *Dermatologic Therapy* Dec 2021

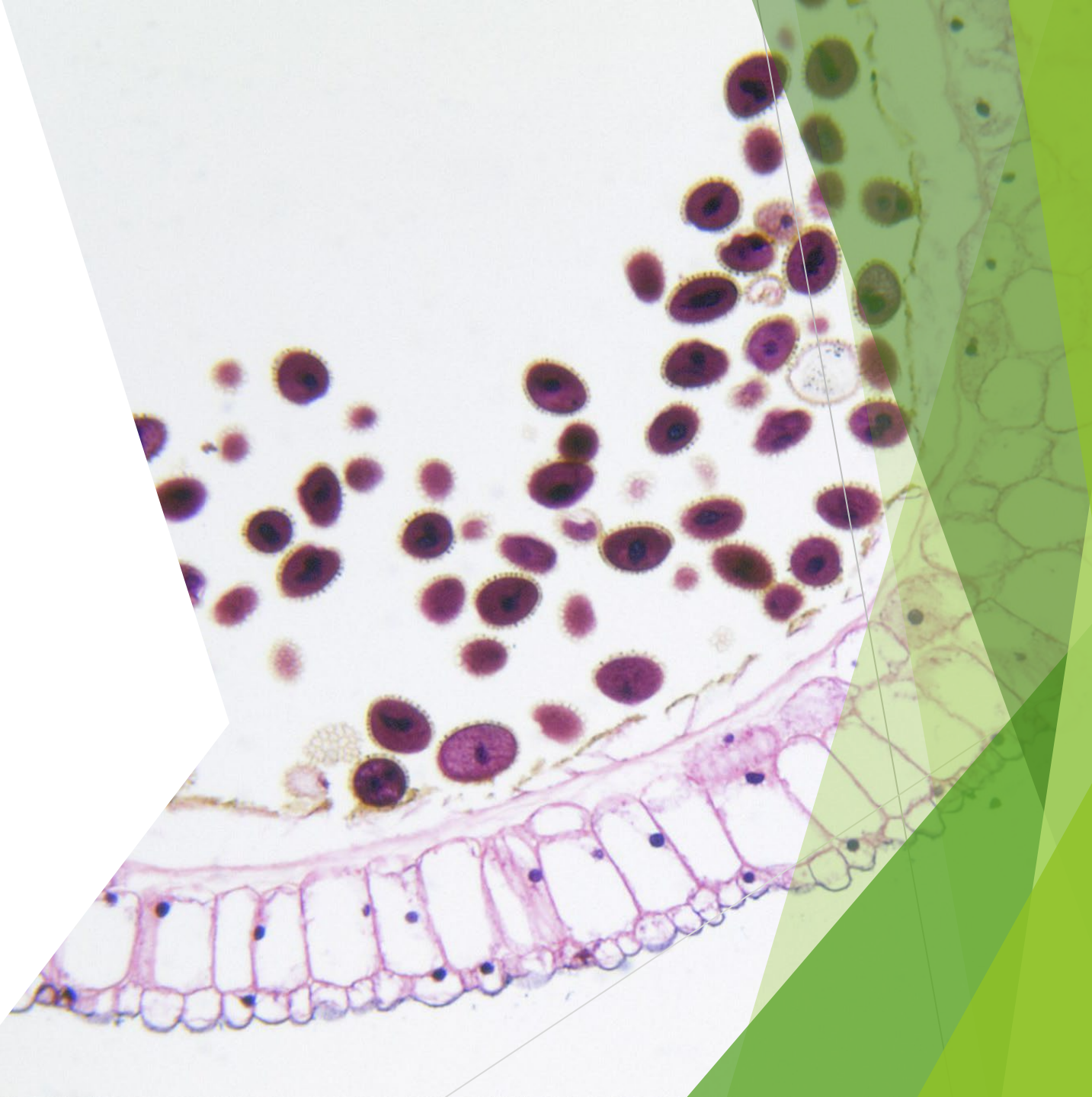
Genetics-follicular structure and its environment

- ▶ Growth
- ▶ Differentiation and maturation
- ▶ Inflammation
- ▶ Cell-cell adhesion
- ▶ Cell signaling
- ▶ Follicular defects



Skin microbiome

- ▶ Different than in normal skin
- ▶ Influence by topical BP
- ▶ Treatment mechanism is not as expected
 - ▶ Increase in *Staph*
 - ▶ Decrease in *C. acnes*
 - ▶ Most significant decrease in *Corynebacterium*

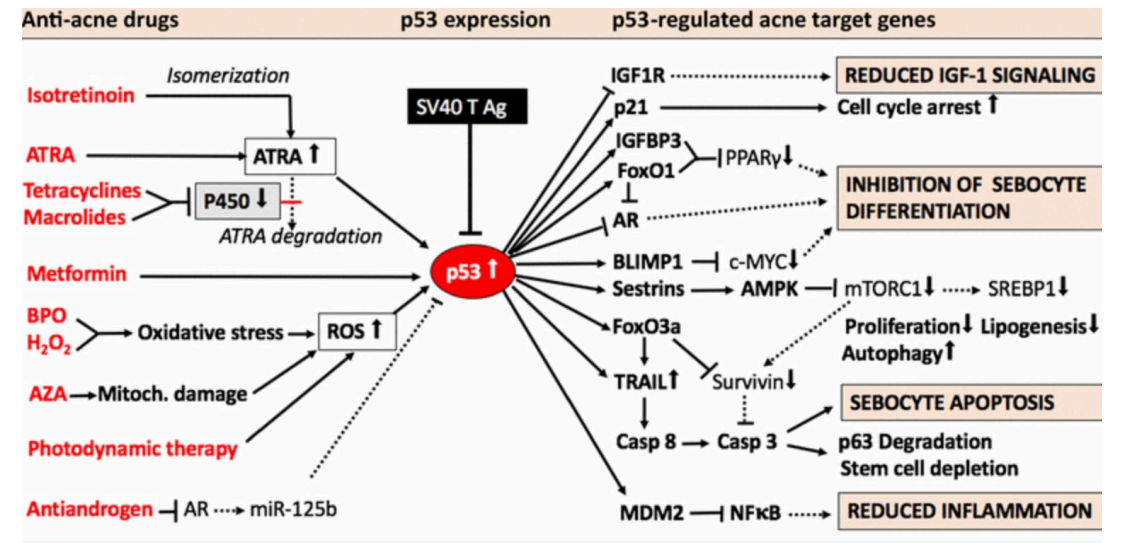


Single Cell Transcription

- ▶ New application to dermatology
- ▶ RNA sequencing-communication between cells
- ▶ Helps differentiate the influence of environments within the hair follicle
- ▶ Subsets of fibroblasts are the active effectors in acne-secrete antimicrobial peptide LL37 (CAMP)
- ▶ Myeloid cells and fibroblast signaling
- ▶ Keratinocytes play minimal role
- ▶ Retinoids induce fibroblast production of AMP
- ▶ Retinoid do not work by inhibiting lipid synthesis

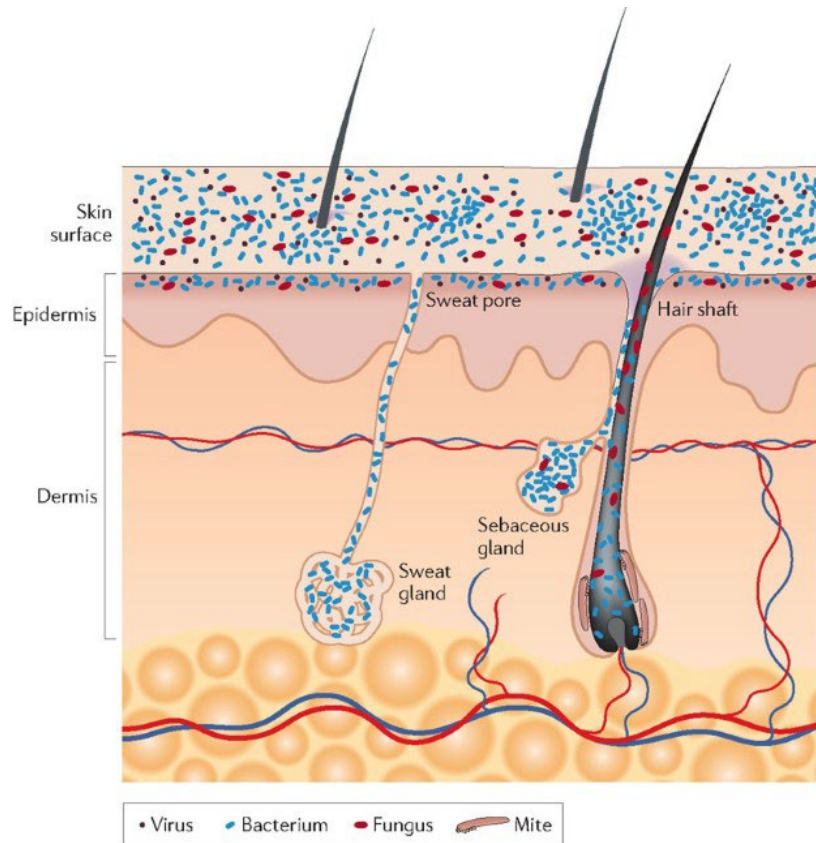
P53 and Therapy

- ▶ P53: key conductor of all anti-acne therapies
- ▶ Melnik, *BC J Transl Med* 15, 195 (2017)
- ▶ <https://doi.org/10.1186/s12967-017-1287-2>





Skin Microbiome



Nature Reviews | Microbiology

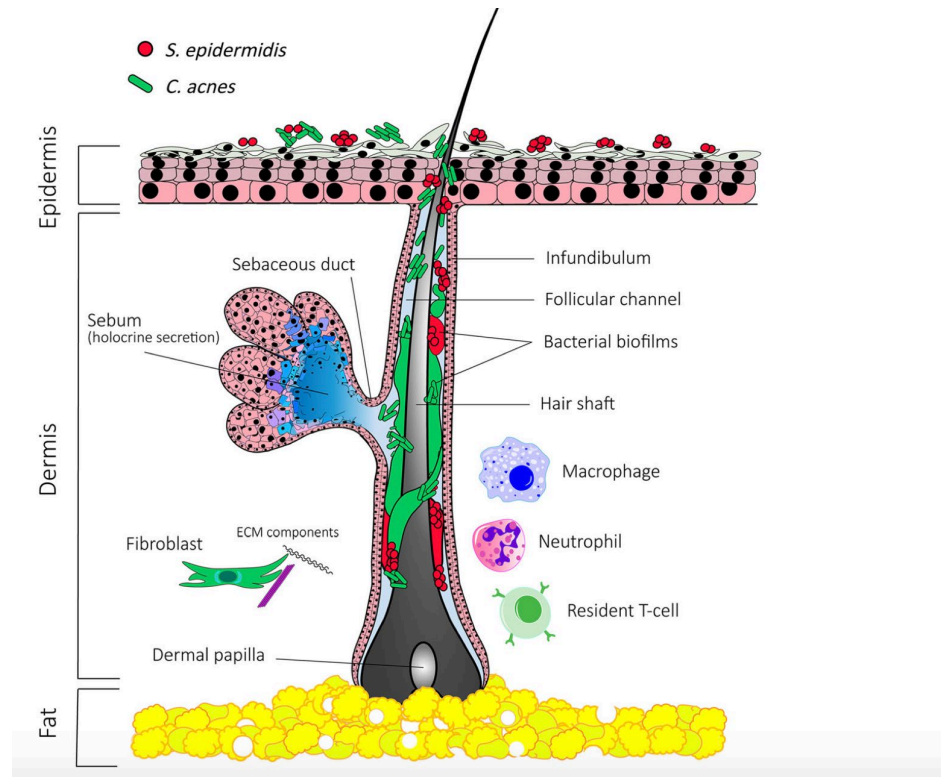
- ▶ *Staphylococcus epidermis* and *Cutibacterium acnes*
- ▶ Large part of microbiome
- ▶ *C. acnes* equally present in acne and non acne skin
- ▶ Differing lineages-non-pathogenic strains are protected from forming biofilms, colonization, and virulence
- ▶ Pathogenic strains produce more virulent proteins
- ▶ Dysbiosis and immunobiology of skin

Cutibacterium Acnes

- ▶ Site specific
- ▶ Major skin commensal
- ▶ Maintains homeostasis of the skin
- ▶ Antimicrobial role
- ▶ Disease does not correlate with overgrowth
- ▶ Co-exists with other *Cutibacterium*, *Staphylococcus*, *Pseudomonas*, *Corynebacterium*, *Malassezia*
- ▶ Interaction with *S. epidermidis*

O'Neil AM, Gallo RL Host Microbiome Interactions and Recent Progress into Understanding the Biology of Acne Vulgaris: *Microbiome* (2018) 6:177 <https://doi.org/10.1186/s40168-018-0558-5>

Fig. 1 Skin organization and representation of the pilosebaceous unit. Major residents of the pilosebaceous unit, *C. acnes* and *S. epidermidis*, coexist on the skin surface and within the follicle as multiphyletic communities that can interact and coexist



O'Neil AM, Gallo RL Host Microbiome Interactions and Recent Progress into Understanding the Biology of Acne Vulgaris: *Microbiome* (2018) 6:177 <https://doi.org/10.1186/s40168-018-0558-5>

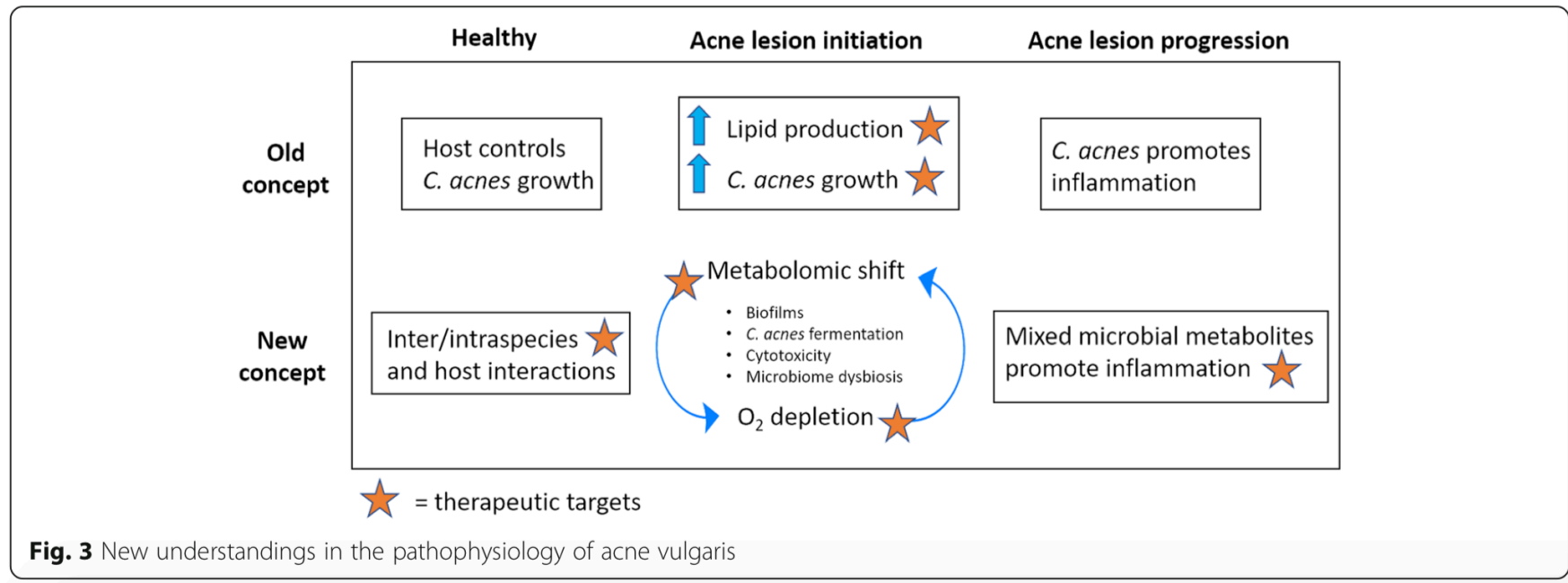
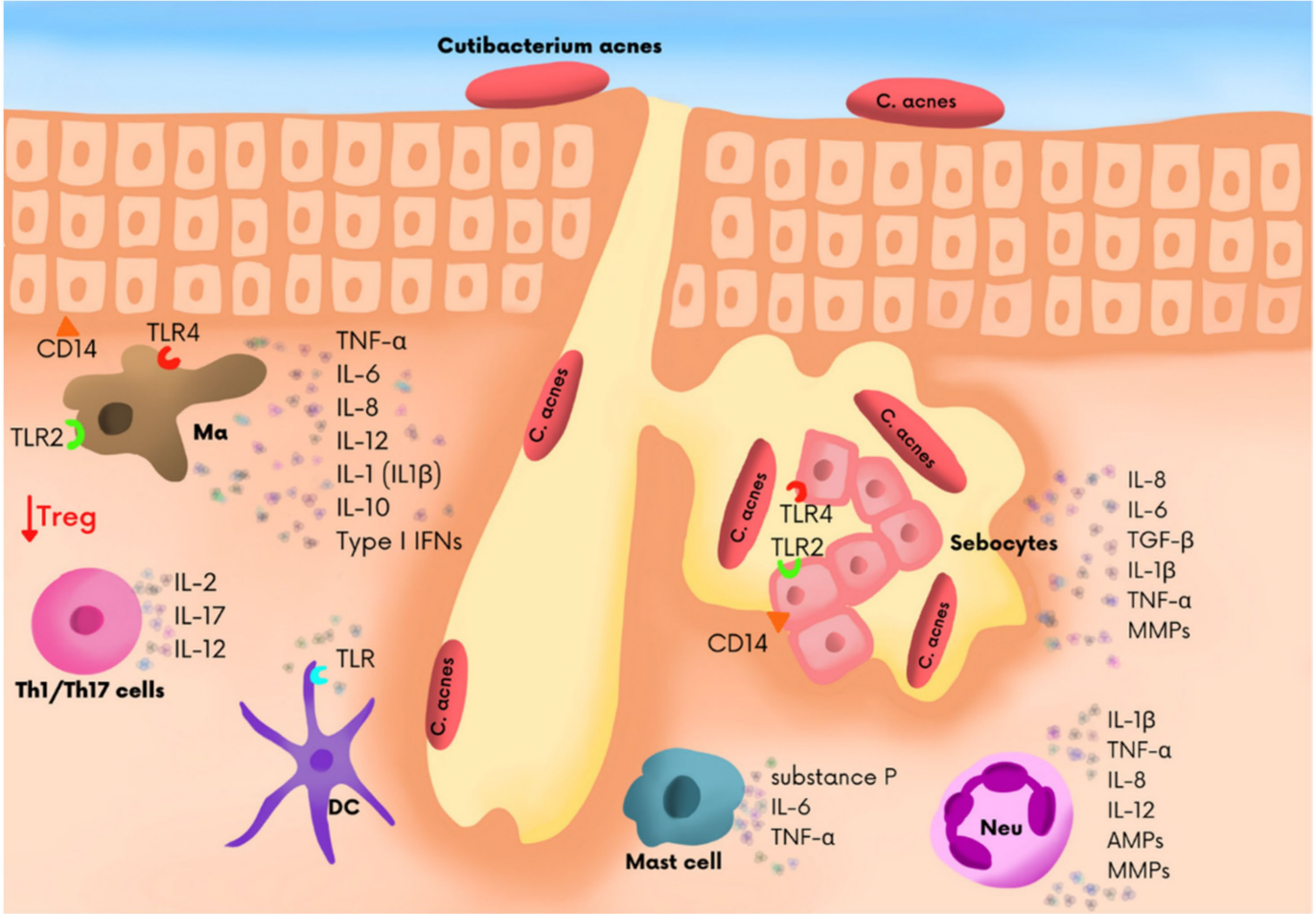


Fig. 3 New understandings in the pathophysiology of acne vulgaris



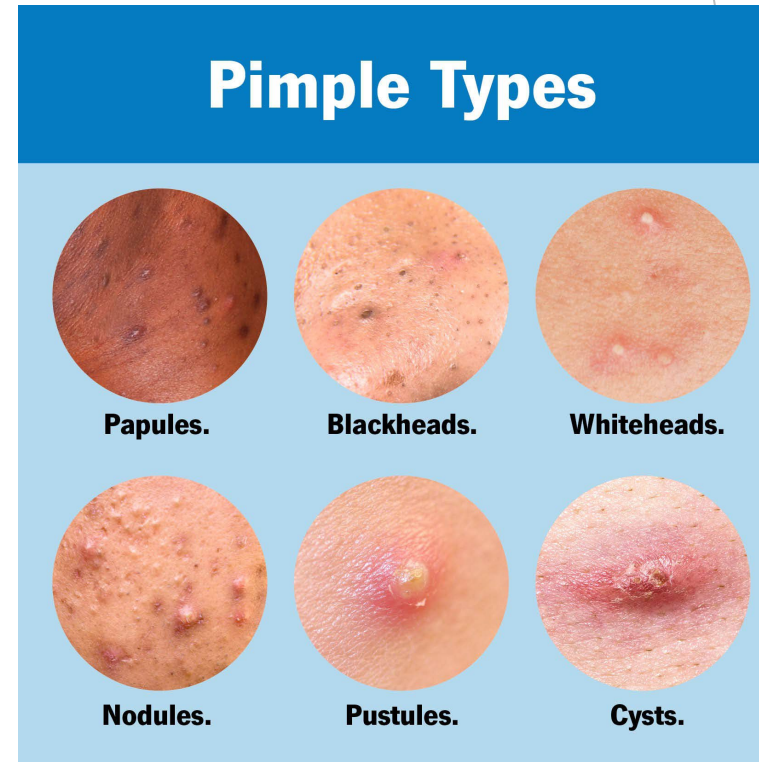
Prevalence

- ▶ Puberty-more in males
- ▶ Adulthood-more in females
 - ▶ 12% women and 5% males at age 25
 - ▶ 5% women at age 45
- ▶ Can be present in infancy when newborn still has maternal hormones-tends to resolve spontaneously

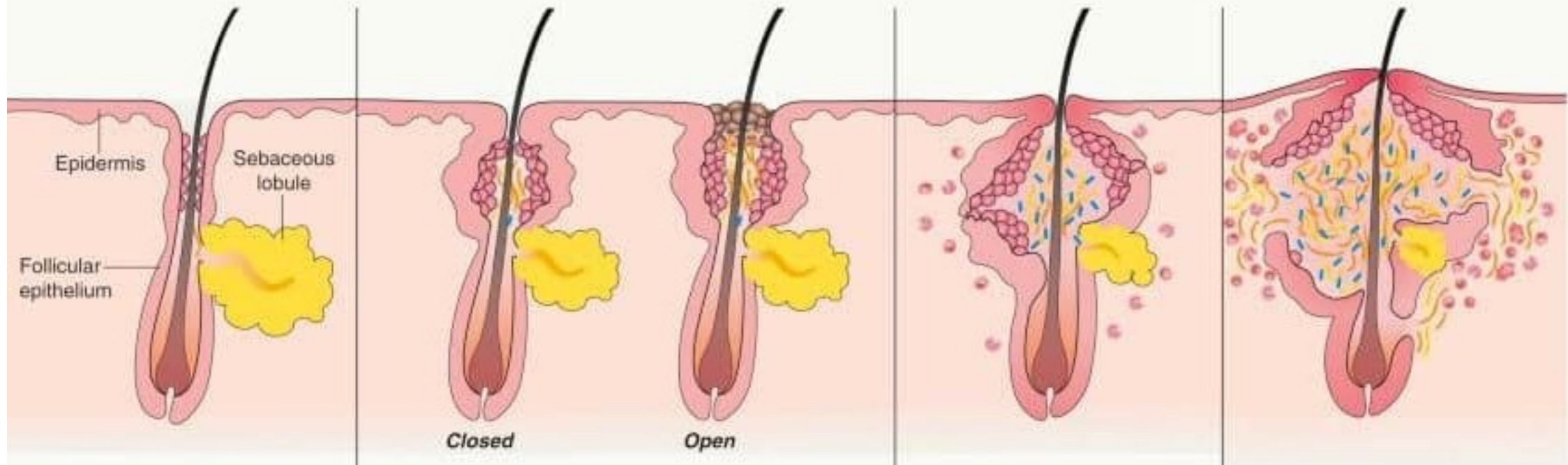


Acne Vulgaris

- ▶ Characterized by comedones, papules and pustules and sometimes nodules
- ▶ Sebaceous distribution-face, upper chest and back and sometimes upper arms
- ▶ Involvement of the above can occur in any combination
- ▶ Local symptoms can include pain and tenderness



PATHOGENESIS OF ACNE



Early comedo

- Hyperkeratosis and \uparrow corneocyte cohesiveness in the upper sebaceous follicle, which lead to microcomedo formation
- Androgen stimulation of sebum production

Later comedo

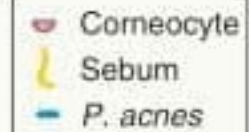
- Accumulation of shed keratin and sebum
- Formation of whorled lamellar concretions
- Comedo may be *closed* (no obvious follicular opening) or *open* (dilated follicular opening; keratin plug darkens due to oxidized lipids & melanin)

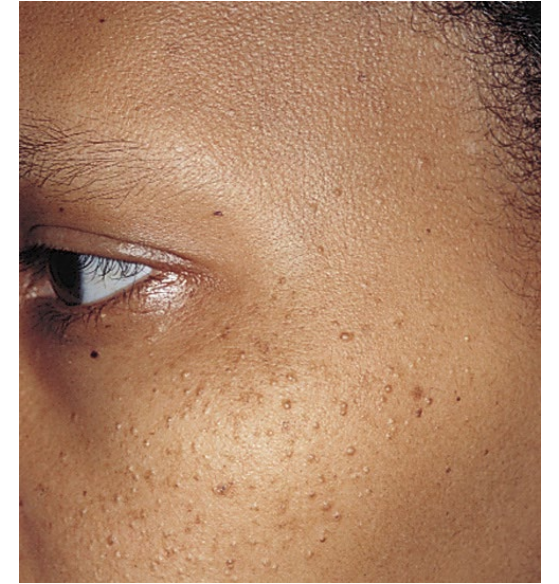
Inflammatory papule/pustule

- *Propionibacterium acnes* proliferation, which upregulates innate immune responses (e.g. via TLRs)
- Mild inflammation (primarily neutrophils), which increases upon rupture of the comedo wall
- Sebaceous lobule regression

Nodule/cyst

- Marked inflammation (primarily T cells)
- May lead to scarring

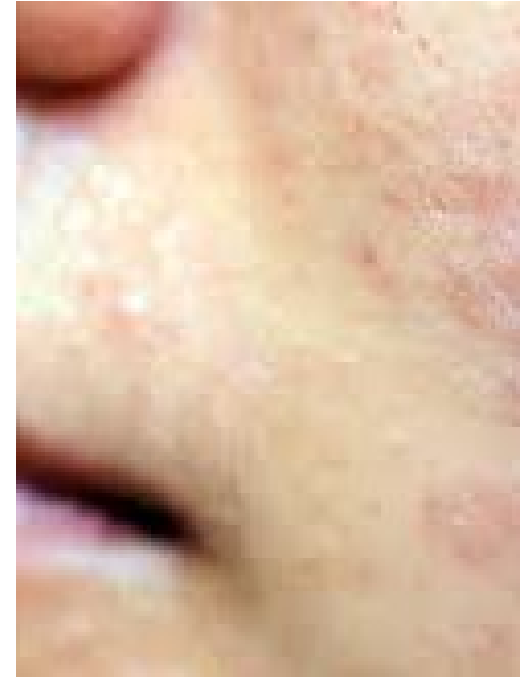




Closed Comedones



Open Comedones



Papules and Pustules



Cystic Nodules



Acne Scarring

Acne Vulgaris

- ▶ Grade I
- ▶ Multiple open and/or closed comedones.
No inflammatory papules or nodules



Acne Vulgaris

- ▶ Grade II
- ▶ Comedones and a few papulopustules



Acne Vulgaris

- ▶ Grade III
- ▶ comedones, inflammatory papules and pustules
- ▶ Greater number of lesions than in mild inflammatory acne



Acne Vulgaris

- ▶ Grade IV
- ▶ Multiple open and closed comedones, papulopustules and cysts
- ▶ Scarring usually present



Diagnosis

- ▶ Clinical diagnosis
- ▶ In cases refractory to treatment, consider culture to rule out gram negative folliculitis
- ▶ In females with dysmenorrhea or hirsutism
 - ▶ Total and free testosterone
 - ▶ Dehydroepiandrosterone sulfate
 - ▶ Luteinizing hormone
 - ▶ Follicle-stimulating hormone
 - ▶ SBG

Severe Acne Vulgaris

Acne Fulminans

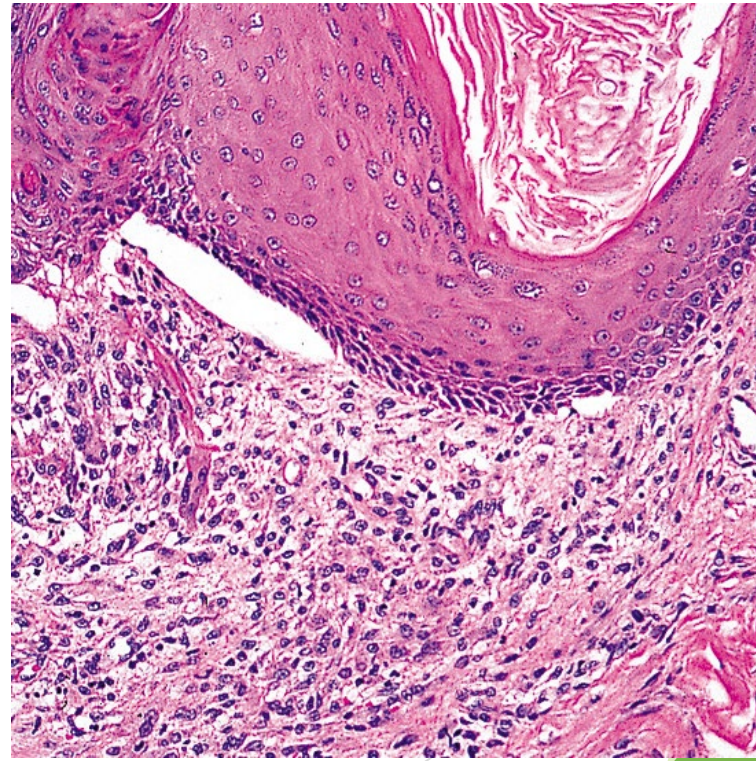
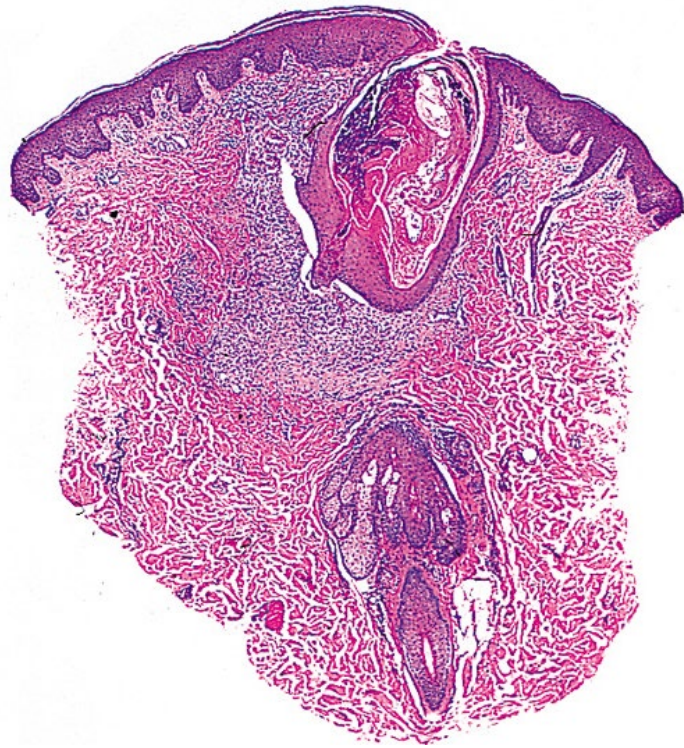
- ▶ Severe acne
- ▶ Fever
- ▶ Arthritis
- ▶ Heals with scarring

Acne Conglobata

- ▶ Severe acne
- ▶ Without systemic symptoms
- ▶ Heals with scarring



Acne Vulgaris



Treatment-topicals

- ▶ Topical BP
- ▶ Topical retinoic acid
- ▶ Adapelene
- ▶ Topical antibiotics
 - ▶ Clindamycin
 - ▶ Erythromycin
 - ▶ Dapsone

Treatment-new topical therapies

- ▶ Tretinoin 0.05% lotion
- ▶ Tazarotene 0.045% lotion
- ▶ Trifarotene 0.005% cream (Aklief)-RAR gamma
- ▶ Microencapsulated tretinoin 0.1%/microencapsulated 3% BP
- ▶ Clindamycin phosphate 1.2%/BP 3.1%/adapalene 0.15% gel
- ▶ Clascoterone 1% cream (Winlevi)-antiandrogen

All are better tolerated and have enhanced penetration

Systemic Therapies

- ▶ Tetracycline class
 - ▶ Tetracycline
 - ▶ Minocycline
 - ▶ Doxycycline
 - ▶ Sarecycline
- ▶ Macrolides
- ▶ Trimethoprim-sulfamethoxazole
- ▶ Spironolactone
- ▶ Isotretinoin
- ▶ Oral contraceptives

Systemic Therapies

Isotretinoin



iPLEDGE™

Committed to Pregnancy Prevention

Isotretinoin

- ▶ 0.5-1 mg/kg/day
- ▶ Dryness
- ▶ Fish oil
- ▶ Antihistamine
- ▶ Lab monitoring
- ▶ Pregnancy prevention







EVERYTHING YOU NEED
TO KNOW ABOUT
HIDRANITIS
SUPPURATIVA



Hidradenitis Suppurativa

hidros=sweat

aden=glans

Hidradenitis Suppurativa

- ▶ Chronic follicular disease
- ▶ Folliculopilosebaceous units (FPSU)



Epidemiology

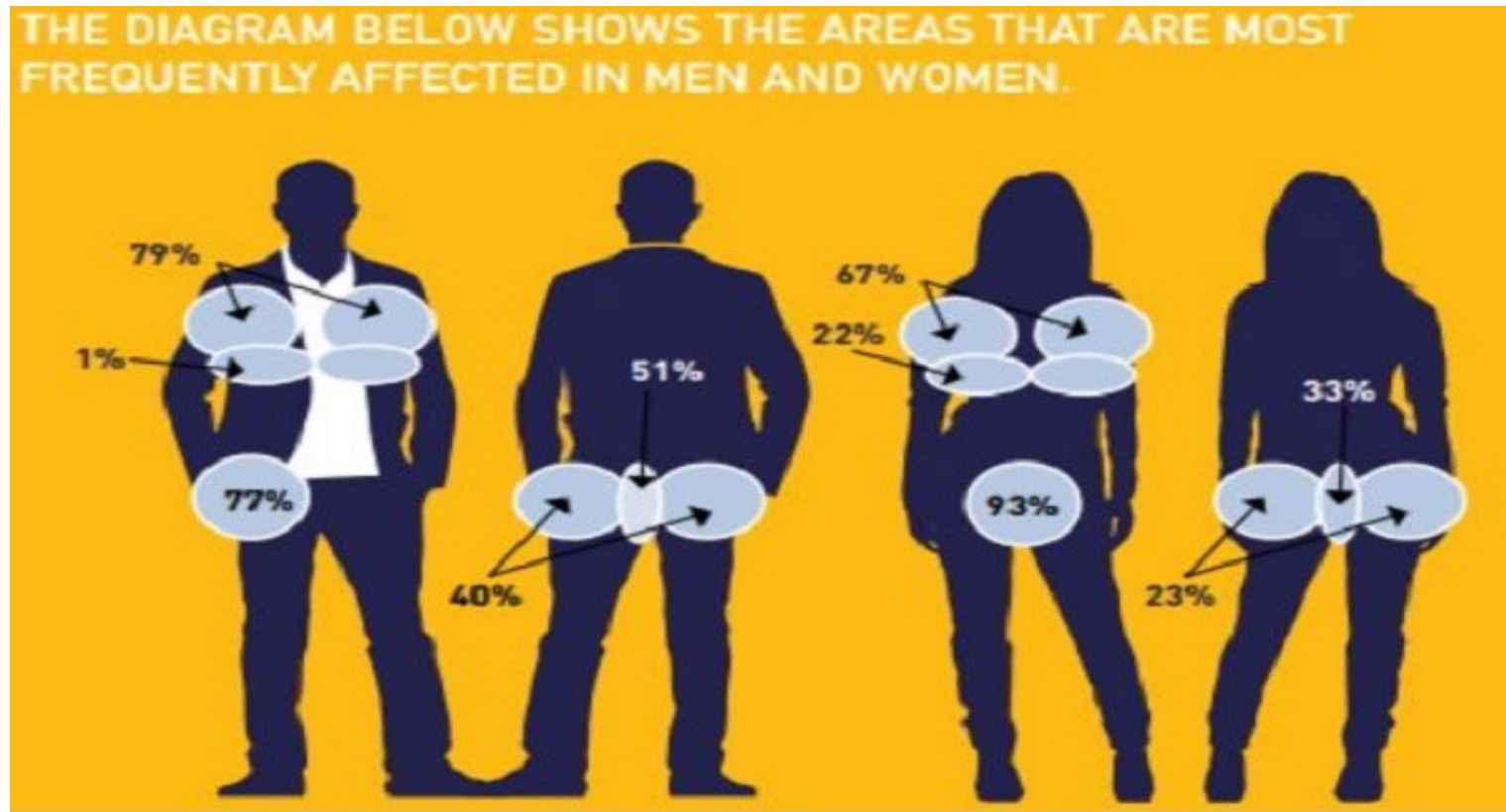
- ▶ The disease that needs more awareness overall in medical and public sectors
- ▶ Overall prevalence 0.1%-1%
- ▶ Female much greater than male
- ▶ 18-40 age group
- ▶ AA affected disproportionately
- ▶ Very impactful disease

Hydradenitis Suppurativa

- ▶ Majority flare monthly
- ▶ Can last up to 10 days
- ▶ That's 1/3 of the year
- ▶ Misdiagnosed as furunculosis



HS-sites of involvement



HS-pathogenesis

- ▶ Follicular occlusion
 - ▶ Hormones
 - ▶ Nicotine
- ▶ Follicular rupture
 - ▶ Follicular duct expands
 - ▶ Friction
 - ▶ Pressure
 - ▶ Heat
- ▶ Immune response



HS



- ▶ Follicular rupture
- ▶ Sinus tract formation
- ▶ Tunnels open unto the skin
- ▶ Chronic inflammation
- ▶ Scarring

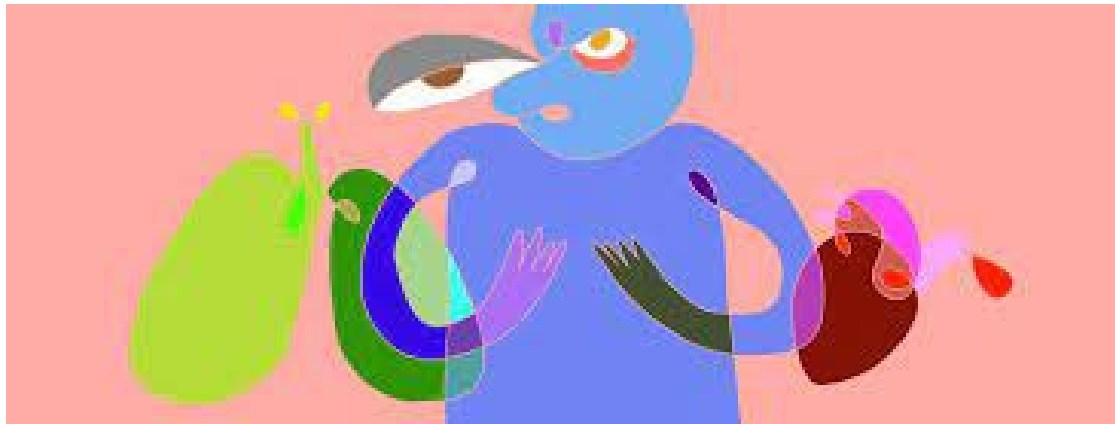


Comorbidities

- ▶ Looking at overall comorbidity with HS vs psoriasis
- ▶ Demographics influence comorbidities
- ▶ Sex and race play a role
- ▶ When matched the above, HS patients overall have a higher burden of comorbidities than psoriasis patients
- ▶ #comorbidities increase mortality
- ▶ Need to address health as a whole

Garget et al Evaluating Patients' Unmet Needs in Hidradenitis Suppurativa: Results from Global Survey on Impact and Healthcare Needs (VOICE) Project. *J Am Acad Dermatol*, 2020;82(2):366-376.

Comorbidities-HS is an independent risk



- ▶ Cardiovascular
- ▶ Stroke
- ▶ Diabetes
- ▶ Crohn's disease
- ▶ PCOS
- ▶ OSA
- ▶ Sexual dysfunction
- ▶ Acne
- ▶ Smoking
- ▶ Obesity

Pregnancy outcomes in HS

- ▶ Higher likelihood of C-section delivery (OR 1.7, 95% CI 1.56-2.02)
- ▶ Preeclampsia (OR 1.36, 95% CI 1.08-1.71)
- ▶ Increased risk of congenital abnormalities (OR 2.00, 95% CI 1.10-3.62)



Althagafi H et al, 497 Pregnancy Outcomes in Patients with Hidradenitis Suppurativa. *Amer J OBGYN: Feb 2021:224(2)S31-S315*

Screening



- ▶ PE
- ▶ Hypertension
- ▶ Diabetes
- ▶ Cardiovascular disease
- ▶ Metabolic syndrome
- ▶ Dyslipidemia



Hurley Staging System



Stage 1
Abscesses with
minimal scarring
No sinus tracts



Stage 2
Sinus tracts
Scarring



Stage 3
Multiple
interconnected
abscesses

Images courtesy of Alexa B. Kimball, MD, MPH.
Hurley J. *Dermatologic Surgery, Principles and Practice*. 1989.



Stage 1

Abscess formation, single or multiple, without sinus tracts and scarring



Stage 2

Single or multiple, widely separated, recurrent abscesses with tract formation and scarring



Stage 3

Diffuse or near-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area

Sartorius score	Description
Anatomical region involved	Axilla, groin, gluteal, or other region, or inframammary region left and/or right: 3 points per region involved
Number and lesion scores	Abscesses, nodules, fistulas, scars: points per lesion of all regions involved: nodules: 2, fistulas: 4, scars: 1, others: 1
Longest distance between two relevant lesions	For example, between nodules and fistulas in each region, or size if only one lesion: <5 cm: 2, <10 cm: 4, >10 cm: 8
Are all lesions clearly separated by normal skin?	In each region: yes: 0, no: 6

Hidradenitis Suppurativa



Follicular Occlusion Triad (Tetrad)

- ▶ Acne (severe)
- ▶ Hidradenitis suppurativa
- ▶ Dissecting cellulitis of the scalp
- ▶ +/- pilonidal cyst



MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.



Treatment

- ▶ Spironolactone
- ▶ Finasteride
- ▶ Metformin
- ▶ Tetracycline class
- ▶ Biologics

Biologics- adalumimab

- ▶ 12 years and older
- ▶ 40 mg weekly or 80 mg every other week
- ▶ See a meaningful reduction in about 12 weeks
- ▶ If do not see success at week 12, continue as 30% of these will get better scores at month 4,5 or 6
- ▶ Only FDA approved biologic

Biologics- others

- ▶ Infliximab- TNF alpha inhibitor-high doses and every 4 weeks (7.5-10mg/kg)
- ▶ Anakinra-IL-1 inhibitor
- ▶ Ustekunimab-IL12/23 inhibitor
- ▶ Etanercept-TNF alpha inhibitor
- ▶ Golimumab

The background features abstract, overlapping geometric shapes in various shades of green, ranging from light lime to dark forest green. These shapes are primarily located on the right side of the frame, creating a modern, layered effect. The text is centered on a white background.

NEW APPROACHES TO MANAGING ROSACEA



ROSACEA

DEMODEX MITES

- ▶ Tiny mites that live in hair follicles
- ▶ Forehead, cheeks, eyelashes, external ear canals, naso-labial folds





ROSACEA

- ▶ Demodex mites are also qualitatively different in patients with rosacea
- ▶ Can directly activate TLR-2
- ▶ Patients also have more mast cells in their dermis
- ▶ This cascade can be option for new treatment paradigms in the future

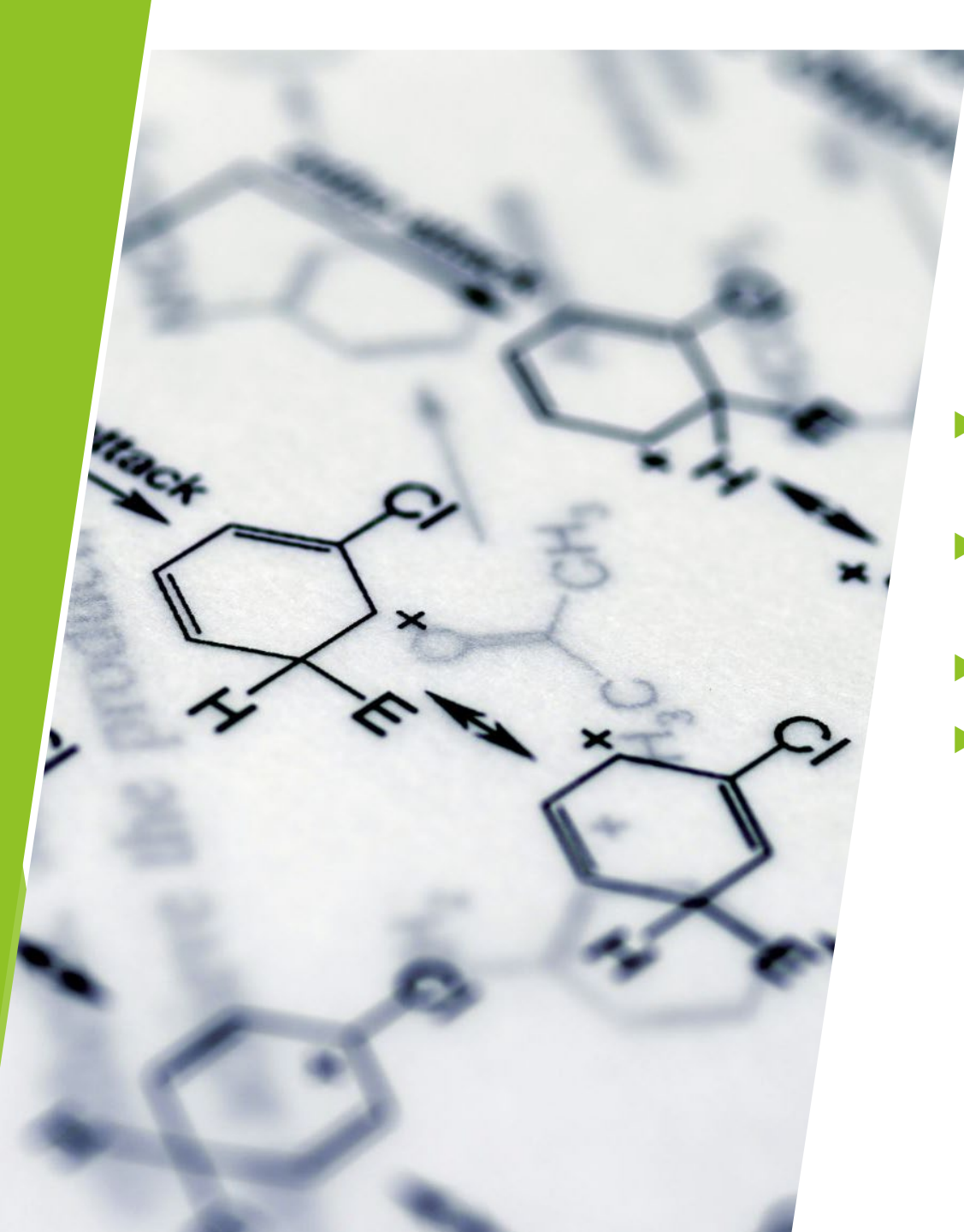
ROSACEA

- ▶ *Demodex folliculorum*-in hair follicles
- ▶ Feeds on skin cells
- ▶ *Demodex brevis*-in sebaceous glands
- ▶ Feeds on gland cells
- ▶ Also found in meibomian glands
- ▶ Can see a 4-fold increase in density compared normal skin



ROSACEA- CATHELICIDIN

- ▶ Cathelicidin (LL-37) is more plentiful in rosacea
- ▶ Of a different molecular weight than in patients without rosacea
- ▶ Promotes angiogenesis
- ▶ Demodex mites can lead to disruption of the skin barrier which also activates cathelicidin

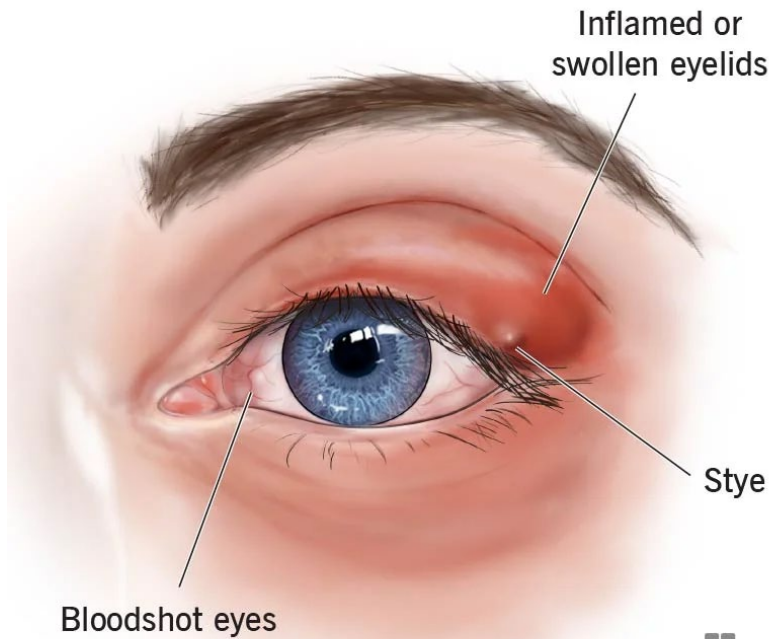


Maskne



- ▶ Increase humidity
- ▶ 10% increase in sebum production for every 1 degree increase in temperature
- ▶ Increased PH
- ▶ Increased friction
- ▶ ACD to textiles, dyes, formaldehyde, rubber
- ▶ Increase Malassezia
- ▶ In health care workers see 14% increase in seborrheic dermatitis

Ocular Rosacea




Cleveland
Clinic
©2022

ROSACEA

- ▶ Mild shampoo on hair and eyelashes
- ▶ Cleanse twice daily with non soap cleanser
- ▶ Avoid oil-based cleansers and greasy makeup
- ▶ Exfoliate periodically to removed dead skin cells
- ▶ PH balanced cleanser and toner
- ▶ Physical defense sunscreens

- ▶ Topical antibiotics-clindamycin, metronidazole
- ▶ Oral low dose tetracyclines
- ▶ Erythromycin topical and systemic
- ▶ Synergistic effect when used topically and systemically
- ▶ Finacea (azelaic acid)
- ▶ Ivermectin cream (soolantra) 1% cream
- ▶ Brimonidine tartrate 0.33% cream (mirvaso)
- ▶ Oxymetazoline 1% cream (Rhofade)
- ▶ Vascular lasers-work very well for the erythema and telangiectasia

TRADITIONAL THERAPIES

Rosacea

Case Reports of what's out there



- ▶ Oral beta blockers
- ▶ Ondansetron
- ▶ Clonidine
- ▶ Low dose naltrexone
- ▶ Vascular lasers

Emerging Treatments

Sarecycline
1.5mg/kg/day

Low dose extended
release
minocycline and
doxycycline

Microencapsulated
BP 5% gel

GI and Skin Connection

- ▶ SIBO
- ▶ Associated with papule and pustular rosacea
- ▶ See gut skin connection in acne as well
- ▶ Rifaximin
 - ▶ Several studies show clear connection with clearance of rosacea

THANK YOU