Acne vulgaris

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DEPARTMENT OF DERMATOLOGY

Acne vulgaris

(*Acne vulgaris, juvenilis*)

It is a disease manifesting of pilosebaceous units.

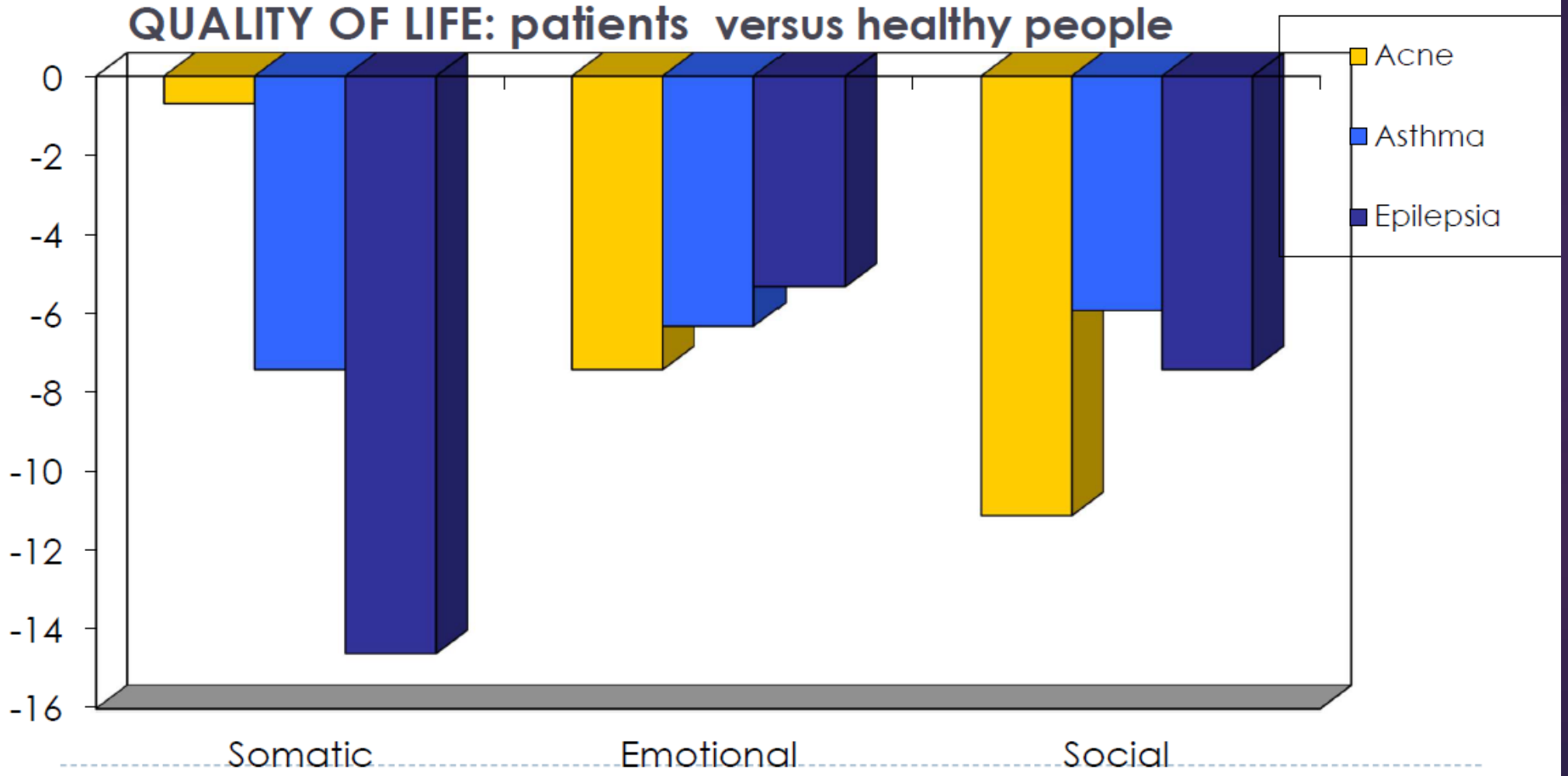
Acne is very common and affects approximately 85% of young people

Lower incidence in Asians and Africans

Localisation of skin lesions

- face - 99%
- back - 90%
- chest - 78%
- shoulders, buttocks (less frequently)

Acne & Quality of life



- Mallon E, et al. *Br J Dermatol*. 1999;140:672-676.

Acne and QoL

- Negative influence on quality of life comparable with other serious diseases:
  - Asthma
  - Epilepsy
- Depression and anxiety
- Lower employment rate
- Lack of self acceptance

Course of acne

- peak morbidity:

  females: 14-17 years of age.

  males: 16-19 years of age.
- More severe in males than in females
- duration: 3-5-10 years (or even longer)

- Recently, we have observed more frequent incidence of acne in patients younger than 11 years old and a longer persistence of lesions in patients older than 25 y.o.

Four key elements of pathogenesis:

(1) follicular epidermal hyperproliferation

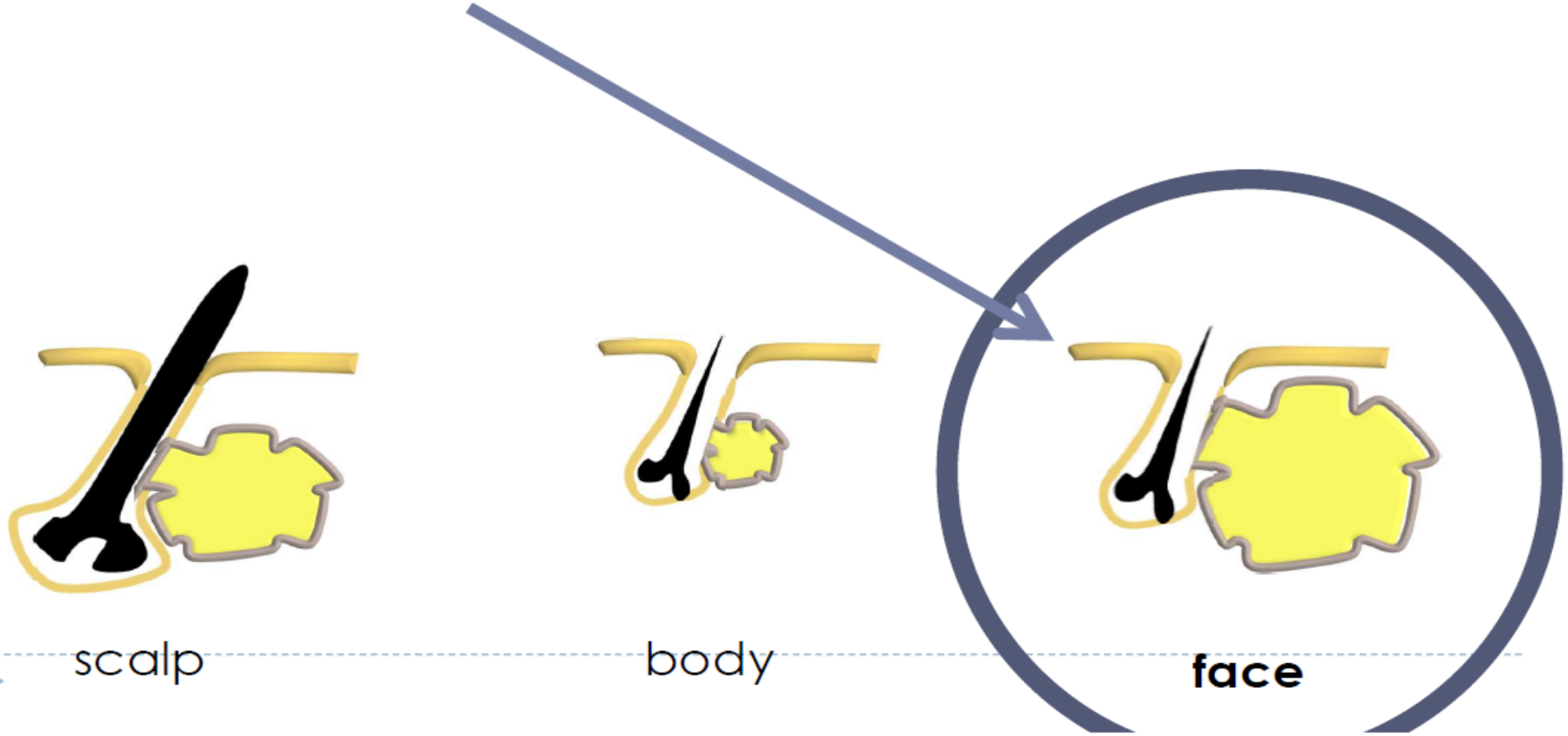
(2) icreased sebum production

(3) inflammation

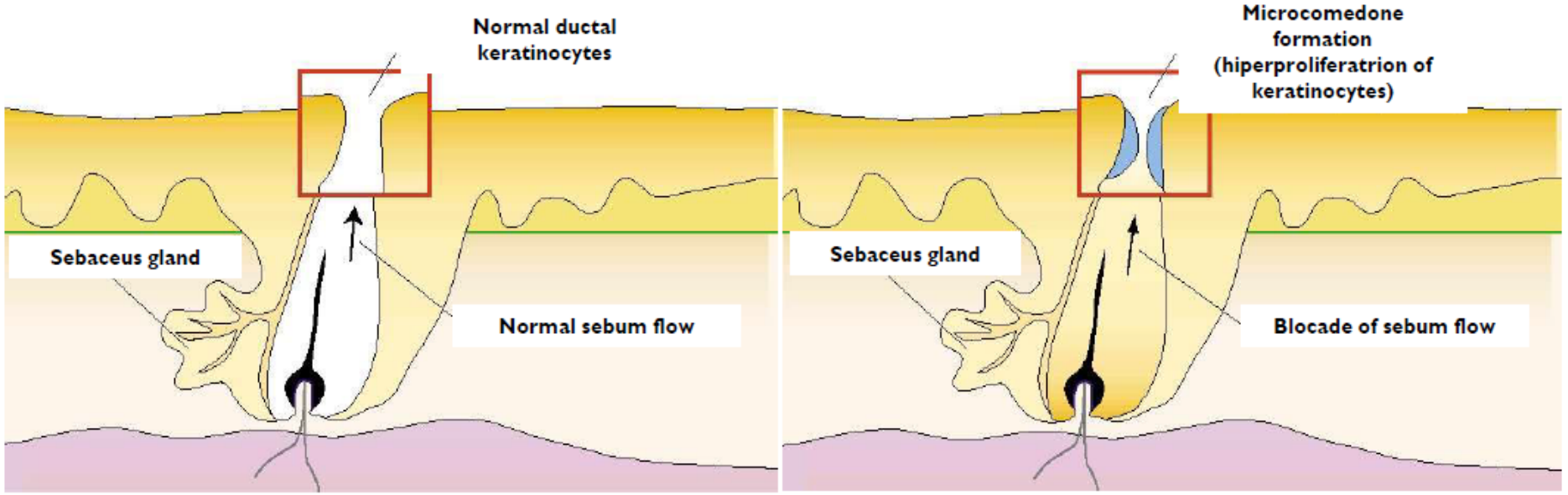
(4) the presence and activity *Propionibacterium acnes*

Acne – pilosebaceus unit

- Only in humans!!!



Acne vulgaris - pathogenesis



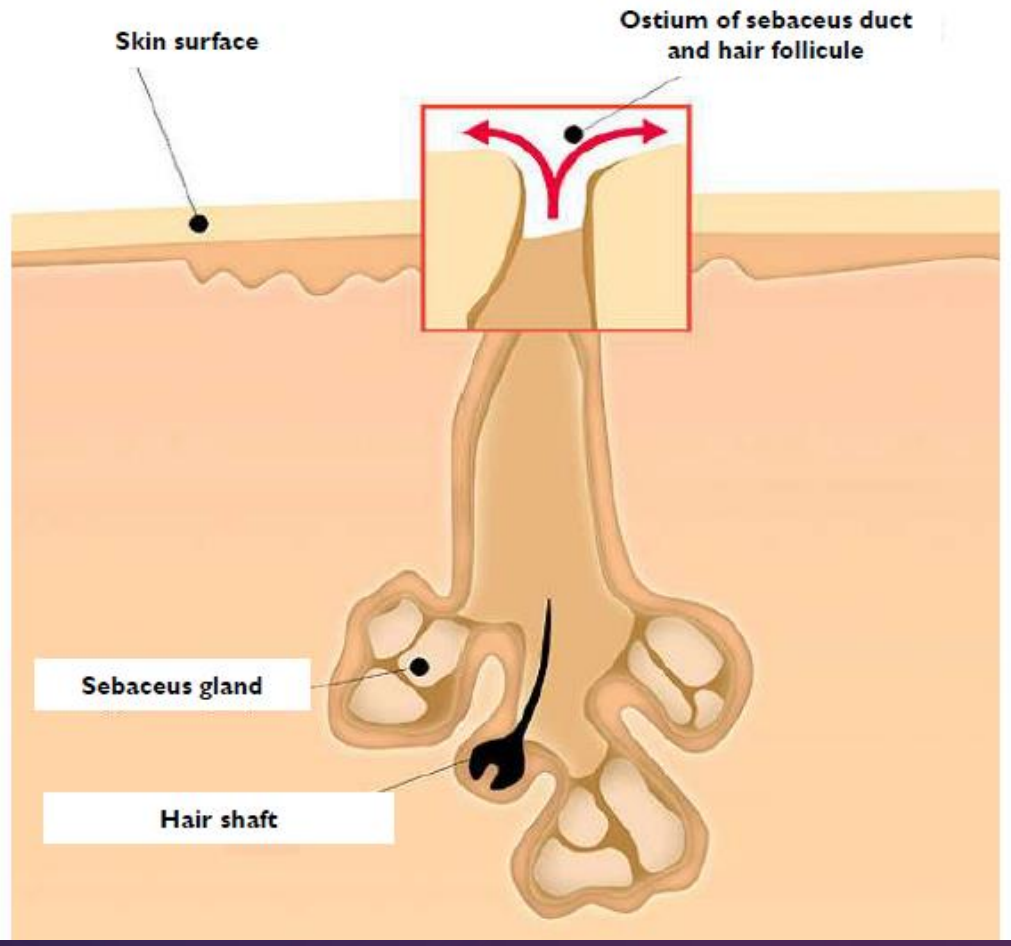
PRIMARY CAUSES: (androgen driven)

- sebum secretion (lipids composition and amount)
- hiperproliferation of keratinocytes

OTHER FACTORS:

- Proliferation of *P. acnes*, inflammation (e.g. TLR2, IL1, IL-6)

Progression of changes



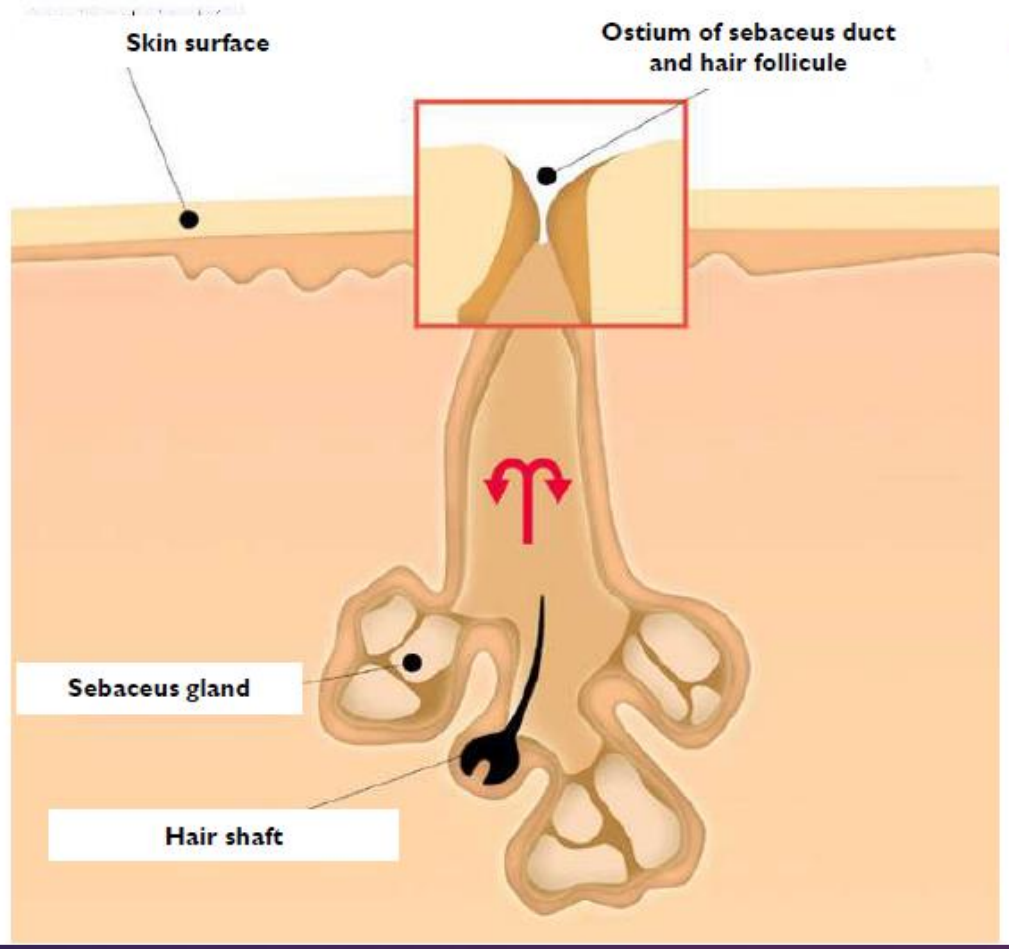
COMEDO:

- Stacked sebo-follicular apparatus
- Accumulation of sebum

VARIATIONS:

- Blackheads
- Whiteheads

Progression of lesions



COMEDO:

- Stacked sebo-follicular apparatus
- Accumulation of sebum

VARIATIONS:

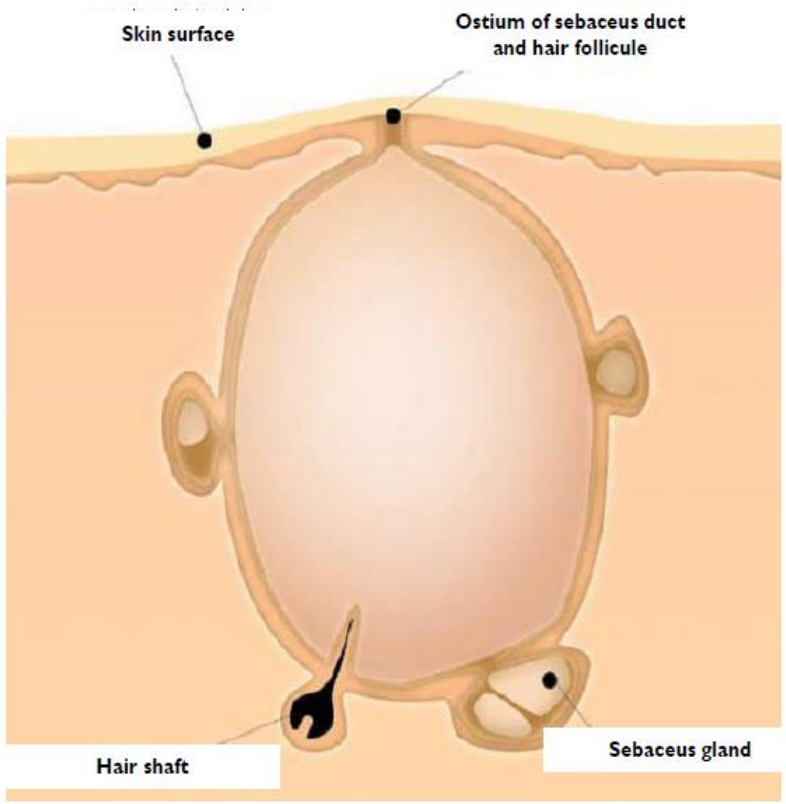
- Blackheads
- Whiteheads

- Another key factor in pathogenesis is bacteria **Propionibacterium acnes**

- Mechanism of action

bacterial lipase converts lipids to fatty acids and produce proinflamatory mediators (IL1, TNF alfa) that lead to an inflammatory response.

Progression of lesions



COMEDO:
- Stacked sebo-follicular apparatus
- Accumulation of sebum

VARIATIONS:
- Blackheads
- Whiteheads

MICROCOMEDO

sebum accumulation

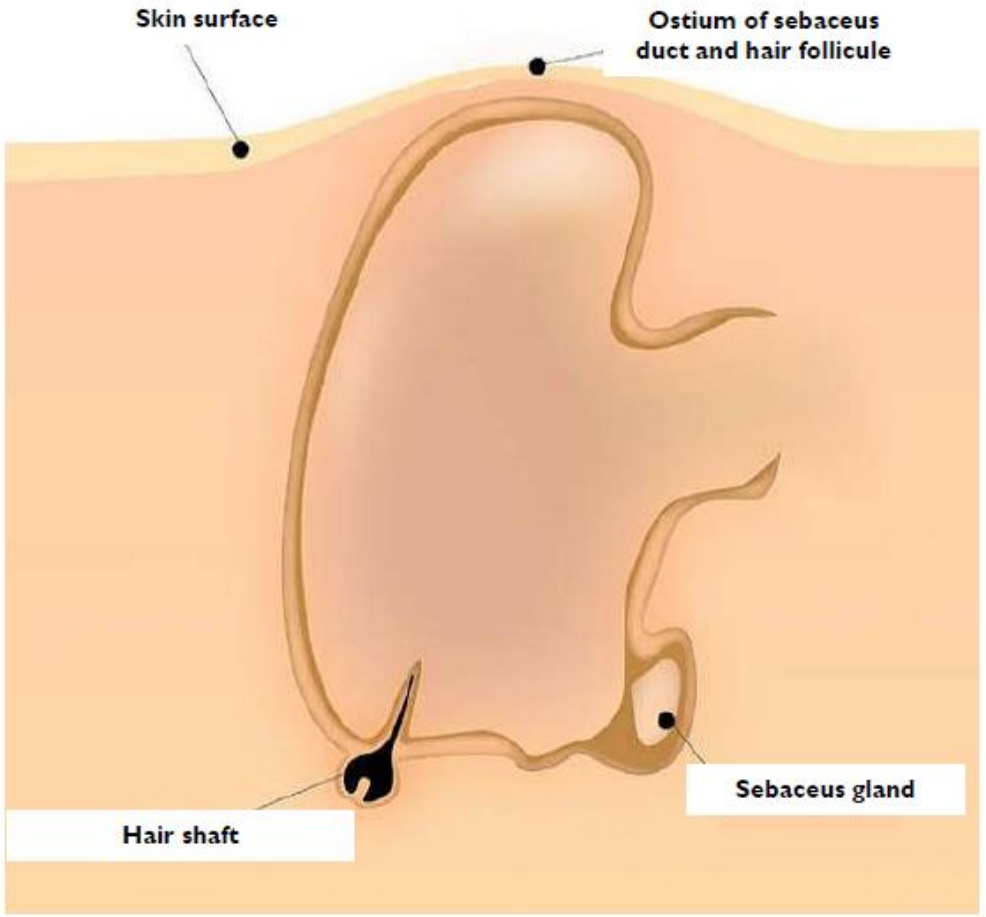
⇓ O_2

P.acnes PROLIFERATION

↓

PERFECT CONDITIONS FOR P. acnes PROLIFERATION

Progression of lesions



INFLAMMATORY LESIONS:

- Prolifferation of P. acnes
- Inflammatory mediators

VARIATIONS:

- Papule
- Pustule
- Nodule
- Cyst

Acne lesions

NON-INFLAMATORY LESIONS

open comedones (blackheads)

closed comedones (whiteheads)

INFLAMATORY LESIONS

papules, pustules,

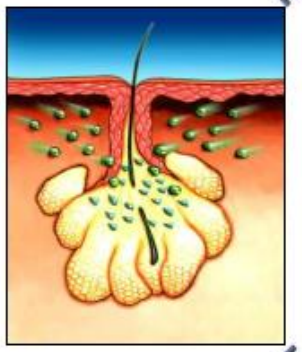
nodules or cysts

Progression of lesions

EPIDERMIS
(STACKED FOLLICLE)
1. Hiperprolifferation
2. False differentiation
3. Decreased scalling

Blackhead

Microcomedo



P acnes
Inflammatory
Mediators

Inflammatory lesion

INCREASED SEBUM EXCRECTION & ALTERED SEBUM COMPOSITION

Whitehead

Hormonal changes in sexual maturation

Androgens cause sebaceous gland hypertrophy and stimulate sebaceous gland to produce more sebum

…have an important role in acne pathogenesis

But the most important role plays:

increased / local expression of androgen receptors

and 5α - reductase activity

→ Total amount of circulating androgens is normal usually !!!!

Testosterone + 5α - reductase

↓

dihydrotestosterone – DHT

The locally active form of androgens is **dihydrotestosterone** (DHT)

It is formed by the **5α-reductase enzyme from testosterone**

DHT receptors are localised in:

hair follicles, sebaceous glands

the 5α - reductase activity is bigger in these areas

Genetic aspects

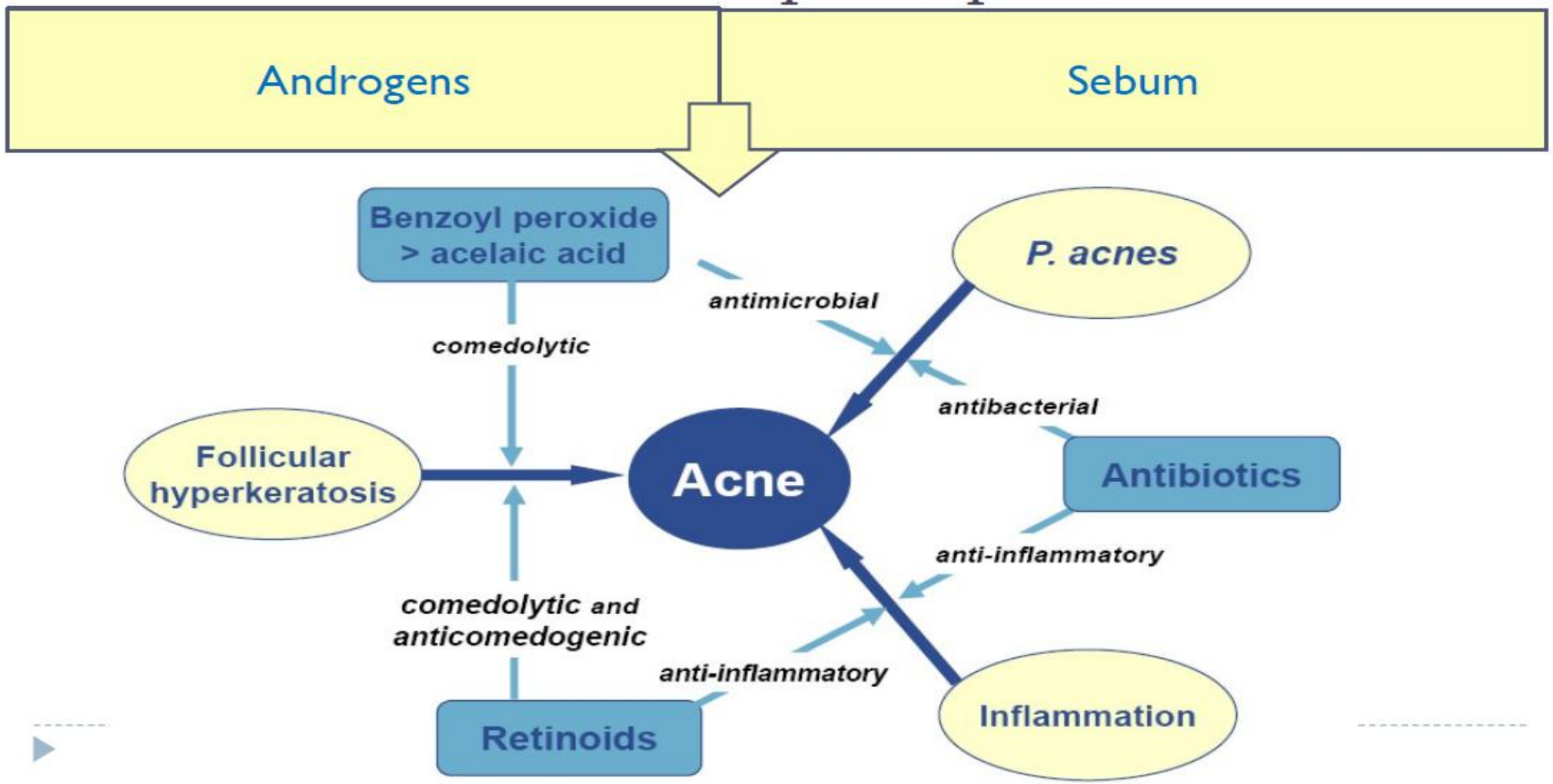
Certain role of genetic background and familial predisposition.

Most patients with severe acne have parents with a history of severe acne.

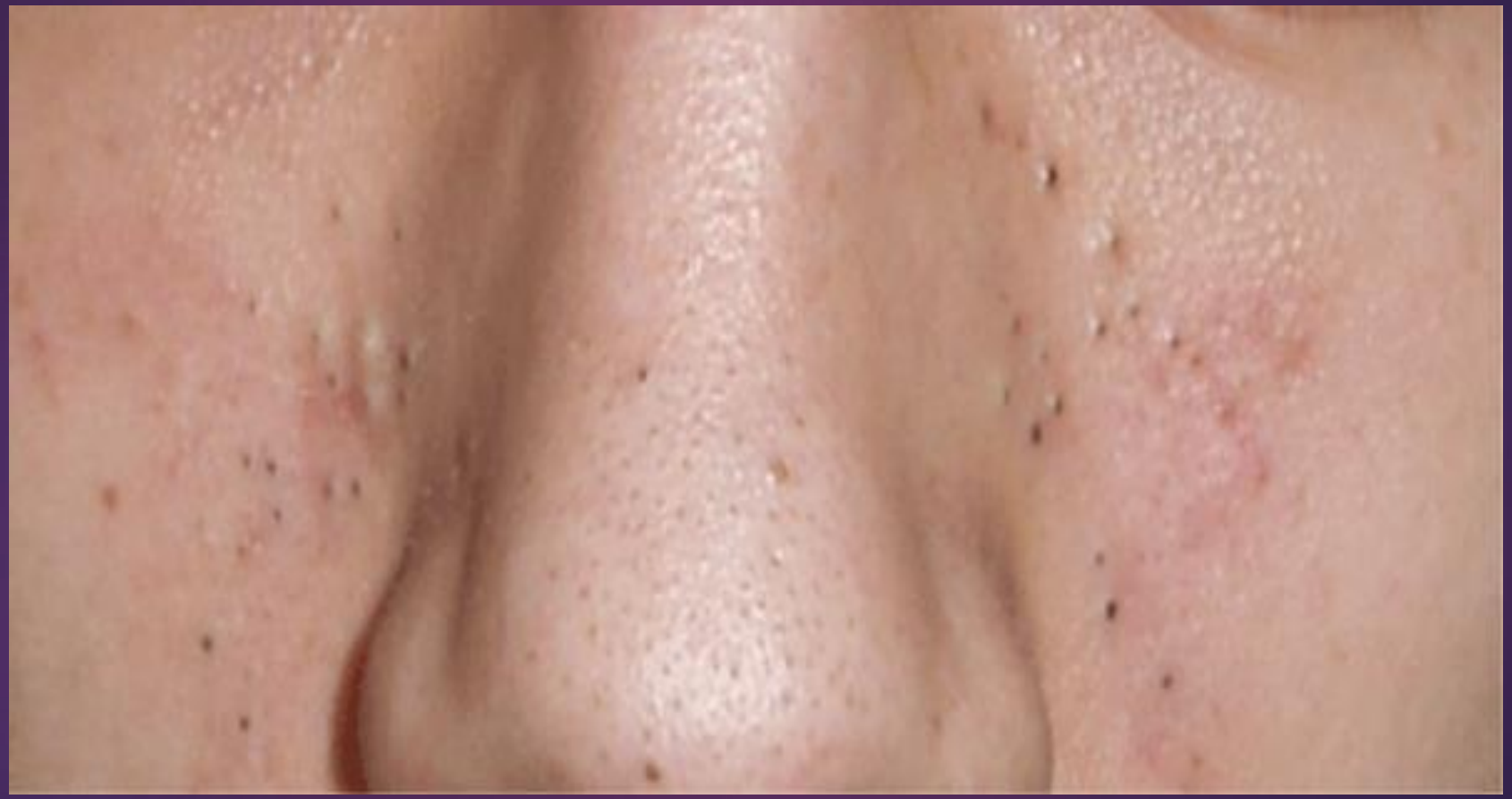
Classification

- Acne vulgaris
  - Acne comedonica (comedonic acne, non-inflammatory acne)
  - Acne papulo-pustulosa (papulopustular acne; inflammatory acne)
  - Acne phlegmonosa (nodulocystica, conglobata)
- Acne fulminans (phlegmanosa + systemic symphtoms)
- Acne inversa (hidradenitis suppurativa)
- Acne excoriae (self induced „picker's acne")

Inflammatory acne
Combined treatment - principals



Comedonic acne (non-inflammatory lesions)



Non-inflammatory acne treatment

- Normalisation of ketratinisation
- Reduction of sebum production

- **Additional treatment**
  - keratolitic
  - Chemical peels

Topical treatment :

1. Retinoids (adapalen, tretinoin , izotretinoin, trifaroten, tazaroten)
2. Benzoyl peroxide
3. Azelaic acid
4. Antibiotics - erythromycin and clindamycin (similar efficacy)

Adverse reactions of topical retinoids:

erythema

exfoliation

burning / itching

Infalmmatory acne

- Benzoyl peroxide
  - Always when antibiotic treatment last for more than a month (↓ *P. acnes resistance*)

Benzoyl peroxide - mechanisim of action:

antimicrobial (anti-inflammatory)

keratolytic action

does not cause drug resistance !!!!

Inflammatory acne
- **topical** antybiotics (antimicrobial, antiinflammatory)

- Ertythromycin
- Clindamycin

Always in combintation with topical retinoids and/or BPO

Topical ANTIBIOTICS

mechanism of action

- **reduce the concentration of free fatty acids (lipase inhibition)**
- **reduce the number of P. acnes**

adverse reactions

- **generally very well tolerated**

but

triggering drug resistance

The principle of topical treatment:

Preparations should be applied to the whole acne-affected area

Acne as a chronic disease requires long-term treatment - for many months or even years

Advantages of combined treatment

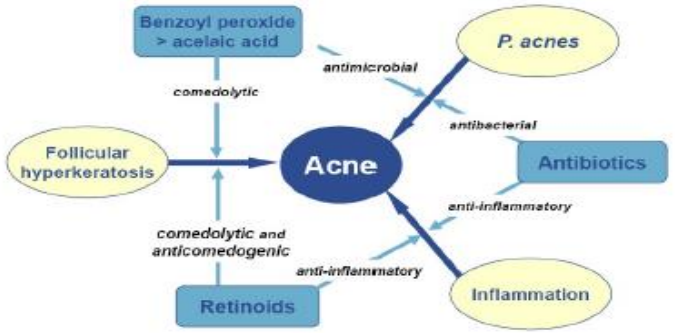
- Synergistic action
- Influence on all causative elements
- Prevention of drug-resistant P.acnes

Inflammatory acne – combined treatment in one tube:

Retinoid + antibiotic

Antibiotic + benzoyl peroxide

Retinoid + benzoyl peroxide

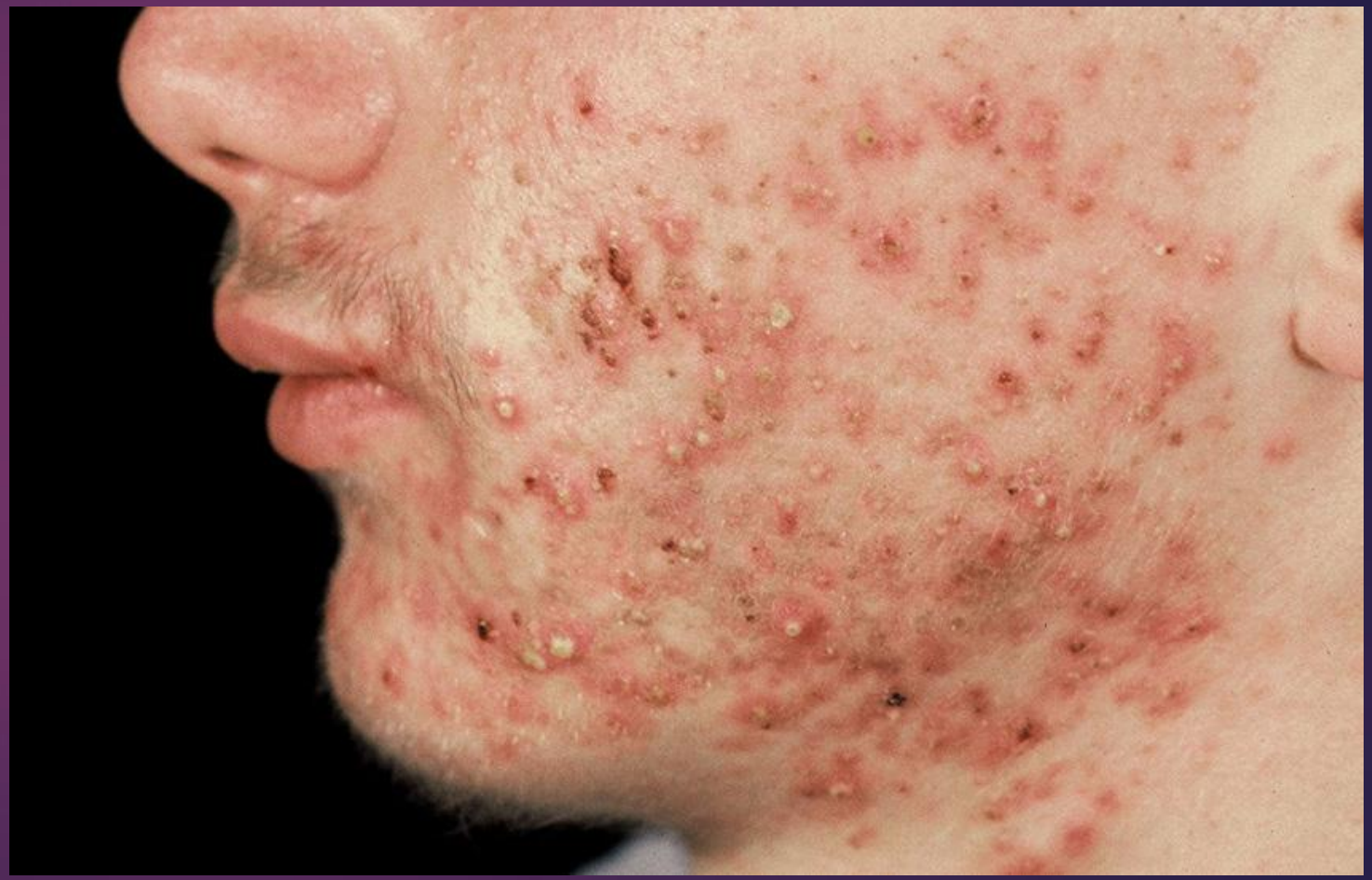


Combined treatment - last developments

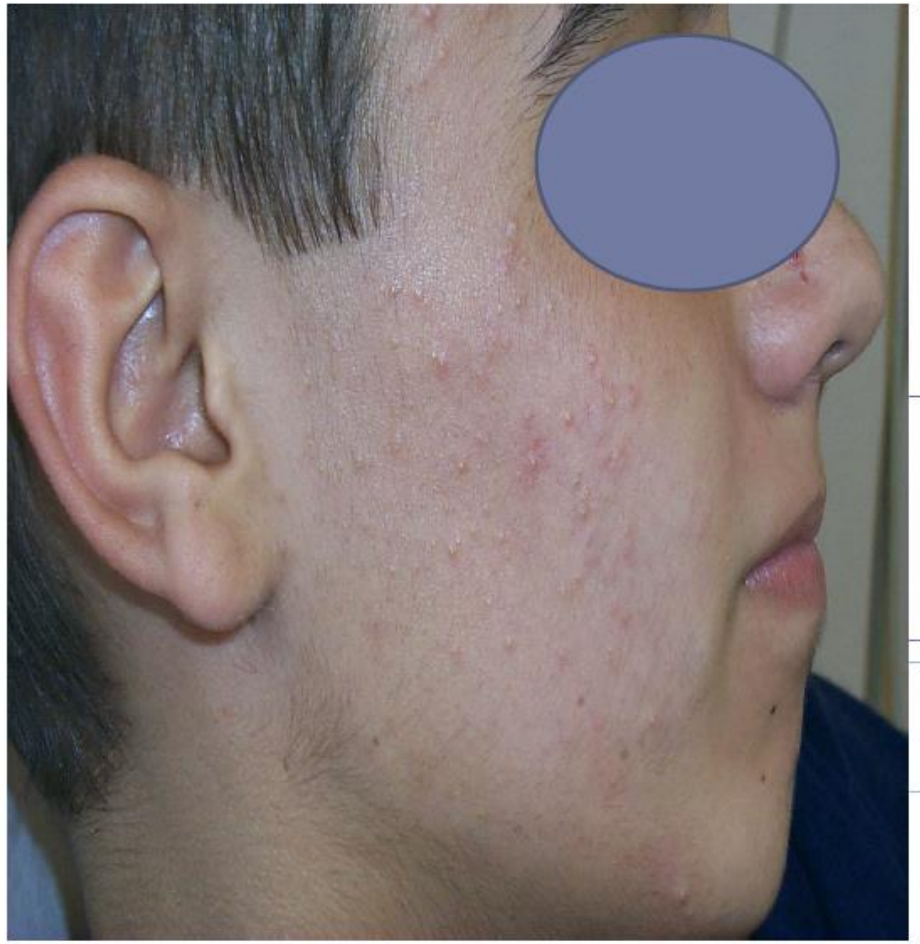
- Modern galenic preparations
- 2 active compouds preparations

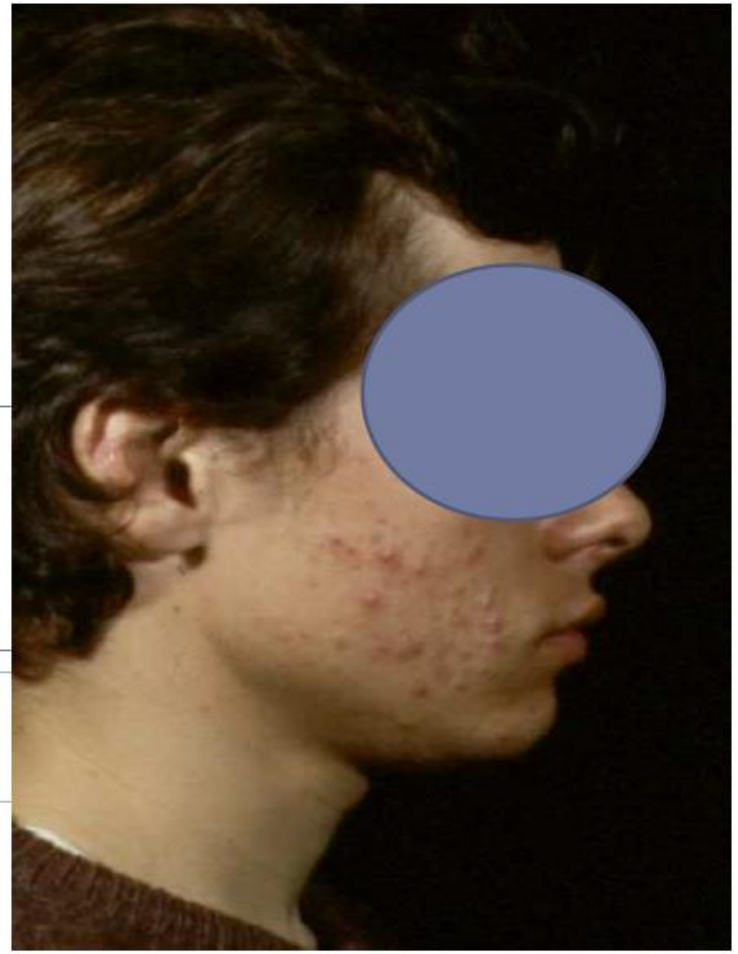
→ Less irritant, once daily treatment, better compliance

Papulopustular acne

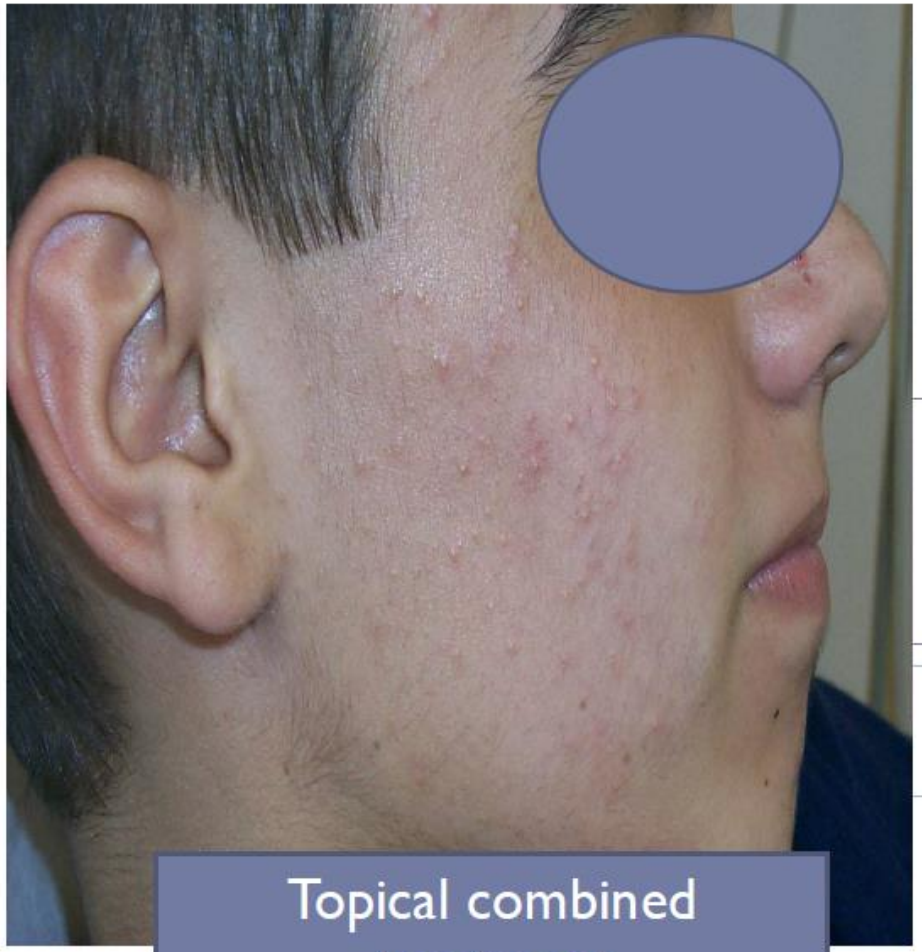


Infalmmatory acne (papulo-pustular)

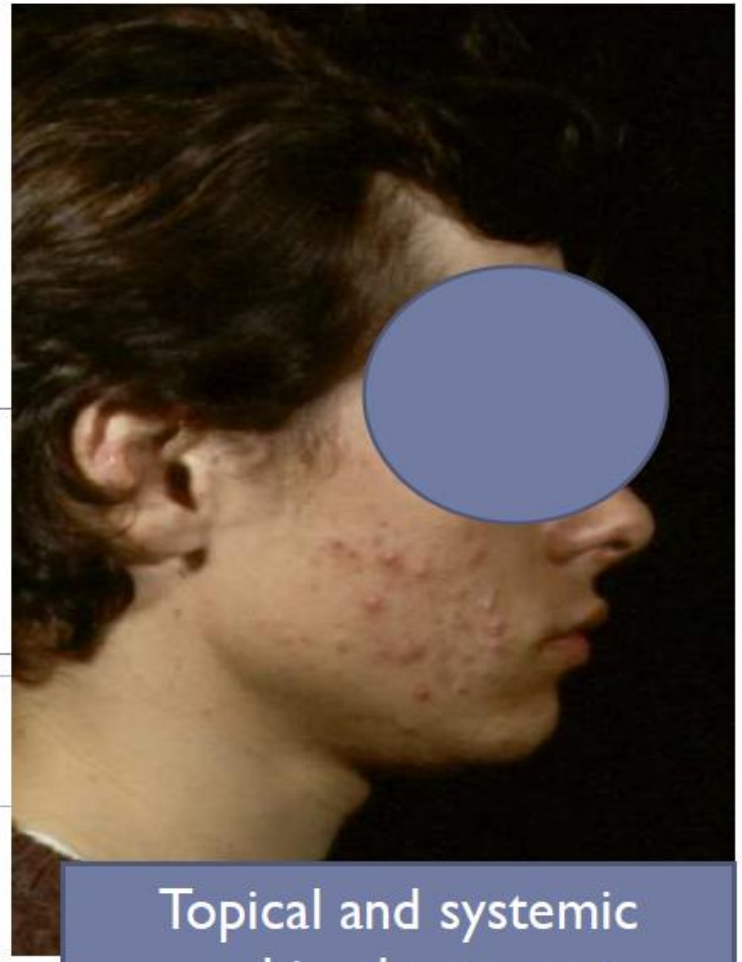




Infalmmatory acne (papulo-pustular)



Topical combined treatment



Topical and systemic combined treatment

Inflammatory acne
- **oral** antybiotics (antimiccrobial, antiinflammatory)

- **Tetracyclins**
  - Tetracyclina, Doxycyclina, Minocyclina, Limecyclin
- Macrolides
  - Erythromycin, Azytromycin

Always in combintation with topical retinoids and/or BPO

Properties:

1. **antibacterial**
2. **direct inhibition of chemotaxis, proinflammatory cytokine production, macrophage activity**

- MACROLIDES (erythromycin, azithromycin) - second-line drugs used in case of:

tetracycline intolerance

in children <10-12 years of age

pregnant women

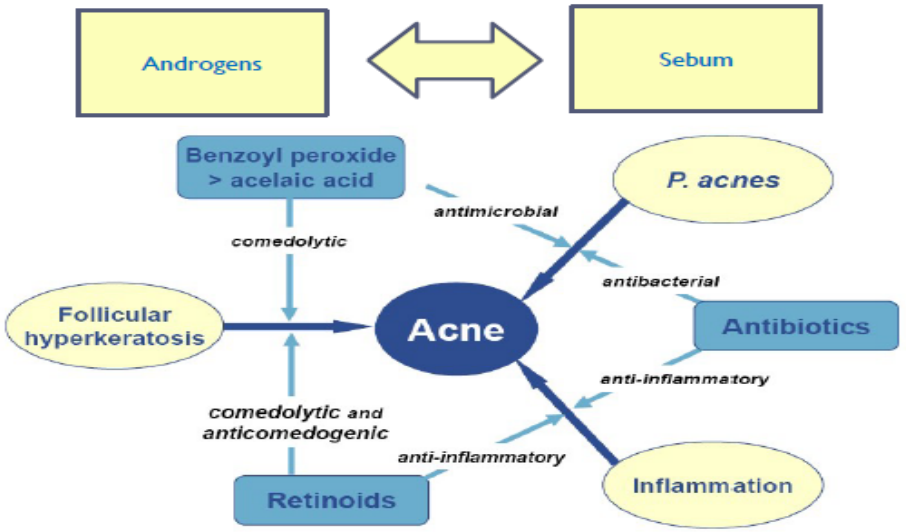
nursing mothers

Oral antibiotics - side effects

- digestive tract intolerance symptoms
- hiperpigmentation around the teeth in children <12 years of age
- phototoxicity
- candidiasis in genital mucosa

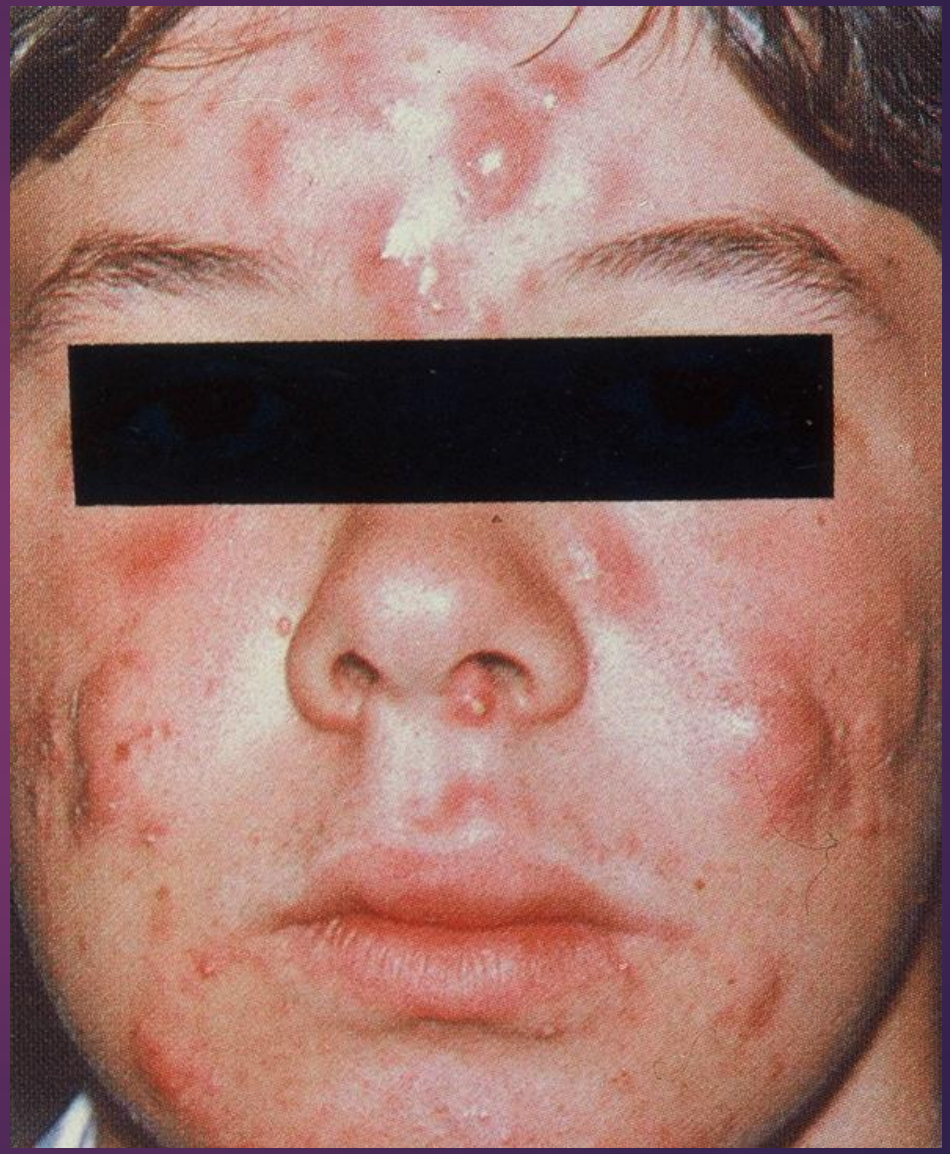
Infalmmatory acne - additional treatment

- Antiandrogens (only females)
  - Oral contraceptives with antiandrogen activity



  - Cyproterone acetate
  - Spironolactone (off label for adult acne)
  - Flutamid

Nodulocystic acne, acne conglobata



Oral isotretinoin

- The only medication which gives permanent results
- Decreases activity of sebum glands
- Not confirmed data on sebum glands atrophy
- Overall dose of 120 mg/kg body weight
- **High teratogenic effect**
  - **Effective ways of contraception are obligatory during the treatment and one month after**

Indications for oral isotretinoin:

severe papulo-pustular acne or nodylocystic acne

acne resistant to antibiotics

psychological aspects (problems with self - acceptance)

acne with significant seborrhea or a high tendency to scarring

Isotretinoin orally - mechanism of action

1. Correct of hyperkeratinization
2. Decrease sebaceous gland activity
3. Decrease the follicular bacterial population of *P. acnes.*
4. Has an anti-inflammatory effect

Oral isotretinoin

oral isotretinoin leads to complete remission in almost all cases, which lasts for months to years in the majority of patients

Recommended dose:

0.5 - 1.0 mg / kg / day

to a total dose of ~ 120 (150) mg / kg

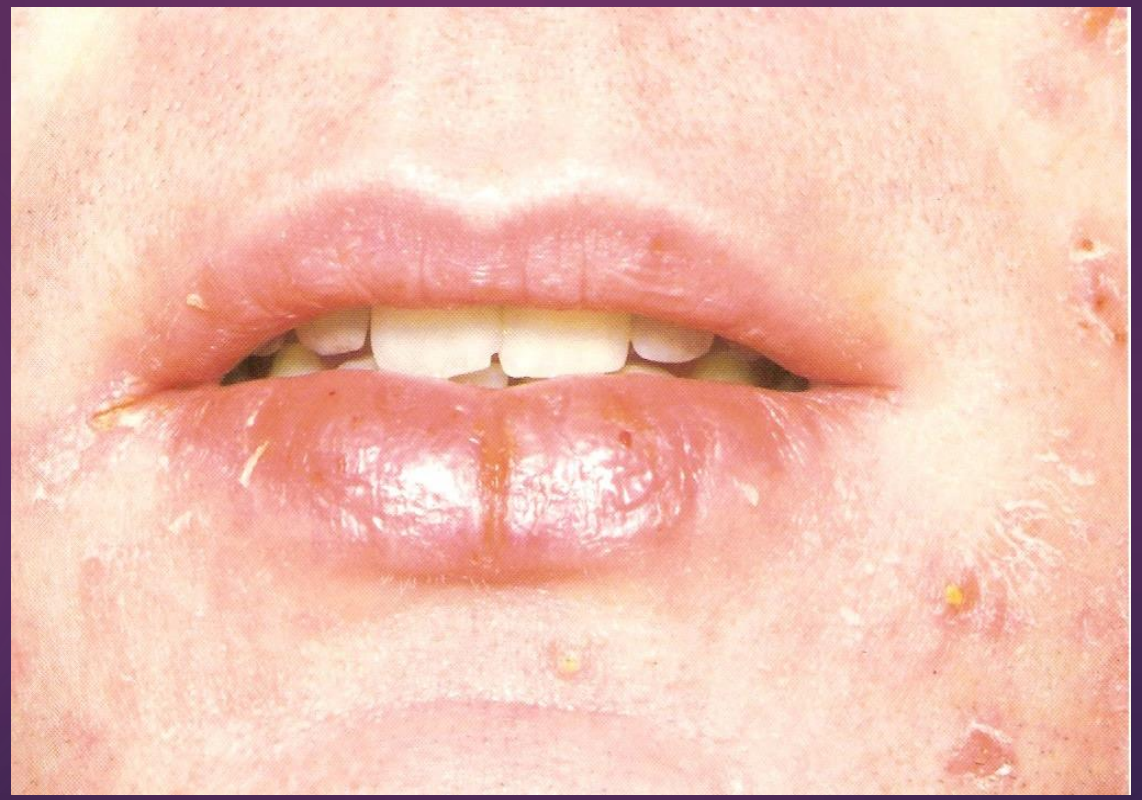
Oral isotretinoin- Side effects:

Isotretinoin is teratogenic and effective contraception is imperative /while treatment and 4 weeks after treatment /

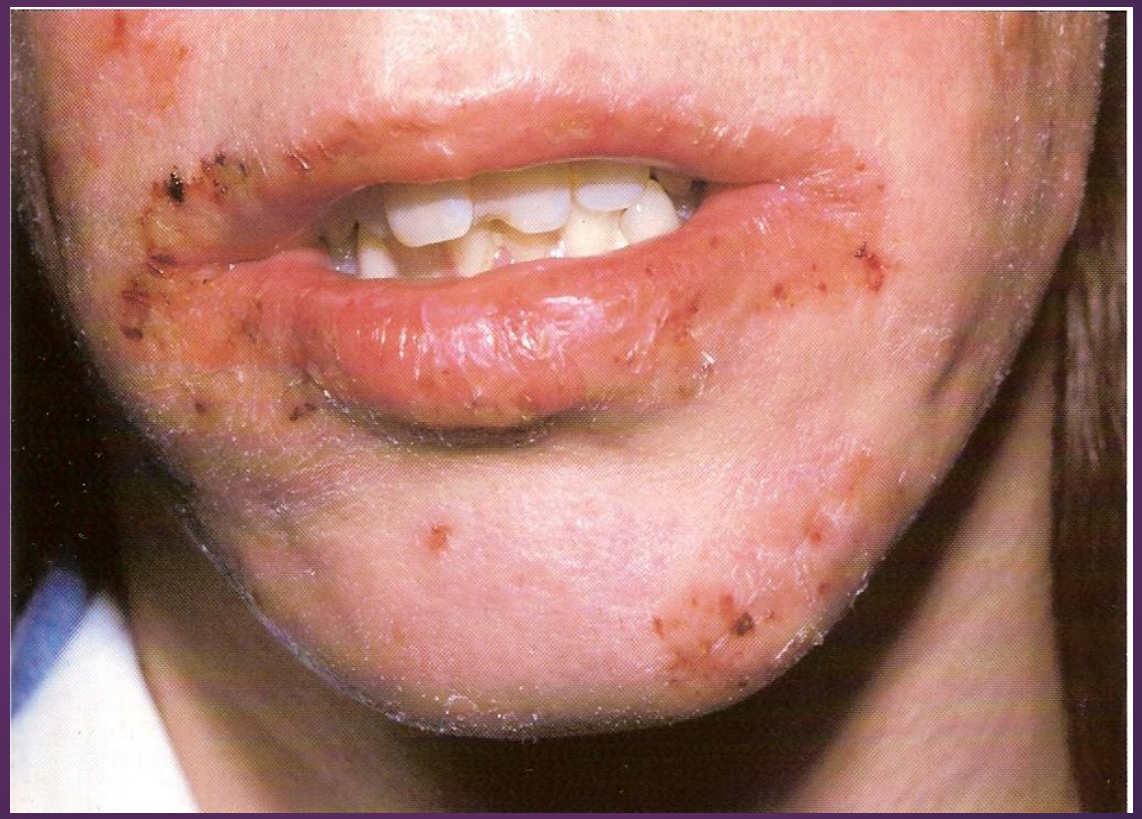
Patients may develop elevation of triglycerides or transaminase levels /dose dependent- normalize with reduction in dose of the drug /

Oral isotretinoin- another clinical adverse events / dose dependent /:

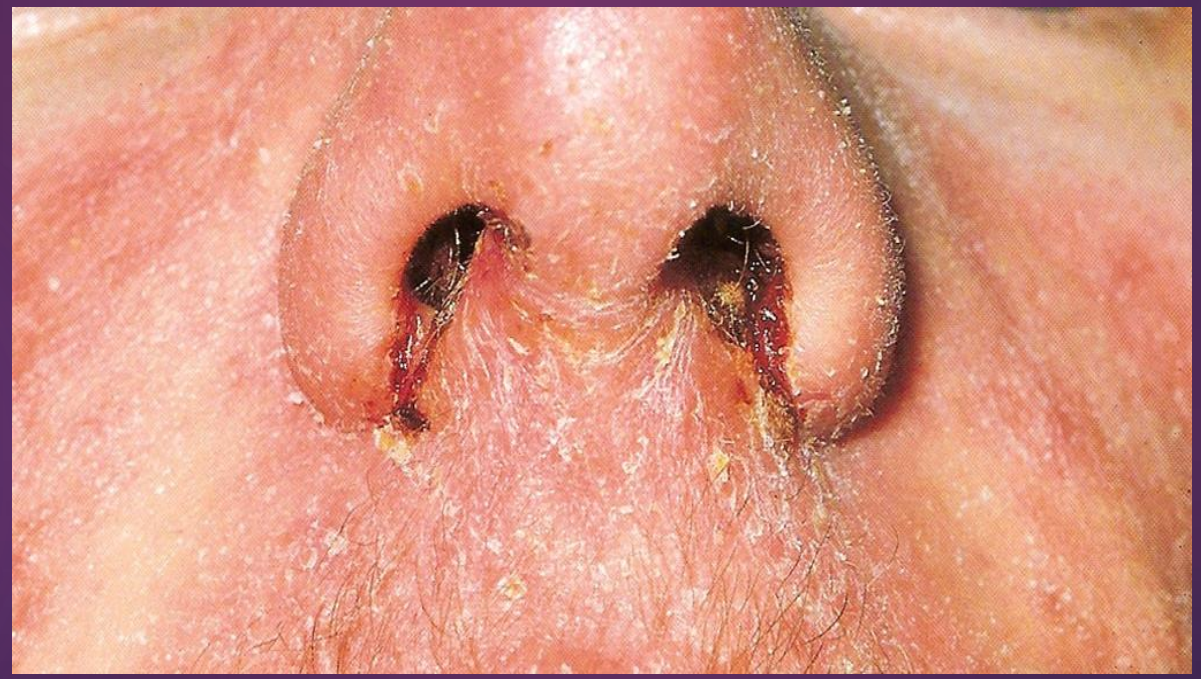
Dry lips and cheilitis 90-100%



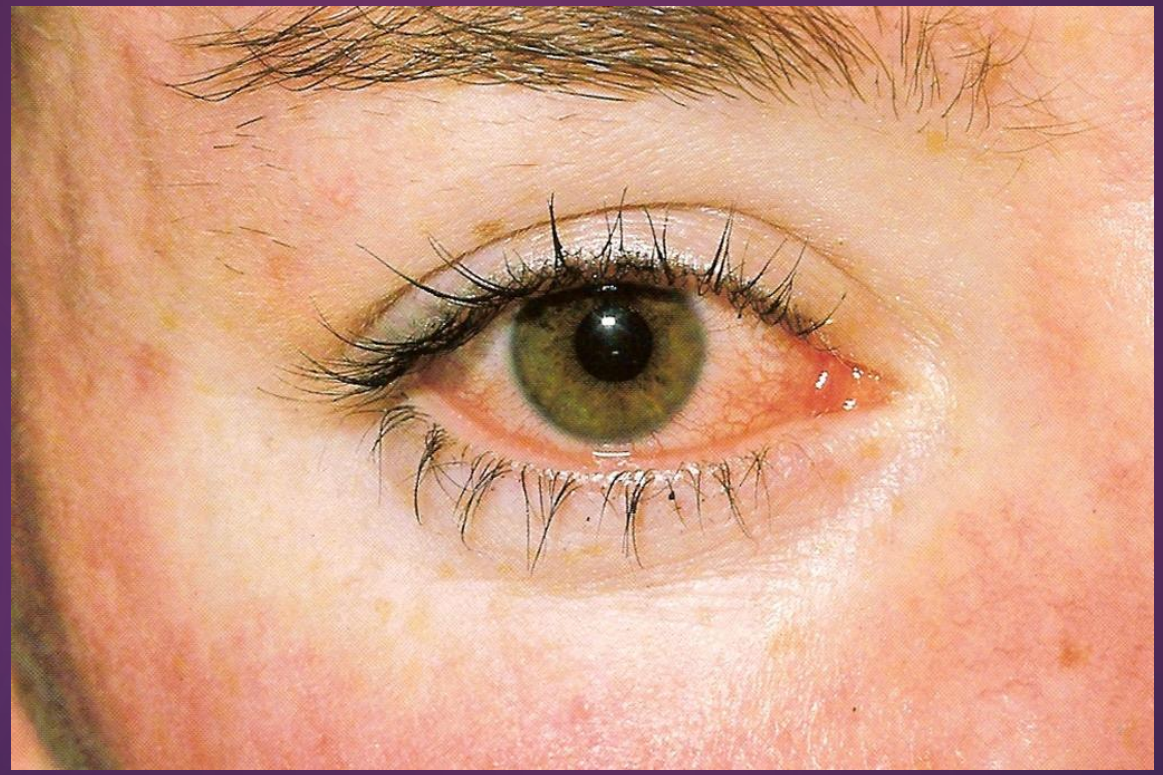
Erythema, dryness, scaling of the face area 40-60%



Dryness of the nasal mucosa, bleeding ~ 20%



Xerophthalmia, conjunctivitis, decreased tolerance to contact lenses 10-15%

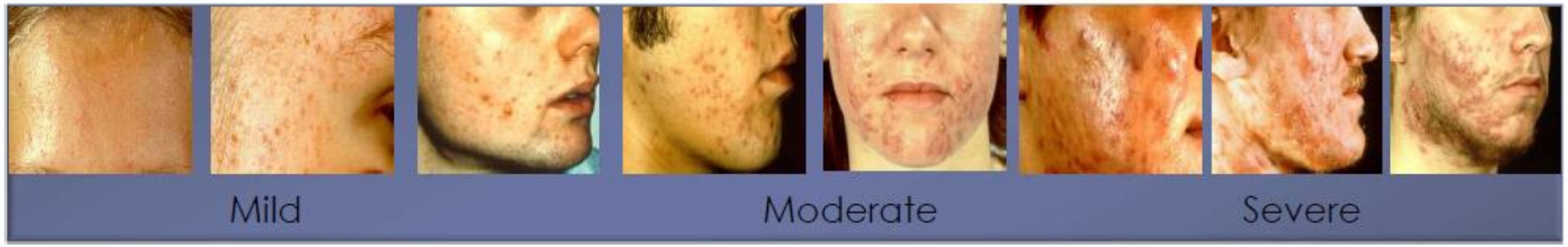


Oral isotretinoin- another clinical adverse events / dose dependent /:

Pain in joints and muscles 20-40%

An eczema-like rash 20-30%

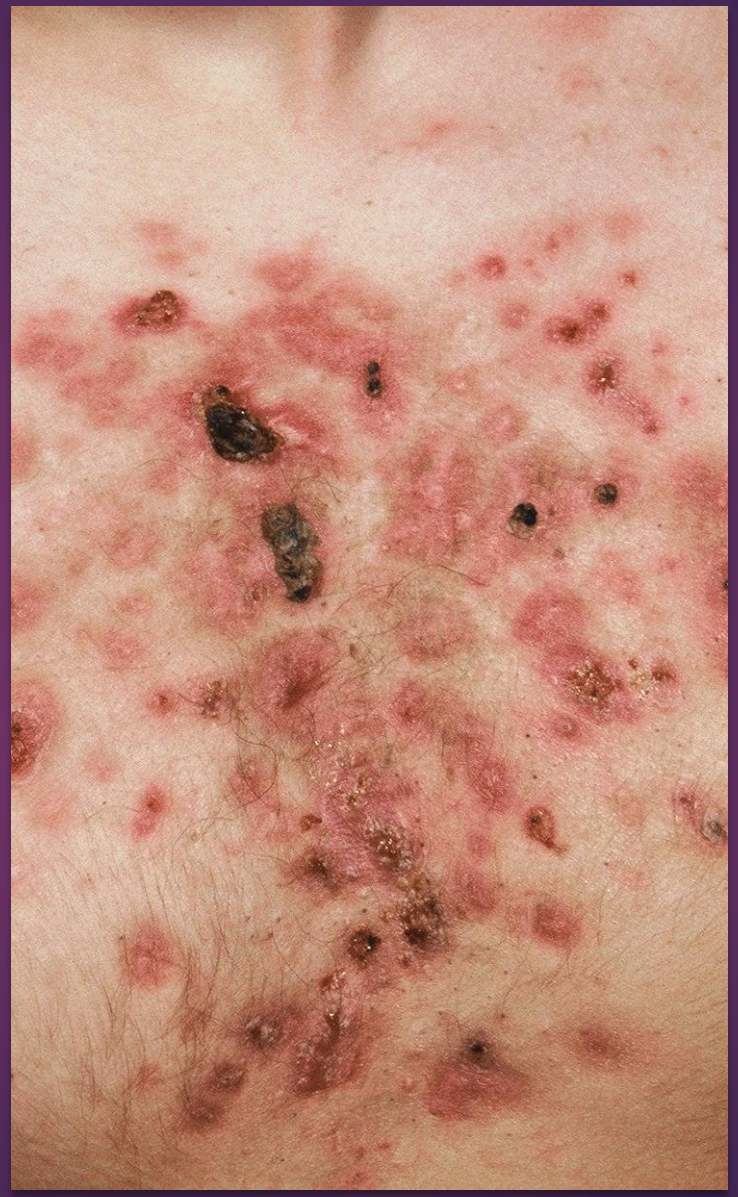
Hair loss ~ 1%

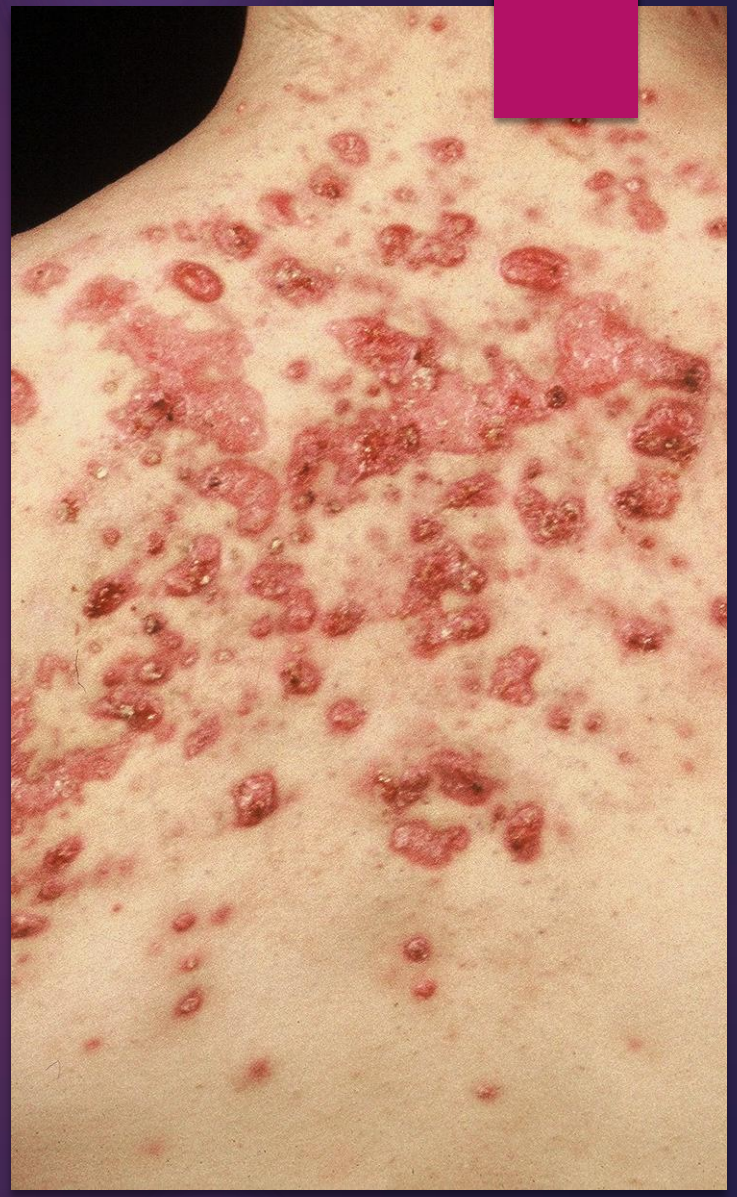


	Mild		Moderate		Severe
	A.comedonica	A.pap.pust.	A.pap.pust	A.pap. pust. nod.	A. conglobata
1st Choice	**Topical Retinoid**	**Top. Retinoid plus topical anti-microbial agent**	**Oral Antibiotic plus topical retinoid +/- BPO**	**Oral Antibiotic plus topical retinoid plus BPO**	**Oral Isotretinoin**
Alternatives	Alt. Top. Retinoid or Azelaic Acid or Salicylic Acid	Alternative top.Retinoid plus Alternative Antimi-crobial agent / Azelaic Acid	Alternative Oral Antibiotic plus Alternative top. Retinoid +/- BPO / Azelaic Acid	Oral Isotretinoin or Alternat. Oral Anitbiotic plus Alt. Top. Retinoid BPO / Azelaic Acid	High Dose Oral Antibiotic + Topical Retinoid + BPO
Alternatives or females	See 1st Choice	See 1st Choice	Oral Antiandrogen plus Top. Retinoid / Azelaic Acid +/- BPO		
Maintenance	Top. Retinoid		Top. Retinoid +/- BPO		

Acne fulminans

- Very rare form
- It occurs mainly in young men
- Relate to the face, chest, back, shoulders
- Lesions are papules, pustules and nodules, often covered with hemorrhagic crusts
- Skin lesions are accompanied by malaise, elevated body temperature, arthralgia
- Leukocytosis and accelerated ESR are observed

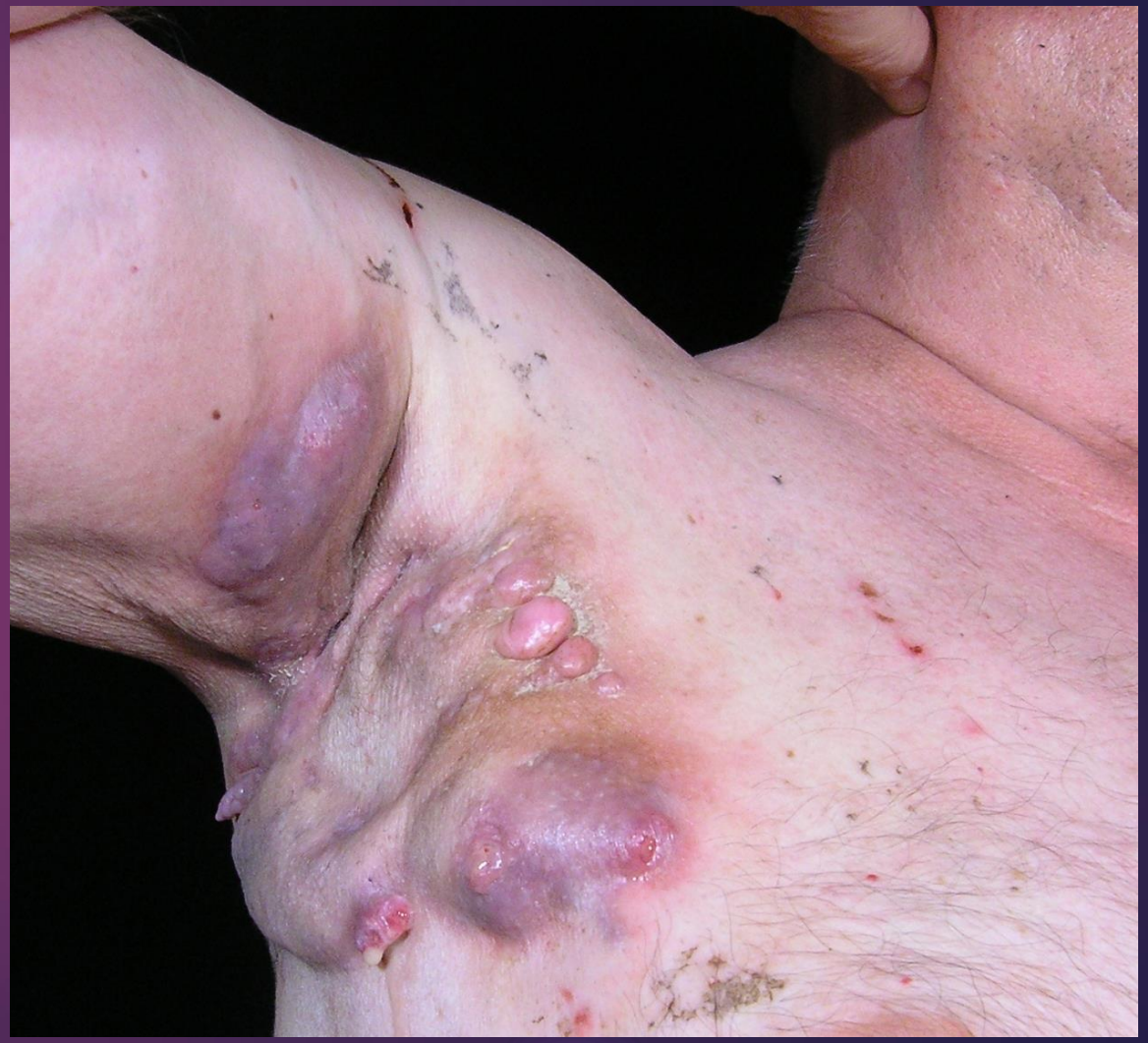




Acne inversa

chronic, suppurative, often cicatricial disease of apocrine glands

involves the axillae, groins and/or anogenital region



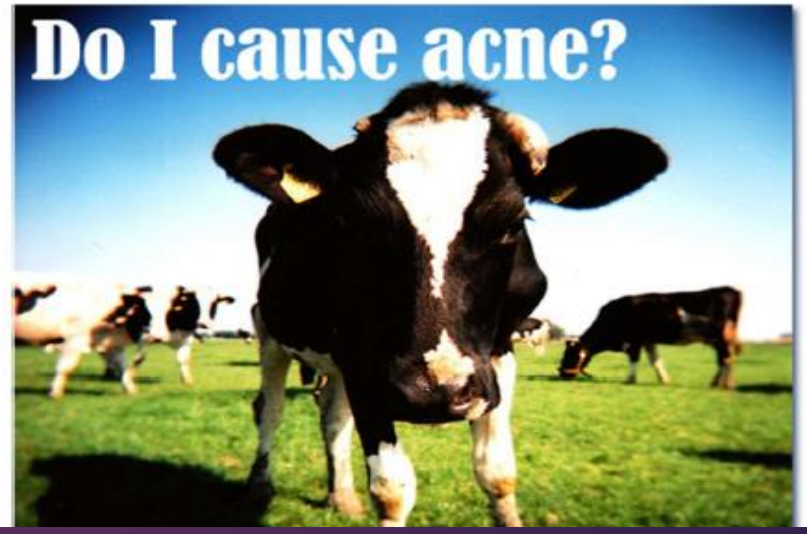
Acne – facts and myths

- Diet – glycemic index, milk
- Weather? -> acne Mallorca
- Cosmetics -> cosmetic acne
- Sexual activity
- Microbiological tests – currently not recomended

- **premenstrual period**
- **drugs (anabolic steroids)**

Diet

- High Glycemic index is inducing acne!
- Milk can induce acne!?
  - not yet fully proven but….



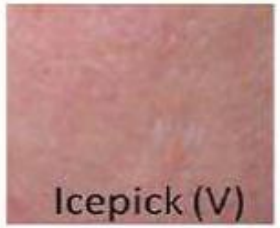
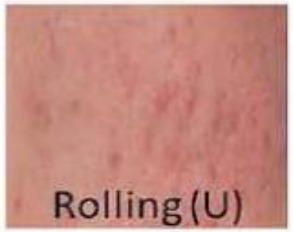
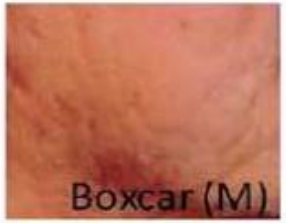
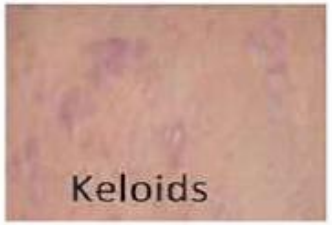
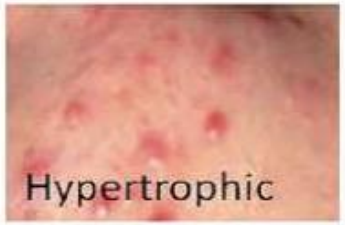
Acne complications

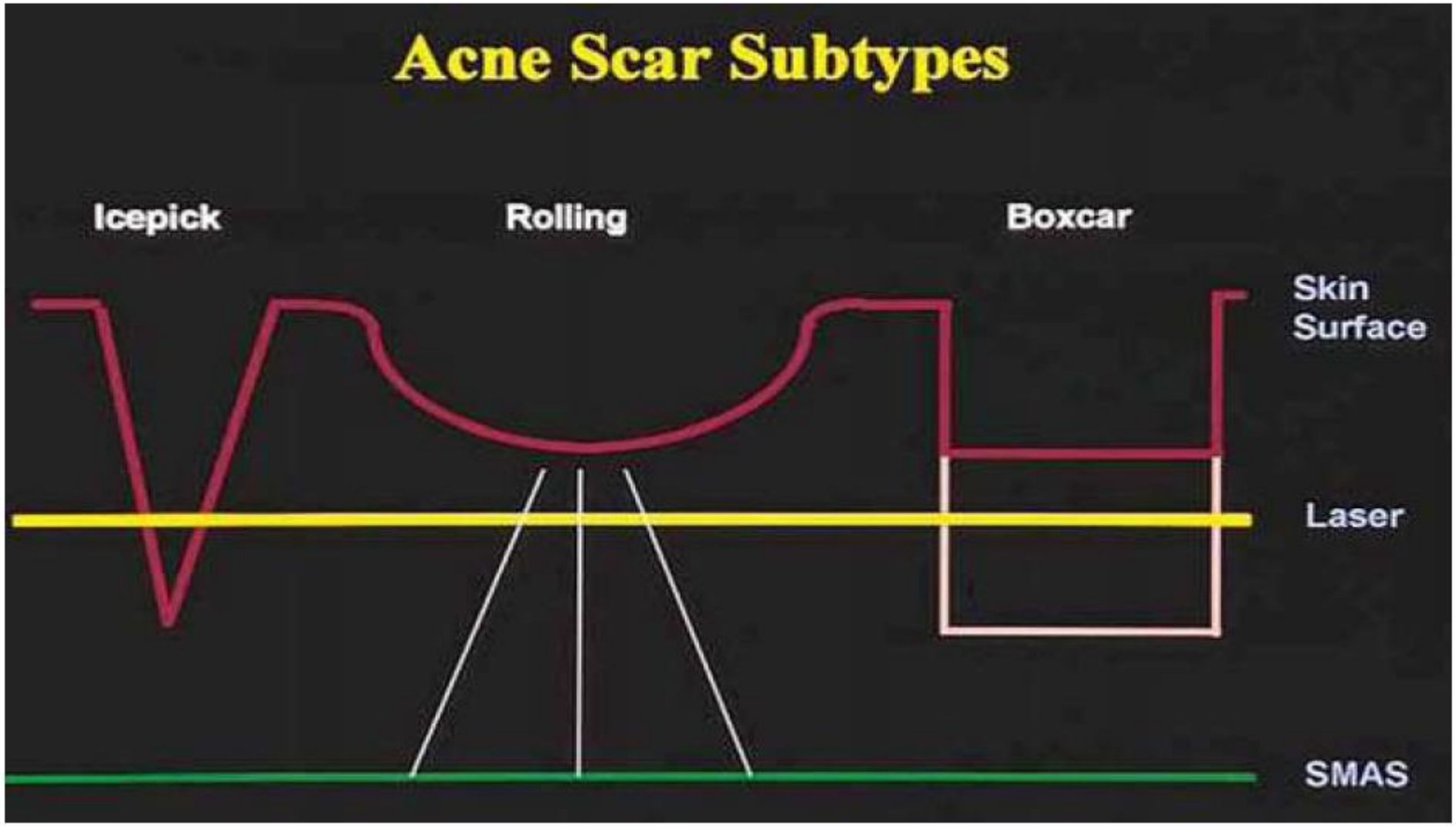
- Hiperpigmentation
- Raised scars
- Keloids
- Atrophic scars

Hiperpigmentation
treatment

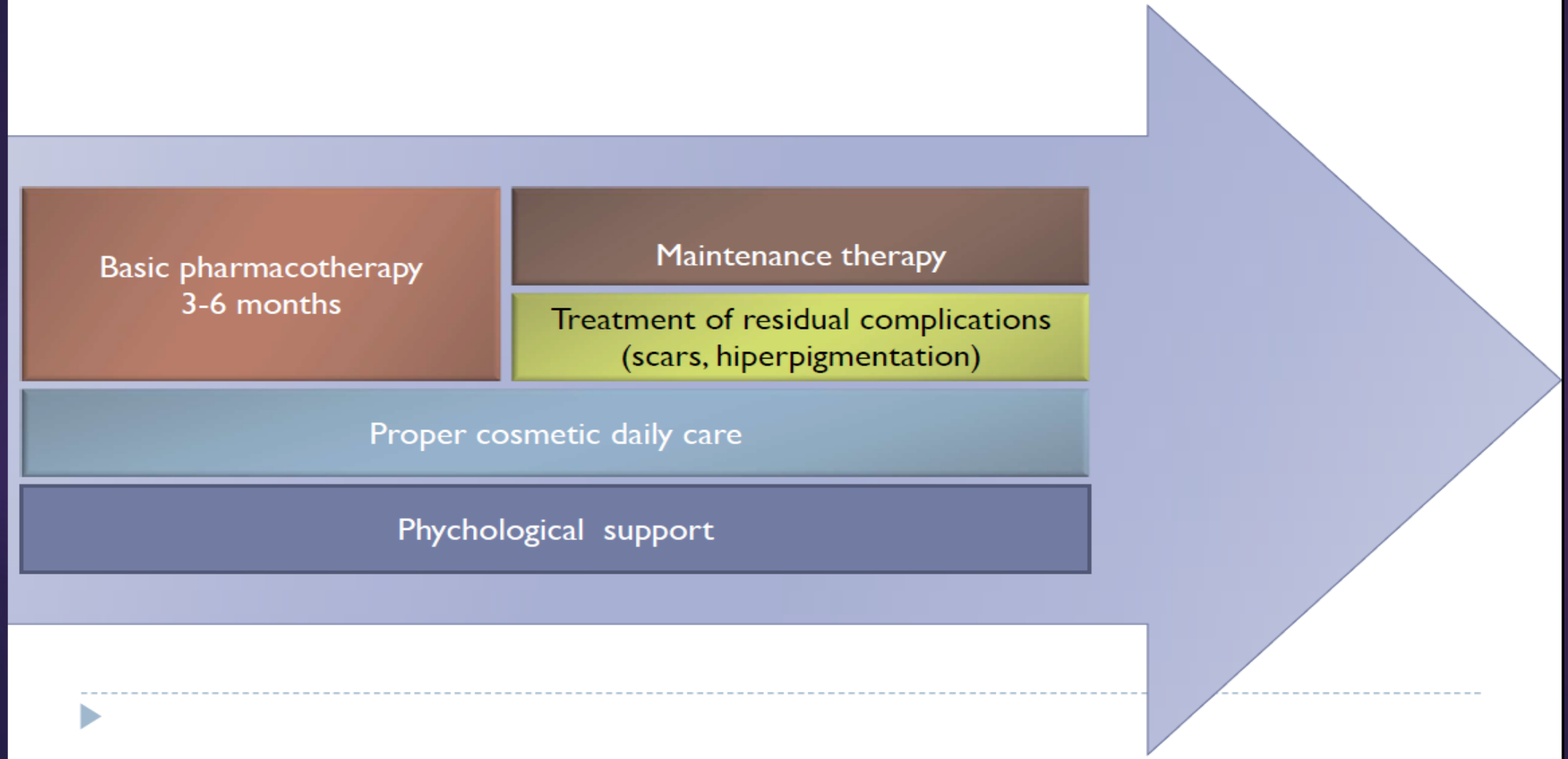
- Sunscreens
- Prolonged use of topical retinoids and a-hydroxyacids
- Azelaic acid
- **Chemical superficial peels (low concentration acids + blanching agents)**
- **Microdermabrasion**
- **Fraxel laser**

Scars

 Icepick (V)	 Rolling (U)	 Boxcar (M)	 Keloids	 Hypertrophic
Punch excision (deep bases) Elevation and grafting Laser resurfacing/ dermabrasion (many scars close together) Spot TCA peel	**Combined therapy** Micrograft and Subcision **+** ± Filler Resurfacing Microdermabrasion *Deep* – spot TCA peel	**Shallow** ≤3mm diameter - Laser skin resurfacing >3mm diameter - Laser skin resurfacing ± punch elevation **Deep** ≤3mm diameter – Punch excision >3mm diameter – Punch excision or punch elevation Fractional thermolysis (deep or shallow) Dermabrasion CO_2 laser resurfacing	Intralesional corticosteroids Intralesional 5-FU Intralesional bleomycin Compression Imiquimod after intralesional excision Cryotherapy Pulsed-dye laser Excision + electrotherapy	Intralesional steroids Intralesional 5-FU Vascular laser Intralesional bleomycin Compression Imiquod after intralesional excision


Acne Scar Subtypes
Icepick
Rolling
Boxcar
Skin Surface
Laser
SMAS

Complexed acne treatment



Thank You