Acne Vulgaris

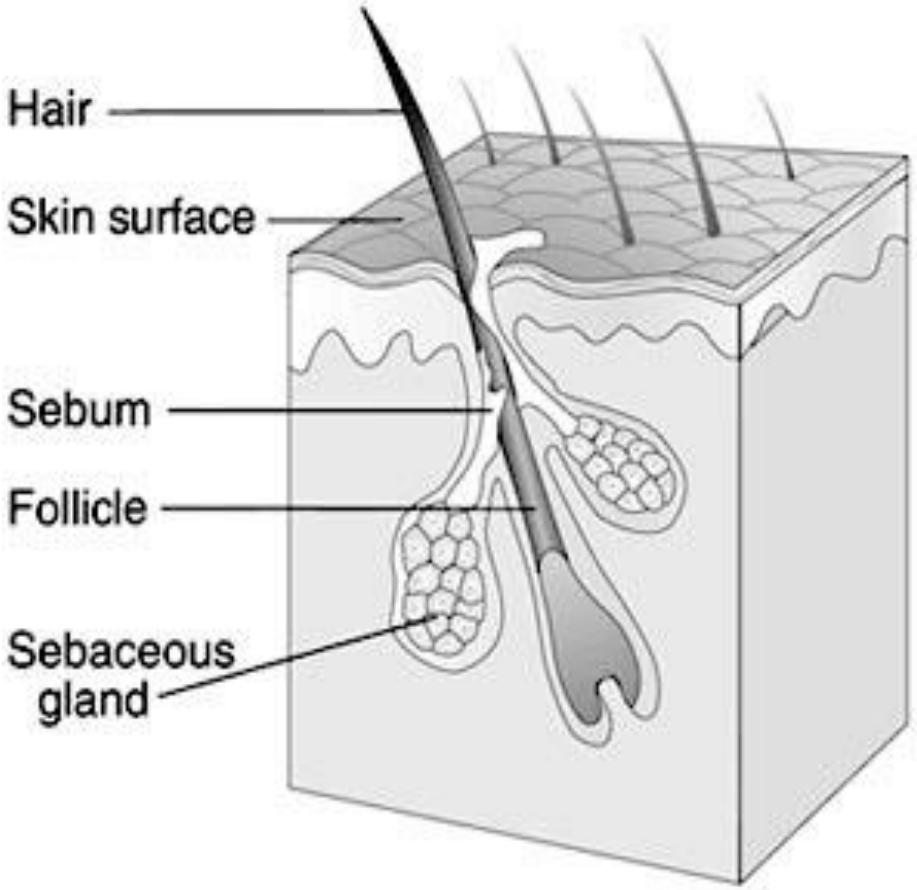
Dr Julia Schofield
Consultant Dermatologist

Acne Vulgaris: learning outcomes

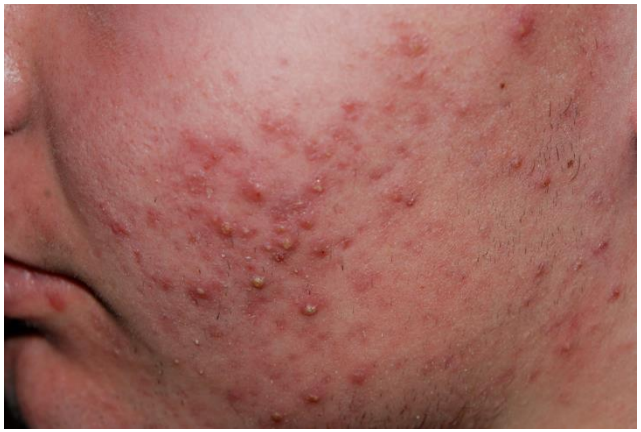
- Clinical presentations
- A bit of pathophysiology
- Treatment
- When to refer

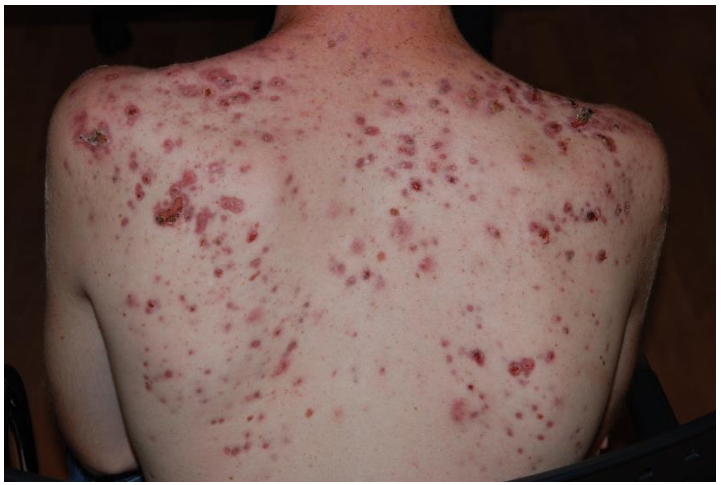
Acne vulgaris

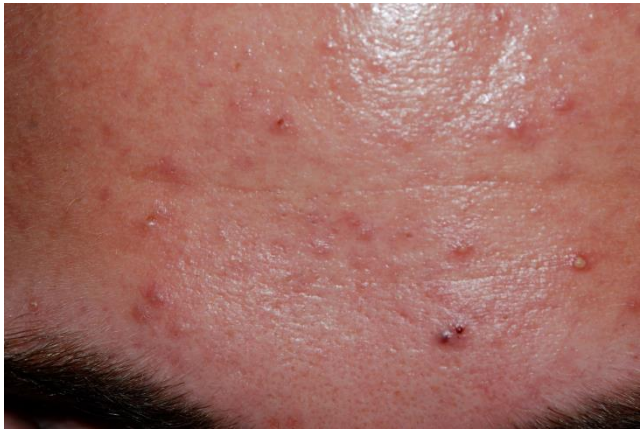
- Chronic, inflammatory disease of the pilosebaceous unit
- Occurs where sebaceous glands most numerous…

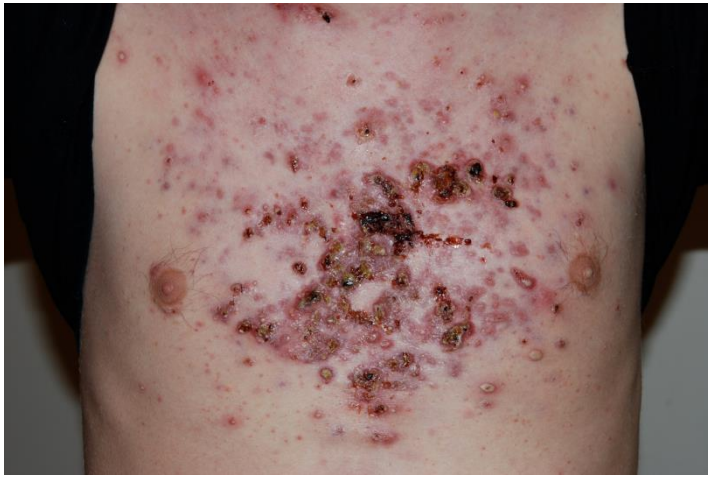


Acne vulgaris - distribution



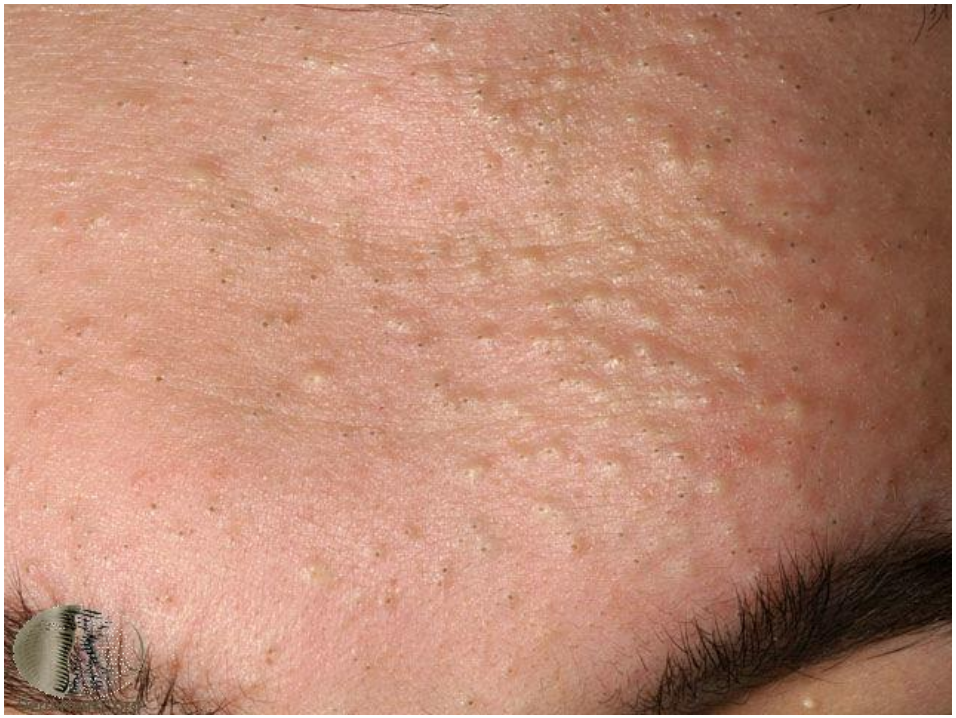






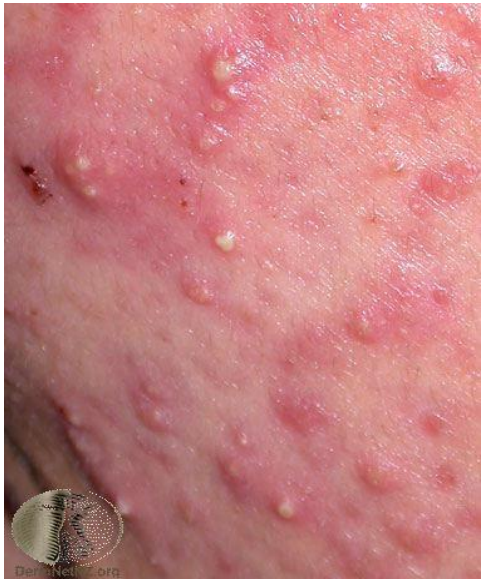
Acne vulgaris- lesion types

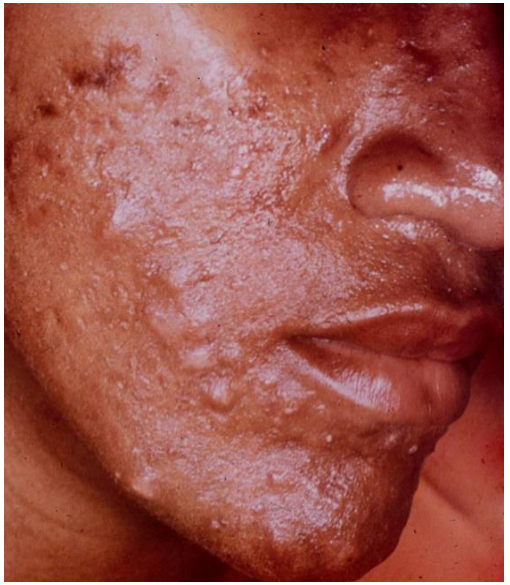
- Seborrhoea
  - Greasiness
- Comedones
  - Non-inflammed
  - Open (blackheads)
  - Closed (whiteheads)
    - Includes macrocomedones



Acne vulgaris- lesion types

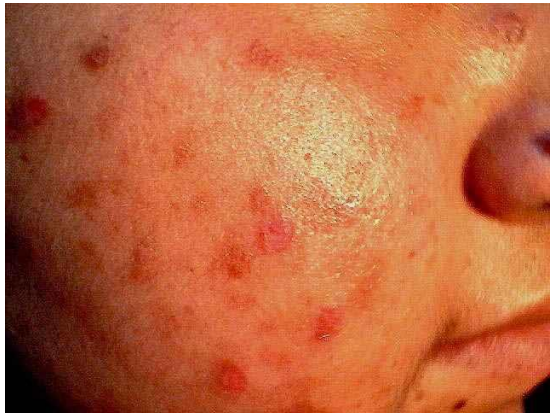
- Inflammatory lesions
  - Papules
  - Pustules (small)
  - Nodules (large)
  - Cysts

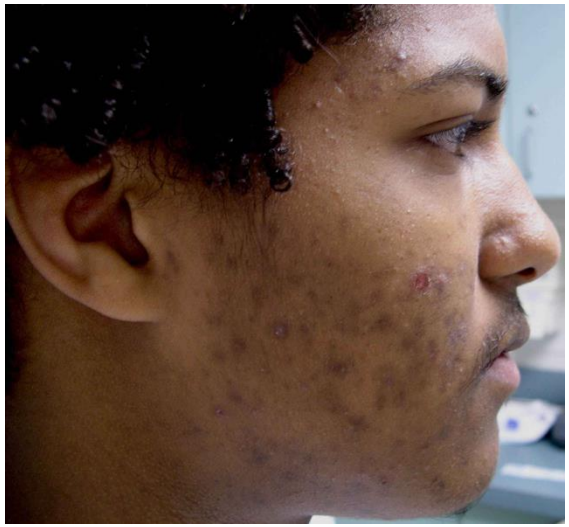




Acne postinflammatory changes

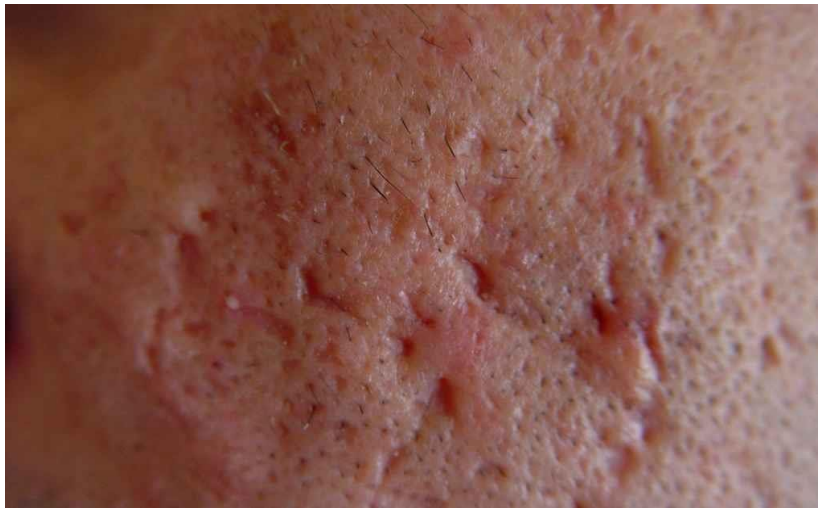
- Post-inflammatory
  - Macular erythema
  - Hyperpigmentation

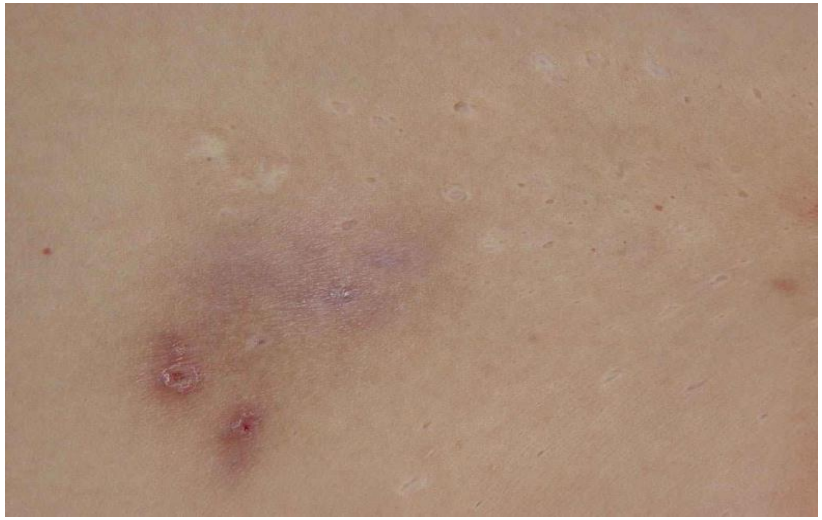




Acne vulgaris: scarring

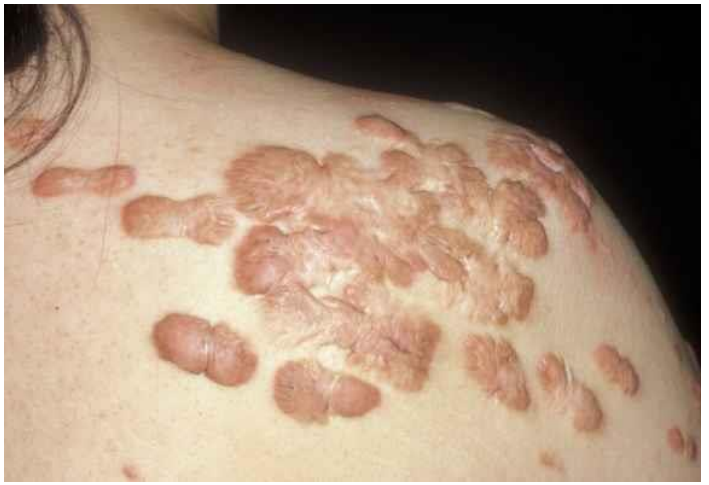
- Scars
  - Atrophic
    - Ice pick
    - Rolling
  - Macular (flat)
    - Macular elastolysis





Acne vulgaris: scarring

- Scars
  - Hypertrophic or Keloidal
    - Especially chest, shoulders
    - People of black or Asian ethnicity much more susceptible
    - May occur after only mild acne
    - Responds to intra-lesional corticosteroid



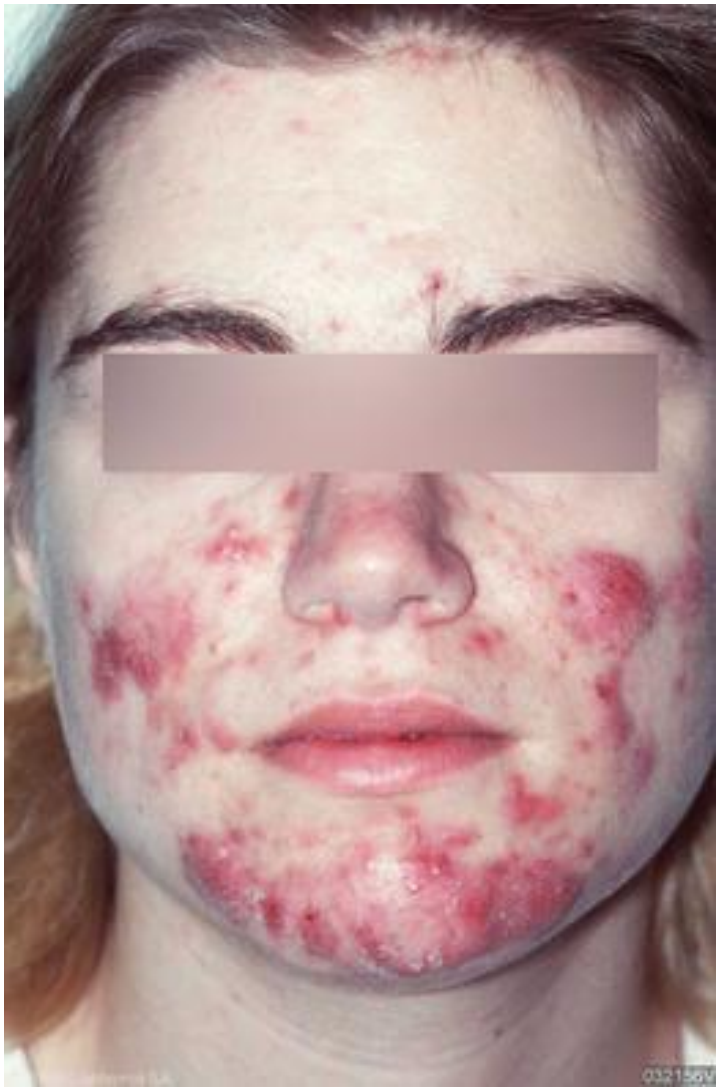
Epidemiology- not just teenagers

Acne Vulgaris; one of the commonest diseases of man

- 16 year olds
  - Males 95%
  - Females 84%
- 25 year olds
  - Males 3%
  - Females 12%
- 40 year olds
  - Males 1%
  - Females 5%

Psychological Consequences

- Shame 70%
- Embarrassment 63%
- Anxiety 63%
- Loss of confidence 67%
- Impaired social contact 57%
- Unemployment
- Comparable QoL effects
  - Asthma
  - Epilepsy
  - Diabetes
  - Arthritis



Why skin disease affects psychological well being

- Appearance has huge role in social communication and functioning
- Physically ‘attractive’ people are attributed more intelligence, friendliness and social skills by strangers than ‘unattractive’ people
- This effect is reinforced by the media, industry and the celebrity culture

Psychological Consequences

- Clinical severity does not correlate with level of psychological impairment

- Extreme example is dysmorphophobia:
  (body dysmorphic disorder)
  - No or little disease
  - Psychologically devastating
  - Risk of suicide (up to 25%)
  - Lack of insight
  - Need more aggressive treatment

Epidemiology- Acne vulgaris and Diet

- There is no proven link between:
  - Chocolate intake and acne
  - Animal fat intake and acne
  - Protein or vitamin intake and acne
  - Sexual activity and acne

Epidemiology- Acne vulgaris and Diet

- Small Randomised Controlled Trial showed low glycaemic-index diets reduced acne vulgaris severity
- Possible association between dairy intake and acne vulgaris
- More research needed

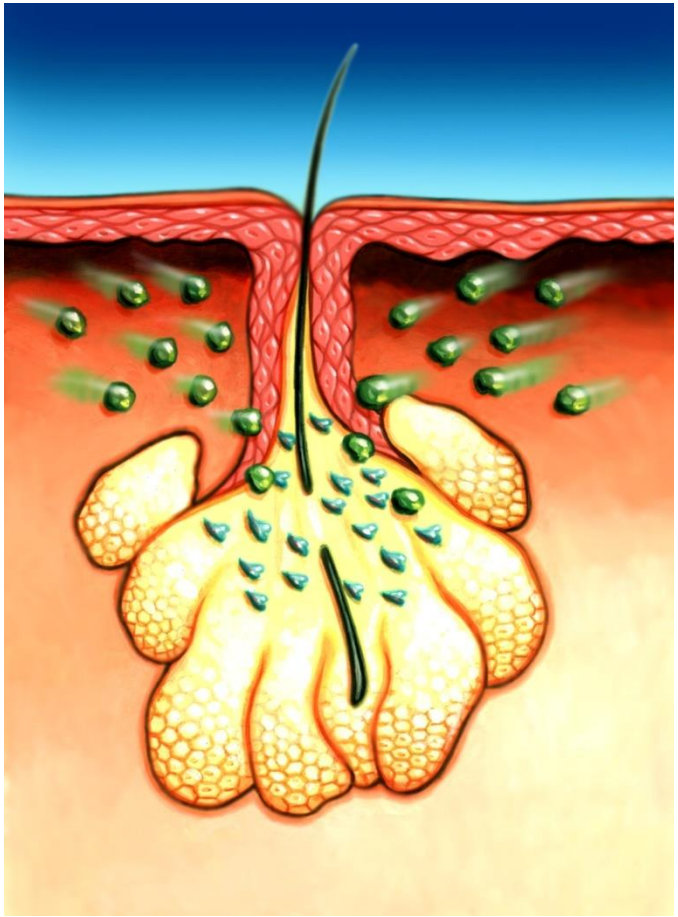
Epidemiology- Sunlight and Acne vulgaris

- Patients and doctors often assume it helps
  - Sunburn causes desquamation and scaling of the skin that gives an impression of reduced oiliness
  - Sun tan has a camouflage effect
  - No evidence at all that it sunlight reduces acne vulgaris lesion counts
  - Artificial UV light (PUVA) can cause acne

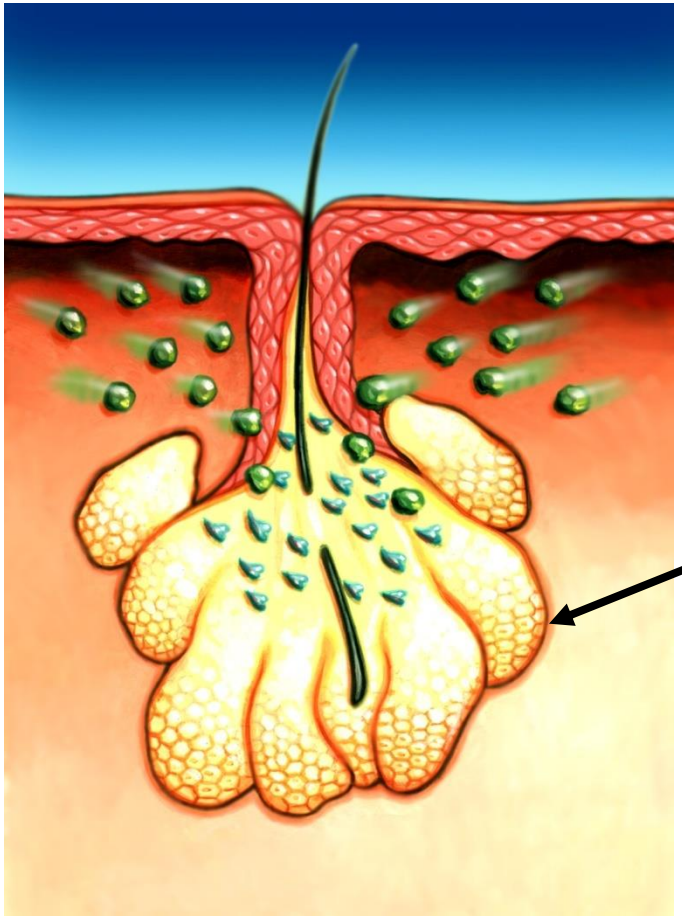
Epidemiology- Smoking and acne vulgaris

- 1000 women 25-50 years old
- 27.7% smokers, 72.3% non-smokers
- 18% prevalence of acne
- 41% of smokers had acne vulgaris
- 9% of non-smokers had acne vulgaris
- Odds ratio = 4.05 (2.6-6.3)

Pathogenesis of Acne vulgaris



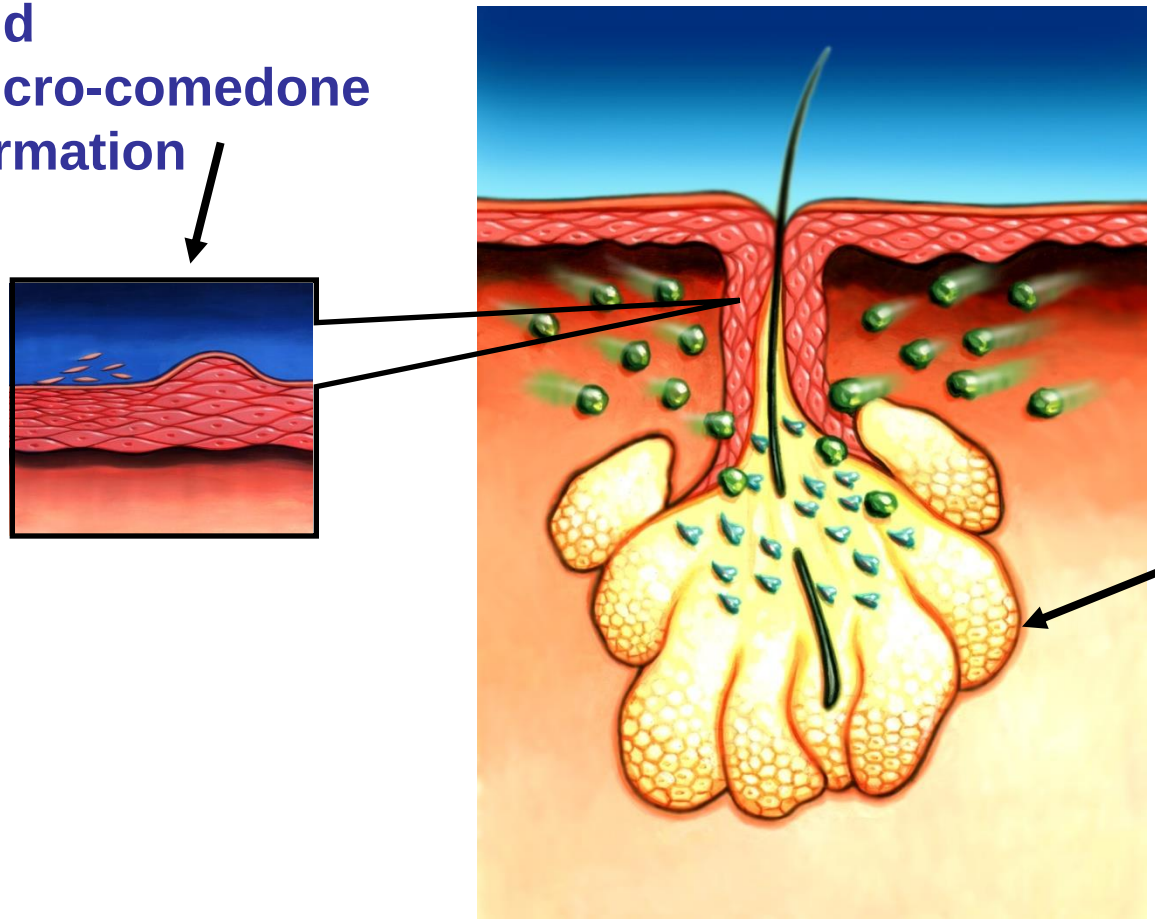
Pathogenesis of Acne vulgaris



1. **Androgen mediated increased sebum production**

Pathogenesis of Acne vulgaris

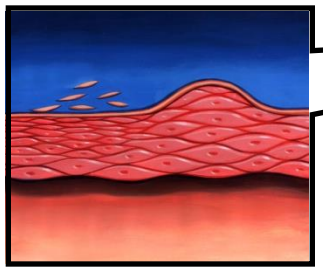
2. Early inflammation and micro-comedone formation

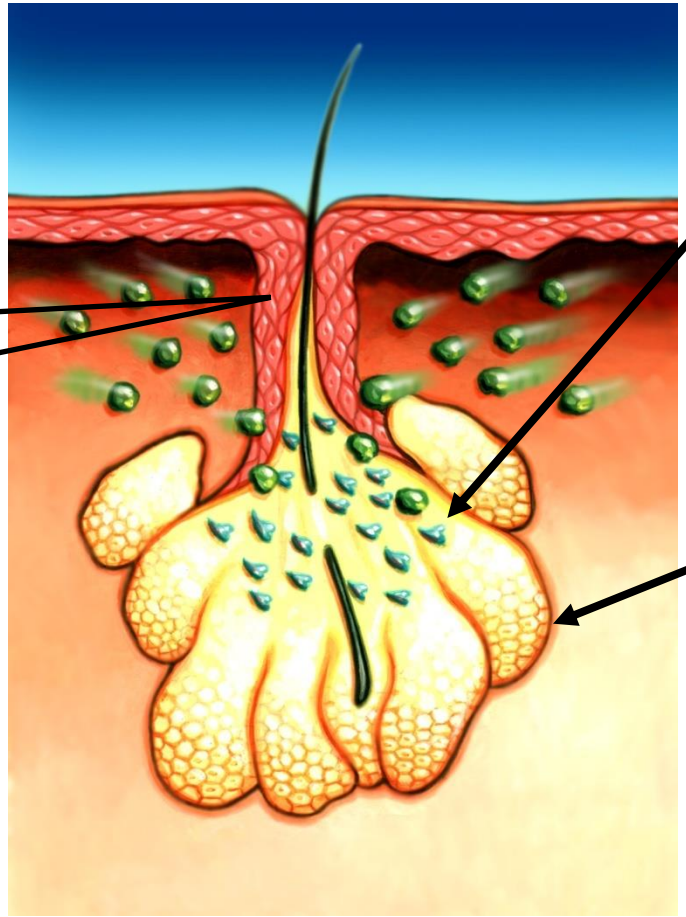


1. Androgen mediated increased sebum production

Pathogenesis of Acne vulgaris

2. Early inflammation and micro-comedone formation



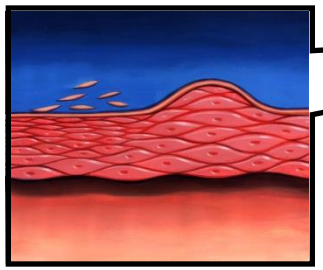


3. *P. acnes* colonisation of follicle

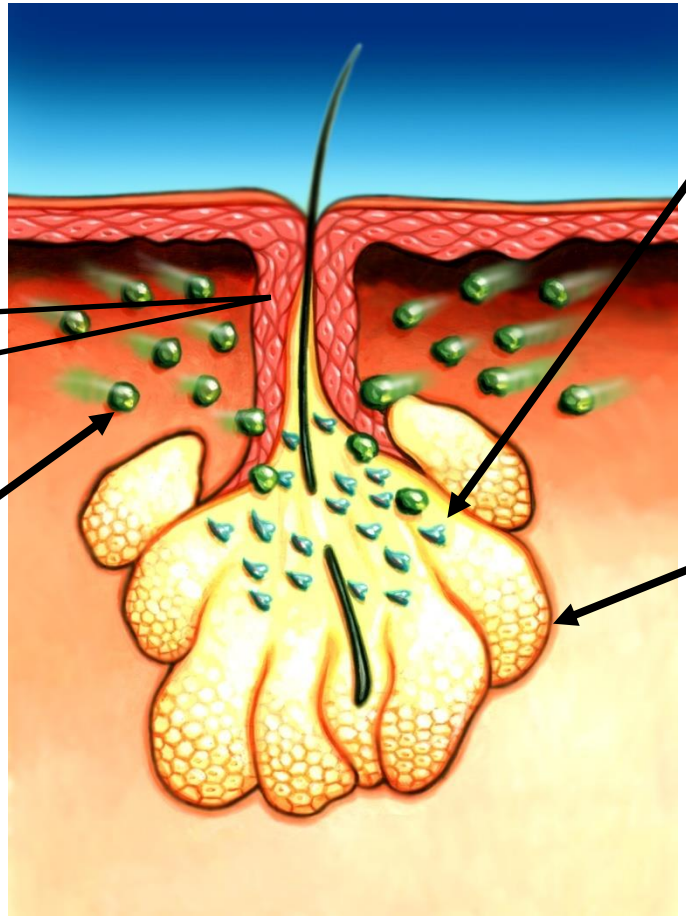
1. Androgen mediated increased sebum production

Pathogenesis of Acne vulgaris

2. Early inflammation and micro-comedone formation



3. *Proprionibacterium acnes* colonisation of follicle

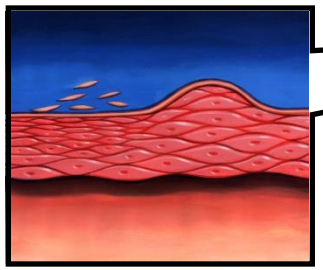


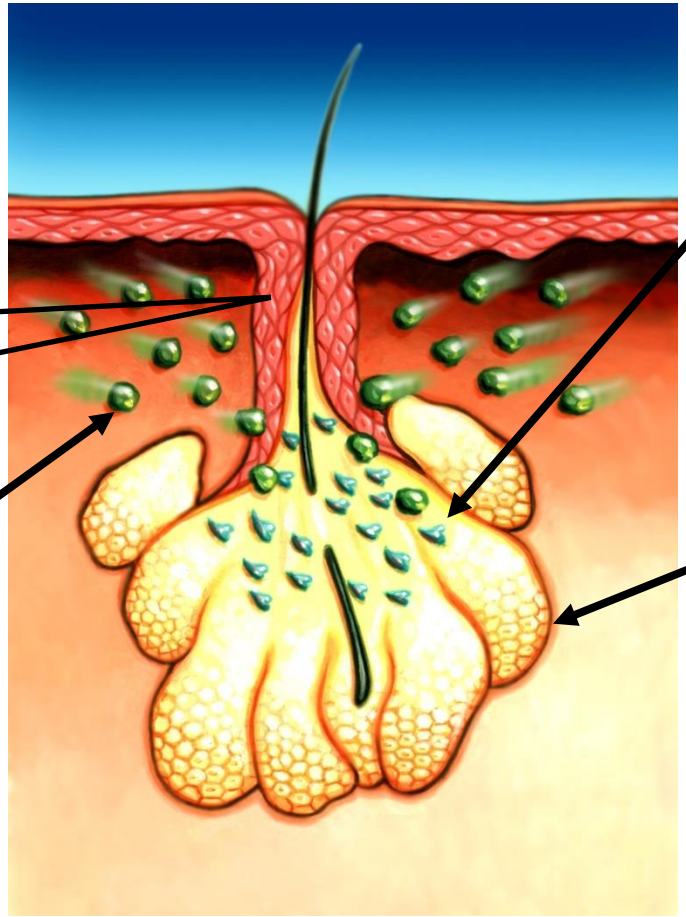
1. Androgen mediated increased sebum production

4. Late inflammation +++

Can you apply this knowledge to treatment selection?

2. Early inflammation and micro-comedone formation





3. *P. acnes* colonisation of follicle

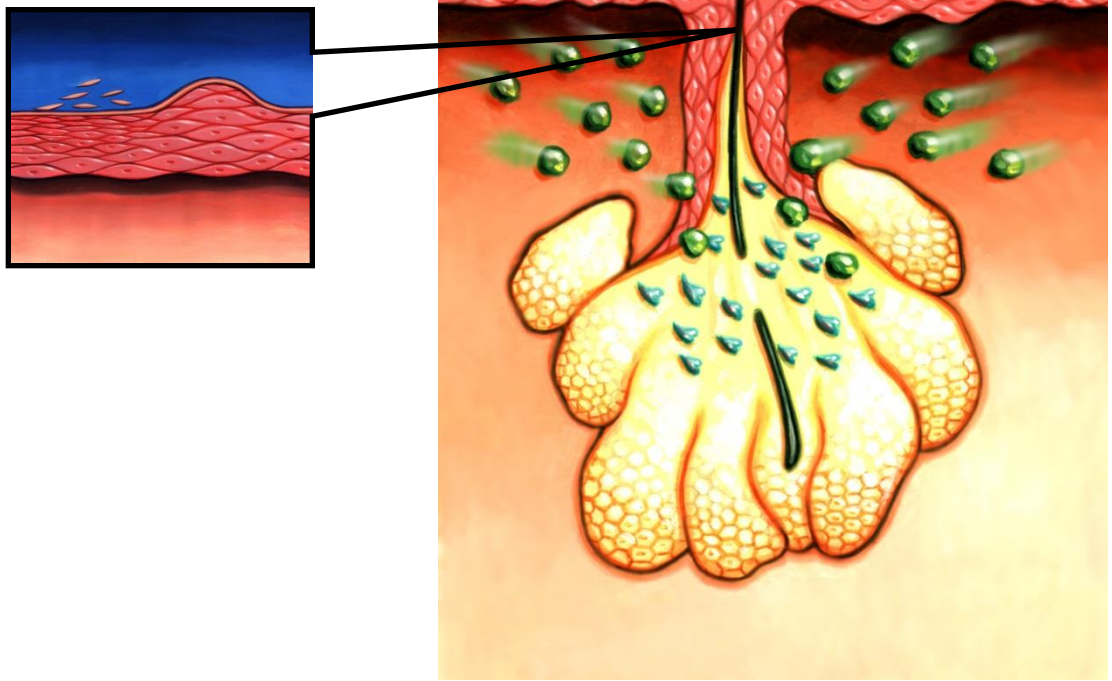
1. Androgen mediated increased sebum production

4. Late inflammation +++

Actions of Anti-Acne Therapies

Topical retinoids:

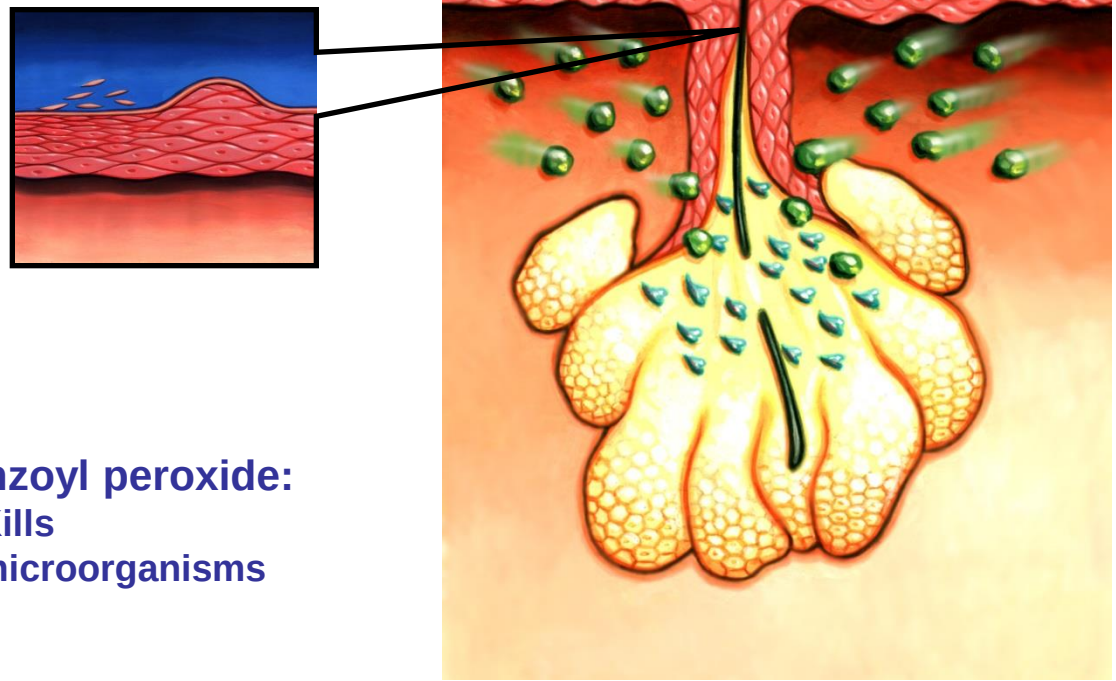
- ✓ **Normalize desquamation**
- ✓ **Reduce inflammatory response**



Actions of Anti-Acne Therapies

Topical retinoids:

- ✓ **Normalize desquamation**
- ✓ **Reduce inflammatory response**



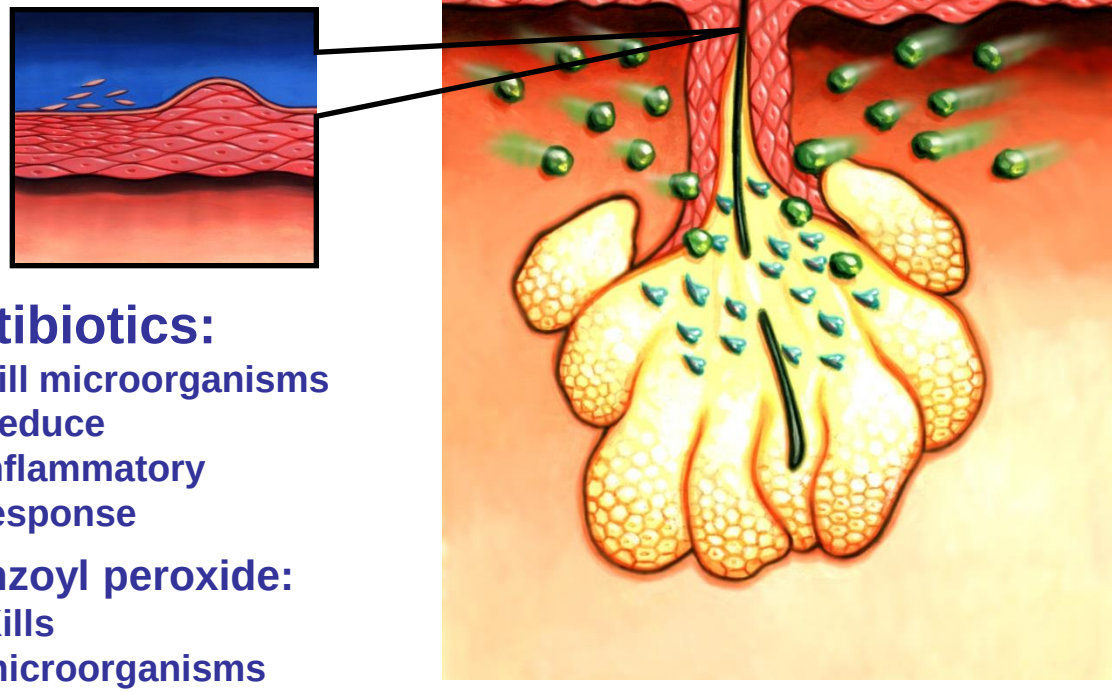
Benzoyl peroxide:

- ✓ **Kills microorganisms**

Actions of Anti-Acne Therapies

Topical retinoids:

- ✓ **Normalize desquamation**
- ✓ **Reduce inflammatory response**



Antibiotics:

- ✓ **Kill microorganisms**
- ✓ **Reduce inflammatory response**

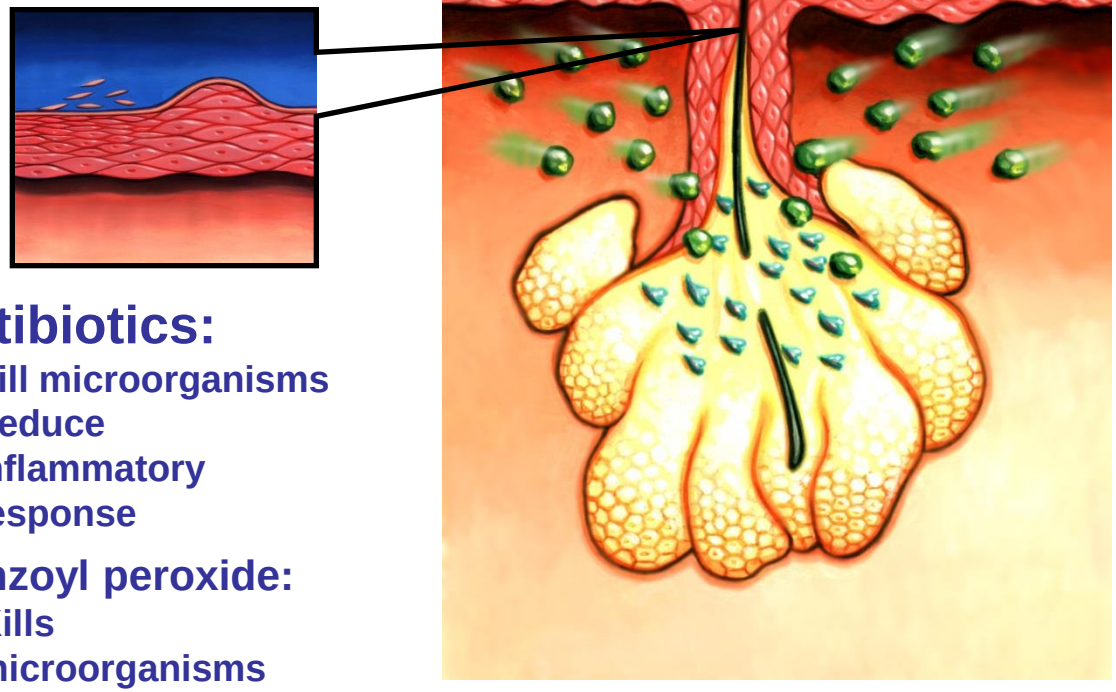
Benzoyl peroxide:

- ✓ **Kills microorganisms**

Actions of Anti-Acne Therapies

Topical retinoids:

- ✓ Normalize desquamation
- ✓ Reduce inflammatory response



Antibiotics:

- ✓ Kill microorganisms
- ✓ Reduce inflammatory response

Benzoyl peroxide:

- ✓ Kills microorganisms

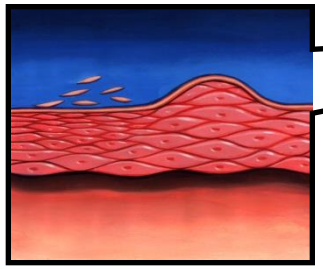
Hormones:

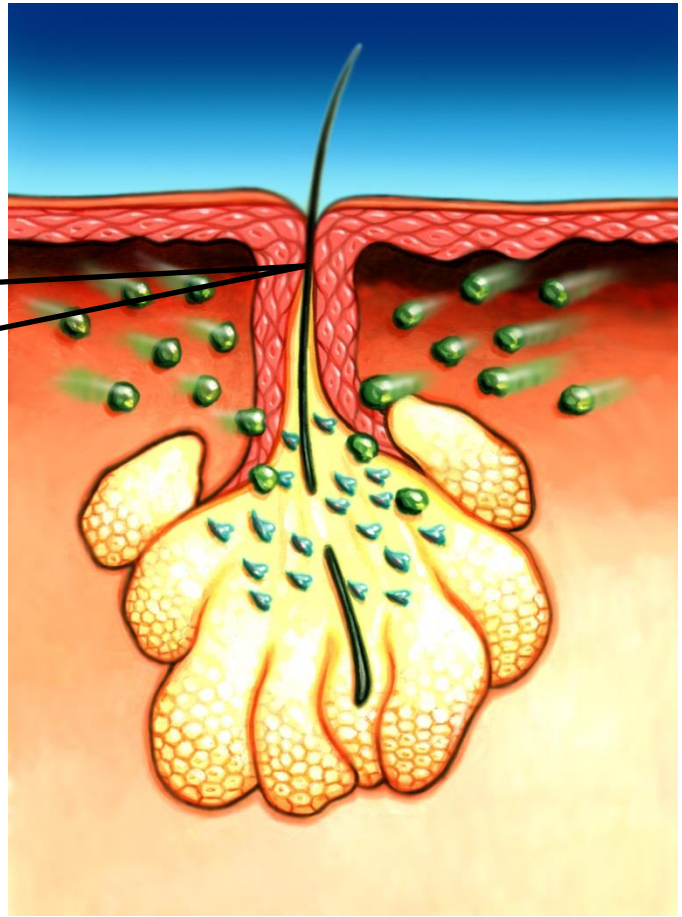
- ✓ Reduce sebum production

Actions of Anti-Acne Therapies

Topical retinoids:

- ✓ Normalize desquamation
- ✓ Reduce inflammatory response





Antibiotics:

- ✓ Kill microorganisms
- ✓ Reduce inflammatory response

Benzoyl peroxide:

- ✓ Kills microorganisms

Oral Isotretinoin:

- ✓ Reduces sebum
- ✓ Normalizes desquamation
- ✓ Inhibits *P acnes*
- ✓ Reduces inflammatory response

Hormones:

- ✓ Reduce sebum production

Treatment of Acne vulgaris

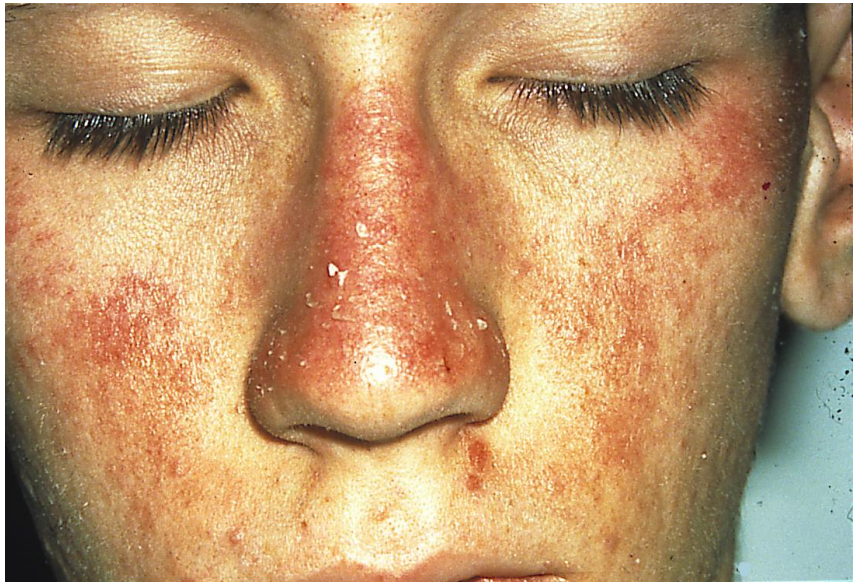
- Use treatments that act on different stages of pathogenesis
- Combination therapy has good evidence base

Treatment of Mild Acne vulgaris

- Topical treatment
  - Topical retinoid plus
  - Topical antimicrobial e.g.
    - Benzoyl peroxide
    - Benzoyl peroxide/ antibiotic combination
    - Antibiotic alone preparation

Management of retinoid dermatitis

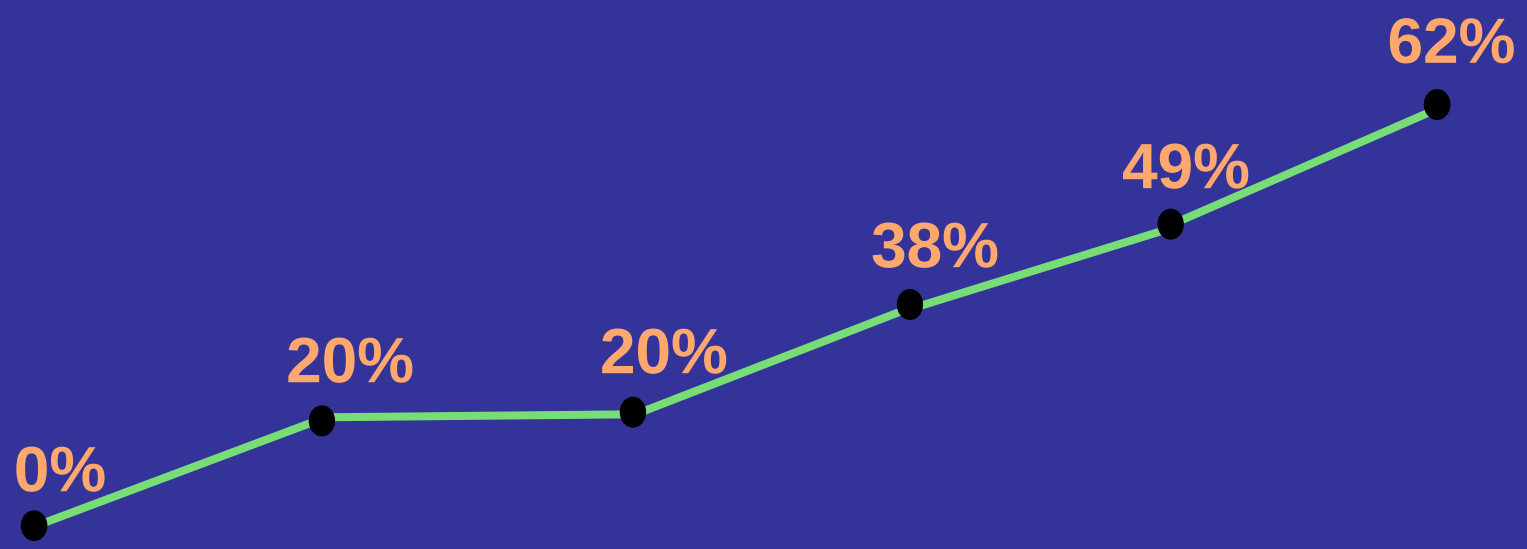
- Warn patients
- Thin application
- Use non-comedogenic mositurizers
- If sensitive
  - < daily application
  - 30 minutes short contact then apply moisturiser



Topical Antimicrobials

- Designed to kill *Proprionibacterium acnes*
- Also have anti-inflammatory effects
- Available preparations
  - Benzoyl peroxide (BPO)
  - Erythromycin (perhaps with BPO or zinc)
  - Clindamycin (perhaps with BPO)

Resistance of *P. acnes* to antibiotics



1976	1978	1988	1993	1995	1996
USA	USA	UK	UK	UK	UK
Leyden	Crawford	Eady	Eady	Jones	Jones
	E.C.T	E.C.T.	E.T.D.Tr.	E.C.T.	E.C.T.

E= Erythromycin C= Clindamycin D= Doxycycline Tr= Trimethoprim T= Tetracyclines

Eady EA. *Dermatology*. 1998;196:59-66.

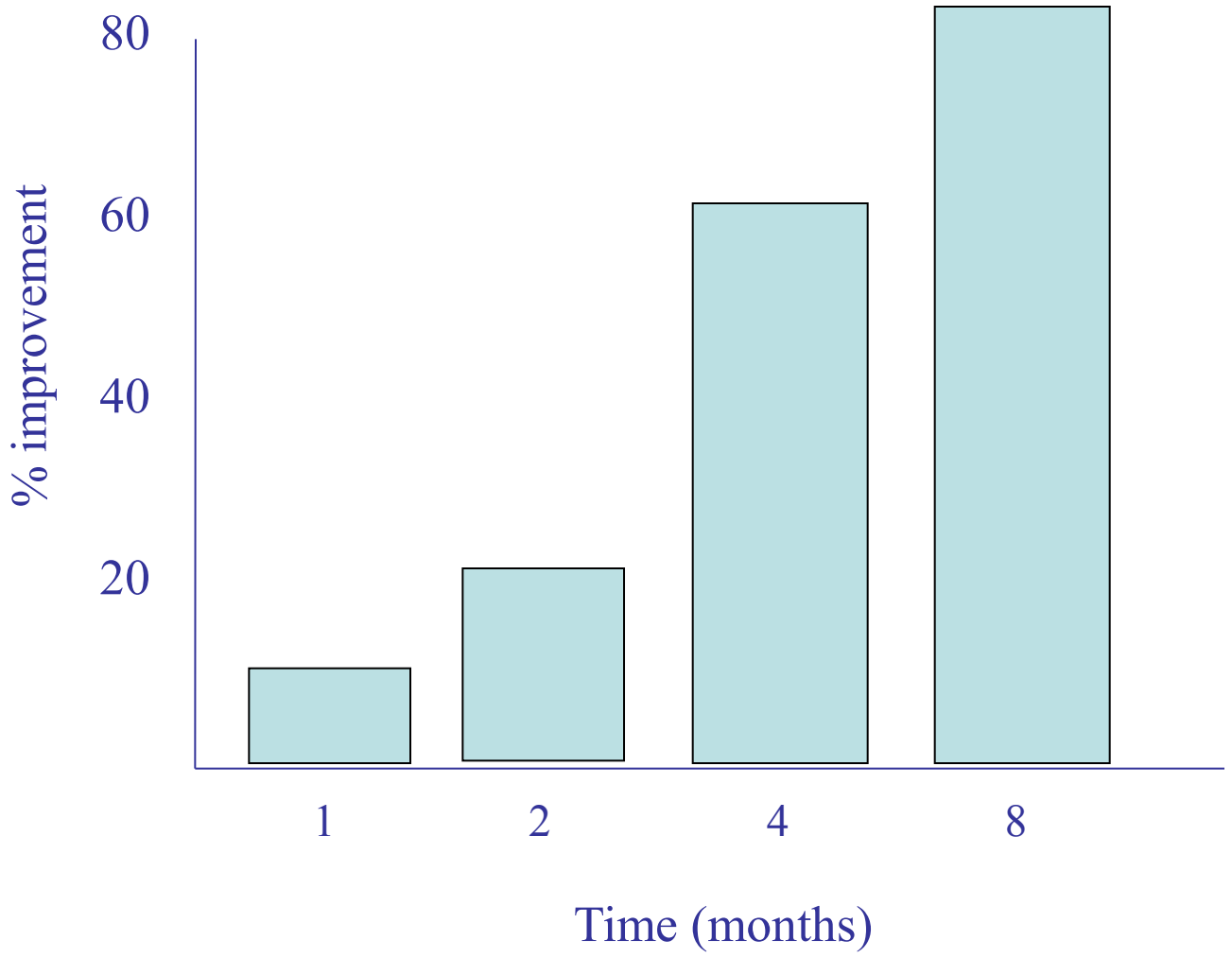
Treatment of mild acne vulgaris

- Comedonal acne
  - Retinoid e.g. adapalene cream
- Mild inflammatory acne
  - Adapalene + BPO combination
  - Or Clindamycin + BPO in mornings and adapalene at night

Treatment of Moderate Acne vulgaris

- Males and females
  - Topical retinoid + benzoyl peroxide
  - PLUS oral antibiotic
    - Tetracyclines
      - Lymecycline 408mg od-bd
      - Doxycycline 100mg od
    - Trimethoprim 200-300mg bd (allergic rash 5%)
    - Macrolides
      - Erythromycin 500mg bd (safe in pregnancy)
      - Clindamycin 150mg bd

The Expected Rate of Response to Acne Therapy (excluding oral isotretinoin)



Moderate acne vulgaris in females

- Persistent acne occurs very commonly occurs in women
- Often perioral
- Premenstrual flares
- Association with cigarette smoking (odds ratio 4)

Managing Adult Female Acne vulgaris

- 81% report failure or oral antibiotics
- 15-30% relapse after oral isotretinoin
- Most have **normal androgen hormone levels**
- Some have abnormal androgen hormone levels
  - Commonest cause:

    polycystic ovarian syndrome

Endocrine Evaluation

- Not routinely useful
- Indications
  - Irregular menses
  - Hirsuitism
  - Severe or late onset acne
  - Failure to respond to therapy
- Tests
  - 1st half of menstrual cycle
  - Stop OCP for 4-6 weeks
  - Testosterone & SHBG
    - Free testosterone raised in PCOS
  - Dehydroepiandrosterone sulphate (DHEAS) &

    17-OH progesterone
    - Raised in congenital adrenal hyperplasia

Oral Contraception and Acne vulgaris

- Avoid progesterone only contraceptives
  - *e.g.* minipill,
    Depo-provera
  - Testosterone-like effect
  - Causes severe flares
- Combined OC
  - Good choice in females with acne
  - Best in < 35 y.o. non smokers
  - Multiple types effective
  - Yasmin and Dianette contain androgen antagonist

    Added benefit

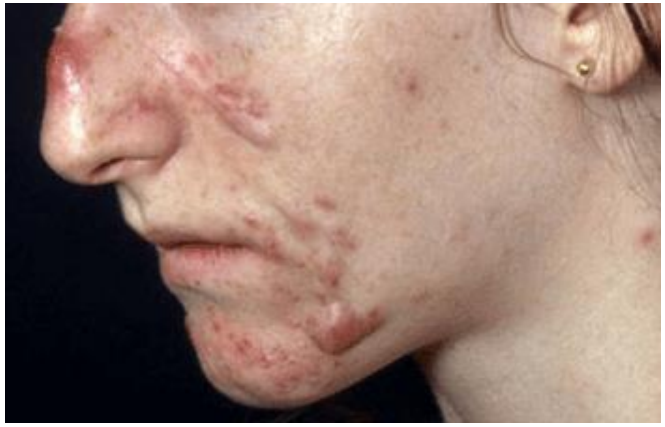
Management of Severe Acne vulgaris

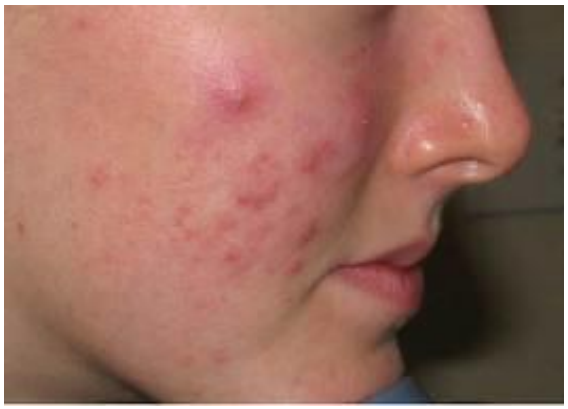
- Oral Isotretinoin (‘*Roaccutane*’)
- Most powerful acne treatment available
- Revolutionised treatment of acne in 1980s
- Mechanism:
  - Powerful effects on cell differentiation/ division
  - Hypoplasia of sebaceous gland (↓ sebum)
  - Reduces comedome formation
  - Indirect killing of *Proprionibacterium acnes*

Oral Isotretinoin- Indications

- Nodulocystic acne
- Moderate acne not responding to two oral antibiotics
- Acne causing significant scarring
- Acne (any severity) associated with severe psychological morbidity

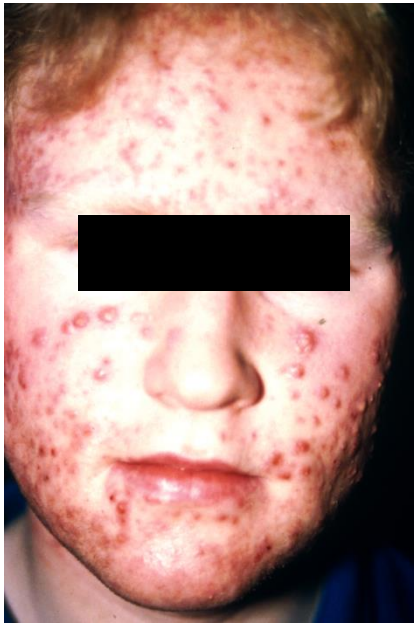
  (including dysmorphophobia)

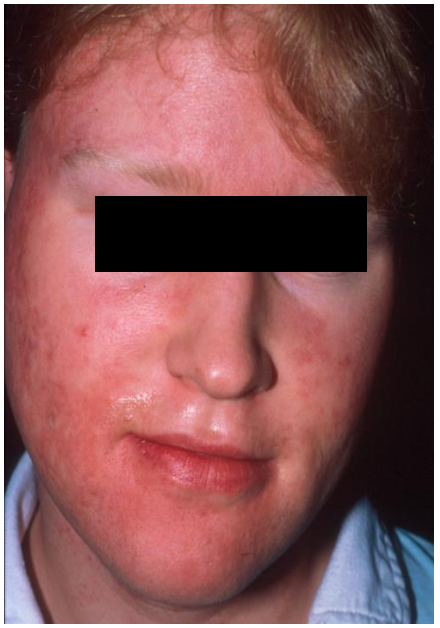




Oral Isotretinoin-Efficacy

- Clears acne in 95%
- Long term remissions occur
- 30-50% will relapse, but usually slowly and after several years





Isotretinoin- Side Effects

- Teratogenic
- Given to women of reproductive age
  - Pregnancy prevention programme
  - Two simultaneous forms of contraception
  - Negative monthly pregnancy tests during course

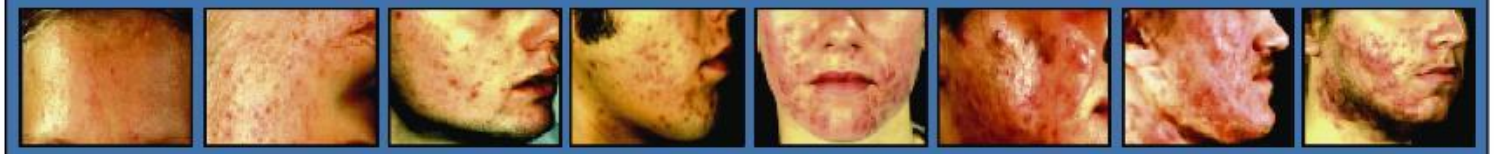
Isotretinoin- side effects

- Lip/skin dryness (chelitis/xerosis) 100%
- Headache 10%
- Arthralgia/ myalgia 10%
- Flare of acne 5-10%
- Elevated LFTs/ lipids
- Hair loss
- Depression/ anxiety/ suicide- idiosyncratic?
  - MUST WARN PATIENTS

Isotretinoin and suicide risk

- Retrospective cohort study
- 5756 patients given isotretinoin 1980-9
- Cause of death registers 1980-2000
- Suicide recorded and compared to standard incidence levels (ag, sex year)

- 128 suicide/ attempted suicide
- 1.57 OR *before* treatment
- 1.78 during/ 6 months after treatment
- 1.04 for 15 years after treatment



	MILD		MODERATE		SEVERE
	Comedonal	Papular/pustular	Papular/pustular	Nodular[2]	Nodular/Conglobate
1st Choice	Topical Retinoid	Topical Retinoid + Topical Antimicrobial	Oral Antibiotic + Topical Retinoid +/- BPO	Oral Antibiotic + Topical Retinoid + BPO	Oral Isotretinoin[3]
Alternatives	Alt. Topical Retinoid or Azelaic acid* or Salicylic acid	Alt. Topical Antimicrobial Agent + Alt. Topical Retinoid or Azelaic Acid*	Alt. Oral Antibiotic + Alt. Topical Retinoid +/- BPO	Oral Isotretinoin or Alt. Oral Antibiotic + Alt. Topical Retinoid +/- BPO/Azelaic Acid*	High Dose Oral Antibiotic + Topical Retinoid + BPO
Alternatives for Females	See 1st Choice	See 1st Choice	Oral Antiandrogen[5] + Topical Retinoid/ Azelaic Acid* +/- Topical Antimicrobial	Oral Antiandrogen[5] + Topical Retinoid +/- Oral Antibiotic +/- Alt. Antimicrobial	High Dose Oral Antiandrogen[5] + Topical Retinoid +/- Alt. Topical Antimicrobial
Maintenance therapy	Topical Retinoid		Topical Retinoid +/- BPO		

[1]Consider physical removal of comedones; [2]With small nodules (>0.5 - 1 cm); [3]Second course in case of relapse; [4]For pregnancy, see text; [5]See text
*There was not consensus on this alternative recommendation, however, in some countries Azelaic acid prescribing is appropriate practice

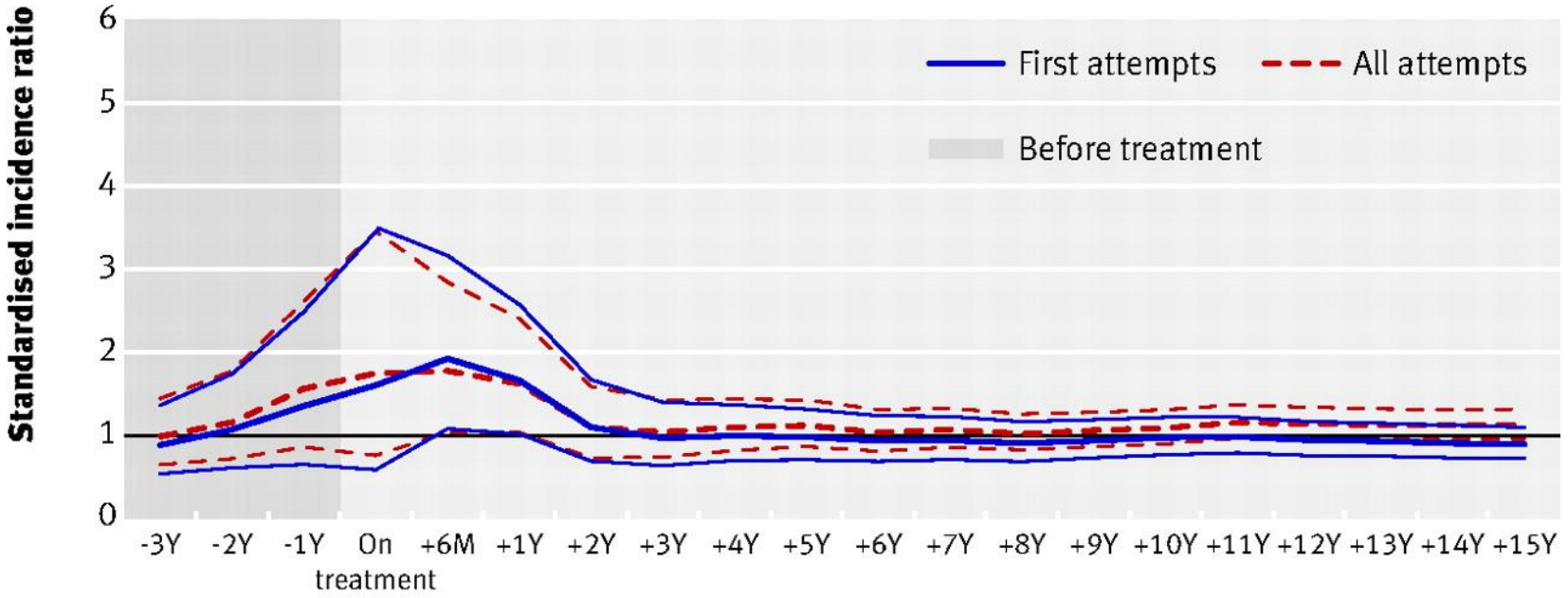
Questions?

Group Discussion

- Who gets acne?
- How do people react when they see someone with acne?
- How do people with acne feel?

- What can people with acne do to help themselves?

Fig 1 Standardised incidence ratios for accumulated first suicide attempts and all attempts from up to three years before (shaded area) to up to 15 years after treatment in all patients.



Cumulative No

First	20	16	10	6	15	20	22	28	37	44	49	56	60	68	77	84	86	90	92	94
All	27	21	14	8	17	24	28	38	52	65	71	85	92	106	119	136	143	149	155	161

Sundström A et al. BMJ 2010;341:bmj.c5812