

ACNE

**Rural GP Conference
Acne Workshop**

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DEFINITION of ACNE VULGARIS

Acne is a skin disease affecting the pilosebaceous unit. It is characterised by comedones, papules, pustules, nodules, cysts &/or scarring, primarily on the face and trunk.

Acne is most common in adolescence, peaking at age 16-20yrs, but can occur at any age. In addition to the physical lesions, acne can have profound psychological and social impact on patients.

AIMS of ACNE PRESENTATION

To discuss:

- Pathogenesis of acne
- Clinical Assessment of a patient with acne
- Psychological morbidity a/w acne
- Acne grading systems
- Diagnostic tests
- Differential diagnoses
- Available treatments
- Maintenance treatment
- Treatment failure
- Criteria for Referral
- Use of oral isotretinoin and its side effects
- Primary and Secondary Prevention

PATHOGENESIS of ACNE

Acne is polygenic and multifactorial.

4 main pathogenic factors contribute to the disease:

1. Sebaceous hyperplasia & excess sebum production- under androgenic stimulus
2. Ductal hyperproliferation & comedone formation
3. *P. acnes* colonisation of the duct
4. Inflammation and immune response.

Assessment of a patient with acne

Pre-treatment

1. **Patient history:** age, skin prototype, current &/or past treatments and their effects, family history, PMHx, present hormonal medication eg. COC, occupation, hobbies and social history.
2. **Examination:** lesions types, acne extent and severity (grading) and scarring.
3. Assess for any **aggravating factors**.
4. **Psychological** assessment as indicated.
5. **Photographic documentation** worth considering

PSYCHOLOGICAL ASSESSMENT

Assessing psychological morbidity:

Disease specific questionnaires:

- **CADI** (Cardiff **A**cne **D**isability **I**ndex)
P score maximum of 15
- **APSEA** (**A**ssessment of **P**sychological and **S**ocial **E**ffects of **A**cne.
Score >90 = significant
(sample of these questionnaires provided)

CADI Questionnaire

(Motley and Finlay, 1992)

1. As a result of having acne, during the last month have you been aggressive, frustrated or embarrassed?
2. Do you think having acne over the last month interfered with your daily social life, social events or relationship with members of the opposite sex?
3. During the last month have you avoided public changing facilities or wearing swimming costumes because of your acne?
4. How would you describe your feelings about the appearance of your skin over the past month?
5. Please indicate how bad you think your acne is now.

Classification of Acne

- No single uniform standardised grading system. Acne is commonly classified by:
- **Type-**
comedones/papular/pustular/nodulocystic
- **Severity-**
mild/moderate /severe/very severe
- **Inflammatory/non-inflammatory** lesions

Acne Grading Systems

Multiple grading systems have been used:

1. Leeds revised acne grading system- grades 1 to 12
2. FDA Global scale- grade 0 to 4
3. Cook's system
4. Pillsbury scale
5. TNRST score (**T**ype, **N**umber, **R**egion, **S**carring, **T**reatments tried)- max score 20

Preferred Simplified Classification

- Comedonal
- Mild
- Moderate
- Severe/nodulocystic























Figure 16.39 Patient with multiple cysts prior to treatment with intralesional triamcinolone.



Figure 16.40 Patient shown in Figure 16.39 after three treatments with intralesional triamcinolone at three-weekly intervals.

Other Presentations of Acne

- Acne conglobata
- Acne fulminans
- Acne mechanica
- Acne excoriee des jeunes filles
- Acnieform eruption caused by drugs
- Infantile Acne





Drugs Causing Acne

- Oral and topical **steroids**
- Male taking **hormonal** treatment for breast enlargement
- **Lithium** carbonate
- **Chloracne**- most well known case is the dioxin poisoning of Viktor Yushenko in 2004.
- **Chemotherapy** with Epidermal growth factor receptor inhibitors- eg. cetuximab and trastazumab (herceptin)





Diagnostic Tests

Investigations are rarely indicated.

- Hormonal assessment in the presence of significant features of hyper-androgenicity- hirsutism, very irregular menses, PCOS or late onset congenital adrenal hyperplasia. Check for elevated total testosterone, prolactin, LH & FSH, DHEA-S, FA index & SHBG. Ovarian USS.
- Bacterial culture if gram negative folliculitis suspected
- FBC/ WBC and ESR- leukocytosis and elevated ESR in acne fulminans

Differential Diagnoses

- Folliculitis
- Gram negative folliculitis
- Perioral dermatitis
- Pyoderma faciale
- Rosacea
- Multiple syringomata
- Acneiform eruptions
- Pomade acne
- Acne keloidalis nuchalis
- Chloracne
- Favre-Racouchet synd
- Adenoma sebaceum (angiofibromas of Tuberous sclerosis)















Complications and Special situations a/w Acne

- Post-inflammatory hyperpigmentation
- Post-inflammatory hypopigmentation
- Atrophic and Ice-pick scars
- Keloidal/hypertrophic scarring
- Psychological scarring

Therapeutic Goals in Acne Treatment

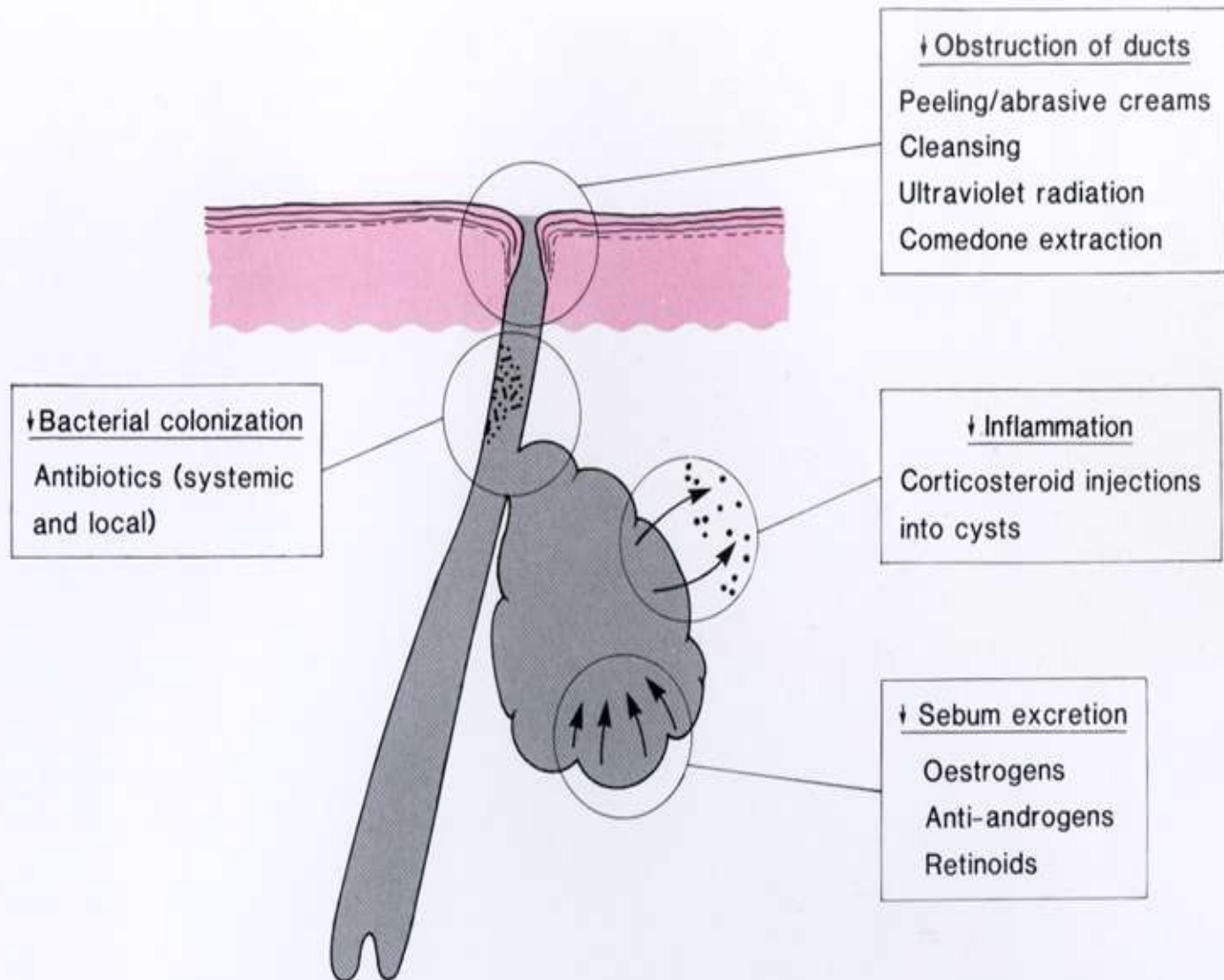
- Resolve existing lesions
- Prevent scarring
- Suppress the development of new lesions

Medication “adherence” has a vital role in the success of treatment

ACNE THERAPIES

Aim of Rx is to:

1. Reduce production of sebum
2. Normalisation of follicular keratinisation, thus unblocking comedones
3. Reduce & prevent growth of *P. acnes*
4. Reduce associated inflammation



Available Treatments for Acne

1. Topical
2. Systemic
3. Combined
4. Hormonal
5. Physical
6. Isotretinoin-considered separately
7. Specific Treatments for acne scarring.

DISCUSSION WITH THE PATIENT

Time spent discussing acne with the patient
will pay dividends in the future

- Very important to ensure patient compliance and to relieve anxiety
- Emphasize:
 - . That acne is a **chronic disease**
 - . **Long term therapy** may be needed
 - . Acne is a **slow responding** disorder with little improvement in the first 3-5/52
 - . Need for **continued compliance**

DISCUSSION CONTINUED

Certain physiological events may influence acne

- Stress may make acne worse
- A premenstrual flare is common in 70% of women
- Sunshine often helps acne but only temporarily

Topical Treatments

Anti-comedonal

- Benzoyl peroxide (BPO)
- Azelaic acid (skinoren)
- Topical retinoids
- Topical salicylic acid preparation

Available **TOPICAL TREATMENTS for ACNE**

Anti-inflammatory

■ **Topical retinoids**

Adapalene (differin), isotretinoin (isotrex) & tretinoin (Retin-A)

■ **Non-antibiotic antimicrobials**

BPO and azelaic acid

■ **Topical antibiotic**

clindamycin, erythromycin, tetracycline

■ **Combination Therapy**

zinc/erythromycin (zineryt), BPO/erythromycin (benzamycin) or, BPO/clindamycin (DUAC), isotretinoin/erythromycin (isotrex).

Side Effects associated with Topical Treatments for Acne

1. Primary Irritant Dermatitis
2. Allergic Dermatitis
3. Drug specific reactions
4. *P. acnes* resistance

S/Es of Topical Acne Rx

Primary Irritant Dermatitis

- Relatively common
- Reduce frequency of application
- Use an oil-free moisturiser
- Low dose topical steroid used for a few days

Allergic Dermatitis

- Very uncommon
- Necessitates withdrawal of the topical agent
- May require patch testing

S/Es of Topical Acne Rx cont'd

Drug specific reactions

- Bleaching of the clothes and hair with benzoyl peroxide
- Topical tetracyclines can make the skin fluoresce under fluorescent lights

P. acnes resistance

- Can occur with topical antibiotics
- Less with combined therapies
- **No resistance of P. acnes to isotretinoin**

Oral Antibiotics

- Doxycycline 50mg to 200mg /day
- Erythromycin 400mg to 500mg bid
- Tetralysal 408mg bid
- Minocycline 50 to 100mg /day
- Trimethoprim 200 to 300mg bid

Reducing dose according to response

Hormonal Treatments

- Estelle 35 (ethinyloestradiol 35 mcg and cyproterone acetate 2mg)
- Yasmin (EE 30mcg/drospirenone 3mg)
- YAZ (3 additional days of EE & drospirenone)
- Spirinolactone 100-200mg/day
- Androcur (cyproterone acetate) 50 to 100mg/day)- specialist

PHYSICAL TREATMENTS

- Physical removal of blackheads using a comedone extractor
- Aspiration of and injection of triamcinolone into new cysts
- Cryotherapy of cysts
- Glycolic acid Rx's –as available at Beauty clinics

Acne Treatment Algorithm

Cunliffe WJ and Gollnick H, 2003, J Am Acad Dermatol. In press



MILD

MODERATE

SEVERE

1st Choice¹

Comedonal

Papular/pustular

Papular/pustular

Nodular²

Nodular/Conglobate

Topical
Retinoid

Topical Retinoid +
Topical Antimicrobial

Oral Antibiotic
+Topical Retinoid
+/- BPO

Oral Antibiotic
+Topical Retinoid
+/- BPO

Oral
Isotretinoin³

Alternatives¹

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/Topical Acid*

High Dose
Oral Antibiotic
+ Topical Retinoid
+BPO

**Alternatives
Females^{1,4}**

See 1st Choice

See 1st Choice

Oral Antiandrogen⁵
+ Topical Retinoid/
Azelaic Acid*
+/- BPO

Oral Antiandrogen⁵
+ Topical Retinoid
+/- Oral Antibiotic
+/- Alt. Antimicrobial

High Dose
Oral Antiandrogen⁵
+ Topical Retinoid
+/- Alt. Topical
Antimicrobial

**Maintenance
Therapy:**

Topical Retinoid

Topical Retinoid+/-BPO

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

PRACTICAL TIPS

- Avoid pregnancy with topical retinoids
- BPO- start @ 2.5%, increase to 5% or 10%. Apply thinly. BPO can cause bleaching
- If using topical retinoid and BPO, use BPO mane and retinoids nocte
- Both groups can cause burning, stinging, itching, redness & scaling
- Do not use near eyes, mouth, lips or inside nose
- Antibiotics can lessen effectiveness of COC in the first month of use

IMPORTANT SIDE EFFECTS OF TREATMENT TO CONSIDER

- **Tetracyclines**:-photosensitivity, onycholysis and benign intracranial hypertension
- **Minocycline**:-headaches (dose-related), pigmentary changes, autoimmune hepatitis/LE like syndrome. Advise monitor LFTs, ANA and pANCA in “at risk” patient when Rx > 6/12
- **Erythromycin**:- GIT upset with diarrhoea or nausea
- **Trimethoprim**:-rare hepatic/renal toxicity and agranulocytosis

Tetracyclines in ACNE

BMJ 2008: 158:208-16

- No evidence one tetracycline any better than another
- Probably anti-inflammatory effect most important
- No justification for minomycin
- Subclinical doss of doxy (40mg/day) seem to be effective

ORAL ISOTRETINOIN

The only Rx which affects the 4 main aetiological factors implicated in acne.

- Reduces sebum excretion by 90% in 6/52's
- Reduces comedones by 90% in 3/12's
- Alters the microenvironment of the intra-follicular duct, reducing *P. acnes* numbers
- Direct anti-inflammatory effect

Prescribing of Isotretinoin

- Start Rx at 0.2-0.5mg/kg/day for 2 to 4 weeks
- then maintenance therapy at 0.1-1 mg/kg/day depending on response and tolerance.

65-70% improvement in 6/52's. Usual course is for 16 weeks. After a second course get a further 10% improvement.

- **Cumulative dose over the treatment course of between 120mg/kg and 150mg/kg** is associated with an increased likelihood of prolonged remission.
- Worsening of acne can occur initially, necessitating a course of erythromycin and oral steroids.

ORAL ISOTRETINOIN

- Not recommended in children < 12yrs
- Pre-therapy pregnancy testing and adequate contraceptive advice.
- Pregnancy C/I on therapy and for 4/52's after stopping Rx.
- LFTs, lipids and renal function checked before Rx & one month after starting Rx & every 3/12's thereafter. Diabetic screen if predisposed to diabetes.
- All forms of peeling & wax epilation should be avoided during therapy and for 6/12 afterwards
- Cannot donate blood during & for 4/52's post Rx

SIDE EFFECTS of ISOTRETINOIN MUCOCUTANEOUS

- Cheilitis—in 90%
- Dry mouth and nose –in 40%
- Facial dermatitis & dry skin- up to 60%
- Nasal crusting & nose bleeds- 40%
- Conjunctivitis and dry eyes– in 40%
- Secondary infection with staph. aureus
- Skin fragility, pyogenic granulomata & excessive sweating
- Hair loss- dose related, reversible- 4%
- Photosensitivity- need good sunscreen





SIDE EFFECTS OF ISOTRETINOIN SYSTEMIC

- Markedly **teratogenic**. Does **not** affect sperm
- Associated with adverse psychiatric events (mood swings & depression) in a small number of patients. Concern about possible increased risk of suicide.
- Headaches. Small risk of benign intracranial hypertension
- Arthralgia & myalgia-16%
- Night blindness-affecting some employment eg.pilot
- Blood disorders- hypertriglycidaemia- risk of pancreatitis or steatohepatitis and neutropenia/thrombocytopenia (1%)
- In children –risk of premature epiphyseal closure and skeletal hyperostosis

Does ISOTRETINOIN Increase Risk of DEPRESSION?

- Some epidemiological evidence of depression
- Many anecdotal reports

Archives of Dermatology 2005: 141: 557-60

101 patients 50: 50 split re isotretinoin or antibiotics.

No difference in depression in two groups

Archives of Dermatology 2000: 136: 1231- 36

No increase in relative risk in depression

Does ISOTRETINOIN Increase Risk of DEPRESSION?

Journal Clinical Psychiatry 2008: 69 (4): 526-32

Editorial in Arch Dermatology 2008: 144: 1197-99

**Conclusion from a Case-crossover study
was a relative risk of 2.68.**

**Need to warn patients there is a possible
association between isotretinoin and
depression.**

Prior to Starting Isotretinoin

- Note any previous psychiatric history or problems of depression
- A history of depression is not an absolute C/I to using isotretinoin but must monitor patient more closely
- Alert patient and their family to the potential risk of mood swings & depression
- Ask about depression and suicidal ideation @ each visit
- Refer if any serious psychiatric symptoms occur
- Make sure appropriate **consent** form is signed.

CONTRAINDICATIONS to using ISOTRETINOIN

- Pregnancy or breast feeding
- Concern that the patient will be non compliant with taking the treatment and returning for followup
- Severe hepatic disease
- Hypervitaminosis A
- Uncontrolled hyperlipidaemia
- Allergy to the drug or its components

Treatment of Acne Scars

- Silicone sheets -expensive
- Occlusive therapy with steroid impregnated tape eg. Haelan tape
- Potent topical steroid applied sparingly over hypertrophic scar x 3/12
- I/L steroids
- Excision of keloid scar -risk of recurrence
- Cryotherapy
- Xray therapy-risk of skin cancer developing later
- Laser Rx- for atrophic and icepick scars
- Injection of collagen and autologous fat

Reasons for Poor Response to Rx

20% of patients show a poor response to Rx

1. The wrong diagnosis
2. Inadequate compliance
3. Inappropriate assessment of the overall acne severity
4. Side effects/intolerance to therapy
5. P. acnes resistance (resistance to erythromycin in 65% & tetracycline in 20% of all acne cases)

Maintenance therapy

After successful Rx of any grade:

- Topical retinoids
- Or, topical retinoids plus benzoyl peroxide (BPO)
- Treatment may need to be continued for some years

General Management

1. Do not pop, squeeze, or pick acne lesions
2. Use "non-comedogenic " skin products. Avoid scrubs
3. Avoid acne irritants such as airborne grease from fast food restaurants, rubbing or friction from sporting equipment
4. Use the amount of product prescribed. More is not better.
5. Acne products can increase photosensitivity. Use sunscreen (factor 30+) daily and wear a hat in the sun

Primary Prevention

Previous studies exonerating “junk food” are now believed to be flawed.

Low glycaemic index (GI), and low fat diets are important in the holistic management of acne.

Secondary Prevention

- Good skin care techniques
- Use non-comedogenic products
- Avoid getting hair products on the face
- Not to pick, squeeze or scratch

CRITERIA for REFERRAL

- Severe variant of acne eg. acne fulminans or gram negative folliculitis
- Severe nodulocystic acne
- Severe psychological problems, or morbid fear of deformity (dysmorphobia)
- At risk of or, are developing scarring despite primary care therapies
- Suspected of having a significant underlying endocrinological cause needing further assessment

Treatment of Acne in Pregnancy

- Reassurance may be all that is required for mild acne during pregnancy. Topical retinoids MUST be avoided, but topical benzoyl peroxide is considered safe.
- For moderate acne during pregnancy topical benzoyl peroxide or topical antibiotic can be used. Tetracycline antibiotics MUST be avoided in pregnancy, but oral erythromycin is considered safe.
- For moderately severe acne during pregnancy where oral antibiotics are considered necessary erythromycin is safe to use. Isotretinoin MUST be avoided in pregnancy.

References & Useful Websites

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