ACNE VULGARIS

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Conflicts of Interest

- Galderma: sponsored meeting attendance, honoraria
- Pierre-Fabre: sponsored research
- Johnson and Johnson: medical advisor
- Nutricia: sponsored meeting attendance and honoraria
“A real girl isn't perfect and a perfect girl isn't real.”

– Harry Styles

One Direction
QUESTION 0

• Which of the following has NOT been shown to be associated with acne?
  – Family history of acne
  – Anticonvulsant medications
  – Dairy products
  – Chocolate
  – Stress
Four primary causes of acne

Treatment should target as many of these factors as possible

- Propionibacterium acnes (P acnes) follicular colonisation
- Alteration in keratinisation process
- Inflammation and immune response
- Sebum production by sebaceous gland


What causes acne?

• Onset often between 8-12 years
• Peaks at 15-18 years
  – 80-100% of adolescents affected
• Usually resolves by 25 years
  – 12% women and 3% men have acne into 30s
What causes acne?

• Risk factors for severe disease
  – Early onset of comedones
  – Family history of scarring acne
• Hormonal factors
  – Androgens, polycystic ovarian syndrome, stress
• Diet
  – Low glycaemic index, milk
  – Not chocolate
• Environmental factors
  – Picking, occlusive skin products, humidity
• Medications
  – Steroids, dioxin, anti-convulsants, gefitinib
Why does acne matter?

• Discussion
Why does acne matter?

• Cosmetic effects
  – Permanent scarring

• Physical discomfort

• Psychosocial effects
  – Impaired self-image & self-esteem
  – Embarrassment
  – Impaired socialisation
  – Reduced participation & enjoyment of social activities
  – Increased unemployment
Acne in New Zealand

• NZ Youth2000 survey
  – Computerised survey of 12000 secondary students
• 67% teenagers report having acne
• 14% report acne to be a ‘really bad’ or ‘terrible’ problem
  – 24% of Pacific female

• Acne prevalence in secondary school students and their perceived difficulty in accessing treatment.
• D Purvis, E Robinson, P Watson. NZMJ 117(1200) Aug 2004
“Have acne or pimples been a problem for you?”

- Not a problem: 33%
- Not too bad: 52%
- Really bad: 10%
- Terrible: 4%

Adjusted percentages:
- Not a problem: 33%
- Not too bad: 52%
- Really bad: 10%
- Terrible: 4%

‘Problem acne’
Depressive symptoms and acne

Odds ratio 2.0 (1.7 - 2.5)  P<0.001
Depressive symptoms and severity of acne

Adjusted percentage

Self-reported acne

'Not a problem' 11
'Not too bad' 13
'Really bad' 19
'Terrible' 36
Anxiety symptoms and acne

No/minimal acne: 4

'Problem acne': 9

Odds ratio 2.3 (1.7 - 3.0)  P<0.001
Suicidal behaviour and acne

Odds ratio 1.8 (1.5 - 2.2)  P<0.001

After controlling for depressive and anxiety symptoms:
Odds ratio 1.5 (1.2-1.9)  P<0.001
Acne in New Zealand

• NZ Youth2000 students with ‘problem acne’ had:
  – 2.0 x incidence of depressive symptoms
  – 2.3 x incidence of anxiety symptoms
  – 1.8 x incidence of suicidal behaviour

• The increased risk of suicidal behaviour was independent of mood symptoms

• Demonstrates association not causality

• Acne, anxiety, depression and suicide: a cross-sectional survey of New Zealand secondary school students.
• D Purvis, E Robinson, S Merry & P Watson J Paed Child Health Dec 2006
Effect of acne treatment

• Treatment of acne improves mood

• Isotretinoin and risk of suicide
  – Anecdotal reports of depression and suicide
  – Not supported by systematic reviews
Retrospective cohort study of 5756 Swedish patients 17 - 49y treated with isotretinoin from 1980-2001
Hospitalisation data for suicide attempt

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
The risk of suicide attempt began to rise three years before treatment with isotretinoin. Increased risk of suicide attempts persists for over a year after treatment has been completed.

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.

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Sundström A et al. BMJ 2010;341:bmj.c5812
Increased suicide risk associated with severe acne
- psychosocial effects of acne
- acne treatment eg tetracyclines
Persists after acne has been treated

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## Types of acne

<table>
<thead>
<tr>
<th>Non-inflammatory</th>
<th>Inflammatory (mild–moderate)</th>
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<th>Nodular/cystic</th>
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<td>Non-scarring</td>
<td>Comedones</td>
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<tr>
<td></td>
<td>• Inflammatory lesions (papules and pustules) • Primarily face</td>
<td>• Inflammatory lesions (papules and pustules) • Extensive involvement trunk and limb</td>
<td>• Inflammatory lesions • Cysts, nodules • Scarring • Often widespread • Possible systemic symptoms • Psychological distress/ depression</td>
</tr>
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Courtesy of 2003 Acne Advisory Board.
• Comedones
  – Open: blackheads
  – Closed: whiteheads
• Scarring unlikely
• Papules
• Pustules
• Scarring unlikely
• Papules and pustules
• Nodules
  – small solid lumps under the surface
• Scarring may occur
- Pustules
- Nodules
- Cysts
- Abscesses
- Scarring present
Global Alliance: acne treatment algorithm

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Only products that are antibiotic free should be used for maintenance therapy

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AB = antibiotic, BPO = benzoyl peroxide

Acne management

• Be guided by the patient’s concern as to whether to treat or not

• Patients often ask about diet
  – Encourage healthy eating

• Wash twice daily with a gently facial cleanser
Treatment options

• Topical
  • Benzoyl peroxide (BPO)
  • Antibiotics - clindamycin, erythromycin
  • Retinoids - retinoic acid, tretinoin*, adapalene*
  • Combinations - BPO/clindamycin, BPO/adapalene

• Oral antibiotics
  • Tetracyclines*, erythromycin*, trimethoprim*

• Oral contraceptives
  • Combined OCPs*
  • Antiandrogenic: Cyproterone acetate with ethinyloestradiol*

• Oral isotretinoin*

• Other
  • Glycolic acid peels, IPL, blue light....
Case 1

• 14 year female attending for asthma inhalers
• Regular menses, not sexually active
• No other health problems
• Multiple >20 open and closed comedones on face
• No inflammatory lesions
QUESTION 1: How would you manage this?

- No treatment indicated
- BPO wash
- Topical erythromycin
- Topical erythromycin/BPO
- Topical adapalene
- Topical adapalene/BPO
Case 2

- 17 year female
- Concerned about her face with upcoming ball
- Not sexually active
- Regular menses
- Open and closed comedones with some papules
- Mild inflammation
- Scarring unlikely
QUESTION 2
How would you manage this?

• No treatment indicated
• Benzoyl peroxide wash
• Topical erythromycin/BPO
• Topical adapalene
• Topical adapalene/BPO
• Oral doxycycline
Case 3

- 13 year old student
- 2 years of increasing acne
- Tried ‘Proactive’
- No other medical problems
- Keen swimmer
- Pubertal but no menarche
QUESTION 3
How would you manage this?

• Benzoyl peroxide wash
• Topical erythromycin/BPO
• Topical retinoid
• Oral doxycycline
• Oral doxycycline + topical retinoid
• Other
Benzoyl peroxide

• Formulations
  – Creams or wash
  – 2.5%, 5%, 10%
• Side effects:
  – Irritation, dryness - dose related; bleaching of clothes/bedding
• 2.5% as effective as 5% & 10%
• Available without a prescription
• Cheap
• Useful for inflammatory acne
Topical antibiotics

Erythromycin, clindamycin
• Less irritation
• Some systemic absorption, avoid in lactation
• Antibiotic resistance increasing
  – Simonart et al, Brit J Dermatol Aug 2005

Clindamycin 1% / BPO 5%
• Results in significantly greater reduction in acne lesions and less P acnes resistance compared with clindamycin alone
  – Cunliffe et al, Clin Therapeutics, Jul 2002
Topical retinoids

Adapalene, tretinoin, isotretinoin

- Side effects: Irritation, dryness, photo-sensitivity
- Initial flaring of acne
- Don’t need to be on contraception but stop if pregnant
- Useful for comedonal acne

Adapalene 0.1% / BPO 2.5%

- Significantly greater reduction in lesions and faster onset of action compared with adapalene or BPO alone
Percentage of patients ‘clear’ or ‘almost clear’

‘Clear’ ‘almost clear’ or ‘mild acne’ at week 12:
75% Adapalene-BPO, 62.5% Adapalene, 58.8% BPO, 52.6% vehicle
Topical acne treatment
- key points

• Effective for mild-moderate acne
  – Apply once or twice daily to affected areas
    • *Not* a spot treatment
  – Use a gentle wash product
  – Non-comedogenic moisturiser, make up and sun protection

• Can cause irritation

• Take 6-12 weeks to see benefit
Case 4

- 15 year old woman
- Acne for 3 years
- Tried clearasil and various beauty products
- Menses heavy
- Iron deficient
- No other medical problems
- Not sexually active
QUESTION 4
How would you manage this?

• Topical erythromycin + BPO
• Topical retinoid
• Oral doxycycline +/- topical retinoid
• Oral contraceptive +/- topical retinoid
• Other
Combined oral contraceptives

- COC decrease circulating androgens and reduce sebum production
- All COC have some effect against acne
- Antiandrogenic (eg cyproterone) may be more effective
  - Consider esp if other androgenising features eg PCOS
- POP, depot or implant progesterone may worsen acne

- Combined oral contraceptive pills for treatment of acne
Case 5

- 17 year young man
- Acne worsening despite topical differin
- Now on back and chest
- Tried oral doxycycline but nauseated, stopped at 2 weeks
- Good health
- Body builder
QUESTION 5
How would you manage this?

- Topical retinoid + BPO
- Oral minocycline + topical retinoid
- Oral erythromycin + topical retinoid
- Oral isotretinoin
- Other
QUESTION 5a

If treating with an oral antibiotic when would you plan to review?

• 1 week
• 1 month
• 3 months
• 6 months
• No routine review
Systemic antibiotics

• Treat Propionibacterium acnes
• Anti-inflammatory effects
• Doxycycline
  – S/E gastrointestinal, photosensitivity, benign intracranial hypertension
• Minocycline
  – Drug induce lupus, pigmentation
• Erythromycin
  – Highest rates of drug resistance
Case 6

- 18 year old student
- 6 month history of untreated acne
- Face, chest and back
- Bleeding at times
- No other medical problems
- Cricket player
QUESTION 6
How would you manage this?

- Topical retinoid
- Oral doxycycline + topical retinoid
- Oral erythromycin
- Oral isotretinoin
- Other
Isotretinoin

• Systemic retinoid (vitamin A analogue)
• Acts in 6-8 weeks to reduce sebum production
• Doses used are now lower than previously so fewer side effects
• Treatment course 3-9 months
  – 75% do not require further treatment
Isotretinoin

• Side effects
  – Dry lips, nose, hair thinning
  – Muscle aches and pains
  – Initial acne flare
  – Photosensitivity
  – Benign intracranial hypertension
  – Hyperlipidaemia
  – Hepatitis
  – Blood dyscrasias
Isotretinoin

• Teratogenic
  – Isotretinoin embryopathy
    • Craniofacial, CNS, cardiovascular, thymic, limb reduction
    • 30% with no gross physical malformations have mental retardation
  – 115 pregnancies while on isotretinoin
    • 21 (18%) spontaneous abortion
    • 26 (28%) malformations consistent with isotretinoin embryopathy
    • 7 (7%) other problems
      – Dai WS et al JAAD 1992
Isotretinoin

• Suicide
  – Subject of intense media coverage and parental concern
  – Rates of suicide on isotretinoin similar to general population
  – Studies have shown improvement of mood symptoms with isotretinoin treatment
  – Idiosyncratic reaction to isotretinoin causing depressed mood in <1%
Case 7

- 32 year old woman
- Erythema, papules and pustules over cheeks and nose
- No comedones
- No medical problems
- History of moderate depression
QUESTION 7

How would you manage this?

- Topical antibiotic
- Topical retinoid
- Oral doxycycline
- Antiandrogenic OCP
- Oral isotretinoin
Differential diagnosis of acne

• Rosacea
  – Erythema, flushing, papules
  – No comedones
  – Onset in adult life

• Perioral dermatitis
  – Papular eruption around mouth and eyes
  – No comedones

• Folliculitis
  – Esp in beard area, trunk
  – Bacterial, Pityrosporum

• Pomade acne
  – Occlusive due to thick topical products
# Global Alliance: acne treatment algorithm

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Summary

• Acne can be associated with significant anxiety, depression and suicidal behaviours
• Topical treatments can be very effective for mild-moderate acne
• Systemic treatments should be considered for unresponsive, severe or scarring acne
• Adherence with treatment is often poor
  – Potential to improve this through education and tailored choice of treatment
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