Dermatology

The use and overuse of antibiotics in dermatology.
Can 6 years of continuous oral antibiotic for acne be 'good therapy?'

Dr Stephen Kownacki
Executive chair, Primary Care Dermatology Society (PCDS)
The use and overuse of antibiotics in dermatology

Can 6 years of continuous oral antibiotic for acne be thought ‘good therapy?’

Dr Stephen Kownacki
Executive Chair Primary Care Dermatology Society (PCDS)
Professor Dame Sally Davies  
Chief Medical Officer  

- **Antibiotic resistance**—a threat to global health security
- **Antibiotic resistance**—a threat to global health security and the case for action
- **UK 5 year antimicrobial resistance strategy 2013 to 2018**
- **Antimicrobial resistance (AMR):**
  - 27 October 2017
  - Collection
  - Defra, DH, VMD, PHE
- Information and resources on the Government’s plans to slow the growth of antimicrobial resistance

Defra, Department for Environment Food & Rural Affairs; DH, Department of Health; PHE, Public Health England; VMD, Veterinary Medicines Directorate.

Department of Health. UK five year antimicrobial resistance strategy 2013 to 2018.  
England's Chief Medical Officer has renewed her warning about what she's described as a ‘post-antibiotic apocalypse’ #r4today
Antimicrobial resistance (AMR) is a major concern and a threat to future healthcare in the UK\textsuperscript{1}

One of the primary causes of AMR is the inappropriate prescribing of antimicrobials\textsuperscript{1–3}

Topics to discuss

- Acne
- Rosacea
- Eczema
Acne

• It’s not uncommon for adult patients to take full-dose oral antibiotics for many years

• Is it due to fear of flare recurrence?

• Or lack of clinical review?

Six years in Harrogate studies, personal communication.
• A recent US study has shown that late-onset acne in women is increasing:\(^1\)
  • 45% of women aged 21–30 years had clinical acne\(^1\)
  • 26% of women aged 31–40 had clinical acne\(^1\)
  • 12% of women aged 41–50 had clinical acne\(^1\)
• Another study has shown that comedonal post-adolescent acne (CPAA) is the most prevalent form of acne in adult women:\(^2\)
  • CPAA was frequently of late-onset and closely correlated with cigarette smoking\(^2\)

Oral antibiotics in dermatology

• Roughly 8% of all antibiotics prescribed in the UK are thought to be for dermatological indications\(^1\)

• Given the emphasis on antibiotic stewardship, no longitudinal studies of topical or oral antibiotic use in acne or rosacea exist\(^1\)

• Recent data from the US indicate that average duration of antibiotic use in acne far exceeds current recommendations\(^2\)

Antibiotic resistance

• Cross resistance between erythromycin and clindamycin:
  • To tetracyclines ~20%
  • To erythromycin ~65%

• Unaffected siblings of patients with acne have been shown to carry resistant strains

Inflammatory > antibiotic

Comedonal > retinoid (or BPO)

BPO, benzoyl peroxide.
Use topical antibiotic therapy if inflammatory, and stop as soon as it improves

- Do not use different antibiotics topically and orally
- Oral antibiotics needed for widespread truncal inflammatory lesions or for severe nodulocystic acne
- Commence topical retinoids with short contact initially and/or less frequent application and continue long term
The anti-inflammatory effect

• Importance of anti-inflammatory activity explains why subantimicrobial doses of doxycycline (40 mg daily) have been used to treat acne

• Two clinical trials confirmed efficacy of these doses in moderate inflammatory acne, with no modification of cutaneous flora and no induction of Propionibacterium acnes-resistant strains

Do not use antibiotics as monotherapy

• Add topical retinoid or BPO
• BPO is strongly bactericidal and its addition to antibiotic therapy minimises resistance at sites of application

BPO, benzoyl peroxide.

14-year-old boy

• Facial and chest inflammatory acne
• Graded mild/moderate with no scarring
• Has tried antiseptic washes with no benefit
• Regards it as nuisance not distressed (mother more worried!)
• Photos on his phone for assessment and progress?
Management

• Family and personal history
• Explanation
• Oral lymecycline as widespread and inflammatory
• Topical BPO 2.5–5% daily, then add adapalene slowly at night (or combination)
• Once inflammation settled (? 3 months), stop oral lymecycline and continue adapalene indefinitely — reducing frequency

BPO, benzoyl peroxide.
Acne: primary care treatment pathway

What is acne?
Acne, an inflammatory disorder of the sebaceous glands, is one of the most common dermatological disorders and is considered a chronic disease. Treatment may be required to improve both the physical appearance and prevent physical and psychological scarring. Whilst it is primarily a skin disorder of the young, often clearing up spontaneously, it can affect up to 12% of women and 3% of men over the age of 25. Treatment options for all age groups and both sexes are largely the same, apart from hormonal therapy.

Important information about treatments
Treatments are effective but take time to work (typically up to eight weeks) and may irritate the skin, especially at the start of treatment. Topical and systemic antibiotics should not be prescribed together, or used as sole treatment as bacterial resistance is a growing concern. All treatments should be routinely reviewed at 12 weeks. In the event of pregnancy, topical retinoids and oral tetracyclines should be discontinued.

At review
If treatment goals are reached at the 12 week review:
- Maintenance therapy should be considered
- Discontinue topical/systemic antibiotics

If treatment goals are NOT reached at the 12 week review:
- Review adherence to treatment(s)
- Consider alternative treatments

Grading acne based on lesion type can help guide treatment

<table>
<thead>
<tr>
<th>Treatment graded by the predominant present</th>
<th>Comedones</th>
<th>Papules</th>
<th>Pustules</th>
<th>Nodules/cysts*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical retinoid</td>
<td>Tretinoin, isotretinoin and adapalene</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>BPO</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Azelaic acid 20% – Skinoren</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Topical antibiotics</td>
<td>++</td>
<td>+++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical retinoid/BPO – Epiduo</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Topical retinoid/antibiotic combination</td>
<td>Treacel</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Topical antibiotic/BPO combination</td>
<td>Duac</td>
<td>++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Oral antibiotics</td>
<td>++</td>
<td>+++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined oral contraceptives (for females only)</td>
<td>+++</td>
<td>Strong recommendation</td>
<td>Moderate recommendation</td>
<td>Low recommendation</td>
</tr>
</tbody>
</table>

Refer immediately if:
- Severe psychological distress
- Uncontrolled acne developing scarring
- Nodulo-cystic acne*
- Diagnostic uncertainty
- Patients failing to respond to multiple therapeutic interventions

*Bulldo/cystic acne
Treatment can be initiated, but patients should be referred

PCDS acne guideline. © PCDS November 2015
Acne: practical advice and maintenance

Practical advice
1. Topical retinoids should be used for all grades of acne. Adapalene is better tolerated than other topical retinoids.
2. The irritant reaction with topical retinoids and BPO can be ameliorated by gradual introduction e.g. by short contact initially and/or less frequent application. Concurrent use with light non-comedogenic emollients may be useful.
3. Azelaic acid may be beneficial in patients with darker skin where acne can lead to hyperpigmentation.
4. BPO can cause bleaching of fabric.
5. Oral antibiotics should not be used as sole treatment. They should be prescribed with a topical retinoid and/or a BPO. Tetracyclines are first line and all show similar efficacy. Lymecycline and doxycycline are likely to have better adherence due to their once daily dosage. Minocycline should not normally be used in view of higher risks. Erythromycin is second line (first line in pregnancy) due to high bacterial resistance. Trimethoprim is an option, but uncommonly used in primary care.
6. Oral contraceptives: unopposed progesterones (including LARCs) can make acne worse. Second and third generation combined oral contraceptives are generally preferred. Co-cyprindiol (Dianette) is used in moderate to severe acne where other treatments have failed and discontinued 3 months after the acne has been controlled
7. Combination Products: Combining topical treatments is recommended for most people with moderate acne (ref: NICE CKS). Combination products improve adherence.

<table>
<thead>
<tr>
<th>Product</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epiduo</td>
<td>No issue with antibiotic resistance</td>
<td>Irritation can be a problem</td>
</tr>
<tr>
<td>(adapalene/BPO)</td>
<td>Anticomedonal</td>
<td></td>
</tr>
<tr>
<td>Treclin</td>
<td>Broad spectrum of action</td>
<td>Antibiotic resistance may limit the duration of treatment</td>
</tr>
<tr>
<td>(clindamycin/tretinoin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duac</td>
<td>Rapid onset of action on inflammatory lesions</td>
<td>No action on comedones</td>
</tr>
<tr>
<td>(clindamycin/BPO)</td>
<td>Two strengths available</td>
<td></td>
</tr>
</tbody>
</table>

Top tips and myth busting
Acne is not caused by a poor diet. However, the role of diet in acne remains controversial and a healthy diet is positively encouraged. There is some evidence that a high GI diet can exacerbate acne.
Poor hygiene is not a contributing factor to acne and aggressive washing is to be discouraged. Patients with acne should be encouraged to wash no more than twice a day using gentle, fragrance free cleanser and dissuaded from picking and squeezing spots (pustules).
Non-comedogenic make up and emollients are recommended.
Acne is not infectious.

Maintenance
Topical retinoids should be used for all grades of acne. Adapalene is better tolerated than other topical retinoids.

Further information for healthcare professionals and patients can be found at:

These comments are the opinions of the contributors, reviewed by the PCDS Executive Committee and do not consider NHS costs and local prescribing restrictions, if any.

BPO, benzoyl peroxide; CKS, clinical knowledge summary; GI, glycaemic index; LARC, long-acting reversible contraception; PCDS, Primary Care Dermatology Society.

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PCDS acne guideline.
Acne treatment: general principles

- Review medications:
  - Lithium, vitamin B12 injections, ciclosporin

- Topicals:
  - Anti-inflammatory
  - Bactericidal: important to prevent AMR:
    - Start for 4 hours at a time and three times per week
  - Apply once daily to all facial or back/ chest skin (not just existing spots)
  - Persistence

- Antibiotics:
  - Topical—never alone to prevent AMR
  - Oral—never alone as need to prevent/treat comedonal element

- Review at 6 and 12 weeks
- Consider COCP for women

AMR, antimicrobial resistance; COCP, combined oral contraceptive pill.

PCDS acne guideline.
Pregnancy

- BPO
- Topical erythromycin
- Oral erythromycin

- Avoid topical retinoids
  - No oral retinoids – teratogenic (patient must be on pregnancy prevention programme)

BPO, benzoyl peroxide.
When to refer?

• Severe psychological distress
• Uncontrolled acne developing scarring
• Nodulo-cystic acne*
• Diagnostic uncertainty
• Patients failing to respond to multiple therapeutic interventions

*Nodules/cysts. Treatment can be initiated, but patients should be referred.
Maintenance

- Use a topical retinoid for long-term maintenance; this may mean years
- Occasional flares may require revisiting previously successful treatments
- Continue co-cyrindiol (Dianette) until skin clear for 3–4 months
- Consider switch to 2nd/3rd-generation COCP if contraception is needed

COCP, combined oral contraceptive pill.

1. PCDS acne guideline.
Rosacea

• No longer called acne rosacea
• No bacteria involved
• So why use antimicrobial antibiotics?
Signs

• Redness affecting the nose, cheeks and chin:
  • this is the most important sign — will be worse when hot, when eating, and with alcohol

• Scattered pustules and papules in the same areas

• Neck, back, and chest spared

• No blackheads, no cysts
Rosacea: subtypes

- Erythematotelangiectatic rosacea
- Papulopustular rosacea
- Phymatous rosacea
- Ocular rosacea
- Note: it is a spectrum and patients may have features from more than one subgroup
- Variant: granulomatous rosacea (non-inflammatory, hard brown, yellow or red papules or nodules)
Differential diagnosis

- Seborrhoeic dermatitis—look for scaling on scalp, naso-labial creases, eyebrows, and ears
- Keratosis pilaris—look at upper arms and thighs
- Acne—look for blackheads; check chest and back
- Lupus erythematosus—follicular plugging, look in the ears
Brimonidine gel

• Causes vasoconstriction
• Works well for some but significant rebound for many
• Use very small quantity and intermittently
• Note: treat papules and pustules first to avoid red lesions on a pale background!
Causation: several theories

- Overactive blood vessels
- Harsh climatic exposure
- Demodex mite
- Skin’s innate immune response
- Genetic factors
Female patient aged 40 years with pustules and papules developing on a permanently red face.
Rosacea: practical advice and maintenance

What is Rosacea?
Rosacea is a chronic disorder of the facial skin characterised by redness, particularly of the central cheeks, chin and forehead sparing the periocular skin. Flushing is common and tends to be prolonged and can be unforeseen on exertion, exercise, food, emotional stimuli and alcohol. In time telangiectasias can develop. Some patients develop acne-like papules and pustules, but comedones are absent. Eye symptoms are common including dryness, grittiness, blepharitis and redness. Rosacea can be seen in all skin types but is more common in fair skin. It affects both sexes and tends to occur in mid-life.

Important Information About Treatments
Treatment is often required because avoiding triggers can be difficult for patients. Use of high factor broad spectrum sunblock (30+) is recommended. Light emollients and camouflage skin care products are beneficial. Topical steroids can exacerbate rosacea and should be avoided. Treatment options are directed by the predominant type of rosacea. Flushing and facial erythema can be helped by topical brimonidine, intense Pulsed Light (IPL) or Pulsed Dye Laser (PDL). More raised/inflammatory changes (i.e. papules and pustules) can be treated with topical agents (tretinoin, azelaic acid or metronidazole gels or creams), or oral antibiotics.

Our guidance is developed mindful of the growing concerns about antibiotic resistance and if possible the use of long term antibiotics should be avoided.

Differential Diagnosis
- Seborrhoeic dermatitis (may co-exist); the patient will usually have history of dandruff, dryness and scale in the naso-labial folds, medial eyebrow and ear
- Acne vulgaris; when presenting with greasiness, comedones and lack of background erythema
- Periodic dermatitis; typically seen in young women, can be asymptomatic or excoriated around the mouth and/or eyes
- Keratosis pilaris rubra; fixed redness of cheeks since childhood with follicular erythema and scale on upper arms and thighs

Practical Advice and Further Information Resources for Doctors and Patients
- Inflammatory rosacea is highly amenable to treatment and patients should be advised that whilst a chronic condition that cannot be cured, it can be very well controlled.
- Long term treatment is generally advisable to minimise the risk of progression of the disease
- Patients may initially require a combination of topical and systemic treatment, but ideally managed on topical treatments in the long term. If significant improvement isn’t experienced at two months, patients should be encouraged to seek further medical advice
- Patients should be reassured that alcohol does not cause rosacea, although it may induce flushing
- We would encourage regular reviews to ensure unnecessary use of antibiotics is avoided

Consider Referral if:
- Severe psychological distress
- Not responding to treatment
- Patient might benefit from: PUL/PDL

PCDS: www.pcds.org.uk
Cochrane Review:
BAD: www.bad.org.uk/for-the-public/patient-information/leaflets
## Rosacea: treatment options

<table>
<thead>
<tr>
<th>Product</th>
<th>Flushing &amp; fixed erythema</th>
<th>Inflammatory papules &amp; pustules</th>
<th>Ocular</th>
<th>Protocol &amp; Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ivermectin 1% Cream (Soolantra®)</td>
<td>+++</td>
<td></td>
<td></td>
<td>Well tolerated, once daily, greater efficacy than metronidazole and no concerns with antibiotic resistance</td>
</tr>
<tr>
<td>Azelaic Acid Gel (Finacea 15%®)</td>
<td>++</td>
<td></td>
<td></td>
<td>Effective twice daily, may cause irritation and no concerns with antibiotic resistance</td>
</tr>
<tr>
<td>Metronidazole Gel or Cream 0.75% (Aczone®, Metrogel®, Metrozole®, Rosacea®, Rozex®, Zynnar®)</td>
<td>+</td>
<td></td>
<td></td>
<td>Twice daily, less effective than ivermectin</td>
</tr>
<tr>
<td>Brimonidine Gel 0.33% (Alvesa®)</td>
<td>++</td>
<td></td>
<td></td>
<td>Effective and fast acting vaso-constrictor; patients should be warned about the possibility of rebound flush which can limit usage</td>
</tr>
<tr>
<td>Eye Lubricants</td>
<td></td>
<td></td>
<td>+++</td>
<td>Lid hygiene and warm eye compresses also important</td>
</tr>
<tr>
<td>Doxycycline MR 40mg (Eracea®)</td>
<td>+++</td>
<td></td>
<td></td>
<td>Once daily. Fewer side effects and equivalent efficacy as full dose (100mg). Sub-microbial dose reduces risk of antibiotic resistance compared to other antibiotics</td>
</tr>
<tr>
<td>Doxycycline 100mg</td>
<td>++</td>
<td>++</td>
<td></td>
<td>Less expensive, more side effects. Well tolerated, once daily</td>
</tr>
<tr>
<td>Oxytetracycline 250-500mg</td>
<td>+</td>
<td>+</td>
<td></td>
<td>Twice daily, avoid taking with meals</td>
</tr>
<tr>
<td>Erythromycin/Zinc Ointment 250-500mg</td>
<td>+</td>
<td></td>
<td></td>
<td>Twice daily, useful in pregnancy</td>
</tr>
<tr>
<td>Isotretinoin</td>
<td>++</td>
<td></td>
<td></td>
<td>Useful in secondary care for resistant cases</td>
</tr>
<tr>
<td>Intense Pulsed Light (IPL)</td>
<td>+++</td>
<td></td>
<td></td>
<td>Limited NHS availability</td>
</tr>
<tr>
<td>Pulsed Dye Laser (PDL)</td>
<td>++</td>
<td></td>
<td></td>
<td>Limited NHS availability and causes significant bruising</td>
</tr>
<tr>
<td>Clindamycin 25-50mg</td>
<td>++</td>
<td></td>
<td></td>
<td>Up to three times daily, improves flushing in some patients</td>
</tr>
<tr>
<td>Propranolol 10-40mg</td>
<td>+</td>
<td></td>
<td></td>
<td>Up to three times daily</td>
</tr>
<tr>
<td>Candesartan 0.125-0.625mg</td>
<td>+</td>
<td></td>
<td></td>
<td>Up to three times a day</td>
</tr>
</tbody>
</table>

**Legend**
- +++ Strong recommendation
- ++ Moderate recommendation
- + Low recommendation

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PCDS Rosacea guideline.
Rosacea: topical treatment

- Topical ivermectin 10 mg/g cream (Soolantra)
- Topical—15% azelaic acid gel twice daily (Finacea)
- Topical metronidazole 0.75% gel or cream twice daily (Rosex)
- Acne treatments (retinoids)
- Green-tinted cream cosmetically helpful
Oral treatments for pustular types

- Lymecycline 408 mg once daily
- Doxycycline 40 mg once daily
- Erythromycin (250–500 mg) twice daily

Secondary care:
- Oral isotretinoin
- IPL/laser for telangiectasia or persistent erythema (not on NHS)
Eczema

• Traditional teaching emphasises the role of *Staphylococcus* toxin in eczema flares
• We have been encouraged to prescribe topical and oral antibiotics
• New evidence suggests/confirms that the anti-inflammatory topical steroid is the prime actor\(^1\)

Conclusion of the ‘CREAM study’

• We found rapid resolution in response to topical steroid and emollient treatment and ruled out a clinically meaningful benefit from the addition of either oral or topical antibiotics.

• Children seen in ambulatory care with mild clinically infected eczema do not need treatment with antibiotics.

So let us consider the treatment for each of these cases
Topical corticosteroid ladder

Mild
Hydrocortisone

Moderate
Eumovate (clobetasone)

Potent
Betnovate (betamethasone)
Elocon (mometasone)

Very potent
Dermovate (clobetasol)

Emollients

PCDS eczema guideline.
Steroid side effects are exaggerated...

But real ones must not be ignored
Topical steroids potency scale

- Mild x 1
- Moderate x 2
- Potent x 10
- Very potent x 50
It’s not just potency but quantity that is needed
Fingertip units

• All steroids in UK have a standard 5 mm diameter nozzle

Topical corticosteroids

• Hydrocortisone is SAFE
• Often better to start strong, review and reduce:
  • e.g. Elocon for a week, then Eumovate, then 1% hydrocortisone ointment
• Weekend-only steroid regimens
• Beware the repeat prescription
• Beware the combination product
Steroids are absorbed at different rates from different parts of the body

- Forearm absorbs 1%
- Armpit absorbs 4%
- Face absorbs 7%
- Eyelids and genitals absorb 30%
- Palm absorbs 0.1%
- Sole absorbs 0.05%
Only prescribe an antibiotic if there is obvious bacterial infection
Questions

www.pcds.org.uk