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Symposium
clinical • aesthetic dermatology

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THE MEDICAL DERMATOLOGY
Summit WWW.LIVDERM.ORG

Oral Therapy Debate: Antibiotics

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Disclosures

Allergan
Procter and Gamble
L'Oreal
Ortho Derm
Aclaris
Revance
Sonoma

Crown
Evolus
Cassiopea
Ferndale
Regimen Pro
CLN
Almirall

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Antibiotics for Acne

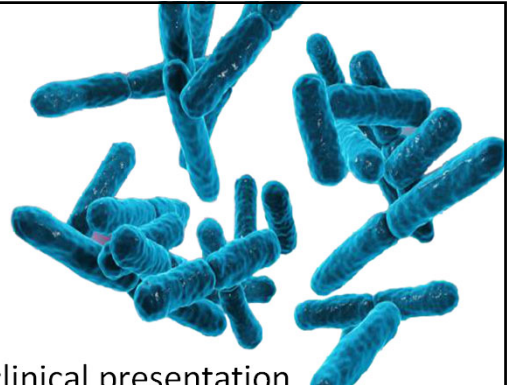
- ❖ Tetracyclines (minocycline, doxycycline) - 1st Line
- ❖ Macrolides
- ❖ Trimethoprim/ Sulfamethoxazole
- ❖ Topicals: Clindamycin, erythromycin



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Propionibacterium acnes

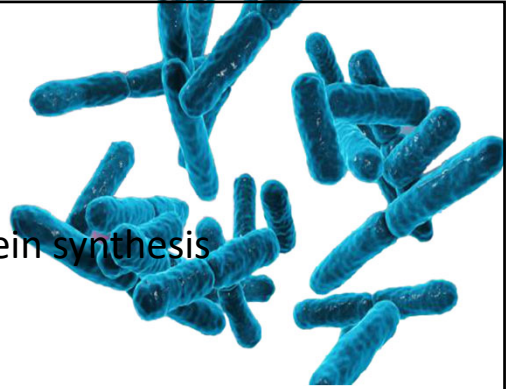
- ❖ Gram positive anaerobic diphtheroid
- ❖ Low pathogenicity
- ❖ Levels elevated in acne patients
- ❖ Hypersensitivity may explain variability of clinical presentation
- ❖ Generates inflammation
 - ❖ FFA hypothesis
 - ❖ Complement
 - ❖ Neutrophil chemotactic factor
 - ❖ Enhanced lymphocytic response



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Tetracyclines

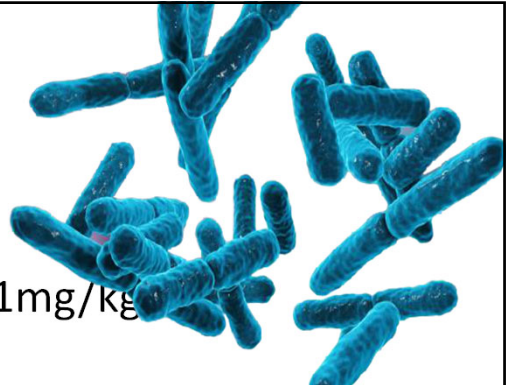
- ❖ Antibacterial – inhibit bacterial protein synthesis
- ❖ Anti-inflammatory – inhibit:
 - Neutrophil chemotaxis
 - Cytokine production (IL-8, TNF-alpha)
 - Macrophage function
 - Neutrophil release ROS
 - MMP's



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Minocycline

- ❖ FDA approved extended release 1mg/kg
- ❖ Lipophilic, least resistance
- ❖ Side effects: Vestibular, pigment, LE syndrome, hepatic, pseudotumor cerebri



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Doxycycline

❖ Side effects:

GI, esophagitis, candidiasis, photosensitivity, ? IBD

❖ Sub antimicrobial:

↓ effect on oropharynx, GI, skin, vaginal flora



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RESISTANCE

Erythromycin > Clindamycin > TCN > Doxycycline > Minocycline

- Can be transmitted to personal contacts



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Systemic Antibiotics – Antibiotic Stewardship

- ❖ Minocycline, doxycycline
- ❖ Limit 3-6 months
- ❖ Use with topical BP
- ❖ Avoid topical antibiotic monotherapy
- ❖ Topicals for maintenance



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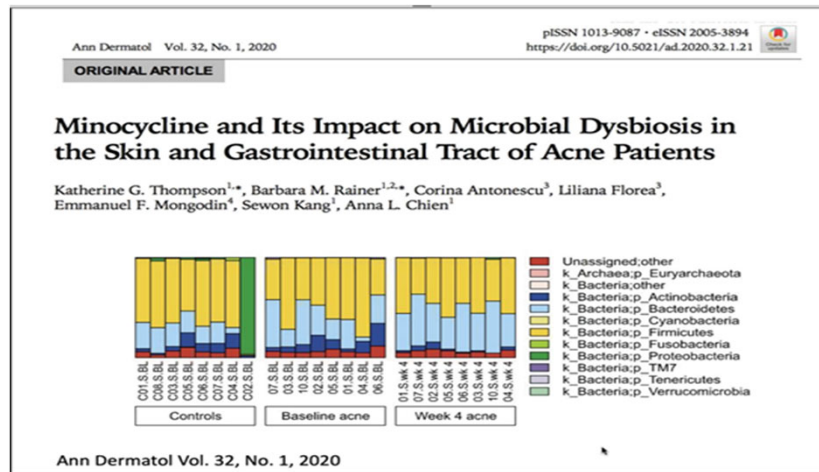
Microbiome

- ❖ Layer of living organisms that coat skin surface
- ❖ Component of epidermal barrier
- ❖ Bacteria, Fungi, yeast
- ❖ Diverse – mostly commensal organisms
 - ❖ bacteria, secrete antimicrobial peptides
 - ❖ regulate immune system and promote immune tolerance
 - ❖ maintain low skin PH
- ❖ Dysbiosis (microbiome alteration) in patients with acne
- ❖ Microbiome “friendly” skin care
 - ❖ doesn’t disturb microbiome
 - ❖ modulate to improve barrier repair and decrease inflammation



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Broad-spectrum: Oral Minocycline



Conclusion: Minocycline produces significant derangements in the microbiota of the skin and gut, including many probiotic species, highlighting the potential for more targeted antimicrobial treatments for acne

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Broad-spectrum: Oral Doxycycline

Journal of Investigative Dermatology
Volume 138, Issue 5, Supplement, May 2018, Page S65

Clinical Research: Epidemiology of Skin Diseases

383 Doxycycline effects on the gut and skin microbiomes and lipidome in acne

K. Haas¹, M. Notay¹, W. Rodriguez², M. Rolston¹, A. Clark¹, W. Burney¹, J. Newman¹, T. Pedersen¹, R. Crawford³, S. Dandekar¹, R. Sivamani¹

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2610 ORIGINAL CONTRIBUTIONS
nature publishing group

BOWEL DISEASE

Potential Association Between the Oral Tetracycline Class of Antimicrobials Used to Treat Acne and Inflammatory Bowel Disease

David J. Margolis, MD, PhD^{1,2}, Matthew Fanelli, MD¹, Ole Hoffstad, MA¹ and James D. Lewis, MD, MSCE^{1,3}

INTERNAL MEDICINE JOURNAL

Association of **doxycycline** use with the development of gastroenteritis, irritable bowel syndrome and **inflammatory bowel disease** in Australians deployed abroad

T. W. Lee,^{1,4} L. Russell,¹ M. Deng² and P. R. Gibson^{1,3}

¹Eastern Health Clinical School and Departments of ²Econometrics and Business Statistics and ³Gastroenterology, Alfred Hospital, Monash University, Melbourne, Victoria and ⁴Department of Gastroenterology, Wollongong Hospital, Wollongong, New South Wales, Australia

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Sarecycline: Modified Structure to Overcome Resistance Mechanism

Broad Spectrum

Narrow Spectrum

➔

1 ST Generation	2 nd Generation		3 rd Generation
FDA: 1953	FDA: 1967	FDA: 1971	FDA: 2018
Tetracycline	Doxycycline	Minocycline	Sarecycline

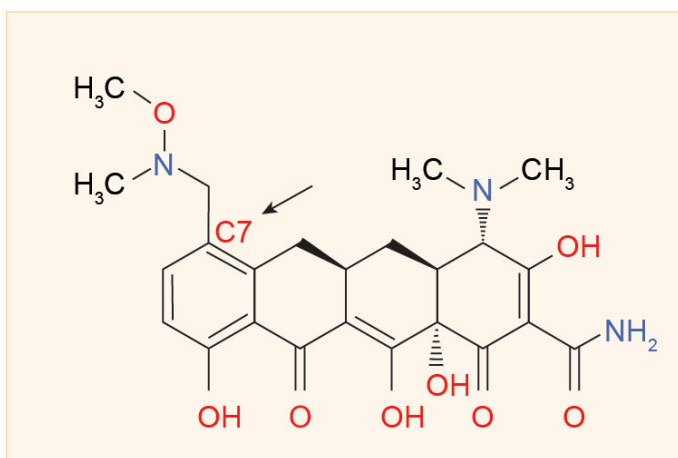
Sarecycline has the longest C7-moiety present in any tetracycline-class drug

The position marked in orange at C-7 has been modified to create tetracycline derivatives to overcome tetracycline resistance mechanisms and to change bacterial ribosome binding

Chemical structure source: ChemSpider: <http://www.chemspider.com/Search.aspx?q=doxycycline>

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Sarecycline: Modified to Overcome Resistance Mechanism



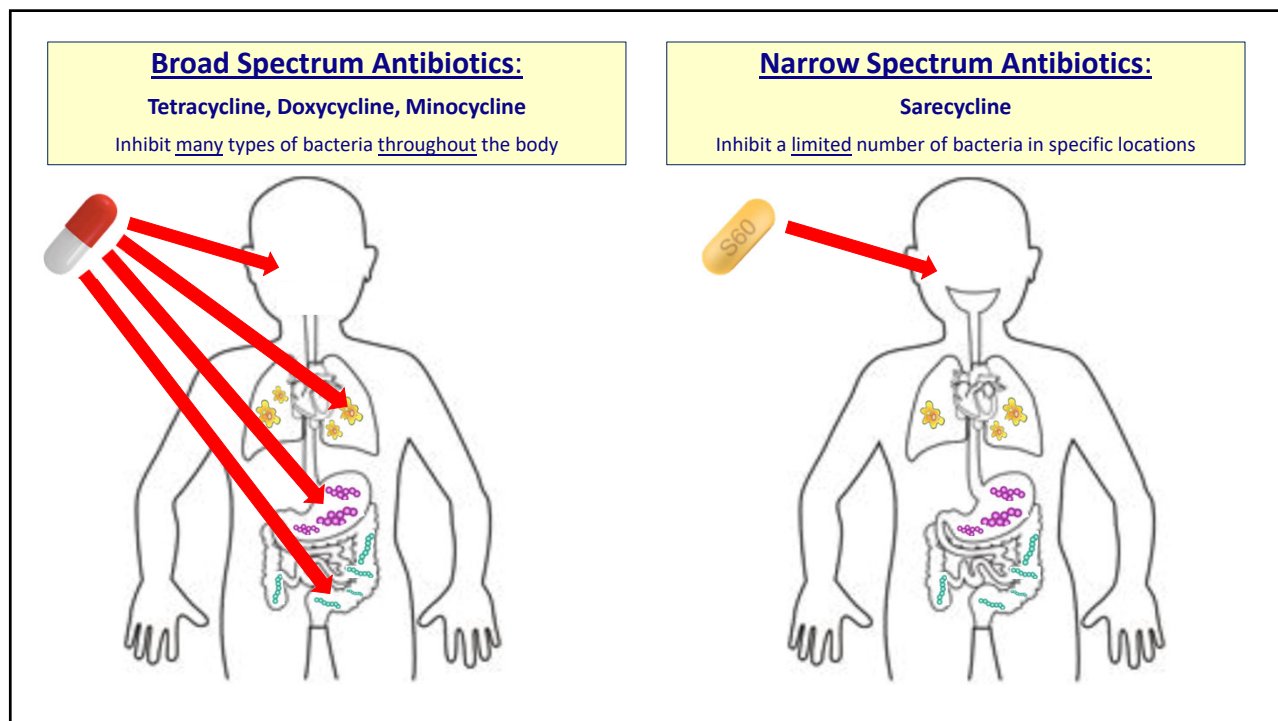
C7 Position Modification
overcomes efflux pump

Sarecycline has the longest C7-moiety present in any tetracycline-class drug

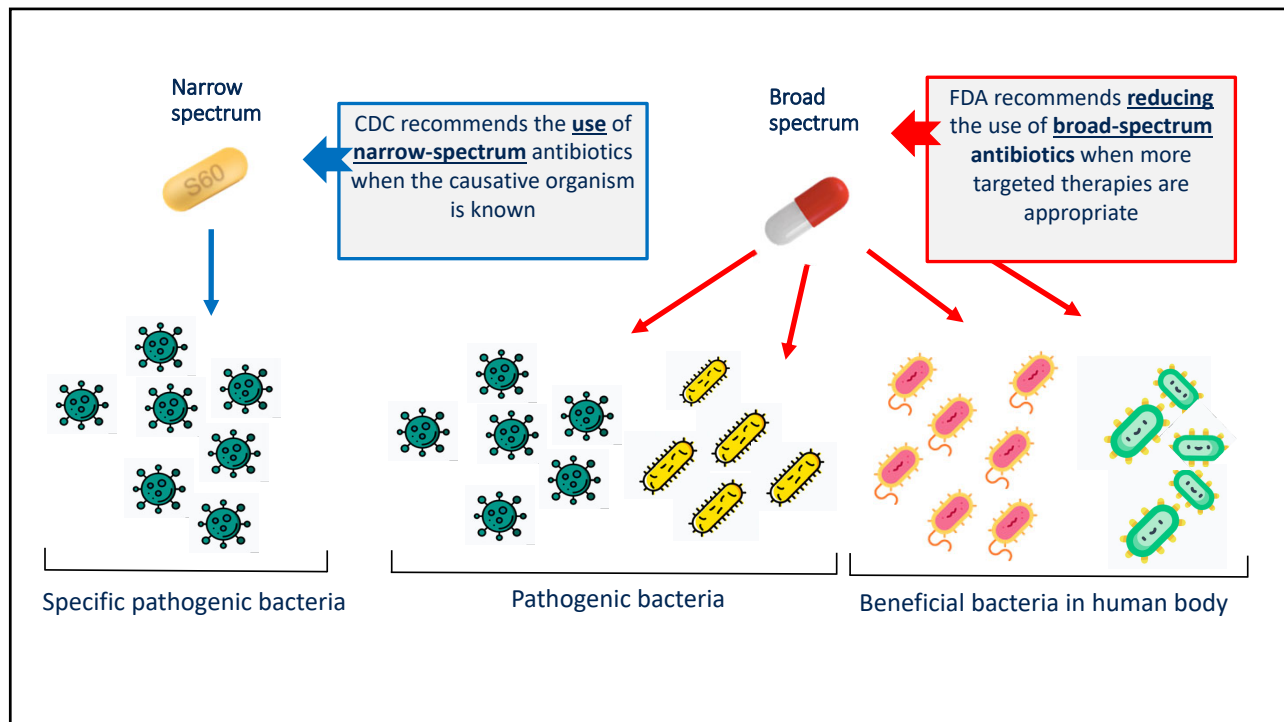
The position marked in orange at C-7 has been modified to create tetracycline derivatives to overcome tetracycline resistance mechanisms and to change bacterial ribosome binding.

1. Zhanel G, Critchley L, Lin LY, Alvandi N. Microbiological profile of sarecycline, a novel targeted spectrum tetracycline for the treatment of acne vulgaris. Antimicrobial agents and chemotherapy. 2019 Jan 1;63(1). 2. Batool Z, Lomakin IB, Polikanov YS, Bunick CG. Sarecycline interferes with tRNA accommodation and tethers mRNA to the 70S ribosome. Proceedings of the National Academy of Sciences. 2020 Aug 12.


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CDC
CENTERS FOR DISEASE
CONTROL AND PREVENTION

Due to concerns regarding antimicrobial resistance, the Centers for Disease Control and Prevention (CDC) has **stressed antibiotic stewardship**. This is an initiative to promote the appropriate use of antibiotics where patients receive the **right dose** of the **right antibiotic** at the **right time** for the **right duration**

Source: Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, Bowie WP, Graber EM, Harper JC, Kang S, Keri JE. Guidelines of care for the management of acne vulgaris. Journal of the American Academy of Dermatology. 2016 May 1;74(5):945-73.

“Promoting narrow-spectrum over broad-spectrum antibiotic use is a common goal of stewardship programs.”

Daniel Livorsi, MD, MSc



Source: ID specialists improve adherence to antibiotic stewardship principles in hospitals

“and facilitate use of narrow-spectrum antibiotics whenever possible” – CDC

Source: Antibiotic Stewardship Statement for Antibiotic Guidelines – Recommendations of the HICPAC

“Core principles of antibiotic stewardship include selecting narrow-spectrum agents when feasible, using antibiotics only when necessary, and prescribing antibiotics for the shortest effective duration,”

Source: <https://www.cidrap.umn.edu/news-perspective/2020/04/stewardship-resistance-scan-apr-09-2020>

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