The new antibiotic mantra: Shorter is better!

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Antibiotic overuse drives AMR

- Key driver of antibiotic overuse: use in syndromes where they are not needed or are of minimal benefit
  - 48% of all Australians have >=1 course of Abs each year
  - URTIs (i.e. colds)
  - Bronchitis
  - (Sore throat/ AOM)
- 2nd most important: longer duration than needed

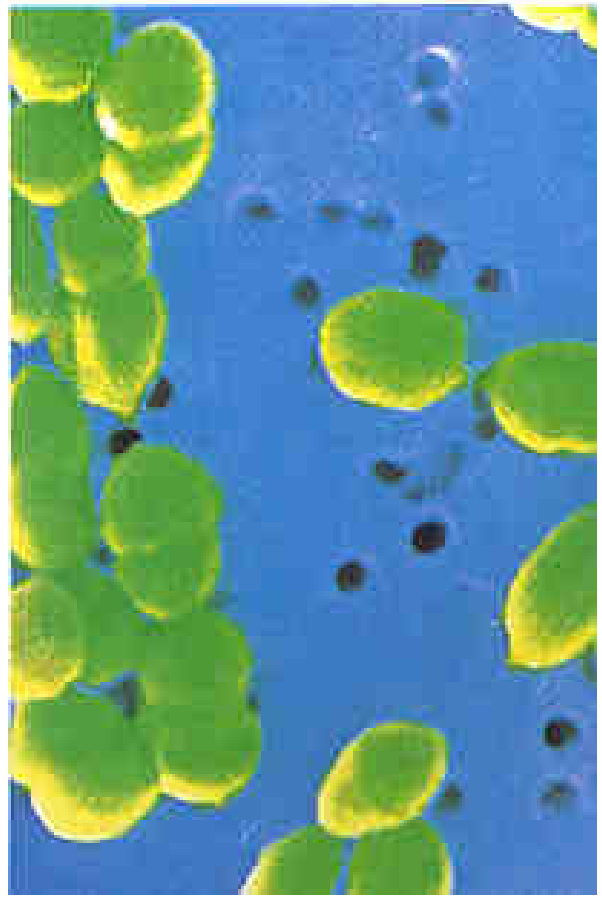
MEGA plate

- https://www.youtube.com/watch?v=plVk4NVIUh8

Respect thy foe: evolution from the bacterial viewpoint

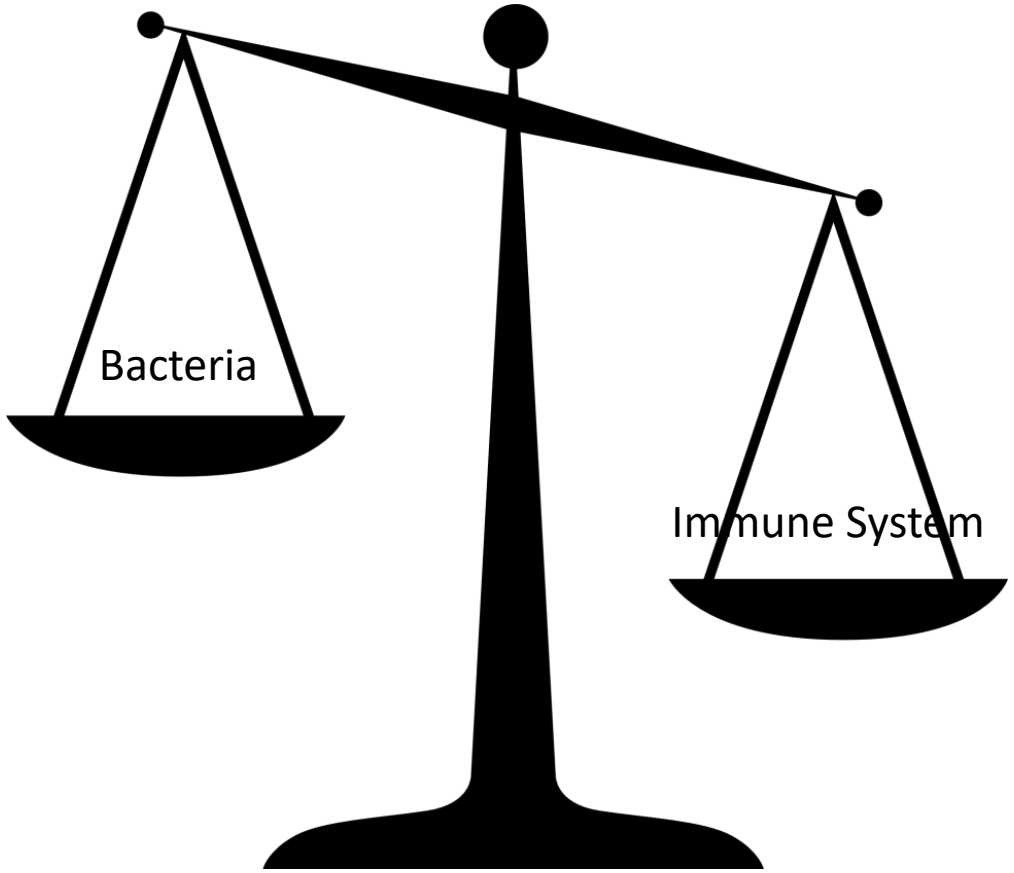
100 years = 1 second

Bacteria	January 1st
Fungi	June 18th
Mammals	December 24th
Humans	23:56hr, Dec 31st
Antibiotic era	23:59, last 0.5 second



90% of the cells in/on a human body are bacteria (and 10% are human)!!

Antibiotics help shift the balance rather than kill all bacteria



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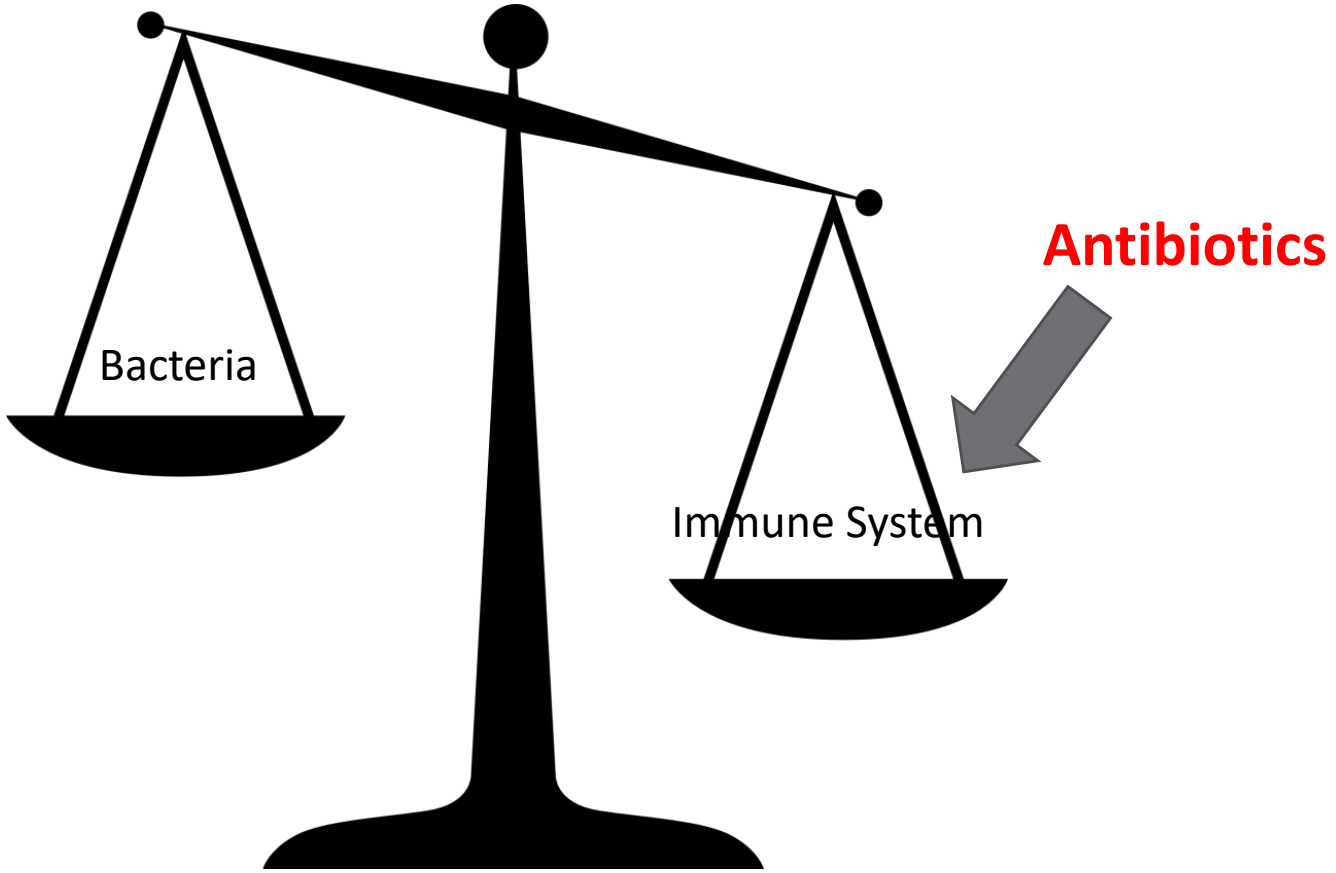

Your mother was wrong!

- Finishing a prescribed course of antibiotics is not necessary
- Most prescriptions are longer than needed
- Ceasing as soon as symptoms improving ==completing whole course
- Longer courses=more exposure=more resistance
- The “antibiotic course” is dead!

What should be the recommended duration of Rx?

- Complicated *S.aureus* bacteraemia
- Mild-moderate community acquired pneumonia
- Cellulitis
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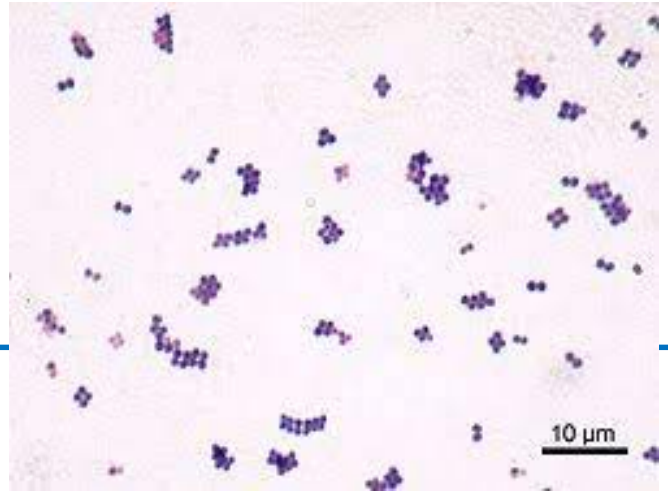

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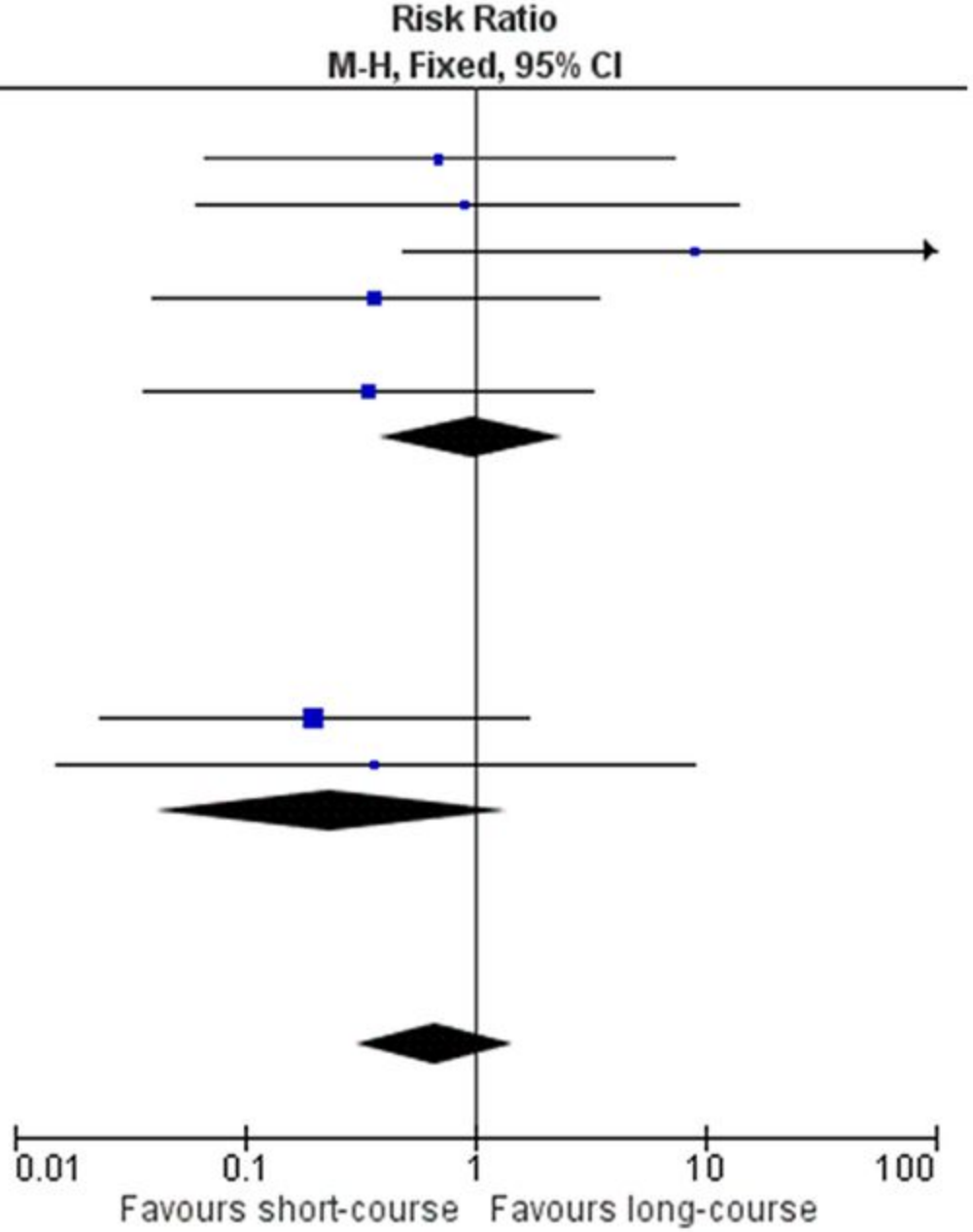
Study or Subgroup	Short-course Events	Total	Long-course Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
1.7.1 3-5 days vs. ≥7 days							
Kinasewitz 1991	1	25	2	35	10.8%	0.70 [0.07, 7.30]	1991
O' Doherty 1998	1	24	1	22	6.8%	0.92 [0.06, 13.79]	1998
Dunbar 2003	4	164	0	166	3.2%	9.11 [0.49, 167.85]	2003
el Moussaoui 2006	1	50	3	56	18.4%	0.37 [0.04, 3.47]	2006
Paris 2008	0	135	0	129		Not estimable	2008
Zhao 2016	1	205	3	213	19.1%	0.35 [0.04, 3.30]	2016
Subtotal (95% CI)		**603**		**621**	**58.4%**	**0.97 [0.38, 2.45]**	
Total events	8		9				
Heterogeneity: Chi² = 3.85, df = 4 (P = 0.43); I² = 0%							
Test for overall effect: Z = 0.06 (P = 0.95)							
1.7.2 Single-dose azithromycin vs. ≥7 days							
Drehobl 2005	1	176	5	177	32.4%	0.20 [0.02, 1.70]	2005
D' Ignazio 2005	0	164	1	182	9.2%	0.37 [0.02, 9.01]	2005
Subtotal (95% CI)		**340**		**359**	**41.6%**	**0.24 [0.04, 1.39]**	
Total events	1		6				
Heterogeneity: Chi² = 0.10, df = 1 (P = 0.76); I² = 0%							
Test for overall effect: Z = 1.59 (P = 0.11)							
Total (95% CI)		**943**		**980**	**100.0%**	**0.67 [0.30, 1.46]**	
Total events	9		15				
Heterogeneity: Chi² = 5.07, df = 6 (P = 0.53); I² = 0%							
Test for overall effect: Z = 1.01 (P = 0.31)							
Test for subgroup differences: Chi² = 1.91, df = 1 (P = 0.17), I² = 47.6%							



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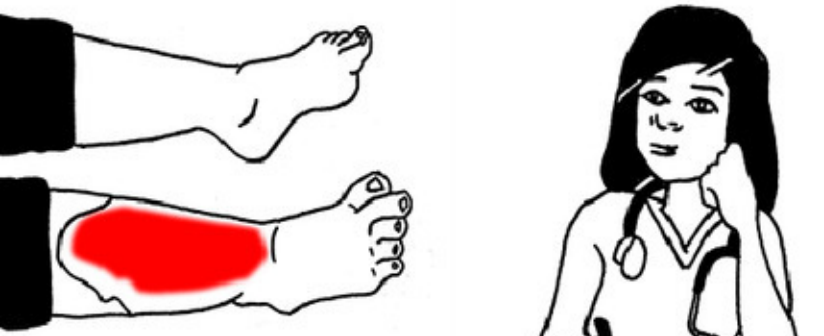
Antibiotic decision making for acute cellulitis – 3 key decisions for clinicians



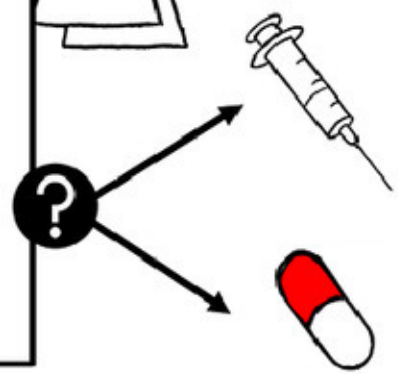
1. Oral or IV antibiotics?

5 RCTs, meta-analysis of 3 trials

Clinical response RR (oral:IV) 1·12 (95% CI 0·98-1·27)

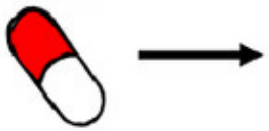
Only 2 trials compared antibiotics from the same class

All studies excluded patients with severe sepsis



2. When to switch from IV to oral?

Single RCT (N=80)
Similar outcomes for <24 vs >72 hours
Too small to demonstrate non-inferiority



3. A shorter or longer duration?

10 RCTs, meta-analysis of 8 trials
Clinical response RR (shorter:longer) 0·99 (95% CI 0·96-1·03)
Only 2 trials compared the same agent in each group

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ORIGINAL ARTICLE

Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection

Table 2. Primary and Major Secondary Outcomes.*

Variable	Control Group (N=260)	Experimental Group (N=257)	P Value
Primary outcome: surgical-site infection, recurrent intraabdominal infection, or death — no. (%)	58 (22.3)	56 (21.8)	0.92
Surgical-site infection	23 (8.8)	17 (6.6)	0.43
Recurrent intraabdominal infection	36 (13.8)	40 (15.6)	0.67

Subgroup	No. of Patients	Days of Antibiotic Therapy *median (interquartile range)*	Proportion with Composite Outcome
Adhered to protocol			
Control	189	7 (5–10)	
Experimental	211	4 (4–5)	

What about bacteraemia other than SAB?

- 7 days probably as good as 14 (3 small RCTs)
- BALANCE trial ongoing (n=3,600)
  - 7 vs 14 days for non-SAB bacteraemias
  - 1ry outcome=90 day mortality
  - Due to complete mid 2023

Australian data from 908 patients

Bacterial species	Number of patients	Median total duration of Rx in days (IQR)	%of Patients receiving 7 days or less	Healthcare setting
Enterobacter cloacae (E. cloacae risk factor study)	159	10 (2-40) days	21%	4 referral hospitals in QLD& NSW
E. coli (Monash Health E. coli cohort study)	566	14 (10-16) days	11%	5 hospitals in the Monash Health Network 2016 (Vic)
ESBLE. coli and Klebsiella spp. (MERINO RCT)	104	14 (10-17) days	9%	Australian + NZ patients in the MERINO study
All pathogens (PRO-GUARD Study)	79	13 (7-26) days	27%	11 Australian ICUs

Shorter Is Better

Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	14
Atypical CAP	1	3	Equal	1
Possible PNA in ICU	3	14-21	Equal	1*
VAP	8	15	Equal	2
cUTI/Pyelonephritis	5 or 7	10 or 14	Equal	9**
Intra-abd Infection	4	10	Equal	2
GNB Bacteremia	7	14	Equal	3†
Cellulitis/Wound/Abscess	5-6	10	Equal	4‡
Osteomyelitis	42	84	Equal	2
Osteo Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2φ
Septic Arthritis	14	28	Equal	1
AECB & Sinusitis	≤5	≥7	Equal	>25
Neutropenic Fever	AFx72h/3 d	+ANC>500/9 d	Equal	2
Post Op Prophylaxis	0-1	1-5	Equal	55Ψ
Erythema Migrans (Lyme)	7	14	Equal	1
P. vivax Malaria	7	14	Equal	1

Total: 17 Conditions >120 RCTs

*Infiltrate on CXR but low CPIS score (≤6), both ventilated and non ventilated, likely CAP, HAP, and VAP combined; **2 RCT included males, the smaller one found lower 10-18 d f/up cure in males with 7 days of therapy but no difference at longer follow-up, larger exclusive male study found no diff in cure; †GNB bacteremia also in UTI/cIAI RCTs; ‡3 RCTs equal, 1 (low dose oral flucox) ↑relapses 2° endpoint; φall patients debrided, in 1 study total bone resection (clean margins); ΨIncludes meta-analysis of 52 RCTs; refs at https://www.bradspellberg.com/shorter-is-better

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