1

ANTIMICROBIAL RESISTANCE IN WOUND CARE

WINDY COLE, DPM, CWSP
Director of Wound Care Research, Kent State University
College of Podiatric Medicine

2

DISCLOSURE OF FINANCIAL RELATIONSHIPS

I have the following relevant relationship(s) to disclose:

- Member of the Speakers Bureau for Organogenesis
- Member of the advisory board: NATROX Wound Care, Biolab Holdings and Sun Scientific

3

WHAT IS ANTIMICROBIAL RESISTANCE (AMR)?

- AMR occurs when microbial pathogens, including bacteria, viruses, fungi or parasites no longer respond to anti-microbial medicines.
- As a result of drug resistance, antibiotics and other anti-microbial medicines become ineffective and infections become hard or impossible to treat.
- This, in turn, increases the risk of severe illness, disability and possibly death.
- AMR is a natural process that happens over time through *genetic changes in pathogens, including but not restricted to elaboration of virulence factors or expression of resistance gene(s).*
- AMR occurs when pathogens undergo adaptive evolutionary changes that enable them to withstand antimicrobials.
- People or animals who encounter resistant pathogens may then suffer infections that can't be treated.
- The pathogens survive, patients get sicker and may die, the cost of medical care rises, and disease continues to spread.

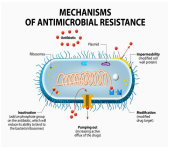


Illustration depicting the mechanisms of antimicrobial resistance
Image source: Shutterstock

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513277/

4

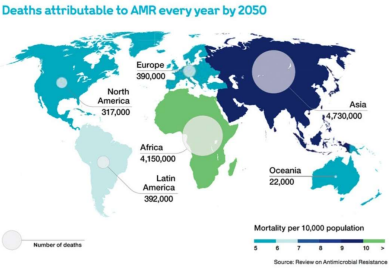
AMR–A FEW KEY FACTS

- **Antimicrobial resistance (AMR) is one of the top, global public health and development threats.**
- **1.27 million deaths were directly attributable to drug-resistant infections in 2019, out of 4.95 million deaths that were associated with antimicrobial resistance Lancet 2022; 399: 629–55**
- **The misuse and overuse of antimicrobials in humans, animals and plants are the main drivers in the development of drug-resistant pathogens.**
- **The World Bank estimates that AMR could result in US$ 1 trillion additional healthcare costs by 2050, $1-3.4 trillion gross domestic product (GDP) losses per year by 2030.**
- **In the USA, antibiotic resistance kills approximately 23,000 patients a year and incurs over $20 billion in additional medical expenses.**

https://www.ncbi.nlm.nih.gov/books/NBK513277/

5

GLOBAL DEATHS ATTRIBUTABLE TO AMR



Antimicrobial resistance: a global threat. UN Environment Programme. 2024. https://www.unep.org/topics/chemicals-and-pollution-action/pollution-and-health/antimicrobial-resistance-global-threat

6

OCCURRENCE AND PREVALENCE OF MICROBIAL PATHOGENS IN CHRONIC WOUNDS

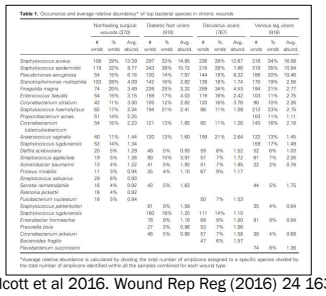


Table 1. Occurrence and average relative abundance* of top bacterial species in chronic wounds

	Nonhealing surgical wounds (233)			Diabetic foot ulcers (918)			Decubitus ulcers (760)			Venous leg ulcers (618)		
	# wnds	% wnds	Avg. abund.	# wnds	% wnds	Avg. abund.	# wnds	% wnds	Avg. abund.	# wnds	% wnds	Avg. abund.
Staphylococcus aureus	106	29%	13.39	297	33%	14.95	226	29%	12.87	316	34%	16.06
Staphylococcus epidermidis	119	32%	9.77	343	38%	10.72	218	29%	7.96	318	35%	10.94
Pseudomonas aeruginosa	94	26%	8.16	193	21%	7.97	144	19%	8.22	186	20%	10.46
Stenotrophomonas maltophilia	103	28%	4.09	142	16%	2.83	139	18%	5.74	170	19%	6.80
Finegoldia magna	71	20%	5.49	226	25%	5.32	259	34%	4.53	194	21%	4.77
Enterococcus faecalis	54	15%	3.16	159	17%	4.03	119	16%	2.42	103	11%	2.76
Corynebacterium striatum	42	11%	3.00	109	12%	2.82	120	16%	3.76	90	10%	2.26
Staphylococcus haemolyticus	62	17%	2.34	194	21%	2.41	86	11%	1.28	213	23%	2.76
Propionibacterium acnes	51	14%	2.25							103	11%	1.11
Corynebacterium tuberculostearicum	54	15%	2.23	121	13%	1.85	85	11%	1.26	145	16%	2.18
Anaerococcus vaginalis	40	11%	1.44	120	13%	1.80	159	21%	2.84	122	13%	1.45
Staphylococcus lugdunensis	53	14%	1.34							158	17%	1.49
Delftia acidovorans	20	5%	1.29	49	5%	0.93	68	8%	1.52	52	6%	1.03
Streptococcus agalactiae	19	5%	1.26	90	10%	3.97	57	7%	1.72	61	7%	2.29
Acinetobacter baumannii	13	4%	1.22	41	5%	1.92	51	7%	1.86	22	2%	0.76
Proteus mirabilis	11	3%	0.94	35	4%	1.10	67	9%	1.17			
Streptococcus salivarius	29	8%	0.93									
Serratia marcescens	16	4%	0.92	43	5%	1.63				44	5%	1.75
Rothia dentocariosa	16	4%	0.92									
Fusobacterium nucleatum	18	5%	0.84				50	7%	1.03			
Staphylococcus pettenkoferi				81	9%	1.58				35	4%	0.64
Staphylococcus lugdunensis				160	18%	1.20	111	14%	1.10			
Enterobacter hormaechei				78	9%	1.16	69	9%	1.00	61	9%	0.94
Prevotella bivia				27	3%	0.96	53	7%	1.66			
Corynebacterium jeikeium				46	5%	0.86	57	7%	1.58	30	4%	0.68
Bacteroides fragilis							47	6%	1.57			
Flavobacterium succinicans										74	8%	1.36

*Average relative abundance is calculated by dividing the total number of amplicons assigned to a specific species divided by the total number of amplicons identified within all the samples combined for each wound type.

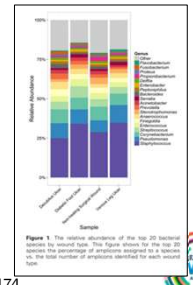


Figure 1. The relative abundance of the top 20 bacterial species by wound type. This figure shows for the top 20 species the percentage of amplicons assigned to a species vs. the total number of amplicons identified for each wound type.

Wolcott et al 2016. Wound Rep Reg (2016) 24 163–174

7

ANTIBIOTIC MISUSE

Healthcare professionals prescribed **236.4 million** antibiotic prescriptions in outpatients setting —equivalent to **709 antibiotic prescriptions per 1000 persons.**

2022

Overuse of antibiotics

- Selective pressure from antibiotic use increases the chance of resistant organisms developing[1]

Below therapeutic levels

- Peripheral vascular disease (chronic) and altered pharmacodynamics (burn) – antibiotics don't always reach the site of injury at correct dose[2-4]
- Low levels of antiseptics such as silver increase chance of developing resistance[5]
- Increasing awareness that biofilms need higher concentrations of antimicrobial to be effective[6]

Incorrect antibiotic choice

- Incorrect antibiotic used in 41.8% skin and soft tissue infections[7]

Inappropriate use

- Use of antimicrobials in non-infected wounds has been reported in 35% of cases[8]

Cole, W Antimicrobial Resistance and Stewardship in Wound Management. Podiatry Management. Aug 2024

8

Patient: I have no medical history
Also patient:

9

- Cole W, et al. *Wounds*. 2025;37(5 Suppl):S1-S24.

10

DETERMINING WOUND INFECTION

Contamination
All wounds may acquire microbes. If unable to evade host defenses, the microbes will not multiply or persist

Colonization
Microbes grow and divide but do not cause damage to host or initiate wound inflammation and infection/biofilm genesis formation

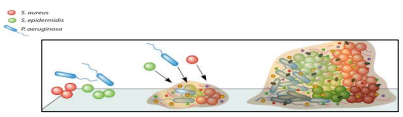
Local Infection ('covert'/sub-clinical)
Focal abundance of hyper-granulated tissue
Bleeding with gentle manipulation
Wound breakdown/enlargement/purulent discharge
Pain and potentially malodorous/biofilm expansion

Overt Local/Spreading Infection (clinical)
Erythema, Lymphangitis
Elevated peri-wound Temperature and Swelling
Wound breakdown, enlargement, Delayed Healing
Pain and Malodorous/Biofilm: Tunneling, Cellulitis and Sepsis

International Wound Infection Institute (IWII) Wound infection in clinical practice. Wounds International 2017.

11

BIOFILM



S.No	Common biofilm forming bacterial species
1	E. coli
2	P. aeruginosa
3	S. epidermidis
4	S. aureus, Staphylococcus epidermidis
5	E. cloacae
6	K. pneumoniae
7	Actinomyces israelii
8	Haemophilus influenza
9	Burkholderia cepacia

Planktonic Bacteria
Opportunistic microbes residing at the wound's surface

Biofilm Genesis

Mature Biofilm
Opportunistic microbes within EPS matrix that shields the microbial community, enabling immuno-protection, drug resistance and virulence factor production

Visuals by Dr. Windy Cole

Muhammad MH, Idris AL, Fan X, Guo Y, Yu Y, Jin X, Qiu J, Guan X and Huang T (2020) Beyond Risk: Bacterial Biofilms and Their Regulating Approaches. Front. Microbiol. 11:928. doi: 10.3389/fmicb.2020.00928

12

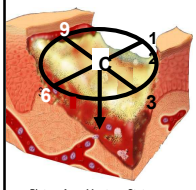
WHEN SHOULD WE OBTAIN A TISSUE SAMPLE?

- Appreciable clinical signs and symptoms of infection
- Wound has not responded to good wound care SOC
- Wound presents with an atypical appearance

- Michael Miller, **Poorly Collected Specimens May Have a Negative Impact on Your Antibiotic Stewardship Program**, *Clinical Microbiology Newsletter*, Volume 38, Issue 6, 2016, Pages 43-48, ISSN 0196-4399.

13

HETEROGENEOUS DISTRIBUTION OF BACTERIA IN CHRONIC WOUNDS



Picture from Montana State University with permission

- The most important rule for clinician colleagues that should be emphasized is:

If it is not infected, don't culture it.

- Culture growth will occur from almost anything due to colonizing normal flora that have no relation to the disease process.
- Wound specimens are a challenge to culture interpretation, and, in fact, not all "wounds" are infected, but they may grow commensal flora when cultured.
- Superficial wounds can easily provide culture results that can confuse the clinician since this specimen that may provide multiple isolates, confusing the interpretation of significance.
- In most instances, **the laboratory needs a specimen, not a swab of a specimen**.
- **Therefore, a properly collected tissue specimen, biopsy, or curetting is more likely to provide relevant results than a swab**.
- In most studies, even those where the authors considered the swabs acceptable, the accuracy of the swabs was only 50-70% compared to the reference biopsy or tissue collection procedure.

Thomsen TR, Aasholm MS, Bjarnsholt T, Givskov M, Kirketerp-Møller K, and Nielsen PH. 2010. The bacteriology of chronic venous leg ulcer examined by culture-independent molecular methods. *Wound Repair Regen*, 18(1):38-49.

14

SYSTEMIC ANTIBIOTICS BEST PRACTICES

- When it is suspected that a wound has become infected, a careful approach should be considered to select appropriate antibiotics and reduce impact of treatment on the rise of AMR

Systemic antibiotics are only recommended in the presence of signs of infection and should not be routinely used as prophylaxis against infections or for local infections.

Table. Signs and Symptoms to Consider When Assessing a Wound for Infection[44]

Subtle Signs of an Infection	Classic Signs of an Acute Infection	Symptoms of a Spreading Infection	Symptoms of a Systemic Infection
Hypergranulation	Erythema	Extending induration	Malaise
Bleeding granulation	Local warmth	Lymphangitis	Lethargy
Epithelial bridging and pocketing in granulation tissue	Swelling	Crepitus	Loss of appetite
Increasing exudate	Purulent discharge	Wound breakdown with or without satellite lesions	Fever
Delayed wound healing beyond expectations	Wound breakdown or enlargement	Spreading inflammation or erythema greater than 2 cm from the wound edge	Severe sepsis
	New or increasing pain		Organ failure
	Increasing malodor		

- Cole W, et al. *Wounds*. 2025;37(5 Suppl):S1-S24.

15

SYSTEMIC ANTIBIOTICS BEST PRACTICES

- When considering antibiotics to select, the clinician should assess for patient risk factors that can increase the risk of a severe infection, the severity of illness, and the likelihood of a multidrug-resistant infection
  - Recent infections
  - Comorbidities
  - Hardware and indwelling devices
  - Immunologic status

- Patient risk factors, including medication allergies and intolerances, drug-drug interactions with other chronic medications, and certain comorbid conditions (eg, impaired renal clearance, liver disease, cardiac arrhythmia, history of vascular aneurysm, advanced age), should also be weighed when choosing the most appropriate antimicrobial drug and dose for an individual patient

- Cole W, et al. *Wounds*. 2025;37(5 Suppl):S1-S24.

16

SYSTEMIC ANTIBIOTICS BEST PRACTICES

- Initial antibiotic prescription is usually provided before return of the microbiologic testing result
- The ideal regimen provides effective activity against pathogenic bacteria without using agents that are unnecessarily broad in spectrum of activity
- This practice protects against drug intolerance, drug interactions, and AMR
- Once culture results return, optimization of regimen is paramount
- Culture-directed therapy should provide the most efficacious agent with the narrowest spectrum of therapy and the lowest toxicity profile

While there is no single best empirical regimen, it is essential to consider a patient's prior culture results, assess risk factors by pathogen type, and review the **local antibiogram** to aid in selecting initial therapy while microbiologic testing is pending.

- Cole W, et al. *Wounds*. 2025;37(5 Suppl):S1-S24.

17

SYSTEMIC ANTIBIOTICS BEST PRACTICES

- Mild-to-moderate infections of the superficial skin and soft tissue structures usually can be successfully treated within 7 to 14 days.
- If deeper soft tissue structures are involved or there is slow or incomplete response within 14 days of appropriate antimicrobial therapy, an intermediate duration of 21 to 28 days may be indicated.
- In cases of osteomyelitis, the standard duration of antimicrobial therapy has traditionally been 6 weeks; however, this may be truncated when aggressive surgical intervention is performed.

The duration of antimicrobial therapy is a complex decision. Consultation with surgical teams and infectious diseases specialists should be considered, especially in the presence of osteomyelitis, retained hardware, and/or extended parenteral therapy

- Cole W, et al. *Wounds*. 2025;37(5 Suppl):S1-S24.

18

ANTIMICROBIAL STEWARDSHIP

- *Antimicrobial stewardship* refers to a set of coordinated strategies aimed at optimizing use of antimicrobial agents through evidence-based selection of most appropriate drug regimen
- In practical terms, it involves ensuring the right antibiotic, for the right patient, at the right time, in the right dose (bioavailability), and via the right route—minimizing harm to both current patient and future populations
- Benefits in wound management: Preserving antibiotic effectiveness, reducing resistance, and improving patient outcomes

Visual by Dr. Windy Cole

- Cole W, et al. *Wounds*. 2025;37(5 Suppl):S1-S24.

19

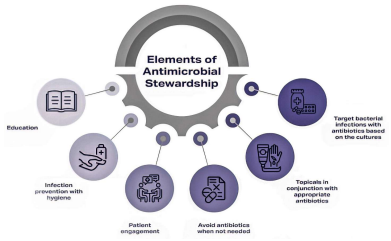
ANTIMICROBIAL STEWARDSHIP

- Avoid antibiotics when not indicated
  - Wound infections should be diagnosed clinically
  - Colonized, uninfected wounds **should not** be treated with systemic antibiotics
- Prescribe an appropriate regimen
  - Narrowest spectrum for likely bacteria present
  - Tailor to culture results
  - Often unnecessary to treat low virulence bacteria in a polymicrobial infection
- Order therapy for the correct duration
  - Just long enough to achieve symptom resolution
  - Consider switching to topical therapy sooner
  - 1-2 weeks for soft tissue, 6 weeks for bone
- Use agents with the least risks/adverse effects

- Cole W, et al. *Wounds*. 2025;37(5 Suppl):S1-S24.

20

ANTIMICROBIAL STEWARDSHIP



- Cole W, et al. *Wounds*. 2025;37(5 Suppl):S1-S24.

21

ANTIMICROBIAL STEWARDSHIP

Case Study: The Cost of Delay – A Chronic Wound and the Rise of Resistance

Patient Profile:

- 68-year-old Male
- **Medical History:** Type 2 Diabetes Mellitus, Peripheral Arterial Disease
- **Presentation:** Chronic non-healing ulcer on the right heel, present for 8 weeks

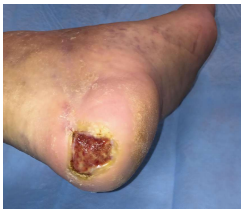


Photo from my medical records used with patient permission

22

ANTIMICROBIAL STEWARDSHIP

Case Study: The Cost of Delay – A Chronic Wound and the Rise of Resistance

Clinical Course:

Week 1–2:

- Initial wound assessment showed signs of colonization but no overt infection.
- Empirical oral antibiotics (amoxicillin-clavulanate) were prescribed without culture.
- No improvement noted.

Week 3–4:

- Wound worsened with increased exudate and odor.
- Swab culture revealed *Pseudomonas aeruginosa* and *Staphylococcus aureus*.
- Switched to ciprofloxacin based on local antibiogram.

Week 5–6:

- Patient developed gastrointestinal side effects; therapy was discontinued.
- Wound culture repeated using tissue biopsy revealed **multi-drug resistant (MDR) P. aeruginosa**.
- Required IV meropenem and hospitalization.

23

ANTIMICROBIAL STEWARDSHIP

Case Study: The Cost of Delay – A Chronic Wound and the Rise of Resistance

Outcome:

- After 3 weeks of IV therapy and advanced wound care, infection resolved.
- However, the patient experienced:
  - **Prolonged hospitalization (21 days)**
  - **Increased healthcare costs**
  - **Reduced mobility and quality of life**
  - **Colonization with MDR organisms**

24

ANTIMICROBIAL STEWARDSHIP

Case Study: The Cost of Delay – A Chronic Wound and the Rise of Resistance

Key Lessons:

1.Inappropriate Empirical Antibiotic Use:

1. Initial antibiotics were unnecessary and likely contributed to resistance.
2. No culture was taken before starting treatment.

2.Delayed Accurate Diagnosis:

1. Reliance on swab cultures delayed identification of MDR pathogens.
2. Tissue biopsy provided more accurate microbiological data.

3.Lack of AMS Principles:

1. No interdisciplinary review of antibiotic use.
2. No de-escalation strategy or reassessment of therapy.

25

ANTIMICROBIAL STEWARDSHIP

Case Study: The Cost of Delay – A Chronic Wound and the Rise of Resistance

Antimicrobial Stewardship in Action: What Should Have Happened

- **Only treating clinically infected wounds**—not colonized ones.
- **Using narrow-spectrum antibiotics** based on culture and sensitivity.
- **Limiting duration** of therapy to the shortest effective course.
- **Engaging a multidisciplinary team** including wound care specialists, pharmacists, and microbiologists.
- **Educating clinicians and patients** on appropriate antibiotic use.

Conclusion:

This case illustrates how **early, evidence-based intervention** and **AMS principles** could have prevented the emergence of resistance, reduced costs, and improved patient outcomes. Embedding AMS into wound care is not optional—it's essential.

26

27

REFERENCES & RESOURCES

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK513277/

https://www.ncbi.nlm.nih.gov/books/NBK513277/

Antimicrobial resistance: a global threat. UN Environment Programme. 2024. https://www.unep.org/topics/chemicals-and-pollution-action/pollution-and-health/antimicrobial-resistance-global-threat

Wolcott et al 2016. Wound Rep Reg (2016) 24 163–174

Cole, W Antimicrobial Resistance and Stewardship in Wound Management. Podiatry Management. Aug 2024

International Wound Infection Institute (IWII) Wound infection in clinical practice. Wounds International 2017.

Michael Miller, **Poorly Collected Specimens May Have a Negative Impact on Your Antibiotic Stewardship Program**. *Clinical Microbiology Newsletter*, Volume 38, Issue 6, 2016, Pages 43-48, ISSN 0196-4399.

Thomsen TR, Aasholm MS, Bjarnsholt T, Givskov M, Kirketerp-Møller K, and Nielsen PH. 2010. The bacteriology of chronic venous leg ulcer examined by culture-independent molecular methods. *Wound Repair Regen,* 18(1):38-49.

Cole W, Greenstein E, Herman IM, Lantis J, Milne C, Pastar I, Beaulieu R, Swanson T, Tickner A, Wahab N. Antimicrobial Resistance in Wound Care: Expert Panel Consensus Statements. Wounds. 2025 May;37(5 Suppl):S1-S24. PMID: 40455938.

28

29