



A Dialogue Between Past, Present, and Future: Combat-Related Injury Infections

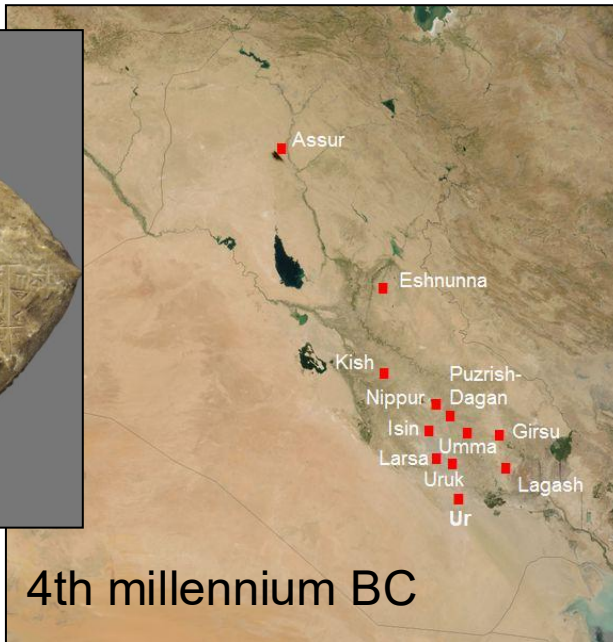
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Major General, U.S. Army
Joint Staff Surgeon
Professor of Medicine, USU



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Historical Overview

- Sumerian Carving > 2000 BC
 - Wound management
 - Rinsing
 - Bandaging

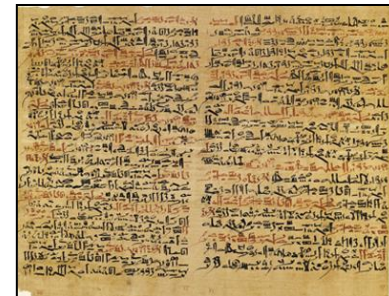


4th millennium BC

- Egypt- 1550-1600 BC
- Edwin Smith and Ebers Papyri
 - Development of differential diagnosis
 - Topical therapy
 - Lint or vegetable fibers- absorbent
 - Grease- barrier to contamination
 - Honey
 - Donkey feces
 - Fly excrement and saliva



Ebers



Edwin Smith-
trauma surgery

Majno 1991; Sipos 2004; Malon 2006

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Historical Overview

Greeks 900 BC

- Homer's Iliad and Odyssey

- 147 wounds

- 106 spears- 80% mortality
- 17 swords- 100% mortality
- 12 arrows- 42% mortality
- 12 slings- 67% mortality



Pikoulis 2004

- Homer's Iliad and Odyssey

- Therapy

- Mechanical debridement with removal of arrow
- Rinse wound with warm water or wine
- Cover wound with bandage soaked in wine
- Applying analgesic
- Applying styptic herbal drugs

Achilles
bandages
the arm of
Patroclus



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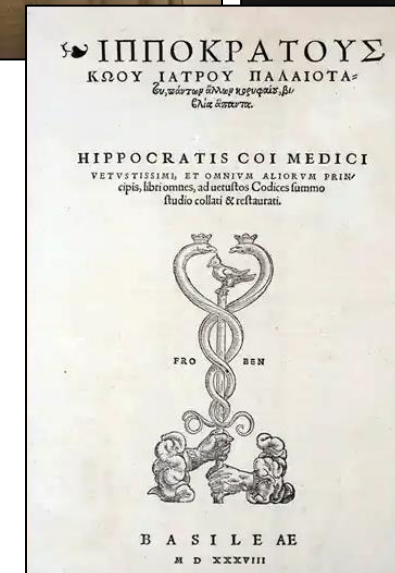
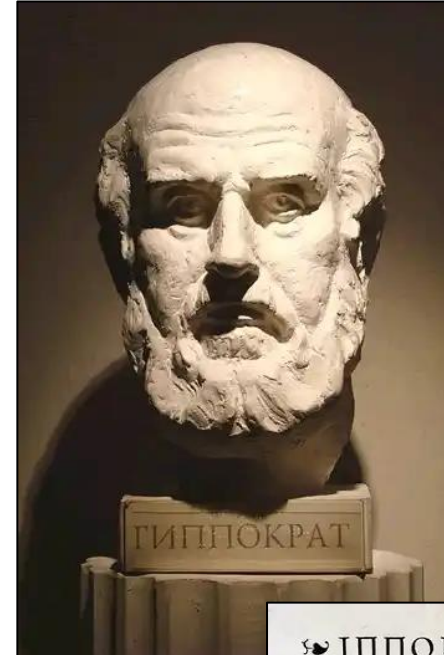


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Historical Overview

Greeks 900 BC

- Hippocrates- Key Findings
 - Surgeon's fingernails length associated with infections
 - Wounds washed with clean water or wine
 - Rest and immobility
 - Sutures sterilized in hot oil prior to use
 - Compound fractures
 - Tight bound bandages to achieve necrosis with limb falling off



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Historical Overview

Romans Galen- 120 AD

- Surgeon to the Roman gladiators
- Authored 400 works
- Introduced concept of laudable pus- held true for 45 generations of surgeons



Majno 1991

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Historical Overview

French

- Ambrose Pare- 1557
 - Improved outcome without cautery of wound with hot oil
 - Used egg yolk, turpentine and rose oil with better results
 - Introduced maggot therapy



Pruitt 2006

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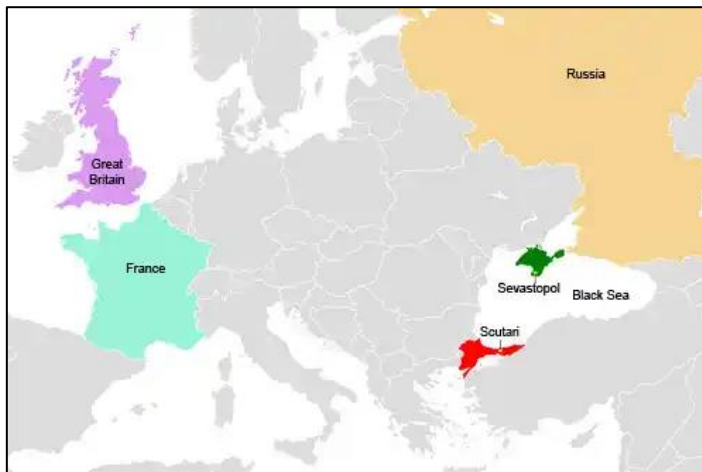


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Historical Overview

Crimean War- Infection Control War Pestilence

- Florence Nightingale and Mary Seacole with their cadre of nurses emphasized sanitation- hygiene, poor nutrition, lack of supplies, stale air, separation of wards/ORs and overworking
- Constantinople (Istanbul, Turkey), 1854



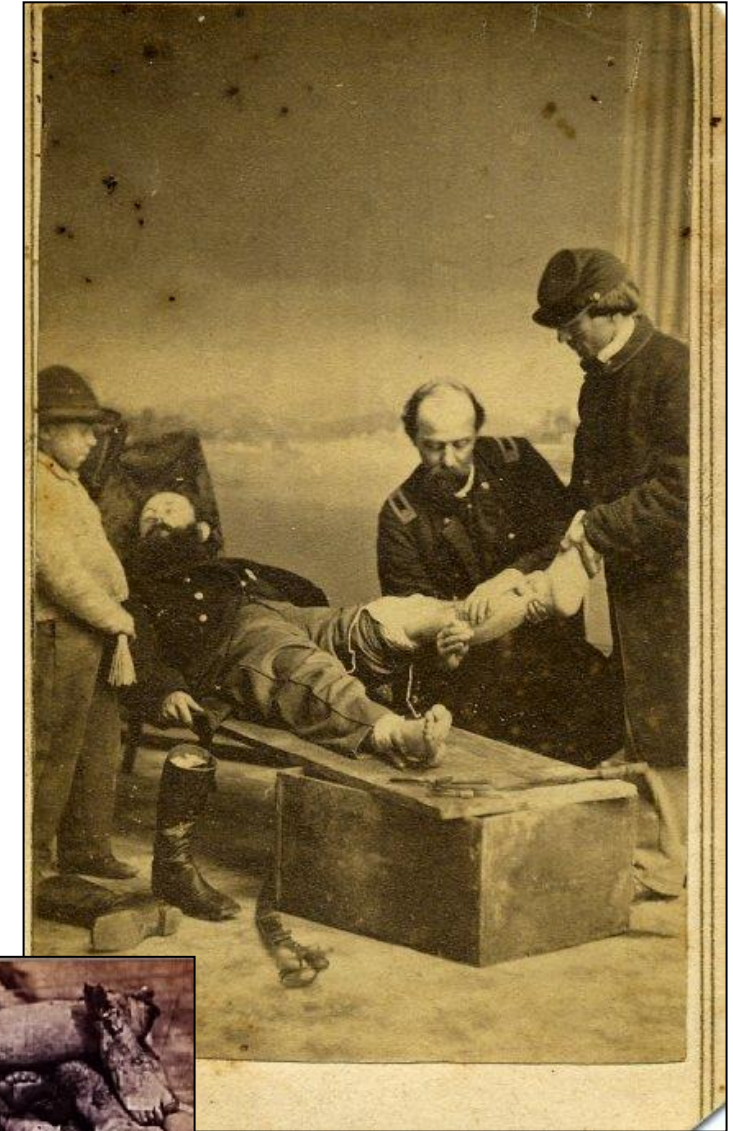
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Historical Overview Civil War

- Laudable pus- thick, creamy would remain localized and not spread
- Malignant pus- thin, bloody exudates resulted in pyemia and blood poisoning with 90% fatality
- Overall wound fatality 14.5%
- Antiseptics- bromine, iodine, carbolic acid
- Hospital gangrene- necrotizing fasciitis from streptococci (erysipelas)
 - Isolating patients with similar wounds together



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Major Advances Impact Infection Rate



Penicillin —————

Masks- 1897 —————

Gloves- 1889 —————

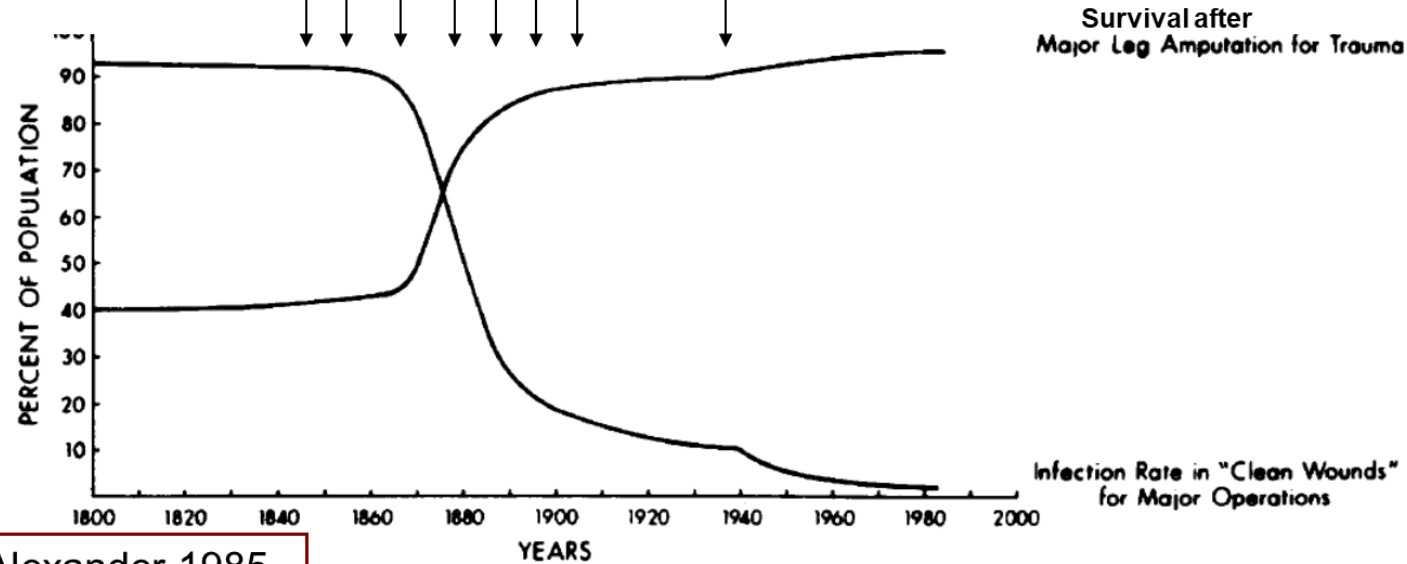
Gowns and Caps 1883 —————

Steam sterilization- 1881 —————

Lister- 1867 —————

Pasteur- 1857 —————

Semmelweis- 1847 —————



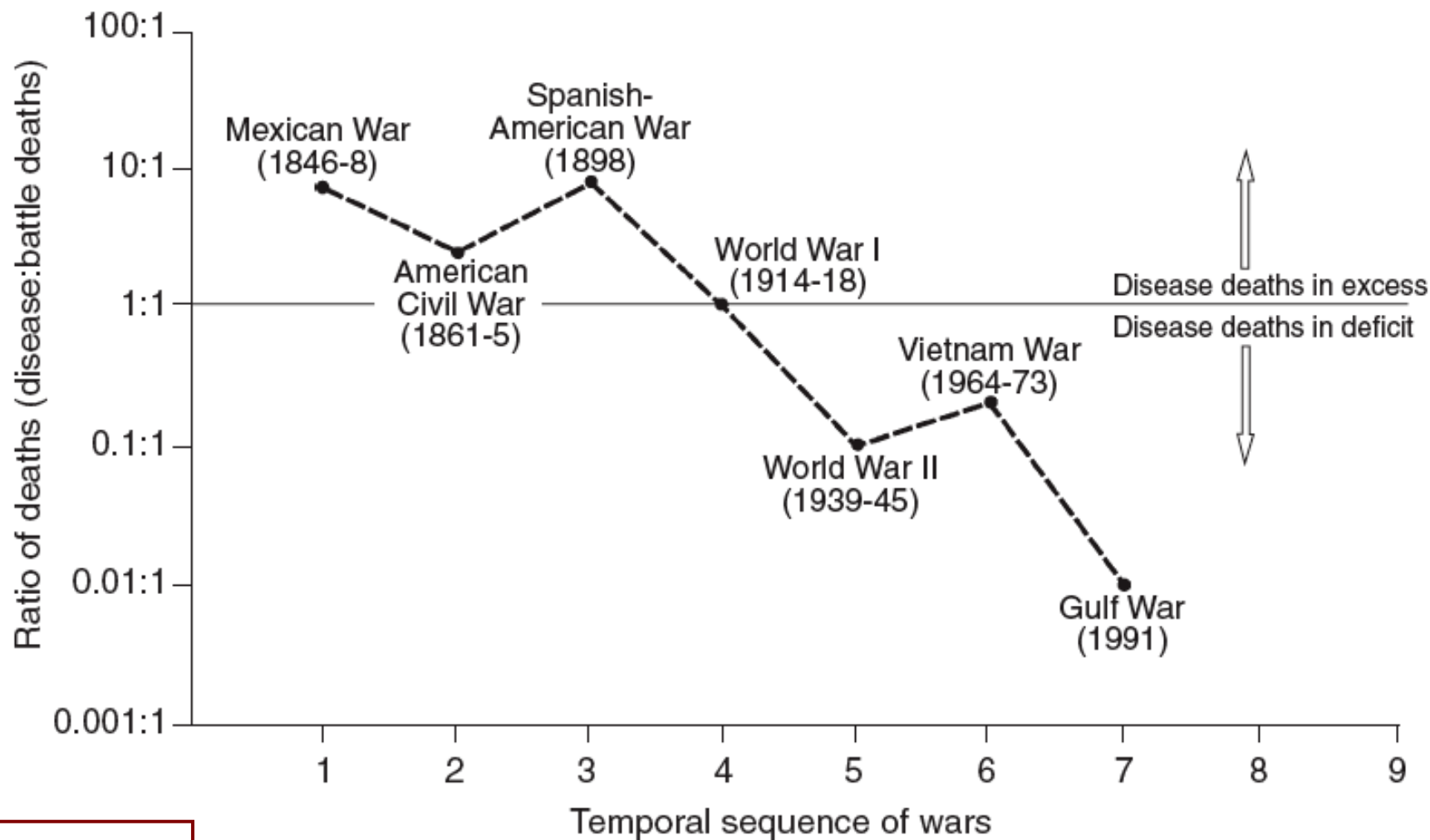
Alexander 1985

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Disease to Battle Deaths Transition from Mexican War



Smallman-Raynor 2004

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World War I

Fleming 1919- Phases of War Wounds

The surgeon- "...it seems a pity that the surgeon should wish to share his glory with a chemical antiseptic of more than doubtful utility." Dakin's Solution

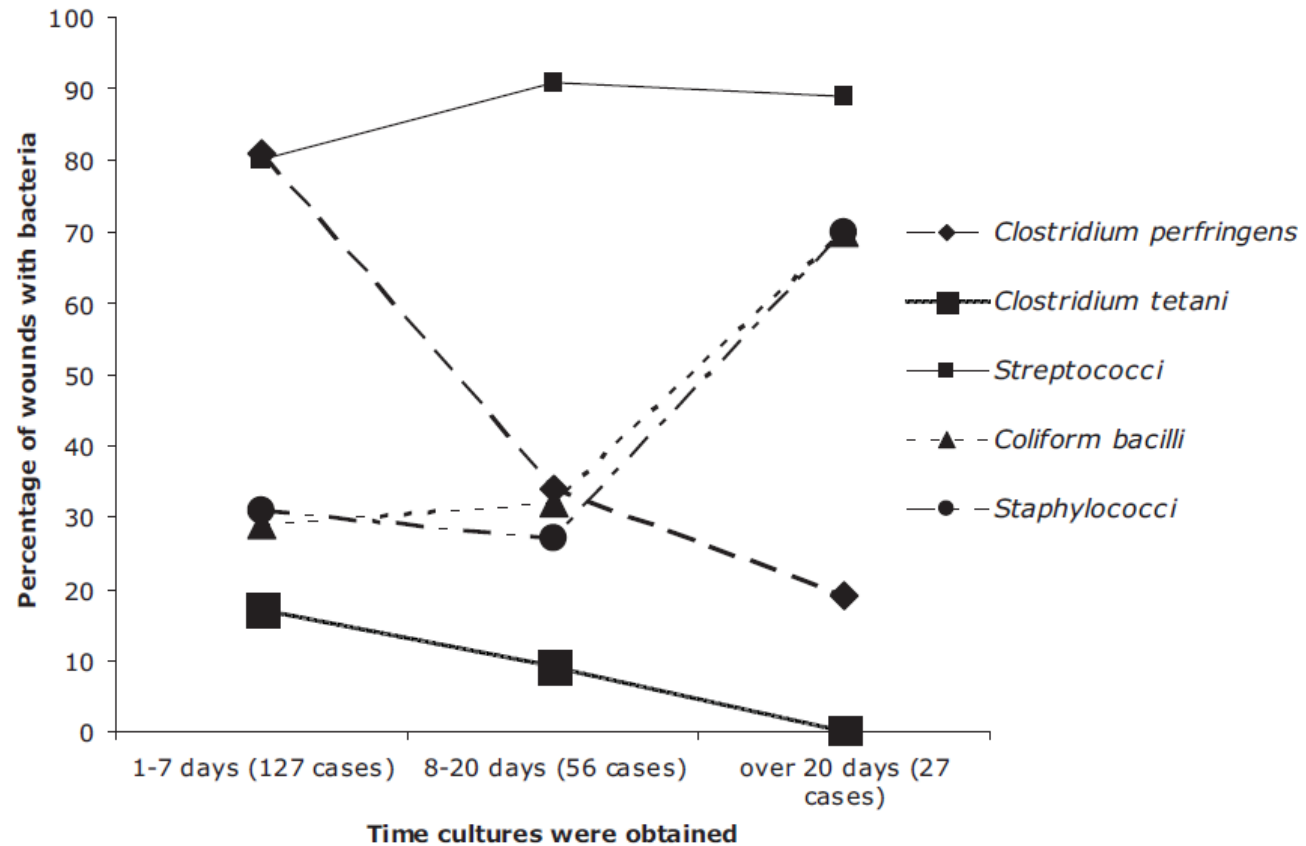
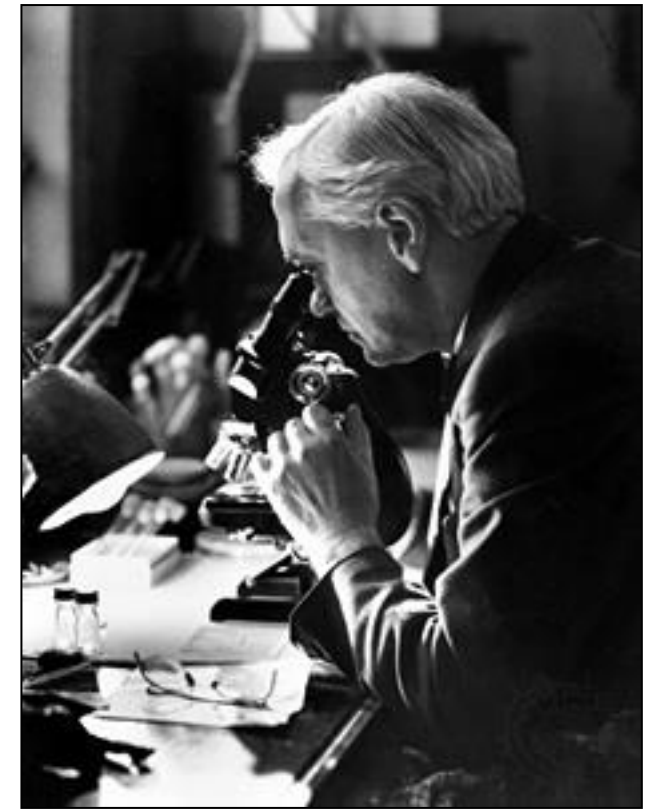


Fig. 1. Bacteria recovered from combat-related injuries during World War I. Adapted from Lancet. 1915;2:638-643.



Fleming 1915, 1919

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History of Modern ID

Era of Antibiotics

- 1936- Sulfanilamide
- 1942/3- Penicillin
 - Oran, African 8 November 1942
 - Hospital ship to Bristol



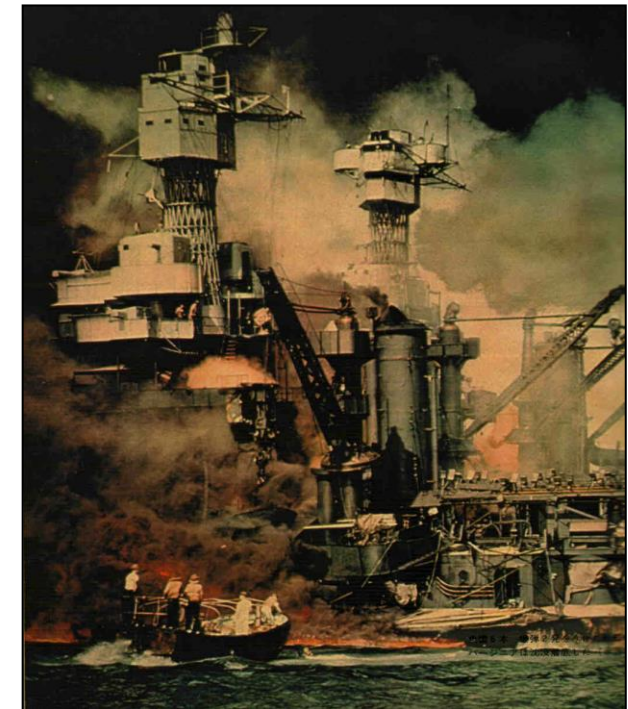
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World War II Pearl Harbor

- November of 1941, Dr. John J. Moorehead, chief surgeon for the New York Subway System, came to Honolulu
- Described the techniques of debridement, topical therapy and delayed primary closure for treatment of large soft tissue wounds
- Only a week later- Pearl Harbor attack occurred and these techniques were applied



Moorhead 1942; Hardaway 1999

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World War II Pearl Harbor

- The immediate reaction “sulfanilamide powder is wonderful”
 - Avoided debridement and delayed primary closure
- The Surgeon General recommended that small packets of sulfanilamide powder be included in the first aid packet of every soldier
- Sulfanilamide powder was dumped in as a lump rather than being sprinkled in so that each grain was separate
- No debridement
- Wounds became infected



Moorhead 1942; Hardaway 1999

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World War II

Nosocomial Transmission

- 5% of wounds were secondarily infected at the time of admission
- 50% were infected after 1 week of hospitalization
- 70-80% were infected after that



Altemeir 1944

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Vietnam War
Wound Bacteria Over Time

Bacteria (63 injuries)	HD 1 (n=189)	HD 3 (n=124)	HD 5 (n=146)
Gram +	48%	39%	27%
Gram -	52%	63%	84%

Bacteria	HD 1 (n=189)	HD 3 (n=124)	HD 5 (n=146)
Gram -	52%	63%	84%
<i>P. aeruginosa</i>	2%	13%	29%
<i>Enterobacter</i>	17%	12%	18%
Mimeae-Herellea- Bacterium-Alcaligenes	15%	11%	11%
<i>E. coli</i>	8%	11%	8%



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Vietnam War

Increasing Bacterial Resistance over Time

Antibiotics and Dose	Staphylococcus		Pseudomonas		Proteus	
	Arrival	After Clinical Infection	Arrival	After Clinical Infection	Arrival	After Clinical Infection
Penicillin (10 unit)	2/33	5/12	0/69	0/18	2/30	9/15
Ampicillin (10 mcg)	1/33	5/12	0/69	0/18	3/20	5/15
Staphcillin (5 mcg)	25/27	9/9	—	—	—	—
Oxacillin (1 mcg)	—	—	—	—	—	—
Erythromycin (15 mcg)	26/30	8/12	30/69	6/18	3/30	3/15
Gantrisin (300 mcg)	—	—	—	—	—	—
Streptomycin (10 mcg)	14/33	0/9	39/69	9/18	9/24	9/15
Chloromycetin (30 mcg)	30/33	12/12	36/66	6/18	11/24	15/15
Tetracycline (30 mcg)	15/30	6/12	17/66	2/15	11/24	0/15
Aureomycin (30 mcg)	—	—	—	—	—	—
Terramycin (30 mcg)	—	—	—	—	—	—
Kanamycin (30 mcg)	23/30	12/12	32/66	11/18	9/27	12/15
Neomycin (30 mcg)	24/30	12/12	57/69	16/18	12/30	8/15
Polymyxin B (30 mcg)	—	—	—	—	—	—
Colymycin (10 mcg)	—	—	63/69	9/18	3/3	—
Keflin (30 mcg)	23/30	6/9	3/60	0/18	0/24	0/9
Nalidixic Acid (30 mcg)	6/6	3/3	9/60	6/18	9/30	3/9
Furadantin (50 mcg)	0/6	3/3	0/60	0/18	20/24	15/15
Tegopen (1 mcg)	23/30	6/6	—	—	—	—
Mandelamine (3 mcg)	33/33	9/9	69/69	18/18	3/3	—
Vancomycin (30 mcg)	6/6	6/6	—	—	—	—

Matsumoto 1969

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Ramadi Iraq, 2003-2004

General Medical Officer



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OIF/OEF

Infections- Trauma ID Outcome Study (TIDOS)

	ICU	Ward	Total
# of patients	64	128	192
# of infections	28 (43.8%)	19 (14.8%)	47 (24.5%)
Bloodstream	12 (18.8%)	6 (3.9%)	17 (8.9%)
Skin & soft tissue	16 (23.4%)	12 (9.4%)	27 (14.1%)
Osteomyelitis	8 (12.6%)	6 (4.7%)	14 (7.3%)

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Afghanistan Resistant Bacteria Bacteremia Burn Patients

Organism	OR	95% CI	p
<i>K. pneumoniae</i>	2.71	1.14 - 6.49	0.025
<i>P. aeruginosa</i>	2.25	0.96 - 5.30	0.061
<i>Acinetobacter</i>	0.48	0.21 - 1.11	0.084
<i>S. aureus</i>	0.79	0.30 - 2.06	0.628
MDR	2.78	1.13 - 6.83	0.026

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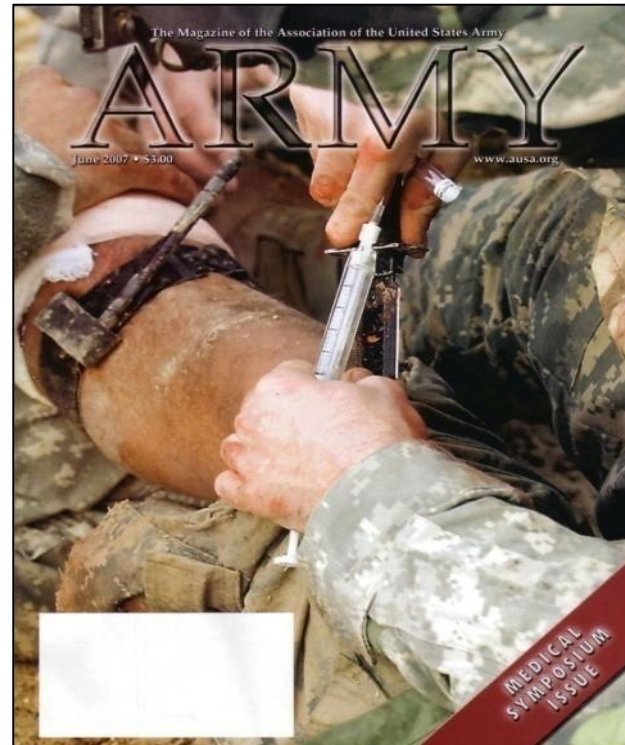


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Source of Bacteria

Epidemiology-Theories

- Pre-injury colonization
- Inoculation at time of injury- environment
- Nosocomial transmission



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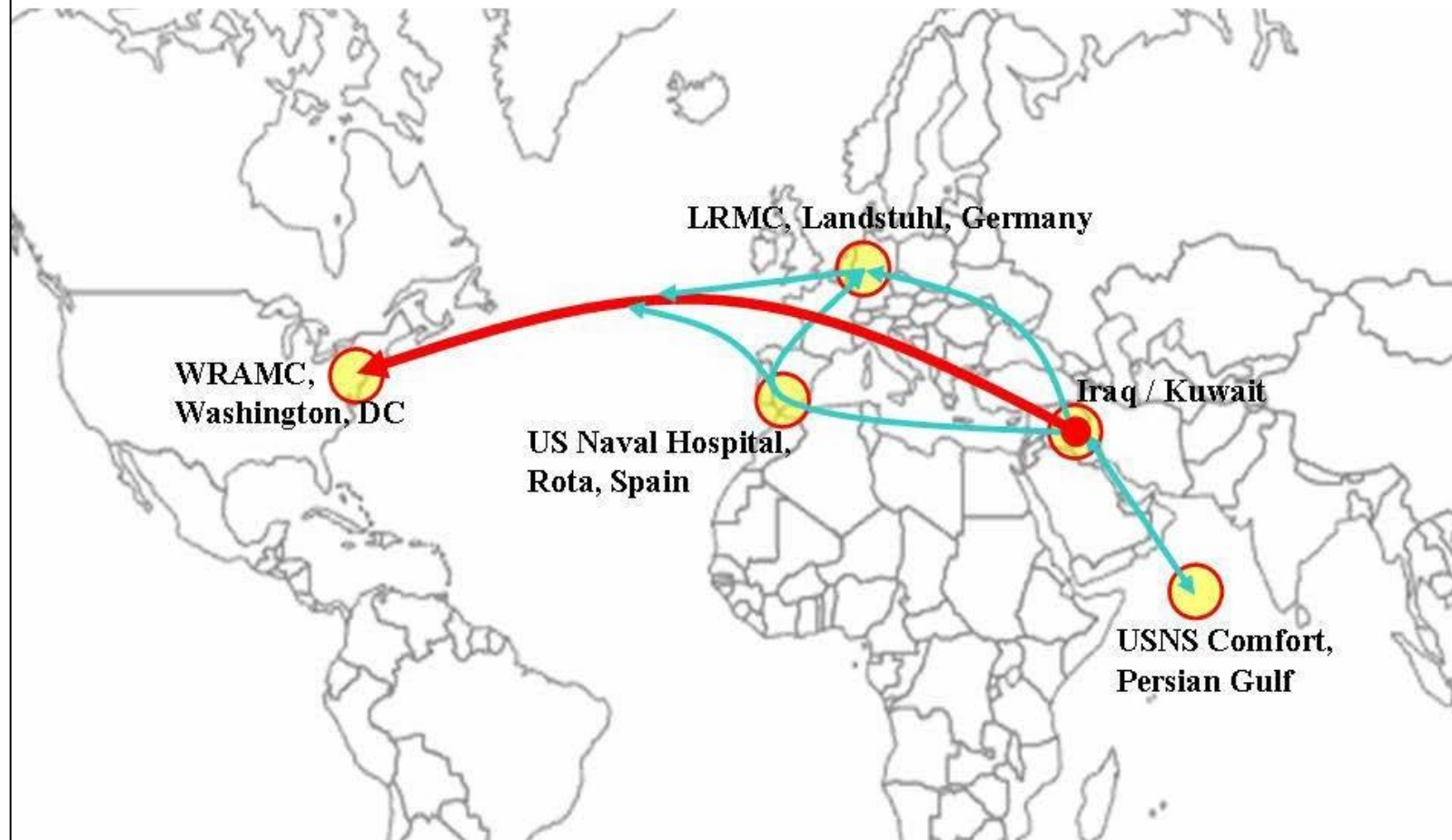


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Resistant Bacteria

Acinetobacter

Aeromedical Evacuation Route for Operation Iraqi Freedom (OIF) Casualties, Iraq to WRAMC



Scott 2007

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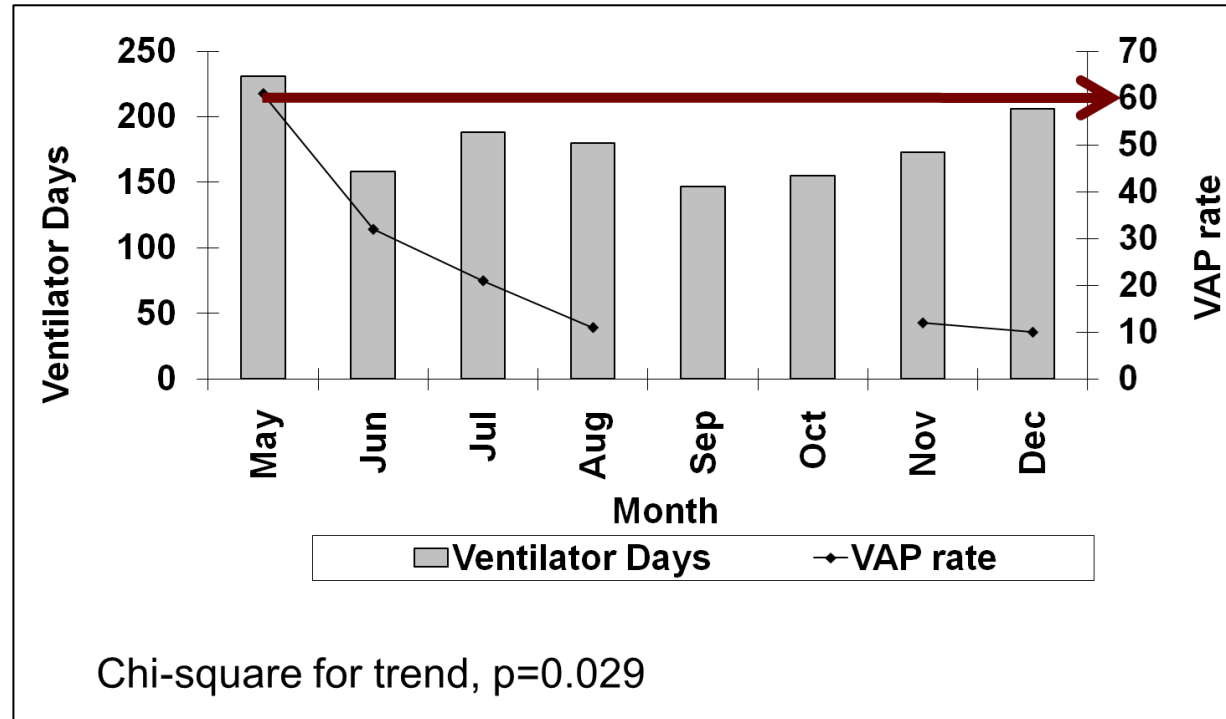
Wars in Iraq/Afghanistan

Controlling the Infection

- Air Force Theater Hospital
- VAP intervention project



Source M Landrum



Landrum 2008

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Ukraine

Battlefield Effects on Medical

- Wound Mechanism: Artillery & UAS munitions (75%)
- Tourniquets: 75% not indicated and loss of extremities due a lack of conversions
- Wound Infection Rates: Near 100%; multidrug resistant organisms



Location of Death *			
POI	Role 1	Role 3	Unclear
40%	30%	5%	25%

Most Common Causes of Death *	
#1	Traumatic Brain Injury (TBI)
#2	Massive Internal Bleeding
#3	Post Tourniquet Syndrome Shock

* Based on autopsy data from 100 casualties

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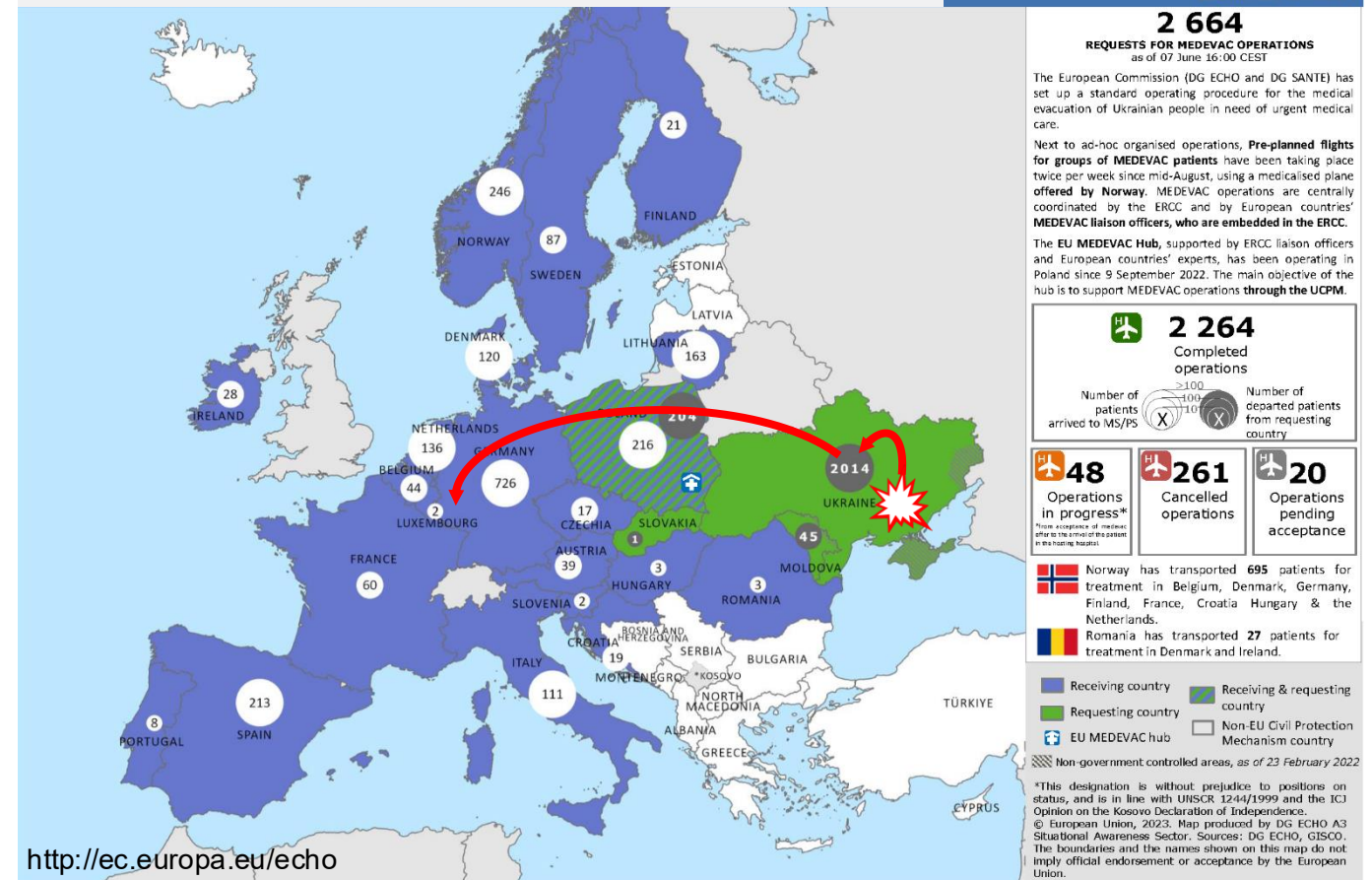


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MDRO Surveillance at Landstuhl Regional Medical Center

- Ukrainian soldier was medically evacuated from Dnipro to Kyiv, then Kyiv to LRMC with ~60% TBSA burns and multiple traumatic injuries 10 days prior to admission
- Clinical cultures obtained + perianal MDRO/CRE screen on admission to LRMC
- Transferred to a German specialty burn center within 24 hours

ECHO MEDEVAC Operations from Ukraine, JUL 2023



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MDRO Surveillance at Landstuhl Regional Medical Center

- Blood culture: **CR-*Pseudomonas aeruginosa***
- MDRO/CRE screen: **4 different Carbapenem-Resistant Organisms**
 - Pseudomonas aeruginosa* x2
 - Acinetobacter baumannii*
 - Klebsiella pneumoniae*
 - VR-*Enterococcus faecium*

Virulence factors encoding the siderophores aerobactin (iuc) and salmochelin (iro), the genotoxin colibactin (Cib), and a hypermucoid phenotype (conferred by the rmpADC locus)



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	PSA (Blood)	PSA #1 (MDRO)	PSA #2 (MDRO)	ACB (MDRO)	KPN (MDRO)
Amikacin	R	R	I		R
Gentamicin	R	R	S	R	R
Tobramycin	R	R	R	R	R
Aztreonam	R	S	S		R
Ceftazidime/Avibactam	R	R	R	R	R
Ceftolozane/Tazobactam	R	R	R	R	R
Meropenem	R	R	R	R	R
Piperacillin/Tazobactam	R	R	R	R	R
Ciprofloxacin	R	R	R	R	R
Levofloxacin	R	R	R	I	R
Tetracycline				S	R
Colistin	I	I	I	I	R
Eravacycline	R	R	R		
Imipenem/Relebactam	R	R	S	R	R
Meropenem/Vaborbactam	R	R	R	R	R
Omadacycline	R	R	R		
Plazomicin	R	R	R	R	R
Tigecycline	R	R	R		I
Cefiderocol	S	S	S	S	R

Species	ST	Major AMR Genes	Hypervirulence Genes
<i>P. aeruginosa</i>	1047	bla _{IMP-1}	
<i>P. aeruginosa</i> #1	773	rmtB4, bla _{NDM-1}	
<i>P. aeruginosa</i> #2	357	bla _{VEB-9}	
<i>A. Baumannii</i>	78	armA, bla _{OXA-23} , bla _{OXA-72} , bla _{CTX-M-115}	
<i>K. pneumoniae</i>	395	armA, bla _{NDM-1} , bla _{OXA-48} , bla _{CTX-M-15}	yersiniabactin (ybt), aerobactin (iucA), rmpA, rmpA2
<i>E. faecium</i>	117	vanA, aac(6')-Ie/aph(2'')-Ia	

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Operation EPIC FURY

Patients Evacuated as of 11 May 2026

- Multidrug resistant bacterial colonization
 - 33 screened (LRMC and WRNMMC)
 - 9 ESBL *E. coli* (4 Kuwait, 1 Iraq, 1 Iran, 1 Saudi Arabia, 1 Bahrain, 1 Oman)
 - 1 ESBL *Enterobacter* (Kuwait)
 - 1 Carbapenem Resistant *Acinetobacter* (Jordan)
 - 1 infected
 - ESBL *E. coli* (Kuwait) poly trauma

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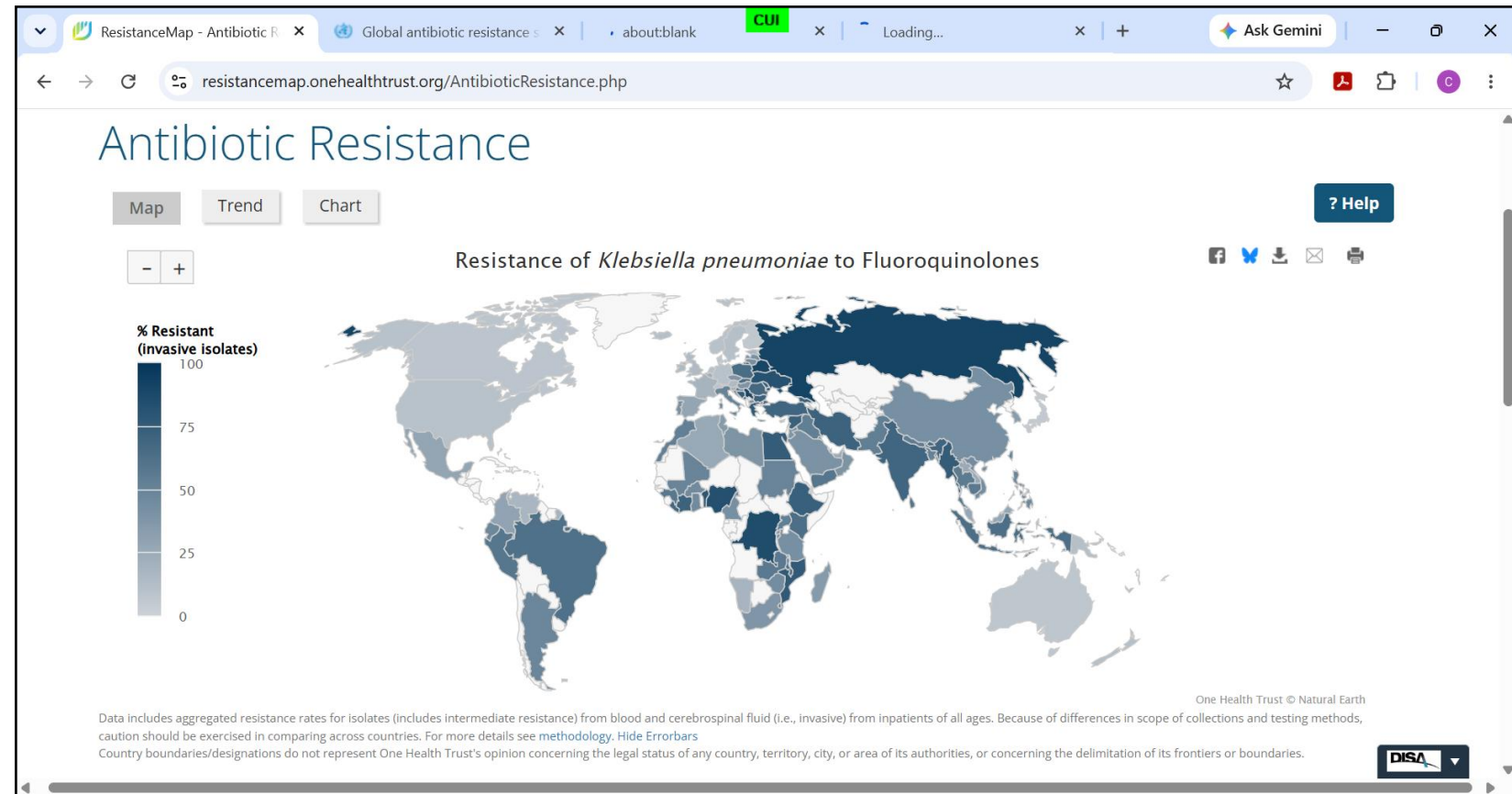
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Multidrug Resistant Bacteria

Need Threat Informed Preventive and Prescriptive Analytics

Joint Warfighter Concept

- **Information Advantage**
- Integrated C2
- Joint/Cross-Domain Fires
- Contested Logistics
- Expanded Maneuver



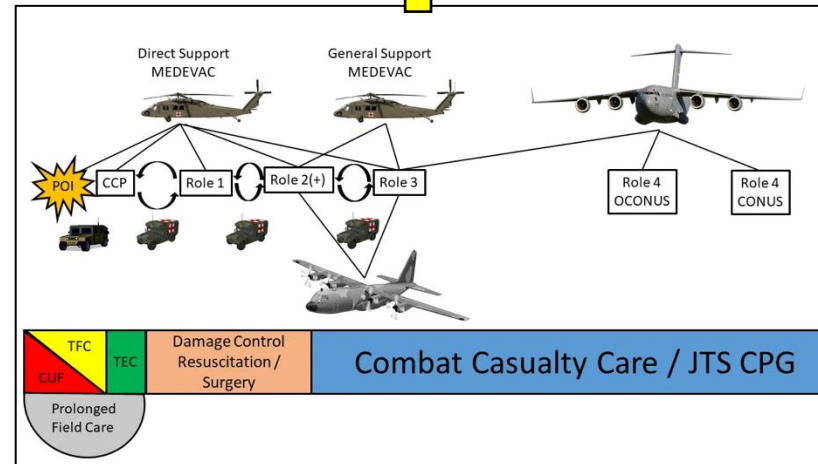
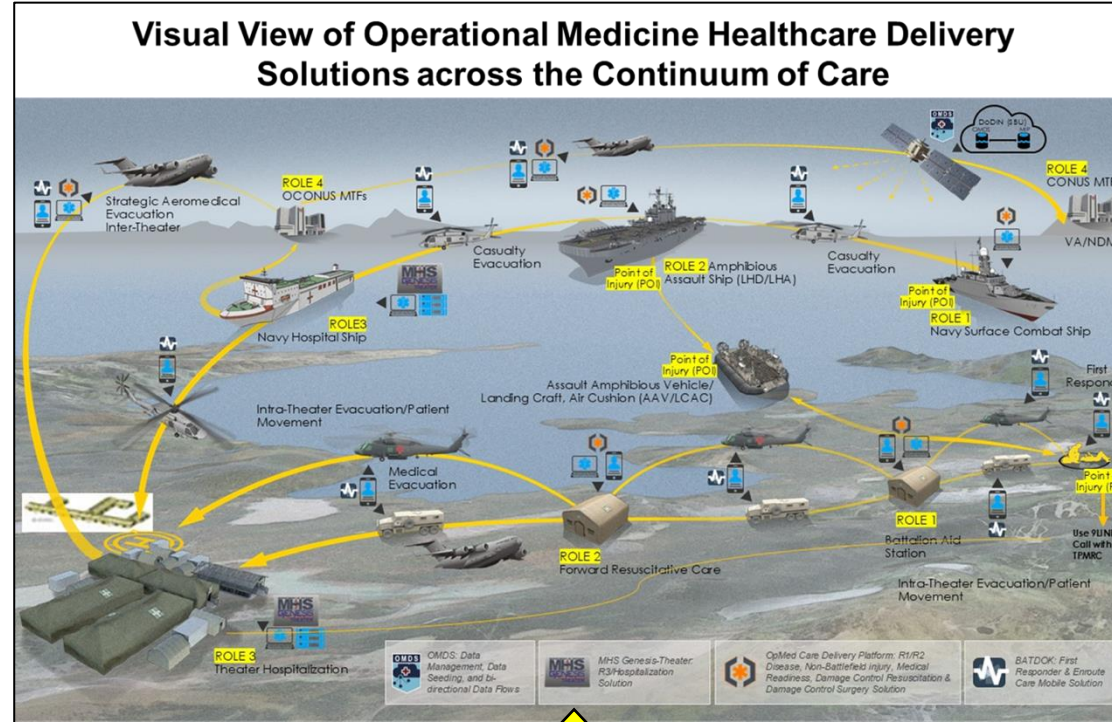
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Continuum of Care is

Transitioning to a Disaggregated Web and then Mesh that is Pulsed





Search Google Maps

- Taipei → Okinawa- 400 miles (350 nm)
- Manila → Guam- 1600 miles (1388 nm)
- Guam → Hawaii- 3800 miles (3303 nm) (C130 can't make it)
 - Army Watercraft ~10 knots/h (35h and 138h)
 - Amphibious Assault Ship (LHD) ~22 knots/h (16h and 63h)
 - Osprey (airplane mode) ~275 knots/h (1.3h and 5h)
 - C-130J (Super Hercules) ~350 knots/h (1h and 4h)

Japan

North Pacific Ocean

HI

Standard max range 280nm
+ 2 200-gal external tanks 400-500nm
1-hour range limit- 40nm

Maps

DoD MTF
VA Polytrauma Ctr

CCRFs: 4

MDR Bacteria- existential threat to the U.S. healthcare system?

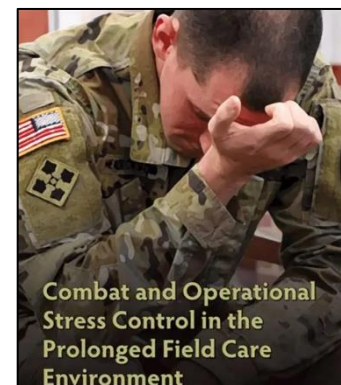
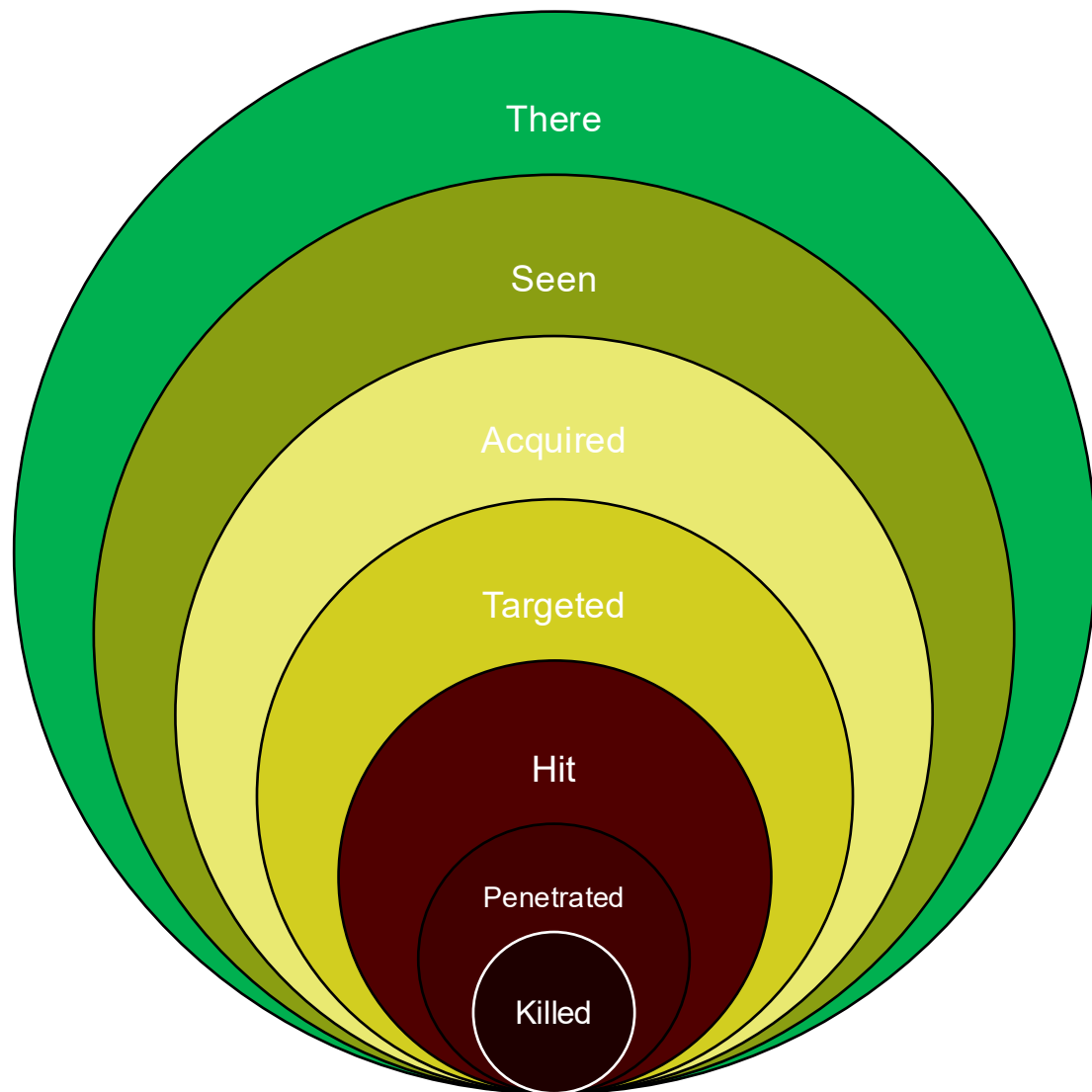
CCRFs: 4
areas- Travis,
JBLM, BAMC,
Walter Reed
(NCR)



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Survivability Onion

Don't Be



Combat and Operational Stress Control in the Prolonged Field Care Environment



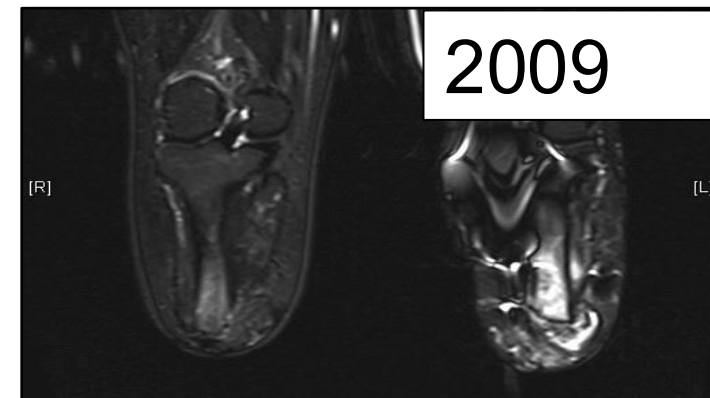
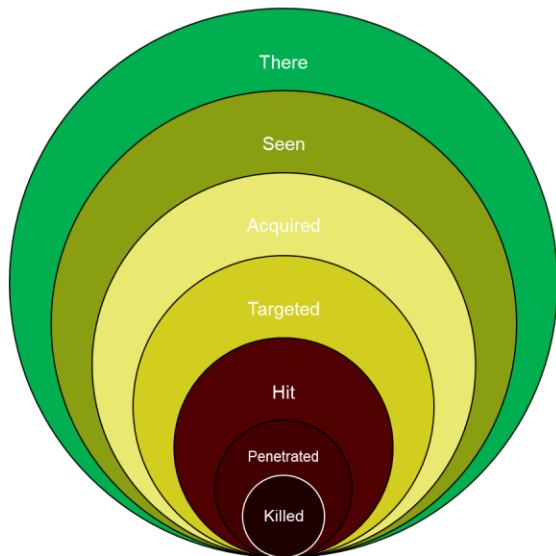
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Survivability Onion

Don't Be



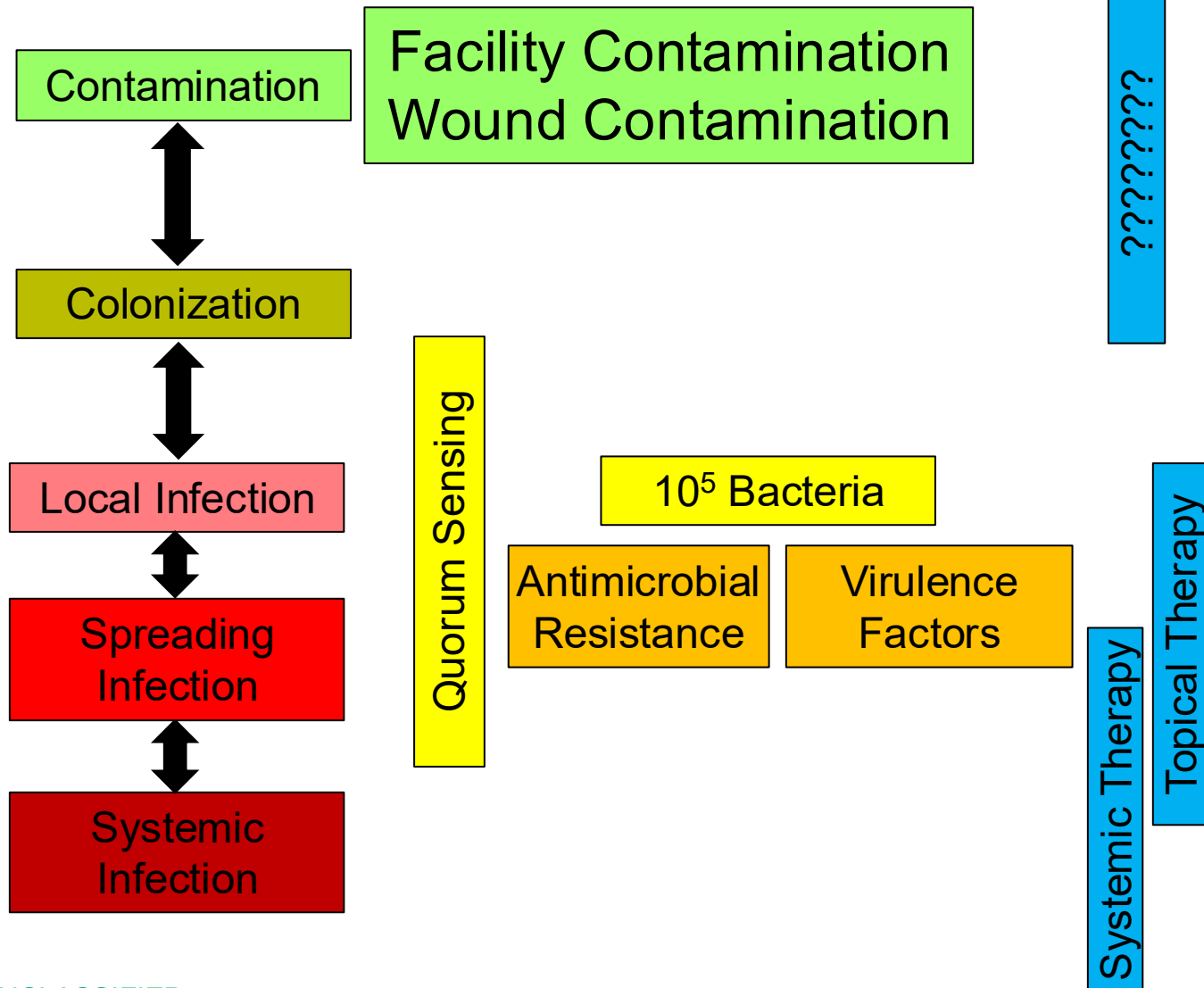
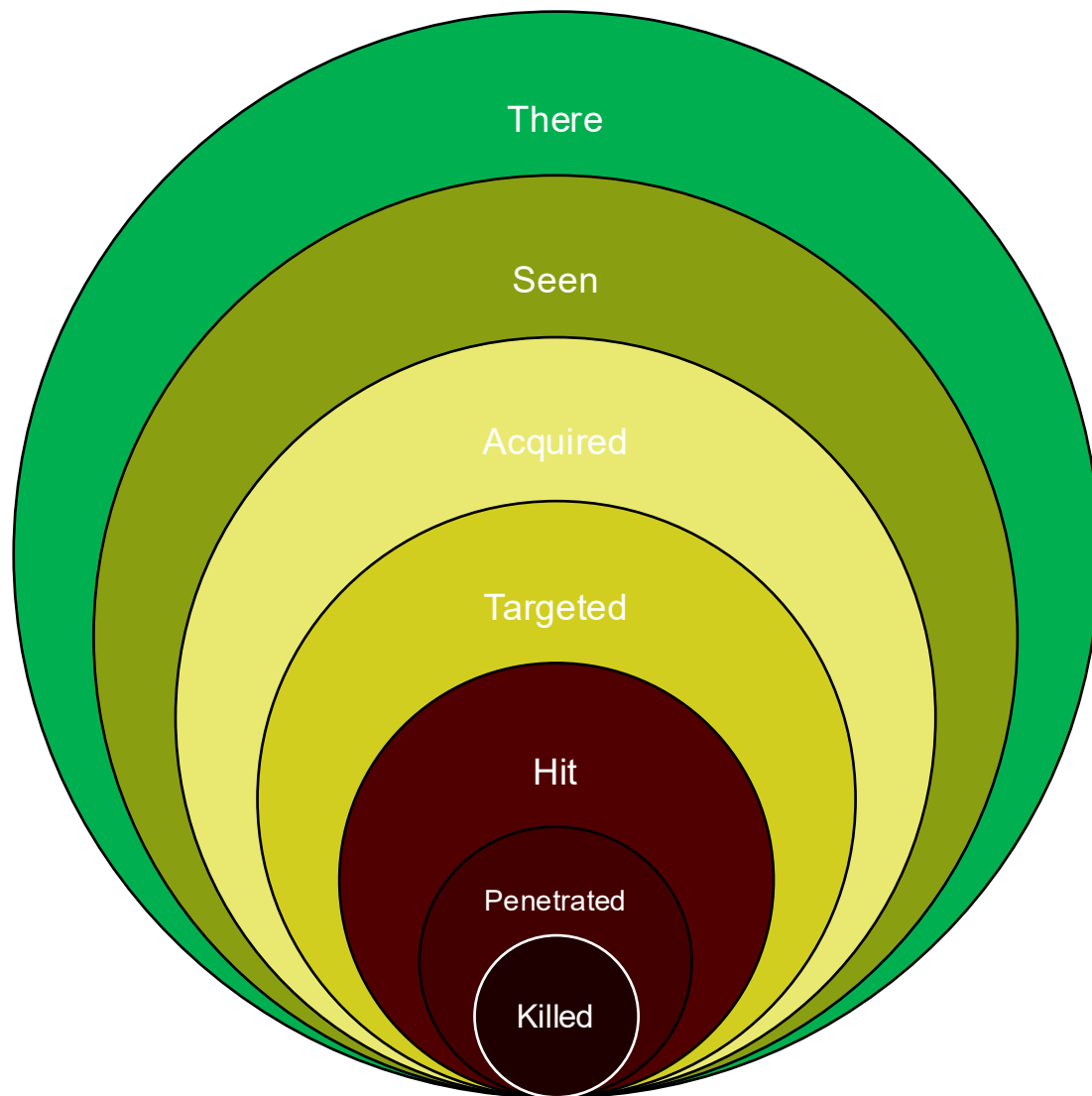
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Survivability Onion

Don't Be



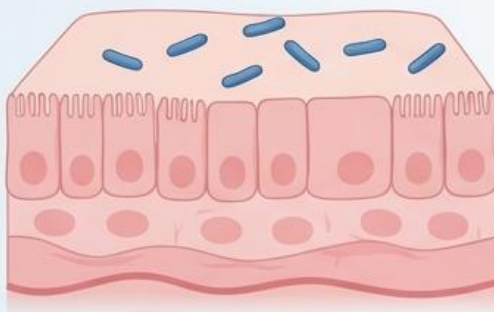
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THE PATH TO INFECTION: DENSITY, COMMUNICATION, AND THRESHOLDS

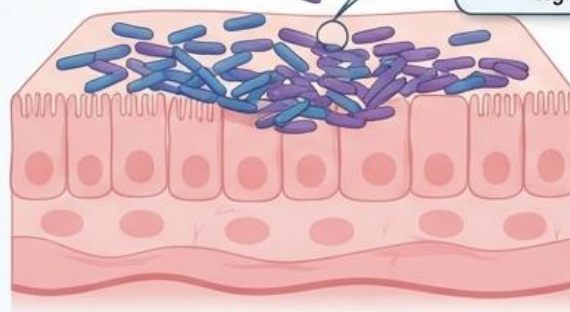
1: Contamination (Low Density)

Few bacteria present.
No host reaction.
Transient presence.



2: Colonization (Increasing Density)

Bacteria adhere and multiply.
Formation of early biofilms.



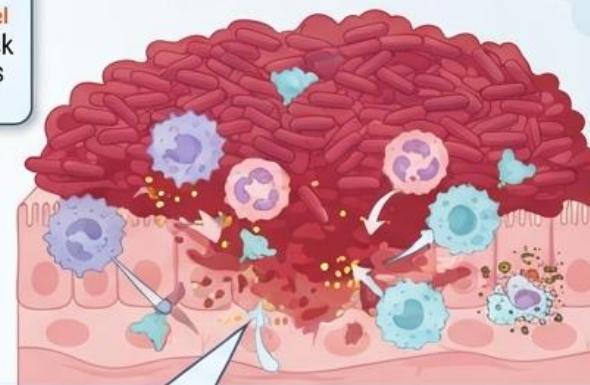
The 10^5 Threshold

CFU/mL 10^5 Critical Level
At $\sim 10^5$ bacteria/g, risk of infection increases significantly.

3: Infection

(High Density & Quorum Sensing)

Tissue invasion and damage.
Host immune response triggered (inflammation)



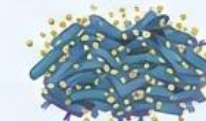
Quorum Sensing in Action.

1 Low Density



Low Autoinducer concentration.

2 High Density (Quorum Reached)



High concentration of Autoinducers binds to receptors.

Trigger: Coordinated



Toxins:
Coordinated expression of Virulence Factors & Biofilm Formation



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Survivability Onion

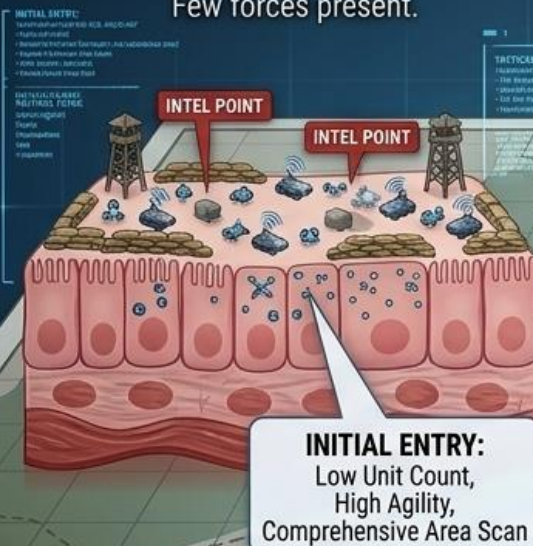
THE PATH TO HOST CONQUEST

OPTIMIZED DEPLOYMENT & STRATEGIC ASSAULT

1: DEPLOYMENT & INTEL GATHERING (RECON)



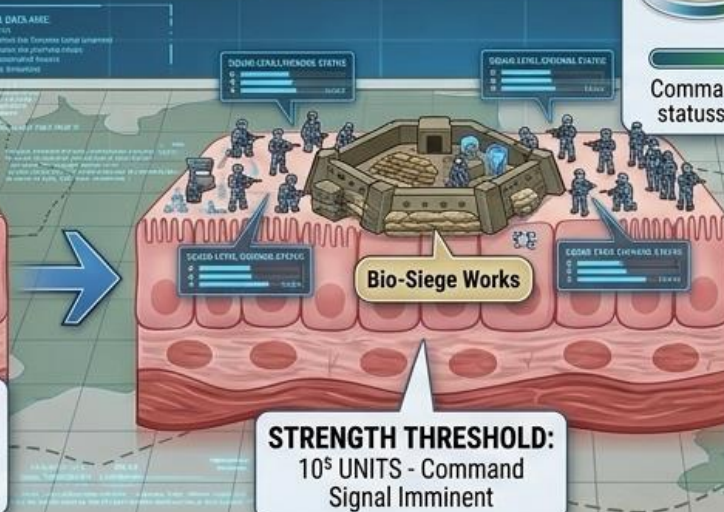
Initial entry. Unit separation.
Gathering intelligence.
Few forces present.



2: LOGISTICAL CONSOLIDATION & SIEGE PREP



Forces multiply and organize.
Establishing forward bases (biofilms).
Reaching Critical Strength Threshold.



The 10⁵ POWER RATING



Command & Control Ready
status units congregate.

3: ALL-OUT ASSAULT (COORDINATED STRIKE)

Coordinated attack.
Breaching defenses.
Tissue degradation.



COORDINATED STRIKE: THE COMMAND NETWORK

1 UNIT DEPLOYMENT (Low Density)



Units scattered. Signals
(autoinducers) too weak
for command recognition.

2 STRENGTH REACHED (COMMAND INITIATED)



Units gathered.
Signal density triggers
command signal.



COMMAND SIGNAL RECPLETE:
Epithelial barrier destroyed,
tissue invasion successful,
systemic host effects initiated.

QUORUM SENSING STATUS: [LOW DENSITY / HIGH DENSITY / COMMAND ACTIVE]

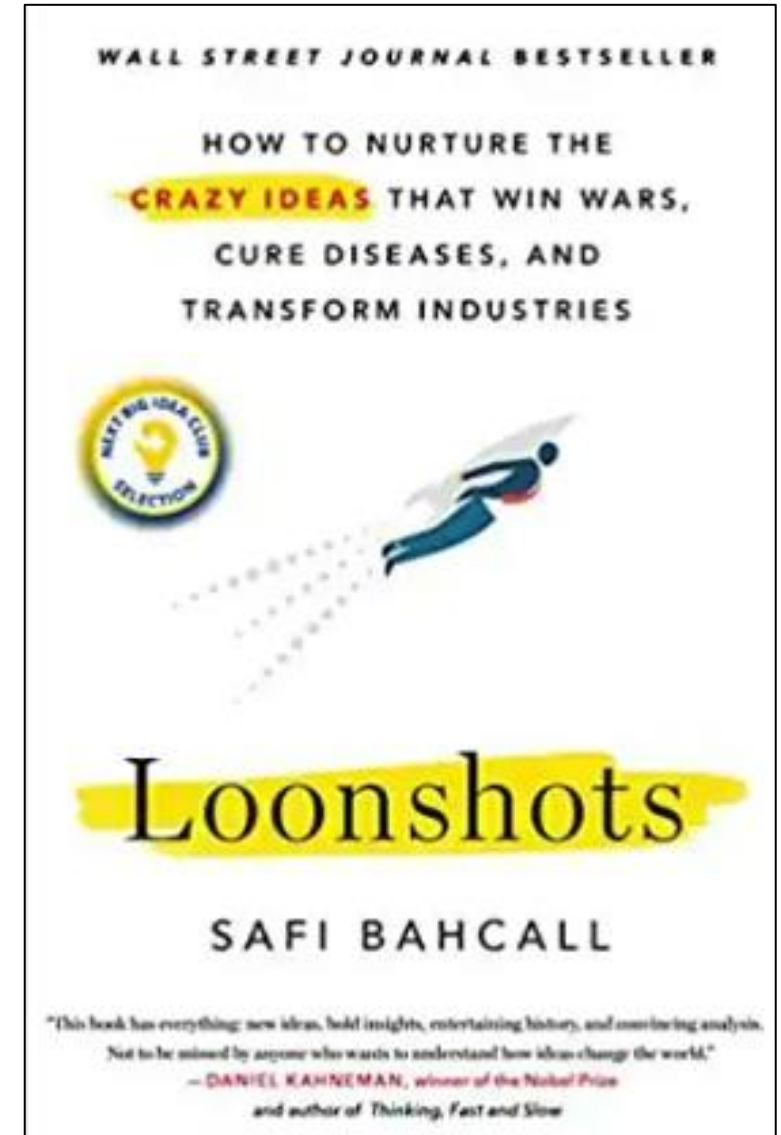
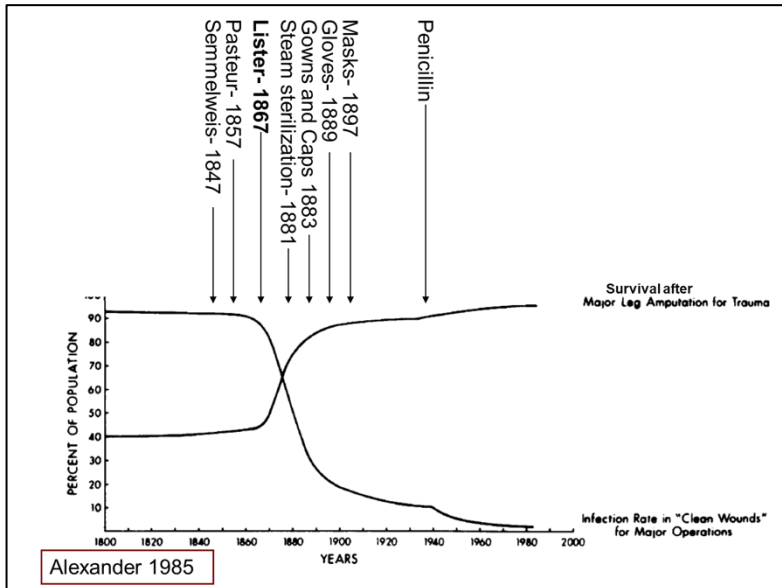
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Thoughts

- Look at it from a different lens
 - Operational lens- tyranny of distance, A2/AD
 - MDR pathogens- Protect, Detect, Treat
 - Patient focused
 - Facility focused- nosocomial transmission
pathogen decontamination



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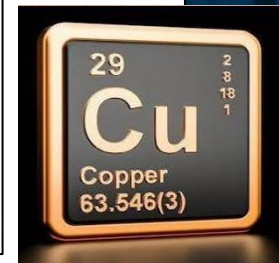
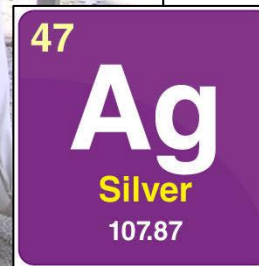


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Operational Loonshot at Scale...Now



*Have We
Advanced?*



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