

WAR TRAUMA, GERM WARFARE



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Acinetobacter baumannii

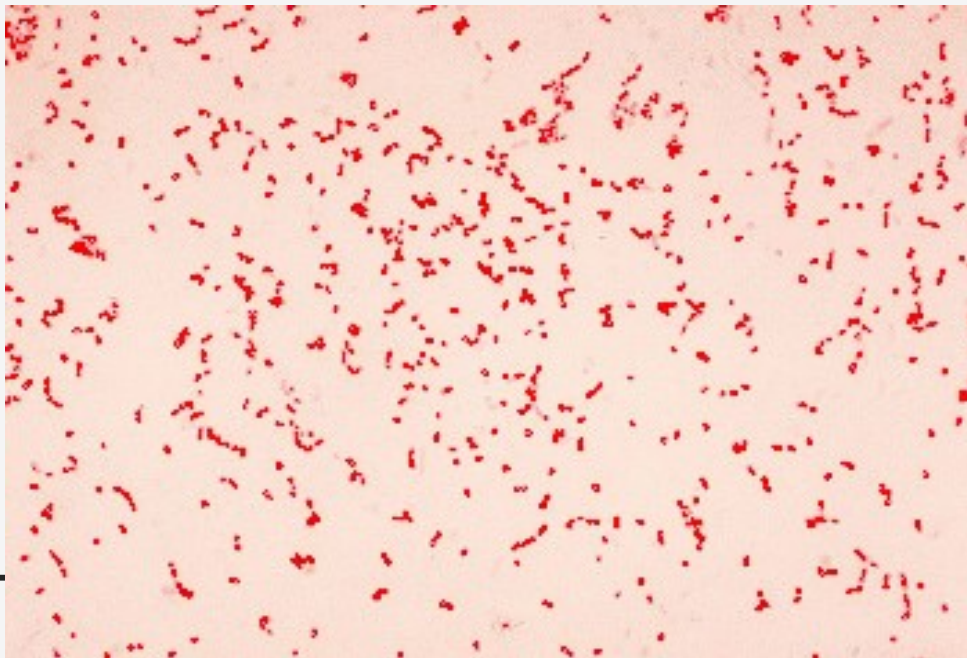
Breeding a new generation of germs

- War trauma (extremity) injury commonly → contamination with environmental debris & severe soft tissue injury
 - Colonization followed by infection with drug-resistant, particularly gram-negative organisms
 - Multi-system infection
 - Very hard to treat
 - Longer hospital stays
 - Very expensive
 - Wounds -> scars, amputations, chronic disability, deaths
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Objectives:

- Know your enemy: *MDR Acinetobacter* (aka *Carbapenem-resistant*)
- From environmental microbe → commensal → superbug
- Understand drivers of resistance
- Use this knowledge to devise effective treatment strategies
- Prevention/ containment/harm reduction



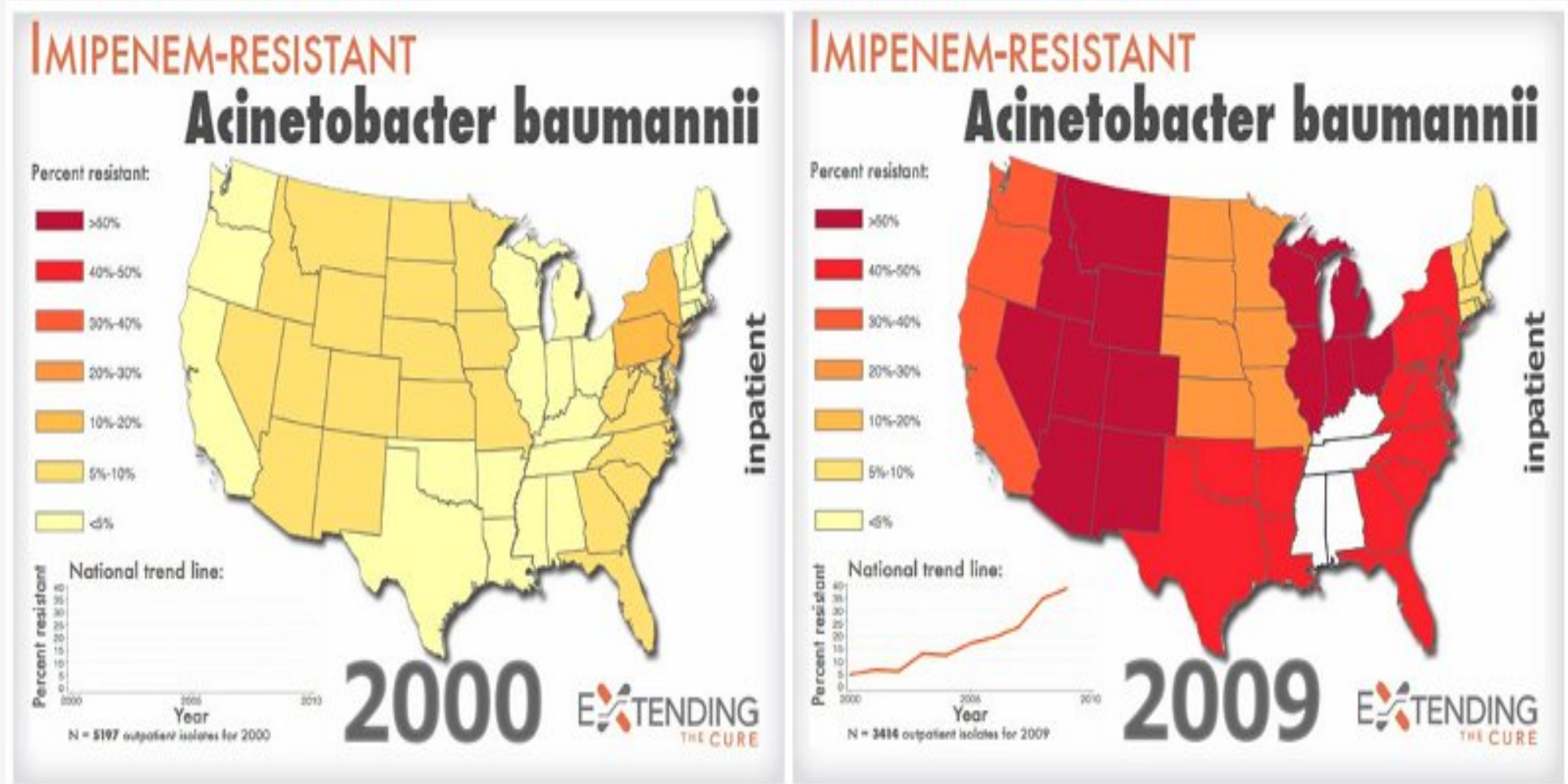
Rise and spread of Acinetobacter baumannii (‘Iraqibacter’)?’

- January 1, 2002 - August 31, 2004,
- 102 US soldiers Afghanistan /Iraq war in 5 military hospitals
- Resistant to :
 - Imipenem
 - Amikacin
 - Ampicillin/sulbactam
 - Piperacillin/tazobactam
 - Cefepime
 - Ciprofloxacin



<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5345a1.htm>
Accessed July 6, 2014

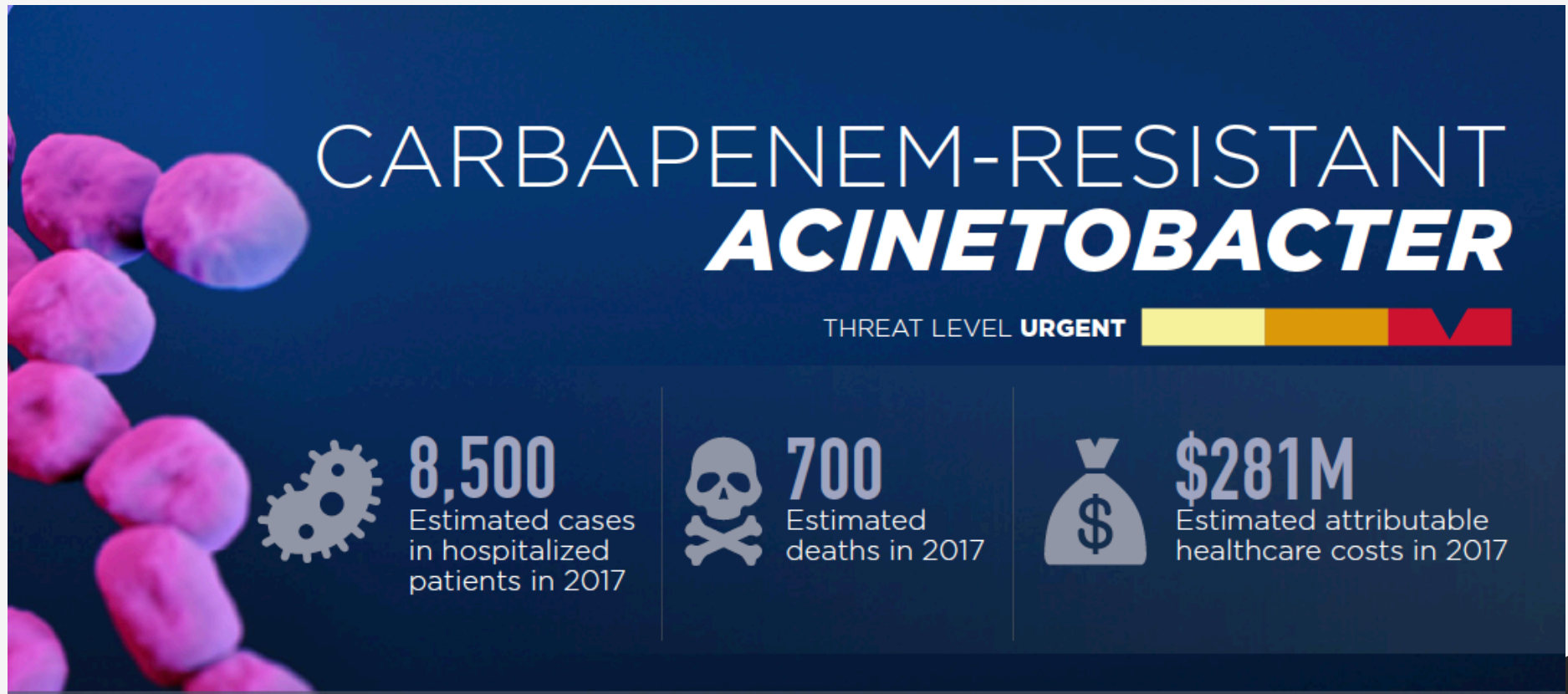
Main driver Acinetobacter = US



Davolterra. <http://www.davolterra.com/content/resistance-antibiotics-rise>. Accessed June 25, 2014

Session 2

CDC Threat Report *2019*



**U.S. Department of
Health and Human Services**
Centers for Disease
Control and Prevention

Acinetobacter: challenge everywhere

Syria: Infection control nightmare

Not 'aggressive' but


- Morbidity increased
- Mortality increased
- Difficult to treat because of antibiotic resistance
- Convergence of resistance and virulence

Underground field hospitals → perfect breeding conditions:

- for germs to acquire resistance
- Patients to acquire infection

Syria Pre-revolution: culture of abuse

- No antibiotic regulation – OTC+++
 - No protocols for infection control
 - Heavy use
 - Few microbiologists
 - I/o training collection samples medical or laboratory personnel
 - Unreliable results

 - Limited to respiratory system:
Acinetobacter - VAP
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Since 2011:

- heavy weaponry
 - multi-system damage
 - penetrating wounds
 - + contamination
 - + shrapnel
 - Unsterile operating environment
 - Little/ no laboratory services
 - Unreliable results
 - Increasing use BSA → resistance
 - Increasing demand → Drug smuggling, fake drugs
 - Hospitals become ifactories
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Facts: Commonly found in

- water, soil, and sewage
- Food (including fruits and vegetables),
- healthy skin and other body sites

grows at

- various temperatures
- and pH environments – acid/alkali
- survives on surfaces for weeks

Virulence factors

Ability of A. baumannii to:

- attach and persist on solid and dry surfaces
 - obtain essential nutrients such as iron
 - adhere to and then destroy epithelial cells,
 - produce gelatinases and proteinases that damage host tissues
 - form biofilms: these assist in colonization, resistance to disinfection and trade of resistant genes
 - colonize the skin of patients of healthy individuals without causing illness
 - Immunosuppressed, esp patients with
 - Diabetes
 - Chronic lung disease
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Sources of colonization and/or infection in hospitals

- Hands of hospital staff
- Food (including hospital food)
- Tap water
- Infusion pumps and Respiratory therapy equipment
- Mattresses, pillows, bed sheets, blankets in vicinity of infected patients
- Soap dispensers
- Fomites like bed rails, stainless steel trolleys, door handles, telephone handles, tabletops
- Hospital sink traps and floors

Risk Factors for MDR A.baumannii Infection

- Exposure to antimicrobial agents esp., carbapenems,
 - mechanical ventilation
 - Prolonged length of hospital stay: hospitals, period.
 - Exposure to an intensive care unit (ICU)
 - Colonization pressure
 - Recent surgery
 - Invasive procedures
 - Underlying severity of illness
 - Environmental contamination
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Transmission

- Person-to-person
- Contact with contaminated surfaces
- Survives for weeks on clothing, bed rails, ventilators, sinks, doorknobs
 - This makes transmission very difficult to control
- Respiratory system is the most prominent route of entry

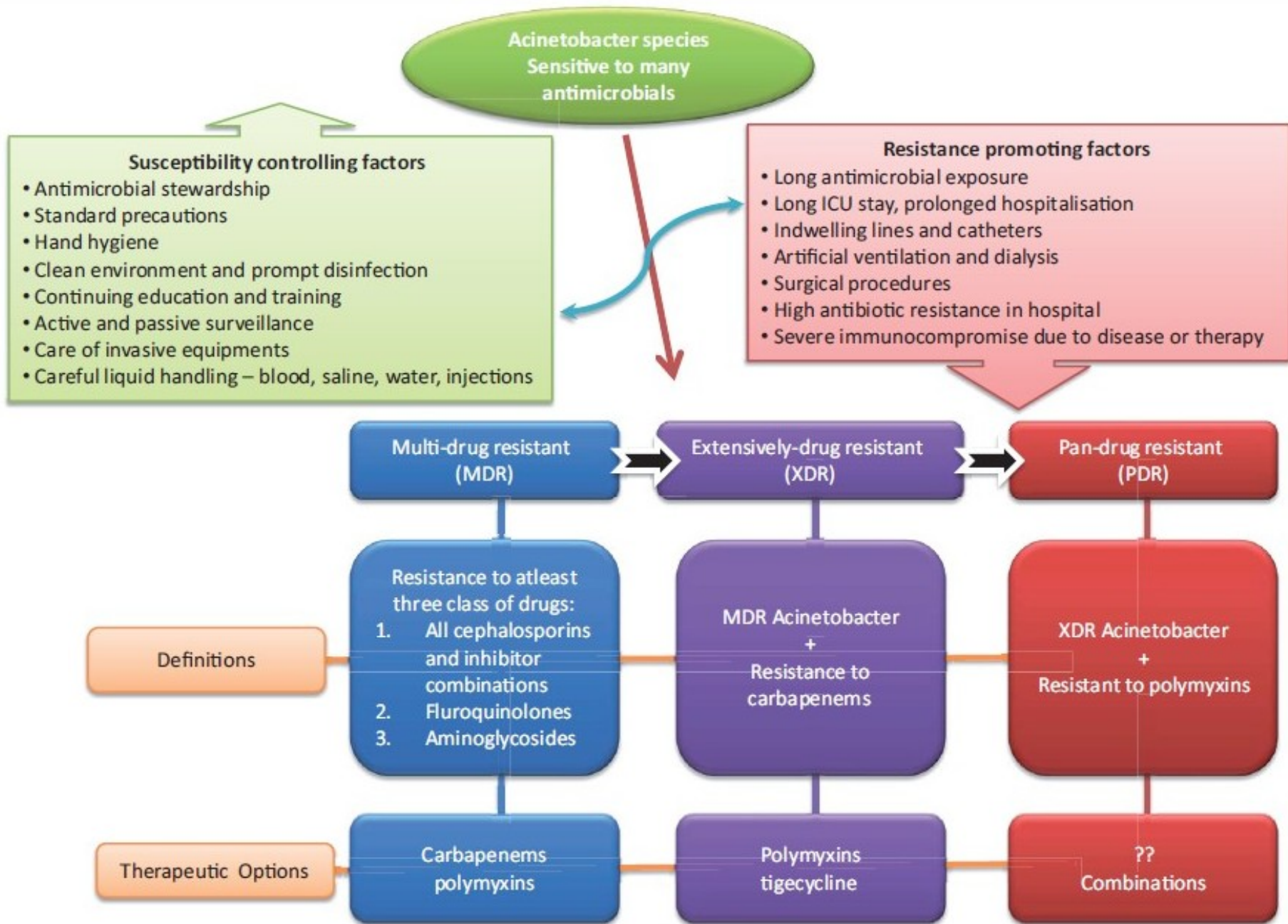


MDR Infections

- Bacteremia
- Pneumonia
- Urinary tract infections
- Wound infections
- Osteomyelitis
- Endocarditis
- Meningitis
- Peritonitis
- Abdominal abscess
- Prolongs mechanical ventilation dependence, ICU stay, and hospital stay


MDR Treatment

- Carbapenem was the treatment of choice:
- Aminoglycosides (tobramycin / amikacin) in conjunction with another active antimicrobial agent
- Ampicillin-sulbactam
- Tigecycline
 - Has bacteriostatic activity against MDRA species
 - High-level resistance to tigecycline has been detected
 - Best reserved for salvage therapy
- Polymyxin B or polymyxin E (colistin)
- Most of the acinetobacter isolates here are becoming resistant to everything with the exception of colistin, tigecycline,
- a very few isolates we are finding also sensitive to doxycycline



Primary tools to fight infection in war trauma:

How to prevent infection by an organism lurking on walls, floors, sinks, tables, sheets, in equipment, on ourselves?

- Aggressive debridement PLUS
 - Wound decontamination & VAC
 - MEBO
 - STOP long broad-spectrum antibiotics:
 - Start culture-directed antimicrobial therapy & talking to microbiologists
 - Strict infection control and a thorough understanding of the organism itself is a critical part of stopping the spread of *A. baumannii* from one ICU to the next.
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Post-traumatic / Chronic OM

Prevention easier than cure

Reducing frequency of COM after open fracture possible with:

- Early debridement and wash-out after injury
- Prophylactic antibiotics
- External fixation
- Soft tissue coverage (envelope for healing, may deter infection)

Once established, post-traumatic COM can be difficult to cure:

- The standard treatment tools widely available for COM in resource-rich settings are not widely available in poor and conflict-affected settings
- MSF approach:
 - Extensive surgical debridement with removal of all necrotic soft tissue and bone (bone clearance margin of ≥ 5 mm)
 - Pathogen-targeted antibiotic therapy up to 12 weeks after definitive debridement
 - Reconstructive surgery in some contexts (eg Amman)



Aggressive Debridement COM

Extent of resection & long-term outcome in COM

Simpson *et.al.* (2001) evaluated 3 surgical strategies for COM (N=50):

- 1) Wide resection, with a bone clearance margin of ≥ 5 mm
- 2) Marginal resection, with a clearance margin of < 5 mm;
- 3) Intralesional biopsy, with only debulking of the infected area.

- All patients antibiotics IV for 6 weeks + PO for a further 6 weeks -

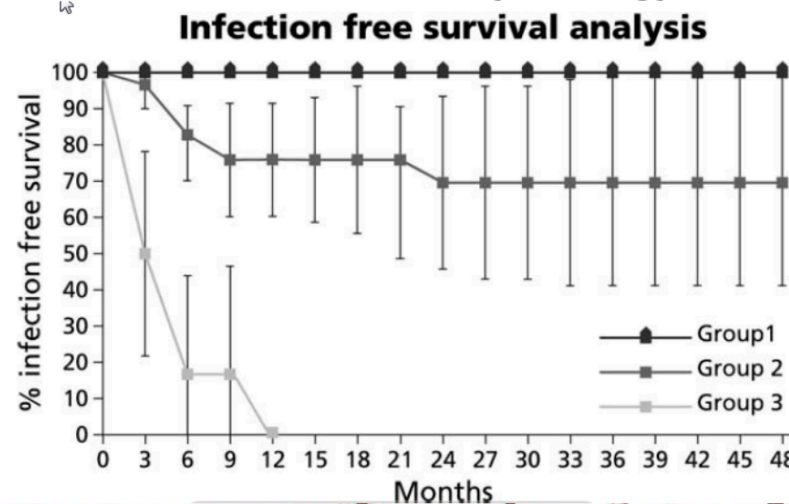
Outcomes:

Group 1 = ≥ 5 mm:
No recurrence (0%)

Group 2 = < 5 mm / marginal
8 of 29 (28%) recurrence.

Group 3 = Debulking
All had a recurrence (100%)
within 1 year of surgery.

Infection free survival by strategy:



Moist Exposed Burn Ointment (MEBO), Honey

dead burned skin, subcutaneous tissue together with viable

MEBO

MEBO (Moist Exposed Burn Ointment) is a Chinese herbal formulation and has been proposed as an efficacious product for the management of partial-thickness burns.



500 × 500 - amic.com.ph

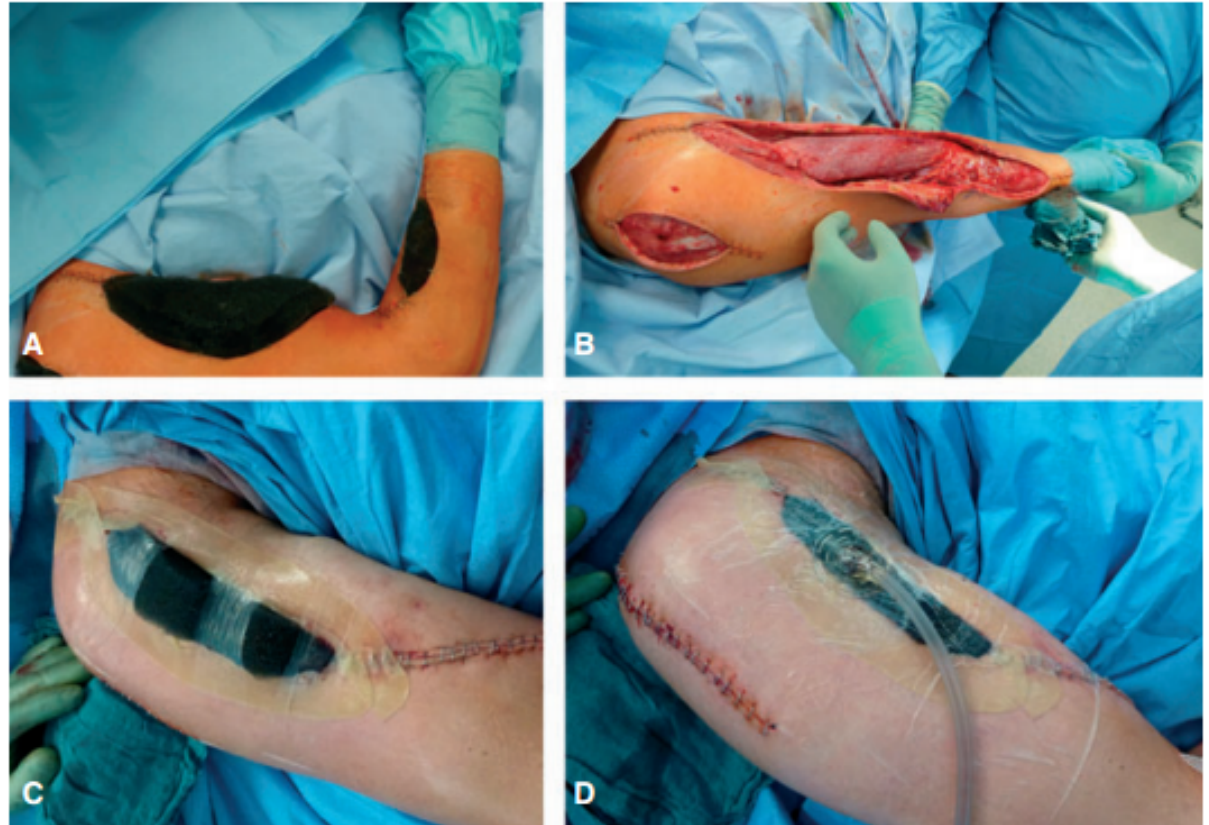


Fig. 6. b. Exposure and dryness of burned skin.



VAC/ Negative pressure wound therapy

- VAC combine with
- local antiseptic wound cleansing



*Patient
innovations
to increase
immunity?*

BCG vaccine or Measles vaccine

Probiotics

Fecal Transplants for C.difficile: -
restoring 'normal bacteria' via fecal
transplants may be an effective
treatment for recurrent, debilitating
CDI: could also improve general
immunity



Environment:

- Culture nose, throat, skin sites – axilla, groin, rectum, open wounds, endotracheal aspirates.
 - Is it the problem or not?
 - Cleansing focus highly contaminated areas:
 - VHP (Vaporized hydrogen peroxide)
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Summary

- Extraordinary challenge against cunning pathogens
 - Get smart: start sampling, get data, know your hospitals and wards OR/ ER/ ICU
 - Use this research – “War trauma, surgical strategies for infection control in conflict”
 - for your patients, for your hospitals to leverage funds/ showcase Syrian expertise/ graduate your residents & medical students
 - Collaborations on offer: but own your data -!
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Case study: 26-year-old pilot



- bilateral closed femur and open tibia fractures
- above the knee amputations and implanted hardware
- Physical exam: soft tissue and bone infections at the surgical sites.
 - debridement
 - started cefazolin and gentamicin
- Fevers persisted, patient developed pneumonia.
 - broadened to vancomycin, piperacillin-tazobactam, and ciprofloxacin

Introducing

• • •



- Cultures from bronchoalveolar lavage and wound debridement grew multidrug-resistant *Acinetobacter baumannii* complex.
- initially susceptible to only colistin
- Started on IV colistin, meropenem, and minocycline
- persistent fever and purulent drainage from the surgical sites

Progress

- multiple surgical debridements and washouts
 - application of wound vacuum-assisted closure (VAC)
 - trial of continuous irrigation of colistin via wound VAC .
 - wounds improved
 - normalization of inflammatory markers
 - Subsequent testing: colistin/rifampin synergy.
 - Finally discharged on meropenem, colistin, & rifampin for 4 more weeks.
 - Transitioned to amoxicillin and doxycycline for chronic suppression of multidrug-resistant organism osteomyelitis due to retained hardware
 - Seven years of follow-up: living independently with bilateral lower extremity prostheses
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