Šta učiniti kod pojave multirezistentnih bakterija?

Multirezistentne bakterije: definicija

MDRO = rezistentni na najmanje jedan antibiotik iz tri ili više grupa antibiotika (ECDC/CDC)

- Mogu uzrokovati infekciju
- Kolonizirati kožu i sluznice

Najznačajnije multirezistentne bakterije

- MRSA
- Enterobacteriaceae-ESBL sojevi (E. coli, Klebsiella pneumoniae)
- Karbapenem rezistentne enterobakterije, Pseudomonas aeruginosa, Acinetobacter spp.
- Vankomicin rezistentan Enterococcus

Trenutna situacija o multirezistentnim bakterijama-WHO

- Antibiotska rezistencija je prisutna u svakoj zemlji
- Pacijenti inficirani multirezistentnom bakterijom su pod većim rizikom od lošeg ishoda i smrti i troše više resursa
- K. pneumoniae rezistentna na karbapeneme proširila se u sve dijelove svijeta. U nekim zemljama kod više od polovine pacijenata inficiranih ovom bakterijom karbapenemi su nedjelotvorni

Trenutna situacija o multirezistentnim bakterijama-WHO

- Rezistencija na colistin javlja se u nekim zemljama (zamjena za karbapeneme)
- Rezistencija E. coli na fluorokinolone (urinarne infekcije) široko je rasprostranjena. U mnogim zemljama više od polovine pacijenata ne može se liječiti ovim lijekovima.
- Pacijenti inficirani MRSA 64% veći rizik od smrtnog ishoda u odnosu na pacijente inficirane osjetljivim S. aureus.

MRSA

- U opštoj populaciji najčešće uzrokuje infekcije kože i potkožnog tkiva, ponekad pneumoniju, rjeđe druge infekcije. Ako se ne liječi može uzrokovati sepsu
- U bolnici najčešće uzrokuje infekciju krvi, pneumoniju i infekciju hirurške rane → sepsu, smrt

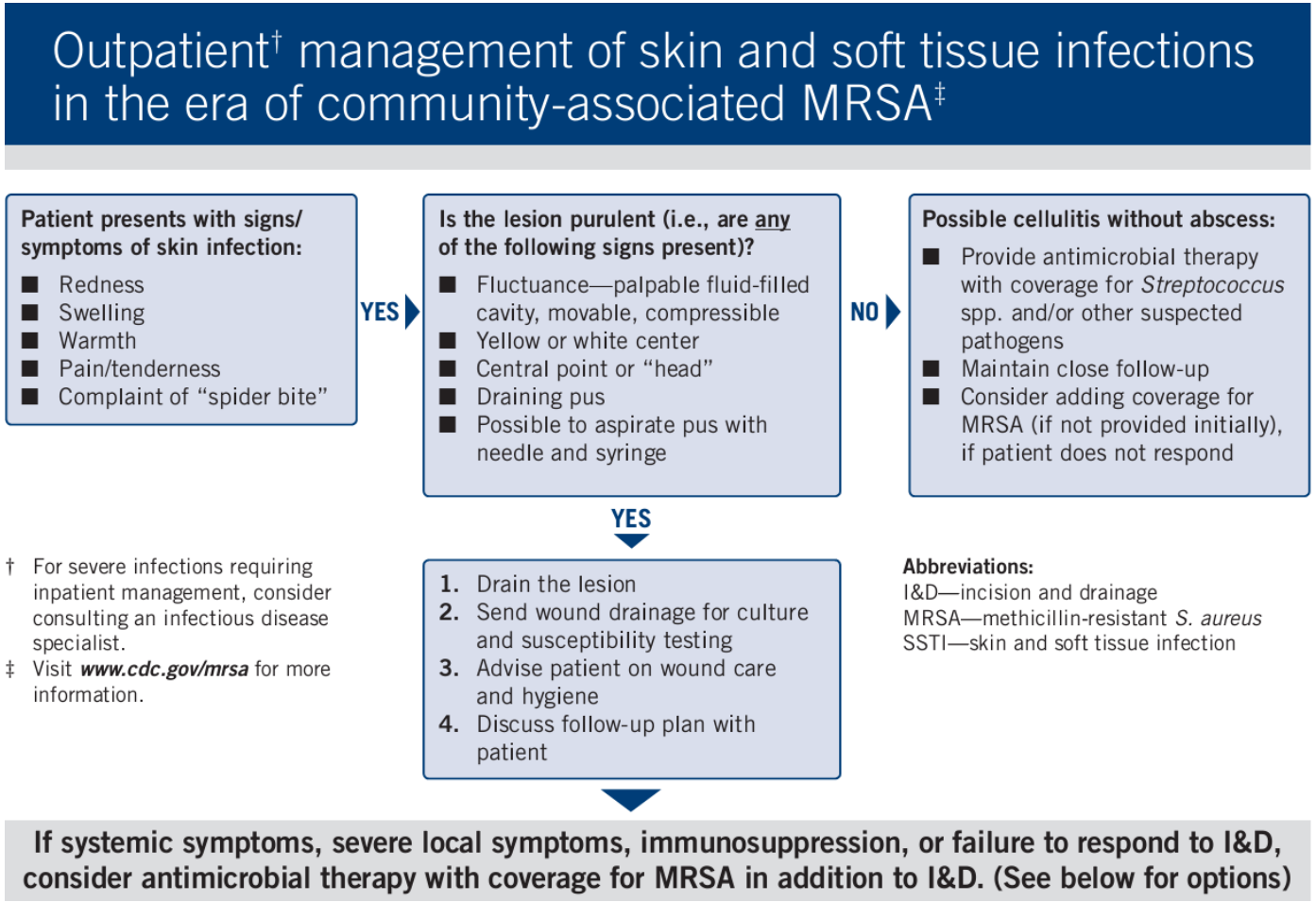
MRSA- opšta populacija

- Procjenjuje se da je 1 od tri osobe kliconoša Staphylococcus aureus (nos)
- 2 od 100 osoba kliconoše MRSA
- Rizik: direktan kontakt sa inficiranom osobom (škole, studentski domovi, vrtići, kasarne, sportski klubovi) ili indirektan (preko pribora za ličnu higijenu-peškiri, brijači...)
- Prevencija: pokrivati inficirane površine, ne dijeliti lični pribor, prati ruke i tijelo, prati prljav veš

MRSA-bolnica

- Rizik: direktan kontakt sa inficiranom ranom, indirektno (kontaminirane ruke-zdravstveno osoblje), kliconoše
- Prevencija: slijediti vodiče, protokole za prevenciju transmisije infekcije, liječenje i sl.

Vodiči za terapiju MRSA infekcija-PZZ



Options for empiric outpatient antimicrobial treatment of SSTIs when MRSA is a consideration*

Drug name	Considerations	Precautions**
Clindamycin	■ FDA-approved to treat serious infections due to *S. aureus* ■ D-zone test should be performed to identify inducible clindamycin resistance in erythromycin-resistant isolates	■ *Clostridium difficile*-associated disease, while uncommon, may occur more frequently in association with clindamycin compared to other agents.
Tetracyclines ■ Doxycycline ■ Minocycline	■ Doxycycline is FDA-approved to treat *S. aureus* skin infections.	■ Not recommended during pregnancy. ■ Not recommended for children under the age of 8. ■ Activity against group A streptococcus, a common cause of cellulitis, unknown.
Trimethoprim-Sulfamethoxazole	■ Not FDA-approved to treat any staphylococcal infection	■ May not provide coverage for group A streptococcus, a common cause of cellulitis ■ Not recommended for women in the third trimester of pregnancy. ■ Not recommended for infants less than 2 months.
Rifampin	■ Use only in combination with other agents.	■ Drug-drug interactions are common.
Linezolid	■ Consultation with an infectious disease specialist is suggested. ■ FDA-approved to treat complicated skin infections, including those caused by MRSA.	■ Has been associated with myelosuppression, neuropathy and lactic acidosis during prolonged therapy.

■ MRSA is resistant to all currently available beta-lactam agents (penicillins and cephalosporins)
■ Fluoroquinolones (e.g., ciprofloxacin, levofloxacin) and macrolides (erythromycin, clarithromycin, azithromycine) are not optimal for treatment of MRSA SSTIs because resistance is common or may develop rapidly.

* Data from controlled clinical trials are needed to establish the comparative efficacy of these agents in treating MRSA SSTIs. Patients with signs and symptoms of severe illness should be treated as inpatients.
** Consult product labeling for a complete list of potential adverse effects associated with each agent.

Role of decolonization

Regimens intended to eliminate MRSA colonization should not be used in patients with active infections. Decolonization regimens may have a role in preventing recurrent infections, but more data are needed to establish their efficacy and to identify optimal regimens for use in community settings. *After treating active infections and reinforcing hygiene and appropriate wound care*, consider consultation with an infectious disease specialist regarding use of decolonization when there are recurrent infections in an individual patient or members of a household.

Vodič za liječenje MRSA infekcija u bolnici

Table 3. Recommendations for the Treatment of Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
Skin and soft-tissue infection (SSTI)					
Abscess, furuncles, carbuncles	Incision and drainage			AII	For simple abscesses or boils, incision and drainage is likely adequate. Please refer to Table 2 for conditions in which antimicrobial therapy is recommended after incision and drainage of an abscess due to CA-MRSA.
Purulent cellulitis (defined as cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess)	Clindamycin	300–450 mg PO TID	10–13 mg/kg/dose PO every 6–8 h, not to exceed 40 mg/kg/day	AII	*Clostridium difficile*–associated disease may occur more frequently, compared with other oral agents.
	TMP-SMX	1–2 DS tab PO BID	Trimethoprim 4–6 mg/kg/dose, sulfamethoxazole 20–30 mg/kg/dose PO every 12 h	AII	TMP-SMX is pregnancy category C/D and not rec ommended for women in the third trimester of pregnancy and for children <2 months of age.
	Doxycycline	100 mg PO BID	≤45kg: 2 mg/kg/dose PO every 12 h >45kg: adult dose	AII	Tetracyclines are not recommended for children under 8 years of age and are pregnancy category D.
	Minocycline	200 mg × 1, then 100 mg PO BID	4 mg/kg PO × 1, then 2 mg/kg/dose PO every 12 h	AII	
	Linezolid	600 mg PO BID	10 mg/kg/dose PO every 8 h, not to exceed 600 mg/dose	AII	More expensive compared with other alternatives
Nonpurulent cellulitis (defined as cellulitis with no purulent drainage or exudate and no associated abscess)	β-lactam (eg, cephalexin and dicloxacillin)	500 mg PO QID	Please refer to Red Book	AII	Empirical therapy for β-hemolytic streptococci is recommended (AII). Empirical coverage for CA-MRSA is rec- ommended in patients who do not respond to β-lactam ther- apy and may be considered in those with systemic toxicity.
	Clindamycin	300–450 mg PO TID	10–13 mg/kg/dose PO every 6–8 h, not to exceed 40 mg/kg/day	AII	Provide coverage for both β-hemolytic streptococci and CA-MRSA
	β-lactam (eg, amoxicillin) and/or TMP-SMX or a tetracycline	Amoxicillin: 500 PO mg TID See above for TMP-SMX and tetracycline dosing	Please refer to Red Book See above for TMP- SMX and tetracycline dosing	AII	Provide coverage for both β-hemolytic streptococci and CA-MRSA
	Linezolid	600 mg PO BID	10 mg/kg/dose PO every 8 h, not to exceed 600 mg/dose	AII	

Table 3. (*Continued*)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
					Provide coverage for both B-hemolytic streptococci and CA-MRSA
Complicated SSTI	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	AI/AII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	AI/AII	For children ≥12 years of age, 600 mg PO/IV BID. Pregnancy category C
	Daptomycin	4 mg/kg/dose IV QD	Ongoing study	AI/ND	The doses under study in children are 5 mg/kg (ages 12–17 years), 7 mg/kg (ages 7–11 years), 9 mg/kg (ages 2–6 years) (Clinicaltrials.gov NCT 00711802). Pregnancy category B.
	Telavancin	10 mg/kg/dose IV QD	ND	AI/ND	Pregnancy category C
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	AIII/AII	Pregnancy category B
Bacteremia and infective endocarditis					
Bacteremia	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	AII	The addition of gentamicin (AII) or rifampin (AI) to vancomycin is not routinely recommended.
	Daptomycin	6 mg/kg/dose IV QD	6–10 mg/kg/dose IV QD	AI/CIII	For adult patients, some experts recommend higher dosages of 8–10 mg/kg/dose IV QD (BIII). Pregnancy category B.
Infective endocarditis, native valve	Same as for bacteremia				
Infective endocarditis, prosthetic valve	Vancomycin and gentamicin and rifampin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BIII	
		1 mg/kg/dose IV every 8 h	1 mg/kg/dose IV every 8 h		
		300 mg PO/IV every 8 h	5 mg/kg/dose PO/IV every 8 h		
Persistent bacteremia	Please see text				
Pneumonia					
	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	AII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	AII	For children ≥12 years, 600 mg PO/IV BID. Pregnancy category C.
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BIII/AII	Pregnancy category B.

Table 3. (*Continued*)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
Bone and joint infections					
Osteomyelitis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII/AII	Surgical debridement and drainage of associated soft-tissue abscesses is the mainstay of therapy. (AII). Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to the chosen antibiotic (BIII). For children ≥12 years of age, linezolid 600 mg PO/IV BID should be used. A single-strength and DS tablet of TMP-SMX contains 80 mg and 160 mg of TMP, respectively. For an 80-kg adult, 2 DS tablets achieves a dose of 4 mg/kg.
	Daptomycin	6 mg/kg/day IV QD	6–10 mg/kg/day IV QD	BII/CIII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII/CIII	
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BIII/AII	
	TMP-SMX and rifampin	3.5–4.0 mg/kg/dose PO/IV every 8–12 h	ND	BII/ND	
		600 mg PO QD			
Septic arthritis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII/AII	Drainage or debridement of the joint space should always be performed (AII).
	Daptomycin	6 mg/kg/day IV QD	6–10 mg/kg/dose IV QD	BII/CIII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII/CIII	
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BIII/AII	
	TMP-SMX	3.5–4.0 mg/kg/dose PO/IV every 8–12 h	ND	BIII/ND	
Prosthetic joint, spinal implant infections	Please see text				
Central nervous system infections					

Table 3. (*Continued*)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
Meningitis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII	Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to vancomycin for adult patients (BIII). For children ≥12 years of age, linezolid 600 mg BID.
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII	
	TMP-SMX	5 mg/kg/dose PO/IV every 8-12 h	ND	CIII/ND	
Brain abscess, subdural empyema, spinal epidural abscess	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII	Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to vancomycin for adult patients (BIII). For children ≥12 years of age, linezolid 600 mg BID.
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII	
	TMP-SMX	5 mg/kg/dose PO/IV every 8–12 h	ND	CIII/ND	
Septic thrombosis of cavernous or dural venous sinus	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII	Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to vancomycin for adult patients (BIII). For children ≥12 years of age, linezolid 600 mg BID
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII	
	TMP-SMX	5 mg/kg/dose PO/IV every 8-12 h	ND	CIII/ND	

NOTE. BID, twice daily; CA-MRSA, community-associated MRSA; DS, double strength; IV, intravenous; ND, no data; PO, oral; QD, every day; TID, 3 times per day; TMP-SMX, trimethoprim-sulfamethoxazole.

[a] Classification of the strength of recommendation and quality of evidence applies to adult and pediatric patients unless otherwise specified. A backslash (/) followed by the recommendation strength and evidence grade will denote any differences in pediatric classification.

Dekolonizacija MRSA?

- Dekolonizacija kod rekurentnih infekcija kože i potkožnog tkiva, kod širenja infekcije na kontakte uprkos higijenskim mjerama i toaleti rane: mupirocin u nos 2 puta dnevno 5-10 dana sam ili u kombinaciji sa topikalnom dekolonizacijom tijela hlorheksidinom 5-14 dana. Razmotriti primjenu antibiotika oralno.

ESBL enterobakterije

- Rezistentne na peniciline, cefalosporine 1.,2.,3. generacije, monobaktame
- Osjetljive na karbapeneme!
- Urinarne, respiratorne infekcije, infekcije rana, infekcije krvi...
- Intrahospitalne i vanbolničke infekcije
- Zbog pojave CRE gube na značaju

CRE

Javnozdravstveni značaj:

a) Smrtnost od invazivnih infekcija uzrokovanih CRE 40-50 %
b) Lako se šire

Povećan rizik za infekciju:

- Mehanička ventilacija
- Urinarni, intravenski kateter
- Tubusi
- Dugotrajna antibiotska terapija

CRE

Liječenje: individualan pristup, prema antibiogramu

Tretman koloniziranih: ne treba antibiotska terapija, što prije se riješiti katetera, tubusa i sl., mjere za sprečavanje prenošenja rezistentnog soja, ev. dekolonizacija sa hlorheksidinom 2%.

CR-Pseudomonas aeruginosa

Rizik od infekcije:
- hospitalizacija
- mehanička ventilacija
- kateteri
- rane (hirurške, opekotine)

Rezervoar infekcije:
VODA I ODVODI!

Tretman:
- individualan pristup, antibiotik prema antibiogramu

CR-Acinetobacter spp.

Rizik od infekcije:

- Hospitalizacija
- Hronične bolesti (pluća, dijabetes)
- Kateteri
- Mehanička ventilacija
- Otvorene rane

Infekcije: krvi, rana, pneumonija

Kolonizira treheostomu i rane!

Terapija individualna, prema antibiogramu!

VRE

Rizik od infekcije:

- hospitalizacija
- dugotrajna primjena antibiotika
- ranija primjena vankomicina
- pacijenti sa oslabljenim imunitetom (jedinica intenzivne njege, onkološki pacijenti, transplantacija)
- hirurške operacije (abdomen, grudni koš)
- kateteri (urinarni, centralni venski i sl.)
- kliconoštvo

VRE

Infekcije:

- krvi
- urinarne
- rana

Tretman:

- individualno, prema antibiogramu
- kolonizirane ne treba tretirati antibiotikom!

Prevencija širenja MDRO

1. Standardne mjere opreza:

- Higijena ruku (nakon skidanja rukavica, između pacijenata, različite radnje kod jednog pacijenta)
- Nošenje rukavica prema riziku
- Zaštita sluznica-oka, nosa, usta kad se očekuje prskanje infektivnog sadržaja
- Nošenje ogrtača kad se očekuje prskanje infektivnog sadržaja
- Adekvatno rukovanje instrumentima i opremom za pacijente (odlaganje, čišćenje, dezinficiranje)
- Adekvatno rukovanje prljavom odjećom i posteljinom (ne zagaditi okolinu, zrak, ljude)

Prevencija širenja MDRO

2. Kontaktne mjere opreza

- Smještanje pacijenta (izolacija, grupisanje)
- Nošenje rukavica i zaštitnog ogrtača (obavezno)
- Reduciranje kretanja i transporta pacijenta (pokriti kolonizirane ili inficirane dijelove tijela)
- Oprema za pacijenta i instrumenti (jednokratna ili čistiti i dezinficirati)
- Pojačano čišćenje pacijentove okoline, posebno dijelova koje češće dodiruje (ormarići, nasloni kreveta, kvake, toalet...)

Prevencija širenja MDRO

3. Druge mjere

- Obezbijediti pacijentu socijalizaciju i rehabilitaciju
- Motivisati pacijenta
- Educirati osoblje
- Kontrola čišćenja (kontrolni brisevi površina oko bolesnika)
- Zatvaranje odjela kod izbijanja epidemije
- Aktivno traganja za MDRO

- Ali i praćenje kolonizacije. Na pr. CRE (zavisi od ekonomskih mogućnosti): kod pacijenata sa pozitivnom istorijom bolesti, kod kontakata, kod pacijenata koji su bili u endemskom području). Uzorak: stolica, rektalni bris, perianalni bris. Koliko često? = jednom do dva puta sedmično. Koliko dugo? = nejasno!

Monitoring, revizija, povratna informacija

- Pratiti svaki korak (evidentiranjem!)
- Revizijom utvrditi nedostatke
- Učiti iz iskustva
- Poboljšati mjere
- Doprinijeti boljoj brizi o pacijentu i kvalitetnom ishodu

Literatura:

1. Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities. Geneva: World Health Organization; 2017.
2. Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of MRSA Infections of Adults and Childrens, 2011
3. ESCMID guidelines for the managment of the infection control measures to reduce transmission of multidrug-resistant Gram negative bacteria in hospitalized patient, 2014

- ecdc.europa.eu/
- www.cdc.gov
- https://www.escmid.org/
- who.int/

Hvala za pažnju!