GUIDELINES FOR THE PROPHYLAXIS & TREATMENT OF MRSA IN THE UK: 2018 UPDATE

N. M. Brown[1], A. Goodman[2], C. Horner[3], A. Jenkins[4], and E. Brown[3]
[1]Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [2]Guy's and St Thomas' NHS Foundation Trust, London, UK;
[3]British Society for Antimicrobial Chemotherapy, Birmingham, UK, [4]Formerly British Society for Antimicrobial Chemotherapy, Birmingham, UK

BRITISH SOCIETY FOR ANTIMICROBIAL CHEMOTHERAPY

INTRODUCTION

- Current UK guidelines for the treatment, management and surgical prophylaxis of methicillin-resistant *Staphylococcus aureus* (MRSA) infections were published in 2009.[1]
- Since then, the prevalence of MRSA in UK hospitals has fallen markedly and serious infection with MRSA is now much less common.[2]
- There is now more evidence to guide use of linezolid and daptomycin, and new antibiotics have been licensed, or are close to market.
- We reviewed the contemporary evidence in order to update the existing guidelines, a brief summary of which is presented here (Table 1).

METHODS

- The Cochrane Library, EMBASE and MEDLINE were searched (2007-2016) for eligible clinical trials/studies that included patients with proven MRSA infection.
- Single, or a combination of agents, or different durations of treatment were compared.
- Studies meeting the inclusion criteria were identified independently by two authors (AJ & EB).
- Primary outcome was clinical and/or microbiological cure.

RESULTS

Table 1. Summary of the recommendations made in the 2008 MRSA guidelines compared with new evidence identified by this review.

Section	#	2008 Recommendation* (summarised)	Update 2018
De-escalation	1	Stepdown to FLU if isolate is later identified as MSSA.	No new evidence identified.
Use of glycopeptides	2	For severe MRSA infection (exceptions listed).	No new evidence identified.
SSTI: Impetigo & boils	3	Topical MUP or FUS.	No new evidence identified.
	4	Antibiotics may not be required after abscess drainage if cellulitis is absent.	3 new studies - antibiotic treatment following drainage of uncomplicated abscess: • No significant difference between oral cephalexin cf. oral CLI (p=0.33). • No significant difference between oral cephalexin cf. placebo (p=0.25). • Higher treatment failure rate in children when TXT given for 3 cf. 10 days (p=0.03).
SSTI: Cellulitis/SSI	5	Non-hospitalized patients: (i) DOX or CLI, unless severe infection and/or high risk of bacteraemia/ endocarditis (ii) GLY, LIN or TXT for DOX- or CLI-resistant isolates. (iii) IV GLY or DAP via OPAT.	24 new studies (largely hospitalized patients): • Most are industry-sponsored, performed for licensing purposes, and powered to demonstrate non-inferiority in comparison with the current standard treatment. • Much heterogeneity in the type of infection studied (e.g. wound infections, erysipelas, cellulitis, burn infections, abscesses, impetigo). • New agents that were non-inferior to VAN: ceftobiprole, lefamulin, oritavancin, telavancin, TD-1992, and ceftaroline vs. VAN+RIF. • New agents that were non-inferior to LIN: avarofloxacin, omadacycline, tednizolid. • Other non-inferior studies: DAL vs. IV VAN followed by oral LIN. • LIN was non-inferior to VAN in 2 studies. • 2 studies found DAP non-inferior to VAN; however, there was significant difference in favour of VAN therapy when compared with high-dose, short course DAP (10mg/kg, 4 days). • Retapamulin ointment (1%) was inferior to oral LIN; likely due to the difference in duration of treatment.
	6	Newly licensed agents (ceftobiprole, ceftaroline, dalbavancin, oritavancin, or telavancin): no recommendations.	
	7	Hospitalized patients: (i) GLY, LIN or DAP in patients with severe SSTIs and/or high risk of bacteraemia. Polymicrobial infection: consider TIG. (ii) Use of combined therapy: no recommendations. Use of RIF plus FUS no longer recommended. (iii) GLY monotherapy treatment failure: no recommendation between adding a second anti-staphylococcal agent (e.g. DOX, RIF or FUS) or switching to LIN or DAP monotherapy. Consider CLI for treatment of ERY-susceptible MRSA.	
SSTI: IV site infections	8	Severe IV site infections: IV GLY or LIN. Mild IV site infections: may respond to oral agents.	No new evidence identified.
Urinary tract infections	9	Simple: use oral agent; NIT, TRI, TXT or TET. Complicated: use IV GLY or DAP.	No new evidence identified.
Bone & joint infections	10	IV GLY +/- RIF or FUS. No evidence that any single agent or combination is superior.	2 new studies: • Statistical power not reached: 1 study • Results not available for MRSA subgroup: 1 study
Bacteraemia & Endocarditis	11	Uncomplicated bacteraemia: IV GLY or LIN (14 days minimum). DAP: alternative to GLY.	5 new bacteraemia studies: • No significant difference: 2 studies (both LIN vs. VAN) • Statistical power not reached: 2 (ceftaroline vs. VAN+AZT) or (TXT+RIF vs. LIN) • High-dose TXT did not achieve non-inferiority to VAN: 1 1 new endovascular study: Results not available for MRSA subgroup.
Respiratory tract infections	12	Bronchiectasis or chronic suppurative lung disease without pneumonia: no recommendation. LIN offers better lung tissue penetration.	8 new pneumonia studies (6 nosocomial pneumonia): • 4 studies: Potential improved outcomes when LIN cf. VAN. • VAN+RIF more effective at treating nosocomial pneumonia cf. VAN alone. • TXT+RIF non-inferior to LIN and TEL non-inferior to VAN • 1 study: TXT cf. VAN: Results not available for MRSA subgroup
	13	MRSA pneumonia: IV GLY or LIN.	
Eye & CNS infections	14	Deep eye or CNS infection: no recommendation. Superficial eye infection: use GEN, FUS or CHL.	No new evidence identified.
Clearance of carriage	15	Oral VAN not recommended. Soft tissue lesions: systemically active oral or parenteral agent, plus an active nasal cream, such as MUP.	Not considered within this review.
Prophylaxis (SSI)	16	IV GLY prophylaxis alone, or in combination with other antibiotics.	5 new studies: • Significant difference in outcome: 2 studies • Statistical power not reached: 3 studies

Key: *Recommendations are based according to in vitro susceptibility of the isolate & allergy status of the patient. CHL, chloramphenicol; CLI, clindamycin; CNS, central nervous system; DAL, dalbavancin; DAP, daptomycin; DOX, doxycycline; ERY, erythromycin; FLU, flucloxacillin; FUS, fusidic acid; GEN, gentamicin; GLY, glycopeptide; IV, intravenous; LIN, linezolid; MSSA, methicillin-susceptible *S. aureus*; MUP, mupirocin; NIT, nitrofurantoin; OPAT, outpatient parenteral antimicrobial therapy; RIF, rifampicin; SSI, surgical site infection; SSTI, skin & soft tissue infection; TEL, telavancin; TET, tetracycline; TIG, tigecycline; TRI, trimethoprim; TXT, co-trimoxazole; VAN, vancomycin.

CONCLUSIONS

- 33 trials were reviewed and treatment with 11 new drugs was described.
- Most studies (n=24) considered MRSA-positive SSTI, several were non-inferiority studies performed for licensing purposes.
- There was no evidence of improved efficacy with high dose daptomycin (10mg/kg) in SSTI.
- There were potential improved outcomes with linezolid in MRSA pneumonia and vancomycin in MRSA bacteraemia.
- Evidence suggests that if an uncomplicated abscess is successfully drained, the patient may not need to be treated with antibiotics.
- A complete review of the evidence will be published soon.

REFERENCES

1. Gould *et al.* (2009) *J Antimicrob Chemother* 2009; **63**: 849-61.

2. Duerden *et al.* (2015) *Open Forum Infect Dis.* 2015 Apr; 2(2): ofv035.

ACKNOWLEDGEMENTS

This work was equally funded by the BSAC, British Infection Association (BIA), Healthcare Infection Society (HIS) and Infection Prevention Society (IPS).

We would like to thank Phil Wiffen for advice and guidance with literature searches & Vittoria Lutje for collection of evidence