S aureus infections: outpatient treatment

Dirk Vogelaers
Dept of Infectious Diseases
University Hospital Gent
Belgium

Table 1 Usual adult dosages of selected antistaphylococcal antibiotics[†]

Antibiotic	Adult dosage/route of administration
Agents active against non-multiresistant MRSA strains (nmrMRSA)[‡]	
Dicloxacillin	250–500 mg q6h (PO) or 0.5–2 g q6h (IV)
Flucloxacillin	250–1000 mg q6h (PO) or 0.5–2 g q6h (IV)
Amoxicillin/clavulanate	1 tablet (500 mg/125 mg or 875 mg/125 mg) PO bid
Ticarcillin/clavulanate	3.1 g IV q6-8h
Piperacillin/tazobactam	2 g/0.25 g–4 g/0.5 g IV q6h-8h
Cephazolin	0.5–2 g q8h IV
Cephalothin	0.5–1 g q6h IV
Cephalexin	250–1000 mg q6h PO
Clindamycin	150–450 mg q6h (PO) or 600–1200 mg/d in 3–4 equal doses (IV)
Co-trimoxazole (trimethoprim/sulphamethoxazole)	1 DS tablet (160 mg/800 mg) PO bid

Intern Med J. 2005 Feb;36(2):142-3

Table 1 Usual adult dosages of selected antistaphylococcal antibiotics†

Antibiotic	Adult dosage/route of administration
Agents active against multiresistant MRSA strains (mrMRSA)§	
Vancomycin	1000 mg q12h or 500 mg q6h (IV) [see section on therapeutic drug monitoring]
Teicoplanin	12 mg/kg loading dose (2 doses in 12 h) followed by 3–6 mg/kg/day as a single daily maintenance dose (IV or IM) [see section on therapeutic drug monitoring]
Rifampicin	300 mg q12h (IV or PO)
Fusidic acid	500 mg q8h-12h (PO or IV)
Ciprofloxacin	500 mg PO q12h or 400 mg IV q12h
Moxifloxacin	400 mg q24h (PO or IV)
Gatifloxacin	400 mg q24h (PO or IV)
Last-line agents	
Linezolid	600 mg bid (IV or PO)
Quinupristin/dalfopristin	7.5 mg/kg q8h-q12h (IV) [*Note:* IV dosing; requires central venous catheter due to occurrence of phlebitis]

Intern Med J. 2005 Feb;36(2):142-3

Treatment of S aureus infections in the outpatient setting

- Consolidation (often sequential) treatment of severe infections with microbiologic documentation after initial hospitalisation

- Empiric outpatient treatment of mild to moderate SSTI with a high likelihood of S aureus infection

Sequential treatment after discharge from hospital

- Clinical trials on SSTI focus on “complicated” SSTI
  - Requiring hospitalisation
  - Requiring surgery
- Often “proof of principle” studies required for registration and not offering information on positioning of drugs in treatment algorithms
  - Daptomycin
  - Tigecycline
- Information on required or optimal duration of therapy lacking

Sequential treatment of documented S aureus infections

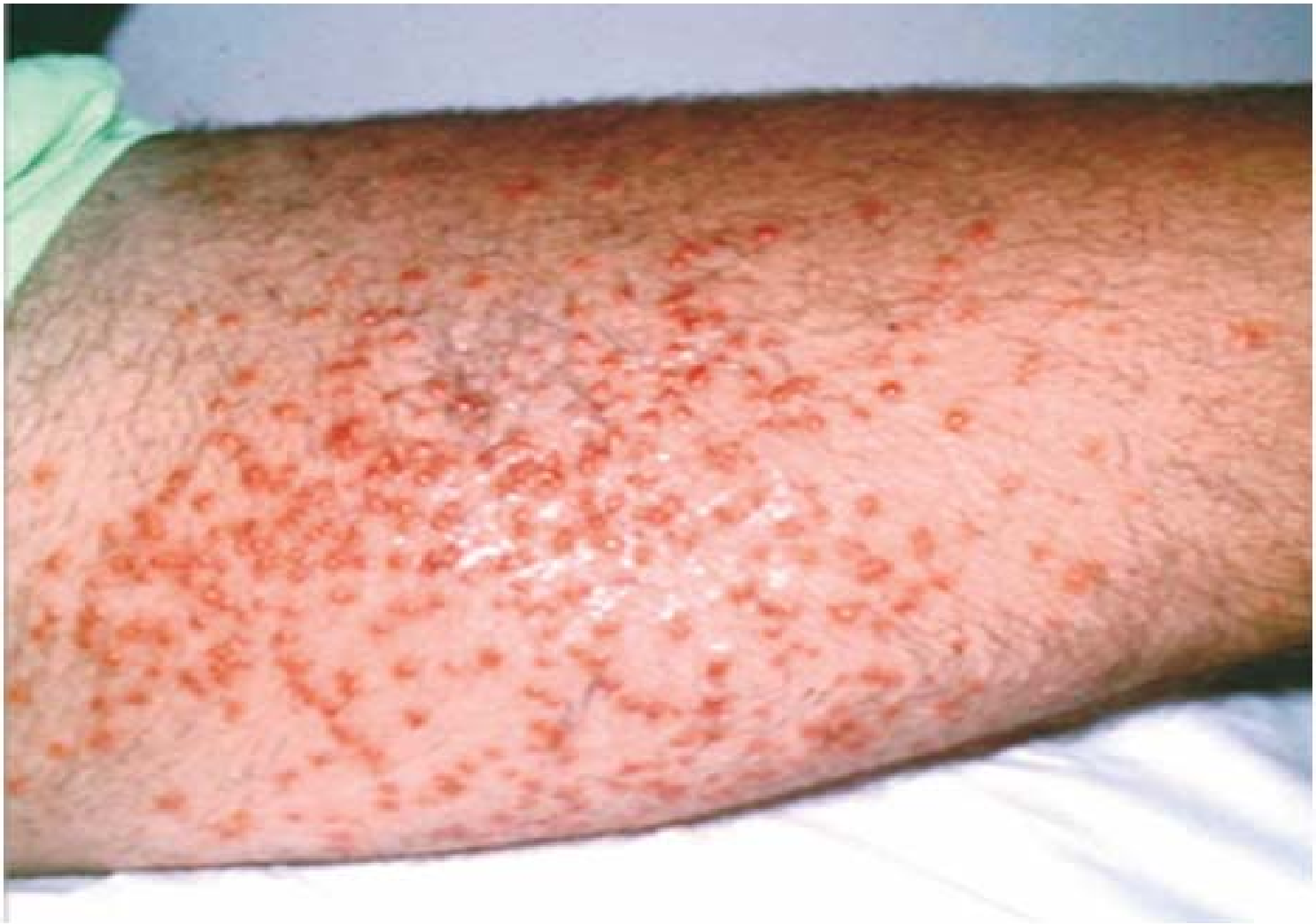
- MSSA
  - PRSP in adequate dosing
    - 4 x 1 g flucloxacillin
- MRSA
  - Teicoplanin IM
  - Teicoplanin IV 3 x/week
  - Linezolid po
  - Cotrimoxazole
  - Clindamycin

Treatment of S aureus infections in the outpatient setting

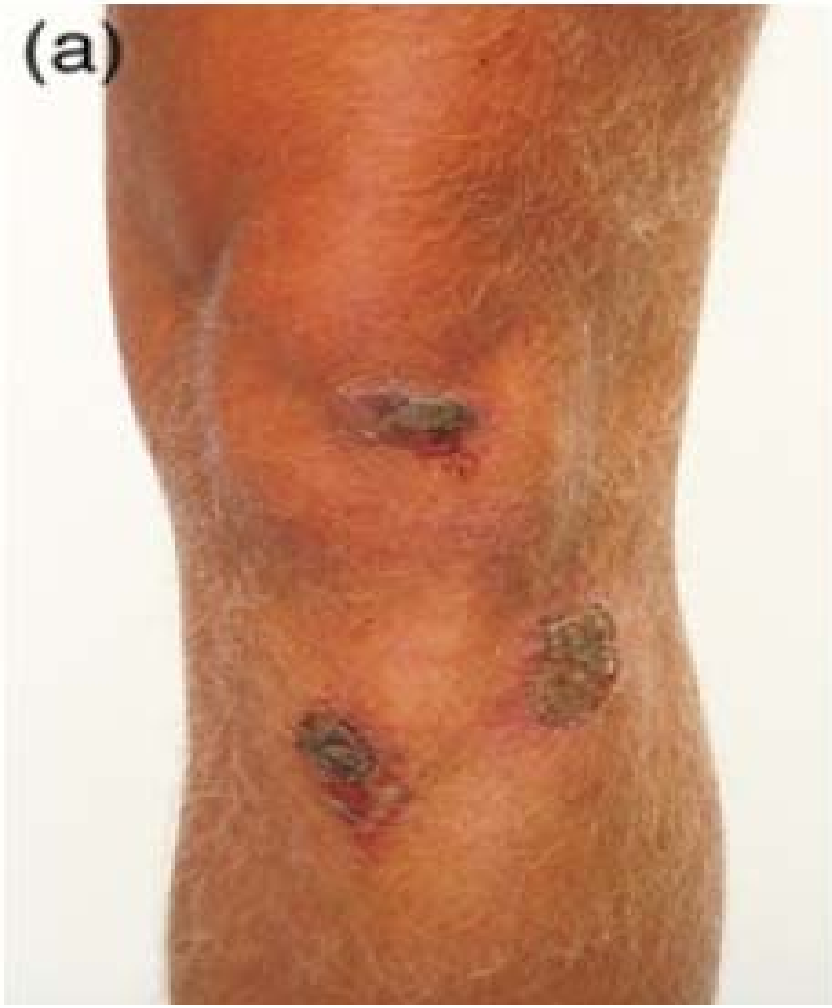
- Consolidation (often sequential) treatment of severe infections with microbiologic documentation after initial hospitalisation

- Empiric outpatient treatment of mild to moderate SSTI with a high likelihood of S aureus infection

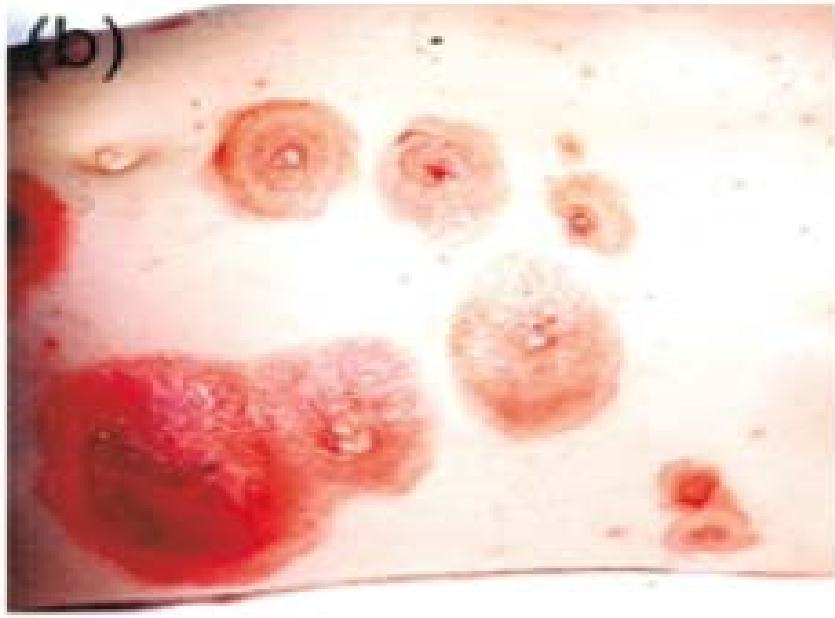
Folliculitis



Non-bullous impetigo



Bullous impetigo



Antimicrobial therapy in impetigo

- Non bullous impetigo (“honey crust”)
  - Group A streptococci, S aureus
    - Topical treatment
    - If extensive, PRSP or cefadroxil
- Bullous impetigo
  - S aureus (phage group II, usually type 71)
    - PRSP
    - In IgE mediated allergy doxycycline, minocycline or TMP-SMX

Furuncles and carbuncles

- Not necessarily indication for antibiotics
  - Application of moist heat sufficient treatment for most furuncles

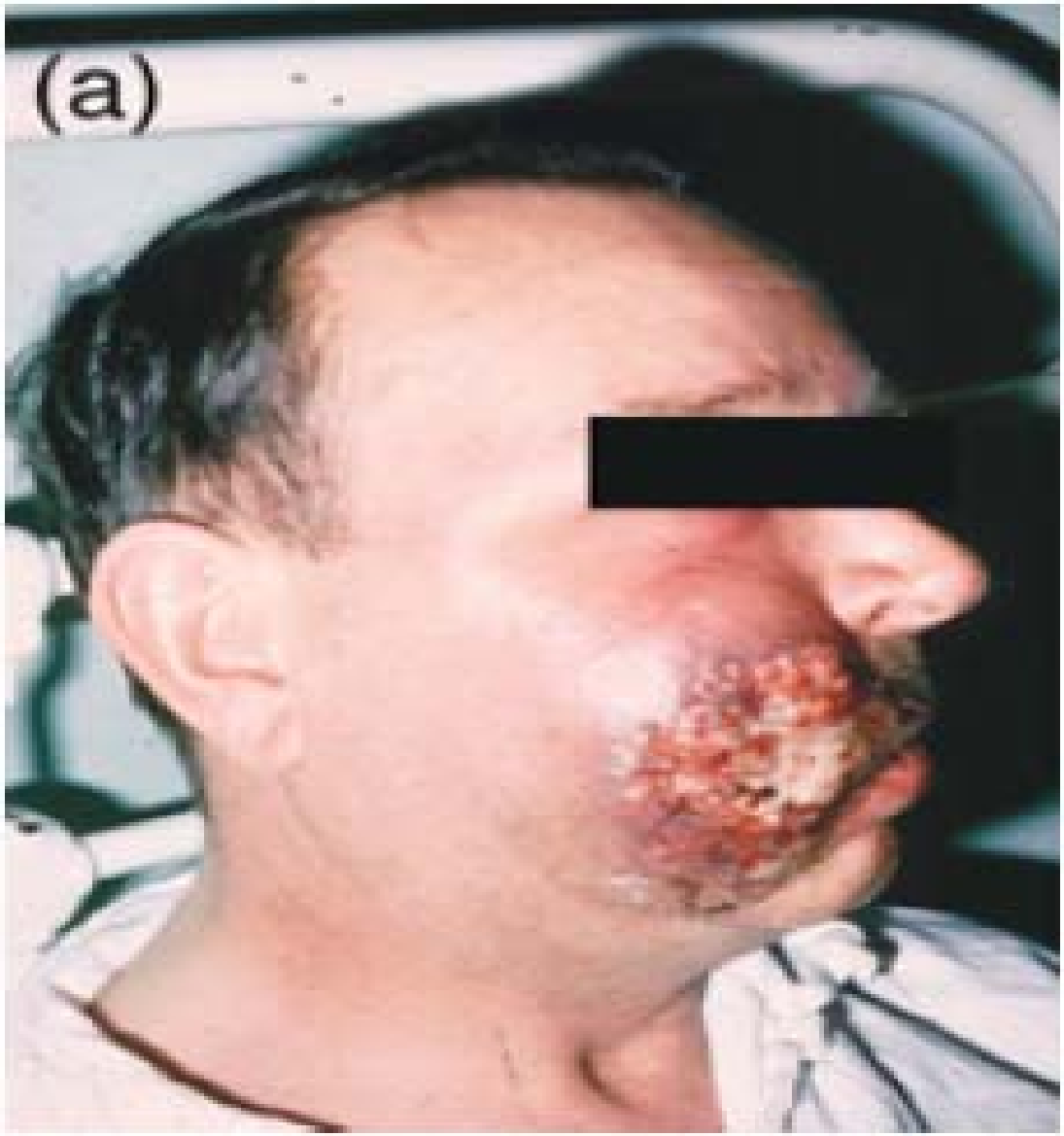
- Antibiotics in
  - Carbuncles
  - Furuncles with surrounding cellulitis or fever
  - Furuncle located about the midface

  → PRSP (250 mg dicloxacillin/6 hrs)
  → clindamycin 150-300 mg/6 hrs in IgE mediated penicillin allergy

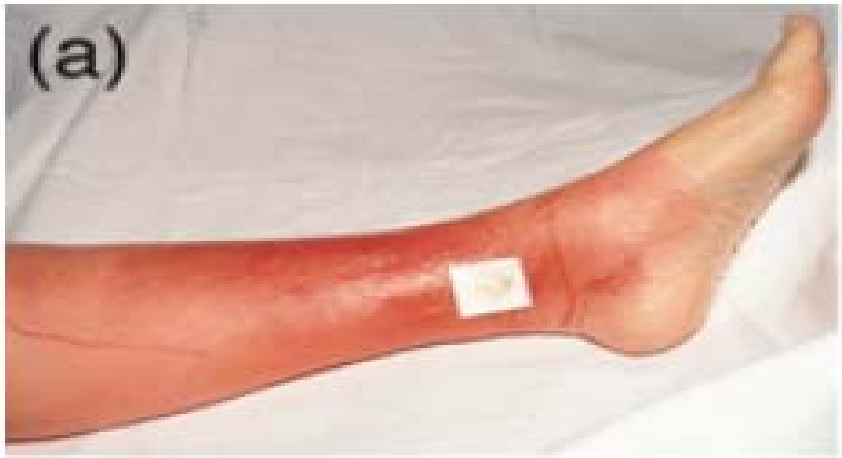
- Surgical drainage of large and fluctuant lesions
  - If < 5 cm diameter without cellulitis or sepsis no indication for antibiotics

- Consider MRSA infection after recent hospitalisation

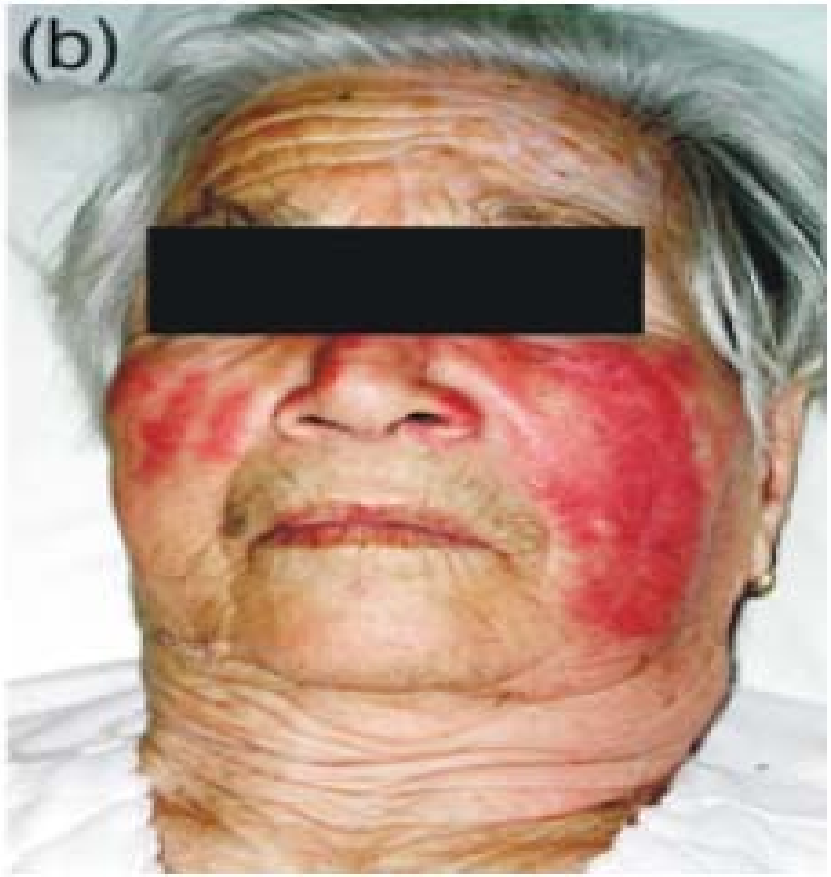
Carbuncle



Cellulitis and erysipelas.



Erysipelas involving face.



Extent to cover S aureus?

- Erysipelas ("non purulent cellulitis")
  - Large proportion to be attributed to group A streptococcus

    (Bernard. Arch Dermatol 1989; 25: 779-82)

  - S aureus as important in frequency distribution of pathogens in prospective assessment (microbiol/serology) of 73 pts with clinical (68 % lower limb) erysipelas
    - 41 % microbiologically documented
    - 15 % group A strep, 12.5 % group G strep (mostly in men > 50 yrs), 10 % S aureus

      (Hugo-Persson. Infection 1987; 15: 184-7)

Erysipelas: treatment

- 10 d IV (downstep to oral) medium dose penicillin standard treatment based on retrospective studies
- Limited evaluation in randomised prospective studies
  - Roxithro vs. IV peni: efficacy 83% vs 76 %, limited patient population (n=69)
    (Bernard, Br J Dermatol, 1992, 127: 755-758)
  - Oral vs. IV peni
    (Jurup-Rönström, Infection, 1984; 12:390-394)
  - Antibiotics + predni : double blind, placebo controlled
    (Bergkvist., Scand J Infect Dis 1987; 25:377-378)
- Pristinamycine vs peni IV $\rightarrow$ oral in hospitalised pts with erysipelas
  (Bernard, BMJ, 2002; 325)
  - As effective in open prospective non-inferiority trial
  - Cure-rate ITT 65 % (90/138) vs. 53 % for penicillin, in protocol-valid pts 81% vs 67 %
  - Possible superiority of 5 %
- Amoxiclav not mentioned in guidelines, but logical in order to cover both GABHS and MSSA
  - Recommendation to cover S aureus in facial erysipelas (risk of sinus cavernosus thrombophlebitis)

Empiric treatment of mild/moderate infections presumably due to S aureus

- Cover most likely pathogens in frequency distribution of microorganisms in particular disease entity
  - Cellulitis without underlying disease
    - Group A, B, C and G streptococci, S aureus
      - PRSP and clindamycin as alternative
      - < 10 % clindamycin resistance in GABHS and S aureus in Belgium
  - Cellulitis with underlying disease
    - Same pathogens + P aeruginosa + Enterobacteriaceae
      - Amoxiclav
      - Clinda + FQ2 as alternative
    - Samples for microbiology warranted (needle puncture through adjacent intact skin or skin biopsy) as more diversity in pathogens involved according to clinical situation/modifying circumstances

Inducible resistance to clindamycin in S aureus

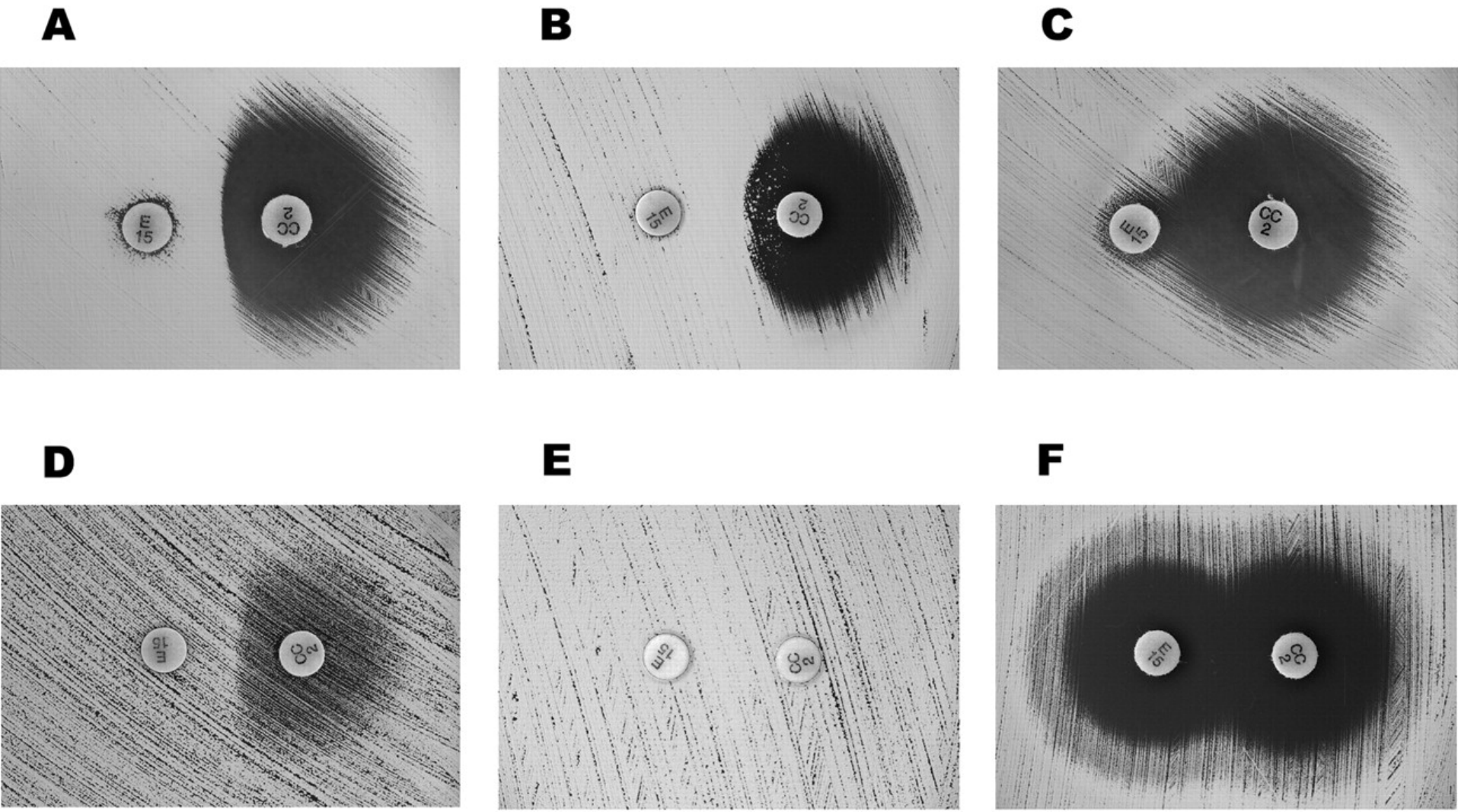
- Present both in MSSA and MRSA with geographic variability
  - 2 % of MRSA / 9 % of MSSA in prospective assessment of causes of SSTI in US emergency depts

    (Moran NEJM 2006; 355:666-74)
  - Need for regional information
- Clindamycin used in treatment of infections with MRSA isolates possessing inducible resistance

  (Martinez-Aguilar. Pediatr Infect Dis 2003; 22: 593-8)
  (Drinkovic. JAC 2001; 48: 315-6)
- Clinical failures reported

  (Siberry. CID 2003; 37: 1257-60)

This figure shows the six phenotypes observed during CLI induction testing of *S. aureus* by disk diffusion. E 15, ERY disk (15 µg); CC 2, CLI disk (2 µg). Top row: D phenotype (A), D+ phenotype (B), Neg phenotype (C). Bottom row: HD phenotype (D), R phenotype (E), S phenotype (F). See text and Table 1 for descriptions of the phenotypes.



J Clin Microbiol. 2005 Apr;43(4):1716-21

Clindamycin in S aureus infections

- Recommendation for testing S aureus isolates with potential for inducible clindamycin resistance (isolates resistant to erythromycin but susceptible to clindamycin on initial testing) for inducible resistance by D-zone disk-diffusion testing (CLS M100-S16, 2006)
- However, no routine microbiologic sampling in outpatient setting
- Regular regional surveillance of MSSA/MRSA → change in guidelines for empirical therapy
  - treshold for change?

Community-acquired MRSA

- High prevalence (59%; 98 % SCC mec type IV; PVL positive) of CA-MRSA (USA300 clone) in prospective study of causes/outcome of SSTI in emergency departments
- No association between patient outcomes and susceptibility of pathogen to antimicrobial agents prescribed (although limited followup information)
- Most skin abscesses can be cured with adequate drainage alone, even when caused by MRSA

(Moran et al. NEJM 2006; 355: 666-74)

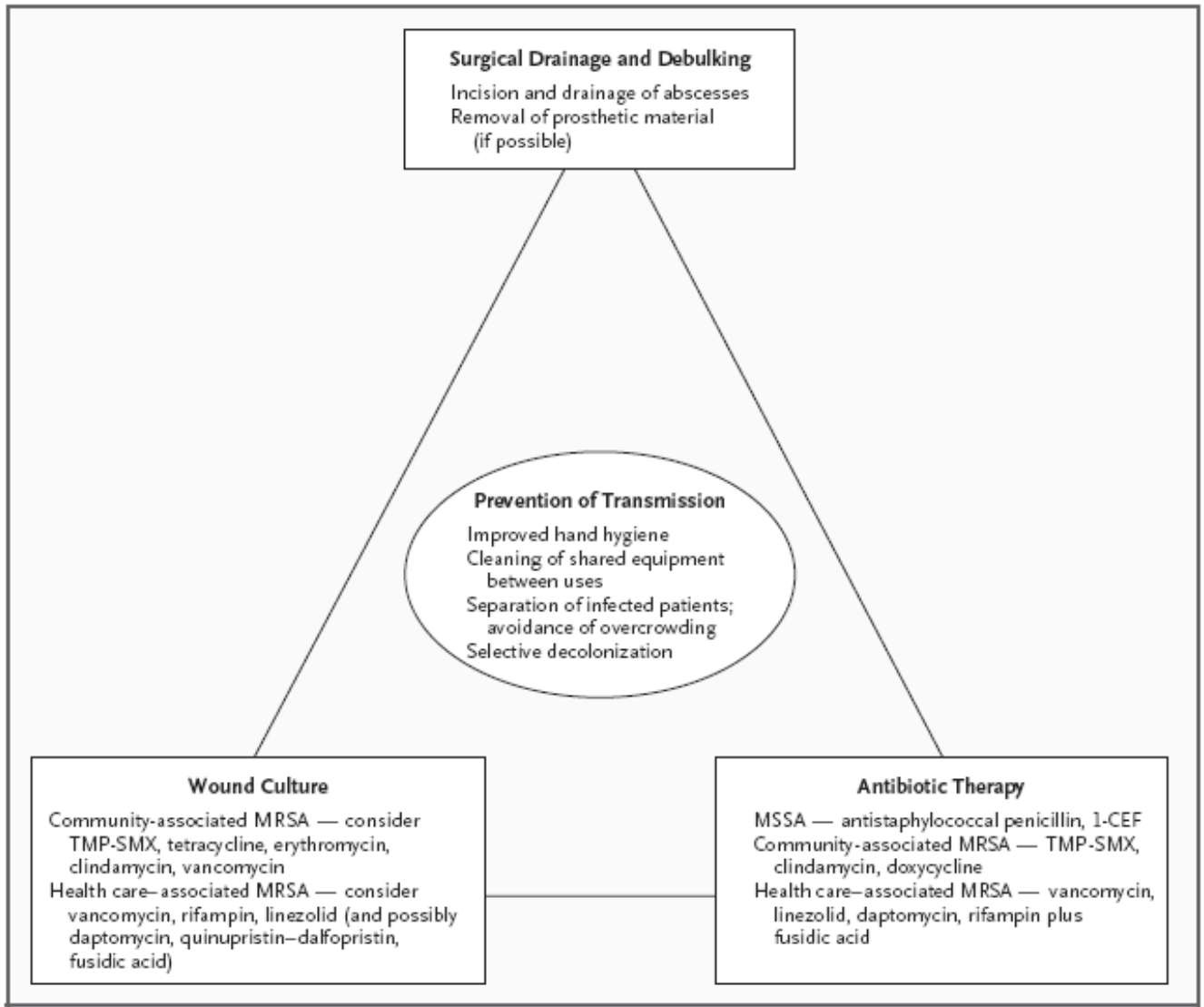


Figure 1. Approach to Suspected Staphylococcal Infections.

GRAYSON NEJM august 17, 2006, 355;5, 724