# Rapid tests for MRSA detection at the hospital admission

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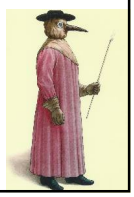
## Prevention strategies for MRSA control

### Complementary strategies

- Early identification of MRSA carriers
  - Active screening
- Reduction of MRSA carriage
  - Decontamination with mupirocin and antiseptic body washing
- Stop transmission
  - Improved compliance with hand hygiene
  - Contact isolation of MRSA positive patients
- Reduction of antibiotic use
  - Education and restriction

Harbarth S. CMI 2006 12:1142



## Rationale for MRSA screening

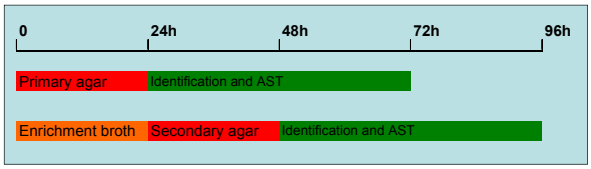
- Colonized patients constitute the main reservoir for nosocomial transmission
- Colonized patients are only detected by active surveillance sampling of muco-cutaneous swabs
- Hospitalized patients carrying MRSA are at high risk to develop a MRSA infection
- High mortality (RR 1.9 vs MSSA, RR > 10 vs no infection) and prolonged hospital stay (2-13 days) is associated with MRSA infections

⇒ MRSA screening for **patients at high-risk of MRSA carriage** and/or in **high risk wards** (ICU, hematology, …)

## Potential benefits for rapid MRSA identification

- **Patient care**
  - Early appropriate treatment with improve clinical outcome
  - Reduced empirical use of glycopeptides
- **Infection control**
  - Early MRSA isolation/cohorting
  - Decrease in nosocomial transmission rate
  - Decrease in MRSA morbidity and mortality
  - Cost saving
    - Shorter patient stay
    - Fewer preventive isolation days
    - Lower medical liability costs

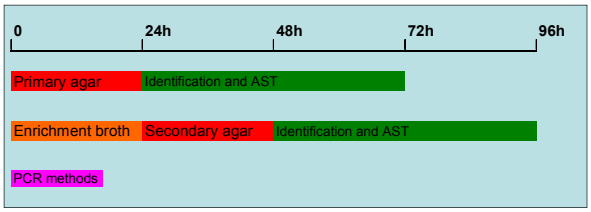
## Conventional method for MRSA detection




- Chromogenic culture for 24 and 48h
- Enrichment broths
- Identification by phenotypic tests and susceptibility using cefoxitin test

**Time to results from 48 to 96h**

## Conventional versus amplification methods for MRSA detection



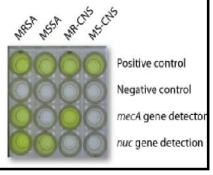

- Amplification for MRSA detection directly in clinical sample

**Time to results few hours**

## Amplification methods for rapid MRSA detection

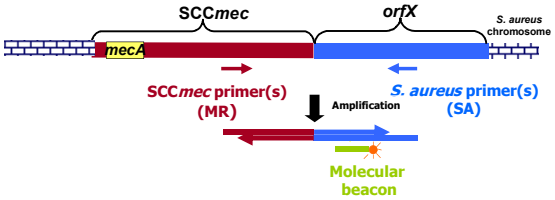
- **First generation**
  - In-house or commercial PCR
  - Target for *S. aureus : e.g. nuc, femA, coa*
  - Target for methicillin-resistance *: mecA*

**High risk of MRSA positive results with mixed flora MR-CoNS and MSSA**




## Amplification methods for rapid MRSA detection

- **Second generation**
  - Detection of the junction between *orfX* (*S. aureus*) and SCC*mec* element (carrying MR determinant)




⇒ **avoids false-positives** from mixed cultures of MR- CoNS and MSSA

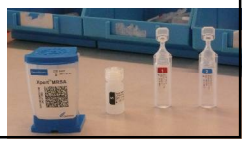
## Commercial assays

- **BD GeneOhm™ MRSA Assay (IDI-MRSA PCR)**
  - Manual procedure
    - Specimen preparation and concentration
    - Lysis and DNA extraction
    - Reconstitution of reagents
  - Real-time multiplex PCR on Smart-Cycler

    ⇒ Full process run time 2 hours

## Commercial assays

- **Xpert™ MRSA (Cepheid)**
  - DNA extraction and real-time PCR combined
  - Random access
  - 75 min assay



## Performance of automated systems for MRSA detection in screening samples

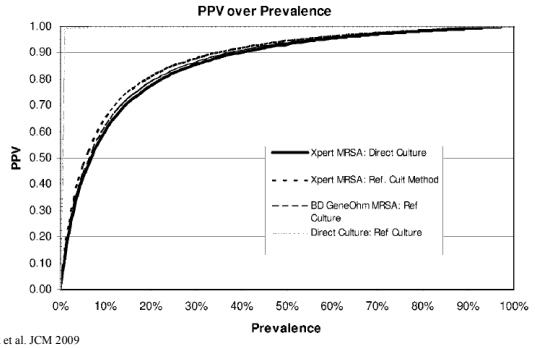
- **Sensitivity 85 – 98%**
  - Nare > other sites
  - False negatives
    - Inhibition (rare)
    - **New variants of SCC*mec* elements**
    - Low inoculum – limit of detection

Bartels et al. JCM 2009

- **Specificity 96 – 98%**
  - False positives
    - **Partial deletion of SCC*mec* element including *mecA***
    - Non viable bacteria – patient under treatment
    - Low inoculum – limit of detection
    - Risk of MRSA infection **not different** from that in patients with PCR and culture negative
  - Low positive predictive value in hospitals with low prevalence

Shore et al. AAC 2008
De San et al. JCM 2007
Herdman et al. JCM 2009

## Changes in the PPV with changes in MRSA prevalence




Wolk et al. JCM 2009

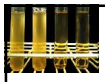
## Comparison of Xpert MRSA and BD GeneOhm MRSA assays versus culture for MRSA colonization

TABLE 2. Comparison of GXP-MRSA and BD-MRSA assay results versus culture results, using CNG swabs for the detection of MRSA colonization

| PCR assay result (n = 210) | MRSA culture result* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Agar alone | | | | | Agar and/or broth | | | | |
| | No. of specimens | | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | No. of specimens | | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
| | Culture positive | Culture negative | | | | | Culture positive | Culture negative | | | | |
| GXP-MRSA | | | | | | | | | | | | |
| Positive | 40[e] | 10 | 87.0 | 93.8 | 80.0 | 96.2 | 42[g] | 8 | 75.0 | 94.7 | 84.0 | 91.1 |
| Negative | 6[d,f] | 152[c] | | | | | 14[d,h] | 144[c] | | | | |
| Unresolved[b] | 0 | 2 | | | | | 0 | 2 | | | | |
| BD-MRSA | | | | | | | | | | | | |
| Positive | 39[i] | 12 | 84.8 | 92.7 | 76.5 | 95.6 | 41[k] | 10 | 73.2 | 93.5 | 80.4 | 90.6 |
| Negative | 7[j] | 152 | | | | | 15[j] | 144 | | | | |
| Unresolved | 0 | 0 | | | | | 0 | 0 | | | | |

- 210 patients screened for MRSA colonization
- 46 MRSA carriers from nose alone (n = 24), groin alone (n = 4) and both sites (n = 18)
- 5/14 false positives were patients under therapy

Kelley et al. JCM 2009



## Performance of commercial methods for MRSA screening

| Methods | TAT hours | Limit of detection CFU/ml* | Costs | Trained personnel | Core lab | Workload |
|---|---|---|---|---|---|---|
| Chromogenic agars | 24-48 | 170 | + | No | No | ++ |
| Enrichment broth | 48-96 | 10 | + | No | No | ++ |
| BD GeneOhm MRSA | 2.5 | 190 | +++ | Yes | No | + |
| GeneXpert MRSA | <1.5 | 60 | ++++ | No | Yes | +/- |

TAT, turnaround time

* Rossney et al. JCM 2009

## Rapid screening at hospital admission

**Observational studies with** GeneOhm MRSA assay

| Authors | Setting | Intervention | Culture | Outcome |
|---|---|---|---|---|
| Cunningham<br>UK - 10M | 2 phases Mixed ICU | Univer. screening<br>Decolonization<br>Contact precaution | Yes | ↓ MRSA transmission |
| Robicsek<br>USA - 3Ys1/2 | 3 phases<br>Baseline, ICU, all admissions | Univer. screening<br>Decolonization<br>Isolation | No | ↓ MRSA infection |
| Jog<br>UK – 1Y | Cardiac surgery | Univer. screening<br>Decolonization | No | ↓ MRSA infection (SSI, bacteraemia) |
| Aldeyab<br>UK | Medical and surgical wards | Decolonization<br>Contact precaution | Yes | No difference |
| Keshtgar<br>UK – 1 Y | Surgical wards | Univer. screening<br>Decolonization | No | ↓ *S. aureus* bacteraemia and MRSA SSI |
| Conterno<br>Canada – 1Y | 1200-bed hospital | High risk patients<br>Contact precaution | Yes | No difference<br>↓ TAT |

## Main limits of published studies using rapid MRSA detection methods for infection control

**Methodological problems**

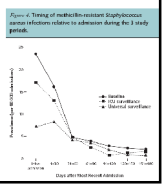
- Systematic screenings not performed at discharge or at follow-up
  - No measure of the rate of nosocomial transmission
- PCR results not confirmed by conventional cultures
  - Risk of "overshooting" (PPV << 75 %)
- Lack of control group
  - No analysis of possible variation in MRSA epidemiology during the study period
- Absence of monitoring of the adherence to infection control procedures
  - decolonization, isolation and hand hygiene

## Evaluation of preventive effect of universal MRSA screening by PCR at hospital admission

- Study design
  - 3 phase before-after study in 3 hospitals
    no screening, ICU screening, universal screening
  - Isolation & decolonisation
- Main findings
  - Prevalence of MRSA infection decreased by 70% (p<0.01) in Phase 3 vs Phase 1
- Conclusions
  - Universal PCR screening was associated with **significant reduction in MRSA disease**

**But** …

- No screening culture before start of the study
- No control group
- PCR not confirmed by conventional cultures
- Highly expensive : >60.000 PCR tests !!!



Robicsek *Ann Intern Med* 2008 148:409

## Evaluation of preventive effect of universal MRSA rapid screening in medico-surgical admission at one hospital

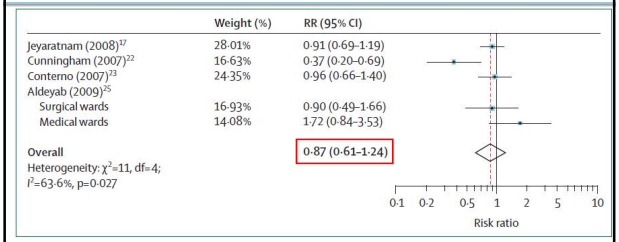
- Study design
  - Cluster-randomised, cross-over study in 10 wards: conventional vs (GeneOhm) PCR universal screening
  - (pre-emptive) isolation & decolonisation
  - Positive patients confirmed by culture
- Main findings
  - Incidence of MRSA acquisition similar
  - phase 2 vs 1 adjusted odds ratio:0.91 (95 % CI, 0.61-1.23)
- Conclusions
  - Universal PCR screening **did not reduce incidence** of MRSA nosocomial acquisition in medical & surgical patients
  - **Reduction in turnaround time** from admission to reporting 21.8 hours versus 46.4 hours

Jeyaratnam *BMJ* 2008 336:9730

BMJ RESEARCH

Impact of rapid screening tests on acquisition of meticillin resistant Staphylococcus aureus: cluster randomised crossover trial

## Effect of molecular tests at hospital admission on MRSA acquisition rate per 1000 patient-days




Tacconelli et al. Lancet Infect. Dis. 2009

## Conclusions

- No evidence that molecular tests decrease significantly MRSA transmission rate in institutions where active screening with conventional cultures and enrichment broth are applied
- Introduction of molecular tests in institution with no active screening might lead to a significantly decreased risk for MRSA bloodstream infections
- Turnaround time is reduced from 4 days for cultures to 1 day for molecular tests

## Issues in routine implementation of rapid molecular testing for MRSA screening

- High heterogeneity related to different study designs, study population and hospital settings
- Need for robust studies in different clinical settings for
  - Which patient groups could benefit most from screening at admission
  - Clinical efficacy, effectiveness and cost-benefit
- Current technologies remain labor intensive and dependent of skilled personnel
- Optimal use requires changes in healthcare systems and modification of professional behaviors toward patient care and infection control