



Infektionskontrolle

➔ Nosokomiale MRSA

➔ Gramnegative Bakterien

➔ Andere Themen



Nosokomiale MRSA

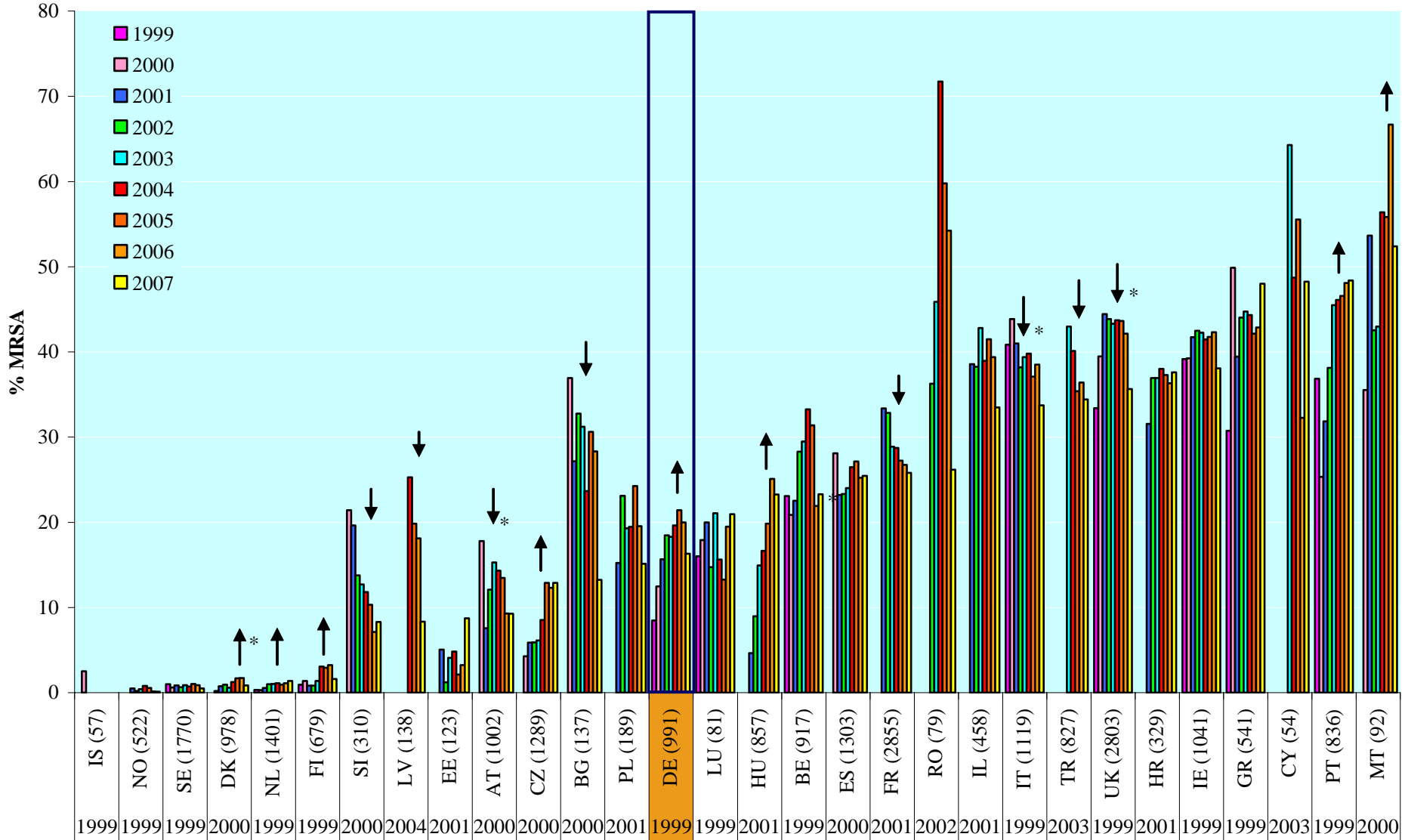
Epidemiologie
Screening
Behandlung des Trägerstatus

Trends in europäischen Ländern

- In mehreren europäischen Ländern wurde eine Abnahme nosokomialer MRSA-Infektionen beobachtet.
- Insgesamt ist eine Trendumkehr zu erkennen.
- **England**
 - ▶ 50% Reduktion der Bakteriämierate nach 5 Jahren landesweiter MRSA-Kontrollkampagne
 - ▶ Kritiker bemängeln die Vernachlässigung anderer dringender Hygieneprobleme (z.B. *Clostridium difficile*) durch die Fokussierung auf MRSA.
- **Frankreich/Belgien**
 - ▶ Keine staatlich verordnete MRSA-Meldepflicht wie in England, dafür gut funktionierende *Surveillance*-Netzwerke, die zum Erfolg beigetragen haben.
- **Deutschland**
 - ▶ Die MRSA-Situation scheint sich stabilisiert zu haben.

MRSA-Bakteriämien in Europa

(European Antimicrobial Resistance Surveillance System 2007)



Ländercode (Mittlere Anzahl der Isolate pro Jahr); Jahr des Beginns der Überwachung

MRSA-Kontrollmaßnahmen

- Länder mit erfolgreicher MRSA-Kontrolle haben vergleichbare Maßnahmenkataloge
- Diese basieren auf den folgenden Konzepten:
 - ▶ Verstärkung der Basishygiene
 - ▶ Förderung der Händehygiene
 - ▶ Gezielte Abstrichuntersuchungen bei Hochrisikopatienten
 - ▶ Kontaktisolierung von MRSA-Patienten mit hohem Übertragungspotential
 - ▶ Bereitstellung von finanzieller Unterstützung und Hilfsmitteln zur flächendeckenden Umsetzung dieser Maßnahmen

MRSA-Screening

- Das systematische MRSA-Screening wird weiterhin sehr unterschiedlich gehandhabt.
- Länder mit erfolgreicher MRSA-Kontrolle (u.a. UK, Belgien, Frankreich) screenen nicht alle Patienten bei Krankenhausaufnahme.
- Die USA scheinen die Bedeutung des allgemeinen MRSA-Aufnahmescreenings (*universal MRSA screening*) zu überschätzen. In mehreren Bundesstaaten sind Krankenhäuser gesetzlich zum Screening verpflichtet.
- Zwei große klinische Studien haben allerdings gezeigt, dass:
 - ▶ ... das schnelle MRSA-Screening mit Dekolonisation in Krankenhäusern mit schlechter Basishygiene und wenig Einzelzimmern die MRSA-Transmissionsrate senken kann (Hawkey et al.),
 - ▶ ... das präoperative Screening vor Elektiveingriffen mit nachfolgender Dekontamination sinnvoll ist, um *Staphylococcus aureus*-Infektionen zu reduzieren (Bode et al.).

Große englische Studie zum MRSA-Screening

Design

- Blockrandomisierte randomisierte *Crossover*-Studie
- Dauer je Studienphase 8 Monate
- Endpunkt: MRSA-Transmissionsrate

Intervention

- PCR basiertes Aufnahmescreening für MRSA versus konventionelle mikrobiologische Standardmethoden
- Erneutes Screening alle 4 Tage bei Langliegern
- Dekolonisation mit Mupirocin und Chlorhexidin für 5 Tage
- Screening aller Patienten bei Entlassung

Studienpopulation

- 12682 chirurgische Patienten in 7 Abteilungen
- Screening-Compliance: 90,8%

Große englische Studie zum MRSA-Screening

Resultate

- 453 (3,6%) Patienten waren MRSA positiv bei Aufnahme
- 268 (2,2%) erwarben MRSA während des Krankenhausaufenthalts
- Nur 17% der MRSA-Patienten waren in Kontaktisolierung
- Nach Berücksichtigung möglicher Störfaktoren ergab die multivariate Analyse, dass das Screening mit konventionellen Methoden die Übertragungsrate **1,5-fach** erhöhte (im Vergleich zur PCR-Methode).

	Standardarm	PCR-Arm
Patientenzahl	6848	5884
MRSA positiv bei Aufnahme	187	266
Nosokomiale MRSA positiv	157	111
Dekolonisation	142	268
Zeit bis zum Resultat (Tage)	3,3	0,9

Große englische Studie zum MRSA-Screening

Beurteilung

- Diese Resultate widersprechen den Ergebnissen von zwei negativen MRSA-Screening Studien, die 2008 publiziert wurden (Harbarth et al. JAMA; Jeyaratnam et al. BMJ) und bestätigen, dass der Vergleich von MRSA-Screening-Studien selbst Experten Kopfzerbrechen bereiten kann.
- Methodische Details der Studie wurden nicht gezeigt, so dass eine endgültige Beurteilung noch nicht möglich ist.

Haut- und Umgebungskontamination bei MRSA-Trägern vor Erhalt der PCR-Resultate der Abstrichuntersuchung

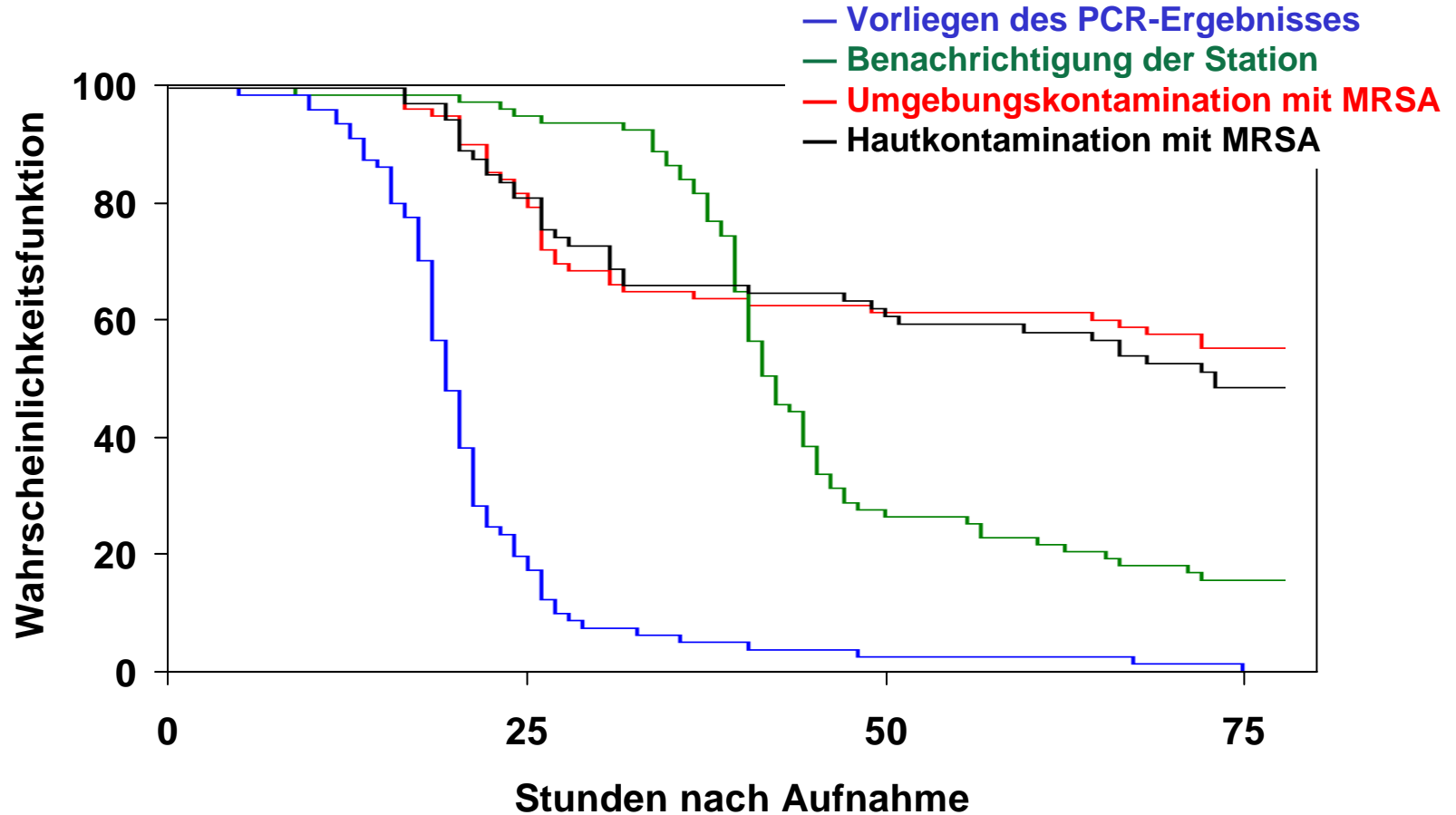
Hintergrund

- Mehrere vor kurzem durchgeführte Interventionsstudien legen nahe, dass die Resultate von PCR-Untersuchungen zur Bestimmung des MRSA-Trägerstatus in der täglichen mikrobiologischen Routine erst nach ca. 20-24 Stunden erhältlich sind.

Studie

- Prospektive 6-wöchige Studie (April/Mai 2008)
- 83 Patienten mit nasaler MRSA-Besiedlung, die in einem Krankenhaus mit allgemeinem PCR-Screening aller Patienten aufgenommen wurden
- Im Intervall zwischen Aufnahme und Erhalt des definitiven Testresultats wurden Haut- und Umgebungsabstriche abgenommen.

Haut- und Umgebungskontamination bei MRSA-Trägern vor Erhalt der PCR-Resultate der Abstrichuntersuchung



Haut- und Umgebungskontamination bei MRSA-Trägern vor Erhalt der PCR-Resultate der Abstrichuntersuchung

Fazit

- Die Rate der Umgebungskontamination vor Erhalt der PCR-Resultate war hoch.
- Es ist nicht auszuschließen, dass eine vorbestehende Raumkontamination nicht ausreichend dokumentiert wurde.
- Die Reinigungspraktiken wurden nicht näher beschrieben.
- Es bleibt unklar, wie viele Patienten vor Einschluss nur nasale MRSA-Träger waren.
- Die Hautbesiedlung war insgesamt überraschend niedrig.
- Präventive Isolation vor Erhalt der PCR-Resultate sollte bei Hochrisiko-Patientengruppen und v.a. auf Intensivstationen erwogen werden.

Große holländische Screeningstudie zur Reduktion postoperativer Infektionen mit *S. aureus*

Design

- Multizentrische, randomisierte Doppelblindstudie

Intervention

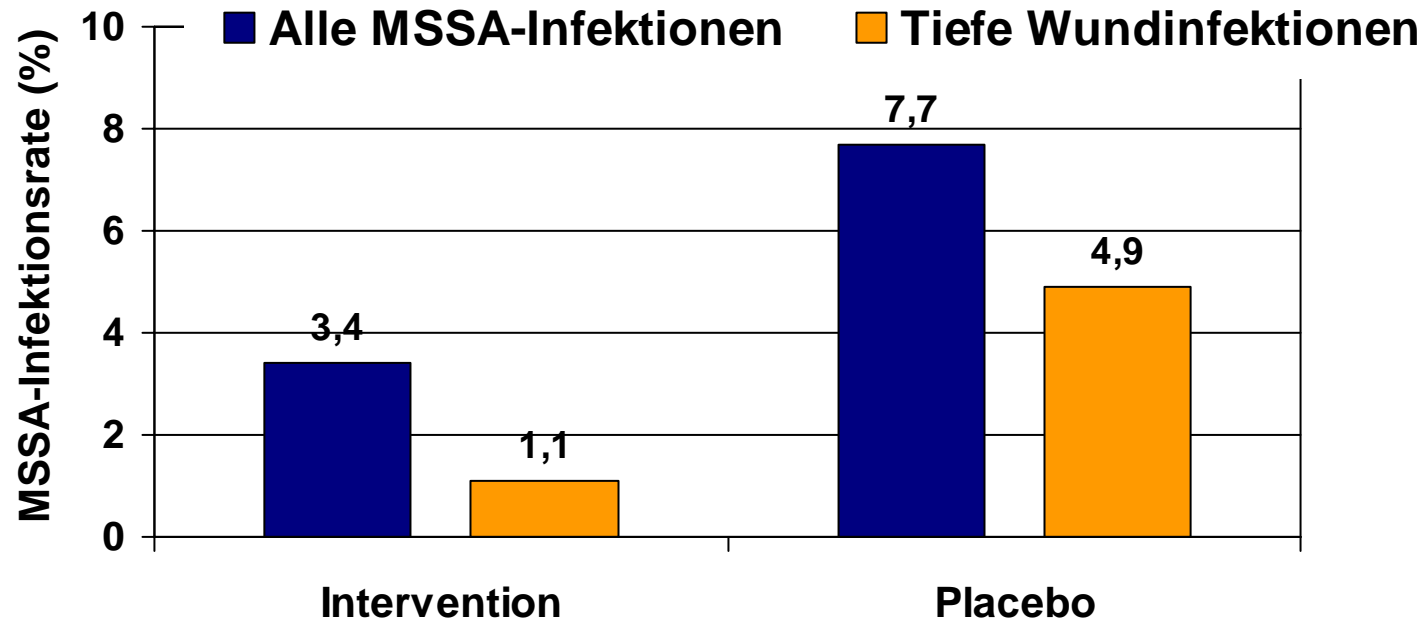
- PCR basiertes Screening auf *S. aureus*
- Mupirocin plus Chlorhexidin für 5 Tage (versus Placebo)
- Beobachtungszeit: 6 Wochen
- Antibiotikaprophylaxe: Cefazolin

Studienpopulation

- 6771 Patienten mit Screening
- 1270 Patienten mit MSSA-Trägerstatus
- 917 Patienten in die Studie eingeschlossen

* MSSA: Methicillin empfindliche *Staphylococcus aureus*

Große holländische Screeningstudie zur Reduktion postoperativer Infektionen mit *S. aureus*



Beurteilung

- Die Studie wurde abgebrochen, nachdem die Interimsanalyse einen eindeutigen Interventionseffekt zeigte.
- Diese Studie enthielt nur 2 MRSA-Träger und ist daher nicht ohne weiteres auf Krankenhäuser mit endemischem MRSA zu übertragen.
- Insgesamt ein überzeugender Beleg für den Nutzen des Screenings auf *S. aureus* vor Elektiveingriffen mit hohem Infektionsrisiko

Weitere Beobachtungen aus Holland

- Richtig durchgeführt kann die MRSA-Dekolonisation bei >90% der MRSA-Träger erfolgreich sein.
- Erst 6 negative Abstrichuntersuchungen, verteilt über mindestens 3-4 Wochen, sind der definitive Nachweis, dass ein Patient dauerhaft MRSA-negativ ist.
- Im häuslichen Umfeld ist die MRSA-Übertragungsrate von Patienten auf Familienmitglieder sehr hoch (44%).
- Die holländische *Search and Destroy*-Strategie ist nach wie vor höchst kosteneffektiv.
- CA-MRSA ist bei landwirtschaftlichem Personal ein zunehmendes Problem, schwere Infektionen sind allerdings selten.

CA-MRSA = *Community-acquired* MRSA

➔ Mollema K-3376

➔ Van Rijen K-3358

➔ Mollema K-1705

➔ Van Rijen K-1712

⬆ Übersicht

MRSA-Trägerstatus und Infektionsrisiko

Fragestellungen

- Wann infizieren sich MRSA-Träger ?
- Wie lange hält der protektive Effekt einer Dekolonisation an ?
- Schützt Mupirocin vor einer MRSA-Infektion ?

Design

- Multizentrische Beobachtungsstudie in Chicago (Evanston Northwestern Healthcare)
- 3 Krankenhäuser mit 850 Betten und 40000 Aufnahmen
- Systematisches Aufnahmescreening aller Patienten

Intervention

- Topische Mupirocin-Behandlung

Patienten

- 1357 Patienten mit MRSA-Besiedlung (ca. 400 Patienten wurden nicht dekolonisiert)

Statistische Analyse

- *Cox Proportional Hazards* Modell

MRSA-Trägerstatus und Infektionsrisiko

Parameter	Ergebnis
Zeitpunkt der MRSA-Infektion nach Besiedlung	Das größte Risiko einer MRSA-Infektion besteht im 1. Monat nach initialer Besiedlung.
Persistierende MRSA-Besiedlung	Mupirocin verringerte das Risiko der persistierenden Besiedlung (bis zu 60 Tage nach Behandlungsende).
MRSA-Infektionsrisiko	Mupirocin verringerte nicht das absolute Risiko einer MRSA-Infektion, aber verzögerte deren Auftreten verglichen mit Patienten, die kein Mupirocin erhielten (Median 50 d vs. 15 d; $p = 0,06$)

Kommentar

- Diese Beobachtungsstudie bestätigt, dass die topische MRSA-Dekontamination zwar einen temporären Effekt auf die Besiedlungsrate hat, aber langfristig nicht ausreichend gegen eine MRSA-Infektion schützt.
- Im Gegensatz zu Deutschland erfolgte hier nur ein Nasenabstrich ohne weiteres Haut-Screening.



Gramnegative Bakterien

Dekolonisierung bei Trägern von *Extended Spectrum Beta-Lactamase*-Bildnern (ESBL)

Hintergrund

- ESBL-Träger werden bisher nicht systematisch dekolonisiert, können aber als Überträger fungieren.

Studie

- Prospektive Kohortenstudie in Basel im Zeitraum 2000 bis 2008
- ESBL-Prävalenz bei *E. coli* < 5%

Intervention

- Dekolonisierung von 100 Patienten mit Paromomycin 500 mg oral 4 x/d für 4 Tage (bei Harnwegsinfektionen plus Nitrofurantoin, Fosfomycin oder Cotrimoxazol)

Ergebnis

- 76% der Patienten wurden erfolgreich dekolonisiert (mediane Beobachtungszeit 24 Monate)

Kommentar

- Diese interessante Pilotstudie zur ESBL-Dekolonisierung sollte Anlass für weitere kontrollierte Studien sein.

Übertragungshäufigkeit von ESBL produzierenden Enterobakterien

Studie

- *Surveillance*-Studie zur Bestimmung der nosokomialen Übertragungsrates von ESBL produzierender Enterobakterien (ESBL-E) in Akutbereich und Langzeitpflege.
- Prospektive Kohortenstudie über 8 Monate.
- Indexpatienten mit positiver klinischer ESBL-E-Probe wurden mittels elektronischem Überwachungssystem identifiziert.
- Alle Zimmernachbarn im Zeitraum vor der Infektion wurden mittels Rektalabstich überprüft.

Resultate

- Identifikation von 31 Indexpatienten und 177 Zimmernachbarn, wovon 8 mit ESBL-E kolonisiert waren.
- 5 Nachbarn zeigten ein identisches PFGE-Muster oder das gleiche Resistenzgen wie ihr Indexpatient.
- Übertragungsrates für ESBL-E: im Akutbereich 4,2/1000 Expositionstage; in der Langzeitpflege 0,4/1000 Expositionstage.

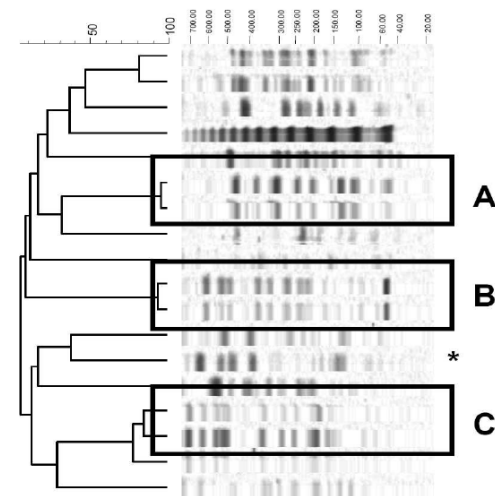
Übertragungshäufigkeit von ESBL produzierenden Enterobakterien

Paar	Pflege	Erreger	Identisches PFGE-Profil	Genanalyse		
				beta-Lactamase	TEM	CTX-M
A	Akut	<i>E. cloacae</i>	Ja	Nein	--	--
B	Langzeit	<i>K. pneumoniae</i>	Ja	Ja	--	15
C	Langzeit	<i>K. pneumoniae</i>	Ja	Ja	--	15
D	Akut	<i>E. coli</i>	Nein	Ja	--	15
E	Akut	<i>E. coli</i>	Nein	Ja	116	15

PFGE = Pulsfeld-Gelelektrophorese

Kommentar

- Die nosokomiale Übertragungsrate war gering.
- Überraschenderweise fanden sich aber mehr Übertragungen im Akutbereich als in der Langzeitpflege.



Carbapenem resistente Klebsiellen

Hintergrund

- Carbapenem resistente Klebsiellen sind in mehreren Ländern mittlerweile endemisch.

Neuere Daten und Beobachtungen

- Ein Patiententransfer aus Israel führte in Miami zu einem größeren Ausbruch.
- Obwohl der Patient bekannter Träger war, wurde er bei Krankenhausaufnahme nicht isoliert.
- Screening und Kontrolle von Carbapenem resistenten Klebsiellen sind technisch anspruchsvoll und aufwendig. Israel hat dazu ein nationales Kontrollprogramm in die Wege geleitet.
- Die Sterblichkeit ist bei Infektionen mit Carbapenem resistenten Klebsiellen deutlich erhöht; die Colistin-Resistenz trägt hierzu entscheidend bei.

Kommentar

- Deutsche Krankenhäuser sollten Patienten, die aus Problemgebieten verlegt werden, auf multiresistente Klebsiellen untersuchen und präventiv isolieren.
- In automatisierten mikrobiologischen Untersuchungen werden diese multiresistenten Organismen nicht immer zuverlässig erkannt.

➔ Castanheira C1-126

➔ Sonnenberg K-4762

➔ Goren C1-135

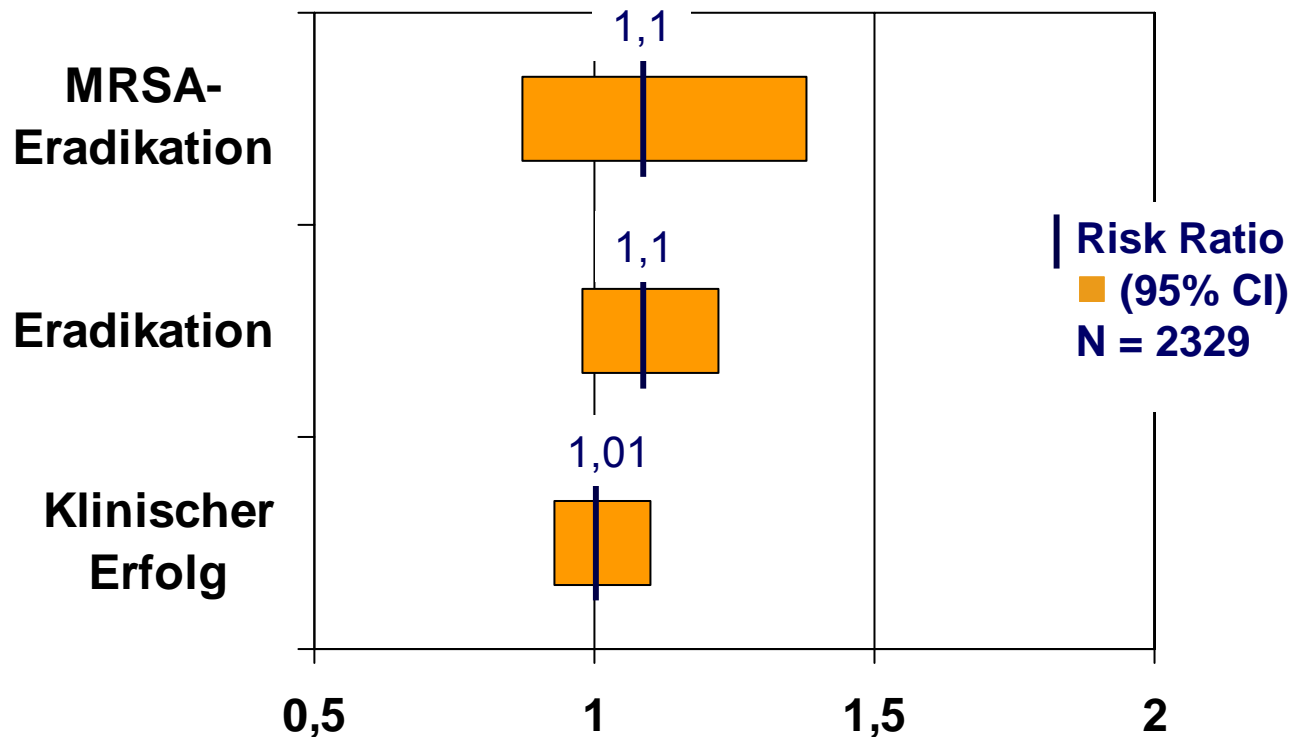
➔ Schwaber K-3509

↑ Übersicht



Andere Themen

Metaanalyse: Linezolid versus Glykopeptide bei nosokomialer Pneumonie



Kommentar

- In dieser Metaanalyse von 9 randomisierten Studien (Vancomycin 7; Teicoplanin 2) zur nosokomialen Pneumonie bestand kein signifikanter Unterschied in der klinischen Wirksamkeit von Glykopeptiden und Linezolid.
- Ob ein Vorteil für Linezolid bei MRSA-Pneumonien besteht, ist noch nicht definitiv geklärt.

Probiotischer Joghurt zur Prophylaxe der Antibiotika assoziierten Diarrhoe?

● Hintergrund

- ▶ Mehrere kleinere Studien und eine Metaanalyse legen nahe, dass Probiotika gegen Antibiotika assoziierten Diarrhoe helfen.
- ▶ Ein probiotischer Joghurt wurde bisher nicht in einer kontrollierten Studie klinisch getestet.

● Studie

- ▶ Prospektive, randomisierte Doppelblindstudie (Madrid, Spanien)
- ▶ Probiotischer Joghurt versus normaler Joghurt (Placebo) versus kein Joghurt (nicht verblindete Kontrollgruppe)
- ▶ 314 Patienten (60% ohne Komorbidität), Beobachtungszeit 1 Monat
- ▶ Antibiotika: Amoxicillin/Clavulansäure oder Levofloxacin (mindestens 1 Dosis)

Probiotischer Joghurt zur Prophylaxe der Antibiotika assoziierten Diarrhoe?

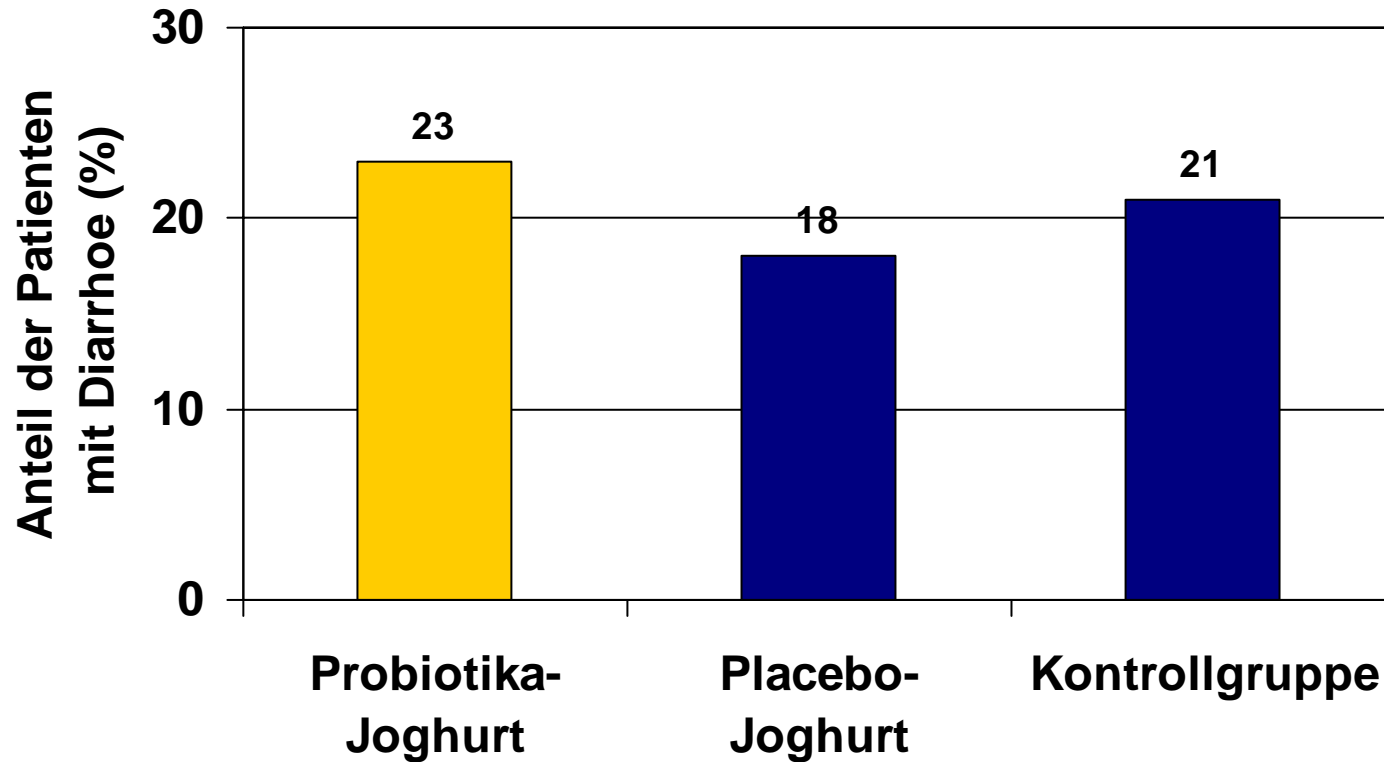
Hintergrund

- Mehrere kleinere Studien und eine Metaanalyse legen nahe, dass Probiotika gegen Antibiotika assoziierte Diarrhoe wirksam sind.
- Probiotischer Joghurt wurde bisher nicht in einer kontrollierten Studie klinisch getestet.

Studie

- Prospektive, randomisierte, Doppelblindstudie (Madrid):
- Probiotischer versus normaler Joghurt (Placebo) versus kein Joghurt (nicht verblindete Kontrollgruppe)
- 314 Patienten (60% ohne Komorbidität)
- Beobachtungszeit 1 Monat
- Antibiotika: Amoxicillin/Clavulansäure oder Levofloxacin (≥ 1 Dosis)

Probiotischer Joghurt zur Prophylaxe der Antibiotika assoziierten Diarrhoe?



Kommentar

- In dieser randomisierten Doppelblindstudie zeigte probiotischer Joghurt keine prophylaktische Wirkung gegen Antibiotika assoziierte Diarrhoe.



Abstracts

C1-126

Increasing Prevalence of KPC-Producers as an Emerging Resistance Mechanism Among Carbapenem Non-Susceptible Isolates: Report from the SENTRY Antimicrobial Surveillance Program

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Background: The dissemination of metallo- β -lactamase (MBL) and serine-carbapenemase (S-Carb)-producing Enterobacteriaceae jeopardize the clinical utility of carbapenems. The prevalence of MBL and S-Carb is still low, but rapidly increasing. We evaluated the occurrence of MBL (IMPs, VIMs) and S-Carb (KPC, IMI/NMC-A, SME, and OXA-48) in a collection of 103 carbapenem-non-susceptible *E. coli* (EC) and *K. pneumoniae* (KPN) from the SENTRY Program.

Methods: 5,357 EC and *Klebsiella* spp. isolates were collected during 2007 from Europe, North and Latin America. Isolates were tested by the CLSI broth microdilution method. Strains showing elevated carbapenem MIC values (≥ 2 $\mu\text{g/ml}$ for imipenem, meropenem or ertapenem) were tested with multiplex PCR approaches for MBL and S-Carb. Amplicons were sequenced and analyzed.

Results: A total of 103 (2% of isolates overall, 7 EC, 96 KPN) isolates showing increased carbapenem MIC values were evaluated. Fifty (49%) isolates were found to harbor bla_{KPC} (49 KPN, 1 EC). These isolates were from the USA (40, mainly east coast), Israel (9) along with one KPC-2-producer from Argentina. KPC-2 was more prevalent than KPC-3. VIM-1 was detected in 6 (6%) KPN; 5 from Italy and 1 from Turkey. IMP-1 was found in 1 isolate from Turkey. OXA-48 was discovered in 2 Turkish KPN. KPC-producing isolates were highly resistant (MIC, ≥ 8 $\mu\text{g/ml}$) to all carbapenems, while MIC values for these agents varied considerably among other enzyme-producers.

Conclusions: MBL are still a problem in certain geographic regions, mainly as causes of local outbreaks; however, KPC-producing isolates are becoming of greatest concern in the USA and are, according to recent studies (including ours), rapidly disseminating worldwide. This is the first report of KPC-2 in Argentina, and of multiple carbapenemases being detected in Turkey.

C1-135

Prevalence and Characterization of Carbapenem resistant *Escherichia coli* (CREC) in Israel (2004-2008)

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Background: Carbapenem resistance in *Enterobacteriaceae* is emerging worldwide. Carbapenem resistant *E.coli* (CREC) in Israel is rare. We aimed to study the molecular epidemiology and molecular mechanisms among *E. coli* in our hospital.

Methods: CREC isolates were collected from 2004 to 2008. Susceptibility testing was performed by Vitek 2 and MICs to carbapenems were tested by agar dilution and E-test. Isolates resistant to at least one carbapenem were studied. Genetic relatedness was analyzed by PFGE. b-lactamases were analyzed by isoelectric focusing (IEF) and hydrolysis. *bla*genes were determined by PCR and sequencing.

Results: 12 CREC single patient isolates were collected and studied (3 blood, 3 urine, 2 synovial fluid, 2 wounds, 2 peritoneal fluid). CREC incidence during 2004-2008 was 0.05%, and no change in incidence during this period was observed. Isolates were multidrug resistant with variable resistance to aminoglycosides, and 11/12 isolates were resistant to quinolones. Not all isolates were resistant to carbapenems; MIC50 and MIC90 to imipenem were 4 and 8 mg/L (range <0.5-32 mg/L), to meropenem were 2 and 8 mg/L (range <0.5-16 mg/L) and to ertapenem were 8 and 12 mg/L (range 4-128 mg/L). Isolates belonged to 7 different pulsotypes, and IEF showed that all produced 3-4 b lactamases. Cell free extracts from all isolates hydrolyzed imipenem. Carbapenem resistance was rendered by production of KPC-2 (10 isolates), KPC-3 (1 isolate from 2008) and a non KPC yet undefined carbapenemase (1 strain from 2007) which hydrolyzed imipenem (hydrolysis rate of 50mU/mg protein compared to 33mU/mg for the KPC producing strains). All 12 strains also carried TEM, 1/12 carried SHV-12 and 6/12 isolates (4 pulsotypes) carried CTX-M-28, firstly detected in Israel. **Conclusions:** CREC occurs rarely in Israel, mostly due to KPC production. This is the first report on KPC-3 in *E. coli* in Israel. Various clones are detected, often carrying also other b lactamases. The co occurrence of KPC-2 and CTX-M-28 in Israel is intriguing.

K-533

Linezolid versus Vancomycin or Teicoplanin for Nosocomial Pneumonia: A Meta-Analysis

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Background: Compared to glycopeptides, linezolid achieves high lung epithelial lining fluid (ELF) concentrations which may correlate with improved efficacy in the treatment of nosocomial pneumonia (NP). However, clinical superiority has not been demonstrated which may be a consequence of sample size in non-inferiority trials. We performed a meta-analysis to test the hypothesis that linezolid may be superior to glycopeptides in NP.

Methods: Prospective, randomized trials which tested linezolid vs. vancomycin or teicoplanin for treatment of NP were included. Heterogeneity was analyzed by I^2 and Q statistics. Relative Risks (RR) were based on the Mantel-Haenszel method. Outcomes analyzed included clinical cure (CC), microbiologic eradication (ME), and side effects.

Results: 8 linezolid trials (6 vancomycin, 2 teicoplanin) were included (N=853). The linezolid vs glycopeptide analysis shows: CC RR=1.01(95% CI 0.93,1.10, p=0.80; $I^2=0\%$; N=853); ME RR=1.10 (CI 0.97,1.23; p=0.11; $I^2=0\%$; N=597); and MRSA population RR=1.14 (CI 0.82,1.58; p=0.44; $I^2=47\%$; N=191). If linezolid is compared to vancomycin only, the CC RR remains 1.01(CI 0.90,1.12), and ME and MRSA RRs are: 1.06 (CI 0.88,1.28) and 1.04 (CI 0.73,1.47), respectively. The risk of thrombocytopenia (RR=1.92 [CI 1.29,2.86]; p=0.001) and GI events (RR=1.90 [CI 1.04,3.48]; p=0.03) were significantly higher with linezolid, but no differences were seen for renal dysfunction (RR=0.82 [CI 0.52,1.27]; p=0.37), or all-cause deaths (RR=0.95 [CI 0.76,1.18]; p=0.63).

Conclusions: Despite a statistical power > 90%, our meta-analysis did not detect clinical superiority of linezolid vs. glycopeptides for treatment of NP. Compared to linezolid, vancomycin was not associated with more renal dysfunction. Linezolid showed a significant increase in the risk of thrombocytopenia and GI events. Available data does not support the claim that linezolid is superior to vancomycin for the treatment of NP.

K-1705

Untreated MRSA Carriership: A Source of Transmission into the Community

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Background: To prevent spreading of MRSA into the community and to prevent recolonisation by MRSA after decolonisation, index patients and their positive household contacts receive eradication therapy simultaneously. We assessed the rate and possible determinants of transmission to household contacts.

Methods: All MRSA positive patients treated or followed up by the Erasmus MC between January 2005 and December 2007 were asked to participate in the study. Screening cultures (nose, throat and perineum) of index patients were obtained. Just before start of MRSA eradication therapy, all household contacts were screened (nose, throat, perineum) to determine whether transmission of index patients to household contacts has occurred. Medical data of index patients and household related data were determined.

Results: 71 MRSA positive index persons and 184 household contacts were included. Transmission from index person to household contacts occurred in 43.7% (n=31) of index persons, who had together 94 household contacts. 62.8% (n=59) of the household contacts were found MRSA positive. MRSA nasal colonisation in combination with other positive MRSA sites was significantly associated with transmission ($p=0.037$, OR 4.125, 95% CI 1.092 - 15.585). Health-care workers were less likely to transmit to their households compared to patients ($p=0.044$, OR 0.300, 95% CI 0.091 - 0.989). Younger persons showed higher transmission rates compared to older persons ($p=0.042$). A positive correlation was observed between transmission rates and exposure time of MRSA positive persons to their household before eradication treatment was started ($p=0.074$).

Conclusions: MRSA transmission to household contacts occurs frequently. To prevent transmission into the community or recolonisation of MRSA through household contacts it is important to screen household contacts. Therefore, index persons and their positive household contacts should be treated simultaneously.

K-1708

How Long After Colonization Does MRSA Disease Occur?

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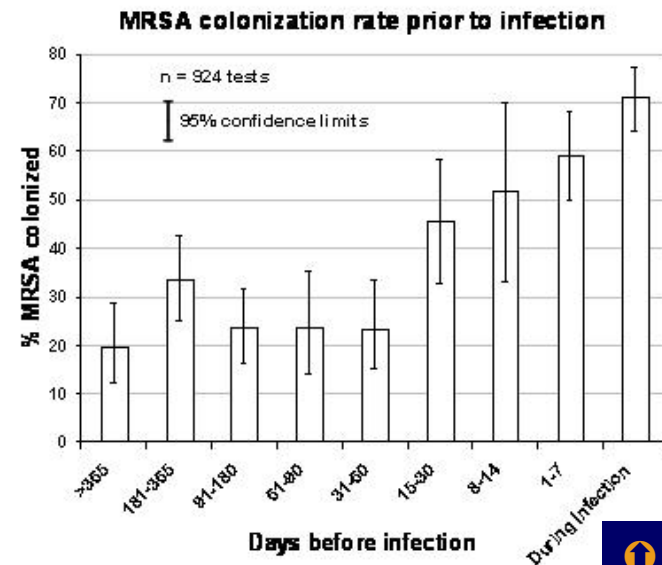
Background: Data regarding the timing of MRSA disease after colonization would aid our understanding of staphylococcal biology and the design of infection control programs.

Methods: From Aug. 2004 - Feb. 2008, 133,221 nasal MRSA surveillance tests were done at our 3-hospital organization as part an infection control program. From Aug. 2005 - Feb. 2008, records of patients with positive MRSA clinical cultures were systematically reviewed to determine whether they had true disease. Study 1: For patients with disease who had surveillance tests done during or prior to disease, the rate of nasal colonization at a series of time points during and prior to disease was determined. Study 2: A cohort of patients was identified from the same timeframe who were initially not colonized, later became nasally colonized but without disease, and still later developed disease. In those patients, the relative risk (RR) of disease in each of the 12 months following acquisition was determined.

Results: Study 1: 396 patients with disease had 924 concomitant or prior surveillance tests. Their rate of colonization with MRSA during and prior to disease is shown in the Figure.

Study 2: 69 patients developed nasal colonization and later developed disease. RR of disease occurring in the first month following colonization was 4.7 (95% CI 2.9, 7.5) compared to the 11 subsequent months.

Conclusion: The greatest risk of MRSA disease occurs in the month following colonization.



K-1711

A Randomized Trial of Admission Screening and Decolonization of *Staphylococcus aureus* Carriers to Prevent Nosocomial *S. aureus* Infections

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Background: Patients who carry *Staphylococcus aureus* (*S. aureus*) have an increased risk of developing nosocomial infections with this microorganism. Decolonization of nasal and extra-nasal sites on admission to hospital may reduce the risk of developing these infections.

Methods: In a randomized, double-blind, placebo-controlled, multi-center trial we assessed whether identification of *S. aureus* carriers by real-time polymerase chain reaction (real-time PCR) on nasal specimens followed by prompt treatment with mupirocin nasal ointment and chlorhexidine gluconate medicated soap reduces the risk of nosocomial *S. aureus* infection in carriers.

Results: From October 2005 to June 2007, 6771 patients were screened on admission to hospital. 917 *S. aureus* real-time PCR positive patients were included in the intention-to-treat analysis. *S. aureus* infection rate was 17/504 (3.4%) in the mupirocin/chlorhexidine treated patients, and 32/413 (7.7%) in the placebo treated group (relative risk for infection 0.42; 95% confidence interval 0.23-0.75). The largest effect was observed for deep surgical site infections (1.1% in the mupirocin/chlorhexidine treated group vs 4.9% in the placebo treated group, RR 0.23; 95%CI 0.09-0.62).

Conclusions: The combination of rapid detection and prompt decolonization of *S. aureus* carriers with mupirocin ointment and chlorhexidine gluconate medicated soap upon admission to hospital significantly reduced the risk of nosocomial *S. aureus* infections, especially the risk of deep surgical site infections.

K-1712

Costs and Benefits of the MRSA 'Search and Destroy' Policy in a Dutch Hospital

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Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) has become an increasingly important pathogen in hospitals and recently also in the community. In Dutch hospitals the 'Search and Destroy' (S&D) policy is applied successfully. The objective of this study was to determine the yearly costs and benefits of the S&D policy over the years 2001 until 2006 in a teaching hospital with 1370 beds.

Methods: Data of the infection control department and from the hospital information system were used to calculate the variable and fixed costs. Variable costs contained costs for isolations, cleaning, treatment, closure of wards and additional costs for coincidental MRSA findings. Fixed costs were divided into costs for building isolation rooms and salary of one full-time infection control practitioner. To determine the benefits of the S&D policy, the number of cases of MRSA bacteremia prevented and its associated costs and mortality were estimated.

Results: In the study period 82 patients and 13 HCW were found to be MRSA positive. Thirty-three different MRSA types were found and one of them had spread in the hospital. This caused a temporary closure of 3 units for a total of 55 days. MRSA carriage of all colonized HCW was treated and together they were not allowed to work for 221 days. Yearly costs of the MRSA policy were estimated at € 215,559, equivalent to € 5.54 per patient admitted to the hospital or € 0.76 per patient day. This is 0.08% of the hospital budget. In the study period there were no patients that had a bacteremia caused by MRSA. Application of this policy was estimated to prevent 64 cases of MRSA bacteremia per year, resulting in annual savings of € 595,584 for the hospital and 15 lives per year (95% CI 9-23).

Conclusions: The S&D policy is highly cost-effective.

K-3358

Pig- and Calf-related MRSA in a Dutch Hospital

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Background: In Dutch hospitals the MRSA 'Search and Destroy' policy is applied successfully. In 2006 a new risk category was added to this control policy. This category includes patients who have professionally direct contact with living pigs or veal calves. Patients who live at a cattle farm are included too. The objective of this study was to determine the number of MRSA positive persons in the new patient group at risk for MRSA carriage, i.e. persons with exposure to pigs or veal calves.

Methods: Data of the infection control department was used to retrieve the total number of patients screened in 2006 and 2007 because of exposure to pigs or veal calves after introduction of this risk category in July 2006 and to retrieve the number of MRSA positive patients found in this category.

Results: In the last six months of 2006, 57 patients with direct exposure to pigs or calves were screened. Eighteen of them were found to be MRSA positive (32%), i.e. 14/39 (36%) with exposure to pigs and 4/18 (22%) with exposure to calves. In 2007, 122 patients from this risk category were screened. 19 (16%) were found to be positive, i.e. 18/90 (20%) with exposure to pigs and 1/32 (3%) with exposure to calves.

Conclusions: Patients with exposure to pigs have an extremely high carriage rate of MRSA. The carriage rate for patients exposed to calves is high, but significantly lower than for those exposed to pigs ($p=0.038$).

K-3376

To Assess Successfulness of MRSA Eradication Therapy: More Than 3 Follow-up Cultures Necessary

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Background: We assessed the rate of success of MRSA eradication therapies by using a strict treatment and follow up protocol and analysed determinants of eradication failure.

Methods: All MRSA positive patients of the Erasmus MC detected between January 2005 and December 2007 were followed up. Only patients, who were treated by or followed up by the Erasmus MC Rotterdam, were included in the study. Through medical chart review, possible risk factors for eradication failure at time of MRSA detection and at time of treatment, eradication regimens and microbiological culture results were collected. Treatment included mupirocine and chlorhexidine bodywash with or without two oral antibiotics for 10 days. Follow up was by 6 colonization cultures. Definition of MRSA negative was by showing 6 negative culture sets.

Results: In 165 patients MRSA was detected, 55 patients were excluded (death, no treatment in our hospital, not eligible for treatment). If postponing of treatment was possible, patients were not treated unless indwelling devices were removed or non-intact skin, whatever reason, was not present anymore. By wait and see, 23 MRSA positive patients became MRSA negative decolonized over time without treatment. By the first antimicrobial treatment attempt 67.8% (n=59) of patients were successfully eradicated. After three eradication attempts an overall succesrate of 79.3% (n=69) was achieved. No significant determinants were discovered which could predict possible therapy failure. No differences in succesrates were found between different oral antimicrobial regimens. After 3 consecutive negative surveillance cultures, 29% of patients turned out to be MRSA positive again.

Conclusions: A standardised protocol can be highly effective in eradicating MRSA by antimicrobial therapy. More than 3 consecutive surveillance cultures are needed to reliable asses the MRSA negative status of a patient.

K-3379b

Skin and Environmental Contamination by Patients with Methicillin-Resistant *Staphylococcus aureus* (MRSA) Occurs Before Admission PCR Results Become Available

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Background:Active surveillance to detect patients colonized with MRSA is increasingly practiced in healthcare settings. However, inpatients may have already become sources of transmission before appropriate precautions are implemented. Here, we examined the frequency of MRSA contamination of commonly touched skin and environmental surfaces before patient carriage status became known.

Methods:We conducted a 6-week prospective study of patients colonized with MRSA at a hospital where active surveillance is performed via nasal PCR screening on admission. Skin and environmental contamination were assessed within hours of PCR completion.

Results:In April-May 2008, 83/113 patients identified via positive admission PCR for MRSA were enrolled. Overall, 38/74 (51%) and 37/83 (45%) patients had skin and environmental contamination, respectively. 75% of samples were collected within 7 hours after PCR completion, and 88% were collected before PCR result notification. By 25 and 33 hours post-admission, at least 18% and 35% of MRSA patients had contaminated their environments, respectively. Among the 32 (39%) patients who had previously shared a room, 13 (41%) had contaminated their environment. Median time from admission to PCR completion and from result to notification were 20 hours (interquartile range (IQR) [18, 23]) and 23 hours (IQR [21-28]). Nasal MRSA density >500 colony-forming units was also associated with skin or environmental contamination (76% vs 40%; P=0.005, and 71% vs 33%; P=0.002).

Conclusions:By the time precautions are implemented, many screened patients have already contaminated their skin and environment with MRSA. First few hours post-admission represent important opportunities to reduce risk of cross-transmission. Strategies to reduce delays, to preemptively identify patients at high risk for disseminating MRSA, or to improve universal precautions are needed.

K-3447

Transmission Rate of Extended Spectrum Beta-Lactamase-Producing *Enterobacteriaceae* (ESBL-E) in Acute vs. Long-Term Care

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Background: Although the incidence of ESBL-E has increased worldwide, there is sparse information about their nosocomial transmission rate in various settings. We therefore conducted a surveillance study to determine the rate of ESBL-E cross-transmission among acute-care (ACF) and long-term-care facility (LTCF) patients at our institution.

Methods: 8-month prospective cohort study of patients with newly detected ESBL-E infection or colonization (=index patients). Patients being in the same or adjacent room at the same time were considered exposed and screened for the presence of ESBL-E. Isolated ESBL-E strains were evaluated for clonal relatedness by PFGE and genotyping. Patient-to-patient transmission was considered to occur if ESBL-E had identical PFGE patterns or the same gene profile.

Colonization pressure was defined as ESBL-E positive-days per 100 patient-days.

Results: 31 index patients and 177 exposed patients were included (118 (57%), LTCF; 90 (43%), ACF). 8 exposed patients were found to be colonized with ESBL-E, 5 of which either had identical PFGE patterns as their index patient (*K.pneumoniae*, 2; *E.cloacae*, 1) or shared the same gene profile (*E. coli*, 2). Genotyping showed that CTX-M-15 was predominant (9/16 [56%]). The overall ESBL-E transmission rate was 0.9/1000 exposure-days. More transmissions were detected in ACF than in LTCF (4.2 vs. 0.4/1000 exposure-days), although exposure time overall was shorter (median days [IQR]: 7 [4-15] vs. 20 [13-33]; $p < 0.001$) and the colonization pressure lower (0.6% vs. 2.2%, respectively). However, exposure time in ACF was longer and similar to LTFC among patients later colonized (medians: 18 (2-23) days and 7 (4-13) days; $p = 0.03$).

Conclusion: Nosocomial ESBL-E transmission was low. More transmission events occurred in ACF despite shorter contact times. As in other European countries, CTX-M 15 was the predominant resistance gene.

K-3455

Gram-Negative Bacteria Expressing Extended-Spectrum beta-Lactamases (ESBLs): Is Eradication Possible?

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Background: Gram-negative bacteria producing ESBLs have emerged worldwide. ESBL colonization can persist for years and is a risk factor for infection. Decolonization (DC) for ESBL is not established, and treatment regimens not standardized. The aim of this study was to determine the effectiveness of systemic antibiotic treatment and a DC regimen for ESBL eradication.

Methods: From 1/2000-4/2007, data from all consecutive patients with ESBL were prospectively recorded. In addition to the site of colonization, a rectal swab, a throat swab and a urine sample were routinely collected before start of DC on patients. The DC regimen included: chlorhexidine 0.2% mouth rinses tid (for throat colonization), neomycin 4x1g od (for rectal colonization) and oral antibiotics for urinary tract colonization. Isolation precautions were stopped after three sets of negative screening samples from throat, rectal, urine).

Results: 150 consecutive patients with ESBL were identified. 50 cases were excluded (death: n=13, ≤ 1 screening sample: n=37). The mean follow-up of the 100 analyzed patients was 30.5 months. The most frequent pathogens were *E.coli* (71%) and *Klebsiella pneumoniae* (25%). ESBL acquisition was nosocomial in 49%, health-care-related in 29% and community-acquired in 22%. 17% (17/100) of patients were colonized and 83% (83/100) were infected with ESBL. The most common sites of infection were urinary tract (57%), wounds (15%) and intraabdominal infections (7%). 82% (68/83) of infected patients were adequately treated with systemic antibiotics and 43% (36/83) subsequently became negative for ESBL. ESBL was successfully eradicated in 73% of non-infected, colonized patients.

Conclusion: Overall, eradication of ESBLs was successful in 58% of all evaluable patients. However, more potent DC regimens are likely needed to successfully control ESBL.

K-3509

Infection Control at the National Level: Containment of an Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP) in Israeli Hospitals

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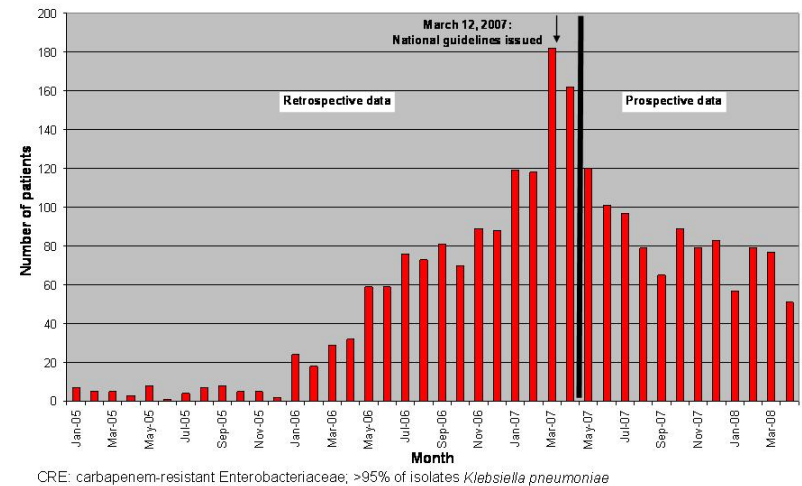
Background: During 2006, Israeli hospitals faced a clonal outbreak of KPC-3-producing CRKP. Local infection control measures failed to contain the spread. Prior to intervention by national public health authorities, over 1000 patients were affected. Crude in-hospital mortality was >40%.

Methods: In early 2007, the Israel Ministry of Health distributed nationwide mandatory isolation guidelines for carriers of carbapenem-resistant Enterobacteriaceae (CRE), and created a task force charged with containing the spread of the epidemic strain. The guidelines mandate physical isolation of carriers and dedicated staffing. The task force pays site visits at each of the nation's general hospitals, and receives a daily census of CRE carriers from each, as well as an itemized report on their degree of compliance with the isolation guidelines.

Results: With the implementation of the guidelines and the creation of the task force, the steady rise in incidence of CRE acquisition was halted, and since then the number of new monthly cases has been reduced by >2/3. Hospitals are given continuous feedback on their performance, and there is direct correlation between compliance and success in containment of spread.

Conclusions: A centrally-coordinated national public health intervention has succeeded in containing, but not yet ending, an outbreak of CRKP after local infection control measures failed.

First-Time CRE Acquisitions in Israeli General Hospitals, Jan. 2005-April 2008



K-3589

Probiotics in the Prophylaxis of Antibiotic-Associated Diarrhea: A Randomized Double-Blinded Controlled Trial

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Background: Meta-analysis suggest that probiotics may be helpful for the prevention of antibiotic-associated diarrhea (AAD), but few large scale randomized controlled trials have been conducted.

Methods: We performed a randomized double blinded clinical trial (ref: AGL2004-07285-C02) in patients admitted to an Internal Medicine Service from june-05 to january-08. Patients who started amoxicilline-clavulanate or levofloxacin were randomized (2:2:1) to receive daily 200 ml of placebo yoghurt (*S thermophilus* 10⁹ ufc/ml, *L bulgaricus* 10⁷ ufc/ml), 200 ml of probiotic yoghurt (previous plus *L. acidophilus* 10⁷ ufc/ml, *B lactis* 10⁸ ufc/ml, *L casei* 10⁷ ufc/ml) or no yoghurt (unblinded control group) from within 48 hours of the beginning of antibiotic therapy up to 5 days after antibiotic stop and followed up for one month. Both yoghurts had a similar taste and external appearance. Neither patients nor attending clinicians were aware of the type of yoghurt. Diarrhea was defined as more than two soft feces per day. Frequency, quality of feces, length and severity of diarrhea and mortality were recorded. Statistical analysis was also carried in a blinded manner.

Results: A total of 314 patients were randomized (122 yoghurt A; 125 yoghurt B and 65 no yoghurt). Follow-up was complete for 307 patients (97.8%). Mean age was 75 years, 46% were women and comorbidities were frequent (40%) without differences among the groups. Diarrhea appeared in 23, 18 and 21% respectively, p>.1. There was no difference in length of diarrhea, maximum number of deposition or prolonged admission because of diarrhea among the three groups. Death was 3, 4, and 7% respectively, p>.1.

Conclusions: Probiotic yoghurt doest not have effect in the prevention of AAD in adults. In these fragile in-patients, probiotic treatment was safe and had no effect on mortality.

K-4762

Carbapenem-Resistant *K. pneumoniae* is a Major Risk Factor for Death Following Liver Transplantation

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Background: Infections with multi-drug resistant bacterial pathogens are associated with morbidity and mortality in hospitalized patients. Patients who receive orthotopic liver transplantation (OLT) are at high risk of acquiring bacterial infections and associated complications. We conducted an historical cohort study to determine the impact of multi-drug resistant bacterial infections following OLT.

Methods: The cohort included all OLT recipients at a large inner-city tertiary care hospital between January 1, 2005 and October 1, 2006. Infection was defined when a pathogen was isolated from a sterile site during the one-year period after OLT. All clinical and demographic data was obtained by review of medical records. We used univariate and multivariable analysis to determine whether specific pathogens or clinical syndromes were risk factors for death within 12 months after OLT.

Results: Of the 175 recipients, 61 (35%) patients had bacterial infections and 32 (18%) died within 12 months following OLT. Of the 61 patients with infection, the most common clinical syndromes were bacteremia in 34 (55%), peritonitis in 26 (43%), and intra-abdominal abscess in 17 (28%); the most common multi-drug resistant pathogens were vancomycin-resistant *E. faecium* in 17 (28%) and carbapenem-resistant *K. pneumoniae* (CRKP) in 14 (23%). In multivariable analysis controlling for sex, age, and MELD score, CRKP was the only pathogen independently associated with death [OR = 11.36, 95% CI (3.04, 42.44), P-value<.001]. Seventy-one percent of the patients with CRKP infection died.

Conclusions: CRKP infection is an independent risk factor for death after OLT. Further studies are needed to define more effective preventive and treatment strategies.