Should all patients harbouring ESBL-producing organisms be isolated?

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Spanish Network for Research in Infectious Diseases (REIPI)
• Guidelines
• Evaluation of evidence
• Evidence-based vs epidemiology-based
• Conclusions
Would you like your mother/father to share a hospital room with another patient who is colonised by ESBL-producing *K. pneumoniae*?

What about ESBL-producing *E. coli*?

What about your mother/father-in-law?
Informal survey among 30 worldwide colleagues
Isolation of patients harbouring ESBL producers

Centers

- 71% All
- 19% Some
- 10% None

Organisms: only Klebsiella, only MDR
Units: ICU, NICU, Haematology
Others: “if possible”
Contact precautions (CDC)

- **Who:**
  - Patients colonised/infected with targeted MDRO

- **Why**
  - To prevent transmission of infectious agents spread by direct or indirect contact with the patient or the patient’s environment

- **How**
  - Gown, gloves at entry and discarding before exiting
  - Patient transport
  - Care equipment and instrument/devices
  - Environmental measures

Contact precautions (CDC)

- A single room is preferred (IB).
  - Prioritize patients with conditions that facilitate transmission (stool incontinence, uncontained drainage) for single room (II)
- If not available: cohort (IB)
- If not possible:
  - Avoid sharing rooms with high risk patients (open wounds, (inmunocompromised) (II)
  - >3 feet (1 m) between beds (II)
  - Change protective attire and perform hand hygiene between patients (IB)

Why isolation?
Why isolation?
Control of MDR gram negatives
ESCMID guidelines (draft)

Outbreak setting
- CP: low/moderate quality evidence
- Isolation: low/moderate quality evidence
- Cohort patients: low quality evidence
- Cohort staff: low/moderate quality evidence

Endemic setting
- CP: low/moderate quality evidence
- Isolation: low/moderate quality evidence
- Cohort patients: no evidence available
- Cohort staff: no evidence available
Lack of evidence should not be interpreted as evidence against
- Scarce or low quality studies
- Different epidemiological situations
- Bundles
- Interpretation of evidence
Premises for CP/isolation efficacy

- **Epidemiology**
  - The colonised patients and/or their close environment must be key reservoirs
  - The organism must be efficiently transmitted by contact
  - Other reservoirs must not be important

- **Once CP/isolation is decided**
  - Compliance!!
Premises for CP/isolation efficacy

HOSPITAL A
- Mostly 3-bed rooms
- Low nurse:patient ratio
- Low cleaning standards
- Low adherence to hand hygiene

HOSPITAL B
- Mostly individual rooms
- High nurse:patient ratio
- High cleaning standards
- High adherence to hand hygiene

High probability of efficacy

Lower probability of efficacy
Tschuding-Sutter et al.
ECCMID 2012 O121

- No CP for ESBL producers
- High adherence to standard precautions
- Nosocomial transmission (PFGE): 2/133 (1.5%) contacts of colonised patients
Looking for evidence in infection control

- Hierarchy in the design of studies
  - Randomized cluster trials
  - Quasi
    - Interrupted time series
    - Before-after
  - Outbreaks reports
Interpretation

- **Eradication/control**
  - Measures used were right to eliminate reservoir(s) and avoid transmission
    OR
  - Unrelated to measures

- **No control**
  - Measures are not useful
    OR
  - Measures were not the right ones or were not adequately performed
Randomisation

Drug A

Drug B

Non-differential bias

Wrong diagnosis

Studies on screening/contact precautions/isolation if patients or their close surfaces are not a key reservoir.
Hospital wide clonal outbreak, ESBL-producing *K. pneumoniae*
Positive environmental samples in kitchen

37% 10% 2% 0

Calbo et al, Clin Infect Dis 2011
Eradication of an extensive outbreak in a neonatal unit caused by two sequential *Klebsiella pneumoniae* clones harbouring related plasmids encoding an extended-spectrum ß-lactamase

C. Velasco a,*, J. Rodriguez-Baño b, L. García b, P. Díaz a, C. Lupión b, L. Durán c, A. Pascual a, d

Randomisation

Drug A

Placebo

Differential bias against Drug A

Studies on screening/contact precautions/isolation if adherence to measures is lower than predicted

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Intervention to Reduce Transmission of Resistant Bacteria in Intensive Care

W. Charles Huskins, M.D., Charmaine M. Huckabee, M.S., Naomi P. O'Grady, M.D., Patrick Murray, Ph.D., Heather Kopetskie, M.S., Louise Zimmer, M.A., M.P.H., Mary Ellen Walker, M.S.N., Ronda L. Sinkowitz-Cochran, M.P.H., John A. Jernigan, M.D., Matthew Samore, M.D., Dennis Wallace, Ph.D., and Donald A. Goldmann, M.D., for the STOP-ICU Trial Investigators*

In a cluster-randomized trial we evaluated the effect of surveillance for MRSA and VRE colonization and of the expanded use of barrier precautions (intervention) as compared with existing practice (control) on the incidence of MRSA or VRE colonization or infection in adult ICUs. Surveillance cultures were obtained from patients in all participating ICUs; the results were reported only to ICUs assigned to the
Figure 2. Use of Hand Hygiene, Gloves, and Gowns by Health Care Providers in Intensive Care Units (ICUs) during Contacts with Patients or Their Immediate Environment.
• Evidence-based approach
  vs
• Epidemiology based approach
Epidemiology of nosocomial pathogens

Mechanism of transmission

Reservoirs → Spread

Facilitators
Although the epidemiological behaviour may be quite predictable for specific organisms, surprises are not that rare...

The hospital environment has probably be underestimated as a source for some enterobacteria (sinks...)
(ESBL-producing) *K. pneumoniae*

- **Ability to cause wide and prolonged outbreaks**
- **Reservoirs**
  - Gut of colonized patients
  - Environment underestimated?\(^1\)
- **Transmission: direct contact**
  - Patient-to-patient\(^2\) through the hands of HCW\(^3\)
  - From environmental sources
- **Antibiotics: facilitators\(^4\)**

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2. Harris CID 2007
*E. coli* as a nosocomial pathogen: the big unknown

- Reservoirs?
- Mechanisms of transmission?
- Outbreaks?
Conclusion: Our data suggest that patient-to-patient is not an important cause of the acquisition of ESBL-producing *E. coli* colonization in the ICU setting.
Nosocomial colonization/infection by ESBL-producing *E. coli*

Rodriguez-Baño et al, CID 2006; 42: 37-45

Hospital Universitario Virgen Macarena y Área
Influx of Extended-Spectrum β-Lactamase–Producing Enterobacteriaceae into the Hospital


Spread of *Escherichia coli* Strains with High-Level Cefotaxime and Ceftazidime Resistance between the Community, Long-Term Care Facilities, and Hospital Institutions

Jesús Oteo, Carmen Navarro, Emilia Cercenado, Alberto Delgado-Iribarren, Isabel Wilhelmi, Beatriz Orden, Carmen García, Silvia Miguélañez, María Pérez-Vázquez, Silvia García-Cobos, Belén Aracil, Verónica Bautista, and José Campos

Hospital Universitario Virgen Macarena y Área
Transmission of genetic mobile elements

Community

Acute care centers

E. coli

Klebsiella, Enterobacter

LTCF

Transmission of genetic mobile elements
Are all colonized patients equally “dangerous”? 
Transfer of antimicrobial resistance plasmids from *Klebsiella pneumoniae* to *Escherichia coli* in the mouse intestine

Susanne Schjørring, Carsten Struve and Karen Al Krogfelt*
Conclusions

- CP and isolation are key infection control measures for MDRO
- The efficacy if CP and isolation depends on the:
  - Epidemiologic behaviour of organism
  - Structural issues, cleaning and standard precautions
  - Adherence to CP measures
- The epidemiology of ESBL-producing organism would need to be characterised to decide/modify infection control practices
- It may be prudent to isolate ESBL-producing *K. pneumoniae* (and Enterobacter)
- It may not be necessary to isolate ESBL-producing *E. coli* (except if patient-to-patient transmission is suspected)
If your mother/father needs to be hospitalised at Hosp Univ V Macarena...

- Will be screened in the ICU
- Will be isolated if colonised or infected by any ESBL-producing *Klebsiella*
- Will not be isolated if ESBL-producing *E. coli*
- Epidemiological data will be collected, and molecular typing performed if transmission is suspected

Your mother/father in law too...