

## The impact of hospitalisation on the epidemiology of antibiotic resistance in the normal oropharyngeal and faecal microflora of hospitalised patients; *background, objectives and methodology of the RADAR-study*

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### **Background**

The RADAR-study (Rotterdam Assessment of Determinants of Antibiotic Resistance) is designed to assess the impact of hospitalisation on the epidemiology of antibiotic resistance in the normal oropharyngeal and faecal microflora and to define the hospital associated risk factors for antibiotic resistance. There are two reasons for interest in the epidemiology of resistance in the normal oropharyngeal and faecal microflora. First many of the bacteria that comprise the normal microflora may cause infections. Knowledge of the prevalence and degree of antibiotic resistance in the normal microflora during hospitalisation will contribute to an optimal choice of empirical therapy in the event of nosocomial infections. The second concern is that faecal bacteria might act as a reservoir of mobile resistance genes. Two major aspects of antibiotic resistance have to be considered: the selection of antibiotic resistant strains from the patients' own microbial flora by the selection pressure of antimicrobial agents and the dissemination of resistance within the hospital setting. Policies to decrease the emergence of resistance should therefore stimulate appropriate use of antibiotics and control the dissemination of resistant bacteria in hospitals. Before starting interventions in these two areas knowledge of the risk factors associated with antibiotic resistance in the local hospital is a prerequisite.

### **Objectives**

#### *Primary objectives*

- To assess whether hospitalisation leads to a) a change in antibiotic susceptibility patterns over time or b) the acquisition of new and resistant strains, in the faecal and oropharyngeal flora.
- To examine whether antibiotic resistance acquired during hospitalisation decreases after discharge.
- To define the risk factors associated with changes in susceptibility patterns during hospitalisation.

#### *Secondary objectives*

- To examine whether changes in susceptibility patterns were derived from a) the selection of resistant variants of mutants from patient's own microbial flora or b) from dissemination of resistant clones (or their resistance genes) in the hospital setting.
- To assess whether colonisation with antibiotic resistant strains precedes infection with the same resistant strains.

### **Methodology**

#### *Study population*

Patients admitted to general wards belonging to the departments of internal medicine, respiratory diseases and neurosurgery and the medical and (neuro) surgical ICU's of the

Erasmus Medical Center Rotterdam. Patients were not eligible for the study if they stayed for <5 days in the participating ward or were referred from another hospital ward (not applicable to the ICU population)

*Collection of specimens and microbiological analysis*

Faecal specimens and oropharyngeal swabs were collected as soon as possible (within 24 hours) after admission, once weekly during hospitalisation and on discharge. One and three months after discharge patients were requested by letter to send a sample of faeces and an oropharyngeal swab. Faecal samples collected during and after hospitalisation were diluted and plated on different agars in order to isolate the following species: Enterobacteriaceae, *Pseudomonas* and *Acinetobacter* spp., *Enterococcus* spp. and *Bacteroides* spp.

Oropharyngeal swabs are analysed for Enterobacteriaceae and *Pseudomonas* and *Acinetobacter* spp. Antibiotic susceptibility testing was performed for all isolates. Shifts over time in susceptibility of isolates were studied by comparing minimal inhibitory concentrations of specific antibiotics. Isolates from patients in whom shifts over time in susceptibility of isolates occurred were studied by pulsed-field gel electrophoresis. Typing patterns from isolates before and after the emergence of resistance were compared. The degree of correspondence between clinical and commensal resistant strains from the same individuals was also assessed by molecular typing.

*Defining risk factors for antibiotic resistance*

Risk factors for a change in susceptibility patterns during hospitalisation were studied by case-control comparison and logistic regression analyses. Risk factors were collected from medical and nursing records and from computerised hospital databases. Risk factors were divided in individual risk factors and risk factors associated with the hospital environment.

**Publications**

Filius PMG, Netten D van, Roovers PJE, Vulto AG, Gysens IC, Verbrugh HA, Endtz HPh. Comparative evaluation of three chromogenic agars for detection and rapid identification of Gram-negative bacteria in stool specimens. *Clinical Microbiology and Infection*, accepted for publication.

Filius PMG, Gysens IC, Vulto AG, Roovers PJE, Verbrugh HA, Endtz HPh. The impact of hospitalisation on the epidemiology of antibiotic resistance in the oropharyngeal and faecal flora of intensive care patients. Abstract P911. *Clinical Microbiology and Infection*. Volume 8, Supplement 1, 2002.

***Preliminary results of the RADAR-study will be presented at the SWAB-symposium***