ERG

Effect of Oral Probiotic Administration on the Intestinal Colonization by Vancomycin-Resistant enterococci in a Mice Model

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Background: Reducing VRE digestive carriage represents therefore a major issue to limit the dissemination. By re-equilibrating the digestive bacterial microflora, oral administration of probiotic bacteria could reduce the VRE intestinal carriage. The aim of this study was to determine the effects of orally administered Lactobacillus rhamnosus Lcr35 on the VRE gastro-intestinal colonization in a mouse model.
Method: Mice feces were screened for VRE 3 days a week for a 3 months period. The duration and density (UFC / gramme of feces) of VRE intestinal colonization were assessed in mice receiving 3 or 7-day-course of Lcr35 (10^8 UFC per day) 7 days after VRE inoculation.
Results: All 13 vancomycin-treated mice were homogeneously (max. 10^{10} UFC, min. 10^7 UFC / g of feces)

Oral administration of Lcr35 for 3 days did not reduce the duration neither the density of VRE colonization,
whereas a seven day treatment reduced, although not statistically, the density of VRE colonization.

Conclusion: We established a mice model in which intestinal VRE colonization was sustained and intense. Although not significant, L. rhamnosus Lcr35 administration reduced the density of colonization but not the duration of colonization.

Probiotiques

- **Méta-analyse Mac Farland A J Gastroenterology 2006;101:812-822**

- **Pb : peu d'étude contrôlée, vs PCB où toutes les modalités de prise du probiotique (et sa description) soient clairs**
- **Aujourd'hui, probiotiques ne sont pas des médicaments et on ne trouve pas toujours dedans ce qui est sensé y être ! OK 4x/30 (13%))**

- **Besselink (hollande) Lancet 2008 : ttt probiotique dans pancréatites aiguës : plus de mort et d'ischémie mésentérique et pas moins d'infection !!!**
- **Autres complications : chez Idep, carence nutritionnelle, diabète : risque infectieux**
  - **Bactériémie à Lactobacillus mortalité 32%**
  - **Endocardites à Lactobacillus mortalité 28%**
  - **Bactériémie à S boulardii mortalité 27%**

SARM

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

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Background: 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: 6-week prospective study. Skin and environmental contamination were assessed within hours of PCR completion.

Results: 83/113 patients identified via positive admission PCR for MRSA were enrolled. 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: Strategies to reduce delays, to preemptively identify patients at high risk for disseminating MRSA, or to improve universal precautions are needed.

CD

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CURRENT AND NOVEL STRATEGIES FOR THERAPY OF *CLOSTRIDIUM DIFFICILE* INFECTION (CDI)

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Stratification of patients into mild or moderate vs. severe disease is critical to selection of the best initial treatment agent. Two randomized, prospective, and blinded trials have shown that oral vancomycin is superior to metronidazole for treatment of severe CDI.

The major unanswered question is how to determine CDI severity as there have been no validated scoring systems published.

Elevated peripheral WBC of >15,000-20,000/mm^3 appears to be one criteria on which to base severity.

Other indicators include presence of pseudomembranous colitis, need for ICU care, hypotension, elevated creatinine, fever, degree of abdominal pain or tenderness, number of stools per day, and CT findings of thickened colonic wall and ascites.

Nitazoxanide (N) vs. Vancomycin (V) to Treat (Rx) *Clostridium difficile* Disease (CDD)

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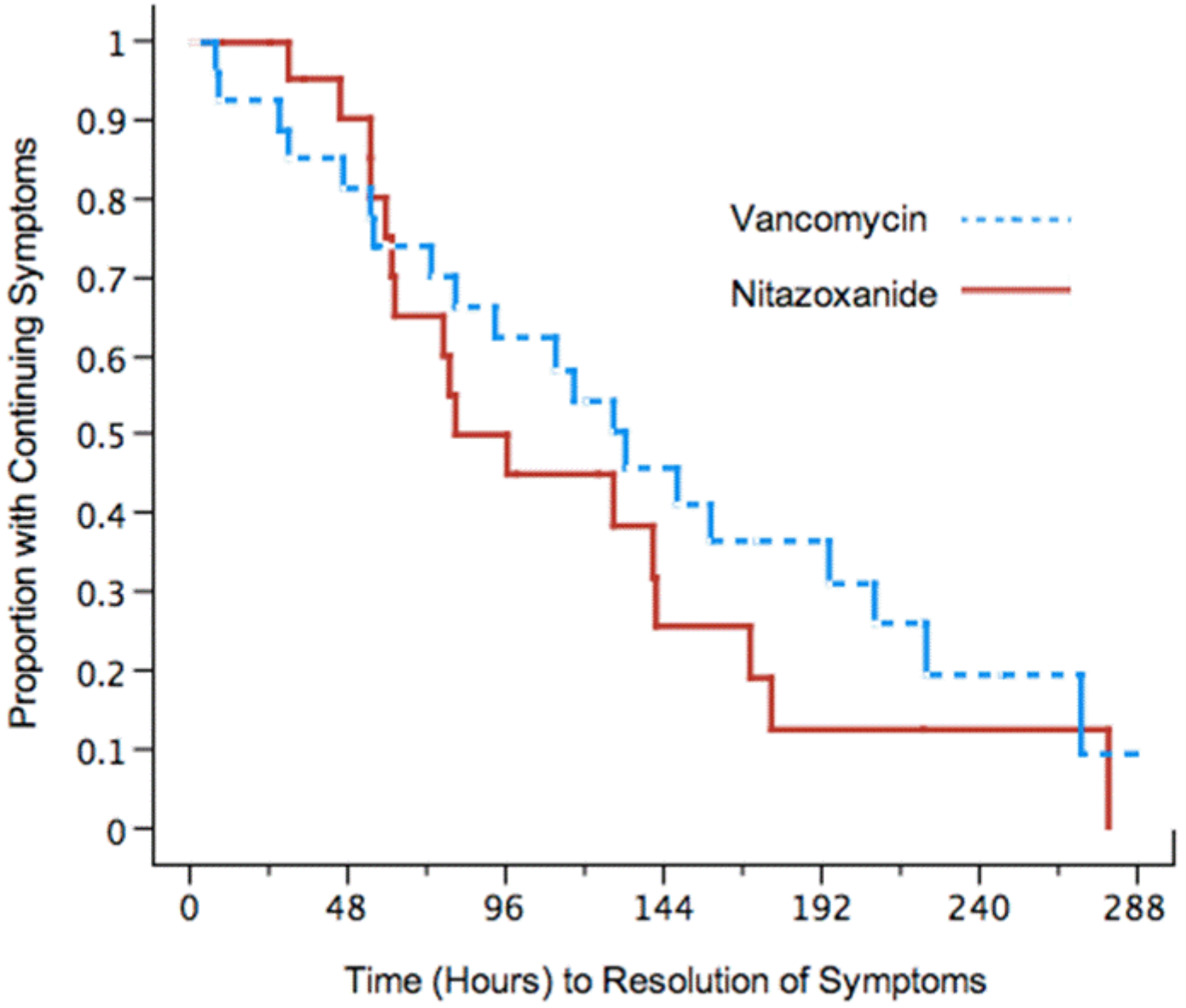
Background: In a randomized clinical trial (RCT), we found that nitazoxanide (N) is at least as effective as M. We now report on a RCT comparing N with V.

Methods: 50 patients (pt) with CDD ($\geq$3 loose stools/24 hr; plus $\geq$1 of the following: fever, abdominal pain, leukocytosis; plus a positive fecal ELISA for *C. difficile* toxins A and B) were randomized to receive V 125 mg 4x daily or N 500 mg 2x daily.

Initial response (primary endpoint) was determined by the absence of Sx of CDD at 12-14 days, and a final response by the absence of all such Sx at 31 days.

Results: 27 pt received V and 22 N. 20 of 27 (74%) treated with V and 17 of 22 (77%) treated with N responded; time to complete resolution of CDD symptoms was similar in the two groups (Figure; P= 0.56). At 31 days, 20 of 23 (86%) V pt and 17 of 18 (95%) N pt were free of symptoms of CDD. After an initial response, two V and 1 N pt relapsed within 31 days. Sustained response rates were, therefore, 18 of 27 (67%) V vs. 16 of 22 (73%) N by intention-to-treat, or 18 of 23 (78%) vs. 16 of 18 (89%) N. None of these differences was significant (P$\geq$0.6).



P = 0.56, Prentice modified Wilcoxon test

E. BSLE

ESBL-Producing *Enterobacteriaceae* in Spain and US: Importance of Community and Healthcare Environments as the Source

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Methods: All ESBL-producing strains of *E. coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca* and *Proteus mirabilis* were identified at the microbiology laboratories of tertiary care hospitals in Seville, Spain and Pittsburgh, U.S. between September, 2006 and March, 2007.

Results: 81 and 89 cases of infections/colonizations due to ESBL-producing organisms were identified in Seville and Pittsburgh, respectively. All but one strain were *E. coli* in Seville, whereas *K. pneumoniae* was predominant in Pittsburgh.

Nosocomial, healthcare-associated and community-acquired cases constituted 27%, 25%, 48% in Seville and 46%, 49%, 3% in Pittsburgh, respectively. All community-acquired cases were due to *E. coli* producing either CTX-M or SHV-type ESBLs (Table).

Distribution of ESBLs according to the sites of acquisition

	E .coli	K. pneumoniae	K. oxytoca	P. mirabilis
Nosocomial Seville	22	0	0	0
Healthcare-assciated Seville	18	1	0	0
Community-acquired Seville	38	0	0	0
Nosocomial Pittsburgh	6	23	4	1
Healthcare-associated Pittsburgh	14	23	0	1
Community-acquired Pittsburgh	3	0	0	0

Epidemiology of Patients with ESBL-Producing *Enterobacteriaceae* at Admission

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New patients admitted in 2005 and 2006 with a positive specimen of ESBLE in the first 48 hours were included.

We compared patients carrying ESBL *E. coli* with other ESBLE, and patients carrying CTX-M ESBLE with TEM/SHV ESBLE.

Results: 116 patients with 122 ESBLE at admission were included : 79 *E. coli* (65%), 26 *Klebsiella sp.* (21%), 15 *Enterobacter sp.* (12%), 3 others. ESBL *E. coli* were different from the other ESBLE : direct admission from home (77% vs 56%; p=0.03), recent lung infection (15% vs 34%, p=0.03) or urinary tract infection (39% vs 16%, p=0.02), cutaneous lesions (16% vs 34%, p=0.03), recent endoscopy (13% vs 31%, p=0.03) or surgery (27% vs 49%, p=0.02), invasive devices at admission (23% vs 38%, p=0.03). 87 ESBLE were analyzed: 57 CTX-M (44 *E. coli*) and 30 TEM/SHV (14 *E. coli*).

Variables associated to TEM/SHV were: transfer from another hospital (39% vs 10%, p<0.01), cutaneous lesions (31% vs 12%, p=0.03), invasive devices at admission (41% vs 21%, p=0.04).

Foreign Travel a Risk Factor for Colonization with ESBL-Producing *Enterobacteriaceae*: A Prospective Study on Swedish Travellers

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Methods: 48 healthy volunteers travelling outside Northern Europe were enrolled. Rectal swabs were collected before and after travelling.

Results: 48 travellers (25 female, 23 male) with a median age of 39 years (range 2-84) completed the study and were included in the analysis.

The median length of stay was 2 weeks (range 1-4).

18 different countries were visited, Africa (n=26), Asia (n=15) Southern Europe (n=3) and South, Central or North America (n=4).

In one case only, ESBL-producing *Escherichia coli* was detected before the trip.

14 travellers with initial negative samples were colonized with ESBL-producing *E. coli* (n=13) or *Enterobacter cloacae* (n=1) after the trip.

Travellers who acquired ESBL-producing *Enterobacteriaceae* were more likely to have suffered from gastroenteritis (11/14) than others (9/33) (p=0.001, Pearson test).

No other significant differences were detected.

Conclusions: This prospective study on Swedish travellers indicates that visits outside Northern Europe is a significant risk factor for colonization with ESBL-producing *Enterobacteriaceae*.

Seagulls of Berlengas Natural Reserve of Portugal as Carriers of Fecal *Escherichia coli* Harboring Extended-Spectrum β-lactamases (ESBLs) of the CTX-M and TEM Classes

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Pigeons as Vectors of CTX-M Dissemination in European Cities?

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CTX-M Type β-lactamases-Producing *Escherichia coli* Isolated from Cattle and Their Environment in Korea

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Factors Affecting Mortality in Extended-spectrum β-lactamase (ESBL) Producing Enterobacteriaceae Bloodstream Infections (BSI): Analysis of 189 Patient Episodes

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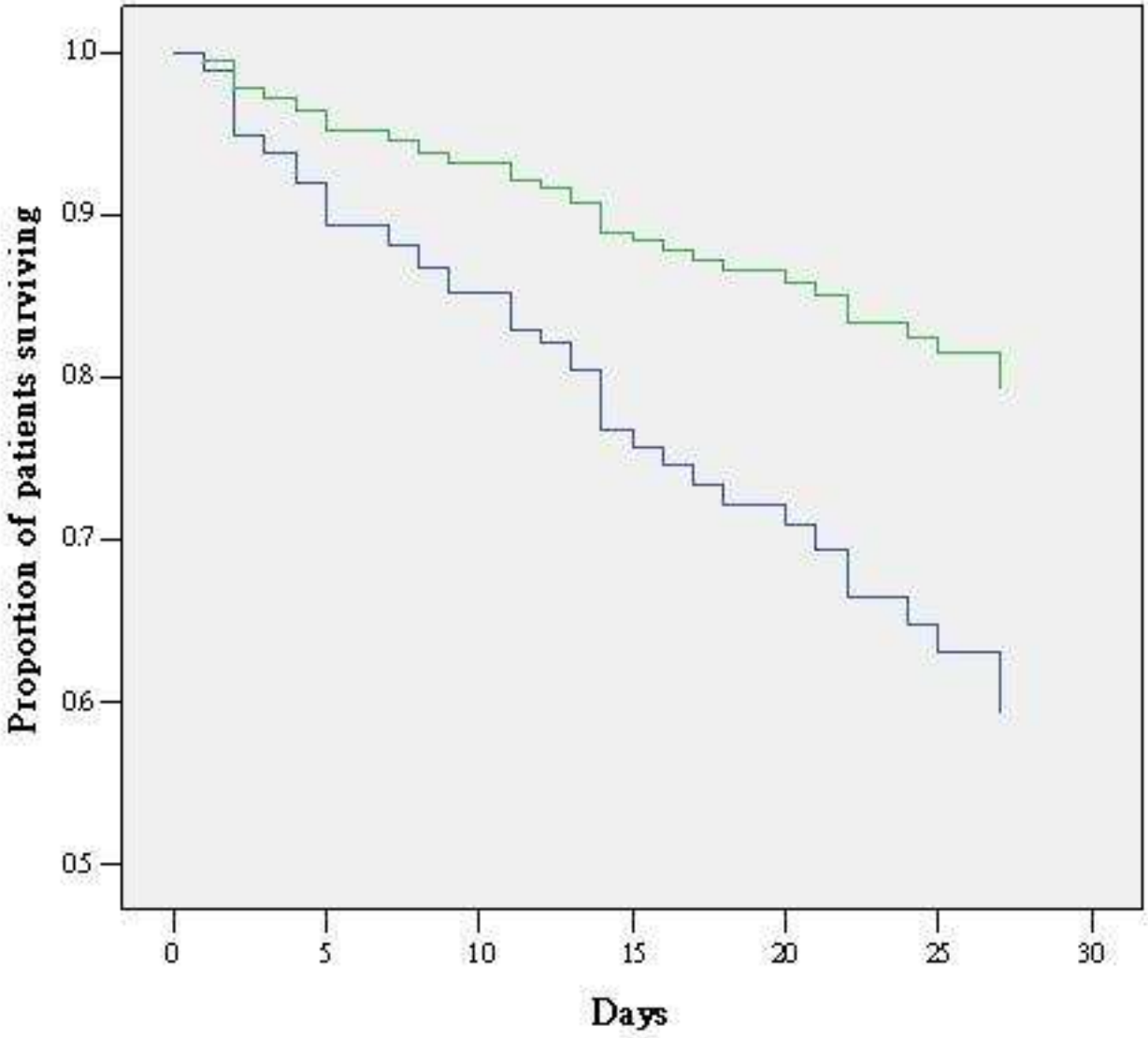
Methods: A retrospective analysis of all episodes of ESBL producing Escherichia coli or Klebsiella BSI in a tertiary-care hospital during 2004-2006 was performed. Factors affecting 30-day all-cause mortality were studied using Cox proportional hazard models.

Results: Among 189 patient episodes [age 67+/-19 yrs, male 54%, healthcare-associated 92%, E. coli 84%; urinary/intra-abdominal sources 43%/34%; ICU care 19%], 87 (48%) received empirical susceptible antibiotic treatment (carbapenems 33%, beta-lactam/beta-lactamase inhibitor combinations 55%); mortality was 26%.

Non-susceptible initial antibiotics (aHR 2.3, 95%C.I. 1.2-4.4, p=0.017), underlying malignancy (aHR 3.8, 95%C.I. 2.0-7.3, p<0.001), and high APACHE II score (aHR 1.1, 95%C.I. 1.1-1.2, p<0.001) were independently associated with death (Figure).

Conclusions: Clinical outcomes of ESBL BSI may correlate with in vitro susceptibility of initial treatment, including beta-lactam/beta-lactamase inhibitor combinations.

Figure. Survival curves of 189 patient episodes of ESBL BSI shown according to initial empirical treatments, with susceptibility tested according to the CLSI (Clinical and Laboratory Standards Institute) guidelines



Susceptible empirical antibiotics included:
β-lactam/β-lactamase inhibitor 55%
Carbapenem 33%
Cephalosporin 7%
Aminoglycoside 5%

Susceptible definitive antibiotics (antibiotics administered after susceptibility results available to clinicians):
Carbapenem 67%
β-lactam/β-lactamase inhibitor 13%
Fluoroquinolone 10%
Others 10%

Multivariate analysis performed by Cox proportional hazard models: Adjusted for age and factors associated with mortality on univariate analysis, including malignancy, non-urinary source of bacteremia and APACHE II score

Oral and Parenteral Therapeutic Options for Outpatient Urinary Infections Caused by CTX-M ESBL-Producing *Enterobacteriaceae*

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Results

	Urine CTX-M ESBLs (n=46) MIC 50 MIC 90 % Susceptible		
Fosfomycin	0.5	64	91.3
Nitrofurantoin	16	64	73.9
Doxycycline	16	16	10.9
Ciprofloxacin	32	32	4.3
Cefdinir alone Amoxicillin-Clavulanate alone Cefdinir + Amoxicillin-Clavulanate	16 32/4 0.25*	16 32/4 2*	0 10.9 89.1
Ertapenem	0.06	0.25	100
*cefdinir MIC in the presence of a fixed concentration of 8 µg/ml amoxicillin and 4 µg/ml clavulanate			

Conclusion Approximately 90% of urinary CTX-M ESBLs were susceptible to fosfomycin and the combination of cefdinir plus amoxicillin-clavulanate. Amoxicillin-clavulanate inhibited the ESBL, maintaining cefdinir activity against most isolates. Nitrofurantoin was active against a majority of isolates. All isolates were susceptible to ertapenem. Testing of the 11 SHV and TEM ESBL strains showed similar results with the exception of nitrofurantoin to which a majority were resistant (data not depicted)

Nitrofurantoin In The Treatment Of Extended-spectrum Beta-lactamase (esbl) Producing *E. Coli* Related Lower Urinary Tract Infection (luti)

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Ege Univ. Faculty of Med., Izmir, Turkey.

Methods: >20 leukocytes/mm^3 in urine microscopy and culture-proven ESBL-producing nitrofurantoin-sensitive *E. coli* in the urine (>10^5 cfu/mm^3); no leukocytosis or fever; and who were treated empirically with nitrofurantoin between January 2006 and May 2008.

All patients had received nitrofurantoin 50 mg capsule and had a control urine culture taken 5 to 7 days after this therapy.

Relapse was defined as isolation of ESBL-producing *E. coli* in the control urine cultures performed 28-31 days after start of the therapy.

Reinfection was defined as isolation of any pathogen in the control urine cultures performed 28-31 days after start of the therapy.

Results: There were 51 patients (aged 56.9±16.5, 29 females, 22 males) who fulfilled the study inclusion criteria. Overall clinical and microbiological success were 66.6% (34/51) and 76.7% (36/51), respectively. Of 36 patients with microbiological success 29 had day 28-31 cultures; and of these 29 one had reinfection and one had relapse.

Conclusions: Our results suggest that nitrofurantoin may be an alternative in the treatment of ESBL producing *E. coli* related LUTI.