Clinical significance and antimicrobial susceptibility of emerging uropathogens Aerococcus urinae, Aerococcus sanguinicola and Actinotignum schaalii: a multicentre prospective study

François Gravey1, Herve Jacquier2, Alban Le Monnier3, Frédérique Le Manach-Kergueris4, Thomas Guillard5, Violaine Walewski6, Etienne Carbonelle7, Philippe Lanotte8, Cécile Le Brun9, Olivier Barraud10, Stephane Corvec11, Asma Jeblaoui12, Laurent Dortet13, Plouzeau Chloé14, Nathalie Soismier15, Vincent Cattoir16, Christophe Isnard*1

1Chu de Caen; Microbiology
2Groupe Hospitalier St Louis Lariboisière-Fernand Widal, Aphp; Service de Bactériologie-Virologie
3Gh Paris Saint Joseph; Clinical Microbiology Laboratory
4Laboratoires Bio 7
5Université de Reims Champagne-Ardenne
6Hôpital Avicenne, Hôpitaux Universitaires de Paris Seine Saint Denis, Aphp; Service de Bactériologie-Virologie, Hygiène
7Hôpital Avicenne,Hôpitaux Universitaires de Paris Seine Saint Denis, Aphp; Service de Microbiologie Clinique
8Université François Rabelais
9Chu de Tours
10University of Limoges; Inserm, Chu Limoges; Laboratoire de Batériologie-Virologie-Hygiène
11Nantes University Hospital; Department of Bacteriology
12Hôpital Bicêtre; Laboratoire de Bactériologie
Background: Aerococcus urinae (Au), Aerococcus sanguinicola (As) and Actinotignum schaalii (Asc) have been for a long time considered as contaminants or misidentified by conventional identification methods. Since the introduction of the MALDI-TOF mass spectrometry and optimized culture conditions, their pathogenic role has been undoubtedly demonstrated, especially in urinary tract infections (UTIs). Because they have been poorly studied so far, the aim of this multicentric prospective study was to investigate clinical significance and antimicrobial susceptibility profiles of these emerging uropathogens.

Material/methods: Over a one-year period, all urine samples positive for Au, As or Asc were prospectively included from 12 French institutions. Clinical data were collected and bacterial identification was done by MALDI-TOF mass spectrometry (Microflex, Bruker Daltonics) or by 16S rRNA gene sequencing. MICs of the following antibiotics were determined by the broth microdilution method using Mueller-Hinton supplemented with lysed horse blood (5%) and β-NAD (20 mg/L) at 35°C for 48h in 5% CO₂ (Au/As) or anaerobic atmosphere (Asc): ampicillin, cefotaxime, cefixime, mecillinam, gentamicin, vancomycin, norfloxacin, ofloxacin, ciprofloxacin, levofloxacin, nitrofurantoin, fosfomycin and cotrimoxazole. When possible, clinical interpretation was performed according to EUCAST breakpoints recommended for viridans group streptococci (Au/As) or anaerobes (Asc).

Results: A total of 261 patients with non-redundant isolates were included, representing approximately 0.3% of all positive urine samples during the study period. The most prevalent species found was Au (n=164, 63%), followed by Asc (n=64, 24%) and As (n=33, 13%). The mean age of patients was 75 years (range, 1-102 years), with a sex ratio F/M at 1.75, regardless of the species. Different underlying comorbidities were noted, such as advanced age (>65 years) (84%), urological disease (32%), immunodeficiency (28%), hypertensive disease (25%), malignancies (19%) and diabetes mellitus (14%). The clinical case was considered as an UTI for 119 patients (46%) including 79 cystitis (66%), 25 pyelonephritis (21%) and 15 prostatitis (13%). All strains were susceptible to amoxicillin (MICs ≤1 mg/L) and vancomycin (MICs ≤1 mg/L). Most of the strains appeared susceptible to cefotaxime (MIC₉₀ ≤2 mg/L) and nitrofurantoin (MIC₉₀ ≤32 mg/L) whereas they usually exhibited elevated MICs for fluoroquinolones (MIC₉₀ ≥1 mg/L). The in vitro activity (MIC₅₀) of cefixime, mecillinam, cotrimoxazole and fosfomycin significantly differs between the species: 4/16/1/32 mg/L, 32/16/16/64 mg/L and 2/2/32/32 mg/L for Au, As and Asc, respectively. A majority of patients (61%) were appropriately treated with a β-lactam.

Conclusions: This first multicentric prospective study confirms the clinical significance of Au, As and Asc as uropathogens. Even though the prevalence of UTIs remains quite low (0.3%), microbiologists and clinicians should be aware about these emerging uropathogens, especially in the elderly, in patients with underlying urological diseases or in case of treatment failure with antibiotics classically used for UTI. A therapy with β-lactams is recommended.