A 12-YEARS MOLECULAR OVERVIEW OF MULDIDRUG-RESISTANT TUBERCULOSIS IN BELGIUM

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Purpose of the study A 12-years (1994-2006) study of multidrug-resistant (MDR) tuberculosis in Belgium, a low TB incidence country (around 12/100.000 inhabitants with 1.2% multidrug-resistant isolates).

Methods Susceptibility testing was conducted on first and second line antituberculous drugs; mutations associated with drug resistance were investigated. Molecular epidemiology (MIRU-VNTR on the recently optimized 15- and 24-locus sets, spoligotyping and IS*6110*-RFLP) enabled characterization of genotype families and detection of strain-clusters.

Results One hundred sixty MDR isolates from 139 patients were analysed. Fourteen patients corresponded to 10 laboratory cross contamination. The 125 remaining MDR-TB patients (67% males, mean age 37±17 years old, 77% foreign-born of which 44% originated from Eastern and Central Europe, 93% pulmonary disease with 75% smear positive) represent 90% of all MDR-TB cases notified to the Belgian register during this 12 years period. One patient was infected by an X-DR strain.

A mutation in the *rpoB* gene (resistance to rifampicin) was detected in isolates of 96% of the patients, a mutation in position 315 of *katG* or in the promoter of *inhA* (resistance to isoniazid) in respectively 68% and 14% of the patients, a mutation in *pncA* in 79% of the 38 pyrazinamid-resistant investigated isolates.

The predominant spoligotype families were T (26% of isolates), LAM (22%), Beijing (20%) and Haarlem (12%).

40 patients (32%) were strain-clustered (13 different clusters) when analysis was based on the 3 genotyping methods all together, yielding to a clustering rate of 22%. The clustering rate decreased to 18% when mutations in resistance genes were included in the analysis. The clustering rates obtained with 15- and 24-locus-based MIRU-VNTR alone were 25% and 23% respectively (24% and 23% when associated with spoligotyping) compared to 22% for IS*6110*-RFLP.

Conclusion This evaluation confirms the foreign origin of most MDR-TB patients identified in Belgium. The 98 distinct patterns of the isolates indicate that most patients were infected in their country of origin but the clustering rate also shows ongoing transmission in Belgium. These results fully justify a reinforced control of MDR-TB (BELTA-TBnet) with the use of molecular characterization even in low incidence countries.