

***Pneumocystis jirovecii*
Genotypes Involved in
Pneumocystis Pneumonia
Outbreaks Among Renal
Transplant Recipients**

TO THE EDITOR—We read with interest the article by Sassi et al published in *Clinical Infectious Diseases* [1]. They investigated *Pneumocystis jirovecii* genotypes involved in *Pneumocystis* pneumonia (PCP) outbreaks among renal transplant recipients. To that aim, they used fragment length polymorphisms of the major surface glycoprotein gene family. This work revealed that the same *P. jirovecii* genotype was involved in 2 outbreaks, 1 in Zurich [2] and 1 in Munich [3], whereas another genotype was linked to a Japanese outbreak [4]. It was likely that the most predominant genotype in the area was not involved in the 2 European outbreaks because unlinked control cases were infected with different genotypes. The authors concluded that there may have been an increased virulence of the outbreak genotypes in renal transplant recipients, and that the Zurich and Munich outbreaks may have had a common source of infection. These observations provided new insights into the transmission patterns of this opportunistic pathogen, but analysis of other outbreaks is needed in order to better understand the issue and improve prevention measures.

We reinvestigated the genotypes involved in 2 other PCP outbreaks among renal transplant recipients that occurred in Europe – 1 in Frankfurt [5] and 1 in Lyon [6]. To compare the genotypes of the different outbreaks, we considered the most frequently used method of typing, which is the sequencing of 4 genomic loci. These loci included the internal

transcribed spacer 1 of the rRNA operon [ITS1], the variable region of the mitochondrial 26S rRNA gene [mt26], the intron of the nuclear 26S rRNA gene [26S], and the β -tubulin intron 6 region [β -tub]; the Japanese outbreak was not investigated using this method and thus could not be compared.

The genotype observed in Frankfurt was reported to harbor the same alleles as the genotype involved in the Zurich and Munich outbreaks for 3 of the 4 loci (B, 7, and 1 for ITS1, mt26, and β -tub, respectively), but a different allele for locus 26S. There was some confusion between 2 close polymorphic positions (296 and 301–305), and after a reassessment of the sequences of the latter locus, it was found that the locus was identical in the 3 outbreaks (with the sequence TTTTACTCTT at positions 296 through 306). The genotype involved in the Lyon outbreak could not be directly compared because another typing method was originally used (single-strand conformation polymorphism of the same 4 genomic loci). Consequently, we sequenced the 4 loci from the DNA of 3 isolates of this genotype that we had stored at -20°C . The results were identical for the 3 isolates, and the genotype proved to be different from that of the Zurich and Munich outbreaks because it harbored different alleles for 3 of the 4 loci (B1 and 8 for ITS1 and mt26, respectively, and a 26S allele with TTTTACTCTT at positions 296 through 306). Thus, the outbreak genotype was the same in Zurich, Munich, and Frankfurt, whereas a different one was involved in Lyon.

Two epidemiological factors may have been important in the variation of the genotype involved in the different outbreaks: (1) the period of time played a role, as the Lyon outbreak occurred from 1994 to 1996, whereas the 4 others took place from 2005 to 2008; (2) the geographical location is relevant because Frankfurt, Zurich, and Munich are relatively close cities, whereas Japan is thousands of kilometers away.

Analyses of a large number of PCP cases showed that the genotype involved in the Lyon outbreak was one of the most prevalent during the period in the area [6], as well as in several European locations, including Zurich [7]. This genotype might have been preferentially transmitted during the outbreak because it has been observed that all suspected cases of interhuman transmission involved this genotype [6]. A particularity of the Lyon outbreak was that it involved not only transplant recipients but also human immunodeficiency virus–infected patients who mostly served as potential donors in the suspected transmission events, with one patient being a recipient. Thus, the data suggested that the Lyon outbreak was linked to a predominant genotype that might be more virulent and/or more transmissible independently of the underlying disease affecting the host. This conclusion differs from that of Sassi et al [1], which hypothesizes that in renal transplant recipients, outbreak genotypes are more virulent but not predominant. Nevertheless, as acknowledged by Sassi et al, it cannot be excluded that typing more isolates from Zurich and Munich may have revealed that the outbreak genotype was, in fact, predominant.

In conclusion, our observations provide additional information suggesting that the genotypes linked to outbreaks may vary according to the geographical location as well as over time. Whether outbreak genotypes are always predominant and whether these harbor specific pathogenicity factors remain open questions.

Notes

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Philippe Hauser,¹ Meja Rabodonirina,² and Gilles Nevez³

¹Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland; ²Université Claude-Bernard, Hospices Civils de Lyon, and ³Université de Brest, France

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Correspondence: Philippe Hauser, Institute of Microbiology, Rue du Bugnon 48, Centre Hospitalier Universitaire Vaudois and University of Lausanne, 1011 Lausanne, Switzerland (philippe.hauser@chuv.ch).

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