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2. Boulous A, Rolain JM, Mallet MN, Raoult D. Molecular evaluation of antibiotic susceptibility of *Tropheryma whippelii* in axenic medium. *J Antimicrob Chemother* 2005;55:178-81.

Retraction: Hussain HM, Hotopf M, Oyeboode F. Atypical Antipsychotic Drugs and Alzheimer's Disease. *N Engl J Med* 2007;356:416.

TO THE EDITOR: A letter that I submitted to the *Journal* was published in the January 25 issue.¹ Because there has been concern about the provenance and authorship of that letter, I request that it be retracted.

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1. Hussain HM, Hotopf M, Oyeboode F. Atypical antipsychotic drugs and Alzheimer's disease. *N Engl J Med* 2007;356:416.

Multiple-Triazole-Resistant Aspergillosis

TO THE EDITOR: The use of voriconazole has become common for the management of invasive aspergillosis. However, therapy with voriconazole still sometimes fails, more often because of unresponsive underlying disease than because of resistance of the fungus. Since the first description of itraconazole resistance in *Aspergillus fumigatus*,¹ three amino acid substitutions in the 14 α -sterol demethylase *cyp51A* gene, which is the target site for azole drugs, have been described.²

Our laboratory receives fungal isolates for identification and susceptibility testing from throughout the Netherlands. Since 2002, using Clinical and Laboratory Standards Institute methodology, we have observed an increase in the number of *A. fumigatus* isolates with elevated minimum inhibitory concentrations of voriconazole (2 to >16 mg per liter), itraconazole (>16 mg per liter), the investigational azole ravuconazole (4 to >16 mg per liter), and posaconazole (0.5 to 1.0 mg per liter). Thirteen isolates were cultured from nine patients from six hospitals in the Netherlands (Table 1). Primary aspergillosis was diagnosed in four patients, and five patients presented with breakthrough invasive aspergillosis.

A new mechanism of resistance, consisting of a *Cyp51A* amino acid substitution at codon 98 (L98H) together with a tandem repeat in the gene

promoter, was found to be responsible for the azole-resistant phenotype. This resistance mechanism was present in 12 of the 13 isolates. Genotyping of the isolates showed no evidence for clonal spread of a single *A. fumigatus* genotype.

The prevalence of multiple-triazole resistance was compared with a previously conducted nationwide survey of 170 *A. fumigatus* isolates collected from 114 patients from 21 Dutch hospitals between 1945 and 1998.⁴ In this period, no patients with multiple-triazole-resistant isolates were found as compared with 10 of 81 patients in the period since 2002 ($P < 0.001$).

Although the emergence of this new resistance mechanism coincides with the approval of voriconazole, the factors that may explain this phenomenon remain unclear. Four patients became infected with a multiple-triazole-resistant strain during long-term prophylaxis with itraconazole, a drug that has been widely available for clinical use since 1991. The recovery of multiple-triazole-resistant strains in patients who had not been previously treated with azoles suggests that alternative sources of azoles, such as the use of azole compounds in agricultural environments, might play a role.⁵

Our observation underscores the need to make an etiologic diagnosis of invasive mold infection