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Cystic Fibrosis Research News

Title:

High airborne level of *Aspergillus fumigatus* and presence of azole-resistant TR34/L98H isolates in the home of a cystic fibrosis patient harbouring chronic colonisation with azole-resistant H285Y *A. fumigatus*

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What was your research question?

Azole-resistant *Aspergillus fumigatus* (ARAF) has become an emerging problem worldwide, and has been associated with treatment failure of fungal infections. Drug resistance is related to the use of azole fungicides in agriculture and is mainly due to mutations of the azoles target gene called *cyp51A*, which encodes for an important enzyme known as lanosterol 14α-demethylase, that is involved in the biosynthesis of ergosterol. TR_{34}/L98H is the most frequent mutation observed.

Why is this important?

Azoles are the first-line antifungals for treatment of allergic broncho-pulmonary aspergillosis, which is characterized by a hypersensitivity response to *A. fumigatus* allergens and affects 2 to 19% of people with cystic fibrosis. In France, it has been reported that 4.6% to 8% of people with cystic fibrosis colonised with *A. fumigatus* have ARAF. A patient's home and close outdoor environment have been recently identified as a potential source of ARAF in an immunocompromised patient who developed invasive aspergillosis. However, the link between domestic environmental exposure and ARAF infection in cystic fibrosis has not been explored so far.

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What did you do?

We assessed the homes of a mother and father of an 18-year-old with cystic fibrosis who had chronic colonisation with ARAF having a H285Y mutation in CYP51A, which is a rare mutation reported in our region (Northern France) and to date has only been identified in an environmental isolate recovered from the home of a person with chronic obstructive pulmonary disease. Since the parents had separated in September 2016, both the mother's and father's dwellings were evaluated. For both homes, air samples were collected from the living room, kitchen and patient's bedroom. Both conventional culture media and azole-containing media (for selection of azole-resistant isolates) were used to isolate any fungi.

What did you find?

In one dwelling, a 4-meter long wall was damp, following rain passing through the roof. Furthermore, old wood windows had been recently replaced with PVC windows to improve isolation, but no ventilation system had been installed to compensate for the loss of natural ventilation. A very high overall fungi concentration was found, (710-7.240 CFU/m^3), in this home with a predominance of *A. fumigatus* (640-6.490 CFU/m^3). A level of 7.240 CFU/m^3 is well above that which defines abnormally high fungi concentrations in dwellings (1.000 CFU/m^3). Furthermore, ARAF showing the most common *cyp51A* mutation (TR_{34}/L98H) was isolated in the patient's bedroom. However, follow-up of the patient showed the persistence of isolates having a H285Y mutation and no acquisition of isolates with the TR_{34}/L98H mutation was observed. Serological follow-up also showed an increase in anti-*A. fumigatus* antibodies after September 2016 but lung function remained quite stable.

What does this mean and reasons for caution?

Our data confirms that dwellings can be a source of ARAF for patients at risk, especially in dwellings with damp, which yields increased airborne fungal concentrations, and thus, increased risk of presence of *A. fumigatus* and ARAF. The absence of H285Y ARAF in the dwellings is consistent witha previous acquisition by the patient of isolates harbouring this mutation in 2012, when ARAF was first detected and when the patient was living in a rural area. The absence of acquisition of isolates with the TR_{34}/L98H mutation could be due to the low proportion of TR_{34}/L98H isolates (<3%) found overall, or the establishment of preventative measures (including patient eviction) and dwelling remediation (removal of mould that was discovered under the wallpaper and replacement of wallpaper, installation of mechanical ventilation) taken after the environmental investigation.

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What's next?

Our data underlines the interest in assessing a patient's home to evaluate *A. fumigatus* exposure and detect ARAF in order to establish preventative measures and limit the risk of *A. fumigatus* exposure and ARAF acquisition.

Original manuscript citation in PubMed

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