Cystic Fibrosis Research News

Title:
An invisible threat? *Aspergillus* positive cultures and co-infecting bacteria in airway samples

Lay Title:
Are we missing *Aspergillus* in airway samples due to bacteria that may also be present?

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What was your research question?
We wanted to know whether using a large group of microbiology results from people with CF could help to determine whether we are missing *Aspergillus* fungal infections on airway cultures.

Why is this important?
Previous studies have shown that *Aspergillus* infection of the airways in CF is associated with reduced lung function, structural airway problems and more CF related complications. We also know that some bacteria, that are commonly found in the airways of people with CF, can reduce the ability of fungi like *Aspergillus* to grow in a laboratory environment. Having a better understanding of the frequency of missed *Aspergillus* infections would help to inform clinicians of when to suspect fungal infection in the absence of positive cultures, and to guide the development of detection methods that do not rely on laboratory culture.

What did you do?
Using 44,554 airway culture results (sputum and bronchoscopy samples) from adults and children with CF at the Royal Brompton Hospital between 2010-2020, we determined the

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frequency of *Aspergillus* infection in samples that did not also grow a bacteria. We then compared this to those samples which did contain bacteria in order to detect any patterns. On some of these samples we also used a laboratory technique that does not rely on culture to determine how many samples contained evidence (DNA) of *Aspergillus* that did not grow.

What did you find?

We found that *Aspergillus* cultures were nearly 40% less likely when a sample also contained *Pseudomonas aeruginosa*, the most common bacterial infection in CF airways. A similar effect was seen with other common infections such as *Burkholderia*, but not with *Staphylococcus aureus*. In samples in which the *Pseudomonas* growth was heavy there was less *Aspergillus* than when there was few *Pseudomonas* grown. Additionally, in samples containing *Pseudomonas*, the chances of finding DNA evidence of *Aspergillus* without a culture growth (a so called 'missed culture') was higher than with other bacteria.

What does this mean and reasons for caution?

The chances of a positive *Aspergillus* culture are lower in the presence of *Pseudomonas,* and the chances of this being a false-negative are higher. We may be missing important fungal disease in some CF patients and interpretation of negative *Aspergillus* cultures in the presence of *Pseudomonas* should be cautious. One caution is the absence of treatment details at the time of sampling, so we may be missing an important antibiotic/antifungal treatment effect. We also excluded cough swabs as they are poor at identifying fungal infection, so these results may not apply to the youngest children with CF.

What's next?

As fungal infections are becoming increasingly common, we need to improve detection in order to improve treatment. This may involve the development of molecular techniques or biomarkers to identify *Aspergillus* in the absence of a positive culture result.

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