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Title:

Establishing the diagnosis of chronic infection with *Pseudomonas aeruginosa* of cystic fibrosis patients: comparison of the European consensus criteria with genotyping of *P. aeruginosa* isolates

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What was your research question?

Patients with cystic fibrosis often suffer from lung infections with a bacterium called *Pseudomonas aeruginosa*. The 'European consensus criteria' are frequently used to determine whether or not patients are at risk of developing a long-term infection. We investigated whether another approach called 'genotyping' could accomplish the same.

Why is this important?

When an infection with *P. aeruginosa* is first noticed, doctors try to treat it with antibiotics in order to get rid of it. After a while however, the lungs of almost all patients with cystic fibrosis become chronically infected with this micro-organism. This means that it stays in their lungs and can cause damage there: the usual antibiotics are not active anymore. When this happens, a different treatment approach is needed. It is however difficult to determine when exactly a patient should be considered 'chronically' infected. Different criteria are used by doctors to try to make this distinction as clearly and rapidly as possible.

What did you do?

Over the course of 14 years, we collected coughed up mucus (expectorations) from patients with cystic fibrosis on a regular basis, and we carried out culture to find out whether

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P. aeruginosa was present. If this was the case, patients were given antibiotics to try to treat the infection and we stored the bacterium in the freezer, for later study by means of genotyping. According to the 'European consensus criteria', the patient will probably not get rid of the bacterium anymore if the micro-organism is found in his/her expectorations on three occasions during a time span of six months. We compared these criteria to our approach called 'genotyping', whereby we look in depth at how similar micro-organisms are at the DNA-level. According to the criteria that we propose, the presence of exactly the same bacterial strain on only two occasions, was sufficient to consider the patient as 'chronically infected'.

What did you find?

When we compared our genotyping approach to the European consensus criteria, we found that both agreed for more than 90% of patients: if the European consensus criteria considered a patient to be chronically infected, genotyping found the same micro-organism in different expectorations of the same patient, indicating that it probably stayed in the lungs despite antibiotic treatment. Most importantly, using genotyping, we could establish probable chronic infection nine months earlier than by using the European consensus criteria alone.

What does this mean and reasons for caution?

First, our study indicates that genotyping could be a useful addition to the existing European consensus criteria: it could help distinguish more rapidly between those cystic fibrosis patients who will probably benefit from antibiotics aimed at getting rid of *P.aeruginosa*, and those who will not. Secondly, the fact that in several cases the bacterium seems to persist in the lungs of patients - even after antibiotic treatment, suggests that the antibiotic treatment that is prescribed is not always successful: it could be that antibiotics sometimes only suppress the micro-organism for a certain period of time, without actually getting rid of it.

What's next?

More studies comparing genotyping to other approaches are needed to confirm the results we found. We also believe that it could be useful to add genotyping to studies investigating the effect of antibiotic treatment on lung infection: in this way, the success - or failure - of the treatment could be more comprehensively evaluated.

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