European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

Changes in Airway Inflammation with Pseudomonas Eradication in Early Cystic Fibrosis

Authors:

Luke W Garratt[1*], Oded Breuer[1,2,3*], Craig J Schofield[1], Samantha A McLean[1], Daniel R Laucirica[1,4], Rabindra Tirouvanziam[5,6], Barry S Clements[1,3], Anthony Kicic[1,3,4,7,8], Sarath Ranganathan[9,10,11,**], and Stephen M Stick[1,3,4,**], for AREST CF[1,4,6,7,8#]

Affiliations:

[1]Wal-yan Respiratory Research Centre, Telethon Kids Institute, University of Western Australia, Nedlands, Australia;
[2]Department of Pediatrics, Pediatric Pulmonary Unit, Hadassah-Hebrew University Medical Center, Jerusalem, Israel;
[3]Department of Respiratory and Sleep Medicine, Perth Children's Hospital, Nedlands, Australia;
[4]Faculty of Health and Medical Sciences, University of Western Australia, Nedlands, Australia;
[5]Department of Pediatrics, Emory University School of Medicine, Atlanta, USA;
[6]Center for CF & Airways Disease Research, Children's Healthcare of Atlanta, Atlanta, USA;
[7]Centre for Cell Therapy and Regenerative Medicine, School of Medicine and Pharmacology, University of Western Australia, Subiaco, Australia;
[8]Occupation and Environment, School of Public Health, Curtin University, Bentley, Australia;
[9]Department of Respiratory Medicine, Royal Children's Hospital, Parkville, Australia;
[10]Murdoch Childrens Research Institute, Parkville, Australia;
[11]Department of Paediatrics, University of Melbourne, Parkville, Australia
[*]Co-first authors; [**]Co-senior authors

What was your research question?

We asked whether lung inflammation persisted after young children with CF were treated with antibiotics to eradicate *Pseudomonas aeruginosa*.

Why is this important?

Germs cause a response by the immune system, otherwise known as inflammation. Lots of studies have established that the inflammation occurring in the CF lung due to infections by germs is a very important factor for lung damage. So treatment approaches with antibiotics that eradicate germs such as *Pseudomonas aeruginosa* are conducted to improve quality of life and prevent lung damage. Whether lung inflammation also immediately resolves when

the germ is gone is not well known and difficult to study in a chronic disease. Since lung inflammation is known to get progressively worse over life with CF, this research question is important for clinical practice.

What did you do?

We utilised the historical data from the Australian Respiratory Early Surveillance Team for CF (AREST CF) program. For 20 years, AREST CF has collected data on newborn children diagnosed with CF annually during their first 6 years of life, particularly to their annual clinical assessments which includes a wash of the lungs, known as bronchoalveolar lavage, and imaging the lungs by CT. We studied 88 cases of *Pseudomonas aeruginosa* infection, some in children as young as 3 months of age. We looked at whether their antibiotic treatment (tobramycin and ciprofloxacin) eradicated *Pseudomonas aeruginosa*, whether they had inflammation after *Pseudomonas aeruginosa* was eradicated, and how the extent of their lung disease had changed by their next annual assessment.

What did you find?

Pseudomonas aeruginosa was eradicated with first treatment in 74 cases and the remaining cases were eradicated after repeat treatment. Although overall inflammation across the 88 cases reduced from the time of *Pseudomonas aeruginosa* infection to their 3-month eradication follow-up, in 33 cases there was still persistent inflammation. These 33 children had two significant outcomes. First, they were 40% more likely to have an infection at their next annual visit and 70% more likely to have *Pseudomonas aeruginosa* again. Secondly, they displayed greater levels of airway damage on their CT scan than children with less inflammation at their 3-month eradication follow-up. We also attempted to study in the laboratory what may be different about the airway conditions between children with or without persistent inflammation. However, we found that the lung washes did not significantly change immune cells in the lab, limiting our ability to study this aspect.

What does this mean and reasons for caution?

Even in very young children with CF experiencing their first *Pseudomonas aeruginosa* infection, lung inflammation can persist following successful eradication. More importantly, this lung inflammation was significantly associated with worse lung health in the near future – both in terms of having another infection and first beginnings of lifelong lung damage. It highlights that not all people with CF have the same biological experience of lung disease, nor the same response to treatment. One reason for caution is that lung washes cannot be

performed regularly in young children, so we cannot rule out additional factors that may have occurred between the yearly assessments.

What's next?

There are two areas of focus next. The first is to validate how lung inflammation can be an important clinical biomarker to monitor CF lung health in addition to eradication of germs like *Pseudomonas aeruginosa*. The goal is to help clinicians personalise care and maximise the prevention of lung damage. The second area is to determine which anti-inflammatories would be most appropriate to reduce lung inflammation and when they should be applied.

Original manuscript citation in PubMed
https://pubmed.ncbi.nlm.nih.gov/33461938/