Mucoid *Pseudomonas* in Cystic Fibrosis

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**Abstract**

Pseudomonas aeruginosa is a frequent and virulent pulmonary pathogen in patients with cystic fibrosis. If colonization is not prevented, *P aeruginosa* becomes permanently established and nearly always mutates into a mucoid strain. The alginate-containing matrix of the mucoid strain is thought to allow the formation of protected microcolonies and provide increased resistance to opsonization, phagocytosis, and destruction by antibiotics. As a result, conversion to the mucoid phenotype is associated with a significant increase in morbidity and mortality. In the microbiology laboratory, mucoid *P aeruginosa* has a distinct Gram stain and culture appearance that can expedite its identification and facilitate appropriate patient management. Important aspects of the mucoid phenotype are reviewed.

It is well established that *Pseudomonas aeruginosa* is a frequent and virulent pulmonary pathogen in patients with cystic fibrosis (CF). After a period of intermittent colonization, the organism becomes permanently established and is difficult to eradicate. Most patients with CF become chronically infected with wild-type *P aeruginosa* strains in early childhood; prevalence increases with age, so that as many as 80% of patients with CF are infected by the time they reach 20 years. During the years following initial colonization, the wild-type strains uniformly mutate into mucoid variants.

Conversion to the mucoid phenotype is thought to be driven by the unique CF microenvironment and provide the organism some protection from dehydration. For patients with CF, this conversion results in a significant increase in morbidity and mortality accompanied by a measurable decline in pulmonary function. The mucoid matrix is believed to allow the formation of protected biofilm microcolonies and provide increased resistance to opsonization, phagocytosis, and digestion. Furthermore, resistance to various antibiotics is increased.

The mucoid strains synthesize a large quantity of alginate exopolysaccharide. Although other virulence factors such as toxins, hemolysins, and proteases are produced, it is alginate production that allows for persistent infection and ultimately establishes the poor prognosis for the patients. The mucoid phenotype is a result of several genes, including *algD* that encodes the enzyme guanosine diphosphate mannose dehydrogenase and catalyzes the last step in alginate precursor synthesis. It is thought that all wild-type *P aeruginosa* strains are capable of synthesizing alginate but that conversion to an overtly mucoid phenotype depends on appropriate host environmental pressures. The mucoid phenotype is not observed...
outside the human host.\textsuperscript{1} Other organisms, including a variety of pseudomonads, may also produce alginate or alginate-like substances; however, \textit{P} \textit{aeruginosa} remains the most frequently isolated pseudomonad from patients with CF.\textsuperscript{1} It is interesting that there is little evidence to suggest that \textit{Burkholderia cepacia}, another important CF pathogen, produces alginate in the respiratory tract of hosts with CF.\textsuperscript{1}

It has long been known that mucoid \textit{P} \textit{aeruginosa} strains may spontaneously convert to nonmucoid forms in culture, indicating that they are the same organism.\textsuperscript{10,11} Studies of serologic group, phage type, and pyocin type confirm this direct relationship,\textsuperscript{10} and mutations controlling the switch between wild-type and mucoid strains have been identified.\textsuperscript{12} Conversion back to a nonmucoid phenotype is now thought to be due to new suppressor mutations, rather than reversal of the original mutations.\textsuperscript{1}

In the microbiology laboratory, mucoid \textit{P} \textit{aeruginosa} can be identified by its distinctive Gram stain appearance: abundant orange alginate material surrounding and separating each gram-negative rod \textbf{Image 1}. Though characteristic, there is a paucity of literature addressing this Gram stain appearance.\textsuperscript{5,11} We have observed a consistent correlation of this orange “capsule” with subsequent growth of a mucoid \textit{P} \textit{aeruginosa} strain \textbf{Image 2}. Although these strains may occasionally be seen with other causes of bronchiectasis and obstructive lung disease,\textsuperscript{1,13} there is a strong association with the clinical diagnosis of CF.\textsuperscript{3} Therefore, we recommend examination of all patients for CF, regardless of age, when a mucoid strain is identified in the laboratory. Recognizing the Gram stain appearance of mucoid \textit{P} \textit{aeruginosa} may allow this examination to start earlier.

In patients with known CF, contemporary management aims to prevent or postpone initial colonization with wild-type \textit{P} \textit{aeruginosa}.\textsuperscript{2} This is achievable through various oral and inhaled antibiotic regimens during the early period of intermittent colonization.\textsuperscript{2} If chronic persistent colonization occurs, transition to the mucoid phenotype may still be delayed with antibiotic prophylaxis and infection control measures such as isolation of patients with a mucoid \textit{P} \textit{aeruginosa} strain.\textsuperscript{1,2}

Mucoid \textit{Pseudomonas} is a predominant source of morbidity and mortality in patients with CF and other forms of bronchiectasis. Through recognition of the characteristic morphologic features and appropriate confirmatory testing, laboratory professionals can provide essential prognostic information to clinicians and patients.

\textbf{References}


