

## Host Defense and Bacterial Genetics in Acute Lung Injury or Ventilator Associated Pneumonia Study (VAPS)

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### Synopsis:

Ventilator associated pneumonia (VAP) is a major clinical problem that is associated with increased length of stay in the intensive care unit and increased mortality. *Pseudomonas aeruginosa* is the most frequent gram-negative bacteria involved in hospital related pneumonia. *Pseudomonas aeruginosa* induced lung infections in ventilated patients have a significantly increased mortality and are difficult to eradicate. Despite the appropriate antibiotic treatment, pneumonias associated with *P. aeruginosa* infections have up to a 60% mortality rate. Also, patients who are chronically infected with *P. aeruginosa* (i.e.: cystic fibrosis, HIV patients and bronchiectasis patients) become resistant to antibiotics and may die from their infections. Knowing when intubated patients get *P. aeruginosa* lung infections is important because this bacterium is difficult to treat in the Intensive Care Unit (ICU).

After years of research in animals, researchers have found that certain *P.aeruginosa* strains are more virulent or dangerous to the lungs of animals. They have recently found that patients can be infected with these virulent *P.aeruginosa* strains and when they are infected with these virulent strains, they are acutely ill and have a greater tendency to die (3). We want to investigate when these virulent *P.aeruginosa* strains infect intubated, critically-ill patients and whether we can detect the genes of the virulent bacteria without doing a standard culture (instead use PCR technology). We also want to determine whether the *P.aeruginosa* utilizes this virulence system throughout the lung infection, or turns the system off and utilizes other virulence systems after the initiation of the infection. The importance of this knowledge is that we intend to block some of the virulence systems of *P.aeruginosa* (as a therapy for patients); however, if virulence systems are turned on and off, we need to know when *P.aeruginosa* utilizes each virulence system during a human lung infection.

The main purpose of this study is to determine the virulence processes of *P. aeruginosa* in lung infections among ventilated critically ill patients, in an attempt to find novel therapies for this condition. As detailed information from all pediatric patients enrolled at CHRCO has been collected, our second aim is to analyze the CHRCO cohort to identify clinical risk factors associated with the development of VAP from all causes in these patients.

Patients have been recruited from the pediatric and neonatal units at University of San Francisco Medical Center and Children's Hospital and Research Center Oakland. All patients who are intubated and mechanically ventilated for > 24 hours were eligible for enrollment. This study is sponsored by the National Institute of Health. The primary investigator is Dr. Jeanine Wiener-Kronish from UCSF Medical Center, Department of Pulmonary Medicine and member of the CVRI. Dr. Heidi Flori and Dr. David Durand are primarily responsible for conducting this study at Children's Hospital and Research Center Oakland (CHRCO).

Consented patients had tracheal aspirate (TA) secretions collected for culture once daily while they were on the ventilator. The TA samples were cultured for *P. aeruginosa*. If positive, the *P. aeruginosa* cultures were sent for more definitive assays. In addition to the collection of tracheal aspirates, one of the researchers reviewed the patient's medical record and recorded information about overall medical course.