

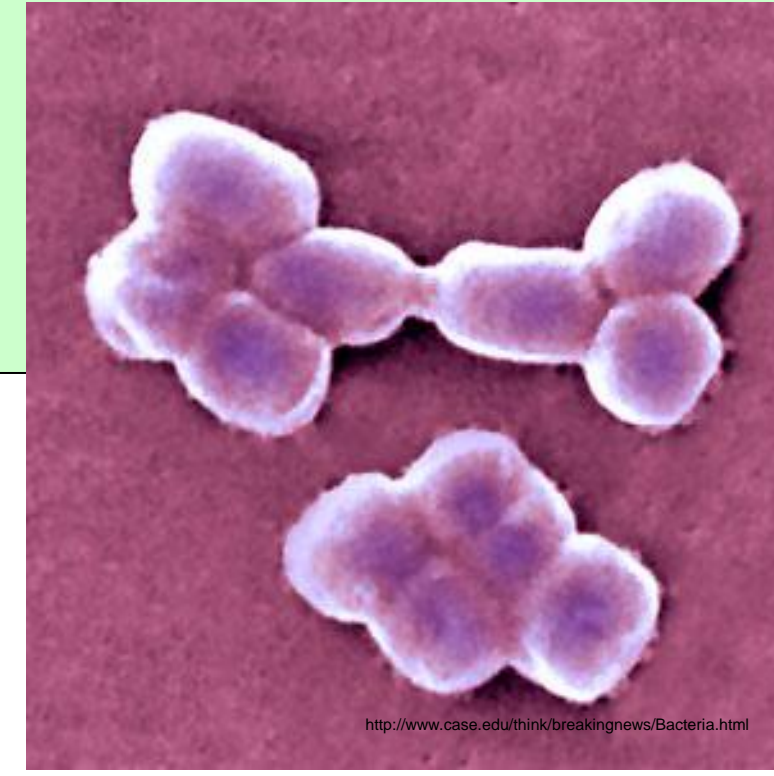
Background:

Acinetobacter baumannii is a gram negative bacterium responsible for both community-acquired and nosocomial infections.

- *A. baumannii* has been cited as the seventh most common isolate recovered from critically ill patients, causing between 5 & 10% of ICU-acquired pneumonias.
- *A. baumannii* is the 10th most common etiologic agent for monomicrobial nosocomial bloodstream infections, most notably from military members injured in Iraq or Afghanistan.
- Over the past decade significant trends have emerged, such as an overall increase in *A. baumannii* infections and its endemic and epidemic occurrence in hospitals, suggesting the development of new multi-drug resistant strains.
- Previously, immunocompromised, fulminantly-infected mice produced via surgical intratracheal inoculation have served as the pneumonia research model, but such models are not realistic relative to human clinical disease.
- The intratracheal mouse model is very labor-intensive and results in staggered start times. It requires general anesthesia and can produce non-uniform, asymmetric deposition. It also has limited research capacity since untreated mice rarely survive longer than 72 hours.

Objective:

To develop a non-acute, progressive model of *A. baumannii* pneumonia which can serve as an alternate and more realistic pneumonia model for evaluation of therapeutic strategies.

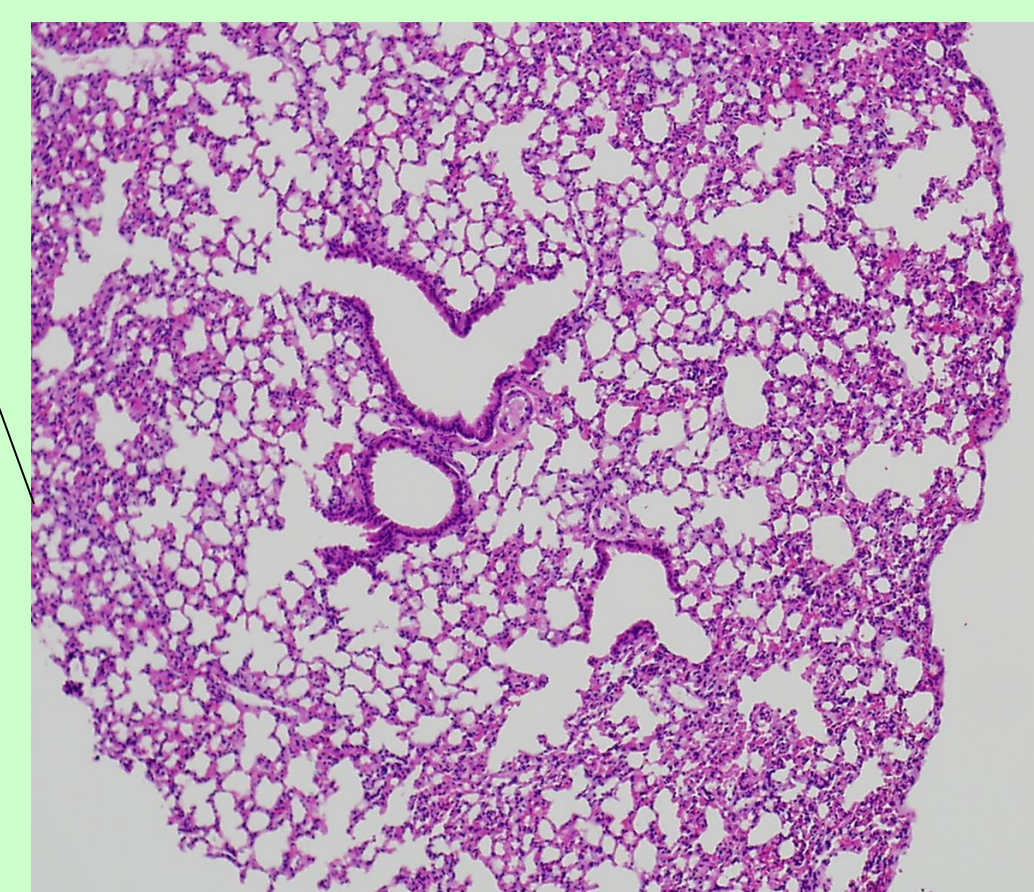


Materials and Methods:

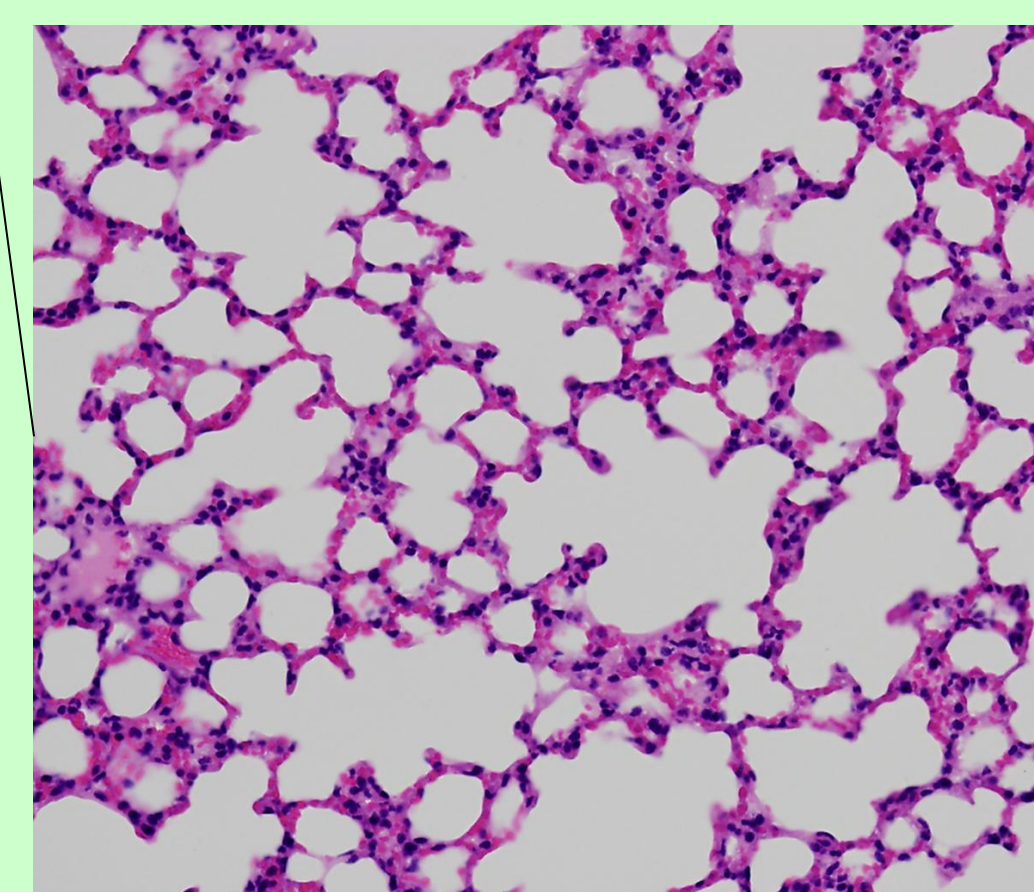
- The *A. baumannii* (ATCC strain) was cultured overnight in broth and then diluted in sterile water for the inoculum.
- The experiment was performed using immunocompetent Balb/c and ICR female mice weighing between 16-20 grams.
- The aerosol challenge was conducted in a chamber of 5 cubic feet with the mice conscious and active using a Glas-Col Inhalation Exposure System (Glas-Col, LLC, Terre Haute, IN).
- A total of 1.5-1.8 x 10⁷ cfu were delivered into the chamber during a 30 minute period.
- Mice were monitored over a 10 day period, after which they were euthanized and their lungs removed using sterile technique.
- The left lung was homogenized and plated overnight for cfu counts, and the right lung was used for histological evaluation.

Results:

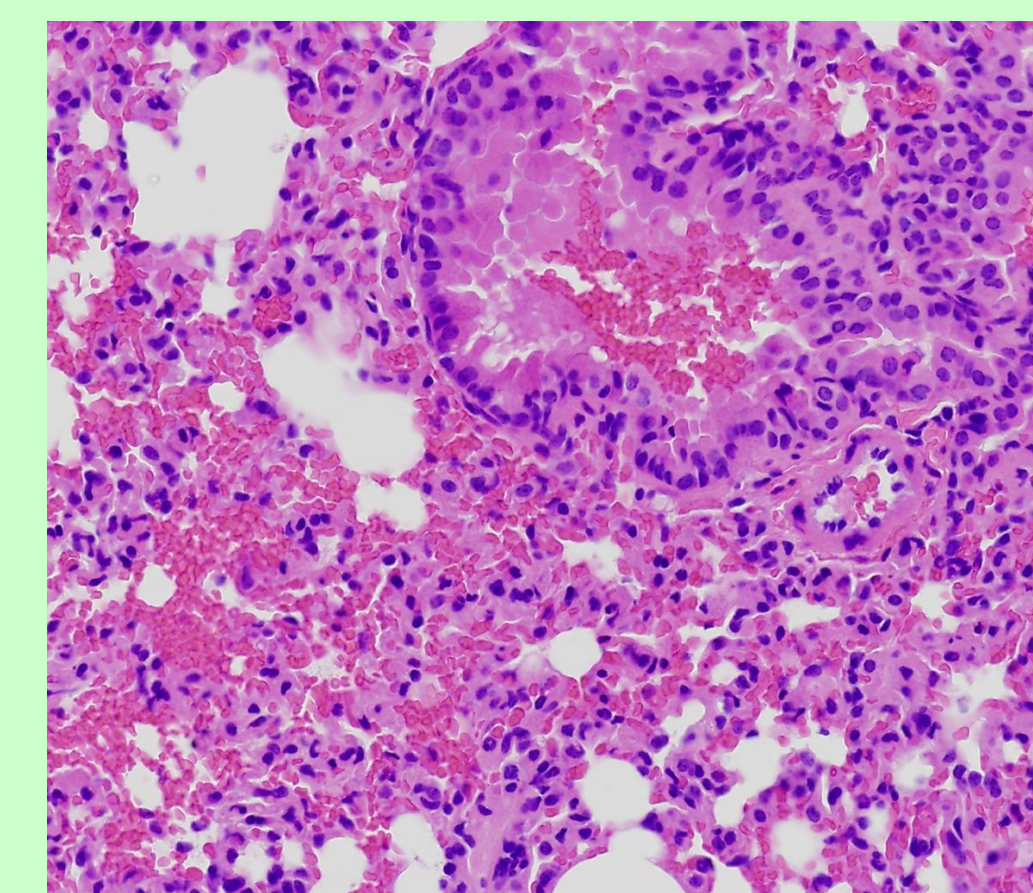
- No clinical disease was observed in any of the mice.
- Histological evaluation showed no clinically significant lesions.
- Colony counts indicated a failure of the bacteria to proliferate.



Above: 10X image mouse lung section H&E staining



Above: 20X image mouse lung section H&E staining



Above: 20X image mouse lung infected with *Francisella tularensis*. Note the mild to severe inflammation and congestion indicative of bronchopneumonia



Above: GlasCol Aerosol Exposure System



Above: Mice in aerosol chamber



Above: Nebulizer containing *A. baumannii* in solution

Conclusions & Future Developments:

- The challenge model was not adequate to induce significant pneumonia.
- It is currently not known whether failure was due to rodent strain, insufficient dose of *A. baumannii*, or a combination of the two factors.
- The variation in virulence among *A. baumannii* strains is an additional factor to consider.
- Parallel experiments using the same aerosol delivery system with *Francisella tularensis* resulted in consistently lethal disease.
- Further experiments involving mucin as an aerosol additive are being considered.
- Development of a soft tissue model is also in progress.

Acknowledgements:

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