| PublisherInfo | | |
|---|---|---|
| PublisherName | : | BioMed Central |
| PublisherLocation | : | London |
| PublisherImprintName | : | BioMed Central |

# New methods to measure the airway surface liquid

| ArticleInfo | | |
|---|---|---|
| ArticleID | : | 1597 |
| ArticleDOI | : | 10.1186/rr-2001-68487 |
| ArticleCitationID | : | 68487 |
| ArticleSequenceNumber | : | 8 |
| ArticleCategory | : | Paper Report |
| ArticleFirstPage | : | 1 |
| ArticleLastPage | : | 3 |
| ArticleHistory | : | RegistrationDate : 2001–9–13<br>Received : 2001–9–13<br>Accepted : 2001–9–13<br>OnlineDate : 2001–9–13 |
| ArticleCopyright | : | Biomed Central Ltd2001 |
| ArticleGrants | : | |
| ArticleContext | : | 129312211 |

Peter Middleton,[Aff1]
Corresponding Affiliation: Aff1

Aff1 Westmead Hospital, Sydney, Australia

## Keywords

ASL, chloride, cystic fibrosis, pH, sodium

# Context

Despite much research into cystic fibrosis (CF) over the last decade, exactly how mutations in CF transmembrane conductance regulator (CFTR) induce lung disease remains unknown. The original, "low volume" theory states that increased sodium absorption and decreased chloride secretion cause hyperabsorption of salt across the airway surface, which leads to a drying and thickening of the airway surface liquid (ASL), causing retention of secretions and subsequent infection; ie ASL is primarily reduced in volume in CF. An alternative, "high salt", theory suggests that the ASL composition is the primary abnormality: mutations in CFTR induce high salt levels in the ASL; high salt concentrations have been associated with reduced bacterial killing by small peptides (defensins). The presence of high salt concentrations in the ASL is, however, controversial. Numerous investigations have attempted to measure volume and composition of the ASL, with varying results. The main difficulty in these measurements is that the collection process itself perturbs the volume and composition of the ASL.

# Significant findings

Two novel approaches were outlined in this paper, confocal microscopy in the measurement of ASL thickness and chloride and sodium fluorescent probes to measure ASL composition. The ASL thickness was 21 ?m in bovine tracheal cell monolayers, decreasing to 8 ?m when the overlying humidified air was replaced with dry air and increasing to ~150 ?m with osmotic loads. In anesthetized wild-type mice the ASL was ~45 ?m (not reported for CF mice). In three human excised bronchial mucosal fragments, the ASL was ~55 ?m. Sodium concentrations were estimated to be 92 mM in the bovine tracheal monolayers, 115 mM and 105 mM in wild-type and CF mice respectively, and 103 mM in the human bronchial specimens. Chloride concentrations were 101 mM in the bovine trachea, 140 mM and 135 mM in wild-type and CF mice respectively, and only 92 mM in the human bronchus. ASL pH values

were 6.94 in the cow, 6.95 and 6.84 in wild-type and CF mice respectively, and 6.78 in the human bronchus. These results, like those in previous publications, suggest that the ASL is slightly hypotonic and acidic with respect to plasma.

# Comments

As the CF mouse model is known to have little lung disease, the mouse data do not necessarily answer the controversy about CF lung disease. The importance of this paper lies in the new noninvasive techniques for measuring ASL thickness and composition. Measurements in human tissues (both normal and CF) using these new techniques will hopefully provide important information concerning CF pathogenesis.

# Methods

Confocal microscopy, fluorescent probes

# Additional information

Boucher RC: **Human airway ion transport. Part one.** *Am J Respir Crit Care Med* 1994, **150**:271-281.

## References

1. Jayaraman S, Song Y, Vetrivel L, Shankar L, Verkman AS: Noninvasive *in vivo*fluorescence measurement of airway-surface liquid depth, salt concentration, and pH. J Clin Invest . 2001, 107: 317-324.