

Biomarkers for Airway Aspiration: Role and relevance?

Stanley Manne
Children's Research Institute*

Mathew Maksimoski MD¹, Michael Gorelik MD², Carolyn Jenks MD², Taher S Valika MD^{1,2}

Ann & Robert H. Lurie
Children's Hospital of Chicago*

Northwestern Medicine*
Feinberg School of Medicine

¹Division of Otolaryngology-Head and Neck Surgery, Ann & Robert H Lurie Children's Hospital of Chicago, 225 E Chicago Ave, Chicago, IL

²Department of Otolaryngology-Head and Neck Surgery, Northwestern University Feinberg School of Medicine, 420 E Superior St, Chicago, IL

Background

In the management of the pediatric airway, aspiration can mean the difference between surgical success and failure.

Bronchoalveolar lavage (BAL) has traditionally been championed prior to major airway reconstruction in order to identify potential aspiration risk and sources.

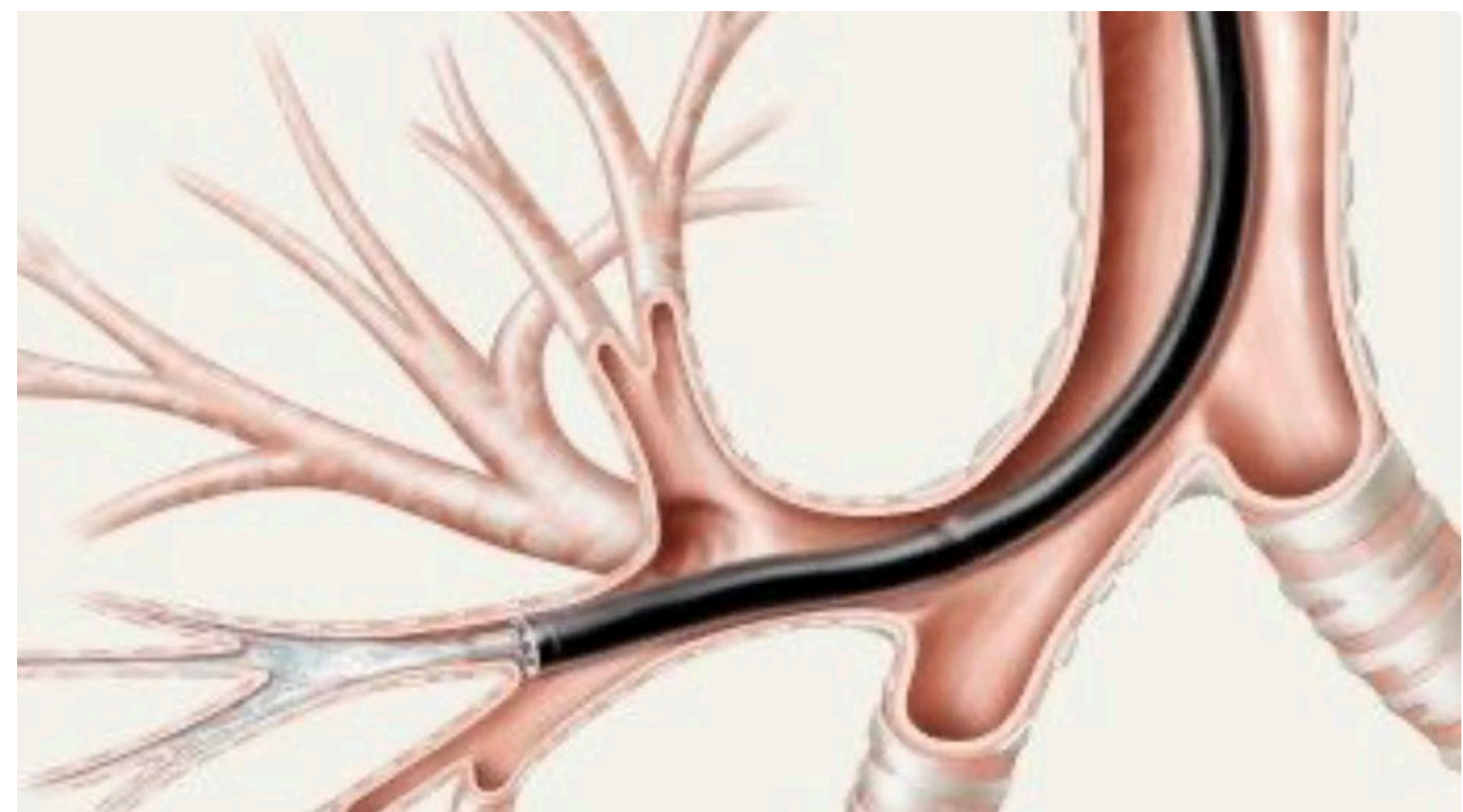


Figure 1: Depiction of bronchoalveolar lavage. Image by Olympus Medical.

This is identified predominantly through the use of two biomarkers: pepsin and lipid laden macrophages (LLM).

Pepsin is a marker of gastric content aspiration, while LLM is a marker for aspiration in general.

We sought to review our data of reconstructive airway surgery and assess the clinical implications of these markers on both surgical planning and reconstructive outcomes.

Methods

- A retrospective review was conducted of laryngotracheal reconstructions (LTR) performed at the home institution from 9/1/2018-9/1/2020.
- Range includes a transition point in the standardization of pepsin collection in the bioassays of BALs.

Results

A total of 38 LTR cases were identified over the two year period.

17 total cases had pepsin assays

- 16 cases were negative for pepsin.

26 cases had testing for the presence of LLM

- 10 cases had positivity for the presence of LLM

There was no difference identified in patient outcomes after halting collection of pepsin or LLM assays.

Additionally, despite having evidence of LLM or pepsin positivity, no further testing was completed in these patients. There was no changes in surgical decision making or preoperative surgical planning. There was one surgical failure in each group requiring reconstruction, both due to a bacterial infection.

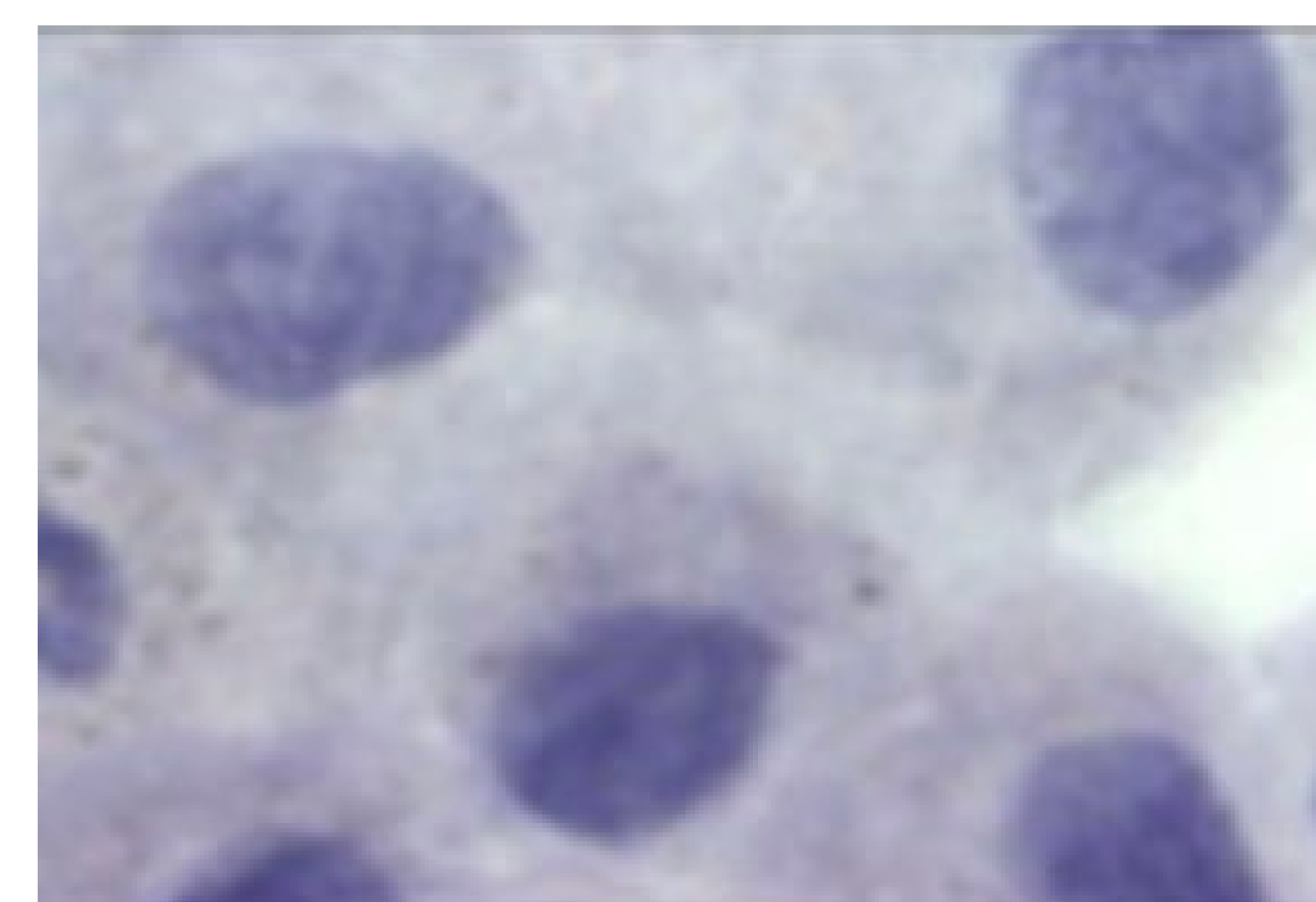


Figure 2: Normal macrophage appearance. Oil red O staining.

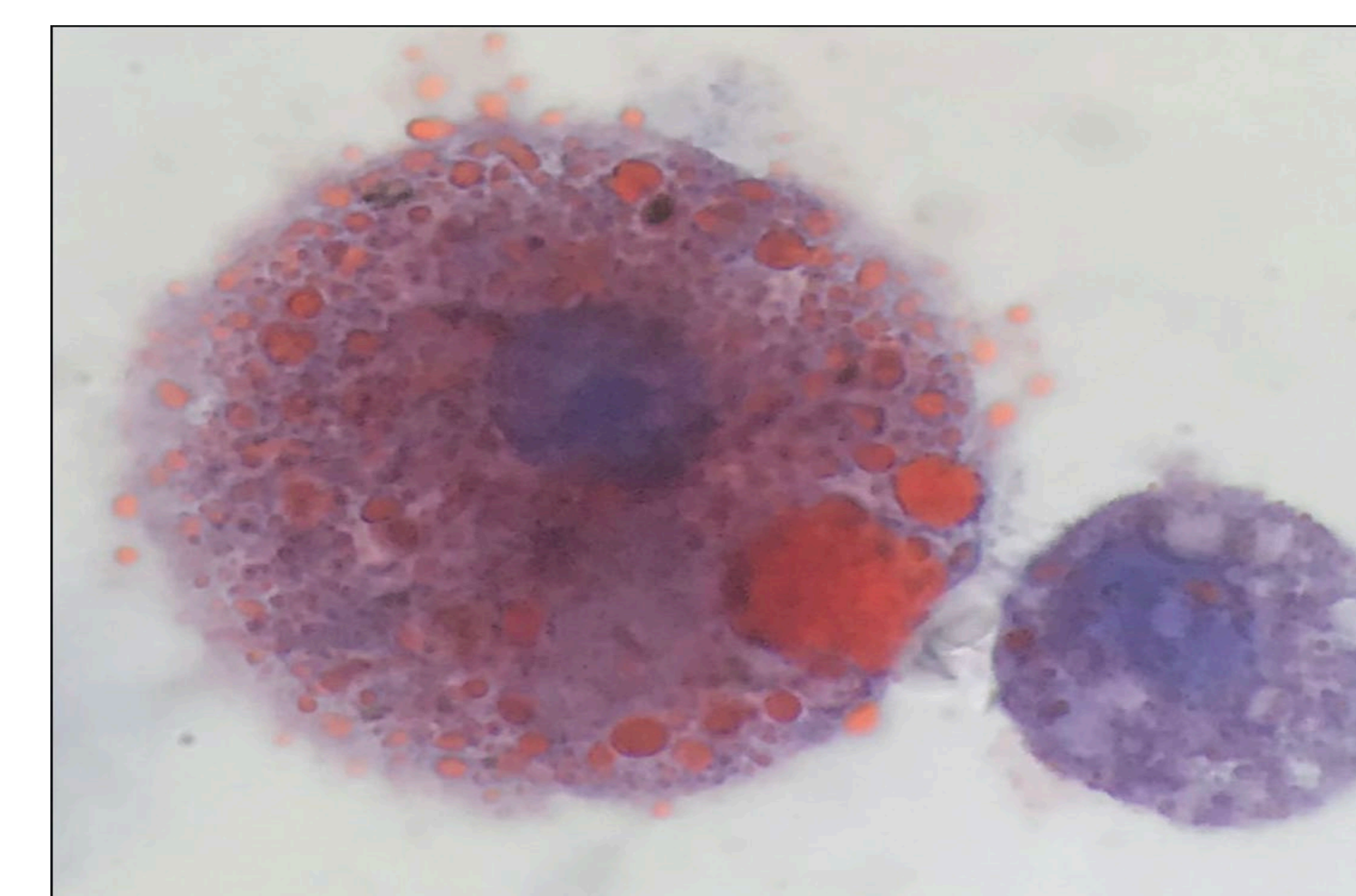


Figure 3: Macrophages containing lipid granules. Note the "foamy" appearance. Oil red O staining.

Discussion

The role of aspiration biomarkers has routinely played a vital prognostic role in pediatric airway surgery.

The question arises though their true clinical value. Despite alerting to the likelihood of aspiration, if there are no clinical factors altered based on the results, what value do they truly have?

Aspiration and more specifically gastric content aspiration can be difficult to manage, especially in the complex airway patient. Targeted work up including pH impedance testing and airway endoscopy may potentially provide more substantiative information than these traditional biomarkers.

Our review shows within our institution their role in treatment impact appears to be limited based on our data. Further research in this area to identify the clinical and diagnostic validity of these markers needs to be investigated.

References

1. Johnston N, Dettmar PW, Ondrey FG, Nanchal R, Lee SH, Bock JM. Pepsin: biomarker, mediator, and therapeutic target for reflux and aspiration. *Ann N Y Acad Sci.* 2018 Dec;1434(1):282-289. doi: 10.1111/nyas.13729. Epub 2018 May 17. PMID: 29774546.
2. Gibbon D, Zhu J, Sogbesan A, Banya W, Rossios C, Saito J, Rocha JR, Hull JH, Menzies-Gow AN, Bhavsar PK, Chung KF. Lipid-laden bronchoalveolar macrophages in asthma and chronic cough. *Respir Med.* 2014 Jan;108(1):71-7. doi: 10.1016/j.rmed.2013.10.005. Epub 2013 Oct 10. PMID: 24172051.
3. Rosen R, Fritz J, Nurko A, Simon D, Nurko S. Lipid-laden macrophage index is not an indicator of gastroesophageal reflux-related respiratory disease in children. *Pediatrics.* 2008 Apr;121(4):e879-84. doi: 10.1542/peds.2007-0723. Epub 2008 Mar 24. PMID: 18362101; PMCID: PMC3293162.
4. De Boeck K, Vermeulen F, Proesmans M. Lipid-laden macrophage index and gastroesophageal reflux-related respiratory disease in children. *Pediatrics.* 2008 Sep;122(3):680-1; author reply 681-2. doi: 10.1542/peds.2008-1144. PMID: 18762545.
5. Ahrens P, Noll C, Kitz R, Willigens P, Zielen S, Hofmann D. Lipid-laden alveolar macrophages (LLAM): a useful marker of silent aspiration in children. *Pediatr Pulmonol.* 1999 Aug;28(2):83-8. doi: 10.1002/(sici)1099-0496(199908)28:2<83::aid-ppul2-3.0.co;2-a. PMID: 10423306.
6. Parameswaran K, Anvari M, Efthimiadis A, Kamada D, Hargreave FE, Allen CJ. Lipid-laden macrophages in induced sputum are a marker of oropharyngeal reflux and possible gastric aspiration. *Eur Respir J.* 2000 Dec;16(6):1119-22. doi: 10.1034/j.1399-3003.2000.16f17.x. PMID: 11292116.

Disclosure

No authors have any contributions or financial disclosures to report in the establishment of this project.