

## Introduction

Otorrhea is the most common complication following tympanostomy tube placement, with an incidence commonly reported at around 20%. Topical otic antibiotic drops are typically used for relief of otorrhea in children with tympanostomy tubes. In children with recurrent otorrhea, gastroesophageal reflux and extraesophageal reflux have been postulated to be involved in the pathogenesis of otitis media with effusion<sup>1</sup>. Middle ear inflammation is thought to be mediated by proteolytic activity of pepsin, as well as by the decrease in pH associated with reflux of gastric acid through Eustachian tube. The goal of this study is to examine the presence of pepsin in post-tympanostomy tube otorrhea.

## Methods

IRB approval for this prospective study was obtained. All subjects were enrolled at Nemours/A.I. Dupont Hospital of Children, a tertiary care institution. After parental informed consent and child informed assent, 28 samples of post-tympanostomy otorrhea were obtained from 23 children. In order to examine the relationship between post-tympanostomy tube otorrhea and pepsin, the fluid was analyzed for color and consistency, and highly sensitive and specific enzymatic assays were undertaken to determine presence of pepsin-A in the otorrhea samples of study patients.

**Table 1: Description of Study Subjects**

Patients	N=23
Sample number	N=28 (5 patients had 2 samples)
Age (years)	2.5±2.9 (range 7mo - 15y)
Gender	14M:9F
Pepsin Positive*	26% (6/23) patients 21% (6/28) samples

\*3 patients had pepsin present <3.0 unit cutoff.

## Results

23 patients were enrolled in this study with a total sample collection from 28 separate ears. Pepsin was found to be positive in 21% of samples (Table 1). The patients' medical histories were also examined for the presence of airway problems, Gastroesophageal Reflex Disorder (GERD), active proton-pump inhibitor (PPI) therapy, and duration of otorrhea. GERD was found to have a positive correlation with presence of pepsin, with 67% of patients with pepsin positive otorrhea also carrying a diagnosis of GERD, while only 12% of patients with pepsin negative otorrhea had a prior reflux diagnosis (p<0.05). Presence of airway problems such as reactive airway disease, wheezing, or sleep apnea were also found to have a positive correlation; 83% of patients with pepsin positive otorrhea compared to 12% of pepsin negative otorrhea patients (p=0.052). No statistical significance was found when controlling for age, gender, active PPI therapy, or duration of illness (Table 2).

**Table 2: Comparing Pepsin Positive and Pepsin Negative Patients**

	Negative (n=17)	Positive (n=6)	P value
Age (years)	2.8±3.6	2.5±2.0	0.876
Gender	12M; 5F	2M; 4F	0.132
Airway Problems*	29% (5/17)	83% (5/6)	0.052
GERD	12% (2/17)	67% (4/6)	0.021
Active PPI Therapy	18% (3/17)	33% (2/6)	0.576
Drainage >6months	35% (6/17)	67% (4/6)	0.347

\*reactive airway disease (RAD); wheezing; sleep apnea

## Discussion

Otitis media with effusion (OME) is the most frequent cause of reversible pediatric hearing loss<sup>2</sup>. The etiology of OME is multifactorial, however, isolation of Pepsin-A in post-tympanostomy tube children and otorrhea provides evidence that reflux plays a role within the pathophysiology of middle ear effusion and inflammation<sup>1</sup>. This is supported by the strong positive correlation of existing GERD diagnosis with pepsin positive otorrhea. Pepsin has been linked to increased rate of otorrhea in children undergoing tympanostomy tube insertion<sup>3</sup>. GERD and OME are both common disorders in young children, and pepsin has been identified previously in middle ear samples retrieved at time of tympanostomy tube placement<sup>2,3,4</sup>. This study is the first to examine the role of pepsin in otorrhea occurring after tympanostomy tube placement.

## Conclusion

Isolation of Pepsin-A in post-tympanostomy tube otorrhea indicates that reflux of gastric pepsin may be an etiologic factor in otorrhea. Further studies are required to examine the exact nature of this relationship, and elucidate its clinical implications for further therapeutic intervention.

## References

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