# Acoustical and Perceptual Voice Profiling of Children With Recurrent Respiratory Papillomatosis

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**Summary: Objectives.** Respiratory papillomatosis is a condition characterized by benign papillomatous (wart-like) growths in the respiratory tract. The condition tends to recur after treatment, requiring multiple procedures to control growth of the lesions. In such cases, the condition is known as recurrent respiratory papillomatosis (RRP). This study aims at providing comparative measures of acoustic as well as perceptual voice analysis of children with RRP.

**Methods.** Ten children with a history of RRP for a minimum of 3 years were selected under purposive sampling. A detailed case history, Clinical Assessment Scale of RRP, and laryngostroboscopy findings were done. This was followed by perceptual voice assessment using Buffalo III Voice Screening Profile, and acoustical voice assessment using *Dr. Speech software* (by Tiger DRS, Inc.). Group statistics and *t* test were used at a significance level of 0.05 (*SPSS* package Version 12.0 is used which is manufactured by IBM Corporation).

**Results.** Both groups with RRP showed substantial difference in habitual  $F_0$ , S/Z ratio, Signal to Noise Ratio (SNR), Harmonic to Noise Ratio (HNR), and Maximum Phonation Time (MPT) voice parameters. On perceptual analysis, all children with RRP had hourse voice quality, and stridors are present.

**Conclusions.** All children with RRP have affected voice parameters in some extent which depend on the period and area of lesion.

Key Words: Recurrent respiratory papillomatosis-Stridors-Hoarse voice quality.

### INTRODUCTION

Respiratory papillomatosis is a condition characterized by benign papillomatous (wart-like) growths in the respiratory tract (larynx, trachea, and rarely lungs). It can affect children and adults, causing voice changes and airway obstruction. The condition tends to recur after treatment, requiring multiple procedures to control growth of the lesions. In such cases, the condition is known as recurrent respiratory papillomatosis (RRP) (National Institute for Health and Clinical Excellence 2012). The papillomata of RRP occur in clusters on the involved mucosa; the fronds of papilloma may be sessile and spread over a wide area of mucosa or they may be pedunculated and localized. The lesions are characteristically nonkeratinizing. It is characteristic that the lesions are multiple; occasionally at the onset of the disease or if the disease is about to become quiescent, only a single lesion may be manifest. <sup>2</sup>

#### Etiology

The etiology of RRP is now known to be infection of the epithelial cells with human papillomavirus (HPV) and is characterized by the proliferation of benign squamous papillomas within the aero-digestive tract. <sup>3–5</sup> HPV belongs to the Papovaviridae family. It is a small, icosahedral (20 sided), capsid virus without an envelope. A distinction has to be made between the so-called low-risk types of the virus (HPV-2, 6, 11, 13, and 32) which can be found in benign oral mucosal lesions, and the high-risk type (HPV-16), which predominantly is found in malignant oral mucosal lesions. <sup>6</sup> HPV

types 6 and 11 are most common which cause RRP. Although electron microscopy has only rarely demonstrated viral particles in papilloma specimens (Incze et al 1977)<sup>7</sup>, immune fluorescent techniques have shown incontrovertible evidence of the footprints of HPV DNA having been incorporated into the cellular DNA (Steinberg et al 1983). Furthermore, it has been shown by electron microscopy and immunofluorescence that apparently normal mucosa adjacent to the papillomata contains intracellular viral DNA of HPV. After removal of the lesions, these infected cells may become activated, leading to the formation of another lesion. This of course explains the difficulty in effecting "a cure" of the disease by using mechanical means of removal alone. This phenomenon has been duplicated in the finding of latent HPV in the normal skin surrounding genital warts (Ferenczy et al 1985). So far, it has not been possible to isolate and propagate the virus.

## **Epidemiology**

RRP can manifest in early childhood (juvenile onset) or in adulthood and is a rare disorder, with an estimated incidence of approximately 4.3 per 100 000 children and 1.8 per 100 000 adults in the United States. RRP puts a heavy emotional burden on to patients and families when repeated surgeries are needed, <sup>10</sup> and its economic cost is high, estimated at \$150 million annually in the United States (Derkay 1995). <sup>11</sup> There is no clear difference in prevalence based on race or ethnicity. Juvenile-onset disease usually presents between the age of 1 year and 4 years and is equally distributed between males and females. Adult-onset disease has a broad peak between the age 20 years and 40 years, but can occur even later, and shows a 2:1 bias toward males. <sup>12</sup>

Presentation in the neonatal period poses higher risk for tracheotomy and attendant morbidity and mortality<sup>13</sup>; Ruparelia, Unger and Nisenbaum 2003).<sup>14</sup> Death of a patient with RRP is usually caused by complications of frequent surgical procedures or respiratory failure because of distal disease progression (Ruparelia, Unger and Nisenbaum 2003).<sup>14</sup>

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#### **Transmission**

The mode of HPV transmission is still not clear. 15 Approximately, a million cases of genital papillomatosis are diagnosed each year in the United States. 16 According to study finding by Bierman et al 1998, HPV infections are found in 43% of sexually active college women over a 36-month period. <sup>17</sup> It has been estimated that approximately 60% of women (81 million) might test positive for HPV antibody, and the virus may be present in the genital tract of up to 25% of all women of childbearing age worldwide. 16 Vertical transmission occurring during delivery through an infected birth canal is presumed to be the major mode of transmitting the infection to children. Clinically apparent HPV infection has been noted in 1.5-5% of pregnant women in the United States<sup>18,19</sup> and overt maternal condylomata are seen in more than 50% of mothers who give birth to children with RRP.<sup>20</sup> Adult onset of RRP has been associated with lifetime number of sexual partners and oral genital sex.21

# **Symptoms**

The vocal folds are usually the first and predominant site of papilloma lesions, and hoarseness is the principal presenting symptom.<sup>22</sup> Unfortunately, particularly in very young children, changes in voice may go unnoticed. Stridor is often the second clinical symptom to develop, initially inspiratory, then becoming biphasic. Less common presenting symptoms include chronic cough, recurrent pneumonia, failure to thrive, dyspnea, dysphagia, or acute respiratory distress, especially in infants with an upper respiratory tract infection. When RRP presents as respiratory distress caused by papillomas obstructing the airway, tracheotomy often must be performed. Shapiro et al 1996<sup>23</sup> noted that these patients tend to be younger and to have more widespread disease, often involving the distal airway. However, it has been suggested that tracheostomy may activate or contribute to the spread of disease lower in the respiratory tract.<sup>24</sup> One of the studies showed tracheal papillomas developing in half of patients with tracheotomy. 25 It is for this reason that a tracheostomy should be avoided if it is possible to establish a normal airway by endoscopic removal of the papilloma.

#### **Characteristics of RRP**

The lesions are notoriously recurrent even after the most radical extirpation. Recurrence may become an airway problem within 2 weeks or nothing may be visible for perhaps 5 or 20 years. The reason for this is that the lesions do not recur from the depth of the wound, but rather from the apparently normal mucosa adjacent to the original lesion. On some occasions, it appears that removal of the papillomata has an enhancing effect on the growth rate of the lesions, 2 so that the recurrence may be larger than the original lesion. RRP is a diffuse diathesis of the mucous membrane of the upper air and food passages; the papillomata may be encountered in the nostrils at the mucocutaneous junction, on the gingiva and lips, on both surfaces of the soft palate and the adjacent tonsillar pillars, in the larynx, in the tracheobronchial tree, and occasionally, in the pulmonary parenchyma and at the

esophageal inlet. The lesions have a predilection for points of airway constriction, where there is increased airflow, drying, crusting, and irritation; this is particularly evident around the tracheostomy site and at the tip of the tracheostomy tube. Most commonly, the larynx is the site of greatest involvement and is often the only site (Strong et al 1976).<sup>26</sup>

#### **Treatment**

At present, there is no "cure" for RRP, and no single treatment has consistently been shown to be effective in eradicating RRP because the natural history of RRP is highly variable and unpredictable. The disease may undergo spontaneous remission, persist in a stable state requiring only periodic surgical treatment, or may be aggressive, requiring surgical treatment every few days to weeks and consideration of adjuvant medical therapy (antiviral modalities, eg, interferon, acyclovir, ribavirin, etc; photodynamic therapy; mump vaccine; HPV vaccine; gene therapy). The current and most prevalent standard of care is surgical therapy with a goal of complete removal of papillomas and preservation of normal structures. The carbon dioxide (CO<sub>2</sub>) laser used for the removal of RRP involving the larynx, pharynx, upper trachea, and nasal and oral cavities is also an alternative. The carbon dioxide and alternative.

#### **Team for RRP treatment**

Surgical therapy for RRP requires a skilled team consisting of otolaryngologists, anesthesia providers, and operating room personnel working together to provide facility properly equipped to manage difficult pediatric airways. Because of voice deviations and thereby occurrence of maladaptive and compensatory vocal symptoms, voice pathologists are important part for the rehabilitation team for patients with RRP. Because of the recurrent nature of RRP and its potential to lead to airway obstruction, restorative vocal rehabilitation done by speech-language pathologists, along with parental support, can be invaluable in maintaining a safe airway and normal voice in children with RRP.

#### Need of the study

Although the exact figure of RRP incidence is difficult to ascertain, incidence of RRP cases reporting in medical setups is on a rise. Limited literature and assessment reports regarding RRP limit and retard the rehabilitation and management procedures of RRP subjects. An exploratory study of such type will provide informative and supportive baseline to voice therapists, otolar-yngologists, and other related professionals regarding its vocal characteristics, vocal habit, and thereby its primary and secondary management options.

#### **AIM**

This study aimed at providing comparative measures of acoustic as well as perceptual voice analysis of children with RRP. As this medical condition is recurrent in nature, it demands periodic routine medical management. Psychosocial needs such as ways to deal with emotional, social, and financial stress by the family members of the suffering children need to be proficiently adhered to.

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