

RRP Medical Reference Service

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Dave Wunrow and Bill Stern

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Preface

The *RRP Medical Reference Service* is intended to be of potential interest to RRP patients/families seeking treatment, practitioners providing care, micro biological researchers as well as others interested in developing a comprehensive understanding of recurrent respiratory papillomatosis.

This issue focuses on a selection of references with abstracts from recent (2008 and later) RRP related publications. These listings are sorted in approximate reverse chronological order as indicated by the "PMID" numbers. Each listing is formatted as follows:

Journal or reference
Title
Language (if it is not specified assume article is in English)
Author(s)
Primary affiliation (when specified)
Abstract
PMID (PubMed ID)

If copies of complete articles are desired, we suggest that you request a reprint from one of the authors. If you need assistance in this regard or if you have any other questions or comments please feel free to contact:

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RRPF Selected Articles and Abstracts

[Curr Opin Otolaryngol Head Neck Surg.](#) 2008 Dec;16(6):536-542.

Recurrent respiratory papillomatosis: update 2008.

[Gallagher TQ](#), [Derkay CS](#).

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PURPOSE OF REVIEW: Recurrent respiratory papillomatosis (RRP) is the most common benign neoplasm of the larynx in children. Over the past several years some exciting new therapeutic options as well as some relevant research into the disease process has emerged that may offer new insight and methods in managing this frustrating disease. **RECENT FINDINGS:** Recent investigations have resulted in the following findings: more accurate prevalence estimates of human papilloma virus in women in the United States; correlation of socioeconomic status and disease severity; the malignant potential of human papilloma virus in head and neck cancer; the role of the host immune system in RRP; the efficacy of a vaccine preventing human papilloma virus; the emergence of pulsed dye laser and potassium-titanyl-phosphate laser as a therapy for RRP; the efficacy of cidofovir as an adjunctive therapy for RRP; and the role of cyclooxygenase-2 in the molecular biology of RRP. **SUMMARY:** The management of RRP is ever evolving. Despite several new therapies discussed in this study, it is still a disease with the potential for high morbidity. As the focus of therapy shifts from treatment to prevention, it will take many years to determine whether prevention strategies are effective in limiting the spread of this disease. In the mean time, further research is needed to gain better control of this disease process.

PMID: 19005325 [PubMed - as supplied by publisher]

[Acta Otorrinolaringol Esp.](#) 2008 Oct;59(8):367-70.

[Risk factors for developing laryngeal cancer in adult population at the hospital español in Mexico city.]

[Article in Spanish]

[Durán de Alba LM](#), [Roa Castro FM](#).

Servicio de Otorrinolaringología. Hospital Angeles Lomas. México DF. México.

INTRODUCTION: Laryngeal cancer is the most frequent head and neck cancer. Considerable geographic differences exist in its incidence by gender. In Spain, there is male predominance (> 90 %). Numerous authors have documented exposure to tobacco and/or alcohol as the main risk factors for laryngeal cancer. Gastroesophageal reflux, genetics, occupational factors and also human papilloma virus are also cited. **PATIENTS AND METHOD:** The present study involved 43 patients diagnosed with laryngeal cancer and 130 healthy control subjects. The goal was to establish the frequency affecting both sexes and to identify the risk factors of those born in Spain but living in Mexico. Odds ratios (OR) for each risk factor were analyzed using univariate analysis. **RESULTS:** A considerable predominance of laryngeal cancer was found in males (90.6 %). Tobacco (OR = 6.56) and alcohol consumption (OR = 3.04) are significant risk factors with a multiplier effect. Gastroesophageal reflux does not show any significant OR. Occupational exposure had a significant OR = 37.28. **CONCLUSIONS:** The main advantage of this type of studies is the ability to design strategies to modify the risk factors. Male predominance and risk factors were no different from other findings reported in Spain, except for the considerable risk relating to occupational exposure.

PMID: 18928671 [PubMed - in process]

[Srp Arh Celok Lek.](#) 2008 May;136 Suppl 2:171-81.

[Virology today and tomorrow]

[Article in Serbian]

Jerant-Patić V.

Virus infections are the most common human diseases, particularly acute respiratory infections (mostly in children and young adults). Virus infections of the upper respiratory tract in children are proved in 77.4%, viral bronchitis in 58.6%, viral pneumonia in 47.6% and febrile conditions with lymphadenopathy in 44.1% patients. Current studies show that virus infections can cause not only acute, but also persistent virus diseases. A certain number of viruses are able to incorporate their nucleic acid into the genome of the host-cell, leading to rearrangement of the cell genes and formation of malignant tumors. In women with cervical changes, by application of hybridization technique in situ, the most frequently identified virus genotypes are human papilloma viruses 16 and 18 (in 21.67%), genotypes 6 and 11 in 8.33% and genotypes 31, 33 and 35 in 3.33% examined women. Viral persistence can cause manifestations of latent or chronic infections, as well as prion-caused slow infections of the central nervous system. Defective particles play an important role in maintaining viral persistence. Viruses are important agents involved in various disorders of

the immunological homeostasis of the organism. Recent knowledge described in SARS infected patients indicates that induction of the so-called TH2 cytokine profile can be responsible for death of infected patients.

PMID: 18924489 [PubMed - indexed for MEDLINE]

[Expert Opin Emerg Drugs](#). 2008 Sep;13(3):393-416.

Emerging antiviral drugs.

De Clercq E.

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Foremost among the newly described antiviral agents that may be developed into drugs are, for the treatment of human papilloma virus (HPV) infections, cPrPMEDAP; for the treatment of herpes simplex virus (HSV) infections, BAY 57-1293; for the treatment of varicella-zoster virus (VZV) infections, FV-100 (prodrug of Cf 1743); for the treatment of cytomegalovirus (CMV) infections, maribavir; for the treatment of poxvirus infections, ST-246; for the treatment of hepatitis B virus (HBV) infections, tenofovir disoproxil fumarate (TDF) (which in the meantime has already been approved in the EU); for the treatment of various DNA virus infections, the hexadecyloxypropyl (HDP) and octadecyloxyethyl (ODE) prodrugs of cidofovir; for the treatment of orthomyxovirus infections (i.e., influenza), peramivir; for the treatment of hepacivirus infections (i.e., hepatitis C), the protease inhibitors telaprevir and boceprevir, the nucleoside RNA replicase inhibitors (NRRIs) PSI-6130 and R1479, and various non-nucleoside RNA replicase inhibitors (NNRRIs); for the treatment of human immunodeficiency virus (HIV) infections, integrase inhibitors (INIs) such as elvitegravir, nucleoside reverse transcriptase inhibitors (NRTIs) such as apricitabine, non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as rilpivirine and dapivirine; and for the treatment of both HCV and HIV infections, cyclosporin A derivatives such as the non-immunosuppressive Debio-025.

PMID: 18764719 [PubMed - indexed for MEDLINE]

[Laryngorhinootologie](#). 2008 Nov;87(11):796-9. Epub 2008 Aug 29.

[Juvenile laryngeal papillomatosis - immunisation with the polyvalent vaccine gardasil(r).]

[Article in German]

[Förster G](#), [Boltze C](#), [Seidel J](#), [Pawlita M](#), [Müller A](#).

Klinik für HNO-Heilkunde/Plastische Operationen des SRH Wald-Klinikums Gera.

Juvenile laryngeal papillomatosis is a rare condition caused by human papilloma virus (HPV). In cases with rapid recurrences permanent impairments of voice and breathing are almost inevitable due to the frequent need of debulking surgeries. Efforts to lower the recurrence rate comprise the adjuvant use of interferon alpha, local cidofovir, photodynamic therapy or mumps vaccination. In the present case we tried to positively influence the aggressive course of disease in a two year old boy by immunisation with the quadrivalent HPV vaccine Gardasil(R). Chromogenic in-situ hybridisation analysis and polymerase chain reaction (PCR) of lesion tissue showed simultaneous infection with the HPV-Types 6 and 11. After the third immunisation the disease became stable. No further surgery was necessary for the last ten months. The risk profile of this adjuvant treatment is low. We think it worth to initiate a multicentre trial to prove a benefit of this treatment even if no complete virus elimination can be achieved.

PMID: 18759217 [PubMed - in process]

[Intern Med.](#) 2008;47(17):1535-8. Epub 2008 Sep 1.

An adult case of multiple squamous papillomas of the trachea associated with human papilloma virus type 6.

[Shibuya H](#), [Kutomi T](#), [Kujime K](#), [Hara K](#), [Hisada T](#).

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A 72-year-old woman with primary biliary cirrhosis complained of dry cough and wheezing. Chest computed tomography showed a tumor arising from the posterior wall of the trachea. Bronchoscopic examination revealed that the tumor was cauliflower-like, with two small polypoid tumors. They were diagnosed as multiple squamous papillomas. The main tumor was recurrent and removed by repeated microwave coagulation therapy (MCT) through bronchoscopy, whereas the two polypoid tumors were likely to disappear spontaneously. Human papilloma virus (HPV) type 6 DNA was detected in the tumor by polymerase chain reaction (PCR) amplification, suggesting that this virus was the cause of her papillomas.

PMID: 18758130 [PubMed - in process]

[Anticancer Res.](#) 2008 Jul-Aug;28(4B):2233-7.

Prevalence of HPV types in a cohort of Greeks with clinical indication of infection.

[Yapijakis C](#), [Adamopoulou M](#), [Antonopoulos G](#), [Koufaliotis N](#), [Vairaktaris E](#).

Department of Oral and Maxillofacial Surgery, University of Athens Medical School, Attikon Hospital, Athens, Greece.

BACKGROUND: Several types of human papilloma virus (HPV) have been associated with increased risk for epithelial malignancies. In light of a recently available vaccine that protects against persistent infection by certain HPV types (6, 11, 16, 18) and resulting neoplasias, the prevalence of HPV types was investigated in a cohort of people with a suspected viral infection. **PATIENTS AND METHODS:** The studied material consisted of genital or oral scrapings obtained from 263 consecutively referred Greeks (aged 18-64 years) with a clinical indication of HPV infection. DNA samples isolated from scrapings were tested by PCR, using consensus primers for at least 50 HPV types. In cases of detected viral DNA sequence, HPV typing was performed by restriction analysis using 4 enzymes and confirmed by DNA sequencing. **RESULTS:** 215/263 (81.7%) of the samples were HPV-positive. HPV types associated with high risk for neoplasias were detected in 91/215 (42.3%), intermediate risk types in 64/215 (29.8%) and low-risk types in 60/215 (27.9%) of the positive samples. A total of 85/215 (39.5%) were positive for one of the vaccine-related types. Furthermore, types 16 and 18 comprised about the same proportion of the high-risk types detected in this study (35/91, 38.5%). **CONCLUSION:** The observed high prevalence rate of high-risk types underlines the importance of testing individuals with an indication of a possible HPV infection. In addition, there is a need for prevention strategies, such as the annual Pap smear screening of women, as well as wider use of HPV molecular screening and vaccines targeted at common HPV types.

PMID: 18751400 [PubMed - indexed for MEDLINE]

[Anticancer Res.](#) 2008 Jul-Aug;28(4B):2169-74.

Follow-up of HPV DNA copy number in cidofovir therapy of recurrent respiratory papillomatosis.

[Major T](#), [Sziklai I](#), [Czeglédy J](#), [Gáll T](#), [Gergely L](#), [Szarka K](#).

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BACKGROUND: Cidofovir is a cytosine nucleoside analogue antiviral drug given as an adjuvant therapy in recurrent respiratory papillomatosis (RRP). **MATERIALS AND METHODS:** Intralesional cidofovir therapy was given to a 14-year-old male patient. The papilloma severity score (PSS) of Derkay et al. was used for follow-up. Serial fresh-frozen biopsies were taken from the lesions in the larynx and soft palate prior to therapy and during its course. After human papillomavirus (HPV) typing and the determination of the genomic physical state, the HPV DNA copy number was estimated with real-time PCR. **RESULTS:** All the papillomas harboured HPV 11 DNA in episomal form. Prior to therapy, the HPV copy number fluctuated with time. In the initial treatment period with 2-week-intervals both the viral load and the PSS decreased and a transient complete remission was observed. Subsequently, when the injections were given at longer intervals, the viral load returned to the initial values or greater, fluctuations reappeared and the RRP recurred at a controlled rate. **CONCLUSION:** The initial treatment period was successful, as the viral load decreased, and long-term effects of cidofovir might account for the controlled disease as the injection intervals were prolonged.

PMID: 18751391 [PubMed - indexed for MEDLINE]

[Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi](#). 2008 May;43(5):355-9.

[Primary study on glycan structure in pathopoiesis mechanism of recurrent respiratory papillomatosis]

[Article in Chinese]

[Wang J](#), [Han DM](#), [Kang HW](#), [Ma LJ](#), [Ye JY](#), [Xiao Y](#).

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OBJECTIVE: To compare the molecular basis difference between recurrent respiratory papillomatosis (RRP) and vocal cord polyp, to analyze the expression of glycan structural genes, and to discuss the pathopoiesis mechanism of RRP. **METHODS:** The gene expressing profile between the 3 groups papilloma and the vocal cord polyp regarded as normal larynx epithelium were compared using mRNA parallel amplify and the human genome gene expressing microarray. Through cluster analysis, Gene Ontology function gene annotation and path way analysis, the relative gene of RRP and HPV infection were acquired.

RESULTS: According to three microarrays results, total 567 expression changed genes related to HPV induce RRP were acquired. A serial change of glycan structure biosynthesis and degradation pathways was significant. The expression of dolichyl-phosphate mannosyltransferase polypeptide 1 (DPM1), asparagine-linked glycosylation 1 homolog (ALG1), fucosyltransferase 8 (FUT8) and alpha-mannosidase 1A (MAN1A) were regulated and beta-hexosaminidase (HEXB), beta1-galactosidase (GLB1), exostosins 1 (EXT1), fucosyltransferase (FUT) reduced expression and heparan sulfate 3-O-sulfotransferase 1 (HS3ST3A1) increased expression. The two related enzymes of the glycosphingolipids which is the main composed of the cell membrane, beta-3-N-acetylglucosaminyltransferase 4 (B3GNT4) and UDP-glucose ceramide glucosyltransferase (UGCG) increase expression, HEXB and GLB1 reduced expression. CONCLUSIONS: The alteration of the coding genes of glycan structure biosynthesis and degradation pathways were significantly and characteristically in pathopoiesis mechanism of RRP. This abnormality may be the beginning of tumor form HPV infection.

PMID: 18717311 [PubMed - in process]

[Ann Otol Rhinol Laryngol](#). 2008 Jul;117(7):477-83.

Cidofovir efficacy in recurrent respiratory papillomatosis: a randomized, double-blind, placebo-controlled study.

[McMurray JS](#), [Connor N](#), [Ford CN](#).

Division of Otolaryngology-Head and Neck Surgery, Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin 53792, USA.

OBJECTIVES: We performed a prospective, double-blind, placebo-controlled, longitudinal adjuvant therapy trial to determine the efficacy of cidofovir in the treatment of severe recurrent respiratory papillomatosis (RRP). Although results of case series suggest that cidofovir may decrease the frequency and rapidity of papilloma regrowth, no blinded placebo-controlled studies have demonstrated efficacy. METHODS: Adults and children (n = 19) with aggressive RRP received either active drug (cidofovir) or placebo. When surgical intervention was needed, drug or placebo was injected into affected areas after surgical removal of disease. The following measures were made at baseline and at 2-month intervals for the course of 12 months: Derkey papilloma severity grading scale, Voice Handicap Index, Health-Related Quality of Life, and total number of procedures performed over 12 months. RESULTS: At 2- and 12-month follow-ups, there was a significant ($p < .05$) improvement in the Derkey Severity Score within the cidofovir and placebo groups, but no difference between groups, and no difference between groups in the number of procedures performed. Significant improvement was found in Voice Handicap Index scores in the cidofovir group at the 12-month follow-up. No differences were seen in Health-Related Quality of Life. CONCLUSIONS: A randomized, blinded, placebo-controlled trial is necessary in the study

of RRP, because the natural history of the disease can include remissions and reactivations. We found a significant improvement in the Derkey Severity Score 12 months after the baseline assessment in patients treated with cidofovir. This effect, however, was also seen in the placebo group. Accordingly, we were unable to provide proof of efficacy of cidofovir in the treatment of RRP.

PMID: 18700421 [PubMed - indexed for MEDLINE]

[Eur Arch Otorhinolaryngol.](#) 2008 Jul 22. [Epub ahead of print]

Surgery and topic cidofovir for nasal squamous papillomatosis in HIV+ patient.

[Capaccio P](#), [Ottaviani F](#), [Cuccarini V](#), [Corbellino M](#), [Parravicini C](#), [Menzo S](#), [Schindler A](#), [Pignataro L](#).

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Intranasal schneiderian exophytic squamous papillomatosis is rare and often secondary to human papilloma virus infection. Treatment usually consists of repeated surgical or endoscopic excisions due to recurrences. The use of intravenous or intralesional or topically applied cidofovir, a cytidine nucleotide analogue suppressing viral replication, alone or as adjuvant therapy has been proposed and described in the literature for the treatment of other human papillomavirus (HPV)-related lesions. We firstly describe a successful combined approach of surgery and topical cidofovir for recurrent nasal HPV-related exophytic squamous papillomatosis in a HIV-infected patient. As no untoward effects were encountered this therapeutical option should be considered in the management of recurrent nasal papillomatosis in HIV-infected patients.

PMID: 18648834 [PubMed - as supplied by publisher]

[Arch Otolaryngol Head Neck Surg.](#) 2008 Jul;134(7):778-80.

Diffuse intranasal papillomatosis and its association with human papillomavirus.

[Bleier BS](#), [Gawthrop CS](#), [Thaler ER](#), [Sewell DA](#), [Montone KT](#), [Marvel DM](#), [Chiu AG](#).

No abstract available.

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PMID: 18645131 [PubMed - indexed for MEDLINE]

[Auris Nasus Larynx](#). 2008 Jul 12. [Epub ahead of print]

Integration of human papilloma virus type 26 in laryngeal cancer of a child.

[Muenscher A](#), [Feucht HH](#), [Kutta H](#), [Teschke S](#), [Wenzel S](#).

University Medical Center Hamburg-Eppendorf, Department of Oto-Rhino-Laryngology, Martinistr. 52, 20246 Hamburg, Germany.

Squamous cell carcinoma (SCC) in larynx is rare with children and adolescents. Usually larynx cancer is common with male smokers in the 7th decade. Among patients with no history of tobacco and/or alcohol consumption several factors can play a role in the outbreak of laryngeal cancer: such as individual predisposition, radiation, gastroesophageal reflux, viral infection, dietary factors and environmental influences. In literature only few cases of laryngeal cancer with children are reported. Recent studies show that the most frequent laryngeal malignancy is the embryonal rhabdomyosarcoma. Besides the recurrent respiratory papillomatosis (RRP) based on an infection with human papilloma virus (HPV) types 6 and 11 (low risk) and types 16 and 18 (high risk) is known for a possible malignant transformation towards a SCC. HPV type 26 is only reported as low risk type HPV associated with cervical cancer. Final diagnosis often takes a long time. Initial symptoms such as hoarseness, cough or shortness of breath are often referred to more typical pediatric diseases or laryngeal development.

PMID: 18621496 [PubMed - as supplied by publisher]

[Mol Med](#). 2008 Sep-Oct;14(9-10):608-17.

Immune dysregulation and tumor-associated gene changes in recurrent respiratory papillomatosis: a paired microarray analysis.

[DeVoti JA](#), [Rosenthal DW](#), [Wu R](#), [Abramson AL](#), [Steinberg BM](#), [Bonagura VR](#).

Feinstein Institute for Medical Research, Manhasset, New York, USA.

Recurrent respiratory papillomas (RRP) are benign airway tumors, caused primarily by human papillomaviruses (HPV) types 6 and 11. The disease is characterized by multiple recurrences after surgical removal, with limited effective therapy. To identify novel targets for future therapy, we established transcriptional profiles for actively growing papillomas compared with autologous, clinically normal, laryngeal epithelia (adjacent tissue). Total ribonucleic acid (RNA) from 12 papillomas and 12 adjacent tissues were analyzed by microarray, and the matched sets of tissues compared by paired t test, to identify differentially expressed genes in papilloma tissues while minimizing variations intrinsic to individual patients. Quantitative polymerase chain reaction (PCR) was used to confirm the relative expression levels for a subset of genes. Within the 109 differentially expressed transcripts whose expression varied at least three-fold were two large groups of genes with related functions. The first group consisted of 18 genes related to host defense, including both innate and adaptive immunity. The second group contained 37 genes that likely contribute to growth of papillomas as benign tumors, since the altered pattern of expression also had been reported previously in many cancers. Our results support our previous studies that document a systemic T(H)2-like adaptive immune response in RRP, and suggest that there is a role for altered innate immunity in RRP as well. We propose that HPV 6 and 11 infection establishes a tumorigenic microenvironment characterized by alteration of both innate inflammatory signals and adaptive immune responses that prevent effective T(H)1-like response, in conjunction with altered expression of numerous genes that regulate cellular growth and differentiation.

PMID: 18607510 [PubMed - indexed for MEDLINE]

[Ann Nucl Med](#). 2008 Jun;22(5):433-6. Epub 2008 Jul 4.

18F FDG-PET/CT findings in recurrent respiratory papillomatosis.

[Pipavath SN](#), [Manchanda V](#), [Lewis DH](#), [Schmidt RA](#), [Martins RG](#), [Godwin JD](#).

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Recurrent respiratory papillomatosis (RRP) is an indolent and primary disease of the larynx and the trachea and rarely extends to smaller airways. F-18 fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (FDG-PET/CT) evaluation in this condition has not been reported earlier. We report FDG-PET/CT findings in a case of RRP that included a large papillomatous lung mass resembling cancer.

PMID: 18600423 [PubMed - indexed for MEDLINE]

[Vaccine](#). 2008 Aug 18;26(35):4513-8. Epub 2008 Jul 1.

The potential health and economic benefits of preventing recurrent respiratory papillomatosis through quadrivalent human papillomavirus vaccination.

[Chesson HW](#), [Forhan SE](#), [Gottlieb SL](#), [Markowitz LE](#).

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We estimated the health and economic benefits of preventing recurrent respiratory papillomatosis (RRP) through quadrivalent human papillomavirus (HPV) vaccination. We applied a simple mathematical model to estimate the averted costs and quality-adjusted life years (QALYs) saved by preventing RRP in children whose mothers had been vaccinated at age 12 years. Under base case assumptions, the prevention of RRP would avert an estimated USD 31 (range: USD 2-178) in medical costs (2006 US dollars) and save 0.00016 QALYs (range: 0.00001-0.00152) per 12-year-old girl vaccinated. Including the benefits of RRP reduced the estimated cost per QALY gained by HPV vaccination by roughly 14-21% in the base case and by <2% to >100% in the sensitivity analyses. More precise estimates of the incidence of RRP are needed, however, to quantify this impact more reliably.

PMID: 18598734 [PubMed - indexed for MEDLINE]

[Asia Pac J Clin Nutr](#). 2008;17(2):352-7.

HPV-induced recurrent laryngeal papillomatosis: dietary fatty acid and micronutrient intakes.

[Louw L](#), [Walsh C](#).

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Human papilloma virus (HPV)-induced recurrent laryngeal papillomatosis (RLP) is a chronic

debilitating disease often encountered among children of poor socio-economic South African groups. There are a few studies and limited evidence as to what extent nutrition may contribute to this disease. To our knowledge this is the first study that gives an account of dietary FA and micronutrient intakes in RLP patients, according to food frequency questionnaires. The dietary FA profile revealed an excessive linoleic acid (LA) intake syndrome and is also marked by high palmitic acid (PA), oleic acid (OA) and SFA intakes. Research revealed that enhanced LA and PA drive, respectively, mitogenic stimuli and apoptotic resistance during tumorigenesis, whilst SFAs are associated with lipid rafts, the Th1 immune response and immunosuppression. Low folate intake, a risk for HPV-infection, and low Zn intake, detrimental for lipid metabolism and immunocompetence, occurred in, respectively, 70% and 20% RLP patients. The poor correlations that were found in RLP patients between essential fatty acids (EFAs) and micronutrients, namely, Mg, Zn and Se, involved in lipid metabolism and immune responses, need proper clarification. Overall, it is plausible that the diet (poor nutrition), a shift in lipid metabolism caused by HPV- infection, environmental smoke and oxidative stress, as well as extra-esophageal acid reflux with secondary inflammation in the larynx are co-factors in the etiology of laryngeal papillomatosis, and that immunocompromised patients are subjected to recurrence. It is imperative to ensure that children with RLP receive proper nutrition and follow a healthy lifestyle to prevent disease recurrence after treatment.

PMID: 18586658 [PubMed - in process]

[Asia Pac J Clin Nutr.](#) 2008;17(2):187-93.

HPV-induced recurrent laryngeal papillomatosis: rationale for adjuvant fatty acid therapy.

[Louw L, Claassen A.](#)

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The course of human papilloma virus (HPV)-induced recurrent laryngeal papillomatosis (RLP) is variable and unpredictable. Some patients experience spontaneous remission, while others suffer from aggressive growth with dire consequences. Unfortunately, HPV DNA can persist in mucosa after treatment and can be reactivated under immunosuppressive conditions. For this reason, these benign tumors are notoriously recurrent. Better understanding of lipid-driven signaling pathways during tumorigenesis and immune responses in RLP patients can contribute to improve therapeutic approaches in an attempt to obviate this disease. Based on a mountain of evidence in the literature that concerns the immunomodulatory potential of certain FAs, it is clear that there is a rationale for adjuvant FA therapy (concurrent application) in the management of RLP. Of particular importance for

immune surveillance is that the Th1 pathway in RLP is down-regulated and it is advocated that conjugated linoleic acid (CLA) and eicosapentaenoic acid (EPA) have the ability to restore the Th1/Th2 balance. Therefore, it is proposed that adjuvant FA therapy with CLA and EPA must be included in the therapeutical regime of RLP, since they are considered excellent anti-viral and anti-tumor agents to improve immune conditions and disease outcome. Immunocompetence plays a pivotal role in the clinical course of RLP and, hence, a new direction with adjuvant FA therapy may be the key to prevent recurrence of this disease.

PMID: 18586635 [PubMed - in process]

[Ear Nose Throat J.](#) 2008 Jun 13;87(6):E8-11.

Recurrent respiratory papillomatosis in pregnancy: a case of emergent airway management.

[Scurry WC Jr](#), [McGinn JD](#).

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Recurrent respiratory papillomatosis is a benign neoplastic process involving squamous epithelium of the respiratory tract, typically the vocal folds. In cases of aggressive growth, or uncontrolled disease, airway compromise and respiratory distress can occur. Human papillomavirus (HPV) is known to be the etiologic agent in this disease process, as well as in condyloma acuminata, or genital warts. Studies have shown that HPV-induced condyloma acuminata can worsen during pregnancy. We present a case of airway obstruction requiring emergent tracheostomy in a pregnant patient with known laryngeal recurrent respiratory papillomatosis. The management of this condition and some theories regarding its response to certain hormonal states are discussed.

PMID: 18561109 [PubMed - indexed for MEDLINE]

[Otolaryngol Pol.](#) 2007;61(5):872-6.

[Functional results after the treatment of laryngeal stenosis]

[Article in Polish]

[Orecka B](#), [Misiolek H](#), [Namysłowski G](#), [Lisowska G](#), [Czeczior E](#), [Sciarski W](#), [Fira R](#),

Sowa P, Misiolek M.

Katedra i Oddział Kliniczny Laryngologii S1.AM w Zabrze.

Six subjects before and after surgery because of the laryngeal stenosis were presented. In 3 cases laryngeal web was recognised which arises after endoscopic removal of infant papilloma. The scar after laser chordectomy due to carcinoma of the larynx occurred in remaining 3 patients. All presented patients simultaneously were undergoing removal of the lesion endoscopically and insertion of silastic separator. AIM: Respiratory and phonatory function assessment in patients who were operated because of the laryngeal stenosis was the aim of this study. METHODS: Treatment effectiveness was estimate on the basis of pre- and postoperative spirometry with flow--volume loop and postoperative phoniatic examination. Ventilatory function was analysis on the basis of the following parameters: PIF, FEV1, FIV1, PEF, FVC. Phoniatic examination was performed after 2 months of outpatient observation and rehabilitation. It consisted of subjective voice assessment using GRBAS scale, videolaryngostroboscopy and assessment of the phonation time. RESULTS: Some of the analysed parameters especially in patients with posterior stenosis were significantly better after surgery. Phoniatic rehabilitation after surgery caused improvement of voice quality and phonatory function of the larynx. CONCLUSION: Thanks to insertion of silastic separator good phoniatic function and ventilation efficiency are possible.

PMID: 18552038 [PubMed - indexed for MEDLINE]

[PLoS ONE](#). 2008 May 28;3(5):e2263.

Age of child, more than HPV type, is associated with clinical course in recurrent respiratory papillomatosis.

[Buchinsky FJ](#), [Donfack J](#), [Derkay CS](#), [Choi SS](#), [Conlev SF](#), [Myer CM 3rd](#), [McClay JE](#), [Campisi P](#), [Wiatrak BJ](#), [Sobol SE](#), [Schweinfurth JM](#), [Tsuji DH](#), [Hu FZ](#), [Rockette HE](#), [Ehrlich GD](#), [Post JC](#).

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BACKGROUND: RRP is a devastating disease in which papillomas in the airway cause hoarseness and breathing difficulty. The disease is caused by human papillomavirus (HPV) 6 or 11 and is very variable. Patients undergo multiple surgeries to maintain a patent airway and in order to communicate vocally. Several small studies have been published in which most have noted that HPV 11 is associated with a more aggressive course.

METHODOLOGY/PRINCIPAL FINDINGS: Papilloma biopsies were taken from patients undergoing surgical treatment of RRP and were subjected to HPV typing. 118 patients with

juvenile-onset RRP with at least 1 year of clinical data and infected with a single HPV type were analyzed. HPV 11 was encountered in 40% of the patients. By our definition, most of the patients in the sample (81%) had run an aggressive course. The odds of a patient with HPV 11 running an aggressive course were 3.9 times higher than that of patients with HPV 6 (Fisher's exact $p = 0.017$). However, clinical course was more closely associated with age of the patient (at diagnosis and at the time of the current surgery) than with HPV type. Patients with HPV 11 were diagnosed at a younger age (2.4y) than were those with HPV 6 (3.4y) ($p = 0.014$). Both by multiple linear regression and by multiple logistic regression HPV type was only weakly associated with metrics of disease course when simultaneously accounting for age. **CONCLUSIONS/SIGNIFICANCE ABSTRACT:** The course of RRP is variable and a quarter of the variability can be accounted for by the age of the patient. HPV 11 is more closely associated with a younger age at diagnosis than it is associated with an aggressive clinical course. These data suggest that there are factors other than HPV type and age of the patient that determine disease course.

PMID: 18509465 [PubMed - indexed for MEDLINE]

[Int J Pediatr Otorhinolaryngol.](#) 2008 Jul;72(7):939-44. Epub 2008 May 27.

Scientific and clinical aspects of the use of cidofovir in recurrent respiratory papillomatosis.

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OBJECTIVE: Cidofovir is the most contemporary adjuvant treatment for recurrent respiratory papillomatosis (RRP) and its use is increasing. Cidofovir is potentially harmful. Otolaryngologists should understand the science of cidofovir and review the current published data on the effects of this therapy. **METHOD:** Pubmed was searched using the terms cidofovir and papillomatosis. Comparisons were made between published articles. **RESULTS:** Thirteen articles were identified between 1998 and 2006, representing the treatment of 142 patients. Cidofovir did result in a significant improvement of papillomatous lesions in the majority (60%) of patients despite the use of different regimes of cidofovir administration. There was no unifying protocol in use. A partial response was demonstrated in 29% of patients. 7.5% had no response however, an additional 3.5% patients were lost to follow-up. No malignant change was reported. **CONCLUSION:** Cidofovir does appear to be effective in improving the outcome of patients with RRP. There are no reports of malignant transformation despite concerns raised by toxicology studies.

PMID: 18502519 [PubMed - indexed for MEDLINE]

[Gynecol Oncol.](#) 2007 Nov;107(2 Suppl 1):S6-13.

The spectrum and clinical sequelae of human papillomavirus infection.

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Infection with the human papillomavirus (HPV) is the most common sexually transmitted disease afflicting approximately 80% of the population. HPV infection is an essential factor in cervical carcinogenesis and cervical carcinoma is the second most common cause of cancer among women worldwide. In addition to cervical cancer, other malignancies in both men and women such as esophageal, oropharyngeal, and anal cancer have been causally associated with this virus. Other gender-specific HPV-related cancers include penile, vulvar and vaginal cancer. HPV-16 is the most common HPV type associated with a malignant phenotype regardless of organ of origin. HPV-16 together with HPV-18 accounts for approximately 70% of cervical cancers. Other non-oncogenic HPV types including HPV types 6 and 11 are associated with over 90% of benign HPV-related lesions such as genital warts and juvenile respiratory papillomatosis.

PMID: 18499914 [PubMed - indexed for MEDLINE]

[Laryngoscope.](#) 2008 Jul;118(7):1236-47.

Recurrent respiratory papillomatosis: a review.

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Recurrent respiratory papillomatosis (RRP), which is caused by human papillomavirus types 6 and 11, is the most common benign neoplasm of the larynx among children and the second most frequent cause of childhood hoarseness. After changes in voice, stridor is the second most common symptom, first inspiratory and then 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. Differential diagnoses include asthma, croup, allergies, vocal nodules, or bronchitis. Reports estimate the incidence of RRP in the United States at 4.3 per 100,000 children and 1.8 per 100,000 adults. Infection in children has been associated with vertical transmission during vaginal delivery from an infected mother. Younger age at diagnosis is associated with more aggressive disease and the need for more frequent surgical procedures to decrease the airway burden. When surgical therapy is needed more frequently than four times in 12 months or there is evidence of RRP outside the larynx, adjuvant medical therapy should be considered. Adjuvant therapies that have been investigated include dietary supplements, control of extra-esophageal reflux disease, potent antiviral and chemotherapeutic agents, and photodynamic therapies; although several have shown promise, none to date has "cured" RRP, and some may have serious side effects. Because RRP, although histologically benign, is so difficult to control and can cause severe morbidity and death, better therapies are needed. The potential for a quadrivalent human papilloma vaccine is being explored to reduce the incidence of this disease.

PMID: 18496162 [PubMed - indexed for MEDLINE]

[Respiration](#). 2008 May 19. [Epub ahead of print]

Airway Stenting for Severe Endobronchial Papillomatosis.

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Severe endobronchial papillomatosis is associated with recurrent respiratory infections and airway obstruction. Current management includes treatment with antiviral and cytotoxic agents to slow papilloma growth and endobronchial therapies to excise the lesions. We report 2 cases of severe tracheobronchial papillomatosis which were managed with endobronchial laser and airway stenting. A 32-year-old man and a 55-year-old woman with known history of tracheobronchial papillomatosis were admitted with hemoptysis and dyspnea, respectively. They presented increasing frequencies of respiratory infections in the preceding year despite therapy with interferon alpha-2A, acyclovir, methotrexate and endobronchial treatment. Moreover, the 2nd patient presented 6 months previously to another institution with central airway obstruction which was treated with a covered metallic stent. Both patients underwent rigid bronchoscopy which revealed airway obstruction by papillomatous lesions. In the 2nd case, the metallic stent was broken due to fatigue and was infiltrated by a giant papilloma. Both patients received laser treatment and airway silicone stenting. After stenting, respiratory infection rate was greatly reduced and no further complications related to the papillomas occurred. This paper highlights the serious complications which may arise if endobronchial management of the disease includes insertion of metallic stents. In contrast, airway stenting with a silicone prosthesis may be useful in refractory endobronchial papillomatosis and may

offer permanent control of symptoms. Copyright © 2008 S. Karger AG, Basel.

PMID: 18487874 [PubMed - as supplied by publisher]

[Am J Obstet Gynecol.](#) 2008 May;198(5):500.e1-7.

Comment in:

- [Am J Obstet Gynecol. 2008 May;198\(5\):487-8.](#)

The economic burden of noncervical human papillomavirus disease in the United States.

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OBJECTIVE: The purpose of this study was (1) to estimate the direct medical costs of 7 major noncervical human papillomavirus (HPV)-related conditions that include genital cancers, mouth and oropharyngeal cancers, anogenital warts, and juvenile-onset recurrent respiratory papillomatosis, and (2) to approximate the economic burden of noncervical HPV disease. **STUDY DESIGN:** For each condition, we synthesized the best available secondary data to produce lifetime cost per case estimates, which were expressed in present value. Using an incidence-based approach, we then applied these costs to develop an aggregate measure of economic burden. **RESULTS:** The economic burden that was associated with noncervical HPV-6-, -11-, -16-, and -18-related conditions in the US population in the year 2003 approximates \$418 million (range, \$160 million to \$1.6 billion). **CONCLUSION:** The economic burden of noncervical HPV disease is substantial. Analyses that assess the value of investments in HPV prevention and control programs should take into account the costs and morbidity and mortality rates that are associated with these conditions.

PMID: 18455524 [PubMed - indexed for MEDLINE]

[Vestn Otorinolaringol.](#) 2008;(2):17-22.

[Gastroesophageal reflux disease and pharyngolaryngeal reflux in children with chronic laryngeal pathology]

[Article in Russian]

[Soldatskiĭ IuL](#), [Onufrieva EK](#), [Pogosova E](#), [Zaviktorina TG](#), [Strygina IuV](#), [Gasparian SF](#), [Shchepin NV](#), [Steklov AM](#).

A prospective non-randomized trial was made to evaluate incidence of gastroesophageal reflux disease (GERD) and pharyngolaryngeal reflux (PLR) in children with chronic laryngeal pathology. A total of 46 children aged 6 to 15 years were examined including 16 patients with recurrent respiratory papillomatosis, 15 patients with acquired laryngotracheal scarry stenosis and 15 patients with vocal nodules and functional dysphonia. Combination of GERD with PLR is a factor of risk for scarry laryngostenosis in a child with recurrent respiratory papillomatosis. If it is impossible to perform 24-h pH-monitoring of the esophagus for detection of GERD or PLR in patients with chronic laryngeal pathology, antireflux therapy is prescribed empirically. It is necessary to establish significant diagnostic criteria of PLR.

PMID: 18454071 [PubMed - indexed for MEDLINE]

[Int J Pediatr Otorhinolaryngol](#). 2008 Jun;72(6):917-20. Epub 2008 Apr 18.

Aggressive recurrent respiratory papillomatosis in a neonate.

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Recurrent respiratory papillomatosis is the most common benign laryngeal neoplasm in children. We report an infant with widespread papillomatosis at the time of diagnosis and rapidly progressive disease as a neonate. This child did not have the usual risk factors for recurrent respiratory papillomatosis, being the second child born by cesarean section to a mother without history of condyloma. Repeated surgical debulking has been used to control the disease, along with adjuvant therapies that included systemic therapy with an epidermal growth factor receptor inhibitor and intralesional cidofovir. We report our experience with these therapies.

PMID: 18423627 [PubMed - indexed for MEDLINE]

[Rev Soc Bras Med Trop.](#) 2008 Jan-Feb;41(1):89-90.

Recurrent respiratory papillomatosis with pulmonary involvement.

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Departamento de Diagnóstico por Imagem, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP.

No abstract available.

PMID: 18368280 [PubMed - indexed for MEDLINE]

[J Chin Med Assoc.](#) 2008 Mar;71(3):143-6.

Cidofovir injection for recurrent laryngeal papillomatosis.

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BACKGROUND: Recurrent laryngeal papillomatosis is caused by the human papilloma virus and characterized by multiple exophytic lesions of the vocal tract; it is a benign disease, but one that tends to recur after removal of growths. Due to the nature of the disease, alternative treatment strategies have focused on antiviral injection at lesion sites that eliminate repeated surgical procedures. The purpose of this study was to evaluate the efficacy of cidofovir injection following initial papilloma excision with a microdebrider. **METHODS:** Cidofovir injections (at a concentration of 7.5 mg/mL) were conducted in 5 patients (1 child; 4 adults). The injection number per patient varied from 2 mL to 6 mL. Repeated cidofovir injections were indicated only if recurrent or newly grown lesions were found in any of 3-week follow-up visits. **RESULTS:** Short-term complete remission was observed with different duration, from 11 to 21 weeks, following initial 2 to 3 cidofovir injections. All patients relapsed eventually, and their recurrent lesions were not successfully eradicated by repeated cidofovir injection. One patient's prognosis was complicated by scarring of both vocal cords. **CONCLUSION:** Surgical excision combined with cidofovir injection failed to prevent relapsing laryngeal papillomatosis. Once lesions recurred, repeated cidofovir injections alone were not able to achieve complete remission, although these procedures might be helpful in lessening the severity of the clinical course. Further studies in determining the dosage, duration of injection, and more long-term follow-up are required to clarify the efficacy of cidofovir for the treatment of recurrent laryngeal papillomatosis.

PMID: 18364266 [PubMed - indexed for MEDLINE]

[Mol Cell Biochem.](#) 2008 Jun;313(1-2):91-102. Epub 2008 Mar 25.

Activation of NF-kappaB by alloferon through down-regulation of antioxidant proteins and IkappaBalpha.

[Ryu MJ](#), [Anikin V](#), [Hong SH](#), [Jeon H](#), [Yu YG](#), [Yu MH](#), [Chernysh S](#), [Lee C](#).

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Alloferon is a 13-amino acid peptide isolated from the bacteria-challenged larvae of the blow fly *Calliphora vicina*. The pharmaceutical value of the peptide has been well demonstrated by its capacity to stimulate NK cytotoxic activity and interferon (IFN) synthesis in animal and human models, as well as to enhance antiviral and antitumor activities in mice. Antiviral and the immunomodulatory effectiveness of alloferon have also been supported clinically proved in patients suffering with herpes simplex virus (HSV) and human papilloma virus (HPV) infections. To elucidate molecular response to alloferon treatment, we initially screened a model cell line in which alloferon enhanced IFN synthesis upon viral infection. Among the cell lines tested, Namalva was chosen for further proteomic analysis. Fluorescence difference gel electrophoresis (DIGE) revealed that the levels of a series of antioxidant proteins decreased after alloferon treatment, while at least three glycolytic enzymes and four heat-shock proteins were increased in their expression levels. Based on the result of our proteomic analysis, we speculated that alloferon may activate the NF-kappaB signaling pathway. IkappaB kinase (IKK) assay, Western blot analysis on IkappaBalpha and its phosphorylated form at Ser 32, and an NF-kappaB reporter assay verified our proteomics-driven hypothesis. Thus, our results suggest that alloferon potentiates immune cells by activating the NF-kappaB signaling pathway through regulation of redox potential. Since NF-kappaB activation is involved in IFN synthesis, our results provide further clues as to how the alloferon peptide may stimulate IFN synthesis.

PMID: 18363038 [PubMed - indexed for MEDLINE]

[Ear Nose Throat J.](#) 2008 Jan;87(1):18-9.

Recurrent respiratory papillomatosis.

[Roy S, Vivero RJ.](#)

Department of Otolaryngology, Leonard M. Miller School of Medicine, University of Miami, Miami, FL, USA.

No abstract available.

PMID: 18357938 [PubMed - indexed for MEDLINE]

[Ann Otol Rhinol Laryngol.](#) 2008 Feb;117(2):113-7.

Histologic review of cidofovir-treated recurrent respiratory papillomatosis.

[Lindsay F, Bloom D, Pransky S, Stabley R, Shick P.](#)

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OBJECTIVES: Recurrent respiratory papillomatosis is currently the most common lesion of the larynx in children. The course of the disease is variable and often requires repetitive surgical interventions to maintain the airway. The predominant concern for disease progression is the possibility of spread to the tracheobronchial tree, as this increases the rates of morbidity and mortality. Cidofovir is an antiviral drug with activity against members of the DNA virus family. Development of local malignant change secondary to use of cidofovir has been a concern. The histopathologic findings from biopsy specimens from children treated with cidofovir have not been previously reported. **METHODS:** We performed a retrospective review of pediatric operative histologic biopsies and charts of patients treated with intralesional cidofovir and untreated study controls from January 1, 1995, through November 1, 2001. **RESULTS:** Ninety-six specimens were evaluated by 2 blinded pathologists. No cases of dysplasia were identified. The most commonly identified finding was an increased nucleus-to-cytoplasm ratio in 8 of 95 cases (8.4%). No cases of abnormal mitoses, prominent nucleoli, or cellular or nuclear enlargement were found.

CONCLUSIONS: This is the first report of pathologically evaluated recurrent respiratory papillomatosis specimens taken before and after treatment with intralesional cidofovir. No dysplasia was identified, and there were no significant dysplastic changes in the specimens analyzed.

PMID: 18357834 [PubMed - indexed for MEDLINE]

[J Postgrad Med.](#) 2008 Jan-Mar;54(1):32-4.

Recurrent respiratory papillomatosis complicated by aspergillosis: A case report with review of literature.

[Kuruville S](#), [Saldanha R](#), [Joseph LD](#).

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Pulmonary extension of recurrent invasive papillomatosis often poses a diagnostic challenge to the examining bronchoscopist, pathologist, radiologist and surgeon, in distinguishing it as a benign lesion that is confined to the mucosa and extending along the branches of the tracheobronchial tree from true invasion of a malignant tumor. We document here a case of recurrent invasive respiratory papillomatosis which initially presented as a laryngeal papilloma. After multiple recurrences, the patient presented with bronchopulmonary involvement, complicated by invasive aspergillosis in a non-immunocompromised setting.

PMID: 18296803 [PubMed - in process]

[Int J Pediatr Otorhinolaryngol.](#) 2008 Apr;72(4):433-52. Epub 2008 Feb 20.

Lung involvement in juvenile onset recurrent respiratory papillomatosis: a systematic review of the literature.

[Gélinas JF](#), [Manoukian J](#), [Côté A](#).

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OBJECTIVES: Determine the exact incidence of pulmonary involvement in recurrent respiratory papillomatosis (RRP); explore available treatments and their effectiveness; determine the characteristics of cases that progress to lung cancer. **DATA SOURCES:** MEDLINE, EMBASE, and the Cochrane Library databases between 1966 and 2007; reference lists of retrieved publication. **STUDY SELECTION:** Studies investigating recurrent respiratory papillomatosis with lung involvement. Age limited to 20 years of age to qualify for the diagnosis of juvenile-onset RRP. **DATA EXTRACTION:** Data pertaining to study design, population demographics, risk factors, site of involvement, investigation including the determination of the human papillomavirus type, treatment, and outcomes including the development of cancer. **DATA SYNTHESIS:** No randomized control trials were retrieved. Hundred and one studies met our inclusion criteria (23 cohorts, 4 case series, 72 case reports,

2 open trials) with 161 cases of lung involvement identified. From the cohort studies we could estimate the incidence of lung involvement in RRP at 3.3%. The incidence of cancer in cases with lung involvement was 16%. We could not draw conclusions regarding treatment effectiveness in lung involvement, as that was not evaluated except in case studies. It would nevertheless appear that Interferon is not effective and the use of intravenous Cidofovir needs to be better evaluated. CONCLUSION: Well-designed, hypothesis-driven randomized control trials and prospective cohort studies are warranted to improve our understanding of the mechanisms underlying the development of lung involvement in RRP, the risks associated with different HPV types, the efficacy of potential therapeutic options as well as the risk of progression to cancer.

PMID: 18281102 [PubMed - indexed for MEDLINE]

[Int J Pediatr Otorhinolaryngol.](#) 2008 Apr;72(4):433-52. Epub 2008 Feb 20.

Lung involvement in juvenile onset recurrent respiratory papillomatosis: a systematic review of the literature.

[Gélinas JF](#), [Manoukian J](#), [Côté A](#).

Respiratory Medicine Division and Otolaryngology Division, The Montreal Children's Hospital, McGill University Health Centre, 2300 Tupper, D-380, Montreal, Canada H3H 1P3.

OBJECTIVES: Determine the exact incidence of pulmonary involvement in recurrent respiratory papillomatosis (RRP); explore available treatments and their effectiveness; determine the characteristics of cases that progress to lung cancer. DATA SOURCES: MEDLINE, EMBASE, and the Cochrane Library databases between 1966 and 2007; reference lists of retrieved publication. STUDY SELECTION: Studies investigating recurrent respiratory papillomatosis with lung involvement. Age limited to 20 years of age to qualify for the diagnosis of juvenile-onset RRP. DATA EXTRACTION: Data pertaining to study design, population demographics, risk factors, site of involvement, investigation including the determination of the human papillomavirus type, treatment, and outcomes including the development of cancer. DATA SYNTHESIS: No randomized control trials were retrieved. Hundred and one studies met our inclusion criteria (23 cohorts, 4 case series, 72 case reports, 2 open trials) with 161 cases of lung involvement identified. From the cohort studies we could estimate the incidence of lung involvement in RRP at 3.3%. The incidence of cancer in cases with lung involvement was 16%. We could not draw conclusions regarding treatment effectiveness in lung involvement, as that was not evaluated except in case studies. It would nevertheless appear that Interferon is not effective and the use of intravenous Cidofovir needs to be better evaluated. CONCLUSION: Well-designed, hypothesis-driven randomized control trials and prospective cohort studies are warranted to improve our understanding of

the mechanisms underlying the development of lung involvement in RRP, the risks associated with different HPV types, the efficacy of potential therapeutic options as well as the risk of progression to cancer.

PMID: 18281102 [PubMed - indexed for MEDLINE]

[Curr Opin Otolaryngol Head Neck Surg.](#) 2008 Feb;16(1):86-90.

Cidofovir: to use or not to use?

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PURPOSE OF REVIEW: Cidofovir is an antiviral agent that has been used increasingly in the last decade as an adjuvant therapy for recurrent respiratory papillomatosis. It has been used in patients with moderate to severe recurrent respiratory papillomatosis requiring frequent surgical intervention or if there is evidence of distal spread. Intralesional administration after surgical debulking delivers the medication directly to the site of disease and is thought to have fewer systemic side effects than intravenous infusion. This review examines recent publications for evidence of safety and efficacy. **RECENT FINDINGS:** Despite its growing popularity, the potential risks related to cidofovir use in recurrent respiratory papillomatosis have not been well documented. It is known to be nephrotoxic when administered intravenously and there remains concern that cidofovir has carcinogenic potential based on animal studies (mammary adenocarcinoma in rats). A review of the literature reveals no randomized controlled trials, one case-control study, multiple case series and case reports only. Study populations are small, however complete response rates have consistently been reported in approximately 60%. **SUMMARY:** Based on current opinion and research, it is likely that intralesional cidofovir will continue to have a role in the management of moderate to severe recurrent respiratory papillomatosis. Further studies are required to assess long-term outcomes.

PMID: 18197029 [PubMed - indexed for MEDLINE]

[Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi.](#) 2007 Sep;21(18):825-7, 830.

[The expressions and significance of CK2 in normal laryngeal mucosa, laryngeal precancerosis and laryngeal squamous cell carcinoma]

[Article in Chinese]

[Wu L](#), [Liu B](#).

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OBJECTIVE: To investigate the expression of protein kinase CK2 and its relationship with the development, progress, invasion and metastasis of squamous cell carcinoma of larynx (LSCC). **METHOD:** Immunohistochemical SP staining method was used to assess the expression of CK2 in 18 cases of normal laryngeal mucosa, 14 cases of polyp of vocal cord, 11 cases of larynx papilloma and 50 cases of LSCC patients. And RT-PCR was used to detect the expression of CK2alpha mRNA and CK2beta mRNA in 50 cases of LSCG patients. The relationship between CK2alpha and CK2p was evaluated. **RESULT:** The positive expression rate of CK2alpha and CK2beta in normal laryngeal mucosa, polyp of vocal cord and tissues close to carcinoma by 1.0 cm, nonmetastatic lymph nodes were lower than that in tissues close to carcinoma by 0.5 cm and laryngeal papilloma. The positive expression rate of CK2alpha and CK2beta in laryngeal carcinoma and metastatic lymph nodes were the highest among the groups. The expression rate of CK2alpha and CK2beta in tissues of laryngeal carcinoma and metastatic lymph nodes of neck was significantly higher than that of laryngeal papilloma and tissues close to carcinoma by 0.5 cm ($P < 0.05$). In the group of LSCC, the expression of CK2alpha in G2 and in G3 was significantly higher than that in G1 ($P < 0.05$). While the age of the patients, TNM stage and lymphatic metastasis didn't change in the expression of CK2alpha obviously. The expression of CK2beta correlates to the differentiation grading and lymphatic metastasis in LSCC patients, but not to the age and TNM stage. The result from RT-PCR was highly consistent with that from immunohistochemical SP staining. There was a positive correlation between the expression of CK2alpha in LSCC patients and that of CK2beta. **CONCLUSION:** The over expression of protein kinase CK2 may be an accelerator to the formation and development of LSCC. Protein kinase CK2 may be one of the predictors for the malignant grade of LSCC. To inhibit the over expression might be new therapeutic methods for LSCC.

PMID: 18062282 [PubMed - in process]

[Tuberk Toraks](#). 2007;55(3):299-302.

Recurrent laryngeal papillomatosis with bronchopulmonary spread in a 70-year-old man.

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Recurrent laryngeal papillomatosis (RRLP) which is characterized by wart like growths in the larynx is a rare benign disease seen in children and young adults and a few cases are reported in old aged adults. The spread of RRLP throughout the respiratory tract occurs rarely; and involvement of the distal bronchi, bronchioles, and lung parenchyma is very rare. We report a case of tracheobronchial and pulmonary spread of RRLP in a 70-year-old man after two previous surgeries. Despite the rarity of this disease in adults, the correct diagnosis may be suggested by a characteristic combination of clinical, radiographic, and pathologic features.

PMID: 17978930 [PubMed - indexed for MEDLINE]

[Laryngoscope](#). 2008 Jan;118(1):50-5.

High incidence of malignant transformation of laryngeal papilloma in Taiwan.

[Lee LA](#), [Cheng AJ](#), [Fang TJ](#), [Huang CG](#), [Liao CT](#), [Chang JT](#), [Li HY](#).

Department of Otolaryngology, Chang Gung Memorial Hospital, Chang Gung University, 5 Fu-Shin Street, Kweishan, Taoyuan, Taiwan.

OBJECTIVES: Papillomas of the larynx include solitary laryngeal papilloma and recurrent respiratory papillomatosis. This study investigated the incidence of malignant transformation and assessed possible risk factors for laryngeal papillomas. **STUDY DESIGN:** A prospective, longitudinal study. **METHODS:** Twenty-six consecutive laryngeal papilloma patients were prospectively studied for 5 or more years, and each patient was periodically examined at 3 to 6 month intervals. A detailed epidemiologic questionnaire was administered at the initial visit. After enrollment, tissue obtained during each laryngeal surgery was examined by polymerase chain reaction assay for human papilloma virus (HPV) and typing. **RESULTS:** During 237 person-years of follow-up, six new, pathologically confirmed cases of laryngeal carcinoma were ascertained (incidence 2.5/100 person-years), and all were associated with HPV-6 or HPV-11. Malignant transformation revealed no correlation with the following: age less than 3 years at diagnosis, sex, history of tobacco use, history of alcohol consumption, family history of laryngeal cancer, or type of laryngeal papilloma. Laryngeal papilloma without demonstrable HPV DNA was the only significant risk factor for malignant transformation ($P < .05$). The cumulative risk of malignant transformation in subjects without demonstrable HPV DNA was significantly higher than that in HPV-positive patients (relative risk, 8.0; 95% confidence interval, 1.1-60.3; $P = .05$). **CONCLUSIONS:** A relatively high incidence of malignant transformation of laryngeal papilloma was noted in Taiwanese patients. Patients without demonstrable HPV DNA require more frequent follow-up and may

benefit from anti-HPV vaccinations.

PMID: 17975511 [PubMed - indexed for MEDLINE]

[Cancer Detect Prev.](#) 2007;31(4):276-81.

Human papilloma virus (HPV)-associated gynecological alteration in mothers of children with recurrent respiratory papillomatosis during long-term observation.

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BACKGROUND: Human papilloma virus (HPV) is one of the most frequently observed sexually transmitted infections. The study' purpose was to investigate the relation between a mother's gynecological history and the local status of her child with recurrent respiratory papillomatosis (RRP). **METHODS:** Forty-two patients enrolled in a prospective multicenter study between 1983 and 1990. The study included patients with juvenile-onset and adult-onset RRP. All patients underwent surgery and treatment with alpha-interferon. Thirty-eight patients were followed up until 31.01.2006. Twenty-five mothers of these patients participated in a parallel prospective study of genital HPV infection. In 1989-1990, all received a routine gynecological examination, an expanded colposcopy, a Pap smear, and a cervical biopsy. The mothers were followed up until February 2006. **RESULTS:** 74% of patients with RRP were the first-born children. Five (20%) mothers had condylomata acuminata, newly diagnosed during pregnancy. Indicators of HPV infection such as koilocytes, koilocytotic dysplasia and condyloma acuminatum were revealed cytologically in 17% of cases and histologically in 71.4% of cases. Six (24%) of mothers had had a hysterectomy. HPV type 11 was prevalent in the children of mothers who had had a hysterectomy. Among the patients with juvenile-onset RRP, the death rate from squamous cell carcinoma of the lung was significantly higher in those patients whose mothers had a hysterectomy ($p=0.028$). **CONCLUSIONS:** Mothers of patients with RRP demonstrated cytological and histological indicators of HPV infection in the genital tract. An adverse outcome of the disease in the child was associated with adverse gynecological history in the mother.

PMID: 17935912 [PubMed - indexed for MEDLINE]

[J Natl Med Assoc.](#) 2007 Sep;99(9):1068-70.

Comment in:

- [J Natl Med Assoc.](#) 2008 Jan;100(1):149.

Pneumomediastinum and retroperitoneal air after removal of papillomas with the microdebrider and jet ventilation.

[Sims HS](#), [Lertsburapa K](#).

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OBJECTIVE: To discuss the complication of pneumothorax from alveolar rupture after transtracheal high-frequency jet ventilation and to present a case of pneumothorax, pneumomediastinum and pneumoperitoneum after jet ventilation coupled with use of the microdebrider. **METHOD:** Detailed case report. **RESULTS:** Unilateral pneumothorax, subcutaneous emphysema, pneumomediastinum and retroperitoneal air discovered after jet ventilation for removal of airway papillomas resolved with conservative management. **DISCUSSION:** We discuss the difference between the respective patterns of air seepage in a peripheral alveolar injury versus a probable microperforation in the trachea. We also review the epidemiology of this rare disorder and its incidence in the African-American community. **CONCLUSION:** The recurrent nature of this disorder mandates multiple surgical procedures. Great care must be taken to eradicate disease and avoid complications. Pneumomediastinum in this setting can be managed conservatively.

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Long-term results of surgical treatment for recurrent respiratory papillomatosis.

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CONCLUSIONS: The presented results add further support to the observation that laser microsurgery is the preferential surgical treatment for recurrent respiratory papillomatosis (RRP). A meticulous follow-up for early recognition of local recurrence and malignant

transformation is recommended. OBJECTIVES: Endoscopic microsurgery continues to be the treatment of choice for RRP. The aim of this study was to evaluate the outcome of patients treated surgically. We focused on demographic data, recurrence rates, and treatment-related complications. PATIENTS AND METHODS: The charts of 194 patients treated at our institution between 1963 and 1993 were analyzed retrospectively. RESULTS: In all, 64 patients (33%) underwent a total of 137 operations using the CO2 laser; 130 patients (67%) underwent a total of 565 microlaryngeal operations by surgery with cold instruments. Five percent of the patients treated with conventional microlaryngeal surgery and none of the patients treated with laser surgery required tracheostomy ($p < 0.05$). Postoperative glottic webs and scar formations were found in 6% of all patients after laser surgery and 20% after conventional surgery ($p < 0.05$). The different methods of treatment did not affect the rate of recurrence ($p = 0.61$) Malignant transformation or secondary airway carcinoma were observed in 4% of all patients.

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[J Paediatr Child Health](#). 2007 Sep;43(9):579-80.

Do human papillomavirus vaccines have any role in newborns and the prevention of recurrent respiratory papillomatosis in children?

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No abstract available.

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[Identification of human papilloma viruses (HPV) in inflammatory states and ear neoplasms]

[Article in Polish]

[Rydzewski B](#), [Goździcka-Józefiak A](#), [Sokalski J](#), [Matusiak M](#), [Durzyński L](#).

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INTRODUCTION: Human Papilloma Virus has a strong relation to oropharyngeal mucosa and is considered to be responsible for a wide range of upper respiratory tract pathologies, like laryngeal papilloma. There's a hypothesis, that it plays a significant role in middle ear chronic inflammations and neoplasm's. MATERIAL AND METHODIC. The examination was carried on a group of 53 patients, 39 of which was suffering from granulation tissue chronic otitis media, 7-cholesteatomatous otitis media, 6--middle ear malignant neoplasm, and 1 middle and/or external ear benign neoplasm. The control group consisted of 5 patients operated on: otosclerosis--4 cases and post-traumatic tympanic membrane perforation--1 case. The material was postoperative tissue, like polyps, inflammatory granulation tissue, cholesteatoma masses and malignant neoplasm's tissue. RESULTS: In the whole group of 53 examined cases, HPV DNA was confirmed in 22 cases (41.5%), in that group oncogenic types 16 or 18 in 12 cases (22.6%), and in 14 cases (26.4%) types 6 or 11. In a group of chronic granulomatous otitis media DNA characteristic for Papilloma was identified in 12 cases (25.6%), in it in 9 cases DNA HPV type 6 or 11 was confirmed, and in 7 cases type 16 or 18. Among cholesteatomatous chronic otitis media HPV DNA types 6 or 11 was identified in 70%. In every case of middle ear malignant neoplasm a presence of high-risk DNA Papilloma types 16 or 18 was confirmed. In any case of control group HPV DNA was detected. CONCLUSIONS: The results has been compared with other authors examinations and it is claimed that they confirm the observation, that Human Papilloma Viruses may be a factor, that might play an important role in pathology of chronic otitis media and ear neoplasm's. It is concluded, that differences in percentages of HPV presence in chronic inflammations (70%) and ear neoplasm's may be explained by viral co-infection during bacterial c. o. m. Viral infection probably evolves carcinogenesis, which leads to a neoplastic growth.

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Genital HPVs in the aerodigestive tract: etiologic association with a subset of oropharyngeal/tonsillar cancers and with recurrent respiratory papillomatosis.

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Gastroesophageal reflux in patients with recurrent laryngeal papillomatosis.

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Evidence of a relation between gastroesophageal reflux and pediatric respiratory disorders increases every year. Many respiratory symptoms and clinical conditions such as stridor, chronic cough, and recurrent pneumonia and bronchitis appear to be related to gastroesophageal reflux. Some studies have also suggested that gastroesophageal reflux may be associated with recurrent laryngeal papillomatosis, contributing to its recurrence and severity. AIM: the aim of this study was to verify the frequency and intensity of gastroesophageal reflux in children with recurrent laryngeal papillomatosis. MATERIAL AND METHODS: ten children of both genders, aged between 3 and 12 years, presenting laryngeal papillomatosis, were included in this study. The children underwent 24-hour double-probe pH-metry. RESULTS: fifty percent of the patients had evidence of gastroesophageal reflux at the distal sphincter; 90% presented reflux at the proximal sphincter. CONCLUSION: the frequency of proximal gastroesophageal reflux is significantly increased in patients with recurrent laryngeal papillomatosis.

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532 nm pulsed potassium-titanyl-phosphate laser treatment of laryngeal papillomatosis under general anesthesia.

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OBJECTIVES: Angiolytic lasers have been shown to be an effective treatment strategy for laryngeal papillomatosis. These lasers precisely target hemoglobin within the microcirculation of papillary lesions. We have previously demonstrated the advantages of the fiber-based pulsed 532-nm potassium-titanyl-phosphate (KTP) laser in an office setting (with local anesthesia). This investigation provides the first report of the pulsed-KTP laser during microlaryngoscopy under general anesthesia. **STUDY DESIGN:** A prospective pilot study was performed in 55 adult patients with laryngeal papillomatosis to determine disease response. **METHODS:** During suspension microlaryngoscopy, a solid-state 532 nm pulsed-KTP laser was used (15 ms pulse width, 5.25-7.5 J/pulse maximum output, 2 Hz repetition rate, 0.4 mm fiber, approximately 20-80 J/cm² fluence) to treat laryngeal papillomatosis. All patients underwent postoperative videolaryngoscopy to assess disease regression based on a previously used rating scale. **RESULTS:** Thirty-seven patients underwent 55 procedures during the 18-month study period. Near-term follow-up with an early postoperative evaluation was available in 23 patients (35 procedures). Fourteen patients (20 procedures) were geographically distant and only returned after developing symptoms with significant disease recurrence. Of the 35 procedures in which near-term follow-up was available, 90% or greater disease regression was achieved in 28 of 35 (80%), 75% to 89% disease regression was achieved in 4 of 35 (11%), and 50% to 74% disease regression in 3 of 35 (9%). Anterior-commissure disease was present in 51 of 55 (93%) cases, and no new webbing/synechia occurred. All patients reported that their vocal function improved after treatment. **CONCLUSIONS:** The 532 nm pulsed-KTP laser was effective for treating recurrent respiratory papillomatosis, which was similar to our experience as an office-based procedure.

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Can zinc be an adjuvant therapy for juvenile onset recurrent respiratory papillomatosis?

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OBJECTIVES: To report a severe case of juvenile onset recurrent respiratory papillomatosis (JORRP) controlled by zinc replacement therapy. To review the contemporary adjuvant therapies used in JORRP. **METHODS:** The trial of zinc was described in terms of its effect on the inter-surgical interval, site score and clinical symptoms. Long-term follow-up with dose adjustment was detailed. Articles reporting trials of adjuvant therapies over the past 20 years were reviewed in terms of regimen used, mode of assessment, side effects and final

outcome. RESULTS: Zinc was effective in decreasing the severity of the disease, the rate of relapse and the need for surgery. There was an obvious relation between the dose used and the degree of improvement. Prolonged treatment seems to be needed to sustain the positive effect. No side effects were noticed over a 45-month follow-up period. The literature does support the role of zinc in modulating the immune system. Eight adjuvant therapies were reviewed as published in 40 reports. Interferon was the most used substance. It is definitely effective but often associated with relapse upon discontinuation. The effect of cidofovir was favorable yet not dramatic as initially expected. Other less commonly used therapies showed humble effects. The HspE7 vaccine seems to be promising awaiting further trials.

CONCLUSIONS: Zinc replacement therapy may benefit JORRP patients with zinc deficiency and should be investigated in more cases. Several adjuvant therapies are available for use in JORRP. They are generally beneficial though mostly not curative.

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Gefitinib therapy for life-threatening laryngeal papillomatosis.

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Respiratory papillomatosis is a potentially life-threatening condition that is caused by a human papillomavirus infection of the respiratory epithelium. Patients whose condition is diagnosed at a younger age are at high risk for recurrent aggressive disease. The primary management approach focuses on the removal of the papillomas by surgical debulking, although persistence of the human papillomavirus genome with subsequent recurrence of disease are the typical outcome. In a minority of patients, surgical management must be supplemented with adjuvant medical therapy, with interferon being the best studied and most commonly used. Other adjuvant treatments include photodynamic therapy, indole-3-carbinol, mumps immunization, ribavirin, and cidofovir. Large controlled trials are lacking for all such treatments other than interferon, making it extremely difficult to assess clinical benefit and risk in a systematic fashion at the current time. As with surgical management, viral persistence occurs after treatment with these adjuvant modalities, further contributing to the challenge of treating patients who have this potentially devastating disease. Because epidermal growth factor receptor (EGFR) is expressed in laryngeal papillomas, we elected to try an EGFR tyrosine kinase inhibitor in a patient with end-stage disease in whom other therapies had failed.

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