Abstract Selection

Primary tracheomalacia and gastroesophageal reflex in infants with cough. Callahan, C. W. Tripler Army Medical Center, (MCHK-PE), Honolulu, HI 96859–5000, USA. Clinical Pediatrics (Clinical Paediatrics (Phila)) (1998), December, Vol. 37 (12). Cough is an uncommon sign in infants. Cough may result from the presence of abnormal secretions in the airway or abnormalities of the central airways that affect the infant's ability to clear normal secretions. Tracheomalacia (TM) and gastroesophageal reflux (GER) can both cause cough in infants. Four infants whose cough began in the newborn period were diagnosed with TM and GER. Symptoms of central airway obstruction (homophonous wheeze or tracheal cough) suggested the diagnoses. In three patients, the diagnosis was made by barium esophagraphy and airway fluoroscopy. The infants responded to conservative and medical therapy for GER and to nebulized bronchodilators. Tracheomalacia and GER cause cough in infants that begins in the newborn period. The diagnosis can often be made with studies available to the primary care provider, and the conditions are often responsive to medical management. Author.

Increase in paediatric acute otitis media diagnosed by primary care in two Finnish municipalities 1994–5 versus 1978–9. Joki-Erkkila, V. P., Laippala, P., Pukander, J. Department of Otolaryngology, Medical School, University of Tampere, Finland. *Epidemiology and Infection* (1998) December, Vol. 121 (3). pp. 529–34

In recent decades, several epidemiological studies have been published on acute otitis media (AOM), indicating that the occurrence of AOM is increasing. However, the comparison between the surveys is complicated and biased by several factors, e.g. variable study demography and design and dissimilar diagnostic criteria. The present study was performed with an identical set-up in 1978–9 and 1994–5 to find out potential changes in the occurrence of AOM. All the attacks of AOM among children under 10 years diagnosed by a physician during the 12-month periods 1 June, 1978 to 31 May 1979 and 1 June 1994 to 31 May 1995 were registered retrospectively in two Finnish municipalities. The incidence rate (total number of AOM attacks per 100 child years) was 19 (95 per cent CI 18–21) in 1978–9 and 32 (95 per cent CI 30–34) in 1994–5. The increase in the occurrence of AOM was 68 per cent (95 per cent CI 53-79 per cent, p<0.0001). Author.

The outcome of patients with upper airway obstruction transported to a regional paediatric intensive care unit. Durward, A. D., Nicoll, S. J., Oliver, J., Tibby, S. M., Murdoch, I. A. Department of Paediatric Intensive Care, Guy's Hospital, London, UK. European Journal of Pediatrics (1998) November, Vol. 157 (11), pp. 907-11. The diagnoses, transfer, management and outcome of patients with upper airway obstruction (UAO) admitted from district general hospitals (DGH) to a regional paediatric intensive care unit were retrospectively reviewed over a 3.5-year period. Sixtyseven patient episodes were analysed. Fifty-two cases (78 per cent) underwent tracheal intubation prior to transport with a low morbidity for both procedures. The most common diagnosis was viral croup (n = 34, 51 per cent) with a median duration of intubation of five days, with subglottic stenosis being the next most common category (n = 10, 15 per cent), median duration of intubation seven days. Inhaled budesonide was used prior to intubation in 12 (35 per cent) of those with croup, and inhaled bronchodilators in 28 per cent, possibly reflecting diagnostic uncertainty. Patients with croup treated with budesonide were significantly less likely to require intubation (p = 0.04). The reintubation rate for patients with viral croup was uncomfortably high at 16 per cent (4/25) despite the routine use of prednisolone throughout the intubation period. Successful extubation of patients with viral croup could not be predicted by age (p =0.31), length of intubation (p = 0.94), endotracheal tube size, (p = 0.60) abnormalities on the chest X-ray (p = 1.0), or presence

of secondary bacterial infection (p=0.23). CONCLUSION: Although viral croup remains the most common diagnostic category presenting at the DGH level with severe UAO, a wide range of other diagnoses is seen. Despite clear evidence of benefit, steroid administration to children presenting at the DGH with viral croup has not become routine practice. Once intubated, no reliable predictors of successful extubation were found amongst this patient group. Author.

Otological problems in children with Turner's syndrome. Stenberg, A. E., Nylen, O., Windh, M., Hultcrantz, M. Department of Otorhinolaryngology, Karolinska Hospital, Stockholm, Sweden. Hearing Research (1998) October, Vol. 124 (1-2), pp. 85-90. Ear and hearing disorders are common problems among girls and women with Turner's syndrome. During infancy and childhood the girls often suffer from repeated attacks of acute otitis media and later in life the women frequently complain of a rapid onset of social hearing problems due to sensorineural hearing impairment. A study of 56 girls aged four to 15 years with Turner's syndrome was performed to investigate the prevalence of eardrum pathology and hearing impairment in young children and teenagers with Turner's syndrome. A possible relation to karyotype was also investigated. A high prevalence (61 per cent) of recurrent acute otitis media was found in the study group and 32 per cent had been treated with ventilation tubes. Fifty-seven per cent showed eardrum pathology, such as effusion, myringosclerosis, atrophic scars, retraction pockets and perforations. Auricular anomalies were noted in 23 per cent of cases, most commonly in the 45, X group. The audiometric analysis showed conductive hearing loss (air-bone gap >10 dB HL) in 43 per cent and the typical sensorineural dip in the middle frequencies was found in 58 per cent of the girls, of whom the youngest was six years old. Four per cent were using hearing aids. The data of this study further confirm that the dip is progressive over time and may be detectable as early as at the age of six, giving a chance to predict a future hearing loss. The findings emphasize the importance of regular otological examinations and audiological evaluations of all girls with Turner's syndrome early in life. Author.

Daily tympanometry in children during the cold season: association of otitis media with upper respiratory tract infections. Moody, S. A., Alper, C. M., Doyle, W. J. Department of Pediatric Otolaryngology, Children's Hospital of Pittsburgh, PA 15213, USA. International Journal of Pediatric Otorhinolaryngology (1998) October 2, Vol. 45 (2), pp. 143–50.

The causal association between otitis media and viral upper respiratory tract infections (URI) suggests that early intervention during the course of a viral URI could prevent many episodes of otitis media. However, the feasibility of this approach can not be assessed at present since many aspects of the epidemiology and natural history of URI-associated otitis media are undefined. To address this deficiency, daily monitoring of middle ear status (tympanometry) and cold symptoms and weekly pneumatic otoscopy were done on a pilot cohort of 20 children. These children, between the ages of two and six, were followed from November 1996 to April 1997. Compliance with symptom diaries was 85 per cent, with tympanograms was 90 per cent, and with weekly physician visits was 70 per cent. During the study period, there were 53 'colds' (average 2.65 per child) and 28 new episodes of middle ear effusion (10 unilateral and nine bilateral). Overall, 47.3 per cent of the tympanograms were Type A, 17.2 per cent Type C1, 9.4 per cent Type C2, and 21.8 per cent Type B. Children who developed MEE during the study spent more time with abnormal MEP (either MEP < -150 or flat) during both cold and healthy days than children who did not develop MEE. Temporally, during colds, high negative pressures preceded the development of Type B tympanograms in children who developed middle ear effusions. Children who did not develop effusions still had high

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negative pressures during colds, but recovered to a normal pressure within days. These observations document the feasibility of this investigational format for study of the sequential changes in middle ear status before, during and after a URI. Author.

Decrease in cranial nerve complications after radiosurgery for acoustic neuromas: a prospective study of dose and volume. Miller, R. C., Foote, R. L., Coffey, R. J., Sargent, D. J., Gorman, D. A., Schomberg, P. J., Kline, R. W. Division of Radiation Oncology, Mayo Clinic and Mayo Foundation, Rochester, MN 55905, USA. *International Journal of Radiation, Oncology, Biology, Physics* (1999), January 15, Vol. 43 (2), pp. 305–11.

PURPOSE: To determine whether tumour control can be maintained, and cranial nerve complications decreased by reducing the radiosurgical dose to acoustic neuromas. METHODS AND MATERIALS: Forty-two consecutive patients with acoustic neuromas were treated prospectively using an initial standarddose protocol in which the tumour-margin dose (50 per cent isodose) was 20, 18, and 16 Gy for tumour diameters < or =2 cm, 2.1-3 cm, and 3.1-4 cm, respectively. After analysis of tumour control and complications, the next 40 patients were treated using a reduced-dose protocol in which the tumour-margin dose was 16, 14, and 12 Gy for tumour volumes $< or = 4.2 \text{ cm}^3$, $4.2-14.1 \text{ cm}^3$, and > or = 14.1 cm³, respectively. RESULTS: Median follow-up was 2.3 years (range 0.1-6) for 80 of 82 patients. The actuarial incidence (Kaplan-Meier) of facial neuropathy at two years was 38 per cent (95 per cent confidence interval (CI), 23-53 per cent) for the standard-dose protocol and eight per cent (95 per cent CI, 0-17 per cent) for the reduced-dose protocol (p = 0.006). Univariate analysis revealed an association between risk of facial neuropathy and use of CT planning, higher radiosurgical dose, and neurofibromatosis, type 2. Multivariate analysis revealed that the only factor associated with increased risk of post-treatment facial neuropathy was a tumour margin dose > or = 18 Gy. The incidence of trigeminal neuropathy at two years was 29 per cent (95 per cent CI, 15-43 per cent) for the standard-dose protocol and 15 per cent (95 per cent CI, three to 27 per cent) for the reduced-dose protocol (p = 0.17). Univariate analysis revealed an association between maximal tumour diameter and increased risk of trigeminal neuropathy; multivariate analysis revealed no additional statistically significant associations between tumour and dosimetric and patient characteristics and risk of trigeminal neuropathy. Two tumours in the standard-dose protocol required salvage surgery for progression. To date, no tumour in the reduced-dose protocol has shown progression. CONCLUSION: Our analysis suggests that a tumour margin dose of > or = 18 Gy is the most significant risk factor for facial nerve complications after acoustic neuroma radiosurgery. Patients receiving a minimal tumour dose of < or =16 Gy are at significantly lower risk for permanent facial neuropathy after radiosurgery. Longer follow-up is required before definitive conclusions can be made about the ultimate rate of tumour control using reduced radiosurgical doses.

Mesothelial cell proliferation in the scala tympani: a reaction to the rupture of the round window membrane. Sone, M. Department of Otorhinolaryngology, Nagoya University School of Medicine, Japan. Nagoya Journal of Medical Science (1998), October, Vol. 61 (3-4), pp. 125-30. The inner layer of the round window membrane is composed of

The inner layer of the round window membrane is composed of mesothelial cells and this mesothelial cell layer extends to the scala tympani. This study describes the histopathologic findings of temporal bone analysis from a patient with bilateral perilymphatic fistula of the round window membrane. The left ear showed proliferation of mesothelial cells in the scala tympani of the basal turn adjoining the round window membrane. This cell proliferation is thought to be a reaction to the rupture of the round window membrane. Author.

Prevalence of various respiratory viruses in the middle ear during acute otitis media (see comments). Heikkinen, T., Thint, M., Chonmaitree, T. Department of Pediatrics, University of Texas Medical Branch, Galveston 77555-0371, USA. New England Journal of Medicine (1999), January 28, Vol. 340 (4), pp. 260-4. Comment in: New England Journal of Medicine (1999) January 28, Vol. 340 (4): 312-4.

BACKGROUND: Vaccines against respiratory viruses may be able to reduce the frequency of acute otitis media. Although the

role of respiratory viruses in the pathogenesis of acute otitis media is well established, the relative importance of various viruses is unknown. METHODS: We determined the prevalence of various respiratory viruses in the middle-ear fluid in 456 children (age, two months to seven years) with acute otitis media. At enrollment and after two to five days of antibiotic therapy, specimens of middleear fluid and nasal-wash specimens were obtained for viral and bacterial cultures and the detection of viral antigens. The viral cause of the infections was also assessed by serologic studies of serum samples obtained during the acute illness and convalescence. RESULTS: A specific viral cause of the respiratory tract infections was identified in 186 of the 456 children (41 per cent). Respiratory syncytial virus was the most common virus identified in middle-ear fluid: it was detected in the middle-ear fluid of 48 of the 65 children (74 per cent) infected by this virus (p < or = 0.04for the comparison with any other virus). Parainfluenza viruses (15 of 29 children (52 per cent)) and influenzaviruses (10 of 24 children (42 per cent)) were detected in the middle-ear fluid significantly more often than enteroviruses (three of 27 children (11 per cent)) or adenoviruses (one of 23 children four per cent)) (p < or = 0.01 for all comparisons). CONCLUSION: Respiratory syncytial virus is the principal virus invading the middle ear during acute otitis media. An effective vaccine against upper respiratory tract infections caused by respiratory syncytial virus may reduce the incidence of acute otitis media in children. Author.

Edema in the upper airway in patients with obstructive sleep apnea syndrome. Anastassov, G. E., Trieger, N. Mount Sinai School of Medicine. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics (1998) December, Vol. 86 (6), pp. 644–7.

OBJECTIVE: The purpose of this study was to investigate the histologic alterations in the upper airway in patients with obstructive sleep apnea syndrome. STUDY DESIGN: Surgical specimens were obtained during non-laser-assisted uvulopalatopharyngoplasty from five adult patients (four male and one female) with polysomnographically confirmed obstructive sleep apnea syndrome. RESULTS: In all of the specimens, interstitial edema was present with mild inflammatory reaction. Fat was not at all prominent. CONCLUSIONS: It is confirmed histologically that there is edema present in the upper airway in patients with obstructive sleep apnea syndrome. It is uncertain whether this edema is one of the causative mechanisms of the obstruction or a consequence of the syndrome. Author.

The relationship between temporomandibular disorders and stress-associated syndromes. Korszun, A., Papadopoulos, E., Demitrack, M., Engleberg, C., Crofford, L. Department of Psychiatry and School of Dentistry, University of Michigan, Ann Arbor 48109–0840, USA. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics (1998) October, ol. 86 (4), pp. 416–20.

OBJECTIVES: The purpose of this study was to determine the comorbidity of temporomandibular disorders and other stressassociated conditions in patients with chronic fatigue syndrome and fibromyalgia. STUDY DESIGN: Of 92 patients who fulfilled the criteria for chronic fatigue syndrome or fibromyalgia (or both), 39 (42 per cent) reported a prior diagnosis of temporomandibular disorder. Further questionnaires were sent to the members of this group, and 30 patients responded. RESULTS: Of the original 92 patients, of whom 42 per cent reported temporomandibular disorders, 46 per cent had histories of irritable bowel syndrome, 42 per cent of premenstrual syndrome, and 19 per cent of interstitial cystitis. Of the patients with temporomandibular disorders, the great majority reported an onset of generalized symptoms before the onset of facial pain. Despite this, 75 per cent had been treated exclusively for temporomandibular disorders, usually with bite splints. CONCLUSIONS: Patients appearing for treatment with chronic facial pain show a high comorbidity with other stress-associated syndromes. The clinical overlap between these conditions may reflect a shared underlying pathophysiologic basis involving dysregulation of the hypothalamic-pituitary-adrenal stress hormone axis in predisposed individuals. A multidisciplinary clinical approach to temporomandibular disorders would improve diagnosis and treatment outcomes for this group of patients. Author.

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Incidence of secretory otitis media following maxillectomy. Talmi, Y. P., Mardinger, O., Horowitz, Z., Yahalom, R., Wolf, M., Peleg, M., Pfeffer, M. R., Teicher, S., Kronenberg, J. Department of Otolaryngology - Head and Neck Surgery, Chaim Sheba Medical Center, Tel Hashomer, Israel. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics* (1998) November, Vol. 86 (5), pp. 524–8.

OBJECTIVE: The prupose of this investigation was to determine the incidence and characteristics of secretory otitis media after maxillectomy procedures. STUDY DESIGN: Retrospective chart analysis was performed with the cases of 49 patients who underwent maxillectomy for tumour in the Departments of Otolaryngology - Head and Neck Surgery and Oral and Maxillofacial Surgery between the years 1990 and 1996. RESULTS: In 10 patients (20 per cent), secretory otitis media manifested itself from one week to six months after surgery; one patient developed a central perforation with chronic otitis media. Nearly one third of patients who underwent total maxillectomy had secretory otitis media. Six patients (eight ears) required insertion of ventilation tubes. CONCLUSIONS: Patients undergoing total and partial maxillectomies are prone to occurrences of secretory otitis media. Insertion of ventilation tubes easily resolves the problem. Preoperative and routine postoperative patient follow-up should always include otoscopy and audiometry, and tympanometry should be performed when warranted. Author.

Otitis media and child development: should we worry? Paradise, J. L. Department of Pediatrics, University of Pittsburgh School of Medicine, Children's Hospital of Pittsburgh, PA, USA. jpar@med.pitt.edu. Pediatric Infectious Disease Journal (1998) November, Vol. 17 (11), pp. 1076-83; discussion 1099-100. Persistent middle ear effusion in infancy and early childhood has been blamed for impairments of speech, language, cognition and psychosocial development later in life. Whether that blame is justified remains unresolved and a matter of controversy, because studies of the relationships involved have been limited and often contradictory and because none was designed so as to address the issue of causality. At issue in particular is the common practice of subjecting infants and young children with persistent otitis media with effusion (OME) to tympanostomy tube placement specifically to reduce the risk of developmental impairment. Currently children younger than age three years undergo an estimated 313000 tympanostomy tube placement operations per year, at a cost of about \$750 million. If a causal association between early life OME and later developmental impairment were to be established, answers would also be needed to be questions whether the adverse effects of OME are linear or threshold, whether they are permanent or transient and whether they are preventable by timely tube placement. A prospective study designed to address all of these questions is currently under way at Children's Hospital of Pittsburgh. The study involves enrolling a large, demographically diverse sample of normal infants before two months of age; monitoring them for the presence or absence of otitis media throughout the first three years of life; identifying those in who OME has persisted for specified minimum periods; randomly assigning those subjects either to prompt tube placement or to delayed tube placement if OME persists; and administering a battery of standardized developmental tests to those subjects and to a sample of the others at ages three, four and six years. Details of the study design and procedures are described in this report. Author.

Otoacoustic emissions as a screening test for hearing impairment in children recovering from acute bacterial meningitis. Richardson, M. P., Williamson, T. J., Reid, A., Tarlow, M. J., Rudd, P. T. Bath Unit for Research into Pediatrics, Royal United Hospital, Bath, United Kingdom. *Pediatrics* (1998) December, Vol. 102 (6), pp.1364–8.

OBJECTIVES: To study the efficacy of otoacoustic emissions (OAEs) as a screening test for hearing impairment in children with acute bacterial meningitis. Hearing tests were performed before discharge from the hospital in an attempt to improve coverage and avoid delays in the diagnosis of postmeningitic hearing loss. METHODS: Children with bacterial meningitis were recruited from 21 centres. In the 48 hours before discharge from the hospital, all patients underwent a thorough audiologic assessment consisting of transient evoked OAEs, auditory brainstem responses (ABRs), otoscopy, and tympanometry. Hearing loss was

defined as ABR threshold >/=30 dB. The results of OAE screening were compared with the gold standard of ABR threshold. RESULTS: Of 124 children recruited, we were able to perform both OAEs and ABRs on 110 children. Seven (6.3 per cent) of the 110 children had ABR threshold >/=30 dB; two had sensorineural hearing loss and five had conductive hearing loss. At follow-up, hearing loss persisted in both cases of sensorineural hearing loss and no new cases were identified. All seven children with hearing loss failed the OAE screening test. Ninety-four children with normal hearing thresholds passed the test, and nine failed. Thus, the screening test had a sensitivity of 1.00 (95 per cent confidence interval, 0.59 to 1.00), a specificity of 0.91 (0.85 to 0.97), a positive predictive value of 0.44 (0.20 to 0.70), and a negative predictive value of 1.00 (0.96 to 1.00). CONCLUSIONS: OAE screening in children recovering from meningitis was found to be feasible and effective. The test was highly sensitive and reasonably specific. Inpatient OAE screening should allow early diagnosis of postmeningitic hearing loss and prompt auditory rehabilitation. Author.

Once-daily therapy for streptococcal pharyngitis with amoxicillin. Feder, H. M. Jr., Gerber, M. A., Randolph, M. F., Stelmach, P. S., Kaplan, E. L. Department of Family Medicine and Pediatrics, University of Connecticut School of Medicine, University of Connecticut Health Center, Farmington, Connecticut, USA. Pediatrics (1999) January, Vol. 103 (1), pp. 47–51.

Pediatrics (1999) January, Vol. 103 (1), pp. 47–51.
OBJECTIVE: An orally administered antimicrobial regimen for the treatment of group A beta-hemolytic streptococcal (GABHS) pharyngitis given once rather than multiple times each day would be more convenient and might result in improved patient compliance. The purpose of this study was to evaluate the effectiveness of once-daily amoxicillin in the treatment of GABHS pharyngitis. PATIENTS: Children presenting to a private paediatric office with GABHS pharyngitis. DESIGN: Patients were randomly assigned to receive orally either amoxicillin (750 mg once daily) or penicillin V (250 mg three times a day) for 10 days. Compliance was monitored by urine antimicrobial activity. OUT-COMES: Outcomes were measured by impact on the clinical course, eradication of GABHS within 18 to 24 hours, and bacteriologic treatment failure rate as determined by follow-up throat cultures four to six and 14 to 21 days after completing therapy. GABHS isolates were serotyped to distinguish bacteriologic treatment failures (same serotype as initial throat culture) from new acquisitions (different serotypes). RESULTS: During the 16 months of this study, 152 children between four and 18 years of age (mean 9.9 years) were enrolled; 79 children were randomly assigned to receive once-daily amoxicillin and 73 were assigned to receive penicillin V three times a day. The children in the two treatment groups were comparable with respect to age, duration of illness before initiation of therapy, compliance, and signs and symptoms at presentation. There was no significant difference in the clinical or bacteriologic responses of the patients in the two treatment groups at the 18- to 24-hour follow-up visit. Bacteriologic treatment failures occurred in four (five per cent) of the 79 patients in the amoxillicin group and in eight (11 per cent) of the 73 patients once-daily amoxillin therapy is as effective as penicillin V therapy given three times a day for the treatment of GABHS pharyngitis, and if confirmed by additional investigations, once-daily amoxicillin therapy could become an alternative regimen for the treatment of this disease. Author.

Metastatic head and neck cancer: role and usefulness of FDG PET in locating occult primary tumours. Assar, O. S., Fischbein, N. J., Caputo, G. R., Kaplan, M. J., Price, D. C., Singer, M. I., Dillon, W. P., Hawkins, R. A. Department of Radiology, University of California Medical Center, San Prancisco 94143, USA. Radiology (1999) January, Vol. 210 (1), pp. 177–81.

PURPOSE: To assess the usefulness of 2-(fluorine-18) fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) of the head and neck in locating occult primary lesions in patients with metastatic cervical adenopathy. MATERIALS AND METHODS: Seventeen patients with metastatic cervical adenopathy of unknown primary origin were referred for FDG PET of the head and neck. All patients had undergone correlative anatomic imaging within one month of FDG PET. Surgical, clinical and histopathologic findings were used to assess the performance of FDG PET. RESULTS: Increased apical lung uptake at FDG PET led to a biopsy-proved diagnosis of primary lung cancer in two

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patients. Of the remaining 15 patients, 10 had a focus of increased activity; directed biopsy of these sites led to confirmation of a primary carcinoma in seven patients. Correlative anatomic imaging failed to demonstrate the primary sites of disease in two of these seven patients. None of the five patients with negative FDG PET studies have manifested evidence of a primary site of disease during follow-up of eight to 42 months (mean, 29 months). CONCLUSION: FDG PET allows effective localization of the unknown primary site of origin in metastatic head and neck cancer and can contribute substantially to patient care. Author.

Criteria for grading in the Llubijana classification of epithelial hyperplastic laryngeal lesions. A study by members of the Working Group on Epithelial Hyperplastic Lesions of the European Society of Pathology. Hellquist, H., Cardesa, A., Gale, N., Kambic, V., Michaels, L. Department of Pathology 2, University Hospital, Linkoping, Sweden. *Histopathology* (1999), Vol. 34, pp. 226–233.

AIMS: To validate histological criteria for the grading of epithelial hyperplastic laryngeal lesions (EHHL) (dysplastic laryngeal

lesions), we used a system that had been devised and tested in Ljubljana, Slovenia over many years and was felt to be more appropriate to laryngeal pathology than is the commonly-used model of intraepithelial neoplasia in the cervix. METHODS AND RESULTS: Vocal cord biopsies of 45 patients with a broad spectrum of EHLL were reviewed. Detailed histological criteria were formulated for each of the four grades of EHLL in the Ljubljana classification, comprising simple hyperplasia (benign spinous layer augmentation), abnormal hyperplasia (benign basal and parabasal layer augmentation), atypical hyperplasia (risk for malignancy) and carcinoma in situ (actually malignant, but without invasion). CONCUSIONS: Using these criteria a high degree of concordance of histological diagnoses of grading levels for the Ljubljana classification was achieved between the pathologists of the Working Group. The system was found to be more precise for routine diagnostic work than the others in vogue. The different grades of the Llubljana classification correspond to significantly different levels yielded in each grade by the semi-objective methods of quantitative morphometry and immunohistochemistry.