

Abstract Selection

Contralateral differences among biomarkers determined by a modified nasal lavage technique after unilateral antigen challenge.

Wihl, J. A., Baumgarten, C. R., Petersson, G. Department of Otorhinolaryngology, Malmo University Hospital, Sweden. *Allergy* (1995) April, Vol. 50 (4), pp. 308–15.

The concentration of biomarkers from vessels and inflammatory cells in nasal lavage fluid reflects the degree of hyperresponsiveness in patients with allergic rhinitis. The lavage has usually been performed of both nasal cavities together after prewashings and administration of decongestants. To improve the technique, we introduced a modification involving lavage of the nasal cavities separately without any prewashings or decongestants. We challenged 20 rhinitic subjects sensitive to timothy unilaterally with timothy extract. In nasal lavages performed before, immediately after, and 6 h after the challenge, we determined the concentrations of albumin, histamine, bradykinin, TAME (N-alpha-tosyl-L-arginine methyl ester)-esterase, and leukotriene C4 (LTC4). In eight subjects, the procedure was repeated one and two weeks later. After the challenge, albumin, bradykinin, TAME-esterase, and LTC4 in the nasal lavage fluid increased on the ipsilateral side but not on the contralateral side. Histamine did not increase after antigen challenge. After 6 h, the biomarkers were not increased. The concentrations of biomarkers did not differ between sides before the challenge and not between visits. Thus, the modified nasal lavage technique is reliable and improved compared to previous methods because it involves reproducible determinations of different biomarkers, and it is simple and easy to perform. Author.

The efficacy and tolerability of fluticasone propionate aqueous nasal spray in children with seasonal allergic rhinitis. Boner, A., Sette, L., Matinati, L., Sharma, R. K., Richards, D. H. Pediatric Department, University of Verona, Italy. *Allergy* (1995) June, Vol. 50 (6), pp. 498–505.

Fluticasone propionate aqueous nasal spray (FPANS) contains fluticasone propionate, which is a new topically active glucocorticoid with approximately twice the potency of beclomethasone dipropionate. In this European multicentre study, 143 children with seasonal allergic rhinitis were recruited: 47 received FPANS 100 micrograms once a day (od), 46 received FPANS 200 micrograms od, and 50 patients received placebo od, for four weeks. Treatment efficacy was assessed using diary card nasal symptom scores for sneezing, rhinorrhoea, blockage and itching, and eye watering/irritation. Patients receiving FPANS 100 micrograms or FPANS 200 micrograms demonstrated statistically significant improvements in median nasal symptom scores in all the symptoms recorded, when compared with placebo. There were no statistically significant differences between the FPANS 100 micrograms and FPANS 200 micrograms groups in improvement in nasal symptom scores. There was no effect on eye watering/irritation symptoms which could be attributed to either FPANS 100 micrograms or FPANS 200 micrograms when compared with placebo. Use of rescue antihistamine medication was significantly reduced in the FPANS 100 micrograms group when compared with placebo. The adverse events profile was similar in all three treatment groups, and the events reported were generally mild and related to the patients' rhinitis. Author.

Difficult direct laryngoscopy in patients with cervical spine disease. Calder, I., Calder, J., Crockard, H. A. Department of Anaesthesia, National Hospital for Neurology and Neurosurgery, London. *Anaesthesia* (1995) September, Vol. 50 (9), pp. 756–63.

Two hundred and fifty-three patients were examined before surgery for cervical spine disease. The grade of glottic visibility was determined at direct laryngoscopy, using the classification

proposed by Cormack and Lehane. The overall prevalence of difficulty (grades 3 and 4) was 20 per cent. Patients with disease that includes the occipito-atlanto-axial complex have a higher prevalence of difficulty than those with disease below the axis vertebra. Occipito-atlanto-axial disease is associated with poor mandibular protrusion. The best single predictor of difficulty was reduced separation of the posterior elements of the first and second cervical vertebrae on lateral radiographs. The Mallampati examination was the best single predictor on physical examination. The Mallampati may be an indicator of poor cranio-cervical extension. Difficulty was rare in patients with class A mandibular protrusion, and invariable in patients with class C protrusion. Author.

A prospective study of anaesthesia for quinsy tonsillectomy. Fagan, J. J., James, M. F. Department of Otolaryngology, Grootte Schuur Hospital, Observatory, Cape Town, South Africa. *Anaesthesia* (1995) September, Vol. 50 (9), pp. 783–5.

A prospective study of 50 adult quinsy tonsillectomy anaesthetics was performed. There were no significant anaesthetic or surgical complications and the mean intra-operative blood loss was 176 ml. The Mallampati score did not correlate with the Cormack and Lehane glottic view and there were no difficult intubations. Pre-operative trismus resolved completely during induction in 77.4 per cent of cases. We concluded that the Mallampati grading system is not applicable in quinsies and in cases with palatopharyngeal arch distortion, that trismus in quinsies is due to muscle spasm and resolves completely during induction in most cases and that pre-anaesthetic drainage of the abscess together with rehydration and antibiotics are important contributing factors to safe anaesthesia for quinsy. Author.

Correct positioning of the epiglottis for application of the Brain laryngeal mask airway. Fukutome, T. Department of Anaesthesia, Kyushu Koseinenkin Hospital, Kitakyushu, Japan. *Anaesthesia* (1995) September, Vol. 50 (9), pp. 818–9.

Positioning of the epiglottis when the Brain laryngeal mask airway is in place was studied in 20 adult patients, using a new technique of insertion. The laryngeal mask was inserted when the anterior displacement of the mandible extended the epiglottis, thereby providing an excellent airway in all patients. In 10 out of these 20 patients, the conventional technique of insertion revealed an incomplete extension of the epiglottis, and inadequate opening of the laryngeal inlet. It was concluded that the anterior displacement of the mandible during insertion of the laryngeal mask enhances the opening of the larynx, the result being an excellent airway. Author.

Cocaine, lidocaine, tetracaine: which is best for topical nasal anaesthesia? Noorily, A. D., Noorily, S. H., Otto, R. A. Department of Otolaryngology–Head and Neck Surgery, University of Texas Health Science Center, San Antonio 78284-7838, USA. *Anesthesia and Analgesia* (1995) October, Vol. 81 (4), pp. 724–7.

The quality of nasal anaesthesia obtained with three local anaesthetic solutions (4 per cent cocaine, 2 per cent lidocaine in oxymetazoline, and 1 per cent tetracaine in oxymetazoline) was evaluated in a randomized study. Each local anaesthetic mixture was applied to the nasal septum of healthy volunteers using medication-soaked pledgets. Measurements of anaesthetic effect (sensation threshold and pain perception) were made with Semmes-Weinstein monofilaments. Measurements were performed prior to local anaesthetic application and 10 and 70 min after local anaesthetic application. Subjects had greater increases in sensation threshold with tetracaine than with lidocaine or cocaine at both 10 and 70 min ($P < 0.05$). Subjects had greater

decreases in pain perception with tetracaine than with lidocaine or cocaine at both time intervals ($P < 0.05$). Tetracaine mixed with oxymetazoline appears to be a superior topical anaesthetic for nasal procedures. Author.

Effect of ibudilast on ciliary activity of human paranasal sinus mucosa *in vitro*. Schwender, D., Conzen, P., Klasing, S., Finsterer, U., Poppel, E., Peter, K. Institute for Anesthesiology, University of Munich, Germany. *Arzneimittelforschung* (1995) August, Vol. 45 (8), pp. 883–6.

The effect of ibudilast (CAS 50847-11-5, 3-isobutyl-2-isopropylpyrazolo(1,5-a)pyridine, KC-404), an anti-asthmatic drug, on ciliary beat frequency (CBF) of human paranasal sinus mucosa was examined *in vitro*. Ciliary activation was observed after a 10-min exposure to 4.6×10^{-6} mol/l ibudilast. Ibudilast dose-dependently increase CBF at the concentrations ranging from 4.6×10^{-7} mol/l to 4.6×10^{-5} mol/l. Propranolol inhibited ciliary activity induced by ibudilast; however, neither indometacin nor verapamil affected the activation of ibudilast on CBF. Platelet activating factor (PAF) and Leukotriene D4 (LTD4) are chemical mediators inducing mucosal dysfunction and damage. Ibudilast prevented ciliary inhibition induced by PAF and LTD4. These findings indicated that ibudilast activates CBF and inhibits the effect of PAF and LTD4 on ciliated cells, and consequently improves the pathogenesis of allergic disorders such as the inhibited mucociliary transport system and airway hyperresponsiveness. Author.

P6 acupressure reduces symptoms of vection-induced motion sickness. Hu, S., Stritzel, R., Chandler, A., Stern, R. M. Department of Psychology, Humboldt State University, Arcata, CA 95521, USA. *Aviation, Space and Environmental Medicine* (1995) July, Vol. 66 (7), pp. 631–4.

PURPOSE: The purpose of the study was to examine the effectiveness of P6 acupressure on nausea associated with visually-induced motion sickness. **METHOD:** There were 64 subjects randomly divided into four groups: P6 acupressure, dummy-point acupressure, sham P6 acupressure, and control. Each subject sat in an optokinetic drum for a 12-min baseline and 12-min drum rotation period. Subjects' electrogastrograms (EGGs) and subjective symptoms of motion sickness were obtained. **RESULTS:** The results indicated that the subjects in the P6 acupressure group reported significantly less nausea ($F(3,60) = 8.16, p < 0.0001$) during drum rotation period than those in the dummy-point acupressure, sham acupressure, and control groups. The scores for symptoms of motion sickness of the P6 acupressure group were significantly lower than those in the sham acupressure and control groups ($F(3,60) = 3.49, p < 0.02$). Also, the subjects in the P6 acupressure group showed significantly less abnormal gastric myoelectric activity, tachyarrhythmia, than those in the sham acupressure and control groups ($F(3,60) = 2.78, p < 0.04$). However, the subjects in the dummy-point acupressure group did not report significantly fewer symptoms and show less tachyarrhythmia than those in the sham acupressure and control groups. **CONCLUSION:** We conclude that P6 acupressure reduces the severity of symptoms of visually-induced motion sickness and gastric tachyarrhythmia. Author.

Benzalkonium chloride in a decongestant nasal spray aggravates rhinitis medicamentosa in healthy volunteers. Graf, P., Hallen, H., Juto, J. E. Department of Otorhinolaryngology, Sodersjukhuset, Karolinska Institute, Stockholm, Sweden. *Clinical Experiments in Allergy* (1995) May, Vol. 25 (5), pp. 395–400.

A randomized double-blind parallel study with 20 healthy volunteers was performed to research the effect of a preservative in a decongestant nasal spray on the development of rhinitis medicamentosa. Ten subjects received oxymetazoline nasal spray with benzalkonium chloride and the others used oxymetazoline nasal spray without the preservative three times daily for 30 days. Before starting the course of treatment and after its conclusion, recordings of the mucosal surface positions were made with rhinostereometry followed by histamine challenge tests. Symptoms of nasal stuffiness were estimated on visual analogue scales (0–100) in the morning and the evening just before using the nasal spray. After 30 days, rebound swelling and nasal stuffiness were found in both groups. In the group receiving oxymetazoline nasal spray with benzalkonium chloride the mean rebound swelling was 1.1 mm and the estimated mean evening symptom score for nasal

stuffiness was 43. In the group without benzalkonium chloride the corresponding variables were significantly less marked, with a mean rebound swelling of 0.5 mm ($P < 0.05$) and a mean evening symptom score of 25 ($P < 0.05$). The increase in histamine sensitivity in both groups was interpreted as a sign of nasal hyperreactivity. A new type of nasal spray bottle was used that has been shown to prevent bacterial contamination. In conclusion, the long-term use of benzalkonium chloride in oxymetazoline nasal spray accentuates the severity of rhinitis medicamentosa in healthy volunteers. Author.

Benzalkonium chloride in nasal decongestive sprays has a long-lasting adverse effect on the nasal mucosa of healthy volunteers. Hallen, H., Graf, P. Department of Otorhinolaryngology, Karolinska Institute, Soder Hospital, Stockholm, Sweden. *Clinical Experiments in Allergy* (1995) May, Vol. 25 (5), pp. 401–5.

Twenty healthy volunteers participated in the present study on the long-term effects of a nasal decongestive spray composed of either a combination of oxymetazoline nasal spray and benzalkonium chloride or of oxymetazoline nasal spray alone. Three months before the present study the participants had undergone treatment with nasal decongestants for four weeks. Ten of the subjects had been treated with oxymetazoline nasal spray without benzalkonium chloride and 10 of them had been treated with oxymetazoline nasal spray with benzalkonium chloride. In a double-blind study the subjects who had been treated with oxymetazoline nasal spray and benzalkonium chloride were again treated with the same combination of substances as before, and the subjects who had been treated with oxymetazoline nasal spray alone were also treated again with oxymetazoline nasal spray alone, but on this occasion only for 10 days. Three variables were studied before and after the 10 days of treatment, i.e. nasal mucosa congestion, nasal reactivity and symptom scores. It was found that only the subjects who were treated with the combination of oxymetazoline nasal spray and benzalkonium chloride had increased nasal stuffiness, estimated by symptom scores and measurements of nasal mucosa swelling after 10 days of treatment. It is concluded that a nasal decongestant spray composed of a combination of vasoactive substance and benzalkonium chloride has a long-term adverse effect on the nasal mucosa. Author.

Esophagopharyngeal distribution of refluxed gastric acid in patients with reflux laryngitis. Shaker, R., Milbrath, M., Ren, J., Toohill, R., Hogan, W. J., Li, Q., Hofmann, C. L. Medical College of Wisconsin Dysphagia Institute, Department of Medicine, Milwaukee, USA. *Gastroenterology* (1995) November, Vol. 109 (5), pp. 1575–82.

BACKGROUND AND AIMS: A variety of otolaryngological abnormalities have been attributed to the contact of gastroesophageal refluxate with respective structures of the aerodigestive tract. The aim of this study was to determine and compare the pharyngoesophageal distribution of gastric acid refluxate between patients with proven laryngitis attributed clinically to gastroesophageal reflux and three control groups. **METHODS:** An ambulatory 24-hour simultaneous three-site pharyngoesophageal pH monitoring technique was used to measure reflux parameters in the pharynx, proximal esophagus, and distal esophagus. **RESULTS:** Between-group comparison showed no significant difference in the reflux parameters in the distal esophagus between the studied groups. A significantly higher percentage of distal reflux episodes reached the proximal esophagus in the laryngitis group than in the control groups ($P < 0.01$), and the number of pharyngeal reflux episodes and time of acid exposure were significantly higher in the laryngitis group than in the control groups ($P < 0.001$). **CONCLUSIONS:** Compared with normal controls and patients with gastroesophageal reflux disease, pharyngeal reflux of gastric acid is significantly more prevalent and the ratio of proximal to distal esophageal acid reflux episodes is significantly increased in patients with posterior laryngitis. Simultaneous three-site ambulatory pharyngoesophageal pH monitoring may provide supporting evidence when the diagnosis of reflux-induced aerodigestive tract lesions is considered. Author.

Scaling of the mammalian middle ear. Nummela, S. Department of Zoology, University of Helsinki, Finland. *Hearing Research* (1995) May, Vol. 85 (1–2), pp. 18–30.

This study considers the general question how animal size limits the size and information receiving capacity of sense organs. To

clarify this in the case of the mammalian middle ear, I studied 63 mammalian species, ranging from a small bat to the Indian elephant. I determined the skull mass and the masses of the ossicles malleus, incus and stapes (M, I and S), and measured the tympanic membrane area, A1. The ossicular mass (in mg) is generally negatively allometric to skull mass (in g), the regression equation for the whole material (excluding true seals) being $y = 1.373 \times (0.513)$. However, for very small mammals the allometry approaches isometry. Within a group of large mammals no distinct allometry can be discerned. The true seals (Phocidae) are exceptional by having massive ossicles. The size relations within the middle ear are generally rather constant. However, the I/M relation is slightly positively allometric, $y = 0.554 \times (1.162)$. Two particularly isometric relations were found; the S/(M + I) relation for the ossicles characterized by the regression equation $y = 0.054 \times (0.993)$, and the relation between a two-dimensional measure of the ossicles and the tympanic membrane area, $(M + I)/2/A1$. As in isometric ears the sound energy collected by the tympanic membrane is linearly related to its area, the latter isometry suggests that, regardless of animal size, a given ossicular cross-sectional area is exposed to a similar sound-induced stress. Possible morphological middle ear adaptations to particular acoustic environments are discussed. Author.

A prospective randomized study of chemotherapy adjunctive to definitive radiotherapy in advanced nasopharyngeal carcinoma (see comments). Chan, A. T., Teo, P. M., Leung, T. W., Leung, S. F., Lee, W. Y., Yeo, W., Choi, P. H., Johnson, P. J. Department of Clinical Oncology, Prince of Wales Hospital, Shatin, Hong Kong. *International Journal of Radiation Oncology, Biology and Physics* (1995) October 15, Vol. 33 (3), pp. 569–77. Comment in: *International Journal of Radiation Oncology, Biology and Physics* (1995) October 15, Vol. 33 (3): 761–3.

PURPOSE: A prospective randomized trial was conducted to compare chemoradiotherapy against radiotherapy alone in the treatment of locoregionally advanced nasopharyngeal carcinoma. **METHODS AND MATERIALS:** Eighty-two patients with histologically proven nasopharyngeal carcinoma who had either Ho's N3 staging or any N stage with a nodal diameter of $>$ or $=$ 4 cm were entered. Seventy-seven patients were evaluated for tumour response and survival. The patients were randomized to receive two cycles of cisplatin 100 mg/m² Day 1, 5-fluorouracil 1000 mg/m² 24-h infusion Days 2, 3, and 4 before radical radiotherapy, and four cycles of postradiotherapy chemotherapy (37 patients) or radiotherapy alone (40 patients). All patients received radical radiotherapy to the nasopharynx and neck. The nasopharynx and upper neck were treated to 66 Gy by conventional fractionation and the lower neck to 58 Gy. Booster radiotherapy (7.5 Gy/two fractions/week) was given to any residual nodes after standard radiotherapy. **RESULTS:** The patient characteristics, including staging, were similar in both arms. The overall response rate to neoadjuvant chemotherapy was 81 per cent (19 per cent complete response, 62 per cent partial response). The rates of radiotherapy for boosting parapharyngeal disease or residual lymph nodes were not significantly different in the two arms. The overall complete response rate to chemoradiotherapy was 100 per cent, and to radiotherapy alone, 95 per cent. Toxicities in the chemoradiotherapy arm were mainly myelosuppression, nephrotoxicity, and nausea and vomiting. The degree of mucositis was not significantly different in the two arms. There was no treatment-related death. The median follow up was 28.5 months. The two-year overall survival was 80 per cent in the chemoradiotherapy arm and 80.5 per cent in the radiotherapy arm. The two-year disease-free survival was 68 per cent in the chemoradiotherapy arm and 72 per cent in the radiotherapy arm, without significant difference between the two arms. The locoregional relapse rate, distant metastatic rate, and median time to relapse were also not significantly different between the two arms. **CONCLUSION:** Despite promising tumour response rates from Phase II trials, this prospective randomized trial has demonstrated no benefit from adjunctive chemotherapy to radiotherapy in the treatment of locoregionally advanced nasopharyngeal carcinoma. Author.

Histochemical and functional characteristics of metachromatic cells in the nasal epithelium in allergic rhinitis: studies of nasal scrapings and their dispersed cells. Otsuka, H., Inaba, M., Fujikura, T., Kunitomo, M. Department of Otorhinolaryngology, Nippon Medical School, Dai 2 Hospital, Kanagawa, Japan. *Journal of Allergy and Clinical Immunology* (1995) October, Vol. 96 (4), pp. 528–36.

BACKGROUND: In allergic rhinitis, metachromatic cells in the nasal epithelium increase in number and are thought to play an important role in nasal allergic manifestation. **METHODS:** To determine immunohistochemical and functional characteristics of the metachromatic cells, nasal scrapings and their dispersed cells from patients with perennial allergic rhinitis were studied. **RESULTS:** Eighty-three per cent of all metachromatic cells in dispersed cell preparations were tryptase-positive mast cells (MCT), 10 per cent were tryptase-chymase-positive cells (MCTC), and 7 per cent were negative (n = 10). The mean histamine chymase-positive cells (MCTC), and seven per cent were negative (n = 10). The mean histamine content per metachromatic cell was 1.9 ± 2 pg. The histamine content and histamine release from nasal surface scrapings of patients sensitized with mite antigen were strongly correlated with the level of serum IgE antibody for mite antigen. The net histamine release from nasal scraping was antigen-dose-dependent ($1:2 \times 10(7)$ to $1:2 \times 10(3)$ dilution), and the antigen stimulated release of up to 17 per cent of cell-associated histamine within five to seven minutes. Histamine release from nasal scrapings induced by calcium ionophore A23187 was up to 21 per cent of cell-associated histamine within two to four minutes, but no histamine release was stimulated by compound 48/80, substance P, or poly-L-lysine. Histamine release from nasal scrapings was inhibited 46 per cent ($10(-5)$ mol/L) to 96 per cent ($10(-4)$ mol/L) by quercetin and 58 per cent ($10(-4)$ mol/L) to 72 per cent ($10(-3)$ mol/L) by sodium cromoglycate. **CONCLUSIONS:** These findings show the predominant characteristics of mast cells in the nasal epithelium in allergic rhinitis, and this information may be useful in relation to a therapeutic approach. Author.

Albumin and immunoglobulin levels in nasal secretions of patients with nasal polyps treated with endoscopic sinus surgery and topical corticosteroids. Biewenga, J., Stoop, A. E., van der Heijden, H. A., van der Baan, S., van Kamp, G. J. Department of Cell Biology, Medical Faculty, Free University, Amsterdam, The Netherlands. *Journal of Allergy and Clinical Immunology* (1995) September, Vol. 96 (3), pp. 334–40.

BACKGROUND: Nasal polyposis is principally treated by surgery, which may be combined with administration of topical corticosteroids to postpone or prevent recurrences. **OBJECTIVE:** In this study endoscopic sinus surgery and subsequent use of topical corticosteroids (budesonide) for one year was evaluated. **METHODS:** Clinical data of 41 patients with nasal polyps were evaluated, and their nasal secretions were compared with those of 26 healthy persons (control subjects). **RESULTS:** The patients had much higher initial total protein, albumin, IgM, secretory IgA (S-IgA) ($p < 0.001$ for all), and IgG concentrations ($p < 0.05$) than the control subjects. Treatment resulted in a significant decrease of S-IgA ($p < 0.001$) within six months. IgM and IgG concentrations decreased more slowly ($p < 0.001$ and $p < 0.05$ at one year, respectively). IgE levels decreased, but we could not demonstrate significance. Relative to total protein levels, the albumin and S-IgA levels decreased within six months ($p < 0.005$ and $p < 0.001$, respectively). The excretion of all proteins remained higher in patients than in the control subjects, even after one year of topical corticosteroid treatments. Clinical evaluation showed slightly higher S-IgA levels in patients with an IgE-mediated allergy than in those without such a condition, and the recurrence rate was highest in the former group (75 per cent vs 48 per cent). **CONCLUSION:** The data support the hypothesis that inflammatory reactions in the nasal mucosa play a role in the pathogenesis of nasal polyps but also suggest an additional causative factor. Author.