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Appropriateness of reducing the number of pollen allergens to three

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Background: Skin prick testing (SPT) is an essential tool in the diagnosis of allergic disorders. The optimal number and type of allergens used in different settings remains undefined. We aim to describe SPT in our clinical practice and propose the appropriateness of reducing the number of pollen allergens to three. The aim is to improve cost-effectiveness and reducing time spent on allergen testing, particularly in the community setting.

Methods: Consecutive patients who attended the private rooms of 2 immunologists and the allergy/immunology clinic in a tertiary referral hospital who required skin prick testing were evaluated from June 2006 to November 2006. Statistical analysis was undertaken with the use of Pearson's Chi-square and Fisher's Exact test to assess for significance. Multivariate analysis was also performed.

Results: There were a total of 273 skin prick test sets performed. There was no significant difference between the rates of SPT positivity with common pollen allergens between the two clinics. A positive SPT to Perennial Ryegass (*Lolium perenne*), Timothy (*Phleum patense*) or Bermuda grass (*Cynodon dactylon*) had a sensitivity of 100% to Bent or Orchard grass (*Dactylis glomerate*), with sensitivities of 97%, 96.3% and 94.8% to English Plantain (*Plantago lanceolata*), Bahia grass (*Paspalum notatum*)and Dock/Sorrel (Rumex sp) respectively. Use of Perennial Ryegrass, Timothy or Bermuda grass also detected tree pollen sensitivity with sensitivities in Birch mix (Betula sp) of 92.6%, Acacia (96.4%), Casuarina (89.1%), Platanus sp (92.3%) and Privet(Ligustrum sp) (88.6%).

Conclusion: The use of 3 common grass pollen allergens in SPTs (*Lolium perenne, Phleum pratense and Cynodon dactylon*) detected 90% of atopic individuals with sensitivity to many pollen types. This information may be useful in defining the most appropriate allergens to determine pollen hypersensitivity in community settings.

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Clinical evaluation of a new allergy lateral flow assay for professional and home use

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Background: Specific immunoglobulin E (sIgE) is a hallmark in the diagnosis of type I allergic reactions and atopic diseases. A new allergy screening test (Allergy Lateral Flow Assay; ALFA^{TM}) for qualitative detection of sIgE in human whole blood, serum or plasma is based on a test device, allowing linkage to a variety of allergens. Objective of our study was the evaluation of ALFA^{TM} for professional and home use.

Methods: Untrained volunteers (n = 96) performed ALFA^{TM} Seasonal Screen (S) [Birch (t3), Bermuda Grass (g2), Rye Grass (g5), Timothy Grass (g6), June Grass (g8), Cultivated Rye (g12), Mugwort (w6) and *Alternaria alternata* (m6)] and ALFA^{TM} Perennial Screen (P) [*D. pteronyssinus* (d1), *D. farinae* (d2), cat (e1), dog (e2), *Aspergillus fumigatus* (m3) and *Aspergillus niger* (m33)] with capillary blood. Each serum was tested for specific IgE to all single allergens contained in both ALFA^{TM} tests by ALLERG-O-LIQ. Furthermore, skin prick tests (SPT, Allergopharma) were performed. Volunteers were defined allergic if patient's history was concordant with SPT and sIgE in-vitro results. ALFA^{TM} results and patient's diagnoses were analyzed by kappa agreement, Chi-square test, positive (PPV) and negative predictive value (NPV) and diagnostic efficiency (DE).

Results: ALFA^{TM} results were obtained from 91 (S) and 83 volunteers (P). 33/91 (36.3%) volunteers, were defined as allergic for seasonal and 16/83 (19.3%) for perennial allergens. Of those, 25/33 and 6/16 showed positive test results in ALFA^{TM} S and P. Agreement between the ALFA^{TM} results and doctor's diagnosis was 94.5% (kappa = 0.75, $p<0.0001$, $\chi^2 = 49.3$) for S and 91.6% (kappa = 0.46; $p<0.0001$, $\chi^2 = 17.3$) for P. Overall agreement was 93.1% (kappa = 0.67; $p<0.0001$, $\chi^2 = 79.1$). Sensitivity, specificity, PPV, NPV and DE were 75.8%, 96.6%, 92.6%, 87.5% and 89.0% (S), 37.5%, 98.5%, 85.74%, 86.8% and 86.7% (P) and 63.3%, 97.6%, 91.2%, 87.1% and 87.9% (combined).

Conclusion: Results, particularly for seasonal allergens, are in good agreement with doctor's diagnosis. Therefore, ALFA^{TM} offers the opportunity for primary care physicians and patients to perform a screening test for early type-I allergy diagnosis.

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Sensitization to five common aero-allergens in children suffering from atopic eczema as examined by atopy patch tests, skin prick-tests and specific IgE

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Background: Although the role of allergy in atopic eczema (AE) is still controversial, some patients with atopic eczema suffer from exacerbation of skin lesions after contact with or inhalation of aeroallergens. From the histological examinations of the skin after contact with aeroallergenes is known that the delayed-type hypersensitivity reactions mediated by allergen-specific T cells can take a part in pathogenesis of atopic eczema. Atopy patch tests (APT) represent a useful tool for detection of such hypersensitivity.

Methods: We examined hypersensitivity to common aero-allergens (birch pollen, grass pollen, cat dander, house-dust mites) using APT, skin prick-tests (SPT) and specific IgE in 27 children suffering from atopic eczema. Results of all methods were then compared.

Results: Delayed-type hypersensitivity was found out (using APT) in 16 patients (59%), immediate type of hypersensitivity was found out (using SPT) in 13 patients (48%), using specific IgE in 15 patients (55%). Only immediate type of hypersensitivity was proved in 5 patients (18%), only delayed-type hypersensitivity in 6 patients (22%). Both types of hypersensitivity occurred concomitantly in 11 patients (41%). In 32 cases the type of hypersensitivity differed in the same allergen. A significant ($p< 0.0005$) positive correlation was found between SPT and specific IgE. Correlation of clinical symptoms of AE and positivity of tests was in 7 patients (26%) in IgE mediated hypersensitivity and in 10 patients (37%) in delayed-type hypersensitivity.

Conclusion: Various aero-allergens can influence substantially the course of atopic eczema not only via specific IgE, but as well by specific T cell-mediated

reactions. Therefore testing for hypersensitivity to aero-allergens both using SPT and/or specific IgE, and atopy patch tests could be useful.

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Complex diagnosis of IgE mediated allergy by in vivo and in vitro methods

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Background: The aim of the study is to assess the diagnostic potential of two in vitro methods for IgE diagnosis and to compare them with the skin-prick test (SPT) as a gold standard.
Methods: 131 patients with positive case history and SPT to grass pollen, house dust mite, moulds, bee and wasp venom suffering of bronchial asthma or allergic rhinitis /hay fever and 10 clinically health controls were studied. The in vitro quantity of serum allergen-specific IgE (UniCap, Pharmacia) and the percentage of allergen-specific basophil's degranulation (FasImmune, BD) were evaluated. The correlation and the percent of coincidence of the results from the three methods were analysed (Statistica 5.5).
Results: Significant statistical correlation between the resuls from the three methods in patients sensitized to grass pollen and house dust mite were found. Strong positive correlation (Spearman, $p<0.05$) between the SPT and the quantity of specific IgE- R=0.67 and R=0.61, between the in vivo test and FasImmune - R=0.66 and R=0.62 and between the both in vitro methods - R=0.67 and R=0.53 were determined. Data from patients, allergic to insect's venom, showed a high percent of coincidence between the three methods - from 70% to 90%. Respectively a cincidence of 60% between the SPT and the quantity of specific IgE in the group sensitized to moulds was established.
Conclusion: The results from the invitro methods represent positive correlation and coincidence with SPT, especially for the allergens of grass pollen, house dust mite, bee and wasp venom. Their application ensures more preceise diagnosis of patients and contributes to the complex assessment of IgE mediated allergy.

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Development and optimization of quartz crystal microbalance immunosensor for the detection of total IgE

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Background: Allergic disease have a significant impact on clinical practice due to their high prevalence. The total IgE quantification is one of the important steps in the classic atopic disease diagnostics.The most widely used methods for IgE detection are time-consuming and complex. Biosensors are interesting tools offering certain operational advantages over standard photometric methods, notably with respect to rapidity, ease-of-use, cost, simplicity, portability, and ease of mass manufacture.
Methods: QCM work as sensors based on the relationship between frequency change and mass loading on the surface of the crystal according to Sauerbrey equation (Sauerbrey, J Phys, 1959). When antigens react with coated antibodies on the surface, a frequency shift occurs and this change is proportional to the mass loading.
Results: The monoclonal anti-IgE were successful immobilize in Nafion polymeric matrix on silver electrodes of piezoelectric quartz resonator. The optimal conditions for anti-IgE immobilization procedure and for piezoelectric immunoassay have been determined. Only 10 microlitres of serum and 45 minutes reaction time is required to measure total IgE. It was found that biosensor is capable to differentiate blood serums of patients with low, intermediate and high level of IgE.
Conclusion: The quartz crystal microbalance immunosensor offers a number of significant advantages over the currentlu available in vitro techniques for the detection of total IgE. It is supposed that such biosensor can be used in laboratory practice for IgE determination.

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Systemic reactions to percutaneous and intradermal skin tests

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Background: The purpose of this study is to determine over 12 months, 2/1/06–1/31/07, the rate of SRs to both P and ID ST, the symptoms reported, and the response to immediate treatment with epinephrine IM.
Methods: A retrospective review over a one year period was conducted to evaluate SRs to P and ID ST to 20 to 50 allergens (trees, grasses, weeds, animals, molds, foods, medications, and Hymenoptera) in 1,456 subjects. A standard form was used to record symptoms, signs, and treatment. No vasovagal reactions were included. Nurses as instructed by the attending physicians administered epinephrine 1:1000 v/v, 0.2mL IM as soon as any signs or symptoms of anaphylaxis occurred.
Results: 52 patients (3.5%) had SRs, 43 (83%) female and 9 (17%) male. The average age of the patients with SRs was 40.6 years (range 13–70, median 35.5 years). 17/52 (33%) had asthma. Symptoms reported: pruritic eyes, nose, and/or pharynx (40%), worsening cough (27%), sensation of difficulty swallowing (17%), worsening nasal congestion (15%), rhinorrhea (13%), chest tightness and/or shortness of breath (13%), generalized pruritus (12%), sneezing (12%), urticaria (4%), and wheeze (4%). No severe asthma, shock, hypotension, unconsciousness, or late phase responses occurred. Treatment: 52 (100%) patients received epinephrine (average dose, 0.2 cc, 1:1000 IM), 48 (92%) oral prednisone, 9 (17%) oral prednisone to take 6 to 8 hours after reaction, 50 (96%) oral antihistamine (H1) , and 6 (12%) nebulized beta agonist.
Conclusion: SRs occurred in 3.5% of patients skin tested and readily responded to early intervention with epinephrine. This early administration of epinephrine by nurses appears to prevent more serious and late phase reactions.

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Clara cell protein in irritating and sensitizing effects of inhaled benzalkonium chloride in rats

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Background: Benzalkonium chloride (BAC) is a bacteriostatic agent used in the pharmaceutical industry as a preservative and is known to cause bronchoconstriction in asthmatic subjects. The aim of our study is qualification of results of inhalation exposure to BAC in rats, with particular reference to the effect on the remodelling of the respiratory system. Conditioned allergic reactions that impair lung function, such as allergic asthma, can be evaluated by specific lung biomarkers. It is known that the irritant fumes affect nonciliated epithelial Clara cells, which release anti-inflammatory and immunosuppressive Clara cell protein (CC16) into the respiratory tract.
Materials and Methods: Female Wistar rats were exposed to BAC aerosol at 30 mg/m3 for 5 days (6h/day) and on day 16 were re-exposed to BAC for 6 h.

After the exposure, bronchoalveolar lavage fluid (BALF) was collected. BALF concentration of total protein, CC16, IgE, MMP-9, hyaluronic acid (HA), IL-6, TNF-α, MIP-2 and activity of lactate dehydrogenase (LDH) were determined. CC16 as the marker of bronchiolar epithelium was assessed by latex immunoassay. In the lung, histological examinations were done and the activity of glutathione S-transferases (GST) was determined. Additionaly total and differential cell number (lymphocytes, neutrophils and macrophages) were measured.

Results: Benzalkonium exposure after challenge induced statistically significant increases of BALF cytokines, LDH and IgE in BALF and serum. CC16 level in BALF was significantly reduced. Significant negative correlation of CC16 concentration in BALF with mediators (IL-6) of inflammatory processes was seen. Huge increase of LDH correlated with the level of total protein, MIP-2 and IgE in serum. Negative relationship was shown to occur between CC16 and LDH. IgE in serum and BALF correlated with MMP-9. In histopathology examination, focal agglomerations of alveolar macrophages were noted as well as proliferation of peribronchial lymphatic tissue.

Conclusion: CC16 play a protective role in allergic inflammation and take part in remodelling effects of low molecular weight sensitizers. CC16 can be used as a diagnostic marker for early detection of impaired respiratory function.

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Pulmonary irritation after inhalation exposure to benzalkonium chloride in rats

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Background: Benzalkonium chloride (BAC) is a quaternary ammonium compound in which the alkyl groups have a chain length from C8 to C18. BAC exerts toxic effects on microorganisms. This property has been utilized in the cosmetic industry and medicine, where it is used as an effective germicide and preservative agent. Various BAC-containing preparations used by people may produce a number of adverse effects on the human body. Bearing in mind that BAC is widely used in different branches of the national economy, its toxic effect may constitute a major health problem.

Materials and Methods: Female Wistar rats IMP: WIST of body weight 165–185 g were exposed to BAC aerosol at the target concentration of 30 mg/m3 in the dynamic inhalation chamber for 6 h and 3 days (6 h/day). After the exposure and 18 h after termination of exposure to BAC aerosol, bronchoalveolar lavage fluid (BALF) was collected from each animal and BALF concentrations of total protein, Clara cell protein, matrix metalloproteinase-9 (MMP-9) hyalurnic acid (HA), immunoglobulin E (IgE) and cytokines (TNF-α, IL-6 and MIP-20) and the activity of lactate dehydrogenase (LDH) and GSH-S-transferase (GST) were determined.

Results: All the rats survived inhalation exposure to 30 mg/m3 BAC. A significant reduction of body weight was noted in the animals exposed repeatedly by inhalation to BAC. Lung weight, total protein, HA level and LDH activity in BALF were higher in rats after single and repeated exposure to BAC, compared to control. Decreased concentrations of CC16 in BALF of rats were observed after the single and repeated inhalation exposure. A significantly higher level of IL-6 and IgE were noted in the BALF from the animals exposed to the single and repeated dose. Concentrations of MMP-9, TNF-α, and MIP-2 in BALF of rats exposed to BAC were similar to those found in the control animals.

Conclusion: BAC showed a strong inflammatory and irritating activity in the lungs of the rats already after 6 hours of inhalation exposure. BAC stimulates the dynamic patterns of IL-6 and IgE production and infiltration of protein from blood circulation system to BALF. Continued exposure resulted in changes involving cellular destruction, statistically increase of LDH activity and a continuous reduction of CC16 concentration in BALF.

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Allergic bronchopulmonary aspergillosis in an asthma clinic using essential minimal criteria

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Objective: Allergic bronchopulmonary aspergillosis (ABPA) occurs in cases of atopic asthma and may result in important lung disease. Early diagnosis is essential as this disease is responsive to corticosteroids. However, there is still no consensus about the diagnostic criteria, because patients in different stages of ABPA may not fulfill the criteria. In this study, we evaluate the prevalence of ABPA or ABPA-like disease in an asthma clinic using essential minimal diagnostic criteria.

Methods: A prospective evaluation of patients with bronchial asthma for ABPA from July 2006 onward. ABPA was diagnosed using essential minimal criteria ?asthma, skin prick testing (SPT) positivity to Aspergillus fumigatus (Af), elevated serum total IgE (CAP), elevated serum Af-specific IgE (CAP), and central bronchiectasis on CT scans.

Results: Ninety consecutive patients with bronchial asthma were enrolled. Forty-four of 90 patients were atopic (49.0%), 7 of 44 (18.0%) were positive to SPT to Af. Five of 44 patients (11.0%) showed only elevated serum Af-specific IgE without positive response to Af on SPT. A secure diagnosis of ABPA, satisfying all essential minimal criteria, was evident in 4 of 12 patients (33.3%).

Conclusion: There is high prevalence of ABPA in asthmatic patients presenting our hospital. Further evaluations are required to differentiate ABPA from asthma patients sensitizing to Af without ABPA. The role of serum Af-specific IgE as a screening tool in diagnosis of ABPA should be redefined.

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Clinical presentation in 12 patints with allergic bronchopulmonary aspergillosis

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Purpose: Allergic bronchopulmonary aspergillosis (ABPA) is an immunologically mediated lung disease charecterise by a Complex hypersensitivity reaction in patients with asthma which occurs when bronchi become colonized

	No. of patients Average	Average
Age (years)		25.3
Cough, wheezes and dyspnea	12	
A history of asthma	12	
Immediate skin test reactivity to Aspergillus antigens	12	
Serum total IgE concentration greater than 1000 ng/mL	10	
Peripheral blood eosinophilia >500/mm3	12	2180
Lung infiltrates	12	
Proximal bronchiectasis	4	
High ESR mm in the first hour	12	64.4

by Aspergillus. Repeated episodes of bronchial obstruction, inflammation, and mucoid impaction can lead to bronchiectasis, fibrosis, and chronic lung disease. Our aim of the study is to increase awareness of this disease.
Methods: We described a study of 12 cases with Allergic bronchopulmonary aspergillosis Twelve patients (6 men and 6 women) were diagnosed in chest department at King Hussien Hospital between 1993–2003. The main criteria for the diagnosis were A history of asthma, immediate skin test reactivity to Aspergillus antigens, Serum total IgE concentration greater than 1000 ng/mL, peripheral blood eosinophilia more than 500/mm3, Lung infiltrates and proximal bronchiectasis.
Results: Demographic data for 12 patients with Allergic bronchopulmonary aspergillosis.
Conclusion: ABPA is a rare disease, diagnosis is depending upon certain criteria.
Clinical Implication: We have to think about the diagnosis of ABPA in any patient with a history of asthma, lung infiltrates and peripheral blood eosinophilia.

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The significance of the diagnostic profile of the ophthalmic allergies in excluding mimicking clinical conditions(MC)* which may pose therapeutic difficulties

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Introduction: Patients with (AC) with/without concomitant allergies in some cases is a therapeutic dilemma.
Methods: In the series of patients, ages 10–35 years usually with intermittently red. eyes(shot redness), intractable itching of eyes, tearing (stringy discharge) with/without seasonal association.

On laboratory investigations, is found raised tears & blood eosinophils counts, total eosinophils counts. Total serum IgE measurement in most of the cases had been higher than 200 to 300 kU/l. supported by, the. rise in titers of allergen-specific IgE, by the radioallergosorbent test (RAST) method, Skin prick test with a mixture of allergenic extracts had a conclusive evidence of an allergy cause for the red eye.

On ophthalmoscope examination. Found pinkish papillae, with a central vessel & characteristics, serous, watery conjunctival secretion.

Conjunctival scrapings, and tear cytology performed after topical ocular allergen challenge to sensitized subjects have shown significant increases in neutrophils and eosinophils, and their presence evidenced a positive diagnostic criterion.
Results: Confirmation of a suspected allergic sensitization by skin prick test for the diagnosis of immediate hypersensitivity is the most sensitive, fastest and cheapest method to confirm an allergic sensitization. However, it carries a small but a significant risk of systemic anaphylaxis.
Conclusion: Challenge tests are the only way to relate the specific allergen to the triggering of ocular symptoms. but with a variable degree of systemic anaphylaxis.

*Bacterial, chlamydial and viral conjunctivitis, superior limbic, phlyctenular, conjunctivitis, keratoconjunctivitis, rosacea-associated conjunctivitis, erythema multiforme, eoiscleritis/scleritis, and ocular cicatricial pemphigoid.

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Electrodiagnostic study of phrenic nerve function in patients with systemic lupus erythematosus

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Objective: 21 patients with SLE were screened for the presence of Phrenic nerve neuropathy and to determine whether neurophysiologic findings correlate to clinical respiratory signs, spirometric abnormalities or serological examination in patients with Systemic lupus erythematosus.
Methods: A total of 21 patients(18 female & 3 male)with systemic lupus erythematosus (SLE) (age range, 16–36 yr) were included and studied by physical pulmonary examination, chest radiography, respiratory function tests, as well as serological examination and bilateral transcutaneous phrenic nerve conduction studies.
Results: 14(66.6%) patient complained of dyspnea ,only one patient showed paradoxical abdominal movement .Pulmonary function tests showed proportional reduction of the forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1), suggesting a restrictive process which was severe in 23% of patients. All patients were on corticosteroids, only 10 (47.6%) patients were on immunosuppressive medication to include methotrexate or cyclophosphamide. Phrenic nerve evaluation using transcutaneous stimulation studies showed delayed latencies of RT, LT & both phrenic nerve in 17 (81%), 19(90%) and 17 (81%) patients respectively confirming a demyelinating neuropathy. Also Phrenic nerve stimulation evoked a low-amplitude response from the right, left and both in 17 (81%), 15 (71%) and 14 (66.6%) of patients respectively confirming axonal neuropathy. There was no significant correlation between electrical phrenic nerve stimulation and serum immune markers, except there was decreased action potential amplitude in SLE group with positive results for Anti DNA as14 (66.6%) of patients had Anti DNA + ve, all showed reduced amplitude of rt phrenic nerve & 13(93%) of them showed reduced amplitude of lt phrenic nerve. Fourteen (66.6%) patients presented with dyspnea and all of them showed abnormal phrenic nerve conduction studies. While 11 patients showed abnormal CXR with small but clear lung fields, no evidence of major parenchymal lung or pleural disease was found. There was no significant correlation between electrical phrenic nerve stimulation and CXR abnormalities.
Conclusion: Diaphragmatic weakness in patients with SLE is both common and is very likely to be caused by a phrenic neuropathy with evidence of bilateral involvement.

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The search engine as a diagnostic tool in complex immunological and allergic case reports: is google useful?

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Background: Web-based search-engines have become an important source of knowledge and communication. Google is the most popular search-engine (64% of all web-searches in March 2007) whilst Yahoo accounted for 21%. Recently Google's value to guide doctors to a correct diagnosis in case records of the New England Journal of Medicine was reported.
Objective: To evaluate the utility of searching clinical information with Google in order to obtain a correct diagnosis of complex immunological and allergic (CIA) case reports.
Study Design: Comparative cross-sectional study.
Methods: Firty-five CIA case reports were randomly selected by an independent investigator from peer-viewed medical journals. Clinical data was presented separately to three observers blinded to final diagnosis. Observer A is a Consultant in Internal medicine and Allergy with an expert knowledge of these fields and basic computing skills. Observer B is a Registrar in Internal medicine and Allergy. Observer C is a research nurse. Both observers B and C had a more familiar knowledge of the regular use of computer search engines. An internet-based search using Google was conducted. In order to perform this, the observers individually studied each text and independently selected five search terms, of their own choosing, from each case record to enter into the standard Google search engine. The observers then recorded for each case the single most prominent diagnosis that

was evident from within the first three results pages of the conducted Google search. Since Google does not necessarily include diagnoses within the search results page itself, observers were permitted to select the diagnosis that best fitted the case record from information after opening each direct results link only. The independent investigator then compared the diagnoses obtained by each observer with the definitive diagnoses as published in the Journals. The main outcome measure of this study was the percentage of correctly obtained diagnoses achieved by each observer.

Results: Observer A identified the definitive diagnosis in 30/45 cases (66%, 95%CI 52–79). Observer B in 39/45 (86%, 95%CI 76–95) and Observer C in 29/45 (64%, 95%CI 50–77). Most diagnostic inaccuracies for both observers were those related to primary immunodeficiency or pediatric cases.

Conclusion: This Google-based search was useful to achieve an appropriate diagnosis in CIA cases. Computer and Internet-based search skills could influence the results.

PHARMACOTHERAPY

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The anti-allergic properties of potassium humate

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Background: Although the anti-inflammatory properties of humate derived from peat, sapropeles and mumie have been described, no clinical studies has been done on the anti-inflammatory effects of humate derived from coal. Leonardite humate compared favourably with prednisolone in suppressing contact hypersensitivity in a rat model. According to a report by the European Agency for the Evaluation of Medicinal Products on toxicity studies (Feb 1999), humic acids extracted from brown coal has no toxic effects on rats in a chronic study at oral dosages as high as 1g/kg BW, whereas the LD50 in rats, after oral administration of humic acids, has been reported to be greater than 11g/kg BW. This report has recently been confirmed by a separate study.

The objective of this study was to establish the safety and therapeutic efficacy of oral potassium humate in reducing the signs and symptoms of hay fever in atopic patients during the grass pollen season.

Methods: In this parallel double-blind placebo controlled phase II study potassium humate was randomly assigned, at a dosage of 1.8g in divided doses/day, to atopic patients (n = 40) presenting with acute symptoms of hay fever. The blood and nasal samples were used to determine the safety and the effects of potassium humate on basophil activation, cytokine levels and eosinophil migration. A skin prick test was used to determine its anti-allergic effects. An in vitro neutrophil adhesion test was used to determine the effects of the product on the adhesion of human neutrophils to ICAM-1expressing baby hamster kidney cells.

Results: A significant decrease in the skin prick test results (presented elsewhere) and eosinophil counts was observed. No significant differences were observed with regard to neutrophil adhesion nor were there any differences observed with regard to the stimulation of basophils. However decreases were observed in the expression of IL-4, IL-5, IL-8 and IL-1â after treatment, although not reaching statistical significance. The product had no effect on neutrophil adhesion to ICAM-1.

Conclusion: This study confirmed, without doubt, that this product possesses anti-inflammatory as well as anti-allergic properties possibly due to a decreased recruitment of eosinopils to the site of inflammation.

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Anti-inflammatory effect of LipoPGE1 on therapeutic intervention for intractable skin ulcer

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Background: Intractable skin ulcer is common in our daily practice. Although patients' QOL is severely impaired by this skin lesion, until now effective treatment protocols have not been established. Wound healing process can be separated into inflammatory phase, proliferating phase, and remodeling phase. Recent reviews have described that prolonged inflammatory phase might partly affect the pathogenic mechanisms of intractable skin ulcer. During the inflammatory phase, various kinds of inflammatory cell infiltrates ware observed in the affected area, and recruited macrophages secrete some inflammatory cytokines including IL-6 and VEGF. Prostaglandin E1 (PGE1)-treatment is believed to be one of the promising treatment for skin ulcers, and LipoPGE1 also demonstrated improvement in a drug delivery system. To note, it has been reported that infiltrated macrophages uptake LipoPGE1. Taken these results together, we hypothesized that LipoPGE1 might have an anti-inflammatory effect and thus contribute to the improvement of intractable skin ulcer.

Methods: Patients with various kinds of intractable skin ulcers were administered with intra-venous injection of 10 microgram/day LipoPGE1 (Palxus®) for two weeks, and the size of the ulcer area and serum concentration of CRP, IL-6, VEGF, and sICAM1 were measured before and after treatment.

Results: LipoPGE1 effectively reduced the size of the ulcer area and the serum inflammatory markers after two weeks of LipoPGE1-treatment.

Conclusion: These results indicated that anti-inflammatory effect of LipoPGE1 might contribute to the improvement of the intractable skin ulcers.

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Comparative efficacy of levocetirizine, desloratadine, clemastine, kvifenadine and sekvifenadine on histamine prick test induced weal reaction, blood perfusion evaluated by laser Doppler flowmetry. Randomized, double-blind, placebo-controlled, crossover design study

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Background: Evaluation of weal reaction and laser Doppler flowmetry are valuable methods for evaluation of efficacy of different pharmacological agents. The aim of our study was to compare the influence of different H1-antihistamines on histamine induced weal reaction, increase of skin blood perfusion and sedation.

Methods: Histamine prick test induced weal area in mm2, percentage of blood perfusion change and area under curve during peak perfusion period (AUCmax) was measured with Periflux System 4000 (Perimed AB, Sweden) 2 hours after intake of 5 mg levocetirizine, 5 mg desloratadine, 1 mg clemastine, 50 mg kvifenadine, 50 mg sekvifenadine and placebo. Sedative effect was measured in mm by visual analogue scale (VAS).

Results: Results were expressed as mean ± 95%CI. Mean weal reaction area was 6.9 (−3.9;+10.7); 17.5 (−12.6;+23.1); 20.2 (−14.9;+26.2); 18.1 (−13.1;+23.9); 17.8 (−12.8;+23.5) and 29.0 (−22.6;+36.1) mm2 respectively. Statistically significant difference was observed between active treatment and placebo ($p<0.05$), and levocetirizine and other H1-antihistamines ($p<0.001$). Increase of blood perfusion was 393.1% (−221.3;+613.8); 626.2% (−403.0;+898.3); 756.5% (−508.8;+1053.2); 741.0% (−496.2; +1339.1); 1001.5% (−712.8;+1339.1) and 1033.2% (−739.6;+1375.8) respectively. Significant decrease of augmentation of blood perfusion was observed after pre-treatment with levocetirizine and desloratadine vs. placebo ($p<0.05$) and levocetirizine vs. kvifenadine, sekvifenadine and clemastine ($p<0.05$). AUCmax was 1298.7 (−781.2;+1947.0); 2197.3 (−1504.5; +3020.9); 2454.3 (−1718.3;+3321.0); 2633.2 (−1868.6;+3528.6); 2551.7 (−1800.0;+3434.2) and 3166.2 (−2321.4;+4141.7) U*s. AUCmax was significantly lower after pre-treatment with levocetirizine vs. placebo and other antihistamines ($p<0.05$). Sedative effect was 24.5 (−17.9;+32.1); 21.1

(−15.1;+28.1); 28.2 (−21.2;+36.2); 17.6 (−12.0;+24.1); 15.1 (−10.0;+21.0) and 19.9 (−14.1;+26.7) mm of VAS. Significant difference of sedation we observed between levocetirizine vs. sekvifenadine, clemastine vs. kvifenadine, sekvifenadine and placebo ($p<0.05$).

Conclusion: Levocetirizine induced significant decrease of weal and flare reaction and skin blood perfusion compared to placebo and other H1-antihistamines. Influence of kvifenadine and sekvifenadine on weal reaction area was similar to desloratadine and clemastine. Sedative effect of clemastine was more pronounced than kvifenadine and sekvifenadine.

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Characterising the pharmacological properties of fluticasone furoate, a novel enhanced-affinity glucocorticoid

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Background: Fluticasone furoate (FF) is a novel enhanced-affinity glucocorticoid developed for topical respiratory use. Its distinct pharmacological properties have been investigated in several in vitro and in vivo studies.

Methods: Binding affinity of FF for the human lung glucocorticoid receptor (GR) was determined by elucidation of association and dissociation rate constants. Molecular interactions of FF with the GR were identified by X-ray crystallography of the GR ligand-binding domain. Cellular onset of action was determined by measuring nuclear translocation in human lung epithelial cells. Measurement of human progesterone (PR), mineralocorticoid (MR), androgen (AR), and oestrogen receptor (ER) activities was used to assess the steroid hormone selectivity of FF. Cellular protection of FF to elastase or mechanical wounding was determined in 16HBe human lung epithelial cells and anti-inflammatory effects of FF in the lung were determined using the Brown Norway Ovalbumin Rat model.

Results: FF has very fast association with, and slow dissociation from, the GR, with a relative receptor affinity (RRA) of 2988±135 with reference to dexamethasone (RRA: 100±5), higher than all other currently available clinical glucocorticoids: mometasone furoate (MF) 2244±142, fluticasone propionate (FP) 1775±130, beclomethasone-17-monopropionate 1345±125, ciclesonide active principle 1212, and budesonide 855. FF has hydrogen bond interactions with the GR through the 3-keto (with Gln570 and Arg611) and the 11β-hydroxy (with Asn564) groups; the 17 β-fluoromethylthioester group also forms a favourable electrostatic interaction with Asn564. FF induces a rapid translocation of GR into the nucleus (<20 minutes to maximum effect) and has high selectivity for GR (30-, 790-, >330,000- and >330,000-fold) versus PR, MR, AR and ER, respectively. FF confers substantial protection against elastase-and mechanically induced damage, with more potent protection than budesonide, FP and MF. FF completely prevents lung eosinophilia, an effect greater than that with FP.

Conclusion: FF has enhanced affinity for the GR compared with other available glucocorticoids, which translates into more potent protection against cellular damage and lung inflammation. Coupled with its fast cellular onset of action and high selectivity for the GR, these properties may contribute to a favourable clinical efficacy and safety profile for FF.

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Downmodulatory effects of cetirizine and levocetirizine on cytokine/chemokine production and CD54 expression in keratinocytes

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Cetirizine is an antihistamic drug of the second generation. Besides its anti-histamic activity various actions have been reported in this anti-histamic. In epidermal keratinocytes, cetirizine inhibits the expression of co-stimulatory molecule ICAM-1 and the MHC class II molecule HLA-DR. Moreover, it exerts anti-inflammation actions by suppressing the production of cytokines and chemokines in various immunocompetent cells. Levocetirizine (L-cetirizine) is the optical isomer of cetirizine and widely used for the treatment of allergic disorders in European countries. In this study, we investigated whether there are differences between cetirizine and levocetirizine in the cytokine and chemokine production by normal human epidermal keratinocytes (NHEK).While NHEK were stimulated with interferon-γ(IFN-γ) and tumor necrosis factor-α (TNF-α) cetirizine or levocetirizine was added to the experimental cultures. Three day-culture supernatants were measured for the concentrations of IL-1α, IL-8, RANTES, Mig, I-TAC and MDC. The IFN-γ/TNF-α-augmented levels of IL-1α, IL-8 and I-TACK were significantly suppressed by the addition of either cetirizine or levocetirizine to the culture in dose-dependent manners (10^{-9} – 10^{-7} M). RANTES, Mig or MDC was not suppressed by cetirizine. To examine the effects of these two reagents on the expression of CD54 (ICAM-1) molecules, NHEK were incubated with IFN-γ with or without cetirizine or levocetirizine for 48 hrs. Cetirizine and levocetirizine at 10^{-8} M downmodulated the expression of CD54 molecules at similar levels to each other.This study demonstrates that cetirizine and levocetirizine have comparable effects on the immunological function of keratinocytes. It is noted that levocetirizine has slightly but significantly stronger effects than cetirizine in the production of RANTES and Mig.

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Efficacy and safety of levocetirizine 5mg as continuous or on-demand treatment for persistent allergic rhinitis over 6 months

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Background: We aimed to document the efficacy and safety of levocetirizine 5mg as continuous (CT) or on-demand treatment (OnD) of persistent allergic rhinitis (PER), as defined by ARIA.

Methods: This was a single-center, randomised, open-label study comparing CT vs. OnD treatment of PER patients with levocetirizine 5mg, once daily, over 6 months. Patients were allowed to have mild asthma treated with a short-acting beta-agonist. Sneezing, rhinorrhea, nasal and ocular pruritus (T4SS=sum of these 4 symptoms) and nasal congestion were measured daily on a 0 (absent) to 3 (severe) scale. Rhinasthma questionnaire (RQ) was used to assess subjects' quality of life (range 0–100; 30 item questionnaire: 1=not bothered at all, 5=bothered very much). Quality of sleep was reported on a VAS scale (0=worst; 10=best).

Results: 31 patients were enrolled per group; 18 in the OnD and 22 in the CT group completed the study. No patients discontinued for drug-related serious adverse events (AEs).

Improvement from baseline in T4SS was significantly higher in favour of CT during months 5 ($p<0.01$) and 6 ($p<0.03$). The maximal T4SS improvement was 80% for OnD and 87% for CT. The maximal improvement in nasal congestion was 75% for OnD and 85% for CT. Quality of sleep considerably improved at end of study: from baseline VAS=5.77 (OnD) and VAS=5.63 (CT) to VAS=7.82 (OnD) and VAS=7.25 (CT). No serious (AEs) were observed. 3.3% of subjects in the CT and 9.4% in the OnD groups reported drug-related treatment-emergent AEs.

Conclusion: Our study confirms previous data that, when taking a potent antihistamine, like levocetirizine, PER symptoms (including nasal congestion) are effectively controlled over a 6-month treatment period. In addition, most of the individual symptoms were controlled significantly better when treated continuously. Regardless of the regimen, levocetirizine improved the patients' quality of life and sleep, and was very well tolerated with fewer patients

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Change from baseline		Month 1 (Adj. Mean)	Month 2 (Adj. Mean)	Month 3 (Adj. Mean)	Month 4 (Adj. Mean)	Month 5 (Adj. Mean) (p-value vs. OnD)	Month 6 (Adj. Mean) (p-value vs. OnD)
Sneezing	OnD	−0.97	−1.22	−1.28	−1.14	−0.95	−0.77
	CT	−0.74	−0.86	−1.26	−1.31	−1.50 (0.004)	−1.41 (0.008)
Rhinorrhea	OnD	−1.32	−1.47	−1.62	−1.51	−1.27	−1.05
	CT	−0.90	−1.07	−1.39	−1.54	−1.75 (0.023)	−1.63 (0.019)
Nasal pruritus	OnD	−1.11	−1.38	−1.63	−1.46	−1.30	−1.14
	CT	−1.02	−1.10	−1.26	−1.47	−1.74 (0.022)	−1.57 (0.081)
Ocular pruritus	OnD	−0.97	−1.11	−1.28	−1.32	−1.18	−1.06
	CT	−0.90	−1.01	−1.16	−1.37	−1.61 (0.016)	−1.51 (0.055)
Nasal congestion	OnD	−1.08	−1.36	−1.54	−1.23	−1.19	−1.03
	CT	−1.11	−1.26	−1.41	−1.55	−1.66 (0.059)	−1.39 (0.210)

		Baseline Mean	Month 1 Mean	Month 2 Mean	Month 3 Mean	Month 4 Mean	Month 5 Mean	Month 6 Mean
RQ Upper Airways	OnD	52.91	30.26	21.53	22.83	29.87	30.56	21.14
	CT	53.11	33.62	29.68	21.71	19.67	22.47	23.86
RQ Lower Airways	OnD	25.19	15.45	11.24	10.54	11.54	11.03	9.40
	CT	29.78	19.19	18.50	12.87	11.92	13.81	14.53

reporting AEs in the CT group. Our results support the long-term continuous treatment of PER with a potent and well-tolerated antihistamine.

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Oxatomide-treated children with atopic dermatitis complicated by food allergy and prevention of asthma development

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Background: Recent epidemiology suggests the increasing prevalence of allergic diseases in the industrialized countries including Japan, which necessitates the analysis of the mechanisms of allergic diseases and development of the effective treatment. Oxatomide (OXM), an antihistaminic drug, has been shown to be clinically effective for the treatment of hypersensitivity and childhood asthma. Its mode of action has been elucidated to increase IFN-g activity as well as anti-histaminic reaction.

Objective and Methods: Peripheral blood mononuclear cells were obtained from 41 patients with atopic dermatitis allergic to hen-egg ranging from 2 months to 2 years 10 months in age. The patients had recurrent eczema, pruritus and positive skin reactions to egg white and/or cow's milk. Patients also had positive responses to the oral provocation test to raw hen egg and or cow's milk. Diagnostic criteria for atopic dermatitis was based on the criteria of Hanifin and Rajk. To clarify the mode of action whereby OXM ameliorates the conditions of the children with food allergy-complicated atopic dermatitis and whether development of bronchial asthma is prevented, OXM-related alterations of the clinical symptoms and examination, seen in patients during the course of 8 months' to 6 years and 10 months' treatment was evaluated.

Results and Discussion: Scores for itching, sleep disturbance and skin lesions (inflammation, lichenification, cracking) was improved from 10 to 2.7 (mean) during the course of 8-16 weeks' treatment with 2mg/kg of OXM in addition to elimination diets, treatment of skin care (shower, Isodine[R], non-steroid ointment), administration of hydroxyzine and/or oral sodium cromoglicate. In further study, OXM efficiently suppressed incidence of asthma to approximately 9% of the patients (control:42.9%) and both of total IgE value and peripheral eosinophils count was not elevated after OXM-treatment and were lower than those in age-matched asthma patients un-treated with OXM.

Conclusion: OXM, which is a significant candidate for one of the therapeutic modalities against children with food allergy-induced atopic dermatitis, and based on the clinical study, was also found to be effective prophylaxis for development of childhood asthma.

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A comparison between intramuscular dexamethasone and fluticasone propionate inhaler in treatment of croup

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Introduction: Croup is a common viral disease in children under 6 years old with incidence rate of 2–6%. The mainstay of treatment is airway management. Treatment focuses on respiratory distress, using cold mist, epinephrine, heliox and corticosteroids. In this study we tried compare the effectiveness of Fluticasone spray with intramuscular Dexamethasone.

Materials and Methods: In this clinical trial, 107 children with croup randomly assigned into two groups. The study group was treated by Fluticasone Propionate and the control group was treated by intramuscular Dexamethasone. Croup scoring was performed at the 6th and 12th hours from initial administration according to Westley croup score.

Results: Improvement was observed in 83% of the study group and 66% of the control group, 6 hours after initiation of treatment. In both groups 10% of the patients didn't respond to treatment ($p = 0.03$). 12 hours after treatment the study group response was 85% and the control group response was 90% ($p = 0.4$).

Conclusion: We found that Fluticasone Propionate and Dexamethasone have similar efficacy in treatment of respiratory distress, considering the simple method of using Fluticasone spray, it can be suggested as a good treatment for croup.

Key words: Croup, Fluticasone Propionate, Dexamethasone, Westley Croup Score.

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Bioequivalency of single doses of desloratadine administered as syrup and tablet formulations in healthy volunteers in China

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Background: Desloratadine (DL) is an oral, non-sedating, selective and potent H1 receptor antagonist that is indicated for the treatment of allergic

rhinitis and chronic idiopathic urticaria in pediatric and adult populations. The clinical and pharmacological profiles of DL have been extensively investigated and DL is available in a number of formulations, including tablets and syrup. The bioequivalence of DL tablets and syrup has not been studied to date in a Chinese population.

Methods: This randomized, open-label, single dose crossover trial studied the pharmacokinetics of DL 5mg administered as a 5mg tablet or 10 ml of 0.5 mg/ml syrup in 24 healthy adult male Chinese subjects. After providing written informed consent and undergoing screening, subjects were admitted to a clinic for baseline assessments. Subjects were randomized to receive one of the two DL formulations in a fasting state. Blood tests for pharmacokinetics were taken over 5 days (subjects remained in the clinic for the first 24 hours), and after a 14 day washout period the subjects were crossed over to the other DL formulation and underwent identical pharmacokinetic analyses. The main pharmacokinetic variables for the two formulations were the log-transformed AUC(I) and the Cmax for DL and 3-OH-DL. Biochemical and hematological tests, ECG data and vital signs were also assessed during the study and adverse event (AE) reports were collected.

Results: DL was safe and well tolerated when administered in the tablet or syrup formulations; no AEs were reported. The Tmax, T1/2, Cmax, and AUC(I) values for DL and 3-OH-DL were similar for both formulations. There were no statistically significant differences between the tablet and syrup DL formulations on the basis of log-transformed Cmax and AUC(I) values for DL and 3-OH-DL (P>0.05). The 90% CIs of AUC, and Cmax were 91.61–103.97% and 86.04–99.92% respectively for DL, and 94.22–101.71% and 88.01–101.35% respectively for 3-OH-DL. The relative bioavailbility of the DL syrup was 99.4% for DL and 98.79% for 3-OH-DL, which met the criteria for bioequivalence of the two formulations.

Conclusion: Both syrup and tablet formulations of DL 5mg were safe and well tolerated. When administered as a syrup formulation DL was bioequivalent to the tablet form of DL in healthy Chinese subjects.

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The pharmacokinetic and safety profiles of desloratadine in healthy korean volunteers

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Background: Desloratadine (DL) is a non-sedating, selective and potent H1-receptor antagonist that is effective and well tolerated in the treatment of subjects with allergic rhinitis and chronic idiopathic urticaria. The pharmacokinetics (PK) of DL have not been studied in a Korean population, to date.

Methods: This was a double-blind, dose escalation study of the PK and tolerability of single doses of DL 5mg, 10mg and 20mg in 36 healthy male Korean subjects. In each dose group 10 subjects received DL and 2 received placebo. Safety was demonstrated at the 5mg DL dose before escalation to the next dose group. Subjects were screened for eligibility during a 3 week pre-baseline period. Subjects were confined on Day -1 and baseline blood/urine tests and ECGs were performed. DL was administered fasting at 9 am on Day 1 and subjects remained confined until Day 3. Blood sampling was performed for biochemistry, hematology and PK from DL administration until Day 8 and the Tmax, terminal T1/2, Cmax and AUClast for desloratadine and it 3-OH-DL metabolite were calculated. Vital signs, physical examinations and ECGs were performed regularly and adverse event (AE) reports were collected.

Results: No clinically relevant changes in vital signs, biochemical, hematological or ECG results occurred. Nine subjects reported 13 AEs during the study. Only dizziness, gingival bleeding and a flu-like illness (all mild in severity) were deemed potentially related to study drug. One subject developed a hemopneumothorax on Day 6 after receiving DL 5mg. This was deemed as being of unknown relationship to study drug. The mean terminal T1/2 for DL was 23.7–31.1 hr across the dose range, while the mean Tmax ranged from 1.75 to 2.0 hr. The Cmax ranged from 2.4 μg/L (DL 5mg) to 9.9 μg/L (DL 20mg); the AUClast ranged from 36.5 μg.hr/L (DL 5mg) to 170.3 μg.hr/L (DL 20mg). The mean AUClast and Cmax values for DL demonstrated moderate intersubject variability (50.6% and 51.1%, respectively) at the 5mg DL dose. The intersubject variability for AUClast and Cmax was less at the 20mg DL dose (21.4% and 25.3%, respectively). The mean AUClast and Cmax for DL and 3-OH-DL demonstrated linear PK.

Conclusion: Single dose DL was well tolerated in healthy Korean volunteers across a dose range from 5mg to 20mg and is consistent with results in other populations. With increasing doses of DL, AUClast and Cmax demonstrated linear PK.

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Cardiac safety evaluation of loratadine in the treatment of allergic rhinitis in elderly patients

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Background: In elderly patients with allergic rhinitis, the second-generation H1-antihistamines have not been adequately studies, although they are widely used and assumed to be safe.

Objective: To evaluate cardiac safety of loratadine in the treatment of allergic rhinitis in elderly patients.

Methods: A total of 40 patients with perennial allergic rhinitis were enrolled in the study. There were 25 males and 15 females, aged 50 to 88 years (mean, 64.4-years-old). 17 cases (42.5%) had a history of cardiovascular diseases and/or presented abnormal ECG parameters, but had no prolonged QT-interval. The subjects received loratadine 10mg once-daily for 30 days. A series of baseline ECG recordings was obtained before treatment. ECG effects of the treatments were then compared with the baseline ECGs.

Results: There were no changes in sinus rhythm in all patients after 30 days treatment by loratadine. No statistically significant difference was found between the heart rates, P durations, PR and QRS intervals at baseline and end-point ECGs (P >0.05), with no significant prolongation of the QT as well as QTc corrected for heart rate using Bazett formula (P>0.05).

Conclusion: The results suggest no cardiotoxicity of loratadine, at the usual recommended dose, in long-term treatment of allergic rhinitis in the elderly.

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Propranolol cytotoxicity on human leukemic MOLT-4 cell line

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Background: Propranolol, a beta-adrenergic blocker has been used for treatment of a large number of cardiovascular diseases. This drug is also an inhibitor of phosphatidic acid (PA) phosphohydrolase and phosphatidic acid biosynthesis. Phosphatidic acid is a growth factor for tumor cells. In addition, the inhibitory effect of Propranolol on the development of a tobacco-induced pulmonary adenocarcinoma and also its cytotoxicity on rat and human lung macrophages and human lung tumor cell line has been reported. The widespread and long-term use of propranolol in lots of heart diseases as well as its cytotoxicity against some tumor cells, prompted us to investigate its cytotoxic effect on a human T leukemic cell line (MOLT-4).

Methods: The MOLT-4 cells were cultured in complete RPMI medium and then incubated with different concentrations of Propranolol (0.0004 –0.4 mM) for 10 and 20 hours. The cytotoxicity was then assessed by 3-[4,5-dimethyl thiazol–2,5-diphenyltetrazoliumbromide (MTT) reduction and also trypan blue dye exclusion methods.

Results: Propranolol induced a significant dose dependent cytotoxic effect on human MOLT-4 cell line in less than 10 hours compared to untreated control cells.

Conclusion: The results showed that human T leukemic cell line was dose dependently sensitive to Propranolol. Further studies investigating the in vivo effect of Propranolol on leukemic patients and also other leukemic cells are warranted.

INFECTION & IMMUNITY

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Human coronavirus infections in Hong Kong children: epidemiology, disease spectrum and relationship with childhood wheezing illnesses

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Background: Human coronaviruses (HCoVs) are enveloped viruses with a large plus-strand RNA genome. Five serologically distinct groups of HCoVs have been described - HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1 and SARS-CoV. The clinical disease spectrum by HCoVs in our population is not clearly defined. Preliminary studies suggested that HCoVs might be related to childhood wheezing. This prospective study investigated the epidemiology and clinical features of HCoV infections in Hong Kong children.
Methods: Nasopharyngeal aspirate (NPA) samples were taken from children who were hospitalised in our university teaching hospital between April 2005 and March 2006. The clinical features, diagnoses and laboratory investigations in these subjects were prospectively collected, and laboratory staff blinded to these details performed low-stringent reverse transcription-polymerase chain reaction (RT-PCR) assays using 12 pairs of primers that detect constant regions of HCoVs (i.e. pancoronavirus).
Results: 1139 subjects (57% males) were recruited, with mean (SD) age being 5.1 (3.6) years. The main discharge diagnoses were pneumonia (n=239), upper respiratory infection (URI; n=227), asthma (n=191), seizure (n=107), bronchiolitis (n=105), roseola infantum (n=98), croup (n=31), and others (n=141). Twenty-eight (2.5%) of these NPA samples were positive for HCoVs. The clinical diagnoses associated with these HCoV isolates included asthma (n=7); seizure (n=6); URI (n=5); bronchiolitis, pneumonia, tonsillitis and roseola infantum (n=2 for each); and croup and otitis media (n=1 for each). HCoV infection was not related to age, highest respiratory rate and maximal temperature (P>0.3). HCoV infection was not associated with wheezing illnesses as defined by 'asthma', 'bronchitis' or 'bronchiolitis' (2.7% *versus* 2.4%; P=0.870) or with lower respiratory infections (the above three plus 'pneumonia'; P= 0.341). HCoV cases were more likely to suffer from seizure (5.6% *versus* 2.1%, P=0.040). Complete blood count and C-reactive protein were not related to HCoV infections (P>0.15).
Conclusion: HCoVs are uncommon yet important pathogens causing seizure disorders in local hospitalised children. On the other hand, HCoV infections are not associated with wheezing illnesses in Hong Kong children.

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Are there predominant strains of Staphylococcus aureus in atopic dermatitis patients? : Genotypic characterization of staphylococcus aureus isolated in adolescent and adult patients with atopic dermatitis

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Background: The colonization of *Staphylococcus aureus* is one of the most important aggravating factors of atopic dermatitis. Until now, the importance of *S. aureus* in atopic dermatitis and a positive correlation between colonization with *S. aureus* and clinical severity / skin barrier function has been demonstrated. Qualitative analysis, especially a genotypic characterization of *S. aureus* isolated from atopic patients, however, has rarely been reported.
Methods: This study aimed to find the genotypic characterization of *S. aureus* from atopic dermatitis patients. We performed newly-developed typing methods - spa typing, multi-locus sequence typing (MLST) and toxin gene assay, by a multiplex polymerase chain reaction, with 165 isolates of Staphylococcus.
Results and Conclusion: The results showed that there was no predominant clone of *S. aureus* with a high heterogenicity of spa typing and MLST. A toxin gene assay showed very interesting results that all *S. aureus* strains had at least two kinds of toxin genes; sea and tsst-1 being the most prevalent.

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Role of primary and secondary low-grade rhinovirus infection in allergic airway inflammation in a murine model of allergic asthma

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Background: Rhinovirus respiratory syncytial virus (RSV) infection is known to develop and exacerbate asthma in young children. In adult, RSV causes recurrent but asymptomatic infections. However, the impact of asymptomatic RSV infection on adult asthma is yet to be determined. The aim of this study was to determine the effects of primary and secondary low-grade rhinovirus infections on allergic airway inflammation in a murine model of allergic asthma.
Methods: A low-grade rhinovirus (2 x 10(3) plaque-forming units/mouse) was inoculated, and this caused neither pulmonary inflammation nor symptoms but induced significant IFN-gamma production in thoracic lymph nodes. To investigate interaction between low-grade virus and Dermatophagoides farinae (Df), airway hyperresponsiveness, lung inflammation and cytokine production from thoracic lymph nodes were compared after primary and secondary low-grade rhinovirus infections in four groups of mice; control, Df allergen-sensitized, rhinovirus-infected and Df-sensitized rhinovirus-infected mice. A direct comparison between low- and high-grade rhinovirus infections was also performed in primary infection. To investigate the role of IL-5 during secondary rhinovirus infection, anti-IL-5 monoclonal antibody (anti-IL-5 mAb) was injected in mice and similar parameters were compared in four groups of mice.
Results: Primary high-grade rhinovirus infection increased allergen-induced airway inflammation, while primary low-grade rhinovirus infection attenuated allergen-induced airway inflammation concomitant with significant IFN-gamma production in lung-draining lymph nodes. In marked contrast, secondary low-grade rhinovirus infection increased both IFN-gamma and IL-5 production, resulting in exacerbation of allergen-induced airway inflammation. Anti-IL-5 mAb treatment in secondary low-grade rhinovirus infection and Df allergen-sensitized mice attenuated virus and allergen-induced airway inflammation.
Conclusion: Low-grade rhinovirus infection per se does not cause pulmonary inflammation, whereas it induces a significant immunological response in the allergen-sensitized host. These results indicate that subclinical and recurrent rhinovirus infection may play an important role in exacerbation and maintenance of asthma in adults, wherein IL-5 is critically involved.

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Serum zinc levels in young children with recurrent wheeze

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Background: Zinc is one of the dietary antioxidants. Previous studies have shown that zinc is crucial for normal development and function of cells mediating non-specific immunity. Recently, zinc supplementation was reported to reduce acute lower respiratory infections and prevent severe pneumonia in children. Our purpose was to examine zinc levels in the serum of the young children who had recurrent early wheeze and evaluate the clinical and laboratory findings in relation to zinc status.

Methods: Seventy-three patients (aged from 8 months to 6 yrs) admitted with acute respiratory infection with wheezing were enrolled. All children had experienced more than 3 episodes of wheezing before admission. Zinc levels were measured in serum samples collected on admission using inductively coupled plasma-optical emission spectrometry (ICP-OES) and the value of < 64 mg/dl was defined as zinc deficiency. Clinical and laboratory findings in the children with zinc deficiency were examined and compared with in the children who had normal values. Zinc levels in sixteen age-matched controls were also studied.
Results: Median value of zinc levels in the patients was significantly lower than in controls ($P<0.001$). 36 patients were found to have zinc deficiency (49.3%), which was significantly higher than in controls (12.5%). Zinc deficiency was observed in 56% of the patients = 2 yrs of age and 40.6% of >2 yrs of age. There was no significant difference in total WBC count, lymphocyte count and atopic status in relation to zinc status in the patients. CD4/CD8 ratio was significantly lower in the patients with zinc deficiency ($P<0.05$), however, other immune profiles were within normal limit.
Conclusion: This study showed that median value of zinc level was significantly lower and zinc deficiency was more frequently found in the patients with recurrent early wheeze compared with in age-matched controls. Our results suggest that zinc deficiency may be associated with frequent respiratory viral infections, a likely trigger for recurrent early wheeze in the young children.

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Persistent cough in patient with infection for mycobacterium avium intracellulare infection

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Aim: Mycobacterium avium intracellulare (MAV) is the atypical Mycobacterium most commonly associated with human disease. The pulmonary disease is the most frequently clinical presentation and appears with higher prevalence in immunosuppressed patients.
Materials and Methods: We present the case of a 46 years old woman, nurse as profession , with cough and dysnea for a period of nine years. No wheezing, fever nor constitutional syndrome were referred. Skin prick tests with common aero-allergens and latex, spirometry and bronchodilatation test were performed. Total IgE, complement study, proteins electrophoresis, immunoglobulins determination, cellular immunity study, HIV, X-ray study and thoracic CT-scan, mantoux, zielh and sputum culture were done.
Results: Positive skin prick test for pollens and dog and cat epithelia were obtained. The patient had normal spirometry values and a negative bronchodilatation test. All the laboratory tests were in normal levels. Determination of total IgE was 483 KU/l. The chest X-ray showed cavities in both lungs with interstitial infiltrates. The CT-scan confirmed these findings. Mantoux, Zielh with 50 BAAR/field and MAV culture were positive. Mycobacterium tuberculosis was excluded by CRP. Cellular immunity, complement, proteins electrophoresis and immunoglobulins determination were in normal range. HIV test was negative.
Conclusion: We present the case of a patient with rhinoconjuntivitis due to pollens hypersensitivity and persistent cough with pulmonary infection for Mycobacteium Avium associated. The Mycobacterium Avium was not described as human pathogen until 1950, when many series described pulmonary infections for MAV. This mycobacterium mainly attacks immunosuppressed patients. This infection is less frequent in patients with normal immunity. Our patient did not have immunosuppression nor risk factors. At the present time she is being treated with antibiotics (ethambutol and claritromicin) and she is in good general condition with no need of hospitalisations.