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The Medical Journal of Malaysia

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E-POSTER PRESENTATIONS

SY-01

Sublingual immunotherapy with allergen specific immunotherapy tablet

Kent Woo, MD

Gleneagles Hospital Kuala Lumpur

ABSTRACT

Allergen specific immunotherapy is now recognized as an allergic disease modifying treatment. Studies have shown that allergen specific immunotherapy (AIT) can prevent new allergic sensitization, reduce medication use in allergic respiratory disease and prevent the development of asthma in patients suffering from allergic rhinitis. The benefits from AIT also translates into lower health care costs. Many society and national guidelines on allergic rhinitis and asthma now endorses the use of AIT in the treatment of patients with allergic sensitization with relevant trigger for their allergic respiratory disease. Patients on AIT are found to mount immunological changes during therapy, there is production of specific IgG4 and induction of regulatory T-cells. The regulatory T-cells are thought to be the key player in modulating the allergic inflammation through the production of IL-10 and TGF-B and is responsible for the prolonged persistent clinical benefits that we see in patients who have completed their AIT treatment. Acarizax is a sublingual immunotherapy product that is FDA approved for the treatment of allergic respiratory disease triggered by house dust mites. This product is a unique fast dissolving sublingual tablet formulation of standardized amounts of the major Group 1 and Group 2 allergens found in house dust mites Dermatophagoides farinae and D.pteronyssinus. There are 3 major well-designed double blinded placebo trials that were conducted on Acarizax in subjects with house dust mite sensitization that demonstrated clinical benefits and the effective dose. One trial, P003 showed that the SQ12 dose reduced allergic rhinitis symptoms in an environmental chamber challenge with onset of effect as early as 8 weeks and demonstrated persistent benefits 1 year after treatment was discontinued. The MERIT trial demonstrated that Acarizax can decrease symptoms scores, medication use with improvement in the Rhinitis Quality of Life Scores. The MITRA trial was conducted in subjects with allergic asthma and demonstrated the ability to reduce medication use in asthma and reduce risk of exacerbations of asthma when inhaled corticosteroids were stopped. In the current Covid-19 pandemic, Acarizax provides an option for patients to safely receive AIT through the sublingual route by self-administration at home. This can help reduce medical visits compared to injection AIT which requires multiple clinic visits for administration along with a 30 minutes observation post injection in a medical setting. Allergen specific immunotherapy is now recognized as an allergic disease modifying treatment. Studies have shown that allergen specific immunotherapy (AIT) can prevent new allergic sensitization, reduce medication use in allergic respiratory disease and prevent the development of asthma in patients suffering from allergic rhinitis. The benefits from AIT also translates into lower health care costs. Many society and national guidelines on allergic rhinitis and asthma now endorses the use of AIT in the treatment of patients with allergic sensitization with relevant trigger for their allergic respiratory disease.

Insights on genetic risk factors of allergic rhinitis

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ABSTRACT

Allergic rhinitis (AR) is common chronic condition, which results from a complex interaction between genetic and environmental factors. Previous studies done on twin siblings showed that there was a higher concordance of the rate of allergic symptoms identified in monozygotic twins, compared to dizygotic twins that demonstrated genetic inheritance of this disease. Studies to identify the genetic risk factors of AR have been performed using three study designs; genome wide association studies (GWAS), candidate gene association studies (CGAS) and family linkage studies. In this review, data from 5 GWAS and 2 meta-GWAS encompassing 137,908 AR cases and 878,758 controls, 121 CGAS and 15 meta-CGAS encompassing 47,853 AR cases and 61,602 controls and 2 family linkage studies encompassing 188 AR individuals from 48 families were evaluated. A total of 56 loci and 89 nearest genes were identified from GWAS/meta-GWAS studies, 80 loci and 112 nearest genes from CGAS/meta-CGAS studies and 2 loci and 5 nearest genes from family linkage studies. Among the nearest genes identified, the majority of candidates (79.1% were common to multiple atopic conditions) while the remaining were specific to AR. The susceptible genes identified showed involvement in the known AR pathogenic pathway, as well as other pathways such as the cell cycle, metabolism, neuronal function, immune regulation, smell function and lung function. I next investigated if ethnic differences influenced the genetic susceptibility to AR. From the genetic variants identified, 18 were replicated across different ethnic groups, while 20 variants from 7 nearest genes were unique between different ethnic populations. The presence of unique variants adds to the complexity in the understanding of AR pathogenesis. The genetic variants identified were next evaluated in terms of its involvement in biological pathways. It was identified that the susceptibility genes of AR were mainly involved in the immune systems pathways. These findings echo the findings from studies done in individuals with other atopic diseases such as asthma and atopic dermatitis. Finally, I evaluated the effects of the gene variants on phenotypic markers involved in AR. A total of 25 nearest genes were associated to IgE levels, 8 genes to eosinophil activity and 4 genes to nasal function. The effects of genes on the phenotype also appears to have ethnic-based variations. This review highlights the need for more genetic susceptibility studies to be done within the Asian population, in order to gain a clearer understanding on the pathological mechanisms of AR.

Skin pH in atopic dermatitis

Kent Woo, MD

Gleneagles Hospital Kuala Lumpur

ABSTRACT

Atopic dermatitis is being recognized as a skin barrier disorder. Filaggrin loss of function mutation has been discovered as one of the key genetic disorders in the pathogenesis of atopic dermatitis. It can lead to barrier dysfunction, increased epidermal water loss and is associated with the atopic march. However, it is important to note that filaggrin does not account for the entire pathogenesis of atopic dermatitis and that the Asian population manifests a more diverse and heterogenous filaggrin mutation as compared to the Caucasian population. Atopic dermatitis (AD) phenotypes also differ among the races, it is found that the Caucasian AD is associated with classical elevated Th2 and Th22 inflammation whereas the Asian AD phenotype closely resembles pediatric AD in which there are elevated Th2, Th22 and Th17 inflammation. The parakeratosis in Asian AD also mimics that which is found in psoriasis, the difference being the absence of Th1 inflammation that is found in psoriasis. Future advances in the research on biomarkers in AD will guide and enable us to use more effective targeted therapy based on the AD phenotype. Normal skin pH is in the acidic range. The skin pH in patients with AD has been found to be in the neutral to alkaline state, and this can be partially attributed to decreased acidic filaggrin breakdown products. We are now starting to recognize the importance of an acidic skin pH mantle in skin barrier homeostasis. Disruption of the skin pH to a more alkaline status will lead to increased skin protease activity causing barrier disruption, itch and decreased antimicrobial defence. Studies have shown that addition of topical acids to reduce skin pH can reduce eczematous inflammation. In particular, lactobionic acid application has been shown to inhibit cutaneous serine protease activity, increase antimicrobial peptide expression and halt eczematous inflammation. More studies are being conducted into the discovery of novel skin pH lowering methods to improve clinical outcomes. Ceradan Advance is a patented novel barrier cream that contains zinc lactobionic acid with a lactobionate buffer to sustainably lower skin pH. Restoration of the disrupted AD skin barrier and lowering of the skin pH should lead to better clinical outcomes.

ENT manifestations of allergy

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ABSTRACT

The ear nose and throat (ENT) specialist often encounter patients suspected to have allergy. A combination of suggestive clinical history, physical examination confirmed by standard allergy testing is needed to make an accurate diagnosis. However, this may be challenging in certain patients without a clear presentation of allergy. Nasal symptoms (sneezing, runny nose, itchy nose or blocked nose) on its own are not specific for allergic rhinitis as it may also be caused by non-allergic nasal pathologies. Physical signs may potentially be used to identify allergy. Middle turbinate oedema was reported to be a specific sign for inhalant allergy and may be a promising clinical marker for allergy. Furthermore, its link with central compartment atopic disease thought to be an allergic phenotype of chronic rhinosinusitis has also been well described. Other classic textbook description of nasal allergy such as pale hypertrophied inferior turbinate has been found to be a non-specific for allergy. Patients may also complain of itchy ears but this symptom is not necessarily due to allergy. Throat symptoms such as globus sensation, voice changes or throat clearing may be due to either allergic laryngitis and laryngopharyngeal reflux. The clinical signs on laryngeal endoscopy between these two diseases also overlap and no distinct clinical sign of allergy has been identified. Therefore, more studies are needed to identify the features which are specific for allergy in the ENT region. This is important for identifying allergy as an underlying cause to enable better patient selection for immunotherapy.

Asthma treatment in 2020: Promise and caution

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ABSTRACT

Asthma is a chronic inflammatory airway disease frequently misdiagnosed or underdiagnosed. The players in the inflammatory pathway are many and they include IgE antibodies, mast cells, eosinophils, dendritic cells and T-helper cells. Acute inflammation leads to bronchoconstriction, chronic inflammation leads to episodes of exacerbations and when the inflammation is persistent, airway remodeling occurs which results in persistent airflow obstruction. The diagnosis of asthma requires demonstration of airway obstruction, variability or detection of eosinophilic inflammation or atopy. The most common investigation is spirometry with demonstration of positive reversibility test. The understanding of asthma has evolved over the years. Treatment options have expanded to include new inhaler devices, biologics and bronchial thermoplasty. The first biologic was Omalizumab introduced in 2003. Since then, they are now many biologics such as Reslizumab, Benralizumab and Dupilumab. In 2019, the GINA guidelines for asthma made changes in the treatment recommendations of mild asthma. Whilst inhaled SABA has been the first-line treatment for asthma for the last 50 years, it is no longer recommended. Regular SABA use is associated with adverse events and adverse clinical outcomes. The recent SYGMA study showed budesonide/formoterol as-needed to be equivalent to budesonide maintenance BID in preventing severe exacerbations with a lower steroid load. In asthma, airway Inflammation involves both the large and small airways. The prevalence of small airway involvement is around 50 to 60%. (4) Studies have shown that particle size plays a part in the deposition in the airways with smaller particle size having a greater deposition. The main types of inhaler devices available are manually-actuated pressurized metered-dose inhalers (conventional puffer), breath-actuated pressurized metered-dose inhalers, dry powder inhalers (multi-dose and capsule types) and mist inhalers. The different inhaler devices and the correct steps to use are adequately outlined in our Malaysian Asthma Clinical Practice Guidelines. There are 5 biologics approved by the FDA for use in severe asthma. They have different mechanism of action, indication and dosages. The evidence suggests a benefit in terms of decrease in exacerbation rates and improvement in quality of life. It is important to remember that asthma is a heterogenous disease and the underlying inflammation needs to be targeted with a move towards earlier use of inhaled corticosteroids and the move away from SABA monotherapy. With the advent of many different types of inhalers with different particle sizes, health care workers need to be familiar with these devices and its components in order to make the correct choice. In addition, inhaler technique should be assessed and corrected at regular intervals during clinic visits.

Allergic sensitization in the tropics – What really matters

Chew Fook Tim, PhD

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ABSTRACT

House dust mite sensitization has frequently been shown to be strongly associated with the presentation of allergic airway diseases, but its significance varies geographically, by ethnicity, age-group and environment. Amongst the tropical regions, Caraballo et al., (2016) summarized the sensitization range to be between 10.8% (in a cross-sectional population in Butajira, southern Ethiopia) to more than 70% (in Singapore). While sensitization is highly prevalent in selected populations, only a proportion of them will present with clinical symptoms. Amongst asthmatic cohorts in the tropics, however, it is common to see mite sensitization prevalence of above 80 or even 90%. A key feature of mite sensitization in the tropics is the larger repertoire of specific mite allergens that the atopic individuals are sensitized to, possibly due to the presence of a more diverse repertoire of mites being co-dominantly present in the environment (e.g., the concurrent presence of both Blomia tropicalis and Dermatophagoides spp.) as well as host genetic factors (with family history being the strongest predictor of allergic diseases). This is in contrast to the predominant Group 1 and/or 2 house dust mite specific responses in the temperate regions (with more than 70% and 80% of house dust mite allergic patients having specific IgE to these allergens, respectively). Nevertheless, Batard et al., (2016) reported that between 20-47% of 1302 house dust mite allergic American, Canadian, European, and Japanese patients evaluated also have IgEs to allergens from groups 4, 5, 7, 13, 15, 21, and 23, and this would have implications for the design, production and standardization of dust mite allergen immunotherapy extracts. Additionally, Soh et al, (2017) demonstrated the presence of an unusual cause of anaphylaxis in mothers triggered by Galacto-oligosaccharides (GOS) added into infant milk formula as prebiotics, which Lee et al., (2019) has linked it to primary sensitization to Blomia tropicalis dust mites. This talk presents the profile of allergen sensitization in our tropical environments and illustrate the significance of these sensitization in disease presentation and outcomes.

Molecular diagnostic testing in food allergy

Narissara Suratannon, MD

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ABSTRACT

Molecular diagnostic testing or component-resolved diagnostic (CRD) is an IgE antibody assay using purified native and recombinant allergenic molecules to detect specific IgE (sIgE) against the individual allergenic molecules. The rationales to use CRD in clinical practice are (1) to detect missing or low abundance allergens, (2) to detect allergenic molecules that identify a risk for clinical reactions and/or predict the likelihood of anaphylaxis, (3) to document IgE cross-reactions (important in "multi-sensitized individuals"), and (4) to identify genuine (primary) sensitization. The aim of this article is to review the recent evidence on using CRD of three food allergens: cow's milk, shrimp and peanut. For cow's milk CRD, even though sIgE testing to casein and beta-lactoglobulin are commercially available, these tests neither predict clinical relevance nor prognosis of cow's milk allergy (2). The reasons are that because (1) each cow's milk component well-presents in cow's milk diagnostic extract, and (2) most patients with IgE-mediated cow's milk allergy were sensitized to several cow's milk allergen components (75% sensitized to two or more components). However, cow's milk CRD might relate to persistent clinical symptoms and can predict reaction to baked milk tolerance in some individuals. For shrimp CRD, shrimp tropomyosin (Pen a1, Pen m1) is the major shrimp allergen that is commercially available. It highly presents in shrimp allergen diagnostic extract. Previous studies and our preliminary results showed that sIgE to shrimp tropomyosin has a similar sensitivity to skin prick test and sIgE to shrimp on predicting shrimp allergy. Yet, it could improve the specificity of the tests even though the frequency of recognition is low. sIgE to shrimp tropomyosin does not predict shrimp anaphylaxis. IgE testing to additional shrimp allergens, including arginine kinase, sarcoplasmic calcium-binding protein, hemocyanin, myosin light chain, might improve the diagnostic yield of the tests. Peanut allergy from different geographic regions reacted to different peanut allergen components. This depends on dietary habits and environmental pollens. Our study from Thailand showed that Ara h2 is the most useful peanut CRD in predicting true clinical reaction. Sensitization to CCD (cross-reactive carbohydrate determinants) related to clinical tolerance, and oral food challenge (OFC) should be performed in this case to avoid unnecessary food avoidance. In conclusion, CRD can be used to optimize the decision for performing OFC, especially in patients who have (1) multiple sensitizations, (2) more than one food is suspected to cause reaction, (3) irrelevant history of food allergic reaction.

Drug allergy testing

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ABSTRACT

Drug hypersensitivity reactions (DHRs) refers to a specific immunologically mediated drug reactions (involve antibodies and lymphocytes) and occurred on re-exposure. It is classified as immediate reactions (IRs) (1-6 hours after drug intake) presented as urticaria, angioedema and anaphylaxis and nonimmediate reactions (NIRs) (>1 hour after drug intake), induce reaction such as maculopapular exanthema (MPE) or fixed drug eruption (FDE), severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS) or drug induced liver disease (DILI). It can be classified as allergic and non-allergic reactions. Allergic reactions are mediated by a specific immune response to a drug acting as hapten that can lead to all types of Coombs and Gell-mediated immune reaction: types I (IgE mediated, produced by B cells), type II (IgG/IgM-mediated cytotoxicity), type III (immunocomplex) and IV (T cell-mediated). The most common are type I and IV, involved in IRs and NIRs, respectively. Non-allergic reactions occurred after drug interaction with mast cells, basophils, and neutrophils through mechanisms such as:1) Over-inhibition of COX-1 inhibition (pharmacological effect) in non-steroidal anti-inflammatory drugs reactions; or 2) Direct stimulation such as the Mas-related G-protein receptor (MRGPRX2) on mast cells by neuromuscular blocking agent (NMBAs). There are 3 main processes by which T cells are stimulated by drug :1) Hapten concept: Haptens are chemically reactive small compounds that bind to peptides to form hapten-carrier complexes (HPC). This HPC presented as hapten-modified peptides to react to T cells; 2) Pro-hapten concept: Pro-haptens are not chemically reactive and cannot form a covalent bond with a peptide. They need to be metabolized to convert into active hapten compound or 3) Pi Concept (pharmacology interaction): A direct pharmacology interaction with immune receptor T cell (TCR) which activate immune cells and cause inflammatory reactions. The following may be used for diagnostic tests: 1) Skin prick test and intradermal are useful for diagnosis of IgE-mediated (Type I) reaction, 2) The measurement of serum Tryptase levels proved useful in confirming acute IgE-mediated reactions in anaphylaxis, 3) Drug patch test to drugs is useful for diagnosis of delayed reaction (Type IV) cutaneous reactions especially to exanthemata but not useful for bullous eruptions (SJS/TEN), 4) Potential role of basophil activation test (BAT) in diagnosis of acute allergic reaction, 5) Potential role of lymphocyte transformation test (LTT) for delayed hypersensitivity and cutaneous drug eruption, 6) Drug provocation test (oral challenge and intradermal test) would be the gold standard and 7) Recently HLA typing has provided an important tool for testing susceptible patient population with certain drug allergy.

Spirometry and pulmonary function testing

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ABSTRACT

Basic respiratory assessment involves some form of lung function assessment. Spirometry is the most common and it measures lung function, specifically the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled. It is helpful in assessing breathing patterns that identify conditions such as asthma, pulmonary fibrosis, cystic fibrosis, and COPD. Every clinic treating patients with respiratory disease should provide this service. Before performing spirometry, basic information needs to be collected from the patient. Any recent illnesses, smoking history, recent surgery, list of medications, weight, height, age. Contraindications to performing spirometry should be noted as well, which includes pneumothorax, aortic aneurysm, recent thoracic or abdominal surgery, recent myocardial infarction among others. Certain clear instructions regarding position and technique will help to get the best results. Giving strong encouragement during the test frequently helps too. Acceptability, repeatability, reproducibility along with knowing common errors will help in validation the test. The shape of the flow loop will provide additional information for diagnostic purposes.

Allergic and non-allergic causes of sinusitis

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ABSTRACT

Simple concepts of allergy, the various allergens that could lead to rhinitis which could progress to the development of sinusitis were discussed along with other non-allergic causes like bacteria, fungi, and chronic granulomatous diseases like tuberculosis and reflux disease were all touched upon. Management is not discussed. A large number of our patients are affected by sinusitis either caused or led to by allergy and others by infective agents of various kinds. Much effort, time and money are spent to treat this disease. Many of our patients don't realise that sinusitis is a slowly developing problem that gradually builds itself up and can quite easily be controlled in the earlier stages without the use of antibiotics. This is a concept we as surgeons need to impress upon our patients that not all patients need antibiotics nor do all our patients need surgery as the initial treatment. There are multiple causes of sinusitis in humans. Some are common and some are not. The concept of inflammation associated with allergy is associated causation of infection within the sinus mucosa. Colonisation of the inflamed, primed mucosa will then lead to the development of sinusitis, acute initially and that progresses to chronic sinusitis. Simple bacterial infections as well as chronic granulomatous infections are all touched upon. The concepts of polyps as part of the process and inferior turbinates development in simple terms is also touched upon. The basic underlying immunologic processes are also discussed, albeit briefly.

Clinical immunologist for Malaysia: Is it all about primary immunodeficiencies?

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ABSTRACT

WHO defines the practice of clinical immunology as a clinical and laboratory activity encompassing the study, diagnosis and management of patients with disease resulting from disordered immunological mechanism. Such conditions are managed by the clinical immunologist, a clinical specialist with further training in immunology. The recommendation states that a country should have 2 clinical immunologists per million. Primary immunodeficiency (PID) in Malaysia began with the first reports of IgA deficiency in 19772. The next flurry of reports came from Noh LM et al in 1988 with congenital hypogammaglobulinemia. The total number of cases from Malaysian Primary Immunodeficiency Network [MyPIN] registry up to 2016 was 235. The average cases rose from 3.7 to 15.7 yearly between the period [1986- 2005] and [2006 – 2016] respectively, an increase of 4.2 time (420 %). PID as a group should not be considered as rare although individually it is [rare defined as less 1per 2000 of population (EU)]. PIDs are under reported in almost all countries; only 2.2 % of expected in Europe and 0.1 % in Africa. For Malaysia, with a likelihood of 1 % of expected [less than Europe,] would compute towards a probable total of 23,500 PID or a prevalence 0.96 per 1200 (similar of 1 :1200 for US 4). The way to verify these figures is to create a National Registry for PID to include all PIDs in Malaysia. Mortality of PID is of concern as it remains high. Preliminary data from a single centre, WCH in Kuala Lumpur recorded a mortality of 17 % compared to Qatar at 21.4% (1998-2012). The substantial volume of PID in Malaysia is sufficient to cause unease amongst the PID population if their needs are not attended which create health issues for Malaysia. There is a need to provide optimum care beginning with creating subspecialty clinical Immunologist which is yet to materialise. The PID parents &patients has form a Patient Group 'MyPOPI' as advocacy for their cause. With the COVID-19 pandemic ablaze, clinical immunologist should be at centre of COVID 19 research activities for Malaysia as the practice in research intensive countries.

HyperIgM but not?

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ABSTRACT

Case Report: TK is currently a 16-year-old boy of Chinese descendant who first presented at the age of 6-years-old to a local state hospital with history of recurrent abdominal pain and chronic coughs for 6-months duration associated with reduced appetite. Extensive investigations at the time for pulmonary tuberculosis, lymphoma and leukemia, connective tissue disease as well as other infections such as retroviral and hepatitis B and C yielded negative results. At the age of about 6.5 years old, a T, B, and NK cell enumeration revealed low B cell (303 x 10^6/L) and low CD8 counts (259 x 10^6/L). Serum immunoglobulin levels showed elevated IgM of 4.7g/l. A CD40 ligand assay was done, which showed slightly reduced levels compared to control and a diagnosis of Hyper IgM syndrome was made. TK was started on 3 weekly intravenous immunoglobulins. Since the age of 11, TK started to have a change in bowel habits whereby he would pass loose stool (Bristol 5-6) 2 to 3 times per day as compared to once daily of soft stools. Physical examination revealed finger clubbing, and occasional crepitation bibasally with presence of enlarged liver of 13cm and spleen of 14 cm with shotty cervical lymph nodes. At the age of 12, molecular studies were done which revealed a missense mutation in the PIK3CD gene causing autosomal dominant pattern of activated phosphatidyl-inositol 3-kinase delta syndrome (APDS). Therapy with sirolimus (Rapamycin) was started after which TK's hepatosplenomegaly has improved and his began passing motion twice a day, Bristol 4-5. **Discussion:** Activated Phosphoinositide 3-kinase δ syndrome (APDS) is a recently recognised primary immunodeficiency disease. It is a type of combined immunodeficiency in which here is T-cell dysfunction as well as B-cell involvement that consequently leads to disease manifestation. APDS is caused by dominant mutations that increase activity of phosphoinositide-3-kinaseδ(Pi3kδ). Activating PI3Kδ mutations cause T cell senescence and lead to impaired B cell function and vaccine responses. Management of cases include anti-infective prophylaxis with Bactrim or Azithromycin, immunoglobulin replacement therapy, immunosuppression / modulation and HSCT for those with lymphomas or life-threatening infections.

Non-IgE-Mediated gastrointestinal food allergies in children: An update

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ABSTRACT

Food allergy refers to immune-mediated adverse food reactions and can either be mediated via IgE or immune mechanisms other than IgE (non-IgE-mediated). Non-IgE-mediated food allergy refers to a symptom complex usually characterized by severe vomiting and diarrhoea caused by non-IgE-mediated allergy. It is fairly common in infants and young children. Allergy to cow's milk and/or other food protein (e.g., soy) are the commonest form of non-IgE-mediated food allergies. Its onset ranges from 1st day to 12 months of life. In addition to cow's milk and soy proteins, hypersensitivities to other food proteins may also be seen. Approximately 40 - 70% of children had atopic background or a positive family history of atopy. Presenting symptoms include severe vomiting, diarrhoea or bloody stools. Other features include oedema, shock and growth faltering. Laboratory features include moderate anaemia, low plasma albumin level, and metabolic acidosis. Serum food allergen IgE and food skin prick tests are both negatives. Treatment include abstaining from offending protein in the diet. Approximately ~ 80% will respond to extensively hydrolysed formula (eHF) while another 20% may require amino acid formula or a brief period of parenteral nutrition.

Practical management of IgE-Mediated food allergy

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ABSTRACT

Food allergy is defined as an adverse immunologic response to a food protein. It is more common in paediatric age group. The increasing prevalence of food allergy is currently being observed worldwide and has significant medical, financial, and social impacts on young children and their families. Although the exact mechanisms responsible for the rise in food allergy are not fully understood, recent findings suggest three main hypotheses for the increase: the hygiene hypothesis, dual allergen exposure hypothesis, and vitamin D hypothesis. Food allergy is categorised into those mediated by IgE antibodies and by non-IgE-mediated mechanisms. IgE-mediated food allergy is the most widely recognised form of food allergy and is characterised by the rapid onset of symptoms, usually within 2 hours after ingestion of or exposure to the trigger. More than 90% of allergic reactions in children are related to eight food allergens, namely cow's milk, eggs, wheat, soy, peanuts, tree nuts, fish, and shellfish. Symptoms of allergic reactions to food may involve the skin, gastrointestinal and respiratory tracts, and cardiovascular system. Anaphylaxis, the most severe form, and life-threatening allergic reaction is a leading cause of death in children with IgE-mediated food allergy. Therefore, referral to an allergist for timely and appropriate diagnosis and treatment is imperative. Diagnosis of food allergy requires a detailed clinical history regarding diet and food exposure, diagnostic tests, such as skin prick tests or serum food-specific IgE and, if indicated, an oral food challenge. Children can have allergic sensitisation without having clinical symptoms. A diagnosis of an IgE-mediated food allergy requires both the presence of sensitisation to and development of specific signs and symptoms on food exposure. Once the diagnosis of food allergy is confirmed, strict elimination of the offending food allergen from the diet is indicated, as well as timely treatment of allergic reactions and good control of atopic co-morbidities to minimise complications. In addition, dietetic and psychological support is also recommended. Oral immunotherapy can potentially be disease-modifying and require further research. In general, this presentation focuses on the epidemiology, pathophysiology, diagnosis, and management of IgE-mediated food allergy, offering advice on how clinicians can avoid common pitfalls and improve patient care.

The role of contact dermatitis in eczema

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ABSTRACT

Contact dermatitis is an exogenous form of eczema as a result of contact to either haptens or irritants. Haptens (low molecular weight substances) will bind to proteins in the skin to form a complete antigen. Susceptibility to skin damage by irritants depend upon the physical and chemical properties of the substance, the degree, duration and frequency of exposure and under hydration or over hydration of the barrier layer due to low or high humidity working environment. In the presence of eczema, it is important to exclude contact dermatitis. The followings should receive adequate attention: 1) The duration of sensitization process and clinical manifestations: In predisposed individuals, sensitization occurs within a few weeks or as short as 10 days with no visible skin changes. On subsequent exposure, the reaction can manifest itself within 24 hours. 2) The role of allergens or irritants: They can be the primary cause or worsen eczema. Avoidance of the offending allergens or irritants can either improve or resolved the eczema. 3) The clinical presentations: Eczema have characteristic features. In the acute form there are pruritus, erythematous papules and vesicles. The chronic form is usually lichenified and hyperpigmented. 4) To recognize common haptens by the sites of contact in both genders. 5) Types of common skin diseases where contact dermatitis may be associated with: These include atopic dermatitis, seborrheic dermatitis and irritant or allergic contact dermatitis among healthcare workers (HCWs) due to personal protective equipment (PPE) and hand hygiene measures. There are many common haptens or irritants that can worsen atopic dermatitis or cosmetics that worsen facial eczema. The prevalence of iatrogenic dermatitis in times of CPVID-19 has escalated from 20-50% to 71-91%. Paraphenylenediamine has the potential to aggravate seborrheic dermatitis. There will always be new haptens in the future with increased usage and therefore there are necessities for continuous monitoring by all interested parties. Patch test plays a very important role to confirm the existence of contact dermatitis. There are various guidelines to recommend when it is necessary such as the Clinical Recommendations Based on Expert Consensus Opinion from the North American Contact Dermatitis Group for atopic dermatitis. Identifying these haptens or irritants is essential for a proper management plan and having high index of suspicion in new or difficult to control eczema is worth the effort for better outcome.

Perioperative anaphylaxis: An approach toward drug allergy

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ABSTRACT

Perioperative anaphylaxis is an acute and potentially life-threatening event. The incidence is estimated to be around 1:353 to 1:18600. In the 6th National Audit Project (NAP6) in UK, the estimated incidence of severe perioperative anaphylaxis is 1:10000. Diagnosis of perioperative anaphylaxis is difficult due to multiple factors and many differential diagnoses can mimic the clinical features of anaphylaxis. Grading of severity is according to the modified Ring and Messmer Scale, consisting of grade 1 to 4. Guidelines on the management of perioperative anaphylaxis include the ANZAAG guidelines published in 2016. Mainstay of treatment remains supportive and early administration of adrenaline, the dose of which depends on the grade of the reaction. Subsequent management include blood investigation (mast cell tryptase) and referral to the anaesthetic allergy clinic. Indications for referral include generalized rash/ urticaria, angioedema, unexplained cardiac arrest, hypotension and or bronchospasm during anaesthesia. The referral should include legible photocopies of anaesthetic record, drug charts, description of reaction and time of onset of reaction in relation to drug administration. The anaesthetic allergy clinic in Hospital Kuala Lumpur is the only testing centre in Malaysia to investigate perioperative anaphylaxis. It was established in March 2014 and receives referrals from across the whole country. At the clinic, skin testing including intradermal test and skin prick test for all suspected agents would be performed, followed by serum testing including total and specific IgEs. Neuromuscular blocking agents (NMBA) remain the commonest or second commonest causative agent in many countries. In Malaysia it is the most commonly identified culprit. Incidence of different NMBAs and cross-reactivities varies between different countries. Chlorhexidine anaphylaxis is also common in many countries including Malaysia where it is the second commonest. In NAP6, antibiotics were the most common culprit for perioperative anaphylaxis, whereas it is the 3rd commonest in Malaysia. A decrease in the incidence of latex allergy has been observed in many countries but is still a problem in Malaysia. Importance of allergy testing following perioperative anaphylaxis has been shown in many studies. Thus, it is important to refer to the anaesthetic allergy clinic following an episode of perioperative anaphylaxis to improve patient safety and outcome in subsequent surgeries and anaesthesia.

IPEX syndrome: The first reported case in Malaysia

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ABSTRACT

Introduction: IPEX (immune dysregulation, polyendocrinopathy, enteropathy, X-linked) syndrome is a rare PID with an incidence of 1:1.6 million people. Herein, we report the first confirmed case of IPEX syndrome in Malaysia. **Case Report:** A 7-month-old Malay male infant, the 3rd born to non-consanguineous parents, presented at 3 months old with chronic diarrhoea (Bristol 7), poor weight gain, hypokalaemia, hypoglycaemia and vitiligo-like rashes over his body. On examination, he was hypotonic and cachexic. He had hypopigmentation over scalp, face, trunk and limbs and hepatomegaly. He had no eczema, enlarged spleen or lymph nodes or respiratory and cardiovascular abnormalities. Colonoscopy and OGDS revealed post-enteritis syndrome with CMV colitis, (severe infiltration and inflammation of the stomach lamina, duodenum, sigmoid and rectum with CMV inclusion bodies). Skin hypopigmentation was likely atrophic vitiligo secondary to CMV infection. He was treated with IV ganciclovir and total parenteral nutrition, despite that his enteropathy did not improve. Initial workup for Omenn syndrome was not suggestive (no erythroderma, normal naïve T cells and eosinophils 0%). Serum IgG, IgA and IgM were normal. Total T, CD4+, CD8+ and NK cells were normal for age. He had low B cells 245 x 10^6/L (normal 500-1500x106/L), high IgE >5000 IU/L, raised inflammatory markers, high ESR >120 and vitamin B12 (1067pmol/L), hyperleukocytosis, thrombocytopaenia and subclinical hypothyroidism. Taken together, all these are suggestive of immune dysregulation. There was decreased percentage of FOXP3+ Treg (CD4+CD25+FOXP3+) cells by flow cytometry. Genetic testing confirmed a pathogenic variant of FOXP3 gene c.2T>A (p. Met1). He was started on rapamycin and corticosteroid and is planned for a matched related donor haematopoietic stem cell transplant. **Discussion:** Despite our patient not having the classical dermatitis and polyendocrinopathy, the presence of colitis and immune dysregulation played an important role in helping to establish the diagnosis. Type 1diabetes in patients with IPEX may develop later in life. Early use of immunosuppressive therapy can significantly improve GI symptoms of IPEX, while awaiting transplant. Common side effects of rapamycin include aphthous stomatitis and hypertriglyceridemia. Hence during initial treatment Rapamycin levels should be monitored every (1-2weekly), maintaining a trough of 8-15 ng/ml.

OP-01

Efficacy of intralymphatic immunotherapy in allergic rhinitis: A systematic review and meta-analysis

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ABSTRACT

Background: Intralymphatic immunotherapy (ILIT) is a potential treatment option for allergic rhinitis (AR). **Objective:** We aimed to determine the efficacy and safety of intralymphatic immunotherapy in the management of patients with AR. **Methods:** An electronic literature search was performed using MEDLINE (1966 to December 2020), EMBASE (1974 to December 2020), and Cochrane Central Register of Controlled Trials CENTRAL (December 2020). A random-effects model was used to estimate the pooled prevalence with 95% confidence intervals. Quality assessment was done using the principles of the Grades of Recommendation, Assessment, Development and Evaluation approach. Heterogeneity was assessed using the I^2 statistic and at face value by comparing populations, settings, interventions and outcomes. This study is registered with PROSPERO (CRD42019126271). **Results:** We retrieved a total of 285 publications between March 2008 and December 2020, of which eleven satisfied our inclusion criteria. There were 467 participants with age ranged from 15 to 58 years old. The allergen was administered via superficial inguinal lymph nodes using ultrasound guidance. ILIT was given in 3 doses with intervals of four weeks between doses in ten trials. One trial gave 3 and 6 doses with an interval of two weeks. There was significant improvement of combined symptoms and medication score post treatment in ILIT group compared to placebo (SMD -0.49, 95% CI -0.91 to -0.06; P = 0.020; I2 statistic= 71%; 4 studies, 99 participants; low certainty evidence) while no differences in other primary outcomes. **Conclusion:** The use of ILIT in the treatment of AR is promising. Trials with better design are required to establish its role in the management of AR.

Risk Factors Associated with Cockroach Sensitization

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ABSTRACT

Background: Sensitization to cockroach allergens is a risk factor for allergic disease development, which causes low quality of life. However, the risk factors for developing cockroach sensitization remains unclear. A systematic review of existing literature was performed to identify the different risk factors that contribute to cockroach sensitization **Methods:** Articles were obtained from six health science databases. We included articles that were longitudinal and cross-sectional studies, published between 1999 to 2020, evaluated sensitization to cockroach allergens based on skin prick test or serum IgE assays and reported the risk factors associated with cockroach sensitization. Quality assessment, data extraction and meta-analysis were also performed. Results: A total of fifty-two studies reporting the prevalence rate and the risk associated with cockroach sensitization were included. In the pooled analysis, male gender (OR 1.89; 95% CI: 1.47-2.43, p< 0.001) was a significant risk factor while higher parental education (tertiary level) (OR 0.69; 95% CI 0.51-0.92, p=0.0123) was a protective factor for cockroach sensitization. No significant associations were identified in relation to ethnicity, area of residence (urban/rural) or tobacco smoke exposure. In the subgroup analysis of cockroach-sensitized individuals with helminth infection, *Trichuris trichiura* infection was a risk factor (OR 1.62; 1.26-2.09, p< 0.002) while hookworm infection was a significant protective factor (OR 0.77; 95% CI 0.63-0.94, p=0.009) for cockroach sensitization. **Conclusion:** Overall, male gender was a risk factor for cockroach sensitization while higher parental education level was protective against cockroach sensitization. The effect of infection of different species of helminth on cockroach sensitization could be attributed to its infection load. A higher parasite load has been shown to induce modified Th2 immune response, which could protect against sensitization to cockroach allergens. More studies investigating environmental factors are needed to gain a better understanding of other risk factors influencing cockroach allergen sensitization.

Lactobacillus may relieve symptoms in children with allergic rhinitis

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ABSTRACT

Background: The effect of probiotics on AR is not consistent. We want to determine the efficacy and safety of *Lactobacillus paracasei* subsp. paracasei LP-33 (GM-080) on the disease severity and immune biomarkers in children with allergic rhinitis (AR). **Methods:** A double-blind, prospective, randomized placebo-controlled study was conducted on 122 children aged 5–16 years with AR. Children are randomized to receive different doses of LP-33 and placebo for 3 months. The scores of severities in each symptom, such as sneezing, rhinorrhoea, nasal pruritus and nasal congestion, Nasal Total Symptom Score (NTSS), and Global Assessment by the Investigator in different groups and at different visits were evaluated by ANOVA and GEE model. Immunological parameters IgE and IFN-γ data were also collected were compared at baseline and after 3 months. **Results:** Children receiving LP-33 showed a significant symptom relief in sneezing than the placebo group after treatment (p= 0.033), and this difference started since week 2. NTSS showed a decrease trend. Global Assessment scores by the Investigator were higher in the LP-33 group than the placebo group after treatment p=0.049). IgE decreased and INF- γ increased after 3 months, though failed to reach statistical significance. **Conclusion:** The supplementation of LP-33 was associated with significant alleviation of symptoms of sneezing in children with allergic rhinitis.

Association between *MBL2* rs7096206 polymorphism and mannose-binding lectin in patients with atopic disease

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ABSTRACT

Background: The serum level of MBL is dependent on single nucleotide polymorphisms in the MBL2 gene. The MBL impairment can lead to immunological damages and autoimmune diseases, however, its pathogenic mechanisms are unclear. **Objective:** The aim was to study *MBL2* rs7096206 polymorphism in patients with atopic disease. **Methods:** A total of 180 patients were recruited in this study including atopic n=90 and non-atopic healthy control n=90. Blood samples were collected from patients in each group and DNA was extracted using gSYNC™ DNA Extraction Kit. The genotype of MBL2 rs7096206 polymorphism was determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Serum MBL levels were measured by an enzyme-linked immunosorbent assay (ELISA). **Results:** The XY genotype distribution in atopic patients were 18.9% (n=17) and 10% in control group (n=9). YY genotype was frequently observed in control group than in atopic group [n=81 (90.0%) vs. n=73 (81.1%); p=0.09]. The median serum levels of MBL were 3793.5±811.01 ng/ml in atopic group and 2665.55±922.23 ng/ml in control group (p<0.001). Additionally, the median of serum levels of MBL was quite higher in the atopic group (3775.4±840.6 ng/ml) than in the control group who has YY genotype (2711.3±945.9 ng/ml; p<0.001). For XY genotype, the median of serum levels of MBL was also significantly higher in the atopic group (3861.0±705.9 ng/ml) than in the control group (2453.9±795.7 ng/ml; p<0.001) those who is carrying XY genotype. There was no relation between YY, XY genotypes, and MBL level (p=0.808, p=0.773) in study groups. **Conclusion:** The frequency of risk X allele was not different between case and control groups. The serum level of MBL was significantly high in the atopic group comparing to controls. Serum MBL level in atopic patients was not differed by MBL2 rs7096206 polymorphism.

Placental proteins proteomic identification is associated with subsequent allergic disease in childhood

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ABSTRACT

Background: Allergic disease has risen to epidemic proportions during recent years. Prenatal events are important in determining disease susceptibility via environmental influences on placental function and fetal programming. We hypothesize that childhood susceptibility to allergy is increased through significant alterations in placental function that exert a programming effect on the fetal immune system. We aim to identify the placental proteins associated with childhood allergy using placental tissue from two populations of women whose children have different risks of allergic disease susceptibility. **Methods:** Placental tissue will be examined using a proteomic approach that involves quantitative label-free comparative MS and data analysis is performed using Mascot database and MaxQuant software. Placental tissue from children without allergy were compared to children with allergic diseases (male n=8, female n=8). **Results:** Three candidate proteins were identified in placental samples associated with subsequent allergic disease in all children that include Human Biglycan (ratio of >2-fold change), Human Amine oxidase [flavin-containing] A and Human Amine oxidase [flavin-containing] B (ratio <0.5-fold change), all relative to non-allergic samples. Moreover, there were 19 proteins significantly altered in placentae of allergic males and 21 proteins altered in placentae of allergic female relative to non-allergic children. Many of these proteins could exert a programming effect on the fetal immune system including Human Ig heavy chain V-I region HG, Human Complement C3, and Human Apolipoprotein B-100. **Conclusion:** The current findings suggest protein expression varies in utero in children who subsequently develop allergy and the altered expression of these proteins vary in a sex specific manner.

EP-01

Prediction of exacerbations of bronchial asthma using fractional exhaled nitric oxide (FeNO) and asthma control test (ACT)

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ABSTRACT

Background: Asthma exacerbations can significantly impact the quality of life of patients. ACT is a questionnaire which is used to assess asthma control by analysing asthma symptoms spanning 4 weeks. FENO is used to monitor eosinophilic airway inflammation which is used for objective assessment of the control of asthma. The purpose of this study was to assess the ability of exacerbation prediction of bronchial asthma using FeNO and ACT. **Methods:** This study was conducted in September 2020 – January 2021 among medical undergraduates with physician diagnosed bronchial asthma in Faculty of Medicine, University of Peradeniya, Sri Lanka. Students who volunteered were given an interviewer-administered questionnaire, which collected information regarding current control of asthma using ACT from which ACT score was calculated. Subsequently, the students underwent FeNO test (using Bedfont NObreath® NBR025079 (Serial No -TMI1850006587)). ACT score >19 was considered as good control whereas <=19 was considered as poor control. FeNO value <50 ppb was considered as good control whereas >=50 ppb was considered as poor control. The subjects were followed-up for 3 months, and asthma exacerbations within that period were obtained. Data was analysed with SPSS utilizing Independent samples T test. **Results:** 30 students participated in the study. Age range 21-25 years. Male 16(53.33%) and female 14(46.67%). According to ACT 16(53.33%) had good control and 14(46.67%) had poor control of asthma. According to FeNO, 21(70.00%) had good control and 9(30.00%) had poor control of asthma. The mean exacerbation of poor control group (according to ACT) was 0.6428 (±0.8419), whereas mean exacerbation for good control group (according to ACT) was 0.688 (±1.9906) (p =0.938). The mean exacerbations of good control group (according to FENO) was 0.190 (±2.4889) whereas Mean exacerbations for poor controlled group (according to FENO) was 1.778 (±2.4889) (p= .007). **Conclusion:** Students who had poor control according to FENO values had significantly higher asthma exacerbations than students who were identified as poor control with ACT. Therefore, FeNO may be considered as a better predictor of asthma exacerbations.

Results about RS1800450 and RS11003125 polymorphisms of MBL2 gene in relatively healthy and bronchial asthmatic subjects

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ABSTRACT

Background: The genetic and environmental factors contribute to the development of bronchial asthma. We aimed to determine the role of rs1800450 and rs11003125 polymorphisms of the MBL2 gene in relatively healthy and asthmatic subjects. **Methods:** Serum samples were collected from 71 healthy Mongolian adult blood donors and 71 bronchial asthma. The extraction of DNA was carried out by the extraction kits of genomic DNA (Geneaid). The mannose binding lectin gene was genotyped by PCR-RFLP method. The data were analyzed by odds ratio (OR) and associated confidence intervals (CI) at 95%. Chi-square test was performed. **Results:** The frequency of risky GA and AA genotypes of the rs1800450 polymorphism were determined respectively 8.4% (6) and 11.3% (8) in a case group and 16.9% (12) and 5.6% (4) in a control group. Also, frequency of GA and AA genotypes of the rs11003125 polymorphism were 33.8% (24) and 2.8% (2) in a case group. In a control group, genotypes were 25.4% (18) and 1.4% (1). Allele G (wild type) of rs1800450 polymorphism was found out in 84.5% of cases and in 85.9% of controls whereas A (mutant allele) was present in 15.5% of cases and in 14.1% of controls. Allele G (wild type) of rs11003125 polymorphism was present, respectively, in 80.3% of cases and in 85.9 of controls whereas C (mutant allele) was present in 19.7% of cases and in 14.1% of controls. **Conclusion:** There was no significant difference between case and control group correlated with rs1800450 and rs11003125 polymorphisms of MBL2 gene.

The role of anti-nuclear antibody indirect immunofluorescence pattern and titration in determining diagnosis of systemic rheumatic autoimmune

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ABSTRACT

Background: The purpose of this study was to determine the correlation between ANA-IIF pattern and titration for the diagnosis of SARDs. **Methods:** A retrospective study was conducted over six months period. All positive ANA-IIF samples were included from patients aged 18 years and above for further analysis. The pattern and titration for ANA-IIF were recorded for each patient. Determination of ANA-IIF pattern and titration was analysed on the NOVA View® platform. The titration was performed at 1:80, 1:160,1:320 and 1:640 dilution. The last positive dilution was taken as the titer for respective sample. The demographic data and final diagnosis of each patient were retrieved. **Results:** A total of 105 patients were included for analysis. The majority of the patients were female (80%) and from Malay ethnicity (66.7%). The mean age was 53.75 years +/- 16.79. Majority of the patients had ANA-IIF titration 160 and less (N=63, 60%). The speckled was observed in 58 patients (55.2%) followed by homogeneous in 34 patients (32.4%). Eighteen patients (17.1%) were finally diagnosed with SARDs. The titration of at least 320 and homogeneous pattern were significantly associated with SARDs ($p<0.0001$). Patients diagnosed with SARDs were significantly younger with mean age of 38.33 years +/- 3.42 ($p<0.001$). Similarly, those with titration of at least 1:320 were younger than those with lower titration (mean age 46.14 versus 56.66 years, $p=0.04$). Multisystemic involvement was significantly associated with the final diagnosis of SARDs ($p=0.14$) but not with ANA-IIF titration of at least 1:320 ($p=0.06$). **Conclusion:** ANA-IIF titration of equal or more than 1:320 and homogeneous pattern were significantly associated with SARDs diagnosis, and this association was perhaps more important in younger patients.

Two novel genotypic markers affecting promoter activity of a CABP1 isoform in allergic rhinitis among chinese population

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ABSTRACT

Background: Allergic rhinitis (AR) affects 30% of the global population and causes heavy economic burden and low quality of life due to its sufferers. While genetic factors play an important role in the pathogenesis of AR, its underlying mechanisms are not fully understood. In this study, we aimed to functionally characterize the CABP1 gene in relation to AR. **Methods:** Genome wide association study was carried out on 2,146 cases (AR) and 2,039 control (non-AR) of Chinese individuals to identify potential single nucleotide polymorphisms (SNPs) associated with AR. Functional prediction was carried out using bioinformatics tools and promoter functional characterization was performed using dual-luciferase promoter reporter assay. **Results:** Logistic regression analyses revealed that the lead SNP (rs11065183) of a quantitative trait locus containing CABP1 gene had a suggestively significant association with AR [OR (95% CI) = 0.7891(0.7120–0.8745), p= 6.25E-06]. Two SNPs (rs12228187 and rs11065189), that were in high linkage disequilibrium (>80%) with rs11065183, were predicted to behave as transcription factor binding sites of a CABP1 isoform. Dual-luciferase promoter reporter assay revealed that CA haplotype (protective allele) of the two SNPs showed a significantly higher promoter expression level compared to TG haplotype (risk allele) at 24h and 48h post infection in the HEK293T cell line (1.42-fold, $p < 0.01$ for 24h; 1.50-fold, $p < 0.0001$ for 48h). **Conclusion:** Two SNPs (rs12228187 and rs11065189) were identified as novel genotypic markers in AR susceptibility among Chinese patients. CA haplotype of these SNPs was identified as the risk factor that demonstrated significantly decreased promoter activity of the CABP1 isoform. CABP1 functions to regulate the activity of a calcium channel subunit, Cav1.2, which is involved in antigen presentation. Further studies on the effect of the SNPs of CABP1 on antigen presentation would provide a better understanding in its role in AR pathogenesis.

Prevalence of food allergy at a single tertiary care centre in Malaysia

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ABSTRACT

Background: Food allergy is increasing worldwide, and Southeast Asian region is no exception. Despite the increasing rates in children, data on the burden of the disease in Malaysia is still lacking. We aimed to determine the prevalence and different types of food allergies at a tertiary care Immunology Clinic in Selangor, Malaysia. **Methods:** A comprehensive chart review was performed on all patients (aged 0-18 years old) referred for allergic diseases to the Pediatric Immunology Clinic from January 2017 to December 2020. **Results:** A total number of 298 patients were referred to our Immunology Clinic from year 2017 to 2020 for allergies. Of these 298 patients, 157 were diagnosed with different types of food allergies. Males to female ratio was 1.2:1 The median age of these patients was 18 months. Most patients have multiple food allergies (%). The most common food allergens that patients were reacted and sensitized to were cow's milk (35.6%) and hen's egg (35.6%), followed by peanut (21.7%), fish (10.2%), soy (8.3%), wheat 7.6%, shellfish 7.6%, and tree nut (1.9%). Other types of foods 16.5% and non-IgE mediated food allergy being 3.2%. **Conclusion:** Food allergy is an important and growing public health problem. Prevalence has increased over the past years. It is important to investigate food allergies among food allergy sufferers as this may help sufferers to identify and to avoid foods that trigger allergic reactions.

Association between allergic diseases and attention-deficit/hyperactivity disorder (ADHD) symptoms in children ages 6 – 12 years old using the Filipino version of the vanderbilt ADHD parent rating scale

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ABSTRACT

Objective: The objective was to determine the association of allergic diseases and ADHD symptoms among children ages 6 – 12 years old based on parental report using the Filipino version of the Vanderbilt ADHD Parent Rating Scale. **Methods:** School-aged children ages 6 to 12 years old with physician-diagnosed allergies (bronchial asthma, allergic rhinitis, atopic dermatitis) were randomly selected. Skin prick test (SPT) to aeroallergens was done. The parents completed the Filipino version of the Vanderbilt ADHD Diagnostic Parent Rating Scale (VADPRS), a screening tool for ADHD. **Results:** Among the 415 patients, 135 (32.5%) screened positive for ADHD symptoms. Upon assessment of the Vanderbilt parent rating subscale responses, 13.49% of the children were categorized as predominantly inattentive subtype, 6.02% as predominantly hyperactive/impulsive subtype, and 13.01% as combined inattention/hyperactivity. Three hundred and seventy-six (91%) children were diagnosed with asthma. Among these asthmatics, 119 (32%) had ADHD symptoms with the following subtypes – predominantly inattentive subtype (13.56%), predominantly hyperactive/ impulsive subtype (5.05%) and combined inattention/hyperactivity (13.03%). Combined inattention/hyperactivity subtype had a significant proportion of severe asthmatics, as compared to mild or moderate asthma (p value = 0.026). Furthermore, 389 (94%) children were diagnosed with allergic rhinitis. Among these patients, 130 (33%) had ADHD symptoms with the following subtypes – predominantly inattentive subtype (13.62%), predominantly hyperactive/ impulsive subtype (6.43%) and combined inattention/hyperactivity (13.37%). However, evidence is not sufficient to demonstrate a difference in ADHD subtypes with allergic rhinitis severity. Lastly, 206 (50%) children were diagnosed with atopic dermatitis. Among these patients, 71 (34%) had ADHD symptoms with the following subtypes – predominantly inattentive subtype (14.56%), predominantly hyperactive/ impulsive subtype (4.85%) and combined inattention/hyperactivity (15.05%). However, there is insufficient evidence to demonstrate a link between ADHD subtypes and atopic dermatitis severity. **Conclusion:** Children with allergies, especially those with severe asthma are more likely to have ADHD symptoms.

Characteristics of atopic dermatitis in vietnamese children - A web-based survey

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ABSTRACT

Background: Atopic dermatitis (AD) is a common allergic disease in children, characterized by chronic, relapsing inflammation with eczematous and pruritic skin condition. Clinical manifestations of AD are affected by multiple factors, including age, environmental factors, food, and skincare routines. **Objective:** This survey investigated the features of AD in Vietnamese children. **Methods:** A web-based survey was conducted with 352 responses from parents whose children were diagnosed with AD by doctors. **Results:** Most responders (89.5%) had their children diagnosed with AD at the age of 0-36 months (23.2% under 1 month, 53.6% of 1-12 months, and 12.7% of 12-36 months). Overall, the AD lesions were found mostly on cheeks (60.2%), leg (40.1%) and arms (39.8%). In children under 12 months of age, AD lesions were commonly found on cheeks; while lesions on arms and legs were frequently reported in older children. 62.2% responders did not know the exact triggers of AD or thought that it was spontaneously exacerbated. The common suspected triggers were extreme weather conditions [hot (28.9%), dry (24.5%) or cold (24%) climates], followed by milk and dairy products (18.2%), and other foods (9.9%). Regarding treatment therapies, 74.9% responders considered skin moisturizing important, followed by frequently bathing (49.9%), avoiding cow's milk or dairy products as well as suspected foods (25.1%), and using topical steroids (20.7%). Only 8.5% and 1.9% responders thought that oral antihistamine and corticosteroids, respectively, are important in AD treatment. More than 50% of responders believed that AD is a chronic disease with flare-ups (52.5%) and will grow out (56.6%); moreover, they believed that children with AD could develop other allergic diseases later in their life (50.8%). **Conclusion:** AD in Vietnamese children has similar clinical characteristics with the general children AD. Hot weather could be a potential AD trigger in Vietnamese children. The knowledge of parents about AD in their children was good. These findings suggested a reasonable application of international AD treatment guidelines in Vietnamese children, with a minor revision due to tropical climate conditions.

The study of osteitic changes in CT paranasal sinus of atopic and non-atopic chronic rhinosinusitis

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ABSTRACT

Objective: To study the osteitic changes in paranasal sinus walls in patient with the atopic and non-atopic chronic rhinosinusitis (CRS) by Computed Tomography (CT) scan evaluation using Lund Mackay staging system and Global Osteitis Scoring System. **Methods:** A retrospective study of 75 CRS patients whom underwent CT paranasal sinus as a part of the disease assessment before any sinonasal surgery from January 2015 until December 2020. Skin prick test is used to determine the atopy among the CRS group. 66 patients that had CT scans within the period and did not have CRS, facial trauma or sinonasal malignancy were included as a control group. The radiological findings for disease severity and osteitic changes in both atopic and non-atopic CRS and the control group were evaluated using Lund Mackay staging system and Global Osteitis Scoring system (GOSS). **Results:** There were more than half of CRS were atopic cases (n=41, 54.7%) with 64% (n=48) osteitis changes were seen in CRS group whereby only 0.03% (n=2) in the control group. The mean score for Lund Mackay was higher in non-atopic group which is 9.03 (SD=5.07) but the mean score for GOSS was higher in atopic group 10.90 (SD=10.50). **Conclusion:** There was no significant association in atopic status for CRS severity and osteitic changes from the radiological evaluation found in this study.

IgE reactivity patterns revealed six IgE epitopes of Der p 2 as potential hypoallergen for dust mite allergic individuals

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ABSTRACT

Background: Studies on dust mites have been confined to very few species in terms of crude extract or purified allergen reactivity, therefore, the relative allergenicity of common indoor dust mite species in the same cohort is unknown. **Objective:** To evaluate the presence of different IgE binding profiles to dust mite crude extracts, purified recombinant group 2 allergens and Der p 2 alanine mutants in the same population. **Methods:** Serum of 458 Singaporeans with allergies were evaluated using purified crude extract and group 2 allergens from 8 dust mite species and 21 alanine mutants of putative IgE epitopes of Der p 2 using immuno dot-blot assay. Reaction signatures were identified based on Ward's minimum-variance using R software and GraphPad Prism. Categorical data were compared using ANOVA test or Fisher-exact testing. Significance was defined as $p \leq 0.05$. **Results:** IgE reactions were observed in 67.9% and 57.1% of the individuals to crude extracts and recombinant group 2 allergens respectively. Individuals were classified into three reactivity-profiles (high mean IgE-reactivity to all dust mites, moderate mean IgE-reactivity to Dermatophagoides spp. and high mean IgE-reactivity to Dermatophagoides spp. but moderate mean IgE-reactivity to storage mites). Similar IgE-reactivity profiles were observed when recombinant group 2 allergens were used. Clinical outcomes did not significantly differ between reactivity profiles. Recognition of Der p 2 IgE epitopes varied among the IgE-reactivity profiles where six IgE epitopes (N10A, H11A, E62A, H74A, K77A and K96A) were common among different reactivity profiles. **Conclusion:** Dermatophagoides spp. and its group 2 allergens were the most important allergens in the indoor environment. Dust-mite allergic individuals displayed three unique IgE-reactivity profiles. Six of 21 IgE epitopes of Der p 2 were recognized by individuals from all three reactivity profiles, suitable to be used in hypoallergen preparations of Der p 2.

Mendelian susceptibility to mycobacterial disease due to IL-12RB1 mutations in two siblings

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ABSTRACT

Background: Mendelian Susceptibility to Mycobacterial Disease (MSMD) is a rare genetic defect that interferes with the synthesis of IFN-γ. Eleven gene mutations (IL12B, IL12Rβ1, ISG15, TYK2, IRF8, SPPL2A, C4BB, IFNGR1, IFNGR2, STAT1, NEMO) has been recognised in MSMD. MSMD patients are at risk of tuberculous infection and less virulent non-tuberculous mycobacterium such as BCG vaccine substrains. Some patients are also susceptible to invasive Salmonella infections and mucocutaneous candida infection. Here, we report a case of siblings with IL12Rβ1 deficiency to investigate the spectrum of clinical presentation. **Methods:** Case notes of the patients were reviewed, and relevant clinical information were summarised and analysed. **Results:** An 8-year-old boy who received Bacille-Calmette-Guerin (BCG) at birth, presented twice at age 4 and 5 months with suppurative left axillary lymphadenitis which requiring surgical excision for the latter. He was subsequently treated with anti-tuberculosis (TB) therapy for 1 year. At age 4, he presented with a left inguinal abscess which was positive for *Salmonella sp.* And he was treated accordingly with no recurrence of illness thereafter. His 6-year-old younger sister, also vaccinated with BCG at birth, had a history of *Salmonella* meningitis at 2 weeks old and suppurative left axillary TB lymphadenitis at age 5 months, cervical TB lymphadenitis at age 9 months, and *Salmonella* septicaemia with disseminated BCG disease at age 21 months. Full blood counts, serum immunoglobulin and T and B cells enumeration were normal for both siblings. Whole exome sequencing results for both siblings showed homozygous mutations of the IL-12Rβ1 gene (missense mutation c.523C>T) consistent with autosomal recessive IL-12Rβ1 which causes MSMD. **Conclusion:** The disease spectrum of MSMD are highly variable from the most severe form of early onset, disseminated, recurrent and life-threatening mycobacterial disease to the least severe form of late onset or silent carrier due to incomplete penetration of the disease.

Nasal provocation test with allergenic extract of *Blomia tropicalis*

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ABSTRACT

Background: The *Blomia tropicalis* mite is a risk factor for allergic rhinitis in Latin America. For the identification of sensitivity to aeroallergens the skin prick test was performed, while the nasal provocation test evaluated the response of the nasal mucosa to specific aeroallergens with high sensitivity and specificity. In Cuba, it is unknown. Our study objective was to evaluate the sensitivity and specificity of nasal provocation test with allergenic extract of *Blomia tropicalis* in patients with allergic rhinitis sensitive to this mite. **Methods:** This experimental, prospective study and diagnostic evaluation was made with patients cared from the department of allergology of the University Hospital "Gral. Calixto Garcia" in the Habana- Cuba. It was carried out from June 2018 to June 2019 with a sample of 100 patients, 50 group A (allergy sufferers) and 50 group B (control) who met the inclusion criteria. Performing the preliminary questionnaire, physical examination, and nasal provocation test (according to the Lebel scale). **Results:** Female sex predominated (Group A 70% and Group B 64%). The skin prick test with allergenic extract of *Blomia tropicalis* it was positive 100% in Group A and negative in Group B. The nasal provocation test with allergenic extract of *Blomia tropicalis* it was positive in 90% of Group A with a response of 34% to the concentration of 20 biological units of the allergenic extract of *Blomia tropicalis* and 100% negative in Group B. A sensitivity of 90% and specificity of 100% were calculated. There were no systemic adverse reactions. **Conclusion:** The nasal provocation test demonstrated high sensitivity and specificity; being a diagnostic method that allows evaluating nasal reactivity resulting in safe, effective, non-invasive, well tolerated, economical and reproducible.

Characterized adverse reactions due to NSAIDs in the University Hospital “Gral. Calixto Garcia”

Aldana D

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ABSTRACT

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely prescribed compounds in the world and the adverse reactions to them are frequently. Hypersensitivity reactions are often confused with those in which an immune mechanism is not involved, which are the most frequent. Our objective was characterized adverse reactions due to NSAIDs in our hospital. **Methods:** Is a descriptive, cross sectional observational study. The sample consisted of 100 patients treated in the allergy department of the University Hospital “Gral. Calixto Garcia” in the Habana- Cuba. Mean age 48,7 years (range between 19 and 75 years). All of them received a medical history and a questionnaire prepared for this study after they gave their written consent. **Results:** The female sex was frequently affected (74%). The drug most implicated was dipyrone (74%). Polypharmacy with NSAIDs was greater for the combination of dipyrone and diclofenac (16%). Cutaneous manifestations were present in 100% of the cases, followed by respiratory manifestations (55%), the majority not mediated by immunological mechanism. 72% of the reactions occurred at home and 100% of the cases improved with the appropriate medication without sequelae. **Conclusion:** Polymedication was present in half of these reactions. Skin manifestations are the most frequent, predominantly urticaria and angioedema. Antihistamines are the most used with satisfactory response to treatment with resolution of symptoms in all cases. Recommend drugs by NSAIDs combinations only in very necessary cases. As a rule, the NSAIDs should only be used by a doctor´s prescription at the appropriate dose and for the time necessary.

Ecthyma gangrenosum as the presenting clinical feature of x-linked agammaglobulinemia: Report of three cases

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ABSTRACT

Background: Children with x-linked agammaglobulinemia (XLA) usually presents with pneumonia and otitis media caused by pyogenic bacteria. Rarely, ecthyma gangrenosum (EG), a known cutaneous manifestation of Pseudomonas septicemia present in XLA as the first presenting features. We report three cases of EG caused by Pseudomonas aeruginosa in previously healthy boys, leading to the diagnosis of XLA. Additionally, we provide a brief literature review on those cases of EG where an underlying XLA was eventually diagnosed. **Methods:** Three paediatric cases admitted to the intensive care unit with *P. aeruginosa* septicemia associated with ecthyma gangrenosum were retrospectively reviewed. Laboratory workup consisted of microbiological, hematological and immunological investigations. **Results:** The three patients were aged 1 year 6 months, 3 years 5 months and 5 years 6 months. All patients had septic shock and required mechanical ventilation. Pseudomonas aeruginosa was isolated in blood and/or skin lesions of all patients. Underlying hypogammaglobulinemia and neutropenia were detected in all patients. Treatment consisted of combined antipseudomonal antimicrobial therapy and surgical debridement. All patients survived. Subsequent B cells measurement and BTK protein and genetic analysis confirmed the diagnosis of XLA. Twelve other similar reported cases were reviewed and analysed based on their clinical presentation, diagnosis and treatment. **Conclusion:** *P. aeruginosa* sepsis should be treated as early as possible. The most common risk factor for ecthyma gangrenosum in XLA patients is neutropenia. In previously healthy children, immunological evaluation is important to rule out an underlying immunodeficiency.

Rheumatoid factor and new generation of anti-cyclic citrullinated peptide antibodies as diagnostic tools in rheumatoid arthritis

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ABSTRACT

Background: Rheumatoid arthritis (RA) is an autoimmune disease which lead to progressive joint damage and affects patient's quality of life. Since rheumatoid factor (RF) has limited diagnostic performance, new generation of anti-cyclic citrullinated peptide (anti-CCP) antibodies were then introduced. This study aims to compare serum RF, anti-CCP2 IgG, anti-CCP2 IgA and anti-CCP3.1 IgG/IgA antibodies status in RA patients and healthy controls. The association between these serological markers and factors associated with functional status of RA patients were also evaluated. **Methods:** This cross-sectional study was conducted among 46 RA patients and 40 healthy controls in Rheumatology Clinic, Hospital USM. Five millilitres of blood were withdrawn. RF was analyzed using Direct Latex, whereas anti-CCP2 IgG, anti-CCP2 IgA and anti-CCP3.1 IgG/IgA antibodies were assayed using Enzyme Linked Immunosorbent Assay. Sociodemographic data, clinical characteristics and serological markers were evaluated for the association with quality of life based on modified Health Assessment Questionnaire (mHAQ) score. The data were analyzed using SPSS version 26.0 with the p value of < 0.05 was considered significant. **Results:** Majority of RA patients had positive status of serum RF (78.3%), anti-CCP2 IgG (63.0%) and anti-CCP3.1 IgG/IgA (63.0%). Significant differences were found in RF ($p<0.000$), anti-CCP2 IgG ($p<0.000$), anti-CCP2 IgA ($p<0.000$) and anti-CCP3.1 IgG/IgA ($p<0.000$) antibodies between RA and control groups. RA patients had mild functional status based on mHAQ score. Significant association were found between pain score ($p <0.000$), anti-CCP2 IgG antibody status ($p =0.049$) and functional status of RA. No significant association between RF and mHAQ score. **Conclusion:** Positive status of RF, anti-CCP2 IgG, and anti-CCP3.1 IgG/IgA antibodies in majority of RA patients indicates the significance of these serological markers in diagnosis and prognosis of RA. Future studies need to be conducted to obtain more understanding regarding the role of new generation anti-CCP antibodies in diagnosis and pathogenesis of RA.

Atypical presentation of the side effect of sublingual immunotherapy - tablet house dust mite allergy immunotherapy in a patient with multiple atopic diseases: Allergic rhinitis, allergic conjunctivitis and atopic eczema

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ABSTRACT

Introduction: House dust mite (HDM) sublingual immunotherapy (SLIT)-tablet is sublingually given as allergy immunotherapy (AIT) for HDM allergic rhinitis and allergic asthma. **Case Presentation:** We report here a 35-year-old female with severe allergic rhinitis, allergic conjunctivitis, atopic eczema, latex and drug allergy, was started on SLIT-tablet AIT and had delayed inflammatory reaction in the oral cavity. She had positive skin prick test to HDM Dermatophagoides pteronyssinus (Der p) and Dermatophagoides farinae (Der f), both with a wheal size of 20mm and 18mm respectively. Total immunoglobulin E (IgE) was raised (644 kU/l) and specific IgE to Der p & Der f were very high (>100 kUA/l). Specific immunoglobulin G4 (sIgG4) were normal. She was started on the first dose of SLIT-tablet at the Ear Nose and Throat operating theatre under latex free environment. Fifteen minutes after administration she had sublingual and throat irritation, choking sensation, followed by heartburn and itchiness over her skin and eyes. Symptoms resolved with levocetirizine and vital signs were normal. She continues the SLIT-tablet daily at home. On third day of SLIT-tablet she developed throat itchiness, discomfort at sublingual area where the drug was placed. She noticed a few small villous like growth on ventral surface of the tongue and some at the floor of the mouth. By day 15 of treatment, the heart burn, the throat, skin and eye itchiness have reduced. At day 52 of treatment, the only reaction was persistent oral cavity discomfort and the presence of tiny villous like growth at the floor of her mouth. She had tolerated the SLIT-tablet without any systemic allergic reaction or anaphylaxis. **Discussion:** The presence of persistent villous like growth over the tongue and floor of mouth after on SLIT-tablet containing HDM allergen could suggest a possibly delayed inflammatory reaction locally over the sublingual region rather than an IgE-mediated allergic reaction.