Immunology, Allergy and Immunodeficiencies Abstracts

Does oral administration of immunoglobulin could reduce diarrheal severity in common variable immunodeficiency

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Background: Common variable immunodeficiency (CVID) is a heterogeneous group of disorders characterized by variety of manifestations especially recurrent respiratory tract infections and diarrhea. Case presentation: Herein a 26-year old woman is presented who suffered from persistent chronic diarrhea and poor weight gain. Giardia lambelia cyst has been constantly present in almost all stool exams since childhood and did not improve with regular treatment. Immunological studies showed hypogammaglobulinemia, while the diagnosis of CVID was subsequently made for the patient. Immunoglobulin therapy via oral consumption was experimentally started for the patient, which led to dramatic relief of diarrheal frequency and severity. Treatment for antibody deficiency syndromes includes either intravenous or subcutaneous administration of immunoglobulin which can reduce the frequency of infections. Further studies on large number of patients with CVID are needed to test the efficacy and safety of oral consumption of immunoglobulin in those with persistent diarrhea.
Keywords: Common Variable Immunodeficiency, Intravenous Immunoglobulin, Diarrhea

Update on classification of primary immunodeficiencies

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Primary immunodeficiencies(PIDs) are heterogeneous group of congenital disorders characterized by different defects in the immune system which lead to increased susceptibility to recurrent infections, autoimmunity, and malignancies. Considering recent advances in identification of novel PIDs, the number of defined PIDs has been increased. While about 200 different types of PID have been reported so far, their number is still rapidly growing. The Expert Committee of the International Union of Immunological Societies(IUIS) classified PIDs into eight categories: 1)combined T and B-cell immune deficiencies, 2)well-defined syndromes with immune deficiencies, 3)predominantly antibody deficiencies, 4)diseases of immune dysregulation, 5)congenital defects of phagocyte number, function, or both, 6)defects in innate immunity, 7) auto-inflammatory disorders, and 8)complement deficiencies. Although there is an effort to re-shape the current classification to more a practical form, all novel PIDs have already go to one of these categories.
Keywords: Primary Immunodeficiency Diseases, Classification

Immune thrombocytopenic purpura as a rare presentation of chronic granulomatous disease

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Background: Chronic granulomatous disease is a rare primary immunodeficiency disorder with various presentations mostly recurrent abscess in skin, lung, brain etc. Auto immune diseases are more prevalent in these patients and their family members than ordinary people. **Case Presentation:** Our patient was a 19 year-old boy who was diagnosed at 8 yr of age when he went under surgery for liver abscess. His parents were 1st cousins and one of his brothers suffered from X- linked CGD as well. During his life he developed Tuberculous uveitis, osteomyelitis in radius bone with Aspergillous spp, Aspergillous pneumonia and chronic bilateral otitis media with perforation. Last year he was admitted with swelling of his elbow due to hemarthrosis and investigations revealed thromcytopenia which was approved as an idiopathic or immune type deficiency. IVIG and high dose steroid could partially corrected platelet numbers and he finally discharged with low dose steroid and Danazole. Up to now he has been admitted twice for bleeding disorders and low platelet numbers. Now, he is stable with low maintenance daily steroid and his platelet count is about 80-90,000/ml. **Conclusion:** Autoimmune disorders are more prevalent among CGD patients and their family members than general population.
Keywords: Chronic Granulomatous Disease, ITP, Autoimmunity

Therapeutic effects of Inhaler corticosteroid and antileukotriene in wheezy child

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Background: Asthma is the common chronic disease of childhood. 10-15% of children are affected and wheezing is the most common chronic symptom of asthma. About 40% of preschool age children have wheezing but only 30% of them go on to have persistent asthma. Antileukotrienes are recommended as alternative treatment for mild persistent asthma.
Methods: During 1 year, 68 children younger than 5 years old with recurrent wheezing(more than 3 times during 1 year) were studied. The patients randomly divided into two groups. Group 1 treated by inhaled corticosteroids while group 2 treated by antileukotrienes and during 6 months the patients were assessed and results of two groups compared with together.
Findings: Both ICS and LTRAS could reduce the frequency of wheezing ($P<0.000$ for both of them), but their efficacy in comparison with each other was not significant.

Conclusion: Regarding therapeutic effects of two drugs in a wheezy child, but more side effects of ICS, it is recommended to use LTRAS as first choice of treatment.
Keywords: Wheezy Child, ICS, LTRAS

Common variable immunodeficiency in a patient with juvenile idiopathic arthritis

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Background: Association of juvenile idiopathic arthritis(JIA) and common variable immunodeficiency(CVID) is rare. Autoimmune disorders affect about 20% of CVID patients and chronic arthritis manifestations such as JIA occur in 1% to 10% of patients with CVID.
Case Presentation: Our patient was a 5 year old girl with a history of chronic polyarthritis in ankles, knees and PIPs. She was treated as a polyarticular JIA for 2 months. She was evaluated for primary immunodeficiency, because of poor response to treatment and lymphopenia. In past history, her immunologic features were recurrent otitis media, pneumonia, and chronic diarrhea. In immunologic evaluation, repeated lymphopenia, hypogamma-globulinemia and abnormal antibody response were detected, but B cell number was normal. Therefore, the patient was diagnosed as CVID and she was treated with monthly IVIG. After this time, joint involvement was considered as a symptom of CVID, so all the treatments for JIA were stopped. However, polyarthritis involvement continued that had exacerbation a few days before periodic IVIg therapy. In this situation and based on clinical and paraclinical findings, polyarthritis JIA considered as an associated disorder with CVID. She was treated with low dose oral prednisolone(daily) and metotraxare(weekly) for 12 months and after clinical improvement, her medications was tapered gradually during 12 months. Finally, her treatment was discontinued after 2 years and she had no flare up in JIA after 3 years. Now she has 10 years old without any joint complication.
Conclusion: Although JIA as a presentation of CVID is rare, but CVID should be suspected in any JIA patient with recurrent sinopulmonary, otitis media infections and lymphopenia.
Keywords: Common Variable Immunodeficiency, Juvenile Idiopathic Arthritis, Hypogammaglobulinemia, Autoimmune Diseases

Multiple epidural abscesses; think about primary immunodeficiency; a case report

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Background: Spinal epidural abscess(SEA) is a rare infection of the epidural space with variable clinical features and etiologies which can lead to cord damage as a result of direct compression, inflammation or vascular compromise. Determining the etiology is important, because epidural abscess may be a component of a systemic disease such as immunodeficiency states. Immune system works as a collaborative cooperation of two main branches: innate(non specific) and acquired(specific). Innate immunity can be considered as the first line of defense against invaders, but acquired immunity works more specifically via cellular and humoral mechanisms in which humoral immunity is responsible for antibody formation and defense against encapsulated bacteria like pneumococci and hemophilus influenza. Abscess formation is unusual in humoral immunodeficiency disorders, but in some circumstances, other factors predispose them to such rare infections.
Methods: This is a review of a case referred to our department.
Case Presentation: A 34 year old female was consulted to our department, because of hypogammaglobulinemia, fever, back pain and history of multiple visceral abscesses. She had back pain with primary normal neurologic exams. Finally according to her immunologic assays common variable immunodeficiency(CVID) was diagnosed and her MRI showed multiple epidural abscesses.
Conclusion: According to catastrophic outcomes of spinal epidural abscess, early diagnosis of this condition especially in immunocompromised patients is important. In the other hand, when we see multiple epidural abscesses, it is necessary to consider primary and secondary immunodeficiency disorders.
Keywords: Common Variable Immunodeficiency, Multiple Epidural Abscesses, Humoral Immunodeficiency, Hypogammaglubolinemia

In vitro comparison of chromosomal radiosensitivity in common variable immunodeficiency and acute lymphocytic leukemia patients

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Background: Common variable immunodeficiency(CVID) is one of the predominantly antibody deficiency disorders in children. Increasing evidence suggests that dose-dependent chromosomal defects are present in these patients. The aim of this study was to investigate the chromosome radiosensitivity in peripheral blood lymphocytes of CVID patients and their first degree relatives and to compare the results with a group of acute lymphoblastic leukemia(ALL) patients and healthy individuals.
Methods: The in vitro radiation sensitivity was measured with the G2 and the G0-micronucleus assays. The results in each group were also compared with ataxia telangiectasia (AT) cases as positive control.
Findings: By two methods of analysis (crude mean and cut off point), the CVID cases were significantly more radiosensitive than healthy control based on the results of the G2 as well as the G0 assays. Patients with parental consanguinity are more prone to irradiation as measured by the frequency of chromatid breaks ($P<0.008$) and rearrangements ($P<0.04$). Surprisingly first degree relatives of CVIDs had similar radiosensitivity to CVID cases in

chromatid breaks which showed significant difference with normal controls.
Conclusion: Results indicate that most of the CVID patients and their first degree relatives are sensitive to ionizing radiation similar to ALL cases. This study may support that chromosome radiosensitivity in CVID patients could be a marker of genetic predisposition to the disease. These patients should be protected from unnecessary diagnostic and therapeutic procedures using ionizing radiation.
Keywords: predominantly antibody deficiency, common variable immunodeficiency, ataxia telangiectasia, acute lymphoblastic leukemia, chromosome radiosensitivity

Complication of 51 Patients with Hyper Immunoglobulin E Syndrome

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Background: Hyper IgE syndrome (HIES) is one of the known primary immunodeficiency presented by recurrent cutaneous and lung infections, eczema, and connective tissue and skeletal abnormalities as well as elevated serum IgE.
Methods: We investigate for recognized aspects of the clinical phenotype and discuss recent genetic and immunologic findings in 51 cases (25 males, 26 females) with HIES who were followed for a total of 240 patient years.
Findings: We documented the molecular, cellular, and clinical features of 17 patients with heterozygous *STAT3* mutations and 1 patient with *DOCK8* mutation. As a result of our survey we found that SCORAD >51 is a good screening test for HIES, however for finding of STAT3 deficient patients, screening NIH score needs to be consider with other parameters especially pneumatocele.
Conclusion: Specific molecular study of *STAT3* and *DOCK8* mutations in patients with HIES clinical manifestations helps physician to definitively characterize the disease and to understand more about the mechanism of eczema, IgE regulation, infection susceptibility, coronary artery disease, scoliosis, and bronchiectasis as well as provide strategy into therapeutic modalities.

How to approach to recurrent infections in children

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Recurrent and chronic infections in children are one of the most common reasons for physicians' visits that make a diagnostic challenge to pediatricians. Although the majority of referred children with recurrent infections are normal, underlying causes of recurrent infection such as atopy, anatomical and functional defects, and primary or secondary immunodeficiency must be considered in evaluation of children with this complaint. Although primary immunodeficiency diseases (PIDs) were originally felt to be rare, it has became clear that they are much more common than routinely appreciated. Early and accurate detection of PIDs in children is essential to institute early lifesaving care and optimized treatments. Therefore in the approach to children with recurrent infections, careful medical history taking and physical examination with more attention to warning PIDs signs and symptoms are essential to distinguish those children with underlying PIDs from those who are normal or having other underlying disorders. If indicated, appropriate laboratory studies including simple screening and advanced tests must be performed.

Morbidity and mortality of Iranian patients with hyperIgM syndrome

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Background: Defects in B cell Class switch recombination (CSR) are a heterogeneous and yet very uncommon group of disorders. These disorders all have a genetic basis and almost uniformly result in hyper IgM syndrome. Due to the rarity of these conditions, a very small number of case studies have been conducted on the affected patients. This study sought to help bring more to light the morbidity and mortality regarding a relatively large cohort of all diagnosed CSR defective Iranian patients.
Methods: This study was performed using the demographic information, laboratory findings and clinical data obtained from an observation of 33 Iranian patients of different ethnicities referred from all medical centers of Iran to the research center for immunodeficiencys, pediatrics center of excellence, Tehran, Iran; of which 28 were males and 5 females.
Findings: Our patients mean age at the onset of their symptoms was 1.86±0.23 years; they were diagnosed with a mean delay of 4.49±3.34 years and followed for a mean time of 5.76±4.84 years. The most prominent clinical features observed were multi organ infections, affecting mostly the respiratory system, followed by lymphoproliferative and autoimmune disorders, the latter being of much higher frequency in our study than the reported frequency in previous literature. The three year survival rate for our enrolled patients was 67.9%.
Conclusion: According to findings of this study the molecular mechanism behind the nature of the patients in Iran are more compatible with autosomal recessive mutations rather than X- linked hyper IgM syndrome in contrast with other large cohorts of patients with CSR defect .
Keywords: HyperIgM syndrome, class switch recombination, morbidity, mortality, clinical manifestation

PID network in Azerbaijan

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Background: Primary Immunodeficiencys (PID) are severe disorders of immune system leads to high morbidity and mortality. Special investigation has been performed for improving the knowledge about PID and organizing registry of these patients. 10 warning signs of PID in native language are used in education programs for pediatric, immunologist and other specialists. The Objective of the study was to educate and increase awareness of PID diagnosis and treatment, also to detect primary immune

deficiency in patients with suspicion on immune abnormalities.
Methods: Three years study was performed with children and adult patients with severe and repeated infections from the different regions of Azerbaijan Republic. Research based on the recommendation of JMF. Data from the patient records were analyzed in relation to age, gender, type of infections and complications.
Findings: 240 patients, children and adults, with repeated and severe infections were suspected on PID and examined during 2010-2012 years. The PID registry was from 2011 and now total 13 clinical immunologists and 4 lab staff are working on PID in the medical centers in Baku.The number of patients being followed is 45, number of patients identified with PID is 28 and 7 patients genetically confirmed and regularreceive IVIG treatment. 17 patient have unspecified diagnose of PID. Patients died in this period were 12. There were published special brochure with algorithm of PID diagnosis and textbook on PID for students and residents.
Conclusion: **S**till there are many undiagnosed immune compromised patients in Azerbaijan. Despite the PID educational program and practical seminars, the investigation of PID in patients is not routinely, most of patients not treated by immunologists and we have no patients received BMT.

Association of Interleukin 10(IL-10) and transforming growth factor β(TGF-β) gene polymorphisms with chronic idiopathic urticaria

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Background: Transforming growth factor β (TGF-β) and interleukin-10 (IL-10) are two anti-inflammatory cytokines that are implicated in pathogenesis of urticaria. This study aimed to examine possible association of polymorphisms of TGF-β and IL-10 genes with susceptibility to chronic idiopathic urticaria (CIU).
Methods: This study was conducted on 90 patients with CIU. Polymerase chain reaction (PCR) was done to determine genotype at 5 polymorphic sites; TGF-β (codon10C/T and codon25G/C) and IL-10 (-1082G/A, -819C/T, and -592C/A).
Findings: Considering allele frequencies, C allele at codon 25 of TGF-β was more prevalent in CIU patients, compared to controls (OR=9.5, 95%CI=5.4-16.8, p<0.001). Genotypes of CT and CG at 10 and 25 codons of TGF-β gene, respectively, and AG, CT and CA for loci of -1082, -819 and -592 of IL-10 gene were significantly higher in CIU patients (p<0.001). In haplotype analysis frequency of haplotypes of only TGF-β were different between patients with CIU and controls; CC haplotype was overrepresented, while CG and TG haplotypes were underrepresented (p<0.001).
Conclusion: These results suggested that TGF-β and IL-10 genetic variability could contribute to susceptibility to CIU. Interestingly, CIU patients seem to have high producing TGF-β and IL-10 cytokine genotypes.

Interleukin-1 family and interleukin-6 gene polymorphisms in recurrent aphthous stomatitis

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Background: Recurrent aphthous stomatitis(RAS) is a common painful, ulcerative oral inflammatory disorder with unknown etiology. Immune system through inflammation process plays a role in outbreaks of RAS ulcers. Interleukin-1 (IL-1) and IL-6 are the most potent proinflammatory cytokines. Single nucleotide polymorphisms(SNPs) of IL-1 and IL-6 genes can affect the secretion of these cytokines. The aim of this study was to investigate the association between RAS and IL-6 and IL-1 in subjects with RAS.
Methods: Genomic DNA was obtained from 60 Iranian patients with RAS. IL-1α C -889 T, IL-1β C -511 T, IL-1β C +3962 T,IL-1R C pst-I 1970 T,IL-1Ra C Mspa-I11100 T,IL-6 C -174 G and IL-6 A nt +565 G polymorphisms were determined using polymerase chain reaction with sequence-specific primers (PCR-SSP).
Findings: The frequency of C -174 C genotype in the patients group was significantly different from the healthy control. No other significant difference was found in genotype and alleles frequencies between the two groups.
Conclusion: These results indicate that certain SNPs of IL-6 gene at position -174 which located in promoter have association with predisposition of individuals to RAS.

Systems biology's applications in diagnosis and classification of immunological diseases

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Unlike classical, reductionist biology, where one or few genes, proteins or traits are investigated at a time, systems biology aims at understanding the normal or pathological structure and function of entire biological systems through high-throughput and high-content experiments followed by rigorous bioinformatics and statistical analyses. This approach has become feasible after the development of

high-throughput technologies including "next generation sequencing" methods, cDNA microarrays and mass spectrometric analyses of proteins, lipids and metabolites. Numerous studies have pointed to the potential role of systems biology in basic and clinical immunology research; where normal or pathological immune reactions are the result of complex intercellular and intermolecular interactions, which are not easily comprehensible through classical approaches. This includes the use of genomic analyses in discovering polymorphisms underlying immunological diseases, application of transcriptomic, proteomic or metabolomic technologies in understanding the pathogenesis of infectious or autoimmune disorders, and the discovery of new immunological biomarkers as well as the development of novel diagnostic and disease classification tools.

Cutaneous reactivity pattern and nasal smear cytology in patients with chronic rhinosinusitis with nasal polyps; is it associated with the course of the disease?

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Background: The objective was to determine the association of hyper reactivity to environmental allergens and mucosal secretion cytology with the course of disease in patients with chronic rhinosinusitis and nasal polyps (CRSwNP).
Methods: A cross sectional study was conducted at Tehran clinic of asthma and allergy in 2010. Adult patients who earned the definite diagnosis of CRSwNP and were free of serious underlying disease were selected. A comprehensive history regarding the course of disease was taken. Success or failure of previous interventions was defined as subsiding the symptoms and no need for further invasive intervention of surgery. Physical examination, pulmonary function test, nasal smear from both nasal cavities and skin prick test were performed for all enrolled subjects. The results were compared among participants with different course of disease.
Findings: A total of 45 patients with mean age of 35.8±11.7 (18 to 60 years) were enrolled. Of the participants, 30 (66.7%) had asthma, medical treatment was failed in 23(51.1%), 25 underwent surgery in whom it was failed in 5 (11.1%). Regardless of course of disease, neutrophilia was the predominant cytology of nasal smear. Of the participants, 17(37.8%) had no sensitization, while, 11 (24.4%) showed mono-sensitization and 17(37.8%) were poly-sensitized. Seasonal allergy was found in 16(35.5%), while, perennial sensitization was in 19 (42.2%). Failures of medical treatment were more sensitized to seasonal allergens (45.2% vs 14.3%, p=0.045). Failures of surgery, were found to have polysensitization to both of perennial and seasonal allergens (66.7% vs 21.1%, p=0.037).
Conclusion: Atopy is frequently present in patients with CRSwNP and pattern of sensitization can affect the outcome of intervention. With respect to different pattern of sensitization among failed and successful interventions, determining the sensitizations prior to any intervention is suggested. Patient counseling regarding the recurrence of disease can be done in accordance with atopic profile.
Keywords: Chronic Rhinosinusitis, Allergy, Asthma, Atopy

Interleukin-6 and tumor necrosis factor-alpha gene polymorphisms in chronic idiopathic urticaria

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Background: This study was performed to evaluate association of gene polymorphisms among proinflammatory cytokines and susceptibility to chronic idiopathic urticaria (CIU).
Methods: Ninety patients with prolonged urticaria more than 6 weeks were included as case group. Single nucleotide polymorphisms (SNPs) of IL-6 (G/C -174, G/A nt565) and TNF-α (G/A -308, G/A -238) were evaluated, using polymerase chain reaction (PCR); and the results were compared to the control group.
Findings: G allele was significantly higher in the patients at locus of -238 of promoter of TNF-α gene($p<0.001$). Frequency of following genotypes were significantly lower in patients with CIU, compared to controls: AG at -308 and GA at -238 of TNF-α gene($p<0.05$ and $p<0.001$, respectively), CG at -174 and GG at +565 of IL-6 gene ($p<0.05$). Additionally, following genotypes were more common among patients with CIU: GG at -308 and -238 of TNF-α gene($p<0.05$ and $p<0.001$, respectively), GG at -174 and GA at +565 of IL-6 gene($p<0.05$).
Conclusion: Pro-inflammatory cytokine gene polymorphisms can affect susceptibility to CIU. TNF-α promoter polymorphisms as well as IL-6 gene polymorphisms are associated with CIU.

Comparison of total IgE and skin prick test results in children with angioedema and allergic rhinitis diseases

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Background: The aim of this study was to compare the level of total IgE and and skin prick results in angioedema and allergic rhinitis patients.
Methods: The method of study was cross-sectional and comparative study. 52 children patients suffered from diseases who had been diagnosed based on diagnostic criteria at Amir al Moemenin hospital of Zahedan city from

2007 up to 2012 were selected. Blood sampling was done for measuring total IgE and skin prick test(SPT) was performed with panel of allergens from Stallergens-France company that were including areoallergens and food allergens. The results were read at 20 minutes and considered positive when the reaction of redness and wheal were observed and analysed statistically in both angioedema and allergic rhinitis patients.
Findings: Our results revealed that 89% allergic rhinitis and 65% of angioedema patients had increased level of IgE. 67.6% of allergic rhinitis had positive reaction to aspergilus (76.1% were males and the rest of them were females) and 89% to alternaria(67.2% were males and the rest of them were females). Only 35.4% of angioedema patientss (47% were males and the rest of them were females) had positive reaction to aspergilus(78.31% were males and the rest of them were females) and 41% had positive reaction to alternaria(51.8% were males and the rest of them were females). Regarding to comparison of positive reaction to other allergens in both patients no significant differences were found. Based on comparison the SPT results of food allergens, 79.4(63% females and the rest of them males) of angioedema had positive reaction to nuts, egg and curry allergens. A few allergic 20.6% (62.4% males and the rest females) rhinitis patients had positive reaction to these allergens.
Conclusion: It was concluded that both diagnostic methods of total IgE and SPT are important factors that play role in the etiology and the complications associated with both angioedema and allergic rhinitis diseases. Thus for controlling of disease we suggest allergen avoidness from such allergens follow immunotherapy need to be done similarly for others allergens in both patients.
Keywords: Total IgE, Skin Prick Test, Angioedema, Allergic Rhinitis

Proinflammatory cytokine gene polymorphisms in autoimmune hepatitis

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Background: Autoimmune hepatitis (AIH) is an inflammatory liver disease, presenting usually with chronic hepatitis, while acute or fulminant hepatitis are not uncommon. In this study, we investigated the pro-inflammatory cytokines gene polymorphisms in a group of pediatric patients with AIH and compared the results with a group of healthy individuals.
Methods: The study group was conducted in 57 pediatric patients with AIH who was referred to the Children's Medical Center Hospital, the Pediatrics Center of Excellence in Tehran, Iran. The studied alleles and genotypes include TNF-α(A/G −308, A/G −238), IL-1α(C/T −889), IL-1β(C/T −511), IL-1β(C/T +3962), IL-1 receptor(IL-1R; C/T Pst-I 1970), IL-1RA(C/T Mspa-I 11100), and IL-6(C/G −174 and A/G nt565).
Findings: The frequencies of the following alleles were significantly higher in AIH patients, compared to healthy controls: TNF-α A allele at position -308(23.7% in AIH patients *vs.* 14.2% in controls, $p<0.035$), IL-6 A allele at position nt565(35.1% in AIH patients *vs.* 18% in controls, $p<0.00042$). The most significant differences in genotype frequency between AIH patients and healthy controls belong to TNF-α AA, GA and GG genotypes at position -238(17.5% in AIH patients *vs.* 0.7% in controls, $p<0.0001$ for AA genotype, 3.5% in AIH patients *vs.* 41.6% in controls, $p<0.0001$ for GA genotype, and 79% in AIH patients *vs.* 57.7% in controls, $p<0.0081$ for GG genotype).
Conclusion: IL-6 and TNF-α polymorphisms are shown to have significant differences between AIH patients and healthy controls, but IL-1 family has no significant correlation.
Keywords: Polymorphisms, Autoimmune Hepatitis, Cytokines

Critical pathways in immunologic regulation of allergic asthma

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Respiratory system is an organ continuously exposed to a diversity of foreign particles. In allergic asthma Th2 cell-driven inflammation is likely to represent an abnormal response to harmless airborne particles in the airways. These reactions are normally suppressed through different non-redundant regulatory pathways. Accumulating evidence supports the pivotal role of $Foxp3^+$ regulatory T cells (Treg) in regulation of the development and outcome of allergic diseases in animals and humans. Other populations of regulatory T cells including Tr1, Th3 might also maintain immunological tolerance in allergic conditions, which are less defined. Besides the production of inhibitory cytokines by regulatory and non-regulatory immune cells are critical in programming effective pulmonary homeostasis. In asthmatic individuals a breakdown in one or different of these regulatory mechanisms is evident. Therefore, the ability to enhance regulatory function in affected individuals may represent an effective treatment for asthma.

How to approach to recurrent infections in children

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Recurrent and chronic infections in children are one of the most common reasons for physicians' visits that make a diagnostic challenge to pediatricians. Although the majority of referred children with recurrent infections are normal, underlying causes of recurrent infection such as atopy, anatomical and functional defects, and primary or secondary immunodeficiency must be considered in evaluation of children with this complaint.Although primary immunodeficiency diseases (PIDs) were originally felt to be rare, it has became clear that they are much more common than routinely appreciated. Early and accurate detection of PIDs in children is essential to institute early lifesaving care and optimized treatments. Therefore in the approach to children with recurrent infections, careful medical history taking and physical examination with more attention to warning PIDs signs and symptoms are essential

to distinguish those children with underlying PIDs from those who are normal or having other underlying disorders. If indicated, appropriate laboratory studies including simple screening and advanced tests must be performed.

Keywords: Recurrent Infections, Immunodefficiency, Children

نقش سایتوکاینها در پاتوژنز بیماری آسم

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آسم بيماري التهابي مزمن مجراي هوايي همراه با تغيير در ساختار و عملكرد است كه منجر به تحريك‌پذيري غيراختصاصي برونش و انسداد مجراي هوايي مي‌شود. التهاب نقش اساسي در پاتوفيزيولوژي آسم ايفا می كند و با واكنش انواع سلول‌هاي ايمني و مدياتورهاي مختلف منجر به تغييرات پاتوفيزيولوژي شامل التهاب برونش و انسداد مجراي هوايي و تظاهرات باليني سرفه، خس‌خس سينه و كوتاهي تنفس مي‌شود. ريسک فاکتورها در بروز آسم شامل فاکتورهای میزبان(ژنتیک، جنس و الگوي سايتوكايني فرد)، فاکتورهای محیطي (آلرژن‌هاي معلق در هوا و ويروس‌هاي عفونت‌زاي تنفسي) و فاکتورهاي ايمونولوژيكي (سلول‌ها و مدياتورهای التهابي و IgE) می باشند. انواع سايتوكاين‌ها بصورت لنفوكاين‌ها، سايتوكاين‌هاي پيش التهابي، سايتوكاين‌هاي مهاري، فاكتورهاي رشد، كموكاين‌ها می توانند در پاتوژنز آسم نقش ايفا مي‌كنند. سلول های التهابی با ترشح سایتوکاین های التهابی و پیش التهابی مثل TNFα، IL-1، IL-6، IL-33، TSLP و سایتوکاین های تیپ 2 از سلول های TCD4+ مثل IL-4، IL-5، IL-9، IL-13 در آسم آلرژیک Mild تا Moderate نقش دارند، در حالیکه فنوتیپ سلولی میکس Th2/Th1 به همراه TH17 با ترشح سایتوکاین هایی مثل-IL 17A/Fدر آسم پایدار مقاوم به استروئید نقش دارد. فاكتورهاي رشد مثل,GM–CSF TGF–β، PDGF از مهمترین مدیاتورها در رمدلینگ شدن بافتي شش افراد آسماتيك محسوب مي شود. كموكاين ها مثل MPC–1، RANTES و MIP–1 و ائوتاكسين وگيرنده های کموکاین ها مثل CCR3، CCR4، CCL11، CCL24، CCL26 نقش مهمی در فراخوانی سلول های التهابی گردشی به مجرای هوایی در بیماران آسماتیک دارد که با افزایش سایتوکاین های TH2 بعد از استنشاق آلرژن نیز ارتباط دارد. از رویکرد های جدید درمانی بیماری آسم، آنتي سايتوكاين درماني با آنتی بادی های بلوکه کننده مثل IL-4، IL-5، IL-9 می باشد که فراخوانی سلول‌هاي التهابي به مجراي هوايي و رمدلينگ شدن مجراي هوايي را كاهش مي‌دهد.