Immunology, Allergy and Immunodeficiencies

The role of infectious agents in acute asthma in children

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Background: The aim of the study was assessing the role of infectious agents as a cause of asthma in children and then evaluating this role in both types of asthma (allergic or no allergic).
Methods: During the period from 01/12/2006 to 01/06/2007, we did a prospective research for the presence of infectious agents in children hospitalized for asthma in the pediatric department in the hospital of Mantes La Jolie, on the outskirts of Paris, all of these cases had been admitted in the emergency department, where they received three doses of aerosol of salbutamol which were not sufficient to allow the shipment to the house; we also studied the allergic situation of these patients according to specific criteria to classify the child in allergic or no allergic asthma.
Findings: During this period 44 children "in accordance" with the terms of our study had been hospitalized with a mean age of 36.4 months. 10 of them were infected by Mycoplasma pneumoniae and 8 by respiratory syncytial virus (RSV); the distribution of infectious agents in both types of asthma was similar.
Conclusion: This study shows that M. pneumoniae is the main infectious cause of an asthma attack, followed by RSV without any differences according to the allergic situation.
Keywords: Asthma, mycoplasma pneumoniae, Respiratory Syncytial Virus

Effect of education on spirometry in the patients referred to Childrens' Medical Center between 2008-2009

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Background: Asthma is a common chronic disease that can cause disability in patients. Studies have shown that patient education plays an important role in asthma control and improving disease. The aim of this study was to investigate the effect of patient education on spirometry.
Methods: In this interventional study, 6-14 years old children with asthma referred to asthma and allergy clinic of Children's Medical Center between 2008-2009 were studied. Patients were divided into two groups; Case and Control, and each group was treated with common and standard therapy of asthma. For case group besides general education, special education was conducted. For each patient two pulmonary function tests(spirometry) on first visit and one year after that have been done. The collected data were analyzed with SPSS software version 18.
Findings: A total of 104 patients were studied. The mean age of patients in case group was 8.01±1.62 and in control group was 8.42±2.08 years. 76.92% of patients had a history of referring to emergency department. The mean changes in FEV1/FVC ratio before training was -3.11±10.55 and after training was 1.15±7.28 that difference was statistically significant (P<0.018). In case group, mean FEV1/FVC ratio before training was 102.97±9.45 and after training was 104.07±9.76 and there was no significant difference (P<0.499). In control group, the mean FEV1/FVC ratio at baseline was 102.85±8.97 and the mean at the end of study was 102.76±11.35, which was not significantly different (P<0.969). In addition, the mean changes in FEV1/FVC ratio at baseline was 0.59±9.37 and the mean at the end of the study was 2.26±13.35 and there was no significant difference (P<0.468).
Conclusion: Pulmonary status did not change much during the study period and the effect of education on patient behavior and lifestyle modification resulted in the prevention of severe attacks and sudden and short-term risky exacerbation episodes. However, a significant reduction in FEV1/FVC ratio changes after training is also indicating the effect of training on this index. Therefore, a training program for asthmatic patients and their families is recommended.
Keywords: Education, Asthma, Children, Spirometry

An etiologic survey of patients with chronic urticaria in Kurdistan provience

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Background: Urticaria, also known as hives, is a very common disorder and is thought to afflict up to 20% of the population at some point in time. Chronic urticaria (CU) generally is defined by the presence of urticaria on most days of the week, for a period of 6 weeks or longer. Approximately 40% of patients with CU have accompanying episodes of angioedema or deeper swelling of dermal or mucosal tissues, whereas 10% have angioedema as their main manifestation.
Methods: We gathered all data of patients with CU. Serum autologous skin test was performed for patients without any specific etiologys.
Findings: 185 Kurd patients with chronic urticarial, 80 male (43.2%) and 105 female (56.8%), who were referred to Kurdistan asthma and allergy clinic were evaluated for causes of CU. The mean (SD) age of the patients was 36.5 (12.8) years. The mean (SD) serum IgE level was 137.5 (151.8). 11 patients (5.9%) had infectious etiologies (Helicobacter pylori, GI fungul infections, chronic viral infections, …). 7 patients (3.7%) had reumathologic diseases and physical triggers were defined in 34 patients (18.3%). 71.1% of patients did not have any etiologies which were classified as idiopathic or spontaneous chronic urticarial. Serum autologous test was performed for patients and was positive on 76 person (41%).
Conclusion: Approximately 20% of patients with CU have a reproducible physical trigger for their skin lesions; this form of the disorder is termed physical urticaria. In the remaining 80% of cases, no external allergic cause or contributing disease process can be identified; accordingly, the condition is termed chronic idiopathic urticaria (CIU). Some guidelines and experts identify a subset of patients

with CIU on the basis of serologic evidence of a presumed autoimmune etiology (observed in 30% to 40% of these patients) and call the condition chronic autoimmune urticaria (CAU).
Keywords: Chronic Urticaria, Serum Autologous Test, IgE Serum Level, Chronic Autoimmune Urticaria

Pneumonia due to Acinetobacter Lwoffii in a patient with X-linked Agammaglobulinemia

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Acinetobacter lwoffii is a nonfermentative aerobic Gram-negative bacillus. It is an opportunistic pathogen in immunocompromised patients and has a cause of nosocomial infections like septicemia, pneumonia, meningitis, urinary tract infections, skin and wound infections. Herein we described a case of pulmonary infection due to Acinetobacter lwoffii in a patient with X-linked agammaglobulinemia.
Case presentation: A 5-year- old boy admitted to hospital with tachypnea, fever and cough of 3 day's duration. He was the a known case of x-linked agammaglobulinemia from infancy. CXR showed infiltration in near heart border in the left lung. Ceftriaxone was started but response to therapy was poor. The culture of sputum obtained during bronchoscopy revealed growth of Acinetobacter lwoffii. A.lwooffi must be considered in severe infections especially in immunocompromised patients.
Keywords: X-Linked Agammaglobulinemia; Immuno-deficiency; Acinetobacter Lwoffii,

Late-onset familial hemophagocytic lymphohistiocytosis with STXBP2 mutations

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare condition, clinically characterized by fever, hepatosplenomegaly, cytopenia, and widespread accumulation of lymphocytes and histiocytes, sometimes with hemophagocytosis, which can either occur sporadically or as part of a familial syndrome (primary HLH). Familial hemophagocytic lymphohistiocytosis (FHL) is a genetically heterogeneous hyperinflammatory syndrome, caused by an uncontrolled proliferation and activation of T-lymphocytes, NK-cells, and macrophages that infiltrate multiple organs, coagulation abnormalities, and inflammatory CNS disease.
Case presentation: Herein, a male patient is presented who was well until 7 years old, when he was hospitalized because of fever and jaundice after 10 days of watery diarrhea. he had ascites and hepatosplenomegaly. Laboratory data revealed high billirubin and liver enzymes. Investigations for viral hepatitis, Wilson were inconclusive. Bone marrow biopsy was normal, but liver biopsy revealed marked interface activity and bridging necrosis and no report of hemophagocytosis, Hence the diagnosis of autoimmune hepatits was made for him and Azathioprine plus prednisolon were started. The patient was well for 6 months until he was admitted to the intensive care unit, because of pneumonia. One year later, he developed sudden onset of ataxia associated with diplopia. Physical examination revealed an atactic speech, nystagmus when gazing to the right side, asymmetric plantar reflexes, and abnormal cerebellum tests. MRI imaging revealed several ring enhancement lesions. fibrinogen, ferritin and triglyceride were normal. Sterotaxic biopsy showed mixed inflammatory cells within a loose necrotic fibrillary background. Immunohistochemical staining was compatible with a reactive inflammatory process. Soluble IL2 receptor was high and CD4+ and CD8+ T cells were highly activated. An NK cell activity assay showed absent degranulation after stimulation with target cells and no recovery of degranulation after stimulation with IL-2.
Conclusion: This case highlights that patients with FHL, especially late-onset ones should be visited in a multi-disciplinary system by expert immunologists, hematologists, and neurologists.
Keywords: Familial Hemophagocytic Lymphohistio-cytosis, STXBP2, Brain Lesions, Autoimmune Hepatitis

Immunometabolism in obesity and its clinical relevance in paeditarics: when immune system meets mitochondria and cellular metabolism

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The human fatty tissue is not just a passive organ to save the excessive energy, but acts as a store for immune cells such as macrophages, neutrophils, T and B cells and produces as an active endocrine unit the biologically active substances, called Adipokine. The human fatty tissue contributes to the innate immune system. The adipocytes are able to detect foreign antigenes via specific receptors on their cell surface and release proinflammatory cytokines and acute phase proteins like tumor necrosis factor α (TNF α), interleukin 6 (IL 6), C-reactive protein (CRP), plasminogen activator inhibitor-1 (PAI-1), vascular cell adhesion molecule-1 (VCAM-1), p-selektin, serum amyloid A3, fibrinogen and angiotensinogen. Obesity shares with most chronic diseases the presence of a permanent local and systemic inflammation which leads to the development of mitochondrial dysfunction, metabolic diseases and insulin resistance. This inflammatory state is reflected in increased circulating levels of pro-inflammatory proteins, and it occurs not only in adults but also in adolescents and children. The chronic inflammatory response has its origin in the links existing between the adipose tissue (AT) and the immune system. Under physiological conditions, the proportion of CD14 and CD31 positive macrophages in stroma cells of fatty tissue amounts to 5-10%. In obese patients the amount of macrophages increases up to 60% in adipose tissue (AT). The number of macrophages in AT correlates positively with BMI and the size of adipocytes.
Macrophages are prime players in the initiation of a chronic inflammatory state in obesity. In response to increases in free fatty acid release from obese adipose depots, M1-polarized macrophages infiltrate adipose tissues. These M1

macrophages trigger inflammatory signaling and stress responses within cells that signal through JNK or IKK β pathways, leading to insulin resistance. If overnutrition persists, mechanisms such as M2 macrophages and PPAR signaling that counteract inflammation are suppressed.
Macrophages are the major origin for production of TNF-alpha and IL- 6 which lead to the insulin resistance. The expression and secretion of TNF- alpha correlate with body weight, especially in visceral AT, compared to subcutaneous fatty tissue. TNF-alpha disturbs insulin signal and leads to insulin resistance by reduction of phosphorylation of insulin receptor substrat-1 (IRS-1) and disturbance of synthesis and translocation of glucose transporters type 4(GLUT-4). On the other hand the increased glucose levels and oxidated low density lipoprotein (LDL) activate the phagocytes and lead to local tissue damages by production and secretion of inflammatory and cytotoxic metabolites. In mouse model, it could be shown a positive correlation between increase of weight and enhancement of expression of mRNA transcript inflammatory genes in fatty tissue. The weight reduction leads significantly to decrease of systemic circulating inflammatory molecules in serum. Recently it could be demonstrated that RBP4, a retinol transporter, is upregulated in insulin resistance and contributes to increased diabetes risk. RBP4 activates macrophage and CD4 T cell. RBP4-overexpressing mice (RBP4-Ox) are insulin resistant and glucose intolerant and have increased AT macrophage and CD4 T cell infiltration. In RBP4-Ox, AT $CD206^+$ macrophages express proinflammatory markers and activate CD4 T cells while maintaining alternatively activated macrophage markers. These effects result from direct activation of AT antigen-presenting cells (APCs) by RBP4 through a JNK-dependent pathway. Transfer of RBP4-activated APCs into normal mice is sufficient to induce AT inflammation, insulin resistance, and glucose intolerance. Thus, RBP4 causes insulin resistance, at least partly, by activating AT APCs that induce CD4 T cell Th1 polarization and AT inflammation.
Summarized, the obesity is a cross-talk that occurs between immune system and metabolism.This article will try to shed a light on the significant importance of research in the field of immunometabolism and its relevance for clinical paediatrics and medicine.
Keywords: Immunometabolism, Immune System, Obesity, Children

Approach to patients with phagocyte defects

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Defects of neutrophil function and/or differentiation, defects of motility, defects of respiratory burst, and Mendelian susceptibility to mycobacterial diseases could be classified as main diseases in the category of phagocytes defects. Severe congenital neutropenia, cyclic neutropenia, glycogen storage disease type 1b, p14 deficiency, Barth syndrome, Cohen syndrome, and poikiloderma with neutropenia are primary immunodeficiency diseases with neutrophil function/differentiation defects. Leukocyte adhesion deficiency (LAD types I-III), Rac2 deficiency, β-actin deficiency, localized juvenile periodontitis, Papillon–Lefèvre syndrome, specific granule deficiency, and Shwachman–Diamond syndrome are classified in group of motility defects. Chronic granulomatous disease (*CYBB, CYBA, NCF1, NCF2, NCF4*) is the prototype of defects of respiratory burst. Mendelian susceptibility to mycobacterial diseases predispose individuals to mycobacterium. Mutations in several gene loci have been detected for MSMD, including *IL-12RB1, IFNGR1, IFNGR2, IL12B, STAT1, CYBB, IRF8,* and *ISG15*. GATA2 deficiency, pulmonary alveolar proteinosis along with autosomal recessive form of IRF8 deficiency are other diseases that have been classified as phagocytes defects.
Keywords: Phagocyte Defects, Mycobacterial Infection, Chronic Granulomatous Disease, Leukocyte Adhesion Deficiency

Idiopathic CD4+ T lymphocytopenia

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Idiopathic CD4+ T lymphocytopenia (ICL) is a rare immune deficiency with heterogeneous clinical manifestations. This syndrome first described in 1992 and defined as absolute CD4+T-lymphocyte count $<300/mm^3$ or less than 20% of total lymphocytes that confirmed at least twice during a period of 1 to 3 months in the absence of HIV-1 infection disease or any other cause of immunodeficiency. Patients with ICL often presents with opportunistic infections, malignancies, or autoimmune disorders and the major risk ICL is unexpected infections, including cryptococus, atypical mycobacterial and pneumocystis pneumonia (PCP). In some patients also additional immunologic defects including CD8+ lymphocytopenia and low immunoglobulin levels was occur. This disease was seen in both children and adults and two genders. At present the etiology of disease is unknown and also it does not appear to be caused by a transmissible agent, such as a virus, but it is widely believed that there is more than one cause. Although in general, prognosis of disease is depends on absolute number of CD4, but in contrast to the $CD4^+$ cell depletion caused by HIV, patients with idiopathic CD4 lymphocytopenia have a good prognosis. The decline in $CD4^+$ T-cells in patients with ICL is generally slower than that seen in HIV-infected patients and in some cases this condition may also resolve on its own. We present 3 cases of ICL with different prognosis.
Keywords: T lymphocytopenia, CD4, Immunodeficiency HIV

Nonhodgkins Lymphoma in a patient with Leukocyte Adhesion Deficiency Syndrome

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Background: Leukocyte adhesion deficiency syndrome type 1 (LAD-1) is a rare autosomal recessive primary immunodeficiency disorder of neutrophil phagocytic function characterized by the deficiency of one or several surface integrins which altered adhesion and cause recurrent infection. Some reports shows association of LADS with malignancy.

Case presentation: We describe a case of a 7-day-old boy who presented with an omphalitis, sepsis, icter and erythematus rashes and characteristic history of recurrent infections, marked leukocytosis and delayed separation of umbilical cord. The diagnosis is based primarily on flow cytometric analysis of neutrophils for the surface expression of CD11, CD18 and CD15s. He developed lymphadenopathy and abdominal mass with diagnosis Nonhodgkins lymphoma (NHL). Our patient represents the first clinically and histopathologically documented association between LADS and NHL. Data could support to the role of tumor genesis of β2 integrins in the human.

Keywords: B-cell non-Hodgkin's lymphoma, Leukocyte adhesion defect, surface integrins, recurrent infections

Vitamin D deficiency in chronic idiopathic urticaria

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Background: Chronic urticarial is one of the most common skin diseases, characterized by as a chronic cutaneous condition which severely debilitates patients in several aspects of their everyday life. CU patients suffer from physical, social, and psychological morbidities resulting in a low quality of life. Vitamin D is known to exert several actions in the immune system and to influence function and differentiation of mast cells, central role players in the pathogenesis of chronic idiopathic urticarial. Recently, an increasing body of literature showed paradoxical relationships between vitamin D and allergic diseases like food allergy, rhinosinusitis, recurrent wheeze, asthma, atopic dermatitis and eczema. This study was performed to evaluate the relationship between vitamin D levels and susceptibility to chronic idiopathic urticarial.

Methods: One hundred and fourteen patients with chronic idiopathic rticarial were recruited in this study along with one hundred and eighty seven sex-matched and age-matched healthy volunteers as the control group. For each patient, urticarial activity score was calculated and autologous serum skin test was done. Vitamin D metabolic statue was measured as 25 hydroxyvitamin D using enzyme immunoassay method.

Findings: Patients with chronic idiopathic urticarial significantly had lower levels of vitamin D ($p<0.01$). Vitamin D deficiency was significantly associated with increased susceptibility to chronic idiopathic urticarial ($p<0.01$). There was a significant positive correlation between vitamin D levels and urticarial activity score ($r=0.2$, $p<0.05$).

Conclusion: This study showed patients with chronic idiopathic rticarial had reduced levels of vitamin D, while vitamin D deficiency could increase susceptibility to chronic idiopathic urticarial.

Keywords: Vitamin D Deficiency, Idiopathic Urticarial, Chronic Urticaria

Phenotyping and follow up of forty seven Iranian common variable immune deficiency patients

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Common variable immune deficiency (CVID) is a heterogeneous syndrome with infective, autoimmune and malignant manifestations. This study describes retrospectively the phenotyping and follow-up of the CVID patients in the allergy and clinical immunology department of Rasol E Akram Hospital of Iran University of Medical Sciences in Tehran until January 2014. The study included forty seven CVID patients with mean age at onset of symptoms and diagnosis of 11.2 and 20.2 years respectively. Phenotyping of our patients was: only infection (62%), cytopenia (26%) and PLI (19 %) and 94% of cases had only one phenotype. We did not find a significant relation between the clinical phenotypes and immunologic or demographic data. Rate of parental consanguinity in our cases was 47%. Parental consanguinity was related to lower age at onset, lower age at diagnosis and higher baseline IgG levels. Patients with malignancy and autoimmunity had significantly higher age at onset. Our patients were followed for 6.9 years and the mortality rate during this time was 6%.

Keywords: Common Variable Immune Deficiency, CVID Phenotype, Iran,

APRIL gene polymorphism and serum sAPRIL and Th1/Th2 cytokines level in children with SLE

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Background: Systemic Lupus Erythematosus (SLE) is a prototypical systemic autoimmune disease diagnosed by the generation of autoantibodies against nuclear and cytoplasmic components that are originated from autoreactive B cells. The etiology of SLE includes immunological disturbances, genetic and environmental factors. Among these, APRIL and Th1/Th2 cytokines (IFN-g, IL-4) have roles in the stimulation and antibody production in B cells. These cytokines were hypothesized to be associated with SLE. Therefore, the aim of this study was to evaluate the hypothesis by assessment of APRIL

polymorphism particularly rs11552708 in addition to the serum levels of APRIL, IFN-g and IL-4 in Iranian children with SLE.
Methods: A single nucleotide polymorphisms (SNP) for rs11552708, of APRIL gene were analyzed by Real-time PCR in 60 SLE Iranian children and 64 healthy controls. DNA samples of patients and healthy controls were extracted from peripheral blood leukocytes by phenol-chloroform. Serum samples obtained from 45 children with SLE and 45 healthy controls were assayed by Enzyme-linked immunosorbent assay (ELISA).
Findings: The G/G genotype (odds ratio (OR) 0.67, 95% confidence interval (CI) 0.22-2.07; P=0.68) and G allele (OR 0.81, 95% CI 0.25-2.56; P=0.89) frequencies of polymorphism at codon 67 (67G) not differ significantly in SLE patients compared with healthy controls. The serum APRIL levels in SLE patients (mean +/- SD=29.27 ng/ml +/- 20.77, range from 0 to 55.33 ng/ml) were significantly higher than in healthy controls (P=0.02). No significant differences in the serum levels of IFN-g and IL-4 were observed between children with SLE and healthy controls.
Conclusion: Our results demonstrated that rs11552708 of the APRIL gene is not associated with SLE susceptibility in Iranian children. Likewise, these findings suggest that APRIL antagonists could be a potential therapeutic target to control of SLE in children.
Keywords: Systemic Lupus Erythematosus, SLE; APRIL

Interleukin-1 gene cluster polymorphisms in inflammatory bowel disease

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Background: Crohn's disease (CD) and ulcerative colitis (UC) are two inflammatory bowel diseases (IBD) in which host-microbiota dysbiosis is expected in a genetically susceptible host. There are conflicting results on role of single nucleotide polymorphisms (SNPs) in IL-1 family members in IBD.
Methods: In this study, SNPs of IL-1 family were investigated in 74 patients with IBD (40 CD and 35 UC), using PCR-SSP method.
Findings: IL-1β -511 CC genotype was significantly less present in UC compared to controls, while IL-1RA-Mspa-I11100 CC was significantly associated with both CD and UC. IL-1α -889 TT genotype was more frequently associated with extraintestinal manifestations. A significant association was observed between IL-1β +3962 TT genotype and the disease activity in IBD. IL-1RA Mspa-I11100 CC significantly less frequent in CD patients who need immunosuppressive therapy. IL-1RA Mspa-I11100 CT was associated with earlier age of onset in IBD, while TT genotype was associated with higher age of onset in IBD.
Conclusion: IL-1 SNPs seem to be associated with IBD and could affect the disease severity as well.
Keywords: Inflammatory Bowel Diseases, Crohn's Disease, Ulcerative Colitis, Interleukin-1

Association of Interleukin 4 Single Nucleotide Polymorphisms with Febrile Seizures

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Background: Interleukin-4 (IL-4) plays a critical role in forming the nature of immune responses. As of its importance in inhibiting the production of proinflammatory cytokines by monocytes and activated T cells, the IL-4 gene polymorphisms were investigated in a group of patients with febrile seizure (FS).
Methods: Ninety patients with febrile seizure were enrolled in this study and compared with 140 controls. The allele and genotype frequency of 3 single nucleotide polymorphisms (SNPs) within the IL-4 gene were determined.
Findings: The frequency of the IL-4 -590/C allele in the patient group was significantly higher than in the control group ($p<0.001$). The most frequent genotypes in patients with febrile seizure were IL-4 (-33) CC ($p<0.01$), IL-4 (-1098) GT ($p<0.046$), IL-4 (-590) CC ($p<0.001$) and IL-4(-33) TT ($p<0.02$). The frequency of the following genotypes was significantly lower in patients compared to controls: IL-4 (-590) TC ($p<0.001$) and IL-4 (-33) TC ($p<0.001$). The most frequent IL-4 haplotypes in the patient group, which were significantly higher than in the control group, were TCC ($p<0.00$), TCT ($p<0.02$), and GTC ($p<0.02$) haplotypes. In contrast, the frequencies of the following haplotypes in the patient group were significantly lower than the controls: GCC ($p<0.01$), TTT ($p<0.009$), and TTC ($p<0.007$).
Conclusion: Certain alleles, genotypes, and haplotypes in IL-4 gene were overrepresented in patients with febrile seizure, which possibly could predispose individuals to this disease.
Keywords: Febrile seizure, gene polymorphisms, interleukin-4, interleukin-4 receptor alpha

Diagnostic approach to primary immunodeficiency disorders

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Primary immunodeficiency disorders (PIDs) are a heterogeneous group of inherited disorders that affect different components of the immune system. During last years, advances in molecular genetics and immunology have resulted in the identification of a growing number of genes causing primary immunodeficiencies (PIDs) in human subjects. Since 1952, more than 220 different PID disorders which have been described. Despite progress in discovery of PIDs and understanding of pathogenesis of these disorders over the last 20 years, many patients remain undiagnosed. Recognition of PIDs may be difficult as

infections are common in young children in particular. Identifying different clinical manifestations of PID is the first most important step of diagnosis of PID. Clues to the diagnosis of PID may be found in history, physical examination. Different diagnostic tools have been developed for diagnosis of primary immunodeficiencies. The investigations are largely guided by the clinical presentation of the patient, the suspected immune defect and the results of initial laboratory evaluation. This review will focus on essential and necessary laboratory approach for diagnosis of suspected cases of PID.
Keywords: Primary Immunodeficiency, Diagnosis

Successful Vp16 desensitization

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Background: Adverse drug reactions are frequent and occur in 10% to 20% of hospitalized patients and approximately 7% of the general population. Reactions to drugs can be divided into two main categories; predictable (type A) and unpredictable drug reactions (type B). The latter one consists only 20% of drug reactions. Drugs are one of the most frequent causes of anaphylaxis, ranging between 8% and 62%.The clinical manifestations of anaphylaxis can involve any organ systems, mainly cutaneous, respiratory, GI , and cardiovascular systems.
Case presentation: A 10 years old girl was treating because of Anablastic T cell lymphoma. During 4th chemotherapy course, she developed urticaria, edema of lips and tongue, dyspnea, and cough (anaphylaxis reaction) while receiving VP16 injection. The medication was discontinued immediately and anaphylaxis treated. She was consulted to our department to receive VP16 in the rest of her chemotherapy courses. As it was necessary in the treatment courses, we decided to desensitize her. Skin tests for VP16 were done according to drug provocation tests protocols 1 month after the reaction. The intradermal test was positive in 1/1000 dilution. Then the desensitization process was started in accordance to the 12 step desensitization protocol.Finally she can tolerate all the VP16 during 6 to 7 hours. Rapid desensitization protocols are available to patients who present with IgE and non-IgE-dependent hypersensitivity to drugs.Temporary toleration which is achieved in hours can be maintained if the drug is administered at regular intervals.
Keywords: Drug Reeaction, Vp16, Desensitization

New protocol for Cow's Milk desensitization based on SPT

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Cow's milk Allergy is one of the most common food allergies. It could be IgE mediate or Non-IgE mediates. As 25% of IgE mediated Food allergies persist up to second decade, avoidance is somehow impossible for most of these patients. Fourteen children over 3 year with history of anaphylaxis to cow's milk, positive skin prick test, and positive OFC were recruited. SPT with Milk extract of Greer, full dilution of milk, 1/10, 1/25, 1/50, 1/100, 1/200, and or 1/500, depends on patient's reaction was performed for all the patients. The dilution of milk which induced 3-5 mm of wheal was selected as a stating dilution. Then it started form 2 drop of the dilution and increased according the protocol. The dose was increased weekly to achieve an intake of 120 mL in approximately 4 months. All doses were administered under medical supervision in a clinical setting. After receiving the dose, children were carefully assessed for positive reactions. Pre and post sIgE to milk and repeated SPT after finishing the protocol were performed for all the patients. In the cases of anaphylaxis the dose returned to the last tolerated dose for one week, then it was increased slower. Finally Full tolerance (120 mL of milk) was achieved in 13 patients (92.8%). Only one child had partially desensitized (64 cc). Six of them had anaphylactic reactions during the protocol that were managed by epinephrine, steroid, and antihistamines, while 2 mild reactions managed only by antihistamines. Prick sizes were significantly decreased in patients after desensitization. Milk desensitization and OIT appear to be efficacious in the treatment of cow's milk allergy. The side-effect profile appears acceptable but requires further study. The permanency of the induced tolerance is still unclear. We propose the second study to survey whether this effect results to OIT.
Keywords: Cow's Milk Allergy, Desensitization

Pregnancy in primary immunodeficiency disorders

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Background: Primary immunodeficiency disorder (PID) refers to a heterogeneous group of disorders characterized by poor or absent function in one or more components of the immune system. More than 200 different disorders have been identified to date, with new disorders continually being recognized. Treatment in PID patients has reduced the mortality and morbidity. Thus, such patients often survive into adulthood. Although it is likely that more women with PID will wish to become pregnant in the future, only a few such cases have been reported to date. In this article pregnancy PID pregnant cases and their management has been evaluated.
Methods: The PID cases that became pregnant have evaluated and followed in clinical immunology clinic of Isfahan medical university between 1997 and 2014. Depend on variety of immunodeficiency, supportive and definitive treatment has been done for pregnant patient.
Findings: Two patients had pregnancy and were followed and managed, the first patient with CGD who treated several times for recurrent infections such as empyema, pneumonia, TB lymphadenitis, cutaneous abscess, mouth ulcer and gingivitis. After normal vaginal delivery, she faced to severe low back pain, sacral fungal osteomyelitis and granulomatous all over lesion in her uterus and liver who has been treated with antifungal and interferon gamma. The second patient with CVID who treated several times for thrombocytopenia and recurrent infection of upper and lower respiratory system. During her pregnancy period and delivery, she has been managed for severe thrombocytopenia by IVIG and platelet infusion.
Conclusion: Ig replacement therapy, antifungal and antibiotic prophylaxis, cytokine replacement, vaccinations and bone marrow transplantation are different treatments for PID patients. Immune regulation switch put provide

more complication and disorders during pregnancy. According to the type of PID, management and treatment of PID patients could be different and future researchers in this area have to be done.
Keywords: Primary Immunodeficiency, Pregnancy, CVID, CGD

The role of Bid pro apopototic gene in Ataxia Telangeictasia

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Background: Ataxia telangiectasia (AT) is an early onset genetic disorder characterized by progressive neurondegeneration, chromosome instability and an extreme sensitivity to DNA damaging agents such as ionizing radiation. An autosomal recessive disorder with signs cerebellar atrophy as the disease progresses including oculocutaneous telangiectasias, immunodeficiency, as well as a predisposition to cancer, particularly lymphoid cancers. ATM plays a central role in DNA damage checkpoint activation that is responsible for arresting cell cycle in order to promote repair and genome stability. However, it is becoming apparent that this is not the only role of ATM in promoting cell survival. One of factor involved in ATM mediated cell survival is the pro apoptotic protein BID. BID is a member of the "BH3 only" factors in the BCL 2 family and is typically found in the cytosol as a full length, inactive form.. However, when phosphorylated, BID becomes resistant to caspase 8 cleavage in what is described as a regulatory event.
Methods: Allelic discrimination assays by Taqman PCR were run on a 7500 FAST Real time PCR Thermocycler. Clustering of three genotypes:common homozygotes, rare homozygous and heterozygous were evaluated for Bid proapoptotic gene between 50 Normal controls of Iranian population and 50 Ataxia Telangiectasia patients.
Findings: Distributaton of genotypes between controls and cases were shown 8 patients were heterozygote and one family was homozygote for BID proapoptotic gene.
Conclusion: In summary, this study raises the novel possibility that the BH3-only BID protein, a molecule that was previously considered to be active only as a proapoptotic factor, may also play a prosurvival role. If BID is indeed playing both a proapoptotic and a prosurvival function in the DNA-damage pathway, then it is an excellent candidate to link DNA repair processes and apoptosis.
Keywords: Ataxia telangiectasia, Bid Proapoptotic Gene Repair

Malignancy or immunodeficiency? A case presentation

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Background: Chediak-Higashi Syndrome (CHS) is a rare primary immunodeficiency. The current treatment consists of hematopoietic stem cell transplantation (HSCT). Untreated patients may experience a lethal malignancy like condition "Hemophagocytic Lympho Histiocytosis (HLH)"
Methods: We present here the clinical and laboratorial features of an undiagnosed case of CHS until he presented with lymphoma like symptoms. Changes on his features in response to treatment were compared using linear regression.
Findings: The patient was a 3-year-old boy who presented with episodes of unexplained fever, pallor, bilateral cervical masses, and abdominal distention from ten days before admission. He had a history of perianal abscess and recurrent upper respiratory tract infections. On physical examination, he had silvery and metallic sheen hairs. Several cervical lymph nodes, liver and spleen were palpable. Initial laboratory investigations revealed hemoglobin of 9.1g/dl, total leukocyte count (TLC) 10600/µl [neutrophil=16% and lymphocyte=84%] and platelet count of 81000 /µl. CT scan of the abdomen showed hepatosplenomegaly and abdominal lymphadenopathy. The lymph node biopsy was highly suggestive of lymphoreticular neoplasm. The bone marrow biopsy also showed lymphoid cell infiltration and in granulocyte cell domain a few giant granules inside them were seen. In the peripheral blood smear giant granules inside the neutrophils was seen and diagnosis of CHS was confirmed. Regarding to the patient's conditions, other laboratory measures indicative of accelerated phase in CHS were performed. The laboratory findings were hemoglobin=6.3 g/dl, TLC=3000/µl [neutrophil=1% and lymphocyte=90%], platelet =28000/µl, triglyceride=381, total cholesterol=466, ferritin>5000, high AST and ALT (>300) and low fibrinogen levels (fibrinogen=70). The patient fulfilled five out of eight diagnostic criteria of HLH. So, he was diagnosed with accelerated phase in CHS and was started on HLH-2004 protocol. After beginning treatment the patient's conditions improved gradually. Improvement in most clinical and laboratory conditions was significant ($p<0.05$), but decrease in splenomegaly wasn't significant statistically. The child now has given HSCT and his condition is good.
Conclusion: The diagnosis of CHS should be suspected in patients with lymphoma like symptoms and any history of Partial albinism, recurrent infections, bleeding tendency and neurodegeneration
Keywords: Chediak-Higashi syndrome, oculo-cutaneous, albinism, accelerated phase, giant lysosomal inclusions

Griscelli syndrome in clinical practice

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Background: Primary immunodeficiencies (PIDs) are a group of diseases based on congenital, genetically determined, functional disorders of the immune system. According to the European Society for Primary Immunodeficiency the epidemiology of PIDs is 1 case per 25,000-100,000 people, selective IgA deficiency occurs with a frequency of 1 case per 500-700 people. Combined deficiency of humoral and cell-mediated immunity is 20-25% of all primary immunodeficiencies. Griscelli syndrome is one of those diseases. As combined immunodeficiencies are rarely occurred in pediatric practice, we consider to describe the case of Griscelli syndrome that was in our department's practice.
Case presentation: Feature of this case was the presence of bleaching eyelashes and hair on the head, persistant

fever, enteropathy, polymorphous exanthem, and lymphadenopathy. The data of laboratory examination includes blood test which showed anemia, mild leukocytosis, thrombocytosis, neutrophilia, accelerated sedimentation (67 mm/h); immunotests showed severe disbalance of subpopulations caused by deep decreasing in the relative number of T helper cells and increasing in the relative and absolute number of T cytotoxic lymphocytes; histology of inguinal lymph node showed the image of chronic granulomatous process; histology of the skinshowed local lymphoid infiltration with clusters of histiocytes. Based on this data primary immunodeficiency Griscelli syndrome was diagnosed. We performed replacement therapy for emergencies by concentrated red blood cells, for passive immunization intravenous immunoglobulin G, antiviral, antifungal, antyplatelete, and antiulcer combination therapy. The only effective treatment for this disease is the transplantation of hematopoietic stem cells. Thus, as shown by this case, caution is needed for primary care pediatricians and pediatric oncohematologists for possible primary immunodeficiency diseases caused by rare genetic abnormalities.

Keywords: Primary Immunodeficiencies, Griscelli Syndrome, Albinism