localization in human nasal mucosa, by polymerase chain reaction (PCR) and immunohistochemistry. Human turbinates were obtained after turbinectomy from 6 patients with nasal obstruction refractory to medical therapy. Total RNA was isolated from human nasal mucosa, and CysLT2 receptor mRNA was detected in these tissues by reverse transcriptase-PCR analysis. To identify the cells expressing CysLT2 receptor protein, double immunostaining was performed using anti-CysLT2 receptor antibody and anti-CD31 (endothelial cell) antibody.

**Results:** Reverse transcriptase-PCR analysis of total nasal RNA demonstrated the expression of CysLT2 receptor mRNA. The immunohistochemical studies revealed that anti-CysLT2 receptor antibody mainly labeled blood vessels.

**Conclusions:** The results suggest a primary role for CysLT2 receptor as the vascular responses in upper respiratory tract.

**PRIMARY IMMUNODEFICIENCY**

**135 Mycobacterial Infections in eChildren With Chronic Granulomatous Disease**

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**Background:** Chronic granulomatous disease (CGD) is a rare primary immunodeficiency caused by inborn errors of the phagocyte NADPH oxidase activity. Affected patients display severe, recurrent and multiple infections from the first year of life onwards, in particular caused by various pyogenic bacteria and fungi. Mycobacterial infections have more rarely been reported in these patients.

**Methods:** We examined the clinical features of mycobacterial disease in 59 CGD patients from 52 kindreds in 16 countries of 4 continents. Tuberculosis or BCGR adverse reactions were identified by culture, staining, biopsy, polymerase chain reaction (PCR), and/or by a combination of clinical criteria with response to treatment. CGD was confirmed by NBT, DHR, cytokrome C reduction assay, or a combination of these. Genetic diagnosis was achieved by means of immunoblotting, flow cytometry, PCR and automated gene sequencing.

**Results:** We found that mycobacterial infections are fairly common in patients with CGD living in certain regions of the world. Twenty-four patients (45%) had tuberculosis, 43 (80%) presented with adverse effects shortly after Bacille Calmette-Guérin (BCG) vaccination; 12 of the patients (21%) had both tuberculosis infection and BCG adverse reactions. Most patients (93%) had also pyogenic and fungal infections; 7% of them, however, presented solely with mycobacterial disease. Most cases were one-time self-limited localized infections, but recurrence (13 patients, 20%), disseminated disease (18 patients, 30%) and even death (5 patients, 8%) were observed. A recurrent finding was early age of presentation for BCG reaction, with a median of 3 months of age; BCG disease was the first manifestation of immunodeficiency in 60% of these patients.

**Conclusions:** Our study offers compelling evidence for an important susceptibility to mycobacterial diseases in patients with CGD, more easily noticed in countries where tuberculosis is endemic and BCG vaccine mandatory. BCG adverse reactions should raise the suspicion of CGD.

**136 Increased Pro-Inflammatory Cytokine Production After Lipopolysaccharide Stimulation in Patients with X-linked Agammaglobulinemia**

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**Background:** X-linked agammaglobulinemia (XLA) is characterized by impaired B-cell differentiation caused by mutations in Bruton’s tyrosine kinase (Btk) gene. Btk is expressed in myeloid cells and recent evidence support that it participates in Toll like receptor signaling, but results regarding its role in XLA patients are contradictory.

**Objective:** To evaluate lipopolysaccharide (LPS)-induced pro-inflammatory cytokine response in peripheral blood mononuclear cells (PBMC) from XLA patients.

**Methods:** Thirteen patients with XLA were included in the study. PBMC LPS-induced TNF-α, IL-1β, IL-6, and IL-10 production was determined by ELISA and compared with that obtained from matched healthy controls. Cytokine production was correlated with the severity of the mutation, affected domain and clinical characteristics.

**Results:** In response to LPS, PBMC from XLA patients produced significantly higher amounts of pro-inflammatory cytokines and IL-10 compared with controls and this production is not influenced by the neither severity of mutation or the affected domain. PBMC from patients with a history of more hospital admissions before diagnosis and patients with lower expression of Btk in monocytes produced higher levels of TNF-α and IL-1β, respectively. PBMC from patients with lower IgA levels showed a higher production of TNF-α and IL-1β. Less severe (punctual) mutations in Btk gene were associated with higher IgG levels at diagnosis.

**Conclusions:** Our results demonstrated a predominantly inflammatory response in XLA patients after LPS stimuli and suggest a TLR signaling dysregulation in absence of Btk. This response may be influenced by environmental factors.

**137 Hypogammaglobulinemia in a Boy: Consider Also X-linked Lymphoproliferative Disease**

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**Background:** X-linked lymphoproliferative disease (XLP) is a primary immunodeficiency presenting with a variety of clinical manifestations, the most common being dysgammaglobulinemia and B-cell lymphoma. The first gene causing XLP, when defective, was termed SH2D1A or SAP for signaling lymphocyte activation molecule (SLAM)-associated protein. The absence of SH2D1A leads to an overwhelming and uncontrolled TH1- shifted cytotoxic immune response, which might, at least in part, explain the severe clinical picture. A second gene, XIAP (X-linked inhibitor of apoptosis), was later identified.

**Methods:** An 8 year old Mexican boy was admitted in June 2008 for bronchopneumonia, with no previous history of recurrent or severe infections. He had a family history of a brother deceased at 7 years from fulminate hepatitis, who was diagnosed with agammaglobulinemia. A laboratory evaluation for primary immunodeficiency was made, including serum immunoglobulins: IgG 30 mg/dL, IgA <5 mg/dL; IgM 8.6 mg/dL; and flow
citometry for lymphocyte subpopulations: CD3+ 2590 mm³ (56%) CD4+ 1004 mm³ (42%), CD8+ 1267 mm³ (53%) CD16/56 171mm³ (41%) CD19+ 1493 mm³ (35%). The patient was started on monthly intravenous gammaglobulin (IVIG) therapy. He was admitted in December 2008 with fever and severe abdominal pain; an exploratory laparotomy revealed a rectal-sigmoid tumor. The biopsy reported an atypical Burkitt lymphoma (Immunophenotype “B”): Bel 2+, CD10+) with surgical margins negative for malignancy. Bone marrow aspirate and biopsy were negative for malignancy. In February 2009, management with chemotherapy was started with the diagnosis of Burkitt’s lymphoma stage III. Patient received 6 courses of chemotherapy with complete response to induction; for consolidation, 4 doses of rituximab were given. PCR amplification and direct automated sequencing by the Sanger method was performed in both genes known to be responsible for XLP in chromosome X.

**Results:** A hemizygous splice-site deletion in SAP was found, in intron 2: c.187_201+1del25, which deletes exon 2 splice donor site, and is predicted to result in the skipping of exon 2, and thus in a truncated, nonfunctional protein. XIAP was also sequenced and no mutation was found.

**Conclusions:** Final diagnosis: XLP. The patient is currently in the program for hematopoietic stem-cell transplantation.

**Background:** Primary immunodeficiencies (PIDs) are genetic diseases in which one or multiple components of the immune system, including cells (i.e. B cells, T cells, natural killer cells, phagocytes, complement components) or molecules (cytokines, chemokines, etc) are affected, leading to a low capacity to eliminate microorganisms and a high susceptibility to infection diseases.

Most of the PID are multifactorial entities were the environmental and multiple genetic factor are involved. The single nucleotide polymorphisms (SNPs) analysis in case and control groups has been increasing the knowledge of the etiopathogenesis of several diseases and the opportunity to identify molecular markers useful in the clinical diagnosis.

**Methods:** We performed a case control study including 19 pediatric patients with IgE deficiency (5 U/mL), and 180 healthy controls. 25 SNPs distributed in the IL-13, IL-10, IL-5, IL-4, FCER1B, INF γ, GM-CSF, STAT3, GATA 3 and TIK-2 were analyzed. Genotyping was performed using sondas TaqMan. Hardy-Weinberg Equilibrium (HWE) and statistical significance were evaluated using FINETTI and STATCAL software.

**Results:** All genotypes, both in cases and controls were in HWE. We documented statistically significant differences in the distribution of the SNPs located in IL-4 (rs4986964, P = 0.018, OR = 14.74, IL-4r, rs18005010, P = 0.018, OR = 2.22, FCER-1B, rs555917, P = 0.00001, OR = 16.9, GM-CSF, STAT3 and GATA-3 genes: GMFCS-130 (P = 4986964, OR = 0.22), STAT3 rs2293152 (P = 0.06 x 10^-9, OR = 6.18), GATA-3 rs2229360 (P = 0.005, OR = 13.52). The highest difference was found in the T allele of rs556917, which was more frequent in cases than controls (42.1 and 1.5%, respectively, P = 0.0001 OR = 16.907, 95% CI, 5.02-54.93). Interestingly, the C allele of 4986964 (IL-4) increased significantly in homozygote genotype (C: OR = 14.74, 95% CI, 2.38-91.234, P = 0.018 to CC OR = 29.4, 95% CI, 1.154-749.32, P = 0.002).

**Conclusions:** Our results suggest that SNPs located in the genes involved in the IgE production are risk genetic factor to IgE immunodeficiency. Increasing of the sample size is currently to get solid conclusions.

**RESPIRATORY INFECTIONS**

**140 Inhibition of AKT Kinase Activity Decreases Replication of Human Respiratory Syncytial Virus**

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**Background:** Human Respiratory Syncytial Virus (RSV) is a leading cause of pediatric pulmonary disease and severe RSV infection predisposes to wheezing later in life. RSV infection has also been shown to be an environmental trigger for asthma. We are investigating whether targeting host factors important for RSV infection is a viable antiviral strategy. Lowering viral burden through these therapies will result in decreased severity of infection and may also prevent the occurrence of pathologic sequelae.

**Methods:** Inhibition of AKT by chemical inhibitors, siRNA, or dominant-negative mutants, was tested for activity against RSV replication in cultured cells. We examined the effect of viral protein expression on Akt activation and downstream signal transduction by Western blot and promoter assay. In addition, we examined the effect of Akt on specific viral processes (entry, macromolecular synthesis, and assembly) and proteins both in vitro and in RSV-infected cells, using kinase assays, Western blotting, and qRT-PCR.

**Results:** We found that AKT inhibition decreases RSV protein expression and viral titers. Expression of RSV NS2 protein activates AKT, leading to NFkB-dependent transcription, and inhibition of AKT blocks this effect. Activated AKT also phosphorylates RSV P protein at a specific site. Interestingly, AKT inhibitors that target the pleckstrin homology (PH) domain of AKT showed decreased efficacy against RSV compared to those that target AKT kinase activity.

**139 Genetic Association Study of the IgE Immunodeficiency in Mexican Population**

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