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ORGANO UFFICIALE DELLA SOCIETÀ ITALIANA DI ALLERGOLOGIA E IMMUNOLOGIA PEDIATRICA

SUPPLEMENTO

ABSTRACT DEL XXII CONGRESSO NAZIONALE DELLA SOCIETÀ ITALIANA DI ALLERGOLOGIA E IMMUNOLOGIA PEDIATRICA 2020

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Editoriale

Marzia Duse
Giampaolo Ricci

Nel corso della pandemia determinata dal COVID-19 tutte le attività associative hanno avuto un blocco totale; così è avvenuto anche per il nostro incontro annuale. Come sapete, il XXII Congresso Nazionale della SIAIP si è svolto via web – in *streaming* e *on demand* – il 23 e 24 giugno 2020 con grande successo non solo per il numero di iscrizioni, ma anche e soprattutto per il numero di Colleghi che hanno partecipato attivamente a tutte le sessioni. Tutto era già pronto per l'incontro di Milano ed erano già stati approvati anche i contributi scientifici inviati da molti Colleghi da tutta Italia. Purtroppo, nell'incontro via web non è stato possibile dare loro spazio per ovvi motivi tecnici. D'altro canto non ci è parso opportuno né trasferirli al prossimo anno (sappiamo bene che questi abstract sono frutto di ricerche ed esperienze *in itinere*, dove la freschezza e la novità dell'argomento rappresentano l'elemento di punta) né inserirli in supplementi cartacei, come abbiamo fatto in passato, in quanto la versione web delle relazioni e delle letture non era accompagnata da versioni scritte.
Il prezioso contributo degli abstract, proprio perché pennellate di scienza "in pillole", è tuttavia innegabile e insieme al Presidente e al Consiglio Direttivo abbiamo ritenuto importante offrire a tutti i soci SIAIP la possibilità di leggere questi contributi scientifici creando un supplemento *online* della rivista.
Sicuramente vi mancherà la discussione diretta sugli argomenti di vostro interesse, momento che è sempre stato una palestra di confronto per i giovani allergologi; tuttavia mettendo in rete questi lavori ognuno potrà interpellare l'autore e, se vorrà, fare un commento o una richiesta di spiegazioni.
Invitiamo tutti a leggere questi lavori; alcuni sono parte di linee di ricerca, altri sono su casi clinici isolati, gestiti e risolti con idee innovative da cui trarre spunto per la propria attività professionale.
Nella speranza che l'anno prossimo il nostro incontro annuale possa svolgersi in presenza e che possiamo quindi tornare a discutere direttamente nella *Poster session*, vi inviamo un caro saluto.

Abstract del XXII Congresso Nazionale della Società Italiana di Allergologia e Immunologia Pediatrica 2020

ID: 6625

Effect of probiotics in children with infantile eczema : a double-blind randomized control trial.

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OBJECTIVE: Probiotics are used in the treatment of several conditions: functional abdominal pain, infantile colic, celiac disease, irritable bowel syndrome, lactose intollerance, food allergy, Hp infection, asthma, atopic dermatitis and infantile eczema. To determine whether oral administration of the probiotic Lactobacillus GG under randomized, double-blinded, placebo-controlled conditions would improve symptoms of infantile eczema in children.PATIENTS AND METHODS: 41 children with infantile eczema were given Lactobacillus GG or placebo for 6 weeks and entered follow-up for 4 weeks. Children entered a randomized, double-blind, placebo-controlled trial.RESULTS: LGG, but not placebo, caused a significant reduction of both frequency ($P < .01$) and severity ($P < .01$) of eczema. These differences still were significant at the end of follow-up ($P < .02$ and $P < .001$, respectively). CONCLUSIONS: Lactobacillus GG was superior to placebo in the treatment of eczema in children. The intestinal microbial flora may contribute to the pathogenesis of allergic diseases, LGG significantly reduces the frequency and severity of infantile eczema and maybe because improves the gut barrier function and reduce the inflammatory response.

ID: 6635

Immunomodulatory action on regulatory T cells elicited by protein fraction of different formulas for cow's milk allergy treatment through epigenetic mechanisms

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Introduction: Regulatory T cells (Tregs) play a pivotal role in immune tolerance. Tregs function is regulated by stable expression the transcription factor "Forkhead box Protein 3" (FoxP3) that requires demethylation of Tregs Specific Demethylation Region (TSDR). Preliminary data suggest the possible influence of dietary protein fractions. We aimed to comparatively evaluate the effects elicited by protein fraction of different formulas available for the dietary treatment of cow's milk allergy (CMA) on Tregs activation. Methods: Five formulas were compared: extensively whey formula (EHWF), extensively hydrolyzed casein formula (EHCF), hydrolyzed rice formula (RHF), soy formula (SOY) and amino acid based formula (AA). Formulas were reconstituted in water according to manufacturer's instructions, and subjected to an in vitro infant gut simulated digestion using a sequential gastric and duodenal static model. Resulting digested protein fractions were purified using C18 reversed phase pre-packed cartridges (Sep-Pak, Waters, Milford, MA, USA), recovered in 70% acetonitrile/0.1% trifluoroacetic acid and finally vacuum-dried. Tregs number and FoxP3 methylation status in TSDR were evaluated in peripheral blood mononuclear cells (PBMCs) from 6 patients, with challenge-proven IgE-mediated CMA (3 males, age range 1-5 yrs, all Caucasians), stimulated with 25 μg/ml digested protein fractions or b-lactoglobulin or bovine serum albumin, as positive and negative control respectively. Tregs were identified as $CD4^+$/$CD25^+$/$Foxp3^+$ cells by flow cytometry analysis. The staining was performed using human Treg detection kit and the results analyzed by BD CANTO II flow cytometer and DIVA software. FoxP3 TSDR methylation analysis was performed by PCR and direct sequencing. Results: Only digested peptides from EHCF were able to significantly increase $CD4^+FoxP3^+$ Tregs number. The effect paralleled with an up-regulation of FoxP3 demethylation rate in TSDR. Digested peptides from other study formulas were unable to modulate $CD4^+FoxP3^+$ Tregs and its demethylation status in PBMCs from CMA patients. Conclusion: The results suggest an epigenetic immunomodulatory action elicited by EHCF-derived peptides on Tregs activation. These results could explain, at least in part, the clinical effects observed on immune tolerance acquisition in CMA patients, and on allergy prevention in children at risk for atopy.

ID: 6636

Exploring the role of T cells population in the pathogenesis of gastrointestinal non-IgE-mediated food allergy

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Introduction: The immune mechanisms involved in the pathogenesis of gastrointestinal non-IgE-mediated food allergy (non-IgE-GI-FA) are largely undefined. We aimed to comparatively evaluate the role of activated Tregs, Bregs and Th17 cytokines response in non-IgE-GI-FAand in healthy controls. Methods: Activated Tregs and Bregs number, and Th17 cytokines (IL-17, IL-22) production were evaluated in peripheral blood mononuclear cells (PBMCs) from 6 non-IgE-GIFA (all subjects affected by cow's milk allergy: 4 food protein-induced enteropathy (FPE), 1 food protein-induced enterocolitis syndrome (FPIES), 1 motility disorder, and from 5 healthy controls. All subjects were male Caucasians and aged between 6 and 24 months. PBMCs were stimulated with cow's milk proteins (CMP) or with bovine serum albumin (BSA) at different doses for 7 days. Tregs and Bregs were identified as $CD4^+/CD25^+/Foxp3^+$ cells and $CD19^+/CD5^+/Foxp3^+$ respectively by flow cytometry analysis.IL-17 and IL-22 production were analyzed by ELISA.Results: After stimulation with CMP (maximal effective dose was 250 mg/ml), PBMCs from non-IgE-GI-FA, but not from healthy controls, showed a significant reduction of $CD4^+/CD25^+/Foxp3^+$Tregs number associated with a significantly higher production of IL-17 and IL-22, without differences among different clinical phenotypes. Activated Bregs remained unchanged in both groups.Conclusions: Our results suggest a potential role of Tregs and Th17 pathways in non-IgE-GIFA. These data could open the way to innovative strategy for the diagnosis and the management of these conditions.

ID: 6637

Formula choice for the management of cow's milk allergy influences other allergic manifestations and the time of immune tolerance acquisition: the Atopic March II study

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Introduction: Children with cow's milk allergy (CMA) have an increased risk to develop other atopic manifestations (AMs).To see whether formula choice for CMA treatment could impact the occurrence of other AMs and the time of immune tolerance acquisition.

Methods: Multicenter prospective open non-randomized trial on a cohort of children with a diagnosis of IgE-mediated CMA in the first year of life, already in follow-up, treated with: EHCF+LGG, rice hydrolyzed formula (RHF), soy formula (SF), extensively hydrolyzed whey formula (EHWF) or amino-acid based formula (AAF).The occurence of AMs (atopic eczema, allergic urticaria, asthma and oculorhinitis) and the immune tolerance acquisition was evaluated during a 36 months follow-up.

Results: 365 subjects completed the study, 73 per group.Demographic and anamnestic features were similar comparing the study cohorts at enrolment.Binomial regression revealed that the estimates of the incidence of the AMs are:EHCF+LGG: 0.22(Bonferroni corrected 95%CI:0.09 to 0.34);RHF:0.52(Bonferroni corrected 95%CI: 0.37 to 0.67);SF : 0.58(Bonferroni corrected 95%CI: 0.43 to 0.72);EHWF:0.51(Bonferroni corrected 95%CI: 0.36 to 0.66);AAF:0.77(Bonferroni corrected 95%CI: 0.64 to 0.89).The incidence of the main outcome in the RHF, SF, EHWF and AAF groups vs.the EHCF+LGG group was always higher than the pre-specified absolute difference of 0.25 and significantly higher at the pre-specified alfa-level of 0.0125(p-value <= 0.001 in all cases).The acquisition of immune tolerance was significantly higher in the EHCF+LGG group comparing to the other groups.

Conclusion: The results of the study suggest thatEHCF+LGG is superior to other formulas for the prevention of AMs and for the acquisition of immune tolerance in children with CMA.

ID: 6638

Tolerogenic effects elicited by a new butyrate releaser in a murine model of cow's milk allergy

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Introduction: The gut microbiota metabolite butyrate has a pivotal role in immune tolerance. It could be a promising new ingredient for innovative formulas for cow's milk allergy (CMA) treatment. Unfortunately, the extremely unpleasant smell and acrid taste lead to an extremely poor palatability of the available butyrate-based products. A new butyrate releaser, (phenylalanine-butyramide, FBA), has been developed. We aimed to investigate the efficacy and the mechanisms of action elicited by FBA added to formulas for the treatment of CMA in a mice model.Methods: Three-weeks old female C3H/HeJ mice were sensitized with 20 mg of cow's milk proteins (CMP), using cholera toxin as adjuvant, on days 0, 7, 14, 21, 28. Two weeks prior to sensitization, mice were given different formulas alone or in combination with FBA (1mM): extensively hydrolyzed whey formula (EHWF), extensively hydrolyzed casein formula (EHCF) or amino acid-based formula (AAF). Solid cow's milk protein-free diet (sensitized group) served as control. One week after the sensitization, mice were challenged with 50 mg CMP, and the anaphylaxis score was monitored. Blood samples were collected to detect serum MCP-1 levels. IL-4, IL-13, IL-10 and IFN-γ concentrations in splenocytes culture were measured by ELISA.Results: FBA addition to the study formulas resulted in a significant reduction of anaphylactic symptom score, serum total IgE, CMP-specific IgE, IgG1 and IgG2a and mMCP-1 compared with control animals and animals treated with formulas alone. The addition of FBA significantly stimulated IL-10 and INFg, and inhibited IL-4 and IL-13 production by splenocytes.Conclusions: FBA exerts a strong stimulation of tolerogenic mechanisms. The effect is independent of the type of formula used. It could be considered as new ingredient, for innovative formulas, able to stimulate the immune tolerance in CMA children.

ID: 6745

Atopic dermatitis and atopic march in children with history of non-IgE mediated gastrointestinal food allergy

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INTRODUCTION: Non-IgE mediated gastrointestinal food allergy (non-IgE-GIFA) are characterized by chronic gastrointestinal symptoms and include food protein-induced: enterocolitis syndrome (FPIES), enteropathy (FPE), allergic proctocolitis (FPIAP), and allergic dysmotility disorders (FPIMD). A casual relationship between atopic dermatitis and non-IgE-GIFA, and the occurrence of other atopic manifestation later in the life (atopic march) are still largely undefined in these patients. We aimed to explore the prevalence of atopic dermatitis and of atopic march in pediatric patients affected by non-IgE-GIFA. PATIENTS AND METHODS: Prospective study evaluating children with non-IgE-GIFA diagnosed according to standard criteria observed at a tertiary center for pediatric allergy (both sex, aged <6 yrs, follow up of at least 12 months after the diagnosis). After collection of the informed consent by the parents, main anamnestic, demographic and clinical data (including presence of atopic dermatitis, time of immune tolerance acquisition, occurrence of atopic march) were collected from all enrolled patients. RESULTS: A total of 43 subjects were enrolled: 46.5% male, mean age (SD) 16.12 (15.85) months (mo), 46.5% with multiple non IgE-GIFA. Non IgE-GIFA manifestations were: FPE(67.4%), FPIES(14%), FPIAP(11.6%), FPIMD(7%). 51.2% of subjects presented atopic dermatitis before the onset of non-IgE-GIFA. Cow's milk allergy was diagnosed in 72.1% of children, and after 12 mo immune tolerance acquisition was achieved in 41.9% of subjects. After 12 mo, the rate of subjects presenting atopic march was 46.5%. CONCLUSION: Our data suggest that atopic dermatitis precedes the development of non-IgE-GIFA, in keeping with a causal relationship, and that these patients present also an increased risk to develop atopic march.

ID: 6771

The Comano score as a caregiver-reported global severity assessment of atopic eczema in children

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INTRODUCTION With its prevalence increasing worldwide, atopic eczema (AE) is the most frequent inflammatory skin disease in infancy. In order to assess the clinical manifestations of AE, several scoring systems have been implemented and both the physician's and the patient's viewpoints were considered. While many standardized scoring systems for adults are available, there are few published options about the expression of a patient/caregiver-centered global severity assessment specifically for AE in children. With this concept in mind, the aim of our study was to evaluate a novel, fast, user-friendly and feasible caregiver-reported global severity assessment of AE in children. We called it the Comano score, a scoring system based on a 0-10 numeric rating scale.
MATERIALS AND METHODS We performed a cross-sectional observational study recruiting 867 patients from 1 to 16 years of age (males 49.5%, mean patient's age 5.9 years, standard deviation ± 3.6 years) who had already been diagnosed AE. These patients underwent balneotherapy at Comano Thermal Center (Comano, Trentino, Italy).
RESULTS We observed a strong correlation between Comano score and SCORing Atopic Dermatitis (SCORAD) ($r = 0.74$, $p < 0.0001$). CONCLUSION According to our results, the Comano score may be a successful novel tool for the definition of a caregiver-reported global severity assessment of AE in children. However, before this scoring system can actually be implemented to manage pediatric AE by health professionals in their everyday clinical practice, further data remain necessary in order to confirm our preliminary findings.

ID: 6774

Anaphylaxis caused by homemade honey in a child: a case report

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Honey is a rare form of food allergy, but it can cause severe systemic allergic reactions. In pediatric age, only few cases have been described in the literature and no allergens have been clearly characterized.
We reported a case of anaphylaxis in a 5-year-old-boy after the ingestion of a homemade honey. The patient was referred to our Hospital Emergency Department for generalized urticaria and breathing impairment. The symptoms occurred 30 minutes after the ingestion of a meal based on salmon and homemade honey. The allergological work-up revealed that prick-by-prick test with implicated honey was positive, while he was tested with salmon and a variety of different commercial honey with negative results. Skin prick test and serum specific IgE resulted also positive for Compositae pollen (ragweed and mugwort). Patients sensitized to weed pollens who ingested bee products may experience an immediate allergic reaction because of cross-reaction between weed pollens and Compositae bee product pollen. In this case, primary sensitization may be due to airborne Compositae pollen. These observations outline the role of Compositae pollen and suggest that the different pollen content of the homemade honey despite the commercial honey was responsible for the allergic reaction in our patient.
This is the first pediatric case of anaphylaxis caused by honey in a child under 6 years of age sensitized to Compositae pollen reported in the literature. Healthcare providers should be aware of the potential risk of severe allergic reactions upon ingestion of bee products, especially in patients sensitized to weed pollens, also in pediatric age.

ID: 6775

Sublingual immunotherapy-related eosinophilic esophagitis: report of two pediatric cases

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Introduction: Little is known about the interplay between eosinophilic esophagitis (EoE) and atopy treatment. An association between EoE and oral immunotherapy for food allergens has been described, but only few reports exist about the role of sublingual immunotherapy (SLIT) for aeroallergens in children. Case Report: We describe the cases of two boys, 11- and 14-year old, diagnosed with EoE while receiving SLIT, respectively for Alternaria and Grass pollen. Both children developed dysphagia, vomiting, and drooling while eating meat, respectively after 15 and 37 months of SLIT. They underwent esophagogastroduodenoscopy (EGD) which revealed endoscopically linear furrowing, mucosal erosion and histologically >100 eos/hpf, suggestive for EoE. According to ESPGHAN guidelines, they were first treated with omeprazole - 1 mg/Kg/die for 8 weeks - and afterwards with swallowed fluticasone propionate - 250 mcg, 1 puff/4 times/day for 8 weeks. EGDs performed after each treatment showed persistence of the disease. Therefore, we decided to switch immunotherapy to injective form in the first patient, and to discontinue SLIT in the latter. At the following EGD, macroscopic examination of esophageal mucosa was normal and eosinophilic infiltration was significantly decreased (respectively 21 and 32 eos/hpf). In both patients EoE symptoms disappeared soon after omeprazole treatment. Conclusions: SLIT may be a potential trigger for EoE due to high antigen exposure of the esophagus. Since SLIT is commonly used, we suggest monitoring for EoE symptoms in patients receiving it. Future studies are needed to better evaluate the role of SLIT in the development of EoE.

ID: 6776

Eosinophilic esophagitis and sublingual immunotherapy: a proposal for a prompt diagnosis

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Introduction
EoE incidence is increasing (1-20/100.000). In pediatric population it is associated with atopy (50-60%), asthma (30-50%), rhinitis (50-75%) and food allergy (15-43%), with best predictive positive value (86%) of milk skin prick test (SPT), followed by egg. In a subset of patients, aeroallergens and SLIT may trigger EoE activating Th2, production of IL5-13 and eosinophils recruitment. Specific disease-risk loci (CAPN14, TSLP) are associated with the molecular pathoetiology of EoE.
Patients
208 SLITs and 4 EoEs (1F, 3M; 11-14 years) between 2018-2020 were analyzed. Medical history, symptoms, esaphagogastroduodenoscopies, SPTs, patch tests, RASTs, allergen components, type of ITS were collected in a database.
Results
All patients with EoE had allergic asthma and were polysensitized to aeroallergens. 3 started SLIT (1 alternaria, 2 grass pollen) lasting respectively 16, 41 and 17 months before EoE diagnosis. After interrupting SLIT: the first switched to SCIT, but EoE with oral itching during egg intake recurred after one year; the second improved without complete histological remission; the third recovered with no need of further ITS. The forth started SCIT (dermatophagoides) after EoE diagnosis.
Conclusion
Aeroallergenes and SLIT may be EoE trigger in susceptible patients. Considering the large amount of SLIT and increasing numbers of EoE, it's important to identify SLIT patients with EoE higher risk. Lacking routine susceptibility genetic test, we propose to administer a gastroenterologic validated symptoms survey (PEESS™ v2.0) quarterly to earlier diagnose EoE in SLIT patients, monthly in case of associated milk-egg allergy. Esophagogastroduodenoscopy and SCIT are recommended if PEESS™ positive.

ID: 6777

UN MYCOPLASMA CHE NON PASSA

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Caso Clinico
Chiara, 10 anni, giunge alla nostra osservazione perchè da circa due mesi presenta febbricola serotina (T max 37,7°C) accompagnata da astenia e malessere generale della durata di qualche ora. In anamnesi storia di polmonite da Mycoplasma trattata con Claritromicina per tre settimane con beneficio clinico e interrotta circa 10 giorni prima. Agli esami ematochimici si evidenzia lieve leucopenia (WBC 5000/mm3) con formula indifferente e PCR negativa. RX torace negativa.Alla luce del dato clinico e anamnestico decidiamo quindi di effettuare un nuovo dosaggio delle immunoglobuline anti-Mycoplasma che risultano positive (sia IgM che IgG) e di escludere eventuali altre cause di febbricola persistente. Il test di Mantoux, la reazione di Widal-Wright, e la sierologia per EBV risultano negativi come il resto degli esami infettivologici. La valutazione delle patologie autoimmunitarie e il dosaggio anticorpale non evidenziano elementi patologici e anche l'assetto tiroideo risulta nella norma. Al fine di escludere problematiche oncoematologiche eseguiamo anche ecografia dell'addome, dosaggio dell'acido omovanillico e vanilmendelico anch'essi risultati nella norma..Escluse le principali condizioni cliniche che potessero giustificare il quadro clinico di Chiara decidiamo di intraprendere un nuovo ciclo di terapia antibiotica con Claritromicina, sebbene fosse stata trattata con lo stesso antibiotico fino a 10 giorni prima, considerando la possibilità che un deficit immunitario di base rendesse l'infezione da Mycoplasma Pneumoniae persistente nonostante il trattamento. Mentre il dosaggio delle sottoclassi immunoglobuliniche non ha mostrato alterazioni, la valutazione delle sottopolazioni linfocitarie ha evidenziato un deficit dei linfociti T helper. Dopo il quinto giorno di terapia gli episodi serotini sono diventati meno frequenti fino a scomparire del tutto.

Discussione
Il Mycoplasma è uno dei più frequenti responsabili di infezioni delle basse vie aeree in età scolare e adolescenziale. Nella maggior parte dei casi, la sintomatologia è lieve o moderata e, spesso, autolimitante. Altre volte quando l'infezione coinvolge le vie aeree inferiori può causare polmonite e febbre. Il trattamento con Claritromicina per 7-10 giorni generalmente risolve il quadro clinico, tuttavia i pazienti con deficit immunologici moderati o severi tendono ad avere infezioni recidivanti e sostenute, necessitando di terapie più prolungate. Sembrano principalmente imputati nell'instaurarsi e il protrarsi dell'infezione, i deficit dell'immunità umorale, sebbene non siano del tutto noti i meccanismi immunologici responsabili.

ID: 6779

A PURPURA SHADE AFTERNOON

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HPS, the most common vasculitis of childhood, affects multiple organs and may have different features at the diagnosis.

Less than 2% of HPS cases develope hemorrhagic vesicles and bullae resulting in cutaneous necrosis and scar. M., a child who experienced HPS 3 years before, was admitted to our hospital because of arthralgia and the evolution of palpable purpura into hemorrhagic vesicles and bullae. CBC, coaugulation, total protein, C3, C4, ANA and serum immunoglobulin were normal; CRP, urine and stool analysis were negative. The most common viral infection were excluded; ASLO 1207 UI/ml. M. was treated with Prednisone, Paracetamol and local Fusidic Acid.

In a limited number of cases, Acute Scrotum is the initial presentation of HPS. P. presented with acute swelling, hyperemia and testicular pain. After scrotum ultrasound, we excluded testicular torsion. After 24 hours, palpable purpura, arthralgia and swelling affected the legs. Coaugulation, total protein, C3, C4, ANA and serum immunoglobulin were normal; stool analysis was negative; ASLO 613 UI/ml; WBC 18,56 x 10^3/mml; CRP 3,51 mg/dl and microhematuria was detected. He was treated with Clavulanate+Amoxicillin and Prednisone with complete resolution.

E. presented with arthralgia, lameness, petechiae, painful lumbar swelling(10 cm)without signs of cutaneous flogosis. Liver and spleen were palpable. Neurological examination was negative. CBC, coaugulation, total protein, C3, C4, ANA and serum immunoglobulin were normal; CRP, urine and stool analysis negative; ASLO 832 UI/ml. E. was treated with Prednisone and Paracetamol with complete resolution within 4 days.

ID: 6780

Variabilità clinica e immunologica di una coorte di pazienti con immunodeficienza comune variabile

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Introduzione: L'immunodeficienza comune variabile (IDCV) è una condizione caratterizzata da ridotti livelli sierici di IgG e di IgA con o senza bassi livelli di IgM, ridotta risposta umorale specifica e/o riduzione delle cellule B memory switch [1]. Dal punto di vista clinico il fenotipo è eterogeneo. I pazienti hanno un'aumentata suscettibilità non solo alle infezioni ma anche a malattie autoimmuni e un'aumentata incidenza di neoplasie. Nell'ambito dell'IDCV sono stati distinti 5 fenotipi clinici: infettivo, autoimmune, con infiltrazione linfocitaria policlonale, enteropatico, neoplastico [2]. Scopo: Descrivere la variabilità clinica e immunologica di una coorte di pazienti con IDCV . Metodi: Sono stati raccolti retrospettivamente i dati clinici e immunologici di 17 pazienti seguiti presso il nostro centro di Immunologia Pediatrica con diagnosi di IDCV, criteri ESID 2014[1]. Risultati: L'età media dei pazienti alla diagnosi è stata 12±4 anni, l'età media attuale è 17,8±4 anni. Dal punto di vista clinico 11 pazienti presentano solo manifestazioni infettive, 2 pazienti, in cui la diagnosi è stata posta sulla base della familiarità per immunodeficit, sono asintomatici, i restanti 4 pazienti presentano, oltre agli eventi infettivi, un fenotipo linfoproliferativo policlonale (2 casi), autoimmune (1 caso), sia linfoproliferativo policlonale che autoimmune (1 caso). Per quanto riguarda l'aspetto immunologico, in 2 casi è stato riscontrato un aumento dell' isotipo M delle immunoglobuline (>2DS per età); questi due pazienti hanno sviluppato, rispettivamente, un fenotipo linfoproliferativo policlonale e un fenotipo esclusivamente infettivo, caratterizzato da ripetute polmoniti. In 3 pazienti il valore dei linfociti B è risultato inferiore al limite della norma per età. In due casi abbiamo riscontrato un aumento della popolazione linfocitaria Natural Killer (NK); i due pazienti hanno sviluppato un fenotipo rispettivamente di tipo linfoproliferativo policlonale e autoimmune. Per quanto riguarda il fenotipo B avanzato, le cellule B memory switch sono ridotte per età nella maggioranza dei pazienti e solo in 3 casi sono risultate nella norma. Questi pazienti hanno presentato solo manifestazioni infettive.Conclusione: Il nostro studio conferma l'ampia eterogeneità clinica della ICVD. In accordo con la letteratura, uno dei due pazienti con aumento delle IgM ha sviluppato un fenotipo linfoproliferativo policlonale; analogamente una riduzione delle cellule B memory switch è osservata in pazienti con fenotipo linfoproliferativo policlonale e autoimmune.
1.European Society for Immunodeficiensis Registry Working Party. Available at: http://esid.org/Working-Parties/Registry/Diagnosis-criteria. Accessed August 10, 2015. 2. Chapel H, et al. Common viarable immunodeficiency disorders: division into distinct clinical phenotypes Blodd 2017;112: 277-286.

ID: 6781

HAZELNUT ALLERGY: COULD THE CO-SENSITIZATION TO BIRCH POLLEN INFLUENCE THE SEVERITY OF ALLERGY SYMPTOMS?

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Introduction

Hazelnut is a widespread food in our culture. This represents a problem for thousands of Italian children who are allergic to hazelnut, who require a taxing exclusion diet, the violation of which involves the occurrence of a wide range of symptoms, from oral allergic syndrome (OAS) to anaphylaxis. Sensitization in many patients results from cross-reactivity with allergens like birch pollen; these patients often show no symptoms after consuming hazelnut. In this study we aimed to summarize the epidemiological and symptomatological situation of hazelnut-sensitized patients from the Pediatric Allergology Center of the Policlinico Umberto I in Rome.

Patients and Methods

We recruited 139 patients (F = 56, M = 89, average age 9 years 10/12) in Allergology Pediatric Department of Policlinico Umberto I with positive Skin Prick Test (SPT) for hazelnut; the symptoms associated with the intake of hazelnut, the therapeutic/preventive measures taken and the co-sensitization detected with SPT were assessed.

Results

Among 139 hazelnut-sensitized patients, 32 (23.02%) never experienced symptoms after hazelnut intake; 30 patients (21.58%) had anaphylaxis; 15 (10.79%) showed urticaria; 7 patients (5%) s.o.a .; 7 (5%) reported gastrointestinal symptoms.

Conclusions

The data of our hazelnut-sensitized patients would seem to indicate that co-sensitization to birch pollen may correlate with lower risk of anaphylaxis. In the situations where OFC is not recommended, the molecular diagnosis might represent the gold standard to identify sensitization to specific, more "dangerous" proteins of hazelnut. A bigger sample size could confirm this hypothesis.

ID: 6782

HOW NITRIC OXIDE CAN HELP IN PDTA OF ALLERGIC RHINITIS?

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Introduction:Nitric oxide is produced from nasal epithelial and inflammatory cells, mediated by inducible nitric oxide synthase.Measurements of FeNO could be used as an objective marker to detect AR inflammation. We aimed to clarify the correlation between mean nasal flow (mNF) using anterior active rhinomanometry (AAR) and nFeNO and the differences between nFeNO in children with AR (group1), asthma(group 2), AR-asthma (group 3), in comparison to healthy children.Materials and methods: We recruited 150 children: 64 with AR, 20 with asthma, 30 with asthma-AR, and 36 controls referring to Allergology of Policlinico Umberto I. All the children performed AAR, measurement of nasal nitric oxide (nFeNo) and exhaled nitric oxide (eFeNo) and a spirometry. Results: The average value of nFeNO concentration is higher in group 1, 2 and 3 and this average assumes a higher value in group 3. Similar observations can be made for eFeNO.ANOVA highlights significant differences between the average of nFeNO and eFeNO regarding the different groups and Post hoc test with Bonferroni shows significant differences between the average of the groups compared two by two.We found a negative Pearson correlation (-0,366) between mNF and nFeNo, a positive Pearson correlation (0, 483) between nFeNo and eFeNo and a negative Pearson correlation (-0,365) between eFeNo and FEV1, all statistically significant ($p<0,001$). Conclusion: Measurement of nFeNO is a non invasive and objective method for the measurement of nasal inflammation in AR children that can be useful in combination with AAR for the management of AR in children.

ID: 6783

OXIDATIVE STRESS AND GUT MICROBIOTA IN PANDAS CHILDREN: NADPH 2 OXIDASE ROLE

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Introduction
PANDAS "Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections" identifies patients with acute onset of obsessive-compulsive disorders and/or tics, related to group A β-hemolytic Streptococcus pyogenes infection.
The aim of our study was to investigate oxidative stress-mediated neuroinflammation and NOX2 activation in children with PANDAS.

Materials and methods
Forty patients (3-16 aged) were consecutively recruited: 20 PANDAS and 20 controls, referring to pediatric neurology and allergology of Umberto I University Hospital in Rome. All patients performed a venous blood sampling for antistreptolysin O title, LPS, serum isoprostanes and soluble NOX2-dp (oxidative stress markers).

Results
Oxidative stress values and serum levels of LPS were each significantly elevated in PANDAS children.
Simple linear regression analysis showed how serum sNOX2-dp levels were significantly correlated with LPS (R: 0.504; $p< 0.001$) and isoprostanes (R= 0.724; ;$p< 0.001$). Serum LPS was significantly associated with isoprostanes (R= 0.722; $p< 0.001$). A multiple linear regression analysis was performed to underline that isoprostanes (SE: 0.008; standardized coefficient β: 0.579; $p< 0.001$) were the only variable independently associated with sNOX2-dp variation. Finally, in PANDAS group, stratified according to the median of LPS, those patients with LPS over the median, had significantly higher levels of sNOX2-dp and isoprostanes.

Conclusion
This study shows an increased NOX2 activity and higher serum LPS in children with PANDAS, potentially implicated in the process of neuroinflammation and neurodegeneration, linked to intestinal dysbiosis.

ID: 6784

Dangerous Bubble

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Introduction: FANS and antibiotics are drugs involved the most in Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The pathogenesis is related to CD8+-T-cells and to a role played by the macrophage/monocyte system. Currently it is not always possible to link the syndrome to particular features or exposure to drugs.
Patients and methods: A 7 year old girl visited our ER for vesicular rash, stomatitis, mucositis, Nicolski sign positive and fever. For the symptoms she was taking Ibuprofen and Amoxicillin/A.Clavulanic without defervescence. The mother reported that the girl had previously taken the drugs without complications. Considering the suggestive physical exam and blood test (thrombocytopenia, high PCR values and hyposodyemia), in the suspicion of an SJS, the therapy was suddenly changed. For the expansion of the rash TEN was diagnosed. A dose of Etanercept was administered without response, so methylprednisolone and IgEV were performed with progressively improvement.
Results: Etanercept was tried in this patient without benefit; glucocorticosteroids and IgEV were more effective, due to the underlying variable immune mechanism of the pathogenesis. After their administration the skin lesions re-epithelized and blood tests were back normal.
Conclusion: Given the rarity of the pathology is hard to conduct clinical trials and follow guidelines. Furthermore it is not always possible to trace the trigger especially in a patient who had already been exposed to the drugs before the event. It is not possible to define the effectiveness of these drugs to modify the clinical course. The origin of SJS/TEN lies probably in the interaction between infections and drugs.

ID: 6785

Allergy in Selective IgA Deficiency (SIgAD)

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Introduction:Selective IgA deficiency (SIgAD) is considered the most common immunodeficiency. Patients with SIgAD may experience recurrent respiratory infections, allergic and autoimmune diseases. Specifically, association between SIgAD and allergy is still debated: while some authors report a similar frequency to that of general population (≈30%), others highlight a greater susceptibility to allergic diseases. Aim of this study is to evaluate the prevalence of allergy in SIgAD patients.
Patients an methods: 48 children aged 4-18 with SIgAD (ESID criteria) were retrospective monitored at Pediatric Immunology and Allergology Centre of Policlinico Umberto I in Rome. Data collection includes age, sex, IgA and IgE serum levels, in vivo or in vitro sIgE detection, gastrointestinal (oral allergy syndrome, nausea, vomiting, GER, diarrhea, recurrent abdominal pain) or allergic (rhinitis, asthma, angioedema /urticaria, atopic dermatitis) symptoms.
Results: 22 patients (45,83%) received diagnosis of allergic rhinitis, 4 patients (8,33%) of allergic asthma, 13 (27,08%) of atopic dermatitis and 6 (12,5%) patients experienced urticaria. In the overall SIgAD(48), only 13 (27,08%) patients shown positivity to in vivo/vitro sIgE for inhalant allergens and 4 (8,33%) for food allergens with gastrointestinal manifestations.
Conclusion: Our study highlight an high percentage of allergic manifestations in patients with SIgAD. To diagnose an allergic diseases can be crucial to improve the quality of life and clinical management of these children already burdened by a greater susceptibility to both respiratory and gastrointestinal diseases. It would be interesting to evaluate how many patients with allergic diseases have undiagnosed SigAD.

ID: 6786

Utility of specific-IgE to egg white and ovomucoid in predicting cooked egg challenge outcome

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Background
Hen's egg is a common cause of childhood food allergy, affecting 0.5-2.5% of children. Oral food challenge (OFC) is the "gold standard" to confirm the diagnosis of egg allergy. The aim of our study was to evaluate the utility of sIgE to egg white (EW) and its dominant allergen, ovomucoid (OVM), in predicting cooked egg challenge outcome.
Method
109 children (mean age 5.3yrs, range 1-16yrs) with clinical history of egg adverse reaction and/or sensitization (positive EW or OVM sIgE), who underwent OFC with boiled egg under medical supervision, were enrolled in this retrospective study. Only patients who had available egg-sIgE within 2 years before OFC were evaluated. According to sIgE, we categorized patients into 4 groups for EWsIgE (E1 <5kUA/L, E2 5-19.9kUA/L, E3 20-29.9kUA/L, E4 ≥30kUA/L) and 4 groups for OVMsIgE (O1 <0.5kUA/L, O2 0.5-4.9kUA/L, O3 5-9.9kUA/L, O4 ≥10kUA/L).
Results
51% of patients had family history of atopic disorders and the majority was affected by other atopic conditions (53% atopic dermatitis, 13% asthma, 13% rhinoconjunctivitis, 56% other food allergies). The onset of egg allergy (mean age 1yr) was characterized by cutaneous symptoms in 68% patients (40% urticaria/angioedema, 28% atopic dermatitis), gastrointestinal ones in 22%, respiratory ones in 6% and anaphylaxis in 11%. 24/109 (22%) patients experienced positive OFCs: 10 (42%) developed anaphylaxis, 18 (75%) cutaneous symptoms, 14 (58%) gastrointestinal symptoms, 5 (21%) respiratory symptoms. Considering EWsIgE in patients with positive OFC outcome, 13/24 (54%) belonged to E1 group, 4/24 (17%) to E2, 3/24 (12%) to E3, 4/24 (17%) to E4. Regarding OVMsIgE, 10/24 (42%) belonged to O1, 9/24 (37%) to O2, 1/24 (4%) to O3, 4/24 (17%) to O4. Children who experienced anaphylaxis during OFC had EWsIgE as following: 5/10 (50%) <5kUA/L, 2/10 (20%) 5-19.9kUA/L and 3/10 (30%) ≥20kUA/L; while OVMsIgE as following: 8/10 (80%) <5kUA/L and 2/10 (20%) ≥10kUA/L.
Conclusion
In our population most children with clinical history of egg allergy and/or egg sensitization passed boiled egg challenge. Althought only few reacted (22%), a significant percentage (42%) developed anaphylaxis. It is noteworthy that the majority of children with OFC positive outcome belonged to lower sIgE groups; in particular, 71% had EWsIgE <20kUA/L and 83% had OVMsIgE <10kUA/L. Therefore, sIgE value was not predictive of OFC outcome or OFC reaction severity, confirming the importance of performing OFC, regardless of sIgE value.

ID: 6787

Food allergy in children with atopic dermatitis

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Background
Oral food challenge (OFC) is still the "gold standard" to confirm or refuse histories of adverse reactions to foods. Children with atopic dermatitis (AD) often show sensitization to trofoallergens and/or aeroallergens, but the prevalence of food allergy (FA) in children with atopic dermatitis has been poorly investigated.

Method
In our study, 103 children with atopic dermatitis (age range 1-18 years old, median age 9,14 years) with sensitization to foods (positive skin prick tests and/or sIgE to one or more food allergens) and/or suspicion of food allergy underwent an oral provocation test under medical supervision. Also subjects who avoided foods for a long time (although previously tolerated) were included, for the risk of adverse reactions. We divided patients into 3 groups: Group A (55/103), patients with positive skin prick tests (SPTs) and/or sIgE and an history of adverse reactions to foods; Group B (22/103), patients sensitized to trofoallergens without reported clinical reactions to foods; Group C (26/103), patients who reported adverse reactions to foods but with no evidence of sensitization to trofoallergens.

Results
Overall, 24/103 patients (23,3%) experienced positive food challenges: 17/24 developed cutaneous symptoms, 8/24 oral itch, 6/24 gastrointestinal symptoms and 15/24 respiratory symptoms, respectively. Among patients who had positive OFCs, 20/24 (83,3%) belonged to Group A (positive SPTs and/or sIgE and history of adverse reactions), 2/24 (8,3%) to Group B (positive SPTs and/or sIgE without reported clinical symptoms) and 2/24 (8,3%) to Group C (history of adverse reactions to foods, without evidence of sensitization to trofoallergens), respectively.

Conclusion
These results highlight the fact that although atopic dermatitis is often associated with single or multiple sensitizations to foods, in most cases a diagnosis of food allergy is not confirmed. In agreement with previous literature data, we found that less than one third of children with AD have concomitant FA. Our data confirm the need to perform an OFC in children with AD sensitized to food, to avoid unnecessary and potentially risky avoidance diets.

ID: 6789

Oxidative stress in Vernal Keratoconjunctivitis

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Introduction
Vernal Keratoconjunctivitis (VKC) is a chronic bilateral conjunctivitis typical of the pediatric age, whose pathogenesis is still under discussion. Oxidative stress is believed to contribute to the damage in VKC; however there are no studies that analyzed this issue. Thus, the aim of this study was to assess oxidative stress in VKC.
Materials and methods
Twelve consecutive children affected by VKC aged between 5 and 12 years of life were enrolled at the Department of Pediatrics, Division of Allergy and Immunology, "Sapienza" University of Rome. Group 0 were six novel diagnosis that didn't have done the gold standard therapy with cyclosporine eyewash and Group 1 were six patients evaluated after 1 month of therapy with good symptoms control. All patients performed tears and blood samples. H2O2 and Nox2 levels were tested in both and H2O2 only in tears.
Results
Our preliminary data show H202 (31,08±5,96 vs 24,23±4,2 , p 0,004), Nox2 (25,12± 7,14 vs 18,72± 4,82 , p 0,017) sera levels and H2O2 tears levels (22,04±6,23 vs 16,03±4,11, p 0,011) are significantly more elevated in Group 0 patients versus Group 1.
Conclusion
Our study shows lower levels of oxidative stress markers in patients after therapy compared with patients without therapy. These markers could be used in future to evaluate the activity disease and therapy response in the patients follow-up. Therefore, further studies are needed.