Abs 01 | Molecular allergological evaluation in pediatric patients

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Introduction: Allergic syndrome diagnosis has been based, for a long time, on a careful clinical-anamnestic evaluation and skin prick test (SPT), with the last one, according to current guidelines, being still the gold standard for its first-level diagnosis. However, it is not always sufficient to identify the specific allergen. In laboratory medicine, the use of second-level molecular diagnostics assays that allows the identification of the genuine allergen is therefore appropriate. The study is aimed to compare the results of SPT with molecular diagnosis, to identify the correlation between positivity to allergen extracts and genuine allergens in a cohort of pediatric patients with respiratory symptoms and positive SPT.

Patients and Methods: We analyzed 30 patients [M = 13; F = 17; mean age: 13 (IQR: 10-15.25) yrs], eligible for molecular diagnostics and willing to participate in the study. At the time of blood sampling, patients were symptomatic and untreated; sera were aliquoted and stored at −20 °C. Investigations for allergen extracts d1 (Dermatophagoides pteronyssinus) and d2 (Dermatophagoides farinae) and for molecular allergens Der p 1, Der p 2, Der p 10 and Der p 23 were performed using a FEIA (Fluorescence Enzyme Immune Assay) method on PHADIA250 (ImmunoCap) instrument (Thermo Fisher Scientific Inc., Uppsala, Sweden), using a cutoff value, <100 KU/L.

Results: Values >100 KU/L were considered positive. Allergen extracts positivity was observed in 30% of patients for d1 and 16.6% of patients for d2. Molecular allergen evaluation showed positive results in 13.3% of patients for Der p 1, 40% for Der p 2 and 23.4% for Der p 23. 100% of patients had specific IgE values between 0-10 KU/L for the cross-reactive Der p 10 molecule.

Conclusion: Our data support the appropriate assessment of molecular allergens, at very early stage, in symptomatic pediatric patients. In this cohort, negative results obtained for the cross-reacting molecule Der p 10 should reflect a better clinical response to an early immunotherapy administration and, thus, a reduced evolution of the allergic march. Laboratory molecular diagnosis has become a pivotal ways sufficient to identify the specific allergen. In laboratory medicine, the use of second-level molecular diagnostics assays that allows the identification of the genuine allergen is therefore appropriate.

Abs 02 | Retrospective analysis of a pediatric population affected by IgE-mediated cow’s milk protein and egg allergy: identification of predictive factors for the development of tolerance

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Introduction: We aimed to identify predictive factors of oral tolerance to cow’s milk and egg and to evaluate differences between cow’s milk protein allergy (CMPA) and egg allergy (EA) in terms of development of tolerance.

Patients and Methods: We retrospectively analyzed data of patients who underwent an oral food challenge to cow’s milk and raw egg in the Pediatric Department of San Raffaele Hospital (January 2011-December 2017). The sample was composed of 70 subjects: 39 had CMPA, 41 had EA (60 patients were allergic to one food, and 10 patients were allergic to both). Statistical analysis was performed using JMP14; Wilcoxon and chi-square tests were used.

Results: 94.88% of patients with CMPA developed complete tolerance vs. 68.29% of patients with EA (P = 0.0197). Median age of tolerance was 1.75 year for cow’s milk and 2.96 year for egg (P = 0.0334). Co-existing EA was associated with a later development of cow’s milk tolerance (P = 0.0135); co-existing CMPA was associated with a lower proportion of development of egg tolerance (P = 0.0249); respiratory allergies were associated with a lower proportion of development of egg tolerance (P = 0.0209); wheezing as a symptom at diagnosis was associated with a later development of cow’s milk tolerance (P = 0.0093) and a lower proportion of egg tolerance development (P = 0.0166); no one with anaphylaxis developed complete egg tolerance (P = 0.0030).

Conclusion: Subjects with a single food allergy, subjects with non-severe symptoms at diagnosis, subjects without respiratory allergy and subjects with CMPA have a more favorable natural history towards food tolerance compared to subjects with EA.

Abs 03 | The predictive value of specific IgE levels as indicator of future tolerance in a pediatric population affected by cow’s milk protein and egg allergy

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**Introduction:** Most patients with cow’s milk protein allergy (CMPA) and egg allergy (EA) develop tolerance during childhood. We wanted to define whether the specific IgE levels at the time of diagnosis of CMPA or EA could be indicators of future oral tolerance to this food.

**Methods:** We retrospectively analyzed clinical data of patients who underwent an oral food challenge to cow’s milk and raw egg in the Pediatric Department of San Raffaele Hospital (January 2011 to December 2017). The sample included 70 subjects: 39 had CMPA, 41 had EA (60 patients were allergic to single food and 10 patients were allergic to both of them). Statistical analysis was performed by using JMP14; Wilcoxon test was used.

**Results:** Lower specific IgE levels at diagnosis were significantly associated with a higher proportion and a more precocious development of food tolerance. Particularly, lower alpha-lactalbumin specific IgE levels were significantly associated with development of cow’s milk tolerance (P = 0.0142); lower egg white and yolk specific IgE levels were significantly associated with development of egg tolerance: median egg white IgE levels of 3.74 kU/L for patients that developed tolerance vs 8.9 kU/L for patients that did not develop tolerance (P = 0.0050), median yolk IgE levels of 0.99 kU/L for patients that developed tolerance vs 3.28 kU/L for patients that did not develop tolerance (P = 0.0236).

**Conclusion:** Our results confirm that subjects with cow’s milk and egg allergy who have lower specific IgE levels at diagnosis have a more favorable natural history towards tolerance.

**Abs 04 | A case of Kawasaki Shock Syndrome: A challenging diagnosis, a challenging inflammatory response**

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A.C., 5 years old boy, was admitted to St. Mary’s Hospital, London with 6 days of fever, persistent on amoxicillin, associated with oral mucosal ulceration, cervical lymphadenopathy, erythematous rash on face and trunk and conjunctivitis. Past medical history was negative. Family history was positive for autoimmune disease: a brother with Juvenile Arthritis, treated with Methotrexate and Infliximab, a sister with Type 1 Diabetes Mellitus. During his initial assessment in the emergency department, the patient became lethargic and hypotensive, requiring fluid resuscitation, peripheral adenolymphatic infusion and tracheal intubation for cardiovascular instability. Blood examination showed Platelets 59,000/mm³, White cell count 3,900/mm³, Neutrophils 2,900/mm³, C-Reactive Protein 263 mg/L, Troponin 39 ng/L. Two main differential diagnoses were considered: Toxic Shock Syndrome and Kawasaki Shock Syndrome (KSS). Broad-spectrum antibiotics, 2 mg/kg of Intravenous Immunoglobulin and Methylprednisolone were administered. As the Echocardiography showed dilated right and left coronary arteries, and, as the patient was still febrile with increased CRP, on Day 3 he received a dose of Infliximab, leading to defervescence and rash resolution. Nasopharyngeal aspirate was positive for Influenza A Virus, Rhinovirus/ Enterovirus, and Parainfluenza 4. The ANA Screening was weakly positive, negative by IIF on HEP2 cells. This patient fulfilled criteria for Kawasaki Disease and presented with shock. Low platelet count, high CRP, and IVIG resistance may be present in KSS. KSS aetiology is unknown, probably intense systemic vasculitis, capillary leak and myocardial impairment are involved. Aberrant inflammatory response due to an underlying host immunological susceptibility is likely, although genetic polymorphisms associated with susceptibility to KSS remain undiscovered.

**Abs 05 | Treatment and follow-up with omalizumab of a refractory case of solar urticaria**

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Solar urticaria (SU) is a rare chronic photodermatosis. It is characterized by urticarial skin lesions at the sites photoexposed. First-line treatment is sun protection, H1-antihistamines and short course(s) of oral steroids. However, SU is often unresponsive. Omalizumab is an anti-IgE antibody, approved for severe, difficult asthma and chronic idiopathic urticaria. We describe the case of a 16-year-old girl with a history of SU unresponsive to conventional therapies but dramatically and fully responsive to omalizumab (4 years of overall treatment), Phototest was positive for UVB. She started therapy with omalizumab on the basis of her initial serum IgE level (228 IU/mL) and her body weight (375 mg/every 2 weeks). Already at first administration, she had an excellent response and the improvement persisted also during the maintenance phase of treatment. After 6 months, we started to reduce the dose of omalizumab (300 mg/month in a single dose in the 7th month, 150 mg in 8th and 9th month of treatment) up to suspension. Since the 4th month of omalizumab washout, the patient had the disease remission. Phototest was negative both for UVA and UVB after 4 months from the suspension of omalizumab (1). During the following 3 years, the patient was treated with 1 cycle/year of omalizumab (300 mg/every 4 week) for 6 months the first two years and 12 months the third year, without adverse events or disease exacerbation. The phototest maintained persistently negative during the follow-up. Therefore, despite the mild relapse of urticaria and the necessity of further courses of therapy, we confirm safety and efficacy of omalizumab in patients suffered of SU not responding to standard pharmacological treatments.
ABSTRACTS

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Introduction: Cow’s milk allergy (CMA) is one of the most common food allergies in the pediatric age, affecting 0.8% of children in Italy. Specific Oral Tolerance Induction (SOTI) is recommended with a grade A of evidence as treatment option in children with CMA (EAACI guidelines 2018). Different protocols are available but no one is standardized and worldwide accepted. Objectives: To compare two different protocols of cow’s milk oral desensitization based on literature evidences.

Methods: We searched on PubMed all cow’s milk oral desensitization studies conducted at the Allergy Unit of IRCCS Burlo Garofalo in Trieste and the Pediatric Allergy Unit of University Hospital “G. Martino” in Messina in the last 15 years.

Results: We found 7 studies. At the Allergy Unit of Trieste, based on tolerance level after positive cow’s milk challenge, specific IgE levels, and type of reactions, patients are eligible before for in-hospital rush-SOTI protocol and after for home-SOTI protocol or directly for home-SOTI protocol, without any other follow-up. At the Allergy Unit of Messina, after positive cow’s milk challenge, patients undergo to in-hospital weekly up-dosing protocol. Percentages of positive outcomes, failures and adverse effects are reported in Table 1.

Conclusion: This comparison shows that both protocols are effective, safe and useful in different contexts. However available literature is too limited and several questions on the best management of these children remain open. A comparison prospective multicentric study could verify successful outcomes, adverse effects, patient’s quality of life, the burden of allergy unit and cost analysis.

Table 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients undergo to SOTI after positive OPT</th>
<th>Children age (years)</th>
<th>Mean of specific IgE levels at baseline (KU/L)</th>
<th>Positive outcomes</th>
<th>Failures</th>
<th>Adverse effects</th>
<th>Protocol used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longo et al 2012 Prospective</td>
<td>118 (at 1-year follow-up)</td>
<td>1.5-14</td>
<td>17.72 (0.30-100.00)</td>
<td>75.4% unrestricted diet</td>
<td>8.5%</td>
<td>During home phase: 4.2% hospital admission 21.2% minor adverse effects* 9.3% major adverse effects**</td>
<td>50 of 175 before in-hospital rush SOTI 122 of 175 direct home SOTI</td>
</tr>
<tr>
<td>Barbi et al 2012 Retrospective</td>
<td>192</td>
<td>3-22</td>
<td>52% tolerance 25 mL 45.4% tolerance 15 mL 2.6% tolerance 1.6 mL</td>
<td>/</td>
<td>During in-hospital phase: 52% mild reactions§ 45.4% moderate reactions§§ 2.6% severe reactions§§§</td>
<td>In-hospital rush SOTI</td>
<td></td>
</tr>
<tr>
<td>Barbi et al 2011 Prospective</td>
<td>132</td>
<td>3-20</td>
<td>55.1 ± 40.5 (SD)</td>
<td>51.9% unrestricted diet 12.4% tolerance 150-250 mL 23.3% tolerance 5-150 mL</td>
<td>12.4%</td>
<td>During home phase: 29.5% from 1 to 5 reactions 23.5% from 5 to 15 reactions 10.7% more than 15 reactions</td>
<td>In-hospital rush SOTI and then home SOTI</td>
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### Table 1 (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients undergo to SOTI after positive OPT</th>
<th>Children age (years)</th>
<th>Mean of specific IgE levels at baseline (KU/L)</th>
<th>Positive outcomes</th>
<th>Failures</th>
<th>Adverse effects</th>
<th>Protocol used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longo et al 2008 DBPCFC</td>
<td>30 (at 1-year follow-up)</td>
<td>5-17</td>
<td>23 patients: &gt;100</td>
<td>36% 150 mL daily</td>
<td>10%</td>
<td>During in-hospital protocol: 100% mild</td>
<td>In-hospital rush SOTI and then home SOTI</td>
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<td>7 patients: 85-100</td>
<td>54% tolerance</td>
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<td>reactions§</td>
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<td></td>
<td>5-150 mL</td>
<td></td>
<td>53.3% moderate reactions§§§</td>
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<tr>
<td>Caminiti et al 2009 Prospective</td>
<td>10</td>
<td>5-10</td>
<td>38.1 ± 7.3 (SD)</td>
<td>70% restricted</td>
<td>20%</td>
<td>80% minor adverse effects* 20% major adverse effects**</td>
<td>In-hospital weekly up-dosing</td>
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<td></td>
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<td>diet</td>
<td>10% tolerance</td>
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<td></td>
<td>&lt;64 mL</td>
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<tr>
<td>Pajno et al 2010 Prospective</td>
<td>13</td>
<td>4-10</td>
<td>32.7 (8.8-124.6)</td>
<td>77% unrestricted</td>
<td>15%</td>
<td>57.8% minor adverse effects* 23% major adverse effects**</td>
<td>In-hospital weekly up-dosing</td>
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<td></td>
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<td></td>
<td>diet</td>
<td>8% tolerance</td>
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<td>100 mL</td>
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<tr>
<td>Pajno et al 2013 Prospective</td>
<td>45</td>
<td>4-13</td>
<td>40.8 (7.5-91.3)</td>
<td>84.5% unrestricted</td>
<td>15.5%</td>
<td>7% minor adverse effects* 15.5% major adverse effects**</td>
<td>In-hospital weekly up-dosing</td>
</tr>
</tbody>
</table>

*Lab does not determine IgE values higher than 100 KU/L, so 100 was the highest possible value.
* Throat and/or tongue itching, mild rhinitis and/or conjunctivitis, urticaria, abdominal pain; ** respiratory symptoms.
§ Clark scale 1 to 3; §§ Clark scale 4; §§§ Clark scale 5.

DBPCFC: Double-blind, placebo-controlled food challenge.
Table 1.

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<tr>
<th></th>
<th>Case group</th>
<th>Control group</th>
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<tr>
<td><strong>N°</strong></td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>10.6 ± 3.8</td>
<td>13.8 ± 3.2</td>
</tr>
<tr>
<td><strong>Sex (%female)</strong></td>
<td>43.8%</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Allergic comorbidities</strong></td>
<td>5 (31.2%)</td>
<td>5 (35.7%)</td>
</tr>
<tr>
<td><strong>Age at onset of T1D (years)</strong></td>
<td>5.9 ± 3.3</td>
<td>7.8 ± 4.1</td>
</tr>
<tr>
<td><strong>CSII duration (years)</strong></td>
<td>2.3 ± 1.8</td>
<td>1.4 ± 1.1</td>
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<tr>
<td><strong>Last year mean value HBa1c (%)</strong></td>
<td>6.8 ± 0.62</td>
<td>6.88 ± 0.77</td>
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</table>

**Patch test positivity**
- Colophonium: 6 (37.5%) vs 2 (14.2%)
- Benzoyl Peroxide: 2 (12.5%) vs 2 (14.2%)
- Formaldehyde: 3 (18.7%) vs 1 (7.1%)
- Corticosteroids Mix: 1 (6.2%) vs 0
- Balm of Peru: 2 (12.5%) vs 2 (14.2%)
- Cobalt Chloride: 0 vs 2 (14.2%)
- Chlorhexidine: 0 vs 1 (7.1%)
- Nickel sulfate: 3 (18.7%) vs 0
- Neomycin sulfate: 0 vs 1 (7.1%)
- Butylacrilate: 1 (6.2%) vs 0
- Sodium disulfate: 1 (6.2%) vs 0
- p-aminobenzoic acid: 1 (6.2%) vs 0
- 1,3 dimethyl methacrylate: 1 (6.2%) vs 0

Abs 08 | Fluticasone furoate in combination with the beta2 agonist vilanterol: our experience

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1Allergologia Pediatrica. Unità Operativa di Pediatria. Università degli Studi di Brescia e ASST Spedali Civili di Brescia; 2Clinica Pediatrica. Unità Operativa di Pediatria. Università degli Studi di Brescia e ASST Spedali Civili di Brescia

**Introduction:** The combination therapy fluticasone furoato with vilanterol has been shown to be beneficial for patients affected with traditional treatment-resistant asthma. Available data are mainly focused on adult patients, especially since the cutoff age for its clinical prescription is 12 years.

**Results:** We report on 12 pediatric and adolescent patients (mean age: 10.6 ± 3.8 years, range: 10.6 ± 3.8 to 13.8 ± 3.2) of our Clinic affected with treatment-resistant asthma. Patients were initially put on inhaled corticosteroid (ICS) followed by ICS + long-acting β2-agonist (LABA) bidaily without good clinical response, as also demonstrated by insufficient increase of FEV1, partially due to incomplete treatment adherence. Thus, affected patients were put on Fluticasone furoate/vilanterol (FF/VI) once daily (OD). During follow-up, the majority of patients (9712; 75%) showed a significant benefit from this treatment, with ACT > 20 e an improvement of spirometry without exacerbations of asthma. The three patients that did not respond in an optimal manner to Fluticasone furoate/vilanterol (FF/VI) once daily (OD) presented comorbidities such as obesity and exercise-induced bronchoconstriction.

**Conclusions:** Although available data in the literature are limited on the efficacy of Fluticasone furoate/vilanterol (FF/VI) once daily (OD) in the treatment of pediatric and adolescent patients with resistant-to-treatment asthma, our data suggest that FF/VI may be a valid option for this age group, both in terms of clinical efficacy and patients adherence to treatment.

Abs 09 | Allergies and pediatric selective IgA deficiency: Long-term single-center follow-up of 184 pediatric patients

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**Introduction:** Selective IgA deficiency (SIgAD) is a primary immuno-deficiency with an estimated incidence of 1:600, characterized by IgA serum levels <7 mg/dL, with normal IgG and IgM and normal lymphocyte subset distribution. Although it has been reported that patients affected with SIgAD present a higher predisposition to allergies, detailed data from long-term follow-up pediatric studies are lacking.

**Results:** In our single-center cohort, 184 pediatric patients were regularly followed with annual visits for a total of 812 patient-years. Mean follow-up time per child was 8.9 years. The mean age at diagnosis was 7.7 years (range 4-17 years). Allergies were present at diagnosis in 42/184 patients (22.8%). Of note, a positive family history for allergies was present at diagnosis in 106/184 cases (57.6%). Allergies included both respiratory and cutaneous manifestations and were dependent on numerous allergens. More than 60% of allergic patients were allergic to more than one allergen. During follow-up, allergies were diagnosed in an additional 30/184 patients (16.3%), leading to the overall presence of allergies in 72/184 patients (39.1%). Of note, within the pediatric SIgAD cohort with allergies, positive family history for allergies was particularly high (85.7%).

**Discussion:** Our data confirm the association between SIgAD and allergies, and also indicate a strong positive family history for allergies within this cohort. Furthermore, our data define for the first time the incidence and type of allergies in pediatric SIgAD during long-term follow-up and underline the need for regular clinical follow-up for affected patients.
Omalizumab is a monoclonal anti-IgE antibody, indicated as an add-on therapy in patients with severe uncontrolled asthma. Aim of this case is to describe off-label treatment with omalizumab in a patient with high total IgE. AE is a 17-year-old boy, followed in our Paediatric Allergology Centre since 2012 for allergic severe persistent asthma. In 2017, his spirometry revealed a Tiffeneau index equal to 90%, severe mixed obstructive ventilatory defect and a positive bronchodilatation test. It was started a 6 months off-label therapy with omalizumab 600 mg every 15 days (weight 77 kg – total IgE 1916 IU/mL) with progressive improvement of spirometry with Tiffeneau index always higher than 70% and negative bronchodilatation tests. Furthermore, he was hospitalised for acute asthma attack. Subsequently, he was treated with fluticasone, montelukast, salmeterol, and nasal steroid cycles. On February 2018, Tiffeneau index was equal to 66% and total IgE were 964.0 IU/mL. On April 2018 omalizumab was restarted at the same dosage. After 6 months off-label therapy with omalizumab, bronchodilatation test was normally (Tiffeneau index equal to 90%). During treatment, he had not symptoms of asthma or treatment side effects. He also lost weight (about 10 kg). Six months after the end of treatment, he maintains clinical well-being. The case suggests how patients with severe allergic asthma can benefit from therapy with omalizumab despite high total IgE. Benefits of Omalizumab seem to remain long-term and they could be boosted by weight loss. Further studies will be necessary to evaluate how long these long-term beneficial effects last.

We report a case of acute meningoencephalitis in a child caused by Streptococcus pneumoniae, complicated with acute disseminated encephalomyelitis (ADEM). 10 years old immunocompetent female presented to our pediatric emergency department with fever, headache, vomiting, altered state of consciousness without signs of meningeal irritation. Cerebrospinal fluid (CSF) examination revealed polymorphonuclear pleocytosis, increased protein level, decreased glucose level and pneumococcal antigen positivity. Ceftriaxone, vancomycin, and dexamethasone were started, with clinical improvement. After three days of treatment, the patient showed neurological deterioration. Brain MRI detected multiple T2-hyperintense lesions suggestive for ADEM. CSF/blood isoelectrofocusing showed polyclonal IgG distribution. Intravenous polyclonal immunoglobulins were started (400 mg/kg/die for 5 days), with initial neurological improvement, but subsequent deterioration on day five. She responded well to high doses intravenous methylprednisolone (IVMP) pulse therapy (1 g/die) for five days and oral tapering over 8 weeks, with complete clinical and neuroradiological recovery. This is the first case of ADEM associated with pneumococcal meningitis in children in the literature. Epidemiological and serological studies suggest that ADEM can be triggered by infections in susceptible subjects (molecular mimicking). Few adult cases of post-pneumococcal ADEM have been reported, highlighting a dramatic clinical and radiological improvement following treatment with IVMP, even in the presence of invasive pneumococcal infection. Clinical history and the evaluation of the immunological status allow to identify susceptibility and risk factors for ADEM. New studies are needed to better define the pathogenetical mechanisms that relate pneumococcal infection to ADEM, and consequently the best therapeutic and preventive strategies.
We found an independent association of the reduction of the symptom scores with a growth velocity SDS ($P = 0.037$).

**Conclusion:** After lactose-elimination diet, our patients with LI showed similar growth velocity SDS as controls. The management of the subjects with LI might focus on the compliance to the lactose-elimination diet to reduce the gastrointestinal symptoms in order to preserve a normal growth. How would have been the growth velocity in the patients with LI without the lactose-elimination diet?

**Abs 13 | The effects of vitamin D supplementation on immune system in children with type 1 diabetes and respective siblings**

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**Objectives:** The aim of this study was to assess a link between 25OHD levels and T-lymphocyte subpopulations in children with T1D and their siblings (S) and to evaluate the impact of vitamin D supplementation.

**Patients and Methods:** 22 T1D, 33 S, and 30 control subjects (CS) were enrolled. At baseline (T0), we evaluated the following biochemical and antibody markers, and genetic haplotypes: fasting glucose, glycated hemoglobin, 25OHD, and T-lymphocyte populations (Th17, Th17/IL17+, Treg, Treg-ICOS+). DR3/DQ2 and/or DR4/DQ8 were categorized as “at risk” (HLA+$^+$), DRB1*1501/1502/DRB1*07 as “no risk” (HLA-$^-$), other haplotypes as “undetermined” (HLA$^+$ID). T1D and S were supplemented with Cholecalciferol 1000 IU/die and revalued after 6 months (T1).

**Results:** Vitamin D hypovitaminosis was frequent (74.4%), with deficiency in 43% of the subjects. T1D and S presented Treg-ICOS$^+$ percentages and glucose levels ($P < 0.01$) higher than CS. Th17/IL17$^+$ and Treg-ICOS$^+$ percentages ($P < 0.05$) were higher in S HLA$^+$ than T1D; Treg-ICOS$^+$ title was higher both in S HLA$^+$ and in S HLA$^-$ than CS ($P < 0.01$). At baseline, a significant increasing trend in Treg and Treg-ICOS$^+$ values ($P < 0.05$) across 25OHD levels were observed. At T1, only T1D and S supplemented showed higher 25OHD levels, and lower Th17 and Treg-ICOS$^+$ percentages ($P < 0.01$) than T0.

**Conclusion:** 25OHD serum levels seem to affect lymphocyte subpopulations according to its immunomodulating role. Furthermore, genetic imprinting might determine a different immunological response in siblings of individuals with T1D.

**Abs 14 | Anaphylaxis to shellfish by inhalation of cooking vapor in a child**

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Crustacean allergy is more common in adults than in children, in which prevalence is less than 0.5% . Allergic symptoms to seafood are usually triggered by ingestion, but can also occur by inhalation of aerosolized proteins during trapping, processing, and cooking. Seafood allergy by inhalation is commonly reported in occupational settings, usually associated with respiratory symptoms, whereas it is rarely reported in children or as a cause of anaphylaxis. Herein, we describe the case of a 10-year-old girl referred to our allergy clinic for an acute episode of urticaria-angioedema of the face and trunk and difficulty breathing a few minutes after breathing in vapors from cooked shrimp, which resolved after administration of intramuscular epinephrine in the emergency department. The girl has a history of atopic dermatitis during early infancy and a few previous acute urticarial reactions involving to the face after ingestion of crustaceans and mollusks, which lead to an elimination diet for these foods without having performed any allergy evaluation. Serum-specific IgE came positive for crab, lobster, oyster, Pen 1 (shrimp tropomyosin and Der p 10 (house dust mites tropomyosin) confirming the diagnosis of IgE-mediated allergy to crustaceans and molluscs. Tropomyosin is the major invertebrate pan-allergen found in all edible crustacean and mollusc species with a highly conserved amino acid sequence, which can cause clinical and IgE cross-reactivity among different invertebrate allergen sources. Tropomyosin is highly heat-stable protein, which can even increase it allergenicity after heat treatment. This feature can explain allergic reaction by inhalation of crustacean cooking vapors.

**Abs 15 | Allergic bronchopulmonary aspergillosis manifesting as recurrent pneumonia in an adolescent: A case report**

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**Introduction:** Allergic bronchopulmonary aspergillosis (ABPA) is a pulmonary disorder caused by hypersensitivity to Aspergillus Fumigatus. The diagnosis is based on sensitization to Aspergillus, associated with clinical, immunological and radiological findings.

**Patient and Methods:** It is a case report concerning a 14-year-old adolescent with history of recurrent episodes of pneumonia involving the right lung, treated with antibiotic therapy. His history did not reveal further significant events. In the evaluation of the history of
recurrent pneumonia, a laboratory and instrumental workup was performed. It documented high total serum IgE and eosinophilic count and the presence of Aspergillus Fumigatus in the bronchial aspirate. Furthermore, asthma, cystic fibrosis, immunodeficiency, and tuberculosis were ruled out. The diagnosis of ABPA was performed and the patient started a six-week treatment with Itraconazole. At follow-up, the culture of bronchial aspirate was negative; moreover, total serum IgE and eosinophilic count were lower, but not normal. The adolescent was never subjected to further episodes of pneumonia.

Discussion: There is no single confirmatory test for the diagnosis of ABPA. In most cases, the diagnosis is suspected in patients with predisposing conditions (asthma or cystic fibrosis) and a sensitization to Aspergillus antigens in the proper clinical and radiographic context. About follow-up, serial measurements of serum total IgE are useful: a decrease of 35 percent is considered a good therapeutic response.

Conclusion: ABPA without asthma or cystic fibrosis is a rare occurrence. Nevertheless, it has to be considered in the evaluation of recurrent pneumonia in paediatric age.

Abs 16 | Selective IgA deficiency as a negative prognostic factor in childhood asthma: A case report

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Introduction: Selective IgA deficiency (sIgAD) is the most common congenital immunodeficiency in childhood age. It represents the comorbidity of multiple diseases, such as asthma; this diagnosis can require different treatment strategies.

Patient and Methods: It is a case report involving a 10-year-old girl, who had a diagnosis of allergic asthma (skin prick testing positive for grass) at the age of 6. Despite the maintenance treatment with medium-dose ICS/LABA, she was subjected to multiple exacerbations of asthma during the winter season, triggered by almost every episode of upper respiratory infection. On the other hand, the patient was not subjected to asthma exacerbation during pollen season. Searching a comorbidity for her poorly controlled asthma, a laboratory workup revealed that IgA serum levels were undetectable (<0.06 g/L); moreover, IgE serum level was low (119 kU/L). The child was discharged with the same maintenance treatment with medium-dose ICS/LABA and the recommendation to start antibiotic therapy as soon as an upper respiratory infection occurs. Using this strategy, the patient was not subjected to asthma exacerbation in the last winter.

Results: sIgAD is a negative prognostic factor in childhood asthma. A defective mucosal barrier due to deficiency of IgA might play a role in asthma exacerbations.

Conclusion: No specific additional treatment is required for asthma related to sIgAD. The only further recommendation is based on a quick antibiotic treatment in order to treat the asthma attack and prevent long-term pulmonary damage induced by recurrent asthma exacerbations.

Abs 17 | Strict cow’s milk-free diet is effective to treat oral immunotherapy-related eosinophilic esophagitis

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Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus due to an immunologic pathogenesis. Therapy includes antigen-free diet and topical steroid treatment. EoE has been described as a rare complication of food oral immunotherapy (OIT). We herein report the case of a 15-year-old boy who developed EoE after cow’s milk OIT. He was diagnosed with cow’s milk protein allergy (CMPA) at the age of 3 months. He underwent a milk OIT at the age of 10 due to persistence of milk allergy. Buildup phase went on slowly due to recurrent reactions characterized by abdominal pain, oral itching, and transient skin rash. Nevertheless, at the age of 12, he managed to achieve a free diet, with daily ingestion of about 200 mL of fresh milk. Three years later, he began experiencing nighttime epigastric pain and heartburn. An eight-week treatment with high-dose proton pump inhibitors was performed three times, failing to induce persistent remission of symptoms. Thus, he underwent an esophagastroduodenoscopy (EGDS) which showed macroscopic and histological signs of EoE (≥ 15 eosinophils/high power field). At the 12 months follow-up, after a cow’s milk-free diet that allowed the ingestion of baked milk products, he achieved clinical, but not histological, remission. No pharmacological treatment was administered. Therefore, a strict cow’s milk-free diet was started. A second follow-up was performed 12 months later, showing persistence of clinical remission, and EGDS revealed a complete macroscopic and histological resolution. Strict elimination diet, without any pharmacological treatment, is effective to treat milk OIT-related EoE.

Abs 18 | HHV7-related acute encephalopathy. Immunological implications and clinical features in a series of pediatric patients

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Introduction: Primary Human herpesvirus 7 (HHV7) infection is almost ubiquitous, and mostly asymptomatic in children, in whom it can present as exanthema subitum. Little is known on the clinical relevance of HHV7 neuroinvasion in immunocompetent children.
**Patients:** This series describes 10 patients (median age 10 years), with acute encephalopathy in whom HHV7-DNA was detected on cerebrospinal fluid (CSF) by RT-PCR results. All patients were healthy before the acute event. 6/10 patients had meningoencephalitis, two of which with acute disseminated encephalomyelitis; 4/10 showed acute neuropsychiatric symptoms. None of them presented the classical skin rash, but five had fever. CSF HHV7 copies ranged between 20 and 3,500 copies/mL (median 66 copies/mL) and mean HHV7 CSF/blood ratio was 0.88. 4/10 patients had pleocytosis on CSF. Polyclonal bands on CSF and sera were found in 5/7 patients, one patient had intratetal IgG synthesis. Total Ig, IgG subclasses, and lymphocyte populations were within normal ranges in all patients. CSF/sera IL-17 dosages were performed in two patients, resulting in the upper range limits. Outcome was favourable in all children, although 3/10 had minor neurological and cognitive sequelae.

**Conclusion:** HHV7 can determine neuroinvasion in immunocompetent children, leading to acute encephalopathy. Blood-brain barrier damage and high CSF/blood viral copies ratio correlated with a more severe presentation. Little is known about the role of cytokine pattern alterations during HHV7 encephalitis. We speculate on the importance of immune-mediated mechanisms in provoking clinical features. Future perspectives will investigate cytokine profiles and the role of the immune system in the pathogenesis of HHV7-related encephalopathy.

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**Abs 19 | Identification of gut inflammation and autoimmunity in murine models carrying Rag1 hypomorphic mutations**

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Hypomorphic Recombination Activating Gene 1 (RAG1) mutations result in residual T- and B-cell development in both humans and mice and have been found in patients presenting with delayed-onset combined immune deficiency with granulomas and/or autoimmunity (CID-G/AI). Recent studies have shed light on how hypomorphic RAG1 mutations alter the primary repertoire of T and B cells, but less is known about their effect on immune dysregulation in targeted organs. In order to investigate the role of these mutations in determining intestinal disease, we set out to evaluate gut immunity and microbiota interplay in Rag1 mutant hypomorphic mice. We evaluated two mouse models carrying homozygous Rag1 mutations (R972Q and R972W), corresponding to human mutations described in patients. On the basis of in vitro studies, the R972Q mutation has demonstrated a moderate effect on Rag1 protein stability while the R972W mutation resulted highly disruptive. Analysis of intestinal pathology in Rag1 mutant mice (NIAID animal protocol LCIM 6E) revealed different degrees of spontaneous colitis, with the most severe inflammatory infiltrate observed in mice carrying the most disruptive mutation, R972W. A significant increase in activated CD44hiCD62L#CD4+ T cells expressing the gut homing receptor α4β7 was observed in mesenteric lymph nodes (MLNs) of both mutant strains and was especially prominent in R972W mutant mice. Additionally, the proportion of MLN CD4+ T regulatory cells was increased in both mouse models. Finally, MLN of mutant mice contained a high number of myeloid cells (CD11b+) along with a decreased number of B220+ B cells, and these abnormalities were also more prominent in R972W than in R972Q mice. In summary, we have shown that Rag1 mutant hypomorphic mice present with different degrees of inflammatory bowel disease, with the mouse model carrying the most disruptive mutation presenting with the most severe phenotype.

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**Abs 20 | High throughput sequencing reveals repertoire restriction of Treg and CD8+ T cells in APDS1 patients**

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**Introduction:** Activated phosphoinositide 3-kinase δ syndrome type 1 (APDS1) is a CID characterized by increased susceptibility to infections, lymphoproliferation, and autoimmunity. Patients display T-cell abnormalities, including increased numbers of memory T cells and T follicular helper cells (Tfh), reduction of naïve T cells and impaired T regulatory cell (Treg) function. We hypothesized that the increased PI3K activity in APDS1 patients would lead to FOXP1 degradation and result in perturbations of the T-cell repertoire.

**Methods:** High throughput sequencing was used to study composition and diversity of T-cell receptor α (TRA) and T-cell receptor β (TRB) repertoire in sorted Treg, conventional CD4+ (Tconv),...
and CD8+ T cells from 4 patients with PIK3CD GOF mutations and healthy controls.

**Results:** \(T_{reg}\) and CD8+ cells of patients with PIK3CD GOF mutations show reduced TRA and TRB repertoire diversity. No repertoire restriction was detected in Tfh, \(T_{conv}\) cells from the same patients. The TRB repertoire of \(T_{reg}\) and CD8+ cells was enriched for the presence of hydrophobic amino acids at positions 6 and 7 of the CDR3, a biomarker of self-reactivity.

**Conclusion:** These data demonstrate that the T-cell repertoire of patients with APDS1 is characterized by a molecular signature that may contribute to the increased rate of autoimmunity associated with this condition. Furthermore, our results support the notion that PI3K pathway is a key regulator of \(T_{reg}\) cell development and homeostasis in humans.

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**Abs 21 | Autoimmune Haemolytic Anemia in a patient affected by WHIM (Warts, Hypogammaglobulinemia, Infections, Myelokathexis) syndrome**

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A 10-year-old girl, WHIM Syndrome, CXCR4 mutation. History: preterm, Tetralogy of Fallot surgically treated, persistent panleukopenia, irregular thrombocytopenia, recurrent respiratory infections. At 8 years old, she presented with severe anemia (Hb 4.6 g/dL) after a recent respiratory infection. Coombs test and anti-red cells antibodies were positive, configuring an autoimmune event. High-dose steroids (Methylprednisolone 2 mg/Kg/die) and IVIg were administered for 5 days with good response. Steroid therapy was continued for 4 weeks and progressively weaned in 6 months. At 10yo she developed a second episode of autoimmune haemolytic anemia (Hb 4.4 g/dL, positive indirect and direct Coombs test). High-dose steroids and IVIg were administered, with no good response (Hb 3.4 g/dL) so an erythrocytes transfusion was needed and steroid and IVIg dosage was increased (Methylprednisolone 3 mg/Kg/die, IVIg 500 mg/kg/die). Steroid therapy was progressively weaned with good response. She is currently on IVIg replacement therapy, antibacterial and antiviral prophylaxes. WHIM Syndrome is a rare primary immunodeficiency caused by gain-of-function CXCR4 mutation, which produces mature neutrophils retention in the bone marrow. Clinic phenotype is variable1,2. This is the first reported case of autoimmune haemolytic anemia in WHIM syndrome. An association with type 1 diabetes is described2. The interaction CXCR4-CXCL12 is important in the immuneregulation, so we can assume that there could be a relation between CXCR4 mutation and the development of autoimmune diseases.


**Abs 22 | Exercise-Induced Asthma as the tip of the iceberg: A case of wheat-dependent exercise-induced anaphylaxis**

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A 9-year-old male (T.L.) presented two episodes of acute and severe asthmatic attacks during physical activity. The child presented cough, dyspnea, pallor and temporary loss of consciousness for 30 seconds while playing tennis. On the first occasion, he was treated with inhaled salbutamol and corticosteroids. His physician prescribed salbutamol before physical activities and set the diagnosis of exercise-induced asthma. During the second attack, he was transported to our emergency room because of the severity and slow recovery that needed Adrenaline administration. Supplementary investigations revealed negative asthma tests and positive IgE for wheat \(\omega-5\)gliadin (Tri a 19). The child revealed that in both occasions he had ingested wheat products before physical activity. In fact, he was advised previously to increase consumption of wheat before childhood tests prescribed by the physician after finding the disease in siblings. The discharge diagnosis was wheat-dependent exercise-induced anaphylaxis (WDEIA). WDEIA is a peculiar form of wheat allergy where a food intake alone does not induce any symptom. However, allergic symptoms are elicited by exercise after ingestion of wheat products and depend on the amount of food ingested. In some cases, cofactors are required for developing a reaction. Noted cofactors include aspirin, cold or warm environment, high humidity, atopic dermatitis, alcohol intake, menstrual cycle. Wheat \(\omega-5\)gliadin and a high molecular weight-gluten subunit have been identified as major allergens in conventional WDEIA.

**Abs 23 | Two Sardinian, unrelated, SCID infants with the same DCLRE1C mutation**

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Artemis, NHEJ protein involved in DNA double-strand breaks repair and V(D)J recombination, is encoded by DCLRE1C gene, whose null homozygous or compound heterozygous mutations cause T B NK SCID. We describe two Sardinian SCID unrelated female infants. CASE 1: 2 months old, born at 39 weeks, normal birth aspect, persistent infections (thrush, rhinitis, otitis, enteritis), fever, generalized...
We describe the case of a male child suffering from pulmonary hemosiderosis and Down's syndrome. Born at term in Romania from normal pregnancy, eutocic delivery with regular peripartum period, small for gestational age. From the first days of life, the presence of polyneea was detected. At the age of 3 months, the child came to Italy where pulmonary hypertension was found in concomitance of interatrial ostium secundum type defect (DIA) and therapy with furosemide, aldactone, and bosentan was started. At 4 months of age, the child was admitted for acute respiratory infection associated with severe interstitial disease, demonstrated by chest TC, which required PICU transfer and respiratory support: the child's status was complicated by severe anemia which needed multiple blood transfusions. Because of clinical presentation (interstitial pulmonary disease, haemoptoysis, and anemia) and blood tests, the clinical suspicion of hemosiderosis was placed; moreover, a cow milk-free diet was started in suspected Heiner syndrome. During the subsequent admission, pulmonary biopsy was performed and hemosiderosis pattern was found. Later, the child performed several hospitalizations and a therapy with hydroxychloroquine and corticosteroids was undertaken. Despite the diet free of milk's derivatives, no respiratory improvement was seen. Possibility of surgery correction of DIA was rejected because of the high anesthesiological risk. The child came to our observation for hemoptysis at 12 month of age: diagnostic blood tests confirmed the diagnosis of pulmonary hemosiderosis. During outpatient follow-up, considering his hemodynamic stability, bosentan was discontinued. Further investigations are currently planned in order to reintroduce milk proteins.

Abs 25 | Sublingual immunotherapy for grass pollen rhinitis in children: 3-year follow-up in a cohort in Southern Italy

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Allergic rhinitis (AR) is a global health problem crucially affecting quality of life. ITS is currently recognized as an effective treatment of AR and it modifies its natural history. We report our experience in order to evaluate the clinical features of patients treated with grass pollen ITS (Grazax® and Oralair®) and the reduction of medication dispensing. From 2015 to 2018, 59 children affected by AR (37 M, 22 F) have been prescribed with ITS, 28 with Grazax® (16M, 12F) and 31 with Oralair® (21M, 10F). Patients underwent to SPT and/or sIgE dosage. Several patients reported comorbidities (18 asthma, 12 AD, 1 urticaria), 34 were polysensitized and 13 were prescribed with additional ITS (8 Df and Dp, 3 O.europea, 2 P.judaica). At reevaluation, performed on 38/59 patients, prevalence of sneezing (86.8% vs 7.9%), similarly to rhinorrea (57.9% vs 23.7%), nose itching (55.3% vs 28.9%) and nasal obstruction (86.8% vs 26.3%) has decreased. Prescription of systemic antihistamines has decreased (86.8% vs 7.9%), as prescription of nasal antihistamines (42.1% vs 18.4%) and nasal steroids (81.6% vs 60.5%). 7/28 Grazax® and 8/31 Oralair® patients intentionally dropped off. Notably, 2/28 Grazax® patients reported labial edema with respiratory distress and dysphagia. ITS represents the only disease-modifying therapy for AR. Sublingual tablets were well tolerated and have improved AR symptoms. Reduction of medication dispensing was observed especially for systemic and nasal antihistamines. A wider cohort will help to evaluate efficacy and to confirm these preliminary findings.

Abs 26 | Pediatric DRESS syndrome for Oxcarbazepine

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Introduction: Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, life-threatening drug-induced hypersensitivity reaction. Classically caused by anticonvulsants and sulphonamides, 2-8 weeks after its introduction. The main clinical symptoms are exanthema, lymphadenopathy, hematological alterations, and organ involvement. It is infrequently seen in the pediatric population. We present an Oxcarbazepine-induced DRESS syndrome in a seven years old boy.
Patients and Methods: Ten days after the patient started treatment with Oxcarbazepine for epilepsy, he presented urticaria and a generalized rash, high fever, lymphadenopathy, eosinophilia, and elevation of cholestasis enzymes. The condition was early detected, the drug was immediately discontinued, and systemic corticosteroid treatment was prescribed. Hospitalization with multidisciplinary management, laboratory tests, and skin biopsies was required. Luckily, the patient did not present any severe visceral involvement.

Results: Corticosteroid led progressively to a good outcome after 4 months with one well-controlled exacerbation after 2 months. Several blood counts showed eosinophilia, (maximum 1.5 x 10e3/μL, 10.4%; range 0-0.5 x 10e3/μL); ALP: 208 U/L; C-Reactive Protein 23.8 mg/L. Serology for CMV, Epstein Barr virus, B19 Parvovirus; and PCR for HV6, HV7 were negative. Skin biopsy showed a superficial and interstitial perivascular infiltrate of small lymphocytes, focal spongiosis and isolated Civatte bodies, with some eosinophils and neutrophils in blood vessels lumen.

Conclusion: DRESS syndrome is a rare condition in children, and the diagnosis is mainly clinical. Doctors should be trained for a rapid diagnostic suspicion and recognition causes the immediate suspension of the offending drug is crucial to avoid complications.

Abs 27 | Efficacy of sublingual allergen-specific immunotherapy in children evaluated by the measurements of bronchial and nasal nitric oxide. Preliminary results

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Introduction: The aim of our study was to establish the efficacy of sublingual immunotherapy (SLIT) by the evaluation of symptoms, lung function tests, bronchial fraction of exhaled nitric oxide (FeNO), and nasal nitric oxide (nNO) after six months of treatment.

Methods: Inclusion criteria: (1) age 6-14 years old; (2) diagnosis of allergic asthma with or without allergic rhinitis; and (3) sensitization towards a single perennial allergen. We compared baseline with six-month treatment values by analyzing symptoms using the visual analogue scale (VAS) and lung function tests.

Results: We enrolled 27 patients (mean age 9.2 ± 2.6), 10 of whom already completed the six-month evaluation. The preliminary results showed an improvement in basal vs six-month treatment values (global VAS 56 vs 5), predicted forced expiratory volume in 1 second ([FEV1]; 88.6 ± 3.6 vs 95 ± 4.4%), a significant reduction in both FeNO and nNO (38.8 ± 10.6 vs 21.8 ± 7.1 ppb and 1264 ± 202 vs 890 ± 73.6 ppb, respectively) after six months. Partial evaluation of the remaining 17 patients showed that a slight improvement in symptoms and FEV1 in addition to a reduction in FeNO and nNO could be demonstrated as early as one month after treatment initiation.

Conclusions: The preliminary results of our study, which is still ongoing, allow us to hypothesize that SLIT may guarantee good results in reducing symptoms of rhinitis and allergic asthma that is objectively confirmed by the reduction of nasal and bronchial eosinophilic inflammation evaluated by the measurement of NO.

Abs 28 | Early inhaled therapy with adrenaline in acute bronchiolitis: A single-center experience on a large cohort of patients

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Introduction: Bronchiolitis is an infectious disease caused by a virus (generally Respiratory Syncytial Virus, RSV) in children under 1 year of age; it is characterized by inflammation, edema, and necrosis of bronchiolar epithelium, with increased mucus production and bronchospasm. The only recommended treatments are oxygen therapy for hypoxia and nasogastric/ intravenous administration of fluids if failure of oral feeding. The aim of our study is to prove through a retrospective analysis the possible efficacy of early inhaled adrenaline treatment in infants who were admitted in the ED of Gaslini Hospital in the 2015-2016 winter period.

Patients and Methods: 374 infants under 6 months of age with diagnosis of “Acute Bronchiolitis from RSV or other Agents” were enrolled; 282 received adrenaline within 72 hours from the onset of symptoms, 92 after. Adrenaline was administered by aerosol at a dose of 0.1 mg/kg/dose 8 times a day. The following outcome indicators were considered: length of hospitalization, need for High Flow Nasal Cannula (HFNC), invasive respiratory support in PICU.

Results: Adrenaline therapy significantly reduced the length of hospitalization (67.2 hours vs 100.4 hours, P < 0.001) if started within 72 hours from the onset of symptoms. Patients with severe clinical presentation (measured with Wang score) treated with early inhaled adrenaline received significantly less HFNC compared to those treated after the first 72 hours (33% vs 58%). No patients needed invasive ventilation.

Conclusion: The results of our study show that early inhaled adrenaline therapy, administered frequently, has statistically significant effect in reducing the length of hospitalization. The beneficial effect is also recorded as a reduced need of HFNC support, in particular among the patients with severe disease.
Abs 29 | Accuracy of component-resolved diagnostics for the diagnosis of cow’s milk and egg allergy in children: A multicenter retrospective study

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Introduction: Cow’s milk allergy and egg allergy are the most frequent food allergy (FA) in children. This study aimed to investigate component-resolved diagnostics (CRD) to cow’s milk and egg proteins, by correlating the level of CRD with outcome of the oral challenge.

Patients and Methods: We analyzed data from 161 subjects, 90 with suspicious of cow’s milk allergy (CMA); median age 5.5 months, and 71 with suspicious of egg allergy (EA); median age 9.5 mo. Data regarding oral food challenges outcome and sensitization data (skin prick test and sIgE to milk and egg components) were collected. We calculated the diagnostic accuracy of CRD, by the ROC curves and derived both the best negative and positive cutoffs for the diagnosis of CM and HE allergy, respectively.

Results: sIgE to beta-lactoglobulin and casein showed better diagnostic accuracy with area under curve (AUC) of 0.8 and 0.84, respectively; casein sIgE showed high SP and PPV, 98% and 91%, respectively, considering a positive cutoff of 9.6 kU/L. For egg allergy, sIgE to ovoalbumin (Gal d 2) had SP and PPV 98% and 80%, respectively, with a cutoff of 8.42 kU/L. sIgE to ovalbumin (Gal d 2) had SP and PPV 96% and 71%, respectively, with a cutoff of 5.91 kU/L. Gal d1 and Gal d2 showed overall diagnostic accuracy with AUC of 0.71 and 0.77, respectively.

Conclusions: Overall, our data indicate that IgE components are not able to replace the oral food challenges as the gold standard in the diagnosis of egg allergy and CMA allergy. However, for CMA, sIgE to casein above specific cutoff could potentially reduce the number of OFC in the considered population.

Abs 30 | Dietary intake, Resting Energy Expenditure (REE) and body composition of children with allergic asthma: A pilot case-control study

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Introduction: Few data exist about growth and dietary habits in children with asthma. We aimed to evaluate REE, anthropometric measurements, body composition and dietary intake in children with allergic asthma.

Materials and Methods: 26 children with allergic asthma were compared to 26 healthy children. Asthmatic children underwent spirometry and nitric oxide measurement. In both groups, anthropometric measurements were taken, and dietary intake was evaluated by a 3-day diet record. REE was measured by indirect calorimetry. Student t test was used to analyse differences between asthmatic children and matched controls.

Results: Asthmatic children show significant higher fat mass ($P = 0.018$) and waist circumference ($P = 0.026$) than controls. Higher intake of arachidonic acid ($P = 0.002$), niacin ($P = 0.001$) and vitamin B6 ($P = 0.029$), and lower fiber g/1000 kcal ($P = 0.003$) and vitamin A intake ($P = 0.037$) have been observed in asthmatic children compared to controls. No differences in terms of anthropometric measurements and REE were observed. Notably, most children in both groups failed to reach the nutritional intakes recommended by the Italian Guidelines.

Conclusion: The observed differences in body composition and dietary intake between asthmatic children vs controls may suggest a possible difference in dietary pattern and lifestyle. These data underline the importance to further investigate dietary habits in asthmatic children to elucidate the role of diet on asthma.

Abs 31 | Effectiveness of omalizumab in two children with severe vernal keratoconjunctivitis

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Introduction: Vernal keratoconjunctivitis (VKC) is a severe form of pediatric ocular allergy, characterized by acute and chronic corneconjunctival inflammation, that usually begins in the first decade of life and tends to resolve spontaneously after puberty. The ocular physical examination is aimed at searching the fourfold signs: conjunctival hyperemia, papillary hypertrophy, giant papillae, papillae in the region of the limbus. Although topical immunosuppressive drugs such as cyclosporine are usually effective, some severe forms may be refractory and require prolonged steroid therapy. In recent years, omalizumab, an anti-IgE monoclonal antibody, has been seen to have promising results in treatment of VKC. Here, we describe 2 cases of children with severe VKC that were poor responsive to conventional therapy.

Case report: We report the cases of 2 children, aged 13 and 10 years old, with high IgE levels (2400 and 1960 Ul/mL, respectively) and positivity for perennial and seasonal allergens, affected by asthma.
and VKC treated with oral and inhaled corticosteroids and topical cyclosporine with poor control. One patient had even requested intrapalpebral depot-steroid injections. Thus, we decided to start treatment with omalizumab by subcutaneous injections every 2 weeks at dosage depending on the weight. After 16 weeks of therapy, there was a general improvement of symptoms of both VKC and asthma with important benefits from the ocular point of view even if they continue the administration of topical cyclosporine.

**Conclusion:** Omalizumab may be an important adjunctive therapy for the treatment of severe forms of VKC associated with allergic diseases.

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**Abs 32 | A strange dermatitis: The lymphoid variant of hypereosinophilic syndromes**

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**Introduction:** The hypereosinophilic syndromes (HES) are a rare, heterogeneous group of disease characterized by hypereosinophilia (>1.5x10⁹/L) for more than six months, associated with eosinophils-mediated organ damage. The lymphocytic form (L-HES) is a reactive HES, due to an increase production of IL-5 by abnormal T lymphocytes, that leads to a polyclonal expansion of eosinophils.

**Case report:** A 7-year-old girl presented with chronic dermatitis characterized by spread erythematous, puritic papules and nodules, with no facial involvement. The first rash appeared at 16 months, with an initial spontaneous regression. At 3 years, blood tests showed marked hypereosinophilia (7280/mmc). Few months later examination of skin revealed Grotton papules over interphalangeal joints, so she was hospitalized for exclusion of dermatomyositis and main causes of hypereosinophilia. Blood test confirmed hypereosinophilia (5000/mmc), so bone marrow aspirate was performed with evidence of increased number of eosinophils and dysgranulopoiesis notes. FISH excluded rearrangements or aneuploidy of PDGFR and PDGFRB genes. Due to worsening of skin lesions, despite antihistamine therapy, and increasingly higher eosinophilic values (maximum 28730/mmc), at 6 years she performed an immunological examination: lymphocyte subpopulations showed a proportion of lymphocytes T CD45(bright)/CD2⁺/CD4/CD5⁺/CD25⁺ (72%)/cyCD3⁺ / CD8⁺/CD7⁺/sCD3⁺, equal to 10%. The examinations performed and the clinical picture were oriented for the diagnosis of L-HES. The girl has currently begun corticosteroids therapy with improvement of cutaneous picture.

**Conclusion:** Patients with L-HES can be poorly symptomatic for years but T-cell lymphomas and organ damage may occur during disease course so they should be closely monitored.

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**Abs 33 | A case of macrolide-resistant Mycoplasma pneumoniae in a 4-years old girl with chronic asthma**

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Asthma is a chronic inflammation of the upper airways, characterized by symptoms of airways reversible obstruction and inflammation such as wheeze, cough, chest tightness, and breathlessness. Trigger of asthma exacerbations may be viral infections, environmental tobacco smoke, aeroallergens, or exercise. The combination of genetic and environmental factors determines the severity of asthma and its exacerbations. C. is a 4-year-old girl with severe chronic asthma, being treated with salmeterol+fluticasone spray, montelukast, and cetirizine, admitted for persistent cough. Her recent medical history saw a change of cough from dry to catarhal, fever and weight loss, treated with cefixime for 7 days and clarithromycin for 14 days. During the hospitalization, first- and second-level exams showed left apical thickening lung and positivity of Mycoplasma pneumoniae(Mp) with the PCR real-time technique, performed by our laboratory. As recommended by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America, she was treated with azithromycin at the dosage of 10 mg/Kg/die for 5 days(with subsequent same antibiotic cycle after 1 week)and, in according with literature, with oral prednisolone(1 mg/Kg/die), with benefit. Differential diagnosis included persistent bacterial pneumoniae, structural anomalies of airways and heart, tubercolosis, etc, excluded during the hospitalization. Macrolide-resistant Mp in children is linked with the excessive use of macrolides treatment. Considering that the severity of Mp infections is largely dependent on the host immune response, in some cases IVIG(intravenous immunoglobulin)or corticosteroids may be added to reduce the immune reaction.


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**Abs 34 | Epidemiological and clinical characteristics of anaphylactic reactions in children: A retrospective study from a tertiary care hospital in Italy**

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**Introduction:** The epidemiological and clinical characteristics of anaphylaxis, especially in children, are not clear and showed diversity in many studies.
Methods: A retrospective case series was developed from children aged from birth to 18 years presenting who had been diagnosed with anaphylaxis between 2003 and 2018 in the Pediatric Department of Immuno-Allergology of Pavia.

Results: We identified 94 cases of anaphylaxis (mean age 6.7 years, 61.7% male). Foods were the most common culprit (88.3%), followed by insect stings (9.6%) and respiratory allergens (2.1%). In the food trigger group, peanut, walnut, and other dried fruits occupied the largest proportion at 52.1%, cow’s milk and hen’s egg at 19.1% and 12.9%, respectively, followed by fish, kiwi, wheat. Asthma and/or allergic rhinitis were the most frequent comorbidities. Cofactors were present in only 3% of patients, mainly exercise. Reactions occurred at home and school most frequently (84%), followed by reactions that occurred in hospital during food challenges (16%). Of 94 anaphylactic events, 90.4% were involved with the cutaneous and mucosal, 71.3% with gastrointestinal, 66% with respiratory, 12.8% with cardiovascular, and 9.6% with neurological systems. Forty-eight (51.1%) children fulfilled the criteria of severe anaphylaxis. Sixty-seven (71.3%) children received a treatment prior to presentation to Emergency Department, but only 22.7% of them received adrenaline. No biphasic reactions and/or fatalities occurred.

Conclusion: Education regarding the more aggressive use of epinephrine in both home and hospital settings is clearly needed to overall improve adherence to anaphylaxis treatment guidelines.

Abs 35 | Off-label treatment with Cyclosporine A in a child with severe atopic dermatitis

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Cyclosporine A (CSA) is used to treat severe atopic dermatitis (AD) where conventional therapy is either ineffective or inappropriate. Although the majority of evidence exists in adult populations, experience in children is limited. We describe the case of a 7-year-old girl with severe AD not responding to conventional treatment. Her AD flares were mainly triggered by Staphylococcus aureus skin infections, which were effectively eradicated with antibiotics in several hospitalizations. Furthermore, specific IgE for milk and nuts were positive and she began a strict elimination diet without clinical skin improvement.

Since her severe AD was not responding to optimized topical therapy, including phototherapy, and other relevant triggers could not be identified, systemic therapy with CSA was considered. Standard pediatric dosing of CSA (3-6 mg/kg/day divided twice daily) was prescribed with an expansive set of baseline laboratory tests including, renal, and liver function. CSA treatment rapidly resulted in a sustained reduction in SCORAD index and a significant clinical improvement of pruritus. However, hypertrichosis and gingival hypertrophy were recorded as side effects. Once in remission (after approximately 0.1% to 0.3% of children and adolescents. Omalizumab is approved as an add-on therapy for the treatment of CSU in patients (aged >12 years) with inadequate response to H1-antihistamine treatment. However, there is limited published information based on real-world experience on the use of omalizumab in the subgroup of adolescents with CSU.

Methods: A single-center retrospective cohort study was performed to assess the efficacy and safety of omalizumab for treatment-refractory CSU in children. Patients previously treated with second-generation antihistamines at a fourfold increased dose without clinical responses at 4 weeks of treatment were selected. The response to therapy was evaluated using urticaria activity score over 7 days (UAS7).

Results: Eight patients (mean age 16 years) received omalizumab 300 mg subcutaneously every 4 weeks for 6 months. A complete response (UAS7 = 0) was observed in 7 (87.5%) children after the first dose of omalizumab and antihistamine therapy was successfully withdrawn. The only non-responder patient showed associated angioedema, which is considered a possible marker of poor response to treatment. No adverse effects occurred in the population treated. Symptom recurrence occurred in 2 patients (25%) at 2 months from the end of the primary therapy. Retreatment with omalizumab was successful without any adverse effects.

Conclusion: Add-on omalizumab therapy for refractory CSU in adolescents seems to be effective and safe with a relatively low incidence of symptom recurrence. Further research should investigate personalized omalizumab dosages and administration intervals, and the identification of biomarkers for future treatment algorithms.
**Abs 37 | Pediatric eosinophilic gastrointestinal diseases: A single-center experience**

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**Introduction:** Eosinophilic gastrointestinal diseases are rare disorders, defined by the abnormal eosinophilic infiltration of different segments of the gastrointestinal tract. They include eosinophilic esophagitis (EoE), eosinophilic gastroenteritis and colitis, namely EGIDs. The aim of this study is to assess the epidemiological and clinical features of EoE and EGIDs in a small cohort of pediatric patients.

**Methods:** A cohort of 19 children and adolescents (3-16 years) was enrolled. At diagnosis, we collected clinical data and all patients underwent endoscopy study. Laboratory investigations included total and specific IgE levels and blood eosinophil count.

**Results:** Of 19 patients, 14 presented with EoE and 5 presented with EGIDs. In both EoE and EGIDs cohorts, male sex is prevalent compared to female sex (85.7% vs 14.3% and 60% vs 40%, respectively). History of allergic diseases was significantly associated to EoE compared to EGIDs patients (P = 0.0052, P = 0.0057 and P = 0.0183, respectively). Levels of total IgE and eosinophilia were significantly higher in EoE patients compared to EGIDs patients (P = 0.0143 and P = 0.0340, respectively). In EoE cohort, patients with severe endoscopic lesions and with food impaction showed higher levels of Eo/HPF compared to patients with mild mucosal lesions at endoscopy and GERD-like symptoms. Moreover, patients responding to therapy had lower levels of Eo/HPF.

**Conclusion:** Pediatric EoE is significantly associated with atopy, higher levels of peripheral eosinophils and total IgE compared to EGIDs. In EoE patients, disease severity might correlate with higher levels of Eo/HPF in biopsy specimens of esophageal tract.

**Table 1.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at diagnosis</th>
<th>Implicated food</th>
<th>Symptoms</th>
<th>Lab tests</th>
<th>Skin Prick test and Specific IgE</th>
<th>Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>N°1</td>
<td>1 month</td>
<td>Cow's milk</td>
<td>Failure to thrive and diarrhea</td>
<td>Hyperchloremic acidosis</td>
<td>IgE for cow's Milk: negative</td>
<td>Aminoacidic formula</td>
</tr>
<tr>
<td>N°2</td>
<td>6 months</td>
<td>Cow's milk</td>
<td>Vomit, lethargy, and hypotonia 5 hours after ingestion of zucchini soup with formula milk</td>
<td>MetaHb 2.8% Increased WBC Normal</td>
<td>None</td>
<td>Breast milk or Hydrolyzed formula</td>
</tr>
</tbody>
</table>

(Continues)
Introduction: Bacille Calmette-Guérin (BCG), the live attenuated vaccine against tuberculosis, is the most commonly administered vaccine in history worldwide and currently licenced for use at birth. Epidemiologic studies suggest beneficial effects of BCG against a broad range of pathogens, possibly reflecting heterologous enhancement of innate immune responses. Manufacturing of BCG under different conditions across the globe has generated divergent BCG formulations that differ in clinical efficacy and scar frequency. Recent studies have indicated that viability of BCG is important to its immunogenicity. We hypothesized that licensed BCG formulations may be divergent in their content of viable mycobacteria and induce distinct age-dependent cytokine production.

Methods: BCG formulations were tested for mycobacterial membrane integrity with flow cytometry, stained for RNA content, and cultured under standardized conditions to determine colony forming units (CFUs). BCG-induced cytokine/chemokine production was measured in cord (N = 4-10) and adult (N = 7-13) whole blood. Formulations tested included BCG Denmark (DEN), Japan (JPN), India (also known as Russia, produced in Pune) (IND), Bulgaria (BUL), and USA (TICE).

Results: BCG India demonstrated significantly decreased membrane integrity (65% intact cells) and significantly lower RNA content (54%) compared to the other formulations. Upon culture, BCG India and Bulgaria demonstrated divergent growth and sensitivity to media composition. BCG-induced whole blood cytokine/chemokine pattern differed significantly by age. IFN-γ showed a delayed response in both age groups, weakest for BCG India. Induction of chemotactic, hematopoietic factors and Th1 cytokines were formulation and dose-dependent: BCG Denmark and Bulgaria produced significantly higher levels at comparable CFU doses, while Denmark and Japan produced significantly higher levels at the human equivalent dose, compared to the other formulations. Whole blood concentrations of BCG-induced pro-inflammatory cytokines and hematopoietic factors correlated with CFU counts, suggesting that BCG viability may be key for immune responses.

Conclusions: Licensed BCG vaccines differ in their content of intact and culturable mycobacterial cells possibly contributing to distinct induction of chemotactic, hematopoietic factors and cytokines in vitro. Age and formulation-dependent BCG activation of innate and adaptive immunity may contribute to distinct clinical effects of BCG.
Abs 40 | Role of ocular cytology in Vernal keratoconjunctivitis

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Introduction: Children with Vernal Keratoconjunctivitis (VKC) present symptoms similar to other ocular allergies, but amplified; they are controlled with local steroids. In order to avoid excessive and extended use of local steroid eye drops, galenic eye drops of cyclosporine with a concentration of 1-2% and tacrolimus at 0.1% were introduced as treatment in severe and unresponsive forms. The aim of this study is to assess which are the most frequent cellular types present in the conjunctiva of children affected by VKC, how ocular treatment can influence them, and if affected children express a typical conjunctival pattern, potentially useful as a patognomonic pattern of VKC, allowing us in the diagnosis of this rare ocular disease.

Materials and Methods: This is a cohort study of 56 children: 17 of them were receiving no treatment at the time of testing, 14 children were assuming steroid eye drops or had taken them in the last 10 days, and 25 were treated with cyclosporine eye drops or tacrolimus eye drops 0.1%.

Results: Children in group 1 (no local therapy) express more epithelial cells, neutrophils, mastcells, eosinophils and lymphocytes than the other two groups, underlying how ocular treatment can influence the composition of the conjunctiva in affected children.

Conclusions: If on one hand the conjunctival cytological examination and the search for eosinophils can help to identify VKC and other ocular allergies, especially when the clinical diagnosis is not clear, on the other hand they could allow monitoring of the progress of the disease and of the response to local treatment.

Abs 41 | Therapeutic options for Vernal Keratoconjunctivitis

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Vernal keratoconjunctivitis (VKC) is a bilateral, asymmetric, chronic, usually seasonally recurrent, inflammation of the ocular surface. VKC is classified among the allergic conjunctivitis, but its immunopathogenesis remains unknown. Antihistamines, mast cell stabilizers, and dual-action drugs eye drops are effective only in mild VKC, with conflicting results in different geographical areas. Topical non-steroidal anti-inflammatory drugs reduce ocular inflammation, but they cannot replace steroids. Steroid eye drops are the most effective treatment for severe VKC, but prolonged therapy could potentially cause glaucoma, cataract, and infections. Sometimes they cannot control the disease. Literature lacks precision about ways and times of using steroids in VKC, and the management of these children is often a dilemma. Steroids are prescribed as oral but also as eye drops, sometimes in short cycles of 3-5 days, repeatable with variable frequency. The shift from steroids to calcineurin inhibitors sometimes occurs in extremely severe VKC, sometimes in less severe cases. This work proposes a therapeutic algorithm with steroids eye drops (2 drops for eye 3 times day) in short cycles (of 3 days each one), repeatable several times in a month. If 3 or more cycles of dexamethasone sodium phosphate 0.15% eye drops are required in a month primarily in spring, it is necessary to assess eye pressure, corneal integrity and the presence of eye infections, but also to evaluate clinical signs VKC and to start therapy with calcineurin inhibitors (cyclosporine at 1% or tacrolimus at 0.1% eye drops).

Abs 42 | Neutralizing high mobility group box-1 provides protection against respiratory syncytial virus infection

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Introduction: HMGB1 has been recently proposed to serve as a potential biomarker elucidating the link between RSV infection and chronic airway dysfunction.

Materials and Methods: Fischer 344 rats were infected with rrRSV. Primary human bronchial epithelial cells and 16HBE14o- were grown in cell culture, and apically infected with rrRSV at an MOI of 1 in the presence or absence of glycyrrhizin, an HMGB1 neutralizing chemical compound.
Results: Analysis of HMGB1 in rat’s lung homogenates by RT-PCR, ELISA, and Western blot analysis revealed higher concentrations of HMGB1 mRNA and protein in the RSV-infected group (P < 0.001). HMGB1 mRNA and protein expression were increased in both primary epithelial cells and 16HBE14o- in response to RSV infection. The peak of mRNA expression measured by real-time PCR was at 3 hours post-infection (P < 0.0001), while Western blot analysis revealed a peak of HMGB1 increase in expression at 6 hours post-infection, which was gradually decreased at 24 hours, with a second peak at 48 hours. Immunofluorescence microscopy showed an increased of HMGB1 expression localized in the nuclei at 3-6 hours post-infection, while a more diffused cytoplasmic pattern was observed at 24-48 h post-infection (fig. 1). Live-cell fluorescent microscopy showed a significant decreased in red fluorescent in the infected cells infected when pretreated with Glycyrrhizin. Pretreatment of polarized epithelial cell cultures with Glycyrrhizin significantly decreased rrRSV mRNA in a dose-dependent manner. Additionally, HMGB1 protein was decreased in cells treated with Glycyrrhizin.

Conclusion: By selectively inhibiting HMGB1 with glycyrrhizin, we documented a significant reduction in viral mRNA expression.

Abs 43 | An uncommon case of food protein induced allergic proctocolitis

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Food protein-induced allergic proctocolitis (FPIAP) is among the commonest causes of rectal bleeding in infants. FPIAP in breast-fed infants is usually caused by cow’s milk, soy, and egg in the maternal diet. A 3-month-old girl was admitted at the pediatrics ward because of blood and mucous in stools since 5 days. She had no other symptoms, except some vomiting episodes in the last few days. She was exclusively breast-fed. She was increasing in weight regularly. On physical examination no abnormalities were found, except for a pale skin. Inflammation markers and abdomen ultrasound were found normal. Due to worsening hematochezia with concomitant anemia, a colonoscopy with biopsy was performed. Microscopical examination revealed a marked increase of eosinophilis (>30 HPF) in the lamina propria, confirming the clinical suspicion of FPIAP. Lab tests revealed eosinophilia (9%, 1,060/mm³). Serum sIgE to cow’s milk, egg, wheat, rice, soy, egg were negative, as well as culture and antigen detection from stool specimens. Maternal diet without cow’s milk proteins was initially started. After two weeks of maternal diet, no clinical improvement was observed and eosinophilia increased (18%); thus, wheat, soy, and egg were also excluded but rectal bleeding continued. At a more accurate history, we found that the infant was given rice-protein hydrolysed milk during the last week as breast milk was insufficient. After stopping rice formula and beginning maternal exclusion diet for rice and corn, the infant began to improve. An elemental formula was introduced. This case highlights the importance of considering other less common allergens as causative agents of FPIAP in exclusively breast-fed infants.

Abs 44 | Neonatal food allergies: A possible triggering role of haemolytic anemia and intestinal hypoperfusion. A case report

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¹Scuola di Specializzazione in Pediatria, Università degli Studi di Siena, Siena; ²UOC Pediatria Neonatale, AOUS “Le Scotte”, Siena

A.P., born at 36 + 2 weeks of gestational age. Admitted in Neonatal Pathology department for GA and a significant tachycardia at birth, the baby did not show initially any sign of respiratory distress. Enteral feeding with breast milk and ev hydration were started. Blood examinations showed severe anemia with reticulocytosis and elevated WBC count. Blood cultures and PCR showed no signs of infection. Maternal indirect Coombs test showed positivity for possible alloantibodies (anti-A and anti-D). Direct Coombs test later revealed positivity for antibodies anti-A and anti-D. Subsequently, clinical conditions significantly worsened with respiratory distress, pallor, tachypnea, peripheral hypoperfusion, melaena and failure to thrive. Echocardiogram excluded cardiac causes. Two blood transfusions were performed with good clinical response. Antibiotic therapy was also introduced. However, a persistent failure to thrive with loss of almost 20% of the initial weight required parenteral nutrition. Abdominal distension and abundant diarrhea were also associated. Further evaluations showed hypereosinophilia, never encountered before, and positive Prist test and Rast test for milk proteins (Table 1). A consistent weight gain, along with an improvement of intestinal signs, was observed after the introduction of hydrolysed milk formula with a complete normalization of the clinical picture and a rapid increase in the Hb levels. Intestinal barrier integrity has a key role in the instauration of tolerance to food antigens and in the prevention of food allergies. A significant and prolonged haemolytic anemia with peripheral hypoperfusion and subsequent intestinal mucosal damage could have had an essential role in triggering a precocious and strong immune response.

### Table 1.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Blood Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow milk IgE</td>
<td>2.01 kUA/L</td>
</tr>
<tr>
<td>Alpha-lactalbumin IgE</td>
<td>0.83 kUA/L</td>
</tr>
<tr>
<td>Beta-lactoglobulin IgE</td>
<td>1.41 kUA/L</td>
</tr>
<tr>
<td>Casein IgE</td>
<td>1.99 kUA/L</td>
</tr>
<tr>
<td>Total IgE</td>
<td>74.8 kU/L (n.v 2.3 kU/L up to 6 w of age)</td>
</tr>
</tbody>
</table>
Case report: We describe the case of a 6-year-old girl with clinical history of recurrent impetigo and cutaneous, dental and articular abscesses. Gastrointestinal disorders (abdominal pain, vomiting, and diarrhea) were also reported from birth, despite long-term gluten, chocolate, tomato, egg and milk exclusion diet. Recurrent vaginal and buccal candidiasis, asthmatic bronchitis and an episode of pneumonia were also reported. She was in follow-up since two months of life because of the diagnosis of Atopic dermatitis. Admitted at hospital due to the onset of vomiting in apyrexia, she performed complete abdominal echography and brain MRI (both negative) and blood testing showing elevated total serum IgE level (15,000 kU/L). Microbiological tests highlighted the presence of Staphylococcus Aureus on ocular and nasal swabs and in sputum. Prophylactic antibiotic therapy with cotrimoxazol was started. Molecular investigation showed mutation of STAT-3.

Discussion: HIES can be misdiagnosed with Atopic Dermatitis (AD), leading to the onset of severe complications. In fact, skin lesions have some similarities with those of Atopic Dermatitis, but distribution and features are different. Early onset of skin lesions, coexistence of eczema and cutaneous abscesses and recurrence of pulmonary infections should suggest to perform first- and second-level immunological screening to exclude HIES.

Abs 47 | Suspicion of allergy to β-lactams in pediatric age: Use of basophil activation test

S. Caimmi; M. De Amici; D. Caimmi; A. Apicella; C. Torre; M. Votto; G. Testa; F. Barocci; G. L. Marseglia

Introduction: The allergy workup for the diagnosis of hypersensitivity to β-Lactams drugs currently requires the execution of correct tests, like skin prick test, intradermal test and oral provocation test, which require an important commitment of resources, in terms of time and money, and a stressful process for young patients. The basophil activation test (BAT) has been proposed as a new diagnostic tool in the allergic workup for the diagnoses of β-Lactams IgE-mediated hypersensitivity in children and adults.

Patients and Methods: Fifty-five childrens, with history of immediate (13) or delayed (42) reactions to Amoxicillin, Amoxicillin-Clavulanate, and various Cephalosporines, were investigated performing BAT, skin prick test, intradermal test, and oral provocation test for the suspect of an IgE-mediated hypersensitivity to this drugs, during years 2015 and 2016.

Results: BAT was positive in 19 patients but only two of these patients had a positive oral provocation test result. One patient
positive to the oral provocation test had a negative BAT. The others 4 patients with a positive drug allergy workup had a negative BAT result. The Negative Predictive Value (NPV) is 97%. The comparison of commercial allergen and drug from pharmacy shows a positive test for 5 out 7 patient tested for the dilution suggested of the commercial ones, and 4 out 8 patients with drug from pharmacy had positive test at all concentration tested, the other where positive only at the highest.

Conclusions: BAT does not seem to be a useful diagnostic exam in an allergy workup for the diagnoses of hypersensitivity to \( \beta \)-lactams in children for a low sensitivity, but it has a good NPV. The research of new diagnostic tools aimed to simplify the allergy workup of drugs hypersensitivity is an important field of study. Extended studies are important to evaluate the appropriate concentration to be used when using homemade preparation of the drug allergens, in order to appropriately set cutoff and reference values.

Abs 48 | A case of SMARCD2 gene mutation with neutrophil-specific granule deficiency and severe cutaneous and respiratory infections

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Introduction: Neutrophil-specific granule deficiency (SGD) is a rare congenital disease. 1 In this condition, the neutrophils lack their specific granules and this leads to an impaired function in controlling infections. 2-3 Neutrophil-specific granules develop during granulocyte differentiation, later than primary granules, and this process requires a specific regulation between different genes and transcription factors. 4 Mutations in these genes lead to an interruption in granulocytes maturation and consequently to an increased susceptibility to bacterial and fungal infections. 5 SMARCD2 has been identified recently as an important gene as regards granulocytes differentiation and granules formation. 6 In 2017, Witzel et al. reported 4 patients with SMARCD2 gene mutation. They all presented with delayed separation of umbilical cord, and severe recurrent bacterial infections. Two of them were successfully treated with hematopoietic stem cell transplantation (HSCT) and 2 died at 1.5 months and 5.5 years, respectively.

6 Case report: We report here the case of M.M.E.D.J., a girl with neutrophil-specific granule deficiency. In June 2018, when the patient was one month old, she was admitted to the hospital of Vicenza because of failure to thrive, persistent mucocutaneous candidiasis, fever, and anemia. A delay in umbilical cord sloughing was also reported. During her stay in the hospital, she developed a perianal abscess and recurrent pulmonary infections with isolation of Klebsiella pneumoniae. Therefore, she was treated with broad-spectrum intravenous antibiotics, but without clinical response. Then the patient was transferred to the Department of Pediatrics, ASST Spedali Civili of Brescia, suspecting an immunodeficiency. Immunological investigations and a bone marrow aspiration were performed showing a morphological alteration of the neutrophils with hypogranulation and hyposegmentation. On the basis of these findings, genetic analysis was performed and a mutation in the SMARCD2 gene (1022_1025delCTTT), coding for a critical regulator of myeloid differentiation, was identified. In November 2018, at six months of age, the patient underwent a HLA-Matched Sibling Donor hematopoietic stem cell transplantation (HSCT) with good response. After the HSCT the cutaneous lesions have progressively healed and she has developed no further infections. She developed a cutaneous and intestinal graft vs host disease, which was treated with systemic corticosteroids, with clinical improvement. Now she is in good condition.

Abs 49 | Possible lymphocyte-mediated mechanisms for swordfish anaphylaxis: A pediatric case report

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Introduction: The exact pathogenic mechanisms of fish allergy are scarcely known.

Patient and Methods: An 11-year-old child was admitted to hospital presenting diffuse urticaria, facial oedema, abdominal pain, vomiting, and hypotension after swordfish ingestion. Blood exams documented: high tryptase value (24.9 \( \mu \)g/L), total IgE 659 KU/L, but no IgE to common fish. Intravenous corticosteroids and antihistamines were administered and patient discharged after 24 hours. A swordfish free diet with consumption of other fish types was administered, with no allergic reactions. Microarray (ISAC test) for food, basophil activation test for dyes and preservatives and swordfish specific IgE were negative, suggesting the absence of hypersensitivity to swordfish. Based on these data, the parents reintroduced by themselves swordfish and anaphylaxis recurred again. Prick tests were not performed due to the recent anaphylaxis episode, so lymphocyte subpopulations and proliferation tests were performed both on the patient and on a healthy donor (HD).

Results: Incubation of patient’s peripheral blood mononuclear cells with raw and cooked swordfish extract, showed B cells proliferation (stimulation index 3.7 and 2, respectively), while no response in the HD. Lymphocyte subpopulations showed higher B memory cells and lower T regulatory cells compared to the HD (14.5% and 1.7% vs 5.3% and 4.9%, respectively) (Table 1).
Conclusion: Swordfish could have induced a non-IgE-mediated anaphylaxis. Clinical data and proliferative response confirm swordfish’s ability to act as antigen to induce a cell-mediated response. Moreover, the documented low levels of Treg lymphocytes could probably predispose to lack of tolerance and to the development of an immune reaction in an IgE-independent way (Table 2 and 3).

**Table 1.**

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Patient %</th>
<th>HD %</th>
</tr>
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<tbody>
<tr>
<td>B CELLS</td>
<td>6.7</td>
<td>6.4</td>
</tr>
<tr>
<td>MEMORY</td>
<td>14.5</td>
<td>5.3</td>
</tr>
<tr>
<td>MEMORY ATIPICHE</td>
<td>8.2</td>
<td>3.9</td>
</tr>
<tr>
<td>REGOLATORIE</td>
<td>16.9</td>
<td>28</td>
</tr>
<tr>
<td>MATUO</td>
<td>47.1</td>
<td>50.4</td>
</tr>
<tr>
<td>PLASMA</td>
<td>2.3</td>
<td>3.6</td>
</tr>
<tr>
<td>CD4+</td>
<td>38.6</td>
<td>49.3</td>
</tr>
<tr>
<td>T REG TOTALI</td>
<td>1.7</td>
<td>4.9</td>
</tr>
<tr>
<td>NAIVE</td>
<td>28</td>
<td>49.1</td>
</tr>
<tr>
<td>EFFECTOR</td>
<td>16.8</td>
<td>17.8</td>
</tr>
<tr>
<td>NK DIM</td>
<td>60.3</td>
<td>74.2</td>
</tr>
<tr>
<td>NK BRIGHT</td>
<td>6.2</td>
<td>3.2</td>
</tr>
</tbody>
</table>

**Table 2.**

Abs 50 | Improvement in nasal reactivity after two years of grass pollen SLIT treatment in children with allergic rhinitis

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Background: The European Academy of Allergy and Clinical Immunology (EAACI) guidelines recommend immunotherapy (AIT) as the only treatment capable to obtain long-term clinical benefits, trying to modify the natural history of allergic diseases. In particular, sublingual immunotherapy (SLIT) offers the possibility of home administration, improving patient comfort and compliance. The primary outcome of this study is to evaluate the change in nasal reactivity after treatment with AIT in children allergic to grass pollen.

Methods: In a period between September 2016 and June 2018, an observational monocentric prospective study was conducted in the Allergy Service of the Pediatric Department of Policlinico Umberto I “Sapienza” Rome. A group of 30 children (aged between 6 and 12 years old) with a persistent allergic rhinitis (PAR) sensitized to grass pollen, were enrolled and divided into the following groups:- treated group (TG): 15 children, that received oral immunotherapy for grass pollen SULGEN® (Roxall, Italy) perlingual spray- non treated group (nTG): 15 children that continued the standard therapy. All children performed 3 visits in total: V0 (September 2016), V1 (June 2017), and V2 (June 2018), during which they performed the dosage of the specific IgE in nasal lavage (Phl p1, Phl p5, Phl p7, Phl p12), the active anterior rinomanometry (AAR) with the evaluation of the mean nasal flow (mNF) and a specific nasal provocation test (NPTs) for grass pollen.

Results: In the nTG we found:- a reduced mNF in V2 vs V0;- NPTs positivized in a percentage like a 30% in V2 vs V0;- increased Phl p1,
Phl p5, Phl p7 and Phl p12 levels in V2 vs V0; In the TG, we observed:- a statistically significant mNF increase in V2 vs V0 and in comparison with the nTG ($P = 0.000$);- NPTs negativized in a percentage equal to 71.43% in V2 vs V0;- Phl p1 ($P = 0.000$), Phl p5 ($P = 0.001$), Phl p7 ($P = 0.002$) and Phl p12 ($P = 0.025$) levels statistically significantly reduced in V2 vs V0.

**Conclusion:** The preliminary analysis of these data suggests to increase the study sample size in order to support, with objective functional parameters, SLIT efficacy on the reactivity of the nasal mucosa and not only in clinical parameters.