

Selections from international journals

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Ann Rheum Dis. 2016;75(3):481-9.

2016 Classification Criteria for Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis: A European League Against Rheumatism/American College of Rheumatology/Paediatric Rheumatology International Trials Organisation Collaborative Initiative.

Ravelli A, Minoia F, Davi S, Horne A, Bovis F, Pistorio A, Aricò M, Avcin T, Behrens EM, De Benedetti F, Filipovic L, Grom AA, Henter JI, Ilowite NT, Jordan MB, Khubchandani R, Kitoh T, Lehmsberg K, Lovell DJ, Miettunen P, Nichols KE, Ozen S, Pachlopnik Schmid J, Ramanan AV, Russo R, Schneider R, Sterba G, Uziel Y, Wallace C, Wouters C, Wulfraat N, Demirkaya E, Brunner HI, Martini A, Ruperto N, Cron RQ; Paediatric Rheumatology International Trials Organisation, the Childhood Arthritis and Rheumatology Research Alliance, the Pediatric Rheumatology Collaborative Study Group, and the Histiocyte Society.

To develop criteria for the classification of macrophage activation syndrome (MAS) in patients with systemic juvenile idiopathic arthritis (JIA). A multistep process, based on a combination of expert consensus and analysis of real patient data, was conducted. A panel of 28 experts was first asked to classify 428 patient profiles as having or not having MAS, based on clinical and laboratory features at the time of disease onset. The 428 profiles comprised 161 patients with systemic JIA-associated MAS and 267 patients with a condition that could potentially be confused with MAS (active systemic JIA without evidence of MAS, or systemic infection). Next, the ability of candidate criteria to classify individual patients as having MAS or not having MAS was assessed by evaluating the agreement between the classification yielded using the criteria and the consensus classification of the experts. The final criteria were selected in a consensus conference. Experts achieved consensus on the classification of 391 of the 428 patient profiles (91.4%). A total of 982 candidate criteria were tested statistically. The 37 best-performing criteria and 8 criteria obtained from the literature were evaluated at the consensus conference. During the conference, 82% consensus among experts was reached on the final MAS classification criteria. In validation analyses, these criteria had a sensitivity of 0.73 and a specificity of 0.99. Agreement between the classification (MAS or not MAS) obtained using the criteria and the original diagnosis made by the treating physician was high ($\kappa=0.76$). We have developed a set of classification criteria for MAS complicating systemic JIA and provided preliminary evidence of its validity. Use of these criteria will potentially improve understanding of MAS in systemic JIA and enhance efforts to discover effective therapies, by ensuring appropriate patient enrollment in studies.

J Clin Immunol. 2015;35(8):696-726.

Primary Immunodeficiency Diseases: an Update on the Classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency 2015.

Picard C, Al-Herz W, Bousfiha A, Casanova JL, Chatila T, Conley ME, Cunningham-Rundles C, Etzioni A, Holland SM, Klein C, Nonoyama S, Ochs HD, Oksenhendler E, Puck JM, Sullivan KE, Tang ML, Franco JL, Gaspar HB.

We report the updated classification of primary immunodeficiencies compiled by the Primary Immunodeficiency Expert Committee (PID EC) of the International Union of Immunological Societies (IUIS). In the two years since the previous version, 34 new gene defects are reported in this updated version. For each disorder, the key clinical and laboratory features are provided. In this new version we continue to see the increasing overlap between immunodeficiency, as manifested by infection and/or malignancy, and immune dysregulation, as manifested by auto-inflammation, auto-immunity, and/or allergy. There is also an increased number of genetic defects that lead to susceptibility to specific organisms which reflects the finely tuned nature of immune defense systems. This classification is the most up to date catalogue of all known and published primary immunodeficiencies and acts as a current reference of the knowledge of these conditions and is an important aid for the genetic and molecular diagnosis of patients with these rare diseases.

Ann Allergy Asthma Immunol. 2016;116(1):49-51.

Venom allergy testing: is a graded approach necessary?

Quirt JA, Wen X, Kim J, Herrero AJ, Kim HL.

BACKGROUND: Many institutions recommend a stepwise approach to intradermal testing for venom allergy. This is costly and uncomfortable for the patient. The rationale for this approach is the risk of potential adverse reactions to testing with the maximal dose alone. **OBJECTIVE:** To evaluate the safety of a single-step approach to venom allergy testing. **METHODS:** The authors retrospectively reviewed the charts of 300 consecutive patients with suspected hymenoptera venom allergy based on history who underwent venom allergy testing in a single allergist's clinic where a single-step protocol had been adopted. All patients had positive skin test reaction to at least 1 hymenoptera venom. Charts were reviewed for testing protocol used, results of testing, and reported immediate and delayed adverse reactions to testing. **RESULTS:** All patients underwent testing with an identical single-step protocol with an intradermal dose of 0.02 mL of a 1.0- μ g/mL concentration of each of the 5 commercially available vespid and bee venoms. Only 1 patient reported an adverse reaction to testing, which was delayed until the morning after his visit. There were no immediate adverse reactions. The patient who had the delayed reaction was successfully started on venom immunotherapy subsequent to his reaction. **CONCLUSION:** A single-step venom allergy intradermal testing protocol with a 1.0- μ g/mL concentration of commercially available extracts is a safe option, which, if adopted into practice, could lead to more streamlined care for patients and cost savings for the medical system.

Allergy. 2016;71(2):149-61.

Drug hypersensitivity in children: report from the pediatric task force of the EAACI Drug Allergy Interest Group.

Gomes ER, Brockow K, Kuyucu S, Saretta F, Mori F, Blanca-Lopez N, Ott H, Atanaskovic-Markovic M, Kidon M, Caubet JC, Terreehorst I; ENDA/EAACI Drug Allergy Interest Group.

When questioned, about 10% of the parents report suspected hypersensitivity to at least one drug in their children. However, only a few of these reactions can be confirmed as allergic after a diagnostic workup. There is still a lack of knowledge on drug hypersensitivity (DH) epidemiology, clinical spectrum, and appropriate diagnostic methods particularly in children. Meanwhile, the tools used for DH management in adults are applied also for children. Whereas this appears generally acceptable, some aspects of DH and management differ with age. Most reactions in children are still attributed to betalactams. Some manifestations, such as nonsteroidal anti-inflammatory drug-associated angioedema and serum sickness-like reactions, are more frequent among young patients as compared to adults. Risk factors such as viral infections are particularly frequent in children, making the diagnosis challenging. The practicability and validity of skin test and other diagnostic procedures need further assessment in children. This study presents an up-to-date review on epidemiology, clinical spectrum, diagnostic tools, and current management of DH in children. A new general algorithm for the study of these reactions in children is proposed. Data are presented focusing on reported differences between pediatric and adult patients, also identifying unmet needs to be addressed in further research.