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## 0787 | Increased values of D-dimer in anaphylaxis: Case series

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**Background**: Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death. One of the pathways of the anaphylaxis is the activation of the contact and the coagulation systems. A pulmonary embolism (PE) is a sudden blockage in a lung artery and the fast test to suspect of PE is measuring concentration of the D-dimer in blood.

**Method**: Four patients were treated for anaphylaxis in Intensive Internal Care Unit (IICU) in Emergency center, Clinical Center of Serbia during 2019.

**Results**: Patient No.1. was 55-year-old Caucasian female who had an anaphylaxis after taking the tablet of Metronidazole. She had following gastrointestinal (GI) symptoms: nausea, vomiting, abdominal pain; respiratory (RES) symptoms: dyspnea, hypoxemia (SO2: 83%); cardiovascular (CV) symptoms: arterial hypotension, loss of consciousness, somnolence; cutaneous (CUT) symptoms: erythema. After admission to IICU, she had an elevated values of D-dimer in blood 4.91 (normal < 0.5 mg/L). Patient No.2. was 61-year-old Caucasian female who had an anaphylaxis after taking Diclofenac tablet. Symptoms: GI: nausea, abdominal pain; RES: dyspnea, hypoxemia (SO2: 84%); CV: arterial hypotension, loss of consciousness, somnolence; CUT: edema and erythema and high D-dimer level: 6.63 mg/L. Patient No.3. was 22-year-old Caucasian male who had an anaphylaxis after meal in restaurant. Symptoms: GI: nausea, vomiting, abdominal pain; RES: respiratory arrest; CV: arterial hypotension, loss of consciousness; CUT: angioedema. Initial sera D-dimer was 8.83 mg/L, which decreased to 0.57 mg/L in two days. Patient No.4. was 35-year-old Caucasian male who had an anaphylaxis after meal at home. Symptoms: GI: abdominal pain; CV: arterial hypotension, syncope; CUT: erythema, angioedema. Concentration of D-dimer at presentation was very high 30.9 mg/L and then decreased to 12.73 mg/L in two days.

All patients had normal ECG. In the case of our first patient due to prolonged hypotension MDCT pulmonary angiography was performed revealing normal result. Control values of the D-dimer after discharge were normal in the first three patients and they did not experienced any thrombotic event. Since the Patient No. 4. was a foreign citizen, he was treated with nadroparin s.c. because of planned trip with high values of D-dimer in blood.

**Conclusion**: Differential diagnosis between anaphylaxis and PE can be difficult due to similar clinical pictures and high values of D-dimer in blood. It can lead to unnecessary testing and prolonged hospitalization.

## 0812 | Changes of antihistamine sales patterns in central Ukraine shows the impacts of both global warming and increased ragweed sensitization

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**Background**: Analysis of the long-term trends of antihistamine sales in central Ukraine shows seasonal peaks of sales of these drugs associated with intense grass and to a lesser extent with tree pollen seasons. The shift of these peaks to earlier periods in 2015-2016 compared with 2008-2009 suggests evidence of global warming and climate change. However, the last two years revealed a new pattern of antihistamine drug sales perhaps due to increased sensitization of the local population to ragweed.

**Method**: Sales data of antihistamines for systemic use (ATC code R06) in the Vinnytsya region of Ukraine for 2008 through 2016 and for 2018-2019 were obtained using system of market research «PharmXplorer» which belongs to the «Proxima Research®» company. Monthly fluctuations of the sales were analyzed. The pollen counts for 2009 through 2016 and 2018-2019 were obtained from the database of the Laboratory for Allergen Investigation at the National Pirogov Memorial Medical University, Vinnytsya, Ukraine. ALEX molecular allergen sensitization blood testing was done on 65 pollen allergic patients in Central Ukraine to assess the sensitization patterns in 2018 and 2019.

**Results**: The greatest sales of antihistamines were seen in May-June or in March-April through years 2008 through 2016 corresponding with intense pollination of trees including alder and birch and of grasses. The pattern of sales in 2018-2019 which coincided, differed from the trends seen in previous years, having gradual increases of antihistamine purchases starting from February through June with a sharp decline in July and followed by significant increase in August. This new pattern may correspond with increased sensitization of the central Ukraine population to ragweed pollen. Examining this hypothesis, results of allergen sensitization obtained by ALEX tests in 2018-2019 showed most Central Ukraine patients (41.5%) were sensitive to grass pollen, 35.4% to tree pollen and 18.5% to weed pollen including *Ambrosia* and *Artemisia*. This is consistent with the sales of antihistamines peaking during seasons of tree, grass and weed pollination.

**Conclusion**: The pattern of antihistamines sales in Central Ukraine supports data showing highest sensitization levels of patients to grass pollen with increases of sales beginning during tree pollination with earlier sales due to climate change. Recent increases of sales during August provides evidence of newly increased sensitization to weed pollen.

## 0815 | The effect of human rhinovirus HRV-16 on angiogenesis and remodeling in 3D cultures of human pulmonary endothelium

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**Background**: In asthma, increased airway angiogenesis and remodeling is observed. Although human rhinovirus (HRV) is engaged in asthma development and exacerbations, its role in angiogenesis is not clear. The aim of the study was to assess the effect of HRV-16 on angiogenesis and expression of angiogenetic and remodeling factors in 3D cultures.

**Method**: Human Lung Microvascular Endothelial Cells (HMVEC-L) were cultured on extracellular matrix (ECM) membrane followed by 3-hour incubation with HRV-16 (MOI 3) in order to assess the new tubule formation in the phase-contrast microscope in hour 24 and 48. Angiogenetic and remodeling factors (VEGF-A, angiopoietin-1, FGF-1, amphiregulin and neutrophillin), receptors (VEGFR1 and VEGFR2) and anti-viral response cytokine (IFN-beta and RANTES) mRNA expression was assessed by Real Time PCR in hour 24, 48, 72 and 96. Proliferation and viability of endothelial cells was analyzed by thymidine incorporation assay and MTT test.

**Results**: HRV-16 significantly inhibited endothelial tubule formation as compared to mock cells in both hour 24 and 48. It was accompanied by the 50% decrease of endothelial proliferation ($P < .05$) and 60% decrease of viability ($P < .05$). At the same time, HRV-16 caused 2-fold increase of both VEGF-A and angiopoietin-1 ($P < .05$), 2-fold increase of VEGFR1 ($P < .05$) and 5-fold increase of VEGFR2 ($P < .05$) as well as the increases of FGF-1 (5-fold), AREG (12-fold) and neurophilin 1 (2-fold) ($P < .05$) of mRNA expression. Enhancement of IFN-beta and RANTES mRNA expression (40-fold and 10.000-fold respectively) and release of 500 pg/mL INF-beta protein ($P < .05$) and 5000 pg/mL of RANTES protein ($P < .05$) confirmed effective infection by HRV-16. Interestingly, the increase of mRNA expression of VEGF-A (2-fold) and angiopoietin-1 (2-fold), IFN-beta (400-fold) and RANTES (800-fold) were confirmed in the material isolated from tubule forming 3D cultures.

**Conclusion**: Human rhinovirus may directly inhibit the new tubule formation; however, it may increase the sensitivity to angiogenic factors and expression of remodeling cytokines.

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## 0851 | Omalizumab in immunotherapy with hymenoptera venom – experience of a portuguese tertiary centre

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**Background**: Venom immunotherapy (VIT) is an effective treatment for Hymenoptera venom allergy. The occurrence of severe hypersensitivity reactions (SHR) during VIT may hamper the achievement of tolerance to insect stings. Pretreatment with omalizumab has been successfully used in patients with previous SHR during VIT. We aimed to present our experience with the use of Omalizumab in patients with previous SHR during bee venom ultra-rush (UR).

**Method**: Retrospective review of the charts of 4 patients with bee venom allergy, with anaphylaxis grade 3/4 based on Muller's classification, positive skin tests and bee venom specific IgE (BV sIgE), double sensitized to Api m1 and Api m10, experiencing a SHR during the UR protocol, proposed by Bimbaum and col. In this protocol, a cumulative dose of 101.1 μg is administered, divided in 6 injections (210 minutes total). Once a SHR during the UR occurred, Omalizumab 300 mg was proposed and administrated subcutaneously every 4 weeks for the first 4 months before the new UR, and afterwards one week before each of the maintenance VIT administrations.

**Results**: All 4 patients were male, mean age 43.5 ± 13.9 years, 3 of them with positivity in prick in addition to the intradermal tests (1-10 μg/mL), with mean values of BV sIgE 20.4kUA/l, Api m1 13.9kUA/l, Api m10 2.8kUA/l, and basal tryptase 5.1 μg/l. Patients were pre-medicated with antihistamine and montelukast and underwent UR. All experienced a SHR (grade 3/4) after the 3rd step of UR (cumulative dose of 11.1 μg). In 3 patients, a second UR was attempted, with no success. Patients then received 4 administrations of Omalizumab 300 mg and underwent an equal UR protocol. All 4 patients were able to conclude the procedure and tolerated the following maintenance doses of VIT (100 μg). Discontinuation of omalizumab was attempted in one patient 15 months later, but he experienced a breakthrough SHR in the 3rd VIT administration and restarted omalizumab with no further SHR. The other patients have received omalizumab for the last 12-24 months with good VIT outcomes, and discontinuation of this monoclonal antibody is currently being considered.

**Conclusion**: Omalizumab therapy seems a promising approach to improve the safety of VIT treatment in patients with previous SHR during the UR, although the ideal dose and length of treatment is still a matter of debate.