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649 CHALLENGE WITH NIMESULIDE , A NEW NSAID, IN PATIENTS WITH REACTIONS TO ASPIRIN AND OTHER NSAIDS. Bernstein M, MD, Rodriguez C, MD.Hospital de Clinicas Caracas, Caracas ,Venezuela.

The use of nonsteroidal anti-inflammatory drugs , has been hampered in a group of patients because of different types of reactions, these is generally thought to be due to its inhibition of prostaglandin's, Nimesulide is a new NSAID with a potent anti-inflammatory , analgesic , and antipyretic effect that appears to be useful in patients that react to Aspirin and other NSAID.We studied 15 patients, all had a clear history of reaction to Aspirin and different NSAID, specially Naproxen and Sodium Diclofenac , the main reaction where angioedema of the eye lids, lips or both. The challenge with Nimesulide was done giving increasing doses of the medication every 30 min, the dose where 5 mg, 10 mg, 15 mg, 25 mg, 30 mg, 40 mg, 50 mg, with a total cumulative doses of 175 mg, the patients where the observed for 2 more hours after the last dose.Of the 15 patients only one reported angioedema of the eye lids after 1 hour of the last dose, but the reaction was less intense then his initial reaction with Sodium Diclofenac.Of the 15 patients 8 have used Nimesulide in different occasion with no problems.

650 **Copolymer–1 (Copaxone®) induces a non-immunologic activation of connective tissue type mast cells.** M Shalit MD, Z Meiner MD, F Levi-Schaffer PhD, Jerusalem, Israel

Copolymer–1 (cop–1) is a mixture of synthetic basic polypeptides, prepared to cross-react immunologically with myelin basic protein. Daily subcutaneous injections of cop–1 were recently shown to be effective in the treatment of patients with relapsing-remitting multiple sclerosis (MS) in a large multi-center double-blind study. The most commonly reported adverse effects of cop–1 are transient erythema, swelling and pain at the injection sites. To investigate the mechanism underlying these reactions, we examined the effect of cop–1 on human skin, human basophils, and rat peritoneal mast cells. Intradermal injections of cop–1 elicited classic wheal-and-flare responses in MS patients treated daily with cop–1, as well as in untreated patients. The skin test reactivity to serial dilutions of cop–1 was similar in the two groups of patients. Ingestion of terfenadine, prior to the intracutaneous administration of cop–1 (2.0 mg/ml and 20 mg/ml), significantly reduced the diameter of the wheals (mm): 9.4±1.5 vs. 4.0±2.6 and 14.5±1.3 vs. 7.6±2.8, respectively, indicating that the reaction was mediated by local histamine release. Cop–1 also induced a dose-dependent activation of rat peritoneal mast cells, starting at 0.1 µg/ml (6.5±1.2% histamine release), with a maximal release of 58.8±4.2%. In contrast, human basophils of MS patients and of healthy subjects were relatively resistant to the drug, releasing only 22–24% histamine at a 1.0 mg/ml concentration. Specific IgE anti-cop–1 antibodies were not detectable in sera of cop–1 treated patients. These results suggest that cop–1 has a direct, IgE-independent, stimulatory effect on connective tissue-type mast cells. The reactions observed at injection sites may be attributable to local histamine release from dermal mast cells.

651 **Interferon beta-1b (IFβ) Hypersensitivity and Desensitization.** MC Young, MD, J Otis, MD, South Weymouth, MA.

A 41 yo WF with mutiple sclerosis (MS) presented with facial and laryngeal edema with subsequent chronic urticaria. She took SQ injections of human recombinant IFβ for MS and also took Klonopin, Zantac, Ditropan, Imodium and Advil. The urticaria persisted despite stopping all oral meds. The IFβ was discontinued and the urticaria resolved. Following a symptom-free period, she resumed the IFβ and the hives and the angioedema recurred. Skin biopsy showed perivascular lymphocytic infiltrate consistent with urticaria. Labs showed normal CBC, diff, ESR, chemistry profile, ANA, RF, C3, C4, Clq binding, cryoglobulins and Lyme titer. Skin tests to preservative-free IFβ were negative with saline and histamine controls. Five normal subjects had negative skin tests to IFβ. Because her MS required the continuation of IFβ, she was desensitized beginning at $0.4X10^6$ IU SQ, increasing by 2X increments to $4X10^6$ IU and tapering to her maintenance dose of $4X10^6$ IU SQ, QOD. She has had no urticaria nor angioedema since, for at least 8 weeks.

Human recombinant IFβ has recently been used to reduce exacerbations of MS. Its exact mechanism of action in MS is unknown. This is the first case of IFβ hypersensitivity. Challenge with IFβ reproduced the symptoms. Although skin tests were negative, an IgE mechanism is not ruled out . This patient's desensitization to IFβ is the first report of this procedure.

652 Acute IgE-mediated generalized urticaria-angioedema after topical application of povidone-iodine. López Sáez MP,MD,Prieto A,MD, Olalde S,MD,Armentia L,Pharm D,Baeza ML,MD, Montoro A,MD,Barrio de M,MD. Madrid. Spain.

Povidone is a synthetic polymer mainly used as a suspending, dispersing, tablet binding, granulating and coating agent. In Spain is widely used as a carrier for iodine in antiseptic solutions. Only a few cases of allergic contact dermatitis to this agent have been reported. We described a patient who developed an acute allergic reaction following topical application of povidone-iodine.

A 27 yrs old male developed itching of the soles, generalized hives and swelling of the face immediately after the first topical use of Betadine™(povidone-iodine 1 mg/ml) on a right arm wound. Successful treatment was established with antihistamines and systemic steroids. Skin prick test were positive with Betadine™ and povidone in PBS (35 µg/ml) in our patient and negative in eight normal controls. Other iodine-containing drugs were tested and resulted negative. Serum specific IgE to povidone was demonstrated by ELISA but not to Betadine™ or other iodinated-containing compounds.

Conclusions: 1) An acute generalized urticaria-angioedema to topical povidone application is reported. Allergic IgE-mediated basis is supported by "in vivo" and "in vitro" tests. 2) We alert Health Authorities the relevance of a full description in drug labels as povidone is not necessarily reported as a part of the excipient in several countries.