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# NEUROLOGY

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## Recent History

An urticarial IgE-mediate...



## An urticarial IgE-mediated reaction to interferon [beta]-1b

[Clinical/Scientific Notes]

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An authoritative review of interferon (IFN) [beta] toxicity in the treatment of MS stated that type I or IV allergic reactions have not been observed or reported. [1](#) Our recent experience provides the opportunity to reexamine this important point. We report a woman with MS who manifested a type I, IgE-mediated, allergic response to the protein IFN [beta]-1b.

## Case report.

A 32-year-old woman had three discrete episodes of nonstereotyped neurologic deficit over 9 years. Her brain and spinal MRI results were consistent with demyelinating disease. Although she declined lumbar puncture, we considered relapsing-remitting MS to be an appropriate diagnosis given her clinical history and imaging data. Shortly after beginning IFN [beta]-1b, the injections evoked multiple side effects: flulike symptoms requiring nonsteroidal anti-inflammatory drugs, urinary urgency with incomplete bladder evacuation lasting 4 hours after each injection, leg cramps, and exacerbation of preexisting asthma. She had previously required albuterol therapy and short courses of antibiotics for asthmatic exacerbations that typically lasted 7 days. After IFN [beta]-1b administration, her asthmatic exacerbations lasted approximately 1 month, were less responsive to albuterol, required longer antibiotic courses, and sometimes required oral steroids. Additionally, she noted more difficulty breathing each day she received her injection. These side effects were all eliminated by decreasing the IFN [beta]-1b dosage by 75%. Thereafter, she gradually resumed the full IFN [beta]-1b dose with fewer problems. Her atopic history was also significant for multiple drug allergies, including both angioedema and urticaria in response to penicillin.

After approximately 9 months of IFN [beta]-1b treatment, she developed urticaria with one of her injections. She had multiple dime- to quarter-sized red, raised lesions distributed over the leg that was injected. These symptoms were successfully treated with diphenhydramine. With our concern for a possible allergic etiology, IFN [beta]-1b was discontinued immediately and she was referred for skin testing. The patient was tested individually with IFN [beta]-1b, IFN [beta]-1a, their respective diluents, and a histamine control by both intradermal and prick administration. Intradermally, she had an immediate 22 × 7 mm wheal and flare response to IFN [beta]-1b at 1:10 dilution and a characteristic response to histamine, but no reaction to undiluted IFN [beta]-1a or to either diluent. Prick testing is about a thousandfold less sensitive than intradermal, and none of the reagents elicited any response. The response to IFN [beta]-1b indicated immunoglobulin (Ig) E specific for this protein. With their similar protein structures and the potential for future cross-reactivity, we recommended that she substitute glatiramer acetate for IFN [beta]-1b rather than using IFN [beta]-1a. Her asthma returned to its baseline characteristics following discontinuation of the IFN [beta]-1b.

## Discussion. 🚩

We report a patient with MS, asthma, and allergic reactions to medications who developed urticaria and exacerbation of her asthma in response to injections of IFN [beta]-1b. Skin testing confirmed an IgE-mediated allergic response to the interferon itself and not to its diluent. Another patient developed severe anaphylaxis after using IFN [beta]-1a for 6 months. [2](#) Corona et al. [2](#) postulated a reaction to the drug vehicle or to a contaminant because there were no previous reports of anaphylaxis to IFN therapy. Although dermatologic side effects are common and diverse, no prior proof of cutaneous type I or IV allergic reactions have been reported, despite suspicion that

these could occur. [1,3,4](#) Skin testing of the IFN and the diluent clearly delineated the nature of the reaction in our patient and provided guidelines for alternative therapeutic options.

Although allergic reactions can occur against endogenous proteins, it seems more likely that structural differences between endogenous IFN [beta] and the synthetic IFN [beta]-1b played a key role in generating the IgE response. To enhance the yield of biologically active synthetic IFN [beta]-1b, serine was substituted for cysteine at position 17. A Met-1 deletion was a consequence of the production method. IFN [beta]-1b also differs from endogenous interferon in that it is not glycosylated. [5](#) IFN [beta]-1a, conversely, is structurally identical to endogenously produced IFN [beta]. The lack of allergic response to skin testing of IFN [beta]-1a may be attributable to the more exact structural replication.

The IFN [beta] therapy appeared to worsen our patient's asthma. We do not think that this was an allergic reaction, but rather was likely secondary to a biological effect of the interferon. Interferons can act as potent proinflammatory compounds. IFN [beta] increases interleukin (IL)-10 activity and reduces IL-12 activity, both potentially aggravating asthma. [6,7](#)

We conclude that IFN [beta]-1b can evoke a specific IgE response with potentially significant clinical manifestations.

Note added in proof. After 11 months of treatment with glatiramer acetate, she developed a generalized urticarial reaction to this agent, thus extending a single prior case report (Bayerl C, Bohland P, Jung EG. Systemic reaction to glatiramer acetate. *Contact Dermatitis* 2000;43:62–63).

## References

1. Walther EU, Hohlfeld R. MS: side effects of interferon beta therapy and their management. Neurology 1999; 53: 1622–1627. [Catalogo Biblioteca ISS Full text \(pacchetto Ovid\) Full text \(sito editore\) Bibliographic Links](#) [\[Context Link\]](#)
2. Corona T, Leon C, Ostrosky–Zeichner L. Severe anaphylaxis with recombinant interferon beta. Neurology 1999; 52: 425. [Catalogo Biblioteca ISS Full text \(pacchetto Ovid\) Full text \(sito editore\) Bibliographic Links](#) [\[Context Link\]](#)
3. Vial T, Descotes J. Clinical toxicity of the interferons. Drug Saf 1994; 10: 115–150. [Catalogo Biblioteca ISS Bibliographic Links](#) [\[Context Link\]](#)
4. Van Rengen A, Goossens A. Local reactions after subcutaneous injections of [beta]-interferon. Contact Dermatitis 1997; 39: 209. [Catalogo Biblioteca ISS Bibliographic Links](#) [\[Context Link\]](#)
5. Runkel L, Meier W, Pepinsky RB et al. Structural and functional differences between glycosylated and non-glycosylated forms of human interferon-[beta] (IFN-[beta]). Pharm Res 1998; 15: 641–649. [Catalogo Biblioteca ISS Bibliographic Links](#) [\[Context Link\]](#)
6. Hohlfeld R. Biotechnological agents for the immunotherapy of MS. Brain 1997; 120: 865–916. [Catalogo Biblioteca ISS Bibliographic Links](#) [\[Context Link\]](#)
7. Borish L, Rosenwasser L. TH1/TH2 lymphocytes: doubt some more. J Allergy Clin Immunol 1997; 99: 161–164. Letter. [Catalogo Biblioteca ISS Bibliographic Links](#) [\[Context Link\]](#)

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