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Delayed Anaphylaxis to the flu vaccine unrelated to known non-viral components

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Vaccine; anaphylaxis; influenza

Summary
On February 4, 2010 the CDC's Advisory Committee on Immunization Practices voted for universal flu vaccination to expand protection against the flu throughout the United States. In addition to this administration expansion, six new influenza vaccines have been introduced into the market possibly introducing new allergenic potentials. We report two cases of delayed anaphylaxis to the flu vaccine.

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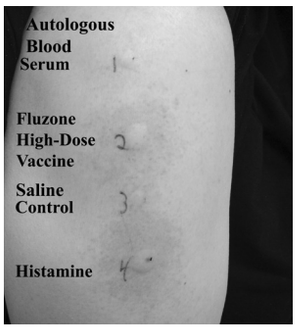
On February 4, 2010 the CDC's Advisory Committee on Immunization Practices voted for universal flu vaccination to expand protection against the flu throughout the United States (1). In addition to this administration expansion, six new influenza vaccines have been introduced into the market since 2012 (2). Although patients are screened for sensitivity to vaccine components prior to administration to avoid Vaccine Adverse Reactions (3,4), we report two cases consistent with multisystem allergy, one 3 hours and the other 5 hours post administration of Fluzone Intradermal and Fluzone High-Dose vaccination, unrelated to known non-viral components. While anaphylactic reactions typically occur within minutes (5), delayed onset reactions have been reported after the administration of omalizumab (6) and Japanese encephalitis vaccine (7) and the ingestion of red meat containing galactose-alpha-1,3-galactose (alpha-gal) (8). Furthermore, it has been reported in the Institute of Medicine Report (9) that there have been 8 reports of anaphylaxis following Fluzone administration, of which the onset interval of 7 of the cases occurred within 24 hrs.

Case 1

A 71-year-old woman received the Fluzone High-Dose vaccine 0.5 mL intramuscularly and reported throat pain, shortness of breath, chest pain, erythematous hands, and generalized urticaria 5 hours post-vaccination. She proceeded to the Emergency Room and was treated with methylprednisolone and diphenhydramine. Symptomatic resolution occurred within 72 hours. She received prior influenza vaccination without incident. Past allergic history is significant for latex for which she reports an immediate rash reaction with no other associated symptoms, and radiocontrast media sensitivity for which she developed flushing and shortness of breath minutes after administration. The patient denies allergic reactions to eggs. Past medical history includes diverticulosis. Medications include Evista 60 mg oral daily, aspirin 81 mg oral daily and a daily multi-vitamin. The components of the Fluzone High-Dose vaccine include 60 mcg HA of A (H1N1), A (H3N2) and B. Other reported in-

gredients include sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde (< 100 mcg) and octylphenol ethoxylate (< 250 mcg), and the vaccine does not contain mercury or other preservatives, antibiotics or gelatin nor does the syringe contain natural rubber latex (10). It contains approximately 0.1 mcg of ovalbumin per dose (11). Intradermal testing showed no reactivity to saline control and a 10 mm wheal and 25 mm of erythema to both Fluzone High-Dose vaccine at 1:100 concentration and histamine 0.1 mg/ml (**figure 1**). Additional skin testing showed no reactivity to latex.

Figure 1 *- Intradermal testing showing high sensitivity to the Fluzone high-dose vaccine.*



Case 2

A 42-year-old woman received the Fluzone Intradermal vaccine 0.1 mL and developed dry cough, chest pain, dyspnea, palpitations and bilateral periorbital angioedema 3 hours post-vaccination. Her symptoms resolved within 24 hours without treatment. She tolerated her first influenza vaccination 2 years prior without incident. The patient reports a rash with amoxicillin but denies allergies to egg or latex. The patient otherwise denies any past medical history and currently does not report taking any medications. The components of the Fluzone intradermal vaccine include 9 mcg HA of A (H1N1), A (H3N2) and B. Other reported ingredients include sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde (< 20 mcg) and octylphenol ethoxylate (< 50 mcg) and does not contain mercury or other preservatives, antibiotics or gelatin, nor does the syringe contain natural rubber latex (12). It contains approximately 0.02 mcg of ovalbumin per dose (11). Prick testing to Fluzone Intradermal and Fluvarin vaccine, an influenza vaccine containing egg proteins (≤ 1 mcg ovalbumin), polymyxin (≤ 3.75 mcg), neomycin (≤ 2.5 mcg), betapropiolactone (not more than 0.5 mcg) and nonylphenol ethoxylate (not more than 0.015% w/v), and the tip caps of the prefilled syringes may contain natural rubber latex (13), both showed a 3-4mm wheal and 10 mm of erythema, and intradermal testing showed a 6-7 mm wheal and 12 mm of erythema for the same at 1:100 concentrations. Prick testing was negative to egg yolk/white. Latex prick testing was negative.

Since 2012, six new influenza vaccines have been approved by the FDA (2). As more variations of the influenza vaccine become available, as developed by different manufacturers, each of the viral components pose potential new allergens, thereby increasing the potential risk of sensitization and reaction as described in the cases above. With new influenza vaccines reaching the market, health care providers who administer vaccinations need to be cognizant of the potential for adverse effect that may occur immediately or delayed.

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