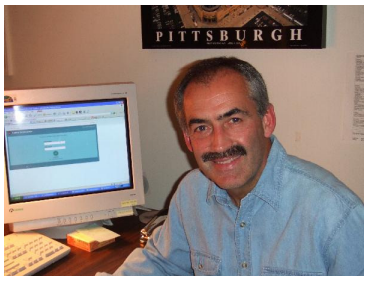
Clinicians Corner



By Dr. Ray Stierer, Pharm D

Flu Season (Again)- September 2008

It's that time of year again, flu season. Many of our patients will receive a flu vaccine. There is conflicting information as to whether or not an interaction occurs with warfarin. Early studies vary from no effect [1,2], to an increase in the INR [3] or decrease in INR [4]. These studies were done in a small number of patients and prior to laboratory standardization of reporting prothrombin times as INRs. This interaction is also listed in the influenza package insert, and implies that warfarin levels may increase, but that this interaction is of little consequence. The insert states, "Although influenza vaccination can inhibit the clearance of warfarin, theophyllin, phenytoin, and aminopyrine therapy, studies have failed to show any adverse clinical effects attributable to these drugs in patients receiving influenza vaccine."[5]

In 2002, Poli et al[6] did the first large study in 73 anticoagulated patients who had received the influenza vaccine. Patients were followed for at least 3 months before and 3 months after vaccine administration. Patients were compared to a control group of 73 anticoagulated patients who did not receive the vaccine. Overall, they found no difference in the overall time spent within, above or below the therapeutic range over the 6 month period. However, for patients over 70 years of age (46.5% of the total number of patients), they observed a statistically significant DECREASE in anticoagulation intensity during the first month after vaccination and persisted for up to 3 months after vaccination. These patients spent a prolonged time below the therapeutic range, 10% before vaccination compared to 27% after, $p = .001$. This effect was not detectable after 6 months. Although not statically significant, 27% of the vaccinated patients > 70 required a $\geq$ 10% increase in warfarin dosage, versus 16% in the controls > 70.

In 2003, Paliani et al[7], obtained an INR in 90 consecutive patients, (mean age of 74), within 7 to 10 days post vaccination. These investigators found that in 49 of 90 patients, the INR INCREASED from 2.64 to 3.85 +/- 0.98.

Two additional studies were published in 2007. MacCallum[8] et al, found that there was NO EFFECT on the INR in 78 patients, average age of 74, when followed for 7 to 10 days post vaccination. Jackson et al[9], retrospectively

followed 4923 patients, 18 years of age or older, for up to 4 weeks post influenza vaccination and found NO EFFECT on the INR, regardless of the age of the patient. These most recent studies suggest that patients who receive the influenza vaccine do not additionally INR monitoring.

So how do we manage our patients who receive the influenza vaccine? Despite conflicting data in the literature, some studies suggest the need for more frequent INR monitoring in elderly patients during the first few weeks and possibly months following influenza vaccination. Personally, I instruct elderly patients to have a follow-up INR within 1 to 2 weeks after receiving the vaccine, although current literature suggests that this may be unnecessary.

1. Lipsky BA, Pecoraro RE, Roben RJ et al. Influenza vaccination and warfarin anticoagulation. Ann Intern Med 1984;100:835-7.

2. Souto JC, Oliver A, Montserrat I, et al. Lack of effect of influenza vaccine on anticoagulation by acenocoumarol. Ann Pharmacother 1993;27:365-368

3. Kramer P, Tsuru M, Cook E, et al. Effect of influenza vaccine on warfarin anticoagulation. Clin Pharmcol Ther 1984;35:416-8.

4. Bussey HI, Saklad JJ. Effect of influenza vaccine on warfarin therapy. Drug Intell Clin Pharm 1988;22:198-201.

5. Fluzone package insert. Swiftwater, PA: Aventis Pasteur Inc; 2007 June.

6. Poli D, Chiarugi L, Antonucci E, et al. Need for more frequent International Normalized Ratio monitoring in elderly patients on long-term anticoagulant therapy after influenza vaccination. Blood Coagul Fibrinolysis 2002;13:297-300.

7. Paliani U, Filippucci E, Gresele, P. Significant potentiation of anticoagulation by flu-vaccine during the season of 2001-2002. Haematilogica 2003;88:599.600.

8. MacCallum P, Madhani M, Mt-Isa S, et al. Lack of effect of influenza immunization on anticoagulant control in patients on long-term warfarin. Pharmacoepidemiol drug saf 2007;16:786-9.

9. Jackson ML, Nelson JC, Chen RT, et al. Vaccines and changes in coagulation parameters in adults on chronic warfarin therapy: a cohort study. Pharmacoepidemiol drug saf 2007;16:790-6.