

Beware Tamiflu!

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I wish to draw readers' attention to some new research on the neuropsychiatric side effects of Tamiflu of which I was unaware when my article "Flu Warning: Beware the Drug Companies!" [NYR, May 12] went to press.

In an article dated December 2010 (but published in March 2011), Toshiharu Fujita and colleagues presented a study of 9,386 influenza patients under the age of eighteen. They found that episodes of loss of consciousness were roughly 80 percent more common among those who had taken Tamiflu compared to those who had not.*

*Toshiharu Fujita et al., "A Pharmacoepidemiological Study on the Relationship between Neuropsychiatric Symptoms and Therapeutic Drugs after Influenza Infection," *Japanese Journal of Pharmacoepidemiology*, December 2010, available at www.jstage.jst.go.jp/article/jjpe/15/2/73/_pdf. Before Fujita died in January 2011, he agreed to share his data and methods with all scientists on request.

This study was exploratory and relied on questionnaires filled out by parents. However, the findings are consistent with at least four animal toxicity studies of Tamiflu, all of which found that the drug caused suppression of the central nervous system in baby rats. Further investigation of the side effects of Tamiflu are therefore urgently needed.

Dr. Fujita was also one of the lead authors of the original study of reactions to influenza medications involving 2,846 children that I described in my article. At first the authors of that study concluded that Tamiflu was not associated with neuropsychiatric events. However, after Rokuro Hama of the Institute of Pharmacovigilance reanalyzed the data and found that the risk of neuropsychiatric events was elevated more than fourfold among the children who had taken Tamiflu, Fujita undertook the second larger study in order to resolve the issue.

When a journalist pointed out that Fujita had received funding from Chugai, Tamiflu's Japanese

manufacturer, the Japanese Ministry of Health Labor and Welfare took the data away from him and commissioned other researchers to analyze it instead. They found no elevated risk of any neuropsychiatric events among the children who took Tamiflu.

However, Rokuro Hama found errors in their analysis that were far more egregious than those in Fujita's original, smaller study. These concerns were raised at a symposium at the Japanese Society of Clinical Pharmacology and Therapeutics in December 2008, after which the ministry returned the data to Fujita. He analyzed it once again and found that the risks of delirium and unconscious episodes were indeed significantly elevated in children who took Tamiflu, especially if they took the drug during the first day or so after influenza symptoms appeared.

This may be because of the expression of cytokines—host molecules expressed during early infection that fight the virus but also weaken the blood-brain barrier, allowing drugs

like Tamiflu to enter the brain. If these results are confirmed, they are especially worrying, since the World Health Organization and the US Centers for Disease Control both recommend that Tamiflu be taken as soon as possible after symptoms appear.

I was not the only one unaware of this important study; neither, apparently, were the World Health Organization, the US Food and Drug Administration, and the US Centers for Disease Control. When I contacted these agencies in January and February 2011, their spokespeople assured me that there was no evidence that Tamiflu causes neuropsychiatric side effects in children.

An additional correction: Rokuro Hama was asked to review the case histories of children with possible neuropsychiatric reactions to Tamiflu in 2005, not 2002. He immediately suspected Tamiflu, rather than influenza itself, because he knew from toxicity studies that the drug caused sudden death in animals. Influenza can kill, but it does not cause sudden death.