Published in final edited form as:

Alcohol Clin Exp Res. 2010 August ; 34(8): 1432. doi:10.1111/j.1530-0277.2010.01227.x.

A Sigh of Relief About Treating Influenza in Individuals With Alcohol-Use Disorders?

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The recent outbreak of so-called “swine flu,” or influenza caused by an H1N1 strain of the influenza A virus, has renewed the public fear (as well as within the medical community) about pandemic influenza. However, we must all remember that seasonal epidemic influenza has always been a serious public health concern. For example, an average of more than 41,000 per year died of influenza in the United States alone between 1979 and 2001 (Dushoff et al., 2006). Although annual vaccinations remain the foundation of public health efforts to limit the severity of seasonal epidemics, many unvaccinated individuals are either exposed to the virus or present with frank influenza illness and are treated with neuraminidase inhibitors such as oseltamivir (trade name Tamiflu) to reduce symptoms and/or transmission of the virus (Moscona, 2005). Although it has long been known that individuals with chronic alcohol-use disorders are at increased risk of a wide variety of community-acquired lung infections, there are no specific studies that have examined the role of alcohol-use disorders on the risks of acquiring and/or spreading influenza. However, studies in animal models have raised concerns; in particular, a study by Legge and colleagues showed that chronic alcohol consumption increased the mortality of influenza infection in a murine model (Meyerholz et al., 2008). In parallel, our group has shown that chronic alcohol ingestion increases the severity of acute edematous lung injury by impairing the normal epithelial barrier in the lung and placing an increased burden on the active transport of sodium and water from the airways to keep the airspaces dry (Guidot et al., 2000; Otis et al., 2008). In parallel, we also determined that the influenza virus interferes with this active fluid transport in the lung (Chen et al., 2004). Taken together, these experimental findings suggest that even otherwise healthy individuals with a chronic alcohol-use disorder could be at increased risk of acute edematous lung injury and death from influenza. Unfortunately, these subjects are also less likely to receive annual vaccinations, and therefore, their survival could depend on the ability of drugs such as oseltamivir to limit the acute illness.

In this regard, the findings by Legge and colleagues (Langlois et al.) in the current issue provide some cautious optimism from their murine model that, at least in otherwise healthy subjects with underlying chronic alcohol use, oseltamivir might remain effective in limiting the severity of acute influenza illness. Specifically, mice given ethanol for 8 weeks in their drinking water and then inoculated with influenza virus had a 60% mortality when compared to a 15% mortality in control mice. In contrast, oseltamivir treatment markedly decreased morbidity and completely prevented any mortality in both control and ethanol-treated mice. Consistent with the elimination of mortality, oseltamivir decreased viral shedding and lung inflammation in both groups. Although one must obviously interpret these experimental

findings cautiously, this study suggests that neuraminidase inhibitors retain their ability to limit the severity of acute influenza pneumonia even in the context of chronic alcohol ingestion. Although it appears for now that the extent and severity of the current H1N1 epidemic has been far less than initially feared, public health officials and clinicians can never drop their guard as epidemic seasonal influenza and intermittent (and unpredictable) pandemics are inevitable. For now, this new study suggests we can remain hopeful that antiviral drugs used to limit the spread of influenza in unvaccinated individuals will retain their efficacy even for those who suffer from chronic alcohol-use disorders.

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