

Tamiflu & influenza vaccines: more harm than good?

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Rapid Response:

TAMIFLU & INFLUENZA VACCINES: MORE HARM THAN GOOD?

Owen Dyer reminds us that we have spent billions on a drug that possibly does more harm than good. (BMJ 2020;368:m626—February 19) The same thing can be said about influenza vaccines.

We hear so much about the vital importance of flu shots that it will come as a nasty surprise to learn that they increase the risk of illness from noninfluenza virus infections such as rhinoviruses, coronaviruses, RS viruses, parainfluenza viruses, adenoviruses, HMP viruses and enteroviruses. This has been shown in at least two studies that have received little attention from public health authorities: A prospective case-control study in healthy young Australian children found that seasonal flu shots doubled their risk of illness from noninfluenza virus infections (unadjusted OR 2.13, CI 1.20—3.79). Overall, the vaccine increased the risk of virus-associated acute respiratory illness, including influenza, by 73% (OR 1.73, CI 0.99—3.03). (Table 2 in Kelly et al, *Pediatr Infect Dis J* 2011;30:107)...A randomized placebo-controlled trial in Hong Kong children found that flu shots increased the risk of noninfluenza viral ARIs fivefold (OR 4.91, CI 1.04—8.14) and, including influenza, tripled the overall viral ARI risk (OR 3.17, CI 1.04—9.83). (Table 3 in Cowling et al, *Clin Infect Dis* 2012;54:1778)....To my knowledge, the foregoing risk figures have not been explicitly published anywhere. They will not be found in the abstracts of the articles, so you have to go to the tables and look at the numbers themselves.

What is going on? We are told year after year that influenza vaccines are 60% effective...30% effective...45% effective...etc. Does this mean that they prevent a significant proportion of all viral respiratory infections? No, these reports are based on non-randomized surveys known as “test-negative case-control studies”; they look only at influenza infections and make no attempt to look at the other 200-plus respiratory viruses. Furthermore, they make no attempt to look at any vaccine adverse effects such as seizures, narcolepsy, Guillain-Barre’ syndrome, or oculorespiratory syndrome.

How can influenza vaccines increase the risk of other infections? There are at least two possible mechanisms: first, influenza vaccines probably alter our immune systems non-specifically to increase susceptibility to other infections; this has been observed with DTP and other vaccines. (Benn et al, *Trends in Immunology*, May 2013) Secondly, there is the phenomenon of “viral interference” in which a virus infection stimulates the innate immune system to provide temporary and non-specific protection against other viruses. By preventing influenza infection a vaccine could prevent this unexpected but positive side effect. The Cowling study discusses this possibility in some detail. A recent study of virus population dynamics found, at least, that influenza A prevented subsequent rhinovirus infections, and influenza B prevented adenovirus infections. (Nickbakhsh et al, *PNAS*, 12 Nov 2019)

In the US seasonal influenza vaccines are now recommend every year for the entire population (excepting infants before 6 months of age). It is important to realize that this policy was instituted without acquiring safety and effectiveness data from randomized controlled trials. When routine vaccination for healthy young children was being contemplated some experts in pediatrics and infectious disease issued warnings. Kenneth McIntosh called for the performance of multi-center randomized trials over several

seasons before such a policy was instituted. In explicit language he worried about adverse effects, and the possibility that the risks of annual vaccination would outweigh the benefits. (Editorial, NEJM 2000;342:275) Twenty years later we must ask, “What harm is done by annual influenza vaccines? Where is the balance between risks and benefits?”

One of the imponderables is the effect of seasonal influenza vaccines on population immunity. Individuals who recover from influenza can have broad and long-lasting protection against an array of influenza viruses. First infections in young children can provide this, a phenomenon known as “imprinting”; this is subverted by childhood vaccination. Furthermore, the protection in adults who still carry the imprint from childhood may be subverted by the seasonal flu vaccine. This was seen in middle-aged adults during the 2018/19 influenza A(H3N2) epidemic in Canada; vaccine recipients suffered a nearly fivefold risk of illness from a drifted strain of A(H3N2), compared with unvaccinated individuals (OR 4.67, CI 1.85-11.82). (Skowronski et al, EuroSurveillance, 14 Nov 2019).....What are we doing to population immunity with wide annual distribution of seasonal flu vaccines? Are our annual epidemics getting milder or more severe? What effect will years of seasonal influenza vaccines have on the next pandemic? Remember the 2009 swine flu pandemic? The risk of severe pH1N1 illness in Quebec increased progressively according to the number of seasonal flu shots received in previous years and was more than threefold in individuals who had received five vaccinations in five years, compared with unvaccinated individuals (adjusted OR 3.24, CI 1.97—5.34). (Table 5 in Skowronski et al, PLoS Medicine, April 2010)

In the US a regular feature of publicity urging annual flu shots are mathematical estimates of deaths caused by influenza, provided by the CDC. Since the 2010-11 season these estimates have ranged between 12,000 and 79,000 US deaths each season. The numbers are far in excess of actual cases documented in death certificates or by surveillance networks reporting on laboratory test-positive cases. While we wait for better numbers, it is not merely academic to ask what we would find if we focused as intensively on other respiratory viruses as we do on influenza. If influenza vaccines increase the overall risk of viral ARIs, as they do in the studies discussed above, would they also increase the overall number of ARI deaths? Tamiflu and influenza vaccines: more harm than good?

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