

## Major flu strain resistant to widely used antiviral drug

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One of the major strains of the influenza virus this season has become resistant to Tamiflu - rendering the mainstay antiviral drug all but impotent and creating tough treatment options for patients who come down with the flu.

On Dec. 19, the federal Centers for Disease Control and Prevention (CDC) alerted local health authorities that an early testing of the most common type of seasonal flu found that it has become virtually impervious to Tamiflu.

The resistance, apparently triggered by a spontaneous mutation in the virus, comes three years after a different subtype of the flu virus became widely resistant to another drug class.

In response, state and local health officials are advising doctors to hedge their treatments by simultaneously prescribing Tamiflu and a second antiviral medicine. The hope is that the combination will work against influenza A virus before doctors have a chance to identify the particular strain.

But doubling up on the medicine not only drives up costs but also could put patients at higher risk for side effects - some potentially serious.

"The decision to treat now is much more difficult," said Dr. Yuan-Po Tu, an associate medical director at The Everett Clinic who oversees its flu shot clinic.

All that underscores the value of getting vaccinated to ward off the flu in the first place, Tu said.

Tu said he was startled at how quickly the virus became resistant to Tamiflu. During the 2007-2008 flu season, 11 percent of the H1N1 virus, one of the two subtypes of influenza A, was found to be Tamiflu-resistant. So far this season, a small sampling tested by the CDC found the resistance has grown to 98 percent.

Since January 2006, Tamiflu has been the only antiviral option for millions of Americans - including all children under 7 - after another influenza A strain, H3N2, became resistant to an older class of antivirals called adamantanessold as amantadine or rimantadine. Adamantanes do not work against a third virus strain, influenza B, but Tamiflu does. Another antiviral, Relenza, is effective against all three strains. But Relenza is not widely available and comes in a powder form that is difficult for some patients to inhale.

What's more, lab tests to distinguish between H1N1 and H3N2 strains can take up to a week, too late for flu patients, who must start antiviral therapy within 48 hours of symptoms (testing for influenza A or B can be done in as little as an hour).

That left Tamiflu as the preferred all-purpose drug because - at least until the new resistance - it worked against all three flu strains and was well tolerated by patients. "We could lose a very, very useful drug very, very quickly," Tu said.

Tu said amantadine, on the other hand, can cause such side effects as disorientation, especially if it's taken for longer than five days. And in rare cases, some patients have reported having suicidal thoughts while taking amantadine. But amantadine is much cheaper than Tamiflu, with a retail price of about \$18 for five days, compared with \$127.

The public-health risks from the Tamiflu resistance will depend on the severity of a flu outbreak and whether H1N1 turns out to be the predominant strain, said Dr. Jeff Duchin, chief of communicable-diseases section of Public Health - Seattle & King County.

Duchin said the Tamiflu resistance won't be a problem for most people who get the flu. But patients in hospitals and nursing homes or others with weakened immune systems face greater danger.

"For a small subset of people, antiviral can be a lifesaver," Duchin said.

The dominant strain can vary from season to season and even from community to community, said Dr. Marcia Goldoft, an epidemiologist with the communicable-diseases section of state Department of Health.

In some years, the flu season is over by the first part of January; other years, it doesn't get going until February, Goldoft said. Normally, flu cases peak in February or March.

Duchin said it's not too late for flu shots, which take about 10 days to build immunity. This year's vaccine is well matched against the current strain. Depending on the years, vaccines can prevent anywhere from 40 percent to 85 percent of people from getting the flu, he said.

"If you are really worried about the flu, vaccination is the best option," Duchin said.

Each year, some 36,000 Americans - the vast majority of them elderly - die of flu. But children, the most efficient transmitters of virus and bacteria, account for the biggest share of flu cases.

Federal guidelines recommend annual flu shots for everyone between 6 months and 18, and 50 and older, as well as pregnant women and people

with chronic medical conditions or weakened immune systems. Health care workers and those who care for small children also are encouraged to get vaccinated.

But only 30 percent of American adults had gotten flu shots by mid-November this season, according to a survey by Rand Health, a research arm of the nonprofit think tank Rand Corp.

Among adults for whom vaccination is recommended, the rate was only slightly higher, at 37 percent.

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