Beat: Health

H7N9 bird flu resistant to antivirals in some cases, worrying experts

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USPA News - Some strains of the new H7N9 bird flu virus that emerged in China this year have developed resistance to the only antiviral drugs available to treat the infection, and misleading test results could help hasten the spread of these resistant strains, researchers have warned. The study, of which the results were published in the online journal of the American Society for Microbiology on Tuesday, characterized viruses taken from the first persons known to be stricken with H7N9 influenza and found that 35 percent of those viruses are resistant to oseltamivir (Tamiflu) and zanamivir (Relenza), both front line drugs used to treat patients suspected or diagnosed with H7N9. But the authors found that lab testing of the viruses, which detects the activity of a viral enzyme, fails to detect that these strains are resistant.

Robert Webster of St. Jude Children`s Research Hospital in Memphis, Tennessee said resistant strains of H7N9 can flourish in patients who are treated with oseltamivir or zanamivir, inadvertently leading to the spread of resistant infections. In the study, the authors tested antiviral susceptibility of an H7N9 strain isolated from the first confirmed human case of H7N9 bird flu using a method that tests the activity of the neuraminidase enzyme. The results showed the strain was susceptible to NA inhibiting antiviral drugs, but it is not. A closer look at the viral isolate revealed it is actually made up of two distinct types of H7N9 viruses. Roughly 35 percent of the viruses carry the R292K mutation, making them resistant to NA inhibitors, and 65 percent are sensitive to these same drugs. Webster said the enzyme-based testing gave misleading results because the functioning wild-type enzymes masked the presence of the non-functioning mutant enzymes. Using NA inhibitors to treat a patient infected with a resistant strain of H7N9 only encourages the virus to proliferate and can lead to enhanced spread of the resistant strain, according to the researchers. They wrote that these results prove that it is crucial to use a gene-based surveillance technique that can detect these resistant influenza strains in a mixed infection. "If H7N9 does acquire human-to-human transmissibility, what do we have to treat it with until we have a vaccine? Oseltamivir," Webster said. "We would be in big trouble." Health authorities have reported a total of 133 laboratory-confirmed cases, all but one of them in China, since the outbreak began in February of this year. The closure of live poultry markets and warmer weather have stopped the spread of the disease, at least for now. Of those infected with the illness, 43 people have died, according to the National Health and Family Planning Commission in China. A recent study found that antiviral treatment failed in two patients infected with a strain of H7N9 influenza that carries a mutation called R292K, and that these patients had a poor clinical outcome. The mutation causes a change in the neuraminidase gene and makes the virus resistant to neuraminidase (NA) inhibitors, including Tamiflu and Relenza. NA inhibitors have been the front line therapeutic option for treating H7N9 influenza because the virus is already resistant to M2 ion channel blockers Amantadine (Symmetrel) and its methyl derivative Rimantadine (Flumadine). The authors of the study have urged experts to continue to evaluate the sensitivity of clinical isolates to NA inhibitors and to monitor for the emergence of resistant variants. Webster said that, if the history of the well-known H5N1 variant is a guide, then H7N9 could rapidly evolve the ability to spread from person to person. He said the situation could become `quite serious` if the virus evolves to spread from person to person and re-emerges this fall. In the event of a widespread outbreak, Webster said Tamiflu and Relenza will `work alright` as treatments, but the development of the R292K mutation puts those options in jeopardy. However, he also pointed out that antiviral resistance is something of a burden for influenza viruses, making the spread of fitter wild-type H7N9 strains more likely. But regardless of whether H7N9 will return in the fall, Webster said the lack of suitable drugs for influenza is a grave cause for concern. "The great need at the moment are additional drugs aimed at additional sites in the influenza genome. There are some in the pipeline, but they are still under testing at the moment," he said. "We`d better get some vaccine seed stocks up and ready. The antiviral option for controlling H7N9 isn`t too good."

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