Why did healthy children fall critically ill in the 2009 H1N1 flu pandemic?

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During the 2009 H1N1 influenza pandemic, many previously healthy children became critically ill, developing severe pneumonia and respiratory failure, sometimes fatal. The largest nationwide investigation to date of influenza in critically ill children, led by Children's Hospital Boston, found one key risk factor: Simultaneous infection with methicillin-resistant *Staphylococcus aureus* (MRSA) increased the risk for flu-related mortality 8-fold among previously healthy children.

Moreover, almost all of these co-infected children were rapidly treated with vancomycin, considered to be appropriate treatment for MRSA. The fact that they died despite this treatment is especially alarming given the rising rates of MRSA carriage among children in the community.

"There's more risk for MRSA to become invasive in the presence of flu or other viruses," says study leader Adrienne Randolph, MD, MsC, of the Division of Critical Care Medicine at Children's Hospital Boston. "These deaths in co-infected children are a warning sign."

The researchers hope their findings, published Nov. 7 by the journal *Pediatrics*, (eFirst pages) will promote flu vaccination among all children aged 6 months and older. (No flu vaccine is currently available for children younger than 6 months.)

"The 2009 H1N1 virus has not changed significantly to date," notes Tim Uyeki, MD, MPH, of the Influenza Division of the National Center for Immunization and Respiratory Diseases, Centers for Disease Control and

Prevention (CDC), a senior investigator on the study. "Infections of children in the U.S. with 2009 H1N1 virus are expected this season and need to be prevented and treated appropriately. Influenza vaccination protects against 2009 H1N1 illness."

With emergency funding from the National Institutes of Health, Randolph and her colleagues in the Pediatric Acute Lung Injury and Sepsis Investigator's Network tracked 838 children admitted to 35 pediatric ICUs around the country with probable 2009 H1N1 influenza from April 2009 to April 2010. Their vaccination status wasn't consistently known, but H1N1 vaccine did not become available until September 2009 or later.

The median age of the children critically ill with H1N1 was 6 years. Most had respiratory failure, two thirds required mechanical ventilation, and some required extracorporeal membrane oxygenation (ECMO) for advanced cardiac and respiratory support. Their disease progressed rapidly, and 75 children (9 percent) died, two thirds of them within two weeks of ICU admission.

"Some children were quickly overwhelmed, and many died despite centers doing everything to save them," says Randolph. "Early in the pandemic, centers were worried that they would run out of ventilators, that they would run out of ICU beds."

While most of the children critically ill with H1N1 had one or more chronic health conditions that increased their risk, such as asthma, neurologic disorders or compromised immune systems, 251 children (30 percent) were previously healthy.

Among these otherwise healthy children, the only risk factor that was identified for death from influenza was a presumed diagnosis of MRSA co-infection in the lung – which increased the risk for mortality 8-fold

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