

OREGON PUBLIC HEALTH DIVISION • DEPARTMENT OF HUMAN SERVICES

A NOVEL H1N1 INFLUENZA VIRUS (NÉ “SWINE FLU”) ARRIVES

*Some say the world will end in fire,  
Some say in ice.  
From what I've tasted of desire  
I hold with those who favor fire.  
But if it had to perish twice,  
I think I know enough of hate  
To say that for destruction ice  
Is also great  
And would suffice.<sup>1</sup>*

EVENTS IN THE H1N1 “swine flu” epidemic are moving so rapidly that it is futile to provide up-to-the-minute information about the current situation in these printed pages. Rather, we hope to provide some useful background information and some orientation to on-line resources for Oregon clinicians. Current recommendations covering a dizzying array of situations are available on line at both the Public Health Division’s and the CDC’s web sites:

<http://www.flu.oregon.gov>  
<http://www.cdc.gov/h1n1flu>

**VIROLOGY**

The influenza virus has a 8-segmented RNA genome. That segmentation allows a wholesale reassortment of constituent genes in addition to mutational sequence changes. Thus, influenza viruses change by what is called “drift” (accumulating point mutations) and “shift” (substitution of whole gene segments). Drift forces vaccine makers to constantly tweak the cocktail of viral antigens in order to maximize efficacy, but shift can punctuate even that tenuous equilibrium. The sudden shift to a quite different antigenic profile can all but wipe the immunological slate clean, stripping away the protections afforded by past exposures and herd immunity.

Influenza viruses are classified into types (A, B, or C) based on internal protein structure.\* Influenza A viruses are subtyped based on immunogenic surface glycoproteins: hemagglutinin (H) and neuraminidase (N). H3N2 and H1N1 serovars circulate widely among humans. The virus in the spotlight today is apparently a novel H1N1 combination—for humans, at any rate—containing

segments of porcine, avian, and human origin. Thus, any “swine flu” label is shorthand for a beast with a complicated pedigree, and another sobriquet may emerge. There is some effort to rebrand this as “H1N1 influenza,” which is certainly accurate, but rather confusing; lots of other H1N1 viruses have been circulating for decades, including this past flu season. The emergence of this virus does not reflect the appearance of a new antigenic type but rather with a novel combination of pre-existing human and animal genomic segments. In any event, the new H1N1 virus is not positive by pre-existing H1 assays; hence it appears to be “H1-negative” or “untypable.” PCR primers specific to the new variant are now in use at Oregon’s Public Health Laboratory.

Influenza—in all its variants—is an acute respiratory illness associated with fever. Other common signs and symptoms include cough, sore throat, body aches, headache, chills and fatigue; GI symptoms (e.g. diarrhea, vomiting) are less common. The full spectrum of illness associated with this new variant is not well characterized. Severe illness (including pneumonia and respiratory failure) with many deaths was initially reported in Mexico, but few of these cases could be lab-confirmed, and there is an increasing consensus (even in Mexico) that the number of severe virus-associated cases may be much lower than initially thought. Elsewhere, including the U.S., most cases to date have been relatively benign—similar to typical seasonal influenza. This could be an artifact of surveillance (e.g., more complete ascertainment in the U.S., more of a focus on hospitalized cases in Mexico); or it could reflect other factors (e.g., exacerbating effects of co-morbidity, delays in seeking sophisticated medical care); time (and better data) will tell.

Of course, even if the average infection is relatively mild, any disease that affects millions of people carries the potential to wreak havoc; there are thousands of people who may find themselves the unhappy outliers on the curve. The incubation period for the new flu is not well defined. Old flu typically

manifests within 1–4 days of exposure—rarely up to a week. Some reports suggest a somewhat longer average for the new H1N1 infections. People typically become infectious a day or so before symptoms manifest, and should be assumed contagious for up to 7 days after clinical onset. Influenza is usually spread by droplet nuclei or exposure to a contaminated fomes (e.g., a doorknob or handrail). Person-to-person transmission, including transmission to health care workers,† has been amply confirmed, although the degree of transmissibility is not well characterized. While the strength of partial immunity from past exposure to homologous viruses is uncertain, it is not a given that it is a flat zero in all age cohorts.

**A BRIEF HISTORY**

The pandemic potential of influenza has been recognized at least since the “Spanish Flu” that flared in 1918–19; earlier pandemics are well known. As many as 20 million people died in that pandemic, with the highest mortality rates among relatively young and thereto healthy adults. The degree to which that extraordinary virulence was due to largely untreatable co-infections, relatively poor supportive care, and social conditions of the time—as opposed to any inherent virulence of the virus—has been long debated. Much smaller but still significant pandemics, each attendant on genomic shifts, were recognized in 1957 (“Asian” flu, the first H2N2 virus) and 1968 (“Hong Kong” flu, the first H3N2).

In February of 1976, an outbreak of H1N1 “swine” flu affected a number of Army recruits at Fort Dix, New Jersey; one died. The confirmation of person-to-person transmission as well as the co-incidence of H3N2 and highly pathogenic H1N1 viruses raised the specter of *in situ* viral miscegenation that could be the harbinger of a pandemic. Those concerns led to a crash program to develop and distribute a vaccine. Beginning in October 1976, over 40 million Americans were vaccinated within just a few weeks. Although the feared pandemic never materialized,

\*Type C viruses rarely cause human illness.

†Doctors are people too.



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hundreds of vaccine-associated Guillain-Barré syndrome cases did. *C'était la guerre*. (Later studies confirmed an association of GBS with that particular vaccine only.)

Over the past few years it has seemed that “bird flu” was going to be the Next Big Thing, and indeed H5N1 avian influenza continues to be a source of great concern. H5N1 infections of poultry were first noted in Asia in 1997, with a small human outbreak (<20 cases) that same year. High-pathogenicity H5N1 influenza re-emerged in 2003 and has caused over 400 human illnesses with at least 250 deaths since then, mostly in Egypt, Indonesia, and other parts of Southeast Asia. Person-to-person transmission of H5N1 has been documented repeatedly, but for whatever reason appears to be of relatively low efficiency; most cases continue to occur among persons having direct contact with infected chickens or other poultry.

The 2009 swine flu outbreak was first recognized in Mexico, but how and where it originated is uncertain. The first confirmed U.S. cases were reported on April 21 in San Diego. Within 14 days, >1000 cases have been confirmed from over 20 countries and 36 states, including Oregon. Available information\* suggests that the virus may have been circulating in Mexico since at least early March. The absence of official reports from many other parts of the world should be interpreted with caution, and even the presumption that this “started in Mexico” is not a given. Case counts are rising rapidly as the epidemic progresses, as testing improves, and as surveillance becomes institutionalized.

#### **SURVEILLANCE**

For over 20 years public health agencies have devoted many resources to pandemic flu planning. A severe influenza pandemic could cause enormous strains on not only

medical care systems but virtually every aspect of social and commercial life.

Disease surveillance is an important part of the public health response. In the initial stage of an influenza epidemic, there is a focus on individual case reporting and follow-up. Case definitions help provide consistency to an otherwise chaotic flow of information. Case definitions are not static and indeed have changed several times already in this outbreak.

Should widespread illness develop, the focus of surveillance shifts from reporting and investigating individual cases to more population-based measures. Traditional influenza surveillance relies on sentinel physician reporting, laboratory testing summaries, and hospitalization and mortality data, and we would expect this eventually during a pandemic. Indeed, this transition is already beginning. Consequent recommendations will change in coming weeks.

At this stage of the outbreak, we recommend H1N1 testing only for patients with acute influenza-like illness whose condition indicates a need for hospitalization.† Collect 2 nasopharyngeal swabs; screen one first with a commercial influenza A test. If that is positive, notify your local health department and send the second swab (refrigerated or on cold packs) to the Public Health Laboratory. More guidance is available through their site: [www.oregon.gov/DHS/ph/phl](http://www.oregon.gov/DHS/ph/phl).

#### **MANAGEMENT**

Treatment with oseltamivir or zanamivir is recommended for patients infected with the new H1N1 virus who are hospitalized or at high risk for complications. For others with suspect or even confirmed infections, we recommend supportive care only. Given the low morbidity and mortality reported to date, such restricted distribution of antivirals makes sense, given the likelihood

of a protracted epidemic. Pre- and post-exposure prophylaxis with oseltamivir or zanamivir is recommended in certain circumstances—refer to the OPHD and CDC web sites for clinical guidance. National stockpiles of antiviral medications have been released to state agencies to distribute in accordance with public health priorities.

In the absence of a vaccine, efforts to curb the spread of this epidemic must focus on infection control: in the hospital and medical office, surely, but also in schools, worksites, and in the home. Specific recommendations are being published on the Oregon Public Health Division's and CDC's web sites. Clinicians can help amplify public health messages about handwashing, “covering your cough,” and isolation of infected persons until the period of communicability is over. Historical evidence suggests that “social distancing” can be an effective adjunct to other infection control strategies. Simply put, this is minimizing face-to-face social interactions. School and office closures, telecommuting, avoiding mass gatherings; these are all examples of social distancing that can blunt the speed and force of viral transmission. Compulsory measures to encourage social distancing would be more or less disruptive, but may be considered should the scope of the epidemic expand. Influenza control measures are planned to have both direct and indirect effects. For example, while pediatric immunizations and school closures reduce the direct burden of illness among children, studies also show that those sweet little lambs can be nasty spreaders of influenza virus to older and often more vulnerable hosts, making collateral benefits at least as important.

#### **REFERENCES**

1. Frost, R. 1920. Fire and Ice. First published in Harper's Magazine; reprinted all over the place.

\*e.g., the New York Times

† This advice does not apply to official sentinel providers.