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[3] *Pandemic warning*
Date: Sat 25 Apr 2009
Source: MSNBC [edited]
<http://www.msnbc.msn.com/id/30398682>

Health officials prepare for swine flu "pandemic"

A new swine flu strain that has killed as many as 68 people and sickened more than 1000 across Mexico has "pandemic potential," the WHO chief said on Saturday [25 Apr 2009], and it may be too late to contain the sudden outbreak. CDC has stepped up surveillance across the United States. "We are worried," said CDC's Dr Anne Schuchat. "We don't think we can contain the spread of this virus," said Schuchat, interim deputy director for the Science and Public Health Program. "We are likely to find it in many other places." Because cases have been detected in California, Texas, and in several sites in Mexico, officials now must work to detect infections and reduce their severity, if possible. "It's time to prepare, time to think ahead and to be prepared for some uncertainty," she told reporters in a telephone briefing on Saturday.

Two dozen new suspected cases were reported Saturday [25 Apr 2009] in Mexico City alone. Schools were closed and all public events suspended in the capital until further notice -- including more than 500 concerts and other gatherings in the metropolis of 20 million. A hot line fielded 2366 calls in its 1st hours from frightened city residents who suspected they might have the disease. Soldiers and health workers handed out masks at subway stops, and hospitals dealt with crowds of people seeking help.

WHO's director-general, Margaret Chan, said the outbreak of the never-before-seen virus is a very serious situation and has "pandemic potential". But she said it is still too early to tell if it would become a pandemic. "The situation is evolving quickly," Chan said in a telephone news conference in Geneva. "A new disease is by definition poorly understood. "This virus is a mix of human, pig, and bird strains that prompted the WHO to meet Saturday to consider declaring an international *public health emergency -- a step that could lead to travel advisories*, trade restrictions and border closures. Spokesman Gregory Hartl said a decision would not be made on Saturday.

Scientists have warned for years about the potential for a pandemic from viruses that mix genetic material from humans and animals. Another reason to worry is that authorities said the dead so far don't include vulnerable infants and elderly. The Spanish flu pandemic, which killed at least 40 million people worldwide in 1918-19, also 1st struck otherwise healthy young adults. This swine flu and regular flu can have similar symptoms -- mostly fever, cough, and sore throat, though some of the US victims who recovered also experienced vomiting and diarrhea. But unlike with regular flu, humans don't have natural immunity to a virus that includes animal genes -- and new vaccines can take months to bring into use.

But experts at WHO and CDC say the nature of this outbreak may make containment impossible. Already, more than 1000 people have been infected in as many as 14 of Mexico's 32 states, according to daily newspaper El Universal. Tests show 20 people have died of the swine flu, and 48 other deaths were probably due to the same strain.

CDC and Canadian health officials were studying samples sent from Mexico, and airports around the world were screening passengers from Mexico for symptoms of the new flu strain, saying they may quarantine passengers. But CDC officials dismissed the idea of trying that in the United States. They noted there had been no direct contact between the cases in the San Diego and San Antonio areas, suggesting the virus had already spread from one geographic area through other undiagnosed people. "Anything that would be about containing it right now would purely be a political move," said Michael Osterholm, a University of Minnesota pandemic expert.

Mexican President Felipe Calderon said his government only discovered the

nature of the virus late on Thursday, with the help of international laboratories. "We are doing everything necessary," he said in a brief statement. But the government had said for days that its growing flu caseload was nothing unusual, so the sudden turnaround angered many who wonder if Mexico missed an opportunity to contain the outbreak.

Across Mexico's capital, residents reacted with fatalism and confusion, anger, and mounting fear at the idea that their city may be ground zero for a global epidemic. Authorities urged people to stay home if they feel sick and to avoid shaking hands or kissing people on the cheeks.

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[4] Suspected outbreak in New York
Date: Fri 24 Apr 2009
Source: WCBS TV News [edited]
<http://wcbstv.com/health/swine.flu.nyc.2.994071.html>

Possible swine flu outbreak at NYC prep school

New York City health officials say that about 75 students at a Queens high school have fallen ill with flu-like symptoms and testing is under way to rule out the strain of swine flu that has killed dozens in Mexico. The Health Department's Dr Don Weiss said on Friday [24 Apr 2009] that a team of agency doctors and investigators were dispatched to the private St Francis Preparatory School the previous day after students reported fever, sore throat, cough, aches, and pains. No one has been hospitalized.

The handful of sick students who remained at the school were tested for a variety of flu strains. If they're found to have a known human strain that would rule out swine flu. Results could take several days. In the meantime, the school says it's postponing an evening event and sanitizing the building over the weekend.

Mexican authorities said 60 people may have died from a swine flu virus in Mexico, and world health officials worry it could unleash a global flu epidemic. Mexico City closed schools, museums, libraries, and state-run theaters across the metropolis on Friday in hopes of containing the outbreak that has sickened more than 900. The US Centers for Disease Control and Prevention (CDC) said tests show some of the Mexico victims died from the same new strain of swine flu that sickened 8 people in Texas and California. It's a frightening new strain that combines genetic material from pigs, birds and humans.

WHO was looking closely at the 60 deaths -- most of them in or near Mexico's capital. It wasn't yet clear what flu they died from, but spokesman Thomas Abraham said "We are very, very concerned. We have what appears to be a novel virus and it has spread from human to human," he said. "It's all hands on deck at the moment."

WHO raised its internal alert system on Friday, preparing to divert more money and personnel to dealing with the outbreak. President Felipe Calderon cancelled a trip and met with his Cabinet to coordinate Mexico's response. The government has 500 000 flu vaccines and planned to administer them to health workers, the highest risk group. There are no vaccines available for the general public in Mexico, and authorities urged people to avoid hospitals unless they had a medical emergency, since hospitals are centers of infection. Some Mexican residents have started wearing blue surgical masks for extra protection, reports CBS News correspondent Adrienne Bard. The federal health minister has warned people not to go near anyone with a

respiratory infection and to avoid kissing -- a traditional Mexican greeting.

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communicated by:
ProMED-mail rapporteur Mary Marshall

[If infection by the novel swine flu virus is confirmed, it will represent a dramatic extension of the range of the outbreak virus from the southern states and Mexico to the north east of the United States. There is no reason to conclude at present, however, that this is anything other than an outbreak of seasonal influenza virus infection (or for that matter another common respiratory virus). - Mod.CP]

[see also:
Influenza A (H1N1) virus, swine, human - N America 20090425.1552
Acute respiratory disease - Mexico, swine virus susp 20090424.1546
Influenza A (H1N1) virus, swine, human - USA (02): (CA, TX) 20090424.1541
Influenza A (H1N1) virus, swine, human - USA: (CA) 20090422.1516
Influenza A (H1N1) virus, swine, human - Spain 20090220.0715
2008

Influenza A (H1N1) virus, swine, human - USA (TX) 20081125.3715
2007

Influenza A (H2N3) virus, swine - USA 20071219.4079
2006

Influenza, swine, human - USA (IA): November 2006 20070108.0077]

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研究報告の概要

CDC は過去のワクチン研究で集めた保存血清サンプルを用いて、2005～06 年、2006～07 年、2007～08 年あるいは 2008～09 年の季節性インフルエンザワクチンの接種前後の小児および成人コホートにおける新型インフルエンザ A ウイルスと交差反応を起こす抗体量をマイクロ中和（MN）法及び赤血球凝集抑制（HI）法により評価した。
その結果、ワクチン接種前では、新型インフルエンザ A ウイルスとの交差反応を起こす抗体量は小児の間では存在しなかった。ワクチン接種前の成人では、18-64 歳で 6-9%、60 歳以上で 33%の人に交差反応を起こす抗体が検出された。
過去にどの 4 種類の 3 価の季節性不活化インフルエンザワクチン又は弱毒化生インフルエンザワクチンの小児への接種において、新型インフルエンザ A との交差反応を起こす抗体産生反応を引き出せなかった。成人では、季節性不活化ワクチンの接種は新型インフクエンザ A(H1N1)と交差反応を起こす抗体産生反応は 18-64 歳では 2 倍に増加させた（季節性の H1N1 に対しての交差反応性抗体産生反応は 12-19 倍増加）。60 歳以上では新型インフルエンザ A と交差反応を起こす抗体産生反応の増加は見られなかった。これらのデータは、最近(2005 年～2009 年)の季節性インフルエンザワクチンは新型インフルエンザ A に対する感染防御抗体反応を起こしそうもないことを示唆する。

報告企業の意見

60 歳以上の人の 33%で新型インフルエンザ A に対する抗体が検出されたこと及び季節性インフルエンザワクチンの接種では小児及び 60 歳以上の人では抗体産生が得られず、成人においても抗体産生が 2 倍の増加にとどまったとする報告である。
インフルエンザ A (H1N1) はオルソミクソウイルス科に属するビリオンは球形で、直径 80～120nm の脂質エンベロープを有する比較的大きな RNA ウイルスである。万一、インフルエンザ A (H1N1) が原料血漿に混入したとしても BVD をモデルウイルスとしたウイルスバリデーション試験成績から、製造工程にて十分に不活化・除去されると考えている。

今後の対応

本報告は本剤の安全性に影響を与えないと考えるので、特段の措置はとらない。

使用上の注意記載状況・その他参考事項等

2. 重要な基本的注意
(1) 本剤の原材料となる献血者の血液については、HBs 抗原、抗 HCV 抗体、抗 HIV-1 抗体、抗 HIV-2 抗体、抗 HTLV-I 抗体陰性で、かつ ALT (GPT) 値でスクリーニングを実施している。更に、プールした試験血漿については、HIV-1、HBV 及び HCV について核酸増幅検査 (NAT) を実施し、適合した血漿を本剤の製造に使用しているが、当該 NAT の検出限界以下のウイルスが混入している可能性が常に存在する。本剤は、以上の検査に適合した血漿を原料として、Cohn の低温エタノール分画で得た画分から人ハプトグロビンを濃縮・精製した製剤であり、ウイルス不活化・除去を目的として、製造工程において 60℃、10 時間の液状加熱処理及びウイルス除去膜によるろ過膜処理を施しているが、投与に際しては、次の点に十分注意すること。

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Serum Cross-Reactive Antibody Response to a Novel Influenza A (H1N1) Virus After Vaccination with Seasonal Influenza Vaccine

As of May 19, 2009, a total of 5,469 confirmed or probable cases* of human infection with a novel influenza A (H1N1) virus had been documented in 47 states and the District of Columbia (*1,2*). In addition, the virus had spread to 41 countries (*3*), with a total of 4,774 cases reported in countries outside the United States. Because producing a novel influenza A (H1N1) virus vaccine will take several months (*4*), determining whether receipt of seasonal influenza vaccine might offer any protection against the novel influenza A (H1N1) virus is important. Therefore, using stored serum specimens collected during previous vaccine studies, CDC assessed the level of cross-reactive antibody to the novel influenza A (H1N1) virus in cohorts of children and adults before and after they had been vaccinated with the 2005–06, 2006–07, 2007–08, or 2008–09 influenza season vaccines. The results indicated that before vaccination, no cross-reactive antibody to the novel influenza A (H1N1) virus existed among children. Among adults, before vaccination, cross-reactive antibody was detected in 6%–9% of those aged 18–64 years and in 33% of those aged >60 years. Previous vaccination of children with any of four seasonal trivalent, inactivated influenza vaccines (TIV) or with live, attenuated influenza vaccine (LAIV) did not elicit a cross-reactive antibody response to the novel influenza A (H1N1) virus. Among adults, vaccination with seasonal TIV resulted in a twofold increase in cross-reactive antibody response to the novel influenza A (H1N1) virus among those aged 18–64 years, compared with a twelvefold to nineteenfold increase in cross-reactive antibody response to the seasonal H1N1 strain; no increase in cross-reactive antibody response to the novel influenza A (H1N1) virus was observed among adults aged >60 years. These data suggest that receipt of recent (2005–2009) seasonal influenza vaccines is unlikely to elicit a protective antibody response to the novel influenza A (H1N1) virus.

Serum specimens were provided to CDC from academic, government, and industry partners for use as part of the public health response to the emergence of the novel influenza A (H1N1) virus. The specimens had been collected from healthy human participants, with written, informed consent. All participants had been vaccinated either 1) intramuscularly with licensed TIV developed for the northern hemisphere 2005–06, 2006–07, 2007–08, or 2008–09 influenza seasons or 2) intranasally with licensed LAIV developed for the northern hemisphere 2005–06 or 2006–07 influenza seasons. The serum specimens were grouped for influenza serology testing by the age of participants and formulation of the vaccines.

Microneutralization (MN) and hemagglutination inhibition (HI) assays were performed at CDC, according to standard MN and HI procedures (*5,6*). As with vaccine production, the seasonal influenza A (H1N1) viruses used in this study (A/New Caledonia/20/1999 [2005–06 and

* Case definitions available at http://www.cdc.gov/h1n1flu/casedef.htm.

INSIDE

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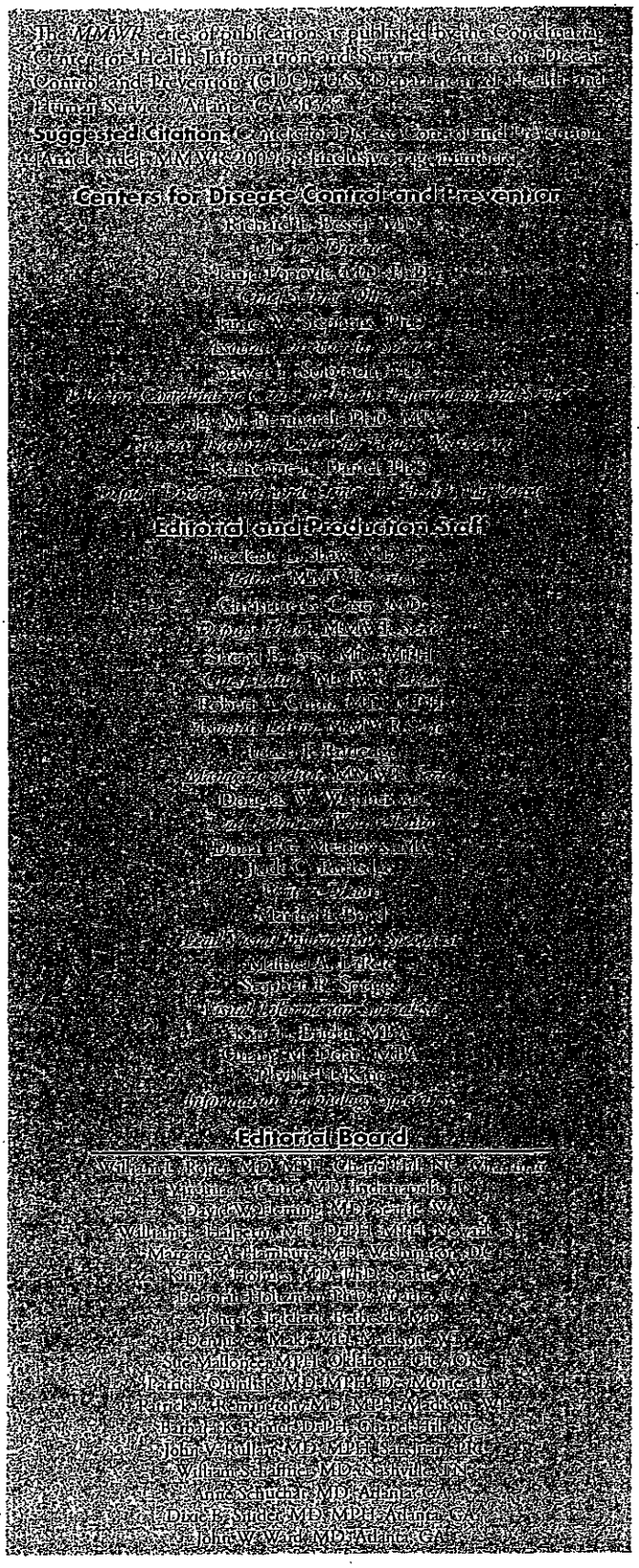

2006–07], A/Solomon Islands/3/2006 [2007–08], and A/Brisbane/59/2007 [2008–09]) were propagated in embryonated chicken eggs. The novel influenza A (H1N1) virus used in the study was A/California/04/2009, which was grown in Madin-Darby canine kidney cells. All procedures were performed in a biosafety level 2 laboratory using biosafety level 3 practices.† The HI assay was performed using 0.5% turkey red blood cells. Serum specimens were treated with receptor-destroying enzymes. Sera containing nonspecific agglutinins were heme-adsorbed and tested at an initial dilution of 1:10. For the MN assay, serum specimens were heat inactivated (at 133°F [56°C], for 30 minutes) and tested at an initial dilution of 1:10. For calculation of geometric mean titer (GMT) estimates, a titer of <10 was assigned a value of 5, and a titer of ≥1280 was assigned a value of 1280. Statistical significance was determined using a paired t-test.

An initial comparison between the HI and MN assays was made for panels of sera from children aged 6 months to 9 years (n = 28), adults aged 18–59 years (n = 30), and adults aged >60 years (n = 42). Although the estimated correlation between HI and MN titers was high (r = 0.82) for the seasonal vaccine strains, the MN assay generally yielded higher titers and detected more seroconversions (i.e., fourfold or greater increases in antibody titers) to A/California/04/2009 than the HI assay. Therefore, the MN assay was used to assess the level of cross-reactive antibody to A/California/04/2009 in populations before and after vaccination with seasonal influenza vaccines. Although serum HI antibody titers of 40 are associated with at least a 50% reduction in risk for influenza infection or disease in populations (*7*), no such correlate of protection exists for MN antibody titers. Therefore, a linear regression model was used to predict the MN titer for seasonal influenza A (H1N1) viruses that corresponded to an HI titer of 40 and to measure titer achievement against the seasonal vaccine strain and the novel influenza A (H1N1) virus. In the pediatric population, an HI titer of 40 corresponded to an MN titer of 40, whereas in the adult population the corresponding MN titer was ≥160.

Among 79 children ranging in age from 6 months to 9 years, little evidence was found of prevaccination cross-reactive antibodies to A/California/04/2009 (Table 1). In addition, after vaccination with seasonal TIV, no seroconversions to A/California/04/2009 virus were detected, whereas seroconversions to the seasonal vaccine strains were detected in 67%–100% of children. Children vaccinated with LAIV also had no seroconversions to the A/California/04/2009 virus.

† Biosafety level information is available at http://www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm.

TABLE 1. Cross-reactive microneutralization (MN) antibody response to novel influenza A (H1N1) virus* in pediatric recipients (aged 6 months–9 years) of seasonal influenza vaccines

Vaccine	Influenza season	Influenza virus	Age group	No.	% with fourfold or greater increase in antibody titer†	% with MN titer of ≥40§		Geometric mean titer (GMT)¶			
						Prevaccination	Postvaccination	Prevaccination (95% CI**)		Postvaccination (95% CI)		Postvaccination to prevaccination ratio
TIV††	2005–2007§§	A/New Caledonia/20/1999	6 mos–9 yrs	33	67	42	94	31	(21–46)	255	(172–378)	8
		A/California/04/2009			0	0	0	5	(4–6)	6	(6–7)	1
	2007–08	A/Solomon Is/3/2006	5–9 yrs	13	85	54	100	42	(22–80)	575	(303–1093)	14
		A/California/04/2009			0	8	8	10	(7–15)	12	(8–17)	1
	2008–09	A/Brisbane/59/2007	6 mos–3 yrs	9	100	0	100	5	(4–7)	285	(202–402)	57
		A/California/04/2009			0	0	0	5	(—)	5	(—)	1
LAIV¶¶	2005–2007§§	A/New Caledonia/20/1999	6 mos–9 yrs	24	25	46	79	33	(17–63)	73	(38–139)	2
		A/California/04/2009			0	0	4	5	(4–6)	6	(5–7)	1

* A/California/04/2009.
† A fourfold or greater increase in antibody titer indicates seroconversion (a response to the vaccine).
§ A linear regression model was used to predict the MN titer for seasonal H1N1 viruses that corresponded to a hemagglutination inhibition (HI) antibody titer of 40. (Serum HI antibody titers of 40 are associated with at least a 50% decrease in risk for influenza infection or disease [7]). In pediatric populations, an HI titer of 40 corresponds with an MN titer of 40.
¶ A titer of 1280 was used for all samples with a titer of ≥1280. The dilution of sera in the first well is based on the combination of a 1:10 serum dilution with an equal volume of diluted virus for a final serum dilution referred to as 1:10. In the statistical models, study participants were treated as random effects sampled from a larger population of study participants, and duplicate samples were treated as random effects nested within each study participant.
** Confidence interval.
†† Trivalent, inactivated influenza vaccine.
§§ 2005–06 and 2006–07 influenza seasons.
¶¶ Live, attenuated influenza vaccine.

Consistent with previous reports (*4*), vaccination of adults with seasonal TIV resulted in seroconversion to the seasonal influenza A (H1N1) vaccine strain in 74% of adults aged 18–64 years, 78% of adults aged 18–40 years, and 54% of adults aged >60 years (Table 2). In contrast, seroconversion to the A/California/04/2009 virus was detected in 19% of adults aged 18–64 years and 3% of adults aged >60 years who received the 2007–08 vaccine and in 12% of adults aged 18–40 years who received the 2008–09 vaccine. Compared with responses to the seasonal influenza A (H1N1) vaccine virus, postvaccination to prevaccination GMT ratios for the response to A/California/04/2009 virus were fivefold to tenfold lower among all adults. However, 6% of adults aged 18–40 years, 9% of adults 18–64 years, and 33% of adults aged >60 years had prevaccination MN titers of ≥160. After vaccination with seasonal vaccine, 7% of adults aged 18–40 years, 25% of adults aged 18–64 years, and 43% of adults aged >60 years had postvaccination titers of ≥160 to A/California/04/2009. The prevaccination GMT of adults aged >60 years against the novel 2009 H1N1 strain was significantly higher than against the seasonal 2007–08 H1N1 vaccine component ($p<0.001$).

Reported by: *J Katz, PhD, K Hancock, PhD, V Veguilla, MPH, W Zhong, PhD, XH Lu, MD, H Sun, MD, E Butler, MPH, L Dong, MD, PhD, F Liu, MD, PhD, ZN Li, MD, PhD, J DeVos, MPH, P Gargiullo, PhD, N Cox, PhD, Influenza Div, National Center for Immunization and Respiratory Diseases, Coordinating Center for Infectious Diseases, CDC.*

Editorial Note: The results in this report suggest that vaccination with recent (2005–2009) seasonal influenza vaccines is unlikely to provide protection against the novel influenza A (H1N1) virus. Although vaccination of adults with seasonal TIV generally resulted in a small increase in antibodies against the novel influenza A (H1N1) virus, whether such levels of cross-reactive antibody provide any protection against infection with novel influenza A (H1N1) virus is unknown. These results are consistent with the substantial degree of genetic divergence of the novel influenza A (H1N1) virus of swine origin from recent seasonal human H1N1 viruses; A/California/04/09 shares only 72%–73% amino acid identity in the HA1 portion of the hemagglutinin molecule with the seasonal viruses used in this study. For comparison, the amino acid sequence identity in the HA1 portion among seasonal vaccine strains used in this study is 97%–98%.

Although the number of sera from children tested in this analysis was small, results indicate that U.S. children are largely serologically naïve to the novel influenza A (H1N1) virus and that vaccination with seasonal TIV or LAIV does not elicit any measurable level of cross-reactive antibody to the novel virus. Results among adults suggest that some degree of preexisting immunity to the novel H1N1 strains exists, especially among adults aged >60 years. One possible explanation is that some adults in this age group have had previous exposure, either through infection or vaccination, to an influenza A (H1N1) virus that is genetically and antigenically more closely related