



Hospitalized Patients with Novel Influenza A (H1N1) Virus Infection – California, April–May, 2009

Since April 15 and 17, 2009, when the first two cases of novel influenza A (H1N1) infection were identified from two southern California counties, novel influenza A (H1N1) cases have been documented throughout the world, with most cases occurring in the United States and Mexico (1–3). In the United States, early reports of illnesses associated with novel influenza A (H1N1) infection indicated the disease might be similar in severity to seasonal influenza, with the majority of patients not requiring hospitalization and only rare deaths reported, generally in persons with underlying medical conditions (2,3). As of May 17, 2009, 553 novel influenza A (H1N1) cases, including 333 confirmed and 220 probable cases, had been reported in 32 of 61 local health jurisdictions in California. Of the 553 patients, 30 have been hospitalized. No fatal cases associated with novel influenza A (H1N1) infection had been reported in California. This report summarizes the 30 hospitalized cases as of May 17, including a detailed description of four cases that illustrate the spectrum of illness severity and underlying risk factors. This preliminary overview indicates that, although the majority of hospitalized persons infected with novel influenza A (H1N1) recovered without complications, certain patients had severe and prolonged disease. All hospitalized patients with novel influenza A (H1N1) infection should be monitored carefully and treated with antiviral therapy, including patients who seek care >48 hours after illness onset (4,5).

Summary of Hospitalized Cases

Beginning on April 20, 2009, the California Department of Public Health (CDPH) and local health departments in Imperial and San Diego counties worked with hospital infection-control practitioners to initiate enhanced surveillance for hospitalized cases of laboratory-confirmed or probable novel influenza A (H1N1) infection at all 25 hospitals in the two counties. Three days later, on April 23, 2009, CDPH extended this surveillance statewide. Cases are reported as either probable (defined as detection of influenza A by real-time reverse transcription–polymerase chain reaction [rRT-PCR] that is unsubtypeable for human influenza virus subtypes H1 or H3)

or confirmed (defined as positive by CDC protocol for rRT-PCR for novel influenza A H1N1).^{*} Approximately 96% of unsubtypeable California specimens subsequently have been confirmed as novel influenza A (H1N1) at CDC or at the CDPH Viral and Rickettsial Disease Laboratory (VRDL).[†]

For this report, a hospitalized case was defined as a confirmed or probable case of novel influenza A (H1N1) infection in a patient who was hospitalized for ≥ 24 hours. Of the 30 hospitalized patients, 26 were confirmed and four were probable (confirmatory testing is in progress); symptom onset ranged from April 3 to May 9. The cases were reported from 11 counties, most of which are located in southern or central California. The largest number of patients, (15 [50%]) resided in San Diego and Imperial counties. Of the 26 patients for whom information on ethnicity was available, 17 (65%) were Hispanic. Ages of the 30 patients ranged from 27 days to 89 years, with a median age of 27.5 years; 21 (70%) were female. Four (13%) patients had traveled to Mexico in the 7 days before onset of illness. None of the 30 patients reported exposure to swine or a known confirmed case of novel influenza A (H1N1) infection.

The most common admission diagnoses were pneumonia and dehydration. Nineteen patients (64%) had underlying medical conditions; the most common were chronic lung disease (e.g., asthma and chronic obstructive pulmonary disease), conditions associated with immunosuppression, chronic cardiac disease (e.g., congenital heart disease and coronary artery disease), diabetes, and obesity. The most common symptoms were fever, cough, vomiting, and shortness of breath; diarrhea was uncommon. Of the 25 patients who had chest radiographs, 15 (60%) had abnormalities suggestive of pneumonia, including 10 with multilobar infiltrates and five with unilobar infiltrates. Six patients were admitted to the intensive care unit (ICU), and four required mechanical ven-

^{*} Additional information available at <http://www.who.int/csr/resources/publications/swineflu/realtimepct/en/index.html>.

[†] Additional information available at [http://ww2.cdph.ca.gov/programs/vrdl/pages/enhancedsurveillanceforinfluenzaa\(h1\).aspx](http://ww2.cdph.ca.gov/programs/vrdl/pages/enhancedsurveillanceforinfluenzaa(h1).aspx).

tilation. Five patients were pregnant. Two of these developed complications, including spontaneous abortion and premature rupture of the membranes; the fetuses were at 13 and 35 weeks gestation, respectively.

Of the 24 patients tested for influenza A in the hospital, the rapid antigen test was positive in 16 and negative in five; three patients tested positive by other methods (direct immunofluorescent antibody [two patients] and culture [one patient]). None of the 30 patients had microbiologic evidence of secondary bacterial infection by blood, urine, or sputum cultures (or endotracheal aspirate or bronchoalveolar lavage cultures in the case of intubated patients). Fifteen (50%) received antiviral treatment with oseltamivir; for five patients, treatment was initiated within 48 hours of onset of symptoms. Among the 15 not treated with antivirals, six sought care >48 hours after illness onset. Of the 22 patients with available history, six (27%) had received seasonal influenza vaccination. As of May 17, 23 patients had been discharged to home, with a median length of hospital stay of 4 days (range: 1–10 days). Seven patients remained in the hospital, with median lengths of stay of 15 days (range: 4–167 days) (Tables 1 and 2).

Case Reports

Patient 3. An infant girl aged 5 months was born prematurely at 27 weeks in early December 2008 with intrauterine growth retardation and congenital heart disease with patent ductus arteriosus and ventricular septal defect. The infant had a complicated hospital course in the neonatal ICU after birth, including development of bronchopulmonary dysplasia and respiratory distress syndrome requiring prolonged mechanical ventilation and multiple courses of steroids, several episodes of clinical sepsis and pneumonia, and chronic anemia and thrombocytopenia. By the fifth month, the infant had been weaned from the ventilator and was doing well on high-flow nasal cannula oxygen. However, on hospital day number 150, she developed a new nonproductive cough and fever, with a new infiltrate of the right lung on chest radiograph that progressed to complete opacification of both lung fields. Multiple blood, urine, and sputum cultures were unrevealing; rapid antigen test was positive for influenza A, with subsequent confirmation at the CDPH VRDL for novel influenza A (H1). The source of the infant's infection is still under investigation. The infant was reintubated and started on broad spectrum antibiotics and oseltamivir at a dose of 2 mg/kg every 12 hours, 3 days after fever. As of May 14, the patient remained hospitalized in critical condition.

Patient 16. A previously healthy woman aged 29 years, who was 28 weeks pregnant, sought care at an emergency department on April 26 with complaints of subjective fever,

productive cough, and increasing shortness of breath during the preceding 10 days. Upon initial evaluation, the patient's vital signs were notable for low grade fever (99.6°F [37.6°C]), a respiratory rate of 38 breaths per minute, blood pressure of 112/57 mmHg, heart rate of 104 beats per minute, and oxygen saturation of 87% on room air. A chest radiograph revealed bilateral perihilar interstitial infiltrates with mediastinal lymphadenopathy. Her complete blood count and chemistries were normal except for an elevated white blood cell count of 11.4 cells/mm³ with a differential of 42% segmented neutrophils, 45% bands, and 9% lymphocytes. The patient was admitted to the ICU and started on broad spectrum antibiotics (azithromycin and ceftriaxone). Serial fetal ultrasounds were normal. Multiple blood, urine, and sputum cultures were unrevealing; rapid antigen test was positive for influenza A, with subsequent confirmation of novel influenza A (H1N1) at the CDPH VRDL. She was not treated with antiviral medications. She gradually improved and was discharged on amoxicillin after 9 days.

Patient 18. A man aged 32 years with a history of obstructive sleep apnea sought care at an emergency department on May 5 with a 3-day history of fever, chills, and productive cough. The patient reported he had been taking amoxicillin for a diagnosis of sinusitis, following complaints of vertigo and dizziness, for the past 2 weeks. His vital signs showed a temperature of 99.1°F (37.3°C), blood pressure of 89/58 mmHg, and heart rate of 84 beats per minute. Physical exam of the chest showed good air movement bilaterally, although chest radiograph revealed bilateral infiltrates. His complete blood count and chemistries were normal except for an elevated white blood cell count of 13.8 cells/mm³ with a differential of 94% segmented neutrophils and 4% lymphocytes. An arterial blood gas showed respiratory acidosis and hypoxemia with pO₂ of 80 mm Hg on room air. The patient was admitted to the ICU on empiric broad spectrum antibiotics and required intubation on the second hospital day for worsening hypoxemia. Initial microbiologic workup and influenza rapid antigen tests were negative; the patient was started on oseltamivir on hospital day 2. A repeat rapid antigen test and bronchoalveolar lavage viral culture were positive for influenza A, with subsequent confirmation of novel influenza A (H1N1). The patient improved, was extubated on hospital day 5, and was discharged on hospital day 10.

Patient 29. A woman aged 87 years with multiple medical problems, including recently diagnosed breast cancer with possible abdominal metastasis, hypertension, diabetes mellitus, coronary artery disease, cerebrovascular disease, chronic renal insufficiency, and obesity, was brought for care at an emergency department on April 21 after being found unconscious by her daughter. The patient had reported onset of fever, cough, and weakness 2 days before admission and also new onset of

TABLE 1. Case characteristics for 30 hospitalized patients with novel influenza A (H1N1) — California, April 15, 2009–May 17, 2009

Case characteristic	No.	(%)
Age group (yrs)		
<5	6	(20)
5-19	7	(23)
20-39	8	(27)
40-59	4	(13)
>60	5	(17)
Chronic comorbid illness*		
Chronic lung disease [†]	11	(37)
Other immunosuppression [§]	6	(20)
Chronic cardiac disease	5	(17)
Diabetes mellitus	4	(13)
Obesity	4	(13)
Seizure disorder	3	(10)
Pregnancy	5	(17)
Symptoms and signs		
Fever	29	(97)
Cough	23	(77)
Vomiting	14	(46)
Shortness of breath	13	(43)
Chills	11	(37)
Sore throat	10	(33)
Body aches	10	(33)
Rhinorrhea	9	(30)
Headache	5	(17)
Conjunctivitis	3	(10)
Diarrhea	3	(10)
Altered mental status	2	(7)
Generalized weakness	2	(7)
Clinical findings and course		
Infiltrates on chest radiograph**	15	(60)
Intensive-care unit admission	6	(20)
Mechanical ventilation	4	(13)
Antiviral treatment	15	(50)

* Conditions listed are not mutually exclusive; certain patients had multiple underlying chronic diseases.

[†] Includes asthma, chronic obstructive pulmonary disorder, bronchopulmonary dysplasia/respiratory distress syndrome, bronchiolitis obliterans organizing pneumonia, Sjogren syndrome, and obstructive sleep apnea.

^{||} Includes congenital heart disease, atrial fibrillation, status-post aortic valve replacement, and coronary artery disease.

[§] Includes immunosuppressive drugs, cancer, and congenital immunodeficiency.

** Out of 25 cases with chest radiographs.

orthopnea and bilateral leg swelling. She was wheelchair bound and had no recent history of travel or known contact with ill persons.. In the emergency room the patient was afebrile, with a blood pressure of 57/39 mmHg, pulse 57, respiratory rate of 14 breaths per minute, and oxygen saturation of 87% on room air. Electrocardiogram was suggestive of non Q-wave myocardial infarction. Chest radiograph showed bilateral pneumonia and congestive heart failure with marked cardiomegaly. Her laboratory abnormalities included an elevated white blood cell count of 13.4 cells/mm³, mild anemia with a hematocrit of 34%, a mildly elevated creatinine at 1.8 mg/dL, alanine aminotransferase of 36 units/L and aspartate aminotransferase

of 160 units/L, and markedly elevated troponin and creatinine kinase levels of 29.43 ng/mL and 653 IU/L, respectively. The patient went into respiratory arrest and was subsequently intubated and started on low dose dopamine, and admitted to the ICU with a diagnosis of myocardial infarction, congestive heart failure, pneumonia and presumed sepsis. A chest computed tomography (CT) scan showed complete atelectasis of the right middle lobe, bilateral ground glass opacities of the upper lobes, and bilateral pleural effusions. A subsequent bronchoscopy identified a large cauliflower-shaped mass in the right lower lobe airway. Multiple blood, urine, and sputum cultures were unrevealing; rapid antigen test was positive for influenza A, with subsequent confirmation of novel influenza A (H1N1) at the CDPH VRDL. The patient remains hospitalized in critical condition under intensive care.

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Editorial Note: Initial surveillance for hospitalized cases of novel influenza A (H1N1) infection in California indicates that the majority of patients were discharged after short hospital stays. Previously healthy patients without underlying chronic medical conditions recovered with an uncomplicated hospital course and a median length of stay of 2.5 days (range: 1–7 days). Although one third of hospitalized patients had abnormal chest radiographs with multilobar infiltrates, only 9% were treated with oseltamivir; nonetheless, most had favorable outcomes. Of five pregnant women, two developed serious sequelae; however, the role that preceding infection with novel influenza A (H1N1) played in these outcomes is unclear.

Certain hospitalized patients in California experienced severe disease and prolonged hospital courses. Of note, three of the six California patients admitted to an ICU continue to require prolonged intensive care. Extremes in age and multiple and debilitating underlying medical conditions might be contributing to the severity of illness in these patients. Although chronic underlying medical conditions and pregnancy classically are associated with a greater risk for complications for seasonal influenza (6), one patient (patient 18) who was relatively healthy with only mild chronic pulmonary disease required intensive care and mechanical ventilation. More data

TABLE 2. Detailed clinical characteristics for 30 hospitalized patients with novel influenza A (H1N1) — California, April 15, 2009–May 17, 2009 (Continued)

Patient no.	Age	Sex	Underlying conditions*	Admission diagnosis	Abnormal complete blood count values	Chest radiographic findings	Intensive-care unit admission	Mechanical ventilation	Antiviral treatment	Length of stay
1	27 days	F	None	Rule out sepsis	None	Normal	No	No	None	3 days
2	6 wks	M	None	Pneumonia	Anemia [†]	Bilateral infiltrates	No	No	Oseltamivir	6 days
3	5 mos	F	Prematurity, intrauterine growth retardation, bronchopulmonary dysplasia, congenital heart disease, chronic corticosteroid administration	Respiratory Distress Syndrome, prematurity	Leukocytosis, [§] anemia [†]	Bilateral infiltrates	Yes	Yes	None	Still hospitalized: day 167
4	17 mos	M	None	Pneumonia respiratory failure	Leukocytosis, [§] lymphopenia [¶]	Bilateral infiltrates	No	No	None	2 days
5	3 yrs	F	None	Dehydration	None	Not done	No	No	Oseltamivir	1 day
6	3 yrs	M	T-cell immunodeficiency	Pneumonia	Leukocytosis, [§] anemia [†]	Bilateral infiltrates	Yes	No	Oseltamivir	5 days
7	7 yrs	F	Asthma, obesity	Asthma exacerbation	Leukopenia ^{**}	Unilobar infiltrate	No	No	None	4 days
8	9 yrs	M	Asthma	Dehydration	Leukopenia ^{**} Lymphopenia [¶]	Hyperinflation, perivascular cuffing	No	No	None	5 days
9	15 yrs	M	Seizure disorder	Dehydration	Lymphopenia [¶]	Normal	No	No	Oseltamivir	1 day
10	15 yrs	M	Cerebral palsy, asthma, seizure disorder	Fever, seizure	Thrombocytopenia ^{††}	Multilobar infiltrates	No	No	Oseltamivir	Still hospitalized: day 11
11	17 yrs	F	Pregnancy	Not available	Not available	Not available	No	No	Oseltamivir	5 days
12	19 yrs	F	None	Acute pharyngitis	Lymphopenia [¶]	Normal	No	No	Oseltamivir	1 day
13	19 yrs	F	Pregnancy	Rule out sepsis	Lymphopenia [¶]	Not done	No	No	None	2 days
14	21 yrs	F	None	Dehydration	None	Normal	No	No	Oseltamivir	2 days
15	26 yrs	F	None	Pneumonia, respiratory failure	None	Unilobar infiltrate	No	No	Oseltamivir	2 days
16	29 yrs	F	Pregnancy	Pneumonia	Leukocytosis [§]	Bilateral infiltrates	Yes	No	None	9 days
17	30 yrs	F	Diabetes melitus, obesity	Viral syndrome, vomiting	None	None	No	No	Oseltamivir	1 day
18	32 yrs	M	Obstructive sleep apnea	Respiratory failure	Leukocytosis, [§] lymphopenia [¶]	Bilateral infiltrates	Yes	Yes	Oseltamivir	8 days

are needed regarding which populations are at greatest risk for hospitalization and severe sequelae after infection with novel influenza A (H1N1).

As of May 15, 2009, 9% of approximately 11,600 clinical specimens submitted for testing to California public health laboratories since April 27, 2009, were positive by rRT-PCR for influenza A; of those, 23% and 28% were subtyped as seasonal influenza A/H1 and A/H3, respectively. These results indicate that seasonal influenza viruses continue to circulate throughout California and might be a cause of influenza-like illness and positive results from rapid antigen tests. Although rapid antigen test results were positive in 67% of tested cases

in this series, anecdotal reports from other cases confirmed at CDPH VRDL, tested mostly in the outpatient setting, suggest that false positive and negative results are common. Accordingly, CDPH has emphasized the importance of testing influenza viruses in the state with rRT-PCR. CDPH also has advised clinicians in California to collect respiratory specimens for rRT-PCR testing, subtyping, and further characterization at public health laboratories from patients who are hospitalized or who die with febrile respiratory illness.

Additional information regarding California testing guidelines is available at [http://ww2.cdph.ca.gov/programs/vrdl/pages/diagnostictestingforswineinfluenzaA\(H1\).aspx](http://ww2.cdph.ca.gov/programs/vrdl/pages/diagnostictestingforswineinfluenzaA(H1).aspx).

TABLE 2. (Continued) Detailed clinical characteristics for 30 hospitalized patients with novel influenza A (H1N1) — California, April 15, 2009–May 17, 2009

Patient no.	Age	Sex	Underlying conditions*	Admission diagnosis	Abnormal complete blood count values	Chest radiographic findings	Intensive-care unit admission	Mechanical ventilation	Antiviral treatment	Length of stay
19	34 yrs	F	Asthma, pregnancy	Dehydration	Leukopenia,** thrombocytopenia ^{††}	None	No	No	None	7 days
20	35 yrs	F	None	Pneumonia	Leukocytosis, [§] anemia [†]	Not done	No	No	None	7 days
21	35 yrs	F	Down syndrome, congenital heart defect, congenital T-cell deficiency	Pneumonia, respiratory failure	Lymphopenia, [¶] thrombocytopenia ^{††}	Bilateral infiltrates	No	No	None	4 days
22	40 yrs	F	Asthma, HTN, obesity	Pneumonia, respiratory failure	Leukocytosis, [§] anemia [†]	Bilateral infiltrates	Yes	Yes	None	Still hospitalized: day 18
23	41 yrs	F	Autoimmune hepatitis/biliary cirrhosis s/p liver transplant, HTN, obesity	Viral syndrome	Leukopenia, [¶] anemia, [†] thrombocytopenia ^{††}	Unilobar infiltrate	No	No	Oseltamivir	6 days
24	42 yrs	F	Asthma, gastrointestinal reflux, pregnancy	Premature rupture of membranes, pre-eclampsia	None	Not done	No	No	Oseltamivir	4 days
25	49 yrs	M	Aortic valve replacement, HTN, lupus nephritis, seizure disorder	Fever	Lymphopenia, [¶] anemia, [*] thrombocytopenia ^{††}	Not available	No	No	None	Still hospitalized: day 15
26	69 yrs	M	COPD, HTN, atrial fibrillation	Respiratory distress	Leukopenia [¶]	Normal	No	No	None	Still hospitalized: day 13
27	72 yrs	F	COPD, BOOP, DM, atrial fibrillation, HTN, chronic corticosteroid administration	Respiratory distress	Leukocytosis [§]	Unilobar infiltrate	No	No	None	10 days
28	73 yrs	F	COPD, HTN	Respiratory distress	Lymphopenia [¶]	Normal	No	No	Oseltamivir	3 days
29	87 yrs	F	CAD, COPD, HTN, breast cancer	Pneumonia, respiratory failure	Leukocytosis, [§] anemia [†]	Bilateral infiltrates and pleural effusions	Yes	Yes	None	Still hospitalized: day 27
30	89 yrs	F	Sjogren syndrome, pulmonary fibrosis, chronic corticosteroid administration, HTN	Not available	Leukocytosis, [§] positive D-dimer	Unilobar infiltrate	No	No	Oseltamivir	Still hospitalized: day 4

* HTN: hypertension. COPD: chronic obstructive pulmonary disease. CAD: coronary artery disease. BOOP: bronchiolitis obliterans organizing pneumonia.

[†] Hematocrit <35%.

[§] Total leukocyte count >10 cells/mm³.

[¶] Total lymphocyte count <800 cells/mm³.

** White blood cell count <5,000 cells/mm³.

^{††} Platelet count <150,000 cells/mm³.

Additional information regarding novel influenza A (H1N1) treatment guidance and other CDC recommendations is available at <http://www.cdc.gov/h1n1flu/guidance>.

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