Winthrop-University Hospital Infectious Disease Division's swine influenza (H1N1) pneumonia diagnostic weighted point score system for hospitalized adults with influenza-like illnesses (ILIs) and negative rapid influenza diagnostic tests (RIDTs)

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BACKGROUND: In spring 2009, a novel strain of influenza A originating in Veracruz, Mexico, quickly spread to the United States and throughout the world. This influenza A virus was the product of gene reassortment of 4 different genetic elements: human influenza, swine influenza, avian influenza, and Eurasian swine influenza. In the United States, New York was the epicenter of the swine influenza (H1N1) pandemic. Hospital emergency departments (EDs) were inundated with patients with influenza-like illnesses (ILIs) requesting screening for H1N1. Our ED screening, as well as many others, used a rapid screening test for influenza A (QuickVue A/B) because H1N1 was a variant of influenza A. The definitive laboratory test i.e., RT-PCR for H1N1 was developed by the Centers for Disease Control (Atlanta, GA) and subsequently distributed to health departments. Because of the extraordinary volume of test requests, health authorities restricted reverse transcription polymerase chain reaction (RT-PCR) testing. Hence most EDs, including our own, were dependent on rapid influenza diagnostic tests (RIDTs) for swine influenza. A positive rapid influenza A test was usually predictive of RT-PCR H1N1 positivity, but the rapid influenza A screening test (QuickVue A/B) was associated with 30% false negatives. The inability to rely on RIDTs for H1N1 diagnosis resulted in underdiagnosing H1N1. Confronted with adults admitted with ILIs, negative RIDTs, and restricted RT-PCR testing, there was a critical need to develop clinical criteria to diagnose probable swine influenza H1N1 pneumonia.

METHODS: During the pandemic, the Infectious Disease Division at Winthrop-University Hospital developed clinical criteria for adult admitted patients with ILIs and negative RIDTs. Similar to the one developed for the clinical diagnosis of legionnaire's disease. The Winthrop-University Hospital Infectious Disease Division's diagnostic weighted point score system for swine influenza H1N1 pneumonia is based on key clinical and laboratory features.

RESULTS: During the "herald" wave of the swine influenza H1N1 pandemic, the diagnostic weighted point score system accurately identified probable swine influenza H1N1 pneumonia and accurately differentiated swine influenza H1N1 pneumonia from ILIs and other viral and bacterial community-acquired pneumonias.

CONCLUSION: In hospitalized adults with ILIs and negative RIDTs, the diagnostic weighted diagnostic point score system, may be used to make a presumptive clinical diagnosis of swine influenza H1N1 pneumonia. (Heart Lung® 2009;38:534–538.)

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Swine influenza (H1N1) pneumonia is caused by a novel influenza A virus containing genetic elements from swine influenza, human influenza, avian influenza, and Eurasian influenza. The current pandemic began in Veracruz, Mexico, and rapidly spread to the United States and then the rest of the world. The "herald wave" of the pandemic in the United States began in the New York area at the end of the seasonal human influenza A season. At that time, other respiratory viruses also continued circulating in the community. The initial cases of H1N1 were epidemiologically linked to individuals with H1N1 in the New York epicenter and to those who had recently returned from Mexico. However, very quickly, there were so many secondary cases that a recent or close-contact history of someone with H1N1 became less clear and therefore less helpful diagnostically. The initial cases were relatively mild, but the number of cases rapidly increased during the pandemic. The immediate clinical problem involved differentiating H1N1 from influenza-like illnesses (ILIs) in admitted adults.[1]

Table I
Swine influenza (H1N1) pneumonia: clinical case definitions in adults

Definite H1N1 pneumonia (laboratory criteria)
ILIs with temperatures > 102°F, severe myalgias, and a CXR with no focal/segmental lobar infiltrates, plus one or more of these positive tests:
• Rapid influenza A test
• Respiratory FA viral panel
• RT-PCR for H1N1
Probable H1N1 pneumonia (clinical criteria)
ILIs with temperature > 102°F, severe myalgias, and a CXR with no focal/segmental lobar infiltrates with negative influenza tests (see above), plus:[†]
• Otherwise unexplained relative lymphopenia
• Elevated CPKs
• Increased serum transaminases (SGOT/SGPT)

†Diagnostic tests negative for other viral CAP pathogens (CMV, SARS, HPS, RSV metapneumoviruses, parainfluenza viruses, and adenoviruses).

RAPID INFLUENZA DIAGNOSTIC TESTS (RIDTs)

Early in the H1N1 pandemic, we realized that the rapid screening test (QuickVue A/B) used in our emergency department was only useful in patients who tested positive for influenza A. However, in adult ILI patients with false-negative rapid-screening influenza A tests (RIDTs), there was great diagnostic difficulty in categorizing patients from a clinical and epidemiologic perspective, i.e., adults admitted with suspected H1N1 pneumonia were placed on influenza precautions and given oseltamivir.[2,3] Early in the pandemic, single/negative-pressure rooms were quickly filled, and it became increasingly critical to devise a clinical diagnostic approach that would differentiate ILIs from the probable H1N1. When it was appreciated that RIDTs were frequently false negative, we used respiratory fluorescent antibody (FA) viral test panels to try to increase diagnostic accuracy. Respiratory FA viral tests had the additional value of detecting not only influenza A and B but other respiratory viruses presenting as ILIs, e.g., metapneumoviruses, parainfluenza viruses, respiratory syncytial viruses, and adenoviruses. Unfortunately, respiratory FA viral test results did not correlate well with results from RIDTs. In most cases, if a rapid influenza A test was positive, the respiratory FA viral panel was also positive for influenza A. However, when a rapid influenza A test was negative (which presented the most difficult diagnostic problem), the respiratory FA viral panel test was not frequently negative as well. When both the rapid influenza A screening test and the respiratory FA viral test were positive for influenza A, the results were highly predictive of a positive reverse transcription polymerase chain reaction (RT-PCR) test for H1N1.

Often there was no way to make a laboratory diagnosis of H1N1, because RT-PCR testing was restricted by the health department, and in the tests performed, the results were often returned long after the information had clinical or epidemiological relevance.[3]

Because laboratory confirmation of H1N1 cases was difficult in admitted adults with ILIs and negative rapid influenza diagnostic tests (RIDTs), diagnostic criteria were developed to provide clinicians with a presumptive clinical diagnosis, pending RT-PCR results. The "herald wave" of the H1N1 pandemic provided an opportunity for the Infectious Disease Division at Winthrop-University Hospital to develop a diagnostic weighted point score system, not unlike the one we had developed for diagnosing legionnaires' disease.[4]

Table II
Swine influenza pneumonia: Winthrop-University Hospital Infectious Disease Division's diagnostic weighted point score system for hospitalized adults with negative RIDTs for H1N1

Adults with ILIs with fever > 102°F with negative and a CXR with no focal/segmental lobar infiltrates plus:*	
• Severe myalgias	+5
• Relative lymphopenia (otherwise unexplained†)	+5
• Elevated CPK (otherwise unexplained)	+5
• Elevated serum transaminases (SGOT/SGPT)	+2
• Thrombocytopenia (otherwise unexplained)	+2
Argues *against* a diagnosis of H1N1 pneumonia:	
• Relative bradycardia (otherwise unexplained)	−5
• Leukopenia alone (otherwise unexplained)	−2
• Atypical lymphocytes	−1
• Highly elevated serum ferritin levels (> 2 × n)	−5
• Hypophosphatemia (otherwise unexplained)	−3
Swine influenza diagnostic point score totals:	Maximum score = 19
Probable H1N1 pneumonia	> 15
Possible H1N1 pneumonia	10-15
Unlikely H1N1 pneumonia	< 10

*Diagnostic tests negative for other viral CAP pathogens (CMV, SARS, HPS, RSV, metapneumo viruses, parainfluenza viruses, and adenoviruses).

†Other causes of relative lymphopenia include: infectious causes, i.e., CMV, HHV-6, HHV-8, HIV, miliary TB, legionella, typhoid fever, Q fever, brucellosis, SARS, malaria, babesiosis, human seasonal influenza, avian influenza, RMSF, histoplasmosis, dengue fever, chickungunya fever, ehrlichiosis, parvovirus B19, HPS, WNE, and viral hepatitis (early) and noninfectious causes, i.e., cytoxic drugs, steroids, sarcoidosis, SLE, lymphoma, RA, radiation therapy, Wiskott-Aldrich syndrome, Whipple's disease, severe combined immunodeficiency disease, common variable immune deficiency, Di George syndrome, Nezelof syndrome, intestinal lymphgiectasia, constrictive pericarditis, tricuspid regurgitation, Kawasaki's disease, idiopathic CD_4 cytopenia, Wegener's granulomatosis, acute/chronic renal failure, hemodialysis, myasthenia gravis, celiac disease, alcoholic cirrhosis, coronary bypass, CHF, acute pancreatitis, and carcinomas (terminal)

RMSF = rocky mountain spated fever; SLE = systemic lupus erythematosis; RA = rhematoid arthritis; CHF = congestive heart failure; HPS = hautavirus pulmonary syndrome; CMV = cytomegalovirus; SARS = severe acute respiratory syndrome.
Adapted from Cunha.[10]

CASE DEFINITIONS: DEFINITIVE OR PROBABLE H1N1

The clinical presentation of H1N1 pneumonia, like that of other infectious diseases, ranges from mild, self-limiting illness to severe life-threatening pneumonia and respiratory failure. The Winthrop-University Hospital Infectious Disease Division's diagnostic weighted point score system was developed to diagnose probable H1N1 pneumonia in hospitalized adults with ILIs, temperatures >102°F and negative RIDTs.

Adult patients considered to have definite (laboratory-based diagnosis) H1N1 pneumonia included those hospitalized with an ILI, fever >102°F and myalgia, plus one or more positive RIDTs, e.g., a rapid influenza A test (QuickVue A/B), a respiratory FA viral test panel, or RT-PCR for H1N1. A probable case (clinically based diagnosis) of H1N1 pneumonia was defined as above, but with negative RIDTs plus otherwise unexplained relative lymphopenia thrombocytopenia, elevated serum transaminases, and elevated CPKs (Table I).

H1N1: KEY CLINICAL DIAGNOSTIC

During the "herald wave" of the H1N1 pandemic, the initial Winthrop-University Hospital Infectious Disease Division's diagnostic weighted point score system was based on the relative diagnostic importance of key features (Table II)[5,6]. Unlike with human seasonal influenza A, Leukopenia was not an isolated finding. If leukopenia occurred, it did so together with relative lymphompenia/thrombocytopniea.[6-8] The Winthrop-University Hospital Infectious Disease Division's proved useful in deciding which adult hospitalized patients with ILIs had probable H1N1 pneumonia (Tables I and II).

Table III
Winthrop-University Hospital Infectious Disease Division's H1N1 pneumonia weighted diagnostic point score system for hospitalized in adults with ILIs, fever > 102°F, negative RIDTs and a CXR with no focal/segmental lobar infiltrates

Clinical Features	Point Scores	Swine Influenza (H1N1) Laboratory Diagnosed	Swine Influenza (H1N1) Clinically Diagnosed	ILIs not swine influenza (H1N1)	CMV CAP	Q Fever CAP	Legionella CAP
• Severe myalgias	+5	+5	+5	0	0	0	0
• Relative lymphopenia (otherwise unexplained*)	+5	+5	+5	0	+5	+5	+5
• Elevated CPKs (otherwise unexplained)	+5	+5	+5	0	0	0	+5
• Elevated serum transaminases (SGOT/SGPT)	+2	+2	+2	0	+2	+2	+2
• Thrombocytopenia (otherwise unexplained)	+2	+2	+2	0	+2	+2	0
Argues *against* diagnosis of (H1N1) pneumonia:							
• Relative bradycardia (otherwise unexplained)	−5	0	0	0	0	0	0
• Leukopenia alone (otherwise unexplained)	−2	0	0	0	0	0	0
• Atypical lymphocytes	−1	0	0	0	0	0	0
• Highly elevated serum ferritin levels (> 2 x n)	−5	0	0	0	0	0	0
• Hypophosphatemia	−3	0	0	0	0	0	0
Swine influenza H1N1 Point Score Total:	Total Points	19	19	0	9	9	12
Probable H1N1 pneumonia > 15							
Possible H1N1 pneumonia 10–15							
Unlikely H1N1 pneumonia < 10							

*Other causes of relative lymphopenia include infectious causes, i.e., CMV, HHV-6, HHV-8, HIV, miliary TB, legionella, typhoid fever, Q fever, brucellosis, SARS, malaria, babesiosis, influenza, avian influenza, RMSF, histoplasmosis, dengue fever, chikungunya fever, ehrlichiosis, parvovirus B19, HPS, WNE, and viral hepatitis (early); and noninfectious causes, i.e., cytoxic drugs, steroids, sarcoidosis, SLE, lymphoma, RA, radiation therapy , Wiskott-Aldrich syndrome, Whipple's disease, severe combine immunodeficiency disease, common variable immune deficiency, Di George syndrome, Nezelof syndrome, intestinal lymphgiectasia, constrictive pericarditis, tricuspid regurgitation, Kawasaki's disease, idiopathic CD_4 cytopenia, Wegener's granulomatosis, acute/chronic renal failure, hemodialysis, myasthenia gravis, celiac disease, alcoholic cirrhosis, coronary bypass, CHF, acute pancreatitis, and carcinomas (terminal).

The Winthrop-University Hospital Infectious Disease Division's weighted diagnostic point scores of cases of adults admitted with ILIs during the H1N1 pandemic are presented in Table III. The Winthrop University Hospital Infectious Disease Division's H1N1 pneumonia diagnostic point score system correctly identified probable cases of H1N1 pneumonia, and differentiated these from other community-acquired pneumonias.

DISCUSSION

In approaching a differential diagnosis from a syndromic prospective, it becomes apparent that certain clinical features are characteristic of a diagnosis, whereas others are only consistent with that diagnosis. The Winthrop-University Hospital Infectious Disease Division's diagnostic weighted point score system is based on this principle, i.e., clinical features that are characteristic and of key diagnostic importance, are given high point scores. During the "herald wave" of the H1N1 pandemic in the spring and summer of 2009 at Winthrop-University Hospital, this approach was used to make a probable diagnosis of swine influenza pneumonia in admitted adults with ILIs, fevers >102°F, CXRs with no focal segmental/lobar infiltrates and negative RITDs. The Winthrop-University Hospital Infectious Disease Division's diagnostic weighted point score system was helpful in differentiating cases of H1N1 pneumonia from ILIs and other causes of viral and bacterial community-acquired pneumonias.[9]

The point scores of actual cases that occurred during the "herald wave" of the pandemic illustrate the practical clinical usefulness of the Winthrop-University Hospital Infectious Disease Division's diagnostic point score system for H1N1 pneumonia. Until more sensitive and specific RIDTs are developed, or until RT-PCR results are more available the Winthrop-University Hospital Infectious Disease Division's diagnostic point score system provides clinicians with an accurate presumptive diagnosis of H1N1 pneumonia in hospitalized adults with ILIs and negative RIDTs. Clinical diagnosis permits early triage of adult hospitalized patients with ILIs and negative RIDTs, to determine which patients should be placed on influenza precautions or treated with oseltamivir.

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