

# Respiratory Research Review™

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## Welcome to the May edition of the Respiratory Research Review.

"Damned if you do-damned if you don't" is the summary of an editorial in Nature on a possible influenza A epidemic, commenting that "The risk is not in hyping the pandemic threat, but in underplaying it." Readers may enjoy reading 'Reflection on the 1976 Swine Flu Vaccination Program' (*Emerg Infect Dis* 2006; 12(1): 29-33) by the people in charge of the mass vaccination programme of 40 million people in 1976. The Influenza epidemic never happened, but an increase in Guillain-Barré syndrome was observed. Readers may wish to monitor the [WHO, Center of Disease Control, New England Journal of Medicine](#) and the [NZ Ministry of Health](#) official websites for current updates.

This month's Research Review focuses on peer-reviewed articles on influenza that describe the virus and compare the NZ pandemic plan with European pandemic plans. The Review will stay with the topic of infectious diseases and report on articles on healthcare-associated pneumonia, pneumonia scoring systems, diagnostic tests and an intriguing article on the possible role of macrolide antibiotics in prolonging the survival rate of patients with pneumonia.

Information technology is essential during this possible flu epidemic. It may also improve the quality of care delivered to individual patients.

Your feedback is as welcome as always.

Kind regards,

**Dr Lutz Beckert**

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## Comparison of the content of the New Zealand influenza pandemic plan with European pandemic plans

**Authors:** Wilson N et al

**Summary:** This comparison of the 16th version of the NZ influenza pandemic plan with 29 European plans available in 2006 revealed that NZ plans had higher scores on border control aspects than the European plans (8.0 vs. 4.9 out of 10.0). NZ and European plans had similar antiviral scores (13.5 vs 10.6 out of 17), but vaccine aspect scores out of 11.0 were lower (4.5 vs. 5.3). However, on another more stringent scoring system, the NZ plan fared worse than European plans for antiviral aspects and the scores were similar for vaccine aspects; this framework probably favoured European plans as the capacity to produce vaccines and antiviral agents is greater. Some deficiencies were highlighted in the NZ plan, such as detail around priority groups for antivirals/vaccines, and consideration of pneumococcal vaccine, and the investigators commented that these could be worth addressing in this year's revision.

**Comment:** This article compares the current NZ influenza pandemic plan on the [MOH website](#) with 29 European pandemic plans. NZ does not fair too badly, particularly in border control and entry screening matters. However, the NZ plan could be improved in operational issues, including prioritisation protocols and consideration of the possible disproportional impact on the Māori population given experience from the 1918 influenza pandemic.

**Bottom line: NZ pandemic planning holds up well compared with European plans despite their higher wealth per capita and own national influenza vaccine production facilities.**

**Reference:** *NZ Med J* 2009; 122(1290): 36-46

<http://www.nzma.org.nz/journal/abstract.php?id=3490>

# COMING SOON to South Africa

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## Triple-reassortant swine influenza A (H1) in humans in the United States, 2005–2009

**Authors:** Shinde V et al

**Summary:** The clinical features of the first 11 cases of triple-reassortant swine influenza (H1) virus infections in humans prior to the epidemic of H1N1 infection were described in this paper. The patients were aged 16 months to 48 years, and 9 had experienced direct (n=5) or indirect (4) exposure to pigs, while human-to-human transmission was suspected in one patient. The incubation period ranged from 3 to 9 days, and among the 10 patients with known clinical symptoms, 10 had cough, 9 had fever, 6 had headache and 3 had diarrhoea. Hospitalisation was required in 4 patients, and two required mechanical ventilation. Two of the 4 patients with complete blood counts had leucopenia, one had lymphopenia and one had thrombocytopenia. Four patients were treated with oseltamivir, and all the patients recovered.

**Comment:** Researchers from the Center of Disease Control remind us that it was a 'swine flu' virus that killed 70 million people in 1918. The current swine flu can be seen as a continuum, and the article provides genetic-based evidence for this. This article, the accompanying editorials, and the reflections on the 1976 swine flu referenced on page 1 provide excellent background information. **Bottom line: The generation of novel influenza viruses through the reassortment of swine influenza may be inevitable and may cause major public health threats. All human infections with influenza viruses of animal origin warrant thorough investigation.**

**Reference:** *N Engl J Med Online May 7, 2009 (10.1056/NEJMoa0903812); scheduled for Jul 2 issue*

<http://content.nejm.org/cgi/content/full/NEJMoa0903812>

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## Emergence of a novel swine-origin influenza A (H1N1) virus in humans

**Authors:** Novel H1N1 Virus Investigation Team

**Summary:** This paper described 642 confirmed cases of novel swine-origin influenza A (H1N1) virus in humans from 41 states in the US. The patients were aged 3 months to 81 years, but 60% were aged ≤18 years. Recent travel to Mexico was identified in 18% of cases with available data, while 16% were from schools where there had been an outbreak. Presenting symptoms included fever (94% of patients), cough (92%) sore throat (66%), diarrhoea (25%) and vomiting (25%). Hospitalisation was required in 36/399 (9%) of patients in whom hospitalisation information was available. Among the 22 hospitalised patients with available data, characteristics conferring an increased risk of severe seasonal influenza were present in 12, pneumonia was present in 11, 8 required an ICU admission, 4 had respiratory failure, and there were 2 deaths.

**Comment:** This article documents the origin of the emerging H1N1 virus, from the first cases in Mexico, the genetic identification, and the WHO pandemic influenza declaration phase 5 (out of 6). This article reports authoritatively on the first 642 cases with an incubation period of 7 days. The article is important reading and 'free for all'. Peter Sandman, a risk communication consultant in New Jersey, gave the best bottom line: **"Anyone who's paying attention gets it that we just don't know if this thing is going to fizzle, hang in abeyance for months, disappear and then reappear, spread but stay mild, replicate or exceed the 1918 catastrophe, or what"** (*Nature 2009; 459(7243): 9*).

**Reference:** *N Engl J Med Online May 7, 2009 (10.1056/NEJMoa0903810); scheduled for Jul 2 issue*

<http://content.nejm.org/cgi/content/full/NEJMoa0903810>

## Respiratory viruses in bronchoalveolar lavage: a hospital-based cohort study in adults

**Authors:** Garbino J et al

**Summary:** This hospital-based study explored the presence of 17 different respiratory viruses in BAL fluid from 299 patients; of the 522 BAL samples analysed, 81% came from immunocompromised patients. Viral nucleic acid was identified in 91 (17.4%) samples at similar rates across the different subpopulations analysed. Identified viruses included coronavirus (32.3%), rhinovirus (22.6%), parainfluenza (19.5%), influenza (9.7%), respiratory syncytial virus (RSV; 8.6%), human metapneumovirus (4.2%) and bocavirus (3.1%). A multivariate analysis revealed that there was an association between the respiratory viral infections and both antibacterial nonresponse (OR 2.2; 95% CI 1.2, 4.1) and radiological infiltrate absence (0.3; 0.2, 0.8). The respiratory viral detection rate was significantly greater in lung transplant recipients with suspected respiratory infection than in other patients (24.4 vs. 13.8%; p=0.02).

**Comment:** This Swiss group investigated 522 lavage specimens from a group of high-risk hospitalised patients systematically with a battery of PCR primers for possible viral infections. They reported on viruses that were found in 17.4% of the samples. 'Common cold' viruses like coronavirus and rhinovirus were more common than the more serious and partially treatable influenza or RSV. **Bottom line: In at-risk patients with respiratory symptoms and a poor response to antibiotics, a respiratory viral aetiology should be considered.**

**Reference:** *Thorax 2009; 64(5): 399–404*

<http://thorax.bmj.com/cgi/content/abstract/64/5/399>

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## Outcomes of patients hospitalized with community-acquired, health care-associated, and hospital-acquired pneumonia

**Authors:** Venditti M et al

**Summary:** This study compared the rates of community-acquired pneumonia (CAP), health care-associated pneumonia (i.e. pneumonia in patients who have recently been hospitalised, had haemodialysis, or received intravenous chemotherapy or reside in a nursing home or long-term care facility) and hospital-acquired pneumonia (HAP) in 362 adults hospitalised with pneumonia during two 1-week surveillance periods. Rates of CAP, healthcare-associated pneumonia and HAP were 61.6%, 24.9% and 13.5%, respectively. Patients with healthcare-associated pneumonia had higher mean SOFA scores than did those with CAP (3.0 vs. 2.0), were more frequently malnourished (11.1% vs 4.5%), and had more frequent bilateral (34.4% vs 19.7%) and multilobar (27.8% vs. 21.5%) involvement on a chest radiograph. Patients with healthcare-associated pneumonia also had higher fatality rates (17.8% vs. 6.7%) and longer mean hospital stay (18.7 vs. 14.7 days). According to logistic regression analysis, factors independently associated with increased intrahospital mortality were depression of consciousness (OR 3.2; CI 15.9, 21.5), leucopenia (6.2; 1.01, 37.6), and receipt of empirical antibiotic therapy not recommended by international guidelines (6.4; 2.3, 17.6).

**Comment:** We know that patients with CAP have better outcomes and a different profile of causative organism than patients with healthcare-associated pneumonia. This study from Italy complements findings from a Japanese study ([Chest 2009; 153\(3\): 633–40](#)) that investigated patients from healthcare facilities (principally rest homes). The prevalence of pneumonia in rest homes was 10.9% in winter, with residents having higher comorbidity, higher risk scores and more complex microbiology. **Bottom Line: Healthcare-associated pneumonia should be considered a distinct subset of pneumonia associated with more severe disease, longer hospital stay and higher mortality rates.**

**Reference:** *Ann Intern Med* 2009; 150(1): 19–26  
<http://www.annals.org/cgi/content/abstract/150/1/19>

*Independent commentary by  
Dr Lutz Beckert, Respiratory  
Physician at Christchurch Hospital.*

## Adrenal response in severe community-acquired pneumonia: impact on outcomes and disease severity

**Authors:** Salluh JIF et al

**Summary:** This study investigated the predictive value of adrenal response in 72 ICU patients with severe community acquired pneumonia. There were significant correlations between baseline cortisol level (18.1 µg/dL) and scores of disease severity (CURB-65, APACHE-II and SOFA;  $p < 0.05$ ). Critical illness-related corticosteroid insufficiency was diagnosed in 40.8% of patients. Patients who survived had lower cortisol levels than those who died, and this was reflected in the findings of a univariate analysis that revealed predictors of death were baseline cortisol, as well as CURB-65 and APACHE II scores. Moreover, baseline cortisol had a better discriminative ability to predict in-hospital mortality than CURB-65, APACHE II and SOFA scores, and levels of D-dimer and C-reactive protein.

**Comment:** This article from a Brazilian group reminds us of the importance of severity assessment of pneumonia. Ten percent of patients admitted with pneumonia will require admission to ICU. These authors concluded that a higher baseline cortisol level had a stronger association with an adverse outcome than the traditional scoring systems. **Bottom line: High baseline cortisol levels may be a marker of adverse outcome. Severity assessment is crucial in the management of pneumonia. Excellent reviews are published in [Respirology 2009; 14\(3\): 327–335](#) and [Q J Med Advance Access online](#).**

**Reference:** *Chest* 2008; 134(5): 947–54  
<http://www.chestjournal.org/content/134/5/947.abstract>

## Incidence and characteristics of viral community-acquired pneumonia in adults

**Authors:** Jennings LC et al

**Summary:** Microbiological testing in 304 patients admitted over a 1-year period to Christchurch hospital with community-acquired pneumonia revealed that 88 (29%) had respiratory viral infections, with  $\geq 2$  pathogens identified in 49 (16%) patients, 45 of whom had both viral and bacterial infections. Rhinovirus and influenza virus were the most common viruses identified. Although reliable clinical predictors of viral pneumonia were not identified, there were associations between myalgia and pneumonia secondary to any respiratory virus (OR 3.62; 95% CI 1.29, 10.12) and influenza virus (190.72; 3.68, 9891.91), and also between severe disease and mixed rhinovirus/pneumococcal infection.

**Comment:** This study reports on data from the Christchurch community pneumonia study. The authors used immunofluorescence, viral culture, serology and PCR testing to determine that viruses were present in 29% of patients admitted. The most commonly identified viruses were rhinoviruses, influenza A and respiratory syncytial virus. It remains unclear whether viruses alone cause pneumonia or whether they act in conjunction with other pathogens. Current management focuses on bacteria because of the lack of specific antiviral agents. However, this focus may change as vaccinations or treatments become available. **Bottom line: Viral-associated pneumonia is common, and mixed infections may be associated with severe pneumonia.**

**Reference:** *Thorax* 2008; 63(1): 42–8  
<http://thorax.bmj.com/cgi/content/abstract/63/1/42>



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### Impact of macrolide therapy on mortality for patients with severe sepsis due to pneumonia

**Authors:** Restrepo MI et al

**Summary:** This retrospective cohort study investigated the effect of macrolides on mortality in patients with pneumonia-related severe sepsis, of whom 104 received treatment with macrolides (at least one dose within 48 hours of admission). Mortality rates at 30 and 90 days were 20.3% and 24.5% respectively. A multivariate analysis showed that use of macrolides was associated with reduced mortality at 30 and 90 days (hazard ratios 0.3; 95% CI 0.2, 0.7 and 0.3; 0.2, 0.6, respectively). The investigators added that further studies are needed to confirm a possible protective effect of macrolides in this patient group.

**Comment:** This intriguing study reports on the impact of macrolide therapy in a cohort of 787 patients admitted with hospital-acquired pneumonia. The authors found that about half of all patients with severe sepsis received macrolide antibiotics during the first 48 hours of admission. The mortality rate of the group not receiving macrolide therapy was almost 30% as expected. However the 30- and 90-day mortality rates in patients receiving macrolide therapy were 11% and 12%, respectively, and were independent of the causative organism. **Bottom line: The authors speculate that macrolides may reduce mortality through immune-modulating activity. This needs to be confirmed in prospective studies.**

**Reference:** *Eur Respir J* 2009; 33(1): 153–9  
<http://erj.ersjournals.com/cgi/content/abstract/33/1/153>

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### Diagnosis of *Streptococcus pneumoniae* infections in adults with bacteremia and community-acquired pneumonia: clinical comparison of pneumococcal PCR and urinary antigen detection

**Authors:** Smith MD et al

**Summary:** A new dual-PCR protocol was compared with the 'Binax NOW' urinary antigen test for diagnosing *Streptococcus pneumoniae* in 58 patients with bacteraemic pneumococcal infections and 51 control patients. Sensitivity was significantly lower for the new dual-PCR test than for the 'Binax NOW' test (53.5% vs. 88%), and specificity was the same (96%). The investigators commented that although the dual-PCR assay was more sensitive than the individual component assays, 'Binax NOW' remains significantly more sensitive, as well as less expensive and time consuming.

**Comment:** This British study reviewed the role of urinary antigen testing in the diagnosis of streptococcus pneumonia sepsis in 58 patients. Although the researchers designed a new, more sensitive PCR methodological method in blood samples, the urinary antigen test was significantly more sensitive with the same, excellent specificity. This outcome must have been disappointing for the authors, and we are grateful that they still published their negative results. **Bottom line: 'Binax NOW' urine antigen test is the nonculture diagnostic method of choice for patients with possible severe pneumococcal infection.**

**Reference:** *J Clin Microbiol* 2009; 47(4): 1046–9  
<http://jcm.asm.org/cgi/content/abstract/47/4/1046>

### Clinical information technologies and inpatient outcomes

**Authors:** Amarasingham R et al

**Summary:** The impact of clinical information technologies on clinical and financial outcomes in 41 US hospitals was assessed using the Clinical Information Technology Assessment Tool. The main findings were: 1) a 10-point increase in automation of notes and records was associated with a reduction in fatal hospitalisations (adjusted OR 0.85; 95% CI 0.74, 0.97); 2) higher order entry automation scores were associated with decreases in mortality associated with myocardial infarction and coronary artery bypass procedures of 9% and 55%, respectively; 3) higher automation scores in decision support were associated with a decrease in complications (adjusted OR 0.84; 95% CI 0.79, 0.90); and 4) costs associated with decision support, order entry and test results were reduced when their automation scores were higher.

**Comment:** The availability of information technology has a significant impact during the surveillance and impact of the influenza epidemic. These American authors reported that the degree of 'wiredness' may also reduce patient mortality, complication rates and costs of patient management. The authors found no increased electronically facilitated errors. By its design, this study can not exclude organisational confounders or chance associations as explanations for the apparent positive impact of information technology. **Bottom line: Clinical information technology promises to improve medicine. More investment in information systems may reduce patient mortality, complications and hospital costs.**

**Reference:** *Arch Intern Med* 2009; 169(2): 108–14  
<http://archinte.ama-assn.org/cgi/content/abstract/169/2/108>

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