The practical experience of managing the H1N1 2009 influenza pandemic in Australian and New Zealand intensive care units

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The influenza A virus undergoes periodic antigen shifts, resulting in new strains. The emergence of new strains provides the necessary conditions for a pandemic,[1] and this occurred in 2009. It was the first pandemic since 1968, and the first to occur in an era of widespread intensive care.[2] The H1N1 2009 virus emerged in the northern hemisphere, and winter outbreaks followed in countries in the southern hemisphere, including Australia and New Zealand (ANZ).[3] The provision of intensive care in these countries is similar to other developed countries.[4] The experience in ANZ may help intensive care clinicians elsewhere to treat critical illness associated with H1N1 2009.

At the onset of the H1N1 2009 influenza pandemic in ANZ, there was no published experience with respect to attack rates, virulence, risk groups, clinical syndromes, management, and risk to staff. This article reports the practical experience of the intensive care community in ANZ. It is an extension of the published experience,[3,5-7] but is largely anecdotal, drawn from the personal experience of us and our colleagues. Focusing only on adult patients, we describe the risk factors, clinical syndromes, diagnosis and

management of the disease. We also discuss infection control issues and management of the increased demand for admissions to intensive care units.

Risk factors

The ANZ Intensive Care Influenza Investigators identified several risk factors for admission to the ICU.[3] Accurate odds ratios for risk factors for severity could not be calculated, as data from patients with confirmed mild disease were not available. It was possible to compare the observed proportion of patients with particular risk factors with the expected proportion using data derived from the general population. These results were consistent with the observations of the intensivists involved.

Among the patients admitted to ANZ ICUs, 9.1% were pregnant, representing a nearly 10-fold higher occurrence than expected.[3] Patients with any form of chronic lung disease, including stable asthma or chronic obstructive pulmonary disease, comprised 32.7% of patients, which is about twice the prevalence in the general population. Among patients in the ANZ Intensive Care Influenza Investigators registry, 28.6% of adults had a body mass index of over 35 kg/m^2, compared with 5.3% in the general population.[3] Indigenous patients were over-represented four-fold in Australia and two-fold in New Zealand. Patients with severe comorbidity (the presence of any APACHE [Acute Physiology and Chronic Health Evaluation] III comorbidity[8]) were also over-represented, and severe comorbidity was reported in 27.9% of patients. Overall, about a third of patients had significant comorbidity, about a third had risk factors such as asthma, obesity or pregnancy but without other severe comorbidity, and about a third had neither risk factors nor significant comorbidity.

Seasonal influenza has the greatest effect on elderly people.[9] The incidence of ICU admission for confirmed H1N1 2009 cases was highest per capita in infants and had an absolute majority among adults aged 25–64 years.[3] Although ICU admission was low in adults aged over 65 years, increasing age was independently associated with death.

Abbreviations

ANZ	Australia and New Zealand
APRV	Airway pressure release ventilation
ARDS	Acute respiratory distress syndrome
BAL	Bronchoalveolar lavage
CAP	Community-acquired pneumonia
CK	Creatine kinase
CXR	Chest x-ray
ECMO	Extracorporeal membrane oxygenation
FIO$_2$	Fraction of inspired oxygen
HFOV	High-frequency oscillatory ventilation
MRSA	Methicillin-resistant *Staphylococcus aureus*
NIV	Non-invasive ventilation
PaO$_2$	Arterial partial pressure of oxygen
PCR	Polymerase chain reaction
PEEP	Positive end-expiratory pressure
SaO$_2$	Arterial oxygen saturation

Clinical syndromes associated with H1N1 2009 influenza

Patients admitted to the ICU usually had one of three pulmonary syndromes: (i) viral pneumonitis, which often met criteria for acute respiratory distress syndrome (ARDS); (ii) secondary bacterial pneumonia; or (iii) airflow limitation. Usually only one syndrome was predominant. Some patients also had one or more extrapulmonary syndromes, including shock, renal failure, abnormal liver function, rhabdomyolysis (quite common), fever (often prolonged and sometimes severe), neutropenia, thrombocytopenia, coagulopathy (including disseminated intravascular coagulation), encephalitis and gastroenteritis. Rarely, extrapulmonary syndromes were the main clinical feature.

About half the patients had viral pneumonitis and 20% had bacterial pneumonia in addition to H1N1 2009 infection.[3] A complete list of the clinical syndromes associated with H1N1 2009 infection is presented in Box 1.

Viral pneumonitis/acute respiratory distress syndrome

Viral pneumonitis/ARDS was characterised by the presence of extensive bilateral alveolar infiltrates on chest x-ray (CXR) (Figure 1), respiratory failure that was often severe and rapidly progressive, and the absence of bacterial pathogens that cause

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Box 1. Classification of syndromes associated with H1N1 2009 influenza

Pulmonary syndromes
- Syndromes of airflow limitation
  - ➢ Exacerbation of asthma
  - ➢ Exacerbation of chronic obstructive pulmonary disease
  - ➢ Croup
  - ➢ Bronchiolitis
  - ➢ Airflow limitation in patients with no history of obstructive lung disease
- Viral pneumonitis with acute respiratory distress syndrome
- Bacterial pneumonia

Extrapulmonary syndromes
- Shock
- Renal failure
- Abnormal liver function tests
- Rhabdomyolysis
- Fever
- Neutropenia
- Thrombocytopenia (with or without coagulopathy)
- Coagulopathy (with or without evidence of disseminated intravascular coagulation)
- Encephalitis
- Gastroenteritis/diarrhoea
- Myocarditis

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pneumonia in lower respiratory tract specimens or blood.

The cardinal manifestation was dyspnoea. Haemoptysis was present in some patients. The most useful investigations were an assessment of oxygenation (saturation or arterial blood gases) and a CXR.

A preceding coryzal illness was common but not universal. The duration of the prodrome varied from 24 hours to a week or more. The viral pneumonitis often had progression of respiratory failure and evolution of infiltrates on CXR over several hours. Most patients who developed confluent pneumonia had an abnormal CXR at presentation, although some presented with hypoxaemia and a clear CXR.

Because illness occurred predominantly in young and middle-aged adults who were often otherwise fit, patients with severe illness frequently "looked better" than they actually were. Care was needed to identify this group, who were at risk of sudden decompensation. The assessment of oxygenation and chest radiography was important to avoid this trap.

Most patients presented from the community. A few acquired nosocomial infections from other patients or from hospital staff or visitors. A diagnosis of influenza cannot be excluded just because a patient has been in hospital longer than the

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Figure 1. Chest x-ray showing confluent viral pneumonitis in a patient with H1N1 2009 influenza
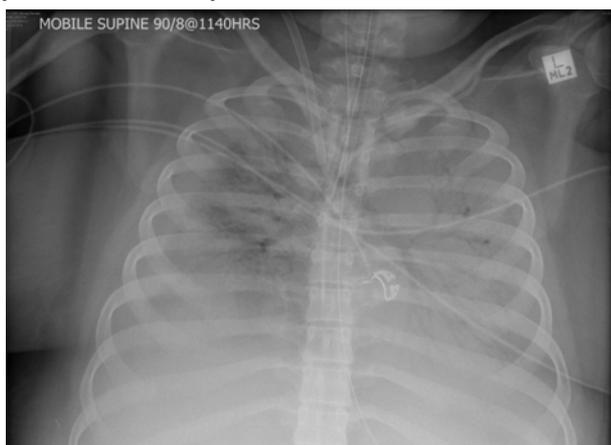

Figure 2. Endotracheal aspirate from a patient with severe H1N1 2009 influenza ("beer lung")

incubation period for the infection.

Most patients with extensive pneumonitis had progressive isolated respiratory failure that required invasive mechanical ventilation. Only a few with extensive CXR changes were successfully managed with high-flow oxygen or non-invasive ventilation (NIV). Some centres avoided NIV because of concern about aerosolisation of the virus and an impression that patients needing NIV would ultimately require intubation. Others reported that NIV sometimes prevented the need for intubation.

There were several unusual features of the ARDS seen in these patients, whose pattern of symptoms has been termed "flu A associated ARDS".[2] Among ventilated patients, lung compliance was often surprisingly normal. Severe shunt and hypoxaemia predominated rather than hypercarbia. Some intubated patients had copious pulmonary secretions, producing up to several hundred millilitres per day of amber or blood-tinged fluid with froth on top (Figure 2). Patients were often difficult to sedate. Coughing was common and could make ventilation difficult.

Recovery was slow, with persisting infiltrates visible on CXR and prolonged hypoxaemia. Patients were observed in whom the arterial partial pressure of oxygen (Pa_{O_2}) was never above 60–70 mmHg for several weeks. During the recovery phase, these patients were particularly fragile. Often even small changes in ventilator settings, reduction in positive end-expiratory pressure (PEEP), or switches from mandatory to triggered modes of ventilation led to deterioration. Reduction in ventilatory support needed to be slower than in most patients with ARDS.

Progression to fibroproliferative ARDS was uncommon, as were pneumothoraces associated with mechanical ventilation. Some patients could be extubated by Day 7 to 10, but many required a tracheostomy and prolonged weaning.

Secondary bacterial pneumonia

Secondary bacterial pneumonia was characterised by lobar infiltrates, which could be patchy and/or multilobar. Bacterial pathogens known to cause pneumonia were present in samples recovered from blood and/or lower respiratory tract samples. The clinical presentation was similar to that of patients with bacterial community-acquired pneumonia (CAP) in other circumstances. Patients with secondary bacterial pneumonia could develop all the usual complications of CAP.

Airflow limitation

In adults with a history of asthma or chronic obstructive pulmonary disease, infection with H1N1 2009 produced an exacerbation of airflow limitation. These patients had similar clinical characteristics and course to patients with usual exacerbations of airflow limitation. Occasionally airflow limitation occurred in patients without any history of obstructive lung disease.

Extrapulmonary manifestations

Shock: Shock was associated with vasodilation rather than impaired cardiac output. The duration of shock was variable. Some patients required vasopressors for several weeks. Some deaths were from multiple organ failure in which the mode of death was refractory shock. At least 35% of patients (and 88% of those in the extracorporeal membrane oxygenation [ECMO] group) required vasopressor support, although these figures are based on incomplete data.[3,5]

Renal failure: Acute renal failure was observed in both viral pneumonitis and bacterial pneumonia. This could present at the time of admission or evolve later. Some patients (5.3%) required acute dialysis or other renal replacement therapy in the ICU.[3]

Fever: Fever was often severe and prolonged. Isolated patients died late in their course from rapidly progressive multiple organ failure, probably secondary to severe hyperthermia. External cooling was used extensively. Despite this, some patients had sustained fevers above 39°C, and some had body temperatures exceeding 41°C.

Abnormal liver function tests: Abnormalities of liver function tests, usually without hyperbilirubinaemia, were common.

Neutropenia: A small proportion of patients with both viral pneumonitis and bacterial pneumonia presented with or developed significant neutropenia.

Thrombocytopenia and coagulopathy: Combinations of thrombocytopenia, coagulopathy or frank disseminated intravascular coagulation were observed. Most were not associated with bleeding.

Rhabdomyolysis: Elevated levels of plasma creatine kinase (CK) were common. The range of elevated CK was wide — from several hundred to tens of thousands of units per litre. Renal failure from rhabdomyolysis alone was rare. The concurrence of elevated CK level and a patient presenting with a clinical illness that was compatible with complicated H1N1 influenza was almost always diagnostic of H1N1 influenza. However, the absence of an elevated CK level could not be used to exclude H1N1 infection. There were isolated reports of severe hyperkalaemia, possibly arising from rhabdomyolysis in patients who required emergency dialysis.

Encephalitis: Encephalitis secondary to pandemic influenza was reported and was clinically little different from other forms of viral encephalitis.

Gastroenteritis: This was reported as being common in patients with H1N1 2009 infection who were managed in the community. It was not prominent in patients admitted to the ICU.

Primary cardiac complications: Myocarditis complicated by cardiogenic shock was observed in association with H1N1 2009 infection. There was also a report of an anterior myocardial infarction being precipitated by an H1N1 2009 infection.

General points

The syndromes of bacterial pneumonia and viral pneumonitis were usually relatively easy to distinguish, based on the combination of infiltrates seen on CXR and microscopy and culture of bacterial pathogens from lower respiratory tract specimens.

In the context of an influenza pandemic, a young patient who has respiratory failure and bilateral lung infiltrates with an elevated troponin level has influenza and not a non-ST-elevation myocardial infarction with pulmonary oedema. Admission to a coronary care unit and/or cardiac catheterisation of such patients did occur. The rapid progression of respiratory failure may not necessarily have been best managed in a coronary care unit.

In the context of a pandemic, pregnant women or people who were morbidly obese with critical illness were very likely to have complications of influenza.

Diagnostic testing

Most ANZ microbiology laboratories had ready access to rapid antigen detection tests, polymerase chain reaction (PCR) testing for influenza A and B and serological assays for influenza antibodies. Except in reference laboratories, viral culture had been phased out. Early experience was that antigen detection tests performed poorly, with false positive and false negative tests occurring frequently. Specific PCR assays to detect H1N1 influenza virus RNA were rapidly introduced into regional reference centres.[10] The PCR assays performed better than antigen detection tests, although probable false negatives were common and PCR could not be relied on to exclude infection. Conventional serology testing for influenza A, most commonly using complement fixation methods, could often detect high or rising titres of antibodies in patients in whom H1N1 2009 had been confirmed by PCR. Serology could only provide a retrospective diagnosis.

PCR for H1N1 2009: The impression of clinicians who interpreted the results of PCR assays was that specificity was high (ie, there were no or few false positive results) but that sensitivity was lower than expected (ie, false negatives were recognised). PCR testing was performed on nasopha-

ryngeal swabs, tonsil or throat swabs, sputum aspirated via an endotracheal tube or expectorated, and bronchoalveolar lavage (BAL) fluid. Clinicians considered that PCR testing on nasopharyngeal swabs was only about 80% sensitive compared with clinical diagnosis.

The clinical diagnosis of viral pneumonitis was uncommon before and after the pandemic. It seems reasonable to presume that, during a confirmed outbreak of H1N1 2009 infection, most patients with an appropriate clinical illness but a negative PCR result have H1N1 2009-induced viral pneumonitis. It was felt that the sensitivity of PCR testing was highest for sputum samples obtained from an endotracheal tube or by BAL and lowest for nasopharyngeal and throat swabs. Further research is required to confirm this observation.

Possible reasons for the poor performance of PCR include inappropriate collection by staff unfamiliar with correct technique and absence of the virus at the site from which the specimen was taken. We postulate that migration of the virus from upper to lower respiratory tract occurred during the evolution of viral pneumonitis, reducing the yield from PCR using upper respiratory tract specimens.

There were still many examples of lower respiratory tract specimens that were likely false negatives on PCR. On occasion, a second or third lower respiratory tract specimen would yield a positive result when tested by PCR. It was not clear if there was a relationship between a false negative result and either preceding antiviral therapy or duration of symptoms. In a patient at high clinical risk, a negative PCR cannot be used to exclude disease, and antiviral medications and infection control measures should be continued as appropriate.

We recommend that PCR be performed in all intubated critically ill patients suspected of having H1N1 2009 infection using samples from nasopharyngeal and throat swabs plus either a sputum or BAL specimen. In patients without an endotracheal tube, nasopharyngeal and throat swabs should be collected, as well as sputum, if the patient can produce it.

We recommend testing in all patients who present with asthma or an exacerbation of chronic lung disease and in all patients with respiratory failure with either focal or generalised lung infiltrates on CXR. The absence of fever or preceding influenza-like symptoms should not preclude testing. In patients with a high clinical index of suspicion, negative PCR tests should prompt repeat testing and antiviral medication should be continued along with infection control measures.

Serology: Serological testing for influenza A, with either complement fixation or enzyme-linked immunosorbent assays, was used in some centres. These assays can only be used to diagnose influenza A and cannot (at this time) be

used to determine the influenza A subtype. The diagnostic validity of serology for influenza A was not known at the beginning, but it became apparent that infection caused by H1N1 2009 was often associated with either high titres at the time of presentation or rising titres over time.

If PCR testing is negative, serology should be performed in all patients as close to the time of presentation as possible and repeated 1–2 weeks later. H1N1 2009-specific serological tests will soon be available, and this will facilitate retrospective testing.

Other testing: Patients should be tested for bacterial superinfection and for alternative infections that may be responsible for their illness. This includes microscopy and culture of sputum or BAL fluid for typical bacterial pathogens, blood cultures, antigen detection tests and/or PCR for atypical bacterial pathogens as well as other respiratory viruses.

The identification of atypical bacterial pathogens or typical bacterial pathogens that are not known to be associated with post-influenza pneumonia (such as enteric gram-negative organisms) was often used as a reason to stop antiviral medications.

If a typical bacterial pathogen such as *Streptococcus pneumoniae, Staphylococcus aureus* or *Streptococcus pyogenes* is identified, antiviral therapy should be continued, along with appropriate antibacterial therapy.

Laboratory issues: Laboratory workload became a significant issue at the height of the outbreak. Many laboratories were inundated with testing, much of which was not clinically indicated (eg, community patients without risk factors for severe disease). Some laboratories found it difficult to prioritise samples for testing or even to track the location of samples to ensure that they were received by laboratories that were able to conduct PCR assays.

Most laboratories spent considerable amounts of money on overtime, and laboratory staff fatigue became a real issue. This delayed the production of results.

"Surge demand" in laboratory services needs to be considered just as it is in clinical services. Investment in resources to deal with a surge in laboratory testing as well as systems to ensure prioritisation of samples from critically ill patents is recommended.

Some ICUs found that the most important specimens for processing were those from patients with a lower clinical likelihood of H1N1 2009 infection but who required isolation for infection control because infection with H1N1 2009 could not be excluded on clinical grounds. Early provision of the results of PCRs in such patients would be useful for optimising the efficient use of limited infection control resources.

Management

This section focuses predominantly on issues that are of particular relevance to patients with H1N1 2009 influenza, rather than on general ICU care.

Antimicrobial treatment: Antiviral therapy against influenza A should be commenced in all patients admitted with a suspicion of H1N1 2009 infection. The most widely used antiviral agent in ANZ ICUs was oseltamivir.[11] Dosing at 75 mg twice daily was common during the initial phase of the outbreak. Higher dosing, at 150 mg twice daily, became common later in the outbreak, especially for patients with viral pneumonitis.

Concerns were expressed at a lack of dosing information in the Product Information regarding critically ill individuals with compromised gastrointestinal tract function or receiving renal replacement therapy. The duration of treatment for most patients was at least 7–10 days, rather than the standard 5 days.

The duration of viral shedding in compromised patients, and the impact of treatment, were unknown. Antiviral resistance studies were not available in real time, although they were being performed on selected isolates by reference laboratories.

There was relatively little experience with zanamivir or other antivirals apart from oseltamivir. Intravenously administered peramivir was not available.

Initial antibacterial therapy for patients with focal or diffuse lung infiltrates was variable. The most important pathogens in patients admitted to ICUs were *S aureus*, *S pyogenes*, *S pneumoniae* and *Haemophilus influenzae*. Patients with lung infiltrates should receive antibacterials active against these pathogens. Ceftriaxone or piperacillin/tazobactam were widely used. In areas where there was known to be community-onset methicillin-resistant *S aureus* (MRSA), an agent such as vancomycin was often part of the empirical regimen. There was some support for use of antibiotics potentially capable of reducing production of Panton–Valentine leukocidin, such as linezolid or clindamycin, but this was not usual practice.

In patients for whom initial lower respiratory tract secretion cultures and blood cultures were negative, some clinicians stopped all antibacterials on Day 3 or 4 because of concern that such patients could develop subsequent infections with more resistant bacteria. Others continued empirical antibacterial treatment for 7–10 days. The duration of antibacterial therapy for patients with confirmed H1N1 2009-associated bacterial pneumonia should be the same as for patients with conventional CAP.

Patients with MRSA or methicillin-sensitive *S aureus* often required long courses of antibacterials, and some patients developed lung cavities, with a risk of late superinfection.

Some patients developed empyaema requiring tube drainage or surgical decortication.

Adjuvant therapies: Glucocorticoids were used sporadically, and some clinicians reported substantial improvement, but there was no general consensus. Many clinicians avoided glucocorticoids because of concerns about complications. Glucocorticoids were administered to 49% of patients receiving ECMO who continued to have severe ARDS. The impression of the clinicians caring for these patients was that glucocorticoid therapy was associated with more marked critical illness neuromyopathy and a slower recovery after separation from ECMO.[5]

We are not aware of any patients being treated with recombinant activated protein C or other adjuvant therapies for severe sepsis. There were isolated reports that some patients had low levels of serum immunoglobulins, but we are not aware that intravenous immunoglobulin was administered to any patient.

Mechanical ventilation

Among patients with acute viral pneumonitis, which was frequently complicated by ARDS, there were unique features related to ventilation that were not seen in ARDS due to other causes.[2]

Initial mechanical ventilation was the same as for any intensive care patient who requiring mechanical ventilation for severe respiratory failure. Generally this was a "lung protective strategy", with stepwise recruitment manoeuvres and PEEP in the range of 15–20 cm water.

Many of these patients had preserved lung compliance and could be ventilated with relatively low ventilator pressures. They were very dependent on recruitment and PEEP, and deteriorated rapidly if the PEEP was reduced or removed. Nursing staff and physiotherapists were advised to minimise suctioning and to not interrupt the breathing circuit unless absolutely necessary.

Early tracheostomy was preferred for patients likely to need prolonged ventilation, but this was often postponed because of the high PEEP and fraction of inspired oxygen (F_{IO_2}) requirements. The median ventilation time was 8 days, but a number of patients required 3–4 weeks of ventilation.

Patients were kept as free of excess fluid as possible, with the use of diuretics and fluid restriction.[12] In some cases renal replacement therapy was required. Significant improvements in oxygenation were not noted with negative fluid balance, perhaps because patients were managed with the least possible fluid from early in the course of their illness.

Agitated delirium was problematic in many ventilated patients. Various agents were used, including combinations of midazolam, opioids, propofol, haloperidol, quetiapine, olanzapine and dexmedetomidine. No one combination

was more effective than others. Often unusually large doses of sedative medication were required, and strategies such as daily cessation of sedation were not practical.[13]

Rescue therapies for severe hypoxaemia

Various rescue techniques were used, depending on the experience of the treating clinicians and availability of necessary equipment. These included prone ventilation, inhaled pulmonary vasodilators, inhaled nitric oxide, airway pressure release ventilation (APRV), high-frequency oscillatory ventilation (HFOV), or ECMO. Unfortunately, there is little firm evidence for the efficacy of these measures on eventual patient outcome.

We recommend that all ICUs that are likely to treat patients with H1N1 2009-associated ARDS develop a predefined plan for employing rescue therapies based on each centre's local expertise.

Prone ventilation: Prone positioning was used in many centres and improved oxygenation in many patients. However, turning patients to the prone position has risks such as extubation, line dislodgement and pressure sores. These must be considered before using this approach. Prone ventilation has the advantage of requiring no special equipment.

Inhaled prostacyclin: Inhaled prostacyclin requires the availability of in-circuit nebulisers that can be run continuously. The exhaled agent does not require scavenging. Some centres reported substantial improvements in oxygenation using this method.

Inhaled nitric oxide: Nitric oxide is expensive and requires special equipment for gas delivery and monitoring, as well as scavenging of the waste gases to prevent pollution of the ICU environment.

Airway pressure release ventilation: APRV was not widely used. At one centre that provides ECMO, at least three patients referred for ECMO were managed successfully with APRV alone. Typical initial settings were a PEEP high of 30 cm water, a time low of 0.6 or 0.7 seconds, and a respiratory rate of 10–12 breaths per minute, sufficient to create an intrinsic PEEP of 12–14 cm water. After an initial period of 12–24 hours, the PEEP high could often be reduced by 2–4 cm water. Patients were weaned by a process of "dip" (reduction in PEEP high) and "stretch" (reduction in respiratory rate). Clinicians with experience in APRV noted that reduction in F_{IO_2} and improvement in CXR appearance were less marked in patients with H1N1 2009 than in other patients.

High-frequency oscillation ventilation: HFOV was not widely available, but adult ICUs that had HFOV available found it effective. Many ICUs felt that the use of HFOV may have saved patients from the need for ECMO. Initial settings

were typically a pressure amplitude of about 60 cm water and frequency 6 Hz, with a mean airway pressure of only 20–25 cm water. These patients were often not significantly hypercarbic, and frequency could be readily increased and pressure amplitude reduced. Patients could return to conventional ventilation when the mean airway pressure was < 25 cm water and the F_{IO_2} 0.4.

Extracorporeal membrane oxygenation: Sixty-eight patients with H1N1 2009 infection were treated with ECMO in ANZ over a 3-month period.[5] This was a 17-fold increase in the use of ECMO compared with the corresponding period in 2008. All patients treated with ECMO met the entry criteria for the CESAR (Conventional Ventilation or ECMO for Severe Adult Respiratory Failure) trial[14] (ie, a Lung Injury Score ≥ 3 or an arterial pH < 7.2). Almost all patients (93%) treated with ECMO received venovenous ECMO. ECMO cannulation was mainly performed using a percutaneous technique.

ECMO was used at 15 sites in ANZ and many patients were transferred long distances to ECMO centres, either on conventional mechanical ventilation or after institution of ECMO at the referral site. ECMO retrievals were conducted up to distances of 900 km. For long-distance retrievals, a jet aircraft was used, with road ambulance transfer between the referring hospital and local airstrip and again from the airport to the other hospital. Initially, road retrievals up to 400 km were performed — a travel time of about 6 hours by ambulance. This frequently necessitated overnight management of the patient on ECMO at the referring hospital by the retrieval team while the ambulance crew rested or change occurred. Later in the course of the pandemic, a helicopter was used for medium-distance retrievals. Having a surgeon on the retrieval team was useful, as regional centres often did not have access to a specialist vascular surgeon.

Optimum management of mechanical ventilation in patients receiving ECMO has not been determined. A modified ARDSnet protocol[15] was adopted, with tidal volumes not exceeding 6 mL/kg but a low respiratory rate. Hypercarbia was rarely problematic. Some mechanical ventilation was maintained because the femorofemoral, venovenous ECMO circuit used early in the pandemic was not able to maintain adequate oxygenation without additional ventilatory support. To prevent back diffusion of oxygen from hyperoxygenated pulmonary arterial blood, the inspired oxygen concentration was not reduced below 60%.

When adequate arterial oxygenation could not be maintained despite maximal possible flows on the ECMO circuit, efforts were made to reduce oxygen demand, including use of deep sedation, neuromuscular blockers and the induction of mild hypothermia (34–36°C).

If these strategies were unsuccessful, an additional venous drainage catheter (usually via the jugular vein) was added to the ECMO circuit to permit increased circuit flows. Later in the course of the pandemic, insertion of the additional jugular venous cannula became routine, especially in patients with a very high body mass index.

Because the patient group was generally young and previously well, the risk of hypoxaemia was thought to be modest. Lower levels of arterial oxygenation (Pa_{O_2} > 50 mmHg, arterial oxygen saturation [Sa_{O_2}] > 85%) were accepted if there was no evidence of tissue or organ hypoxic stress (eg, acidaemia, lactataemia, renal or hepatic dysfunction). This allowed lower ECMO circuit flows.

Additional strategies to manage lung oedema included high-level PEEP (15–20 cm water) and diuresis. Often large amounts of fluid could be cleared (3 L or more) without the need for inotropes or vasopressors to maintain adequate ECMO flow.

During the pandemic, there were many referrals for consideration for ECMO from district and regional intensive care specialist colleagues. Occasionally the need for ECMO could be prevented by emphasising protective ventilator management strategies and rescue therapies.

Infection control and isolation

Infection control issues had an impact on ICU workflow, staff and visitors. Patients with suspected or proven H1N1 infection were generally kept in single rooms. Some ICUs cohorted patients in separate but open areas at the height of the outbreak.

Face protection, eye protection, impervious gowns and gloves were worn by staff when caring for patients with suspected or proven H1N1 2009 infection. Controversy existed about the need to wear N95 masks versus simple surgical face masks.[16] While some units had strict protocols for all patients, others required the use of face protection only for those caring for patients with open breathing systems (ie, oxygen masks, nasal prongs or non-invasive ventilation). Fit-testing of N95 masks was not undertaken for all personnel, but fit-checking to ensure a good seal was uniformly recommended.

Procedures were developed to ensure that staff members would not contaminate themselves while removing their protective attire. This involved particular attention to not touching the front of the face mask.[16]

Alcohol-based hand gel was used for skin disinfection before and after patient care when gloves were worn. Routine hand washing was used in instances when gloves were not used or hands were visibly soiled. Staff needed frequent reminders to maintain adherence.

Fatigue was accelerated by the wearing of N95 masks and impervious gowns, as they are hot and retain sweat. Some consideration needs to be made for relieving staff to combat this problem.

An unresolved issue was the frequency with which masks needed to be changed. The consumption of disposable masks, gowns and hand gel was high and required vigorous efforts to keep adequate stock in the unit.

The duration of implementation of infection control measures was quite variable, although this was not noted to increase the risk of nosocomial transmission or acquisition by staff. Strategies included cessation of infection control measures (i) after 3 days of antiviral medication; (ii) when the patient had been afebrile for more than 24 hours; or (iii) when the patient left the ICU. There were reports of patients testing positive with PCR for up to 30 days in an ICU, even in the absence of immune suppression. The significance of PCR positivity with respect to infectivity is not known. As far as we are aware, no units used sequential PCR or viral culture to determine the duration of infection control measures.

Most ICUs adopted specific infection control measures and tested all patients admitted with respiratory failure associated with lung infiltrates in whom an alternative cause was not present, as well as all patients with an exacerbation of asthma or chronic obstructive pulmonary disease. Many patients who turned out not to have H1N1 2009 infection were subject to strict infection control measures. This approach was necessary, as infection was confirmed in some patients thought initially to be at low risk.

Among staff with confirmed H1N1 2009 infection, an analysis of potential exposure indicated that many cases were acquired outside the workplace. Some emergency departments advocated universal use of surgical masks in all patient encounters. Staff who were pregnant or had immune suppression were not allocated to care for patients with confirmed or suspected H1N1 2009 infection. This required some circumspection by those managing staff allocations to protect the individual's privacy. Staff who were ill with suspected influenza were asked to telephone before attending work and, if influenza was likely, they were referred to staff health for swabs and provision of antiviral medication. Policies with respect to return to work were varied and included return after 3 days of antiviral treatment, return when afebrile, or return only when both criteria were met.

H1N1 infection affected the availability of staff, with some hospital departments being markedly short of staff and relying on overtime work. Systems need to be designed to deal with fatigue management in depart-ments experiencing unusual levels of absenteeism and overtime. It must be noted that most hospitals had lower rates of absenteeism than in typical "influenza seasons".

Nosocomial transmission did occur. Potential sources were other patients, staff members and visitors. Staff and visitors were notified of the likely symptoms of H1N1 2009 infection, such as cough, fever and sore throat. Staff and visitors were asked to stay away from the hospital while they had symptoms. All patients with suspected or confirmed influenza remained on respiratory precautions and antiviral drugs until negative tests or after 5 days of anti-viral treatment. The rapid provision of diagnostic results helps to reduce this workload, although the diagnostic tests are not perfect.

Impact on ICU services, and surge capacity

There was substantial uncertainty about the severity of the pandemic as it emerged, and this made planning difficult. It became apparent that initial pandemic plans — prepared for a virulent H5N1 avian influenza infection — were not appropriate for this pandemic. A revised plan, termed PROTECT, was implemented in Australia. This included assumptions of a 20% attack rate and a 0.14% case-fatality rate.[17] This would have corresponded to about 6000 deaths and would have rapidly overwhelmed the available intensive care capacity.

Despite these assumptions being in the public domain, there was little engagement of the intensive care community by public health authorities before the first surge in ICU cases. Although the epidemic was relatively mild, the surge of cases associated with H1N1 2009 placed a severe strain on the provision of intensive care services. At peak, up to 20% of ICU beds in some regions were occupied by patients with confirmed H1N1 2009, with another 5% of beds occupied by patients with strong clinical suspicion of having the infection, including many with serological evidence of influenza A, but in whom confirmatory tests for H1N1 2009 were negative.

The surge in cases was accommodated by the cancellation of elective surgery that would have required ICU admission, by the transfer of patients with critical illness not due to H1N1 2009 from public-hospital ICUs to ICUs in private hospitals, and the urgent opening of physical ICU bed spaces that were not funded. A few hospitals ventilated patients outside the ICU or reduced patient–staff ratios (in ANZ, ventilated patients are usually nursed at a ratio of one nurse to one patient).

It was apparent at all sites that the main limit on expansion of ICU services was the availability of nursing staff who had sufficient experience to care for ventilated patients. Plans were developed at some sites to allow for

the rapid training of ward nurses to be competent to care for ventilated patients, but these were not needed. There were also attempts at some sites to review staff records to identify nurses who had had ICU training but were no longer working in the ICU.

Plans were considered for triage of patients to not receive ICU support if the expanded capacity of the ICU was overwhelmed, but at no point were these plans required.

The peak in ICU demand generally occurred about 4–6 weeks after the first ICU admission. The total duration of the outbreak was 8–10 weeks in most regions.[3] Some public health authorities undertook modelling to predict the timing and magnitude of the peak of the epidemic, and the sharing of the results of these models was of use to ICU managers or clinicians. Information was also collected by public health authorities on the level of activity of the infection in the community, including the number of presentations to general practitioners or emergency departments with influenza-like illness. Real-time sharing of these data with ICU clinicians may assist in the optimal management of ICU bed capacity.

Systems that allowed ICU clinicians to know the number of available ICU beds throughout their region were useful in identifying where patients transferred from smaller hospitals could be admitted.

There are several registries that aim to collect information on new cases admitted to ICUs. We encourage all clinicians to enter data on these patients, as this information can be used to model the evolution of an outbreak and, in combination with published data about length of stay and outcomes,[3,18,19] can be used to make local estimates of ICU bed requirements as any local outbreak evolves.

Conclusion

We have described the intensive care response to the winter H1N1 2009 pandemic in ANZ. Up to 25% of intensive care beds were occupied with proven or suspected cases, which significantly stressed but did not overwhelm the system. The clinical manifestations of H1N1 2009 influenza were in many ways different to those seen in seasonal influenza, particularly with respect to the number of young and middle-aged patients with severe respiratory failure and the number who needed advanced rescue therapies, including ECMO, for severe ARDS. Despite the availability now of a specific H1N1 vaccine, it is likely that there will be a recurrence of H1N1 2009 influenza in ANZ in winter 2010. The information presented here may help during future pandemics.

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