



Noninvasive mechanical ventilation in high-risk pulmonary infections: a clinical review

Antonio M. Esquinas¹, S. Egbert Pravinkumar², Raffaele Scala³, Peter Gay⁴, Arie Soroksky⁵, Christophe Girault⁶, Fang Han⁷, David S. Hui⁸, Peter J. Papadacos⁹ and Nicolino Ambrosino¹⁰ on behalf of the International NIV Network¹¹

Affiliations: ¹Intensive Care Unit, Hospital Morales Meseguer, Murcia, Spain. ²Dept of Critical Care, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA. ³Pulmonary and Respiratory Intensive Care Unit, S. Donato Hospital, Arezzo, Italy. ⁴Dept of Pulmonary, Critical Care and Sleep Medicine, Mayo Clinic, Rochester, MN, USA. ⁵General Intensive Care Unit, Assaf Harofeh Medical Center, Ramat Aviv, Israel. ⁶Dept of Medical Intensive Care, Charles Nicolle Rouen University Hospital, UPRES EA 3830-IRIB, Institute for Biomedical Research, Rouen University, Rouen, France. ⁷Dept of Pulmonary Medicine, The People's Hospital, Beijing University, Beijing, China. ⁸Dept of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, SAR, China. ⁹Critical Care, University of Rochester, Rochester NY, USA. ¹⁰Pulmonary and Respiratory Intensive Care Unit, Cardio-Thoracic Dept, University Hospital Pisa, Pisa, Italy. ¹¹For a full list of the International NIV Network collaborators see the Acknowledgements.

Correspondence: Antonio M. Esquinas, Intensive Care Unit, Hospital Morales Meseguer, Avenida Marques de Los Velez, s/n, Murcia, 3088-Spain. E-mail: antmesquinas@gmail.com

ABSTRACT The aim of this article was to review the role of noninvasive ventilation (NIV) in acute pulmonary infectious diseases, such as severe acute respiratory syndrome (SARS), H1N1 and tuberculosis, and to assess the risk of disease transmission with the use of NIV from patients to healthcare workers.

We performed a clinical review by searching Medline and EMBASE. These databases were searched for articles on “clinical trials” and “randomised controlled trials”. The keywords selected were non-invasive ventilation pulmonary infections, influenza-A (H1N1), SARS and tuberculosis. These terms were cross-referenced with the following keywords: health care workers, airborne infections, complications, intensive care unit and pandemic. The members of the International NIV Network examined the major results regarding NIV applications and SARS, H1N1 and tuberculosis. Cross-referencing mechanical ventilation with SARS yielded 76 studies, of which 10 studies involved the use of NIV and five were ultimately selected for inclusion in this review. Cross-referencing with H1N1 yielded 275 studies, of which 27 involved NIV. Of these, 22 were selected for review. Cross-referencing with tuberculosis yielded 285 studies, of which 15 involved NIV and from these seven were selected. In total 34 studies were selected for this review.

NIV, when applied early in selected patients with SARS, H1N1 and acute pulmonary tuberculosis infections, can reverse respiratory failure. There are only a few reports of infectious disease transmission among healthcare workers.



@ERSpublications

NIV in high risk pulmonary infection management can prevent respiratory failure in ICUs with well trained staff <http://ow.ly/wSpqx>

Received: Dec 21 2013 | Accepted after revision: May 11 2014

Conflict of interest: None declared.

Provenance: Submitted article, peer reviewed.

The present work was previously presented as a poster presentation at the American Thoracic Society 2010 International Conference (New Orleans, LA, USA).

Copyright ©ERS 2014. ERR articles are open access and distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0.

Introduction

Noninvasive ventilation (NIV) as an early option in selected contagious patients with severe acute respiratory syndrome (SARS), H1N1 and tuberculosis (TB) infections that can avert or reverse respiratory failure and, therefore, decrease complications when implemented in units with well-trained staff. Currently, there are only a few reports of infectious disease transmission among healthcare workers. Practical precautions and protocols to protect healthcare workers during NIV use in high-risk pulmonary infections are necessary.

NIV is an essential component in both emergency and intensive care medicine [1]. In the 1950s, the widespread use of the iron lung during the polio epidemic increased the survival of patients with respiratory failure [2, 3]. Although the use of NIV and the number of articles on NIV have been rapidly growing over the past decades [3–5], there are still insufficient data concerning the use of NIV during pulmonary infections, especially in pandemic respiratory infections. NIV was used in patients with SARS in 2002–2003 and also during the H1N1 epidemic in 2009. However, in recent years NIV use has been extended to patients with respiratory failure due to a wide spectrum of infectious diseases. These include, but are not limited to, SARS and pandemic avian influenza (H5N1). However, some concern has been raised with the use of NIV in patients with contagious diseases. Studies from Mexico, Canada, Spain, and Australia have reported experiences with treating H1N1 influenza patients with respiratory failure [5, 6]. A significant proportion of these patients were treated with NIV. There were no reports of disease transmission with the use of NIV from patients to healthcare workers in these studies, but all involved healthcare workers were not routinely screened for infection. Nevertheless, the World Health Organization (WHO) has included NIV among aerosol-generating procedures in which the risk of pathogen transmission is possible [7, 8].

The aim of our study was to conduct a systematic review to determine the effectiveness of NIV in high-risk pulmonary infections, including pandemic infections, and to explore the risk of infectious spread among healthcare workers with the use of NIV. In order to perform this review, we formed an international working group comprised of experts in infectious pathology and NIV from Asia, Europe, Latin America and the USA. This network is a permanent working group that evaluates technological implications concerning NIV for future pandemics and mass disaster causalities. We selected key topics related to pertinent methodological and technical issues in NIV and infectious diseases. Our study centred on the use of NIV in pulmonary infections, especially during pandemics, to determine the risk of transmission of infection to healthcare workers. The international members of this network participated in the careful review of selected studies in order to provide recommendations for protocols and guidelines, and subsequently to the writing of this manuscript.

We conducted a search in Medline (PubMed) for published randomised and non-randomised control trials, as well as observational studies (cohort, case–control or case series) in adult patients between January 1990 and March 2012, and in EMBASE from 1966 to June 2012.

The keywords selected were: non-invasive ventilation, pulmonary infections, influenza A (H1N1), SARS and tuberculosis. These terms were cross-referenced with the following keywords: health care workers, airborne infections, complications, intensive care unit and pandemic. Bibliographies of the selected articles were hand searched for additional relevant articles. We did not include paediatric studies.

Effectiveness of NIV in pulmonary infections and pandemics

NIV in SARS

SARS, caused by the novel coronavirus (SARS-CoV), emerged in November 2002 and was first identified by the WHO in mid-March 2003. SARS is a severe and progressive disease with ~25% of patients developing respiratory failure [9].

In order to reduce endotracheal intubation (ETI) and its associated complications, NIV was commonly employed in the SARS outbreak in China, including Hong Kong. The use of NIV has become part of the standard treatment protocol for SARS [10]. A summary of clinical studies and corresponding recommendations are described in [table 1](#).

NIV does not demonstrate absolute benefit among non-chronic obstructive pulmonary disease (COPD) patients with acute hypoxaemic respiratory failure or acute respiratory distress syndrome (ARDS), *e.g.* in SARS patients [8, 9, 11–17]. It is well known that ETI is associated with higher risk of disease transmission and associated complications. The use of NIV as initial ventilator support for respiratory failure in the presence of SARS appears to be a reasonable option, albeit under strict infection control measures.

TABLE 1 Published data on noninvasive ventilation (NIV) during severe acute respiratory syndrome (SARS) infections

First author [ref.]	Year	Country	Study design	Interface	Received NIV	NIV failure	Transmission among HCW#	Mortality	Observations
LIN [11]	2003	China	Retrospective, single centre	Face mask	n=40 (51.9%)	n=8 (10.3%)	No	9%	70 (90.9%) patients were clinically cured
CHEUNG [12]	2004	China	Case series, single centre (n=31)	Face mask	n=20	n=14 (70%)	No	0%	
FOWLER [13]	2004	Canada	Retrospective, single centre	Face mask	0	n=38	No	50% after NIV failure	Affected patients had primarily single organ respiratory failure
SUNG [14]	2004	China	Prospective, single centre (n=37)	Face mask	n=15	n=21 (15.2%)	No	n=15 (10.9%)	Most patients had significant comorbidities
YAM [8]	2005	China	Retrospective, single centre	Face mask	n=21	n=8 (38%)	No	n=9 (35%)	Early application of NIV as initial support for SARS-related ARF appeared to be associated with significantly reduced need for ETI and mortality

HCW: healthcare workers; ARF: acute respiratory failure; ETI: endotracheal intubation. #: instances of transmission of SARS among HCW.

NIV in influenza A H1N1 infection

Pandemic influenza A (pH1N1) is a new strain of influenza virus that was first identified in Mexico and the USA in the early part of 2009 [18–30]. The pH1N1 virus originated from the swine influenza (H1N1) virus circulating in North American pigs [23].

Animal studies have shown that the novel influenza virus caused increased morbidity and replicated to higher titers in lung tissue; thus, explaining its pathogenicity and ability to invade the lower respiratory tract in humans, resulting in rapid and fulminant respiratory failure [19]. Such clinical deterioration is characterised by sudden and rapidly progressive respiratory failure with persistent and refractory hypoxia, bilateral diffuse pulmonary infiltrates and a low arterial oxygen tension (P_{aO_2})/inspiratory oxygen fraction (F_{IO_2}) ratio reaching ARDS criteria [20–22, 25, 26, 31, 32]. Severe respiratory failure is common during the first week and the incidence decreases over time. Refractory hypoxia was the major cause of death, followed by multi-organ failure and shock [26–28, 32].

About 10–30% of hospitalised patients required admission to the intensive care unit (ICU) during the pH1N1 epidemic [27, 28, 32]. Comorbidities were noted in 32–84% of cases admitted to the ICU. These included obesity, COPD, diabetes mellitus, asthma, immunosuppression, chronic kidney disease and heart failure [27–30, 32]. The overall ICU mortality rate for critically ill cases of pH1N1 was close to 17% [19–33]. Factors that were independently associated with mortality included requirement for invasive mechanical ventilation (IMV) and a low P_{aO_2}/F_{IO_2} ratio at ICU admission, the presence of comorbidities and older age [19, 20, 22, 23]. Autopsy findings showed three distinct pulmonary pathologies: diffuse alveolar damage, necrotising bronchiolitis, and diffuse alveolar damage with alveolar haemorrhage [21, 23, 24, 31]. If we analyse ventilatory management, IMV with lung protective ventilatory strategy and fluid restriction is recommended as the initial approach for managing patients with pH1N1 infection complicated by ARDS [21, 24, 26, 27, 32, 33].

Based on the guidelines from the European Respiratory Society (ERS)/European Society of Intensive Care Medicine (ESICM), WHO, the UK National Health Service, Hong Kong Lung Foundation and the American Association for Respiratory Care (AARC), NIV is not to be used as first-line therapy in pH1N1-associated respiratory failure for the following reasons. 1) Poor clinical efficacy in severe respiratory failure that rapidly progresses to refractory hypoxaemia and ARDS. 2) The prevalent pattern of hypoxaemic failure instead of hypercapnic respiratory failure in patients with pH1N1. 3) Concern about aerosol droplet particle dispersion and spread of infection [10, 19, 34, 35].

A summary of published studies on NIV in pH1N1 is shown in table 2 [19–33, 36–48]. Of the 22 studies included in table 2, the majority were case series reports. The contribution to pH1N1 case series according to country is shown in table 3. There is only one international study [37] that has shown a favourable result with the use of NIV in pH1N1. Five of the studies, most of which were case series applying a face mask for NIV, yielded a failure rate of 10–15%. A full face mask was the NIV interface choice in all but one study; in which the NIV helmet and face mask were used as an alternative. The results regarding the success of NIV were highly variable. Among the causes of NIV failure are refractory hypoxaemia and shock, with multi-organ failure being the most unfavourable. As shown in table 2, mortality is clearly lower in the group treated with NIV *versus* the IMV group. While the Chinese and European studies appear to argue in favour of NIV use, the Canadian study did not support its use. These studies do not report on significant complications for patients and healthcare workers and in none of these studies do the authors report cases of infection transmission to healthcare workers.

Based on the review of these reports our conclusions are as follows. NIV has a role in the management of early respiratory failure due to pH1N1 infection; however, in a strictly controlled environment with close monitoring of healthcare workers and with adequate precautions for prevention of infection transmission [20, 22, 24–26, 29–33, 36–48]. NIV has no role in severe respiratory failure and ARDS related to severe pH1N1 infection. These patients must undergo ETI and IMV [26, 30, 32, 33, 42–44, 46].

NIV in pulmonary TB

NIV remains an option for ventilatory support in both acute and chronic respiratory failure secondary to pulmonary TB [49–54]. In acute situations, judicious use of NIV in carefully selected patients can potentially obviate the need for IMV [49–53, 55–58]. NIV can be regarded as a simple and suitable solution not only for the provision of long-term and domiciliary-assisted ventilation in patients with sequelae of pulmonary TB, but also for acute exacerbations of pulmonary TB [50, 54, 59, 60]. The concern with the use of NIV in such acute situations is linked with the potential risk of the transmission of TB [49, 56]. Whether or not NIV should be considered a high-risk procedure in infectious diseases like TB continues to be a controversial issue [49, 56]. However, the limited availability of invasive ventilators and/or ICU beds,

TABLE 2 Published data on noninvasive ventilation (NIV) during pandemic influenza A H1N1

First author [ref.]	Year	Country	Study design	Interface	Received NIV	NIV failure	Transmission among HCW ^a	Mortality	Observations
KAUFMAN [21]	2009	Australia	Multicentre, prospective cohort (n=3)	Face mask	0	100%	No	n=7	22 HCW were treated with oseltamivir. None were hospitalised.
PEREZ-PADILLA [22]	2009	Mexico	Retrospective, multicentre cohort (n=98)	Face mask	n=18 (IMV: n=12)		Yes		None of the secondary infections among HCW were severe.
RELLO [23]	2009	Spain	Multicentre cohort (n=32)	Face mask	n=8 (33%)	75%	No	n=8	24 (75.0%) required IMV.
DIBRE [28]	2009	France	Case 1: pregnant	Face mask	1	0%	No	0	Pregnancy population.
KUMAR [24]	2009	Canada	Prospective, observational, multicentre cohort (n=168)	Face mask	n=55 (33%)	85%	No		136 (81.0%) patients received IMV.
DOMÍNGUEZ-CHERIT [31]	2009	Mexico	Prospective, observational, multicentre cohort (n=58)	Face mask	0	0	No	0	
MILLER [29]	2009	USA	Monocentre, observational cohort (n=47)	Face mask	n=13 (3%)	85%	No	17%	Severe ARDS with MOF in the absence of bacterial infection was a common clinical presentation.
LI [26]	2010	China	Retrospective, monocentre cohort (n=75)	Face mask	n=33 (44%)	n=10 (30%)	No	10%	
KOEBELEBERG [30]	2010	South Africa	Monocentre, observational cohort (n=19)	Face mask	n=6 (66%)	66.6%	No	n=13 (68.4%)	
WIKICK [36]	2010	Portugal	Case report (n=1)	Face mask	n=1	0	No		
ESQUINAS [37]	2010	International NIV Network Survey	Prospective, international, observational cohort	Face mask			No		
HAAJAR [38]	2010	Brazil	Monocentre cancer patients, observational study cohort (n=8)	Face mask	n=8 (50%)	n=5 (62.5%)	No	100%	Cancer patients highlight the severity of the H1N1 pandemic in this vulnerable population and the urgent need to establish specific protocols of care and management strategies designed to face this healthcare challenge.
LOURIZ [40]	2010	Morocco	Observational, prospective, multicentre cohort (n=186)	Face mask	n=10	n=10 (100%)	No	30%	
ANGÜZEL [32]	2010	Turkey	Observational, monocentre cohort (n=19)	Face mask	Nasal cannula: n=4 (21.1%)		No		First study to include nasal cannula.
NIH [39]	2011	Spain	Multicentre, observational, prospective cohort (n=96)	Face mask	n=43 (45%)	77%	No	50% global	High mortality, primarily due to refractory hypoxia.
RÍOS [25]	2011	Argentina	Retrospective, observational, monocentre cohort (n=62)	Face mask	n=49 (28%)	94%	No	n=4 (6.5%)	Hypoxaemia, MOF, and a requirement for IMV.
LIU [43]	2011	China	Prospective, observational, monocentre cohort (n=14)	Face mask	n=23	n=3	No	2.1%	
TIMENETSKY [46]	2011	Brazil	Prospective, observational, monocentre cohort (n=19)	Face mask	85.7%	58.4%	No		
GRASSELLI [45]	2011	Italy	Retrospective, observational, monocentre cohort (n=19)	Face mask	n=13	n=11	No		Frequent IMV.
BELNGUER-MUNCHABAZ [47]	2011	Spain	Retrospective, observational, monocentre cohort	Face mask and helmet	n=10	0	No	0	First study to use a helmet and a face mask.
MASCLANS [48]	2012	Spain	Prospective, observational, multicentre registry cohort	Face mask	n=177	n=105 (59.32%)	No	0	Best outcome in low APACHE II and SOFA, no vasopressor, lower chest radiograph quadrants and shorter ICU stay.
ZHANG [33]	2012	China	Retrospective, observational, monocentre cohort (n=394, including 1 pregnant subject) (IMV (n=186))	Face mask	n=83	n=45 (24.32%)	No	n=24 (28.91%)	Pregnancy population.

HCW: healthcare workers; IMV: invasive mechanical ventilation; ARDS: acute respiratory distress syndrome; MOF: multi-organ failure; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; ICU: intensive care unit. ^a: instances of transmission of influenza A H1N1 among HCW.

TABLE 3 Contribution to pandemic influenza A H1N1 case series (total n=23) based on country

European countries	n=9
Spain	n=5
Italy	n=1
France	n=1
Portugal	n=1
Turkey	n=1
Asia	n=3
North America	n=1
Australia	n=1
Canada	n=1
Latin America	n=6
Mexico	n=2
Brazil	n=2
Chilean-Uruguay	n=1
Argentina	n=1
South Africa	n=1
North Africa (Morocco)	n=1

especially in developing countries where TB incidence remains high, is an important constraint in managing patients with TB and acute respiratory failure by means of NIV.

The medical literature offers very few published reports concerning the use of NIV in contagious TB patients. This is due to the fact that there is a limited number of published articles where NIV was used in exacerbations of chronic respiratory failure in patients with TB sequelae [50, 54, 59, 60], and even fewer reports were available about the use of mechanical ventilation in acute respiratory failure due to active pulmonary TB [56, 57].

In the seven published studies dealing with patients suffering acute exacerbations of pulmonary TB sequelae, nasal mask was the most frequently used interface for delivery of NIV (used in four studies). These studies suggest no apparent complications for patients and workers and report no cases of death in treated patients. Continued applications at home following the acute phase yielded similar results. A summary of published data on NIV in acute exacerbation of pulmonary TB is shown in table 4.

In summary, the practitioner who has to decide whether to initiate NIV or IMV in acute respiratory failure due to pulmonary TB has to take into account several factors, such as: the prolonged period of infectiousness of these patients; the lag time for noticeable clinical improvement following initiation of treatment; and the risks related to positive pressure ventilation, such as pneumothorax and haemoptysis [49].

Risk of aerosol droplet generation and infection spread with NIV

Cough represents the most important airway defence reflex and one of the main symptoms of respiratory diseases [7, 61, 62]. During coughing and sneezing, particles of mucus can be expelled to a distance of up to 9 m [14, 13, 62]. Therefore, various pathogens, when present, could infect surrounding people and animals, thus markedly contributing to the massive dissemination of airborne infections [62]. It was shown that, during a 3-h flight, ~80% of passengers could potentially become infected by a coughing patient with influenza. Subsequently, these passengers could disseminate the infection at their destinations worldwide [14, 63]. Urgent protective and therapeutic actions are considered necessary for pH1N1, SARS and TB, which mostly affect immune-compromised populations [8, 12, 16, 47].

Currently, available recommendations are mainly based on published studies and experiences from the first SARS epidemic in 2003 [8, 11–17]. The pivotal study arguing that NIV poses a high risk for spread of infection is based on the assessment of particle dispersion using an experimental model. Smoke was introduced into the lungs of a mannequin while NIV was being performed. Plumes of smoke emerging from the vented mask were photographed for particle dispersion. As yet, there have been no studies evaluating particle dispersion in human beings. Much debate has risen since the SARS epidemic as to whether a mannequin-based study on particle dispersion simulates a real patient using NIV. Many experts argue that the NIV mask may in fact offer protection from secretions that would otherwise disperse from the infected patient during coughing, sneezing and speaking. Furthermore, there is no controlled data comparing particle dispersion between individuals receiving NIV and those who did not [9, 62].

Guidelines from ERS/ESICM, WHO, the UK National Health Service, Hong Kong Lung Foundation and the AARC, have considered NIV as a high-risk procedure during respiratory pandemics. This has led to

TABLE 4 Noninvasive ventilation (NIV) in acute exacerbations of pulmonary tuberculosis (TB) sequelae

First author [ref.]	Year	Country	Study design	Type of ARF-TB	Interface	NIV failure	Transmission among HCW#	Mortality	Observations	Home MV after AEPTS
Tsuboi [51]	1996	Japan	Prospective cohort (n=17)	AEPTS in mixed groups	Nasal mask	0	No	0		Yes
Machida [53]	1998	Japan	Retrospective survey (n=58)	AEPTS	Nasal mask	0	No	0		Yes
Prats Soro [60]	1999	Spain	Case report (n=1)	AEPTS	Nasal mask	0	No	0		Yes
Schulz [54]	1999	Germany	Prospective cohort (n=26)	AEPTS	Nasal mask	0	No	0		Yes
Agarwal [56]	2005	India	Cases series cohort (n=3)	ARDS and <i>Mycobacterium tuberculosis</i> AEPTS	Face mask	0	No	0		No
Utsui [57]	2006	Japan	Case report (n=1)	ARF, military TB and AEPTS	Face mask	0	No	0		No
Aso [58]	2010	Japan	Prospective cohort (n=58)	AEPTS	Face mask	13.8%	No	1.7%	0	No

ARF-TB: acute respiratory failure associated with TB pulmonary infection; HCW: healthcare workers; MV: mechanical ventilation; AEPTS: acute exacerbations of pulmonary TB sequelae; ARDS: acute respiratory distress syndrome. #: instances of transmission of *Mycobacterium tuberculosis* among HCW.

overuse of ICU beds and strain on available resources, in addition to an increase in IMV-related complications. Further validation of the association between NIV and infection spread by particle dispersion is needed for planning the best strategy for future pandemics [5, 10, 19, 34, 35, 47, 63].

Technical issues should also be considered in the strategic planning of guidelines that could be used by NIV teams for the management of suspected or proven cases of acute respiratory failure caused by contagious diseases [34, 63]. When considering the choice of ventilators, physicians should give preference to machines equipped with a dual-limb circuit without an unfiltered expiratory port (*i.e.* plateau exhalation valve, anti-rebreathing valve, *etc.*) [7, 13, 18, 34, 36]. Such technology avoids the dispersion of expired air contaminated by infected particles through a circuit leak. Such leaks are caused by bias flow necessary to prevent rebreathing in single-limb circuits and are magnified by the high positive end-expiratory pressure levels that are often required in the treatment of acute hypoxaemic respiratory failure [7].

A recent study reported that the use of certain standard face masks for NIV in patients with infectious diseases might be associated with a substantial exposure to infectious organisms in the exhaled air occurring within a distance of 1 m [7]. The dispersion of infected respiratory droplets may be amplified by an increase in mask leakage, and can be aggravated with higher inspiratory pressures [7, 62].

Regarding interface selection, full face or total face masks might be preferred to nasal masks in order to theoretically prevent the potential spread of contaminated exhaled air particles from unintended air leaks through the mouth. Therefore, choosing the brand and size of mask that best fits the anatomy of the patient's facial contours and at the same time allows delivery of adequate pressure levels is crucial to minimise unintended air leaks around the interface. However, currently there is no published data to confirm this theoretical strategy as having a positive impact in clinical situations [7, 62].

Recently, in Europe, a helmet interface has become available for delivering NIV [3]. In the majority of patients, a helmet is better tolerated than a face mask [64]. It is speculated that the use of a helmet interface, where available, for NIV together with negative pressure rooms equipped with high-efficiency particulate air filters, may decrease the dispersion of infected respiratory droplets.

Risk of infection spread with NIV in pandemics

During the SARS pandemic, nearly half of all SARS victims were healthcare workers, highlighting the occupational risks associated with the care of infectious pneumonias and pandemic infections [11–14]. Evidence related to airborne transmission of the SARS virus and the potential risk of aerosol generation with the use of NIV in SARS still remain controversial [8, 9, 11–17].

FOWLER *et al.* [13] examined transmission rates in healthcare workers caring for SARS patients who required ETI and IMV. This study showed a greater risk of developing SARS in physicians and nurses performing ETI (relative risk 13.29 (95% CI 2.99–59.04); $p=0.03$). Although nurses caring for infected SARS patients who are on NIV may have been at increased risk of droplet infections (RR 2.3 (95% CI 0.25–21.76)), this theoretical health-related risk was not translated into statistically significant clinical events ($p=0.5$). Two other reports analysed cases of SARS in Hong Kong, China, and there were no reported cases of SARS among healthcare workers caring for patients treated by NIV. However, it is unclear how this surveillance was carried out [8, 12, 17, 34].

YU *et al.* [17] conducted a case–control study to investigate nosocomial spread of SARS by identifying “super spreading events” in multiple hospitals in China, including Hong Kong [8, 12, 16, 17]. The results were of importance since 71.1% and 74.8% of the infections were attributable to super spreading events in Hong Kong and Singapore (Malaysia), respectively. In the final multiple-logistic model, the use of NIV was one of the six factors found to be associated with the risk of dissemination [20, 21]. However, the significance of NIV as a contributing factor to a rapidly spreading healthcare event could not be established [8, 12–14, 15–17].

To date, there are no reports demonstrating an increased risk of NIV-related dissemination in healthcare workers treating infected patients [10]. During the SARS outbreak, a study performed in Hong Kong by CHEUNG *et al.* [12] examined the efficacy of NIV in early ARDS and also evaluated the infection risk among healthcare workers who had direct contact with patients on NIV. A total of 22 (25%) patients needed NIV and a total of 155 healthcare workers, including doctors, nurses and healthcare assistants, were exposed to these patients on NIV therapy and were regularly screened for signs of infection. Coronavirus serology was obtained in 97% of healthcare workers. NIV equipped with expiratory bacterial and viral filters was provided in isolated cubicles in the ward or ICU, which were centrally air-conditioned, and fitted with exhaust ventilation fans to achieve negative pressure flow. This study concluded that NIV was not only effective in preventing IMV in 70% of patients with acute respiratory failure due to SARS but effectively reduced the ICU length of stay or avoided ICU admission. Moreover, no infection was noted in any of the

155 healthcare workers. Their serology tests for coronavirus were negative. The potential risk of particle dispersion and spread of infection due to NIV must not be overlooked, even though, at present, the data remains inconclusive.

In pulmonary TB, the majority of patients have a relatively long period of infectiousness (weeks to months), until the diagnosis is established and an effective anti-TB therapy is initiated [49]. There are certain characteristics in TB patients that increase the risk for infectiousness: presence of cough, cavitation on chest radiograph, sputum smear-positive for acid-fast bacilli, and failure to cover the mouth and/or nose during coughing or with cough-inducing and aerosol-generating procedures [49, 50, 56, 58].

Mycobacterium tuberculosis is carried in airborne particles as droplet nuclei that can be generated when persons with pulmonary or laryngeal TB cough, sneeze, shout or sing. The infective particles are ~1–5 µm in diameter and are maintained in the air and spread throughout the room/building by air currents. Therefore, TB infection is transmitted by air, not by surface contact. Contact with ocular/nasal secretions, saliva or other fluids from the patient do not represent a mode of transmission of *M. tuberculosis* [58, 60].

High-risk infections and healthcare worker protocols

The AARC recently issued a statement concerning ventilation in mass casualty situations, including pandemics [63]. The recommendation is against the use of NIV in pandemic influenza as the disease often progresses to ARDS, for which NIV is not the standard of care [63]. The development of infection control protocols for healthcare workers is essential to avoid the risk of acquiring contagious diseases [10, 18, 19, 34, 35, 49, 63, 65]. Protocols should be established in advance, before the onset of a crisis. Protocol should

TABLE 5 Summary of recommendations for noninvasive ventilation (NIV) during severe acute respiratory syndrome (SARS), H1N1 and tuberculosis (TB) infections

Specific NIV recommendations

NIV in TB

- TB patients are contagious for a relatively long period of time after starting anti-TB treatment (at least 2 weeks)
- NIV needs a long period of time to improve the respiratory condition in severely ill TB patients
- NIV patients are exposed to a higher risk of pneumothorax and/or haemoptysis and the lowest pressures should be set

NIV in SARS and H1N1

- Selection in early stages and mild forms of ARF, such as minimal pulmonary infiltrates and arterial oxygen tension/inspiratory oxygen fraction >250
- Exclude in shock or multi-organ failure

HCW general recommendations for NIV[#]

- TB patients with contagious forms of the disease should be isolated in airborne infection isolation (All) rooms
- Air cleaning technologies, such as HEPA filtration and UVGI, should be used
- HCW entering a room with an infectious TB patient should wear at least a N95 disposable respirator (preferably a FFP3 mask)
- Negative pressure rooms should be equipped with HEPA (where available) and have anterooms
- Use full protective clothing as per all aerosol generating procedures including a FFP3 mask when available (N95 masks are second choice), eye protection, a gown, gloves and an apron
- Strict personal protection equipment for HCW
- Minimise the number of individuals caring for the patient
- Strict monitoring of HCW for signs and symptoms of infection

Equipment and setting recommendations for NIV[#]

Viral/bacterial filter (99.9997 efficiency)

- These should be used between the mask/interface and the expiratory port, and at the outlet of the ventilator. In order to reduce the risk of contaminating the ventilator, a bacterial filter should be placed at the expiratory side of the breathing circuit or between the mask and the circuit. It is recommended to choose a model to filter particles 0.3 µm in size

Ventilators

- Double hose tubing (inspiratory and expiratory limb) may be advantageous. Avoid high flow face mask CPAP (open exhalation port)

Interface

- Helmet is preferred if applicable and available; if not, a non-vented face mask may be used
- For TB patients, select long-term nasal mask ventilation
- Apply and secure mask before turning on the ventilator

Pressure setting

- Use the lowest possible pressures, e.g. EPAP 5 cmH₂O and IPAP <10 cmH₂O titrated to respiratory rate and arterial blood gas tensions.
- When applying the helmet, inspiratory pressures may be at least twice the pressures used with a standard face mask
- Turn off the ventilator before removing the mask

ARF: acute respiratory failure; HCW: healthcare workers; HEPA: high-efficiency particulate air; UVGI: ultraviolet germicidal irradiation; CPAP: continuous positive airway pressure; EPAP: expiratory positive airway pressure; IPAP: inspiratory positive airway pressure. #: these apply to SARS, H1N1 and TB.

include handling procedures pertaining to aerosol-generating devices such as NIV, environment, equipment disinfection, and transport of infected patients. The designed protocol should be multidisciplinary in nature and involve doctors, nurses, physical therapists and technical personnel [10, 18, 19, 34, 35, 49, 63, 65]. However, these protocols are not intended to supplant physician judgment with respect to special clinical situations or individual patients. NIV must be managed under strict isolation measures in patients suspected of or diagnosed with highly contagious infections, with adequate protection of the healthcare workers who attend to the patient [10, 18, 19, 34, 35, 49, 63, 65].

Infected patients should be isolated in rooms with negative pressure, and visits should be restricted. The isolation time will depend on: the period of replication of the microorganism; comorbidity of the patient, such as immunosuppression; and availability of scientific information [10, 18, 19, 34, 35, 49, 63, 65]. Healthcare workers must wear personal protective equipment, as recommended by the Centers for Disease Control and Prevention's guidelines. These include N95 masks, gloves, gowns, caps, and face shields or goggles, complemented by strict hand hygiene before and after entering the room and after managing the patient [10, 18, 19, 34, 35, 49, 63, 65]. It is essential that the healthcare workers are familiar with NIV and should have received adequate training for the use of NIV in contagious patients. They should also adhere strictly to the use of personal protective equipment to avoid the risk of acquiring contagious diseases. Recommendations for NIV in SARS, pH1N1 and TB are summarised in [table 5](#).

Conclusion

NIV use in the management of acute respiratory failure in pulmonary infections, especially in pandemics, can avert or reverse respiratory failure and, therefore, decrease the rate of ETI in selected groups of contagious patients [10, 18, 19, 34, 35, 49, 63, 65]. However, its use as first-line therapy is not recommended in severe pH1N1 infections, severe respiratory failure with ARDS or in pneumonia. Although only a few reports have been published to date on infectious disease transmission among healthcare workers who manage patients receiving NIV therapy, it is crucial that reasonable and adequate precautionary steps are followed in order to protect healthcare workers from an infectious spread, as well as other patients and family members. The International NIV Network recommends further research is conducted in this area to determine whether currently proposed NIV protocols are effective in reducing infectious particle dispersion and spread of disease to others.

Acknowledgements

The International NIV Network collaborators are as follows. Henry Kwok (Hospital Authority Head Office, Queen Elizabeth Hospital, University of Hong Kong, Hong Kong, China), Anca Macri (Clinica de Pneumologie U.M.F. "Carol Davila", Institutul de Pneumologie "Marius Nasta", Bucharest, Romania), Ritesh Agarwal (Dept of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India), Benan Bayrakci (Dept of Pediatrics, School of Medicine, Hacettepe University Pediatric Intensive Care Unit, Ankara, Turkey), Dominic Dellweg (Dept of Respiratory and Critical Care Medicine, Kloster Grafschaft, Schmalleberg, Germany), Emilio Curiel (Intensive Care Unit, Hospital Carlos Haya, Malaga, Spain), Francesco Mojoli (Servizio di Anestesia e Rianimazione I, Fondazione IRCCS Policlinico S. Matteo, Pavia, Italy), Paolo Feltracco (Dept of Pharmacology and Anesthesiology, University Hospital of Padova, Padova, Italy), Praveen Neema (Dept of Anaesthesiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India), Stephan Steiner (Dept of Cardiology, Pneumology and Angiology, Heinrich Heine University Düsseldorf, Düsseldorf, Germany), Alexander Zarbock (Dept of Anesthesiology and Critical Care Medicine, University of Münster, Münster, Germany), Wei-Erh Cheng, (Division of Pulmonary and Critical Care Medicine, Dept of Internal Medicine, China Medical University Hospital, Taichung, Taiwan, China), Viliam Donic (Dept of Physiology and Sleep Laboratory, Faculty of Medicine, University of Pavol Jozef Safarik, Kosice, Slovakia), Pieter Depuydt (Dept of Intensive Care Medicine, Ghent University Hospital, Ghent, Belgium), José Luis Sandoval Gutiérrez (Medicina Interna-Medicina Crítica-Neumología, Departamento de Medicina Crítica y Terapia Intensiva, Centro de Investigación en Enfermedades Infecciosas, Instituto Nacional de Enfermedades Respiratorias (INER), Distrito Federal, Mexico), Yoshinori Matsuoka (Dept of Anesthesiology and Critical Care, Saga Medical School Hospital, Saga, Japan), Ana Paula Goncalves (Intensive Care Unit, Unidade Local de Saúde-Hospital, Guarda, Portugal), Belén Estébanez (Unidad de Cuidados Intensivos, Hospital del Tajo, Madrid, Spain), Güniz Koksall (Dept of Anaesthesiology and Reanimation, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey), Cenk Kirakli (Dept of Pulmonary and Critical Care, Intensive Care Unit, Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital, Izmir, Turkey), Killen Harold Briones Claudett (Pulmonology Dept, Military Hospital, Guayaquil, Ecuador), Aurelio Rodriguez Fernandez (Unidad de Medicina Intensiva y Emergencias, Hospital "Saturnino Lora", Santiago de Cuba, Cuba), Rogelio García Torrentera (Jefatura de Terapia Respiratoria, Centro de Investigación en Enfermedades Infecciosas, Instituto Nacional de Enfermedades Respiratorias (INER), Distrito Federal, Mexico), Jaime Zevallos Vásquez (Unidad de Cuidados Intensivos, Hospital Almenara, Lima, Peru), David Chiumello (Dipartimento di Anestesia, Rianimazione e Terapia del dolore, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy), Roberto Consentini (Emergency Medicine Dept, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy), and Zoltan Tomori (Dept of Physiology and Sleep Laboratory, Faculty of Medicine, University of Pavol Jozef Safarik, Kosice, Slovakia).

We would like to thank Mark Ryder (Istanbul American Academy, Istanbul, Turkey) for grammatical review of this article.

References

- 1 International Consensus Conference in Intensive Care Medicine: noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med* 2001; 163: 283–291.
- 2 Kallet R, Diaz J. The physiologic effects of noninvasive ventilation. *Respir Care* 2009; 54: 102–111.
- 3 Ambrosino N, Vaghegghini G. Noninvasive positive pressure ventilation in the acute care setting: where are we? *Eur Respir J* 2008; 31: 874–886.
- 4 Levitt J, Matthay M. Treatment of acute lung injury: historical perspective and potential future therapies. *Semin Respir Crit Care Med* 2006; 27: 426–438.
- 5 Harper SA, Bradley JS, Englund JA, et al. Seasonal influenza in adults and children – diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Disease Society of American. *Clin Infect Dis* 2009; 48: 1003–1032.
- 6 Kallet R. Noninvasive ventilation in acute care: controversies and acute emerging concepts. *Respir Care* 2009; 54: 259–263.
- 7 Hui DS, Hall SD, Chan MT, et al. Noninvasive positive-pressure ventilation: an experimental model to assess air and particle dispersion. *Chest* 2006; 130: 730–740.
- 8 Yam LY, Chan AY, Cheung TMT, et al. Noninvasive versus invasive mechanical ventilation for respiratory failure in severe acute respiratory syndrome. *Chin Med J (Engl)* 2005; 118: 1413–1421.
- 9 Fowler RA, Lapinsky SE, Hallett D, et al. Critically ill patients with severe acute respiratory syndrome. *JAMA* 2003; 290: 367–373.
- 10 WHO Interim Guidelines. Infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care. Geneva, World Health Organization, 2007.
- 11 Lin L, Xu YJ, He DP, et al. A retrospective study on clinical features of and treatment methods for 77 severe cases of SARS. *Am J Chin Med* 2003; 31: 821–839.
- 12 Cheung TM, Yam LY, So LK, et al. Effectiveness of noninvasive positive pressure ventilation in the treatment of acute respiratory failure in severe acute respiratory syndrome. *Chest* 2004; 126: 845–850.
- 13 Fowler RA, Guest CB, Lapinsky SE, et al. Transmission of severe acute respiratory syndrome during intubation and mechanical ventilation. *Am J Respir Crit Care Med* 2004; 169: 1198–1202.
- 14 Sung JJ, Wu A, Joynt GM, et al. Severe acute respiratory syndrome: report of treatment and outcome after a major outbreak. *Thorax* 2004; 59: 414–420.
- 15 Lew TW, Kwek TK, Tai D, et al. Acute respiratory distress syndrome in critically ill patients with severe acute respiratory syndrome. *JAMA* 2003; 290: 374–380.
- 16 Han F, Jiang YY, Zheng JH, et al. Noninvasive positive pressure ventilation treatment for acute respiratory failure in SARS. *Sleep Breath* 2004; 8: 97–106.
- 17 Yu IT, Xie ZH, Tsoi KK, et al. Why did outbreaks of severe acute respiratory syndrome occur in some hospital wards but not in others? *Clin Infect Dis* 2007; 44: 1017–1025.
- 18 McCracken J. Should noninvasive ventilation be considered a high-risk procedure during an epidemic? *Can Med Assoc J* 2009; 181: 663–664.
- 19 Pandemic H1N1 2009 influenza: Clinical management guidelines for adults and children. London, Department of Health, 2009. http://web.archive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_107769
- 20 Lum ME, McMillan AJ, Brook CW, et al. Impact of pandemic (H1N1) 2009 influenza on critical care capacity in Victoria. *Med J Aust* 2009; 191: 502–506.
- 21 Kaufman MA, Duke GJ, McGain F, et al. Life-threatening respiratory failure from H1N1 influenza 09 (human swine influenza). *Med J Aust* 2009; 191: 154–156.
- 22 Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. *N Engl J Med* 2009; 361: 680–689.
- 23 Rello J, Rodríguez A, Ibañez P, et al. Intensive care adult patients with severe respiratory failure caused by influenza A (H1N1) in Spain. *Crit Care* 2009; 13: R148.
- 24 Kumar A, Zarychanski R, Pinto R, et al. Critically ill patients with 2009 influenza A(H1N1) infection in Canada. *JAMA* 2009; 302: 1872–1879.
- 25 Ríos FG, Estensoro E, Villarejo F, et al. Lung function and organ dysfunctions in 178 patients requiring mechanical ventilation during the 2009 influenza A (H1N1) pandemic. *Crit Care* 2011; 15: R201.
- 26 Li H, Ma RC. [Clinical analysis of 75 patients with severe influenza A H1N1 in Qinghai Province]. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue* 2010; 22: 164–165.
- 27 Ramsey CD, Funk D, Miller RR, et al. Ventilator management of hypoxemic respiratory failure attributable to H1N1 novel swine origin influenza virus. *Crit Care Med* 2010; 38: Suppl. 4, 58–65.
- 28 Djibré M, Berkane N, Salengro A, et al. Non-invasive management of acute respiratory distress syndrome related to influenza A (H1N1) virus pneumonia in a pregnant woman. *Intensive Care Med* 2010; 36: 373–374.
- 29 Miller RR 3rd, Markewitz BA, Rolfs RT, et al. Clinical findings and demographic factors associated with ICU admission in Utah due to novel 2009 influenza A (H1N1) infection. *Chest* 2010; 137: 752–758.
- 30 Koegelenberg CF, Iruen EM, Cooper R, et al. High mortality from respiratory failure secondary to swine-origin influenza A (H1N1) in South Africa. *QJM* 2010; 103: 319–325.
- 31 Domínguez-Cherit G, Lapinsky SE, Macias AE, et al. Critically ill patients with 2009 influenza A(H1N1) in Mexico. *JAMA* 2009; 302: 1880–1887.
- 32 Adıgüzel N, Karakurt Z, Kalamanoğlu Balci M, et al. Influenza A (H1N1) virus pneumonia in intensive care unit. *Tuberk Toraks* 2010; 58: 278–285.
- 33 Zhang PJ, Li XL, Cao B, et al. Clinical features and risk factors for severe and critical pregnant women with 2009 pandemic H1N1 influenza infection in China. *BMC Infect Dis* 2012; 12: 29.
- 34 Conti G, Larsson A, Nava S, et al. On the role of non-invasive (NIV) to treat patients during the H1N1 influenza pandemic. http://dev.ersnet.org/uploads/Document/63/WEB_CHEMIN_5410_1258624143.pdf Date last updated: November, 2009. Date last accessed: February 1, 2011.
- 35 World Health Organization. Avian Influenza, including influenza A (H5N1), in humans: WHO interim infection control guidelines for health care facilities. Geneva, World Health Organization, 2007.

- 36 Winck JC, Marinho A. Non-invasive ventilation in acute respiratory failure related to 2009 pandemic Influenza A/H1N1 virus infection. *Crit Care* 2010; 14: 408.
- 37 Esquinas A. International survey acute respiratory failure in H1N1 infection. *Am J Respir Crit Care Med* 2010; 181: A6117.
- 38 Hajjar LA, Mauad T, Galas FR, et al. Severe novel influenza A (H1N1) infection in cancer patients. *Ann Oncol* 2010; 21: 2333–2341.
- 39 Nin N, Soto L, Hurtado J, et al. Clinical characteristics and outcomes of patients with 2009 influenza A (H1N1) virus infection with respiratory failure requiring mechanical ventilation. *J Crit Care* 2011; 26: 186–192.
- 40 Louriz M, Mahraoui C, Azzouzi A, et al. Clinical features of the initial cases of 2009 pandemic influenza A (H1N1) virus infection in a university hospital of Morocco. *Int Arch Med* 2010; 3: 26.
- 41 Adlhoch C, Wadl M, Behnke M, et al. Pandemic influenza A(H1N1)pdm09 in hospitals and intensive care units – results from a new hospital surveillance, Germany 2009/2010. *Influenza Other Respir Viruses* 2012; 6: 162–168.
- 42 Hui DS, Lee N, Chan PK. Clinical management of pandemic 2009 influenza A (H1N1) infection. *Chest* 2010; 137: 916–925.
- 43 Liu L, Zhang RF, Lu HZ, et al. Sixty-two severe and critical patients with 2009 influenza A (H1N1) in Shanghai, China. *Chin Med J (Engl)* 2011; 124: 1662–1666.
- 44 Martin-Loeches I, Diaz E, Vidaur L, et al. Pandemic and post-pandemic influenza A (H1N1) infection in critically ill patients. *Crit Care* 2011; 15: R286.
- 45 Grasselli G, Bombino M, Patroniti N, et al. Management of acute respiratory complications from influenza A (H1N1) infection: experience of a tertiary-level intensive care unit. *Minerva Anestesiol* 2011; 77: 884–891.
- 46 Timenetsky KT, Aquino SH, Saghabi C, et al. High success and low mortality rates with non-invasive ventilation in influenza A H1N1 patients in a tertiary hospital. *BMC Res Notes* 2011; 4: 375.
- 47 Belenguer-Muncharaz A, Reig-Valero R, Altaba-Tena S, et al. Noninvasive mechanical ventilation in severe pneumonia due to H1N1 virus. *Med Intensiva* 2011; 35: 470–477.
- 48 Masclans JR, Pérez M, Almirall J, et al. Early non-invasive ventilation treatment for severe influenza pneumonia. *Clin Microbiol Infect* 2013; 19: 249–256.
- 49 Jensen PA, Lambert LA, Iademarco MF, et al. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR Recomm Rep* 2005; 54: 1–141.
- 50 Sekino H, Ohi M, Chin K, et al. [Long-term artificial ventilation by nasal intermittent positive pressure ventilation; 6 cases of domiciliary assisted ventilation]. *Nihon Kyobu Shikkan Gakkai Zasshi* 1993; 31: 1377–1384.
- 51 Tsuboi T, Ohi M, Chin K, et al. [Outcome of long-term nasal intermittent positive pressure ventilation in 41 patients with hypercapnic respiratory failure]. *Nihon Kyobu Shikkan Gakkai Zasshi* 1996; 34: 959–967.
- 52 Kondoh Y, Taniguchi H, Ikuta N, et al. [Outcomes of noninvasive positive-pressure ventilation in patients with acute hypercapnia complicating chronic respiratory failure]. *Nihon Kyobu Shikkan Gakkai Zasshi* 1997; 35: 960–964.
- 53 Machida K, Tanaka T, Tsuboi T, et al. [Report of national survey on death due to tuberculosis in 1994 in national hospitals and the treatment and prognosis of tuberculosis patients with mechanical ventilation]. *Kekkaku* 1998; 73: 739–745.
- 54 Schulz MR, Herth FJ, Wiebel M, et al. Intermittent positive pressure ventilation in post tuberculosis syndrome. *Pneumologie* 1999; 53: Suppl. 2, S116–S119
- 55 Machida K. [Management of respiratory failure in patients with pulmonary tuberculosis]. *Kekkaku* 2003; 78: 101–105.
- 56 Agarwal R, Gupta D, Handa A, et al. Noninvasive ventilation in ARDS caused by *Mycobacterium tuberculosis*: report of three cases and review of literature. *Intensive Care Med* 2005; 31: 1723–1724.
- 57 Utsugi M, Ishizuka T, Hisada T, et al. Acute respiratory failure associated with miliary tuberculosis successfully treated with sivelestat sodium hydrate. *Intern Med* 2006; 45: 1069–1070.
- 58 Aso H, Kondoh Y, Taniguchi H, et al. Noninvasive ventilation in patients with acute exacerbation of pulmonary tuberculosis sequelae. *Intern Med* 2010; 49: 2077–2083.
- 59 Chin K, Ohi M, Kuno K. [Noninvasive ventilatory support on chronic respiratory failure with hypoventilation]. *Bull Chest Dis Res Inst Kyoto Univ* 1989; 22: 50–57.
- 60 Prats Soro E, Escarrabill Sanglas J, Farrero Muñoz E, et al. Ventilación mecánica a domicilio como tratamiento de las secuelas de la cirugía de la tuberculosis [Home mechanical ventilation as a treatment of the sequelae of tuberculosis surgery]. *An Med Interna* 1999; 16: 35–37.
- 61 Guerin C, Girad R, Chemorin C, et al. Facial mask noninvasive mechanical ventilation reduces the incidence of nosocomial pneumonia. *Intensive Care Med* 1997; 23: 1024–1032.
- 62 Hui DS, Chow BK, Ng SS, et al. Exhaled air dispersion distances during noninvasive ventilation via different respiratoric face masks. *Chest* 2009; 136: 998–1005.
- 63 American Association for Respiratory Care. AARC SARS page. www.aarc.org/resources/sars/index.asp Date last accessed: December 4, 2008.
- 64 Antonelli M, Conti G, Esquinas A, et al. A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome. *Crit Care Med* 2007; 35: 18–25.
- 65 Centers for Disease Control and Prevention. Interim recommendations for infection control in health-care facilities caring for patients with known or suspected avian influenza. www.cdc.gov/flu/avian/professional/infect-control.htm Date last updated: May 21, 2004. Date last accessed: September 18, 2012.