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Healthcare Acquired Respiratory Infections-Considerations and Strategies for Prevention and Control

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Abstract

This paper provides a critical review of existing procedures and practices, including surveillance methods and systems for identifying patients' risk of acquiring healthcare associated respiratory infections, in different settings. The burden of healthcare associated respiratory infections afflicting patients and healthcare workers is underappreciated. Infection control measures for TB control have been strictly applied in the United States and have decreased rates of disease acquisition below that of the general population. However, in most other countries healthcare workers are at a greater risk of acquiring TB and other infections. The principles of these TB and general infection control measures can be applied in resource scarce settings and should reduce the transmission of TB in particular but may provide protection from other respiratory infections as well. As facilities vary widely in the complexity of care they provide, a framework of risk assessment should be used to identify and apply engineering controls, work practice controls, administrative controls, personal protective equipment, and education. Novel and creative solutions, including use of telemedicine and mHealth solutions should be further explored.

As care becomes more complex in resource constrained settings, the necessary infrastructure related to water, energy, medical records, ability to do preventive maintenance and sterilize (reprocess) devices must be put into place so that the benefits of invasive care exceed the risks to the patients. The volume of water available per patient and family in hospitalized patients is a crude indicator of the quality and sophistication of care that can be provided. As we seek to improve infection control as much as possible with simple interventions, it is important to realize that once again, limits are reached without a broader system infrastructure strengthening.

Safe care does not harm the patient, the provider or the community. Implementation of safe care requires risk assessments, provision of appropriate ventilation, and adequate volumes of water. Because the preconditions for a safe environment of care cannot be assumed in resource scarce settings, there may be limitations in the effective application of US infection control "bundles". Infection control measures will have to be tested prior to implementation. Unlike in the United States, the impact of infection control measures may have to be extrapolated from studies done at sentinel sites. Measures can then be applied to facilities and evaluated with process control measures. Examples of process control measures include compliance with respiratory symptom screening, available volumes of water, hand hygiene monitoring, employee absenteeism, presence of crowds in areas with low air exchanges, ventilation, and indications for treatment among others.

Keywords: Tuberculosis; Respiratory Infections; Healthcare settings; Infection Control

Introduction

A number of important lessons have been learned from efforts to prevent Healthcare-Associated Respiratory Infections (rHAI) in the United States (US), which may provide examples for application in resource-limited settings. Healthcare associated infections are infections that are not present on admission that the patient is exposed to during their healthcare. The infection may manifest while the patients is still present in the hospital or

it may occur days, months, or years later. For example, a patient who comes to deliver a baby may get infected with influenza from a care worker and become ill in a period of days, a patient may be exposed to tuberculosis while waiting for 6 hours in a waiting room of a clinic and not develop the disease for years, or an elderly women treated for a broken leg may get colonized from methicillin resistant Staphylococcus aureus (MRSA) and not have an infection develop for 18 months later.

It is important to note that while developments have been made in the United States to put in place infection control tools to prevent respiratory infections, their use has shown a very limited capability to prevent the transmission of respiratory illnesses in healthcare settings, and therefore deep concern remains over the potential for an influenza, Severe Acute Respiratory Syndrome (SARS), or polio-like enteroviral outbreak. Healthcare providers are aware of historic difficulties preventing transmission of any respiratory infection which presents with non-specific symptoms.

Infection control is more challenging for pathogens for which we do not have available diagnostic tests, an effective vaccine, or treatment. While theoretically hand hygiene and avoiding contact with ill children or visitors helps [1], in practice most US healthcare facilities have not strictly implemented restrictions on age of visitors, restricted ill visitors, or been able to enforce strict hand hygiene for patients and visitors. One barrier is the Centers for Medicare and Medicaid (CMS) use of Press Ganey surveys to evaluate care. These patient-reported scores place patient satisfaction above patient safety or disease outcome measures, and work against U.S. facilities who wish to restrict ill visitors or require strict mask use or use of gowns and gloves.

For a variety of reasons, North American hospitals have not been able to prevent the transmission of either mild illnesses such as the common cold, or severe illnesses such as SARS. Even with vaccination, few facilities are able to lower staff absenteeism from respiratory illness during seasonal flu outbreaks [2]. A clear example occurred during the SARS outbreak where in Toronto, despite a declared international emergency, a few SARS imported cases spread to hundreds of patients and staff in healthcare settings. When emergency measures ceased and facilities resumed their usual level of respiratory infection control, a second wave of infection occurred:

These examples underline a primary lesson around the importance of routine, continuous application of existing tools to prevent respiratory infection, which can reduce transmission of disease, if applied. Or at least, in the absence of untested alternatives, existing tools should be fully implemented and their efficacy tested. In the U.S., for example, there was no transmission from the eight cases of SARS to US healthcare workers [3]; although skeptics would argue there were perhaps fewer high-risk exposures (intubations), or less infectious patients. In the above study, it is notable that authors commented that many infections in Toronto happened not because the tools were ineffective but because they were inconsistently applied.

The same basic and well-known Tuberculosis (TB) Infection Control principles are proposed to control respiratory Healthcare-Acquired Infections (rHAI) but with the following caveat: TB infection control is more consistently applied in all healthcare facilities the United States than in Africa or Asia. National, state and local health departments have been continuously funded to provide statutory oversight to infection control programs in hospitals, schools, and workplaces. They ensure that controls are applied and investigate gaps when transmission occurs.

Discussion: Can application of U.S. TB and respiratory infection controls reduce healthcare acquired respiratory infections in resource-scarce settings?

Adaptation of the principles of TB infection control applied to all healthcare facilities may reduce rHAI. In the U.S. these practices have reduced disease transmission in the community and in healthcare facilities, decreased patient deaths and prevented TB disease in healthcare workers.

Not only have TB rates in the general population decreased, but occupational acquisition of TB infection in nurses and medical students, which were 10 to 100-fold higher than the general population in the 1950's, has decreased to levels below those of the general population [4]. In contrast to the United States, healthcare workers in other settings have excessive occupation disease to TB when compared to the general population (Table 1) [5,6].

Table 1: Excess occupational risk of TB among healthcare workers in low and middle-income settings.

Work location	TB incidence rate ratio in health care workers relative to general population
Outpatient facilities	4.2 – 11.6
General medical wards	3.9 – 36.6
Inpatient facilities	14.6 – 99.0
Emergency rooms	26.6 – 31.9
Laboratories	78.9

Source: [5] Joshi R, Reingold AL, Menzies D, Pai M. Tuberculosis among health-care workers in low- and middle-income countries: a systematic review. PLoS Med 2006 Dec3(12):e494.

While the risk of acquiring TB in healthcare facilities has improved, US healthcare workers remain at risk of contracting other respiratory infections and transmitting them to patients. This problem is twofold; first, employees may get exposed at work and, second, employees, patients and visitors acquire respiratory

infections in the community and bring these infections into healthcare settings. One study by Loeb et al. [7]. unintentionally illustrated the problem of acquisition of rHAI. Researchers randomized hospital employees to use respirators or surgical masks and monitored their use. They found masks to be non-inferior to respirators in presenting influenza. However, in the study of about 460 participants, about 23%, of both groups developed lab confirmed influenza, a rate that does not indicate safety.

Another study also illustrated the risk of respiratory illness in U.S. healthcare workers [8]. This randomized control trial evaluated the impact of flu immunization on work place absenteeism from influenza and other respiratory illnesses in immunized and unimmunized workers. Vaccinated healthcare workers had 9.9 work absences from influenza per 100 workers compared to 21.1 per 100 unvaccinated workers. However, those vaccinated against influenza still reported 28.7 days of febrile respiratory illness compared to 40.6 days in the control group. While it is both biologically plausible and encouraging that immunization would reduce other respiratory co-morbidities, the significant burden of respiratory infection in healthcare workers in healthcare settings is alarming.

Infection control measures used to reduce respiratory transmission in the U.S. are shown in Table 2. Facilities should first conduct a risk assessment to identify the respiratory hazards in their areas and the procedures that put patients at risk. These should assist to prioritize the engineering controls, work practice controls, Personal Protective Equipment (PPE), vaccination, education, surveillance and evaluation, or other measures that will be most effective for the identified hazards. In practice, facilities apply a variety of different measures with variable compliance. In comparison to facilities in less developed settings, though, they are applied in settings with a controlled environment of care. The actions taken by US healthcare workers happen in settings, sometimes with statutory mandates, with unlimited volumes of high grades of water (potable, deionized, distilled, sterile, pyrogen free), unlimited volumes of continuous energy, existence of mechanical ventilation equipment and staff to monitor and maintain air exchanges, humidity and dust. Staff have unlimited access to masks/respirators/powered air purifying respirator cover gowns, disinfectants, and cleaning supplies. High quality sterilization or disinfection of medical equipment is provided. Highly reliable products and medications are available. Medical records exist that can record and communicate patient history, status, and risk over time. Laboratory systems have diagnostic tests with rapid turnaround times to identify or exclude treatable pathogens in patients with non-specific symptoms. Means of communication exist to contact patients at remote locations. Medical waste, waste water and solid waste are managed with minimal healthcare worker action. In hospitals, staff dedicate time to supervise infection control. Staff are routinely paid wages and given benefits, including sick leave. In short, a safe environment of care is provided that requires little attention of the immediate clinical staff.

In summary, many long standing respiratory infection control tools exist which may be effective if consistently applied. But the same efficacy of these tools when used in ideal settings compared and in resource scarce settings should not be assumed.

Table 2: Measures to Prevent Respiratory Healthcare Associated Infections in US.

Notifications	**Medical records or notifiable illness reports of severe respiratory disease**
	Case and contact investigations
Restrictions	Quarantine (social distancing) of exposed individuals
	Isolation of symptomatic and confirmed cases
	Screen and restrict visitation from children and visitors with respiratory symptoms
Engineering controls	Having private rooms
	Having isolation rooms with negative pressure
	Mapping ACH and air flow in cubic feet per minute
	Mapping patient flow to reduce non-essential exposure
	Ventilation: appropriate use of negative or positive pressures
	Ventilation: increasing number of exchanges per hour to the outside air
	Ventilation: eliminating indoor waiting areas

	Building design: including directional airflow
	Ventilation: use of UV light to disinfection air and air handling systems
Employee protection	Paid sick leave for workers with respiratory symptoms
	Employee health pre-employment TB screening and treatment of latent infection
	Evaluation of interventions and reporting back to staff and admin
Transmission controls	Transmission-based precautions, e.g., airborne, droplet, contact precautions
	Staff education about respiratory transmission
	Glove, mask and gown use to reduce transmission
	Restrict cough-inducing procedures to negative pressure rooms with at least 12 Air Changes per Hour (ACH)
Vaccinations	Mandatory influenza vaccine programs for staff where cost effective
	Influenza and pneumococcal vaccine programs for patients where cost effective
Sterilization and cleaning	Reprocess devices in contact with respiratory secretions at least to high level disinfection: nasal cannulas, masks, intubation devices, ambu bags, etc.
	Do not reuse single use devices on multiple patients
	Supervise reprocessing if single use respiratory devices are used on multiple patients
	Humidifier: use sterile water
	High level disinfection of mist tents and all item used on mucous membranes
Respiratory etiquette	Masking symptomatic persons, hand hygiene
	Screening for signs of respiratory illness at point of entry to the facility
	Cover your cough reinforced (can use cloth handkerchiefs if no masks for indoor facilities)
	Masks available at all entry, use reinforced by staff
Facility Information (signs)	Signage at entry
	Greetings that avoid handshakes
Clinical care	Oral hygiene and Chlorhexidine Gluconate (CHG) mouth swabbing (ventilated patients)
	Ventilator care bundle (See Table 3)
	Large volume nebulizers with sterile solutions
	Suctioning with sterile or at least clean gloves and sterile water
	Oral 0.12 % CHG before heart surgery
	Sink guards (to prevent Acinetobacter on supplies on counters near sink)
	Separating hand hygiene sink from dirty utility sinks
Laboratory	Laboratory biosafety practices (hoods) especially for microscopy
	Hand hygiene for patients and staff
Programmatic	Coordination between animal and human health for severe pathogens
	TB screening and control programs

Factors that increase the risk of acquiring rHAI

Whether a patient acquires rHAI depends largely on their susceptibility and exposure. At the moment of care, facilities can reduce exposure, but not change susceptibility. However, proactive early and routine efforts to identify patients who are susceptible may help to prioritize application of measures to reduce exposure for those patients.

In general, susceptibility can be decreased through immunization, immunity acquired from past infection, having a healthy immune system, having a healthy biome, avoiding unnecessary antibiotics, as well as by maintaining the ability to remove pathogens including by bathing and coughing, by intact lungs and skin and mobility, by managing and reducing comorbidities, and by maintaining blood sugar levels within normal limit.

Exposure can be influenced by a variety of factors and their interaction. The burden of infectious disease in the general population also increases the risk of exposure in hospitals. The effectiveness of interventions may vary in high and low prevalence settings. Fragile patients in very invasive settings such as intensive care units [9], are also highly exposed to respiratory pathogens.

Factors which affect exposure include:

- The patient's biome (many nosocomial infections come from the patients' own organisms)
- The duration and type of contact in the healthcare setting
- The duration and type of invasive procedures (shorter surgery versus longer surgery)
- Use of safe care practices (coughing and deep breathing, head of bed up in ventilated patient, sedation vacations, etc.)
- Contact with medical equipment or devices that have not be reprocessed between patients
- Sharing space with infectious patients or staff
- Air that has low air changes per hour and intakes vents that bring in contaminated air
- Contaminated items and surfaces
- Contaminated food
- Contaminated medications, e.g. prepared from a common intravenous fluid bag or nebulized medications made from surface water
- Environmental factors that increase or decrease the survival of pathogens in the environment
- Level of implementation of control strategies
- Burden of exposure due to local epidemics

Factors that increase susceptibility and exposure increase the risk of infection. Important patient level factors which impact susceptibility are summarized in Table 3.

The greatest exposure to rHAI is present in patients on a ventilator, whose use may increase the rate of acquisition of Ventilator Associated Pneumonia (VAP) 6 to 21 fold [10].

Surveillance systems to identify patients' risk of rHAI

In the United States, surveillance systems to detect respiratory epidemics exist at the facility or organizational level and in the public health sector's regional, national and international levels. Public health surveillance is not exclusively focused on healthcare acquired infections, but aids the identification of rHAI via documentation of the prevalence of infections circulating in the community [11]. Public health laboratories also conduct diagnostic tests for emerging infections of public health importance when commercial tests do not exist. Public health systems may also administer, monitor, and standardize systems for tracking rHAI in facilities.

Table 3: Factors Increasing Patient Susceptibility for rHAI.

Note: Factors are not independent and may be synergistic or markers of other underlying causal factors [12,13, 14]	
General factors	Age (very young and > 50* with increased risk > 70)
	Immunization status (MMR, polio, influenza, HIB, pneumococcus, recent pertussis)
	Lack of immunization for flu, pneumococcal, or Hib (children)
	Malnutrition status including vitamin A deficiency
Existing or prior conditions	Prior hospitalization 90 days or nursing home placement
	Burn or trauma patient
	Neoplastic disease
	Congestive heart failure
	Liver, cerebrovascular disease or renal disease
	Other respiratory illness, chronic respiratory condition or lung abnormality
	Prior colonization with MRSA
	Hemodialysis patient
	Pregnancy
	Alcohol or opioid use disorders [15]
	Allergies
	Diabetes
	HIV or immunocompromised
	Prior use of antibiotics, especially broad spectrum
	Stroke
Lifestyle or environmental factors	Smoking status
	Exposure to secondary smoke and air pollution
	Occupational exposure (asbestos, silica, young children)
Factors associated with treatment and care	Healthcare wound care therapy
	Therapy with H2 blockers, proton pump inhibitors, antacids
	Recent bronchoscopy
	Immobility
	On steroids
	Post-surgical procedure
	Use of general anesthesia
	Use of 4 or more units of blood
	Altered mental status
	Tube feeding
Other health system factors	Lack of treatment for TB infection
	Occupying room whose prior patients had drug resistant or respiratory infections
	Contact of lab confirmed case of respiratory illness
	Duration of intubation
	Duration of hospitalization

Local, regional, national and international surveillance systems

Examples of these public health surveillance systems related to rHAI are:

- Laboratory-based surveillance systems such as the National Respiratory and Enteric Virus Surveillance System of the Centers for Disease Control and Prevention (CDC).
- Armed Forces Health Surveillance Center, which conducts respiratory surveillance on a variety of populations including military recruits, zoonotic-human interfaces on a variety of common respiratory pathogens.
- The National Syndromic Surveillance System, which uses electronic data from emergency rooms to detect mass events including epidemics of respiratory infections.
- Respiratory surveillance systems for influenza from the Council of State and Territorial Epidemiologists.

- U.S. Outpatient Influenza-Like Illness Network (ILINET), which is a sentinel surveillance networks of 1800 outpatient settings in 50 states, the US Virgin Islands, Puerto Rico, and the District of Columbia. The system reports the weekly percentage of outpatient visits for influenza-like illness.
- The Influenza Hospitalization Surveillance Network (FluSurv-NET), which covers approximately 9% of the US population. This system reports hospitalizations and deaths.
- The 122 Cities mortality reporting system (CDC), which tracks the portion of mortality associated with pneumonia and influenza.
- The Influenza-Associated Pediatric Mortality Surveillance System.
- The public health laboratories and World Health Organization collaborating laboratories in the United States.
- Reporting occupational acquisition of TB and other infections on the U.S. Occupational Safety and Health Administration (OSHA) log used with workman's compensation programs.
- World Health Organization (WHO), Department of Communicable Disease Surveillance Response, maintains a Disease Outbreak News web site (http://www.who.int/csr/don).
- National Health Safety Network, the largest US system to report HAI in the United States, with more than 13,000 hospitals and ambulatory surgery centers participating.
- ProMED-mail (Program for Monitoring Emerging Diseases), a non-governmental reporting network of news, science, and member reports sponsored by the International Society for Infectious Diseases (http://www.promedmail.org).

Hospitals participate in the National Health Safety Network system to track complications of mechanical ventilation, post-operative infections, and flu immunization status. The complications of ventilation include ventilator associated events, death, pulmonary edema, sepsis, Acute Respiratory Distress Syndrome (ARDS), pulmonary embolism, and barotrauma. Facilities are motivated to participate through various levers including:

1. Reporting certain metrics is a condition for participation in Centers for Medicaid and Medicare Services programs and requirement for payment for Medicare and Medicaid patients.
2. State and local health jurisdictions may require participation.
3. Accrediting bodies, e.g., Det Norske Veritas (DNV), the Joint Commission, or the Accreditation Association for Ambulatory Healthcare (AAAHC), require facilities to report with a standardized system.
4. Facilities participate to use data to compare the quality of care internally and externally.

Intermediate between facility level and governmental surveillance systems to detect nosocomial respiratory infections are research or quality consortiums. They often test interventions and may have private or government funding. Examples include the Washington State Hospital Association's "Safe Tables," the Institute for Healthcare Improvement's Project Joint, and the multi-organization consortium's Surgical Care Improvement Project (SCIP). Organizations such as Qualis Health have governmental funding and offer consulting services to reduce adverse events including ventilator-associated pneumonia.

Facility level surveillance systems

At the facility or organizational level, hospitals adopt a variety of surveillance systems to detect and control the transmission of nosocomial respiratory illnesses. For examples, healthcare facilities use the CDC TB risk assessment to identify occupational clusters of TB infection and level of risk. This practice helps facilities develop strategies appropriate to their level of TB risk for screening employees and identifying transmission from patients: http://www.cdc.gov/tb/publications/guidelines/AppendixB_092706.pdf. In other cases, individual facilities may volunteer to become a site in the influenza sentinel surveillance systems. In the United States, care increasingly includes very short length of stay for almost all patients. Hospitals are largely centers for highly invasive procedures and monitoring, and patients may be discharged in hours or days to other care facilities. This reduces the risk of exposure to respiratory infections but also limits the ability to detect infections that may not develop for 30 or 90 days.

Facilities will employ various levels of screening, employing a number of different tools at different levels or at different points in the process of care. These include:

- Screening on first contact or admission to a facility.

Screening may occur in a phone call for an appointment, by computer kiosk, by patient phone app, by secure email, or by receptionist or volunteer. The condition screened for, and the questions to detect it, vary by institutional priority and by existing health alerts. They may screen for temperature, infections present on admission, immunization status, MRSA history or Multi-Drug Resistant Organisms (MDRO) test results. Patient may also be screened for presence of a rash and fever illness, fever of unknown origin, or influenza-like illness. During outbreaks, patients may be screened for additional conditions including travel to impacted areas. In the United States, most facilities screened for travel due to the 2014 Ebola emergency and to a lesser degree for travel to countries with transmission of the Middle Eastern Respiratory Syndrome Corona Virus. Hospitalized patients with respiratory syndrome and acute flaccid myelitis or paralysis (AFP) in the

United States are screened for enterovirus D68; elsewhere in the world persons younger than 15 years of age with AFP would be screened for polio infection.

- Screening on entrance to a unit.

Within a facility, individual departments may conduct additional screening for respiratory conditions when they admit a patient. For example, patients admitted to HIV care wards may be screened for TB; patients admitted to Intensive Care Unit (ICU) may have screening cultures for nasal, rectal, and wound culture for MRSA and or other multiple drug resistant infections. Patients admitted to stem cell or transplant services may be screened for a broad array of conditions. Preoperative patients facing major surgery may have chest X-ray and a history and physical taken that can identify respiratory conditions and be used to defer surgery. Mothers presenting for delivery may have themselves and family in attendance screened for respiratory illnesses.

- Active screening for respiratory conditions.

Some facilities screen patients and visitors for respiratory symptoms to identify patients who may need isolation or special precautions. Patients are usually actively screened and visitors are actively questioned or undergo self-screening at a check-in kiosk.

U.S. facilities may screen healthcare workers prior to the first day of work for immunizations, annual flu shot, and by law, for TB infection or disease. By law, health facilities are required to:

1. Conduct annual symptom surveys for employees with latent TB infection, and
2. Repeat tuberculin testing (Tuberculin skin testing or Interferon-Gamma Release Assays (IGRAs) for staff in high-risk departments.

- Surveillance for ventilator related pneumonia or ventilator related events.

Hospitals report ventilator-associated pneumonia in the National Healthcare Safety Network. While the definition and data requirements are standardized, individual facilities develop their own systems to obtain the required data.

Reporting ventilator-related pneumonia requires tracking all patients put on a ventilator in a given unit and then monitoring the number of ventilator-days, which becomes the denominator. For example, if at 8 AM, 10 patients are on a ventilator in an Intensive Care Unit (ICU), this would be counted as 10 ventilator-days. Obtaining the denominator data (ventilator-days) is almost always a manual process and is done daily, or for a sample of days. Staff review charts to exclude patients with pneumonia present on admission, then track lists of patients on ventilators to see if they develop a reportable event attributable to use of the ventilator.

Different facilities use different systems to do this. Some have data mining software, or program algorithms to help identify possible infections. While these systems reduce the chart review, due to the difficulty of diagnosing pneumonia, patients still need to be reviewed individually to see if they meet the definition for ventilation-related pneumonia.

- Surveillance of post-operative pneumonia to report rates pneumonia following surgery.

Starting with a list of patients who have undergone a surgical procedure, patients are followed for 30 days. Patients with respiratory infections present on admission are removed, then patients are stratified by ventilated and non-ventilated patients, and patients are then tracked to see if they develop infections meeting the definition in the follow-up period. Systems with active surveillance send letters, texts, phone or e-mail to patients and families asking if they developed infections in the post-op period; those indicating in the affirmative are usually interviewed directly. Alternately, letters may be sent to the surgeons or physicians providing follow-care.

- Surveillance in non-surgical settings.

Non-surgical hospitals may determine their highest risk patient population and track pneumonia developing more than 48 hours after admission. For example, hospitals may track the development of respiratory illness in stroke patients, trauma patients, burn patients, in patients with tube feeding, and in patients with tracheostomies on a ventilator.

- Tracking infections following exposures to lab confirmed infections of public health importance.

Most hospitals have a system in place to notify patients, staff, and public health authorities of infections acquired during their care. During high priority outbreaks, health departments or CDC staff will step in. During the SARS outbreak for example, CDC dedicated more than 800 staff to surveillance and containment efforts. Hospitals try to identify exposures to limit future transmission, to remove infectious staff from duty, and to provide prophylaxis or treatment.

Existing tools for identifying rHAI

Standard Comprehensive References: Three organizations, the Curry International Center, CDC and WHO have published very clear, exceptionally well done, evidence-based tools for the control of TB in Healthcare settings. Applying the principles of these guidelines and adapting the procedures to other respiratory diseases would likely contribute to the control of a variety of respiratory infections. Because of that, this review strongly recommends their use as primary references and resources, with additional focus on hand hygiene, and provision of large volumes

of water to all facilities doing invasive procedures. All three organizations have developed training material related to these guides that are simple, clear, and appropriate for a wide variety of settings:

- WHO Policy on TB infection control in Health-Care Facilities, Congregate Settings and Households 2009. WHO/HTM/TB/2009.419. http://whqlibdoc.who.int/publications/2009/9789241598323_eng.pdf?ua=1
- Francis J. Curry National TB Center. TB Infection Control, A Practical Manual for Preventing TB. 2011. http://www.currytbcenter.ucsf.edu/sites/default/files/ic_book_2011.pdf
- CDC. Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005 MMWR 2005; 54 (No. RR-17).

In addition, the 225 page HICPAC 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings remains the US standard guiding practice on the use of transmission-based precautions for both respiratory syndromes and pathogen-specific infections. The evidence base and duration of application for many of the isolation precautions remain widely debated in the United States. As better diagnosis tools evolve for viral pathogens, more advocacy is seen for the use of both respiratory (airborne or droplet) and contact precautions (e.g., gowns, gloves and mask and eye protection) [16], for a broader range of diseases [17].

The last classic reference is the 2003 federally appointed Healthcare Infection Control Practices Advisory Committee (HICPAC) guideline (Guideline for Preventing Healthcare-Associated Pneumonia) [18], which remains the most evidence dense reference for preventing healthcare associated pneumonia. It includes guidance for preventing ventilation-associated pneumonia (events), tube feeding risk reduction, and an extensive literature review.

References for outbreak investigations: While the resources needed to conduct an analysis of an outbreak investigation may be outside of the budget, time availability, and expertise of many healthcare providers, there are some basic principles which can be applied to detect and define that a problem exists, even if the plan is then to request external help. Some countries have WHO sponsored field epidemiology courses which can provide training or assistance in outbreaks. CDC provides assistance for outbreaks with novel or unknown risk factors or the potential for multi-country spread. The CDC Healthcare Associated Infection Outbreak Investigation Toolkit contains outbreak abstraction forms and guidance on contains general information or 'variables' that might be collected during HAI outbreak investigations in a variety of different settings. An outline of the steps to take is described in Infection Control in Ambulatory Care.

Tools, trainings, forms, program descriptions and best practices: Table 3 provides a list of specialized guides, job aids, and case studies related to the measures discussed in Sections I-III above, for different healthcare settings and disease areas. These include commonly used forms, trainings, signs, calculators, sample legislation, and new approaches that may be useful for control of respiratory infections. These should not be regarded as 'ready to use' guides, but as illustrations of principles that could be adapted to reduce the susceptibility and vulnerability of patients to rHAI in other settings.

Implications for practice in limited resource settings

To be successful in halting transmission, infection control measures need to match the complexity of care provided. The more complex the care that is provided, the more important system-level facility enhancements become. At the lowest level, relatively simple measure like implementation of alcohol hand gel or provision of sterile syringes can have important benefits, since at dispensaries or health posts the most common invasive procedures done may be injections. Even for sterile syringes to be successful, it will be necessary to have systems for stock management, medical waste, supervision, and cost recovery. As care becomes more complex, however, system wide health strengthening in infection control is necessary or care will not be safe. A dispensary may prevent the spread of blood borne pathogens with the use of single-use syringes. A dialysis facility may implement use of sterile syringes but will still spread hepatitis C (HCV) and B unless they institute a variety of measures including water systems, adequate volumes of water, reverse osmosis, cleaning protocols, ability to separate patients, strict reprocessing guidelines for dialysis filters. To prevent respiratory transmission within the healthcare setting, system level changes will most likely be necessary.

As worldwide levels of HIV and HCV rise, infection control measures to prevent blood borne infections are of increased importance as they are transmitted by unsafe care in the workplace by percutaneous and mucous membrane exposures.[19]

U.S. government requires healthcare programs to have a bloodborne pathogen control programs. These have a number of key elements, as outlined below. These elements parallel the principles of a respiratory infection control program as well.

1) Conduct a risk assessment to identify where exposure to blood will occur and to whom

2) Develop a plan for prevention, control and treatment of bloodborne exposures

- Implement engineering controls:
- Provide sterile devices for injections; offer safety devices where available

- Eliminate injections and sharps whenever possible
- Use sharps containers
- Institute medical waste systems to prevent reuse of contaminated devices by facilities or public.

3) Introduce Personal Protective Equipment (PPE) for staff and patients

These should be made available to employees at greatest risk rather than those of highest status (e.g. midwifes and surgeons should have the same level of PPE.)

- Gloves, gowns, masks and eye protection
- Closed toe shoes

4) Implement work practice controls

- Remove blood from the environment though effective cleaning
- Provide cleaners with water, cleanable buckets, brushes, detergent and disinfectants.
- Launder textiles in safe ways
- Institute a biosafety program in the lab to minimize blood contact
- Reprocessing of instruments between patients appropriate to contact with skin, mucous membranes or parenteral use
- Ban recapping of used sharps
- Supervise use and storage of medications with potential for abuse

5) Require vaccinations for healthcare workers and patients (especially HBV)

6) Implement exposure management system for workers including testing and treatment; provide compensation for work related illness and injuries

Core principles of airborne TB control

The principles of TB control can be adapted to reduce the nosocomial transmission of other respiratory pathogens. These principles and suggested modifications include:

1) Conduct a risk assessment to define hazards and select control measures appropriate to the hazard, risk and location.

2) Engineering controls

- Design facilities to avoid recirculation of unfiltered or untreated air
- Design the patient flow to minimize the time infectious patients spend in public waiting rooms or settings without adequate ventilation
- Provide enhanced ventilation for higher risk procedures including cough inducing procedures
- Place waiting rooms outdoors and/or in areas that vent to the outside, eliminate waiting in corridors
- Provide lab fume hoods for microscopy and cultures
- Use appropriate diagnostic tests to confirm need medications and ensure prudent use of antimicrobials.
- Use directional air flow including appropriate use of negative pressure and positive pressures.
- Apply evidence based treatment regimens
- Use of a combination of mechanical ventilation systems, filters, upper air UV light, fans, and non-recirculating exhaust systems when natural ventilation is not possible

3) Administrative Controls

- Use the least restrictive setting possible including care at home.
- Avoid purchasing devices that the setting cannot main or reprocess.
- Transition from financing programs by the sale of medications as this promotes inappropriate use of medications.
- Select an improvement priority based on regional risks and track progress with process indices.

4) Work practice controls

- Screen new employees for infection and disease
- Screen for infectious cases in staff, visitors and patients in all settings
- Screen for respiratory symptoms and mask those upon entry to facility (or provide cloth handkerchiefs)
- Isolate infectious cases from public areas and shared workplaces
- Investigate persons with significant exposure to serious and treatable illnesses to prevent additional transmission (SARS, MDR-TB, MERS-CoV, ARDS)
- Use respiratory hygiene (cover coughs, mask persons with respiratory illness)
- Match therapy to drug susceptibility, avoid broad treatment when possible.

5) Immunization

- Use vaccines as appropriate and cost effective including pneumococcal, flu and Hib

6) Personal Protective Equipment (e.g. masks, gowns, gloves)

- Provide and supervise staff use of appropriate PPE when working with infectious patients
- Promote patient use of masks, and facility provided handkerchiefs or tissue

7) Exposure Management

- Treat latent TB infection
- Use directly observed or monitored therapy to ensure completion
- Evaluate rates of occupational illness and treatment failures to improve the program

Expectations of lowered efficacy when applying TB control measures to other respiratory pathogens

TB control practices reduced transmission of TB in U.S. healthcare facilities. The same approaches are likely to have some, but less effect on the control of other respiratory infections and in other countries for a number of reasons. For example, the rate of untreated HIV/TB and MDR TB infections are higher in many countries [20]. HIV increases the progression of TB disease, changes the detection by skin testing or CXR, and increases the reactivation rates of TB. A high prevalence of HIV in the population makes it likely additional infectious TB patients are present in healthcare facilities during childbirth, emergency care such as car accidents, and for all other medical treatments [21]. HIV also increases vulnerability to other respiratory infections.

When applying TB control measures to other rHAIs, there are other reasons to expect lower efficacy. Unlike TB, many respiratory pathogens are infectious before the onset of symptoms: staff unknowingly come to work while infectious [22]. This limits the sensitivity of screening measures to identify infectious cases. Subclinical infections can also be infectious, whereas for TB, not all clinical infections are infectious.

Second, TB control programs in the United States are often supported by law, externally funded and audited, and have standard measures of proven efficacy. Program evaluation measures have also been standardized. Hospital control programs for other infectious respiratory illnesses are not externally funded, but are sometimes monitored by state or local departments of health.

Research money and interest also exists to test TB control measures, including in resource scarce settings. In contrast, the majority of viral infections transmitted in facilities (e.g., RSV in adults and metapneumovirus) are often ignored as a cause of nosocomial infection. Clinicians do not test for them if there is no targeted therapy; diagnostic tests done for screening are not billable. Diagnosis of VAP and pneumonia is difficult [23,24], variable, and unreliable in both developed and developing country settings, making the evaluation of pneumonia control measures more difficult.

In addition, TB control is an identified priority due to the high case fatality rates and burden of disease. National, bilateral organizations, and foundations fund consensus strategies. The same is not true for many of the other poorly understood respiratory adverse events.

As TB also has a lower attack rate than many pathogens [25], it does not overwhelm healthcare facilities the way RSV or influenza epidemics can. A very high rate of TB would be 280 per 100,000 persons per year, as occurs in Southern Africa (In contrast, the US rate in 2014 was 3/100,000 [26]), whereas during a flu season more than three quarters of children may be infected. It is not uncommon during the peak of a seasonal flu outbreak to have more than 10% absenteeism in the U. S. work place.

Even in the United States, lab diagnosed rHAI can only be verified in funded research or sentinel sites; clinical hospitals monitor process indicators rather than outcome indicators except for VAP. Readily available and affordable diagnostic tests exist for TB, but not for most of the other causes of respiratory pathogens which are predominantly viral. This limits the identification of pathogen specific causes for early triage into isolation.

Finally, except in HIV positive persons, healthcare acquired TB disease may take months to years be become visible. The onset of other healthcare acquired infections may be considered at 48 hours after admission or within the incubation period of known pathogens.

Prioritizing tools for use in limited resource settings

Infection Control practices and experience are underrepresented in the professional literature and some of the comments to follow are based on unpublished data from the author's experience managing a 38 facility infection control program, a university affiliated trauma hospital serving five states, and community hospitals.

Measure ventilation: air exchanges per hour and airflow

The most effective baseline intervention would be to do a facility review of the indoor and outdoor spaces and how they are used, including identifying the paths of patient flow and where the high hazard procedures are done, and documenting the ventilation air changes per hour, where the intake and exhaust vents are located, the use of fans, bio-safety cabinets, and where cough inducing procedures, and the lab are located. When identifying the air intakes and exhaust locations include the opened space of windows, not the size of the glassed window, which can then be used to identify the areas that need more ventilation, and the locations that have enhanced (> 12 ACH), normal (6 ACH), and

poor ventilation rates. The highest priorities would be to eliminate crowded internal waiting rooms, such as outside of an X-ray machine, changing the flow to separate infectious patients from low risk settings, and maximizing natural ventilation. Technical guides are available to help locate intake and exhaust vents and to size them to provide safe air.

Locate high risk services in settings with adequate ventilation (ACH and air exchanges per hour)

Services with a high risk of respiratory transmission should be located in areas with enhanced ventilation. However, all patients presenting for care should be assumed to be possibly infectious with respiratory illnesses. Surgery, autopsies, intensive care units, sputum induction, waiting, bronchoscopy, childbirth, toilets, laundry, laboratory, microscopy, central sterile supply, and pulmonary therapy are among the services that should be conducted in areas with enhanced ventilation and with at least two air exchanges per hour to the outside and no recirculated air.

Much disease transmission occurs, however, in patients admitted for non-respiratory conditions. It is the pregnant woman with her persistent cough, the child with a broken leg with influenza like illness, the febrile family caregiver of a malaria patient who, unnoticed by staff, may be a super-spreader of respiratory illness. Adequate ventilation without recirculation in all settings is the only way to provide safe care.

Ensure that adequate volumes of suitable water is readily available

A point worth emphasizing is that effective infection control requires the provision of large volumes of water. Hand hygiene, patient bathing, cooking, reprocessing of linen and medical instruments, not to mention cleaning of the environment, all require large volumes of water. Even when alcohol hand rubs have been fully implemented, water remains an essential component for care. Conversely, facilities without water should not implement services that cannot be safely provided without large volumes of water, e.g., hemodialysis, bronchoscopy, endoscopy, and surgery.

Water needs to be prioritized for persons doing instrument reprocessing, including steam sterilization. If water is not available, invasive procedures will not be safe.

Use process monitoring coupled with existing outcome measures to evaluate compliance with infection control measures

In resource-limited settings it may be useable and feasible to track some outcomes that are less specific to rHAI than the US National Health Safety Network (NHSN) measures. For example, departments can track death rates beyond 48 hours of admission, all-cause employee absenteeism, and diagnosis of TB disease in employees (or preferably conversion of latent TB infection). In settings without a system to replace ill staff, it may be useful to do periodic, anonymous symptom surveys at work to detect respiratory symptoms. Patient death rates by unit and, if possible, by disease are also useful to detect serious problems. Because most facilities do not have dedicated staff who can compile and present statistics, facilities should only track measures that can be acted on to improve quality.

Employees, even those vaccinated with BCG can be screened for latent infection by tuberculin. Those with mm reading > 14 are predictive of TB disease, and the size of the induration is also lessened after 15 years [27]. In high prevalence settings these would need to be compared with community acquisition rates. However, identification of infected employees and provision of prophylactic treatment is important to preserve and protect valued, trained staff as well as to identify units where transmission is greater than expected.

Share data and learn from peers

The International Infection Control Consortium is an ongoing working group that shares data and interventions to improve care in middle-income economies. Settings that are willing to share and discuss what issues and data they have, including discussing problems arising, are better able to develop interventions realistic to their settings. Facilities can also use applicable published work as a benchmark for rates or rHAI. For example, Ndegwa et al. [28], surveyed patients twice a week in several Kenyan hospital wards for hospital onset (>48 hrs) of fever, hypothermia, and signs of respiratory infection such as cough. They then took naso-pharyngeal swabs. They established a base rate of 9 per 10000 patient days with ICU having the greatest rates. While this strategy was 5 fold lower than systems that sampled patients every day, it did verify the problems of viral rHai, the problem in ICU, and pediatric wards. Rather than replicating this expensive and labor intensive prevalence study on an ongoing basis, facilities can now focus on monitoring interventions including the onset of influenza-like illnesses in staff, hand hygiene monitoring, cleaning validation, volumes of water used, volumes of hand hygiene gel used, etc., to address a known problem.

ICUs with staff who have administrative time can monitor the bed position of ventilated patients and track the portion of afebrile patients who develop a fever or purulent sputum beyond 48 hours (not specific to rHai), as well as track the duration of ventilation, sedation vacations, and the duration of central line or urinary catheter placement. The goal is to decrease the duration of invasive measures. Most simply, this can be done on paper at the head of the bed (then verified by a checklist) by recording the date of admission and date on and off a ventilator. It can also be done on daily ward rounds for patients on the unit. Institute for Healthcare Improvement (IHI) and University Research Co., LLC (URC) have adapted simple run chart tools that can be used to identify when the population based rates are “out of control” or

statistically significant.

Additional means of preventing rHAI in resource scarce settings

Anticipating concerns that the 'easy' infection control measures may have already been applied, and understanding that most off-the-shelf measures cannot necessarily be used without the same environment of care, several recommendations can nevertheless be made to improve infection control, especially against respiratory infections. These include undertaking risk assessment: identify high-risk patients and high-risk procedures, and measure existing ventilation to ensure the setting matches the need. Equally important is the need to provide water in adequate volume and quality for staff and patient hand hygiene, instrument reprocessing, facility cleaning, laundry, food preparation, bathing, and laundry. Improving these two elements of care: safe air, safe water can provide broad improvements in patient care. No facility can safely provide invasive procedures without them.

In conjunction with these measures, sites should select a process improvement goal based on regional priorities and use quality assurance techniques to track its resolution. Depending on the risk profile for the facility, some process goals might be:

- Increase the rate of HIV and TB testing in patients with pneumonia who are not improving with antibiotics;
- Improve the TB screening rate for employees with cough greater than two weeks;
- Track the rate of fever, cough and increased respiratory rate in patients with nasal gastric feeding tubes,
- Decrease the number of patients with sinusitis who are treated with antibiotics;
- Decrease the number of patients presenting with upper respiratory infection who are treated with antibiotics etc.

Beyond these measures, additional steps which can be taken include the following:

Antimicrobial stewardship

In support of overall with infection control, the importance of promoting rationale antimicrobial use is paramount. Worldwide, flu and pneumonia remain among of the 10 top causes of mortality, and preserving antibiotics for treatment is essential.

It is not uncommon for clinicians to prescribe antibiotics and multiple medications to many patients a day, often without diagnostic tests, detailed history, record review or examination. While patients are satisfied when they receive medications often after expensive and long travel to the clinic, and the clinic benefits from the access fee and sale of medications, it cannot be assumed that this care is better than no care, Such care contributes to drug resistance and may be no better than random distribution of medication. For example, in the US case of prescribing opioids, providing medication to meet patient demand led to tens of thousands of deaths a year. The CDC, Infectious Disease Society of America (IDSA), the WHO Rational Drug Program and US Agency for International Development (USAID) have well developed programs promoting rationale drug use. The US program guides presume that there is no public ability to purchase antimicrobial medications without a prescription, and that existing medications are not counterfeit. Internationally, key challenges relate to developing consensus around a new "post-Bamako Initiative" that finances primary care without the sales of antibiotics, restricting public access of antimicrobials (i.e., street vendors), and instituting prescriptive authority over antibiotics while maintaining appropriate access for remote populations. However, facilities should not wait for sweeping programmatic changes. In the meantime, and possibly as part of a regional initiative they can apply the rational drug use work of WHO focused on:

- Developing antimicrobial treatment criteria that are accepted by clinicians, patients and administration
- Using the shortest effective therapy
- Auditing antibiotic prescribing for defined conditions
- Incentivizing providers to adhere to evidence based practice rather than independent decision making in opposition to evidence
- Educating providers and the public on treatment of viral conditions including flu, upper respiratory infections, simple diarrhea and sinusitis for which universal antibiotic treatment is considered a medical error.

Develop, test and implement better diagnostic tests

Large-scale syndromic treatment programs lead to drug resistance. More specific criteria are needed. For example, Amiriv and others [29, 30] are also reconsidering the use of respiratory rate as the diagnostic criteria for bacteria pneumonia in children, due to the low predictive values that lead to the unnecessary use of antimicrobials. To preserve the effectiveness of antibiotics for future years, and to reduce the harms of unnecessary antibiotic use, diagnostic tests should be implemented when cost effective. This cost, however, should consider not just the current patient's costs, but the cost to society if there is no effective or affordable treatment in future years. Implementation of diagnostic tests can improve care, and programs should promote the use of rapid diagnostic tests where appropriate for HIV, malaria, TB and possibly in some situations for Strep, syphilis and other conditions, so inappropriate antibiotics use is reduced. New work with small scale multi-organism molecular diagnostics may be able to detect organisms within hours. This development work should be guided by needs in developing countries.

Where possible, facilities can support the design and evaluation of new diagnostic measures that can better diagnose pneumonia including new ultrasound and pulse oximeters or other new technologies. This is important as the community dispensing programs for pneumonia use an algorithm that is insensitive for pneumonia and contributes to drug resistance. While pediatric populations may benefit for the first years from community-based distribution, it remains likely that the rapid drug resistance that is developing for cotrimoxazole will eliminate this as a low cost treatment option.

Vaccinate against respiratory infections

As respiratory pathogens develop drug resistance, the cost-effectiveness of pneumococcal vaccines and Hib may increase in developing country settings.

Use mobile phone and computer technology to expand virtual access in remote settings

In resource-limited settings, a large proportion of patients' out of pocket costs are for travel to health sites. Where available, increasing the use of mobile technology should be explored. Telehealth visits can convey lab results, send pictures to monitor wound care, report patient status, promote medication compliance, send immunization reminders, and in general improve communication between patient and provider.

Important programmatic models are developing in the US and elsewhere. In the Northwest US, rural providers cover a five-state area including Alaska. Weekly telemedicine sessions are conducted following the University of New Mexico's Project ECHO (Extension for Community Health Care Outcomes) model [31], with expert practitioners who coach group sessions of providers in treatment of such specialty conditions as HCV, pain, rheumatoid arthritis, mental health and HIV. Provider to Provider sessions allow the rural provider to present their case for expert advice. Providers join from their laptop (requiring no travel costs) and have video sessions. The result is to support both patient treatment and continuous provider education. The model has been so successful expanding specialty care to remote areas that Project Echo website currently reports expansion to 37 countries and 677 programs. The U.S. Indian Health services [32], has expanded the use of telehealth services to allow patients to consult with providers via secure video and audio links so providers can be in cities and patients in their rural communities. This type of consultation also reduces exposure to infections for both the provider and patient.

Conclusion

It is an unfortunate truth that Infection Preventionists can more easily prevent Ebola in their facilities than the spread of a typical respiratory infection. However, implementing risk assessments for procedures and populations with high associated risk of infection combined with a critical review of existing control strategies can assist to reduce transmission. Engineering controls (e.g. placing waiting areas outside or with enhanced ventilation, use of safety hoods) will be more effective than those requiring workers and patients to change their behavior. As demonstrated by the experience in the US, the routine application of well-known TB control measures to prevent respiratory disease when applied in non-TB settings can be effective. Screening and isolation of persons with respiratory symptoms, improving ventilation and PPE use can likewise reduce transmission. There is no existing solution for provision of enough PPE in resource scarce settings, so this needs innovation. Staff might use cartridge masks rather than N-95 as they last longer and the lifetime cost is lower. Process measures should be applied to evaluate the consistency of the infection control interventions. Hand hygiene and enough water for reprocessing of surgical instruments used on multiple patients, hand washing, cleaning and laundry are important. Public and provider education, while popular recommendation, are necessary but not sufficient measures. Adequate control of healthcare acquired respiratory infections will benefit from use of the additional measures mentioned above.

Disclaimer

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Conflict of interest

None

Definitions

Airborne infections: Used by US CDC to refer to diseases thought to be transmitted largely by nuclei < 5 microns that can travel more than 1 meter from the source. These include disease such as measles, chickenpox, tuberculosis, and Hanta virus.

Droplet infections: Used by US CDC to refer to disease spread by pathogens on aerosolized particles larger than 5 microns which usually fall out of the air close to the patient emitting them. Historically it was thought that separating patients by 3 feet was enough to prevent the spread of disease transmitted by droplet infections. These include diseases such as influenza, common colds, influenza, parainfluenza virus, adenovirus, respiratory syncytial virus, and human metapneumovirus.

Efficacy: Results achieved under research or ideal conditions.

Effectiveness: Results achieved under real world settings.

Healthcare-associated infections: Infections acquired as an unintended consequence of receiving healthcare. Depending on the causative organisms, infections may present from 1 day to 18 months or decades (TB) after the exposure during the healthcare visit.

Respiratory infections: Used in this document to refer to pathogens infecting the respiratory tract that may be transmitted by a variety of routes including fecal-respiratory, droplet, airborne and contact.

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