

Antonio Matías Esquinas *Editor*

# Humidification in the Intensive Care Unit

The Essentials

 Springer

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Antonio Matías Esquinas, M.D., Ph.D., FCCP  
International Fellow AARC  
Intensive Care Unit  
Hospital Morales Meseguer  
Avd Marques Velez s/n  
Murcia, Spain  
antmesquinas@gmail.com

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## Preface

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### **Humidification in Intensive Care Medicine: A New and Ancient Science Evolving**

For several decades, we have realized the complexity of maintaining adequate respiratory function in critically ill patients, particularly during mechanical ventilation (MV), both invasive (IMV) and noninvasive (NIV), and have managed to maintain a reasonable balance between the patient and the ventilator in different scenarios [1–5].

Humidification is an essential part of any successful ventilatory strategy in critically ill patients. Nevertheless, the importance of this strategy and its probable impact on prognosis, weaning, control of bronchial secretions, gas exchange and complications, such as ventilator-associated pneumonia (VAP), are still under-recognized by many practitioners [6, 7]. We have not yet identified the ideal level of humidification needed for different clinical scenarios in critically ill patients, or the impact of external factors that may influence the level of absolute and relative humidity. Despite the fact that we have made significant developments in the technology of heated humidifiers or heated moisture exchangers, a great need for large clinical trials in patients with different types of respiratory diseases still exists.

The new advances in the technology of IMV and NIV have increased the need for proper assessment of the requirements of ventilated patients for humidification, the appropriate time and mechanism for the application of humidification, and the potential interactions between physical factors, such as ventilator mode, and patient-related factors. These issues are unresolved and open for future research to help specialists develop clinical guidelines for the indications for and effectiveness of humidification in NIV.

The science of humidification in critically ill patients is still an unresolved dilemma, with a strong pathophysiological basis and technological challenges, which the critical care physician is still discovering.

The authors and editor of this book wanted to make a critical summary of the main practical points pertaining to humidification in NIV in adult and pediatric patients, and try to answer the question of when and how to start humidification. We have highlighted the relationship between humidification and VAP, summarizing the aspects of prevention and treatment of ventilator-associated pneumonia (VAP), a clinical situation that merits further analysis and research.

Chapters were structured in a simple, practical way, covering different clinical scenarios and targeting intensivists, pulmonologists, anesthesiologists, pediatricians and respiratory care therapists.

I want to thank all authors for their great efforts and contributions that tried to summarize available data and develop a bridge between science and clinical practice. We hope that this book will serve as a reference for practitioners and respiratory therapists involved in managing patients on NIV and will stimulate researchers to explore unresolved areas.

We hope that this book will meet the requirements and expectations of its readers and create innovative new ideas in the science of humidification.

As Marco Aurelio Valerio Majencio said,

“what is not useful for the hive, it is useful to the bee.”

(Roman leader, *Marcus Aurelius, Rome*). –278–312

Murcia, Spain

Antonio Matfás Esquinas, M.D., Ph.D., FCCCP

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## Section I

# Humidification and Physiology

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# Physiology Humidification: Basic Concepts

# 1

Jens Geiseler and Julia Fresenius

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## 1.1 Introduction

Conditioning of inspired air and filtration of airborne particles with a diameter  $>3 \mu\text{m}$  are the main tasks of the upper airways with regard to respiration. Under normal circumstances the inspired air is warmed up to body temperature with 100% relative humidity when entering the gas-exchanging parts of the lungs, thus preventing damage from the organism. In the following chapters the anatomy of the upper airways and their properties of warming and humidifying inspiratory air are described.

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## 1.2 Anatomy

The respiratory tract can be divided into two parts: the conducting airways and the gas-exchanging part, the alveoli. The conduction airways can be subdivided into the upper airways – nose, mouth, and pharynx – and the lower airways containing the larynx, trachea and bronchi that extend while branching several times to the respiratory bronchioles. The boundary between the upper and lower airways is the larynx.

### 1.2.1 Anatomy of the Nose

The nose is divided by the nasal septum in two separated airways, extending from the nostrils to the posterior nares. The surface of the nose is increased by the turbinates up to an area of 100–200  $\text{cm}^2$  [1], while at the same time the lumen is narrowed, thereby facilitating close contact of the inspired air with the nasal mucosa

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J. Geiseler (✉) • J. Fresenius  
Department of Intensive Care Medicine and Long-Term Ventilation,  
Asklepios Fachkliniken München-Gauting,  
Gauting, Germany  
e-mail: j.geiseler@asklepios.com; j.fresenius@asklepios.com

and generating more turbulent flow, which alleviates deposition and trapping of inhaled particles on the nasal mucosa.

The vestibular region of the nose has a surface of thin squamous epithelium that is covered at the nostrils by short stiff hairs acting as receptors for mechanical stimuli and inducing sneezing. At the posterior parts of the nose the epithelium changes to a columnar ciliated respiratory epithelium [2]. The glands of the mucosa produce a secretion film composed of a low-viscous phase at the surface and a superposed high-viscous gel phase. The submucosa lying between the epithelium and basement membrane has abundant blood vessels. The arteries and arterioles have dense adrenergic innervation. Mucosal capillaries join to form confluent veins that establish the sinusoids or cavernous plexus.

The regulation of the perfusion of the mucosa is important for conditioning of inspired air. Due to vasoconstriction of the arteries induced by the sympathetic drive or application of local sympathomimetic drugs, the perfusion of the mucosa is reduced, and therefore the capacity of the mucosa to condition inspiratory air is decreased. Contrarily, an increase in perfusion with swelling of the mucosa may lead to an increase in the nose's resistance, leading to a preference for mouth breathing and hindered conditioning of the inspiratory air. Infections and inflammations of the mucosa, or therapy with continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV) via a nasal mask can cause swelling of the mucosa.

## 1.2.2 Anatomy of the Lower Airways

The trachea begins below the larynx. The shape is stabilized by cartilage rings in the form of a horseshoe, so at the dorsal part of the trachea there is only a membrane. The cartilage prevents collapse of the trachea during increases of intrathoracic pressure. The length of the trachea is about 10–12 cm and ends at the bifurcation into the two main bronchi. The mucosa contains ciliated respiratory epithelium with glands creating a fluid line on the surface of the epithelium.

The bronchi contain cartilaginous rings for stabilization. The right and left main bronchi divide and form segmental bronchi that keep branching and form up to 23 generations of smaller bronchi. The more distant from the main bronchi, the less cartilage can be found in the walls of the bronchi. Lastly, the bronchi pass on to acartilaginous bronchioles. Finally, the conduction airways end at the terminal bronchioles.

The epithelium resembles that described for the trachea.

---

## 1.3 Function of the Upper Airways Regarding Conditioning of Inspiratory Air

The main objectives of the nose are smell, filtering the inspired air, and humidification and heating – the so-called conditioning of inspired air. During expiration some heat and moisture are recycled, thus minimizing the loss of water and temperature.

### 1.3.1 Warming of Inspiratory Air in Humans

Most conditioning of the inspiratory air takes place in the nose. The temperature of the nasal mucosa is in the range from 30°C to 36.6°C depending on the method of measurement, the location of the measurement and the time point during the breath cycle at which the measurement is done [3]. Data from healthy subjects reveal that the end-inspiratory temperature of air is already increased in the anterior parts of the nasal cavity compared to ambient air [4] and reaches 34°C in the nasopharynx. The end-inspiratory temperature of the nasal mucosa is thereby lowest at the end of inspiration and highest at the end of expiration. The degree of warming inspiratory air is clearly dependent on the ambient temperature. Webb published data of pharyngeal temperatures of only 27°C when the ambient air temperature was only 7°C [5]. The short contact time of the inspired air with the nasal mucosa seems to be long enough to allow a warmth transfer by convection and radiation from the nasal wall to the air [6]. Preconditioning therefore allows the mucosa to have great potential for regulating blood perfusion to counterbalance its heat loss during inspiration to prevent damage of the mucociliary clearance, which is temperature-dependent [7]. As mentioned above, the temperature of the inspired air when leaving the nose is about 34°C. Further warming up to 37°C takes place in the lower airways, so the air entering the gas-exchanging area has body temperature and is 100% saturated.

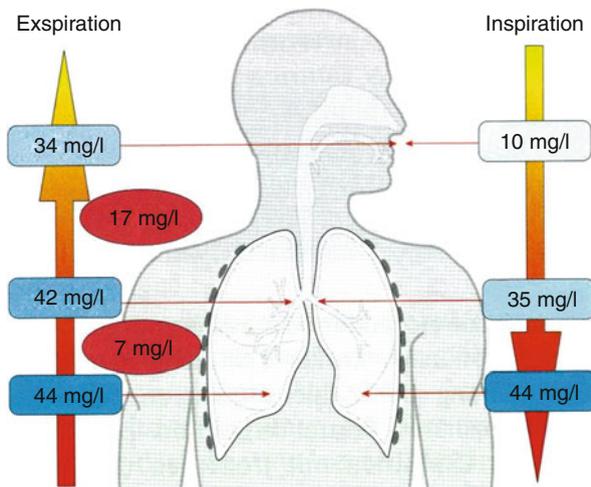
During expiration heat is partially conserved by condensation of the water vapor at the mucosa because of large temperature differences mainly in the nasal cavity, but nevertheless about 35 kcal of heat are lost each day [8] – air is expired at a temperature of about 32°C.

There are no exact data about the conditioning capacity of the upper airways during mouth breathing – a situation that is almost always occurring in patients with severe dyspnea. The mucosa of the oral cavity and the pharynx has some warming and humidification capacity, but clearly less than the nose, mainly because of the much smaller surface area. The air entering the conducting lower airways is warmed to body temperature and fully saturated by tracheal and bronchial mucosa, so nevertheless the gas-exchanging parts of the lung should not be compromised.

### 1.3.2 Humidification of Inspired Air

One of the main tasks of the conducting upper and lower airways is to fully saturate the inspired air to 100% body humidity. If this physiological mechanism fails, negative consequences for mucociliary clearance may result: damage of ciliated epithelium, inspissation of secretions in the lower airways and, as a life-threatening complication, occlusion of an endotracheal tube or tracheal cannula while being dependent on mechanical ventilation.

The main location of humidification is the upper airways, especially the nose and nasopharynx.



**Fig. 1.1** Conditioning of inspired air while breathing at rest through the nose. *Numbers* mean content of water of in- and expired air while breathing ambient air (temperature 22°C, absolute humidity 10 mgH<sub>2</sub>O/L). Isothermic boundary shortly behind the main bifurcation. Colors are equal to temperature (With permission of: [10])

Humidity means the amount of water vapor in a specific gas, for example, inspired air. The content of water vapor depends on temperature, with higher absolute values at higher temperatures. Absolute humidity means a relative humidity of 100%, is expressed as mgH<sub>2</sub>O suspended in a liter of gas and equals a water content of nearly 44 mgH<sub>2</sub>O/L air at a body temperature of 37°C [9]. The moisture originates from fluid loss of the mucosa of the nasal cavity and pharynx/trachea, creating a water content of about 42 mgH<sub>2</sub>O/L air at the main bifurcation of the trachea, and increases up to 44 mgH<sub>2</sub>O/L air at the level of the alveoli (see Fig. 1.1). The so-called isothermic boundary is normally located 5 cm below the main bifurcation [11] and indicates the location where the body temperature of 37°C is achieved in combination with a relative humidity of 100%, which equals an absolute humidity of 44 mgH<sub>2</sub>O/L air. The position may vary because of changes in the heat and moisture content of the gas and the tidal volume [12]. Moisture is conserved from expiratory air (content of water about 34 mgH<sub>2</sub>O/L in air expired), but 250 mL of water are lost per day as saturated vapor in the expiration gases [13].

Medical gases delivered by a ventilator are normally totally dry, with a relative humidity of nearly 0%, and reach the patient via a noninvasive interface (mask ventilation) or an invasive interface (endotracheal tube or tracheal cannula). Especially invasive ventilation causes depletion of the normal mucosal moisture content by bypassing the location of the physiological humidification and heating of the air (upper airways), and may harm the lower airways by increased mucus viscosity and functional loss of the cilia. The consequences and measures to prevent such damage are discussed in the following chapters.

## 1.4 Work of Breathing

A decrease in negative intrathoracic pressure (values lowering from  $-5$  cm  $H_2O$  at end-expiration to  $-8$  cm  $H_2O$  at end-inspiration) is necessary during inspiration while breathing spontaneously to create a pressure difference from the mouth to the alveoli that allows air flow to and from the alveoli, thereby promoting oxygen uptake and carbon dioxide elimination.

The work of breathing necessary to overcome the resistive and elastic properties of the airways, lung and thoracic cage is provided by the respiratory muscles, with the diaphragm being the main inspiratory muscle. Expiration during rest occurs passively by return of the stretched lung and thoracic cage to the volume at the start of inspiration (functional residual capacity).

The elastic properties of the lungs are determined by compliance ( $C$ ) and tidal volume ( $V_T$ ), according to the following equation [14]:

$$P_{el} = V_T / C,$$

whereby  $P_{el}$  is the pressure necessary to overcome the elastic properties during spontaneous breathing.

The resistive properties of the lung ( $P_{res}$ ) are determined by flow ( $V'$ ) and airways resistance ( $R$ ), described by the following equation [14]:

$$P_{res} = V' * R$$

The pressure that must be built up by the muscles to create a pressure difference between the mouth and alveoli can be described by the following equation:

$$P_{mus} = V_T / C + V' * R$$

Work of breathing must be carried out for spontaneous breathing, and also for some modes of mechanical ventilation. Triggering the ventilator during assisted/controlled or pressure support ventilation demands muscle activity of the patient, thereby creating a drop in flow or pressure in the circuit of the ventilator. This signal is sensed by the ventilator and releases an increase in pressure to deliver a preset volume or pressure to the patient. The work of breathing of the patient depends on the sensitivity of the inspiratory trigger and the settings of the ventilator, e.g., ramp of increase of pressure. Contrarily, during controlled ventilation a mandatory breath is initiated, limited and cycled exclusively by the ventilator, and all work of breathing is done by the ventilator.

The complete measurement of work of breathing under mechanical ventilation is complex, for both inspiration and expiration, because not only the properties of the respiratory system itself, but also properties of the circuit and added devices have to be considered. The best method is using an esophageal catheter to measure simultaneously pressures above (esophageal pressure that equals pleural pressure) and below (intra-gastric pressure that equals intra-abdominal pressure) the diaphragm and so

calculating the pressure time product (PTP) of the diaphragm. The exact value per breath must finally be corrected for the volume inspired. For a more detailed discussion, see the ATS/ERS Statement on Respiratory Muscle Testing, published in 2002 [14].

Humidification and warming of inspiratory air during invasive and also noninvasive ventilation require the addition of either a heated humidifier (HH) – active conditioning of inspiratory air – or a heat and moisture exchanger (HME) – passive conditioning of inspiratory air. The mechanical properties of both devices and efficiency regarding conditioning are discussed in the following chapters. Both devices exhibit resistive properties, thereby possibly increasing the resistive load of the inspiratory limb of the circuit, which could influence triggering properties and the work of breathing of the patients during assisted ventilation. In case of HME also an increase in resistance caused by abundant secretions plugging the filter must be considered.

In some studies examining the influence of different devices for conditioning inspiratory air (heated humidifier versus HME), simpler methods have been implemented to calculate the work of breathing, e.g., noninvasively with the least square fitting method described by Iotti in 1995 [15] in intubated patients [16]. Work of breathing also has been measured during noninvasive ventilation by esophageal catheter by Lellouche and coworkers [17]. The reader should have in mind that the accuracy of the measurement of work of breathing is highest with invasive methods. The results of the studies will be discussed in the following chapters.

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# Airways: Humidification and Filtration Functions

# 2

Maire Shelly and Craig Spencer

The upper airway extends from the nose to the major bronchi. It fulfils two major functions; firstly it humidifies and heats inspired gas. Secondly it filters and expels particles via the muco-ciliary elevator. The upper airway provides the alveoli with relatively warm, moist, particle-free gas.

---

## 2.1 Humidification

During inspiration, water evaporates from the moist mucous epithelium of the nose, larynx, trachea and major bronchi, increasing the humidity of inspired gas. Heat energy is added by convection. The upper airway heats inspired gas to 37°C and 100% relative humidity/44 mg/l absolute humidity. During expiration, cooling occurs by convection, transferring energy to the relatively cool nasal mucosa. Expired gas loses the capacity to hold water, which condenses, returning a smaller amount of water and energy to the system. However, overall, this is an energy-requiring process – the greater part in providing the latent heat of vaporisation, with a lesser amount required to heat inspired gas by convection. This process results in a net loss of 250–300 mL of water and around 180 kcal/day in a normal adult [1].

The point at which gas is fully heated and saturated is usually just distal to the carina and is known as the Isothermal Saturation Boundary (ISB). Temperature and humidity are constant distal to the ISB. The location of this boundary will vary with the temperature, humidity and volume of inspired gas, and may move significantly distally if the upper airway is bypassed by an endo-tracheal tube. A degree of compensation is possible under extreme conditions such as upon inspiration of cool, dry medical gases or in a cold climate. Under such circumstances the gradients of the

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M. Shelly (✉) • C. Spencer  
Acute Intensive Care Unit,  
University Hospital of South Manchester Foundation Trust,  
Wythenshawe, Manchester, UK  
e-mail: m.shelly@nwpqmd.nhs.uk

counter-current exchanger increase, and the ISB is still achieved before gas reaches the respiratory bronchioles. In warm, dry environments, the upper airway will still require expending a significant amount of energy in humidifying air and so may act as an organ of thermoregulation and homeostasis. In warm, humid environments, this potential role is greatly reduced.

---

## 2.2 Filtration

Filtration, in this context, refers to the filtration of aerosolised particles from inspired gases. An aerosol is a suspension of solid or liquid particles in a gas. Solid aerosolised particles tend to have varying shape and size (described as polydisperse). Liquid particles are usually spherical due to surface tension and can potentially contain pathogens. It is clearly advantageous to the body to filter and expel both inert particles and pathogens.

Particles generally contact surfaces when they are unable to follow gas flow as it changes direction around obstructions. Aerosolised particles generally adhere to any surface they come into contact with, especially if that surface is coated in viscous respiratory mucus. Where airflow becomes turbulent, such as around the turbinates, the likelihood that the particle will contact the mucous membrane increases. There are five main mechanisms by which it contacts the surface [2]:

1. *Inertial impaction*. The particle cannot follow a change in gas direction because of its inertia. This is an important mechanism of deposition of large particles in the upper airways.
2. *Interception*. The particle has low inertia but makes partial contact with a surface because of the particle's large diameter.
3. *Brownian motion*. Small particles move in a widespread, apparently random pattern under the influence of surrounding gas molecules. Due to this phenomenon, they appear to occupy a much larger diameter. This is an important mechanism of deposition of small particles throughout the airways.
4. *Gravitational settling*. Large particles deviate from a gas stream under the influence of gravity.
5. *Electrostatic deposition*. Particles deviate from the gas stream because of electrostatic attraction.

Once particles become trapped in respiratory mucus, they begin to be transported cranially in the muco-ciliary elevator.

---

## 2.3 Muco-Ciliary Elevator

The ciliated pseudostratified columnar (respiratory) epithelium of the nose, sinuses, trachea and bronchi contains many goblet cells. These secrete droplets of respiratory mucus formed of proteoglycans, glycoproteins and lipids onto their epithelial surface. This is further hydrated by secretions from serous cells, moisture in the airway and transudation of water. The mucous layer is around 10  $\mu\text{m}$  deep and consists of

two layers. The deep (sol) layer is watery and contains many antibacterial substances such as lactoferrin and lysosyme. The superficial (gel) layer is more viscous and capable of trapping inhaled particles.

Embedded in this mucous layer are finger-like projections – cilia. They are 5–6- $\mu\text{m}$ -long projections consisting of a microtubular ultrastructure. Dynein (ATPase) cross-links between adjacent microtubules allow them to bend. Cilia bear a number of short claw-like projections near their tips that allow them to ‘grip’ the viscous superficial (gel) mucous layer. Each columnar ciliated epithelial cell has around 200 cilia; each cilia has a basal foot, which is aligned with the others originating in that cell, allowing the unidirectional coordinated beating of cilia. During each beat cycle the cilia tip grips the viscous layer, propelling it forward. It then undergoes a recovery stroke, bending sharply at the base, moving through the deep watery layer. By beating around 1,000 times per minute, in a coordinated fashion, this ‘Mexican wave’ transports respiratory mucous cranially at around 12–15 mm/min [3].

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## 2.4 Coughing

Particulate matter in respiratory mucous in the trachea can be cleared by coughing. The afferent impulse is mainly transmitted by unmyelinated C fibres in the vagus nerve to the brainstem. Rapid inspiration to a high lung volume is followed by closure of the glottis and the compressive phase. Active expiration and elastic recoil cause a rapid increase in intra-thoracic pressure that drives gas flow upon glottic opening and compresses airways, increasing velocity. Rapid expulsion of gas at up to 12 l/s causes sheering and expectoration of secretions.

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## 2.5 Altered Muco-Ciliary Function

Altered function may result from abnormal mucous consistency or volume, or from a reduction in ciliary numbers or function. It may be congenital such as in primary ciliary dyskinesia or as in cystic fibrosis where respiratory mucous is viscous, promoting bacterial colonisation. This is due to a failure to secrete chloride and water due to a defective trans-membrane chloride channel. Altered function may be acquired as in inflammatory lung disease (e.g. chronic bronchitis, asthma), which is characterised by mucous gland hypertrophy, mucous accumulation, and a reduced watery peri-ciliary layer with reduced efficacy of the ciliary stroke. Smokers have reduced ciliary beat frequency and efficacy. Ciliary loss occurs in ventilated critically ill patients. Pathogens such as *Pseudomonas aeruginosa* may reduce ciliary beat frequency too.

Mucus flow is significantly reduced below a relative humidity of 50% (22 mg/l) at 37°C such as occurs with prolonged use of dry medical gases. Mucosal inflammation, loss of cilia, epithelial ulceration and necrosis may occur. Hyper-viscous secretion may obstruct bronchi or endo-tracheal tubes. Encrustation may occur, causing sputum

retention, infection, atelectasis, reduced functional capacity, ventilation/perfusion mismatch and reduced compliance. Over-humidification is harmful too. It removes a potential source of heat loss and homeostasis. Condensation of water may occur in the airway, leading to reduced mucosal viscosity, inefficient transport, increased resistance, risk of pulmonary infection, surfactant dilution, atelectasis and ventilation/perfusion mismatch. Inhalation of hot, humid gases may cause direct thermal injury to the epithelium, resulting in tracheitis.

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## 2.6 Major Key Points

1. The upper airway acts as a counter-current heat and moisture exchanger, with transfer of heat and moisture by evaporation and convection.
2. The point at which inspired gas reaches 37.0°C and 100% relative humidity is called the Isothermic Saturation Boundary (ISB). It usually lies in the major bronchi, but moves distally with cold, dry gas and/or an endotracheal tube.
3. Inhaled particles are filtered when they contact and adhere to respiratory mucous when they cannot follow gas flow.
4. Respiratory mucous is formed of a thick superficial layer and a deep watery layer. This allows the tips of the cilia to 'grip' mucous and propel it cranially on a forward stroke, yet pass back through it on the recovery stroke. This is the basic unit of the muco-ciliary elevator.
5. The function of the muco-ciliary elevator may be impaired in congenital or acquired conditions. These are due to altered mucous volume or consistency, or reduced ciliary efficacy or numbers.

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## Section II

# Humidification and Devices

Varun Gupta and Surendra K. Sharma

## Abbreviations

ARDS	Acute respiratory distress syndrome
HH	Heated humidifier
HME	Heat and moisture exchanger
ICU	Intensive care unit
ISB	Isothermic saturation boundary
ISO	International Organization for Standardization
NIV	Noninvasive ventilation
VAP	Ventilator-associated pneumonia

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## 3.1 Introduction

The inspired air is warmed and humidified by evaporation of water from the surfaces of the mucous membranes during nasal respiration. The air in the pulmonary periphery thus gets saturated with water vapor. The point at which gases reach 37°C and 100% relative humidity (corresponding to an absolute humidity of 44 mg/l) is called the “isothermic saturation boundary” (ISB). The ISB is located well below the carina during quiet breathing. The evaporation leads to a loss of energy that results in cooling down of the mucous membranes. This fall in mucous membrane temperature allows the recovery of water and heat through condensation in the subsequent expiration. This occurs primarily in the nasopharynx. Delivery of cool and dry gases to the patient with a bypassed upper airway can lead to adverse consequences, including alterations in tracheobronchial structure and function. Common findings include

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V. Gupta • S.K. Sharma (✉)

Division of Pulmonary, Critical Care & Sleep Medicine, Department of Medicine,  
All India Institute of Medical Sciences,  
New Delhi, India

e-mail: sksharma@aiims.ac.in, surensk@gmail.com

inspissation of secretions, mucus plugging of airways, ciliary dyskinesia, epithelial desquamation and tracheal tube occlusion [1].

Humidification of respired gases during mechanical ventilation is a standard of care. It is always necessary when the ISB has been shifted towards the periphery of the lungs, i.e., when the upper airways are bypassed with a tracheal tube. The humidification of respiratory gases should be started as early as possible, and should not be dispensed with, even during short-term postoperative mechanical ventilation, patient transport or other emergency room situations. Two systems are commonly used to humidify and warm inspired gases: heated humidifiers (HHs) and heat and moisture exchangers (HMEs), also called “artificial noses.” This chapter will discuss HHs. Refer to Chap. 4 for details on HMEs.

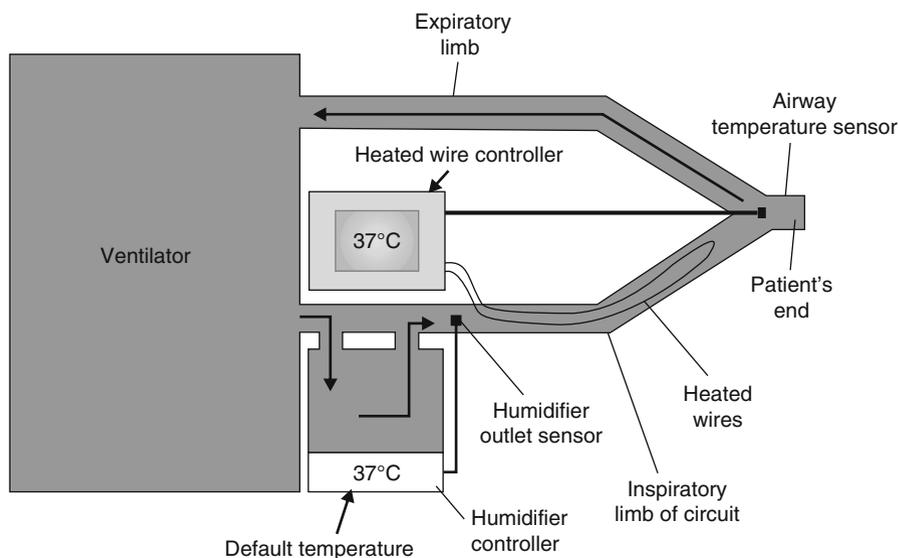
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## 3.2 Device Description

The HH is an active humidifier that adds water vapor and heat to the inspiratory air from temperature-regulated water reservoirs independently of the patient. The humidifiers are usually connected to the inspiratory end of the breathing circuits. These are often microprocessor controlled, which monitors the readings from the various sensors and makes the necessary adjustments for maintaining a set humidity and temperature. If one or more parameters are out of range, the microprocessor sends a signal to activate the audible or visual alarms. The humidifier can also be used in conjunction with a servo controller and a heated breathing circuit for reducing the humidified air condensation in the breathing circuit. The respiratory gas is warmed inside the humidification chamber to a set target temperature. This must be achieved by an additional heating device. The warmed gas is then humidified by addition of water vapor from the heated water reservoir. The larger the area of contact between water and gas, the more opportunity there is for evaporation to occur. Inspiratory circuit tubing containing a heated wire is then used to maintain or slightly raise the gas temperature before it reaches the patient. This helps to prevent water rainout in the circuit and the consequent fall in gas temperature. An HH system is depicted in Fig. 3.1. Different methods can be used to evaporate water in HHs. These will be discussed subsequently.

### 3.2.1 Cascade Humidifiers

The flow is passed beneath the surface of the water in a heated reservoir. It is, in principle, a bubble-through humidifier (see Fig. 3.2) that utilizes the bubble-diffusion technique. In this, a stream of gas is directed underwater, where it is broken up into small bubbles. As the gas bubbles rise to the surface, evaporation increases the water vapor content within the bubble. The smaller the bubble is, the greater the water/air surface-area ratio. A sintered filter can be used to reduce the bubble size and increase the surface area for evaporation (see Fig. 3.2). Spraying water particles into the gas is an alternative to dispersing gas bubbles in water. This is accomplished



**Fig. 3.1** Heated humidifier system. The default temperature setting of 37°C is shown here. The temperature is kept constant throughout the inspiratory limb of circuit by the dual sensor system. The heating unit should shut off automatically at temperatures above 41°C (Adapted from Fink [5])

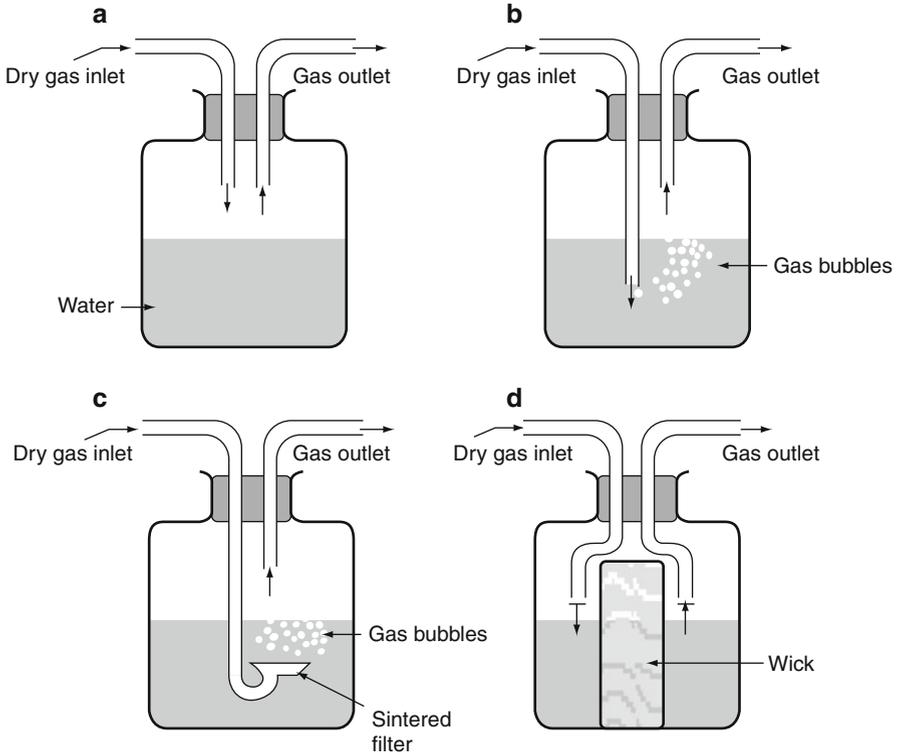
by generating an aerosol in the gas stream. The water content of the inspired air can be adjusted by varying the temperature of the water in the reservoir. Assuming that water vapor saturation is achieved, estimation of the humidity can be done merely by measuring the temperature of the gas at the tracheal tube. The cascade humidifier exhibits the highest measured inspiratory flow resistance. Therefore, it cannot be recommended for use in intubated and spontaneously breathing patients.

### 3.2.2 Passover Humidifiers

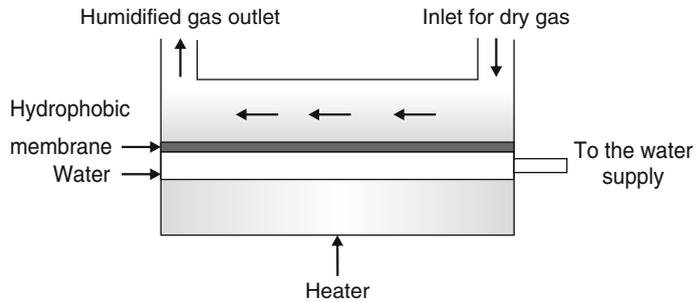
The airflow is directed over a water surface. These humidifiers offer several advantages compared to bubble humidifiers. First, the inspiratory air does not need to be passed beneath the water surface of the reservoir. Thus, airway resistance is reduced compared with cascade humidifiers. Second, unlike bubble devices, they can maintain saturation also at high flow rates. Third, they do not generate any aerosols and thus pose a minimal risk of spreading infection. There are three common types of passover humidifier:

The simple reservoir type directs gas over the surface of a volume of heated water. The surface for gas-fluid interface is limited.

In wick humidifiers (see Fig. 3.2), the accessible surface area is increased by means of a wick made of water-absorbent blotting paper. The wick is placed upright with the gravity-dependent end in a water reservoir and surrounded by a heating element. The water is continually drawn up from the reservoir by means of capillary action and



**Fig. 3.2** Schematics of various humidifiers. (a) Simple bottle humidifier, (b) bubble-through humidifier, (c) bubble-through humidifier with sintered filter, (d) wick humidifier (Adapted from Ward [6])



**Fig. 3.3** Membrane-type heated humidifier (Adapted from Fink [5])

keeps the wick saturated. The dry gas entering the chamber flows around the wick, picks up heat and humidity, and leaves the chamber fully saturated with water vapor.

The third is a membrane-type humidifier (see Fig. 3.3). It separates the water from the gas stream by means of a hydrophobic membrane. Water vapors can pass easily through this membrane, but liquid water and hence the pathogens cannot.

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### 3.3 Requirements for a Humidification Device

#### 3.3.1 Operating Range

The device must ensure physiological conditions in the respiratory tract and avoid pulmonary water losses of greater than 7 mg/L due to ventilation with dry gases. According to the International Organization for Standardization (ISO) 8185:1997, the moisture output of an HH should be at least 33 mg/L (= 75% of the saturation humidity of 44 mgH<sub>2</sub>O/L at a body temperature of 37°C). Most humidifiers have humidity settings from 0 to 100%. The humidifier's heating unit should shut off automatically at temperatures above 41°C to avoid heat damage to the trachea. Ventilation with oversaturated gases should also be avoided. One should also remember that these devices influence the inspiratory and expiratory resistance as well as the functional dead space in different ways. This is especially important in spontaneously breathing patients to avoid additional work of breathing and hypercapnia. Resistance values for defined flows can be obtained by referring to ISO 8185:1997 for HHs. The inspiratory flow resistances of most HHs range between 0.5 hPa/L/s and 1.5 hPa/L/s [2].

#### 3.3.2 Safety Features

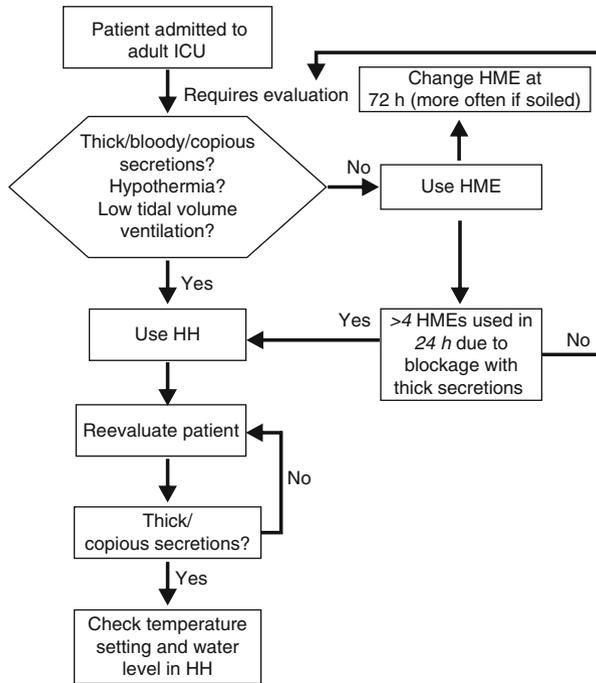
The device should have means to prevent any possible adverse effects (see Sect. 3.6) to the patient and the operator. For example, the humidifiers should have a high and low temperature alarm and an alarm for faulty sensor connection, etc. These devices should also have automatic shut down mechanisms that can cut off the device or parts of the device to ensure patient safety. For example, the power to the heating filament should be cut off if the safety temperature is exceeded. The device should also have a fuse or a circuit breaker for protection against power surges. Proper grounding of the device must also be ensured.

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### 3.4 Common Concerns with the Use of HHs

Most users do not know the function of the humidity correction control knob on some devices. This leads to a high risk for an incorrect setting, which, in turn, can result in insufficient humidification. There is insufficient knowledge among critical care physicians with regard to the optimal inspiratory gas temperature. A permanent default temperature setting of 37°C can simplify this and simultaneously increase patient safety. In any case, there is no clinical necessity for the reduction or elevation of temperature to a level higher than body temperature. Faulty operation is another area of concern. For example, in some devices no alarm is given in case of initiating the operation without or with too little water.

**Fig. 3.4** Algorithm for selection of humidification devices in an adult ICU. Thick secretions refer to secretions that remain stuck to the walls of suction catheter after it is rinsed with saline during two consecutive suctioning procedures. Bloody secretions refer to hemoptysis that is more than small streaking. Copious secretions, as seen in those with pulmonary edema or pneumonia, may occlude the media. Low tidal volume ventilation refers to ventilation with a tidal volume  $\leq 6$  mL/kg predicted body weight. *HH* heated humidifier, *HME* heat and moisture exchanger (Adapted from Branson [1])



### 3.5 Clinical Decision Making for the Use of Humidification Under Specific Conditions

The selection of the device to be used on a given patient should be based on the patient's underlying lung disease, ventilator settings, intended duration of use, the presence of leaks, body temperature, etc. [1]. An algorithm for the selection of humidification devices for an adult intensive care unit (ICU) is provided in Fig. 3.4.

#### 3.5.1 Acute Respiratory Distress Syndrome (ARDS)

A significant improvement in  $\text{PaCO}_2$  is associated with the switch to an HH from an HME in patients who have ARDS [3]. Compensation for HME dead space is possible by increasing the set tidal volume. This compensation, however, increases peak airway pressure and mean airway pressure, which may not be acceptable in ARDS patients [1]. Therefore, if low-tidal-volume ventilation is used, such as in the case of ARDS and hypercapnia, an HH is the humidification system of choice.

#### 3.5.2 Weaning from Mechanical Ventilation

During spontaneous-breathing trials, the use of an HME (with a dead space of 100 mL) results in an increased ventilator requirement and an increase in the work

of breathing compared with HH. The use of an HME results in higher PaCO<sub>2</sub> despite attempts by patients to compensate by increasing their minute ventilation [4]. Thus, for weaning that includes spontaneous-breathing trials, an HH should be used.

### 3.5.3 Humidification During Noninvasive Ventilation (NIV)

The high flows delivered during NIV quickly result in oral and nasal dryness, which can proceed over time to mucosal cracking, bleeding and pain. The addition of humidity seems to reduce symptoms of airway dryness. The use of an HME during NIV is not advisable for two reasons. Firstly, the leaks around the mask and built-in leaks for CO<sub>2</sub> clearance prevent the movement of expired gas through the HME and thereby cause ineffective function of the HME. Secondly, the HME adds to dead space and can reduce the efficacy of NIV [1]. Therefore, humidification during NIV should be accomplished with an HH.

### 3.5.4 Hypothermia

Patients who have hypothermia are often treated using superheated inspiratory gases. This practice has no scientific basis. Although heating gases to 44°C seems to have few acute adverse effects, it seems to be of little use in humans [1]. Attempts at whole-body rewarming through the respiratory tract are not supported by the literature.

### 3.5.5 Very Low Birth Weight Infants

The safety and efficacy of HME for very low birth weight infants have not been established conclusively. Thus, an HH should be used in this group.

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## 3.6 Potential Complications with the Use of an HH [7]

### 3.6.1 Electrical Shock

There is a risk of electrical shock to both the patient and the operator if the device is not properly grounded.

### 3.6.2 Burning of the Patient's Airway

There is also a risk of burning of the patient's airway with the use of an HH if *excessive* heat is introduced to the patient; however, low humidity and high flow of air can also contribute to this situation.

### **3.6.3 Water Entering the Breathing Circuit**

Some humidifiers have an elevated water supply source. In these humidifiers, water flows down from the water supply to the heating chamber to be evaporated. If the amount of water supplied is more than the evaporation rate, sufficient water can enter the breathing circuit and limit the air passage.

### **3.6.4 Bacterial Colonization of Respiratory Tubing and Ventilator-Associated Pneumonia (VAP)**

Although HHs do not influence occurrence of VAP, they are associated with rapid bacterial colonization of respiratory tubing. This contamination bears the potential for cross-contamination.

### **3.6.5 Burns to Care Providers**

The potential for burns to care providers from the hot metal of HH exists.

### **3.6.6 Hypothermia**

Hypothermia can occur in patients undergoing mechanical ventilation with dry gases.

### **3.6.7 Under-Humidification and Impaction of Mucus**

There is a risk of mucus plugging of airways due to under-humidification of inspired air. This can lead to increased resistive work of breathing, hypoventilation and/or alveolar gas trapping.

### **3.6.8 Pooled Condensate in the Patient Circuit**

Pooling of condensate in the patient circuit can take place. This can lead to inadvertent tracheal lavage, elevated airway pressures, patient-ventilator dyssynchrony and improper ventilator performance.

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## **3.7 Contraindications [1, 7]**

*There are no contraindications to the use of an HH.*

**Table 3.1** Precautions and warnings pertaining to a heated humidifier

Precautions	Warnings
1. When mounting a humidifier, always ensure that it is <i>positioned lower</i> than the patient	1. <i>Do not</i> fill the chamber above the maximum level as liquid could enter the breathing circuit if the chamber is overfilled
2. The water traps should be arranged at the lowest point of the circuit so that the condensate drains away from the patient	2. <i>Never</i> drain the condensate back into the humidifier reservoir as it is considered infectious waste
3. Inspection of the device should be done with every ventilator system check and condensate removed from the circuit	3. Never use a device for patient care that fails to perform according to the manufacturer's specifications

### 3.8 Precautions and Warnings

The critical care team should be aware of the warnings and precautions pertaining to the use of an HH. These are summarized in Table 3.1.

### 3.9 Active HMEs

“Active” HMEs combine an HME with an integrated HH. However, their use can cause problems because of their complexity. One of the indications for use is in cases of large tidal volume (>1 L) ventilation as well as in patients with a lung fistula where parts of the exhaled gas are lost.

### 3.10 Conclusion

The heated humidifier is an active humidifier that adds water vapor and heat to the inspiratory air independently of the patient. Passover humidifiers offer several advantages compared to bubble humidifiers. An HH is preferred over an HME in patients with ARDS, during NIV, during weaning from mechanical ventilation, in very low birth weight infants and in those with contraindications for HMEs. Common problems with HHs include condensation, cross-contamination, burning of the patient's airway and ensuring proper conditioning of the inspired gas. A temperature alarm, automatic shut down mechanisms and sometimes a permanent default temperature setting of 37°C can also help increase patient safety.

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Jean-Damien Ricard, Alexandre Boyer,  
and Didier Dreyfuss

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## 4.1 Heat and Moisture Exchangers

HMEs were first described in the mid 1950s and the early 1960s, and have undergone considerable development since the beginning of the 1970s [1]. The basic principle of all HMEs lies in their capacity to retain heat and moisture during expiration, and deliver these to the incoming dry medical gas during the subsequent inspiration. This passive function can be achieved by different mechanisms.

The first HMEs were simple condensers, made with metal elements with a large surface area such as rolled wire gauze or stainless steel tubes. Because of the high density and thermal conductivity of metal, no effective temperature gradient was achieved across the device. Metal elements of the condenser were then replaced by disposable foam, plastic or paper. Increased moisture output was further achieved by coating the condenser element with a hygroscopic chemical (calcium or lithium chloride), which chemically adsorbs expired water vapor that is then returned to the inspired gas. These HMEs were called hygroscopic condensers. Deriving from the field of filtration, hydrophobic HMEs were also used to heat and humidify inspired gas. The very large surface area of pleated, water-repellent ceramic of the first hydrophobic HMEs along with its low thermal conductivity enabled an important temperature gradient to develop within the HME that favored heat and moisture

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J.-D. Ricard (✉) • D. Dreyfuss  
INSERM U722, UFR de Médecine,  
Université Paris Diderot, Paris 7,  
Paris, France

Assistance Publique - Hôpitaux de Paris, Hôpital Louis Mourier,  
Service de Réanimation Médico-chirurgicale,  
178, rue des Renouillers, F-92700 Colombes, France  
e-mail: jean-damien.ricard@lmr.aphp.fr

A. Boyer  
Service de Réanimation Médicale, CHU Bordeaux,  
3 place Amélie Raba Léon, 33076 Bordeaux cedex, France

retention. Finally, hygroscopic and hydrophobic elements were used in a single HME to create a “combined” HME. Hygrometric performance of these various HMEs differs considerably, with hydrophobic HMEs exhibiting the poorest humidity outputs (risk of endotracheal tube occlusion) and combined HMEs the highest, although recent measurements indicate that some purely hygroscopic HMEs provide comparable values of absolute humidity to that of combined HMEs [2, 3].

### 4.1.1 Active Heat and Moisture Exchangers

New devices have been designed to boost humidifying performances of HMEs [4]. Briefly, these devices, which are added to the circuit between the HME and the endotracheal tube, consist of a ceramic heating element fed by an electrical energy source that vaporizes water (fed into the system by a side port) into the airway. They enable a 3–4 mgH<sub>2</sub>O/l increase in absolute humidity delivered by the HME [4], although the actual clinical benefit of this increase has, to date, not been demonstrated.

### 4.1.2 Clinical Use

Apart from certain specific situations, HMEs or heated humidifiers can equally be used to heat and humidify inspired gases [1]. Despite this, practices differ considerably among countries [5, 6]. A survey found that HMEs were used for all patients in 63% of French ICUs, whereas this was the case in only 13% of Canadian ICUs [6]. Conversely, heated humidifiers were primarily used in 60% of Canadian ICUs and in only 20% of French ICUs. These results may account for some of the difference in cost of mechanical ventilation between the two countries [5]. Rationalizing the choice of a given humidifying device should help decrease costs in mechanical ventilation without impeding quality of care.

### 4.1.3 Efficacy

Several important aspects must be taken into account when analyzing the effectiveness and outcome of inspired gas conditioning. These include:

- The avoidance of endotracheal tube occlusion (which is the worst and most feared complication of inadequate gas conditioning), and this aspect is directly linked to the performance of the humidifying device in terms of heat and humidity delivery.
- The avoidance of spreading microorganisms (and in particular multidrug-resistant organisms), and this is directly linked to the humidifying device’s capacity to prevent respiratory tubing contamination.
- The addition of minimal resistance and dead space.
- The practicability of using the device.

- The minimal maintenance necessary to ensure optimal use of the device.
- The minimal cost associated with the purchase and the long-term use of the device.

According to this list, the ideal humidifier can be defined as a device providing adequate levels of humidification whatever the ventilator and patient conditions, in an automatic manner, that is safe (i.e., electric-shock free, with no or limited connections that could be faulty), protects the environment from the patient's pathogens, is easy to use, maintenance free and inexpensive.

#### 4.1.4 Ensuring Adequate Humidification

The adequate level of humidification can be defined as a level where there is no excessive heat or water loss by the respiratory tract. The difficulty arises when one tries to set the minimum value of absolute humidity a device should deliver. This may be useful when selecting and comparing different devices. Although ranges as wide as 25–35 mgH<sub>2</sub>O have been suggested in the past, the figure of 30 mgH<sub>2</sub>O/l is recommended [7]. That is, a clinician wishing to select an appropriate humidifying device should make sure that this device delivers at least 30 mgH<sub>2</sub>O/l absolute humidity. Another definition of adequate humidification includes avoiding endotracheal tube occlusion. Some may argue that restricting adequate humidification to the risk of endotracheal occlusion is overly simplistic. One must bear in mind, however, that it is the worst and most feared side effect of insufficient humidity, and can be sometimes fatal [8].

There is no doubt that 20 years ago, HMEs and heated humidifiers were not equivalent in terms of humidity output. In 1988, Cohen et al. alerted clinicians of the risk of endotracheal tube occlusions associated with the use of HME [9]. Two years later, Martin et al. reported a fatal case of endotracheal tube occlusion with an HME [8]. Several other publications confirmed the increase in endotracheal tube occlusion risk with HMEs in comparison with heated humidifiers. These studies, however, all used purely hydrophobic HMEs whose performances, when measured, display low values for absolute humidity [2, 10].

It has been shown that endotracheal tube occlusion occurs after a gradual reduction in the tube's inner diameter by clots of secretions along the inner surface of the tube [11]. This reduction was found to be significantly greater with a purely hydrophobic HME than with a heated humidifier or a combined (hydrophobic and hygroscopic) HME [11]. Although hygrometric measurements were not performed simultaneously in this study [11], it seems evident that inner diameter reduction (and thus ultimately endotracheal tube occlusion) is dependent on the amount of humidity delivered by the humidifying device. Indeed, humidity measurements of the devices used by Villafane et al. [11] have been made by others, and the results are consistent with their findings (i.e., the hydrophobic HMEs that suffered the greater inner diameter reduction displayed the poorest humidity output [10]). This leads to the question of hygrometric and clinical performance.

**Table 4.1** Endotracheal tube occlusion rates in studies comparing heated humidifiers and heat and moisture exchangers

First author, year	No. of patients	No. of ETT obstructions	
		HH	HME
Branson, 1993	120	0	0
Dreyfuss, 1995	131	0	1
Branson, 1996	200	0	0
Villafane, 1996	23	1	0
Boots, 1997	116	0	0
Hurni, 1997	115	1	0
Kollef, 1998	310	0	0
Thomachot, 1998	29	0	0
Kirton, 1998	280	1	0
Lacherade, 2002	370	5	1
Jaber, 2004	60	2	1

HH heated humidifier, HME heat and moisture exchanger

Although heated humidifiers undisputedly deliver greater values for absolute humidity than HMEs [10], there is to date no evidence for any benefit of these greater values in terms of clinical outcome, including endotracheal tube occlusion. Table 4.1 displays the incidence of endotracheal tube occlusion reported in recently published studies. It is important to note that: (1) endotracheal tube occlusion rates have drastically dropped in comparison with earlier studies [9, 12, 13], (2) endotracheal tube occlusion is also reported with the use of heated humidifiers, and (3) the incidence of endotracheal tube occlusion no longer appears to be greater with HMEs than with heated humidifiers. In one study, the incidence was greater with heated humidifiers than with HMEs [14].

To conclude, HMEs have considerably evolved since their first appearance on the market. They are no longer associated with more frequent endotracheal tube occlusion than heated humidifiers, and ensure safe and efficient inspired gas conditioning [15]. Their practicability and cost-effectiveness are by far superior to heated humidifiers, explaining why they should be used in first intention in most patients requiring mechanical ventilation.

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# Heat and Moisture Exchangers and the Booster® System: Technology and Clinical Implications

# 5

Fabrice Michel, Marc Leone, and Claude Martin

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## 5.1 Introduction

The importance of delivering warm, humidified gas to patients ventilated through an endotracheal or tracheostomy tube is widely accepted [1–7]. Mechanical ventilation with endotracheal intubation or tracheostomy bypasses the upper airway and the normal heat and moisture exchanging process of inspired gases (Fig. 5.1). A continuous loss of moisture and heat occurs and predisposes patients to serious airway damage [1–7]. In addition, medical gases are dried to avoid condensation damage to valves and regulators in the distribution network. Complications after ventilation with dry and cold gases can be prevented by the addition of exogenous heat and humidity by the use of heated hot water systems, i.e., vaporizers or nebulizers. Heated humidifiers (HH) have some disadvantages, namely condensation of water that can be a source of infection, malfunctions, high maintenance costs, and increased workload for nursing staff [8]. The use of modern artificial noses or heat and moisture exchangers (HME) made of recently developed material could be a solution to both the problems of humidification and heat preservation [9–13]. The heat and moisture exchangers preserve the patients' heat and water levels; globally, they recover 70% of expired heat and humidity.

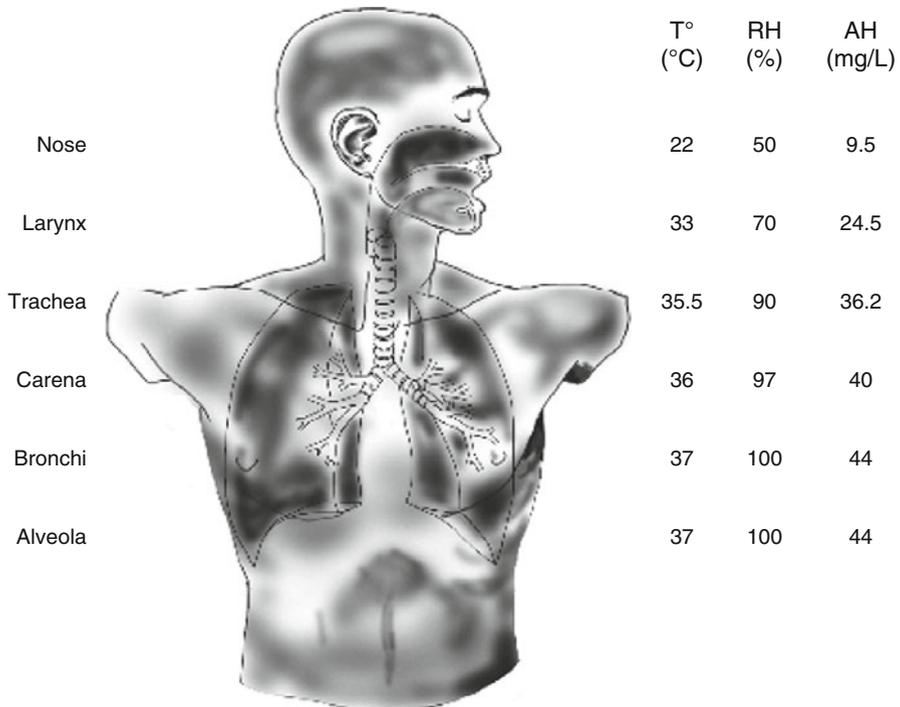
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## 5.2 Heat and Moisture Exchangers

HMEs are placed between the intubation tube and the Y piece (Fig. 5.2) or the facial mask. Advantages of HMEs over HHs are numerous (Table 5.1). Characteristics of an ideal HME are presented in Table 5.2.

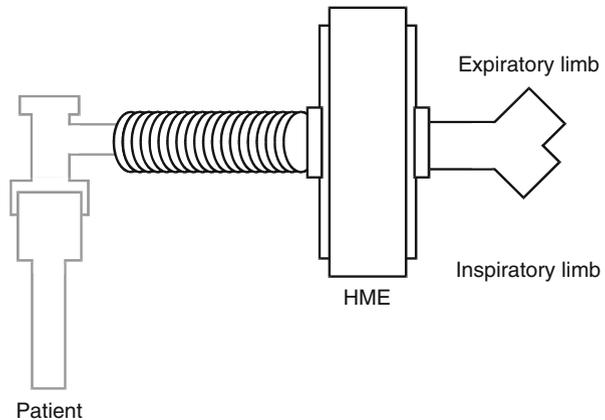
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F. Michel • M. Leone • C. Martin (✉)  
Service d'Anesthésie-Réanimation, Hôpital Nord,  
Bd Pierre Dramard, 13915 Marseille cedex 20, France  
e-mail: claud.martin@ap-hm.fr



**Fig. 5.1** Conditioning of inspiratory gas in upper and lower respiratory systems

**Fig. 5.2** HME in the ventilatory circuit



### 5.2.1 Hydrophobic HMEs

Hydrophobic HMEs are constituted of a porous membrane of approximately  $0.2 \mu\text{m}$ . Gas and vaporized water can go through porines, but not liquid water. Hydrophobic HMEs work as the human nose, capturing vaporized water and energy of expired gas, restituting them during the following inspiration. Air leaving the lungs has a temperature

**Table 5.1** Advantages and disadvantages of HME and HH

	Advantages	Disadvantages
HME	No electric hazard No over humidification Low cost No maintenance Easy to use	Increased resistance Increased dead-space Risk of under humidification
HH	Adequate humidification Good temperature control Easy to use  Possibility to treat hypothermia	Electric hazard Condensed water in limbs Temperature monitoring needed Bacterial contamination Over humidification Hyperthermia and risk of burned mucosa. Cost

**Table 5.2** Ideal HME*European requirements (ISO 9360/1992(E))*

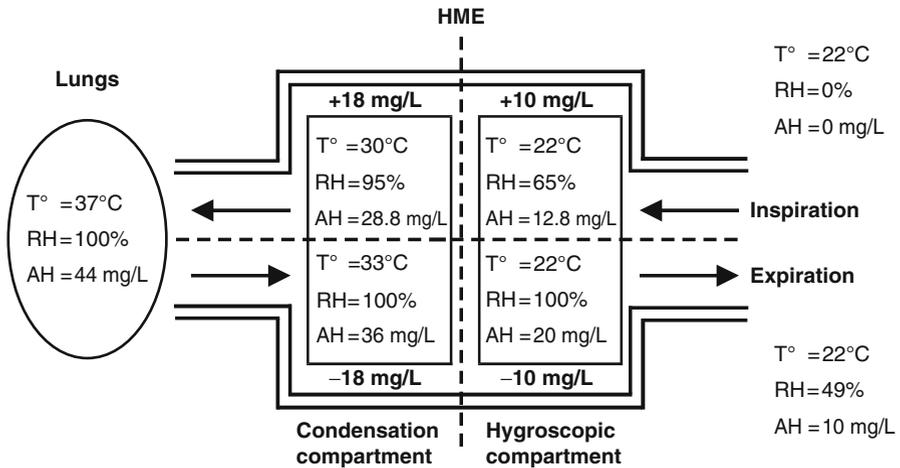
- Gas leak < 25ml/min at a pressure of 30 cmH<sub>2</sub>O
- Pressure drop < 5 cmH<sub>2</sub>O for a gas flow of  
60 l/min (adult)  
30 l/min (children)  
15 l/min (neonates)
- Single use
- Individual packaging

*Required characteristics*

- Dead space < 50 ml
- Conditioning of end-expiratory gases for a VT between 200 and 1000 ml:  
AH > 32 mgH<sub>2</sub>O/l  
Temperature > 32°C  
RH > 95%
- Weight < 40 g
- Bacterial filtration > 99.999%
- Connexion to capnometer

of 37°C and 100% relative humidity (RH) (Absolute humidity – AH – is 44 mgH<sub>2</sub>O/l). Expired air reaches the end of the intubation tube (or the mouth) at a temperature of 33°C. RH is still 100%, but AH is only 36 mg/l. Thus, 8 mgH<sub>2</sub>O/l was condensed on the way from the lungs to the mouth. When expired gas reaches the HME, water condenses on the surface of the condenser compartment (Fig. 5.3), which releases latent heat of vaporized water. This energy heats the HME. When the expired gas leaves the filter at around 20°C, AH of the gas is 18 mgH<sub>2</sub>O/l (Fig. 5.3). Thus, 18 mg of water per liter is left in the HME. The higher the difference in temperature between the patient side and the ventilator side of the HME, the more heat and humidity are preserved in the HME.

At the following inspiration, the HME transfers heat and humidity preserved during the expiration, 18 mgH<sub>2</sub>O/l. Upper and lower airways will transfer an additional



**Fig. 5.3** How does an HME work?

26 mgH<sub>2</sub>O/l to reach the physiological values of alveolar gas: 44 mgH<sub>2</sub>O/l and a temperature of 37°C.

## 5.2.2 Hygroscopic HMEs

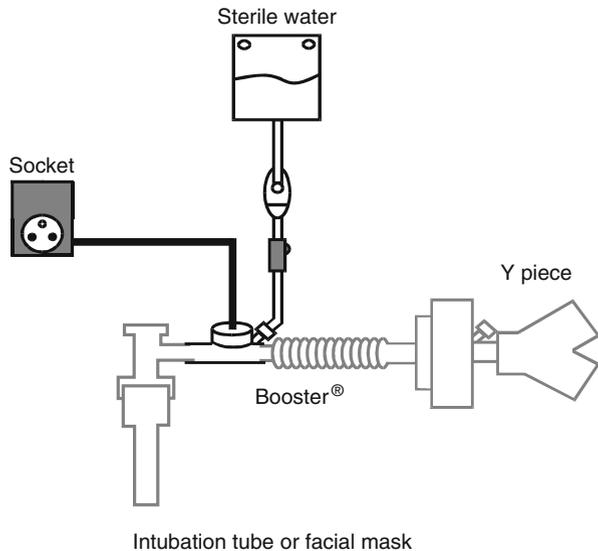
To the simple physical process of the hydrophobic HME is added a chemical trapping of water in the hygroscopic compartment (Fig. 5.3). The hygroscopic layer is made of wool or plastic foam impregnated with a hygroscopic substance as the active element: calcium or lithium. Hygroscopic HMEs preserve patients' heat and water better, and globally they recover 70% of expired heat and humidity (Fig. 5.3).

## 5.3 Booster® Technology (Fig. 5.4)

The Booster® brings active heating and humidification, in addition to those of HMEs. The device is placed between the HME and the intubation tube or the facial mask. The Booster® is mainly constituted of a ceramic electric heating element. Water is delivered to the system via a Gore Tex® membrane. The heating element vaporizes water on the membrane. Vaporized water goes through the membrane to the inspiratory limb of the ventilatory circuit where it is mixed with inspired gas, already conditioned by the HME. The Booster® device increases the temperature and humidity delivered by the HME.

## 5.4 Mechanical Effects of HME

Placement of an HME in the ventilatory circuit affects the ventilatory function. Expected modifications are the following [14].

**Fig. 5.4** Booster® System

- increased dead space
  - no change in inspiratory resistance
  - increase in expiratory resistance
  - decrease in compressible volume
- Potential consequences for ventilation are:
- increased minute ventilation
  - dynamic pulmonary inflation
  - intrinsic PEEP (iPEEP)
  - increased ventilatory workload

#### 5.4.1 Effects on Inspiratory Resistance

HMEs are devices with low resistance: 0.5 to less than 4 cmH<sub>2</sub>O/l/s for a ventilatory flow of 60 l/min. Resistive load can be evaluated by comparing peak pressure and plateau pressure with and without the HME. A minimal increase in respiratory workload can be expected.

#### 5.4.2 Expiratory Resistance and iPEEP

By increasing expiratory resistance, the HME will reduce the speed of the expiratory flow with a risk of dynamic pulmonary hyperinflation and increased iPEEP. A moderate increase in iPEEP has been shown in patients with no chronic obstructive pulmonary disease (COPD) [15, 16]. Contrarily, in patients with COPD, use of HMEs was not accompanied by an increase in iPEEP [17]. This phenomenon could be explained by the fact that the external resistance induced by the HME counteracts the bronchial collapse during expiration, the net result being no change in dynamic pulmonary inflation. Table 5.3 summarizes the mechanical effects of HMEs and HHs.

**Table 5.3** Mechanical effects of HH and HME

	HH	HME
Compressible volume	+++	+
Dead space	0	++
Inspiratory resistance	±	+
Expiratory resistance	0	++
Intrinsic PEEP	0	+
Ventilatory load	0	++

## 5.5 Changing HMEs: 24 h, 48 h or 7 Days?

Heat and moisture exchangers can be used safely for long-term mechanical ventilation and must be changed every 24 h, as recommended by the manufacturers' instructions [18, 19]. Several investigations found that the same HME could be employed for up to 48 h without increasing a patient's risk for VAP or other adverse outcomes [20, 21]. Another investigation reported that the technical performances of HMEs were not affected when used for 96 h [22], and Davis and colleagues showed that the same HME can be used for <120 h with no adverse effects [23]. In an open study, Ricard and coworkers [24] concluded that mechanical ventilation can be safely conducted using an HME changed only once a week. Kollef and colleagues [25] showed that the initial application of an extended use HME, up to the first 7 days of mechanical ventilation, was safe and cost effective. One limitation of this study was that HMEs could be used only for the first days of ventilation. After 7 days, patients were switched to heated water humidification.

A randomized study demonstrated that adequate airway humidification can be delivered with the same HME used up to 7 days, and this is in agreement with the conclusions of other reports. For Ricard and coworkers [24], tracheal tube occlusion never occurred during the 377 days of mechanical ventilation they studied. Davis and colleagues [23] also reported no cases of tube obstruction in the 120 patients ventilated with the same HME for a mean duration of 4 days. Similar observations were made by Kollef and coworkers [25] in their 163 patients ventilated with the same HME for their first 7 days in the ICU.

An important finding that can be drawn from these studies is that endotracheal tube occlusion is a very rare event when humidification is provided by extended (up to 7 days) use of HMEs. This observation is probably due to the strict protocols for the monitoring of patients followed by the different ICU teams. Several points should be emphasized for the patients' safety:

1. Patients with contraindications must be excluded (hypothermia, bronchopleural fistula);
2. Tube patency must be checked by repeated suctionings;
3. HMEs must be changed when they are visibly soiled;
4. HMEs should be placed vertically above the tracheal tube, and nurses and doctors should repeatedly check the position. Indeed, reducing costs by extending the duration of HME use should not be done at the expense of the patient's life.

Thus, the available literature demonstrates that an extended-use HME (up to 7 consecutive days) is a safe and more cost-effective alternative method of providing humidification compared to the standard 24 h change. This is obtained without an increased risk of pneumonia and with no deleterious effects on secondary outcome, such as duration of mechanical ventilation, ICU length of stay, or mortality.

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## 5.6 Conclusion

Delivery of warm, humidified gas to patients is of primary importance. Medical gases are dried to avoid condensation damages to valves and regulators in the distribution network. HMEs, preferably hygroscopic HMEs, are a simple solution to the problems of conditioning respiratory gases. Hygroscopic HMEs preserve patients' heat and water, and globally they recover 70% of expired heat and humidity.

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# Active Versus Passive Humidification: Efficiency Comparison Between the Methods

# 6

Jens Geiseler, Julia Fresenius, and Ortrud Karg

## Abbreviations

CPAP	Continuous positive airway pressure
HH	Heated humidifier
HME	Heat and moisture exchanger
HMEF	Heat and moisture exchanger and mechanical filter
IMV	Invasive mechanical ventilation
NIV	Noninvasive ventilation
p0.1	Mouth occlusion pressure 0.1 s after start of inspiration
pCO <sub>2</sub>	Partial pressure of carbon dioxide
VAP	Ventilator-associated pneumonia
WOB	Work of breathing

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## 6.1 Introduction

Physiological conditioning of ambient air occurs in the upper airways at a temperature of 37°C and a relative humidity of 100% (absolute humidity 44 mgH<sub>2</sub>O/l) in the alveoli. During invasive or noninvasive mechanical ventilation dry air is delivered by the ventilator to the patient with high flow and high pressure.

While there is a clear indication for humidification and heating during invasive mechanical ventilation as a consequence of bypassing the upper airways that normally humidify and warm inspiratory air, comparable recommendations for noninvasive mechanical ventilation are lacking. Maybe this is because the upper airways humidify

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J. Geiseler (✉) • J. Fresenius • O. Karg  
Department of Intensive Care Medicine and Long-Term Ventilation,  
Asklepios Fachkliniken München-Gauting,  
Robert-Koch-Allee 2, 82131 Gauting, Germany  
e-mail: j.geiseler@asklepios.com; j.fresenius@asklepios.com; o.karg@asklepios.com

the inspiratory air so problems with under-humidification exist only with high inspiratory flows.

In principle, there are two different methods of humidifying and heating inspiratory air, either by heated humidifier (HH), the so-called active method, or by heat and moisture exchanger (HME), the so-called passive method.

In this chapter the performance of the two principle methods of artificial humidification of inspiratory air during mechanical ventilation is discussed regarding the efficiency of humidification and differences in work of breathing (WOB) and carbon dioxide (CO<sub>2</sub>)-elimination, for invasive as well as noninvasive ventilation.

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## 6.2 Humidification During Invasive Mechanical Ventilation

The devices for invasive mechanical ventilation are either an endotracheal tube or a tracheal cannula. Both devices bypass the upper airways and allow direct access to the trachea. Therefore, dry inspiratory air may reach the lower airways, causing damage to the ciliated epithelium, higher non-physiological water loss from the lower airways, and inspissations of secretions or occlusion of the endotracheal tube. To prevent negative effects, external heating and humidifying of the inspiratory air are absolutely necessary. The conditioning of the airways should start immediately after the beginning of invasive mechanical ventilation.

Nowadays, HMEs are the most commonly used devices for humidification in intensive care medicine, at least in France [1]. The formerly constructed hydrophobic HMEs, e.g., the Pall BB2215 filter (Pall Biomedical; Saint-Germain-en-Laye, France), with insufficient humidification properties and a high risk of tube occlusion [2], have been replaced by modern hydrophobic and hygroscopic HMEs that often also have antibacterial filtering properties (heat and moisture exchanger and mechanical filter, HMEF). For HMEs the European Norm EN ISO 9360-2:2001 calls for a minimum humidity of 30 mH<sub>2</sub>O/l [3]. The efficiency of the HMEs decreases with increasing tidal volumes [4]. An actual study compared 48 different HMEs and HMEFs by a bench test apparatus that simulated real-life physiological ventilation conditions [5]. Only 37.5% of the tested devices performed well (>30 mgH<sub>2</sub>O/l, according to the ISO requirements), while 25% of the devices performed poorly (<25 mgH<sub>2</sub>O/l). There were also considerable differences between measurements and manufacturers' data, with a mean difference of 3.0 mgH<sub>2</sub>O/l, but in some cases up to 8.9 mgH<sub>2</sub>O/l. The authors concluded that not all so-called HMEs should be really used as HMEs. The performance of the HMEs and HMEFs needs to be assessed independently, and may in many cases be lower than in the manufacturer's data. Manufacturers recommend a change of HME every 24 h, but there are data that show a persistent efficacy of HMEs with regard to humidification for up to 7 days [6].

The alternative for conditioning inspiratory air is a heated humidifier. The minimal necessary humidity delivered by such devices in case of bypassing the upper airways is 33 mgH<sub>2</sub>O/l, according to the actual ISO 8185 standard [7]. Principally, these devices use a heating plate to generate water vapor, and act either with or

without an electrically heated breathing tube. Normally, these humidifiers work with a feedback loop that responds to the temperature of the humidifier chamber and the Y-piece. The heat is supplied either by the heated water vapor from the humidifier (non-heated-wire humidification) or the heated water vapour from the humidifier plus a heated wire in the circuit (heated-wire humidification). A recently published *in vitro* bench model [8] stated that water vapor delivery with non-heated-wire circuits was higher over a wide range of minute volume, while using a heated wire circuit with the same temperature at the Y-piece (35°C) did not reach full saturation at 37°C at a minute volume > 6 l/min. Therefore, the usually performed measurement of the temperature of the Y-piece of the ventilator circuit may not be sufficient to assure adequate humidification. Differences between devices according to the method by which air is humidified are: “bubble-through” humidifiers that can potentially produce infectious micro-aerosols [9] and convection-type (“passing-over”) humidifiers that at least in a bench model with continuous airway pressure devices (CPAP) do not generate water aerosols but only water vapor, with no risk of carrying infectious agents [10].

A new development – the so called counter-flow type heated humidifier – has an inner structure with a specially developed surface coated with water, thereby enhancing adsorption of water by passing through air [11]. In a bench study the efficiency of humidifying air was greater than with conventional heated humidifiers, and contrary to the former device, was flow- and rate-independent.

According to these data, the efficiency of the HH in humidifying inspiratory air is better than that of the HME. However, the devices are more expensive, and an elevated risk of infection due to contamination of the water of the HH is possible.

Irrespective of the properties and differences of these two types of humidifiers in bench models, from a clinical point of view the following problems are relevant during invasive mechanical ventilation: adequate humidification of inspiratory air, the rate of tube occlusion, influence on work of breathing, elimination of CO<sub>2</sub> and risk of infection.

### 6.2.1 Adequate Humidification of Inspiratory Air

Both devices are principally suitable to deliver adequately warmed and humidified air to the lower airways during invasive mechanical ventilation. With HMEs, especially older ones with a poor performance, endotracheal tube occlusion, a serious problem with potentially fatal outcome, has been reported. A recently published randomized controlled trial [12] showed no difference in the rate of tube occlusion comparing the properties of the HH MR 730 (Fisher & Paykel Healthcare Ltd., Auckland, New Zealand) and the well-performing HME filter DAR Hygrobac filter device (Tyco Healthcare/Nellcor, Pleasanton, California, USA). According to the theoretically higher humidification properties of the heated humidifiers we favor these devices in case of abundant tenacious secretions, e.g., during exacerbation of COPD, but consistent data that prove substantial superiority of one device over the other are lacking.

### 6.2.2 Work of Breathing

Both HMEs and HHs add extra resistance to the circuit of the ventilator, which must be overcome by ventilator settings, especially during assisted ventilation, in order not to increase the WOB. The resistance of the HH extends from 0.5 to 4.4 cmH<sub>2</sub>O/l/s; the expiratory flow resistances of the devices are low [13]. The airway resistance of so-called “bubbling” or cascade devices is so high that it should no longer be used in intubated patients. The HME and HMEF add a resistance of between 1.5 and 2.9 cmH<sub>2</sub>O/l/s to the circuit.

Iotti and colleagues analyzed the mechanical properties of the HH and HME in ten patients with acute respiratory failure; none of them suffered from COPD [14]. The resistance of the HH was lower than that of the HME (0.50 cmH<sub>2</sub>O/l/s for HH, 1.57 cmH<sub>2</sub>O/l/s for HME, 2.86 cmH<sub>2</sub>O/l/s for HMEF), and the additional dead space was 0 ml for the HH, 60 ml for the HME and 100 ml for the HMEF, according to the position of these devices in the circuit, the inspiratory limb of the circuit (HH) versus between the Y-piece and endotracheal tube (HME). The authors reported a significant increase in airway resistance with both types of HME/HMEF, and an increase in total WOB to maintain the same level of pCO<sub>2</sub>, because of a significant increase in tidal volume with the HMEF. Similar results were reported by Pelosi et al., who examined 14 patients with acute respiratory failure. With two different HME devices they observed an increase in WOB that could be overcome by increasing inspiratory pressure in the range of 5–10 cmH<sub>2</sub>O [15]. Girault et al. examined the mechanical effects of different humidification devices in difficult to wean patients [16]. In comparison to HHs, HMEs significantly increased transdiaphragmatic pressure and inspiratory WOB, which could be partly counterbalanced by elevation of inspiratory pressure of the ventilator by ≥8 cmH<sub>2</sub>O.

The conclusion is that HMEs can decrease the efficiency of mechanical ventilation because of an increase in airway resistance and dead space. Therefore, adjusting ventilatory settings (volume delivered or pressure applied) to overcome these negative effects is absolutely necessary, especially in patients with reduced inspiratory muscle strength, e.g., in prolonged weaning.

### 6.2.3 Elimination of CO<sub>2</sub>

Le Bourdelles et al. [17] reported significantly higher pCO<sub>2</sub> values during pressure support breathing in the course of weaning while using an HME instead of an HH1. Their patients only increased breathing frequency and not tidal volume during the study phase with HMEs, leading to elevated dead space ventilation and diminished alveolar ventilation. Similar results were observed by Prin et al. [18]: change from an HME to an HH in hypercapnic patients with ARDS resulted in a significant decrease of pCO<sub>2</sub> in the range of  $-11 \pm 5$  mmHg, while the ventilator setting was not adapted.

To conclude, while using the HME instead of the HH, alveolar hypoventilation might occur because of an increase in dead space. A careful observation of blood

gases is necessary, and in case of rising  $p\text{CO}_2$  either an increase in inspiratory pressure or change to an HH device will have favorable effects.

### 6.2.4 Effect of HH/HME on the Risk of Ventilator-Associated Pneumonia (VAP)

In the literature there are conflicting data: Kirton et al. reported a significant reduction in late-onset VAP while using an HME instead of an HH in a group of 280 trauma patients [19]. Similar effects regarding early-onset VAP could not be observed. Also a meta-analysis published 4 years ago by Kola et al. [20] found a significant reduction in the incidence of VAP in patients humidified with HMEs during MV, particularly in patients ventilated for a minimum of 7 days. This is contrary to the results from a published randomized controlled trial [21] that found no significant difference in the incidence of pneumonia, length of mechanical ventilation and intensive care mortality with regard to the humidification system used.

Presently, there is no clear evidence that the use of an HME either without or in combination with antibacterial filters decreases the incidence of ventilator-associated pneumonia. The possible anti-infective action of an HME might simply depend on the fact that these devices considerably reduce condensate accumulation in the ventilator circuit. But the pathophysiology of ventilator- or tube-associated pneumonia is complex, not only depending on contamination of the circuit, but also on other factors, e.g., micro-aspiration.

## 6.3 Humidification During Noninvasive Mechanical Ventilation

Different interfaces are used for noninvasive mechanical ventilation in acute respiratory failure: a nasal mask, naso-oral mask, total-face mask or helmet. With the exception of the latter device, all masks have a risk of leakage of in- and expiratory air, making an HME less effective compared to invasive ventilation. On the one hand, not all humidity and heat of expired air can be stored in the filter during expiration because of leakage, and on the other hand, inspiratory leaks are counterbalanced by rising inspiratory flow that decreases the efficacy of the HME. A physiological study published in 2009 [22] measured hygrometry of the air applied during NIV in healthy people using different strategies: with HMEs, with HHs and without humidification. HHs and HMEs showed a comparable efficiency in humidifying air to a water content of 25–30  $\text{mgH}_2\text{O/l}$  without leaks, but with increasing leakage the performance of HMEs got worse, reaching only an absolute humidity of 15  $\text{mgH}_2\text{O/l}$ . Toleration of air with a water content of 15  $\text{mgH}_2\text{O/l}$  was equivalent to 30  $\text{mgH}_2\text{O/l}$  – this may be because additional normal humidification during NIV in the upper airways occurs. Whether these data can be transferred to patients with acute exacerbation of COPD with often abundant secretions remains to be examined. Jaber et al. [23] and Lellouche and co-workers [24] published two articles in 2002 dealing with

HHs versus HMEs in patients being ventilated noninvasively with pressure support ventilation via full-face mask. An HME during NIV with the same settings was associated with significantly higher values of  $p\text{CO}_2$  in spite of higher minute volume and higher mouth occlusion pressure  $p_{0.1}$  in the study of Jaber. Lellouche reported that inspiratory efforts were markedly increased in hypercapnic patients with HMEs; furthermore, NIV with HME and zero end-expiratory pressure failed to unload inspiratory respiratory muscles compared to spontaneous breathing, contrary to an HH.

These data favor the use of HHs in the acute care setting to minimize WOB and to maximize  $\text{CO}_2$  clearance; even so, a study in long-term home mechanical ventilation showed similar tolerance and adverse effects for HMEs and HHs [25].

The helmet has a high internal gas volume around the patient's head that can store humidity of the patient's expired alveolar gases. Thus, it is believed that additional humidification of air is not necessary during helmet ventilation but may be dangerous because of a high degree of condensed water in the helmet. Chiumello et al. [26] examined the temperature and humidity of inspiratory gases during helmet ventilation with and without a heated humidifier, while offering low- or high-flow CPAP by an ICU ventilator, to nine patients with acute respiratory failure and ten healthy volunteers. They concluded that the helmet acts as a humidification chamber that renders active humidification unnecessary during ventilator CPAP.

Data regarding a difference in VAP during NIV with regard to the type of humidification are lacking. NIV is known to dramatically reduce the rate of nosocomial infections in comparison to invasive mechanical ventilation, and therefore it may be impossible to detect differences between the two conditioning devices in the future.

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## 6.4 Key Recommendations

- Conditioning (heating and humidification) inspiratory air is absolutely necessary in case of invasive mechanical ventilation and in our opinion should be considered in patients on NIV in case of an anticipated ventilation time of longer than 6 h or thick secretions.
- The HH device has a physiologically higher efficiency in humidifying inspiratory air during IMV, but clinically there are no significant differences, so both devices can be used during controlled mechanical ventilation.
- HMEs and HMEFs add dead space to the circuit, so the elimination of  $\text{CO}_2$  may be worse than with HHs. To overcome this problem, a higher minute ventilation with elevated WOB is necessary. During pressure support ventilation, due to rising resistance, WOB is increased. The levels of inspiratory pressure should be customized, especially in patients with inspiratory muscle weakness.
- In NIV HH is the preferred method for conditioning inspiratory air in the acute care setting.

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# Main Techniques for Evaluating the Performances of Humidification Devices Used for Mechanical Ventilation

# 7

François Lellouche

Evaluation of gas hygrometry allowed an improvement and progressive diversification of the humidification devices used. The main techniques to evaluate the performances of the heat and moisture exchangers (HME) and of the heated humidifiers (HH) in terms of humidification are mainly used within the framework of research. The technique of visual evaluation of condensation on the flex-tube or on the humidification chamber's wall is feasible at the patient bedside but has several limitations. Many techniques to measure the moisture of gases exist. The most frequently used in the clinical setting are the psychrometric method and the capacitance hygrometers usable on patients (during invasive or non-invasive ventilation) or on benches. Gravimetry (used by the standard ISO 9360) has technical limitations and can be used only on bench. Psychrometry and gravimetry are generally used for clinical research, whereas the manufacturers of the humidification systems often use gravimetry. This may explain the differences in performance evaluation found for humidification device assessment [1, 2].

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## 7.1 Visual Evaluation of Condensation

### 7.1.1 Condensation in the Flex-Tube

A simple way to evaluate if the gases administered to the patients are correctly humidified is to visually examine whether condensation exists in the flex-tube of the endotracheal tube. Indeed, if there is a difference between gas temperature in the circuit and room temperature, the gas cools in the circuit, causing an increase in the relative

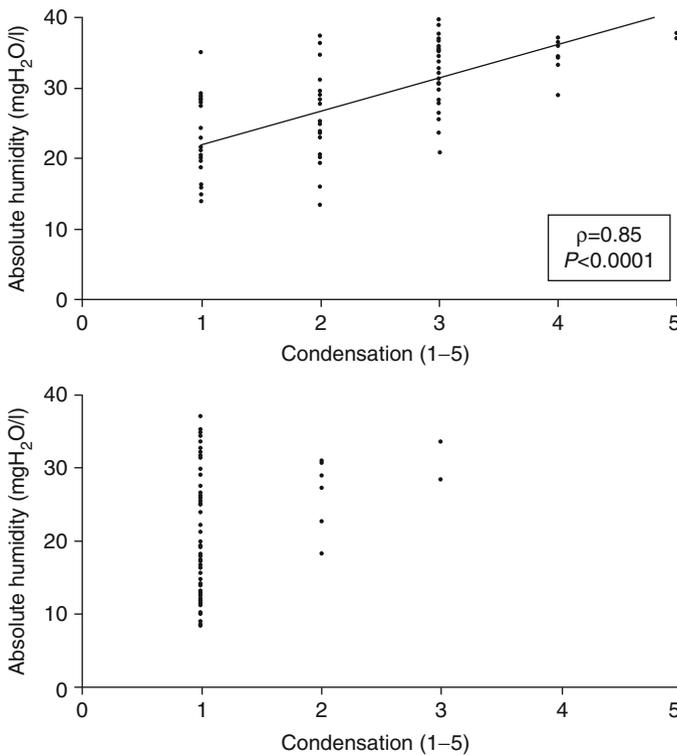
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F. Lellouche  
Institut Universitaire de Cardiologie et de Pneumologie de Québec,  
Centre de recherche, Hôpital Laval,  
2725, chemin Sainte-Foy, G1V4G5 Québec, QC, Canada  
e-mail: francois.lellouche@criucpq.ulaval.ca, fllellouche@free.fr

humidity and possibly condensation on the wall if the dew point temperature is reached. This technique was validated by two teams; they showed a good correlation between condensation and the absolute humidity of gases delivered by the tested HME [3, 4]. This simple technique can be used for both HMEs and HHs, but it remains vague and can only give an idea of the level of relative humidity of gases. Under no circumstances, however, does it allow accurately evaluating the gas water contents.

### 7.1.2 Condensation on the Humidification Chamber's Inner Wall

With heated humidifiers, it is possible to determine indirectly if the gas has reached a high relative humidity by examining condensation on the walls of the humidification chamber. This technique was validated for relatively low room temperatures



**Fig. 7.1** (a, b) Visual evaluation of condensation on the heated humidifier humidification chamber [5]. A close correlation exists between visual evaluation of the condensation (based on a condensation scale, see below) and heated wire humidifier performance [absolute humidity (mgH<sub>2</sub>O/l) of inspiratory gases] when ambient air is low enough (22–24°C) (a). However, there is no correlation when ambient air is high (28–30°C) (b). *Scale for visual evaluation of condensation:* the level of condensation on the humidification chamber wall can be assessed by visual inspection as follows: 1 dry, 2 vapor, 3 vapor with a few small droplets, 4 numerous droplets not covering the entire wall, 5 numerous droplets covering the wall almost completely. This scale has been used in several studies [4, 5]

(between 22°C and 24°C) [5]. Indeed, low room temperatures are required to get a sufficient difference of temperature with the gas circulating in the humidification chamber. While cooling by contact with the wall, the relative humidity of the gas can rise and condensation on the wall will occur at the dew point. On the contrary, with high room temperature, the delta between ambient and chamber temperature is not enough to lead to condensation. In this case, there is no correlation between condensation on the wall and the level of gas humidification [5] (Fig. 7.1).

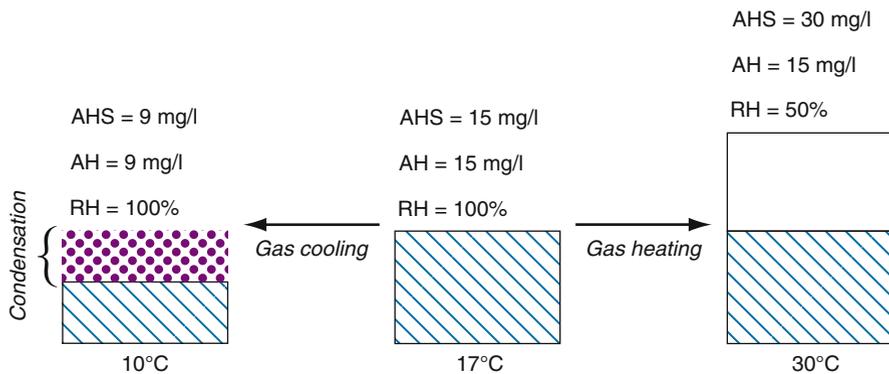
## 7.2 Techniques to Measure the Hygrometry of Gases During Mechanical Ventilation

### 7.2.1 What Is Hygrometry?

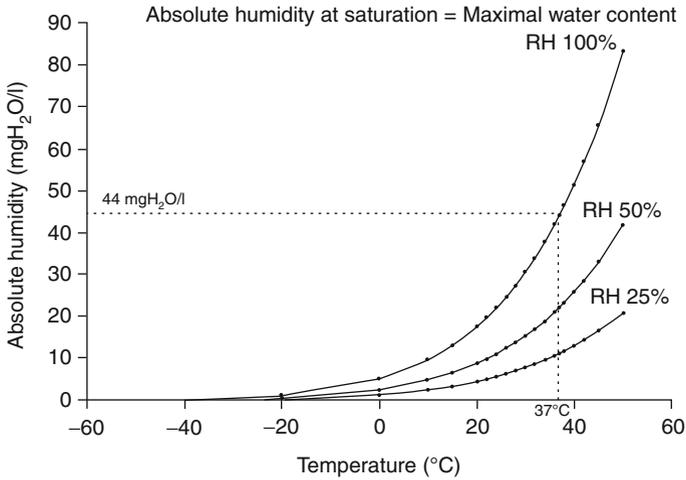
Hygrometry characterizes the quantity of moisture in the air, namely the quantity of water vapor present in the air (or in another gas). It does not take into account the water present in liquid or solid form.

Definition of humidity: humidity or moisture expresses the presence of a mixture of dry air and water vapor in ambient air. In general, moisture refers to the “rate of moisture” expressed in percentage, which refers to the relative humidity. The determination of this measurement is related to conditions, such as the temperature and the pressure. The rate of moisture in a volume of air is generally expressed by one of the following parameters (Fig. 7.2):

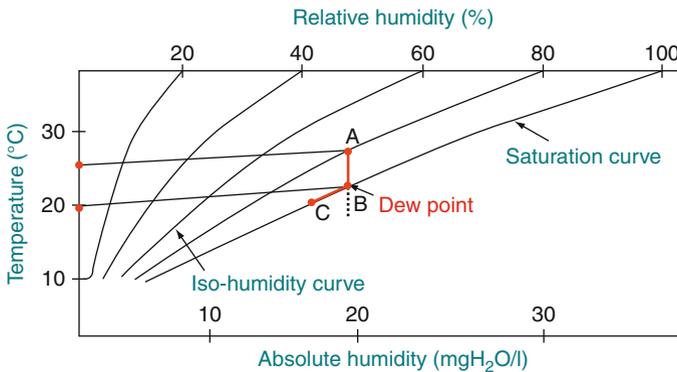
- *Absolute humidity (AH)* or water content of a gas, which defines the quantity of water vapor (i.e., gaseous state or steam) contained within a certain volume of



**Fig. 7.2** Schematic representation of relative humidity (*RH*), absolute humidity (*AH*) and absolute humidity at saturation (*AHS*) with different temperatures. At 17°C, a gas is completely saturated with water vapor; the water content (*AH*) is equal to *AHS*. This temperature corresponds to the dew point. By cooling down of the gas at 10°C, condensation occurs. By warming up the gas, the water content (*AH*) remains the same, but since gas can contain more water with a higher temperature, the relative humidity diminishes. The *hatched lines* represent the quantity of water vapor in comparison with the complete volume of gas. This volume is artificially separated from the rest of the gas (*in white*), which is a volume of dry gas without water vapor



**Fig. 7.3** Presentation of the air water contents [i.e., absolute humidity (in mgH<sub>2</sub>O/l)] according to its temperature and according to the relative humidity of the air (RH). The curves of 25, 50 and 100% of saturation or relative humidity (RH) are represented. At 100% of relative humidity, the water content corresponds to the maximum water contents [i.e., absolute humidity at saturation (AHS)]. At 37°C, the gas water content is 44 mgH<sub>2</sub>O/l with 100% relative humidity (gas completely saturated with water vapor); it is 22 mgH<sub>2</sub>O/l to 50% of RH and 11 mgH<sub>2</sub>O/l to 25% of RH



**Fig. 7.4** Mollier's diagram. Let us assume that a gas has a temperature of 25°C with relative humidity of 80% (point A on the diagram). If the temperature is cooled down to 20°C, the relative humidity will increase and attain the dew point (100% of relative humidity) (according to point B). Between A and B, only relative humidity varies, while absolute humidity is constant. If the gas is further cooled, condensation appears: the relative humidity remains at 100%, but absolute humidity will be reduced (passage from point B toward point C)

this gas. It is generally expressed in mgH<sub>2</sub>O/l. The maximum water content of a gas increases with its temperature (Fig. 7.3).

- *Dew point temperature*: This is the temperature for which, at constant pressure, it is necessary to cool down a mass of humid air to reach the saturation of this steam gas. When the gas is further cooled, condensation appears. Knowing this

temperature makes determining the humidity of air possible, thanks to tables and diagrams such as the Mollier diagram (Fig. 7.4). A parameter associated with this concept is the *absolute humidity at saturation* (AHS, or maximal water content), which corresponds to the absolute humidity or water content when the gas is saturated. The absolute humidity at saturation depends on the gas temperature (Fig. 7.3) [6].

- *Relative humidity* (RH) is defined as the ratio of absolute humidity with the absolute humidity at saturation of this gas:  $RH = (AH/AHS) \times 100$ .

A gas containing steam contains a quantity of energy (enthalpy) or latent heat, which will be released at the time of the passage of the gas state to the liquid state (condensation). On the contrary, during the evaporation of gas, energy is required and the temperature of the gas decreases.

## 7.2.2 Psychrometry

### 7.2.2.1 Working Principles of Psychrometry

The psychrometric method comes from the exploitation of the Mollier diagram. The work of Mollier, completed in the nineteenth century, highlighted the relation between temperature and humidity relative to a given pressure. Mollier's diagram directly resulting from this research shows this relation. In spite of the limited means of its author at the time of this research, the Mollier diagram is still used as a reference. In particular, the psychrometric method that is used for the majority of hygrometric measurements presented here is based on this work. The diagrams are valid for a given pressure. The influence of the pressure on a clinical application is negligible because of the low amplitude of the barometric variations. Thus, measurements to be carried out only take into account the temperature as a variable.

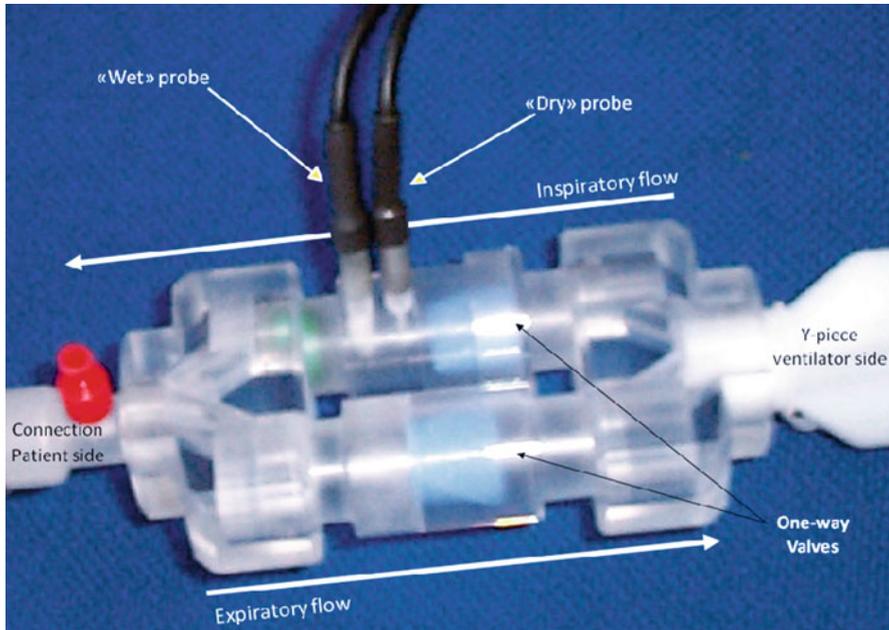
A great number of moisture sensors exist, which rely on very complex principles (reserved for applications in the laboratory), such as the hygrometer with radioactive isotopes, and on very simple principles, such as the hair hygrometer, based on the principle of lengthening of a hair with moisture [7].

The psychrometer is one of the oldest hygrometers, invented by Regnault around 1845. Its principle is based on the Mollier diagram and the measure of the difference in temperature between a “dry” and a “wet” temperature sensor.

A psychrometer consists of two temperature probes, wet and dry, placed in the gas for which humidity is assessed. One of the thermometers, called the “wet” thermometer, is kept wet with the help of a cloth soaked in water. The other, called the “dry” thermometer, measures the temperature of air. Through contact with air, the water of the fabric evaporates if the gas is not already saturated with water, which causes a cooling of the wet thermometer until it reaches a balanced temperature. Knowing these two temperatures makes it possible to determine the rate of humidity relative to the abacuses means, derived from the Mollier diagram.

In the medical field, which interests us, psychrometry has been used in many studies [2, 4, 8–25] and its technique well described [12, 21].

Two temperature sensors – dry and wet – are placed on the inspiratory path (generally in the event of measurement of inspired gas hygrometry) or on the expiratory



**Fig. 7.5** Flow separator used for psychrometric studies. This separator is required because of the low response time of this hygrometer. It allows analyzing only inspiratory (most often) or expiratory gas without mixing of the flows. The additional dead space is minimal as the gases are separated; however, resistive proprieties must be taken into account during the measurements

path (in the event of measurement of expired gas hygrometry). The temperatures must be measured after the steady state is reached, after 15 min to 3 h (in particular when measurements relate to heated humidifiers with compensation systems). The psychrometric method is based on the comparison of the dry and wet temperatures. The dry probe is placed first (ventilator side), and the humid probe, encircled with a sterile piece of cloth soaked in water, is placed about 1 cm ahead of the dry probe (patient side) (Fig. 7.5). The vaporizing of the water on the humid probe depends on the relative humidity of the gas (the dryer the gas, or if it has a low relative humidity, the more vaporization occurs, leading to the cooling of the probe). The gradient of temperature between both probes varies in a converse manner proportional to the relative humidity of gas. There is no gradient of temperature between the dry and humid probe when gas is saturated with a relative humidity of 100%.

Relative humidity (RH) is calculated in reference to a psychrometric diagram taking into account differences between the temperatures of the two probes [26]. The absolute humidity at saturation (AHS) is acquired by the following expressions:

$$\text{AHS} = 16.451563 - 0.731 T + 0.03987 T^2 \text{ (mgH}_2\text{O/l)}, \text{ for a dry temperature from } 24.1^\circ\text{C to } 38^\circ\text{C.}$$

$$\text{AHS} = 6.0741 + 0.1039 T + 0.02266 T^2 \text{ (mg H}_2\text{O/l)}, \text{ for a dry temperature from } 10^\circ\text{C to } 24.1^\circ\text{C.}$$

where  $T$  is the temperature of the dry probe.

Absolute humidity (AH) is acquired by the following formula, and by knowing the relative humidity (RH) and absolute humidity at saturation (AHS):

$$AH = (AHS \times RH) / 100 \text{ (mgH}_2\text{O/l)}.$$

The response time of this psychrometer for a gas at a speed of 1 m/s was measured in 1.25 s for 50% of equilibration and 4.1 s for 90% of equilibration of the temperature. The response time (63% of the equilibrium time) is in the order of 2 s [12]. Considering that the relatively long response time does not allow the separation of inspiration and expiration in normal breathing conditions, a flux separator should be used, allowing separating inspiratory gases from expiratory gases (Fig. 7.5). It allows the non-“pollution” of inspiratory gases with expiratory gases during measurement.

The temperature probes are placed on the inspiratory or expiratory paths, according to the type of measurement. The calibration of this machine is based on the calibration of the temperature probes. Furthermore, before every series of measurements, the measured temperatures by the two temperature probes of the psychrometer (prior to the soaking in water of the humid probe) should be compared with the standard temperature acquired with a high-precision thermometer placed at the same level as both assessed temperature probes. The value of the highest temperature in the inspiratory canal should be considered in the course of several cycles after equilibrium. Certain teams use the medium inspiratory temperature [12, 21].

## 7.2.3 Comparison of Psychrometry with Other Techniques

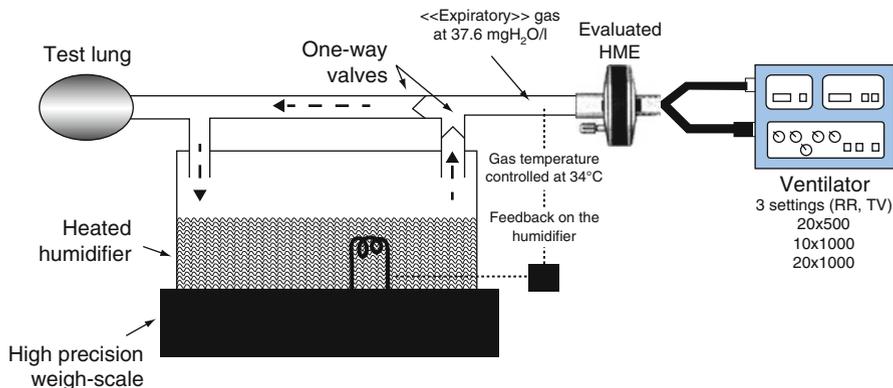
### 7.2.3.1 Studies Using the Psychrometry

The psychrometric technique has been used by numerous teams [2, 4, 8–25]. The first measurements that we acquired with the psychrometric method showed very good reproducibility of measurements compared with data published previously for identical systems of humidification. For instance, the hygrometric performance evaluation of the Hygrobac DAR HME made by different teams found very similar data [4, 21, 27]. Also, within our laboratory, the reproducibility of measurements carried out on the same system was very good with weak standard deviations (normally lower in 1 mgH<sub>2</sub>O/l) [1, 5, 28–30].

By comparing the psychrometric measurements provided in the literature with other techniques to measure hygrometry, a good correlation appears between measurements accomplished with psychrometry and those performed with other techniques. Most frequent alternative techniques to measure the performances of the humidification systems are gravimetry (bench studies only) and the capacity hygrometer, which also allows taking measurements in mechanically ventilated patients.

### 7.2.3.2 Studies Using Gravimetry

Gravimetry is one of the techniques used for evaluation of the humidification systems. A method was developed and recommended by Norm ISO 9360 [31]. It is based on the weight difference of a semi-closed system over a given period (normally of 2 h) and assesses the loss of water in the system, which consists of a lung, the humidification system to be tested [25, 32–37] and a model simulating a patient



**Fig. 7.6** Gravimetric method to measure hygrometry according to Norm ISO 9360 [32]

with saturated expiratory gas (Fig. 7.6). Results are normally expressed in mgH<sub>2</sub>O/l of water loss/h. Knowing the value of exhaled humidity and minute-ventilation, it is possible to determine the absolute humidity of the delivered gas.

This method is used mainly by the producers to test the humidification systems on the bench. The major limitation of this technology is that it cannot be directly used on patients. The other limitation is that it requires high-precision equipment for weighing the system, and for measurements of inspired and expired volumes at different levels of temperature and humidity. The study of Branson and Davis is the most exhaustive among those having used this technology [32]. These authors assessed the performances of 21 HMEs with the gravimetric method according to Norm ISO 9360. It was possible to make a comparison with our bench study [1] for four HMEs tested in the same conditions of ventilation (tidal volume of 500 ml, respiratory rate of 20 breaths/min) (Table 7.1). Most of the other HMEs were different or had a reference that did not allow certain identification.

The most important difference in measurements was with the Hygroster (−7.5%), but remained weak. For other HMEs, the difference was minimal: Hygrobac (−2.5%), Hygrobac S (+4.2%) and Portex 1200 (+0.2%).

The main advantage of psychrometry is that it can be used on patients as well as on the bench, allowing clinical validation of the model.

### 7.2.3.3 Studies Using Capacitance Hygrometer

This hygrometer was described for use for humidification system evaluation by Tilling in 1983 [38]. The sensor is a fine polymeric film with electrodes positioned

**Table 7.1** Comparison of the results for absolute humidity measurements (in mgH<sub>2</sub>O/l) acquired for several HMEs evaluated with gravimetry [32] and psychrometry [1]

	Hygrobac	Hygrobac S	Hygroster	Sims Portex 1200
Branson [32]	32.5	29.6	33.2	27.2
Lellouche [1]	31.7	31.2	30.7	27.8

**Table 7.2** Comparison of results obtained from identical HMEs with a capacitance hygrometer [18, 39, 41, 42] and with the psychrometric method [1]

	Humid-Vent Light	Pall-Ultipor BB50	Maxipleat
Martin [18]	Mean: $32.9 \pm 3.1$ Minimum: $29.0 \pm 5.0$	Mean: $31.0 \pm 3.8$ Minimum: $22.0 \pm 6.6$	
Thomachot [42]	Mean: $29.3 \pm 3.4$		
Thomachot [41]	Mean: $32.6 \pm 2.5$		
Boisson [39]			Maximum: $34.0 \pm 2.4$ Mean: $22.9 \pm 2.8$
Lellouche [1] (psychrometric method)	$30.8 \pm 0.3$	$21.8 \pm 1.5$ (BB2215)	$20.1 \pm 0.6$

For data coming from the capacitance hygrometer, the available maximum, mean or minimum values of absolute humidity (in  $\text{mgH}_2\text{O/l}$ ) are displayed. The Pall filter tested was BB2215, whose performances are very close to those of the BB50 [4]

on each side. According to the relative humidity, the water steam is absorbed on the polymeric film, which changes its capacitance. These hygrometers are usually not expensive. Their main flaw is having significant drift, which often requires frequent calibrations. Moreover, considering that the response time is very quick, given values (maximum, minimum and medium value) make the analysis of results very difficult.

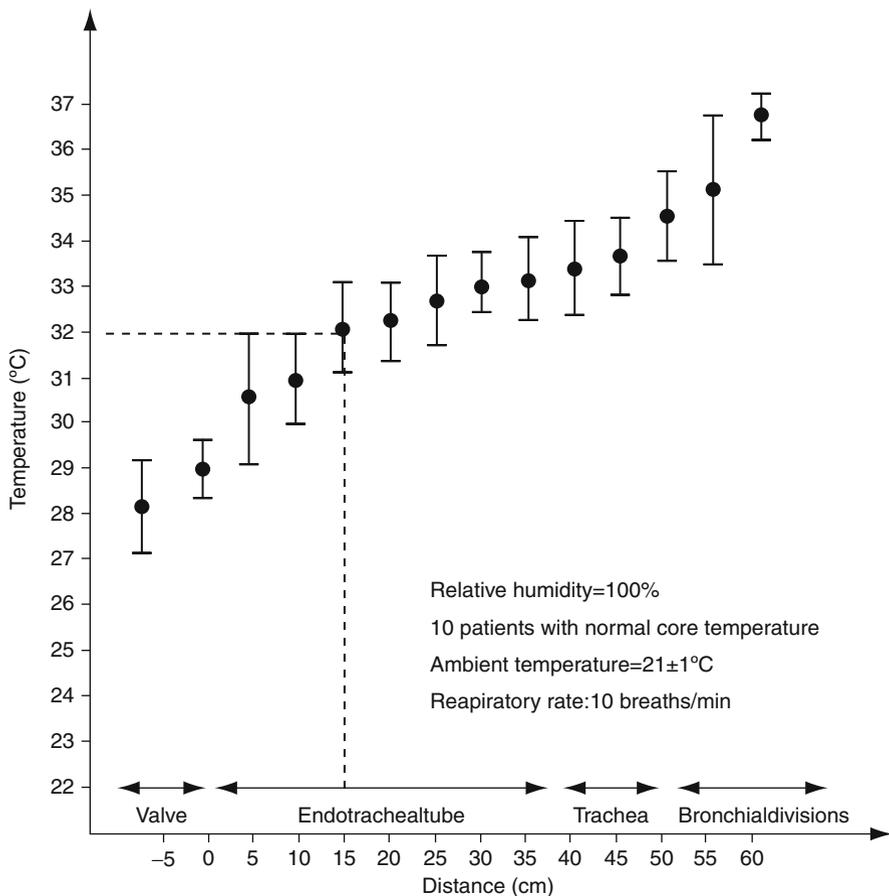
This hygrometer has been used by several teams [18, 39–42], but the results are difficult to compare with other hygrometers considering the quick response time of this hygrometer, the values of absolute humidity being given in maximum, minimum or average (Table 7.2). It seems that the medium value is the one that comes closest to most psychrometric data, except in the case of the Pall-Ultipor used in the study of Martin et al. [18].

### 7.2.4 Limits of the Psychrometric Method

The psychrometric method nevertheless has some limits that need to be known. It is possible that the ambient temperature has an influence on measurement. Indeed, at the level of the separator of flux, there can be thermal exchanges between the gas passing in this piece and surrounding air, particularly when the difference in temperature between these gases is important. To restrict this phenomenon, it is possible to use isothermic foam around the separator of flux. The use of the medium rather than maximum temperature can also restrict this phenomenon. Another problem linked to the piece that separates inspiratory gases from expiratory gases is the high resistance, especially in the inspiratory path. Inspiratory resistance was measured at  $19.6 \text{ cmH}_2\text{O}$  for 1 l/s and expiratory at  $4.8 \text{ cmH}_2\text{O}$  for 1 l/s. Due to inspiratory resistance in patients ventilated with assist control ventilation in volume, the peak pressures increase in patients ventilated with a pressure mode, and the volumes delivered by the ventilator are reduced with the presence of the flow separator. In the first case, it is necessary to set the high pressure alarms; in the second event, it is necessary to increase the level of assistance to about 5–10  $\text{cmH}_2\text{O}$  to obtain an

equivalent tidal volume. Due to the expiratory resistances, there can be a risk of expiratory flow limitation. Usually the duration of the measurements does not exceed 15 min to attain the steady state, which limits this potential issue. In practice, we did not have problems with poor tolerance in the course of numerous measurements, probably due to the selection of the patients. The patients included had to have a relative respiratory stability ( $FiO_2 \leq 80\%$ ) as well as hemodynamic stability (epi- or norepinephrin  $\leq 2$  mg/h).

Another limitation shared by most of the hygrometric measurements is the inability to assess systems producing nebulizations. Indeed, psychrometry measures the vapor of water contained in a gas, while nebulization draws away micro-droplets under liquid form. These droplets make the dry probe wet, which distorts measurements. This limitation also exists with other methods using sensors (hygrometer with capacitance, dew point hygrometers).

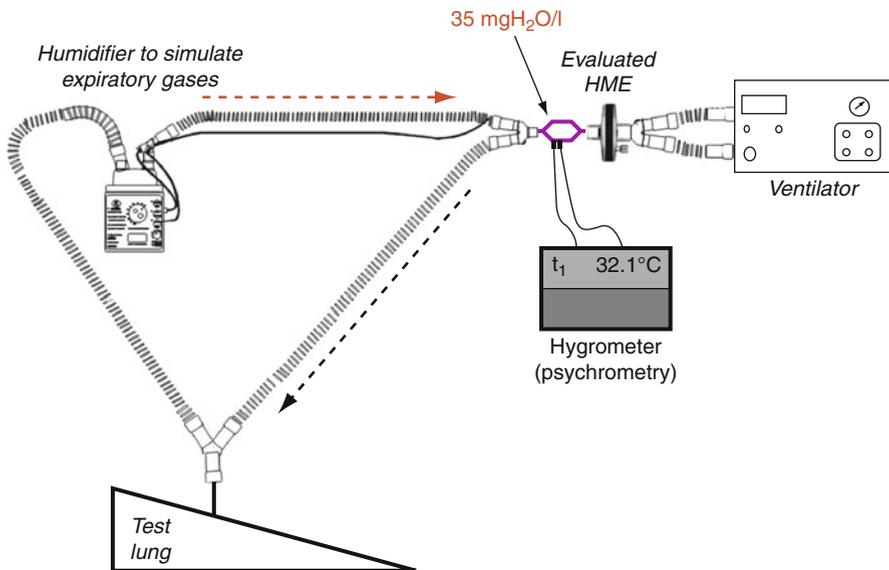


**Fig. 7.7** Expiratory gas temperature in ten patients during anesthesia. *Dotted lines*: gas temperature in the endotracheal tube at the level of the teeth. Adapted from Dery et al. [44]

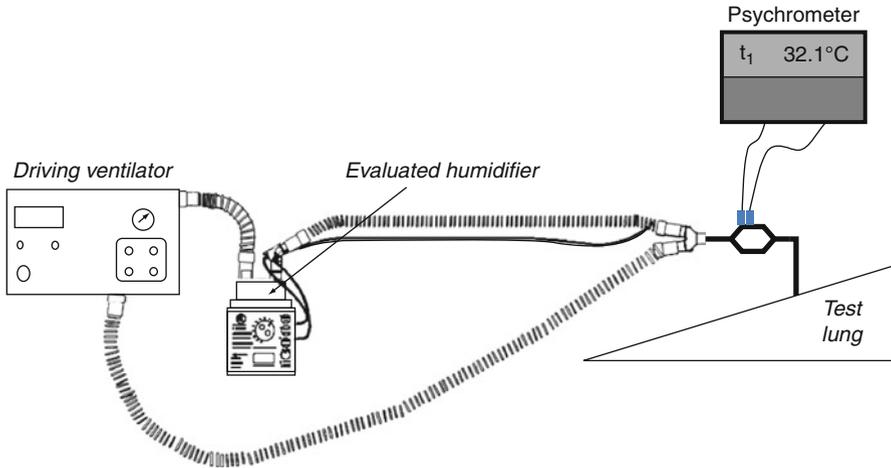
### 7.3 Benches for Measurements of Hygrometry (for HME, “Active” HME and for Heated Humidifiers)

The bench evaluation of HME and “active” HME requires simulating a physiological model that provides saturated exhaled gas as for a patient with a normal core temperature. According to the literature data, exhaled gases are saturated with water vapor at 32°C in the endotracheal tube at the tooth level [43, 44], which corresponds to a water content of 34 mgH<sub>2</sub>O/l (Fig. 7.7). These absolute expiratory humidity values are concordant with those found in the study assessing expiratory humidity in patients with hypothermia and normal core temperatures [29]. The simulation of saturated expiration can be performed with a heated humidifier (Fig. 7.8).

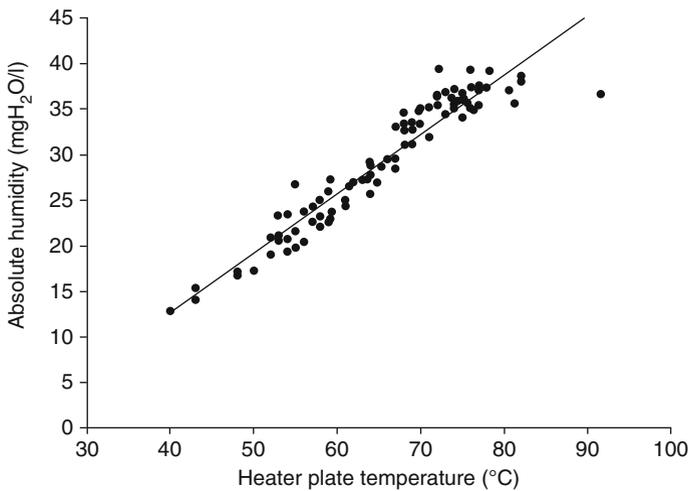
Several studies have been published using a model with simulation of expiratory saturated gases going from 32°C to 37°C, which corresponds to gas absolute



**Fig. 7.8** Hygrometric bench test apparatus used to measure the humidification performances of HMEs and antibacterial filters. A driving ventilator delivered controlled cycles (respiratory rate set at 20 breaths/min with a tidal volume of 500 ml and a positive end-expiratory pressure of 5 cmH<sub>2</sub>O). A heated humidifier (MR 730) was connected to the expiratory limb of the model and was set to deliver gases with a water content of 35 mgH<sub>2</sub>O/l at the Y-piece. A circuit with heated wire was used after the humidification chamber. The (ambient) temperature should be maintained constant between 24.5°C and 25.5°C. The system can be installed in an isolated space (like an incubator) to keep this constant temperature. Ideally, isothermic insulating foam should surround the flow separator to avoid heat variations on this level and condensation in the hygrometry part. For all the bench studies, the number of measurements carried out for each studied condition must be preset (between 3 and 6 measurements). This bench can be used for study of the humidifier filters and active filters [1, 28]



**Fig. 7.9** Bench study of psychrometric measurements used during different studies for the evaluation of the heating humidifiers



**Fig. 7.10** Relationship between heater plate temperature of the humidifier and absolute humidity of the inspiratory gases (unpublished data). However, this relationship can vary with minute ventilation and ambient temperature, and these data are not currently available. (Data obtained on bench with MR 850, Fisher&Paykel)

humidity between 34 and 44 mgH<sub>2</sub>O/l [25, 32–37, 45–48]. We performed a bench study to compare different filters and HMEs in stable and controlled situations [1] (Fig. 7.8).

The bench evaluation of the *heated humidifiers* performances is easier. The heated humidifier to be tested is installed on a ventilator with different settings (Fig. 7.9). The circuit of the ventilator is connected to a test lung (at the Y-piece), the latter being changed regularly to avoid the accumulation of water. Different

temperatures are measured (ambient temperature, ventilator output temperature, inlet chamber temperature) by a high precision thermometer, and temperatures measured by the humidifier are also recorded (heater plate temperature, outlet chamber temperature, temperature at the Y-piece) [5].

---

## 7.4 Use of the Heated Humidifier' Heater Plate Temperature

The recent heated humidifiers usually display the Y-piece temperature and the humidification chamber outlet temperature. Also, other interesting data used by the humidifier for closed loops are available only by accessing the sub-menu. The most interesting “hidden” datum is the heater plate temperature from the prospective of humidification evaluation. Indeed, a good correlation was shown to exist between the heater plate temperature and the absolute humidity of the inspiratory gases (Fig. 7.10) [5]. This temperature is not currently used, but may be helpful to assess the performances of the humidifiers online. However, there are only few data on the accuracy of this indirect measurement. Due to differences of the heat dissipation based on ambient temperature, the relationship between the absolute humidity and heater plate may vary slightly. More data are required to rely on the heater plate temperature, but it may be helpful in the future.

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## Section III

# Humidification and High-Flow Oxygen Therapy

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# Main Topic Related with Humidification: Discomfort Associated with Underhumidified High-Flow Oxygen Therapy in Critically Ill Patients

# 8

Gerald Chanques and Samir Jaber

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## 8.1 Pain, Discomfort and Stress Response were Associated with an Increased Morbidity in Critically Ill Patients

Critically ill patients hospitalized in the intensive care unit (ICU) frequently report pain and discomfort symptoms whose etiology may be diverse, such as the medical history, but is also related to care procedures and devices [1]. ICU stressors have been associated with an increased morbidity, explained in part by an increased stress response, a worse quality of life and unpleasant memories in survivors. It has been shown that a systematic pain and agitation assessment in a mixed population of medical-surgical ICU patients was associated with an improvement of ICU morbidity [2].

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## 8.2 High Flow Oxygen Therapy may cause Discomfort Symptoms

Oxygen therapy has long been a common treatment for patients who suffer from an organ dysfunction and are hospitalized in the ICU. Non intubated critically ill patients are often treated by high-flow oxygen therapy (HFOT) above 4 l/min using a face mask. The face mask is used in place of a nasal cannula because patients with acute respiratory failure (ARF) breathe preferentially through an open mouth rather than the nose. Given that oxygen delivered to the patient is dry, humidifying the oxygen is recommended when above 4 l/min in the ICU setting, because the humidification function of the nasal mucosa can be insufficient at high oxygen flow rates and/or the critically ill patient with ARF often breaths through the mouth. Although

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G. Chanques (✉) • S. Jaber  
Intensive Care and Anesthesiology Department “B” (SAR B),  
Saint Eloi Hospital, CHU de Montpellier University,  
80, Avenue Augustin Fliche, 34295 Montpellier Cedex 5, France  
e-mail: g-chanques@chu-montpellier.fr

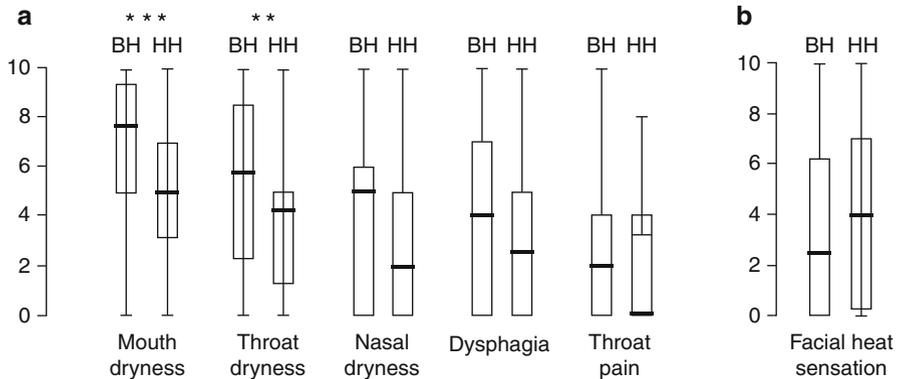
HFOT is commonly practiced in the ICU, there is a paucity of studies on the humidification of HFOT for this population of patients. We studied 30 consecutive ICU patients (70% surgical) treated with a median oxygen therapy of 8 l/min [5–11] delivered by a face mask for 48 to 72 h [3]. HFOT was humidified either by a bubble humidifier (BH) (HAD 2; AGA medical, Rueil-Malmaison, France) or a heated humidifier (HH) (MR850; Fisher & Paykel Healthcare, Panmure, New Zealand); these were randomly assigned and changed every 24 h in a cross-over design. After each study day (24 h of humidification with either device), and after a period of 2 h without noninvasive ventilation (NIV), aerosol therapy or oral care, the clinical parameters of discomfort were assessed by a blinded observer asking the patient to rate his/her discomfort symptoms using an enlarged ICU-adapted numerical rating scale (NRS) from 0 (no discomfort) to 10 (maximum imaginable discomfort) [2]. The discomfort symptoms were determined for the dryness of the delivered oxygen (dryness of the mouth, throat, nose, difficulty to swallow and throat pain) and for its warmth (facial heat sensation). We also evaluated a total dryness score, which pooled all five dryness symptoms. The last day of the study, the patient was asked to rate his or her preference for the humidification device used, with respect to the humidification of the upper airway mucosa and the warmth of the mask, using a 5-point verbal scale: +2 = much better than the other device, +1 = better, 0 = no preference, -1 = worse and -2 = much worse. Finally, the level of vapor condensation on the inner side of the face mask was recorded each day by the blinded observer, as either present or absent. The main result was that 56% of patients experienced moderate to severe discomfort symptoms whichever humidification device was used [3].

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### 8.3 Discomfort Associated with Oxygen Therapy Decreased with its Humidification

In our study [3], the intensity of symptoms was less important when HFOT was humidified. These findings are supported in three different ways.

Firstly, the discomfort symptoms associated with the dryness of the mouth and throat were significantly lower when an HH was used (Fig. 8.1). The median intensity of the total dryness score was significantly lower with an HH than with a BH (3.1 [1.7–4.8] vs. 4.8 [2.0–6.4],  $P < 0.01$ ). The decrease of discomfort was more important for mouth and throat dryness. The fact that only trends towards lower discomfort with an HH were observed for other symptoms, such as nasal dryness, throat pain and difficulty to swallow, could be explained by the high rate of using a nasal-gastric catheter (63%), mainly in patients recovering from digestive tract surgery. No significant difference in facial heat sensation was observed between the two humidification devices (Fig. 8.1). Upon the last day of the study, patient preference was significantly higher for HHs than BHs with respect to humidification of the upper airway mucosa (1.0 [0.0–1.3] vs. 0.0 [-1.0–0.3],  $P = 0.02$ , respectively), whereas no significant difference was observed regarding the warmth of the mask (0.0 [0.0–1.3] vs. 0.0 [-1.0–0.0],  $P = 0.17$ ).



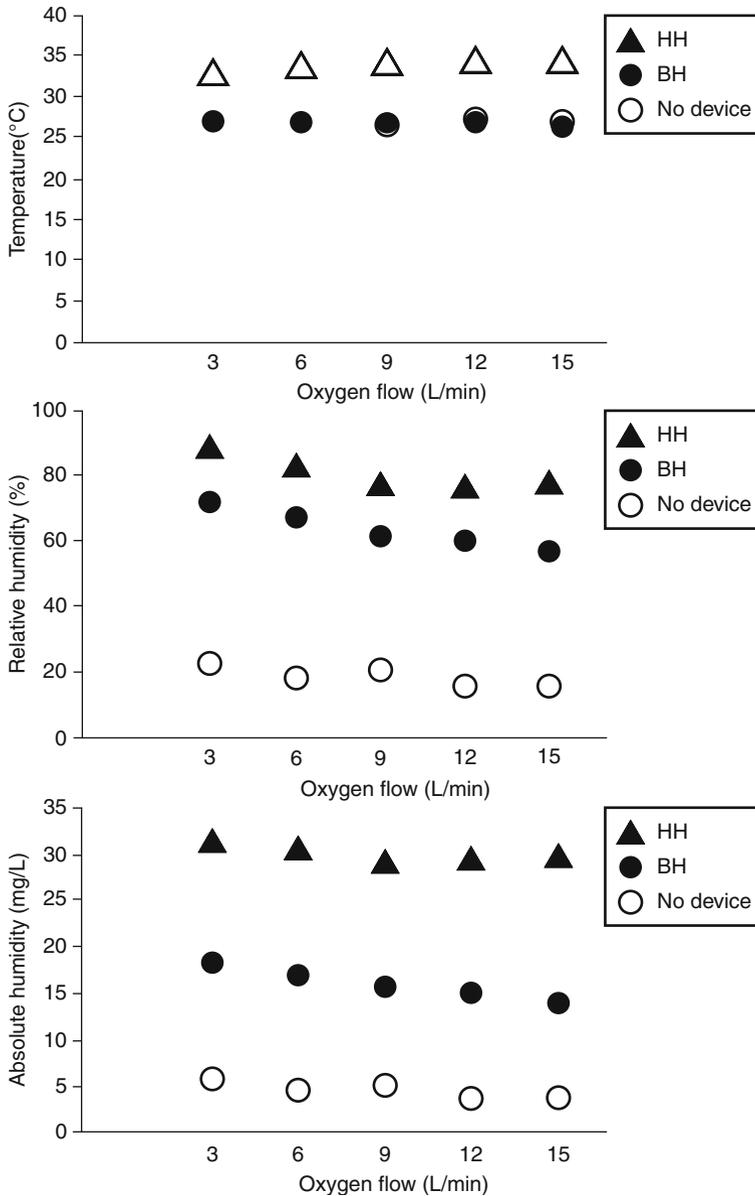
**Fig. 8.1** Intensity of each discomfort symptom evaluated for each of the two humidification devices, from [3]. This figure shows that the intensity of all dryness discomfort symptoms (a) decreased with heated humidification compared to the bubble humidifier. The difference was significant only for mouth and throat dryness and trended towards significance for the others ( $P$  values  $\leq 0.12$ ). The facial heat sensation (b) was not significantly greater with the heated humidifier ( $P=0.20$ ). Medians are expressed as horizontal bars, 25–75th percentiles as boxes and maximal-minimal values as \*\*\*  $P < 0.001$ ; \*\*  $P < 0.01$

Secondly, the presence of vapor condensation on the inner side of the face mask was dramatically more frequent when an HH was used compared to a BH (90 vs. 18%,  $P < 0.001$ ). This has been suggested as an index for adequate levels of humidity delivered to the patient. As reported in mechanically ventilated ICU patients, the visual evaluation of vapor condensation provides a very accurate estimation of the humidifying efficacy of the humidification device when compared to the psychrometric method.

Thirdly, we performed a bench test study to measure, by the psychrometric method, the hygrometric properties of oxygen therapy humidified with either the BH or the HH, and without any humidification device. The measures supported the main findings of the clinical study because the delivered oxygen had higher hygrometric properties when an HH was used compared to a BH. The mean absolute humidity was two times greater with an HH than with a BH (Fig. 8.2).

#### 8.4 Beyond the Discomfort Symptom Associated with Underhumidified Oxygen Therapy, What are Other Benefits of Interests to Better Humidifying Oxygen?

Our study demonstrates that increasing absolute humidity of the gas breathed by critically ill patients requiring HFOT is associated with an improvement of mouth and airway mucosa dryness. Consequently, this could contribute to a better preservation of the mucociliary transport system and reduced airway resistance. This is an important factor in critically ill patients who frequently develop atelectasis and nosocomial



**Fig. 8.2** Hygrometric properties of oxygen delivered at increasing flow rates, without and with a bubble or heated humidifier, measured with the bench test, from [3]. This figure shows the hygrometric measurements of the bench study. The median temperature measured with the heated humidifier (HH) was significantly higher than with the bubble humidifier (BH) (34.1 [33.7–34.3] vs. 26.7 [26.4–26.8] °C), as were the median relative humidity (77.6 [77.3–82.4] vs. 60.7 [59.7–66.3] %) and the median absolute humidity (29.7 [24.4–30.6] vs. 15.6 [14.9–16.9] mg/l), all *P* values < 0.05, Wilcoxon’s rank tests. The median relative and absolute humidity levels measured without humidification device at a temperature of 26.7 [26.6–26.9]°C were respectively 17.3 [14.6–19.8] % and 4.4 [3.7–5.0] mg/l. For the two conditions, all the measurements were obtained at constant room air conditions (temperature = 26°C; relative humidity = 73%; absolute humidity = 18 mg/l)

infections, such as sinusitis and pneumonia. Regarding the findings of this study, better humidification could be considered in critically ill patients treated by HFOT delivered with a face mask because these patients often breathe through the mouth and/or the humidification capacity of the nasal mucosa could be insufficient at high flows of oxygen, as reported for patients treated by noninvasive ventilation for ARF. In the same way, improved humidification of hospitalized patients' airways could be of interest so as to avoid the sick building syndrome associated with air conditioning, which is often reported by health caregivers and could be particularly important in critically ill patients who commonly have high minute ventilation and/or breathe frequently through the mouth. Further studies are needed to measure the clinical impact of humidification devices on respiratory function and associated outcomes in these critically ill patients, taking into account also the cost-effectiveness of more widespread use.

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### **8.5 Waiting for Further Studies, What Humidification can we Recommend for ICU Patients Treated by Oxygen Therapy?**

First, discomfort symptoms should be systematically assessed in ICU patients, such as pain and agitation, because all these symptoms are frequent in critically ill patients. Second, because the bubble humidifier is more cost-effective than heated humidifiers, and because its hygrometric properties are not nil (Fig. 8.2), it should be used first in patients treated with HFOT above 4 l/min who experienced no or light discomfort symptoms. In other patients, those who experienced moderate to severe discomfort and/or suffer from atelectasis, the use of an HH should be considered. In ICUs whose ventilators are equipped with an HH, the use of the same HH that was used for mechanical ventilation is common sense and probably more cost-effective than the use of another device, such as a bubble humidifier.

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## Section IV

# Humidification and Noninvasive Ventilation

David Chiumello, Antonella Marino,  
and Elisabetta Gallazzi

## 9.1 Introduction

The humidification and heating (i.e., the conditioning) of medical gases is now a well-established clinical practice in intubated patients receiving invasive ventilatory support [1]. Under normal circumstances at a temperature of 20–22°C, room air is only partially humidified, with a relative humidity (RH) around 40–50% with an absolute humidity (AH) of 18–20 mgH<sub>2</sub>O/l. Through the nose and upper airways, particles and microorganisms are filtered from the inspired air, which is warmed to body temperature (37°C) and fully saturated [2]. This can ensure optimal gas exchange and respiratory function, maintaining the gas mixture within the lower airways and alveoli constant at 37°C with AH of 44 mgH<sub>2</sub>O/l (i.e., RH 100%). Nasal mucosa and turbinate bones in the nose have the main role in these mechanisms. The nasal mucosa is always moist because of its high vascularization and high concentration of mucous glands [3]. The surface area of the turbinates, which are covered by the mucosa, has convolutions that can increase the turbulence of gas flow. Both of these factors increase the contact between the gas and mucosa [4]. As a result, inspiratory flow arriving in the oropharynx is already heated at a temperature of 30–32°C and almost fully saturated (AH 28–34 mgH<sub>2</sub>O/l, corresponding to 90–100% RH) [5]. During the passage in the trachea, the gas is further heated at body temperature and charged with water vapor until the isothermic saturation boundary [6].

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D. Chiumello (✉)

Dipartimento di Anestesiologia, Terapia Intensiva e Scienze Dermatologiche,  
Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena di Milano,  
Università degli Studi di Milano, Via F. Sforza 35, 20122 Milan, Italy  
e-mail: chiumello@libero.it

A. Marino

Dipartimento di Anestesiologia, Terapia Intensiva e Scienze Dermatologiche,  
Università degli Studi di Milano, Milan, Italy

E. Gallazzi

Dipartimento di Anestesia, Rianimazione (Intensiva e Subintensiva) e Terapia del Dolore,  
Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico, Milan, Italy

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**Table 9.1** Temperature, absolute and relative humidity of gases from 21% to 100% oxygen

Oxygen fraction (%)	Temperature (°C)	Absolute humidity (mgH <sub>2</sub> O/l)	Relative humidity (%)
21	24.0	3.9	18
30	23.6	3.9	18
40	23.5	2.8	13
50	23.3	2.5	12
60	23.2	2.4	12
70	23.0	2.4	12
80	23.0	2.5	12
90	22.9	2.8	14
100	22.7	2.9	14

During expiratory phase, heat and water are in part recovered by the mucosa membrane, although this recovery is not complete, and the expired air is hotter and more humidified than the inspired one, resulting in a physiological net loss of heat and water [3, 7].

Recommendations for the conditioning of medical gases during NIV are lacking [8]. In patients during NIV, we have to consider that we are delivering medical compressed gases to the nose and mouth. The temperature of medical gases depends on the hospital gas storage location and room temperature, whereas the humidification is always low (Table 9.1). Consequently, medical compressed gases will remain excessively dry until delivered to patients. As shown in Table 9.1, medical gases present a low AH, while the temperature is within acceptable ranges. When dry gases are inspired, a humidity deficit (the difference between the alveolar and ambient air water content) is generated [2, 6]. This may lead to moisture depletion of the mucosa, a reduction in the ciliary activity and functional alteration of the upper airway epithelium [2, 6]. On the other hand, the indiscriminate use of humidification devices, currently used in intubated mechanical ventilated patients, can lead to inappropriate overhumidification and excessive air heating, which can result in severe patient discomfort with possible premature interruption of NIV. Both these situations (deficit or excess in conditioning) can worsen a precarious clinical status, resulting in a failure of NIV requiring endotracheal intubation and invasive ventilatory support.

## 9.2 The Conditioning of Medical Gases During Noninvasive Ventilation

The two most commonly used humidifying devices are the heated humidifier (HH) and the heat and moisture exchanger (HME). HMEs are relatively efficient and usually have a microbiological filter. During the expiratory phase, the patient's expired heat and moisture condense on the HME membrane, which then returns the expired heat and moisture during the next inspiration. HMEs are generally preferred for their simplicity and low cost, but can increase the dead space and resistance to flow. In a cross-over study comparing HHs and HMEs on arterial blood gases and patient effort in patients with acute respiratory failure, despite similar carbon dioxide levels,

the minute ventilation was found to be significantly higher with HMEs compared to HHs [9]. In addition, the use of HMEs was associated with a greater increase in work of breathing and indices of patient effort.

The first application of NIV was in chronic pulmonary disease patients, but nowadays it is broadly applied in any kind of acute respiratory failure from severe acute respiratory failure to cardiogenic pulmonary edema [8]. Failure of NIV has been reported in between 20% and 50% of patients [10], and some of these failures could be due to poor tolerance of the technique [11]. Compared with invasive mechanical ventilation, the upper airways, the main structure responsible for gas conditioning, are not bypassed during NIV.

The last consensus conference on NIV stated that: “inadequate humidification may cause patient distress, especially if pipeline or cylinder gas is used;” based on the paucity of available data, no specific recommendations were made [8]. At the present time there is no information on the optimal level of humidity of inspired gases during NIV. The American National Standards Institute suggested, although not directly for NIV, that 10 mgH<sub>2</sub>O/l of AH is the lowest acceptable level needed to minimize mucosal damage in the upper airways [12].

Life-threatening inspissated secretions due to inadequate conditioning were reported in a patient during NIV [13]. In patients with obstructive sleep apnea (OSA) treated with continuous positive airway pressure (CPAP), a possible complication due to the air leaks is formation of a high unidirectional flow that passes through the nose. If this high gas flow is not conditioned, it may cause an increase in the inflammatory mediators [14] and in nasal airway resistance [15]. Richards et al. showed that during CPAP with mouth leaks the active conditioning of the inspired gases, using a heat and water bath humidifier, attenuated the increase in airway resistance [16]. This study confirmed that mucosal dryness due to high gas flow can cause an increase in nasal resistance. Similarly, Martins de Araujo et al. evaluated the impact of heated and humidified gases on relative humidity compared to dry gases during CPAP in OSA patients [17]. Compared to spontaneously breathing patients without CPAP, the RH was significantly reduced when CPAP was started (80 vs. 63%) and further decreased when patients simulated air leaks (39%). The conditioning of gases significantly increased the RH to similar values of spontaneous breathing (82%). Most importantly, the authors also evaluated the RH when CPAP was delivered by a face mask. Using the face mask and dry gases, the RH was similar to spontaneous breathing. The face mask is able to mix the inspired dry gases with the heated and humidified expired gases, establishing an optimal humidity gradient and thus avoiding the need for additional conditioning.

However, dyspneic patients often breathe through their mouths, causing air leakage and decreasing the efficacy of NIV when the nasal mask is used [18]. NIV delivered by face mask failed in a significant number of cases because of technical problems, such as gas leaks around the mask [18, 19], skin lesions [20] and mask discomfort [21, 22]. A new device, the “helmet,” has been introduced in clinical practice to deliver NPPV [23, 24]. The helmet is a transparent plastic hood of 12–15 l internal volume depending on the size originally used to deliver the desired oxygen fraction during hyperbaric oxygen therapy. The helmet compared to the face mask, because of the absence of any contact with the patient’s face, avoids skin

lesions and may increase patient comfort with the possibility of longer delivery of NIV. In addition, the helmet can be used in difficult anatomic situations such as in edentulous patients or patients with facial trauma. Several studies describing the use of the helmet in delivering NIV in patients with acute respiratory failure showed a lower rate of NIV interruption because of the discomfort of the interface compared to the face mask [23]. Differently from the face mask, the higher internal volume of the helmet (12–15 l vs. 0.3 l) generates a mixing chamber between the expired and inspired medical gases, thus increasing the level of temperature and humidity. This could raise the levels of heat and humidity of the medical gases, thus avoiding the need for a heated humidifier. The final humidity inside the helmet will depend mainly on two factors: the amount of humidity in the patients' expired gases and the flow of fresh medical gases into the helmet.

We evaluated the temperature and humidity of respiratory gases within the helmet with and without an active humidifier during CPAP in a high and low flow system and by a common critical care ventilator. The application of the heated humidifier during all CPAP modes tested significantly raised the temperature, and absolute and relative humidity compared with CPAP without the heated humidifier. Temperature and absolute and relative humidity were significantly higher with ventilator CPAP with and without the heated humidifier compared with continuous high-flow CPAP and continuous low-flow CPAP (with the exception of temperature for low-flow CPAP). Continuous low-flow CPAP exhibited a significantly higher temperature, absolute and relative humidity compared with continuous high-flow CPAP (Table 9.2). These data show, at least during the short term, that the use of a heated humidifier during ventilator CPAP, continuous low-flow and high-flow CPAP significantly increased the temperature and humidity of the gases within the helmet. Taking 10 mgH<sub>2</sub>O/l as the absolute minimum humidity required for medical gases during NPPV, this level was achieved without use of the heated humidifier only during ventilator CPAP. Third, patients with acute respiratory failure and healthy individuals exhibited similar abilities to condition the medical gases. We must remember that it is not possible to use the HME with the helmet because there is no expiratory flow passing through the HME.

Considering the face mask, because of the very low dead space, a conditioning system is recommended; the HH should always be used in the presence of severe leaks, or in patients with hypercapnic respiratory failure or high work of breathing.

**Table 9.2** Temperature and humidity of medical gas with and without the heated humidifier in patients with acute respiratory failure

	Temperature (°C)	AH (mgH <sub>2</sub> O/l)	RH (%)
Ventilator CPAP with HH	32.4 ± 1.4	34.1 ± 2.8	98.1 ± 1.8
Ventilator CPAP without HH	29.5 ± 2.0	18.4 ± 5.5	61.4 ± 14.7
Low-flow CPAP with HH	32.3 ± 1.0	33.9 ± 1.9	98.0 ± 1.0
Low-flow CPAP without HH	28.5 ± 1.7	11.4 ± 4.8	40.4 ± 15.5
High-flow CPAP with HH	29.4 ± 1.1	24.2 ± 5.4	82.3 ± 18.3
High-flow CPAP without HH	27.4 ± 1.2	6.4 ± 1.8	24.6 ± 6.9

### 9.3 Conclusions

The conditioning of medical gases is a common practice in intubated patients, but during NIV there are no defined guidelines.

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Antonio Matías Esquinas and Ahmed S. BaHamam

## Abbreviations

AH	Absolute humidity
AHRF	Acute hypoxemic respiratory failure
ARF	Acute respiratory failure
AWR	Airway resistance
BPAP	Bi-level positive airway pressure
COPD	Chronic obstructive pulmonary diseases
CPAP	Continuous positive airway pressure
EPAP	End expiratory airway pressure
Ex-pha	Expiratory phase
FiO <sub>2</sub>	Fraction of inspired oxygen
HH	Heated humidifier
HWH	Heated wire humidifier
IPAP	Inspiratory positive airway pressure
NIV	Noninvasive mechanical ventilation
OSAS	Obstructive sleep apnea syndrome
PIF	Peak inspiratory flow
RH	Relative humidity

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A.M. Esquinas (✉)

International Fellow AARC, Intensive Care Unit, Hospital Morales Meseguer,  
Avd Marques Velez s/n, Murcia, Spain  
e-mail: antmesquinas@gmail.com

A.S. BaHamam

University Sleep Disorders Center, College of Medicine, King Saud University,  
Riyadh, Saudi Arabia  
e-mail: ahammam2@gmail.com

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## 10.1 Introduction

Although humidification of inspired gas during invasive ventilation is an accepted standard care, there are no clear guidelines for the use of humidification during noninvasive mechanical ventilation (NIV). Normally, the respiratory system warms and humidifies inspired gas so that alveolar gas is at body temperature, atmospheric pressure and saturated with water vapor (BTPS) [1]. NIV disturbs the normal physiological system that warms and humidifies inspired gases. NIV increases minute volume ( $V_E$ ) and changes the characteristics of inspired air into cool and dry air at high volume and flow. If NIV is supplied through an ICU ventilator that utilizes anhydrous gases from compressed wall air and oxygen, the risk of dryness increases. In addition, patients with acute respiratory failure (ARF) tends to breathe through the mouth during NIV, which is a less efficient route than nasal breathing with regard to heat and moisture of the inspired gas [2]. Obstructive sleep apnea syndrome (OSAS) is one of the most important indications for chronic use of NIV at home. Available data suggest that up to 60% of patients with OSAS who use CPAP therapy experience nasal congestion and dryness of the mouth and nose [3–5]. Therefore, humidification of the inspired gas in NIV appears to be important for patient comfort and better compliance with therapy.

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## 10.2 Hygrometry and Noninvasive Mechanical Ventilation

Recently, there has been growing interest in determining the best hygrometry level during NIV and its potential influence on outcome (tolerance, efficacy, comfort, complications, etc.) after the incorporation of new technologies in mask design and mechanical ventilator. However, few clinical studies have analyzed the optimal level of relative humidity (RH) and how hygrometry measurement can give us the needed information about humidification efficacy, especially in situations of ARF. Currently, hygrometry has not been recommended as an optimum standard or gold standard of care for the majority of common indications of NIV.

Review of the available bench and clinical studies allow us to categorize the major results into the following areas: (a) hygrometry and physical factors that interact with AH stability; (b) hygrometry and adaptive or subjective response; (c) hygrometry and gas exchange; (d) hygrometry and short-term clinical outcome (for example, failure of NIV); (e) hygrometry and indirect complications (atelectasis, ventilator-associated pneumonia, difficult endotracheal intubation, etc.) during NIV.

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## 10.3 Bench Studies

The majority of traditional studies come from bench analysis with controlled physical conditions and very stable situations. Hygrometry measurements have been done by direct measures (nostrils) or indirect techniques (thermometers) [6, 7]. Under these conditions, correct interpretation of hygrometric behavior must take

**Table 10.1** Factors related with hygrometry levels during NIV

1. Level of air leaks
2. Design of the interface (dead space)
3. Respiratory pattern
4. Design of the ventilator (for example, high inspiratory flow CPAP system)
5. Setting of the IPAP/EPAP levels
6. Inspiratory oxygen fraction ( $\text{FiO}_2$ )
7. Place of the sensor

into account a number of physical and inherent variables of NIV that can interfere with the correct interpretation of hygrometry measurement. From these studies, we can observe that the major physical variables that can influence AH are: (1) environmental temperature and humidity: temperature of the inspired gas, which should not exceed 32–34°C [8]; (2) atmospheric pressure level, (3) airflow: level and characteristics; (4) the humidification system selected; (5) the inherent characteristics of the selected NIV technique (interface, ventilatory mode, positive pressure setting.). These aspects are summarized in Table 10.1 (hygrometry and NIV elements).

## 10.4 Where Do We Measure Hygrometry? Inspiratory Gas, Expiratory Gas or Both?

For correct interpretation, there must be a system that distinguishes between measures of the AH (or RH) in the inspiratory and expiratory phases as it has different interpretations and implications (inspiratory or expiratory respiratory cycles). Details of such a system are shown in Fig. 10.1. Following this schema, we can analyze the factors related to NIV that can influence the hygrometry values and their implications for the interpretation and application of humidification during NIV.

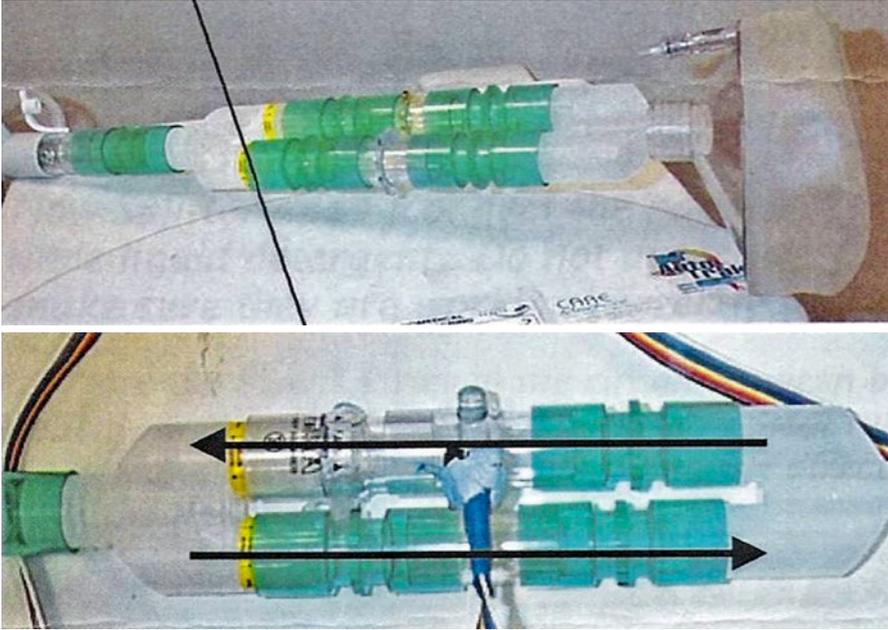
When analyzing the factors that can influence hygrometry, it is necessary to differentiate pure physical variables from specific variables related to the condition of the patient with ARF.

### 10.4.1 Physical Variables

The variables that can influence the operation of the hygrometer are summarized in the following.

#### 10.4.1.1 NIV Ventilator

Traditionally, NIV was applied utilizing intensive care ventilators (ICU ventilators), and then portable ventilators were introduced for home care of patients with OSAS and other disorders. Positive pressure was delivered as a continuous positive airway pressure (CPAP) that delivers high flow and provides a high peak inspiratory flow rate or as a bi-level positive airway pressure (BPAP), with a variable oxygen inspiratory fraction ( $\text{FiO}_2$ ) to compensate for the inspiratory demand in patients with ARF and to reduce work of breathing (WOB).



**Fig. 10.1** Hycall system, hygrometry

Few bench studies have addressed this aspect and demonstrated a negative impact of NIV on AH; hence, early use of humidification devices is recommended [9, 10].

The first analysis of hygrometry behavior was carried out by Wiest et al. using conventional intensive care ventilators, which showed that the use of ICU ventilators provided a low level of AH in the range of 5 mg H<sub>2</sub>O/l for specific ventilator turbines (13 mgH<sub>2</sub>O/l) [11]. According to Wiest et al., the AH level below which complications can be expected is in the range of less than 5 mgH<sub>2</sub>O/l [11].

Holland et al., in a recent broader bench study, analyzed the effects of mechanical ventilation parameters and the HHW system on RH, AH and ventilator performance during NIV [12]. Without humidification, RH in the NIV circuit (range 16.3–26.5%) was substantially lower than the ambient RH (27.6–31.5%) at all ventilatory settings [12]. Another important finding was that the increases in inspiratory positive airway pressure (IPAP) cmH<sub>2</sub>O setting induced a significant decrease in RH (Spearman's  $r=0.67$ ,  $p<0.001$ ), which returned back within normal values when an HHW was applied [12]. This observation could be explained by the increase in temperature (t°C) of the inlet humidification system itself from the mechanical ventilator, or the increased airflow or speed of the turbine to generate more airflow and positive pressure. This physical effect induced a slight decrease in the target level of IPAP (0.5–1 cmH<sub>2</sub>O). The selected ventilatory parameters, respiratory rate, and airflow and the relationship between inspiratory: expiratory (I:E) ratio can modify the final RH. Oto et al., in a recent bench study, demonstrated that the AH

was significantly influenced by EPAP [9]. As EPAP increased, the average base flow increased and AH decreased [9].

#### 10.4.1.2 Airflow Inlet Humidification Chamber

The features of the airflow entering into the humidification chamber have some impact on hygrometry measurement. The first description of this physical phenomenon was made by Wenzel et al., who analyzed the factors influencing hygrometry's ability to have a variable range of airflow rates (20, 55 and 90 l/min) [13].

#### 10.4.1.3 Mask Design

The mouth opening induces a constant loss of AH especially with a nasal mask and influences hygrometry stability. We know that the nasal interface is associated a constantly higher level of leakage and leads to a loss of moisture and consequently leads to an increase in the upper nasal resistance.

Recently, Chiumello et al. compared the hygrometric values in a helmet system during CPAP with or without a HHW, delivered by either a mechanical ventilator or a continuous low (40 l/min) or high (80 l/min) flow in nine patients with ARF and ten healthy subjects [14]. The results revealed that the HHW system increased the AH level, both during ventilator CPAP (from  $18.4 \pm 5.5$  mgH<sub>2</sub>O/l to  $34.1 \pm 2.8$  mgH<sub>2</sub>O/l) and with CPAP at low flow (AH =  $11.4 \pm 4.8$  mgH<sub>(2)</sub>O/l to  $33.9 \pm 1.9$  mgH<sub>(2)</sub>O/l) and high flow (AH =  $6.4 \pm 1.8$  mgH<sub>(2)</sub>O/l to  $24.2 \pm 5.4$  mgH<sub>(2)</sub>O/l). Without the heated humidifier, the absolute humidity was significantly higher with ventilator CPAP (AH =  $18.4 \pm 5.5$  mgH<sub>(2)</sub>O/l to  $34.1 \pm 2.8$  mgH<sub>(2)</sub>O/l) compared with continuous low-flow and high-flow CPAP. The level of comfort was similar for all three modes of ventilation with or without the heated humidifier. The findings in healthy individuals were similar to those in the patients with ARF. We can conclude from this study that the effect of the flow applied to CPAP systems itself has an impact as a limiting factor on the intra-helmet AH measured level. Unlike when the NIV helmet is applied with a conventional mechanical ventilator, early use of HH is recommended with continuous flow CPAP systems.

#### 10.4.1.4 Airleakage

Most of the previous studies did not analyze the amount of air leakage (l/min), and its impact on the clinical efficacy of NIV. Air leakage has a negative impact on humidity, which results in lower hygrometry levels and an exponential increase in the risk of NIV failure, as described in other chapters. Although we cannot establish or define what and where the “critical” level or condition of leakages is, a drop in the AH is a constant and relevant situation in any ranges of leakage.

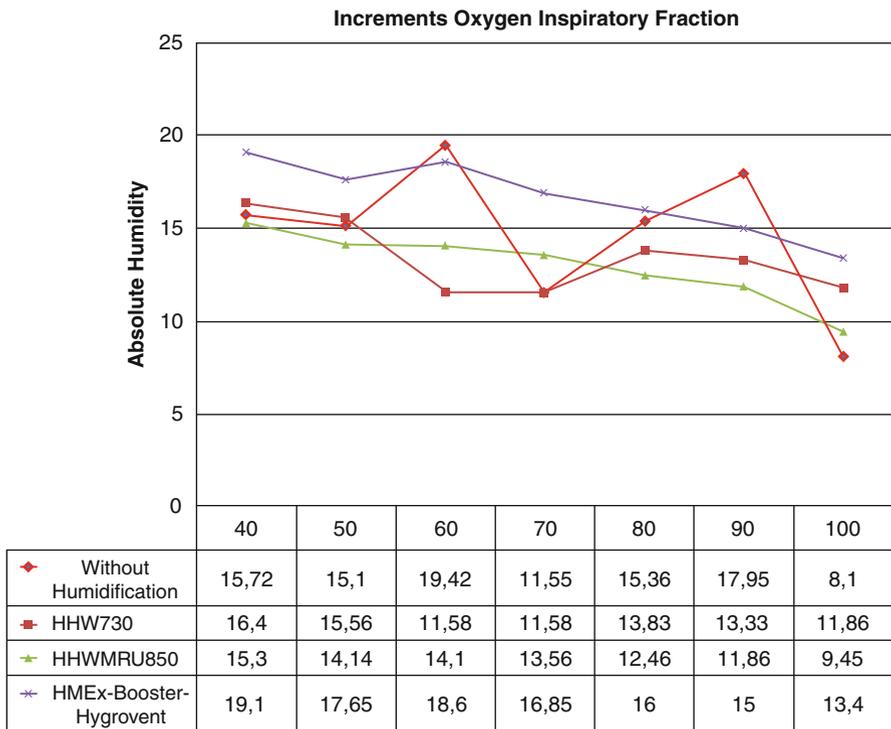
#### 10.4.1.5 Humidifiers

There is no clear consensus or recommendation concerning the best and most effective humidifier system with regard to the optimal humidity levels achieved. The hygroscopic humidifier produces physiological levels of AH (25–30 mgH<sub>2</sub>O/l), which are adequate for the functioning of the airways. However, the “effectiveness” of different humidification systems (moisturizing performance) can be variable

depending on the respiratory frequency range and the level of airflow, as Schumann et al. have described [15].

Currently, it is not known how different systems of active humidification (HH) with or without electrical wires, passive (or filter) or mixed systems (Booster technology) can influence the control of humidity.

Recently, Esquinas et al. analyzed the AH values in 12 patients with hypoxemic ARF, receiving NIV administered by means of BPAP ventilator and a face mask under a wide range of oxygen inspiratory fractions ( $FiO_2$ ) in four different NIV environments: (1) without humidification; (2) with HHW-MR850; (3) with HHW-730; (4) with a HME-Booster specific hygrometry (model Hycal) (Figs. 10.1 and 10.2) [16]. Average ranges of respiratory parameters were: mean respiratory rate:  $25.54 \pm 8.9$ ; levels of IPAP =  $21 \pm 4.7$  cmH<sub>2</sub>O; level of EPAP =  $7.8 \pm 2.5$  cmH<sub>2</sub>O; tidal volume ( $V_T$ ) =  $350 \pm 240$  ml; minute volume ( $V_E$ ):  $11.13 \pm 5.7$  l/min; level of leakage =  $42 \pm 33.00$  l/min. The level of IPAP was superior to that used by Holland et al. [12]. Patients were analyzed with an increment in  $FiO_2$  (40, 50, 60, 70, 80, 90 and 100%) in four different humidification conditions and devices (Fig. 10.2).



**Fig. 10.2** Hygrometry with increments of oxygen inspiratory fraction in differents ranges and conditions [16]: (a) NIV without humidification; (b) NIV with Fisher@Paykel-MR730 humidifier; (c) NIV with Fisher@Paykel MR850 humidifier; (d) NIV with humidifier (modelo Hygrovent, Medisize)

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## 10.5 Conditions of Heated Wire Humidifier (HWH)

The main purpose of applying an electrical guide is to prevent condensation of water and therefore better moisture. The systems that provide heated water without a wire induce molecules of water (droplet, not gas), which predispose to water condensation and as a result affect the level of humidification.

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## 10.6 Booster Technology

This is a mixed system (such Booster technology) where airflow and  $\text{FiO}_2$  enter a column of warm water (liquid) inside the chamber. The column of liquid water gives a greater proportion of molecules per inch, so the AH is higher, as shown in our study [16]. However, these devices can result in an increase in internal resistance that may be clinically relevant.

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## 10.7 Humidification Systems (Mixed Type Booster) Versus Humidification Systems with Electrical Guide

Another important aspect is the mixed heating system, where the range of AH that has been reached is higher. When we compared HWH and HME-Booster systems, the AH level was higher when NIV was applied with the latter; however, the HME-Booster was associated with a higher degree of patient-ventilator asynchrony and an increase of  $\text{PaCO}_2$  values [16].

For better physical control, temperature and humidity maintenance using HWH should match the inspiratory flow and inspiratory oxygen fraction. This will produce fewer condensation phenomena and less resistance, and a lower risk of re-breathing (less dead space). In general, passive humidifier moisture exchange (HME) or Booster technology is very effective but gives rise to a greater internal airway resistance (AWR), which can be potentially dangerous, particularly in patients with airway respiratory problems such as chronic obstructive pulmonary diseases (COPD). Other chapters examine these systems and their best known clinical indications.

### 10.7.1 Inspiratory Oxygen Fraction

In our study [16], initially parameters measured with our hygrometer were examined for the range and extent of AH with a progressive increase of  $\text{FiO}_2$ , observing the behavior of the AH in two extreme situations [(low fraction of inspired oxygen (0.21) and one with an inspired oxygen fraction of (1.0)].

In our observational clinical study that analyzed the value of the AH in the inspiratory phase of a breathing circuit in a series of patients on NIV by face mask,

it was noted that there is an inverse relationship between the level of inspired oxygen fraction and the value of AH. The relationship between the two variables is reversed ( $1/\text{FiO}_2 = \text{AH}$ ). An increase in  $\text{FiO}_2$  leads to a lower level of AH and the temperature distally. Oto et al. in a bench study reported similar findings with a significant inverse relationship between AH and  $\text{FiO}_2$  [9].

This observation implies that the value of AH in a given patient on NIV will be influenced by the  $\text{FiO}_2$  level. The absence of  $\text{FiO}_2$  control leads to the development of adverse effects in the upper respiratory tract, such as cilia damage and respiratory mucosa cell damage, which have potentially deleterious effects in critically ill patients with ARF. If we add mouth breathing, which is common among patients with ARF, this implies that the endogenous moisture conservation system in the airway will be ineffective in maintaining optimum moisture. Holland et al. and Oto et al. described under laboratory conditions that changes in the levels of PAP and  $\text{FiO}_2$  can influence the level of humidity in the airway circuit [9, 12]. The interpretation of this observation could be related to an increase in temperature generated by the ventilator as a result of the increment in the rotation of the turbine to generate more airflow and maintain higher PAP, which leads to a higher temperature of the breathing circuit and therefore a further decrease in RH. However, these observations have been made in the laboratory under controlled conditions, which did not account for some of the most important variables that influence the level of humidity in real patients with ARF, such as the levels of air leakages, higher levels of IPAP (20  $\text{cmH}_2\text{O}$ ), the ventilator and its behavior with a variable range of  $\text{FiO}_2$ .

Our group has analyzed the AH values in 12 patients with hypoxemic ARF receiving NIV administered by means of BPAP ventilator and a face mask under a wide range of  $\text{FiO}_2$  [16]. To do this as described in our methodology, a device was placed between the breathing circuit and the mask that measured the AH in the inspiratory and expiratory phase independently (Fig. 10.1).

Following implantation of this device, the patient was exposed to  $\text{FiO}_2$  in a progressively increasing pattern, and the AH was measured in a time interval immediately after the elevation of the  $\text{FiO}_2$ . The measurements were analyzed using a statistical analysis that compared the variables in each observation sequence (Fig. 10.2).

Our observations demonstrate that increases in concentration of  $\text{FiO}_2$  result in a significant decrease of the AH measured by the hygrometer at the interface. The largest decrease occurs in patients with NIV without a humidifier (scenario A), especially when the  $\text{FiO}_2$  setting was above 60% (Fig. 10.2). This can be defined by a “critical area of  $\text{FiO}_2$ ” with NIV in ARF. The present data suggest that as  $\text{FiO}_2$  increases, the absolute humidity significantly decreases. This has practical implications for deciding the best humidifier for different settings of  $\text{FiO}_2$ . With respect to the practical question, what are the ranges of  $\text{FiO}_2$  that are critical in patients with NIV? Probably, a range of  $\text{FiO}_2$  of more than 50% (60% for others) justifies the early use of humidification. This study confirms the observations of Holland et al. and Oto et al. [9, 12] where a rise in the level of IPAP and  $\text{FiO}_2$  contributes to a greater need for NIV humidification.

With respect to the optimal levels of AH or RH, there is no previously published evidence related to the optimal levels during NIV. Currently, there is no consensus on what is the best level for humidity in different NIV systems.

## 10.7.2 Factors Related to Patient Respiratory Pattern

### 10.7.2.1 Respiratory Pattern, Respiratory Rate

Tachypnea also implies a lower humidification in the inspiratory phase and a greater loss of AH due to the shorter expiratory phase (conservative phase).

### 10.7.2.2 Mouth Breathing

This perpetuates the loss of moisture and at a certain point the airway cannot compensate for the loss of moisture (expiratory phase).

### 10.7.2.3 High Peak Inspiratory Flow (PIF)

The inspiratory airflow affects AH and RH. As the PIF increases the AH decreases. Several variables affect the inspiratory flow pattern, including ventilatory volumes ( $V_T$ ), I:E ratio and the severity of respiratory failure (ARF).

### 10.7.2.4 Tidal Volume ( $V_T$ )

The changes in tidal volume can affect the interpretation and level of AH. Physiologically, the reduction in AH can be attributed to a greater volume of air/oxygen that needs to be humidified in the respiratory tract. Humidification therapy seeks to balance this increased humidification needs.

In our study [16], the average  $V_T$  was high compared to previous studies conducted in patients on NIV, particularly on nasal CPAP therapy among OSAS patients. In our study,  $V_T$  and minute volume ( $V_E$ ) were higher than that used in the Holland et al. study ( $V_T = 350 \pm 240$  ml;  $V_E: 11.13 \pm 5.7$  l/min). This shows that the interpretation of the hygrometry measurements in patients with ARF can be difficult, and can vary based on the patient's condition, and the NIV system and settings. In summary, available data suggest that the higher the  $V_T$  and respiratory rate are, the lower the humidity of the inspired air. This factor should be taken into consideration when managing patients on NIV [16].

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## 10.8 Expiratory Humidity: Clinical Implications

Most of the previous studies did not directly measure the moisture of the nasal cavity/oropharynx/hypopharynx. In our study, we performed a measurement of AH in the expiratory phase, and found that changes in the level of AH inversely correlated with the  $FiO_2$  (loss of endogenous humidification conservation phenomenon) [16]. Expiratory phase (Ex-pha) is considered a “conservative” or “moisture-saving” phase. Therefore, the expiratory values of AH should always be recorded and be maintained in a lower range in order to avoid moisture loss,

which can have significant clinical and physiological implications. Contrarily, significant air leakage can lead to a greater expiratory AH, which in turn can enhance moisture loss.

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## 10.9 Limitations of Hygrometry Studies

### 10.9.1 Inspiratory Oxygen Fraction

We used increasing values of  $FiO_2$  as our patients were in a range of hypoxemic ARF that could not be treated with a low  $FiO_2$ . This is an aspect to consider when studying the behavior of moisture in a gas or gas mixture in bench models.

Oto et al. [9] in a recent study assessed the effect of  $FiO_2$  on gas humidity both clinically and in a bench model. In an  $FiO_2$  range of 0.3–0.5, they could not find a relationship between  $FiO_2$  and humidity or oral dryness in the clinical study. However, in the bench study, they demonstrated that as  $FiO_2$  increased, the AH significantly decreased [9].

### 10.9.2 Sensor Technology

The signal recorded by the hygrometer sensor used has a wide range of variability (not known).

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## 10.10 Conclusions

1. It is essential to know the technical limitations of the humidification systems used and the implications of the environmental conditions, and the inherent characteristics of the used ventilator.
2. Results obtained from bench studies cannot be extrapolated and directly applied to the clinical setting in patients on acute or chronic NIV therapy as there are several factors that may influence the AH in the clinical setting, which bench studies do not account for. More studies are needed to assess the different factors that can affect AH of the inspired gas in real patients.
3. There is no clear consensus on the following: (1) When and what are the optimal roles of humidification in NIV in the acute setting or home use? (2) What are the recommended humidity levels? (3) What is the effectiveness of the current systems?
4. Few studies have analyzed the relative humidity measurements in patients with NIV, especially in patients with hypoxemic ARF.
5. Studies should use a system of specific humidity with separate measures of inspiratory and expiratory AH.

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# Practice of Humidification During Noninvasive Mechanical Ventilation (NIV): Determinants of Humidification Strategies

Antonio Matías Esquinas, Suhaila E. Al-Jawder,  
and Ahmed S. BaHammam

## Abbreviations

AH	Absolute humidity
ARF	Acute respiratory failure
BIPAP	Bilevel airway pressure
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
CPE	Cardiac pulmonary edema
ETI	Endotracheal intubation
FEV <sub>1</sub>	Forced expiratory volume in the first second
H1N1	H1N1 flu virus
HME	Heat and moisture exchanger
HWH	Heated wire humidifiers
ICU	Intensive care unit
IMV	Invasive mechanical ventilation
MV	Mechanical ventilation

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A.M. Esquinas (✉)  
International Fellow AARC, Intensive Care Unit,  
Hospital Morales Meseguer, Avd Marques Velez s/n,  
Murcia, Spain  
e-mail: antmesquinas@gmail.com

S.E. Al-Jawder  
Department of Medicine, Salmaniya Medical Complex,  
Manama, Kingdom of Bahrain

A.S. BaHammam  
University Sleep Disorders Center, College of Medicine,  
King Saud University, Riyadh, Saudi Arabia

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NAWR	Nasal airway resistance
NIV	Noninvasive mechanical ventilation
RH	Relative humidity
SAOS	Sleep apnea obstructive syndrome
SARS	Severe acute respiratory syndrome
VAP	Ventilator-associated pneumonia
VT	Volume tidal

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## 11.1 The Development of the NIV and Humidification

The provision of heat and humidity during mechanical ventilation (MV) is a standard of care worldwide [1]. There is an international consensus on the importance of humidification during invasive mechanical ventilation. The two humidification methods used during invasive MV are: the heated humidifier and the heat-and-moisture exchange (HME).

Noninvasive mechanical ventilation (NIV) is increasingly used in intensive care units (ICU) and emergency departments. Currently, it is the standard of care in the treatment of acute exacerbation of chronic obstructive pulmonary disease (COPD), acute cardiogenic pulmonary edema (CPE), and immunocompromised patients [2, 3]. Furthermore, NIV is available for home use for patients with sleep-related breathing disorders and chronic respiratory failure.

The routine use of humidification during NIV is controversial. There is no consensus statement defining the indications, patient selection, device selection, etc. The literature provides some evidence in terms of improving patient comfort and some other physiological parameters. However, well-designed studies are necessary to provide clear evidence to support or discourage the use of humidification in NIV [4, 5].

This chapter focuses on the use of humidification in NIV especially when applied to patients with acute respiratory failure (ARF). The physiological aspects of humidification have been covered thoroughly in other chapters of this book. The available data in the literature will be reviewed in order to develop an adequate strategy for the use of humidification in NIV.

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## 11.2 Humidification in NIV

The available data in this field are very scant. In addition, the published studies have a number of limitations that make their interpretation and the development of a clear approach for humidification difficult.

The following challenges are facing the development of a standard approach to humidification in NIV:

1. Absence of a consensus statement in this regard despite the availability of statements and recommendations that guide the overall use of NIV [2, 4].
2. Clinical and bench studies do not always reflect the actual practice because of the interaction of many variables in real patients [6–8].

3. No comprehensive survey has been conducted among practitioners [5].
4. Finally, the development of proper clinical practice guidelines depends to a large extent on the availability of randomized clinical trials in well-defined populations [9, 10]. Such data are missing at this stage.

Initial reports that alerted practitioners to the importance of humidification in patients on NIV came from observational studies conducted on patients with ARF. Those reports drew the attention of practitioners to the beneficial effects of applying humidification in NIV and the potential complications of inhaling dry gas [11–13].

The international consensus document on NIV published in 2001 did not thoroughly address the use of humidification in NIV because of insufficient data at that time, especially in applying NIV to patients with ARF [2]. In the last decade, there has been a major technological breakthrough in the manufacturing of humidifiers and a better understanding of how to incorporate these new humidifiers into the conventional devices of NIV. For example, with some of these humidifiers, some potential beneficial effects were described on the control of hypercapnia and work of breathing (WOB) [13]. Furthermore, a form of agreement that humidification of inspired gases should be a standard of care has begun to evolve among specialists [1]. Since 2005, a growing number of studies on the use of humidification in NIV have been published. In this chapter, we discuss the international survey we conducted in 2008 in 15 hospitals to explore the practice of incorporating humidification in NIV [5]. This chapter focuses on three key questions:

5. Who will benefit from humidification?
6. When to apply humidification?
7. How to incorporate humidification into NIV?

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### 11.3 Humidification in Early/Short-Term Use of NIV

NIV has been accepted worldwide as a standard of care for a number of respiratory disorders with clear indications in the emergency or home settings [1]. However, the practice of using humidification with NIV is not practiced routinely. Today, we understand that NIV may adversely influence the normal humidification system in the body and hence decrease moisture of the inspired gas [4].

Evaluating the response of the upper and lower airways in asthmatic patients hyperventilating cold air and breathing through the mouth demonstrated a decrease in FEV1 and an increase in nasal resistance [4]. Additionally, controlled asthmatics who are mouth breathers are also found to have an increase in nasal airway resistance [14]. Perhaps in obstructive crisis, when patients breathe through the mouth, insufficient moisture can play an important role, though this has yet to be documented.

One of the objectives of early use of humidification during noninvasive ventilation is to enhance tolerance and subsequent compliance with NIV. Discomfort or intolerance of NIV devices can result from different factors. Dryness of the mucous

membranes is one of the major contributing factors. Clinical trials are needed to determine whether the application of humidification can improve tolerance and enhance compliance to NIV [11, 14].

Humidification requirements should be tailored to the clinical characteristics and needs of each patient. Therefore, it is necessary to consider conditions that influence the moisture of the airway such as diseases of the respiratory mucosa, nasal septum deviation, medications, ventilator setting, and types of interfaces [14]. Nasal masks promote mouth leaks and therefore high unidirectional nasal flow, which results in increased nasal resistance and mouth opening, which in turn perpetuate mouth leak [14, 15]. Heated humidification as discussed in other chapters of this book acts by increasing the relative humidity (RH) of the air, reducing nasal resistance, and possibly increasing adherence to NIV.

The available literature lacks large-scale studies that evaluate the use of humidification for early and acute application of NIV. In clinical practice, it has been observed that some complications have developed in the absence of humidification and have contributed directly or indirectly to NIV failure and difficulties in endotracheal intubation [16]. The literature also lacks information about the frequency of this problem in patients with ARF on NIV. However, the application of a heated humidifier has proven to be useful and safe in the control of associated symptoms such as mucosal dryness, and therefore may contribute to improved comfort and compliance, especially in patients with chronic stable respiratory diseases [17, 18]. The development of an algorithm that stratifies patients into different risk groups is essential. Knowledge of the above-mentioned information and training and experience of the medical team applying the NIV are necessary to create a successful algorithm that can provide proper NIV application strategies.

Some factors that can influence the decision for early use of humidification are:

1. *Cost-effectiveness:*

The economic aspect and the cost of implementing humidification strategies is another considerable factor that can influence the selection of the humidifier to treat patients on NIV. A status of balance between the cost and the benefits of humidification should be achieved particularly when considering short-term use of NIV [18]. With regard to invasive mechanical ventilation (IMV), clinical aspects such as the duration of IMV, the increased risk of developing ventilator-associated pneumonia and weaning difficulties are well identified and important outcomes that favor the routine and early use of humidification [19, 20]. Unfortunately, in the case of NIV such clinical outcomes are not well identified and studied. Nevertheless, the development of complications as a result of not using proper humidification in patients with ARF treated with NIV will add to the cost of ARF treatment. Furthermore, failure of NIV for any reason will lead to a more costly intervention, such as endotracheal intubation. Therefore, it would be reasonable to identify patients on NIV at a moderate to high risk of developing complications if not using humidification and provide them with early humidification. One of the serious complications is the difficulty experienced with endotracheal intubation, which is attributed to the dryness of the upper airway mucosa [5, 8, 16, 21].

2. *Type of respiratory disease:*

The use of an early humidification strategy is required in respiratory failure secondary to some respiratory diseases, such as COPD and asthma, where the introduction of humidification has shown favorable effects [12, 14].

3. *Type of ARF:*

When discussing the available data pertaining to humidification in NIV, we have to categorize ARF into hypoxemic and hypercapnic. In patients with hypoxemic ARF, data supporting the use of humidification are available for those requiring  $\text{FiO}_2$  greater than 0.60 and those who are expected to require a prolonged use of NIV (>2 h) [15, 16].

In patients with hypoxemic ARF, data supporting the use of humidification are available for those requiring  $\text{FiO}_2$  greater than 0.60 and those who are expected to require a prolonged use of NIV (>2 h) [22] and characteristics of bronchial secretions [12, 23].

4. *Ventilatory parameters:*

The use of ventilatory parameters influences moisture loss. The higher the tidal volume ( $V_T$ ) and the higher the peak inspiratory flow rate, as with the NIV-CPAP systems, the greater the moisture loss is. Therefore, these physical conditions should be considered when applying NIV. Early institution of humidification reduces the effects of  $V_T$  and flow rate on humidity [12, 24].

5. *Bronchial secretion clearance:*

The rheological property of the viscosity of bronchial secretions is an important determinant of the early humidification strategy, especially in critically ill patients, as discussed in other chapters of this book [25]. The loss of these characteristics leads to retention of the bronchial secretions, especially in the distal airways of the bronchial system that are difficult to draw from, and results in increased airway resistance, impaired gas exchange, and airway obstruction, etc. [6, 15, 21]. The early combination of proper humidification with cough-assist techniques is useful and can improve the outcome of the NIV. Other factors that can encourage an early implementation of humidification include: older age, increased nasal resistance, mucociliary dysfunction, medication that can cause dehydration of the mucosa, chronic nasal or respiratory diseases, mouth breathing, and bronchial hypersecretion, especially if associated with COPD or bronchiectasis [21, 23, 25]. Despite the long list of proposed benefits of humidification in NIV, it is usually used without humidification, and controversy still exists regarding humidification efficacy [1, 4]. More studies are needed to document the benefits of humidification in patients with ARF who require NIV. Although we still need more evidence, the application of humidification in the above-discussed conditions is encouraged.

Contrarily, some factors deter the routine use of humidification in NIV. These factors include:

1. Absence of a consensus on the criteria needed to identify the appropriate candidates and indications for early humidification use.
2. In some cases, the humidifier model used can induce asynchronization problems via different mechanisms [6, 13, 19, 26, 27]:
  - I. Increasing the largest dead space,
  - II. Increasing work of breathing,

- III. Rebreathing problems,
  - IV. Causing a drop in inspiratory positive pressure.
3. Humidifier use may increase the cost of treatment with NIV [18].
  4. Concerns with cross-infection may limit the use of humidifiers. Heat-moisture exchange (HME) use for short-term NIV in patients with ARF is associated with less cross-infection [28]. The heated humidifier may carry a greater risk of spreading aerosols of respiratory viral infections (SARS, H1N1) or *Mycobacterium tuberculosis*. Nevertheless, the currently published work of the International Network Group, which was analyzed during the H1N1 pandemic, did not demonstrate such an association [29]. However, with the long-term use of NIV at home for OSAS, a potential risk of colonization and infection was described [30].

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## 11.4 Current Practice of Humidification in NIV

### 1. *Hospital organization.*

In some institutions, the decision to use humidification in NIV depends on the setting where the NIV is applied, such as emergency departments, intensive care units, or outpatient settings. Humidification is recommended when high-flow NIV-CPAP is used in patients at high risk even if it is going to be used for a short time [24]. Such practice is mostly seen in critically ill patients in the medical ICU or postoperative recovery units [31].

### 2. *Geographical data.*

The differences in humidity among countries would suggest a variation in the practice of humidification use. Nevertheless, the International Survey in Humidification Practice did not suggest these geographical factors to be important in the practice of humidification [5]. The European Survey of Noninvasive Ventilation Practices showed that humidification practice is common in Europe [3].

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## 11.5 The International Survey of Humidification Practice

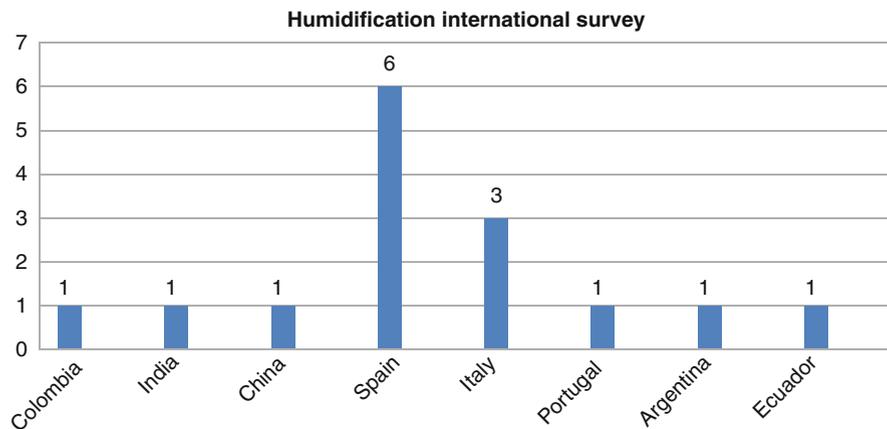
Surprisingly, no epidemiological survey has been conducted analyzing the practice of NIV humidification and its effects on short-term outcomes that can guide humidification practice [3, 5, 31]. Below is a summary of the available data.

### 1. *Types of humidifiers*

There are no data to support one humidification system over the other or to demonstrate the superiority of one over the other in terms of hygrometry efficacy or absolute humidity. The selection of the humidification system depends on other factors such as the interface (nasal, facial, helmet) [32], and the type of mechanical ventilator (home mechanical ventilator, high flow CPAP systems or ICU mechanical ventilators) [3, 5, 24, 31].

#### i. *Heated humidifier (HH)*

The HH acts as an active system to increase the AH to acceptable levels with a minimal effect on the set inspiratory positive airway pressure (IPAP) (on average



**Fig. 11.1** Countries participating in the International Survey-NIV

IPAP can decrease by a value of 0.5–1 cmH<sub>2</sub>O [20]. Currently HHs are preferred when the air is dry and cold with retention of bronchial secretions [26]. Unidirectional flow causes nasal mucosal dryness, promotes the release of inflammatory mediators, and increases nasal resistance [15, 21]. The HH increases the RH in the air, reduces nasal airway resistance, and may increase adherence to the NIV compared to HMEs [6, 8, 9, 17, 26, 33].

ii. *Heat and moisture exchanger (HME)*

As defined in other chapters, the HME acts by conserving moisture endogenously in the breathing circuit and is used when the patient has sufficient capacity to maintain AH of the inspired air. It is recommended to be applied early, but not recommended with all types of interfaces (nasal mask or face mask). They are ideal for the helmet system. Chanques et al. found that the humidifiers most commonly used are HMEs (52%), followed by HHs (26%), both (4%), and neither (19%) in postoperative resuscitation units.

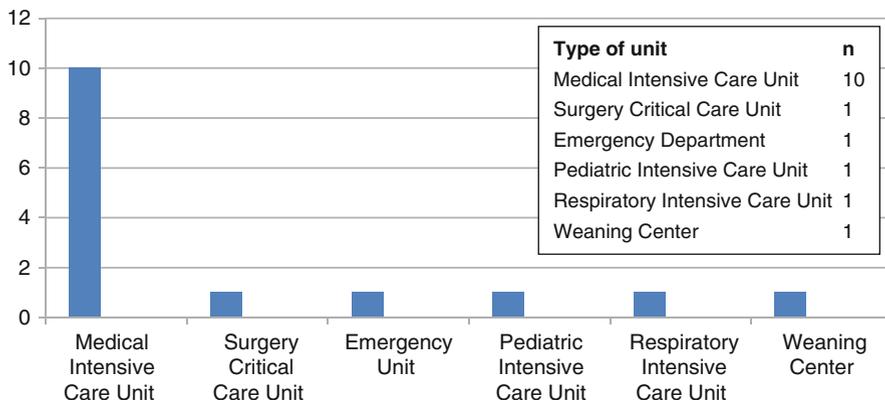
In our international survey, we analyzed the information from 15 hospitals including information on 1635 patients who had been treated with NIV in 2008 [5] (Fig. 11.1). When the results were analyzed in relation to the humidification system used, we found that the heated wire humidifier (HWH) was used most frequently (46.6%). No differences between countries, types of hospital settings, or acute care units were observed. This is different from the results of Chanques et al., who analyzed data collected from post-surgical observation units [31].

2. *Humidifier availability.*

Humidifier availability is influenced by several factors, including hospital area (acute care units, general wards, or out-patient setting), the type of ARF, the type of ventilator and interface used, and the number of patients treated simultaneously with NIV. The above are factors that determine the availability and type of humidifier to be selected [3, 5].

3. *Protocols of humidification.*

In our survey, we observed that 40% of the surveyed hospitals do not have written protocols to guide the use of humidification in NIV. The utilization of



**Fig. 11.2** Type of units in the NIV humidification practice survey

Protocols and centers		
(15 centers)		
Type humidifiers during NIMV		
<b>HWH</b>	<b>Never use humidifiers</b>	<b>HHW and HME</b>
<i>n</i> = 8	<i>n</i> = 6	<i>n</i> = 1
(53.33%)	(40%)	(6.6%)

**Fig. 11.3** Protocols of humidification practice and type of humidifiers used. *HWH* heated wire humidifier, *HME* heat and moisture exchanger. Models *HWH* used: hwh-fp-mru830-1; hwh-fp-(\*mr730, and others models = 1); hwp-fp= (410s, 810s) = 1. FP = fisher@paykel models

humidification in NIV seems to depend to a large extent on the practitioner's experience and preference. There are no large epidemiological studies to analyze other factors associated with humidification and response to NIV. [5] (Figs. 11.1, 11.2 and 11.3).

#### 4. Education.

Education is of paramount importance to achieve proper implementation and optimal results of humidification in NIV [26]. Our survey revealed that there was no formal training or education for NIV and humidification in the surveyed hospitals.

## 11.6 Conclusion

There are no large epidemiological studies to determine the best strategy for humidification in NIV. However, based on the available data, the best strategy to ensure proper application of humidification in NIV is to first identify the factors that may affect humidification and enhance moisture loss in patients with ARF, and then to apply the proper humidification system that suits each case based on the patient's

clinical condition, the ventilator parameters, and the interface used. Early application of humidification may benefit patients with hypoxemic respiratory failure or obstructive pulmonary diseases, and patients on high-flow CPAP systems, or who need prolonged use of NIV. Multi-center studies with large numbers of patients are needed to identify the patient groups who are likely to benefit from the addition of humidification to NIV therapy and to assess the effect of humidification on adherence to NIV, and its effect on different outcome measures.

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Antonio Costa and Ricardo Reis

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## 12.1 Introduction

Sullivan et al. [1] first introduced nasal continuous positive airway pressure (nCPAP) therapy in 1981, and since then this therapy has become the treatment of choice for obstructive sleep apnea.

Nasal CPAP is not only the specific antidote for the imbalance between excessive negative airway pressure and inadequate upper airway dilating forces that occur during sleep and lead to an obstructive airway, it is also noninvasive. However, despite being an effective therapy, treatment compliance is limited, ranging from 46% to 85%.

Many factors are thought to influence the use of CPAP, including the intensity of patient support and follow-up, mask claustrophobia [2], previous palatal surgery and perceived lack of benefit. However, the major obstacles to compliance seem to be the side effects associated with the use of nasal CPAP, such as nasal congestion, nosebleeds, dry nose or dry and sore throat, affecting between 30% and 50% of OSAS patients [3]. However, the appearance of serious complications that require stopping this technique are rare (e.g., severe epistaxis).

At present, therapies aimed at reducing the incidence and magnitude of these side effects include avoidance of drying medications, use of nasal corticosteroids, nasal moisturizing solutions, full-face masks and humidifiers. Of these, heated humidification has proven to be superior in reducing the adverse effects at the same time improving patient comfort.

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A. Costa (✉)  
Serviço de Pneumologia,  
Centro Hospitalar do Alto Ave, Guimarães, Portugal  
e-mail: amsantoscosta@gmail.com

R. Reis  
Serviço de Pneumologia,  
Centro Hospitalar Trás-os-Montes e Alto Douro, Vila Real, Portugal  
e-mail: ricardomcreis@gmail.com

## 12.2 Physiology

Inhaled air is conditioned in the nasal airways passages, where particulates are removed, and the air is warmed and humidified by the nasal mucosa because of the close apposition of highly vascular erectile sinusoid tissue and a slightly turbulent airflow distributed over a relatively large surface area. In fact, considering the size of the human nasal airway, the velocity of airflow, and the absolute amount of heat and water exchange that occurs, its efficiency is remarkable, recovering approximately one third of water delivered to the inspired gases from expired gases. Such function also requires maintenance, so every few hours, one of the nasal airways is responsible for air conditioning, while the other, because of its decreased airflow, replenishes the mucosa. This process is important for the maintenance of the conditioning process because unless heat and humidity are replenished to the mucosa, it becomes prone to desiccation, and nasal obstruction and morphologic alteration of the respiratory lining develop. Consequently, the primary nasal functions of humidification and removal of airborne particulates become much less efficient [4]. In addition, medications, anatomic abnormalities, various disease states and physiological factors, such as being in the supine position, reduce the ability of the nose to condition cold dry air [5].

## 12.3 Physiopathological Effects of Positive Pressure in the Upper Airways

During nasal CPAP administration, the relative and absolute humidity of inspired air are decreased, especially with high inspiratory pressure, compared to spontaneous breathing. This was well demonstrated by Holland et al., who found that increasing the IPAP leads to a rise in gas temperature (probably because of the action of the compressor) and consequently to a decrease in the relative humidity of the gas, unless additional water vapor is added to the respiratory circuit. The same study showed that the effects of the tested humidifier on the delivered pressure were small and probably not clinically important [6].

This decrease in humidity is further exacerbated by the presence of a mouth leak, which causes high unidirectional nasal airflow that overwhelms the capacity of the nasal mucosa to heat and humidify inspired air, leading to progressive drying of the upper airway mucosa as the nasal mucosa cannot recover water delivered to inspired gases during expiration. Besides dryness of the nasal mucosa, the presence of mouth leaks also decreases or terminates ciliary function, increases mucus viscosity, enhances nasal mucosal inflammation, and increases nasal mucosal blood flow and nasal congestion [7–11]. These mechanisms promote further mouth breathing, which may also increase pharyngeal obstruction due to relaxation of the mandibular muscles, increasing unidirectional high airflow through the nose and mouth, further drying the respiratory lining. Even in normal awake persons, simulation of a mouth leak while breathing with CPAP produces a subjective feeling of mouth and nose dryness, nasal congestion and an increase in nasal resistance. And although these

adverse effects of inadequate humidification may be partially reversible, they are directly proportional to the duration of the exposure and to the properties of the gas.

In this manner, treatment with positive pressure in the airways can affect nasal function and consequently alter CPAP therapy effectiveness. Although several mechanisms may be potentially involved in the development of nasal discomfort, mouth leaks during the use of nCPAP seem to be particularly important. Also, we know that a great percentage of patients submitted to chronic CPAP treatment have conditions that favor the appearance of mouth leaks, such as nasal septum deviation, chronic rhinitis, nasal polyps and uvulopalatoplasty, that make the daily use of CPAP very uncomfortable.

And so, the use of heated humidification of inspired air can attenuate the increase in mucosal blood flow and nasal resistance under experimental conditions and diminish adverse upper airway symptoms in OSAS patients chronically treated with nCPAP [12–14].

However, many questions about humidification treatment remain unanswered, e.g., the level of absolute humidity required for optimal treatment results is not clear, nor is the precise identification of patients who need humidifier-assisted treatment nor heated breathing tube humidification.

Room temperature and relative humidity information is usually forgotten in clinical trials, making it difficult to extrapolate the results to other populations where these variables are different for climatic or quality of life related reasons.

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## 12.4 Indications

In theory it seems logical to humidify non invasive mechanical ventilation (NIMV) gas, as we now know that an inadequate humidification increases mucus viscosity and retained secretions, resulting in increased airway resistance, thus leading to subjective feelings of discomfort that diminish patients therapy compliance and can also reduce the efficiency of CPAP use.

However, NIMV has traditionally been used without humidification, and questions remain as to who will benefit from NIMV humidification. In fact, the consensus statements and guidelines for NIMV use, contain conflicting recommendations regarding added humidification [15–17], which reflects the paucity of published data.

However, the use of humidification, especially heated humidification, has proven to be a safe and efficient way to relieve secondary nasal symptoms caused by mucosal dryness associated with cold air, thereby improving comfort with the ventilator and increasing compliance to CPAP therapy.

Another option to reduce nasal symptoms and mouth leaks is the use of facial masks; however, despite their many advantages, this interface is considered less comfortable by the patients and thus reduces patient therapy adherence. Other methods, such as the use of nasal relievers, nasal corticosteroids or nasal moisturizing solutions, have sparse scientific evidence.

In clinical practice, humidification is usually reserved for patients who complain of persistent and severe side effects related to upper airway symptoms, and its introduction may be delayed for several weeks or months.

Waiting for the development of upper airway symptoms may identify the patients most likely to benefit from humidification, but delaying its introduction may reduce potential benefits of compliance. Indeed, patients who become irregular CPAP users (defined as extreme variability in use averaging 4 h/night) can be identified by the fourth day of treatment [18].

Although the use of routine humidification is not recommended, the following factors can be considered as predictors of the need to eventually use of humidification:

- Advanced patient age, as with increasing age there is progressive nasal resistance and reduction in mucociliary activity of the airways;
- Medical treatment with drugs that can contribute to mucosal dehydration, e.g., antihypertensive and antidepressant medication;
- Previous nasal conditions that favor nasal inflammation and nasal dryness, and promote mouth leaks, such as chronic rhinitis, polyposis, sinusitis and nasal septum deviation;
- Uvulopalatopharyngoplasty – due to the frequent presence of mouth leaks;
- Patients with bronchial hypersecretion, in conditions such as COPD and bronchiectasis, especially when airway dryness and retention of secretions are a concern.

In regard to the influence of humidification in the adherence to CPAP therapy, Massie et al. [12] have demonstrated a small but important increase in the use of CPAP (an average of more 30 min per day) with the use of humidification. Although showing a small increase in patient adherence, the use of humidification in CPAP therapy also seems to increase patient satisfaction.

Other studies have evaluated the benefit of heated humidification during initial CPAP titration use and its effect on upper airway dryness, CPAP compliance and patient comfort in the short term without finding significant benefit of with use of humidification.

In conclusion, the initial introduction of heated humidification in CPAP therapy seems to provide no benefit concerning compliance or side effects. Therefore, heated humidification should be reserved for symptomatic treatment of nasal complaints. Patient education and support remain the only initial interventions that increase compliance.

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## 12.5 Contraindications

No absolute contraindications exist to the use of humidification in CPAP. The use of humidification does not seem to produce new or more side effects from CPAP therapy; in fact the few problems relative to the addition of a humidifier are not of a clinical nature. One problem is due to the increased cost of nCPAP therapy with added humidification that also complicates the practical modalities (like transport,

cleaning, etc.). Also, the patient needs to be informed about the hassle associated with the condensation forming within the mask and/or tubing that drips on the patient's face, which can be particularly bothersome. This condensation is caused by cooling of the temperature of the air traveling within the delivery tube, due to the cooler room temperature, thereby reducing the maximum level of humidity the air can hold, resulting in an accumulation of water in the breathing tube, or condensation, and consequently reducing the level of humidity delivered to the patient's mask. For that reason many patients who require a heated humidifier complain of condensation forming in the tube of the CPAP device, especially during winter. However, this inconvenience can be easily avoided with the use of controlled heated breathing tube humidification technology, which prevents the condensation of water in the tubing.

The use of humidification also brings new concerns, such as the risk of infection, especially given reports of microbes contaminating ventilator tubing, humidifiers and nebulizers. In an attempt to resolve this concern, manufacturers have eliminated older "bubble-through humidifiers" because of the fear that aerosolized water particles could transport bacteria and increase the risk of respiratory tract infection. However, a more recent study has demonstrated that heated convection humidifiers, as used in current CPAP systems, do not aerosolize water droplets [19]. Instead, these systems produce molecular water vapor, which cannot transport bacteria or other microorganisms.

In conclusion, the use of humidification seems to be a safe therapy, with the only contraindication being the non-adaptation or discomfort of the patient.

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# Pros and Cons of Humidification for CPAP Therapy in the Treatment of Sleep Apnea

# 13

Arschang Valipour

Obstructive sleep apnea (OSA) is a disorder characterized by episodic collapse or narrowing of the upper airway during sleep. Closure of the upper airway results in hypoxemia accompanied by incremental breathing efforts that culminate in arousal, re-opening of the upper airway and brief hyperventilation followed by return to sleep. OSA affects 4% of men and 2% of women, and if left untreated has considerable deleterious effects, including excessive daytime sleepiness, neurocognitive deficits, increased incidence of motor vehicle accidents, as well as associations with hypertension, myocardial infarction and stroke.

Introduced in 1981, nasal continuous positive airway pressure (nCPAP) therapy has since become the treatment of choice for OSA. nCPAP acts as a “pneumatic splint” by delivering a predetermined constant positive pressure during both inspiration and exhalation. The result is an increased cross-sectional area of the upper airways, particularly with respect to the oro- and hypopharynx, which prevents upper airway obstruction during sleep.

Multiple beneficial effects of nCPAP treatment have been documented, including improvement of OSA symptoms, such as daytime sleepiness, quality of life, and a reduction of risk for cardiovascular morbidity and mortality associated with sleep apnea. Furthermore, regular nCPAP use has been associated with a reduction in the risk for future motor vehicle accidents. Initial acceptance rates for nCPAP treatment, however, vary between 50% and 90%, with an average of approximately 80%. Of those using nCPAP, adherence rates (more than 4 h use for 70% of days) have varied from 40% to 80%, with the highest figures reported for studies with a systematic educational program for nCPAP treatment. The most frequently reported factors associated with low acceptance and adherence rates include side effects

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A. Valipour

Department of Respiratory and Critical Care Medicine,  
Ludwig-Boltzmann-Institute for COPD and Respiratory Epidemiology  
Otto-Wagner-Spital, Sanatoriumstrasse 2, 1140 Wien, Austria  
e-mail: arschang.valipour@wienkav.at

associated with treatment, such as nasal congestion, dry nose or throat, and discomfort associated with cold air, which are reported by as many as 65% of patients using nCPAP [1].

Particularly chronic nasal congestion can compromise a patient's ability to successfully utilize nCPAP. The nasal mucosa has a considerable capacity to heat and humidify inspired air. This capacity, however, can be overwhelmed at high flow rates in association with nCPAP application and under conditions of unidirectional flow such as mouth leaks. The flow of cold air through the nose dries the mucosa, which results in the release of vasoactive and proinflammatory mediators. These mediators increase superficial mucosal blood flow and engorgement of deeper capacitance vessels, leading to increased nasal resistance [2]. Increased nasal resistance in turn promotes mouth breathing, creating a pathologic vicious circle. Martins de Araujo and co-workers [3] previously demonstrated that patients complaining of nasal discomfort experience major mouth leaks up to 30% of the total sleep time during nCPAP. The authors furthermore observed a significant reduction in humidity of inspired air during periods of mouth leak.

The above-mentioned complications can be largely prevented by humidifying inspired air. A humidifier usually consists of a hot plate, which raises the temperature of the water in the humidification chamber in order to increase water vapor production. Humidification is generally employed to alleviate dryness and congestion of the upper airways in OSA patients. The use of humidifier devices, however, is also associated with a number of disadvantages, such as the need for more space, higher costs, more servicing, cleaning and transport effort. Some of these factors may result in an increased likelihood of operating errors by the patients and infections due to colonization of the humidifier by pathogens. In fact, Sanner and co-workers [4] previously reported that the use of humidification was associated with an increase in infectious complications in association with nCPAP treatment for sleep-disordered breathing.

Thus, it appears reasonable that adding a humidifier to nCPAP treatment should be reserved for carefully selected patients. In this context there are a number of questions that need to be addressed: What is the optimal timing of initiating humidification? Does humidification result in increased nCPAP compliance rates? Is there a clinical difference between cold-passover and heated humidification? How does heated humidification work in a cold environment? Are there alternatives to humidification in preventing upper airway side effects in association with nCPAP treatment for OSA? Only few reports have attempted to provide an answer to some of these questions, which are summarized below.

Wiest and co-workers [5] investigated whether, during the initiation phase of nCPAP treatment in the sleep laboratory, prophylactic humidification would result in improved initial patient comfort and acceptance. In 44 consecutive, previously untreated OSA patients with no history of upper airway dryness, nCPAP titration with and without humidification was performed on 2 consecutive nights in a randomized order. The patients were interviewed after each treatment night in order to establish the comfort of the treatment, and, after the second treatment, they were asked which of the 2 nights they considered more pleasant, and which treatment they would

prefer for long-term use. Summarizing their results, the use of a humidifier system under the circumstances described above failed to improve initial acceptance and comfort of treatment. Using a randomized cross-over design with OSA patients being randomized to either heated humidification or placebo humidification, Neil et al. [6] similarly observed no significant difference in treatment satisfaction with prophylactic humidification when initiating nCPAP treatment. Duong et al. [7] extended these findings by demonstrating that the use of heated humidification during the initial titration study of nCPAP offered no additional benefit with respect to nasal airway resistance, nasal symptoms and therapeutic CPAP level. They furthermore observed no significant difference in the overall acceptance of therapy with prophylactic humidification assessed over a period of 1 year compared to addition of heated humidification only when patients complained of relevant upper airway symptoms that were unresponsive to simpler measures (e.g., intranasal steroid application, temporary use of local vasoconstrictors, etc.). The latter reflects the most useful approach in clinical practice. Thus, humidification should be reserved for patients who complain of persistent and severe side effects related to upper airway symptoms with nCPAP. Nevertheless, it appears reasonable to identify predictors that are most likely to require humidification when initiating nCPAP therapy. In their report Rakatonanahary and co-workers [8] observed that patients older than 60 years of age and those with conditions promoting mouth leakage, such as deformity of nasal septum, chronic nasal mucosal disease, polyposis and/or previous uvulopalatopharyngoplasty, are most likely to require humidification in clinical practice. According to this report, 50% of the overall population required humidification. About one half of these patients were successfully treated with cold-passover humidity, which resulted in improved upper airway symptoms; however, the daily use of nCPAP was not significantly modified. The other patient group with persistent upper airway symptoms despite cold humidification was changed to heated humidification after 4 weeks. The symptoms disappeared in almost all of the patients with increased nCPAP compliance rates.

Massie and co-workers [9] used a different approach to assess the benefits of cold versus heated humidification systems. The authors studied 38 patients who were randomized to heated or cold passover humidity using a cross-over study design. There were no differences between randomized groups in age, gender, body mass index (BMI), sleep apnea severity or nCPAP pressure. Humidification in this study was supplied to all eligible patients starting nCPAP, and it was initiated during pressure titration. Seventy-six percent of the patients preferred the heated humidifier to the cold passover humidifier. The authors also observed higher compliance for nCPAP use with heated humidity ( $5.5 \pm 2.1$  h/night) compared to nCPAP use without humidity ( $4.9 \pm 2.2$  h/night;  $p=0.008$ ), but no difference was observed between CPAP use with cold passover humidity and CPAP without humidity, or between heated and cold passover humidity. Similar results were observed for specific side effects that compromised nCPAP use, such as dry nose, mouth or throat. This suggests that the increased compliance with heated humidity was a result of fewer adverse side effects. Furthermore, heated humidity, but not cold passover humidity, was associated with feeling more refreshed on awakening.

When using a conventional humidifier, it has to be acknowledged that the level of humidity delivered to the patient may be influenced by ambient room temperature. Thus, cool room temperatures can affect the delivery of humidity to the patient by cooling the temperature of the air travelling within the delivery tube, thereby reducing the maximum level of moisture the air can hold. The result is an accumulation of water in the breathing tube, or condensation, and consequentially, a level of humidity delivered to the patient's mask that is lower than that desired. During the winter months, many patients who require a heated humidifier to encounter nasal/oral or pharyngeal problems complain of condensation forming in the tube of the CPAP device. On the basis of the current literature, there is no consistent evidence that this condensation reduces effective CPAP pressure due to the reduction of the CPAP delivery tube's effective lumen; however, individual patient reports suggest more frequent awakenings due to condensation, particularly during the winter months. Nilius and co-workers [10] demonstrated a CPAP device with an integrated humidifier consisting of a heater plate and water chamber in addition to a heated breathing tube. The internal algorithm of the humidifier takes into consideration a number of inputs, such as set pressure, ambient temperature and flow, and using these inputs adjusts the power to the heated breathing tube in order to maintain the individually adjustable heat and humidity all the way from the chamber output to the patient's mask. Using this system the authors were able to reliably avoid a considerable amount of condensation in the CPAP mask and tubing system. The latter resulted in significantly improved sleep quality and subjective experience. Due to higher treatment costs associated with this system, it should be reserved for those who regularly report problems of condensation due to cool room temperature.

Finally, nCPAP therapy with heated humidification may in some cases not fully correct mucosal dehydration caused by mouth leaks. To resolve this problem the use of a face mask has been empirically proposed as an adjunct method to prevent airway dryness during nCPAP in OSA patients. A face mask maintains the saturated gas returned during the expiratory phase, and therefore counterbalances the difference between dry inspired gas and saturated expired gas at each cycle, establishing an optimal airway humidity gradient [3]. Despite the advantages of a full face mask to reduce nasal symptoms, most patients with OSA prefer a nasal mask than a face mask [11]. In the author's experience a full face mask should be preferably used in patients with "chronic" mouth breathing, those with CPAP pressures greater than 12 cmH<sub>2</sub>O, or those receiving bilevel ventilatory support because of concomitant obesity hypoventilation or COPD.

Increasing usage of modern CPAP variants, such as auto-adjusted and/or expiratory pressure relief positive airway pressure (EPR-PAP), is usually associated with lower average therapeutic CPAP pressures, and thus lower flow rates and fewer upper airway side effects. EPR-PAP was developed to improve patient comfort by allowing the airway pressure to fall below the prescribed airway pressure in early expiration with a return to the prescribed level at end exhalation. We recently observed a significantly lower number of humidifier prescriptions in patients receiving EPR-PAP compared with conventional CPAP despite similar severity of sleep disordered breathing and baseline clinical characteristics [12].

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## **Section V**

# **Humidification and Invasive Mechanical Ventilation**

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# Humidification in Intensive Care Medicine: General Approach to Selected Humidification Devices and Complications of Mechanical Ventilation

# 14

Pedro F. Lucero, David W. Park, and Dara D. Regn

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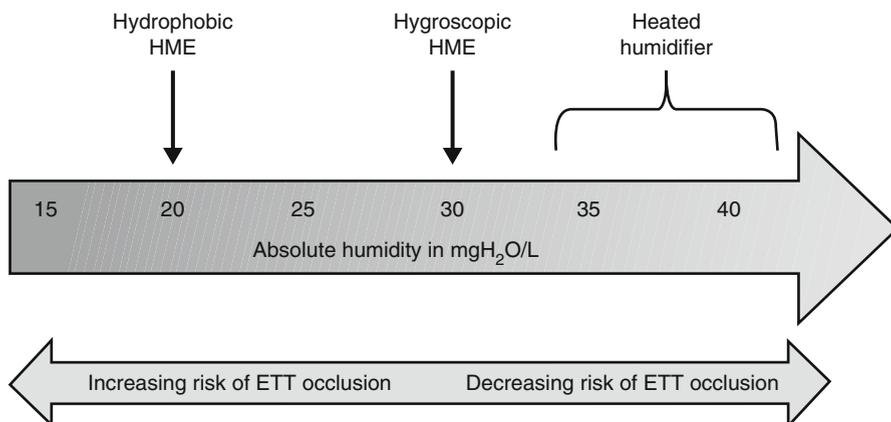
## 14.1 Introduction

When the tracheal mucosa is bypassed via endotracheal tube (ETT) intubation or from a surgically placed tracheostomy, humidification is essential to preserve tracheobronchial mucosal integrity [1]. Without humidification, the tracheal mucosa will lose ciliary function, develop inspissated secretions, and the underlying connective tissue will undergo structural changes [2–5]. Williams et al. performed a meta-analysis evaluating the relationship between the humidity and temperature of inspired gas and airway mucosal function [6]. They developed a model suggesting above or below optimal temperature, and humidity conditions can lead to impaired airway mucosal dysfunction, or, vice versa, that adequate mucociliary function is an indicator of ideal humidification. Oostdam et al. showed animals that inspired dried air demonstrated a significant reduction of extravascular water of the loose connective tissue of the airways and an increase in airways resistance to histamine [2]. ETT occlusion secondary to thickened or dried secretions is also strongly linked to suboptimal humidification [5, 7]. The most common way to avoid these and other potential complications (Box 1) is accomplished by applying humidification from non-heated-wire humidifiers, heated-wire humidifiers, or a heat and moisture exchanger (HME) [4, 8]. The goal of each of these humidification devices is to provide tracheal humidification consisting of heat and moisture to the inspired gas with a minimum of 30 mgH<sub>2</sub>O/l or 100% relative humidity with a delivered gas at 30°C [4, 5].

Non-heated wire humidifiers are becoming increasingly less popular because of the concerns over respiratory condensation [8]. In patients requiring long-term

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P.F. Lucero • D.W. Park • D.D. Regn (✉)  
Pulmonary/Critical Care/Sleep Medicine, Wright-Patterson AFB Medical Center,  
Uniformed Services University of the Health Sciences and Wright State University,  
Boonshoft School of Medicine,  
2517 Acorn Dr, Kettering, OH 45419, USA  
e-mail: drregn@hotmail.com



**Fig. 14.1** Recommendation of Lellouche et al.

mechanical ventilation >96 h, the heated-wire humidifiers are the device of choice [4, 8]. Other indications for heated humidifiers include contraindications for HMEs as listed in Box 2 [4]. Heater humidification devices are capable of delivering gases with 100% relative humidity near 37°C body temperature. However, heated humidifiers are more expensive than HMEs, and have been associated with a potential for electrical shock, hyperthermia, thermal injury, and nosocomial infections [4, 9, 10]. Inappropriate settings of temperature or humidification can also lead increased resistive work of breathing due to mucous plugging and/or life-threatening occlusions of endotracheal or tracheostomy tubes [8, 11].

HMEs are disposable devices that function by passively storing heat and moisture from the patient's exhaled gas and releasing it to the inhaled gas (an artificial nose) [4, 9]. Their regulation of humidity is slightly lower than that of heat humidifiers, but their clinical efficacy is similar [12]. HMEs are hydrophobic, hygroscopic, or a combination of both. Hydrophobic HMEs have the best antimicrobial properties and lower humidity retention [9]. Hygroscopic HMEs have less antimicrobial filtration but better humidity qualities, and all HMEs are able to absorb moisture in the expired air. HME humidity and temperature settings are predetermined by the manufacturer based on in vivo studies. The optimal HME performance specification is not well defined; however, Lellouche suggests an absolute humidity <30 mgH<sub>2</sub>O/l is associated with a risk of ETT occlusion (Fig. 14.1) [13]. The airway resistance has been shown to be less in hygroscopic models compared to hydrophobic or combination HMEs [14].

HMEs are more attractive than heated humidifiers for patients requiring mechanical ventilation of short duration because they are less costly and easier to use [9–11]. They are recommended for shorter durations <96 h or during patient transport, and have been used safely for up to 7 days [4, 10]. Most manufacturers recommend changing HMEs every 24 h despite a plethora of literature supporting use for 96 h except in COPD patients [10]. HMEs appeared to lose the ability to maintain humidity for more than 48 h in patients with COPD. They do not require electricity,

and there is no risk of thermal injury or concerns about excessive condensation. Like heated humidifiers, they possess a unique set of complications, i.e., hypothermia, hypoventilation due to increased dead space, impaction of secretions, and increased work of breathing. HMEs also have contraindications (Box 2) [4].

HMEs that possess a large dead space present another problem that clinicians need to be aware of, particularly when using low tidal volume for lung protective strategies [3]. Resultant hypercarbia and/or increased minute ventilation may ensue. Some experts recommend removing HMEs in patients with acute respiratory distress syndrome and changing to heated humidifiers.

Ventilator-associated pneumonia (VAP) has received much attention over the past several years and has been related to multiple variables, including humidifiers [15]. Other etiologies with stronger relationships to VAP include microaspirations from around the endotracheal cuff, colonization of the GI tract, poor provider hand hygiene, inadequate oral care, prolonged sedation, and patients in recumbent positions of less than 30° [15]. Nevertheless, the humidifier can be a real threat if not managed correctly. Routine inspection of the humidification device for secretions and or condensate in the patient circuit should be scheduled [4]. Increasing evidence is showing that the rate of VAP is lower when using a passive (HME) rather than active humidification device at a relative risk of 0.7 [16]. The risk of occlusion from secretions, hypothermia, and prolonged intubation often prohibits the continued use of HMEs. The exact mechanism by which HMEs reduce VAP is not entirely clear, but most experts recommend HMEs in all patients when there are no contraindications.

Once the selected humidification device has been chosen, determining the best level of heat and humidification, as previously mentioned, is difficult. Sottiaux and Branson suggest a minimum of 32°–34°C and 100% relative humidity [5]. The AARC recommends that the absolute humidity cutoff should probably be <30 mgH<sub>2</sub>O/l; however, there is no evidence that any specific humidity level improves outcome [3]. Nevertheless, the deviation of tracheal mucosa function relative to suboptimal humidity cannot be ignored [1, 16]. The AARC recommends the ideal inspired gas temperature should be near the patient's airway opening and the inspiratory gas should not exceed 37°C [4]. In general, HMEs probably improve baseline variables of humidification and temperature, but whether they perform according to specification is arduous to actually measure [3].

Lemmens et al. reviewed three different HMEs during routine anesthesia practice to determine whether the devices actually performed according to the manufacturers' specifications [17]. Their main findings showed that following the manufacturers' specifications did not reliably predict performance during routine anesthesia procedures. Only one HME performed according to specifications. The other two performed at less than the values specified by the manufacturers, but did provide humidification. Solomita evaluated non-heated-wire humidification, heated-wire humidification, and HMEs to determine the effects of humidification on the volume of airway secretions in mechanically ventilated patients [8]. Their results revealed that measurement of temperature alone was inadequate to predict humidification and non-heated-wire humidification was associated with a greater secretion volume. In practice, humidity is measured by a combination of temperature

and arbitrary clinical observation of secretion accumulation because formal measurements of humidity are limited by technology and cost [3, 5].

**Box 1**

Complications of mechanical ventilation with suboptimal humidification:

**Cyto-morphologic airway modifications**

Decrease in sol phase depth

Hyperviscosity of airway secretions

Tracheal inflammation

Deciliation, epithelial ulceration, and then necrosis

**Functional airway modifications**

Decrease in the humidification capabilities

Downward shift of the ISB

Decrease in mucus transport velocity, secretions retention

Decrease in the bronchospasm threshold

Alteration of the ciliary function, ciliary paralysis

Airway obstruction and increase in airflow resistance

**Pulmonary, mechanical, and functional alterations**

Atelectasis

Decrease in functional reserve capacity and compliance

V/Q mismatching, increase in intrapulmonary shunt, hypoxemia

Pulmonary infection

*Source:* Ref. [5]

**Box 2****HME contraindications in patients with:**

Thick, copious, or bloody secretions

Expired tidal volume less than 70% of the delivered tidal volume (e.g., those with large bronchopleurocutaneous fistulas or incompetent or absent endotracheal tube cuffs).

Body temperatures less than 32°C

High spontaneous minute volumes (>10 l/min)

When the patient is receiving aerosol treatments when the nebulizer is placed in the patient circuit

*Source:* Ref. [4]

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## 14.2 Conclusion

The tracheal mucosa and ciliary function can be severely impaired without adequate humidification in patients who are mechanically intubated or undergo tracheostomy [1]. Resultant complications can occur from increased secretions and infection, or

endotracheal tube occlusions can ensue [2, 5]. Although the exact amount of humidification and temperature has not been defined, there is a large body of literature supporting that the minimal physiological conditions of 32°–34°C and 100% relative humidity should be maintained [5]. Objective assessment of humidity is difficult to make, so routine monitoring of the quantity of secretions is recommended [4]. HMEs are generally preferred if there are no contraindications in patients who require mechanical intubations of short duration [4, 10]. If mechanical ventilation is prolonged, optimal humidification is required to ensure tracheal mucosal function. Ultimately, the humidification devices and target settings will change as more studies emerge, but the indications will remain the same.

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Michael J. Morris

## Abbreviations

COPD	Chronic obstructive pulmonary disease
HH	Heated humidifier
HME	Heat and moisture exchanger
MV	Mechanical ventilation
PaCO <sub>2</sub>	Partial pressure of carbon dioxide
PS	Pressure support
RR	Respiratory rate
V <sub>D</sub> /V <sub>T</sub>	Dead space ventilation
V <sub>E</sub>	Minute ventilation
V <sub>T</sub>	Tidal volume

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## 15.1 Introduction

The application of heat and humidification to inspired gases during mechanical ventilation (MV) is necessary to prevent hypothermia, airway secretions, and destruction of the airway [1]. Warming and humidification are either accomplished through the use of heated humidifiers (HH), or alternatively heat and moisture exchangers (HME), both hygroscopic and hydrophobic. The preference of a HH versus an HME varies depending on the type of patient, length of MV, cost, or choice by respiratory therapists. In general, the use of an HME is more common in surgical patients and those patients with potential short-term MV because of concerns for airway obstruction [2]. There are some recommendations that stipulate the type of

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M.J. Morris  
Pulmonary/Critical Care, Department of Medicine, Brooke Army Medical Center,  
Fort Sam Houston, TX 78234, USA  
e-mail: michael.morris@amedd.army.mil

humidification where HHs are preferable and HMEs are contraindicated: copious amounts of secretions, very small or very large tidal volumes [expired tidal volume ( $V_T$ ) < 70%, high minute ventilation ( $V_E$ ) > 10 l/min], low synchronized intermittent MV rates, and hypothermia [3]. A recent meta-analysis by Siempos et al. evaluated 13 randomized controlled clinical trials of HH compared to HME and found no differences in the incidence of ventilator-associated pneumonia, mortality, intensive care unit stay, duration of ventilation, or airway occlusion [4]. Despite the lack of outcome differences, the use of either modality (HH vs. HME) may have varying effects on respiratory mechanics in the ventilated patient. This section explores the available data on the effect of airway humidification devices on airway mechanics such as respiratory rate (RR),  $V_T$ , and  $V_E$ , and its measurement in the ventilated patient.

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## 15.2 Heated Humidifiers Versus Heat Moisture Exchangers

The general principle of the HH is to heat water contained in a humidification chamber with inspired gas passing through it. Cooling of humidified gases prior to entry into patients can lead to abundant condensation in the tubing; this is prevented by electric heater wires in the circuit that maintain heating. There is no increase in dead space with HH and consequently no effect of respiratory mechanics, such as  $V_T$  and partial pressure of carbon dioxide ( $\text{PaCO}_2$ ). The HME is an in-line device that contains either a hygroscopic condenser or a hydrophobic element to maintain warming and humidification. It is commonly referred to as an “artificial nose” in the literature. Newer HMEs contain both types of condensers to maintain the highest humidification levels. Differing from the HH, an important concept in the use of HMEs is the increase in dead space in the ventilator circuit due to the HME internal volume, which can be as large as 95 ml. This may potentially affect carbon dioxide retention,  $V_E$ , and increased work of breathing due to the increased dead space and internal resistance of the HME. In most cases, this can be overcome by increasing the level of pressure support, but is a potential contraindication for HME use.

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## 15.3 Comparison Studies of Respiratory Mechanics

Pelosi et al. [5] performed the first study comparing HH with two different hygroscopic-hydrophobic HMEs (each with different dead space and resistance) on 14 patients on MV using PSV. Patients were divided into two groups and completed a 90-min period with the HH and the HME apiece. As expected, there was a significant increase in  $V_E$ , RR, and work of breathing. Increase in  $V_E$  was reported due to increase in  $V_T$  ( $0.49 \pm 0.13$  vs.  $0.56 \pm 0.14$  l in group 1;  $0.38 \pm 0.12$  vs.  $0.44 \pm 0.12$  l in group 2). Tidal volume decreased with a decrease in PSV of 5  $\text{cmH}_2\text{O}$  and increased with an increase of 5  $\text{cmH}_2\text{O}$  over baseline values [5].

Le Bourdelles et al. [6] tested 15 patients with an HME and a HH in a random order during spontaneous weaning trials with inspiratory pressure support. The HME gave a significantly greater  $V_E$  than the HH ( $9.3 \pm 0.8$  vs.  $8.1 \pm 0.8$  l/min;

$p < 0.005$ ), because of increased RR ( $21 \pm 2$  vs.  $19 \pm 2$  breaths/min;  $p < 0.05$ ). Tidal volume was unchanged for HME and HH ( $470 \pm 32$  ml vs.  $458 \pm 39$  ml). A higher PaCO<sub>2</sub> with HME than with HH revealed an insufficient alveolar ventilation response to the increase in dead space. The authors commented on the need to increase  $V_E$  in spontaneous ventilation when an HME is used, especially for difficult weaning from mechanical ventilation [6].

Iotti et al. [7] compared the effects of an HH with a hygroscopic HME and a hygroscopic HME with a mechanical filter on ten patients on assisted ventilation with PSV. Pressure support was adjusted via feedback to maintain a constant inspiratory work of breathing; patients generally reached a steady state at 25 min. There was found to be a progressive and significant increase in  $V_D/V_T$  and airway resistance with the use of HH vs. HME vs. filtered HME. Accordingly, the level of PS increased from  $12.8 \pm 6.4$  cmH<sub>2</sub>O for the HH group,  $14.8 \pm 5.4$  cmH<sub>2</sub>O for the HME group, and  $17.6 \pm 5.6$  in the filtered HME group. While RR remained constant for each group, the required  $V_T$  increased significantly from  $398 \pm 111$  to  $423 \pm 96$  to  $463 \pm 98$  ml. In this study, there was increased inspiratory resistance, dead space ventilation, and dynamic hyperinflation that were overcome by the increase in PSV [7].

Campbell et al. [8] compared three humidification devices, an HH, a hygroscopic HME with a dead space of 28 ml, and a hygroscopic HME with a dead space of 90 ml, in two groups of patients. One group consisted of spontaneously breathing patients on PS ventilation, and the other group was paralyzed postoperative patients on a fixed ventilator mode. The three humidifiers were used in random order for an hour each with measurements taken of respiratory mechanics. Addition of HMEs in spontaneously breathing patients resulted in increased dead space ventilation ( $V_D/V_T$ ), but alveolar ventilator was maintained by an increase in RR [ $22.1 \pm 6.6$  breaths/min (HH) vs.  $24.5 \pm 6.9$  breaths/min (HME-28) vs.  $27.7 \pm 7.4$  breaths/min (HME-90)] with a significant overall increase in  $V_E$  ( $9.1 \pm 3.5$  vs.  $9.9 \pm 3.6$  l/min vs.  $11.7 \pm 4.2$  l/min). Notably, there was a slight decrease in  $V_T$  in the first HME-28 group from  $411 \pm 61$  ml to  $400 \pm 52$  ml with an increase to  $428 \pm 67$  ml in the second HME-90 group. In the controlled ventilation group, there were no changes among the three humidifiers for RR,  $V_T$ ,  $V_E$ , or  $V_D/V_T$  [8].

Girault et al. [9] compared HH and HME (combined hydrophobic-hygroscopic with  $V_D/V_T$  of 84 ml) devices in 11 patients with chronic respiratory failure defined as greater than 48 h. Each patient was subjected to four pressure support (PS) ventilation sequences with each humidifier at two different levels of PS (7 and 15 cmH<sub>2</sub>O). While there was a significant increase in  $V_E$  between devices at both levels of PS (7 vs. 15 cmH<sub>2</sub>O), there were not any differences in RR ( $28 \pm 7$  vs.  $29 \pm 7$  breaths/min;  $26 \pm 7$  vs.  $28 \pm 7$  breaths/min) or  $V_T$  ( $468 \pm 143$  vs.  $457 \pm 143$  ml;  $516 \pm 126$  vs.  $516 \pm 150$  ml). There was increased work of breathing and an increase in PaCO<sub>2</sub> in the HME group at the lower PS level that was compensated by an increase in the PS to 15 cmH<sub>2</sub>O. The authors concluded that there is a negative influence by the HME in spontaneously breathing patients unless there is a compensatory increase in the PS to overcome the dead space and increased resistance due to an HME [9].

These five crossover studies have compared HH and HME to measure the effect on  $V_E$ ,  $V_T$ , and respiratory rate (RR). These studies were systematically reviewed in a Cochrane database to evaluate the effect on each parameter [10]. For  $V_E$ , there were the above five studies with 76 participants. The analysis showed significant higher  $V_E$  in the HME group at the low, moderate, and high correlation estimates. Tidal volume was measured in the same five studies. There was no difference between the HH or HME groups at the low or moderate correlation estimates, but  $V_T$  was significantly higher at the high correlation estimate for the HME group. Respiratory rate was reported in only four of the above crossover trials ( $n=65$ ). The RR was significantly higher in the HME group at the low correlation estimate, but there was no significant difference between groups at moderate or high correlation estimates.

There is only a single crossover study that evaluated differences between HH and HME in short-term non-invasive ventilation. Jaber et al. compared HH vs. HME in non-invasive ventilation in 24 patients with a single device used for two consecutive periods of 20 min. Their study noted there was both an increased  $V_E$  (14.8 vs. 13.2 l/min) and an increased RR (26.5 vs. 24.1 breaths/min) with the HME, but no significant change in  $V_T$  (674 vs. 643 ml) [11]. These findings correlate with the previous studies in MV showing increases in  $V_E$  and RR.

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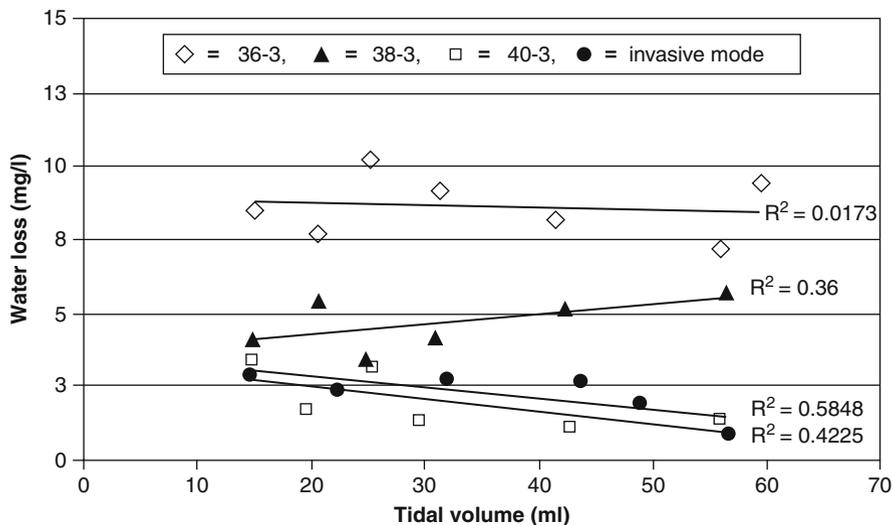
## 15.4 Comparison of Different HMEs' Tidal Volumes

There have been several studies comparing specific differences in HME devices on airway measurements in MV. Boyer et al. evaluated two hygroscopic HMEs in long-term MV for 48 h. The two HMEs had internal dead space measurements of 34 and 90 ml, respectively. In addition to demonstrating safety efficacy for the two humidification devices, the study showed no differences in  $V_T$  or positive end-expiratory pressure for the two devices [12]. Sottiaux et al. [13] compared three HMEs (two hygroscopic) in 29 surgical patients on postoperative mechanical ventilation for short-term use less than 24 h. While the primary outcome was airway humidification, where the hygroscopic HME performed better, there were no differences in the  $V_T$  or RR among all three groups [13]. The final study conducted a comparison of two HMEs for 7 days in long-term, ventilated chronic obstructive pulmonary disease (COPD) and non-COPD patients primarily to study the effect of airway humidification. As a secondary measure, no differences in  $V_T$  ( $531 \pm 76$  vs.  $536 \pm 37$  ml;  $498 \pm 59$  vs.  $510 \pm 55$  ml) between COPD vs. non-COPD patients with both types of HME [14].

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## 15.5 Effect of Humidification on Tidal Volume

There is a theoretical effect of airway humidification of expiratory  $V_T$ , and several studies have addressed this issue in artificial lung models. Large tidal volumes with the use of HME are reported to significantly decrease the humidification of inspired

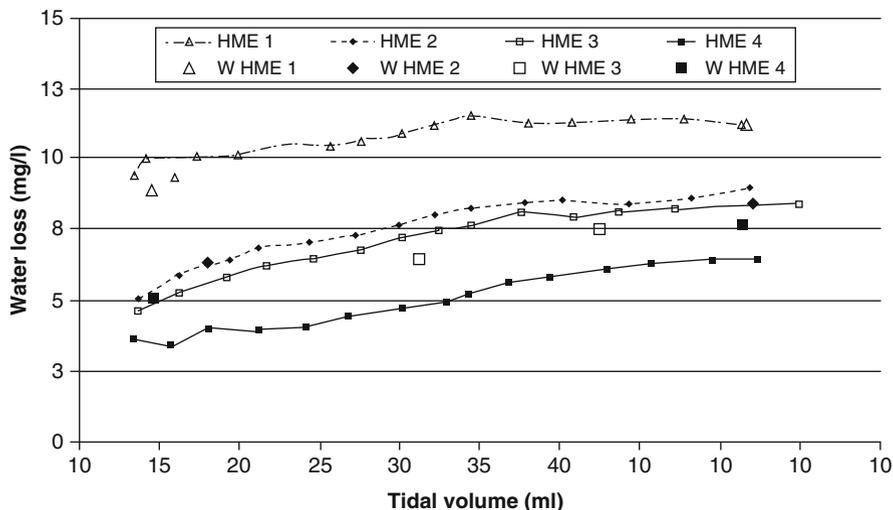


**Fig. 15.1** Tidal volume and heated humidification (Reproduced with permission from Schiffmann [18])

gases. Eckerbom and Lindhold evaluated six commonly used devices and found that the hygroscopic devices were significantly better than hydrophobic devices at all ranges of  $V_E$  [15]. This finding was confirmed by Bethune and Mackayas who demonstrated that with a  $V_T$  of 1.0 l and a RR of 20 breaths/min the hydrophobic HME provided humidification at 17 mgH<sub>2</sub>O/l, while a hygroscopic HME was able to provide humidification at 31 mgH<sub>2</sub>O/l [16]. Similarly, another artificial model demonstrated the superior humidification of four hygroscopic HMEs at higher  $V_T$  [17]. Using a neonatal lung model, Schiffman et al. compared different temperature settings in HH and four different HMEs (see Figs. 15.1 and 15.2). The amount of expiratory water loss was influenced by various ventilatory parameters. With HH use, increases in temperature by 4° resulted in a decrease of expiratory water loss (9–1.5 mg/l); further expiratory water loss was decreased by higher tidal volumes. For all HMEs, increasing the  $V_T$  resulted in increases in expiratory water loss (below 7–9 mg/l in 3 of 4 devices tested) [18]. These studies demonstrate the superiority of hygroscopic condenser humidifiers compared with conventional hydrophobic HMEs with respect to airway humidification, but underscore the potential limitations based on large  $V_T$ .

## 15.6 Conclusion

Clinicians should be made aware that the choice of device for airway humidification can play an important role in respiratory mechanics during MV. The use of an HH may have less effect on  $V_T$ , but may also be less useful in humidification of the airway. In general, the application of an HME and its specific type will definitely increase the  $V_D/V_T$ , but numerous studies and a Cochran analysis failed to demonstrate



**Fig. 15.2** Tidal volume and heat and moisture exchangers (Reproduced with permission from Schiffmann [18])

a significant difference in  $V_T$  or likewise the RR or  $V_E$ . However, specific clinical situations such as high  $V_E$  or low  $V_T$  may dictate the use of an HH because of these potential limitations. Additionally, there is a paucity of data on the effect on airway humidification devices on the in-line measurement of  $V_T$ , which can potentially negatively affect the delivered volume to patients.

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# Humidification During Invasive Mechanical Ventilation: Selection of Device and Replacement

# 16

Jean-Damien Ricard

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## 16.1 Which Device for Which Patients

As stated earlier on, adding heat and moisture to the inspired gas during invasive mechanical ventilation is mandatory. This can be adequately achieved both by HMEs and heated humidifiers [1].

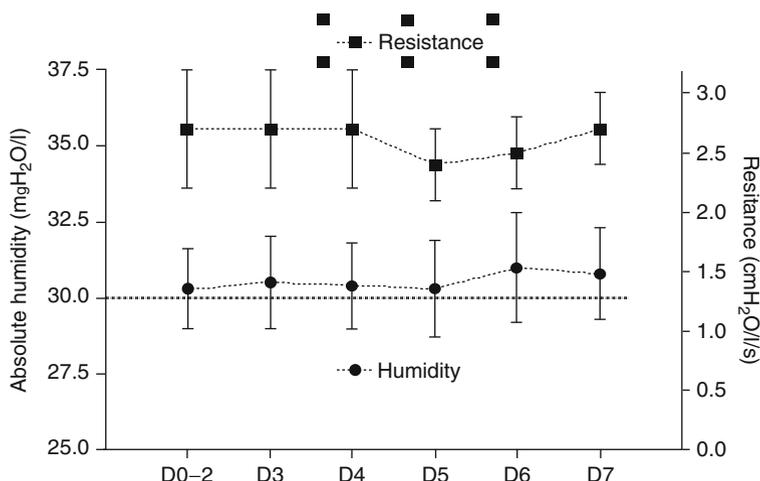
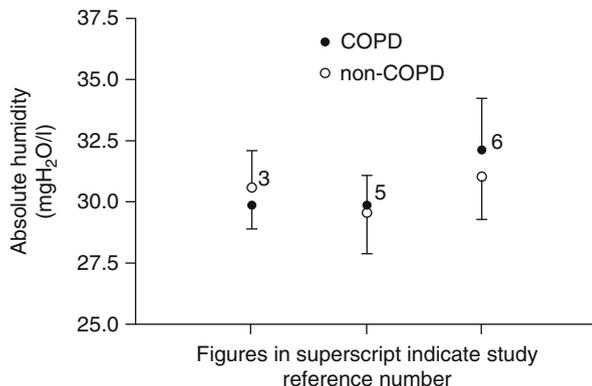
There are very few and rare contraindication to the use of HMEs. Because they act passively, the amount of heat and moisture they deliver to the inspired gases depends on the amount of heat and moisture they retain during expiration. Therefore, patients with profound hypothermia or important bronchopleural fistula should preferably be ventilated with a heated humidifier. In addition, a heated humidifier may be preferable in patients ventilated for acute asthma or acute respiratory distress syndrome, in whom a drastic tidal volume reduction induces extreme respiratory acidosis (to avoid increased dead space with HMEs) [2] until improvement in the patient's respiratory condition enables the use of a HME. Apart from these specific situations, HMEs should be considered first to heat and humidify inspired gases of all mechanically ventilated patients. As mentioned earlier, they are as effective clinically as heated humidifiers, and they are much cheaper and much easier to use. Importantly, medical as well as surgical patients can benefit from them. Indeed, despite former algorithms that tended to restrict their use to patients without a history of respiratory disease and for the first 5 days of mechanical ventilation only, several studies have clearly shown that they can be

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J.-D. Ricard  
INSERM U722, UFR de Médecine,  
Université Paris Diderot, Paris 7,  
Paris, France

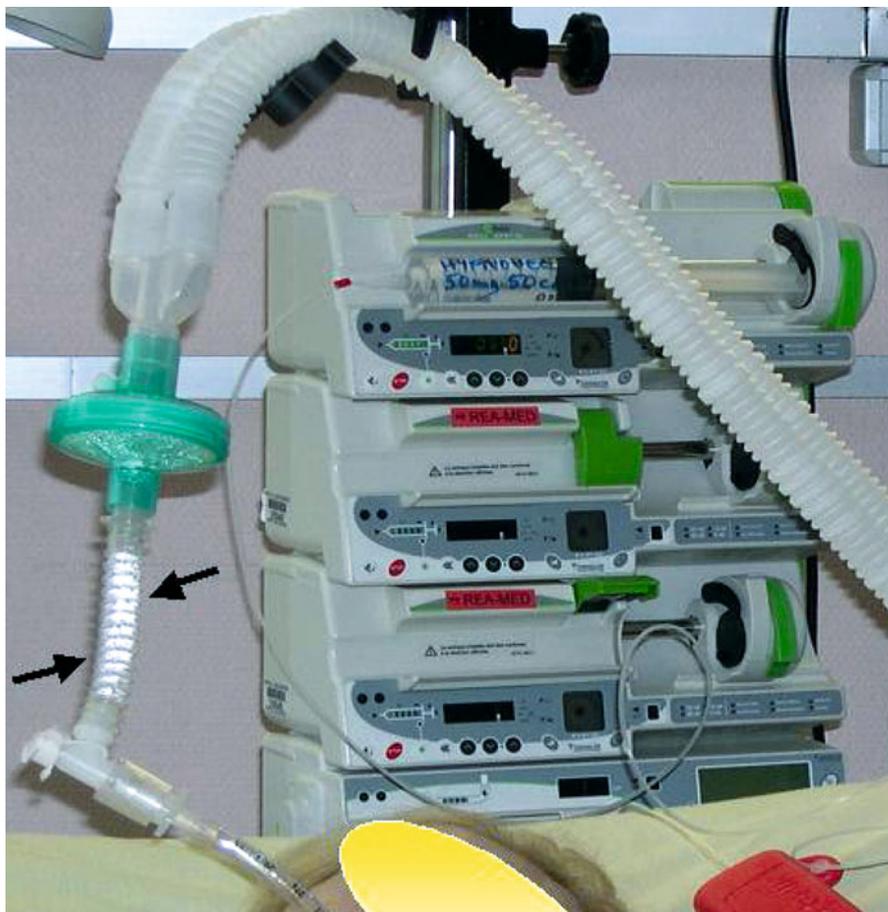
Assistance Publique – Hôpitaux de Paris, Hôpital Louis Mourier,  
Service de Réanimation Médico-chirurgicale,  
178, rue des Renouillers, F-92700 Colombes, France  
e-mail: jean-damien.ricard@lmr.aphp.fr

**Fig. 16.1** Comparison of levels of absolute humidity delivered by HMEs in COPD and non-COPD patients in three different studies. Very similar levels are obtained, indicating that HMEs can be used in COPD patients



**Fig. 16.2** Levels of absolute humidity (*left Y axis*) and resistance (*right Y axis*) measured with HMEs kept during 7 days in mechanically ventilated patients. Both parameters remained remarkably stable during the 7 days of use (reproduced from Ricard JD [3])

used in any patient requiring mechanical ventilation, even in patients with COPD and for any length of mechanical ventilation. Because patients with COPD represent the most important subgroup of mechanically ventilated ICU patients in the United States and because their duration of ventilation is longer than that of other patients, adequate humidification is probably more critical in such patients than in those ventilated for shorter periods of time. Numerous studies have shown that long-term mechanical ventilation can be safely conducted in such patients with HMEs [3–6]. Three studies have specifically compared the humidity output of HMEs in COPD and non-COPD patients, and consistently found that values for absolute humidity measured in COPD and non-COPD patients were very similar (Fig. 16.1) [3, 5, 6].



**Fig. 16.3** Photograph of an HME and its flextube in a mechanically ventilated patients. Black arrows show the presence of abundant condensation in the flextube. The flextube and the HME are positioned vertically above the endotracheal tube, so as to limit secretions reaching the HME

## 16.2 Frequency of HME Replacement

There is now considerable evidence that HMEs can be used for longer than the 24 h recommended by the manufacturers (reviewed in [7]). These compelling results stem either from rigorous clinical evaluation [8, 9] or extensive bed side measurement of humidity delivery [3–6, 10]. Figure 16.2 shows that humidity delivery of a combined HME (Hygrobac®, DAR, Miranda, Italy) used for 7 days without change was remarkably stable during this period of time. Progressive clogging of the device with tracheal secretions (that seriously increase its resistance to airflow) could have been a potential drawback to the prolonged use of the HME. Repeated measurements of the resistance of the HME over 7 days indicate that this phenomenon did not

occur [3] (Fig. 16.2). Maintaining the HME vertically above the tracheal tube (Fig. 16.3), as well as having nurses and doctors repeatedly check the position of the HME, prevents secretions from refluxing from the tracheal tube and obstructing the HME [3, 5]. Use of HMEs can be extended in both medical patients (including those with COPD [3–6]) and surgical patients [10–12]. This practice is now widely accepted, and recommendations have been made to change HMEs only once a week [13]. In our own published [3, 6] and unpublished experience, we have been changing HMEs only once a week since 1997, and haven't encountered endotracheal tube occlusions.

### 16.2.1 Bedside Adjustment

Assessing adequate humidification at the bedside is desirable if not essential for at least two reasons: (1) a potentially life-threatening tracheal tube occlusion [14] may occur without any precursory clinical signs of insufficient humidification; (2) devices may not deliver, in some instances, the heat and humidity that is expected from them, either because they are malfunctioning or because performances measured in the clinical setting do not attain those publicized by the manufacturer [6].

There are two aspects to this assessment: (1) Is the device delivering enough heat and humidity (according to the standards)? (2) Is the amount of heat and moisture delivered appropriate for a given patient?

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## 16.3 Assessing HMEs and Heated Humidifiers at the Bedside

A simple means of evaluating the humidity delivered by a given device is to rate the amount of condensation seen in the flex tube that connects either the Wye piece (when using a heated humidifier) or the HME to the endotracheal tube [15]. Indeed, a positive correlation has been found between the amount of condensation seen in the flex tube (black arrows, Fig. 16.3) and the absolute humidity measured at the bedside [15]. When, with a given device, the flex tube is constantly dry over time or if only very few droplets of water are seen, then the absolute humidity delivered by this device is probably below 25 mgH<sub>2</sub>O/l and the patient at risk of endotracheal tube occlusion. On the other hand, when numerous droplets are seen in the flex tube or when it is dripping wet, then the device is more likely to deliver an absolute humidity sufficient to avoid endotracheal tube occlusion [15].

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## 16.4 Assessing Adequacy of Inspired Gas Conditioning

Though it is conceivable that some patients have special humidification needs, the prevailing literature indicates that heated humidifiers and HMEs equally meet the humidification requirements of the vast majority of mechanically ventilated

patients. Therefore, monitoring the aspect of the secretions (thick and tenacious, or on the contrary watery and abundant) in order to detect insufficient or excessive humidification may be of limited value, since changes in the mucus aspect may be entirely due to the patient's condition (respiratory status, fluid balance, etc.) and not the consequence of the humidifying device. As a matter of fact, it has been shown that air humidification with either an HME or a heated humidifier had similar effects on mucosal rheological properties, contact angle, and transportability by cilia in patients undergoing mechanical ventilation. Finally, results from a recent meta-analysis indicate that both HMEs and heated humidifiers should be considered the gold standard of humidification since no difference in outcome was found between patients ventilated with an HME and those with heated humidifiers [1, 16]. For obvious practical and economic reasons, HMEs should be systematically used in the first place.

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# Humidification During Invasive Mechanical Ventilation: Hygrometric Performances and Cost of Humidification Systems

# 17

François Lellouche

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## 17.1 Introduction

The deleterious impact of dry gases on airway mucosa was described very early [1]. Abundant literature on humans and animals is available demonstrating a relationship among airway mucosal dysfunction, inflammation and atelectasis, and (1) the level of gas humidity delivered during invasive mechanical ventilation and (2) the duration of exposure to this gas [2]. An ongoing debate centers on the optimal level of inspiratory gas humidity. Several recommendations have been published on the optimal level of humidification required during invasive mechanical ventilation. Most of these publications are not recent. In general, it is recommended that the humidification systems should provide at least 30 mgH<sub>2</sub>O/l for inspiratory gases [3–6]. Many studies were published that allow us to better determine what a safe level of humidification is. If we consider as a clinical requirement to avoid obstruction of the endotracheal tube, slightly lower levels of humidity may be sufficient [7]. Few authors recommend using levels of gas humidity corresponding to the water content in the alveoli, or 44 mgH<sub>2</sub>O/l, which corresponds to 100% relative humidity at 37°C [8]. These latter requirements are not usually obtained with the humidification systems used so far [7, 9]. Until now, no study has really compared stable systems delivering 40 mgH<sub>2</sub>O/l with stable systems delivering 30 mgH<sub>2</sub>O/l. In some clinical situations, such as patients ventilated with ARDS or severe asthma, other criteria than the level of humidification should be considered, in particular to take into account the mechanical characteristics of the different humidification systems (especially the dead space). Finally, the issue of the humidification systems' cost cannot be set aside at the time of the choice.

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F. Lellouche

Institut Universitaire de Cardiologie et de Pneumologie de Québec,  
Centre de recherche, Hôpital Laval,  
2725, chemin Sainte-Foy, G1V4G5 Québec, QC, Canada  
e-mail: francois.lellouche@criucpq.ulaval.ca, flellouche@free.fr

## 17.2 Hygrometric Performances of the Main Humidification Systems

### 17.2.1 What Is the Optimal Level of Humidification During Invasive Mechanical Ventilation?

This difficult question has been debated for a long time, and although the answer is now more accurate, it has not changed much since 1969. In this year, Chamney defined the targets that were required by the humidification systems used in intubated or tracheostomized patients [10]. Among these conditions, the author recommended that the gases reaching the trachea should be between 30 and 36°C in the range of 30–40 mgH<sub>2</sub>O/l. In an editorial in 1987, “A rational basis for humidity therapy,” Chatburn proposed to provide saturated gas at 32–34°C (33.9–37.7 mgH<sub>2</sub>O/l), which is the humidity level of the gas at the trachea in healthy subjects [11]. He also concluded in the same editorial that there was no rationale for proposing to issue gas saturated at 37°C.

Several different organizations have provided recommendations for humidifying gases during invasive mechanical ventilation. The British Standards Institute recommended providing an absolute humidity of 33 mgH<sub>2</sub>O/l in 1970 [3]. In 1979, the ANSI (American National Standards Institute) recommended a minimum level of moisture delivered at 30°C at 100% relative humidity (i.e., 30.4 mgH<sub>2</sub>O/l absolute humidity) with the heated humidifier [4]. In addition, the AARC (American Association of Respiratory Care) recommended 30 mgH<sub>2</sub>O/l and has extended this recommendation to all humidification systems [6]. The ISO 8185 also recommended 30 mg/l for humidification systems in 1988 [5]. Finally, in 1997, the ISO 8185 standards recommended 33 mgH<sub>2</sub>O/l (6.8.4), but this standard “does not concern heat and moisture exchangers” (1.1) [12].

### 17.2.2 Risk Scale for Endotracheal Tube Occlusion

The hygrometric performance of the humidification devices is the first parameter to consider when assessing such systems. There are several hygrometric techniques that make the comparison of the humidification devices difficult. Using the same technique (psychrometric method), we had the opportunity to measure the hygrometric performances of a wide variety of humidification systems currently available on the market, the majority of heated humidifiers of previous generations as well as the most recent ones, many heat and moisture exchangers (HME) and the majority of active HMEs available on the market [7]. Comparing our results with those in the literature (Table 17.1) [13–30], we designed a risk scale for endotracheal tube occlusion according to the humidification systems used and their conditions of use (Fig. 17.1). We discuss here the main characteristics of the humidification proprieties of the currently available humidification devices.

**Table 17.1** Summary of published studies comparing HMEs and heated humidifiers (upper table) or evaluating only HMEs (lower table) for which the frequency of catheter occlusion is reported [13–30]

First author [reference]	Heated humidifiers				Heat and moisture exchangers				Absolute humidity (psychrometry) in mgH <sub>2</sub> O/l
	Device	Included patients/occlusions	Percentage of endotracheal tube occlusions	Device	Included patients/occlusions	Percentage of endotracheal tube occlusions	Percentage of endotracheal tube occlusions		
Cohen [13]	Cascade	81/1	1.2	BB2215	170/15	8.8	21.8		
Martin [14]	HHBW (32°C)	42/0	0.0	BB2215	31/6	19.4	21.8		
Misset [15]	MR 450 (32–34°C)	26/2	7.7	BB2215	30/4	13.3	21.8		
Roustan [16]	Aquapor (31–32°C)	61/0	0.0	BB2215	55/9	16.4	21.8		
Branson [25]	Conchaterm III (32–34°C)	32/0	0.0	Aqua+	88/0	0.0	ND		
Dreyfuss [20]	MR 450	70/0	0.0	Hygrobac	61/1	1.6	31.7		
Villafane [17]	MR 310 (32°C)	7/1	14.3	BB2215	8/3	37.5	21.8		
Boots [19]	MR 730 (37/35)	41/0	0.0	Hygrobac	8/0	0.0	31.7		
Hurni [21]	F&P (32°C)	56/1	1.8	Humid Vent Light	75/0	0.0	30.8		
Kirton [23]	Marquest	140/1	0.7	Hygroster	59/0	0.0	30.7		
Kollef [30]	MR 730 (35–36)	147/0	0.0	BB100	140/0	0.0	26.8		
Thomachot [24]	Cascade 2 (32°C)	20/0	0.0	Duration	163/0	0.0	ND		
Jaber [26]	MR 730 (37/40)	34/2	5.9	Humid Vent Light	9/0	0.0	30.8		
Lacherade [22]	MR 730 (37/40)	185/5	2.7	Hygrobac	26/1	3.8	31.7		
Boots [18]	MR 730 (37/40 or 37/35*)	191/0	0.0	Hygrobac	185/1	0.5	31.7		
	Total HH	1133/13	1.1%	Humid Vent Light	190/0	0.0	30.8		
				Total HME 1	1298/40	3.1%			
				Total HME 1 (excluding BB2215)	814/3	0.4%			
Thomachot [29]				Humid Vent Light	66/1	1.5	30.8		
Thomachot [28]				BB100	70/1	1.4	26.8		
				Humid Vent	77/1	1.3	30.8		
				Clear Therm	63/0	0.0	26.2		

(continued)

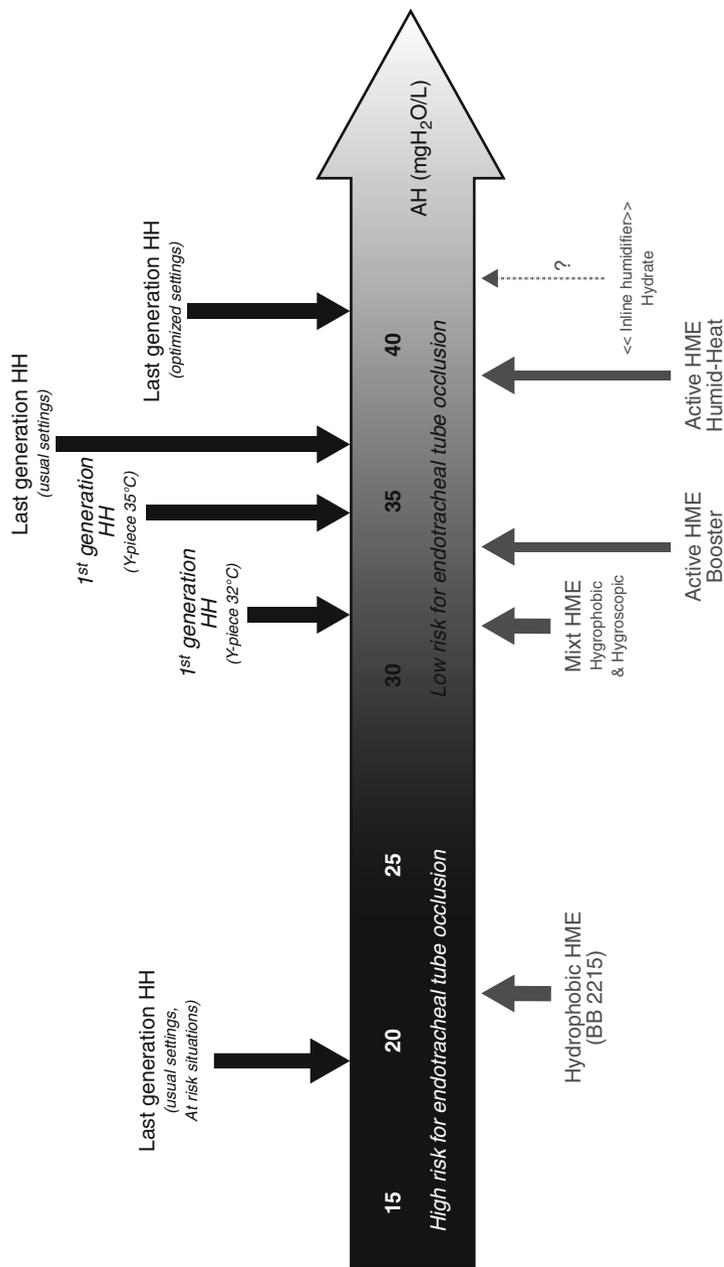
Table 17.1 (continued)

First author [reference]	Heated humidifiers			Heat and moisture exchangers			Absolute humidity (psychrometry) in mgH <sub>2</sub> O/l
	Device	Included patients/occlusions	Percentage of endotracheal tube occlusions	Device	Included patients/occlusions	Percentage of endotracheal tube occlusions	
Boisson [46] Davis [58]				Maxipleat Aqua+ (24 h) Duration (120 h) Aqua+ (120 h)	12/0 100/0 60/0 60/0	0.0 0.0 0.0 0.0	20.1 ND ND ND
Markowicz [81]				Hygrobac Humid Vent Clear Therm	21/0 20/0 20/0	0.0 0.0 0.0	31.7 30.8 26.2
Ricard [57] Thomachot [27]				Hygrobac Thermovent Hepa+ (1j) Thermovent Hepa+ (7 days)	33/0 84/0 71/0 71/0	0.0 0.0 0.0 0.0	31.7 27.8 27.8 27.8
Boyer [89]				Editiflex Hygrolife	22/0 21/0	0.0 0.0	ND ND
				Total HME 2	800/0	0.4%	
				Total HME 1 + 2	2098/43	2.0%	
	Total HH	1133/13	1.1%	Total HME 1 + 2 (excluding BB2215)	1614/6	0.4%	

The humidification systems are reported. For HMEs, performance measured by the psychrometric method is reported [7]

NA not available

\*Temperature at the humidification chamber/temperature at the Y piece



**Fig. 17.1** Psychrometric risk scale. Position of different humidification systems in connection with their humidification performance based on the same technique of measurement (psychrometric method) (personal data combined with the literature data) [7, 9, 33, 34, 49, 51, 92]. Between 25 and 30 mgH<sub>2</sub>O/l of absolute humidity is a grey zone where the risk of occlusion exists but is less known. Under 25 mgH<sub>2</sub>O/l, that risk is probably important [13–17], and above 30 mgH<sub>2</sub>O/l the risk is low [20, 22, 57, 80]. Furthermore, there is a potential risk of over-humidification with systems with the highest performances in terms of hygrometry [93]. However, this risk is currently difficult to estimate. The last generation HH stands for HHs with heated wires and specific regulation loops. The “at risk situations” are high ambient or ventilator temperatures, which are associated with low humidification performances with these devices. Data with the new “inline vaporizer” are preliminary and will require confirmation. HH Heated humidifiers, HME heat and moisture exchangers

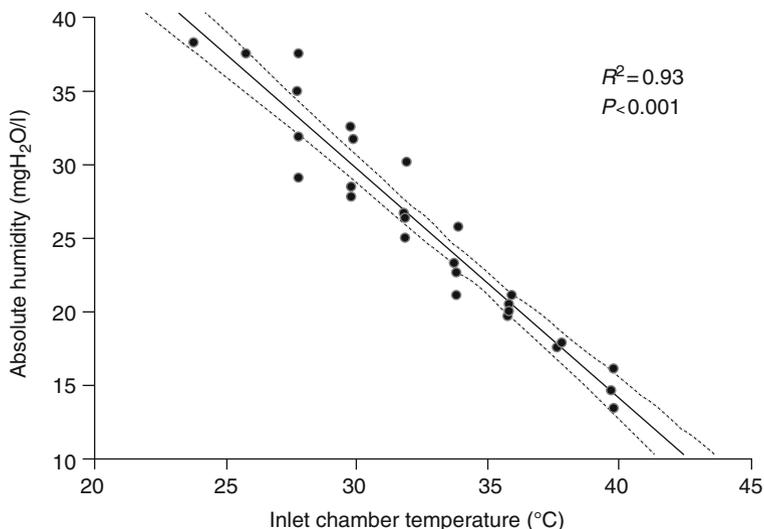
### 17.2.3 Heated Humidifiers' Humidification Performances

Heated humidifiers are usually considered the most efficient systems in terms of humidification performances. This statement must be qualified. It has been shown that the performances of heated humidifiers with heated wires vary widely from 20 to 40 mgH<sub>2</sub>O/l and are influenced by external conditions, particularly ambient and ventilator outlet temperatures [9]. When these temperatures are high, the inlet chamber temperature is high, leading to the reduction of the heater plate power. Indeed, with these humidifiers the regulation of the heater plate power aims at maintaining a constant humidification chamber temperature (usually 37°C). The temperature of the water in the humidification chamber is related to the heater plate power. Water with a low temperature will not produce moisture. Consequently, there is a strong inverse relationship between the inlet chamber temperature and the humidification performances (Fig. 17.2) [9]. Thus, the very low humidity levels (around 20 mgH<sub>2</sub>O/l and even lower), described as being likely to cause endotracheal tube obstruction, are delivered by these systems in the most adverse conditions (high ambient temperature, turbine ventilators and high minute ventilation). These humidity levels are comparable to or even lower than those measured with the HME BB2215, with which the incidence of endotracheal tube occlusions ranged from 10 to 20% [13–17]. Furthermore, even in favorable situations (normal ambient and ventilator temperatures), the measured performances are below what is advertised by the manufacturers (44 mgH<sub>2</sub>O/l) [9, 31]. This again calls for an independent evaluation of the humidification systems [7, 32].

In another study, we evaluated the influence of ambient temperature and ventilator output temperature for many heated humidifiers, particularly those of previous generations without heated wires (requiring water traps in the ventilator circuits) [33]. This study showed for settings equivalent to heated humidifiers with heated wires (35 and 37°C at the Y-piece) that the heated humidifiers without heated wires (1) performance was more stable with little influence from external conditions and (2) delivered gas with inspiratory absolute humidity levels above 30 mgH<sub>2</sub>O/l. In contrast, (3) for more traditional settings (32°C), the performances of these systems were near the limit of 30 mgH<sub>2</sub>O/l and sometimes below.

More recently, we evaluated heated humidifiers with different technologies (counter-flow heated humidifier) and devices incorporating an algorithm to reduce the risk of under-humidification [34]. We found significant improvements with the new algorithm of the MR 850 (Fisher&Paykel) and good performances with the humidifier HC 200 (Hamilton Medical) to obtain an inspired water content between 35 and 40 mgH<sub>2</sub>O/l, with only a moderate influence of the ambient and ventilator temperatures, flows and tidal volumes used [34]. Similar data have been published for counter-flow heated humidifiers [35].

Even if the performance improves with the most recent heated humidifiers (with compensation algorithms and counter-flow heated humidifiers), the problem of condensation in the circuit remains in spite of the heated wires. This question has long been raised concerning the heated humidifiers [36], and the use of heated wires was intended to limit the consequences. Yet, the frequency of condensation in the



**Fig. 17.2** Correlation between heated wire humidifier performance and inlet chamber temperature. A very close correlation was found between humidifier performance (absolute humidity [mgH<sub>2</sub>O/l] of inspiratory gas) and inlet chamber temperature (°C). A good correlation was also found between humidifier performance and heater plate temperature in that study [9]

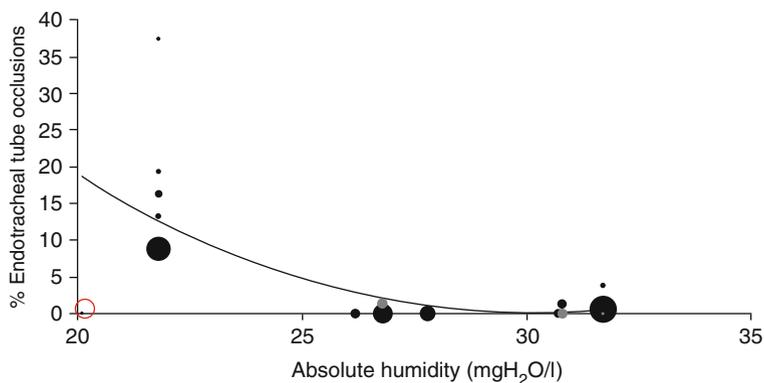
inspiratory circuit is high [37], especially in the turbine ventilators and in case of low ambient temperature [38]. New “porous” expiratory circuits limit the problem in the expiratory circuit, whereas in the inspiratory circuit, the issue remains. Interest in the “porous” circuits derives from the potential to reduce the water content in the expiratory limb, which could limit the risk of condensation of gases that could potentially interfere with measures of expiratory flow with some pneumotachographs [39].

Clinicians must be aware of these technical issues to interpret specific clinical situations (i.e., thick secretions or endotracheal tube occlusion or sub-occlusion in spite of heated humidifier use). When used in normal conditions, heated humidifiers are performing systems. Normal conditions mean (1) stable and moderate ambient temperature (south-facing rooms with sun on the humidifier can be a problematic situation!) and (2) moderate output ventilator temperature with a specific precaution in case of turbine ventilator use.

## 17.2.4 Heat and Moisture Exchangers’ Humidification Performances

### 17.2.4.1 Comparison with the Literature on the Risk of Tracheal Occlusion

Heat and moisture exchangers (HMEs) are the most commonly used humidification devices in Europe [40] and are being increasingly used in North America [41] (Fig. 17.3).



**Fig. 17.3** Frequency of endotracheal tube occlusions reported in the literature with heat and moisture exchangers [13–30, 57] in relation with the absolute humidity delivered by the HMEs measured using the bench test apparatus (see Table 17.1) (from [7]). One study (*red circle*) is an outlier [46] with no endotracheal occlusions despite very poor humidification. However, this study only included 12 patients, which is not enough to reach a conclusion about the safety of the device tested. A hydrophobic HME (Pall BB2215), which delivered a measured absolute humidity of  $21.8 \pm 1.5$  mgH<sub>2</sub>O/l, has been associated with high rates of endotracheal tube occlusions in five previously published studies [13–17] (Table 17.1). A number of studies are represented by *grey dots* to make them stand out. The sizes of the dots are proportional to the number of patients in the studies

As for heated humidifiers, many technological improvements have led to the emergence of new models of performing HMEs on the market. The very first metallic HMEs were not disposable and generated significant resistance [42–44]. The first disposable HME was available in 1976 and was used during anesthesia [45]. The first HMEs proposed for ICU patients (hygroscopic HME) had insufficient humidification performances, which were responsible for their poor reputation [13–17]. This poor reputation is not justified anymore. Improved materials have reduced the size of HMEs and improved their performances. We conducted a large-scale evaluation of the humidification performances of 48 devices (HME, HMEF, antibacterial filters) [7]. The main result was the heterogeneous performances of these systems. Antibacterial filters should not be used to humidify gases. However, some of the filters have fairly similar appearances compared with HMEs or HMEFs, but the water contents are very different, with the possibility of confusion. The most efficient HMEs provide a humidity of inspired gases above 30 mgH<sub>2</sub>O/l, but some systems proposed for airway humidification provide water contents below 25 and sometimes below 20 mgH<sub>2</sub>O/l. Moreover, comparing with data from manufacturers, we have observed some significant differences, again calling for independent evaluations.

We used data from this study and from the literature to try to assess the humidification level associated with a risk of endotracheal tube occlusions. The BB2215 device with performance of about 22 mgH<sub>2</sub>O/l resulted in a significant increased risk of occlusions [13–17]. HMEs providing absolute humidity above 25 mgH<sub>2</sub>O/l seem to be at lower risk. Although there is limited few data for humidification

systems with intermediate performance (between 25 and 30 mgH<sub>2</sub>O/l), the few studies available show that the risk of catheter occlusion is also low in that zone [23, 27, 29]. However, it is likely that this risk is directly linked to the hygrometric performances. Although no formal data exist on the risk of occlusion near 25 mgH<sub>2</sub>O/l, caution is advisable when approaching or exceeding 30 mgH<sub>2</sub>O/l to minimize these risks.

In the literature, there are several conflicting studies with the latter results. In the study of Boisson et al. [46], no occlusion occurred when a low performing hydrophobic HME was used (absolute humidity just above 20 mgH<sub>2</sub>O/l). But this study had included only 12 patients. While the main issue is safety, we cannot make a positive conclusion considering the small number of patients. Moreover, Kapadia et al. [47, 48] reported the incidence of catheter occlusions for a series of nearly 8,000 patients during a period of 5 years. While the HMEs used were the BB2215 (22 mgH<sub>2</sub>O/l) and Cleartherm (26 mgH<sub>2</sub>O/l), the frequency of occlusions was “only” 0.16%. In analyzing the results, it appears that the average duration of mechanical ventilation was less than 2 days, which probably explains the low rate of occlusion in this study. The duration of ventilation must obviously be taken into consideration when analyzing the risk of endotracheal tube occlusion. Thus, these discordant publications should not be reassuring.

#### 17.2.4.2 Impact of External Conditions on HME's Hygrometric Performances

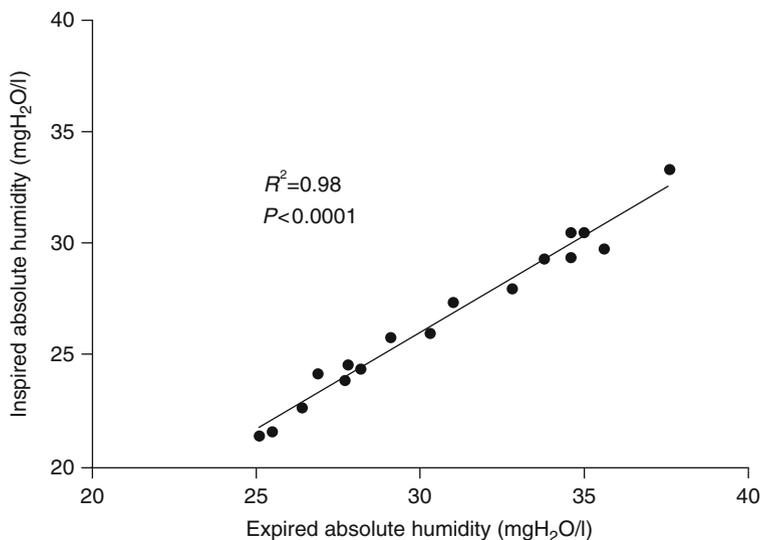
HMEs are more stable and less influenced by environmental conditions, but can be influenced by the patient's core temperature. We studied the impact of ambient temperature on HMEs and showed that high ambient temperature did not affect HME performance [49]. Croci et al. showed that low ambient temperature (20°C vs. 26°C) slightly reduced the efficiency of hydrophobic HMEs (21 vs. 23 mgH<sub>2</sub>O/l) [50].

HME performance can be significantly influenced by the patient's core temperature. Indeed, with these devices, the quantity of water delivered to the patient during inspiration is highly dependent on the amount of water present in the exhaled gas (Fig. 17.4). In patients with induced hypothermia to 32°C [51], the expiratory water content is about 27 mgH<sub>2</sub>O/l, while it is about 35 mgH<sub>2</sub>O/l in patients with a normal core temperature [51, 52]. Therefore, even the best performing HMEs can only deliver inspiratory gases with a water content of around 25 mgH<sub>2</sub>O/l during hypothermia. In this situation, even heated humidifiers provided non-optimal levels, and the moisture target was uncertain during hypothermia.

HME performance can be reduced in case of high minute ventilation [53, 54]. This has been described with hydrophobic HMEs, but most recent hydrophobic and hygroscopic HMEs do not seem to be influenced by the level of minute ventilation [49].

#### 17.2.4.3 Other Parameters to Evaluate Airway Humidification Impact

Furthermore, we must wonder about the value of this clinical parameter, the occlusion of the endotracheal tube, which is used in most studies. This parameter is easy to detect, but it represents only the easily visible part of the problem. Studies using other parameters are difficult to interpret because they compare humidification systems with similar performances, and few provide humidification measurements to



**Fig. 17.4** Correlation between inspired and expired absolute humidity of the gas (expressed in mgH<sub>2</sub>O/l) with heat and moisture exchangers. A strong correlation exists between inspired and expired gas hygrometry with heat and moisture exchangers. With the high performing heat and moisture exchangers used in this study, the rate of inspired humidity corresponded to 87% of expired humidity [51]

allow a better understanding of what is effectively compared. Studies from Hurni et al. [21] and Nakagawa et al. [55] used original techniques (cytology of bronchial cells in one case and rheological properties of secretions in another) and compared HMEs with first generation heated humidifiers. But the performance of these systems are very similar (probably within 5 mgH<sub>2</sub>O/l), which does not allow demonstrating a significant difference. Moreover, the study of Jaber et al. [26], using the acoustic method to evaluate the resistance of endotracheal tubes with HME and HH (with heated wire), did not provide humidity data. Again, this makes it difficult to interpret these results, especially as humidifiers used in this study had no compensation system and their humidification performances were highly variable [9]. Of note, at the same time, a study showed a non-significantly increased risk of endotracheal tube occlusion with heated wire humidifiers compared to HME (2.7% vs. 0.5%,  $P=0.12$ ) [22]. In these studies comparing the HME to HH, and more generally in the literature, there is an implicit starting premise that HHs outperform HMEs. We have shown that this cannot be presumed to be true, especially for humidifiers with heated wires [56].

Another issue with HMEs is their obstruction or occlusion with plugged secretions. In the study by Ricard et al. with HMEs elevated above the endotracheal tube to limit the passage of secretions in the device, this risk was 10% despite a period of prolonged use of HMEs of up to 7 days [57]. The replacement rate of HMEs secondary to obstruction was 15% in the study of Kollef et al. [30]; again, HMEs could

be used up to 7 days. In the study by Davis et al. where there were no specific precautions, the frequency of partial occlusion was 3% when the HMEs were changed every 24 h and 9% when the HMEs were changed every 5 days [58]. In the same study, resistances of 12 partially occluded HMEs were measured [58]. The devices' resistances increased from a mean of 1.1 before use to 2.8 cmH<sub>2</sub>O/l/s. The highest resistance involved two cases of partial occlusion by hemorrhagic secretions where the resistance went from 0.85 before use to 5.8 cmH<sub>2</sub>O/l/s. This increase in resistance of the HME or of the endotracheal tube associated with inadequate humidification or thick secretions may delay weaning patients and remains a real problem.

### 17.2.5 Active HMEs and Innovative Systems

The place of active HMEs is more difficult to define. This type of device was first described in 1992 by Kapadia et al. [59]. The Booster™ is positioned between the HME and the patient. A metal part is covered with a membrane that allows heating external water. The membrane made of Gore-Tex™ allows the production of water vapor. This system can be used with any HME in order to improve its performance [60]. Another system, the Humid-Heat™, is based on a similar principle, with a heated humidifier piece surrounding a specific HME, also with a supply of extra water [61]. A third “active” HME has been described, the “performer,” based on the same principle [62]. The latter was evaluated with the psychrometric method in the study conducted by Chiumello et al., which allows a comparison with our results. The system delivered inspiratory gases with a water content from 3 to 5 mgH<sub>2</sub>O/l above HMEs with good performance [49, 62]. The active HME tested had higher humidification performances in comparison with effective HMEs avec, a gain of approximately 3 mgH<sub>2</sub>O/l with the Booster™ and about 5 mgH<sub>2</sub>O/l with the Humid-Heat™ under standard conditions of use. However, the clinical benefit to increase humidity from 30 to 35 mgH<sub>2</sub>O/l is not clear in the literature.

The Hydrate OMNI (Hydrate Inc., Midlothian, VA), a new original humidification system, is now available on the market, but few data are available. This system is neither a heated humidifier nor a passive or active HME, but a humidification device based on water vaporization in contact with a heated piece of ceramic. According to the manufacturer, humidification performances of this inline vaporizer are very high, and our very first evaluation reached a similar conclusion (unpublished data). There are no data concerning the impact of external conditions on this system. The other advantage of this device is the absence of additional dead space as it is positioned just behind the Y-piece (ventilator side). Also, theoretically there is no condensation in the inspiratory limb, but water traps or porous circuits should be used for the expiratory limb. However, there is currently no clinical evidence to recommend a system that provides 40 mgH<sub>2</sub>O/l or even more vs. 30 mgH<sub>2</sub>O/l. Also, clinicians must be aware that there is very little experience with devices that can deliver humidity above 40–45 mgH<sub>2</sub>O/l or even more, and with these new products, particular attention should be paid. The cost/benefit is another factor to consider with such systems.

### 17.3 Mechanical Properties of Humidification Systems (Resistances and Dead Space)

In addition to the humidification properties, mechanical aspects of HME and HH (especially resistance and dead space) must be taken into consideration in specific clinical situations. There is significant heterogeneity of the dead space and resistance among humidification devices [7, 63–66]. The dead space should be considered more than the resistance between HMEs and HHs. Indeed, humidification system resistances are fairly similar [67]. The HH circuit's resistance is not negligible, especially if the heated wire is in the circuit. Resistance is probably less if the heated wire is integrated into the wall. Several studies showed that during assisted ventilation, HMEs increased the work of breathing and the minute ventilation, and decreased alveolar ventilation in comparison with HHs [68–73]. During controlled ventilation, HMEs decrease the alveolar ventilation in comparison with HHs [73–78]. In patients with ARDS, it is possible to obtain the same alveolar ventilation with lower tidal volumes when using heated humidifiers because of the reduction of the instrumental dead space. In Moran's study, when replacing the HME by a heated humidifier, with the same alveolar ventilation target, it was possible to reduce the tidal volume from  $521 \pm 106$  to  $440 \pm 118$  ml ( $P < 0.001$ ) without significant changes in  $\text{PaCO}_2$ , and plateau airway pressure decreased from  $25 \pm 6$  to  $21 \pm 6$   $\text{cmH}_2\text{O}$  ( $P < 0.001$ ) [75].

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### 17.4 Comparison of Humidification Devices Cost

Several studies have compared the costs of different humidification systems [15, 19–21, 25, 30, 57, 80–82]. Comprehensive studies are difficult to perform and should take into account (1) the costs of devices and circuits, (2) the human costs, such as time to set up heated humidifiers, time to change HMEs and time to empty the water traps (when heated wires are not used), and (3) miscellaneous costs, such as cleaning, storage and maintenance of humidifiers, water used in humidifiers, water traps, etc.

Not surprisingly, most evaluations have shown that the costs associated with heated humidifiers are much larger compared with those for the HMEs. Branson et al.

**Table 17.2** Daily cost for different humidification devices (in US dollars, from [82])

Humidification device	Day 1	Day 2	Day 3	Day 4	Day 5
HME	5.2	4.6	4.5	4.4	4.7
HH with heated wire	30.2	16.1	12.6	9.9	9.0
HH without heated wire	27.8	21.7	19.6	18.6	18.0

HH heated humidifiers, HME heat and moisture exchangers

compared HMEs with heated humidifiers with and without heated wires [82]. In this study, the use of heated humidification without heated circuits caused a heavy workload in relation to water trap emptying (on average 9 times per 24 h), a procedure whose duration was estimated at 5 min. Therefore, 45 min per day was spent to empty water traps with this system. The cost of using heated humidifiers (with or without heated wires) was much larger than for HMEs in this study (Table 17.2). Moreover, during this study, HMEs were changed every 24 h. With less frequent changes (every 2–3 days and up to 7 days), the daily cost of these devices is even lower [27, 57, 58, 80, 81].

The duration of ventilator circuit use was 24 h in the study of Craven who challenged this practice [36]. Other studies followed and showed that the spacing change and even the lack of change for the same patient resulted in a reduction of costs and especially the rate of ventilator-acquired pneumonia [83–87], which went against the generally accepted idea. The question of HME use duration follows the same path, but there is still a fear of prolonged use of these devices based on the risks of poorer humidification performance and of increased resistance of the HMEs. Most manufacturers recommend changing these devices every 24 h. Yet many studies have argued for lifetimes greater than 24 h [24, 27, 30, 46, 57, 58, 80, 81, 88, 89] and up to 7 days [27, 30, 57]. With prolonged use, humidification performances do not change a lot with the most efficient filters, with the exception of the results in Ricard et al.'s study, which in three COPD patients over 10 showed a reduction over time of HME effectiveness with an absolute humidity below 27 mgH<sub>2</sub>O/l (with a minimum of 24.9 mgH<sub>2</sub>O/l in a patient on day 5) after several days of use [57]. However, among 23 other patients without COPD included and in the majority of COPD patients, the values of absolute humidity measured daily remained stable during the 7 days of use. Similarly, no endotracheal tube occlusion occurred with this practice. In this same study, the resistances of the devices were not significantly different after use [57].

In addition to the maximum duration of a single HME, the issue of the maximum duration of use of this humidification system has been raised for patients with prolonged ventilation. Branson et al. proposed an algorithm that limited HME use to a maximum of 5 days [25, 90], replacing them with a heated humidifier after this period. There are currently no clear data for limiting the duration of HME use. Numerous studies have demonstrated that prolonged use of HMEs did not result in any particular risk for patients [20, 22, 91]. Especially in the study conducted by Lacherade et al., who compared HMEs and HHs in terms of the rate of ventilator-acquired pneumonia, duration of use was 2 weeks on average in the HME group ( $n=185$ ) without specific problems being noted [22]. The rate of ventilator-acquired

**Table 17.3** Advantages and drawbacks for different humidification devices

Humidification device	Humidification performances	Circuit condensation (I/E)	Dead space	Resistance	Cost
Passive HME	– to ++	0/0	+ to +++	+	–
Active HME	++	0/0	++	+	+
Heated humidifier	– to +++	0 to ++/0 to +	0	0 <sup>a</sup> to +	+
Inline vaporizer	+++ ?	0/?	0	+/-	+?
This system does not exist	+++	0/0	0	0	–

HME heat and moisture exchangers

<sup>a</sup>If heated wires are within the circuit wall

pneumonia (28.8% vs. 25.4%,  $P=0.48$ ), the duration of mechanical ventilation ( $14.9 \pm 15.1$  vs.  $13.5 \pm 16.3$ ,  $P=0.36$ ) and the mortality (34.2% vs. 32.8%, NS) were similar. A trend for more endotracheal tube occlusion was noted in the heated humidifier group in comparison with HME group (6 vs. 1,  $P=0.12$ ).

## 17.5 Conclusion

The choice of a humidification system during mechanical ventilation should of course take into account the humidification performance, but also the mechanical properties and finally the cost of the device (Table 17.3). For the majority of patients, well-performing HMEs can be used when mechanical ventilation is initiated. For specific situations, when instrumental dead space reduction is considered, heated humidifiers may be a better choice. Clinicians have to be aware of the impact of external conditions, especially ambient or outlet ventilator temperature (heated humidifiers) or patient core temperature (heat and moisture exchangers), on humidification device performance.

*Heated humidifiers with heated wires* have very reduced performance if the inlet temperature of the humidification chamber is high, which can happen when the ambient temperature is high (absence of air conditioning or a humidifier “in the sun”) or when the outlet temperature of the ventilator is high (using turbine ventilators). This issue is partially improved by a compensation algorithm and specific technologies (counter-flow humidifiers), but these systems are not available in all countries. The performances of *humidifiers without heated wires* are influenced by the settings as expected, but are much less influenced by external conditions. Recommended settings with these humidifiers (Y-piece temperature around 30–32°C) deliver gas at around 30 mgH<sub>2</sub>O/l or slightly above.

*Heat and moisture exchangers* have very heterogeneous humidification performances, and only a few models attain 30 mgH<sub>2</sub>O/l. Systems with similar external appearance can have very different humidification performances, which can cause potentially serious confusion. HME performance is mainly influenced by the expiratory humidity, which is mainly related to the patient’s temperature. In hypothermic patients whose expiratory gas water content is lower than that of normothermic

patients, HMEs perform poorly. However, there is a lack of clinical data for short-term periods of hypothermia (as for therapeutic hypothermia after cardiac arrest, which is usually used for 24 h). The additional instrumental dead space with HMEs causes a reduction in alveolar ventilation. This may have an impact particularly on patients requiring a protective ventilatory strategy (low tidal volume and high respiratory rate). In these cases, heated humidifiers should be used. Also, HMEs can increase the work of breathing during assisted ventilation, which can be an issue for severe COPD patients, and the minimal level of pressure support used for spontaneous breathing trials should be 10–12 rather than 5–7 cmH<sub>2</sub>O if an HME is used.

The current role for *active HMEs and new systems (the inline vaporizer)* is not clear, and more data are required to better define their potential advantages and drawbacks. Also, with new systems, the question of over-humidification needs to be raised, and clinicians must be aware of this potential risk, which did not exist with previous systems.

Independent data on humidification system performance in addition to the other factors that differentiate HME and heated humidifiers (mainly mechanical properties and costs) must be known by the clinician in order to choose the optimal humidification system for patients on mechanical ventilation.

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Leonardo Lorente

Of the major complication groups in postoperative patients, that of pulmonary difficulties is one of the most frequent causes of increased morbidity and mortality. A preventive strategy is necessary to reduce the incidence of pulmonary complications and minimize their clinical repercussions. Atelectasis is a frequent complication in postoperative patients. During mechanical ventilation, atelectasis can occur because medicinal gases are cold and dry. Atelectasis can cause hypoxemia and increase the risk of nosocomial pneumonia. Adequate airway humidification can help prevent the occurrence of atelectasis. The decision to use a heat and moisture exchanger (HME) or heated humidifier (HH) should be made for each patient, based on cost assistance, infection control, and other medical considerations. The decision about the use of HMEs can generally be considered based on cost savings; however, in patients with the presence of specific circumstances (such as hypothermia, atelectasis, thick secretions or hemoptysis), the use of HHs can be considered.

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## 18.1 Introduction

Pulmonary difficulties comprise a group of major complications in postoperative patients and are one of the most frequent causes of increased morbidity and mortality in these patients [1]. Among the pulmonary complications are the following: acute lung injury (ALI), acute respiratory distress syndrome (ARDS), pleural effusions, atelectasis, nosocomial pneumonia, pulmonary embolism and phrenic nerve dysfunction.

The risk of pulmonary complications is higher in specific patients, such as those having abdominal surgery, cardiothoracic surgery, emergency surgery, general

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L. Lorente  
Intensive Care Unit,  
Hospital Universitario de Canarias,  
La Laguna, Tenerife, Spain  
e-mail: lorentemartin@msn.com

anesthesia, a dependent functional status, history of chronic obstructive pulmonary disease (COPD), and impaired sensorium or neurologic deficits, and those who smoke or are elderly.

Atelectasis is a frequent complication in postoperative patients [2–5]. During anesthesia induction, the functional residual capacity (FRC) decreases below the lungs' closing volume and can result in micro- and macroatelectasis. In addition, during mechanical ventilation atelectasis can develop because medicinal gases are cold and dry. Atelectasis can cause hypoxemia and increase the risk of nosocomial pneumonia.

Strategies must be developed in the perioperative period to reduce the appearance of atelectasis and minimize its clinical repercussions, such as adequate postoperative pain control, adequate hydration, the use of incentive spirometry for lung expansion, elimination of respiratory secretions, early mobilization when possible and adequate airway humidification.

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## 18.2 Need for Humidification

The use of mechanical ventilation with an artificial airway requires conditioning of the inspired gas [6]. This is because medicinal gases are cold and dry, and when the upper airway is bypassed it cannot contribute to the natural heat and moisture exchange process of inspired gases.

At low levels of inspired humidity, water is removed from the mucus and periciliary fluid by evaporation, causing increased viscosity of mucus and loss of the periciliary fluid layer. Thus, mucociliary clearance decreases since thick mucus is difficult for cilia to remove and, besides, mucociliary transport is impaired because of the decreased cilia beat rate. Continuous desiccation of the mucosa causes cilia paralysis, cell damage, decreased functional and residual capacity, and atelectasis may develop.

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## 18.3 Appropriate Level of Humidification

There is controversy about what constitutes the optimal humidity level of the inspired gas and about the appropriate humidification system. Some authors have advocated absolute humidity levels of 26–32 mg of water vapor/l of gas and recommend the use of a heat and moisture exchanger (HME) because these devices provide these levels. However, others advocate an absolute humidity level of 44 mg of water vapor/l of gas and recommend the use of heated humidifiers (HH) because they can condition inspired gas to this humidity level (programmed to deliver medicinal gas at a temperature of 37°C and a relative humidity of 100%). These authors believe that using an HME delivering 26–32 mg of water vapor/l of gas to humidify inspired gas results in a 12–18-mg water vapor/l humidity deficit and an associated high rate of water loss from the periciliary fluid layer. Thus, the inspired gas is not conditioned to body temperature and saturated with water vapor until the

third generation of the airways, and the sections of the airway prior to this point are desiccated, causing mucociliary dysfunction and moisture loss from the periciliary fluid layer. These authors claim that a humidity of 32 mg/l is the minimum humidification level, below which significant dysfunction occurs (ciliary paralysis and cell damage) and recommend HH because these devices can condition inspired gas to 44 mg water vapor/l of inspired air, thus avoiding periciliary fluid layer and mucus water loss, and preserving mucociliary clearance.

In the review by Williams et al. [6], 200 articles/texts on respiratory tract physiology and humidification were considered. Each published study was scrutinized for sufficient data (explicit or implied) on the measure of the inspired air temperature and humidity, patient core temperature, period of exposure to each humidity level and sufficient information to allow the assignment of a dysfunction score to the result of each exposure period. The data from the relevant studies were plotted on a humidity exposure map with each measurement from each study represented as a single point. The dysfunction state observed at each measurement was coded. From the position of these data points, it is possible to derive the boundaries of the successive dysfunction states. This review reveals that there are few humidity, temperature and mucosal function studies of human subjects and that the duration in most of them was only 12 h. The trend in the data suggests that mucociliary dysfunction can occur after 24–48 h with an absolute humidity level of <32 mg water vapor/l (the humidification delivered by HME devices) and that the optimal humidification model of inspired medicinal gas should be at body temperature and 100% relative humidity, containing approximately 44 mg water vapor/l of gas (which can be achieved with HH devices). However, further research with longer exposure times than 24 h is needed to fully verify this proposition.

In the study by Hurni et al. [7], 115 patients who required mechanical ventilation for 48 h or more were randomized to receive inspired gas conditioned either by an HH at 32°C and a relative humidity of 100%, or by an HME. In 41 patients receiving mechanical ventilation for 5 or more days, the morphologic integrity of the respiratory epithelium, obtained by endotracheal aspirate, was evaluated on day 1 and day 5 of mechanical ventilation. Recognizable respiratory epithelial cells were scored using a six-point scale, one point being assigned for the normal appearance and zero points to an abnormal appearance of each of the following characteristics: cilia, end plate, cytoplasm color, cell shape and cytoplasm texture, nuclear size, and nuclear shape and texture. The scores of 200 epithelial cells were added to obtain a final score with a maximum possible value of 1,200 (indicating maximum cytological integrity) and a minimal value of 0 (indicating maximum damage). In both patient groups, the scores significantly decreased from day 1 to day 5 (in the HH group from  $787 \pm 104$  to  $745 \pm 88$  and in HME group from  $813 \pm 79$  to  $739 \pm 62$ ;  $p < 0.01$  for both groups). Besides, in the patient group with HMEs the reduction of the epithelium score was greater, although not significantly so, than in the patient group with HHs. The authors noted that they could not exclude some contribution of inadequate tracheal temperature and humidity to this progressive reduction in cytological score. In our opinion, the absence of significant differences can be attributed to two causes: (1) the limited sample size of only 41 patients,

and (2) in the HH group, the inspired gas was conditioned to a relative humidity of 100% and a temperature of only 32°C (but what should the result be with a temperature of 37°C, which ensures the delivery of approximately 44 mg of water/l of gas?).

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## 18.4 Types of Humidifiers

Artificial humidification of medicinal gases can be active or passive. In the active humidifiers, called heated humidifiers (HH), the inspired gas passes across or over a heated water bath. Passive humidifiers, called artificial noses or heat and moisture exchangers (HMEs), trap heat and humidity from the patient's exhaled gas and returns some of them to the patient on the subsequent inhalation.

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## 18.5 Advantages and Disadvantages of the Different Types of Humidifiers

There is also controversy concerning the possible influence of these systems on the incidence of ventilator-associated pneumonia (VAP). In the meta-analysis published in 2007 by Siempos et al. [8], which included 13 randomized controlled trials with 2,580 patients, there was no difference between the HME and HH patient group in the incidence of VAP (OR 0.85, 95% CI 0.62–1.16), ICU mortality (OR 0.98, 95% CI 0.80–1.20), length of ICU stay (weighted mean differences, –0.68 days, 95% CI –3.65 to 2.30), duration of mechanical ventilation (weighted mean differences, 0.11 days, 95% CI –0.90 to 1.12) or episodes of airway occlusion (OR 2.26, 95% CI 0.55–9.28). Although HMEs were cheaper than HHs in each of the randomized controlled trials, a subgroup analysis was performed by including only the five RCTs in which the used HHs contained heated wire circuits (which markedly reduce the formation of condensate and thus the risk of VAP). This analysis showed no difference in the development of VAP between patients undergoing MV managed with HMEs and those managed with HHs with heated wire circuits (OR 1.16, 95% CI 0.73–1.84, 1,267 patients). The subgroup analysis of the seven RCTs in which heated circuits were not employed demonstrated that use of an HME was associated with fewer episodes of VAP than use of HHs without heated circuits (OR 0.61, 95% CI 0.42–0.90, 1,073 patients). Finally, three RCTs in which the mean duration of MV was >7 days and the used HHs contained heated wire circuits revealed no significant difference between patients managed with passive and active humidifiers regarding the incidence of VAP (OR 1.32, 95% CI 0.65–2.68, 870 patients).

In addition to VAP, there are other important issues that must be considered when a passive humidifier is used. The results of several studies suggest that HH humidification is preferable, reporting a lower incidence of tube occlusion, thick bronchial secretions and atelectasis than with HMEs [9]. Besides, the use of HME is associated with increased airway resistance and dead space; thus, HMEs could entail increased work of breathing [10–12].

## 18.6 Recommendations About the Type of Humidification in Recently Published International Guidelines

Recommendations for the preferential use of either an HME or HH have not been established by several published guidelines on the prevention of VAP.

The guidelines of the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) published in 2008 did not review the issue of humidification systems [13].

The guidelines of the Canadian Critical Care Society published in 2008 do not make a recommendation about humidification systems because there is no difference in the incidence of VAP between both systems of humidification [14].

The guidelines of the British Society for Antimicrobial Chemotherapy published in 2008 recommended the use of HMEs rather than HHs in patients who have no contraindications to their use (e.g., patients at risk of airways obstruction), as HMEs are more effective in reducing the incidence of VAP [15]. However, the UK guidelines did not include the meta-analysis published in 2007 by Siempos et al. with a larger number of studies and of patients showing that there was no difference between the HME and HH patient groups in the incidence of VAP, ICU mortality, length of ICU stay, duration of mechanical ventilation or episodes of airway occlusion [8].

The European Task Force provided by four European societies (Respiratory, Intensive Care Medicine, Clinical Microbiology and Infectious Diseases, and Anaesthesiology) published in 2009 recommended the use of HMEs over HHs [16].

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## 18.7 Conclusions

Of the major complication groups in postoperative patients, that of pulmonary difficulties is one of the most frequent causes of increased morbidity and mortality.

A preventive strategy is necessary to reduce the appearance of pulmonary complications and minimize their clinical repercussions.

Adequate airway humidification can help prevent the occurrence of atelectasis. The use of HMEs or HHs should be established for each patient, and this decision should be based on cost assistance, infection control and other medical considerations.

The use of HMEs can generally be decided upon based on cost savings (since HMEs were cheaper than HHs in several studies), but not on VAP reduction (according to the results of the more recently published meta-analysis). However, in patients with the presence of specific circumstances (such as hypothermia, atelectasis, thick secretions or hemoptysis), the use of HHs can be considered.

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# Humidification During Laparoscopy Procedures: Key Topics Technologic and Clinical Implication

# 19

## Humidification in Laparoscopy

Guniz Meyanci Koksals and Emre Erbabacan

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### 19.1 Introduction

Laparoscopy is now a common minimally invasive technique with an increasing number of benefits for the patient and to some degree for the delivery of health care [1]. It is associated with a shorter length of hospital stay, less postoperative pain, fewer pulmonary complications, and earlier return to normal activity [2]. To perform laparoscopic surgery, it is necessary to create a pneumoperitoneum by insufflating carbon dioxide into the abdominal cavity. Pneumoperitoneum causes reductions in cardiac output, and systemic carbon dioxide absorption influences splanchnic, renal and cerebral blood flow during minimally invasive procedures [1, 2].

Carbon dioxide (CO<sub>2</sub>) is used almost universally as the insufflation gas of choice. Medical grade CO<sub>2</sub> is supplied as a compressed liquid in cylinders with a release temperature of approximately -90°C [3]. Laparoscopic procedures use CO<sub>2</sub> gas at a temperature of -19–21°C with a relative humidity approaching 0% at the point of entry into the peritoneal cavity, which is not identical to the normal physiological condition of the peritoneal cavity (36°C and virtually 100% relative humidity). Experimental and clinical studies of short duration laparoscopic insufflation have demonstrated that cold, dry CO<sub>2</sub> insufflation can lead to peritoneal consequences (structural, morphological and biochemical changes in the peritoneal mesothelial surface layers) and result in numerous detrimental outcomes, including hypothermia, increased postoperative pain and narcotics consumption, as well as prolonged delayed recovery [3, 4].

Hypothermia causes significant perioperative morbidity, and it is an important concern of anesthesiologists. We have noted in our daily practice that prolonged

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G.M. Koksals (✉) • E. Erbabacan  
Department of Anesthesiology and Reanimation,  
Cerrahpasa Medical Faculty, Istanbul University,  
Istanbul, Turkey  
e-mail: gunizkoksals@hotmail.com; emreerbabacan@gmail.com

abdominal laparoscopy is responsible for a significant drop in core body temperature. This results from the combination of specific heat losses, particularly via convection and evaporation, leading to energy loss from the body due to the insufflated gas and nonspecific heat losses caused by the imbalance of thermoregulatory mechanisms during general anesthesia [5]. The warm abdomen and the organs therein provide a large internal surface area for heat exchange, and because gas is constantly circulating and being renewed, there is a significant energy transfer from the patient to the intraperitoneal gas as the gas is warmed [6]. Many studies have focused on evaluating the postoperative outcomes of pain and narcotic use in patients having different kinds of procedures, comparing conventional dry-cold, dry-warmed and humidified-warmed gas in prospective, randomized, controlled studies.

Sammour et al. [7] conducted a multicenter, double-blinded, randomized controlled trial investigating warming and humidification of carbon dioxide insufflation in laparoscopic colonic surgery in 82 patients. No statistically significant difference was obtained in postoperative opiate analgesia usage, intraoperative core temperature, or the peritoneal or plasma cytokine response between groups. Therefore, warming and humidification of insufflation gas are not recommended in laparoscopic colonic surgery.

Savel et al. [8] performed a randomized double-blind, prospective, controlled clinical trial of 30 patients undergoing laparoscopic Roux-en-Y gastric bypass. Patients received postoperative analgesia from morphine, delivered via a patient-controlled analgesia pump, and pain scores and the amount of morphine used were measured postoperatively. Their trial was unable to provide evidence of any significant reduction in postoperative pain as measured by either morphine requirements or pain scores with the use of warmed humidified CO<sub>2</sub>. They were able to demonstrate a statistically significant increase in end-of-case temperature with the use of this device, but this result was not clinically significant.

Wong et al. [9] showed that CO<sub>2</sub> pneumoperitoneum resulted in severe peritoneal acidosis in a porcine model, and it was unchanged by heating and humidification or the addition of bicarbonate. Peritoneal acidosis may play a role in promoting tumor cell implantation during laparoscopic oncological surgery.

Farley et al. [10] showed that while patients undergoing laparoscopic cholecystectomy with warmed (35°C) and humidified CO<sub>2</sub> (95% relative humidity) had several advantages that were statistically significant but not clinically between groups. They recommended carrying out better and larger randomized blinded trials.

Mouton et al. [11] advocated that the use of humidified insufflation gas reduces postoperative pain following laparoscopic cholecystectomy, but the heat-preserving effect of humidified gas insufflation was not significant.

Peng et al. [12] suggest that heated (37°C), humidified (95% relative humidity) insufflation results in significantly less hypothermia, less peritoneal damage and decreased adhesion formation as compared with cold, dry CO<sub>2</sub> insufflation.

Benavides et al. [13] compared the use of warm, humidified gas with cold, dry gas and showed that in laparoscopic surgery humidified (95% relative humidity), warmed (35°C) gas improved clinical outcomes significantly up to 10 days by reducing postoperative pain and the use of morphine equivalents, and by improving quality of life immediately in the postoperative recovery.

Sammour et al. [14] performed a meta-analysis on the effect of warm humidified insufflation on pain after laparoscopy including several randomized controlled trials (RCTs). This meta-analysis demonstrated a reduction in postoperative pain with heated, humidified insufflation CO<sub>2</sub> in major laparoscopic surgery; this appeared to be consistent at different intervals in the postoperative period, whether measured by Visual Pain Score (VAS) or analgesic requirements.

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## 19.2 Conclusion

It has been proved that the use of cold and dry CO<sub>2</sub> in laparoscopic surgery causes an increase in postoperative pain, hypothermia and acidosis in the peritoneum, and a decrease both in preoperative and postoperative patient comfort. The loss of heat during the perioperative period causing hypothermia is an important concern for anesthesiologists and intensivists. Hypothermia not only causes metabolic changes, but also prolongs the recovery time after anesthesia, resulting in the increased use of supplies and drugs, which can lead to the patient needing to be in the ICU. All of these issues will result in increased lengths of hospital stays, morbidity and costs. To avoid this, we try to keep the patients' temperature within physiological limits by warming patients perioperatively. During laparoscopic surgery it is not possible to keep the patients' temperature within normal values with external heating because the surgeons prefer to use cold and dry CO<sub>2</sub>. Although many studies on the warming and humidification of CO<sub>2</sub> have been carried out in the past decade, two different opinions still exist, one supporting warming and humidification, and the other against it. The most important factor in these two different opinions is the discrepancy among the study protocols. The warming temperature and rate of humidification, patient groups, type and duration of operations differed in the study groups. It would be more appropriate to standardize the patient groups, and the warming and humidification rate of the gas in prospective, blind clinical trials. In these studies, different warming levels and different concentrations of humidification that are suitable for human physiology must be used. As is commonly accepted, the results of the animal trials are not thoroughly concordant with the human studies. Especially in studies where the pain and the amount of analgesic used are evaluated, using animal models may not be correct. This discordance is more evident in small animals like rats. Which surgeon is doing the laparoscopic surgery is also an issue. The use of laparoscopic surgery has increased dramatically in the last decade because of cosmetic concerns and its lower surgical stress. It is essential that the surgical team is experienced in the procedure, the patient is in a proper position and the gas is thoroughly emptied. All of these factors affect the postoperative waking from the anesthesia, pain, amount of analgesic used and hemodynamics of the patient. Hence, the study protocols dealing with the warming and humidification of CO<sub>2</sub> in humans must be accomplished by skilled teams.

In future studies, the techniques of warming and humidification must also be evaluated. Different techniques will surely affect the results of the studies. Nowadays different techniques, such as the HME-Booster, Modified-Aeroneb and Pall system, are being worked on, but still no significant benefit compared to the others has emerged for any of the techniques.

Wang et al. [9] demonstrated in a pig model that the acidosis created in the peritoneum by CO<sub>2</sub> gas in laparoscopy increased the implantation of tumor cells, and the warming and humidification of CO<sub>2</sub> or buffering with bicarbonate did not decrease this impact. Therefore, a detailed study is needed on the consequences of CO<sub>2</sub> insufflation in laparoscopic surgery in oncological patients.

As a result, although there are negative concerns about the warming and humidification of the CO<sub>2</sub> used to raise the abdominal wall during laparoscopic surgery, a large series of human studies is needed to examine which different physiological temperatures and humidification concentrations are required to eliminate the side effects of cold and dry gas.

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### 19.3 Key Major Messages

1. Today, laparoscopic procedures are increasingly preferred because they have better cosmetic results and the surgical stress is lower when compared with conventional techniques.
2. The cold (−21°C) and dry (0%) CO<sub>2</sub> used in laparoscopic surgery causes an increase in postoperative pain and need for analgesics, and a decrease in both perioperative and postoperative patient comfort accompanied by morphological and metabolic changes in the peritoneum.
3. Cold and dry CO<sub>2</sub> causes the patient to be hypothermic, and external heating is insufficient to prevent hypothermia.
4. Warming and humidification of CO<sub>2</sub> are an order of the day, although some studies suggest that warming and humidification do not prevent the effect of cold, dry gas.
5. The side effects of cold and dry CO<sub>2</sub> must be prevented. New prospective, blind clinical studies need to be carried out on the different techniques of warming and humidification, and different temperatures and humidification concentrations using consistent large patient groups by skilled surgical and anesthesia teams.

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## Section VI

# Humidification and Ventilator Associated Pneumonia

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# Respiratory Filters and Ventilator-Associated Pneumonia: Composition, Efficacy Tests and Advantages and Disadvantages

# 20

Leonardo Lorente

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## 20.1 Introduction

Respiratory filters (also known as bacterial or microbial filters) are devices with a high capacity to prevent the passage of microorganisms [1] and are placed in the breathing circuit in order to protect the patient from possible respiratory infections carried by the respirator.

The use of respiratory filters was proposed after the reports between 1952 and 1972 of several outbreaks of respiratory infection attributed to contamination of anesthesia machines [2–4].

However, the results of later studies showed no contamination of patients by anesthesia machines, and vice versa [5–9], and that they could have undesirable effects [10] and did not decrease the incidence of ventilator-associated pneumonia (VAP) in clinical studies [11–13]; therefore, its usefulness is questioned.

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## 20.2 Composition of Respiratory Filters

The internal component of the filters can be composed of different materials [1]: wool, foam, paper, polypropylene, polysulfone, ceramics or glass fibers.

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## 20.3 Mechanisms of Filtration Microbiological Respiratory Filters

Filters can have different mechanisms of microbial filtration [1]: (1) mechanical filtration, (2) electrostatic filtration and (3) filtration bactericides.

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L. Lorente  
Intensive Care Unit, Hospital Universitario de Canarias,  
La Laguna, Tenerife, Spain  
e-mail: lorentemartin@msn.com

1. Mechanical filtration is determined by several aspects. First, the size of the filter's pores causes the organisms to be retained on a relatively large filter surface. Second, the provision of nonlinear irregular pores determines the course of air-flow and causes an increase in inertial force that traps the microorganisms within the mesh. The pore size can allow interception of organisms larger than 1  $\mu\text{m}$  and thanks to the nonlinear arrangement of the pores increases their ability to filter microorganisms larger than 0.5  $\mu\text{m}$ . This principle has the limitation that the mesh of tiny pores has high resistance to airflow.
2. The electrostatic filter is produced by the fibers of the internal components of the filter being subjected to an electric field. Bacteria and viruses also have a surface electric charge, either positive or negative, and remain trapped in the dipole electric fields of the filter screen.
3. The bactericidal filter is made by impregnating the filter material with bactericidal agents. Their action allows the growth of bacteria within the filter. For this purpose, antiseptic substances such as chlorhexidine acetate have been used. They are not recommended because they can dissolve in the condensate circuit and reach the tracheobronchial tract.

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## 20.4 Efficacy Tests of Respiratory Filters

Microbial filtration efficiency of the filters is assessed by challenge with a microbial aerosol [1]. An aerosol with a microorganism and a known concentration is generated, then the aerosol is passed through the filter and the concentration examined after passing through the filter. Filter efficiency is analyzed by an aerosol with different organisms; a comparison is made of the concentration of microorganisms in the gas applied to the filter and the effluent gas after it has passed through the filter.

The filtration efficiency is evaluated for bacteria and viruses. Bacterial filtration of tiny *Pseudomonas* or *Serratia marcescens*, which have a diameter of 0.3  $\mu\text{m}$ , was evaluated. Viral filtration efficiency was evaluated with the hepatitis C virus, which has a diameter of 0.03  $\mu\text{m}$ .

Many experimental studies have verified the ability of antimicrobial filters to prevent the passage of microorganisms. Some filters examined in the filtration efficiency tests in vitro reached values of bacterial filtration efficiency greater than 99.999% [1].

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## 20.5 Insertion in the Respiratory Circuit

Respiratory filters are inserted in the breathing circuit with a conical socket of 15 mm diameter (in the area of the patient) and a conical plug of 22 mm diameter (in the area of the respirator). This prevents the disconnection of the breathing circuit, which would endanger the patient's life.

## 20.6 Functions of the Filters According to Their Location in the Breathing Circuit

The functions of microbial filters vary depending on their location in the breathing circuit: (1) In the inspiratory limb, they can prevent antegrade infection of the patient by the respirator; (2) in the expiratory limb, they can prevent the retrograde infection of the patient by the respirator; (3) interposed between the “Y” part and the endotracheal tube, they can have both functions.

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## 20.7 Disadvantages of the Respiratory Filters

Antimicrobial filters involve some undesirable effects [10]: (1) increased resistance to inspiratory airflow, (2) increased resistance to expiratory airflow and (3) an increase in the dead space of the breathing circuit.

1. The antimicrobial filters cause an increase in expiratory flow resistance, which can promote air trapping within the patient’s lungs. Pulmonary air trapping can have different implications: (a) hemodynamic deterioration, (b) risk of pneumothorax and (c) impaired gas exchange. Pulmonary air trapping leads to increased intrathoracic pressure, which causes the venous return, and therefore can decrease cardiac output and blood pressure. One of the mechanisms of the production of pneumothorax is increased intrathoracic pressure, and this increase appears with air trapping. Moreover, this can also cause air trapping impaired gas exchange because of changes in ventilation/perfusion of the lung, and therefore lead to the development of hypoxemia and/or hypercapnia. This effect could appear when the filter is interposed between the “Y” part and the endotracheal tube or is located in the expiratory limb (immediately before the expiratory valve of the respirator).
2. Respiratory filters produce an increase in inspiratory flow resistance, which may have implications for the patient and the respirator. This increase in inspiratory flow resistance increases the work of breathing of the patient to initiate inspiration and may hinder weaning from mechanical ventilation. Besides, this increase in inspiratory flow resistance also increases the work of breathing for inspiration, and positive pressure can damage the mechanism of the respirator. This effect can appear when the filter is interposed between the “Y” part and the endotracheal tube or is located in the inspiratory limb (immediately after the ventilator inspiratory valve).
3. The bacterial filters generate an increase in dead space because the air space does not participate in gas exchange and can lead to hypoventilation and the development of hypoxemia and/or hypercapnia. This effect can appear when the filter is interposed between the “Y” part and the endotracheal tube.

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## 20.8 Advantages and Disadvantages of the Different Types of Respiratory Circuits Based on the Location of the Filters

The different breathing circuits used, based on the location of respiratory filters in the circuit, have different advantages and disadvantages. In a breathing circuit with one filter, the filter is interposed between the “Y” part and the endotracheal tube. The advantage of a filter circuit with one filter is that the initial economic cost is lower (because there is only one filter). The disadvantages of using one filter are the increased dead space in the circuit and that the filter has to be changed often as it gets contaminated by patient secretions from coughing.

In a breathing circuits with two filters, one is placed in the inspiratory limb (immediately after the ventilator inspiratory valve) and another in the expiratory limb (immediately before the expiratory valve of the respirator).

The advantages of circuits with two filters are that there is no increasing dead space and no risk of having to change filters because of contamination by patient secretions. The disadvantage of using two filters is that the initial breathing circuit is more expensive (because there are two filters).

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## 20.9 Contribution of Anesthesia Machines in Respiratory Infection

The issue of whether contaminated ventilators and anesthesia machines are the origin of nosocomial pneumonia is controversial, with some data implicating them [2–4] and others not [5–9].

Reports from 1952 to 1972 on several outbreaks of respiratory infections attributed the contamination to anesthesia machines [2–4]. However, none of the reports presented a bacteriological demonstration of a cause-and-effect relationship; however, the study by Tinne et al. reported that the same isolate of *Pseudomonas aeruginosa* responsible for an outbreak of postoperative pneumonia was cultured from the corrugated tubing of an anesthesia machine and from Ambu bags [3].

Contrarily, several studies have shown no contamination of the patient by the anesthesia machine and vice versa [5–9]. In some studies [5, 6] of anesthetized patients with and without respiratory infection, samples were taken from several sites of the anesthesia machine and breathing circuits before and after anesthesia, and no differences were found in the contamination of the anesthesia machine and breathing circuits in either patient group. Other studies [6–9] have simulated the contamination of an anesthesia machine by intentional contamination of the expiratory limb of the breathing circuit with an inoculum of an organism, after the sterilization of the anesthesia machine and the entire respiratory circuit, and with continued contamination of the anesthesia machine and breathing circuit inspiratory limb. The authors suggest that the absence of contamination of the anesthesia machine and breathing circuit inspiratory limb is because microorganisms cannot live in the

breathing circuits, because the circulating gas is cold and dry (characteristic of medicinal gases), which hinders the survival of microorganisms.

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## **20.10 Efficacy of the Respiratory Filters to Reduce the Incidence of Ventilator-Associated Pneumonia (VAP)**

In an attempt to prevent ventilator-associated pneumonia by contamination of respirators and anesthesia machines, inserting respiratory filters in the breathing circuits has been proposed.

Some authors have suggested that respiratory filters could reduce the incidence of respiratory infections associated with mechanical ventilation because of a reduction in the incidence of infections acquired by exogenous pathogenesis [4], i.e., those infections that are caused by microorganisms that do not colonize the oropharynx at the time of diagnosis. This decrease in exogenous respiratory infection processes could be due to the fact that microbial filters in respiratory circuits could reduce the risk of exogenous microorganisms reaching the patient antegradely from the inspiratory valve of the respirator or retrogradely from the exhalation valve of the respirator.

However, in clinical studies respiratory filters have failed to reduce the incidence of ventilator-associated pneumonia in patients on anesthesia machines [11, 12] and in critically ill patients [13]. In 1981, Garibaldi et al. [11] examined 520 patients on anesthesia breathing circuits with filters (inspiratory and expiratory) or without filters, and found no difference in the cumulative incidence of ventilator-associated pneumonia (16.7% vs. 18.3%). In 1981, Feeley et al. [12] studied 293 anesthetized patients, a group with a filter circuit in the inspiratory limb and one without filters, and no differences in the cumulative incidence of ventilator-associated pneumonia between the two groups (2.2% vs. 2.5%) was found. In one study carried out by our team, 230 critically ill patients were randomized to receive mechanical ventilation with and without respiratory filters. We did not find significant differences between patients with and without respiratory filters in the percentage of patients who developed VAP (24.56% vs. 21.55%), in the incidence of VAP per 1000 days of mechanical ventilation (17.41 vs. 16.26 without BF) or in the incidence of exogenous VAP per 1000 days of mechanical ventilation (2.40 vs. 1.74) [13].

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## **20.11 Recommendations of the International Guidelines for the Use of Antimicrobial Filters in Respiratory Circuits**

In the guidelines of the Centers for Disease Control and Prevention (CDC) for the prevention of VAP published in 2004 [14], no recommendation was made for or against the use of respiratory filters in breathing circuits of respirators, either with hot water humidifiers or with heat and moisture exchangers, or in breathing circuits of anesthesia machines, because there is insufficient evidence or consensus on their effectiveness.

The guidelines of the Canadian Critical Care Society published in 2008 did not recommend using respiratory filters [15].

The guidelines of British Society for Antimicrobial Chemotherapy published in 2008 recommended the use of expiratory filters for patients suffering from highly communicable infections (e.g., human coronavirus) and who require mechanical ventilation to reduce the contamination of ventilator circuits (although they do not reduce the VAP risk) [16].

In the guidelines published in 2008 by the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) [17] and in those published by two different European working groups in 2009 [18] and 2010 [19], there were no reviews of the issue of preventing VAP.

The CDC guidelines for preventing the transmission of *Mycobacterium tuberculosis* recommend the use of respiratory filters in patients with suspected or confirmed bacillary pulmonary tuberculosis undergoing mechanical ventilation [20].

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## 20.12 Conclusion

Outbreaks of VAP were associated with the contamination of anesthesia machines from 1952 to 1972; however, none of the reports presented a bacteriological demonstration of a cause-and-effect relationship.

Bacterial filters have been interposed in respiratory circuits to avoid VAP caused by contamination of ventilators and anesthesia machines.

The use of respiratory filters has not decreased the incidence of VAP in patients using anesthesia machines and in critically ill patients.

Besides, respiratory filters could have some undesirable effects, such as an increase of resistance to inspiratory airflow, increase of resistance to expiratory airflow and increase of dead space in the breathing circuit.

The use of respiratory filters is not routinely necessary; however, they should be used in patients with suspected or confirmed highly communicable respiratory infections (such as bacillary pulmonary tuberculosis) and who require mechanical ventilation.

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# Efficacy of Heat and Moist Exchangers in Preventing Ventilator-Associated Pneumonia (VAP): Clinical Key Topics

# 21

Patrick F. Allan

The opinions or assertions contained herein are the private views of the author and are not to be construed as reflecting the views of the Department of the Air Force, Army, Navy, or the Department of Defense.

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## 21.1 Introduction

Heat and moisture exchangers or HMEs (also known as artificial noses) are a form of passive humidification of the ventilator circuit designed to mimic the natural humidification process in the upper airways. In the HME system that is placed between the Y-connector of the ventilator tubing and the tracheal tube, the patient's exhaled gases pass through the exchanger, heating a filter and condensing the water in it. During inhalation the gas passes through the same filter, and is thereby heated and humidified in the process achieving approximately 30–33°C and greater than 23–32 mg/l H<sub>2</sub>O. One of the advantages of the HME system is to reduce contaminated condensate in the ventilator circuit where the microorganisms that colonize the ventilator predominate. These microorganisms that colonize the ventilator circuit have been found to originate from the patient [1]. Advantages of the HME system include lower costs, and particularly lower workload with the recent improvements in the performance characteristics of HMEs that prolong the frequency of changing the device to 7 days, which also reduces septic handling [2, 3]. Disadvantages of the HME system include potential for artificial airway occlusion by tenacious secretions, which may also increase resistance in the circuit, and the increased dead space volume of the system. Contraindications to the use of certain

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P.F. Allan  
Department of Pulmonary, Critical Care, and Sleep Medicine,  
Landstuhl Regional Medical Center,  
CMR 402, Box 307, APO AE 09180 Landstuhl, Germany  
e-mail: patrick.allan@amedd.army.mil

types of HMEs include tenacious or bloody secretions, copious secretions, obstructive airway disease (COPD) or increased airway resistance, high minute ventilation, bronchopleural fistula and hypothermia.

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## 21.2 Hydrophobic and Hygroscopic HMEs

Hydrophobic HMEs are associated with bacterial filtration and not so much by humidification properties, whereas hygroscopic HMEs (HHME) are characterized by humidification properties and not so much bacterial filtration. A variant of hygroscopic HMEs is the hygroscopic condenser humidifiers or HCHs, which are coated with lithium chloride or calcium chloride to improve heat and moisture exchange. Some hygroscopic HMEs also have bacterial-viral filter membranes in addition to their humidification compounds (HHMEF or HCHF).

In a comparison of hygroscopic HMEs changed every 24 h, hydrophobic HMEs changed every 120 h and hygroscopic HMEs changed every 120 h in a surgical ICU setting in patients ventilated for more than 48 h, the frequency of nosocomial pneumonia among the groups was unchanged, and changing out the HME after 120 h did not diminish efficiency, increase resistance or alter bacterial colonization [4].

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## 21.3 Risk of Airway Occlusion

An important consideration in the selection of the HME system is the patient's risk of airway occlusion. The earlier humidification studies [5–8] looking at VAP used purely hydrophobic HMEs, which demonstrated higher rates of endotracheal occlusion compared to HHs. Hess et al. [9] also reported a greater risk of airway occlusion with passive than active humidifiers (RR 3.84, 95% CI 1.92–7.69). These findings led to the recommendation that clinicians avoid HMEs in patients at risk of airway occlusion, such as those with hemoptysis or tenacious secretions, and this recommendation was applied in the most recent RCTs [3, 10–14]. However, the newer generation of HMEs with hygroscopic properties has proven to be safer than hydrophobic HMEs [8, 15, 16]. As a result most recently several experts have strongly advised that HMEs can be safely used in patients with COPD who have copious and tenacious secretions or patients with high minute ventilation.

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## 21.4 Summary

The newer generation of hygroscopic HMEs has been shown to be equivalent to HH-HWCs in the incidence of VAP and can now be safely used even in patients with COPD and copious secretions. They are seen as a cost effective alternative; however, this benefit depends on the frequency of exchange of the device and the provider's time.

## **21.5 Effects of Active Humidification on Ventilation-Associated Nosocomial Pneumonia**

### **21.5.1 Introduction**

Heated water humidifiers or HHs, or heated humidifiers and heated wire circuits (HH-HWC) are a form of active humidification of the ventilator circuit. An advantage of the HH system is the ability to achieve higher humidity levels in the inspired gas than HMEs, thereby preserving mucociliary clearance. In the active systems, external water sources and electricity are used to heat blended gas mixtures to simulate body conditions (temperature of  $>35^{\circ}\text{C}$ , water content  $>40$  mg/l). Inspiratory air passes over the heated water bath and cools as it approaches the patient, which can result in rainout. Rainout or condensate that collects in the ventilator tubing is a reservoir for bacterial contamination and impedes good airflow. If the contaminated condensate drains back to the patient's respiratory tract, VAP can result, particularly as a result of turning the patient or raising the bed rail [12, 17]. To prevent this, the HH-HWC system consists of a heater wire intended to reduce formation of ventilator tubing condensate, which has been blamed for increasing VAP development [18, 19]. The heater wire is located inside the inspiratory tube downstream from the humidifier.

### **21.5.2 HH-HWC Compared with HH**

In a trial consisting of medical and surgical ICU patients categorized as ineligible for HME use because of prolonged ventilation, pre-existing lung disease or thicker secretions, the HH-HWC was compared to the HH. The circuits were changed out every 7 days, and the mean duration of ventilation was longer than 7 days. No significant difference in VAP was found between the trial groups [10]. This study was included in Siempos et al.'s [18] subgroup analysis of five RCTs [3, 10, 12–14] in which HHs of the HH-HWC type were compared, and they concluded there was no difference between patients managed with HMEs and HHs in regards to VAP incidence or mortality. This was also found in the subgroup analysis of the three RCTs [12–14] that used HH-HWCs, and the mean duration of ventilation was  $>7$  days. However, in the subanalysis of seven RCTs [5, 6, 11, 17, 20–22] with the use of HHs without HWCs, there were more episodes of VAP than with HMEs.

### **21.5.3 Summary**

An advantage of the traditional HH system has been the ability to achieve higher levels of humidity; however, this advantage had resulted in the disadvantage of accumulation of condensate in the ventilator tubing that predisposed MV patients to VAP. However, with the advent of the use of HH-HWCs, this disadvantage has been overcome, and they have been shown to be equivalent to HMEs in the incidence of VAP.

## 21.6 Global Result Effects of Humidification on the Incidence of VAP

### 21.6.1 Introduction

Mechanical ventilation (MV) following endotracheal intubation bypasses the natural physiologic heat and moisture exchanger of the upper airway, and within 48 h can lead to inflammation and dry airway epithelia [2, 19, 23]. In addition pathogens from the patient's own oropharyngeal and gastrointestinal flora, which colonize the upper airway, can pool around the endotracheal tube and then be aspirated into the lung. These risk factors place MV patients at great risk for ventilator-associated pneumonia (VAP), which is defined as pneumonia occurring 48 h after endotracheal intubation and initiation of MV, and which increases mortality, lengthens ICU stays and increases hospitalization costs [24]. It has been well established that a means of heating and humidifying inspiratory air is therefore needed in the ventilator circuit to reduce mucosal injury and VAP; however, the best means of achieving this continues to be debated, particularly with the development of the new generation of HMEs with good humidification and bacterial-viral filtration properties.

By the early 2000s, there was a growing body of evidence, including several meta-analyses comparing HMEs with HHs in mechanically ventilated patients, showing a trend toward lower VAP incidence in the use of the HMEs or passive humidifiers compared with the HH or active humidifier. The first of these meta-analyses was by Hess et al. [9] and included six randomized controlled trials (RCTs) [3, 5, 6, 10, 20, 21] with the combined effect of showing a lower incidence of VAP with the use of passive rather than active humidifiers. In a non-randomized prospective study by Kranabetter et al. [25], all patients admitted to an ICU consisting of primarily abdominal and thoracic surgical cases admitted during a 21-month time period were placed on active (1887 patients) humidification, followed by all patients (1,698) admitted for a 21-month period being placed on passive humidification. Kranabetter et al. found no difference in the incidence of VAP, and in the subgroup of patients on MV for >2 days, found a lower incidence of VAP in the HME group. This was followed by another meta-analysis by Kola et al. [26] in 2005, which included many of the same studies [3, 5, 6, 10, 20, 21] as Hess et al. [3, 5, 6, 10, 20, 21] plus two additional studies [11, 22] [9], and reached the same conclusion that the use of HMEs in mechanically ventilated patients reduced the incidence of VAP also in patients ventilated for >7 days. However, both of these meta-analyses favored passive humidification because of the Kirton et al. [21] study, which was a relatively larger study including 280 patients in a trauma ICU setting that showed HMEF significantly reduced the incidence of late-onset VAP, but not early onset VAP, compared to conventional HH-HWC, whereas the previous RCTs only showed a slightly lower VAP rate with passive humidification. Factors that were not examined by these meta-analyses include the impact on mortality, duration of mechanical ventilation and ICU length of stay.

Most recently, Siempos et al. [18] did a systematic review of 13 RCTs (2397 patients) comparing passive and active humidification that included the eight studies included in the Kola et al. meta-analysis [3, 5, 6, 10, 11, 20–22, 26] plus five addi-

tional studies [12–14, 27, 28], three [12–14] of which had recently been published. This most recent review was also intended to examine the effect of these devices on mortality, length of intensive care unit stay and duration of mechanical ventilation. In summary, the group found that passive humidifiers did not significantly reduce the incidence of VAP (14 versus 16%, OR 0.85, 95% CI 0.62–1.16, 2341 patients), mortality (25 versus 26%, OR 0.98, 95% CI 0.80–1.20, 2104 patients), length of ICU stay (–0.68 days of ICU stay; 95% CI –3.65 to 2.30, 1291 patients), duration of mechanical ventilation (weighted mean differences, 0.11 days of MV; 95% CI –0.90 to 1.12, 2397 patients) or episodes of airway occlusion (OR 2.26, 95% CI 0.55–9.28, 2049 patients).

## 21.6.2 Summary

With the wide array of humidification systems available, there is a lack of large-scale, blinded, high-quality randomized controlled studies in the literature with specific definitions of VAP, which would ideally include quantitative cultures rather than just clinical and radiographic criteria, and uniform VAP preventive strategies. Preventative strategies that also need to be addressed include: prevention of occlusion of the ventilator circuit by secretions, environmental and health care workers' hand hygiene in handling the circuit, and frequency of exchange of the humidifier. Based on the most recent study findings, the following organizations have concluded that neither active nor passive humidification should preferentially be used in the prevention of VAP in patients undergoing mechanical ventilation: the American Thoracic Society and Infectious Disease Society of America [23], Centers for Disease Control and Prevention [29], the American Association for Respiratory Care [9], American Burn Association [30] and European Task Force on VAP [31]; however, the Canadian Critical Care Trials Group and Canadian Critical Care Society in their published guidelines recognized the slightly decreased incidence of VAP with HMEs compared to HHs, but advocated the use of HMEs primarily based on cost issues.

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# Humidifier Type and Prevention of Ventilator-Associated Pneumonia: Chronological Overview of Recommendations

# 22

Sonia Labeau and Stijn Blot

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## 22.1 Introduction

Ventilator-associated pneumonia (VAP) is defined as pneumonia occurring 48 h after endotracheal intubation and initiation of mechanical ventilation [1]. In intubated patients, VAP is an important cause of morbidity and mortality, and of prolonged hospital and intensive care unit (ICU) stay. Additionally, VAP is associated with considerable costs for both society and the individual afflicted [2].

Preventing VAP is a key priority among ICU healthcare professionals. Several authoritative organizations have issued evidence-based guidelines to assist clinicians in their prevention efforts, the most recent being published jointly by the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) as part of their 2008 compendium of strategies

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S. Labeau (✉)  
Faculty of Healthcare,  
University College Ghent,  
Ghent, Belgium

Faculty of Medicine and Health Sciences,  
Ghent University, Ghent, Belgium  
e-mail: sonia.labeau@hogent.be

S. Blot  
Faculty of Healthcare,  
University College Ghent,  
Ghent, Belgium

Faculty of Medicine and Health Sciences,  
Ghent University, Ghent, Belgium

General Internal Medicine and Infectious Diseases,  
Ghent University Hospital, Ghent, Belgium

to prevent healthcare-associated infections in acute care hospitals [3]. The document highlights practical recommendations for the implementation of a number of VAP prevention strategies. It nevertheless refers to previously published evidence for more detailed guidance in specific VAP prevention issues such as, for instance, which type of airway humidifier to choose in intubated patients.

Below, the current state of the science regarding which type of airway humidifier is recommended in terms of preventing VAP is summarized.

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## 22.2 The Importance of Airway Humidification

Airway humidification can be defined as the addition of heat and moisture to inspired gases delivered to the mechanically ventilated patient via an artificial airway. During normal breathing, inspired air is warmed, humidified and filtered by a mucous membrane in the upper respiratory tract. In intubated patients, however, the upper airway is bypassed by the presence of an endotracheal tube, thus impeding the natural heat and moisture exchange processes. Consequently, the mechanically ventilated patient is at risk for inspissation of airway secretions, destruction of airway epithelium, and inflammation. The natural defense mechanisms that, in normal circumstances, protect the lung from infection are deficient. The medical gases inspired through the ventilator are, moreover, dry and cold. Conditioning of these gases is thus of utmost importance to adequately protect the mechanically ventilated patient from pernicious complications.

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## 22.3 Airway Humidification Devices

Artificial humidification of medical gases can be accomplished using either a heated humidifier (HH) or a heat and moisture exchanger (HME).

HHs operate actively to increase the heat and water vapor content of inspired gases by forcing the gases to pass across or over a heated water bath before they are inhaled by the patient. The warmed gas is nevertheless cooling while passing from the HH to the patient's airway, resulting in condensate that is accumulating within the ventilator circuit and that is associated with an increased risk for VAP [2, 4, 5]. Indeed, condensate in the ventilator tubing not only hinders adequate airflow, but is also known to attract bacterial contamination, and may contaminate the environment and the hands of the clinicians who remove the condensate manually from the tubing [4]. Flushing the condensate into the lower airway may also increase the risk of VAP [5]. The combined use of HHs with a heated wire circuit may reduce the formation of this condensate.

HMEs, also known as artificial noses, are passive humidifiers that function by storing heat and moisture from the expired gas and returning them to the patient via the inspired gas during the subsequent inhalation. They mimic the natural mechanisms and processes of the upper respiratory tract. HMEs are placed between the Y-connector of the ventilator tubing and the endotracheal tube, thus diminishing the accumulation of condensate in the circuit to a great extent.

Different types of HMEs are available. While the function of hydrophobic HMEs is mainly bacterial filtration, hygroscopic HMEs and hygroscopic condenser humidifiers are treated with hygroscopic salts that increase their humidification capacity. Hygroscopic condenser humidifiers are very similar to hygroscopic HMEs, but their surface is additionally coated with lithium chloride or calcium chloride to improve chemically the heat and moisture exchange [4]. Also, bacterial filters are integrated in some hygroscopic devices.

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## 22.4 The Optimal Humidity Level

There is an ongoing debate on what constitutes the optimal humidity level of the inspired gases. Some authors promote absolute humidity levels of 26–32 mg of water vapor per liter of delivered gas with a concurrent use of HMEs, as these devices deliver the humidity levels mentioned. Others support the use of absolute humidity levels of 44 mg of water vapor per liter of delivered gas and simultaneously recommend the use of HHs for their ability to condition inspired gases to this higher humidity level. Further studies with bigger sample sizes would be of interest to come to more conclusive statements concerning the optimal humidity level [2].

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## 22.5 Type of Humidifier and VAP Prevention

The potential impact of the type of airway humidifier on the incidence of VAP has been a controversial issue in the various evidence-based VAP prevention guidelines that have been issued over the years, and in the conclusions of systematic reviews and meta-analyses investigating this topic. So far, no unanimous recommendations exist. Table 22.1 provides a chronological overview of the different recommendations of evidence-based guidelines and conclusions of reviews of the literature on which humidifier type to prefer in terms of VAP prevention.

In the 2001 evidence-based guidelines by the European Task Force (ETF) [6], an outline was provided of the key VAP prevention issues that were under debate at that time. A distinction was made between issues that were ‘still controversial’ and ‘not controversial.’ In these guidelines, the issue of which humidifier type to recommend is categorized as being ‘still controversial.’ Randomized studies that were conducted at that time demonstrated a comparable incidence of VAP using HMEs and HHs, and it was questioned whether this was due to the reduction of condensed fluid in the expiration circuit or to the bacterial filtration properties of the devices.

Three years later, in 2004, both the Centers for Disease Control and Prevention (CDC) [7] and the Canadian Critical Care Society (CCCS) [8] issued evidence-based guidelines that provided extensive and well-substantiated recommendations for VAP prevention. In the CDC guidelines the question whether to recommend HMEs or HHs in terms of preventing VAP is considered an unresolved issue [7] because of contradicting findings from the referenced studies. The CCCS recommendations [8], however, state that the use of HMEs can be associated with a slightly decreased

**Table 22.1** Chronological overview of recommendations/conclusions concerning humidifier type in terms of VAP prevention

Year	Author	Recommendation/conclusion
2001	ETF [6]	Still controversial
2004	CDC [7]	Unresolved issue
2004	CCCS [8]	HMEs recommended
2005	ATS-IDSA [9]	No preferential use of HME or HH
2005	Kola et al. [1]	Significant reduction in VAP incidence using HMEs, particularly in patients ventilated for at least 7 days
2007	WIP [4]	No preferential use of HME or HH
2007	Lorente et al. [2]	Use of HME in patients expected needing mechanical ventilation for 24–48 h, and HH in patients expected requiring more prolonged ventilation
2008	IDSA-SHEA [3]	Issue not covered
2009	Torres et al. [5]	Preference of HMEs over HH

incidence of VAP compared with the use of HHs based on the evidence from seven trials with at least one of the following characteristics: concealed randomization, blinded outcome adjudication, an intention-to-treat analysis, or an explicit definition of VAP. The CCCS therefore recommend the use of HMEs over HHs, clarifying, nevertheless, that this recommendation is not only based on clinical, VAP preventing advantages, but that also cost considerations favor the use of HMEs.

The 2005 guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia by the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) [9] make no recommendation for the use of HMEs or HHs. They state that, although HMEs have demonstrated to decrease ventilator circuit colonization, they have not consistently succeeded in reducing the incidence of VAP and therefore cannot be considered as a pneumonia prevention tool.

A meta-analysis conducted in the same year (2005) by Kola et al. evaluated the available evidence on the efficacy of passive compared to active humidification in preventing VAP [1]. In this study, eight RCTs between 1990 and 2003 met the inclusion criteria of the analysis. As a result, a significant reduction in the incidence of VAP in patients humidified by HMEs during mechanical ventilation was found, particularly in patients ventilated for 7 days or longer. This finding is nevertheless limited by the exclusion of patients at high risk for airway occlusion from some of the studies. The authors suggest that more RCTs are needed to investigate the wider applicability of HMEs [1].

The findings of this meta-analysis were nevertheless criticized in a systematic review that was conducted 2 years later, in 2007, by the Dutch Working Party on Infection Prevention (WIP) [4] and that resulted in deviating findings. WIP systematically reviewed all (quasi-) randomized trials, systematic reviews and meta-analyses that compared humidification methods in ventilated ICU patients to identify which humidification policy is best in terms of preventing VAP. Ten trials that, overall, were found to be of poor quality were included in the review.

As a result, WIP does not recommend either passive or active humidifiers to prevent VAP, nor do they make recommendations concerning the type of passive humidifiers of choice. Regarding active humidification, WIP recommends the use of heated wire circuits [4]. The rationale behind this recommendation is that less condensate reduces colonization and subsequently the risk of spread in the ICU when removing condensate. According to WIP, the main reason for the difference between their own findings and those of Kola et al. [1] is that the latter resulted from the summary of too many diverse trials, with a treatment group incorporating all types of HMEs, i.e., hydrophobic and hygroscopic with or without filtering, and a control group including HHs both with and without heated wire circuits. Moreover, WIP questioned the current relevance and up-to-datedness of the results reported by Kola et al. [1], as of the eight trials that were included in the meta-analysis, seven dated from 1998 or earlier.

Also in 2007, Lorente et al. [2] made a comparison of the evidence-based VAP prevention guidelines that had been issued since 2001, updated with the further most recent evidence at that time. As for the type of airway humidifier recommended, the authors emphasize the lack of unanimity concerning this issue. Of the publications they reviewed, a considerable diversity in findings was shown, with one study reporting lower VAP rates associated with the use of HMEs, several studies not finding significant differences between HMEs and HHs, and three studies describing a lower incidence of VAP with the use of HHs. Although the authors [2] suggest that more research is needed to determine which airway humidifier is most efficient in preventing VAP, they recommend the use of HMEs in patients who are expected to need mechanical ventilation for 24–48 h, and of HHs in patients expected to require more prolonged ventilation.

As previously mentioned, the 2008 recommendations jointly issued by the IDSA and the SHEA [3] do not provide clear guidance concerning the type of airway humidifier of choice, but refer to previously published guidelines for recommendations on this issue.

Recently, three European Societies, the European Respiratory Society (ERS), the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and the European Society of Intensive Care Medicine (ESICM), jointly established a manuscript in which the European perspective on the management and prevention of VAP was elucidated [5]. The authors review in depth topics that were not covered by the last IDSA/ATS guidelines [9] and controversial issues, such as which type of humidifier is recommended in terms of VAP prevention [5]. The authors refer to the evidence as summarized by the CCCS [8] to substantiate their recommendation in favor of using HMEs over HHs [5].

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## 22.6 Additional Considerations

The focus of this chapter is on the relationship between the type of airway humidifier and the prevention of VAP. However, some other important concerns that must be taken into account when considering a specific type of humidifier are the potential

risk for tube occlusion, thick bronchial secretions, atelectasis, increased airway resistance and dead space, and thus increased work of breathing, which have been reported with the use of HMEs [2]. These issues, nevertheless, are beyond the scope of the current topic.

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## 22.7 Conclusion and Key Messages

There is still a lack of unanimity concerning which type of airway humidifier best succeeds in preventing VAP in mechanically ventilated patients. More high-quality randomized controlled trials with large sample sizes are needed to obtain more consistent conclusions. In these, besides VAP, mortality and cost-effectiveness should be incorporated as primary outcomes. Moreover, uniformity in the definition of VAP is required, as well as a comprehensive description of the comparisons included.

The present authors recommend the use of HMEs in patients who are expected to need mechanical ventilation for 24–48 h, and HHs in patients expected requiring more prolonged ventilation.

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# Humidification on the Incidence of Ventilator-Associated Pneumonia: Evidence and Guidelines on the Prevention of VAP for the Use of HME or HH

# 23

Leonardo Lorente

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## 23.1 Introduction

When the upper airway is bypassed, it cannot contribute to the natural heat and moisture exchange process of inspired gases. The medicinal gases are cold and dry; thus, the use of mechanical ventilation with an artificial airway requires conditioning of the inspired gas [1].

In situations of low levels of inspired gas humidity, water is removed from the mucus and periciliary fluid by evaporation, causing increased viscosity of mucus and loss of the periciliary fluid layer. Continuous desiccation of the respiratory mucosa causes cilia paralysis and respiratory cell damage; thus, mucociliary clearance decreases since thick mucus is difficult to remove for cilia and also because mucociliary transport is impaired because of the decreased cilia beat rate. All these events facilitate the appearance of atelectasis, and the presence of atelectasis increases the risk of ventilator-associated pneumonia (VAP).

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## 23.2 Types of Humidification

There are two types of artificial humidification of medicinal gases, the active and the passive system. Passive humidifiers, called artificial noses or heat and moisture exchanger (HMEs), trap heat and humidity from the patient's exhaled gas and return some of that to the patient on the subsequent inhalation. In the active humidifiers, called heated humidifiers (HH), the inspired gas passes across or over a heated water bath. There are different types of HME: (a) the purely hydrophobic HME, with high antimicrobial filtration properties, but that performs poorly in terms of

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L. Lorente  
Intensive Care Unit, Hospital Universitario de Canarias,  
La Laguna, Tenerife, Spain  
e-mail: lorentemartin@msn.com

humidity output; (b) the hygroscopic HME, which has better humidifying qualities than the hydrophobic HME, but does not possess antimicrobial filtration properties; and (c) the hydrophobic and hygroscopic HME, which has both satisfactory humidity outputs and antimicrobial filtration properties.

There is controversy about what constitutes the appropriate humidification system and the optimal humidity level of the inspired gas. Some authors have advocated an absolute humidity level of 44 mg of water vapor/l of gas and recommend the use of heated humidifiers (HH) because they can condition inspired gas to this humidity level (programmed to deliver medicinal gas at a temperature of 37°C and a relative humidity of 100%). These authors believe that using an HME, delivering 26–32 mg of water vapor/l of gas to humidify inspired gas, results in a 12–18 mg water vapor/l humidity deficit and an associated high rate of water loss from the periciliary fluid layer. Thus, the inspired gas is not conditioned to body temperature and saturated with water vapor until the third generation of the airways, and the sections of the airway prior to this point are desiccated, causing mucociliary dysfunction and moisture loss from the periciliary fluid layer. These authors claim that a humidity of 32 mg/l is the minimum humidification level, below which significant dysfunction occurs (ciliary paralysis and cell damage), and recommend HHs because these devices can condition inspired gas to 44 mg water vapor/l of inspired air, thus avoiding the periciliary fluid layer and mucus water loss and preserving mucociliary clearance. However, other authors have advocated absolute humidity levels of 26–32 mg of water vapor/l of gas and recommend the use of a heat and moisture exchanger (HME) because these devices provide these levels.

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### **23.3 Evidence from the Literature on the Relationship Between the Use of an HH or an HME and the Incidence of Ventilator-Associated Pneumonia**

There is also controversy concerning the possible influence of these systems on the incidence of ventilator-associated pneumonia (VAP). One study reported a lower incidence of VAP associated with the use of HMEs [1]. On the other hand, several studies found no significant differences in VAP incidence between the two systems. Finally, there are also studies that found a lower incidence of VAP associated with HHs [2–4].

In the study by Kirton et al. [1] 280 trauma patients were randomized to receive an HME or HH. The VAP incidence was lower in the HME than in the HH group [9 of 140 (6.43%) vs. 22 of 140 (15.71%),  $p=0.02$ ]. The authors suggest that this difference can be attributed to two mechanisms: (a) the inclusion of an HME filter, which is suggested to protect the patient from exogenous VAP, and (b) reduced contaminated condensate in the HME circuit. With respect to the first mechanism, we believe that currently there are not sufficient data to support the role of gas filtration in reducing the incidence of VAP. Previous studies evaluating the effect of gas filtration in anesthesia machines and in ventilators were unable to demonstrate differences in the incidence of VAP between the patient groups with and without filters [5–7]. With respect to the second mechanism, we agree that entry of the contaminated

condensate circuit into the airway may explain the higher incidence of VAP reported with the HH system. Therefore, we recommend a new heated humidifier type, the servo-controlled humidifier, that is currently available, which differs from cascade humidifiers in that: (a) it has a dual-heated circuit and thus the mobile circuit condensate is minimal, (b) it has an auto-feed chamber (eliminating the need to open the circuit to refill the chamber with water), which minimizes the possibility of exogenous microorganisms entering the circuit and causing exogenous VAP.

In the study by Cohen et al. [2], for an 8-month period 170 patients on mechanical ventilation received an HME, and for the following 4 months, 81 patients received an HH as humidification system. The endotracheal tube occlusion rate was higher in the HME than in the HH group [15 of 170 (8.8%) vs. 1 of 81 (1.2%),  $p < 0.01$ ], and the increase in the endotracheal tube occlusion rate was associated with an increased incidence of VAP ( $p < 0.001$ ), atelectasis ( $p < 0.01$ ) and duration of mechanical ventilation ( $p < 0.01$ ).

In the study by Blin et al. [3], the incidence of VAP was studied for 24 months in six ICUs in France. A total of 1415 patients from four ICUs received HMEs and 373 patients from two ICUs received HHs. The incidence of VAP was higher in the HME than in the HH group [184 of 1415 (13.0%) vs. 29 of 373 (7.8%),  $p < 0.01$ ].

In 2006, our group published a randomized study [4] of 104 patients requiring mechanical ventilation for more than 5 days; we analyzed the incidence of VAP associated with the use of an HH or HME, finding it to be lower in the HH group [8 of 51 (15.69%) versus 21 of 53 (39.62%);  $p = 0.006$ ]; in addition, multivariate Cox regression analysis showed HMEs to be a risk factor for VAP (hazard ratio = 16.2, 95% confidence interval = 4.54–58.04,  $p < 0.001$ ). We believe that the reduction of VAP found in our study when using an HH as compared to an HME can be attributed to three causes: (a) The previously mentioned improvement of the HH system (with a dual-heated circuit and an auto-feed chamber). (b) The study analyzed patients on mechanical ventilation for more than 5 days, and the mean duration of mechanical ventilation (20 days) was higher than in previous studies (4–14 days). (c) With HHs it is possible to deliver higher levels of humidity to the airway (44 mg of water vapor/l of gas) than with HMEs (lower than 33 mg of water vapor/l of gas), and thus they can facilitate maximal mucociliary clearance. This study had several limitations. First, we did not perform the direct assessment of gas heating and humidification in the patients, so airway temperature and humidity were not monitored (the reliability of the data reported by the manufacturers was assumed). Second, we did not perform an indirect assessment of gas heating and humidification in the patients, so secretion characteristics or possible epithelial bronchial damage was not assessed.

A meta-analysis published in 2005 by Kola et al. [8], with 1378 patients from eight trials found that the use of HMEs decreased the VAP rate (relative risk = 0.7; 95% CI = 0.50–0.94). Only one of the studies included in the meta-analysis, the study by Kirton et al. [1], reported a significantly lower incidence of VAP with HMEs compared to HHs. This meta-analysis did not include the non-randomized studies by Cohen et al. [2] and Blin et al. [3]. After the meta-analysis, two recent randomized studies published by Lacherade et al. [9] and Boots et al. [10] found no significant differences in pneumonia rates associated with the use of HHs or HMEs. One

randomized study reported a lower VAP incidence with HHs in patients requiring mechanical ventilation for more than 5 days (15.69% versus 39.62%;  $p=0.006$ ) [4].

Afterward, in 2007, another meta-analysis by Siempos et al. was published [11], which included 13 randomized controlled trials with 2580 patients. There was no difference between HME and HH patient groups in the incidence of VAP (OR 0.85, 95% CI 0.62–1.16), ICU mortality (OR 0.98, 95% CI 0.80–1.20), length ICU stay (weighted mean differences,  $-0.68$  days, 95% CI  $-3.65$  to  $2.30$ ), duration of mechanical ventilation (weighted mean differences,  $0.11$  days, 95% CI  $-0.90$  to  $1.12$ ) or episodes of airway occlusion (OR 2.26, 95% CI 0.55–9.28). However, HMEs were cheaper than HHs in each of the randomized controlled trials. A subgroup analysis was performed by including only the five RCTs in which the used HHs contained heated wire circuits (which markedly reduce the formation of condensate and thus the risk of VAP). This analysis showed no difference in the development of VAP between patients undergoing MV managed with HMEs and those managed with HHs with heated wire circuits (OR 1.16, 95% CI 0.73–1.84, 1267 patients). The subgroup analysis of the seven RCTs in which heated circuits were not employed demonstrated that use of an HME was associated with fewer episodes of VAP than use of HHs without heated circuits (OR 0.61, 95% CI 0.42–0.90, 1073 patients). Finally, of three RCTs in which the mean duration of MV was  $>7$  days and the used HHs contained heated wire circuits revealed no significant difference between patients managed with passive and active humidifiers regarding the incidence of VAP (OR 1.32, 95% CI 0.65–2.68, 870 patients).

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### **23.4 Recommendations of Recently Published Guidelines on the Prevention of VAP with the Use of HMEs or HHs**

Recommendations for the preferential use of either HME or HH have not been established by recently published guidelines on the prevention of VAP.

The guidelines of the European Task Force published in 2009 provided by four European societies (the European Respiratory Society, the European Society of Intensive Care Medicine, the European Society of Clinical Microbiology and Infectious Diseases, and the European Society of Anaesthesiology) recommended the use of HMEs over HHs [12].

The guidelines of the British Society for Antimicrobial Chemotherapy, published in 2008, recommended the use of HMEs rather than HHs in patients who have no contraindications to their use (e.g., patients at risk of airway obstruction), as HMEs are more effective in reducing the incidence of VAP, with a recommendation grade A [13]. However, they suggested that the benefit of using HMEs versus HHs should be established for each patient and this decision should not be based solely on infection control considerations. The grade A for the recommendation of HMEs rather than HHs is based on the results of two meta-analyses [8, 14] and one systematic review [15]. The meta-analysis published in 2003 by Hess et al., including six trials and 1013 patients, concluded that although the available evidence suggests a lower VAP rate with HMEs than with HHs (relative risk = 0.65; 95% CI = 0.44–0.96), other issues related to the use of passive humidifiers (resistance, dead space volume,

airway occlusion risk) preclude a recommendation for the general use of HMEs [14], and the decision to use an HME should not be based solely on infection control considerations (recommendation, grade A). The meta-analysis published in 2005 by Kola et al. [8], with 1378 patients from eight trials, found that the use of HMEs decreased the VAP rate (relative risk=0.7; 95% CI=0.50–0.94), and also suggested that some contraindications to the use of HMEs must be considered (tenacious secretions, obstructive airway disease, hypothermia). In the systematic review published in 2004 by Dodek et al. [15], seven trials were included, and using HMEs in patients who have no contraindications (such as hemoptysis or a requirement for high minute ventilation) was recommended because they may be associated with a slightly decreased incidence of VAP. In that review, the authors expressed a concern about endotracheal tube obstruction associated with the use of HMEs, although this issue was not confirmed later. However, the UK guidelines did not include the meta-analysis published in 2007 by Siempos et al. with a higher number of studies and of patients showing that there was no difference between the HME and HH patient groups in the incidence of VAP, ICU mortality, length ICU stay, duration of mechanical ventilation or episodes of airway occlusion [11].

The guidelines of the Canadian Critical Care Society published in 2008 did not make a recommendation about which humidification system to use because there is no difference in the incidence of VAP between patients whose airways are humidified using an HME and those whose airways are humidified using an HH [16].

The guidelines of the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) published in 2008 did not review the issue of humidification systems [17].

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## 23.5 Conclusions

Much controversy exists about what constitutes the appropriate humidity level for inspired gas.

Thus, controversy also exists concerning the possible influence of the different humidification systems on the incidence of VAP. While one study reported a lower incidence of VAP associated with the use of HMEs, several studies found no significant differences between the two systems, and others have found a lower incidence of VAP associated with HHs.

The decision to use HMEs can generally be considered based on cost-saving considerations, but not on VAP reduction. However, in specific patients (such as those with hypothermia, atelectasis, thick secretions or hemoptysis), the use of HHs can be considered.

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# Humidification Devices and Ventilator-Associated Pneumonia: Current Recommendations on Respiratory Equipment

Jean-Damien Ricard, Alexandre Boyer, and Didier Dreyfuss

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## 24.1 Introduction

Ventilation-acquired pneumonia (VAP), defined as lung parenchyma inflammation caused by infectious micro-organisms, complicates the ICU course of 20–30% of mechanically ventilated patients [1]. Pneumonia develops after microbial invasion of the normally sterile lower respiratory tract and lung parenchyma. Among the risk factors for VAP, bacterial contamination of respiratory equipment (that can be an important reservoir for bacteria that can reach and infect the lung parenchyma) has been long recognized as a potential source of VAP [1]. Older inhalation therapy equipment posed a considerable challenge in the past (reviewed in [2]), and despite considerable improvement in respiratory equipment, the impact of humidification devices on the occurrence of VAP is still a matter of debate [2, 3]. Choice of equipment [4] and of VAP prevention policy may differ among countries [5] and perhaps impacts on costs of mechanical ventilation. This chapter will review past and recent data related to airway heating and humidification, and analyze its relationship with VAP.

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J.-D. Ricard (✉) • D. Dreyfuss  
INSERM U722, UFR de Médecine, Université Paris Diderot,  
Paris 7, Paris, France

Assistance Publique - Hôpitaux de Paris, Hôpital Louis Mourier,  
Service de Réanimation Médico-chirurgicale,  
178, rue des Renouillers, F-92700 Colombes, France  
e-mail: jean-damien.ricard@lmr.aphp.fr

A. Boyer  
Service de Réanimation Médicale, CHU Bordeaux,  
3 place Amélie Raba Léon, 33076 Bordeaux cedex, France

## 24.2 Circuit Contamination During Mechanical Ventilation

It has been suggested that contamination of respiratory tubing used with heated humidifiers may be a risk factor for VAP [6, 7]. This hypothesis stemmed from the rapid and considerable bacterial colonization of respiratory tubing encountered when heated humidifiers are used [8]. Craven et al. studied ventilator-circuit colonization during the first 24 h after a circuit change. They found that 33% of circuits were colonized at 2 h and 80% at 24 h. The median level of colonization at 24 h was  $7 \times 10^4$  organisms/ml [6]. Bacteria isolated in respiratory tubing condensates correlated with (and originated from) the microorganisms found in patients' tracheobronchial secretions [6, 9, 10]. The respiratory equipment becomes contaminated first and most heavily at sites near the patient [6]: in Craven et al.'s study [6], over 90% of swivel adapters were contaminated, whereas this figure was only 33% for the distal tubing. Similarly, 70% of the contaminated swivels grew above 1000 CFU, compared with 53 and 43% of the contaminated Y-junction and proximal tubing, respectively. The rate of condensation formation in the circuit was rapid (30 ml/h), and the level of colonization in the condensate was high (median level:  $2 \times 10^5$  organisms/ml). Obviously, such high levels of microorganisms posed an important threat of cross-contamination during the emptying of these condensates, but were also considered as a potential risk factor for VAP [6]. In a subsequent study, Craven et al. evaluated risk factors for VAP in over 200 patients requiring mechanical ventilation and found that respiratory tubing changes every 24 h rather than every 48 h was one of them. This finding questioned the appropriateness of changing respiratory tubing every 24 h, as was commonly done at the time. Larreau et al. were the first to show that increasing the length of use of respiratory tubing from 8 to 24 h was not associated with an increase in VAP or level of circuit contamination [11]. This original finding was confirmed by Craven et al. who showed the same level of circuit colonization whether these were changed every 24 or 48 h. It was then demonstrated that, in fact, respiratory circuits did not require any change at all during the entire period of mechanical ventilation of a given patient [12]. In this study, 73 patients requiring mechanical ventilation were randomized to have their circuits changed either every 48 h or not at all. Exhaustive bacteriological sampling showed similar rates of circuit contamination, and, importantly, similar VAP rates between the two groups. These pioneer results were confirmed by several teams (reviewed in [8]), leading to a radical evolution in the CDC guidelines for the prevention of nosocomial pneumonia, from a recommendation to change respiratory circuits daily [13] to one for no routine change, unless the circuits are visibly soiled or mechanically malfunctioning [14]. Obviously, such a policy results in considerable cost savings [12].

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## 24.3 Prevention of Circuit Colonization

As seen above, respiratory circuits get rapidly and heavily contaminated when heated humidifiers are used [6, 15, 16]. In that respect, HMEs provide a major advantage over humidifiers. Indeed, several studies have consistently shown the

reduction of breathing circuit contamination with HMEs in comparison with heated humidifiers. Martin et al. found that 11% of breathing circuits were contaminated when an HME was used compared with 54% with a heated humidifier ( $p < 0.01$ ) [17]. When patients had a positive bronchial specimen, the same pathogen grew on the Y-piece in 10% of cases with the HME and in 65% with a heated humidifier ( $p < 0.001$ ). Very similar and consistent results have been found by others [18–20]. As stated above, bacteria found in the circuits originate from the patients' respiratory flora, explaining why pharyngeal and tracheal colonization was found to be similar in patients ventilated with an HME compared to those ventilated with a heated humidifier [19].

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#### 24.4 Influence of Humidification Devices (Heated Humidifier or HME) on VAP

Because respiratory tubing contamination has been considered as a risk factor for VAP [6, 7], and because HMEs efficiently prevent this bacterial contamination in comparison with heated humidifiers [17], it has been suggested that use of HMEs may help decrease the incidence of VAP in mechanically ventilated ICU patients. The first comprehensive study that specifically compared HMEs and heated humidifiers in terms of VAP rate found no difference in VAP incidence between the two devices [19]. In this relatively large study, patients were randomized to receive mechanical ventilation either with an HME ( $n=61$ ) or with a heated humidifier ( $n=70$ ). Incidence of VAP was similar with the two devices (6/61 with HMEs and 8/70 with heated humidifiers). Similarly, bacterial colonization of the pharynx and trachea was identical in both groups. The strength of this study resided not only in the method used to diagnose VAP (quantitative culture of protected brush specimen), but also in the control for potential confounding factors. Several studies (reviewed in [8]) confirmed these findings and are summarized in Table 24.1.

The only study that apparently contradicted the initial findings was published by Kirton et al. in *Chest* in 1997 [21]. This single-center study randomized 280 trauma patients to receive mechanical ventilation either with a hydrophobic HME (BB100, Pall Incorporation) changed every 24 h or with a conventional heated wire humidifier (Marquest Medical Products). Circuits were changed every 7 days and inline suction catheters every 3 days. VAP (according to the Centers for Disease Control criteria) was diagnosed in 9/140 (6.4%) patients ventilated with the HME and in 22 (15.7%) patients with the heated humidifier ( $p < 0.05$ ). These seemingly compelling results call, however, for several remarks, as already alluded to [22]: first, the study population was exclusively trauma patients, and whether or not these results can be extended to medical ICU patients remains unknown; second, the VAP rate in this population was surprisingly low in comparison with reported figures in the same setting of trauma patients (17.5% in a large US database, [23]); third, the diagnosis of ventilator-associated pneumonia was not based on invasive bacteriologic sampling. Finally, the HME tested (BB100, PALL) is a poor-performing HME in terms of humidity delivery [24]. One can therefore hypothesize that tracheal secretions

**Table 24.1** Studies comparing incidence of VAP according to the humidification device used

Study	Number of patients		VAP rates <sup>a</sup>		RR (95% CI) with HMEs
	Heated humidifier	HME	Heated humidifier	HME	
Martin, 1990	42	31	19% (8)	7% (2)	0.34 (0.08–1.49)
Roustan, 1992	61	51	14.7% (9)	9% (5)	0.66 (0.24–1.86)
Branson, 1993	32	88	9% (3)	6% (5)	1.65 (0.42–6.51)
Dreyfuss, 1995	70	61	11.4%	9.8%	0.86 (0.32–2.34)
Branson, 1996	49	54	5.5% (3)	6% (3)	1.1 (0.23–5.21)
Boots, 1997	41	75	17% (7)	18.6% (14)	1.09 (0.48–2.49)
Kirton, 1998	140	140	15.7% (22)	6.4% (8)	0.36 (0.17–0.79)
Kollef, 1998	147	163	10.2% (15)	9.2% (15)	0.90 (0.46–1.78)
Memish, 2001	120	123	15.8%	11.5% 5	0.72 (0.38–1.37)
Lacherade, 2005	184	185	28.8 (53)	25.4 (47)	0.88 (0.63–1.23)

HME heat and moisture exchanger

<sup>a</sup>VAP rates are expressed as percentages. Figures in parentheses are the absolute numbers of VAP

were too dry to be suctioned, thus underrating the prevalence of nosocomial pneumonia in the HME group. Following this controversial study, two multicenter RCTs compared the incidence of VAP in patients ventilated either with an HME or with a heated humidifier [25, 26]. In 243 mechanically ventilated ICU patients, Memish et al. found no difference in VAP rate (11.5 in the HME group vs. 15.8 in the heated humidifier group,  $p=0.3$ ). Consistently, Lacherade et al., in the most recent study on the subject, found similar rates of VAP between HME and heated humidifier ventilated patients (25.4 vs. 28.8, respectively,  $p=0.48$ ). This is strictly consistent with the results of the smaller study by Dreyfuss et al. [19]. Interestingly, Lacherade et al. reported a significantly greater number of polymicrobial VAP in patients ventilated with a heated humidifier in comparison with HME patients (10 vs. 0,  $p<0.01$ ). Unfortunately, this point is not addressed by the authors in the discussion. Whether this latter finding is related to a greater percentage of patients with pathogens isolated in their tracheal aspirates when heated humidifier are used – as reported by Memish et al. [25] but not by others [19] – or to an important percentage of patients with multiple species of bacteria isolated in their respiratory tract [6] remains unknown. Taken together, results from these two large RCTs confirm the original findings, and all but one (with the methodological reservations explained above) study consistently found no influence of the humidification device on VAP rate in mechanically ventilated ICU patients.

## 24.5 Prolonged HME Use and Circuit Contamination and VAP

Because duration of use of HMEs can be safely prolonged up to a week without any change in their humidifying performances [27], one can legitimately question if such a policy is not associated with a decrease in circuit protection with the concurrent risk of an increase in VAP. Djedaini et al. were the first to study the prolonged

use of HMEs in terms of circuit contamination and VAP rate [28]. They compared two periods, one where HMEs were changed every 24 h (as recommended by the manufacturers); and the other where the change occurred every 48 h. Clinical evaluation showed no difference between the two periods in terms of quality of humidification; circuit colonization and VAP rates were very similar between the two groups. These findings were later confirmed and extended by several studies [22, 29–33]. For example, Davis et al. [31] compared the rate of circuit colonization and of VAP in patients ventilated with an HME changed either every 24 h or every 120 h, and found no difference between the two periods. Their study also confirmed the possibility of prolonging the use of these disposable devices without altering their humidifying properties [31]. Thomachot et al. found no difference in VAP rate when HMEs were changed either every 24 h or every 7 days [33].

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## 24.6 Influence of HME Type on Circuit Colonization and VAP

The filtering media contained in HMEs is considered the source of the antimicrobial properties of these devices, enabling them to block the bacteria present in the gas flow from contaminating the breathing circuits. Different types of filtering media are available (paper, foam, ceramic fiber), but do not influence occurrence of circuit contamination or of VAP [22, 31, 34, 35].

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## 24.7 Cross Contamination

Although, as discussed above, use of heated humidifiers is not associated with a greater incidence of VAP, these devices do have the potential for cross infection [15]. Findings by Craven et al. detailed above on the rapid and significant contamination of respiratory circuits and on the important formation rate and massive contamination of condensates in these circuits support this concern [6]. These highly contaminated condensates should therefore be handled as infectious waste and regularly emptied [6]. Repeating these septic maneuvers several times a day obviously increases the risk of cross infection, especially when patients are colonized with multidrug-resistant bacteria.

Preventing respiratory tubing condensates and contamination confers on HMEs a great advantage over heated humidifiers [19, 20, 22]. Attempts have been made to reduce the formation of condensation in the circuits of heated humidifiers by heating both the inspiratory and the expiratory limb of the circuit. Such new equipment needs to be evaluated in the clinical setting. Indeed, Lellouche et al. have showed that an increase in inlet chamber temperature induced by high ambient temperature markedly reduced the performance of these heated-wire humidifiers, leading to a risk of endotracheal tube occlusion [36]. In addition, a preliminary report found that condensation still occurred in up to 50% of patients ventilated with these heated circuits [10], leading to substantial bacterial colonization, with multidrug resistant bacteria in some instances.

## 24.8 Current Recommendations on Respiratory Equipment and VAP

Several recommendations have been recently published from review articles [37–39], to a consensus conference [40] and guidelines [14, 41]. Unfortunately for the clinician, and despite the use of the same available data, some of these recommendations diverge considerably. Whereas the 2003 CDC guidelines state that “no recommendation can be made for the preferential use of either HMEs or heated humidifiers to prevent pneumonia in patients receiving mechanically assisted ventilation,” others, on the contrary, “recommend the use of HMEs in patients who have no contraindications” [38]. In between, undecided opinions argue that “although the available evidence suggests a lower VAP rate with passive humidification than with active humidification, other issues related to the use of passive humidifiers (resistance, dead space volume, airway occlusion risk) preclude a recommendation for the general use of passive humidifiers” [41]. This latter recommendation has not, however, taken into account the fact that airway occlusion is no longer a problem with HMEs [42]. The most indecisive statement comes from the Fourth International Consensus Conference in Critical Care on ICU-acquired pneumonia (ICU-AP): it first says that “there is no evidence that active (wick or cascade) humidifiers increase the risk of ICU-AP” (which seems reasonably straightforward), but the next sentence, “Heated wire humidification may result in a higher incidence of ICU-AP than HMEs,” leaves the clinician in a state of uncertainty.

Several metaanalyses have recently been published. Surprisingly (or not), they do not convey the same result! Hess et al. [41] and Kola et al. [43] report a reduced risk of VAP with HMEs, whereas Siempos et al. find no effect [44]. It may not be necessary to try to reconcile discordant metaanalyses in this area given – as acknowledged by Siempos et al. and others [2, 45] – the absence of pathophysiological rationale behind humidification devices and VAP. Therefore, a negative result (i.e., no influence of devices on VAP) of the most recent metaanalysis is rather predictable. There is, indeed, no direct link between the devices and the pathophysiology of VAP (silent aspiration of contaminated oropharyngeal and/or gastric secretions).

Although heated humidifiers do not increase VAP, they are associated with rapid and important bacterial colonization of respiratory tubing. This contamination bears the potential for cross contamination, whereas, conversely, HMEs prevent this risk. Given the scarcity of randomized studies on the subject, this intuitive aspect is overlooked by the metaanalyses.

Siempos et al.’s metaanalysis demonstrates that mechanical ventilation and the outcome of ICU patients is not affected by the type of humidification device. There is no doubt that heated humidifiers deliver greater humidity than HMEs [24], but does that make any difference to the patient? If the 5–8 mgH<sub>2</sub>O/l difference in absolute humidity between the devices were clinically relevant, then Siempos et al. would have brought to light a longer duration of mechanical ventilation (because of repeated episodes of atelectasis and airway occlusion) and increased rate of lung infection (facilitated by bronchial and alveolar injury

because of insufficient humidity), but they found none of that. Both devices have their drawbacks: HMEs should be avoided during prolonged hypothermia [46] or severe hypercapnia with respiratory acidosis [47], whereas worrisome shut down of ventilators has been reported with heated humidifiers [48, 49], and these should be avoided in patients bearing multidrug-resistant bacteria in their respiratory tract or highly transmissible lung infections (tuberculosis, SARS, avian or AH1N1 flu).

Findings of the most recent metaanalyses highlight the fact that active humidification should no longer be considered as the gold standard for inspired gas conditioning during mechanical ventilation. Because passive humidification with HMEs is safe, efficient, simple and cost-effective, it should be considered in the first place for heating and humidifying inspired gas of most patients. This policy reduces staff workload, reduces the potential risk of cross contamination and enables substantial cost savings.

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## Section VII

# Humidification Tracheostomy

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# A Portable Trachea Spray for Lower Airway Humidification in Patients After Tracheostomy

# 25

Tilman Keck and Ajnacska Rozsasi

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## 25.1 Introduction

In patients after tracheostomy, respiratory problems, such as excessive sputum production, coughing, crusting and recurrent tracheobronchitis, are frequently observed. To sufficiently prevent excessive crusting and blockage of the upper and lower trachea, humidification via inhalation has been recommended in tracheostomized patients as part of early postoperative care after tracheostomy or laryngectomy.

Several forms of water delivery are feasible. Water can be delivered in molecular form (vapor), particulate form (aerosol), or bulk form (liquid). The water volume in a vapor stream is low (approximately  $30 \text{ mgH}_2\text{O/l}_{\text{Air}}$ ); in an aerosol stream it is approximately  $60\text{--}400 \text{ mgH}_2\text{O/l}_{\text{Air}}$ . In a recent study of Rozsasi et al. two forms of water delivery to the lower airways in tracheotomized patients were investigated [1]. One type of humidity supply was humidity in molecular form at normal conditions of air entering the tracheobronchial region. The other type of humidification was particulate form between ambient and tracheobronchial conditions. The result of their study was that, after use of both a vaporizing humidifier (molecular form) and an aerosol spray (particulate form), the total water content and water gradient in the trachea increased significantly compared to baseline values before humidification. The tracheal humidity remained on a higher level after application of humidity via aerosol spray compared with delivery of water by use of a vaporizing humidifier [1].

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T. Keck (✉)

Department of Otorhinolaryngology, Head, Neck, and Facial Plastic Surgery,  
Elisabethinen Hospital GmbH, Academic Hospital of the Medical University of Graz,  
Elisabethinergasse 14, 8020 Graz, Austria  
e-mail: kecktill@aol.com

A. Rozsasi

Department of Otorhinolaryngology, University Hospital of Ulm, Ulm, Germany

**Fig. 25.1** Humidity can easily be delivered in particulate form in an aerosol stream via a portable hand spray (trachea hand spray, Heimomed GmbH, Kerpen, Germany)



In a following study of the same working group, the moisturizing effect of a commercially available vaporizing humidifier, supplying molecular water, was compared with a newly available portable trachea spray, supplying particulate water to the lower airways [2].

## 25.2 Trachea Spray

Using a newly designed trachea hand spray (Heimomed GmbH, Kerpen, Germany, Fig. 25.1), particulate water can be applied to the upper and lower trachea. The hand spray is filled up with 20 ml NaCl 0.9% and cannot be re-filled when empty for hygienic reasons. In the study of Keck et al. moisture was delivered in an aerosol stream via two puffs of a previous type of the new trachea hand spray (Trachea hand spray HeimoAIR, Heimomed GmbH, Kerpen, Germany; 26°C and 90% relative humidity;  $300 \mu\text{H}_2\text{O}/\text{l}_{\text{air}}$ ) four times daily for 1 week.

## 25.3 Vaporization

In tracheostomized patients, humidity is often delivered in molecular form in a vapor stream (approximately 32°C and 100% relative humidity;  $30 \mu\text{H}_2\text{O}/\text{l}_{\text{air}}$ ). In the study of Keck et al. an inhalation device (SUPER tracheal inhaler®, Heimomed GmbH, Kerpen, Germany) was used for 20 min four times daily for 1 week.

## 25.4 Efficiency of the Trachea Spray

No differences in visual analogue scoring and in endoscopic scoring among five patients who performed inhalation therapy and five patients who applied the new hand spray were observed. No subjective symptom reached moderate or unacceptable severity. Overall, the patients were more satisfied with the trachea spray because of its easy handling and immediate humidification effect [2].

After both inhalation (five patients) and spray (five patients), the total water content, measured in the upper trachea using an experimental setup for conditioning measurement [3], increased non-significantly compared to baseline values before delivery of moisture. The water gradient, calculated from the values measured in the trachea and in front of the tracheal opening, after spray application for 1 week increased significantly. The water gradient after inhalation for 1 week was non-significantly higher than before vaporization therapy.

In summary, no relevant differences of the impact of water in molecular or particulate form on the tracheobronchial respiratory mucosa have been found. Aerosols delivered by a trachea spray that deposits in the lower airways seem to sufficiently provide humidity that can be evaporated to condition subsequent breaths.

In the study of Keck et al. no clinical signs of serious tracheobronchial irritation or subjective complaints after both forms of humidity supply were found. After administration of the trachea spray, a short irritation, accompanied by coughing, occurred in the patients. After the 1 week study period, no negative effect on the mucociliary function of the respiratory mucosa and no clinical signs of disturbance of the ion-associated and osmotically driven water transport of the respiratory mucosa of the lower airways were observed. After both moisturizing therapies, the water content of the respired air is increased, with an increased amount of water that can be transferred to the tracheobronchial mucosa and with possible impact on mucociliary clearance [4]. The patients with hand spray humidification therapy were even more satisfied than the patients after vapor humidification and asked to continue the spray therapy because of a subjectively increased feeling of tracheobronchial comfort.

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## 25.5 Conclusion

The results of the study of Keck et al. indicate that humidification via a vaporizing humidifier and trachea spray is effective in tracheostomized patients after at least a 1 week period of use. Molecular water, delivered as a vapor stream ( $30 \text{ mgH}_2\text{O/l}_{\text{Air}}$ ), is not superior to particulate water delivered via an aerosol stream ( $60\text{--}400 \text{ mgH}_2\text{O/l}_{\text{Air}}$ ), because of the temperature and humidity increase after both forms of water delivery. Because of its easy use, portability, and significant moisturizing effect, a portable trachea spray may offer additional options in postoperative tracheostomy and laryngectomy care.

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## **Section VIII**

# **Humidification, Mucus Transport and Secretion Clearance**

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# Humidification and Mucus Transport in Critical Patients: Clinical and Therapeutic Implications

# 26

Naomi Kondo Nakagawa, Juliana Araújo Nascimento,  
Marina Lazzari Nicola, and Paulo Hilário Nascimento  
Saldiva

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## 26.1 Introduction

An adult man inhales more than 12,000 l of air per day, which may contain particles and microorganisms. The epithelium of the conducting airways, from the nose to the bronchioli, are anatomically and physiologically designed to protect the alveoli by providing clean, warmed and fully saturated air at this level, where an efficient gas exchange must occur, and by providing specific defense mechanisms, such as trapping particles and microorganisms in the mucus and mucociliary transport of these agents in the direction of the oropharynx, where they will be swallowed or expectorated. Mucociliary transport (MCT) is an important respiratory defense mechanism, which efficiency depends on the equilibrium among three major components: ciliary beating, airway surface liquid (the periciliary liquid and mucus), and the interaction between cilia and mucus. In the intensive care unit (ICU) and emergency department, many factors can increase the risks of mucus transport dysfunction. Among them, artificial inspired air conditioning is a basic factor with physiological and clinical impact in critically ill patients.

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N.K. Nakagawa (✉) • J.A. Nascimento • M.L. Nicola  
Department of Physiotherapy, Communication Science and Disorders,  
Occupational Therapy, LIM 34, Faculdade de Medicina,  
Universidade de São Paulo, São Paulo, Brazil

Department of Pathology, LIM 05, Faculdade de Medicina, Universidade de São Paulo,  
São Paulo, Brazil  
e-mail: naomikondo@uol.com.br

P.H.N. Saldiva  
Universidade de São Paulo, São Paulo, Brazil

Department of Pathology, LIM 05, Faculdade de Medicina, Universidade de São Paulo,  
São Paulo, Brazil

## 26.2 Artificial Inspired Air Conditioning in Mechanically Ventilated Patients

This efficiency occurs even under extreme atmospheric conditions. During normal respiration, the inspired air is heated and moisturized primarily by the mucous membrane of the nose and the nasopharynx (approximately 75% total performance), and of the trachea (approximately 25% total performance). Two centimeters before bifurcation, there is a virtual place in the trachea called the isothermic saturation boundary (ISB), where the inspired air reaches an approximate moisture content of 35 mgH<sub>2</sub>O/l at a temperature of 37°C with almost 100% relative humidity. At the alveoli, the inspired air contains a moisture content of 44 mgH<sub>2</sub>O/l at a temperature of 37°C with 100% relative humidity. During exhalation, a restricted recovery of water and heat (approximately 30%) occurs at the nasopharynx and trachea.

However, in the ICU and emergency room, patients may need intubation and mechanical ventilation (MV) for oxygenation improvement or treatment of acute respiratory failure. The artificial tube bypasses the upper airways and shifts the ISB to the bronchial branches that are not adequate or sufficient for air humidification and heating. Insufficiently humidified and dry air damages the mucosa and the epithelium, including the mucociliary apparatus, and also cause mucus plug formation and endotracheal tube occlusion, which in turn can be fatal if not released or removed [1, 2]. In addition, the medical respiratory gases do not contain any moisture and are cooler than the normal ambient air. Therefore, artificial inspired air conditioning is required during invasive MV, immediately subsequent to intubation, even during short-term MV during the postoperative period or patient transportation between units or places.

There are two main types of artificial humidifiers for invasive MV, heated humidifiers (HH) and heat moisture exchangers (HME). The HH is a heated water bath system mounted beside the main ventilator circuit, and needs an external source of energy (electrically or electrical-electronically powered) and also a continuous or intermittent water source repositioning, as well as, additional ventilator circuits, and it involves time-consuming handling (particularly for removing condensation from the circuits and water source repositioning). Heating of the water bath is carried out by three major methods: (1) not servo-controlled (the temperature setting however is not the exact temperature), (2) servo-controlled (exact temperature setting at the Y-circuit) and (3) servo-controlled with a heated wire inside the circuit (exact temperature setting at the Y-circuit and internal heating to increase absolute humidity). The International Organization of Standardization 8185 recommendations for HH are: a maximum temperature of 41°C at the Y circuit and a minimum water content of 30 mg/l [16].

The HME, also called the “artificial nose,” is a device mounted directly between the artificial airway and the Y tube of the ventilator circuit. The HME passively conditions the inspired air with part of the water content and heat collected during the last expiration. It is independent of external energy and water sources. However, it is dependent on the host’s hydration and temperature, as well as on the device characteristics. There are three types: (1) the hydrophobic HME (a hydrophobic

coating substance and/or bacteriostatic substance covers the main material, which repels water molecules and induces water drop formation around the hydrophobic coating); (2) the hygroscopic HME (salts like magnesium, calcium and lithium chloride cover the main material and bind water molecules, increasing the water-retaining capacity); (3) an HME with hygroscopic and hydrophobic characteristics. The main material can be paper, cellulose sponges, and polyurethane or polyethylene foams.

The studies focusing on the efficiency of inspired air heating and moistening, mucus transport as well as total dead space, flow resistance, and respiratory colonization and infection during MV are shown in Table 26.1. However, no consensus and no sufficient evidence exist concerning the best choice of artificial inspired air conditioning system for all patients. The choice should be individualized for each patient.

Non-invasive mechanical ventilation (NIV) has been widely used in patients with a number of acute and chronic conditions, such as some forms of acute respiratory failure, and particularly in chronic respiratory failure caused by restrictive thoracic diseases and exacerbation of COPD; these patients get a clear benefit with this therapeutic device. However, very few studies focusing on the effects of artificial inspired air conditioning systems during NIV have been performed in ICU patients (Table 26.2). It seems that the HH is more comfortable for some patients, and the HME increases the minute ventilation and work of breathing in others.

From the physiological point of view, NIV is provided to patients through a face, nasal or total mask, which means that the conducting airways are preserved. However, a subjective aspect can be taken into account, the patient's comfort. If the respiration of dry and cooler air from the MV is unpleasant, the use of humidification systems is recommended.

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## 26.3 Conclusions

The efficiency of HMEs decreases with increasing tidal volumes. HMEs increase inspiratory and expiratory airway resistance, particularly during spontaneous breathing, and should not be associated with vaporizers. HMEs with lithium coatings can induce a possible hazard of lung absorption of a potentially toxic substance. HMEs should be avoided in patients undergoing long dehydration therapy, or with dehydrated or elastic mucus or bloody mucus.

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## 26.4 Key Messages

1. Mucociliary clearance is a crucial defense mechanism of the respiratory tract that is under increased risk of dysfunction in critically ill patients [17].
2. External (artificial airway, suctioning, mechanical ventilation, artificial inspired air conditioning systems, diuretics) and host factors (smoking habit, age, inflammation,

**Table 26.1** Clinical and therapeutic implications of HH and HME during invasive MV

Author/journal/ year	Number and clinical aspects of patients	Setting	Types of humidifi- cation systems	Variables analyzed	Clinical and therapeutic implications
Martin et al., <i>Chest</i> , 1990 [3]	N = 73 patients MV > 24 h	ICU	N = 2 (a) HME (b) HH	(a) Humidity  (b) Temperature (c) Number of suctioning procedures (d) Quantity of saline instillations during suctioning (e) Endotracheal tube occlusion (f) Ventilator circuits contamination (g) Incidence of pneumonia	HH was more effective than HME in humidification  HME was more effective than HH in contamination control of ventilator circuits and reduced the incidence of pneumonia. However, HME increased incidence of endotracheal tube occlusion in patients with tidal volume > 10 l/min
Sottiaux et al., <i>Chest</i> , 1993 [4]	N = 29 post-operative patients	ICU	N = 2 (a) HYG (b) HYD	(a) Inspiratory gases temperature (b) Inspiratory gases absolute humidity	HYG provides the temperature and absolute humidity of the inspiratory
Nakagawa et al., <i>Crit Care Med</i> , 2000 [2]	N = 21 patients with acute respiratory failure	ICU	N = 2 (a) HME (b) HH	(a) Mucociliary transport (respiratory mucus properties): – Rheology – Transportability by cilia – Transportability by cough – Contact angle	No differences between HME and HH on mucus rheological properties, contact angle, and transportability by cilia. However, HME decreased transportability by cough after 72 h of MV

<p>Ricard et al., <i>Am J Respir Crit Care Med</i>, 2000 [5]</p>	<p>N = 33 patients</p> <p>(a) COPD (N = 10)</p> <p>(b) Other pulmonary diseases (N = 13)</p> <p>(c) Non-respiratory diseases (N = 10)</p>	<p>ICU</p>	<p>N = 1 HYG-HYD</p>	<p>(a) Tracheal absolute humidity</p> <p>(b) Tracheal relative humidity</p> <p>(c) Tracheal temperature</p> <p>(d) Number of suctioning</p> <p>(e) Quantity of saline instillations during suctioning</p> <p>(f) Peak pressure following suctioning</p> <p>(g) Airway resistance</p> <p>(h) Colonization in Y-circuit and HME after 7 days</p>	<p>Changes of a HYG-HYD only once a week is safe and effective in heating and humidification of the inspired air</p> <p>For COPD patients, circuits should be changed every 48 h</p>
<p>Girault et al., <i>Crit Care Med</i>, 2003 [6]</p>	<p>N = 11 patients with chronic respiratory failure:</p> <p>(a) COPD (N = 7)</p> <p>(b) Others (N = 4)</p>	<p>ICU</p>	<p>N = 2</p> <p>(a) HME</p> <p>(b) HH</p>	<p>(a) Diaphragmatic muscle activity</p> <p>(b) Breathing pattern(b) Breathing pattern</p> <p>(c) Gas exchange</p> <p>(d) Respiratory comfort</p>	<p>In difficult weaning process of chronic respiratory failure patients, HME increased respiratory effort, respiratory acidosis and discomfort. These effects were avoided by the use of pressure support ventilation (15 cmH<sub>2</sub>O)</p>

(continued)

Table 26.1 (continued)

Author/journal/year	Number and clinical aspects of patients	Setting	Types of humidification systems	Variables analyzed	Clinical and therapeutic implications
Jaber et al., <i>Anesthesiology</i> , 2004 [7]	N = 60 patients MV > 48 h	ICU	N = 2 (a) HME (b) HH	(a) Endotracheal tube volume (b) Endotracheal tube resistance	After 9 days of MV, HME reduced endotracheal tube volume and increased resistance compared with HH
Cinnella et al., <i>Minerva Anesthesiol</i> , 2005 [8]	N = 20 patients undergoing elective surgery	Surgical center	N = 2 HYG-HYD (a) Dead space = 84 ml (b) Dead space = 55 ml	(a) Tracheobronchial ciliated cells morphology after intubation and before extubation	HME with more dead space (84 ml) induce more changes in cilia of the ciliated cells. No changes on cytoplasm or nucleus morphology
Lacherade et al., <i>Am. J. Respir. Crit. Care Med.</i> , 2005 [9]	N = 370 patients MV > 48 h	ICU	N = 2 (a) HMEF (b) HH	(a) Incidence of VAP (b) Duration MV (c) Mortality (d) Length of ICU stay (e) Rate tracheostomy (f) Endotracheal tube occlusion	No differences between HMEF and HH
Lourente et al., <i>Critical Care</i> , 2006 [10]	N = 104 MV > 5 days	ICU	N = 2 (a) HME (b) HH	(a) Incidence of VAP	The incidence of VAP was higher with HH than HME

Siempos et al., <i>Crit Care Med</i> , 2007 [11]	N = 2580 13 randomized controlled trials	ICU	N = 2 (a) HME (b) HH	(a) Incidence of VAP (b) Mortality (c) Length of ICU stay (d) Endotracheal tube occlusion (e) Cost	HME requires lower costs than HH Incidence of VAP was similar between groups
Solomita et al., <i>Respir Care</i> , 2009 [12]	N = 7 patients	ICU	N = 3 (a) HME (b) HH (c) NHH	(a) In vitro delivery of water vapor (b) In vivo volume of airway secretions	NHH was more effective in more water vapor production at different minute ventilation NHH increased the volume of secretion

MV Mechanical ventilation, HME heat and moisture exchanger, HH heated humidifier, HMEF heat and moisture exchanger combined with a microbiological filter, NHH non heated humidifier, HYD hydrophobic HME, HYG hygroscopic HME, HYG-HYD hygroscopic and hydrophobic HME, VAP ventilator-acquired pneumonia, ICU intensive care unit

**Table 26.2** Clinical and therapeutic implications of HH and HME during NIV

Author/journal/year	Number and clinical aspects of patients	Setting	Types of humidification systems	Variables analyzed	Clinical and therapeutic implications
Lellouche et al., <i>Intensive Care Med</i> , 2002 [13]	N=9 patients with acute respiratory failure  (a) COPD (N=7) (b) Heart disease (N=1) (c) Post-operative phrenic paralysis (N=1)	ICU	N=5 (a) HME +PEEP (b) HME+ZEEP (c) HH + PEEP (d) HH + ZEEP (e) sHME	(a) Ventilatory parameters (b) Arterial blood gases (c) Inspiratory work of breathing	HME increased minute volume and the inspiratory work of breathing
Nava et al., <i>Eur Respir J</i> , 2008 [14]	N=14 patients with stable hypercapnic respiratory failure  (a) COPD (N=7) (b) RTD (N=7)	Homecare	N=2 (a) HME (b) HH	(a) Compliance with long-term NIV  (b) Airway symptoms (c) Incidence of side-effects (d) Hospitalization (e) Pneumonia	No differences in incidence of side effects, hospitalization pneumonia and compliance. However, 10 patients chose to continue with HH at the end of the trial  HME induced more often dry throat complaint
Boyer et al., <i>Intensive Care Med</i> , 2010 [15]	N=50 patients with acute respiratory failure	ICU	N=4 (a) HME (b) HME + flexible tube (c) HH (d) HH + flexible tube	(a) Ventilatory parameters (b) Arterial blood gases	No differences between HME and HH

NIV Non-invasive ventilation, HME heat and moisture exchanger, HH heated humidifier, PEEP positive end expiratory pressure, ZEEP positive end expiratory pressure of 0 cmH<sub>2</sub>O, sHME small dead space, COPD chronic obstructive pulmonary disease, RTD restrictive thoracic disease, ICU intensive care unit

hypovolemia, hypoperfusion, severity of the underlying disease) can be associated with MCT dysfunction.

3. Artificial inspired air conditioning is essential during invasive MV. The type of artificial system should be individually determined.
4. Artificial inspired air conditioning is optional during NIV. Comfort and adherence should guide the choice.

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# Secretion in Patients with Neuromuscular Diseases. Key Major Topics, Technology and Clinical Implications

# 27

Jens Geiseler, Julia Fresenius, and Ortrud Karg

## Abbreviations

AARC	American Association of Respiratory Care
FIV	Forced inspiratory volume
IPPB	Intermittent positive pressure breathing
LIAM	Lung insufflation assist maneuver
MIC	Maximum insufflation capacity
MI-E	Mechanical insufflator-exsufflator
NMD	Neuromuscular disorder
PCF	Peak cough flow
S <sub>a</sub> O <sub>2</sub>	Oxygen saturation (in arterialised blood)
SMA	Spinal muscular atrophy
VC	Vital capacity

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## 27.1 Introduction

Secretion accumulation in the lower airways can have serious consequences for patients with neuromuscular diseases. These consequences are listed in Table 27.1.

There are principally two mechanisms of secretion clearance in healthy people: mucociliary clearance and cough. The secretion formed by the tracheobronchial mucosa is transported cephalad by the ciliated epithelium. In case of abundant mucus, e.g. in viral or bacterial infection of the tracheobronchial system or due to

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J. Geiseler (✉) • J. Fresenius • O. Karg  
Department of Intensive-Care Medicine and Long-Term Ventilation,  
Asklepios Fachkliniken München-Gauting,  
Gauting, Germany  
e-mail: j.geiseler@asklepios.com; j.fresenius@asklepios.com; o.karg@asklepios.com

**Table 27.1** Consequences of abundant secretions in lower airways

- Atelectases
- Increase in work of breathing
- Increase in ventilation-perfusion-mismatch with hypoxemia
- Infection
- Failure of noninvasive ventilation
- Failure of extubation after invasive mechanical ventilation

aspiration, the mucociliary clearance capacity is not sufficient for effective removal of mucus, and cough is the main mechanism. In neuromuscular diseases cough can be impaired by affection of inspiratory, bulbar or expiratory muscles, alone or in combination.

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## 27.2 Normal Cough

A normal cough is a complex procedure initiated by irritation of cough receptors mainly located in the proximal airways. A deep inspiration up to 85–90% of vital capacity (VC) – at least 1–1.5 l of VC is necessary – is followed by active closure of the glottis with concomitant contraction of expiratory muscles leading to intrathoracic pressures up to 140 mmHg. Subsequent active opening of the glottis, while contraction of expiratory muscles persists, results in a high expiratory flow of air with a velocity of 6–20 l/s. Narrowing of the airways by protrusion of the pars membranacea of the airways and properties of mucus also are important factors that influence cough clearance.

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## 27.3 Diagnosis of Impaired Cough Capacity

Anamnestic clues to impaired cough capacity are recurrent infections of the lower airways, dyspnoea, swallowing difficulties and symptoms of hypoventilation. Body examination can reveal use of accessory respiratory muscles, paradoxical movement of the diaphragm, and in case of atelectasis diminished or absent breath sounds on auscultation.

A vital capacity of lower than 1–1.5 l is a strong predictor of impaired peak cough flow. The peak cough flow can be measured by a pneumotachograph, as is used for normal spirometry. For some patients, e.g. bed-ridden, complete spirometry is difficult to perform, and measurement of the peak cough flow can be done with simple peak-flow meters using a mouthpiece or, in case of inability of mouth closure, a face mask. Although the accuracy of the values is lower than measured with a pneumotachograph, for clinical purposes this method is sufficiently accurate.

**Table 27.2** Measures to improve secretion expectoration in NMD patients

- Augmentation of inspiration, e.g. by air stacking
- Manually assisted cough
- Mechanically assisted cough (intermittent positive pressure breathing, mechanical insufflator-exsufflator)

## 27.4 Measures to Improve Cough Clearance

In general two distinct aims have to be considered separately in patients with neuromuscular diseases: measures to improve secretolysis and measures to improve secretion expectoration. The last one especially in case of lower airway infection is much more important in NMD patients because impaired cough strength is one of the main problems.

### 27.4.1 Secretolysis

The role of mucolytics or mucokinetics in patients with neuromuscular diseases has not been studied intensively. In general, the published data are not sufficient to clearly show convincing evidence of usefulness, with the exception of rh-DNAse in cystic fibrosis. In case of thick mucus, inhalation of hypertonic NaCl solution has been shown to improve mucociliary clearance in patients with cystic fibrosis in an experimental design.

Endobronchial oscillating devices, e.g., the RC Cornet™, often used in COPD patients, are usually not suitable for NMD patients with respiratory muscle weakness. A high-frequency chest wall oscillation system, TheVest® Airway Clearance System (Hill-Rom Co., Batesville, IN, USA), applies oscillations of various frequencies and intensities. First reports advocate a possible role of this device also in NMD patients [1].

### 27.4.2 Measures to Improve Secretion Expectoration

There are several possibilities to improve peak cough flow in NMD patients; these are listed in Table 27.2.

#### 27.4.2.1 Augmentation of Inspiration

A deep inspiration is an indispensable precondition to achieve sufficient peak cough flows. In NMD patients with inspiratory muscle weakness additional air can be insufflated into the lungs by air stacking. Air stacking is a specific technique to allow a patient to stack consecutively delivered volumes from a volume-cycled ventilator or manual self-inflating resuscitator bag into his lungs. This procedure requires a functioning glottis closure between the additional volumes applied. Nowadays, pressure-controlled ventilation is the mode preferred for noninvasive ventilation in NMD by most home mechanical ventilation centres, so the easiest way to perform air stacking



**Fig. 27.1** Manual resuscitator bag with tubing, one-way-valve and mouthpiece. 1 mouthpiece, 2 one-way valve (Passy Muir valve™, Passy-Muir Inc., Irvine, CA, USA), 3 ventilator tube, 4 bacterial filter, 5 manual resuscitator bag

is by a manual resuscitator using a mouthpiece or a face mask as interface. A one-way valve, e.g. the Passy-Muir-valve, inserted in the ventilator tubing, can alleviate the air stacking manoeuvre (see Fig. 27.1). A nose clip may be necessary in patients that have no capacity of preventing air leakage through the nasopharynx. The resulting intrathoracic volume achieved by air stacking is called the maximum insufflation capacity (MIC) and can be measured spirometrically. The greater the difference between VC and MIC, the higher is the peak cough flow.

A new development in a specific home mechanical ventilator (VENTIlogic LS™, Weinmann Geräte für Medizin GmbH+Co.KG, Hamburg, Germany) is the LIAM (lung inflation assist manoeuvre) function, which inflates the lungs with high pressure of up to 50 mbar. Advantageous is that active glottis closure is not a prerequisite for this lung inflation, and the time needed to perform is much shorter. Preliminary data show a sufficient improvement in peak cough flow with this technique.

Comparable effects can be achieved with the mechanical insufflator-exsufflator, which can create pressures up to 60 mbar, but needs an additional device supplemental to the ventilator.

**Fig. 27.2** CoughAssist™ (Philips Respironics Inc., Murrysville, PA, USA)



### 27.4.2.2 Assisted Coughing

#### Manually Assisted Coughing

This is an old physiotherapeutic technique that applies an abdominal thrust timed to the glottic opening as the patient initiates cough. In case of exclusive expiratory muscle weakness, e.g. in paraplegia patients with damage below the cervical spinal cord or in spinal muscle atrophy (SMA) type II, this technique may be sufficient alone. In most cases concomitant inspiratory muscle weakness requires augmentation of deep inspiration by the above-mentioned techniques before manual cough assistance.

#### Mechanically Assisted Coughing

There are several devices that have been tested in patients with NMD to improve secretion expectoration. Best of all, the mechanical insufflator-exsufflator has been examined. But also an intermittent positive pressure breathing device has been shown to be effective in cough augmentation in paediatric patients.

#### Mechanical Insufflator-Exsufflator

The electromechanical insufflator-exsufflator first was developed by J.H. Emerson about 60 years ago as an aid for NMD patients with impaired cough. In 1953 the first device, called the Cof-flator, was distributed in the USA. Nowadays two similar devices are available in Europe: the CoughAssist™ (Philips Respironics Inc., Murrysville, PA) (see Fig. 27.2) and the Pegaso™ (Visisol Srl, Monza, Italy) (see Fig. 27.3). The insufflator-exsufflator simulates and supports physiological cough

**Fig. 27.3** Pegaso™ (Vivisol Srl, Monza, Italy)



by providing deep insufflations with positive pressure and shifting this positive pressure rapidly into a negative pressure that supports exsufflation. The pressure shift from positive to negative occurs in a short time (0.02 s) and is guided by a magnetic valve [2]. The MI-E can be cycled manually or automatically. Automatic mode requires programming of inspiratory and expiratory times; in the manual mode the switch between in- and expiration is done by hand. In- and expiratory pressures up to 60 mbar are possible. An older publication of Chatwin et al. [3] examined in- and expiratory pressures of  $25 \pm 16$  mbar and  $26 \pm 22$  mbar respectively, with the result of peak cough flows of  $235 \pm 111$  l/min. Recently, Fauroux et al. [4] have shown in a population of NMD children that in average in- and expiratory pressures of more than 35 mbar are necessary to achieve an insufflation of the lung of more than 1.5 l and a peak cough flow of  $192 \pm 99$  l/min. With lower pressure levels the cough augmentation was not as effective. Our own experience supports the concept of use of sufficient high in- and expiratory pressures, between 35 and 45 mbar each, that are tolerated by most of the patients after a phase of familiarization.

Especially important is the right choice of adequate inspiratory and expiratory times. With deep inspiration the mucus is displaced to the periphery of the airways so the expiratory time that allows cephalad movement of the mucus must be at least as long as the inspiratory time.

The MI-E is the most effective, but also the most expensive possibility of improving cough flows in NMD patients. Comparison of the maximum expiratory flows achievable with different methods clearly showed superiority of the MI-E [5].

The MI-E can be applied in patients either with a mouthpiece or with a full-face mask; also the usage in tracheostomized patients is possible via the tracheal cannula [6].

Although the MI-E is generally well tolerated, specific complications can occur, and one must be aware of when using this device: the large swing in intrathoracic pressure can compromise cardiac function, especially in patients with right heart insufficiency, because of long-lasting alveolar hypoventilation. The consequence can be profound hypotonia. Starting with low in- and expiratory pressures and slowly increasing these pressures can overcome this problem in most patients. A report on another rare complication – pneumothorax, which has been observed by us and other HMV centres – has been published recently by Suri et al. [7].

Contraindications for the MI-E are a history of pneumothoraces or severe right heart insufficiency.

### **IPPB-Assisted Coughing**

In NMD children hyperinsufflation with an IPPB device (Salvia Lifetec a 200c, Hoyer, Bremen, Germany) has been examined by Dohna-Schwanke et al. [8]. In nearly all patients IPPB-assisted hyperinsufflation resulted in significant improvement of intrapulmonary volume from FIV  $0,68 \pm 0,40$  l to an MIC of  $1.05 \pm 0.47$  l with a consequent increase in peak cough flow from  $119.0 \pm 57.7$  l/min to  $194.5 \pm 74.9$  l/min.

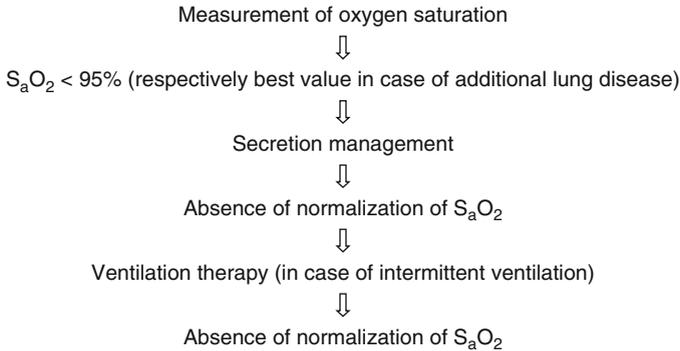
### **27.4.2.3 Secretion Management in Neuromuscular Disorders**

Management of abundant secretions is essential in NMD patients to prevent morbidity and mortality, to prolong the time of noninvasive ventilation if needed and to avoid the necessity of tracheostomy and invasive ventilation. The secretion management is not a simple action but rather a bundle of actions that must be performed regularly and correctly to achieve the best results.

First of all, an early detection of cough impairment is necessary. In case of diminished peak cough flows, i.e. PCF lower than 270 l/min, the applicability of air stacking manoeuvres should be tested and, if adequate and sufficient in normalising or at least improving PCF, prescribed regularly at least three times a day. In case of infection of the upper and lower airways, an increase in the frequency of air stacking is of importance, but nevertheless not sufficient in many cases.

If air stacking alone is not effective in improving PCF, manually assisted coughing should be implemented. Many patients, especially with slowly progressive NMDs, can be treated with these means for many years.

If bulbar muscles are weak, manual air stacking will often be ineffective, and mechanical air stacking, e.g. with the MI-E or with modern ventilators, can offer an effective alternative treatment. But in many patients the results regarding the PCF will be suboptimal, and the applicability of the MI-E should be tested. There are some situations that prevent the use of MI-E: first, hyperreagible vocal cords that paradoxically close during high inspiratory flow, and second, instability of the pharynx due to muscle weakness that leads to a near total collapse of the upper airways during the exsufflation phase and therefore to ineffectiveness in clearing the lower



**Fig. 27.4** Oxymetry feedback protocol

airways from mucus. This phenomenon has been described especially in patients with amyotrophic lateral sclerosis [9].

The oxymetry feedback protocol (Fig. 27.4) developed by J.R. Bach [10] can guide caregivers and patients concerning when to use assisted cough techniques: patients with NMDs usually have healthy lungs and therefore, in the absence of hypoventilation or secretions in the airways, oxygen saturation measured selectively with an oxymeter will normally reveal an oxygen saturation above 95%. The main causes for lower values are secretion retention and alveolar hypoventilation. Therefore, affected patients should first start with assisted coughing, and if normalisation of oxygen saturation is not achieved, should be ventilated if already placed on intermittent ventilation. If these measures are not effective, advanced diagnostic procedures should be done, most often as outpatients or inpatients in a hospital specialised in home mechanical ventilation to exclude, for example, pneumothorax, pneumonia, heart insufficiency, etc.

If the patient has been tracheostomised the MI-E can be used as well, most often in combination with endotracheal suctioning at the end of the procedure. It is important to perform strictly endotracheal suctioning to avoid damage of the bronchial mucosa caused by deep suctioning that can lead to increased mucus production, according to the published guidelines of the AARC [11].

## 27.5 Conclusion

The early diagnosis of a weak cough in NMD patients is important for the timely start of existing and effective measures for improving the capacity of elimination of secretions – air stacking, manually assisted cough and mechanically assisted cough. Education and training of patients and caregivers is essential for a correct application. Although there is no high degree of evidence, we believe that morbidity and possibly mortality can be affected in a positive manner.

## 27.6 Key Recommendations

1. Regular measurement of cough capacity is critical in NMD patients with possible affection of respiratory or bulbar muscles for early detection of impaired peak cough flow.
2. Air stacking, manually assisted coughing and mechanical assisted coughing are successful in improving peak cough flows in many NMD patients.
3. Education and training of patients and caregivers is essential for correct application of the different measures to improve cough strength.
4. The oxymetry feedback protocol should be used to guide the frequency of assisted cough procedures.
5. Physicians caring for NMD patients must know contraindications and possible complications of the different devices.

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# Automated Airway Secretion Clearance in the ICU by In-line Inexsufflation: Clinical Implications and Technology

# 28

Eliezer Be'eri

## Abbreviation List

ET	Endotracheal
IL-IE	In-line inexsufflation
MIE	Mechanical inexsufflation
PEEP	Positive end expiratory pressure
VAP	Ventilator-associated pneumonia

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## 28.1 Background

Mechanical inexsufflation (MIE) is a method for clearing airway secretions by simulating the airflow characteristics of a natural cough: a deep inspiration (insufflation) followed immediately by a rapid expiration (exsufflation). An exsufflation airflow velocity of at least 160 l/min is required to effectively move secretions up the airways [1]. During the polio epidemic of the 1950s, MIE was used extensively for secretion clearance in paralyzed patients being ventilated in iron lungs, with the iron lung performing the deep insufflation and rapid exsufflation. Studies of the technique at that time, in both animal models and humans, (and confirmed in more recent surveys [2]) established its efficacy and safety. With the advent of invasive ventilation via endotracheal (ET) tubes in the 1960s, however, MIE was largely abandoned in favor of catheter suction, which has remained the gold standard for ICU airway management until the present time.

Catheter suction, however, suffers from many drawbacks. As an invasive modality it can cause scarring and bleeding of the tracheal mucosa [3], and can precipitate

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E. Be'eri  
Department of Respiratory Rehabilitation,  
Alyn Rehabilitation Hospital, Jerusalem, Israel  
e-mail: ebeeri@alyn.org

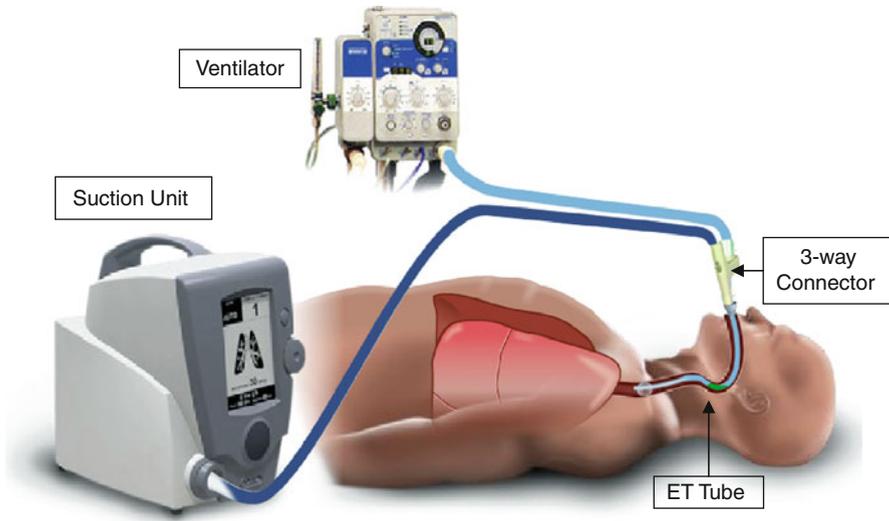
hemodynamic deterioration and oxygen desaturation. Furthermore, passage of a catheter through the biofilm-coated lumen of an endotracheal tube may be important in the pathogenesis of ventilator-associated pneumonia (VAP) [4]. Because of these potential side effects, catheter suction is generally performed only when absolutely necessary, i.e., when airway secretions have accumulated to the point of being clinically obvious and/or are impacting on oxygenation. Even then, catheter suction is of limited efficacy, because the catheter can only suction up secretions with which it comes into direct contact. Secretions beyond the mainstem bronchi are therefore out of range, and the left mainstem bronchus itself is missed by the catheter about 90% of the time [5].

MIE would appear to be preferable to catheter suction as a means for clearing airway secretions in ventilated patients, who are often unable to cough effectively [6]. MIE is non-invasive, is well tolerated hemodynamically [7], generates airflow from as deep as the fifth generation bronchi, and clears secretions from the left side of the bronchial tree with equal efficacy as from the right. However, current MIE devices, such as the CoughAssist (Philips Respironics, Murrysville, PA), are unsuited for acute ICU applications as they interrupt the patient's ongoing mechanical ventilation. This is because attaching the MIE device to the patient entails first disconnecting the patient from the ventilator. As a consequence, during MIE treatments the patient's inhalation parameters and  $\text{FiO}_2$  may differ significantly from those titrated while on the ventilator, and the patient does not receive PEEP at all. In addition, repeatedly disconnecting and reconnecting the patient and the ventilator is labor-intensive. As a result, MIE is rarely used in the ICU arena. In-line in-sufflation (IL-IE), however, is a method for performing MIE in ventilated patients that is ideally suited for ICU use, as it is fully automatic and does not interrupt ongoing ventilation.

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## 28.2 Technology of IL-IE

An IL-IE device (Innovent Medical Solutions, Jerusalem, Israel) comprises a suction unit that is connected in-line with the patient's ventilation circuit and ET tube via a disposable, three-way connector (Fig. 28.1). The three-way connector incorporates a pressure/flow sensor that feeds pressure and airflow data to the suction unit and a pneumatically operated membrane valve that closes off the ventilation circuit when activated. The device performs MIE by initiating a sudden suction exsufflation immediately after the ventilator has completed an inhalation, in the following manner: The device monitors the pressure and airflow received by the patient, identifies the onset of exhalation, commences high-flow suction at that time, and continues the suction until exsufflation airflow starts approaching zero. Throughout the duration of exsufflation the membrane valve in the three-way connector is activated, closing off the ventilation circuit so that the ventilator itself is not exposed to the exsufflation suction force at all. When exsufflation has terminated, the membrane valve deactivates, re-exposing the ventilator to the patient and allowing ongoing ventilation to continue uninterrupted. A single treatment comprises several MIE



**Fig. 28.1** Schematic representation of an IL-IE system (not to scale)

cycles in a row (typically six). After the treatment, secretions that may have migrated up into the ET tube are removed by performing shallow suction (confined to the ET tube) with an in-line suction catheter, if needed. The device can be programmed to perform MIE treatments automatically at regular intervals (such as every 15 min) in an ongoing fashion, and/or can be activated by a button push by the nurse, or even by the patient, whenever desired. The system can work with both invasive ET-tube ventilation and non-invasive face mask ventilation.

### 28.3 Potential Advantages and Disadvantages of IL-IE

IL-IE has the following potential advantages for ICU ventilatory management:

1. Avoidance of the traumatic and hemodynamic side-effects of catheter suction.
2. Better secretion clearance, particularly from the left lung and more distal airways.
3. Less VAP, because of less biofilm embolization and better clearance of pathogenic bacteria.
4. The possibility of using non-invasive ventilation on more patients: those with an impaired ability to clear secretions (for whom non-invasive ventilation would currently be contra-indicated).
5. The possibility of performing secretion clearance “prophylactically” at frequent regular intervals, to avoid secretion buildup and desaturation, as opposed to the current paradigm of ad hoc catheter suction only once respiratory distress is already evident.
6. Savings in staff time.

IL-IE may be particularly useful following neurosurgical procedures, when catheter suction is often avoided because of its tendency to precipitate a cough reflex and consequent spike in intracranial pressure. IL-IE could facilitate effective secretion clearance without such risk in these patients.

The potential drawbacks of IL-IE relate to its impact on both the patient and the ventilator. IL-IE is contraindicated following recent airway surgery or trauma, in cases of acute spinal shock (due to dysautonomic bradycardia, which can be precipitated by changes in intrathoracic pressure), and in cases of ARDS or cardiac failure that are dependent on high levels of PEEP. Despite concerns that negative-pressure exsufflation might cause atelectasis, this has not been found in any of the more than 6,000 cases of MIE reported in the literature to date [8, 9]. Nor should airway collapse be expected, given that the transmural pressure changes induced by IL-IE (a pressure change of about 90 cmH<sub>2</sub>O) are less than those of a forceful natural cough (more than 200 cmH<sub>2</sub>O).

During normal functioning, the primary impact of IL-IE on the ventilator is that during each exsufflation the ventilator does not sense an expired tidal volume at all (as all exsufflated air flows towards the suction unit, rather than towards the ventilator's exhalation valve). This may transiently activate the ventilator's "low minute volume" alarm if the alarm parameters have not been adjusted accordingly. In addition, after each exsufflation the subsequent inhalation delivered by the ventilator may be of a larger volume than usual, because the lung's residual volume post-exsufflation is less than that after a regular breath. This may result in a transient "high tidal volume" alarm, depending on how the alarm parameters have been configured. As the patient's ventilation tubing is closed off by the IL-IE membrane valve only during the expiratory phase of the ventilation cycle, and remains fully open throughout the inspiratory phase, IL-IE does not interfere with mechanical inspiration at all.

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## 28.4 The Feasibility of IL-IE in the ICU

The feasibility of IL-IE as an ICU secretion clearance modality was studied in a large, multidisciplinary ICU over the course of 3 months in 2009 [10].

### 28.4.1 Methods

An Innovent IL-IE device was connected to the ventilation tubing of an Evita 4 ICU mechanical ventilator (Dräger Medical, Lubeck, Germany) in each of ten adult patients being ventilated for acute respiratory decompensation (Fig. 28.2). In all patients the cycling mechanism was pressure controlled. The IL-IE device operated automatically, performing six coughs in a row every 10 min for up to 8 h. During this time the nursing staff performed catheter suction whenever they felt it was clinically indicated, as per the ICU's institutional protocol. Continuous video monitoring of the transparent ET tubes was performed so as to evaluate whether IL-IE could



**Fig. 28.2** An intubated patient connected to an IL-IE device

be seen to generate secretion movement. The impact of IL-IE on the patients' respiratory status was assessed by monitoring the following parameters:  $O_2$  saturation,  $O_2$  requirement, ventilator parameters, delivered minute volume, and lung compliance. Ventilator function and alarms were monitored continuously.

### 28.4.2 Results

The patients' diagnoses included pneumonia, pulmonary emboli, COPD, atelectasis, pulmonary edema and lung tumor. All in all, the 10 patients received 393 IL-IE treatments and required 41 catheter suction treatments. Once the nursing staff had become familiar with the new IL-IE device (after the third patient), the need for catheter suction was approximately once per 20 IL-IE treatments. IL-IE could be seen to actively move secretions up the ET tube in eight out of the ten patients. In addition, in two instances IL-IE cleared large mucous plugs that catheter suction immediately beforehand had missed.

Table 28.1 summarizes the impact of IL-IE on the patients' respiratory status. One of the ten patients underwent elective extubation 2 h into the study, which precluded meaningful evaluation of the clinical impact of IL-IE in this case. Of the remaining nine patients, over the course of the 8 h oxygenation improved in four patients, remained stable in four patients, and deteriorated in one patient. This patient was being ventilated because of cardiogenic pulmonary edema and was withdrawn from the study when it became evident that the patient was dependent on

**Table 28.1** Percentage change in respiratory indices during 8 h of IL-IE treatment

Patient#	Minute volume	Tidal volume	Compliance	Resistance	Saturation	FiO2
1	↑50%	↑44%			↑6%	↔
2	↑38%	↑20%			↔	↓33%
3	↑25%	↑30%			More stable during sxn	↓25%
4	↑51%	↔	↑trend	↓trend	↔	↔
5	↓39%	↓37%	↔	↔	↓3%	↔
6	↑trend	↔			↔	↓20%
7			↓43%	↑44%	↔	↔
9	↔	↑20%	↑34%	↔	↔	↔
10	↔	↔	↑42%	↔	↔	↔

<b>Key:</b>	<span style="display:inline-block; width:15px; height:15px; background-color:red; border:1px solid black;"></span>	Deterioration
	<span style="display:inline-block; width:15px; height:15px; background-color:green; border:1px solid black;"></span>	Improvement
	<span style="display:inline-block; width:15px; height:15px; background-color:white; border:1px solid black;"></span>	No change or no data
	trend	Seen on graphic trend graph

high PEEP. Minute volume and/or compliance improved in seven and deteriorated in two patients (one of whom was the PEEP-dependent patient with pulmonary edema) during the 8 h of the study. All the patients remained hemodynamically stable throughout the trial. In seven out of the ten patients the ventilator alarmed for either “low minute volume” or “high tidal volume” during IL-IE treatments, until such time as the ventilator’s alarm settings were adjusted. During three particularly prolonged IL-IE treatments the ventilator went into a backup ventilation mode. Adjustment of the setup parameters for apnea time for triggering backup ventilation prevented this problem from recurring. There were no instances of acute ET tube obstruction necessitating urgent medical intervention, and no instances of accidental disconnection of the three-way connector.

### 28.4.3 Discussion

IL-IE actively cleared secretions from the airways of intubated patients and was well tolerated in all patients who were not dependent on high PEEP. No significant detrimental impact on ventilator function was noted. The trend towards an improvement in oxygenation, compliance and minute ventilation during the 8 h trial period suggests the possibility that continuous and pro-active secretion mobilization might be more beneficial to a ventilated patient’s respiratory status than is occasional catheter suction when secretions have accumulated excessively.

## 28.4.4 Conclusions

The findings of this initial observational study indicate that automated IL-IE is feasible for use in appropriately selected ICU ventilated patients. It may decrease the need for catheter suction and enhance secretion clearance and pulmonary function, and therefore potentially reduce time on ventilation. IL-IE potentially has all the advantages of MIE, without being labor intensive or disruptive of ventilation. As such it may be a realistic alternative or adjunct to catheter suction for airway management in the ICU.

Disclosure of conflict of interests: The author is the Chief Scientific Officer of Innovent Medical Solutions, Ltd.

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# Effect of Humidification on Lung Mucociliary Clearance in Patients with Bronchiectasis

# 29

Amir Hasani and Roy E. Smith

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## 29.1 Humidification

Theory supports the use of a highly humid or mist atmosphere in therapy of airway disease. In patients, the incidence of postoperative pulmonary complications decreased as the humidity of administered anaesthetic gases increased. A similar relationship was found between the amount of inhaled moisture and the damage to the ciliated epithelium of the tracheobronchial tree. These results appear to indicate that a high inspired humidity is beneficial for operations on normothermic patients, and that cellular damage caused by dryness is a possible contributory factor in the production of the pulmonary atelectasis that follows stoppage of the mucociliary transport system in the immediate postoperative period.

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## 29.2 Mucus Clearance

The importance of mucociliary clearance as a first-line defence mechanism of the bronchial tree is well established. Clearance by cough comes into play when mucociliary clearance is impaired. Whether achieved by mucociliary clearance or by cough, active removal of microbial matter and host-derived inflammatory products is essential if a vicious cycle of microbial colonisation is to be avoided. Clearly the role of water, as a main constituent of mucus, can be crucial to the composition of mucus and to its transportability. Recent work has shown that airway surface liquid is controlled by airway epithelial cells via the reciprocal regulation of active  $\text{Na}^+$  absorption and  $\text{Cl}^-$  secretion and that mucus transport increases with increasing

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A. Hasani (✉) • R.E. Smith  
Department of Medical Physics, Royal Free Hospital,  
London, UK  
e-mail: amer.alhasani@royalfree.nhs.uk

airway surface liquid volume. Moreover, it seems likely that mucosal function may be optimal at 37°C and 100% relative humidity.

Given the problems patients experience from mucus retention, such as bronchiectatics, and given a desire to offer them a relatively robust and sustainable treatment option, we have investigated the clearance effectiveness of warm air humidification treatment relative to a control (baseline) assessment. Whilst a considerable variety of inhaled agents could be postulated to influence mucociliary transport, we considered that if “optimal” humidification *per se* proved effective, then future work on inhaled agents should include consideration of the extent to which humidification and temperature factors might be contributory. Moreover, we hypothesised that if both an underlying mechanism and evidence of clinical effectiveness could be established for a patient-acceptable warm air humidification approach, then such an approach might prove helpful to the future care of patients with various mucociliary clearance disorders.

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### 29.3 Radioaerosol Technique for Measuring Mucus Transport

Polystyrene particles, 5 µm in diameter, were firmly labelled with the radionuclide <sup>99m</sup>Tc and produced by a spinning top generator located inside an airtight tank. Each patient inhaled the radioaerosol particles by taking discrete breaths of 0.45 l from the resting level of the lung, which was ascertained by using a pneumotachygraph linked to a dedicated computer [1].

The initial radioaerosol lung deposition was measured and its subsequent clearance was monitored by two collimated scintillation detectors positioned posteriorly and anteriorly to the chest. The detectors measured the radioactivity emitted by the inhaled particles from both lungs. Measurements were commenced immediately following the radioaerosol inhalation and repeated at 30-min intervals up to 6 h and then at 24 h. The remaining activity of radioaerosol particles in the lungs at 24 h (corrected for radioactive decay) was used to estimate alveolar deposition (AD) which was taken to represent the amount of particles deposited in the non-ciliated airways and thus unavailable for mucociliary clearance.

Tracheobronchial clearance was assessed by measuring the area under the tracheobronchial retention curve (AUC), which was generated by subtracting the AD from the total lung burden, for the entire 6-h monitoring period. The retention of radioaerosol particles at 6 h was also used as a measure of tracheobronchial clearance (TBC<sub>6</sub>). During the 6-h monitoring period, patients were encouraged to avoid coughing. However, any involuntary coughs were recorded and sputum samples (when produced) were collected and weighed over this period.

The initial distribution of the radioaerosol particles within the lungs was assessed by a gamma camera [2]. This distribution was expressed in terms of a penetration index (PI), which is the ratio of the amount of radioaerosol particles in an outer to an inner region of the lungs divided by the same ratio of krypton gas (<sup>81m</sup>Kr).

**Table 29.1** Lung clearance, radioaerosol distribution, and lung function indices for the ten patients at baseline and following treatment

Variable	Baseline	Post-humidification	P-value
AUC (%.h)	319 ± 50	271 ± 46	0.007
TBC <sub>6</sub> (%)	35 ± 10	27 ± 9	0.017
AD (%)	58 ± 6	63 ± 5	0.114
PI	0.78 ± 0.11	0.79 ± 0.10	0.759
AIFR (l/min)	27 ± 2	26 ± 3	0.859
FEV <sub>1</sub> (l)	1.69 ± 0.21	1.74 ± 0.22	0.092
FVC (l)	2.35 ± 0.26	2.46 ± 0.26	0.155
PEF (l/min)	323 ± 37	325 ± 40	0.838
FEF <sub>50</sub> (l/min)	1.88 ± 0.37	1.89 ± 0.35	0.236
FEF <sub>25</sub> (l/min)	0.62 ± 0.11	0.66 ± 0.12	0.721

AUC Area under the TBC curve over 6 h, TBC<sub>6</sub> tracheobronchial clearance over 6 h, AD alveolar deposition, PI penetration index, AIFR aerosol inhalation flow rate, FEV<sub>1</sub> forced expiratory volume in 1 s, FVC forced vital capacity, PEF peak expiratory flow, FEF<sub>xx</sub> forced expiratory flow at xx% of functional residual capacity

Data are presented as means ± SE values

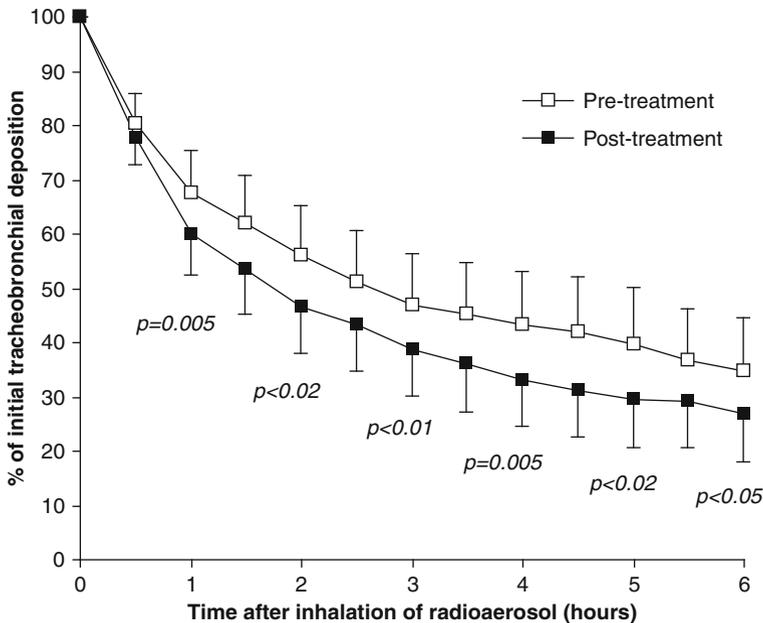
## 29.4 Humidification System

The humidification system used for this purpose was MR880 (Fisher & Paykel Healthcare, Auckland, NZ), which provides humidified air, fully saturated at 37 °C delivered via nasal interface at a flow rate between 20 and 25 l/min. Each patient was provided with a new nasal interface, heated breathing tube, humidification chamber, air delivering tube to connect the humidification chamber with a blower HC211 (Fisher & Paykel Healthcare, Auckland, NZ) plus a bag of sterile water. One of the investigators personally took the system to each patient's home and gave instruction in its daily use. Patients were asked to operate the system and use it for a short period of time to make sure they were comfortable with it. Each patient was instructed to use the system for 3 h/day for 7 days. Compliance with the treatment regime was assessed electronically, as usage time of the blower, which provides air to the humidifier, is recorded automatically.

## 29.5 Effect of Humidification on Mucus Clearance

Ten patients (3 males and 7 females) with bronchiectasis completed the study with a mean ± SE age of 63 ± 4 years. Three patients were ex-smokers with tobacco consumption of 5.8 ± 2.5 pack years. All but one of the ten patients exceeded the planned 'target' of 21 h humidification. Median duration of humidification was 25.0 h (range 14.9–26.9). All patients found the humidification procedure very acceptable.

One of the measures of initial tracer aerosol deposition, PI, changed little as indicated in the Table 29.1. The other AD changed relatively more. But in neither



**Fig. 29.1** Mean tracheobronchial retention curves at baseline and following humidification. Data are mean and standard error values

case was there any significant change. There was however a significant change in AUC and tracheobronchial retention. Humidification resulted in significant enhancement of clearance compared to baseline assessment. The enhancement of clearance was sustained at statistically significant levels throughout the 6-h monitoring period as seen in the Fig. 29.1.

After 7 days of treatment the number of coughs was slightly (non-significantly) reduced. During both 6-h monitoring periods, three patients had no coughs. The median number of coughs in the other seven patients was five coughs (3–37) with sputum wet weight of 1.8 g (0.0–2.9) at the baseline assessment and four coughs (0–13) with sputum wet weight of 1.4 g (0.0–8.2) during the post-treatment assessment.

Although differences were statistically non-significant, all lung function indices slightly improved following humidification compared to baseline assessment as indicated in Table 29.1.

## 29.6 Discussion

Maintenance of a sufficient airway surface liquid volume is crucial to preserving effective mucociliary defence of the airways. Hydration of the airways has for some time been suggested as a step towards facilitating mucus clearance and as a rational

component of some therapeutic approaches. Cell culture studies have shown that airway epithelia regulate both the periciliary and the mucus levels of airway surface liquid and both layers tend to be transported together. Current research findings highlight the complexity of the possible factors influencing airway surface liquid volume, but do place an emphasis on  $\text{Na}^+$  absorption and  $\text{Cl}^-$  secretion. Procedures adding extra liquid onto proximal airway surfaces may stimulate  $\text{Na}^+$  absorption.

The mucociliary clearance test we used – tracheobronchial aerosol retention – serves as an overall test of mucociliary function summing clearance from both bronchial and bronchiolar airways. It is potentially influenced by cough as well as by mucociliary transport. Cough has been shown to be a very important clearance mechanism in patients with chronic airways obstruction [3], but the mean number of coughs over the 6-h monitoring period was lower in the present study than in other studies we have conducted. Given also that cough frequency decreases slightly (albeit not significantly) on treatment, we suggest that the change we measured in radioaerosol clearance was a reflection of improved mucociliary clearance.

Inhaled tracer can only reach ventilated regions of the lung. Bronchiectasis patients – particularly those with severe disease – may have a very heterogeneous distribution of ventilation such that some elements of lung volume are completely inaccessible to any inhaled agents. These regions are likely also to have little or no effective mucus clearance (either by mucociliary clearance or cough). Our data can obviously shed no light on the long-term effects humidification therapy might have on these regions. Nevertheless, an improvement in clearance for the ventilated regions can of itself be a mechanism underlying an improvement in patient well-being. Arguably (but beyond any present proof) it might offer conditions favourable to some eventual partial recovery in adjacent non-ventilated regions. In bronchiectasis, as in chronic obstructive pulmonary disease, recurrent exacerbations may well reflect an overwhelmed defence system. They also serve as landmarks in the vicious cycle of infection and damage – and in so doing also provide evidence of stages in the patient's progression at which a clear need exists for an effective repair process.

In conclusion, our results suggest a positive effect from humidification. Further clinical trials of humidification therapy should indicate whether the short-term promise can be maintained in the longer term. This may then lead to the possibility of considering humidification therapy for other patients with disorders known to affect the mucociliary transport process adversely.

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## **Section IX**

# **Humidification in Critically Ill Neonates**

Alan de Klerk

Delivering appropriately conditioned inspired gas is widely recommended and practiced during invasive respiratory support of neonates, although no consensus exists regarding optimal temperature and humidity.

The lining of the infant's airway functions to prevent pulmonary infection and to serve as a countercurrent heat and moisture exchanger. Mucociliary clearance of the airway is dependent upon effective airway humidification in which inspired gas is heated and humidified by the respiratory tract during spontaneous breathing until at body temperature and pressure saturated (BTPS). Inadequately conditioned inspired gas typically produces a number of deleterious effects on the mucociliary transport system in mechanically ventilated infants.

During ventilatory support via an artificial airway in which the upper airway is bypassed, it becomes necessary to heat and humidify the inspired gas. This is most effectively achieved via a heated humidifier (HH), although careful attention to detail is needed to optimize effectiveness. Passive gas conditioning via a heat and moisture exchanger (HME) may also be used, but only in limited circumstances because of technological limitations. There is little evidence to support their safe and effective use in neonates, in particular for long-term ventilation.

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## 30.1 Introduction

The provision of heated and humidified gas is widely regarded as standard of care during respiratory support of the newborn infant, and is routinely practiced in neonatal intensive care units (NICUs). However there is no absolute consensus concerning the optimal temperature and humidity of the inspired gas used for neonates undergoing mechanical ventilation [1].

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A. de Klerk  
Department of Neonatology/BirthCare Center,  
Florida Hospital Memorial Medical Center, Daytona Beach, FL, USA  
e-mail: alan.deklerk@fhmmc.org

## 30.2 Anatomy and Function of the Airway Lining

The lining of the infant's airway is designed anatomically and physiologically to prevent pulmonary infection and to serve as a countercurrent heat and moisture exchanger. The luminal surface of the entire upper respiratory tract and the tracheobronchial tree down to the level of the respiratory bronchioles is covered by three layers: [2–4]

### 1. A basal cellular layer

With the exception of areas of the larynx and pharynx covered predominantly by squamous epithelium, this basal layer consists of ciliated epithelium of a number of different cell types, including columnar ciliated cells, mucus-producing goblet cells, serous cells, Clara cells, brush cells, neuroendocrine cells, and basal cells. Each columnar epithelial cell carries up to 200 cilia ranging from 6  $\mu\text{m}$  in length in the proximal airway to 4  $\mu\text{m}$  in the peripheral airway. Human cilia beat at 12–15 Hz at body temperature in a two-part movement cycle, swinging close to the cell 180° backward during the recovery stroke, then extending and moving through their effective stroke in a plane perpendicular to the cell surface. This effective stroke engages the overlying mucus, advancing it forward. The cilia then bend down toward the cell surface, disengaging from the mucus layer, and repeat the sequence. During the backward recovery stroke, cilia engage other resting cilia, stimulating them to begin a recovery stroke and resulting in a coordinated beating of airway cilia to produce effective mucociliary clearance in a cephalad direction [2–4].

### 2. A periciliary sol layer of thin nonviscous secretion. This bathes the basal portion of the cilia and allows the cilia to move in a low resistance environment during the backstroke of their movement cycle. If this layer is too thick, cilia are unable to effectively engage the overlying mucus. If too thin, disengagement of cilia from the mucus layer during the recovery stroke is adversely affected, and ciliary motion is impeded. The periciliary layer also plays a role in mucus hydration, thereby lessening mucus viscosity. Of note in neonates, mucociliary clearance is slow, and this is believed to be at least in part due to increased periciliary fluid secretion. With maturing secretory function in neonates, mucus transport rates increase to adult values by 4–8 weeks of life [2–4].

### 3. A viscoelastic mucus layer. This consists of glycoproteins, proteoglycans, immunoglobulins, other proteins, lipids, and, with airway inflammation or infection, significant amounts of DNA, which can increase mucus viscosity substantially. Mucus is formed in the Golgi apparatus of goblet cells and submucosal mucous glands, and secreted by exocytosis as globules of 1–2 $\mu\text{m}$ size. Water is rapidly absorbed from the periciliary fluid layer with swelling of the mucus globules. In the smaller distal airways, mucus appears as smaller droplets or plaques in response to particle deposition. These droplets gradually coalesce as they are moved up the tracheobronchial tree, forming a continuous, progressively thicker, blanket-like layer in the larger airways that continues to trap inhaled particles, bacteria, macrophages, and cell debris [2–4].

Mucociliary transport rates are higher in the proximal than the distal airway, averaging 4–5 mm/min in the trachea versus less than 0.4 mm/min in the bronchioles. Mucociliary clearance occurs in two distinct but simultaneous phases, an initial rapid phase in the tracheobronchial tree with a half-life of approximately 4 h, and a slow phase of alveolar clearance by non-mucociliary transport mechanisms that may last weeks to months. Of particular relevance to the neonatal population, mucociliary function is suboptimal at birth but develops and matures over several weeks before becoming adultlike [4].

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### 30.3 Physiology of Airway Humidification and Thermoregulation

With regard to physiological airway humidification, inspired gas (typically 22°C with a water content of 9–10 mg H<sub>2</sub>O/l and relative humidity of 50% under normal circumstances) is heated and humidified by the respiratory tract during spontaneous breathing until at body temperature and fully saturated with water vapor, often referred to as body temperature and pressure saturated (BTPS) [1, 5]. This process occurs predominantly in the nasopharynx and proximal trachea, and is progressive in nature as gas moves down the intact airway. Entering the trachea, inspired gas typically reaches temperatures of 29–32°C and full saturation, ultimately reaching the isothermic saturation boundary (defined as the point at which gas reaches 37°C and 100% relative humidity, corresponding to an absolute humidity of 44 mg H<sub>2</sub>O/l) just below the carina at the level of the mainstem bronchi in the normal adult during quiet breathing of room air. The exact location of the isothermic saturation boundary is influenced by a number of factors, including the temperature and humidity of the inspired gas, breathing pattern, and the airway used (oral or nasal). It moves proximally with slow and shallow breathing, and distally when breathing cold dry air, with oral breathing rather than nasal breathing, when minute ventilation is high, and when the upper airway's ability to heat and humidify inspired gas is compromised, for example, in the patient with a tracheostomy. Below the isothermic saturation boundary, temperature and humidity are constant, whereas above this boundary, the gradient between the cooler, dry inspired gas and the airway itself results in countercurrent heat and moisture exchange, with inspired gas gaining heat and water vapor from the upper airway lining. During expiration, expiratory gas above the isothermic saturation boundary is cooled, leading to recovery of heat and water from the expired gas as it loses heat and water condenses on the upper airway lining. This recovery is only partial, with expired gas ranging from 32°C to 34°C at 100% relative humidity during normal breathing. Heat and moisture exchange occurs as long as the thermal and moisture gradient between the gas and the airway mucosa is maintained, and the greater the gradient, the greater the transfer of heat and water [2, 5].

The net result of the complex cycling process described above is a predominantly evaporative loss of water and heat from the respiratory tract. This evaporative loss ( $H_{\text{evap-r}}$ ) is dependent on the respiratory water loss (the difference between the water content of inspired and expired gas), which in turn depends on the humidity of

inspired gas, with lower losses at higher humidity. Insensible water loss from the respiratory tract (IWL<sub>r</sub>) has been shown to decrease from 9 to 5 g/kg/24 h in term infants when ambient humidity is increased from 20% to 80%. Although respiratory water loss (RWL) is higher in more preterm infants when compared to term infants, the RWL per breath is almost the same, suggesting that the higher losses in preterm infants are the result of a higher respiratory rate. Respiratory water loss relative to transdermal loss is also affected by gestation, being almost equal in term infants, whereas respiratory losses in preterm infants are proportionately smaller than transdermal losses [1]. Respiratory heat loss in infants can account for 3–10% of the total heat production from metabolism and about 40% of the insensible heat loss [4]. Most of the energy requirement of spontaneous breathing is needed for humidification of inspired gases, with warming consuming relatively little energy [1]. A small amount of convective heat transfer ( $H_{\text{conv-r}}$ ) also occurs in the respiratory tract, related to the gas volume ventilated per unit time and to the temperature difference between inspired and expired gas. If an infant is nursed in an environment where the ambient temperature is not substantially lower than that of expired air (such as an incubator), convective losses are very small [6].

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## 30.4 Principles of Heat and Humidity Exchange

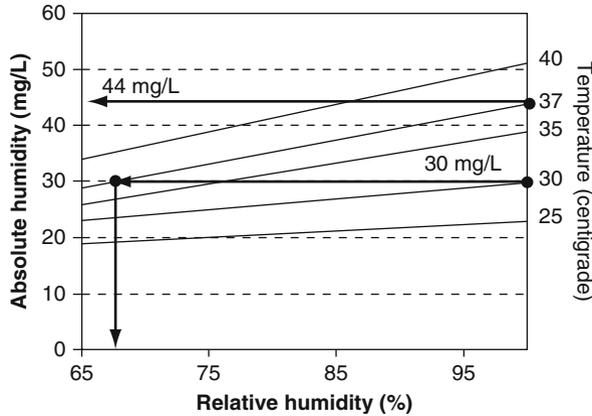
Broadly speaking, there are two important ways to deliver water to the airways via inspired gases [2, 3].

### 1. Vaporization

This is produced using heated humidifiers or heat and moisture exchangers, and results in an invisible molecular distribution of water in air. Fully saturated air (100% relative humidity) at 37°C has a gaseous partial pressure of water vapor of 47 mmHg, corresponding to an absolute humidity of 44 mg water per liter of gas. The relationship among absolute humidity, relative humidity, and temperature is shown in Fig. 30.1. It is the provision of this vaporized water as humidification during mechanical ventilation that is the principle focus of this chapter.

### 2. Nebulization

A dispersion of small droplets of water in air is generated using jet or ultrasonic devices. These droplets of approximately 0.5–5 μm in size are visible as mist and are of sufficient size to carry infectious agents. The smaller the droplet size, the further they may penetrate toward the lung periphery before depositing on the tracheobronchial lining. Due to droplet size, the resultant airway deposition by impaction of larger particles and sedimentation of smaller particles, the inability of an aerosol to contribute significantly to gas conditioning beyond the isothermic saturation boundary, the water burden on the mucosa with perturbation of mucociliary clearance, and the potential for increased airway resistance and occlusion of small airways, water or normal saline nebulization does not offer significant benefit for inspiratory gas conditioning [1, 2], and will not be discussed in further detail in this review. It should be noted that nebulization devices may be necessary and useful for the delivery of pharmacologic agents to neonates and infants via the airway.



**Fig. 30.1** The relative humidity of a gas depends on its absolute water content and gas temperature. At 37°C and 100% relative humidity, the respiratory gas has 44 mg/l absolute water content. If the gas is saturated (100% relative humidity) at 30°C, its water content is only 30 mg/l. When the gas is then warmed to 37°C, its relative humidity falls to less than 70% (Reprinted from Schulze [2]. Copyright (2007). With permission from Elsevier)

Heat exchange between the newborn and the environment occurs primarily through the skin, but also to a lesser extent through the respiratory tract. Basic mechanisms of heat loss in neonates include conduction, radiation, evaporation and convection, although only the last two of these play a significant role in respiratory tract heat exchange [7].

The relationship between water content of inspired gas and heat content is an important one when considering heat loss (or gain) during respiration. Total energy content of air consists of two components, sensible and latent heat. Air temperature alone represents sensible heat, and adds minimally to the total energy content of inspired gas in the absence of water vapor. Thus, adding dry heat to fully humidified gas in the inspiratory limb of a ventilator circuit has little effect on the total energy content and would not risk thermal injury to the airway. Conversely the latent heat content is represented in the water vapor mass, and vaporization of fluid from the airway lining to humidify dry inspired gas consumes considerable energy and results in cooling of the airway with consequent heat as well as water loss. Condensation of water vapor in the patient airway may in turn generate energy [2, 3].

### 30.5 Impact of Inadequate Humidification and Warming of Inspired Gases

Although providing adequate heat and humidification of inspired gas during invasive ventilation is generally accepted as standard of care, there is no clear consensus on either the optimal or the minimal acceptable levels of temperature and humidity. Various minimum absolute humidity levels have been proposed for

inspired gas in patients whose supraglottic airway is bypassed, including 33 mg/l in the UK and by the International Organization for Standardization [1], and 30 mg/l at 30°C in the US [8].

The mucociliary transport system is highly sensitive to changes in inspired gas humidity and temperature, and a number of deleterious effects may result from inadequately conditioned inspired gas. Due to its ability to warm and humidify inspired air, nasal mucus transport is not significantly affected by changes in humidity or temperature, but tracheal ciliostasis occurs if gas of less than 30% relative humidity is breathed [4]. Non-humidified inspired gas leads to dehydrated mucus, slowing cilia beat frequency and mucociliary transport rate, and to thinning of the periciliary sol layer impairing the recovery stroke of the cilia. Mucosal inflammation and sloughing may follow, with impairment of the heat and moisture exchange function of the upper airways. As a result, the isothermic saturation boundary is displaced distally, progressively extending the area of mucosal damage toward the lung periphery [1–5]. In a preterm lamb model, 3 h of ventilation with cold and dry gas versus with heated and humidified gas produced no differences in pulmonary mechanics or markers of inflammation, but did result in ciliary damage and dysfunction on electron microscopy, especially if also exposed to hyperoxia [9]. The progressive and cumulative effects of these changes may result in one or more of the following:

1. Inspissation of airway secretions
2. Impaired mucociliary clearance
3. Inflammation and necrosis of the airway epithelium
4. Heat loss and hypothermia
5. Impaired surfactant activity
6. Nosocomial infections
7. Increased risk for airway obstruction, atelectasis, and air leak

Inadequate humidification has been identified as a common problem in mechanically ventilated neonates with increased risk for respiratory complications in very low birth weight infants (less than 1,500 g birth weight) [1]. Although rehumidification may allow recovery of ciliary function and mucociliary clearance, prolonged cessation of ciliary activity has been shown to result in irreversible mucosal damage and sloughing [2]. Recovery of normal epithelial architecture may take up to several weeks if denudation occurs to the level of the epithelial basement membrane [4].

Increased osmolarity of the airway lining fluid due to water loss has been demonstrated to induce bronchial smooth muscle contraction in patients with exercise-induced asthma, although the mechanism of this action is unclear, as is its possible role in chronic lung disease in premature infants. Mechanically ventilated preterm infants exposed to suboptimally heated and humidified inspired gas in the first 4 days of life were noted to have more air leaks and more severe chronic lung disease [2]. That this finding was not noted in more mature infants suggests that gestational age may play an important role.

It should be noted that excessive heat and humidification of inspired gas may also have significant consequences [1, 3]. These include:

1. Airway thermal injury with potential for pulmonary edema and airway stricture formation

2. Condensation of water and accidental lavage of airways with contaminated condensate and potential for subsequent pneumonia
3. Surfactant inactivation with decreased compliance
4. Impaired lung function and hemodynamics
5. Impaired mucociliary clearance

Given these concerns, the American Association for Respiratory Care recommends that the inspiratory gas temperature should not exceed 37°C at the airway threshold [8], although no similar recommendations are made for maximum humidity levels.

All of these potential adverse consequences need to be considered in the context of their additive, and in some cases synergistic, effects to those of mechanical injury. Mechanical ventilation and interventions such as endotracheal intubation and suctioning produce inflammatory changes with epithelial flattening and denudation, and loss of goblet cells and cilia. Bronchopulmonary dysplasia following positive pressure support results in similar changes extending to the terminal and respiratory bronchioles [4]. Any exacerbation of these adverse mechanical influences on the exquisitely sensitive airway epithelium and mucociliary transport function by the use of inadequately conditioned respiratory gases should be avoided.

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## 30.6 Humidification Devices and Clinical Use

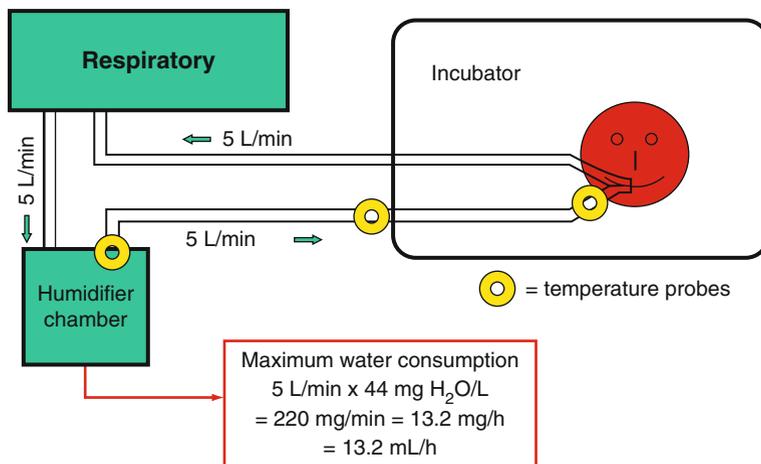
During ventilatory support via an endotracheal tube (ETT) or tracheostomy, the normal humidifying and conditioning function of the upper airway is bypassed, and it becomes necessary to heat and humidify the inspired gas. This is achieved in one of two principle ways, either actively via a heated humidifier (HH) or passively via a heat and moisture exchanger (HME), also known as an artificial nose.

### 30.6.1 Heated Humidifiers

These are able to provide a wide range of temperature and humidity [10]. The most common generic device of this type consists of a humidification chamber with a water reservoir and heating element along with a temperature control unit (including temperature probe and alarms). The humidification chamber heats the respiratory gas to a set target temperature while adding water vapor from the heated water reservoir. The water surface area and temperature of the chamber are the principle determinants of its vaporizing capacity. The water consumption rate of a humidifier is indicative of its efficiency, and can be used to calculate the absolute and relative humidity at the chamber outlet if the continuous gas flow rate is known for a ventilated patient [2, 3]. Typically, a heated wire in the inspiratory limb of the respiratory circuit delivers a more precise gas temperature to the patient airway, and either maintains or, more commonly, raises slightly the gas temperature to prevent condensation (“rainout”) in the circuit proximal to the patient [2, 10]. Assuming fully water saturated gas at the chamber outlet, any cooling of the gas en route to the Wye adaptor results in condensation and loss of moisture from the respiratory gas.

The degree of cooling (and the resultant amount of condensation) is affected by tubing size (smaller diameter tubing has a relatively large outer surface area for heat exchange, especially if corrugated), ambient room temperature and cooling drafts, and by gas flow rates (lower flows result in longer contact time with the surrounding environment for heat exchange). It is important to recognize that this rainout is reflective of underhumidification of the delivered gas rather than effective humidification. Aside from the adverse effects of inadequately conditioned gas previously described, rainout may also result in airway lavage with contaminated condensate, and may affect ventilator function, including autocyling in patient-triggered ventilators. When ventilating neonates, it is generally recommended that the humidifier chamber temperature be set to 37°C in order to fully saturate the gas with 44 mg/l of water vapor (100% relative humidity). If the target gas temperature at the Wye adaptor is then set at 39°C, moisture loss in the inspiratory limb of the heated circuit will be minimized, and the gas should arrive at close to full saturation [2]. As previously discussed, the dry sensible heat added in the inspiratory circuit dissipates very rapidly once beyond the heated wire segment of the inspiratory tubing.

Most humidifiers used in the NICU are servo-controlled. The operator sets the desired gas temperature, and the temperature probe close to the patient interface monitors the respiratory gas temperature and aims to maintain the set gas temperature by adjusting the heated wire output [10]. Critically ill neonates are commonly managed in incubators or on radiant warmers, and the delivered gas is exposed to two different temperatures, room temperature and the temperature in the incubator or under the radiant warmer. As a result, servo-control of the heated wire circuit becomes more complex. If the distal temperature probe is in a heated field (either the incubator or under the direct radiant heat of a radiant warmer) in which the temperature is higher than the targeted gas temperature, the radiant or convective heat from that environment may cause it to record a higher temperature than the actual temperature of the respiratory gas, and to signal the servo-control to decrease the heating output of the ventilator circuit. This will then cause a loss in gas temperature and rainout. One way to minimize this effect, in particular under a radiant warmer, is to protect the temperature probe with a light reflective patch. If the patient is in a heated incubator in a relatively high ambient temperature, the temperature probe may be placed outside the incubator, if necessary using an unheated extension tube distal to the probe. As the high ambient temperature maintains the temperature of the gas in the circuit within the incubator, the heated wire is less essential. Theoretically, if the incubator temperature is substantially higher than the airway temperature, the gas temperature may increase with a subsequent decrease in the relative humidity of the inspired gas, and the risk of epithelial drying [1]. In a cooler incubator with temperature less than approximately 34°C, a heated wire along the entire inspiratory limb to as close to the patient interface as possible is preferred. Insulating of the respiratory circuit with wrapping or drapes is practiced by some as a way to further reduce rainout, but has been associated with melting or charring of circuit components [2]. Although not commonly used in NICUs, circuits with two temperature probes, one outside the heated field and one close to the Wye adapter at the patient, can be very useful for patients in incubators. The heated-wire



**Fig. 30.2** Position of three temperature probes of a heated-wire humidification system for infants. The user sets the target temperature to be reached at the endotracheal tube adaptor. This temperature is commonly set at or slightly greater than 37°C. The temperature inside the humidifier chamber must be high enough to vaporize an amount of water near the absolute water content of gas saturated at 37°C (44 mg/l). The water consumption rate of a humidifier chamber required to reach a target respiratory gas humidity can be calculated from the circuit flow rate. Observation of this water consumption rate can be used as a simple test of the efficiency of a humidifier (Reprinted from Schulze [2]. Copyright (2007). With permission from Elsevier)

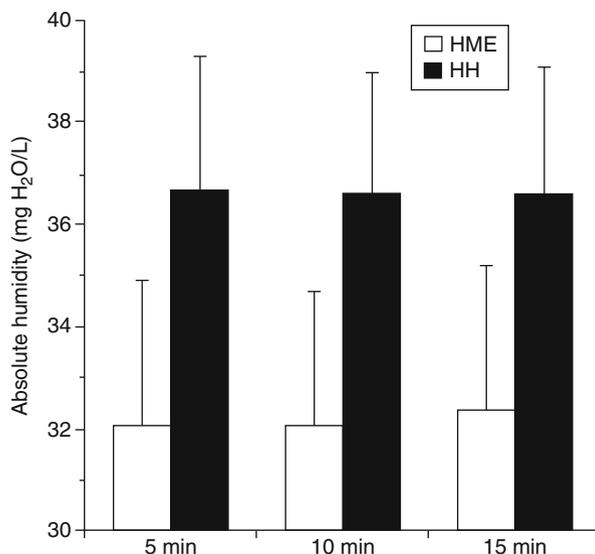
servo-control is programmed to use the lower of the two temperatures to control the power output, and is thus capable of appropriately regulating inspired gas temperature over a wider range of incubator temperatures (Fig. 30.2).

Even very early and short-term use of conditioned inspired gas may have clinically significant effects. The use of heated and humidified gas during respiratory support of very preterm neonates in the delivery room reduced the postnatal decrease in temperature typically seen in these patients [11]. Further studies are needed to investigate whether any additional short-term and/or long-term effects, either positive or negative, are associated with this strategy.

Mode of ventilation may impact the effectiveness of HHs. The mean absolute humidity and relative humidity at the patient end of the respiratory circuit at a humidifier setting of 37°C during high-frequency ventilation were less than 35 mg/l and 65%, respectively, compared with 42.3 mg/l and 96.8%, respectively, with conventional intermittent positive pressure ventilation [12]. In another study comparing HH and HME humidification in an artificial lung model, increasing expiratory water loss was observed with increasing oscillation amplitude and low oscillation frequency with both devices [13].

It is important to consider inherent limitations in the technology of heated humidifiers as currently manufactured and utilized. A study of ventilated neonates found that the temperature at the circuit temperature probe may not accurately reflect the temperature at the airway opening [14]. With the chamber temperature

**Fig. 30.3** Mean ( $\pm$  SEM) temperatures at circuit temperature probe site (*Circuit*), ETT-circuit manifold (*T1*), and ETT adaptor (*T2*) (Reprinted from Davies et al. [14]. Copyright (2004). With permission from John Wiley and Sons)



set at 36°C and the circuit temperature set at 37°C, the mean temperature at the airway opening in infants nursed in incubators was 34.9°C, compared with radiant warmers where the mean was 33.1°C (Fig. 30.3). The mean difference in temperature from the circuit temperature probe to the airway opening was greater under radiant warmers, with a mean drop of 3.9°C compared with 2.0°C in the incubators. The authors speculated that it may be prudent to measure temperature closer to the patient than typical current practice, and that unless this is done, setting the circuit temperature higher should be considered as a way to compensate for the drop in temperature from the circuit temperature probe site to the airway opening.

In a subsequent experimental lung model study, the inspired gas temperature was shown to drop when passing from the circuit temperature probe site (40°C) to the proximal end of the ETT (37°C) [15]. The temperature dropped further as it traveled through the exposed part of the ETT (34°C), but then warmed again so that the gas entering the airways and lungs was at the desired 37°C. The authors again suggested that unless the temperature is measured closer to the patient, it may well be worth setting the temperature at the circuit temperature probe site even higher at >40°C to compensate for the drop in temperature from the circuit temperature probe site to the exposed part of the ETT.

The benefits of HHs in terms of their ability to condition respiratory gases effectively need to be weighed against recognized actual and potential drawbacks of these devices, including: [10, 16]

1. Increased cost relative to HMEs
2. Over-heating/-hydration with resultant lung damage
3. Condensation with bacterial contamination
4. Increased inspiratory workload

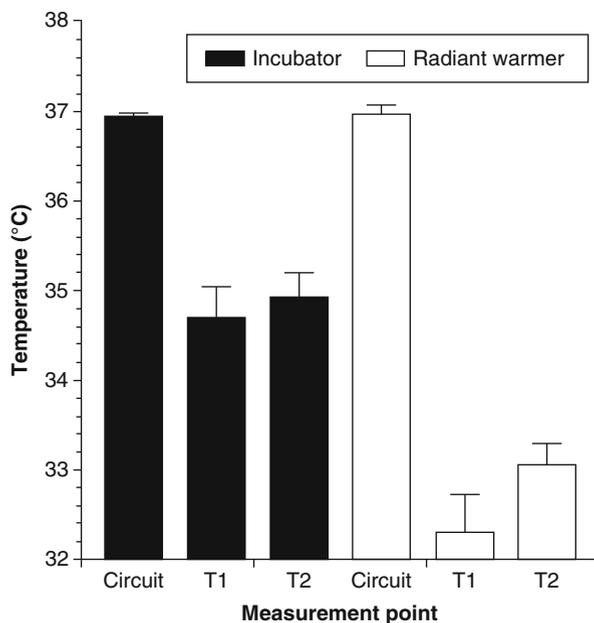
Despite theoretical concerns and demonstrated colonization of humidifier chambers, nebulizer reservoirs, and circuit condensate with infectious agents, there is no good evidence of increased risk for nosocomial pneumonia or sepsis with appropriately conditioned respiratory gases [2]. In addition, the optimal rate of ventilator circuit changes in neonates and infants has not been established. Since disrupting ventilation for circuit changes may have adverse effects and has not been shown to have any clear cut advantages, weekly respiratory circuit changes or none at all except between patients has been recommended [3].

### 30.6.2 Heat and Moisture Exchangers

These are also known as artificial noses because of the similarity in function to the human nose. They are passively acting humidifiers that utilize a low thermal conductivity sponge material to collect part of the expired heat and moisture and return it during the following inspiration. Since only a portion of the expired humidity is returned, the use of HMEs always involves a net loss of heat and humidity. Simple HMEs use only physical principles of heat and moisture exchange. Some are coated with bacteriostatic substances and have viral filters added, and are referred to as heat and moisture exchanging filters (HMEFs). Hygroscopic condenser humidifiers (HCHs) contain a hygroscopic salt (such as calcium or lithium chloride) to further enhance the moisture-conserving performance of the HME by absorbing water vapor during expiration and releasing it during inspiration [2, 10, 16]. A filter can also be added to these latter devices (HCHF). As with all of these device types, the addition of a filter increases the resistance of the device [10].

Small HMEs/HCHs designed for use in neonates are available, and it is likely that technological and commercial advances will increase their availability, effectiveness, and safety, but there are few data to date to support their use in this population. HMEs integrated into the tracheal tube connector are available for small neonates to minimize additional dead space. Due to concerns related to the increased resistance imposed by HMEs and the potential for increased work of breathing, especially as spontaneous breathing increases when weaning from ventilatory support, it has been recommended that a body weight of 2,500 g or more be used as a reasonable minimum for the use of HME humidification [1]. However, modern ventilator technology and techniques such as pressure support ventilation may mitigate this problem, and short term use of HMEs in neonates weighing as little as 610 g has been reported [17]. In the latter study comparing HH and HME humidification in conventionally ventilated neonates, absolute humidity of 28 mgH<sub>2</sub>O/l or more and a temperature of 30°C or more were achieved with HMEs. Higher values of absolute humidity and temperature were obtained with HH use (Fig. 30.4). Using a neonatal HME with high frequency oscillatory ventilation in a neonatal lung model provided more than 35 mg/l of mean humidity at the proximal end of the ETT adapter, and dampened the oscillatory pressure less than an ETT of 3.5-mm internal diameter [13].

**Fig. 30.4** Mean values  $\pm$  SD of absolute humidity of inspired gas. Absolute humidification was higher at the three measurement periods with heated humidifiers (HH) than with heat and moisture exchangers (HME) (Reprinted from Fassassi et al. [17]. Copyright (2007). With permission from Springer-Verlag)



Advantages of HMEs include lower cost, simplification of the ventilator circuit, passive operation, and elimination of condensate with lower risk of circuit contamination [3, 10, 17]. A Cochrane review comparing HH and HME use in ventilated adults and children found no overall effect on artificial airway occlusion, mortality, pneumonia, or respiratory complications, although PaCO<sub>2</sub> and minute ventilation were increased and body temperature was lower when HMEs were used. There was some evidence that hydrophobic HMEs may reduce the risk of pneumonia and that blockages of artificial airways may be increased with the use of HMEs in certain subgroups of patients. In addition, the cost of HMEs was lower in all studies that reported this outcome. However only 2 of the 33 studies included in the metaanalysis in the review were carried out in children (weighing between 5 and 10 kg in one study and between 5 and 30 kg in the other), and another 1 of the 33 reported data from a neonatal population. In two neonatal studies excluded from the metaanalysis, no differences were found in humidity, body temperature, PaCO<sub>2</sub>, pneumothorax rates, tube blockage, duration of ventilation, or oxygen requirement. Of relevance in the NICU, the review concluded that HMEs be used with caution in patients at risk of airway obstruction, including neonates, and that insufficient data are available to recommend the widespread use of HMEs in the pediatric and neonatal populations [16].

The Cochrane review findings and recommendations have specific implications in the NICU. Neonates are at increased risk for hypothermia because of their large surface area to body weight ratio, immature skin with high evaporative loss, inability to shiver, and high respiratory heat loss secondary to their respiratory minute volume relationship to body surface area being twice that of adults [17]. A clinically significant reduction in body temperature with HME use versus HH use, while

likely not clinically relevant in adults, may be very important in neonates and children. Due to the mechanism of action of HMEs, minimizing leaks around the ETT is important [1, 17]. Sufficient moisture retention capability has been demonstrated if the leak fraction around the ETT is less than 15% [18]. This is particularly relevant in neonates as uncuffed ETTs are typically used in this population.

In addition to the general concerns regarding HME use in the neonatal population, it has also been recommended to avoid HME use in patients with copious, thick sputum, grossly bloody secretions, hypothermia, bronchopleural fistula, or prolonged ventilation (>5 days), or those requiring frequent medication delivery via small volume nebulizer, whether adults or children. However, some advocate prolonged use of HMEs in the adult population depending on clinical circumstances, and they have been used for periods as long as 30 days or more [10]. Safety and efficacy for long-term ventilation in neonates have not been established, and they are more appropriately used for short term mechanical ventilation in this population [3].

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### 30.7 Summary

It is widely recognized that neonates and infants undergoing mechanical ventilatory assistance via an artificial airway such as an ETT should have inspiratory gases appropriately conditioned with heat and humidification. The anatomic and functional integrity of the airway lining, most importantly the mucociliary clearance function, are dependent on maintaining the temperature and humidity gradients along the airway. Although limited evidence and no consensus exists for the optimal temperature and humidity for this population in these clinical circumstances, it is common practice to deliver gas at or near body temperature and pressure saturated (BTPS: 37°C and 100% absolute humidity, equivalent to 44 mg H<sub>2</sub>O/l absolute humidity). Heated humidifiers are able to deliver this safely and for prolonged periods, and also have the capability to deliver conditioned gas over a wide range of temperature and humidity if clinically indicated. Heat and moisture exchangers designed for use in neonates and infants can provide sufficient moisture output during short-term ventilation, and have some benefits related to cost and simplicity. However concerns exist with the use of HMEs in segments of this population, and safety and efficacy in preterm infants, in low birth weight infants, and during long-term ventilatory support have not been established. Future technological advances may extend their availability, effectiveness, and safety.

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# Measurement of Inspired Gas Temperature in the Ventilated Neonate

# 31

Luke Anthony Jardine, David Cartwright,  
Kimble Robert Dunster, and Mark William Davies

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## 31.1 Introduction

Ventilated neonates routinely have their inspired gases warmed and humidified via a humidifier and a heated inspiratory line as part of the ventilator circuit. The normal physiological temperature of the neonatal airway is largely unknown, as are the optimal temperature and humidity of the inspired gas. The main roles of warming are to achieve adequate levels of humidification and reduce heat loss through the lungs. High levels of humidity are technically difficult to measure; sensors are costly, fragile and when saturated with condensed water give inaccurate measurements. Indirect assessment via calculation from water consumption, gas flow and

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L.A. Jardine (✉) • M.W. Davies  
Grantley Stable Neonatal Unit, Royal Brisbane and Women's Hospital,  
Brisbane, Queensland, Australia

Department of Paediatrics and Child Health,  
The University of Queensland, Royal Children's Hospital,  
Brisbane, Queensland, Australia  
e-mail: luke\_jardine@health.qld.gov.au

D. Cartwright  
Grantley Stable Neonatal Unit, Royal Brisbane and Women's Hospital,  
Brisbane, Queensland, Australia

K.R. Dunster  
Institute of Health and Biomedical Innovation, Queensland University of Technology,  
Brisbane, Queensland, Australia

Grantley Stable Neonatal Unit, Royal Women's Hospital,  
Brisbane, Queensland, Australia

Critical Care Research Group, Department of Intensive Care Medicine,  
The Prince Charles Hospital,  
Brisbane, Queensland, Australia

temperature would provide, at best, a crude long-term average measure of humidity. Temperature probes are slow, durable and inexpensive, and as a result airway temperature, as measured by a probe placed in the inspiratory limb of the ventilator circuit, is routinely used as a proxy measure of humidity. However, these temperature measurements are usually measured at the circuit temperature probe, which is at least 8 cm from the airway opening and even further from the infant's lungs. The temperature measured by the circuit temperature probe at the distal end of the inspiratory line may not be the temperature of the gas entering the infant's lungs. The total amount of water going into the inspiratory limb of the ventilator circuit is fixed once the gas leaves the humidifier; therefore changes in temperature will cause changes in humidity, leading to either inadequate humidification or condensation in the circuit. An increase in temperature will reduce the relative humidity, but maintain absolute humidity. If the relative humidity is already 100%, a decrease in temperature will maintain relative humidity at 100% and lead to condensation. Condensation of water droplets in the circuit can lead to their delivery to the lungs and resulting injury. Ventilated neonates routinely have their inspired gases warmed and humidified via a humidifier and a heated inspiratory line as part of the ventilator circuit. The normal physiological temperature of the neonatal airway is largely unknown, as are the optimal temperature and humidity of the inspired gas. The main roles of warming are to achieve adequate levels of humidification and reduce heat loss through the lungs. High levels of humidity are technically difficult to measure; sensors are costly, fragile and when saturated with condensed water give inaccurate measurements. Indirect assessment via calculation from water consumption, gas flow and temperature would provide, at best, a crude long-term average measure of humidity. Temperature probes are slow, durable and inexpensive, and as a result airway temperature, as measured by a probe placed in the inspiratory limb of the ventilator circuit, is routinely used as a proxy measure of humidity. However, these temperature measurements are usually measured at the circuit temperature probe, which is at least 8 cm from the airway opening and even further from the infant's lungs. The temperature measured by the circuit temperature probe at the distal end of the inspiratory line may not be the temperature of the gas entering the infant's lungs. The total amount of water going into the inspiratory limb of the ventilator circuit is fixed once the gas leaves the humidifier; therefore changes in temperature will cause changes in humidity, leading to either inadequate humidification or condensation in the circuit. An increase in temperature will reduce the relative humidity, but maintain absolute humidity. If the relative humidity is already 100%, a decrease in temperature will maintain relative humidity at 100% and lead to condensation. Condensation of water droplets in the circuit can lead to their delivery to the lungs and resulting injury.

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## 31.2 Role of Humidification and Airway Temperature

Insufficient humidification of the inspired gases can promote drying of the mucosal surface, which will inhibit mucociliary clearance, make secretions thick and viscous, lead to plugging of the large airways and, in extreme cases, cause death [1].

Low inspired gas temperatures may not just be associated with inadequate humidification and drying of the airway mucosa, but may also lead to poor temperature control. High temperatures may also perturb the infant's temperature control and can potentially burn the respiratory epithelium [2]. Adequate inspired gas temperatures are associated with a lower incidence of pneumothorax and a decreased severity of chronic lung disease in ventilated very low birth-weight infants [3].

### 31.3 Temperature Changes from Humidifier to Patient

Davies et al. studied inspired gas temperature in ventilated neonates using the normal ventilator circuits and the humidifier settings that were standard at the time (chamber temperature set at 36°C and circuit temperature set at 37°C) [4]. The temperature set on the humidifier did not reflect the temperature of the gas at the airway opening [i.e., the proximal end of the endotracheal tube (ETT)] [4]. This is because the gas temperature dropped as it passed from the inspiratory circuit, beyond the heating wire, to the airway opening. To allow for this temperature drop, it is recommended that the humidifier chamber temperature be set to 37°C and the circuit temperature set to 40°C.

In a subsequent experimental bench-top model, Jardine et al. showed that the temperature drops further – down to 34°C – as it travels through the exposed part of the ETT, but then warms again so that the gas entering the airways and lungs is at the desired 37°C [5]. The eventual temperature that enters the infant's lungs will be dependent on the temperature of the gas coming from the ETT-circuit manifold (having been heated in the inspiratory line), the temperature of the environment through which the exposed ETT travels, the rate of flow of gas down the ETT and the temperature of the infant. The decrease in temperature is presumably secondary to radiant loss to the environment. This large decrease might be prevented if the environmental temperature were increased (e.g., the room temperature or the temperature around the circuit in an incubator or under a radiant warmer) or the flow rate increased. It is reassuring that the inspired gas is re-warmed as it flows down the ETT. This increase in temperature as the airway enters the model lung is thought to be secondary to radiant and conductive warming from the lung model itself (representing the patient temperature). This re-warming must require energy expenditure from the infant.

It may be worthwhile heating the gas more in the inspiratory circuit so that the gas that finally enters the ETT inside the patient is at 37°C, and less energy expenditure is required by the infant. Safety may become an issue if unanticipated environmental changes cause overheating of the inspired gas. Factors that increase or decrease flow in the ETT and the ambient temperature may then become important. This could therefore impact on an infant's energy expenditure. Unless the temperature can be measured closer to the patient, it may well be worth setting the circuit temperature even higher to compensate for the drop in temperature from the circuit temperature probe site to the exposed part of the ETT. However, this needs to be studied further, and the effect of the ambient temperature also needs to be considered. It would seem prudent to keep the temperature of the inspired gas in the presumed physiological range (i.e., 36.6–37.4°C) until more data are available.

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## 31.4 Conclusion

Clearly, for optimal respiratory management, there is a need to measure both temperature and humidity as close as possible to the patient. Measuring the temperature closer to the patient than current practice allows would circumvent the drop in inspired temperature in the exposed part of the ETT. The temperature of the inspired gas should be kept in the physiological range (i.e., 36.6–37.4°C) until more data are available.

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## 31.5 Key Major Messages

1. Airway temperature is measured as a surrogate marker for humidity.
2. Inadequate humidification increases the risk of pneumothorax and chronic lung disease.
3. Excessive airway temperatures can cause burns to the respiratory epithelium.
4. Gas temperature drops as gas travels from the circuit heater to the patient.
5. The temperature of the inspired gas should be kept in the physiological range (i.e. 36.6–37.4°C) until more data are available.

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# Humidification During Noninvasive Respiratory Support of the Newborn: Continuous Positive Airway Pressure, Nasal Intermittent Positive Pressure Ventilation, and Humidified High-Flow Nasal Cannula

Alan de Klerk

Various modes of noninvasive respiratory support have evolved in an attempt to minimize lung damage associated with invasive respiratory support of the neonate.

Continuous positive airway pressure (CPAP), delivering positive airway pressure that is consistent, predictable and regulated, has long been the mainstay of noninvasive respiratory support in neonates. The device used and application technique may influence CPAP efficacy significantly. More recently, technological advances have resulted in increasing use of synchronized and non-synchronized noninvasive positive pressure ventilation (NIPPV). Humidified high-flow nasal cannula (HHFNC) therapy, with its ease of use, is being widely adopted despite limited evidence of safety and efficacy.

There is no widely accepted standard for heated humidification of gases during non-invasive ventilatory support, in which the upper airway is not bypassed and can continue to contribute effectively to gas conditioning. However, studies in adults and limited neonatal clinical evidence support the role of effective conditioning of inspired gases when delivering non-invasive respiratory support, as a means to optimize efficacy of support and minimize adverse effects on airway and pulmonary function. Minimal and optimal temperature and humidity settings remain to be elucidated.

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## 32.1 Introduction

Pulmonary disorders are among the most common in neonatology, and respiratory support of preterm or critically ill neonates has long been a mainstay of neonatal care. Intermittent positive pressure ventilation (IPPV) of preterm infants via an

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A. de Klerk  
Department of Neonatology/BirthCare Center,  
Florida Hospital Memorial Medical Center, Daytona Beach, FL, USA  
e-mail: alan.deklerk@fhmmc.org

endotracheal tube (ETT) began in the 1960s, but was associated with high rates of pulmonary morbidity and mortality [1]. As a result, various modes of noninvasive respiratory support and methods for delivering it have evolved over the ensuing decades in an attempt to minimize lung damage and improve survival. Balancing the need for appropriate support with the potential for lung damage frequently caused by such support is one of the key factors in selecting the desired mode of support, as well as how and for how long it is applied [2].

This chapter will outline the most common methods of providing noninvasive respiratory support to neonates, and will describe the importance of appropriate conditioning of associated inspiratory gases. For a review of the anatomy and function of the airway lining and of the physiology of airway humidification and thermoregulation in newborn infants, readers are referred to Chap. 30.

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## 32.2 Methods of Noninvasive Respiratory Support

Noninvasive respiratory support refers to the delivery of respiratory support using techniques that do not require an invasive artificial airway (ETT or tracheostomy tube), and is being used with increased frequency in a variety of clinical situations. Since its use in newborns was first described in 1971 [3], continuous positive airway pressure (CPAP) has long been the mainstay of noninvasive respiratory support in neonates. More recently, technological advances with improvements in sensors and flow delivery systems have resulted in increasing use of a variety of other types of noninvasive positive pressure ventilation (NIPPV) techniques [4], all of which are characterized by the provision of assisted ventilation that delivers positive pressure throughout the respiratory cycle with additional phasic increases in airway pressure, without the presence of an invasive artificial airway in the trachea [5]. Over the past decade, the use of humidified high flow nasal cannula (HHFNC) therapy in neonatal intensive care units (NICUs) has become widespread. These three primary modes of noninvasive respiratory support in neonates will be described in more detail, with a subsequent review of the role of humidification in the optimal application of each.

### 1. CPAP

CPAP refers to positive pressure applied to the airways of a spontaneously breathing patient throughout the respiratory cycle [6]. It may be generated via continuous flow or variable flow of gas, which is typically heated and humidified, in principle via a closed circuit (that is, one in which pressure is maintained by gas flow through a sealed or “closed” respiratory circuit from the point of gas inflow to the terminal outflow, while some is inhaled and exhaled by the patient). Continuous flow CPAP is generated using a constant flow of gas throughout the respiratory cycle directed against the resistance of the expiratory limb of the circuit. Commonly used methods of generating continuous flow CPAP include ventilator-derived (using variable resistance in a valve), bubble or water-seal devices, and, in some countries, the Benveniste gas-jet valve (Dameca, Copenhagen, Denmark). Variable flow CPAP generates CPAP at the airway proximal to the nares, and utilizes a number of principles of physics and

**Fig. 32.1** Neonate on binasal prong bubble continuous positive airway pressure (CPAP). The relatively bulky interface, typical of most effective CPAP devices, can make comfortable and appropriate handling and positioning a challenge (Adapted and reprinted from De Klerk [2]. Copyright (2008). With permission from Wolters Kluwer Health)



physiology to provide a constant airway pressure at flows that vary with inspiration and expiration, thereby decreasing certain components of work of breathing when compared with continuous flow CPAP. Variable flow CPAP devices include the Infant Flow Nasal CPAP System (VIASYS Healthcare Inc.) and the ARABELLA infant nasal CPAP system (Hamilton Medical AG). At least in design, the aim of each of these devices is to deliver positive airway pressure that is consistent, predictable and regulated. The most commonly used interfaces between the CPAP circuit and the neonate are nasal prongs and/or nasal masks [2].

The primary goal and effect of CPAP, when effectively applied, is to provide low-pressure distention of the lungs and prevent collapse of the alveoli and terminal airways during expiration [6]. Essentially this serves to recruit alveoli and to increase and/or maintain the functional residual capacity (FRC) of the lungs, with secondary benefits including increased lung compliance, conservation of surfactant, decreased intrapulmonary shunting, and increased airway diameter.

Difficulties with successful application of CPAP are principally related to the relatively bulky patient interface leading to problems maintaining proper position and effectiveness (Fig. 32.1). Unless well-designed equipment is appropriately selected, carefully applied and maintained, leaks around the nares and via the mouth can result in inconsistent airway pressure generation, increased work of breathing, and respiratory instability with increased oxygen requirements and risk of respiratory failure. Similarly, poor system design, prong selection, or application, along with the inherently bulky nature of most CPAP interfaces, can predispose patients to nasal irritation and trauma [2].

Although the scope of this chapter does not include a detailed review of the techniques and applications of CPAP, the following general points summarize much of what is currently known regarding CPAP use in neonates:

- A. In preterm infants with respiratory distress, CPAP use is associated with reduced respiratory failure and reduced mortality [7].

- B. Early versus delayed application of CPAP in the treatment of respiratory distress syndrome (RDS) reduces subsequent use of intermittent positive pressure ventilation (IPPV) [8].
  - C. Prophylactic surfactant followed by mechanical ventilation does not result in improvements in major clinical outcomes when compared to stabilization in the delivery room either with CPAP or with prophylactic surfactant and extubation to CPAP [9, 10].
  - D. Prophylactic surfactant with rapid extubation to CPAP has not been shown to be superior to CPAP and early selective surfactant in decreasing the need for subsequent mechanical ventilation and the incidence of main morbidities of prematurity in spontaneously breathing very preterm infants [10–12].
  - E. CPAP is effective in preventing respiratory failure in preterm infants following a period of endotracheal intubation and IPPV [13].
  - F. CPAP has not consistently been shown to influence the rate of bronchopulmonary dysplasia (BPD) whether defined as supplemental oxygen dependency at 28 days of age or at 36-week corrected gestational age [9–13].
  - G. CPAP of 5 cm H<sub>2</sub>O or more appears to be more effective than CPAP at lower pressures [13], but optimal CPAP levels have not been well defined and may depend on the condition treated.
  - H. Short binasal CPAP prongs are more effective than single prongs in the treatment of RDS and in reducing the rate of re-intubation [14].
  - I. Variable flow CPAP (VF-CPAP) may have some work of breathing (WOB) and breathing asynchrony advantages over continuous flow CPAP (CF-CPAP), whether underwater bubble CPAP or ventilator driven, and bubble CPAP may in turn have some similar advantages over ventilator CPAP [15]. However, limited clinical outcome studies to date either have not proven either VF-CPAP or CF-CPAP to be superior [16], or have shown bubble CF-CPAP to be more effective than VF-CPAP post-extubation [17].
  - J. Minimizing leaks around the nares and via the mouth by employing techniques to maintain mouth closure during CPAP augments CPAP transmission [18], and may improve CPAP consistency and efficacy.
2. NIPPV

Given the significant overlap in the equipment used, the patient interface, the clinical roles of CPAP and NIPPV, and the likely similarities in humidification requirements, a brief overview of this respiratory support modality follows. NIPPV uses intermittent ventilator inflations to augment CPAP by adjusting peak inspiratory pressure (PIP), inflation rate (IR) and inspiratory time (Ti) over a baseline positive end-expiratory pressure (PEEP; equivalent to CPAP). This enhances transpulmonary pressure during inspiration and may augment inspiratory reflexes and sigh breaths [5]. The terminology nasal intermittent positive pressure ventilation (NIPPV) is used here as a catch-all for the multiple variations in how this method of support can be applied, with many non-standardized terms and acronyms. These include synchronized NIPPV (SNIPPV), nasal ventilation (NV), nasal intermittent mandatory ventilation (NIMV), synchronized NIMV

(SNIMV), nasal bi-level positive airway pressure (nBiPAP), non-invasive pressure support ventilation (NI-PSV), and many others.

This modality of support can be delivered via similar patient interfaces to CPAP (single or binasal prongs, or nasal-/facemask), but facemasks are not recommended secondary to concerns about associated cerebellar hemorrhage [5], and it is reasonable to assume the benefits of binasal prongs that have been shown for CPAP use would apply to NIPPV as well. As such, short, wide binasal prongs are likely to provide the most effective interface. Most standard ventilators can be used or adapted to provide nonsynchronized NIPPV. Due to limitations of triggering and flow-sensor devices in neonates, and the phasing out of production of the Infrasonics Infant Star ventilator (SOMA Technology, Bloomfield, CT), options are much more limited for providing synchronized NIPPV. However, there are devices available for this purpose, including the Infant Flow SiPAP Ventilator and Infant Flow SiPAP Comprehensive Ventilator (Viasys Healthcare, Yorba Linda, CA), the Hamilton C2 device (Hamilton Medical AG, Bonaduz, Switzerland) in their nCPAP-PS mode, and the Puritan Bennett 840 ventilator (Puritan Bennett inc. Pleasanton, CA) via their NeoMode Software Option. Although there are theoretical advantages of synchronizing NIPPV and patient breaths, no clinical studies have compared synchronized and nonsynchronized NIPPV in neonates.

The following summarizes much of the current evidence basis for the use of NIPPV when compared with CPAP in neonates:

- A. NIPPV may deliver larger tidal and minute volumes, and may result in lower respiratory rates, respiratory effort, thoraco-abdominal asynchrony, and carbon dioxide ( $\text{CO}_2$ ) levels [5].
  - B. When used from birth to prevent the need for invasive ventilation, NIPPV decreases the need for endotracheal tube ventilation [19].
  - C. The use of NIPPV after extubation augments the beneficial effects of CPAP in preterm infants and reduces the incidence of symptoms of extubation failure [20].
  - D. Despite concerns related to higher pressures generated with NIPPV, increased gastrointestinal side effects (in particular bowel perforation) have not been demonstrated to date [20].
  - E. NIPPV may reduce the frequency of apnea more effectively than NCPAP [21].
3. HHFNC

Until the relatively recent development of HHFNC devices, the provision of nasal cannula gas at flows greater than 2 l/min in neonates was not recommended [22] nor considered practical. In addition, humidification of flows  $\leq 4$  l/min was not recommended [22]. Both of these recommendations by the American Association for Respiratory Care (AARC) are based on the limited evidence available, and although neither has changed or been adapted, HHFNC therapy has nonetheless become widely utilized and increasingly popular. Although there is no single universally accepted definition for what constitutes HHFNC therapy in neonates, a widely used and reasonable definition would be optimally warmed and humidified respiratory gases delivered by nasal cannula at flow rates between

2 and 8 l/min [2]. Flow rates should be sufficient to exceed patient inspiratory flow rates at various minute volumes.

The first device approved in the US for the provision of HHFNC in neonates was the Vapotherm 2000i in 2004, and it has since attained widespread international use along with a related device, the Vapotherm Precision Flow. Similar products have since been released in various markets, including the Fisher & Paykel Healthcare (Auckland, New Zealand) RT329 Infant Oxygen Delivery System and the Hudson Comfort Flo Humidification System (Teleflex Medical, Research Triangle Park, NC). Given the growing popularity of HHFNC therapy in neonates, it is likely that additional HHFNC devices will be available in the near future.

Although differences exist in the specifics of HHFNC devices, they share the following basic design attributes: [2]

- A. A heated humidifier to effectively warm and humidify respiratory gases.
- B. A respiratory circuit with a means to maintain the temperature – and, by extension, the humidity, thereby preventing excessive condensation or “rain-out” – of the delivered gas until the distal end of the circuit. Vapotherm devices achieve this by means of a sleeve of recirculated warmed water encasing the delivery tube, and the F&P RT329 and Hudson Comfort Flo systems by means of a heated wire coil that extends to the distal end of the circuit.
- C. A nasal cannula with an adapter that connects to the delivery circuit. Of note, the cannula design is such that there is little or no excess tubing between the end of the delivery circuit and the actual nasal prongs, thereby minimizing further any potential for gas cooling and precipitation.

No uniformly accepted guidelines exist for cannula size selection, and this reflects the dearth of good clinical evidence in this regard. However the manufacturers of both the F&P RT329 and the Hudson Comfort Flo systems recommend that cannula prongs should be of an external diameter no greater than 50% of the internal diameter of the nares in order to prevent an occlusive seal between prongs and nares that might predispose to excessive airway pressure generation. It is unknown how closely users follow this recommendation. Gas flow rate is adjusted according to clinical response, generally being increased for increasing respiratory distress or oxygen requirement and decreased for improving respiratory distress or decreasing oxygen requirement.

The precise mechanism of action of HHFNC remains to be elucidated. Aside from the basic concept of being able to provide higher flows of humidified respiratory gases and an increased fractional inspired oxygen concentration, it has been speculated that HHFNC may work by, among other mechanisms, providing airway pressure, nasopharyngeal purging of expired gases, improving mucosal perfusion, or stimulation of respiratory drive [2]. It seems clear from multiple studies that HHFNC therapy does produce positive airway pressure, and that this pressure is variable (and may range from trivial to excessive), relatively unpredictable, unregulated, related to flow, prong size and patient size (and likely to effective heated humidification), and may be sufficient to produce clinical effects and/or changes in pulmonary function [2]. Concerns have been expressed regarding the variable pres-

**Fig. 32.2** The lighter and less cumbersome patient interface with humidified high flow nasal cannula (HHFNC) can make handling, feeding, and interacting with neonates much easier (Adapted and reprinted from De Klerk [2]. Copyright (2008). With permission from Wolters Kluwer Health)



tures seemingly generated by HHFNC, and large multicenter randomized controlled trials are needed to clarify safety and efficacy questions.

The exact role of HHFNC has not been well defined, but it has become increasingly popular as a support modality in situations when CPAP might traditionally have been used, such as primary treatment in respiratory distress syndrome, as a post-extubation modality to prevent the need for reintubation, during the sometimes prolonged convalescent phase in premature neonates when relatively low-grade ongoing respiratory support may be needed before weaning to room air, or as a treatment for apnea of prematurity. The trend to provide HHFNC instead of CPAP appears at least in part due to the perceived greater ease of use of the former, as well as reports of improved patient tolerance and possibly greater efficacy with HHFNC. The expectation is that the heat and humidity should prevent airway water loss, airway cooling, thickened secretions, and nasal irritation, allowing high flows without nasal drying or bleeding. The lighter and easier-to-apply interface (when compared with most traditional CPAP interfaces) might lessen nasal septal damage while allowing practitioners and family members to handle and care for infants more easily (Fig. 32.2) [2].

Given the lack of good quality evidence from clinical trials regarding HHFNC use in neonates and infants, concerns that have been or might reasonably be expressed include excessive airway pressure generation (as previously mentioned), incidence of infection, local trauma, and other as yet unidentified adverse effects. None of the limited publications to date have noted an increased incidence of infection, but in the US, the VapoTherm device was recalled from the market in 2006 following a Centers for Disease Control (CDC) investigation into multiple cases of colonization and infection with a gram-negative bacteria (*Ralstonia* spp.), as well as other organisms, associated with the device usage. Cultures of unused VapoTherm

cartridges performed by two hospitals also yielded *Ralstonia* [23]. The product was approved to return to the market in 2007 with new instructions for use, including the recommendation to utilize only sterile water in the system. This experience suggests that, at the very least, centers using the reintroduced Vapotherm device (or other similar devices) should monitor closely their infection rates and the occurrence of any unusual infections until large randomized controlled trials have addressed this potential problem satisfactorily.

It is anticipated that high-quality evidence to support or refute the efficacy and/or safety of HHFNC should be forthcoming in the next few years as a number of large, multicenter randomized controlled trials are currently under way or in the late stages of planning. These include trials comparing HHFNC to both CPAP and NIPPV, and comparing these strategies as an initial therapy, immediately post-extubation, and/or during the convalescent phase in premature neonates. Until this evidence is available, HHFNC should best be regarded as a potentially valuable respiratory support modality, being easier to use with the possibility of being better tolerated with fewer adverse effects such as local trauma, but also as an unproven respiratory support modality until concerns regarding infection risk, airway pressure and other as yet unrecognized possible adverse effects are adequately addressed.

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### 32.3 Humidification with Non-invasive Respiratory Support

Although effective conditioning of inspired gas is widely regarded as standard of care in invasive ventilation of neonates and infants, there is no consensus regarding the optimal temperature and humidity of the inspired gas. Given this, it is unsurprising that there is little quality evidence and even less agreement concerning the need for, or specifics of, heated humidification of gases during non-invasive ventilatory support.

The infant's airway is designed anatomically and physiologically to prevent pulmonary infection and to heat and humidify inspired gas via a complex countercurrent heat and moisture exchange mechanism. A detailed summary of this anatomy and process can be found in Chap. 30." From a humidification standpoint, the primary difference between invasive (that is, via an endotracheal tube or tracheostomy) and non-invasive ventilatory support is that in the latter the upper airway from the nares to the level of the proximal trachea is not bypassed and can continue to contribute effectively to gas conditioning. In spontaneously breathing adults, inspired gas is heated and humidified to body temperature and pressure saturated (BTPS), occurring predominantly in the nasopharynx and proximal trachea such that entering the trachea, inspired gas typically reaches temperatures of 29–32°C and full saturation. This process continues with inspired gas typically reaching the isothermic saturation boundary (defined as the point at which gas reaches 37°C and 100% relative humidity, corresponding to an absolute humidity of 44 mgH<sub>2</sub>O/l) just below the carina [24]. The limited data on the role of humidification during the provision of the most commonly used specific non-invasive respiratory support modalities is discussed below.

## 1. CPAP

Due to an extreme dearth of good data in neonates, much of what little we do know regarding humidification of gases during CPAP use has to be extrapolated from the adult literature. Therapy with positive airway pressure can adversely affect nasal airway function and effectiveness of nasal CPAP. Inadequate humidification can be associated with respiratory mucociliary dysfunction, nasal mucosal inflammation, increased nasal mucosal blood flow, and increased nasal congestion. When used in adults for sleep apnea, extensive data support the role of heated humidification in improving CPAP comfort and tolerance, and likely compliance [24]. There is also evidence that nasal airway resistance and, by extension, CPAP effectiveness may benefit from effective humidification. A brief period of nasal CPAP with an open mouth has been shown to lead to an increase in nasal mucosal blood flux [25] that was not seen with nasal CPAP with the mouth closed. Even with a mouth leak, the change in nasal mucosal blood flux could be prevented by warming and humidifying the inspired air. Surprisingly, this study did not find a fall in nasal volume and cross-sectional area in combination with the increase in nasal mucosal blood flux, which had been expected. However, in another study in adult volunteers, nasal CPAP with a mouth leak resulted in a three-fold increase in nasal airway resistance that was substantially attenuated by effective humidification [26]. This elevated nasal airway resistance would result in a substantially lower effective CPAP pressure being transmitted to the nasopharynx and subsequently to the distal airway. The importance of humidification is highlighted by the latter study, as the inevitable leaks around the nares and mouth that are experienced with neonates contribute to a significant unidirectional airflow component with CPAP in the neonatal population, and this unidirectional flow exacerbates drying of airway mucosa and secretions. The same study found that as much as 70% of effective CPAP may be lost as a result of the increased resistance produced by the mouth leak (in the absence of humidification), and noted that the smaller the cross-sectional area of the nasal airway to begin with, the greater this relative loss of effective CPAP would be. This would carry obvious implications for the small nasal airway of the premature and even full term neonate. However, the addition of heated humidification to an acute rat model of CPAP therapy both with and without a mouth leak did not reduce nasal inflammation as evidenced by percentage of neutrophils in the nasal mucosa [27].

The optimal level of humidification has not been determined. However an absolute humidity of 30 mg/l was sufficient to attenuate the increase in nasal airway resistance associated with simulated mouth leaks in adults on CPAP [26], and increased nasal mucosal blood flow with mouth leaks was effectively ameliorated with inspired air warmed to 29°C and a relative humidity of 70% [25]. Furthermore, it appears as if mucosal drying plays more of a role in increasing nasal airway resistance than does mucosal cooling [26]. No significant differences were observed when comparing the physiologic responses of preterm infants using two humidifier settings (33–35°C and 36–37°C) on CPAP [28].

The relatively high gas flows used with non-invasive ventilation in neonates and infants, coupled with the inherent problems related to leaks around the nares and, in particular, the mouth, make the use of heat and moisture exchangers (HMEs, also known as artificial noses) with CPAP ineffective as they require to-and-fro gas flow with exhaled gas humidified by the lung. As a result, humidification for CPAP in neonates is almost universally achieved with heated humidifiers. A fuller discussion of heated humidifiers and heat and moisture exchangers can be found in the chapter in this book titled, "Physiology of Humidification in Critically Ill Neonates."

The relationship among the application of CPAP, any resultant increase in mucosal blood flux, inflammation, nasal mucosal edema, airway resistance, and effectiveness of CPAP, as well as the role of inspired gas humidification in affecting these processes, remains somewhat unclear. However, it seems that delivering air to the nose with a minimum absolute humidity of around 30 mg/l and a minimum relative humidity of around 80–90% at a minimum temperature of around 30°C may be advisable. Whether providing conditioned gas at or close to BTPS can provide additional benefits or be more optimal is not currently known, but this is common practice in NICUs.

## 2. NIPPV

In general, NIPPV is provided to neonates and infants via the same interfaces as CPAP, with short binasal prongs and nasal masks being the most commonly used. Standard ventilators or dedicated NIPPV devices, such as those listed under Section 32.2 Methods of Noninvasive Respiratory Support, are used to provide synchronized or non-synchronized NIPPV. All of these devices typically come with or are used with heated humidifiers for appropriate gas conditioning.

Unfortunately, there is even less evidence regarding the need for and specifics of heated humidification with NIPPV than there is for CPAP. No randomized controlled studies of NIPPV in neonates have independently examined the questions of whether to heat and humidify inspired gas, and if so, to what temperature and humidity. Given the similarities between the interfaces and devices used for these two modalities of support, it may be prudent to apply the same recommendations for humidification with NIPPV as for CPAP above. If anything, the generally higher flows needed to provide NIPPV, and the presumed increased oral and nasal leaks with the higher flows and generated pressures, may require greater attention to meticulous conditioning of inspired gases in order to avoid the known consequences of breathing non-conditioned gas in these circumstances.

## 3. HHFNC

As noted above, HHFNC systems generally provide heated and humidified inspired gas via nasal cannula to neonates and infants at flows that vary from 0.3 to 8 l/min. The first such device on the market was the Vapotherm 2000i, which, along with a more recent similar device, the Vapotherm Precision Flow, uses patented membrane technology to deliver molecular vapor with 95–100% relative humidity at body temperature through nasal cannula at flows from 5 to 40 l/min. A Vapor Transfer Cartridge allows use at 1–8 l/min in neonates. The Fisher & Paykel (F&P) RT329 system, used in tandem with the F&P MR850 humidifier,

is designed to deliver humidified gas at BTPS (37°C, 44 mg/l) via nasal cannula at flows between 0.3 and 8 l/min [2]. The Hudson Comfort Flo System (including the Hudson RCI Neptune heated humidifier) provides similarly humidified gas [29] at flows from 1 to 8 l/min.

Limited data exist comparing these different devices. An abstract-only study achieved 95.75% relative humidity with the F&P system versus 98.75% with VapoTherm at flows of 1–8 l/min, although the F&P system was not set up according to manufacturer recommendations [30]. A similar study with heater temperatures set to 37°C produced relative humidities of 79%, 92%, and 97% with the F&P, VapoTherm, and Hudson RCI Neptune humidifiers, respectively [29]. These variable results may have been affected by different testing conditions in these two studies, but all three devices appear to condition gases effectively.

VapoTherm has recently introduced an interesting variation of their neonatal and infant cannula, the Insolare [31]. This cannula has a single patent and functional airflow tube from the proximal cannula to the nasal prongs. The second tube with no lumen is non-functional, but loops behind the opposite ear to give the cannula similar characteristics to a regular nasal cannula for application and attachment. Since the same flow of gas is delivered as if a regular cannula were being used, but the flow is all passing via one side of the cannula, the residence time of the delivered gas in the unheated cannula is reduced by half. At least in theory, this should reduce heat loss and rain-out, in particular at relatively low flow rates.

Most studies of HHFNC have compared the support modality to CPAP in such settings as post-extubation or as a primary mode of support following delivery. As such, there is little evidence regarding the specific benefits of using heated and humidified gas at flows defined as high flow. However, one retrospective chart review study found that the use of non-heated and non-humidified gas via nasal cannula in preterm neonates was associated with increased nasal secretions and bleeding (which would likely increase the work of breathing) and with a non-statistically significant trend to increased coagulase-negative *Staphylococcus* sepsis [32].

Another study compared two methods of delivering high flow gas therapy by nasal cannula following endotracheal extubation in a prospective, randomized, masked, crossover trial [33]. Thirty moderately preterm neonates averaging 31–32 weeks gestation were extubated to VapoTherm for 24 h, then standard high flow nasal cannula (HFNC) for 24 h, or to standard HFNC for 24 h, then VapoTherm for 24 h. Standard HFNC was not described in detail other than as being provided by a “standard high-flow system”, presumably without effective humidification. Uniform nasal cannulae manufactured by VapoTherm were used for both VapoTherm and standard HFNC support. The nasal gas flow (mean  $\pm$  SD) used on VapoTherm was  $3.1 \pm 0.6$  l/min compared with  $1.8 \pm 0.4$  l/min on standard HFNC based on what was considered to be optimal individual support to each patient as judged by the neonatal care team. VapoTherm performed better than standard high flow nasal cannula in maintaining normal appearing nasal mucosa, a lower respiratory effort, and averting reintubation, with no recognized complications. The better respiratory effort scores were felt to be due at least in part to

the higher gas flow used on Vapotherm, with the improved nasal mucosa on Vapotherm the result of the higher humidity and temperature of the gas. As intrathoracic pressures were not measured, it is unclear whether or not the improved respiratory effort scores on higher Vapotherm flows were related to any potential generated airway pressure differences between groups.

Although much remains to be proven in well-designed clinical studies, it is likely that optimally conditioned inspired gas delivered as HHFNC may contribute to the prevention of airway water loss and cooling, thickened secretions, and nasal irritation. This support modality is more user friendly and easier to apply than CPAP, and may decrease nasal septal damage and facilitate feeding and parental interactions with their baby. As such, HHFNC use in neonates and infants is likely to continue to grow in popularity. It is highly desirable that optimal settings for flow, temperature, and humidity be tested and proven as this increasing use evolves.

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## 32.4 Summary

Non-invasive respiratory support of the neonate and infant has experienced a substantial increase in use over the past decade. Nasal CPAP, NIPPV, and HHFNC are the most commonly used modalities of non-invasive support. Both CPAP and NIPPV have a considerable body of evidence to support their use in different clinical situations. The evidence basis for HHFNC is less robust, but limited evidence to date suggests a significant role for this modality of support, and higher quality evidence is gradually being developed. Very few data are available regarding the need for and specifics of heated and humidified inspired gas during the provision of non-invasive respiratory support in neonates. However, evidence extrapolated from the adult literature and limited evidence in neonates suggests that appropriate conditioning of inspired gas is desirable and should help to optimize non-invasive respiratory support and limit adverse effects. Further research is needed to confirm the need for such gas conditioning, and to define optimal temperature and humidity settings.

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