PART TWO CHAPTER THREE
A DISCUSSION ON NOSOCOMIAL PULMONARY INFECTION

CAUSE and EFFECT

THERAPEUTIC CONSIDERATIONS

The following is an abstraction from a "periodical review" relating to Nosocomial (in hospital) infections, revealed in part by a study undertaken by Utah's Intermountain LDS Hospital system (Forbes).

"Another rampant problem is ventilator-associated pneumonia, which afflicts anywhere from 10% to 25% of patients on the machines. The longer the patients remain on the ventilator the greater the odds that germ-laden gunk from the back of the throat will get sucked down into the lungs. Some embarrassingly low-tech steps can make a difference, if only hospitals would make the effort to do them. One is tilting the bed to 30 degrees so secretions are less likely to bubble into the lungs. Another is minimizing the time patients are on ventilators, removing sedation once a day in order to assess whether the patients are ready to be weaned."

Whether one would agree in total or in part or not at all with the preceding abstraction, a clinician involved in general mechanical cardiopulmonary management well realizes the potentials for nosocomial pulmonary infections. In order to address these potentials for "in-hospital pulmonary infections," the following factors could be considered and prophylactic ally acted upon.

A discussion of the overall respiratory tract secretion generation and clearance mechanisms consists of the following:

The nasal structures provide for filtration and the major component of humidification of all spontaneously inspired air. Particulate matter which is turbulently precipitated by the nasal turbinates etc. is propelled by ciliated mucus membranes into the pharynx, where they are swallowed or expectorated. Essentially, the nasal filtration and humidification system functions in opposition to the endobronchial ciliary escalator, with both systems delivering their exudates into the pharynx for clearance. The majority of the endobronchial structures are lined with Goblet cells which manufacture secretions consisting of water, polysaccharides and proteins.

In the adult, the Goblet cells collectively secrete about a liter of edobronchial secretions daily. These endobronchial secretions are continuously propelled upward in a cephalad (headward) direction by a ciliary escalator into the Pharynx where they are continuously swallowed, thus recovering proteins.

From birth the healthy human species is close to a mandated nose breather. Normally the nasal turbinates serve to filter (through turbulent precipitation and adhesive forces) the total spontaneous tidal exchange. Additionally, the nasal mucosa nominally saturates (at body temperature) the 350 to 450 cc tidal exchange some 14 times per minute, before it enters the pharyngeal structures.
Even under strenuous exercise with partial or total mouth breathing (it is believed) the oral mucosa alone is capable of providing a very effective meniscus to help saturate the inhaled air.

Water delivery from the mucosa of the nasal structures can be increased by drinking hot soup or eating super cold ice cream, demonstrating there must be a thermal sensor capable of controlling, in part, the ability of the nasal mucosa to nominally saturate the inhaled air. Likewise, the inhalation of dry super cold or hot air serves to excite the nasal mucosa in terms of musosal water delivery rates.

Beyond potential thermal sensing above the carina, the relative humidity of the inspired air must function in concert with other carinal sensing considerations, which are directed toward control over the endobronchial Goblet cell water balance.

In health, the viscosity of the lower pulmonary airway secretions is consistent with the ability of the beating endobronchial wall cilia to create a continuous endobronchial secretion clearance (flow), negating the retention of endobronchial secretions. A major factor related to secretion clearance is the viscosity of the secretions being excreted by the Goblet cells.

The viscosity of the Goblet cell secretions, consisting of water, polysaccharides and proteins, must be physiologically regulated because the relative humidity of the inspired respiratory gases can be constantly changing. These changes affect the core cooling as well as the water removal (dehydration) of the mucous being propelled upward by the ciliary escalator.

One might postulate that the water balance of the endobronchial secretions is under the control of the relative humidity of the inspired gases.

For example, a seashore resident on a humid warm day could experience a potential bronchorea causing the secretions to become so wet that the ciliary escalator can not effectively sweep the secretions out of the airways. It follows that a desert resident on a dry hot day, with a very low relative humidity, could experience inspissations secondary to the increased viscosity of the endobronchial secretions.

If the optimal water balance is not maintained, secondary to disease etc., the increased viscosity of the secretions can reduce the effectiveness of the ciliary escalator, leading to the retention of endobronchial secretions.

It is logical to expect that the "thermally coupled relative humidity" of the inspired respiratory gases could serve to trigger some physiological auto regulatory mechanism which controls the water, polysaccharide and protein balance of the Goblet cell excretion. These physiological thermally coupled humidity sensors are most likely located in the

sensitive carinal areas to control any saturation deficits not satisfied by the nasal humidification system.

When a healthy subject travels from a high humidity seashore environment to a dry hot desert climate with a very low relative humidity, a near immediate Goblet cell compensation occurs which is directed toward maintaining a near optimal Goblet cell secretive water balance.

In chronic COPD patients who are subjected to acute decreases in the relative humidity of the inspired gases, this rapid compensation has been observed to be compromised, which can lead to an increased level of endobronchial inspissations when going from warm wet to hot dry environments.

When the potential upper airway sensors are bypassed by an endotracheal tube insertion, what influence does that have upon the water, polysaccharides and protein viscosity secondary to Goblet cell excretion? It is reasonable to expect that thermally coupled humidity sensors controlling the water balance of the Goblet cells do co exist in sensitive carinal areas along with the cough reflexes etc. Therefore, these physiological reflex sensors would be located below the tip of the indwelling airway catheter and would respond to the thermally coupled relative humidity of mechanically delivered ventilator gases.

When the first red rubber endotracheal tubes were used during anesthesia for the delivery of the typical very dry anesthetic gases (in the semi open breathing circuits), Atropine was used to decrease the flow of endobronchial secretions. Would this not suggest that thermally controlled humidity sensors located below the indwelling tip of the endotracheal tube served to increase the endobronchial Goblet cell water, as opposed to polysaccharides and protein?

Another observed phenomena in many long term ventilator patient populations is an endobronchial secretion retention in the presence of the delivery of a saturated water vapor (100% saturated relative humidity) at body temperature during the mechanical ventilation of the lung. This is verified by a continual requirement for mechanical airway aspiration.

In theory, with the maintenance a 100% relative humidity within the tracheobronchial tree (as in health) during CMV, there should be zero water loss from the lung. Therefore, the endobronchial secretion viscosity should remain near optimal for ciliary escalator transport. The question then becomes why endobronchial secretions become more viscid during extended CMV with a body temperature saturated respiratory gas delivery.

If the auto regulatory system controlling endobronchial Goblet cell water balance is based upon the thermal governed relative humidity of the inspired respiratory gases, the following logic could apply during CMV:

During CMV with a heated humidified delivery employed to maintain a saturated water vapor (100% R.H.) into the proximal airway, a carinal humidity based auto regulatory system could command the Goblet cells to decrease the water component of the water, polysaccharide, protein exudate. This could serve to make the endobronchial secretion blanket more viscid.

Technically, if a nasal bypassed saturated water (molecular) vapor is delivered into the tracheobrochial tree at existing airway temperature, a major source of core cooling is obtunded because of the diminished intra airway evaporative process.

In order to deliver any degree of bulk water within the tracheobronchial tree during CMV, the respiratory gases would have to be supersaturated; which is not likely. Therefore, there would not be an exogenous water deposition upon the endobronchial walls to hydrate the potentially dehydrated Goblet cell exudates. This can serve to embarrass the ciliary escalator functions; leading to the retention of endobronchial secretions.

It follows that the high protein endobronchial secretion retention provides a near perfect incubator for pathogenic organisms, leading to intrapulmonary inflammatory processes. In heath, with a normal cilliary escalator providing for a continuous endobronchial secretion clearance (wash out) as well as a cough reflex, the normal flora of mixed pathogenic organisms contained in the inspired respiratory gases are washed out of the respiratory tract to be controlled during expectoration and/or the digestion of the swallowed Goblet cell exudates.

The potential for a reverse flow of any retained upper or lower endobronchial airway wall secretions during CMV tidal delivery is minimized because of a potential for an induced counter gas flow. Therefore, seeding of the retained endobronchial airway secretions would most likely be from an airborne source and not from an upper airway aspiration or deposition. Mechanical regression of airway pathogens would be more likely to be provoked within the upper airways during mechanical aspiration.

A major understanding of the saturation of inspired respiratory gases with a 100% relative humidity at maximum intra pulmonary temperatures and/or the intrapulmonary deposition of topical aerosols can only be functionally elucidated by one who possesses a unique understanding of physics involving meteorology, fluid dynamics, and cardiopulmonary pathophysiology among other basic sciences.

Much of the confusion and published oversimplifications are created by the inability to meaningfully measure with a high degree of accuracy the diffusive levels of endobronchial humidification.

<u>There is a vast difference between the humidification of inspired respiratory gases and the deposition of topically active endobronchial aerosols.</u>

When humidification is discussed, one is referring to the molecular saturation of a gas with water at a given temperature (relative humidity) or the amount of water content in a given volume of a gas (absolute humidity). The science of aerosolization is related, in part, to the spectrum and volume of particulate generation and the endobronchial suspensional transport, which are physically explained primarily using Archimedes laws of buoyancy and the many factors creating endobronchial turbulent precipitation.

The "sloughing of water molecules" from the aerosolized particulate body (during endobronchial travel) is an automatic meteorological function controlled primarily by the meniscus (liquid gas interface) and the humidity deficit of the transporting gases. The

endobronchial sites of mass rain out are primarily determined by particulate size and invoked turbulent precipitation within the tracheobronchial tree.

The physical design of a nebulizer (aerosol generator) employed by a trach-positive pressure therapeutic delivery system must address the specific gravity and cohesive forces of the solution to be aerosolized in terms of creating a particulate spectrum as well as the valence and other factors which control the desired levels of endobronchial deposition.

The delivery of "vasodilator aerosols" would be favored by nebulizers which would produce major rain out within the upper airways for systemic absorption.

The delivery of "peripheral vasoconstrictor aerosols" delivered within edematous peripheral airways to reduce mucosal and sub mucosal edema would primarily depend upon the diluent in terms of osmotic pressures to provide transport across the mucosal membranes of the endobronchial structures. For example, if an aqueous solution of racemic epinephrine was employed as an alpha as well as a beta in an approximate 2.5% solution; a water diluent would be more effective in providing cross transport than a physiological or hypertonic saline diluent.

The site delivery of therapeutic aerosols within the tracheobronchial tree have long been surveyed by radioactive tagging employing isotopes such as (technetium) and thoracic scanning.

The primary rationale for the isotope studies was to determine in part the effectivity of the aerosol transport system to deliver topically active peripheral aerosols. Systemic uptake has also been a component of these typical evaluations.

In the mid 1950's A. Cometto pioneered a therapeutic heated humidification system (Mistogen) which was clinically evaluated by W. F. Miller. This became timely as Engstrom and others delivered their volume oriented ventilators for use in "post heart patients" etc. In order to "near accurately" measure tidal exchange (during CMV); the exhaled gases could not be "leveraged" by other cumulative "non physiological expiratory flows" from nebulizers etc.

It was recognized that mechanical humidifiers, saturating inspired respiratory gases at or below ambient temperatures, could not provide for the saturation of inspired gases as they entered the tracheobronchial tree (bypassing the nasal mucosa); while experiencing a physiological temperature increase.

As the volume oriented ventilators proliferated into the Surgical Intensive Care facilities (SICU's) in the 1960's and 70's, the need for saturating the inspired respiratory gases without upsetting tidal volume measurement created a need for (safe) heated humidifiers to automatically deliver inspiratory respiratory gases into the physiological airways.

It was believed that saturated respiratory gases (100% relative humidity) had to be delivered endobronchially at the maximum internal airway temperatures to prevent water loss leading to dehydration of the endobronchial secretions. This soon became the "state of the art".

Whenever a saturated gas at a given temperature experiences a "cool down," condensation occurs as the transporting gas molecules experience contraction. This condensation serves to deliver bulk water in both the mechanical inspiratory and expiratory tubings of the ventilator breathing circuits. Water traps required a degree of supervision by the attending with a major threat of "back flow" to Neonates. To this end, Engstrom developed the first medical ultrasonic nebulizer capable of delivering bulk particulate water into the physiological airways (for humidity resolution) without adding to the physiological exhaled tidal volumes.

The major ultrasonic aerosol spectrum was about 0.5 microns. Generally circulated claims insinuated that the valance on the ultrasonically generated aerosol particles "was so positive" they failed to discharge sufficiently within the tracheobronchial tree to provide adequate rain out, creating an endobrochial humidity deficit.

Later in the 1970's, F. M. Bird experimented with a heated inspiratory tubing, creating a temperature rise from the humidifier to the proximal airway which negated the undesirable rain out in the inspiratory tubing. In the 1990's, several thermally governed tubing systems became available to control condensation within CMV breathing circuit tubings.

As often is the case, a habit to correct a cause and effect relationship becomes "state of the art".

It is undeniable that beyond several definitive applications, the initial requirement for a heated humidifier during volume oriented mechanical ventilation of the lung was mandated by "state of the art" expiratory volume measuring techniques and not a clinical rationale. These applications included:

1. To minimize core (evaporative) cooling within the pulmonary structures of a neonate being ventilated in an open (convenience) incubator with surface heat loss.

2. A hypothermic "rescue type patient" where intrapulmonary core cooling during the clinical warm up period could be undesirable.

Core (evaporative) intrapulmonary cooling in a patient with a near normal body temperature might not be a major clinical factor; however, if a patient with an elevated body temperature were to loose their pulmonary core cooling it might be contraindicated.

From a clinical rationale, what does a heated humidifier add to or subtract from a general level of clinical efficacy in the average patient? Clinicians who do not have an extensive physical background relating to humidification versus nebulization appear to base their argument more upon emotion than upon fact.

At this point in this discussion, a review of the subject might be useful in terms of understanding the difference between humidification and aerosolization.

Physically, the saturation of "trach-positive tidal volume deliveries" with the capabilities of producing a near zero water loss from the endobronchial airways can only be accomplished by the delivery of gases with a 100% relative humidity into the pulmonary airways at the maximum existing endobronchial temperature. This serves only to provide exogenous water in molecular form to prevent evaporation of water from the endobronchial secretion meniscus. The mechanical saturation (humidification) of the inspired gases satisfies any existing gaseous humidity deficit in the tidal gases only, without adding any bulk reserve water.

The heated humidification logic is directed toward preventing the viscosity of the endobronchial mucoid secretions being transported in a cephald direction (by the ciliary escalator) from becoming viscid and impeding their physiological airway clearance.
Among the vast array of therapeutic nebulizers, there are only several which are expressly designed to be integrated into the breathing circuit of a ventilator providing for humidification as well as to effect the peripheral delivery of a therapeutic aerosol.

An aerosol generation system designed to precisely match the physiological inflow of a specific medical ventilator, in terms of particulate spectrum and volume, has sufficient meniscus (liquid gas interface) to satisfy any humidity deficit in the inspired gases as well as to provide for bulk water delivery to be deposited upon the cephald moving endobronchial secretion blanket.

The deposition of bulk water upon the mucoid endobronchial wall secretions will tend to hydrate differentially, in proportion to the salinity of the secretions and the topical aerosol deposition. In order for the aerosolized pharmaceuticals to be delivered across the mucoid secretions, through the cilia into the mucous membranes of the endobronchial airways, a favorable osmotic gradient must exist.

If one applies the rationale suggesting that the viscosity of the Goblet cell secretions is directed by the relative humidity of the inspired respiratory gases (as earlier explained), it would be valid to expect that the mechanically saturated tidal gases (with a 100% relative humidity) would direct the Goblet cells to secrete less water as opposed to polysaccharides and proteins thus increasing their viscosity. This could well explain why endobronchial secretion retention continues to be manifested during ventilation with "state of the art" volume oriented ventilation supported with exemplary heated humidification systems. Therefore, it is likely that "secretion viscosity management" during conventional mechanical ventilation (CMV) can contribute to endobronchial secretion retention.

Emotional arguments as well as classical beliefs continue to support those who believe in pure "state of the art" heated humidification protocols. Less argument exists with a continuous heated humidification system enhanced with aerosol delivery. However, there are those who honestly believe that aerosol delivery alone without a saturated vapor leads to inspissations.

Supporters of "unheated dense aerosol delivery systems" continue to be challenged by those reporting inspissations. Investigations of reported inspissations frequently point toward lassitude by attending who allow the aerosol (nebulization) systems to become void of fluid refill for hours on end.

It is typical for a clinician to leave a patient well hydrated with an unheated aerosol delivery system in the evening, only to discover inspissations in the morning; more than likely due to hours of mechanical ventilation "without nebulizer fluid re-fill". Of course this is usually denied by the "swing shift attending".

In sectional summary, arguing pros and cons relative to heated humidification systems may be a futile experience with little valid scientific support in either direction. However, one must agree that the propagation of pathogenic organisms must be enhanced within breathing circuits as temperatures are increased in warm, high humidity physical environments.

The incidence of nosocomial infections among patients on ventilators with heated humidified breathing circuits can not be denied. However; because of the universal use of this heated humidification technique, little or no data in terms of endobronchial contamination could be produced to compare heated humidifiers against ambient aerosolization employed for humidification concomitant with pharmaceutical delivery.

For well over a decade Intrapulmonary Percussive Ventilation (IPV®) has been employed adjunctively with conventional CMV ventilatory systems to maintain higher pulmonary compliances. The role of supportive IPV® during CMV most likely centers around three factors. They are:

1. Aerosolized bulk water is rained out upon the peripheral endobronchial wall mucoid secretions, lowering their viscosity to a more optimal level for cephalad ciliary functions.

2. The concomitant percussive endobronchial sub tidal IPV® deliveries provide for a "Newtonian counter pump" to enhance the upward mobilization and transport of retained endobronchial secretions.

3. The intrathoracic physiological lymph pump can be mechanically enhanced by the "vesicular peristalsis" provided by the repetitive IPV® percussive sub tidal volume deliveries, which serve to clear protein congestion from the interstitial spaces via the lymphatics, thus reducing tendencies toward an interstitial edema.

NOTE: See publications (available through Percussionaire Corporation) directed toward the physical and physiological understanding of Intrapulmonary Percussive Ventilation (IPV®) conceived by Bird F. M. and correlated by the Bird Institute of Biomedical Technology .

IN SUMMARY

In health, the daily liter or so of nasal and Goblet cell secretions consisting of water, polysaccharides and protein are constantly propelled downward and upward into the pharynx where they are swallowed or expectorated. This prevents the accumulation of airway secretions which could serve as a warm high protein garden for inspired airborne organisms to colonize.

Under stress or disease, impairments to the intrapulmonary ciliary escalator which interfere with continuity or alter the Goblet cell water, polysaccharide, protein balance can alter the viscosity of the secretions thus reducing the efficacy of the ciliary escalators, leading to airway secretion retention.

The longer any mass of endobronchial secretion is retained within the endobronchial structures, the greater the opportunity for a virulent incubation of airborne deposited pathogenic organisms.

It is generally believed that the nasal turbinates can filter particles above 0.5 microns. Therefore, airborne particles below this level can either rain out (by turbulent precipitation) or be exhaled. For example, It is believed that cigarette smoke is about .3 microns and enters and leaves the pulmonary alveoli.

Endobronchial secretion retention, however caused, can lead to infection, airway inflammation, mucosal and sub mucosal edema, with resultant airway caliber encroachment. It follows that any therapeutic means with sufficient clinical efficacy to maintain patent airways, without inflammatory encroachment secondary to endobronchial secretion retention, can decrease pneumonic tendencies.

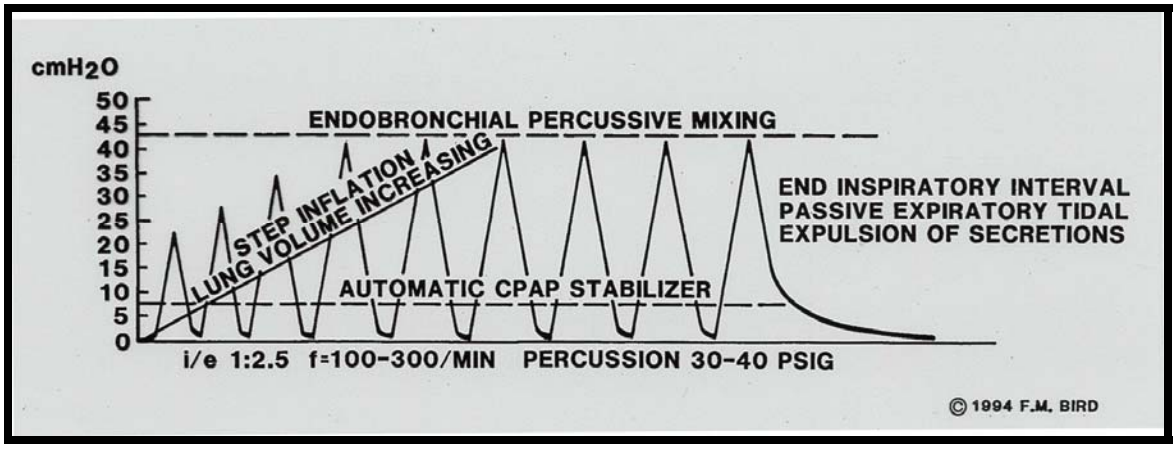
Patients with chronic or acute cardiopulmonary diseases with overriding infections are constantly entering institutional facilities with a broad spectrum of pathogenic organisms which serve to contaminate the facilities with airborne and/or fluid transmittable contaminants.

When a hospitalized patient with a reduced immune response becomes infected with an "institutional pathogenic organism" it is called a nosocomial (in hospital) infection.

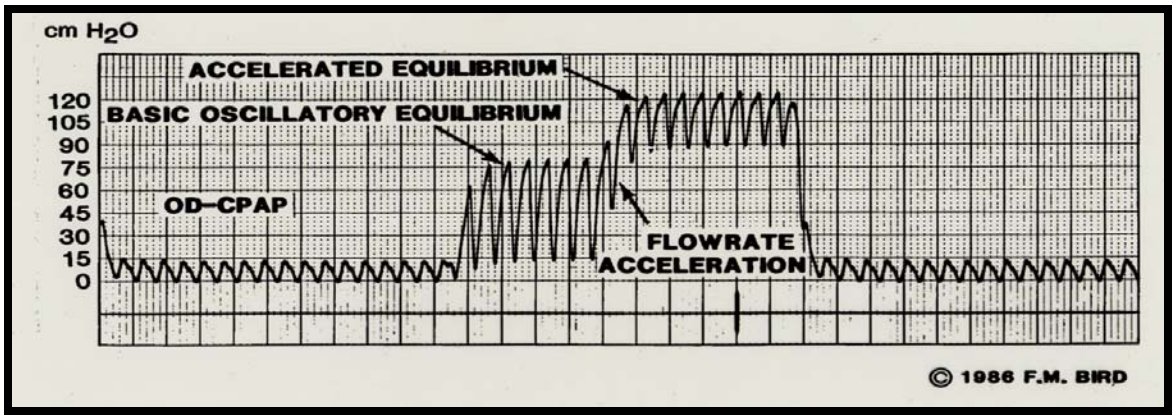
Hospitals are rampant with transmitters of pathogenic organisms from patients, attending, visitors as well as a wide variety of contents. Aseptic protocols, no matter how well projected, can not filter against all cross contamination. Therefore, prophylactic therapeutic means can play a major role in insulating patients from cross infection. Auto infection from emesis can be a source in certain de-compensated patients. Any patient with retained endobronchial secretions is at major risk for a nosocomial infection.

A therapeutic means directed toward the mobilization and raising of endobronchial secretions may serve to minimize the potentials for major transient pulmonary infections. With or without antibiotic resistant organisms, pneumonia is always a major threat to any institutionalized patient receiving long term mechanical ventilation. It must be recognized that it is very difficult, at best, to provide a ventilator patient with a "closed loop positive pressure ventilator breathing circuit with sterile respiratory gas delivery" while maintaining a warm humid breathing circuit requiring water refill. A possible initial airborne or surface contamination of a breathing circuit may not be revealed for days as the organism colonizes. Most patients will require airway aspiration, which can negate the maintenance of a closed loop positive pressure isolated breathing circuit. Aseptic procedures follow a circuitous pathway over time as each new generation of institutional personnel seem to try an old NEW aseptic protocol.

Intrapulmonary Percussive Ventilation (IPV®) is a therapeutic modality directed toward the daily mobilization and raising of retained endobronchial secretions in all institutionalized patients, thus reducing the potential for the retention of endobronchial secretions which can start a vicious cycle toward infective processes leading to nosocomial ventilatory pneumonias.

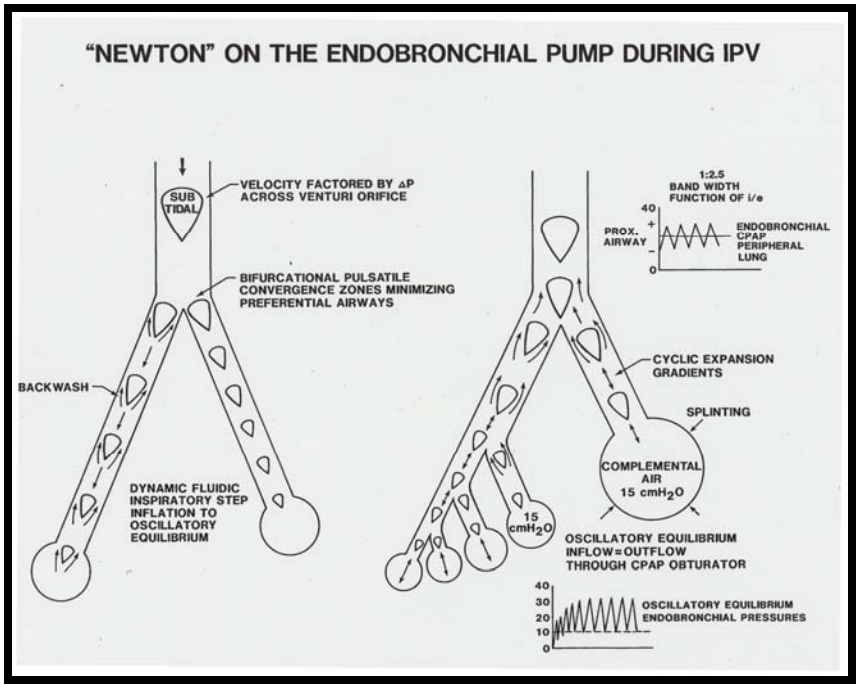


The IPV® format employed for Intrapulmonary Percussive Ventilation.



Volumetric Diffusive Ventilation (VDR®)

VDR® is the Intensive Care version of Intrapulmonary Percussive Ventilation (IPV®) employing a constant percussive intrapulmonary sub tidal delivery with an "endobronchial wall counter-flow" to move "endobronchial airway secretions" or matter, upward past a partially cuffed endotracheal tube, for Pharyngeal oral aspiration.



It is important to understand why, by employing Newton's third law which essentially states "for each action there is an equal and opposite reaction," this unique form of "percussive endobronchial therapy" serves to mobilize and raise retained endobronchial secretions. By utilizing "NEWTONIAN PUMP" logic; a unique endobronchial fluid exchange becomes a component of Intrapulmonary Percussive Ventilation (IPV®) and/or Volumetric Diffusive Ventilation (VDR®).

Essentially, retained and/or aspirated endobronchial secretions and/or matter are propelled from the periphery upward in a cephalad direction into the pharynx for aspiration or expectoration.

It is imperative to read and understand the publication entitled

HISTORICAL REVIEW OF INTRAPULMONARY PERCUSSIVE VENTILATION (IPV®)

IPV® and VDR® ventilatory protocols are unique from any other form of mechanical ventilation (CMV) of the lung in terms of preventing any potential aspiration of pharyngeal secretions and/or matter, while maintaining a continual cephalad endobronchial airway clearance by maintaining a "Newtonian" pumping action during a programmed continuous "endobronchial intrapulmonary percussion" during spontaneous or controlled respiration.