Ventilator-associated Pneumonia

Atefeh Sadeghizadeh,MD
PICU Assistant Professor

- VAP is a type of pneumonia that **develops ≥۴۸ hours after endotracheal intubation.**

PATHOGENESIS

- Microaspiration of organisms that have colonized the oropharyngeal or gastrointestinal tract
- Direct contact with environmental reservoirs, including respiratory devices and contaminated water reservoirs
- Disposable tubing used in respiratory circuits or tracheostomy or endotracheal tubes may become contaminated in the process of routine nursing care or via the contaminated hands of hospital personnel.
- The near sterility of the stomach and upper gastrointestinal tract may be disrupted by alterations in gastric pH due to illness, medications, or enteric feedings. For this reason, much attention has been paid to the possible adverse effect of ulcer prophylaxis regimens that raise the gastric pH
- Inhalation of infectious aerosols or from bacteremia originating in a distant focus

MICROBIOLOGY

- **Aerobic gram-negative bacilli** (eg, *Escherichia coli*, *Klebsiellapneumoniae*, *Enterobacter* spp, *Pseudomonas aeruginosa*, *Acinetobacter* spp)

- **Gram-positive cocci** (eg, *Staphylococcus aureus*, including methicillin-resistant *S. aureus* [MRSA], *Streptococcus* spp)

DIAGNOSIS

- A new lung infiltrate plus clinical evidence that the infiltrate is of infectious origin, which includes the new onset of fever, purulent sputum, leukocytosis, and decline in oxygenation

- Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: ٢٠١٦ Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis ٢٠١٦; ٦٣:e٦١.

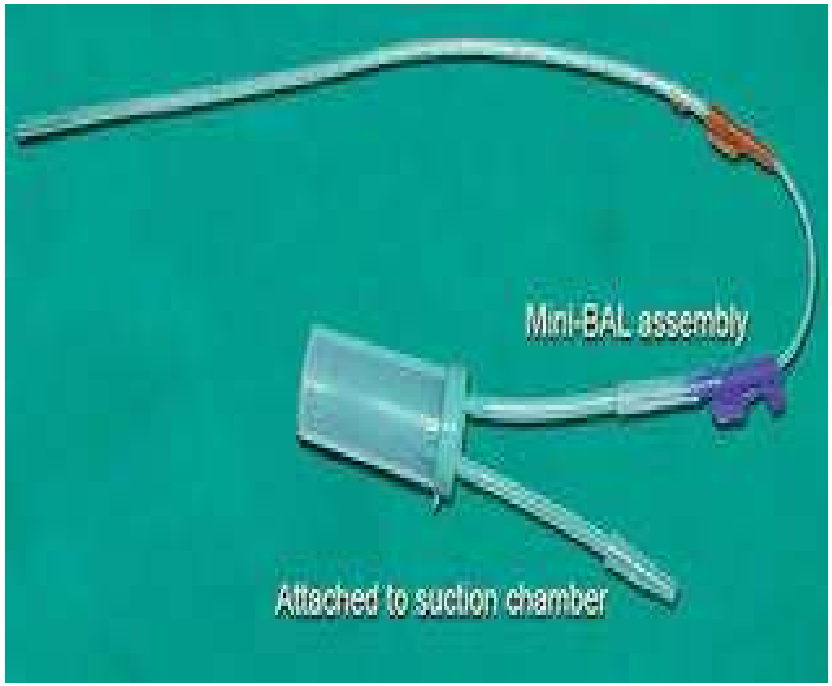
- **Symptoms** – dyspnea
- **Signs** – fever, tachypnea, increased or purulent secretions, hemoptysis, rhonchi, crackles, reduced breath sounds, bronchospasm
- **Ventilator mechanics** – reduced tidal volume, increased inspiratory pressures
- **Laboratory findings** – worsening hypoxemia, leukocytosis
- **Imaging** – new or progressive infiltrate on chest radiograph or computed tomography (CT)

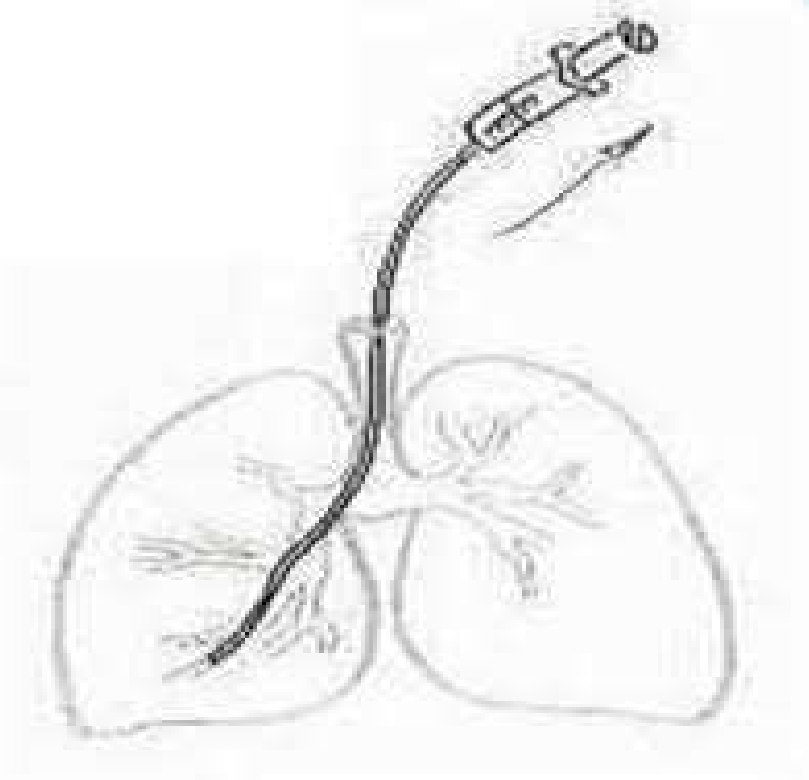
“None of these features are sensitive or specific for the diagnosis”

- **The diagnosis is confirmed when lower respiratory tract sampling identifies a pathogen**

- **Invasive sampling methods** (Mini-BAL, Bronchoscopic BAL, or protected specimen brush [PSB]) with **quantitative cultures**

Torres A, Niederman MS, Chastre J, et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT). Eur Respir J ۲۰۱۷; ۵۰.





- ***Alternative approach*** — **Noninvasive sampling**

(ie, endotracheal aspirates) **with semiquantitative cultures**

- **Noninvasive sampling** with **semiquantitative** cultures has **not** been shown to **affect important clinical outcomes** when compared with quantitative invasive techniques

- **Quantitative cultures:** Bacteria can be counted on any respiratory specimen. As examples, Staphylococcus epidermidis and most Gram-positive bacilli (except actinomycosis and nocardia) should **not** be counted.

- Typical thresholds include the following

- **Endotracheal aspirates – ١’٠٠٠’٠٠٠ (cfu)/mL**
- **Bronchoscopic- or mini-BAL – ١٠’٠٠٠ cfu/mL**
- **PSB – ١٠٠٠ cfu/mL**

- **Semiquantitative cultures:** are typically reported as showing **heavy, moderate, light, or no bacterial growth.**

- The amount of growth suggests VAP has not been firmly established, but most experts consider moderate or heavy growth to be positive.

VAP is a ***clinical diagnosis*** based upon the identification of a new or progressive **lung infiltrate** on imaging with clinical evidence that the infiltrate is of **infectious origin** (eg, fever, purulent sputum, leukocytosis, and decline in oxygenation), **together** with a **positive pathogen** identified on microbiologic respiratory sample

- We and others **do not include use** of the entities of ventilator-associated conditions (VAC) and infection-related ventilator-associated complications (IVACs), which were introduced by the CDC

EMPIRIC THERAPY

local pathogen

Risk factors for MDR pathogens

- The United States Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC) have developed standard terminology for antimicrobial-resistant gram-negative bacilli:

- Multidrug-resistant (MDR) refers to acquired nonsusceptibility to at least one agent in three different antimicrobial classes.

Ventilator-associated pneumonia: Risk factors for multidrug-resistance in adults

Risk factors for MDR pathogens:
▪ IV antibiotic use within the previous 90 days
▪ Septic shock at the time of VAP
▪ ARDS preceding VAP
▪ ≥5 days of hospitalization prior to the occurrence of VAP
▪ Acute renal replacement therapy prior to VAP onset

Risk factors for MDR *Pseudomonas* and other gram-negative bacilli:

- Treatment in an ICU in which >10 percent of gram-negative isolates are resistant to an agent being considered for monotherapy
- Treatment in an ICU in which local antimicrobial susceptibility rates are not known
- Colonization with OR prior isolation of MDR *Pseudomonas* or other gram-negative bacilli

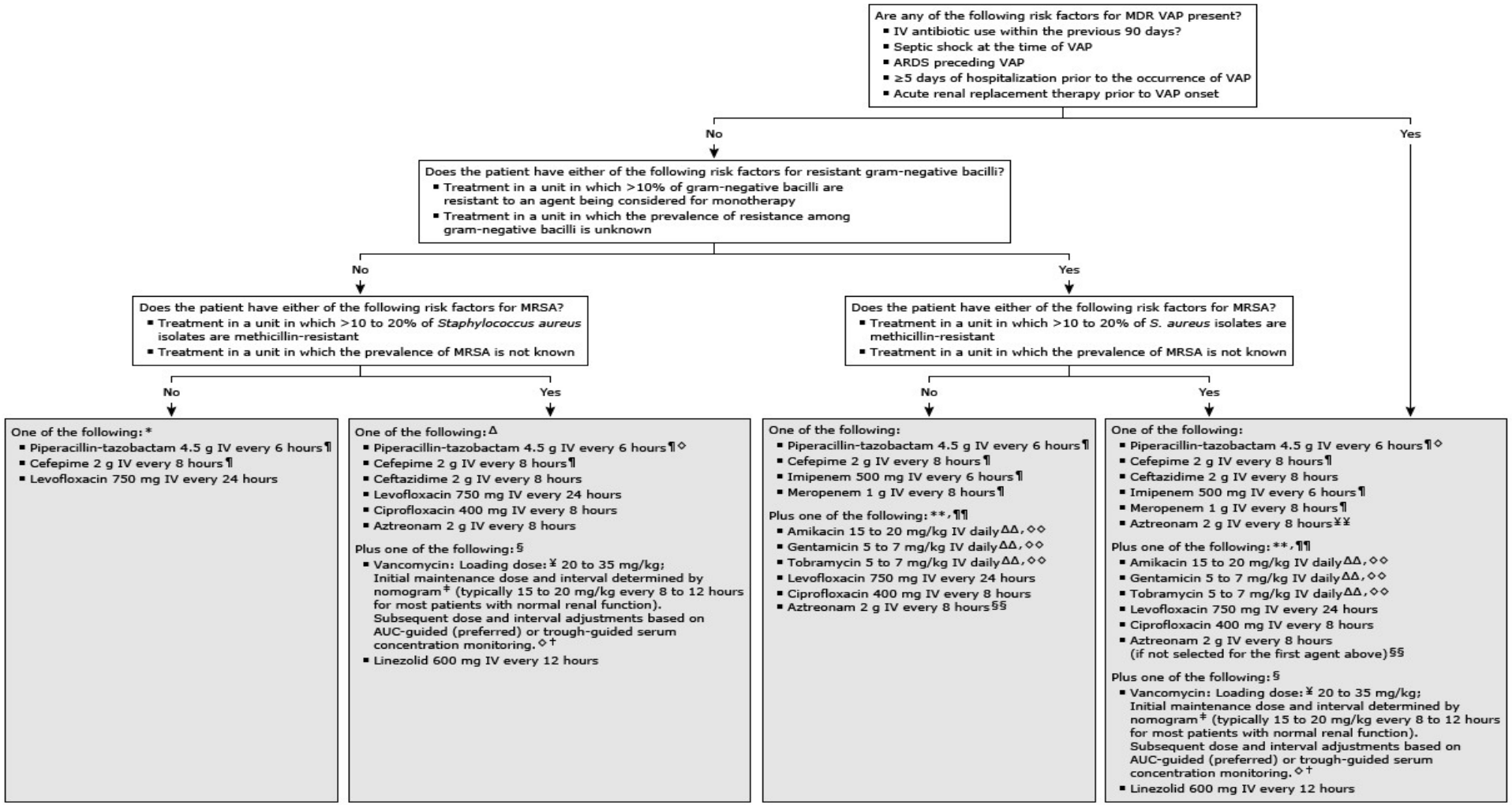
Risk factors for MRSA:

- Treatment in a unit in which >10 to 20 percent of *Staphylococcus aureus* isolates are methicillin resistant
- Treatment in a unit in which the prevalence of MRSA is not known
- Colonization with OR prior isolation of MRSA

Table 3. Suggested Empiric Treatment Options for Clinically Suspected Ventilator-Associated Pneumonia in Units Where Empiric Methicillin-Resistant *Staphylococcus aureus* Coverage and Double Antipseudomonal/Gram-Negative Coverage Are Appropriate

A. Gram-Positive Antibiotics With MRSA Activity	B. Gram-Negative Antibiotics With Antipseudomonal Activity: β-Lactam–Based Agents	C. Gram-Negative Antibiotics With Antipseudomonal Activity: Non-β-Lactam–Based Agents
Glycopeptides[a] Vancomycin 15 mg/kg IV q8–12h (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	Antipseudomonal penicillins[b] Piperacillin-tazobactam 4.5 g IV q6h[b]	Fluoroquinolones Ciprofloxacin 400 mg IV q8h Levofloxacin 750 mg IV q24h
OR	OR	OR
Oxazolidinones Linezolid 600 mg IV q12h	Cephalosporins[b] Cefepime 2 g IV q8h Ceftazidime 2 g IV q8h	Aminoglycosides[a,c] Amikacin 15–20 mg/kg IV q24h Gentamicin 5–7 mg/kg IV q24h Tobramycin 5–7 mg/kg IV q24h
	OR	OR
	Carbapenems[b] Imipenem 500 mg IV q6h[d] Meropenem 1 g IV q8h	Polymyxins[a,e] Colistin 5 mg/kg IV × 1 (loading dose) followed by 2.5 mg × (1.5 × CrCl + 30) IV q12h (maintenance dose) [135] Polymyxin B 2.5–3.0 mg/kg/d divided in 2 daily IV doses
	OR	
	Monobactams[f] Aztreonam 2 g IV q8h	

The recommendations in this algorithm are generally in keeping with the 2016 IDSA/ATS guidelines for the management of HAP and VAP. These regimens are intended for the initial treatment of patients in whom the microbiologic cause has not yet been identified. The doses below are intended for patients with normal renal function; dosing will need to be adjusted for patients with renal dysfunction. Empiric treatment choices should be influenced by the local distribution of pathogens causing VAP and their antimicrobial susceptibility patterns (ideally using an antibiogram that is specific to the hospital's ICU population). Antimicrobial selection should also be based upon the patient's risk factors for MDR pathogens, including recent antibiotic therapy, the presence of underlying diseases, and available culture data (including prior microbiology data). Additional considerations include potential toxicities, potential drug interactions, cost, availability, and clinician familiarity with the medications. Once the results of pretherapy cultures are available, therapy should be narrowed based upon the susceptibility pattern of the pathogens identified and the potential toxicities of the regimens.



- Once VAP is suspected clinically, antimicrobial therapy should be started ***as soon as possible***.

- In patients with sepsis or septic shock, antibiotics should be started within one hour

- Delaying treatment and failing to give a regimen with activity against the causative pathogens are associated with higher mortality rates in patients with VAP

- **Reassessing** a patient's ***status ٧٢ hours after*** the initiation of therapy and to discontinuing antibiotics or narrowing the regimen **(deescalating therapy)** based upon culture results

- Broader regimens and longer treatment courses increase the risks of adverse drug effects, Clostridium difficile infections, and antimicrobial resistance.

DURATION OF THERAPY

- Recommend a ***seven-day*** course of antimicrobial therapy rather than a longer duration regardless of the pathogen

- Although they state that a **shorter or longer** duration may be indicated, depending upon the rate of improvement of clinical, radiologic, and laboratory parameters

- Failure to **improve at ٧٢ hours** should prompt a search for **infectious complications**, **other diagnoses**, or **other sites of infection.**

- A longer duration than seven days is warranted for patients with other factors such as ***S. aureus bacteremia, concern for metastatic infection, or more severe disease***

PROGNOSIS

- Serious illness at the time of diagnosis
- Bacteremia
- Severe underlying comorbid disease
- Infection caused by an organism associated with multidrug resistance
- Multilobar, cavitating, or rapidly progressive infiltrates on lung imaging
- Delay in the institution of effective antimicrobial therapy

RISK FACTORS

- Older age
- Chronic lung disease
- Depressed consciousness
- Aspiration
- Chest or upper abdominal surgery
- Agents that increase gastric pH (H^2 blockers, antacids, proton pump inhibitors)
- Previous antibiotic exposure, especially broad spectrum
- Reintubation or prolonged intubation
- Paralysis
- Mechanical ventilation for acute respiratory distress syndrome
- Frequent ventilator circuit changes
- Total opioid exposure
- Multiple trauma
- Number of central venous catheter placements and surgeries
- Use of muscle relaxants or glucocorticoids
- The presence of an intracranial pressure monitor
- Malnutrition, chronic renal failure, anemia, previous hospitalization

PREVENTION

- Avoiding intubation when possible (eg, noninvasive ventilation)
- Minimizing transport while ventilated (when feasible)
- Implementation of weaning protocols
- Minimizing sedation
- Maintaining and improving physical conditioning
- Minimizing pooling of secretions above the endotracheal tube cuff
- Elevating the head of the bed
- Maintaining ventilator circuits

Klompas M, Branson R, Eichenwald EC, et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals: ۲۰۱۴ update. Infect Control Hosp Epidemiol ۲۰۱۴; ۳۵:۹۱۵. **(recommended by SHEA/IDSA)**

PREVENTION-Role of gastric pH

- We **avoid agents** that **raise gastric pH** in patients who are not at high risk of developing a stress ulcer or stress gastritis.

- Some meta-analyses have found decreased rates of pneumonia in critically ill patients using sucralfate for stress ulcer prophylaxis compared with H blockers and PPIs

Recommendation	Rationale	Intervention	Quality of evidence
Basic practices	Good evidence that the intervention decreases the average duration of mechanical ventilation, length of stay, mortality, and/or costs; benefits likely outweigh risks	Use noninvasive positive pressure ventilation in selected populations	High
		Manage patients without sedation whenever possible	Moderate
		Interrupt sedation daily	High
		Assess readiness to extubate daily	High
		Perform spontaneous breathing trials with sedatives turned off	High
		Facilitate early mobility	Moderate
		Utilize endotracheal tubes with subglottic secretion drainage ports for patients expected to require greater than 48 or 72 hours of mechanical ventilation	Moderate
		Change the ventilator circuit only if visibly soiled or malfunctioning	High
		Elevate the head of the bed to 30 to 45°	Low*
Special approaches	Good evidence that the intervention improves outcomes but insufficient data available on possible risks	Selective oral or digestive decontamination	High ¶
	May lower VAP rates but insufficient data to determine impact on duration of mechanical ventilation, length of stay, or mortality	Regular oral care with chlorhexidine	Moderate
		Prophylactic probiotics	Moderate
		Ultrathin polyurethane endotracheal tube cuffs	Low
		Automated control of endotracheal tube cuff pressure	Low
		Saline instillation before tracheal suctioning	Low
		Mechanical tooth brushing	Low
Generally not recommended	Lowers VAP rates but ample data suggest no impact on duration of mechanical ventilation, length of stay, or mortality	Silver-coated endotracheal tubes	Moderate
		Kinetic beds	Moderate
		Prone positioning	Moderate
	No impact on VAP rates, average duration of mechanical ventilation, length of stay, or mortality Δ	Stress ulcer prophylaxis	Moderate
		Early tracheotomy	High
		Monitoring residual gastric volumes	Moderate
		Early parenteral nutrition	Moderate
No recommendation	No impact on VAP rates or other patient outcomes, unclear impact on costs	Closed/in-line endotracheal suctioning	Moderate

PREVENTION-Preventing aspiration

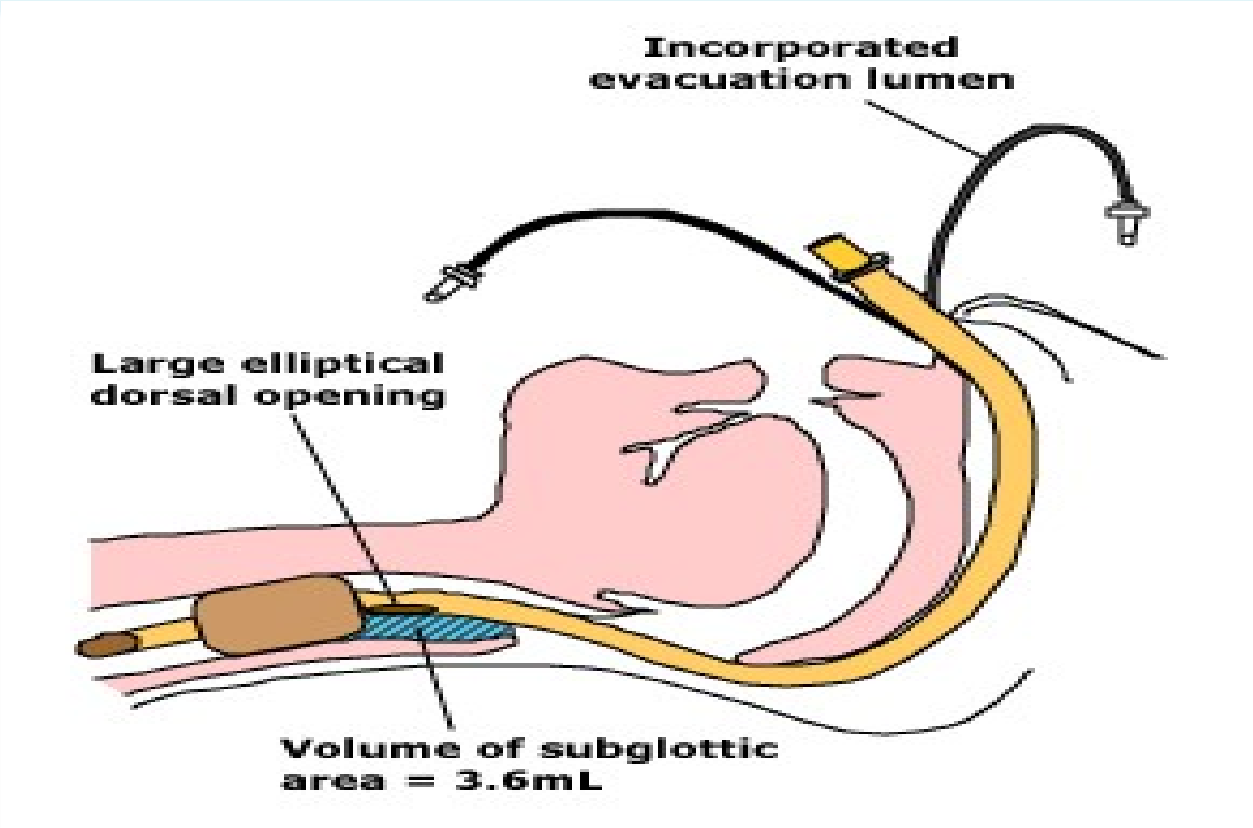
Aspiration is a major predisposing mechanism for both HAP and VAP.

- **Elevating the head of the bed,**
- **Minimizing sedation,**
- **Draining subglottic secretions in ventilated patients,**
- **Maintaining endotracheal tube airway cuff pressure (٢٠ to ٣٠ cmH٢O)**
- **Application of positive end-expiratory pressure are measures that have been proposed to minimize aspiration**

PREVENTION-Preventing Aspiration

- **Patient positioning** :Supine positioning appears to predispose to aspiration and the development of HAP, particularly in patients receiving enteral nutrition. The head of the bed should therefore be elevated to ٣٠ to ٤٥°

- **Subglottic drainage** : Drainage of subglottic secretions that pool above the endotracheal tube cuff may lessen the risk of aspiration of secretions around the cuff and thereby decrease the incidence of VAP.


Incorporated
evacuation lumen
Large elliptical
dorsal opening
Volume of subglottic
area = 3.6mL

PREVENTION-Decontamination of the oropharynx and digestive tract

- Chlorhexidine
- Selective decontamination of the oropharyngeal tract (SOD) with nonabsorbable antibiotics applied in the oropharynx,
- Selective decontamination of the digestive tract (SDD) with nonabsorbable antibiotics applied to the oropharynx and administered orally, with or without intravenous antibiotics.

PREVENTION-Probiotics

- Available results do not provide sufficient evidence to draw conclusions regarding the efficacy or safety of probiotics for the prevention of VAP.
- We therefore do not use probiotics for the prevention of VAP.