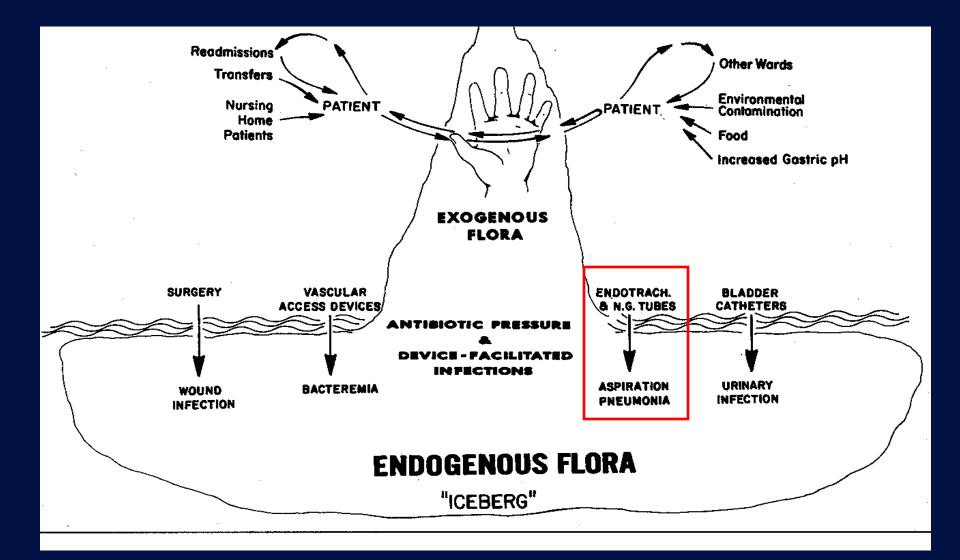
HEALTHCARE-ASSOCIATED PNEUMONIA: EPIDEMIOLOGY, MICROBIOLOGY & PATHOPHYSIOLOGY

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HAZARDS IN THE ICU



Weinstein RA. Am J Med 1991;91(suppl 3B):180S



GOALS OF LECTURE

Understand the epidemiology of nosocomial pneumonia

- Impact
- Incidence
- Risk factors for acquisition and mortality
- Review the microbiology of HAP & VAP
- Understand the pathophysiology of HAP & VAP
 - Diagnosis
 - Treatment

DEFINITIONS

Table 1. Pneumonia classification for patients in the intensive care setting

HCAP

NHAP

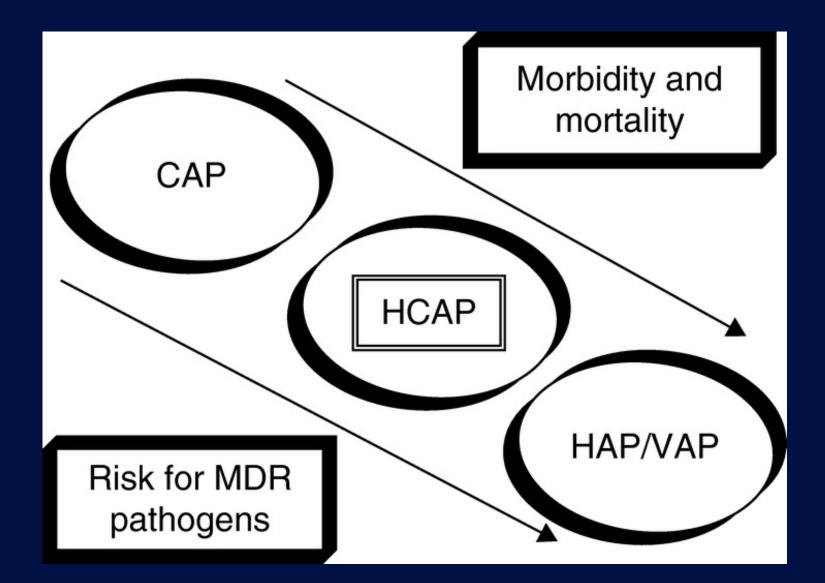
HAP

VAP

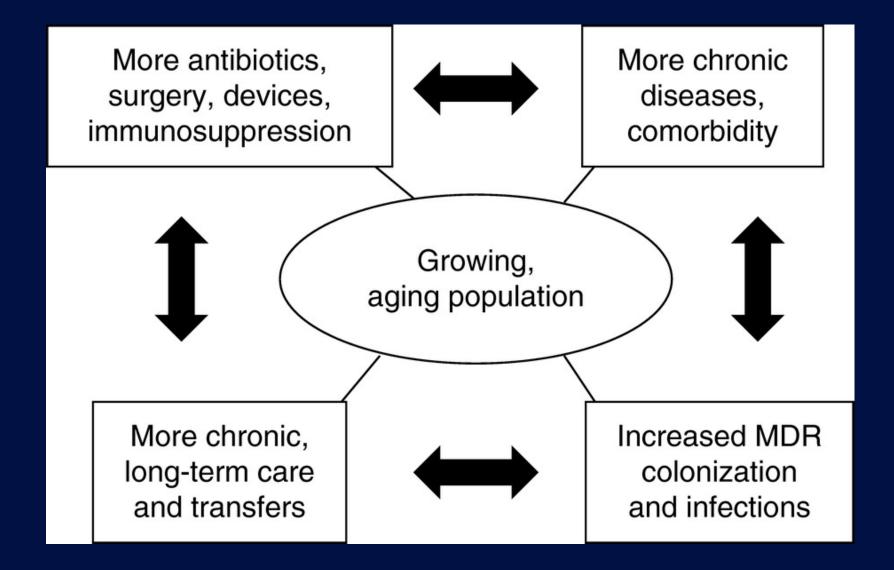
- CAP
 Infection present at hospital admission in patients who do not meet the criteria for HCAP
 - Pneumonia present at hospital or ICU admission in patients with at least one of the following risk factors:
 - Hospitalization for ≥2 days in an acute care facility within 180 days of infection
 - Residence in a nursing home or long-term care facility
 - Antibiotic therapy, chemotherapy, or wound care within 30 days of current infection
 - Hemodialysis treatment at a hospital or clinic
 - Home infusion therapy or home wound care
 - Family member with infection due to MDR bacteria
 - Significant immune suppression (corticosteroids, HIV, organ transplant)
 - Pneumonia occurring during residence in a nursing home or rehabilitation facility
 - Pneumonia occurring typically ≥48 hrs after hospital admission in a nonintubated patient
 - Pneumonia occurring typically >48 hrs after hospital admission and endotracheal intubation

CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; ICU, intensive care unit; HIV, human immunodeficiency virus; MDR, multidrug resistant; NHAP, nursing home-associated pneumonia; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia.

Marrow LE, Kollef MH. Crit Care Med 2010;38[suppl]:S352-S362



Chroneou A, et al. Expert Opinion 2007;8:3117-31



HEALTHCARE-ASSOCIATED PNEUMONIA

• HAI

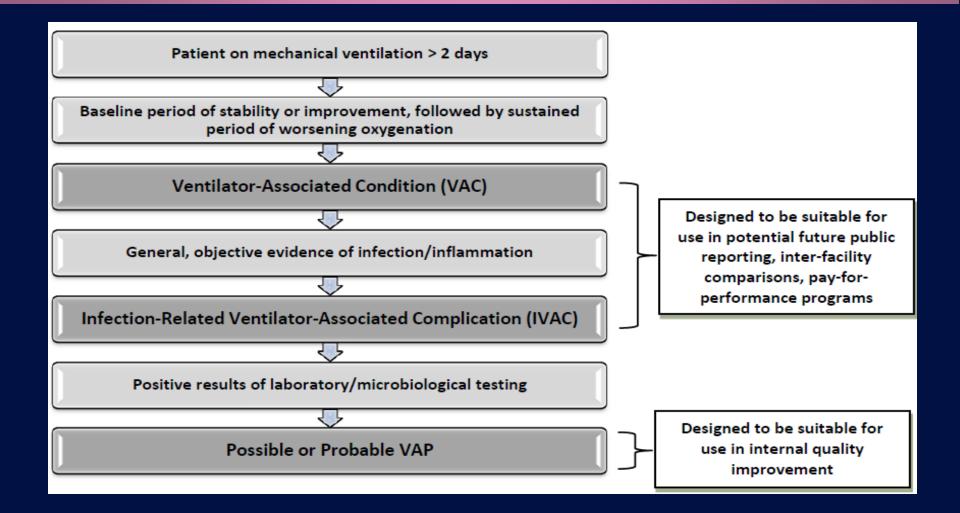
An infection is considered an HAI if ALL elements of a CDC/NHSN sitespecific criterion were first present together on or after the 3rd hospital day (day of admission is Day 1). For an HAI, an element of the infection criterion must be present during the first 2 hospital days as long as it is also present on or after Day 3. All elements used to meet the infection criterion must occur within a timeframe that does not exceed a gap of 1 calendar day between elements

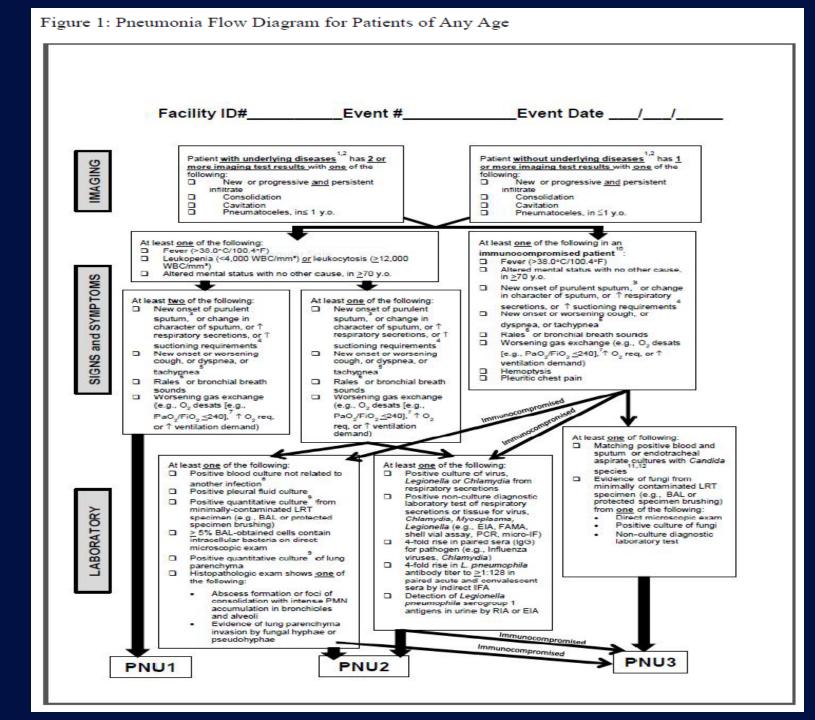
Pneumonia (PNEU)

Pneumonia is identified using a combination of radiologic, clinical and laboratory criteria. For VAP the date of the event is the date when the last element used to meet the pneumonia criteria are occurred.

http://www.cdc.gov/nhsn/acute-care-hospital/vae/index.html

VENTILATOR-ASSOCIATED EVENT (adult patients >18 years of age



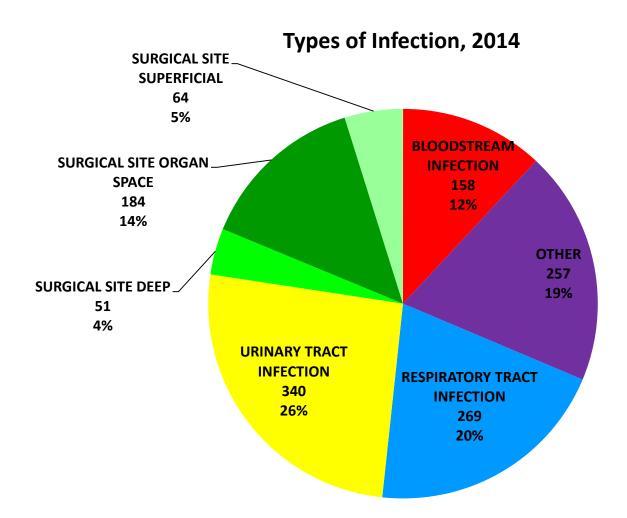


EPIDEMIOLOGY

HAP & VAP: IMPACT

Potential complications of mechanical ventilation

- Pneumonia, acute respiratory distress syndrome (ARDS), pulmonary embolism, barotrauma, pulmonary edema, and death
- Incidence
 - >300,000 patients receive mechanical ventilation each year in the US
 10% TO 20% develop VAP
 - 2011, an estimated 157,000 healthcare-associated pneumonias in US
- Mortality (VAP)
 - Patients 15-19 years, 24%; patients >80 years of age, 60%
 - Attributable mortality ~10%



Proportion of infection types were similar to 2013.

Urinary tract infections increased by 13%; surgical site infections decreased by 12%. Bloodstream, respiratory tract and other infections were within 5% of previous year's numbers.

Table 4. Estimated Numbers of Major Types of Health Care-Associated Infection in the United States in 2011.						
Type of Infection	Infections Identified in Survey	Surveyed Patients with Type of Infection	Estimated Infections in the United States*			
All health care_associated infections	no.	% (95% CI)	no. (95% CI)			
Pneumonia	110	24.2 (20.6. 28.5)	157 500 (50 800 281 400)			
		24.3 (20.6-28.5)	157,500 (50,800-281,400)			
Surgical-site infection	110†	24.3 (20.6-28.5)	157,500 (50,800-281,400)			
Gastrointestinal infection	86	19.0 (15.6-22.8)	123,100 (38,400-225,100)			
Urinary tract infection	65	14.4 (11.4–17.9)	93,300 (28,100–176,700)			
Primary bloodstream infection	50	11.1 (8.4–14.2)	71,900 (20,700–140,200)			
Eye, ear, nose, throat, or mouth infection	28‡	6.2 (4.2–8.7)	40,200 (10,400-85,900)			
Lower respiratory tract infection	20	4.4 (2.8–6.6)	28,500 (6900–65,200)			
Skin and soft-tissue infection	16	3.5 (2.1–5.6)	22,700 (5200–55,300)			
Cardiovascular system infection	6	1.3 (0.5–2.7)	8,400 (1200–26,700)			
Bone and joint infection	5	1.1 (0.4–2.4)	7,100 (1000–23,700)			
Central nervous system infection	4	0.9 (0.3–2.1)	5,800 (700–20,700)			
Reproductive tract infection	3	0.7 (0.2-1.8)	4,500 (500–17,800)			
Systemic infection	1	0.2 (0.01-1.1)	1,300 (0-10,900)			
Total			721,800 (214,700-1,411,000)			
Infections in non-neonatal intensive care units						
Catheter-associated urinary tract infection	25	5.5 (3.7-7.9)	35,600 (9100-78,000)			
Central-catheter-associated primary bloodstream infection	11	2.4 (1.3-4.2)	15,600 (3200-41,500)			
Ventilator-associated pneumonia	35	7.7 (5.5–10.5)	49,900 (13,600–103,700)			
Surgical-site infections attributed to Surgical Care Improvement Project procedures§	46	10.2 (7.6–13.2)	66,100 (18,700–130,300)			
Hospital-onset infections caused by specific pathogens						
Clostridium difficile infection¶	56	12.4 (9.6–15.7)	80,400 (23,700-155,000)			
MRSA bacteremia	7	1.5 (0.7–3.0)	9,700 (1700–29,600)			

Magill SS, et al. New Engl J Med 2014;370:1198

PREVALENCE: ICU (EUROPE)

• Study design: Point prevalence rate 17 countries, 1447 ICUs, 10,038 patients • Frequency of infections: 4,501 (44.8%) <u>Community-acquired: 1,876 (13.7%)</u> Hospital-acquired: 975 (9.7%) ICU-acquired: 2,064 (20.6%) ♦ Pneumonia: 967 (46.9%) Other lower respiratory tract: 368 (17.8%) ♦ Urinary tract: 363 (17.6%) ♦ Bloodstream: 247 (12.0%)

Vincent J-L, et al. JAMA 1995;274:639

PREVALENCE: ICU (WORLDWIDE)

- Study design: Point prevalence, 8 May 2007
 - **75** countries, 1265 ICUs, 13,796 adult patients
- Frequency of infections: 7,087 (51%)
 - Sites of infection
 - ◆ Respiratory tract:: 4,503 (63.5%)
 - ◆ Abdominal: 1,392 (19.6%)
 - ◆ Bloodstream: 1,071 (15.1%)
 - Renal/urinary tract: 1,011 (14.3%)
- Antibiotic therapy: 71%
- Pathogens of infected patients: 47% GPC, 62% GNR, 19% fungi
- Infected patients had higher ICU (25.3% vs 10.7%) and hospital mortality (33.1% vs 14.8%)

Vincent J-L, et al. JAMA 2009;302:2333-2329

VENTILATOR-ASSOCIATED PNEU RATES, NHSN, 2012

Table 6

Pooled means and key percentiles of the distribution of ventilator-associated PNEU rates and ventilator utilization ratios, by type of location, DA module, 2012

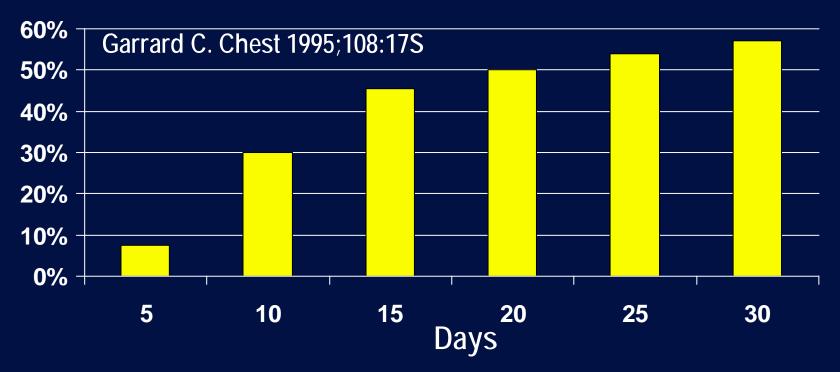
Ventilator-associated PNEU rate*							Percentile		
Type of location	No. of locations [†]	No. of VAP	Ventilator-days	Pooled mean	10%	25%	50% (median)	75%	90%
Acute Care Hospitals									
Critical Care Units									
Burn	36 (34)	86	19,503	4.4	0.0	0.0	1.1	6.7	10.9
Medical									
Major teaching	112 (111)	205	212,392	1.0	0.0	0.0	0.5	1.6	2.9
Medical									
All other	223 (197)	191	206,731	0.9	0.0	0.0	0.0	1.3	3.4
Medical cardiac	178 (170)	135	139,864	1.0	0.0	0.0	0.0	1.5	3.6
Medical/surgical									
Major teaching	152 (145)	372	234,972	1.6	0.0	0.0	0.9	2.2	3.9
Medical/surgical									
All other 15 beds	841 (660)	419	383,926	1.1	0.0	0.0	0.0	1.2	3.6
Medical/surgical									
All other >15 beds	405 (400)	666	711,280	0.9	0.0	0.0	0.4	1.3	2.8
Neurologic	23	62	20,859	3.0	0.0	0.0	0.2	2.5	7.0
Neurosurgical	76 (74)	210	98,026	2.1	0.0	0.0	1.5	2.9	3.8
Pediatric cardiothoracic	20	9	36,187	0.2	0.0	0.0	0.0	0.2	0.6
Pediatric medical	16 (9)	2	6,634	0.3					
Pediatric medical/surgical	142 (132)	113	147,441	0.8	0.0	0.0	0.0	0.9	2.4
Pediatric surgical	5 (4)	1	2,328	0.4					
Respiratory	7	4	6,037	0.7					
Surgical									
Major teaching	81 (80)	280	127,251	2,2	0.0	0.6	1.5	3.1	5.6

VENTILATOR-ASSOCIATED PNEU RATES, NHSN, 2012

Ventilator-associated PNEU rate*							Percentile		
Type of location	No. of locations [†]	No. of VAP	Ventilator-days	Pooled mean	10%	25%	50% (median)	75%	90%
Surgical									
All other	93 (88)	192	96,388	2.0	0.0	0.0	0.9	2.8	5.9
Surgical cardiothoracic	207 (203)	319	190,785	1.7	0.0	0.0	0.6	2.5	5.1
Trauma	75 (74)	508	141,314	3.6	0.0	0.8	2.6	6.0	9.4
Specialty Care Areas/Oncology									
Hematopoietic stem cell transplant	5	0	1,951	0.0					
Step-Down Units									
Adult step-down (post-critical care)	102 (82)	31	42,462	0.7	0.0	0.0	0.0	0.0	1.8
Pediatric step-down (post-critical care)	5 (4)	1	5,813	0.2					
Step-down NICU (level II)	7(1)	0	119	0.0					
Inpatient Wards									
Medical	39 (22)	3	6,472	0.5	0.0	0.0	0.0	0.0	1.4
Medical/surgical	64 (35)	22	25,731	0.9	0.0	0.0	0.0	0.0	1.3
Pediatric medical	6 (5)	0	2,026	0.0					
Pediatric medical/surgical	11 (8)	0	3,146	0.0					
Pulmonary	9 (8)	7	7,241	1.0					
Surgical	8(1)	0	107	0.0					
Telemetry	10 (5)	1	1,770	0.6					
Critical Access Hospitals									
Critical care units [‡]	67 (14)	3	2,964	1.0					
Non-critical care units [§]	9(1)	4	2,660	1.5					
Long-Term Acute Care Hospitals									
Adult critical care	18 (17)	8	12,544	0.6					
Adult ward	195 (190)	103	316,632	0.3	0.0	0.0	0.0	0,3	1.4

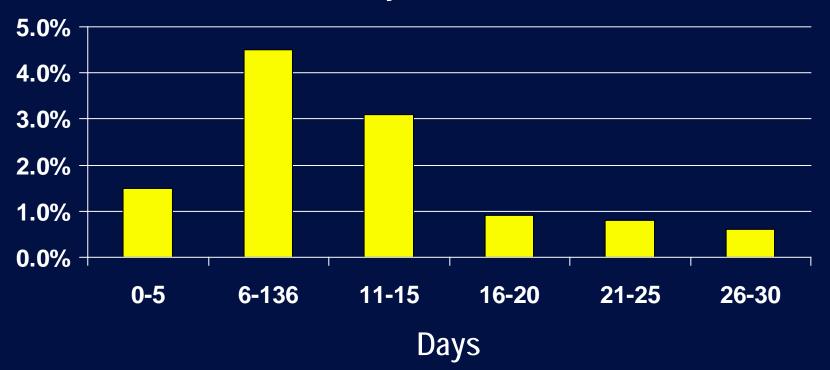
VAP: TIME COURSE

Cumulative Incidence ICU VAP



VAP: TIME COURSE

Mean Daily Risk Of VAP



MICROBIOLOGY

CAUSES OF LOWER RESPIRATORY TRACT INFECTIONS IN ADULTS

		Aspira		
Organisms	Inhalation	Community- acquired	Hostital- acquired	Hemato- genous
Haemophilus influenzae				
Streptococcus pueumoniae	8			
Oropharyngeal streptococci and anaerobes				
Staphylococcus aureus	8			
Enterobacteriaceae				
Pseudomonas aeruginosa				
Legionellaceae				
Mycoplasma pneumoniae				
Chlamydia pneumoniae				
Viruses				
Histoplasma capsulatum				
Blastomyces dermatitidis				
Coccidioides immitis				
Mycobacteria				

Table 3. Reported Causative Pathogens, According to Type of Infection.*

Pathogen	All Health Care– Associated Infections (N=504)†		Pneumonia (N=110)	Surgical-Site Infections (N=110)	GI Infections (N=86)	UTIs (N=65)	Bloodstream Infections (N=50)
	no. (%)	rank			number (percent)		
Clostridium difficile	61 (12.1)	1	0	0	61 (70.9)	0	0
Staphylococcus aureus	54 (10.7)	2	18 (16.4)	17 (15.5)	1 (1.2)	2 (3.1)	7 (14.0)
Klebsiella pneumoniae or K. oxytoca	50 (9.9)	3	13 (11.8)	15 (13.6)	1 (1.2)	15 (23.1)	4 (8.0)
Escherichia coli	47 (9.3)	4	3 (2.7)	14 (12.7)	1 (1.2)	18 (27.7)	5 (10.0)
Enterococcus species‡	44 (8.7)	5	2 (1.8)	16 (14.5)	5 (5.8)	11 (16.9)	6 (12.0)
Pseudomonas aeruginosa	36 (7.1)	6	14 (12.7)	7 (6.4)	1 (1.2)	7 (10.8)	2 (4.0)
Candida species§	32 (6.3)	7	4 (3.6)	3 (2.7)	3 (3.5)	3 (4.6)	11 (22.0)
Streptococcus species¶	25 (5.0)	8	7 (6.4)	8 (7.3)	2 (2.3)	2 (3.1)	2 (4.0)
Coagulase-negative staphylococcus species	24 (4.8)	9	0	7 (6.4)	0	1 (1.5)	9 (18.0)
Enterobacter species	16 (3.2)	10	3 (2.7)	5 (4.5)	0	2 (3.1)	2 (4.0)
Acinetobacter baumannii	8 (1.6)	11, tie	4 (3.6)	2 (1.8)	0	0	0
Proteus mirabilis	8 (1.6)	11, tie	1 (0.9)	5 (4.5)	0	1 (1.5)	0
Yeast, unspecified	8 (1.6)	11, tie	3 (2.7)	0	1 (1.2)	4 (6.2)	0
Stenotrophomonas maltophilia	8 (1.6)	11, tie	6 (5.5)	0	0	2 (3.1)	0
Citrobacter species	6 (1.2)	15, tie	2 (1.8)	1 (0.9)	0	1 (1.5)	0
Serratia species	6 (1.2)	15, tie	2 (1.8)	0	0	2 (3.1)	0
Bacteroides species	6 (1.2)	15, tie	0	5 (4.5)	1 (1.2)	0	0
Haemophilus species	6 (1.2)	15, tie	2 (1.8)	2 (1.8)	0	0	0
Viruses	3 (0.6)	19, tie	1 (0.9)	0	0	0	0
Peptostreptococcus species	3 (0.6)	19, tie	0	2 (1.8)	0	0	1 (2.0)
Klebsiella species other than K. pneumoniae and K. oxytoca	2 (0.4)	21, tie	1 (0.9)	0	0	0	1 (2.0)
Clostridium species other than <i>C. difficile</i>	2 (0.4)	21, tie	0	2 (1.8)	0	0	0
Prevotella species	2 (0.4)	21, tie	0	1 (0.9)	0	0	0
Morganella morganii	2 (0.4)	21, tie	0	1 (0.9)	0	1 (1.5)	0
Lactobacillus species	2 (0.4)	21, tie	0	0	1 (1.2)	0	1 (2.0)
Other organisms**	13 (2.6)	_	1 (0.9)	6 (5.5)	0	1 (1.5)	3 (6.0)

McGill NEJM 2014; 370: 1198

ETIOLOGIC AGENTS ASSOCIATED WITH HAP: NNIS vs INVASIVE DX

Pathogen	NNIS	INVASIVE DX
<i>S. aureus</i> (ORSA 55.7%)	19%	20.4%
S. Pneumoniae	NA	4.1%
Streptococcus spp.	3%	8.0%
Coagulase-negative staphylococcus	2%	1.4%
Enterobacteriaceae	26%	14.15
Pseudomonas aeroginosa	17%	24.4%
Acinetobacter spp.	4%	7.9%
Stenotrophomonas maltophilia	<1%	1.7%
Hemophilus spp.	7.1%	9.8%
Neisseria spp.	<1%	2.6%
Anaerobes	2%	0.9%
Fungi	7%	0.9%
Other (<1% each)		3.8%

Chastre J, Fagon J-Y. Am J Respir Crit Care Med 2002;165:867-903

MICROBIOLOGY

- Determinants of pathogens
 - Setting
 - Prior antibiotic use
 - Duration of hospitalization
 - Early (<5 days): S. pneumoniae, H. influenzae, MSSA</p>
 - ◆ Late (≥5 days): P. aeruginosa, MRSA, Gram (-) bacilli
 - ICU stay
 - Colonization

COMMON PATHOGENS BY PRESENCE OR ABSENCE OF RISK FACTORS FOR MDROs

Table I. Common pathogenic organisms in ventilator-associated pneumonia according to presence or absence of risk factors for multidrugresistant organisms^[10]

Risk factors	Commonly isolated organisms
No risk factors	Streptococcus pneumoniae Haemophilus influenzae Antibacterial-sensitive enteric Gram-negative bacilli Escherichia coli Klebsiella pneumoniae Enterobacter spp. Proteus spp. Serratia marcescens
Late onset (>5 days) or one of the following risk factors: antimicrobial therapy in preceding 90 days, current hospitalization of ≥5 days, high frequency of antibacterial resistance in the community or in the specific hospital unit, presence of risk factors for HCAP (hospitalization for ≥2 days in the preceding 90 days, residence in a nursing home or extended care facility, home infusion therapy [including antibacterials], chronic dialysis within 30 days, home wound care, family member with multidrug-resistant pathogen), immunosuppressive disease and/or therapy	As above plus: <i>Pseudomonas aeruginosa</i> <i>K pneumoniae</i> (ESBL) <i>Acinetobacter</i> spp. Methicillin-resistant <i>Staphylococcus aureus</i>

ESBL = extended-spectrum β-lactamase; HCAP = healthcare-associated pneumonia.

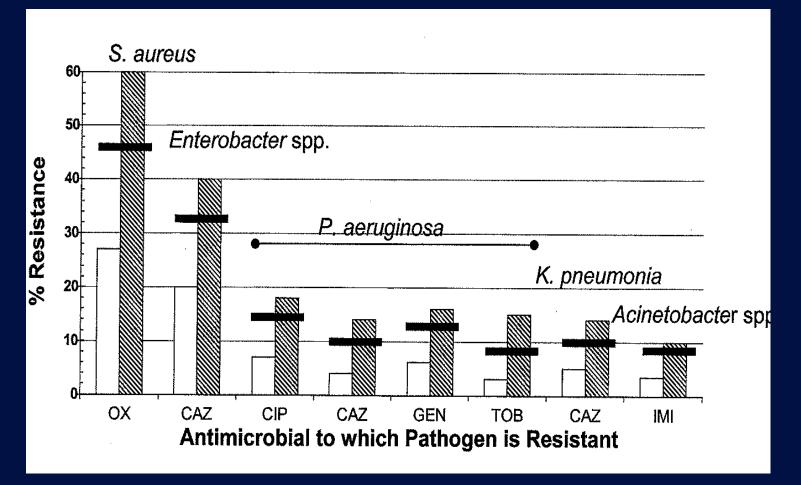
Vincent JL, et al. Drugs 2010;70:1927-1944

No. (%) of isolates Patients with VAP^a Patients with HAP^b Pathogen, by class ICU Non-ICU ICU Non-ICU Gram-positive cocci Staphylococcus aureus Oxacillin-susceptible 35 (9.59) 2(5.71)13 (12.87) 23 (13.61) Oxacillin-resistant 69 (18.90) 2(5.71)13 (12.87) 42 (24.85)^c Streptococcus pneumoniae 7 (1.92) 1(2.86)7 (6.93) 8 (4.73) Gram-negative bacilli Enterobacter species 0 (0.00) 6 (3.55) 9 (2.47) 2(1.98)Escherichia coli 10(2.74)5 (14.29)° 3 (2.97) 5 (2.96) Klebsiella pneumoniae 6 (1.64) 2(5.71)5 (4.95) 8 (4.73) Serratia marcescens 8 (2.19) 2(5.71)3 (2.97) 2(1.18)Acinetobacter species 29 (7.95) 2(5.71)4 (3.96) 5 (2.96) Stenotrophomonas maltophilia 25 (6.85) 2(5.71)2(1.98)1(0.59)Pseudomonas aeruginosa 60 (16.44) 10 (28.57) 11 (10.89) 14 (8.28) Moraxella catarrhalis 6 (1.64) 0 (0.00) 2(1.98)5 (2.96) 0 (0.00) Hemophilus species 18 (4.93) 4 (3.96) 2(1.18)Total, all pathogens 365 35 101169

TABLE 3. Relative Frequency of Isolation of Selected Pathogens From Patients With Ventilator-Associated Pneumonia (VAP) and Nonventilated Patients With Hospital-Acquired Pneumonia (HAP), as a Function of Hospital Location of Care

Weber DJ, et al. ICHE 2007;28:825-831

ICU (NNIS, 1989-99): Ventilator-Associated Pneumonia



Open bars <a> 7 days hospitalization Closed bars >7 days hospitalization

Fridkin SK. Crit Care Med 2001;29:N67

PATHOGENS AS A FUNCTION OF DURATION OF HOSPITALIZATION

TABLE 4. Frequency of Isolation of Selected Pathogens from Patients With Ventilator-Associated Pneumonia (VAP), as a Function of Duration of Hospitalization

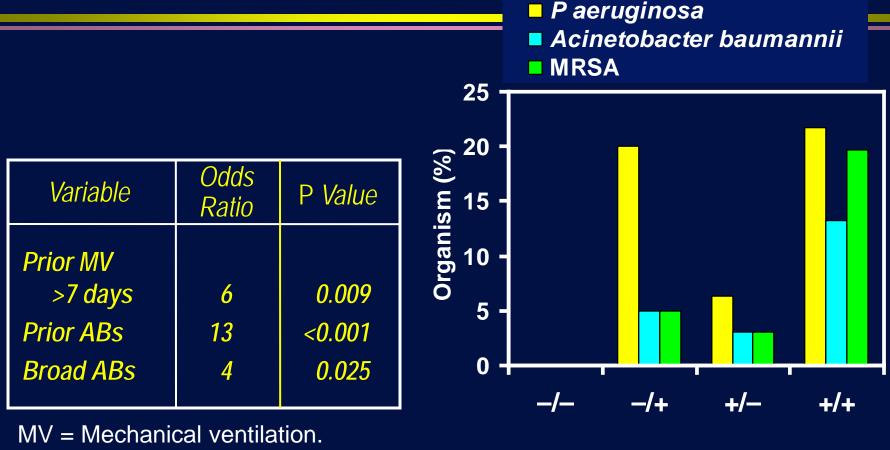
	No. (%)		
Pathogen, by class	Patients with early-onset VAP	Patients with late-onset VAP	Р
Gram-positive cocci			
Staphylococcus aureus			
Oxacillin-susceptible	12 (18.75)	24 (7.19)	.006
Oxacillin-resistant	8 (12.50)	63 (18.86)	.149
Streptococcus pneumoniae	4 (6.25)	4 (1.20)	.026
Gram-negative bacilli			
Enterobacter species	1 (1.56)	8 (2.40)	.561
Escherichia coli	2 (3.13)	13 (3.89)	.556
Klebsiella pneumoniae	1 (1.56)	7 (2.10)	.623
Serratia marcescens	2 (3.13)	8 (2.40)	.497
Acinetobacter species	0 (0.00)	31 (9.28)	.003
Stenotrophomonas maltophilia	1 (1.56)	26 (7.78)	.049
Pseudomonas aeruginosa	8 (12.50)	61 (18.26)	.176
Moraxella catarrhalis	2 (3.13)	4 (1.20)	.176
Hemophilus species	12 (18.75)	10 (2.99)	<.001
Total, all pathogens	64	334	

TABLE 5. Frequency of Isolation of Selected Pathogens From Nonventilated Patients With Hospital-Acquired Pneumonia (HAP), as a Function of Duration of Hospitalization

	No. (%)	of isolates	
Pathogen	Patients with early-onset HAP	Patients with late-onset HAP	Р
Gram-positive cocci			
Staphylococcus aureus			
Oxacillin-susceptible	13 (19.40)	22 (11.00)	.063
Oxacillin-resistant	8 (11.94)	47 (23.50)	.028
Streptococcus pneumoniae	8 (11.94)	7 (3.50)	.015
Gram-negative bacilli			
Enterobacter species	2 (2.99)	6 (3.00)	.639
Escherichia coli	1 (1.49)	7 (3.50)	.361
Klebsiella species	3 (4.48)	12 (6.00)	.454
Serratia marcescens	2 (2.99)	3 (1.50)	.369
Acinetobacter species	2 (2.99)	7 (3.50)	.598
Stenotrophomonas maltophilia	1 (1.49)	2 (1.00)	.581
Pseudomonas aeruginosa	2 (2.99)	23 (11.50)	.026
Moraxella catarrhalis	3 (4.48)	4 (2.00)	.244
Hemophilus species	4 (5.97)	4 (2.00)	.122
Total, all pathogens	67	200	

Weber DJ, et al. ICHE 2007;28:825-831

Antibiotic-Resistant VAP



MRSA = Methicillin-resistant *S* aureus.

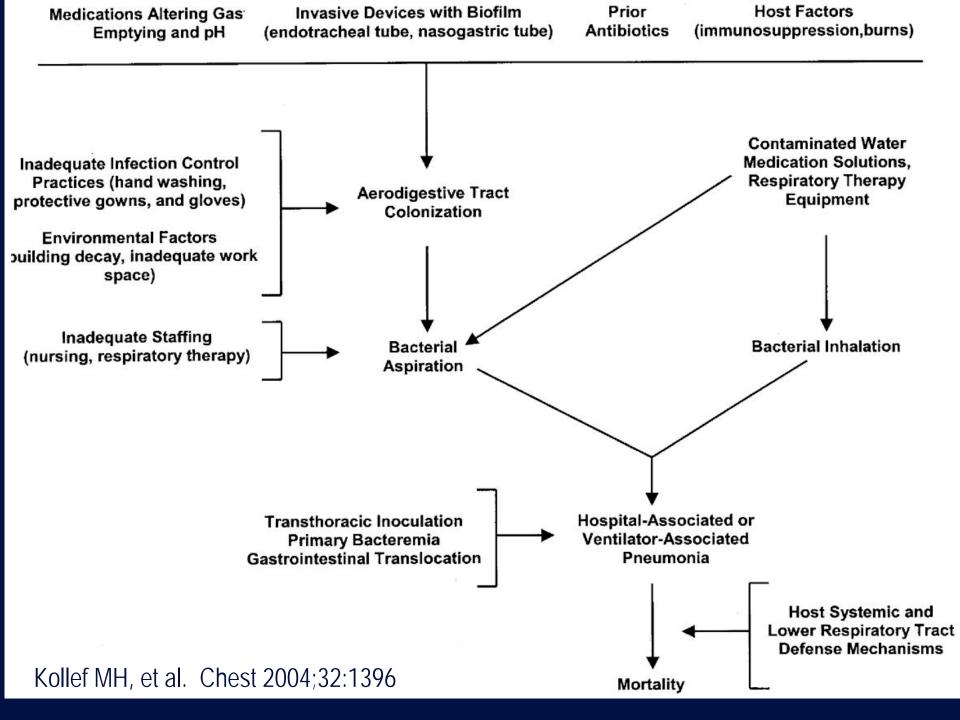
MV>7 Days/Prior Antibiotics

Trouillet JL, et al. Am J Respir Crit Care Med. 1998;157:531-539.

PATHOPHYSIOLOGY

PATHOGENESIS

- Colonization, aspiration, pneumonia in the setting of impaired host defenses
- Inhalation
- Instillation
- Bacteremic spread
- Contiguous spread



VAP: RISK FACTORS

Intrinsic Risk Factors

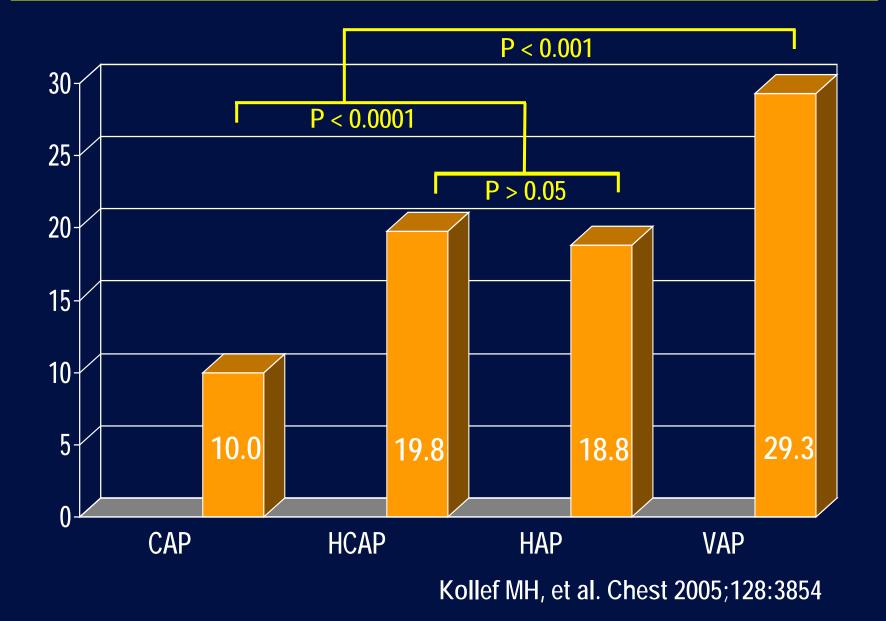
- Chronic lung disease/COPD
- Severity of illness
- ARDS
- Witnessed aspiration
- Age >60 years
- Coma
- Head trauma/ICP monitoring
- Upper abdominal surgery
- Thoracic surgery
- Fall-winter season

Extrinsic Risk Factors

- Duration of intubation
- Emergent intubation
- Reintubation
- Elevated gastric pH
- Prior antibiotic therapy
- Nasogastric tube
- Enteral nutrition
- Supine head position
- Patient transport out of ICU

Kollef M. Crit Care Med 2004;32:1396 (adapted)

%Hospital Mortality by Classification



RISK FACTORS FOR MORTALITY (VAP)

- High risk pathogens: *P.aeruginosa, Acinetobacter, S. maltophilia* 65% (Kollef, Chest 1995;108:165)
- Severity of underlying illness; shock
- Age
- Inappropriate antibiotic therapy
- Bilateral infiltrates
- Duration of prior hospitalization
- Prior antibiotic therapy
- Supine head position in ventilated patients

CONCLUSIONS

- Nosocomial pneumonia remains an important cause of patient morbidity and mortality in the US
- Nosocomial pneumonia results in a more prolonged hospital stay and increased cost

THANK YOU

