Pneumonia

המצגת הוכנה ע"י אסא טל

סטודנט שנה 4

בית הספר לרפואה

אוניברסיטת תל-אביב

מחלקה פנימית ג'

המרכז הרפואי שיבא

טיוטור: דר' חוסם קאסם

Case report

A 65-year-old man with hypertension and degenerative joint disease presents to the emergency department with a three-day history of a productive cough and fever. He has a temperature of 38.3°C (101°F), a blood pressure of 144/92 mm Hg, a respiratory rate of 22 breaths per minute, a heart rate of 90 beats per minute, and oxygen saturation of 92 percent while breathing room air. Physical examination reveals only crackles and egophony in the right lower lung field. The white-cell count is 14,000 per cubic millimeter, and the results of routine chemical tests are normal. A chest radiograph shows an infiltrate in the right lower lobe. How should this patient be treated?

Definition:

Pneumonia is an infection of the pulmonary parenchyma. Despite being the cause of significant morbidity and mortality, **pneumonia** is often misdiagnosed, mistreated, and underestimated.

Classification:

- community-acquired pneumonia (CAP)
- health care–associated pneumonia (HCAP):
  - -hospital-acquired pneumonia (HAP) and
  - -ventilator-associated pneumonia

Epidemiology

- One of the most common infectious diseases in the world.
- 12/1,000/year, about 600,000 hospitalization cases per year (in the U.S.).
- The 6th leading cause of death in the U.S.
- The most common cause of death due to infectious disease.

-N Engl J Med 1995; 333:1618-24

Pathophysiology

Proliferation of microbial pathogens at the alveolar level and the host's response to those pathogens.

Microorganisms gain access to the lower respiratory tract in several ways:
- Aspiration from the oropharynx – sleep / ⬇ consciousness.
- Inhaltion of contaminated droplets.
- Hematogenous spread (e.g., from tricuspid endocarditis - RARE) or by contiguous extension from an infected pleural or mediastinal space.

Mechanical factors are critically important in host defense

Hairs in nares
Branching architecture
Mucociliary clearance
Antibacterial factors
Gag reflex + cough
Normal flora

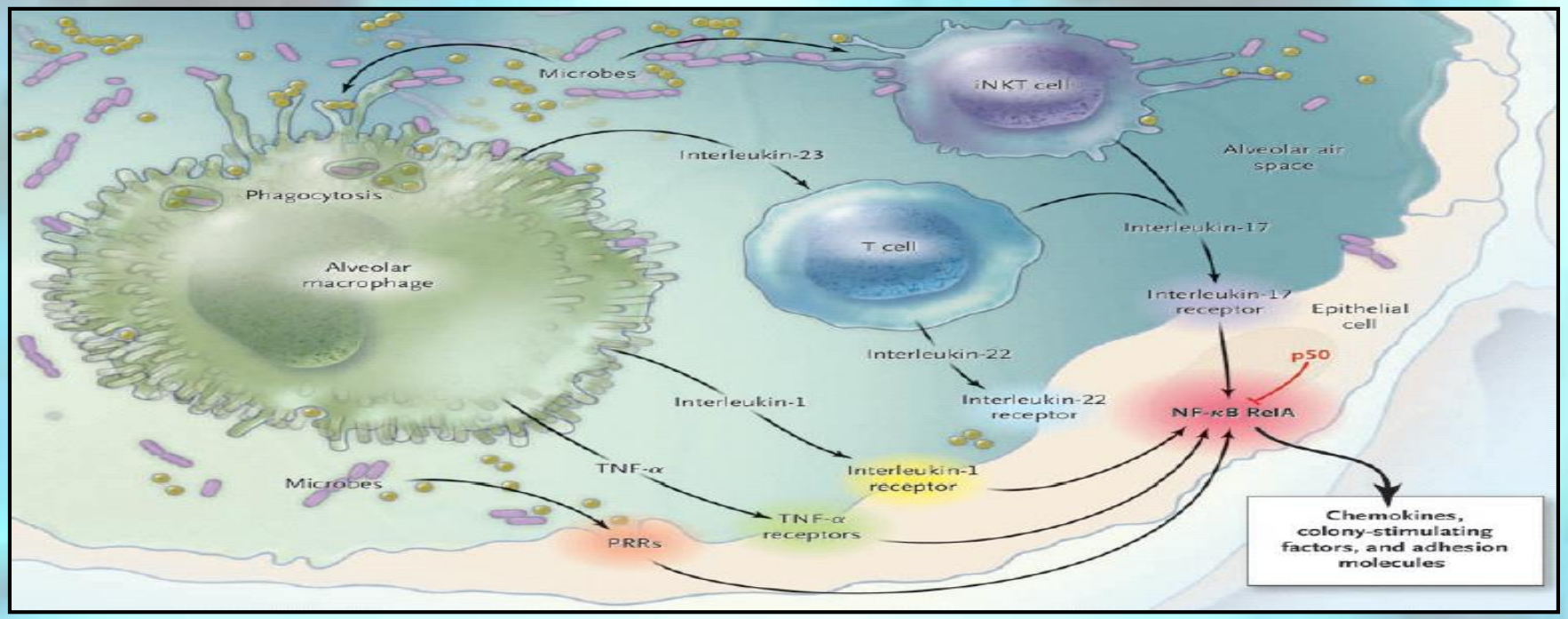
Immune factors come into action

Resident alveolar MQ
Local proteins (Surfactant A&D) – opsonization

But when all of these fail:

MQ release inflammatory mediators leading to clinical syndromes of Pneumonia:

Interleukines & TNF - Fever
Chemokines (IL-8 & G-CSF) – Leukocytosis
Alveolar capillary leak (Neutrophils, Erythrocytes) – Hemoptysis, Hypoxemia



Pathology

edema, with the presence of a proteinaceous exudate—and often of bacteria—in the alveoli. Rapid phase!

red hepatization, The presence of erythrocytes in the cellular intraalveolar exudate (neutrophils are also present).

gray hepatization, The neutrophil is the predominant cell, fibrin deposition is abundant, and bacteria have disappeared. successful containment of the infection and improvement in gas exchange.

resolution, MQ cleans up the mess.

CAP

Etiology

Table 6. Most common etiologies of community-acquired pneumonia.

Patient type	Etiology
Outpatient	*Streptococcus pneumoniae* *Mycoplasma pneumoniae* *Haemophilus influenzae* *Chlamydophila pneumoniae* Respiratory viruses[a]
Inpatient (non-ICU)	*S. pneumoniae* *M. pneumoniae* *C. pneumoniae* *H. influenzae* *Legionella* species Aspiration Respiratory viruses[a]
Inpatient (ICU)	*S. pneumoniae* *Staphylococcus aureus* *Legionella* species Gram-negative bacilli *H. influenzae*

Clinical Manifestations

- Typical presentation
- Atypical presentation
- (Overlapping)

Clinical Manifestations

- ***Typical presentation***
  - Advenced age
  - Chronic underlying disease: COPD,CHF,DM,AIDS,etc.
  - Productive cough (>90%)
  - Sudden onset of fever (80%)
  - SOB (66%)
  - Rusty sputum production (66%)
  - Pleuritic chest pain (50%)
  - Signs of pulmonary consolidation (dullness, increased fremitus, egophony, bronchial breathing sound, rales)
  - Systemic symptoms: nausea, vomiting, and/or diarrhea. fatigue, headache, myalgias, and arthralgias

Clinical Manifestations

- ***Atypical presentation***
  - Younger patients
  - Environmental history: exposure to young children and sick people. Exposure to birds, sheep, goats, cattle, domestic animals. Exposure to air coolers,
  - Minimal findings on physical examination
  - Sore throat and hoarseness
  - Gradual onset
  - Dry cough
  - Extrapulmonary symptoms
    - *Legionella*-CNS, heart, liver, GI and GU
    - *M.pneumoniae*- upper RT, GI, skin

Diagnosis

Prompt and accurate diagnosis of CAP is important, since it is the only acute respiratory tract infection in which delayed antibiotic treatment has been associated with increased risk of death!

When confronted with possible CAP, the physician must ask two questions:

Is this pneumonia?

•Clinical diagnosis & radiographic methods

What is the etiology?

•Laboratory techniques

Clinical Diagnosis

Table 8. Epidemiologic conditions and/or risk factors related to specific pathogens in community-acquired pneumonia.

Condition	Commonly encountered pathogen(s)
Alcoholism	*Streptococcus pneumoniae*, oral anaerobes, *Klebsiella pneumoniae*, *Acinetobacter* species, *Mycobacterium tuberculosis*
COPD and/or smoking	*Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Legionella* species, *S. pneumoniae*, *Moraxella catarrhalis*, *Chlamydophila pneumoniae*
Aspiration	Gram-negative enteric pathogens, oral anaerobes
Lung abscess	CA-MRSA, oral anaerobes, endemic fungal pneumonia, *M. tuberculosis*, atypical mycobacteria
Exposure to bat or bird droppings	*Histoplasma capsulatum*
Exposure to birds	*Chlamydophila psittaci* (if poultry: avian influenza)
Exposure to rabbits	*Francisella tularensis*
Exposure to farm animals or parturient cats	*Coxiella burnetti* (Q fever)
HIV infection (early)	*S. pneumoniae*, *H. influenzae*, *M. tuberculosis*
HIV infection (late)	The pathogens listed for early infection plus *Pneumocystis jirovecii*, *Cryptococcus*, *Histoplasma*, *Aspergillus*, atypical mycobacteria (especially *Mycobacterium kansasii*), *P. aeruginosa*, *H. influenzae*
Hotel or cruise ship stay in previous 2 weeks	*Legionella* species
Travel to or residence in southwestern United States	*Coccidioides* species, *Hantavirus*
Travel to or residence in Southeast and East Asia	*Burkholderia pseudomallei*, avian influenza, SARS
Influenza active in community	Influenza, *S. pneumoniae*, *Staphylococcus aureus*, *H. influenzae*
Cough >2 weeks with whoop or posttussive vomiting	*Bordetella pertussis*
Structural lung disease (e.g., bronchiectasis)	*Pseudomonas aeruginosa*, *Burkholderia cepacia*, *S. aureus*
Injection drug use	*S. aureus*, anaerobes, *M. tuberculosis*, *S. pneumoniae*
Endobronchial obstruction	Anaerobes, *S. pneumoniae*, *H. influenzae*, *S. aureus*
In context of bioterrorism	*Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia)

Etiologic Diagnosis

When susspecting pneumonia – START IMMIDIATLY EMPIRICAL TREATMENT!

However, Identification of an unexpected pathogen allows narrowing of the initial empirical regimen, which decreases antibiotic selection pressure and may lessen the risk of resistance.

Pathogens with important public safety implications, such as *Mycobacterium tuberculosis* and influenza virus, may be found in some cases.

Finally, without culture and susceptibility data, trends in resistance cannot be followed accurately, and appropriate empirical therapeutic regimens are harder.

Etiologic Diagnosis

- Gram's Stain and Culture of Sputum
- Blood Cultures (low yield)
- Antigen Tests (detect pneumococcal and *Legionella* antigens in urine)
- PCR
- Serology (IgM antibody)

Community-Acquired Pneumonia: Treatment

- Site of care - Home? Hospital? (1/20 cost)

PSI

Nursing Home Resident

Comorbid Diseases :

Renal Disease, Liver Disease, CHF, Cerebrovascular Disease, Neoplasia

Physical Exam :

Altered Mental Status, SBP < 90

Temp < 35 or >= 40 , RR >= 30 , HR >= 125

Labs :

PH < 7.35, PO2 < 60 or Sat < 90

NA < 130 HCT < 30

Gluc > 250

BUN > 30 Pleural Effusion

CURB-65 AND CRB-65 SEVERITY SCORES FOR COMMUNITY-ACQUIRED PNEUMONIA

Clinical factor	Points
Confusion	1
Blood urea nitrogen > 19 mg per dL	1
Respiratory rate ≥ 30 breaths per minute	1
Systolic blood pressure < 90 mm Hg or Diastolic blood pressure ≤ 60 mm Hg	1
Age ≥ 65 years	1
Total points:	

CURB-65 score	Deaths/total (%)*	Recommendation†
0	7/1,223 (0.6)	Low risk; consider home treatment
1	31/1,142 (2.7)	
2	69/1,019 (6.8)	Short inpatient hospitalization or closely supervised outpatient treatment
3	79/563 (14.0)	Severe pneumonia; hospitalize and consider admitting to intensive care
4 or 5	44/158 (27.8)	

CRB-65 score‡	Deaths/total (%)*	Recommendation†
0	2/212 (0.9)	Very low risk of death; usually does not require hospitalization
1	18/344 (5.2)	Increased risk of death; consider hospitalization
2	30/251 (12.0)	
3 or 4	39/125 (31.2)	High risk of death; urgent hospitalization

Table 7. Recommended empirical antibiotics for community-acquired pneumonia.

Outpatient treatment

1. Previously healthy and no use of antimicrobials within the previous 3 months

   A macrolide (strong recommendation; level I evidence)

   Doxycycline (weak recommendation; level III evidence)

2. Presence of comorbidities such as chronic heart, lung, liver or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; or use of antimicrobials within the previous 3 months (in which case an alternative from a different class should be selected)

   A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg]) (strong recommendation; level I evidence)

   A β-lactam **plus** a macrolide (strong recommendation; level I evidence)

3. In regions with a high rate (>25%) of infection with high-level (MIC ≥16 μg/mL) macrolide-resistant *Streptococcus pneumoniae*, consider use of alternative agents listed above in (2) for patients without comorbidities (moderate recommendation; level III evidence)

Table 7. Recommended empirical antibiotics for community-acquired pneumonia.

Inpatients, ICU treatment

A β-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) **plus** either azithromycin (level II evidence) **or** a respiratory fluoroquinolone (level I evidence) (strong recommendation) (for penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended)

Special concerns

If *Pseudomonas* is a consideration

An antipneumococcal, antipseudomonal β-lactam (piperacillin-tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin (750 mg)

or

The above β-lactam plus an aminoglycoside and azithromycin

or

The above β-lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for above β-lactam)

(moderate recommendation; level III evidence)

If CA-MRSA is a consideration, add vancomycin or linezolid (moderate recommendation; level III evidence)

Pathogen-Directed Therapy

Table 9. Recommended antimicrobial therapy for specific pathogens.

Organism	Preferred antimicrobial(s)	Alternative antimicrobial(s)
Streptococcus pneumoniae		
Penicillin nonresistant; MIC <2 μg/mL	Penicillin G, amoxicillin	Macrolide, cephalosporins (oral [cefpodoxime, cefprozil, cefuroxime, cefdinir, cefditoren] or parenteral [cefuroxime, ceftriaxone, cefotaxime]), clindamycin, doxycyline, respiratory fluoroquinolone[a]
Penicillin resistant; MIC ≥2 μg/mL	Agents chosen on the basis of susceptibility, including cefotaxime, ceftriaxone, fluoroquinolone	Vancomycin, linezolid, high-dose amoxicillin (3 g/day with penicillin MIC ≤4 μg/mL)
Haemophilus influenzae		
Non–β-lactamase producing	Amoxicillin	Fluoroquinolone, doxycycline, azithromycin, clarithromycin[b]
β-Lactamase producing	Second- or third-generation cephalosporin, amoxicillin-clavulanate	Fluoroquinolone, doxycycline, azithromycin, clarithromycin[b]
Mycoplasma pneumoniae/Chlamydophila pneumoniae	Macrolide, a tetracycline	Fluoroquinolone
Legionella species	Fluoroquinolone, azithromycin	Doxycyline
Chlamydophila psittaci	A tetracycline	Macrolide
Coxiella burnetii	A tetracycline	Macrolide

Pathogen-Directed Therapy

Enterobacteriaceae	Third-generation cephalosporin, carbapenem[c] (drug of choice if extended-spectrum β-lactamase producer)	β-Lactam/β-lactamase inhibitor,[d] fluoroquinolone
Pseudomonas aeruginosa	Antipseudomonal β-lactam[e] **plus** (ciprofloxacin or levofloxacin[f] or aminoglycoside)	Aminoglycoside **plus** (ciprofloxacin or levofloxacin[f])
Burkholderia pseudomallei	Carbapenem, ceftazadime	Fluoroquinolone, TMP-SMX
Acinetobacter species	Carbapenem	Cephalosporin-aminoglycoside, ampicillin-sulbactam, colistin
Staphylococcus aureus		
Methicillin susceptible	Antistaphylococcal penicillin[g]	Cefazolin, clindamycin
Methicillin resistant	Vancomycin or linezolid	TMP-SMX
Bordetella pertussis	Macrolide	TMP-SMX
Anaerobe (aspiration)	β-Lactam/β-lactamase inhibitor,[d] clindamycin	Carbapenem
Influenza virus	Oseltamivir or zanamivir	
Mycobacterium tuberculosis	Isoniazid plus rifampin plus ethambutol plus pyrazinamide	Refer to [243] for specific recommendations

Duration of Antibiotic Therapy

32. Patients with CAP should be treated for a minimum of 5 days (level I evidence), should be afebrile for 48–72 h, and should have no more than 1 CAP-associated sign of clinical instability (table 10) before discontinuation of therapy (level II evidence). (Moderate recommendation.)
33. A longer duration of therapy may be needed if initial therapy was not active against the identified pathogen or if it was complicated by extrapulmonary infection, such as meningitis or endocarditis. (Weak recommendation; level III evidence.)

Table 10. Criteria for clinical stability.

Temperature ≤37.8°C
Heart rate ≤100 beats/min
Respiratory rate ≤24 breaths/min
Systolic blood pressure ≥90 mm Hg
Arterial oxygen saturation ≥90% or pO_2 ≥60 mm Hg on room air
Ability to maintain oral intake[a]
Normal mental status[a]

Other treatment considerations

35. Hypotensive, fluid-resuscitated patients with severe CAP should be screened for occult adrenal insufficiency. (Moderate recommendation; level II evidence.)

37. Low-tidal-volume ventilation (6 cm^3/kg of ideal body weight) should be used for patients undergoing ventilation who have diffuse bilateral pneumonia or ARDS. (Strong recommendation; level I evidence.)

Assessment of Nonresponders

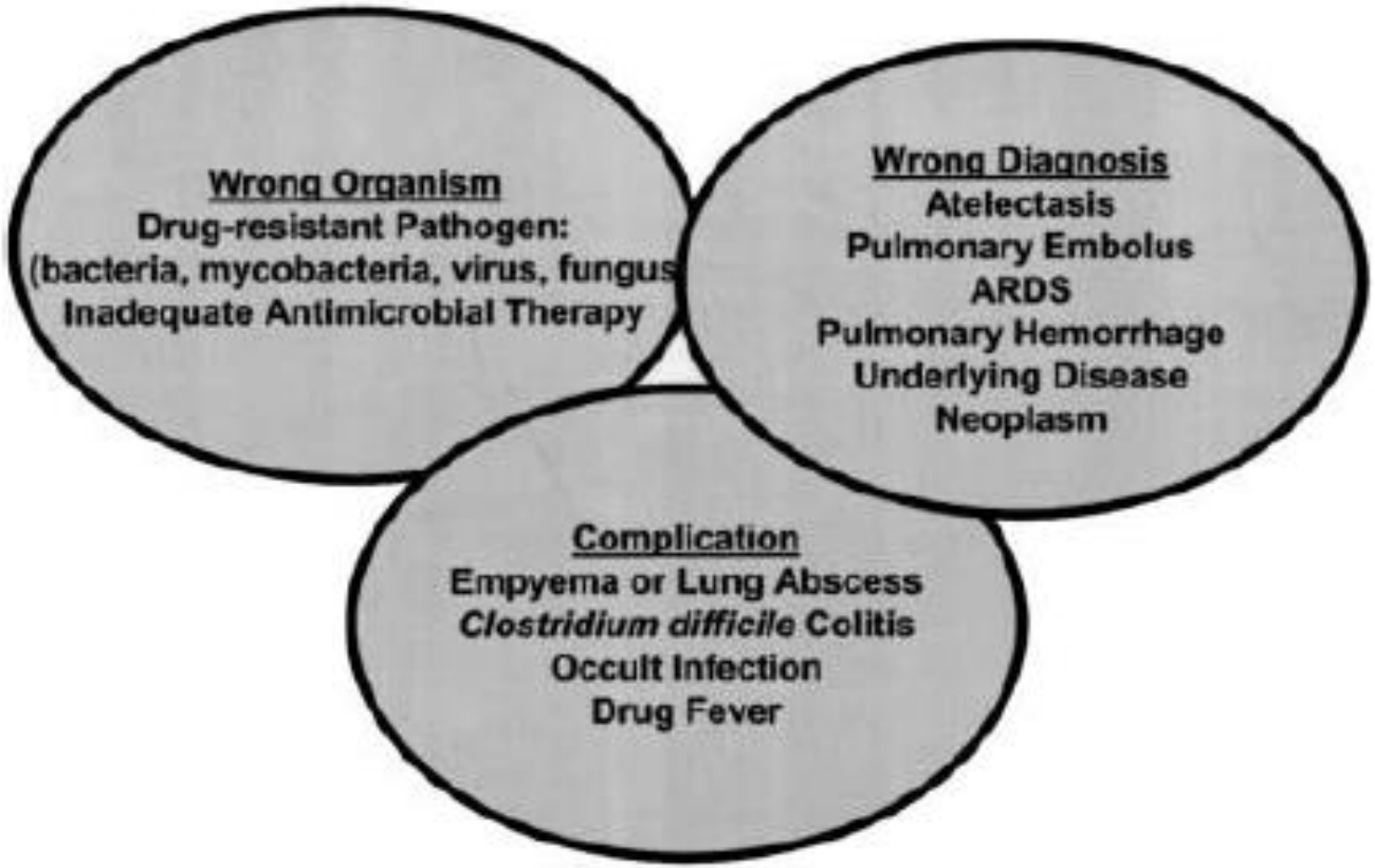


Table 12. Factors associated with nonresponding pneumonia.

	Overall failure[a]		Early failure[b]	
Risk factor	Decreased risk	Increased risk	Decreased risk	Increased risk
Older age (>65 years)	…	…	0.35	…
COPD	0.60	…	…	…
Liver disease	…	2.0	…	…
Vaccination	0.3	…	…	…
Pleural effusion	…	2.7	…	…
Multilobar infiltrates	…	2.1	…	1.81
Cavitation	…	4.1	…	…
Leukopenia	…	3.7	…	…
PSI class	…	1.3	…	2.75
Legionella pneumonia	…	…	…	2.71
Gram-negative pneumonia	…	…	…	4.34
Fluoroquinolone therapy	0.5	…	…	…
Concordant therapy	…	…	0.61	…
Discordant therapy	…	…	…	2.51

Prevention

Table 13. Recommendations for vaccine prevention of community-acquired pneumonia.

Factor	Pneumococcal polysaccharide vaccine	Inactivated influenza vaccine	Live attenuated influenza vaccine
Route of administration	Intramuscular injection	Intramuscular injection	Intranasal spray
Type of vaccine	Bacterial component (polysaccharide capsule)	Killed virus	Live virus
Recommended groups	All persons ≥65 years of age	All persons ≥50 years of age	Healthy persons 5–49 years of age,[a] including health care providers and household contacts of high-risk persons
	High-risk persons 2–64 years of age	High-risk persons 6 months–49 years of age	
	Current smokers[b]	Household contacts of high-risk persons	
		Health care providers	
		Children 6–23 months of age	

HCAP

Clinical Conditions Associated with and Likely Pathogens in HCAP

	Pathogen			
Condition	MRSA	Pseudomonas aeruginosa	Acinetobacter spp.	MDR Enterobacteriaceae
Hospitalization for 48 h	X	X	X	X
Hospitalization for 2 days in prior 3 months	X	X	X	X
Nursing home or extended-care facility residence	X	X	X	X
Antibiotic therapy in preceding 3 months		X		X
Chronic dialysis	X			
Home infusion therapy	X			
Home wound care	X			
Family member with MDR infection	X			X

TABLE 2. RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS CAUSING HOSPITAL-ACQUIRED PNEUMONIA, HEALTHCARE-ASSOCIATED PNEUMONIA, AND VENTILATOR-ASSOCIATED PNEUMONIA

- Antimicrobial therapy in preceding 90 d
- Current hospitalization of 5 d or more
- High frequency of antibiotic resistance in the community or in the specific hospital unit
- Presence of risk factors for HCAP:
  - Hospitalization for 2 d or more in the preceding 90 d
  - Residence in a nursing home or extended care facility
  - Home infusion therapy (including antibiotics)
  - Chronic dialysis within 30 d
  - Home wound care
  - Family member with multidrug-resistant pathogen
- Immunosuppressive disease and/or therapy

Major Points for Pathogenesis

1. Sources of pathogens for HAP include healthcare devices, the environment (air, water, equipment, and fomites), and commonly the transfer of microorganisms between the patient and staff or other patients (**Level II**) (3, 9, 12, 13, 27, 66, 92, 93).
2. A number of host- and treatment-related colonization factors, such as the severity of the patient's underlying disease, prior surgery, exposure to antibiotics, other medications, and exposure to invasive respiratory devices and equipment, are important in the pathogenesis of HAP and VAP (**Level II**) (40, 93, 94).
3. Aspiration of oropharyngeal pathogens, or leakage of secretions containing bacteria around the endotracheal tube cuff, are the primary routes of bacterial entry into the lower respiratory tract (**Level II**) (95–98).

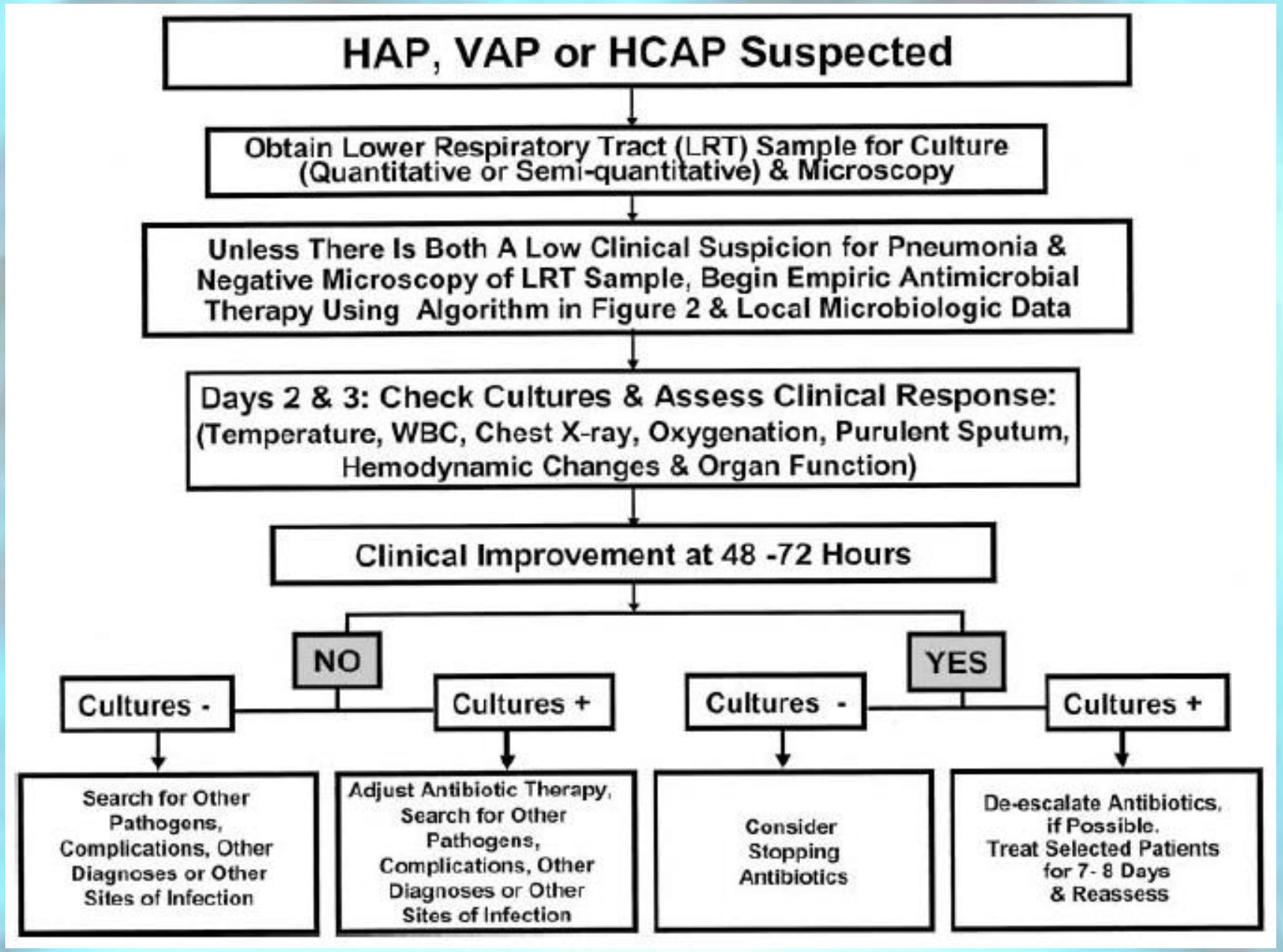

HAP, VAP or HCAP Suspected
Obtain Lower Respiratory Tract (LRT) Sample for Culture (Quantitative or Semi-quantitative) & Microscopy
Unless There Is Both A Low Clinical Suspicion for Pneumonia & Negative Microscopy of LRT Sample, Begin Empiric Antimicrobial Therapy Using Algorithm in Figure 2 & Local Microbiologic Data
Days 2 & 3: Check Cultures & Assess Clinical Response: (Temperature, WBC, Chest X-ray, Oxygenation, Purulent Sputum, Hemodynamic Changes & Organ Function)
Clinical Improvement at 48 -72 Hours
NO
YES
Cultures -
Cultures +
Cultures -
Cultures +
Search for Other Pathogens, Complications, Other Diagnoses or Other Sites of Infection
Adjust Antibiotic Therapy, Search for Other Pathogens, Complications, Other Diagnoses or Other Sites of Infection
Consider Stopping Antibiotics
De-escalate Antibiotics, if Possible. Treat Selected Patients for 7- 8 Days & Reassess

TABLE 3. INITIAL EMPIRIC ANTIBIOTIC THERAPY FOR HOSPITAL-ACQUIRED PNEUMONIA OR VENTILATOR-ASSOCIATED PNEUMONIA IN PATIENTS WITH NO KNOWN RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS, EARLY ONSET, AND ANY DISEASE SEVERITY

Potential Pathogen	Recommended Antibiotic*
Streptococcus pneumoniae†	Ceftriaxone
Haemophilus influenzae	*or*
Methicillin-sensitive *Staphylococcus aureus*	Levofloxacin, moxifloxacin, or ciprofloxacin
Antibiotic-sensitive enteric gram-negative bacilli	*or*
Escherichia coli	Ampicillin/sulbactam
Klebsiella pneumoniae	*or*
Enterobacter species	Ertapenem
Proteus species	
Serratia marcescens	

TABLE 4. INITIAL EMPIRIC THERAPY FOR HOSPITAL-ACQUIRED PNEUMONIA, VENTILATOR-ASSOCIATED PNEUMONIA, AND HEALTHCARE-ASSOCIATED PNEUMONIA IN PATIENTS WITH LATE-ONSET DISEASE OR RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS AND ALL DISEASE SEVERITY

Potential Pathogens	Combination Antibiotic Therapy*
Pathogens listed in Table 3 and MDR pathogens *Pseudomonas aeruginosa* *Klebsiella pneumoniae* (ESBL$^+$)† *Acinetobacter* species†	Antipseudomonal cephalosporin (cefepime, ceftazidime) *or* Antipseudomonal carbepenem (imipenem or meropenem) *or* β-Lactam/β-lactamase inhibitor (piperacillin–tazobactam) *plus* Antipseudomonal fluoroquinolone† (ciprofloxacin or levofloxacin) *or* Aminoglycoside (amikacin, gentamicin, or tobramycin) *plus*
Methicillin-resistant *Staphylococcus aureus* (MRSA) *Legionella pneumophila*†	Linezolid or vancomycin‡

Major Points and Recommendations for Optimal Antibiotic Therapy

1. Empiric therapy of patients with severe HAP or VAP requires the use of antibiotics at optimal doses, to ensure maximum efficacy (**Level I**) (240, 242–247). Initial therapy should be administered to all patients intravenously, with a switch to oral/enteral therapy in selected patients with a good clinical response and a functioning intestinal tract. Highly bioavailable agents, such as the quinolones and linezolid, may be easily switched to oral therapy in such patients (**Level II**) (248, 253, 254).

3. Combination therapy should be used if patients are likely to be infected with MDR pathogens (**Level II**) (21, 205). No data have documented the superiority of this approach compared with monotherapy, except to enhance the likelihood of initially appropriate empiric therapy (**Level I**) (262).

4. If patients receive combination therapy with an aminoglycoside-containing regimen, the aminoglycoside can be stopped after 5–7 days in responding patients (**Level III**) (235).
5. Monotherapy with selected agents can be used for patients with severe HAP and VAP in the absence of resistant pathogens (**Level I**) (240, 242–247). Patients in this risk group should initially receive combination therapy until the results of lower respiratory tract cultures are known and confirm that a single agent can be used (**Level II**).
6. If patients receive an initially appropriate antibiotic regimen, efforts should be made to shorten the duration of therapy from the traditional 14 to 21 days to periods as short as 7 days, provided that the etiologic pathogen is not *P. aeruginosa*, and that the patient has a good clinical response with resolution of clinical features of infection


"Thats all Folks!"