Pneumonia

Term	Definition
Classification by site of acquisition	
Community-acquired pneumonia (CAP)	An acute infection of the pulmonary parenchyma acquired outside of health care settings
Hospital-acquired pneumonia (HAP)	Pneumonia acquired ≥48 hours after hospital admission; includes both HAP and VAP
Ventilator-associated pneumonia (VAP)	Pneumonia acquired ≥48 hours after endotracheal intubation VAP also includes HAP that occurs within 48 hours of extubation
Classification by etiology	
Atypical pneumonia	Pneumonia caused by "atypical"¶ bacterial pathogens including ***Legionella*** spp, ***Mycoplasma*** *pneumoniae*, ***Chlamydia*** *pneumoniae*, *Chlamydia psittaci*, and ***Coxiella*** *burnetiid*
Aspiration pneumonia	Pneumonia resulting from entry of gastric or oropharyngeal fluid, which may **contain bacteria and/or be of low pH, or exogenous substances** (eg, ingested food particles or liquids, mineral oil, salt or fresh water) into the lower airways
Chemical pneumonitis	Aspiration of substances (**acidic gastric fluid**) that cause an **inflammatory reaction** in the lower airways, **independent of bacterial infection**
Bacterial aspiration pneumonia	An active **infection** caused by inoculation of large amounts of **bacteria** into the lungs via orogastric contents

Community-acquired pneumonia (CAP)

Risk factors

- age ≥65 years
- chronic comorbidities
- concurrent or antecedent respiratory viral infections
- impaired airway protection
- smoking
- alcohol abuse
- lifestyle factors (eg, crowded living conditions)

Microbiology

The most commonly identified causes of CAP include :

- respiratory viruses
  - particularly coronavirus during the pandemic
- typical bacteria
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - *Moraxella catarrhalis*
- atypical bacteria
  - *Legionella* spp
  - *Mycoplasma pneumoniae*
  - *Chlamydia pneumoniae*

Pseudomonas and methicillin-resistant *Staphylococcus aureus* (MRSA) are less common causes that predominantly occur in patients with specific risk factors

Risk factors for specific pathogens in adults

Condition	Commonly encountered pathogen(s)
Alcohol use disorder	**Streptococcus pneumoniae** **oral anaerobes** **Klebsiella** pneumoniae **Acinetobacter** species Mycobacterium tuberculosis
COPD and/or smoking	**Haemophilus influenzae** **Pseudomonas** aeruginosa **Legionella** species **S.pneumoniae** **Moraxella** catarrhalis, **Chlamydia** 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	**Chlamydia** psittaci
Exposure to farm animals or parturient cats	**Coxiella** burnetti (Q fever)
Hotel or cruise ship stay in previous two weeks	**Legionella** species
Structural lung disease (eg, bronchiectasis)	**P. aeruginosa** S. aureus Burkholderia cepacian
Injection drug use	**S. aureus** Anaerobes M. tuberculosis S. pneumoniae

Risk factors for MRSA and *Pseudomonas* in adults

	MRSA	*Pseudomonas*
Strong risk factors*	Known MRSA colonization	Known *Pseudomonas* colonization
	Prior MRSA infection	Prior *Pseudomonas* infection
	Detection of gram-positive cocci in clusters on a good-quality sputum Gram stain	Detection of gram-negative rods on a good-quality sputum Gram stain
		Hospitalization with receipt of IV antibiotics in the prior 3 months
Other factors that should raise suspicion for infection¶	Recent hospitalization or antibiotic use, particularly hospitalization with receipt of IV antibiotics in the prior 3 months	Recent hospitalization or stay in a long term care facility
	Recent influenza-like illness	Recent antibiotic use of any kind
	Necrotizing or cavitary pneumonia	Frequent COPD exacerbations requiring glucocorticoid and/or antibiotic use
	Empyema[Δ]	Other structural lung diseases (eg, bronchiectasis, cystic fibrosis)
	Immunosuppression	Immunosuppression
	Risk factors for MRSA colonization, including: End-stage kidney disease Crowded living conditions (eg, incarceration)[Δ] Injection drug use[Δ] Contact sports participation[Δ] Men who have sex with men[Δ]	

Making the diagnosis

clinically compatible syndrome (eg, fever, dyspnea, cough, and leukocytosis).

with

an infiltrate on chest imaging in a patient

a posteroanterior and lateral chest radiograph is sufficient.

Computed tomography scan is reserved for selected cases.

Determining severity of illness

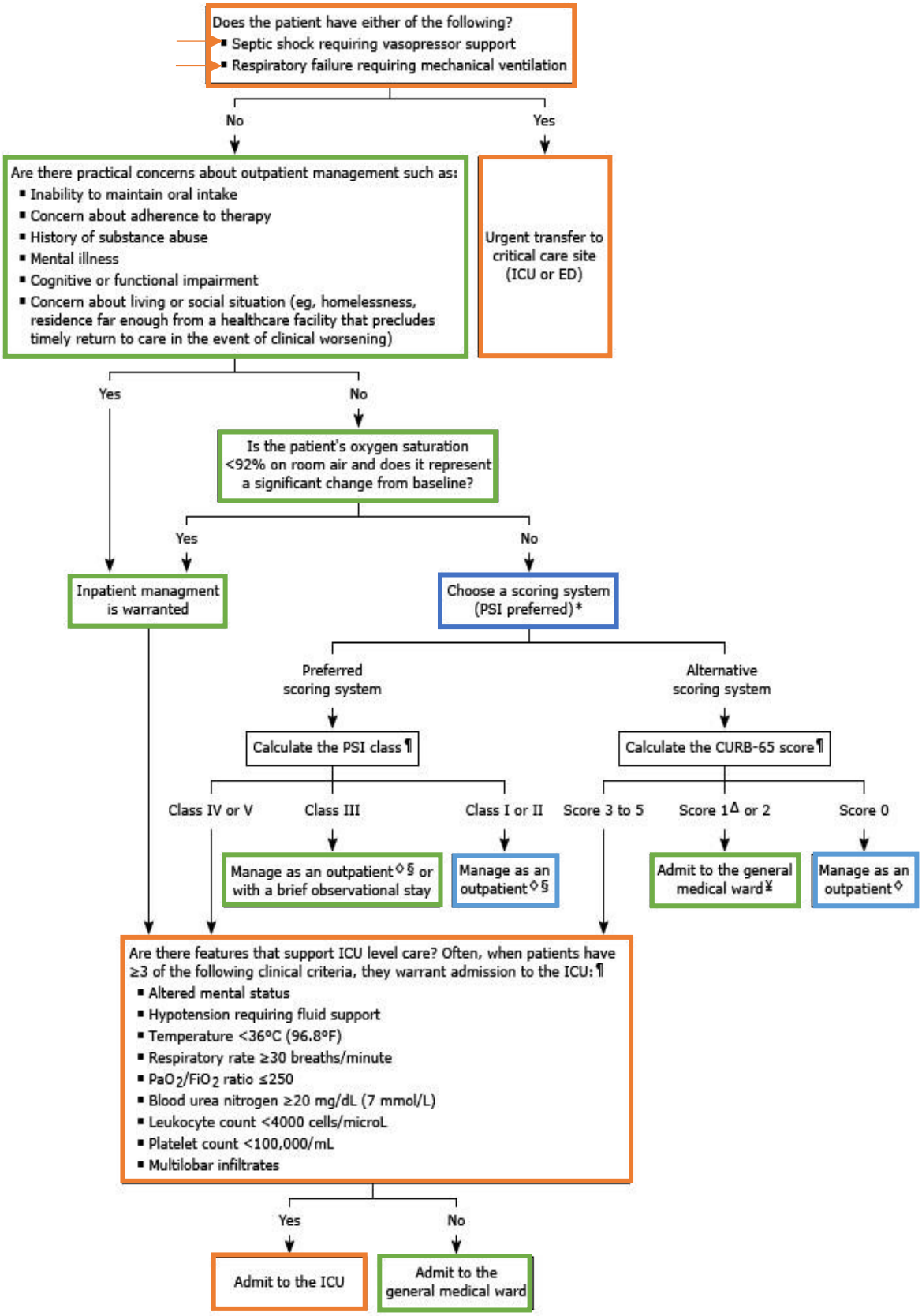
the initial steps in management are

defining the severity of illness

and

determining the most appropriate site of care

Determining the appropriate site of treatment in adults



Δ Using the CURB-65 score, if the patient has a score of 1 because he or she is **≥65 years of age** and he or she has **no major comorbidities**, hospital admission is **not** necessarily indicated

Pneumonia Severity Index

Risk factors	Points
Demographic factors	
Age for a man	Age (in years)
Age for a woman	Age (in years) – 10
Nursing home resident	+10
Coexisting illnesses	
Neoplastic disease (active)	+30
Chronic liver disease	+20
Heart failure	+10
Cerebrovascular disease	+10
Chronic renal disease	+10
Physical examination findings	
Altered mental status	+20
Respiratory rate ≥30/minute	+20
Systolic blood pressure <90 mmHg	+20
Temperature <35°C or ≥40°C	+15
Pulse ≥125 beats/minute	+10
Laboratory and radiographic findings	
Arterial pH <7.35	+30
Blood urea nitrogen ≥30 mg/dL (11 mmol/L)	+20
Sodium <130 mmol/L	+20
Glucose ≥250 mg/dL (14 mmol/L)	+10
Hematocrit <30%	+10
Partial pressure of arterial oxygen <60 mmHg*	+10
Pleural effusion on chest radiograph	+10

Class	Points	Mortality (percent)
I	No predictors	0.1
II	≤70	0.6
III	71 to 90	0.9
IV	91 to 130	9.3
v	>130	27.0

we determine our approach to microbiologic testing based on this assessment

	Severity score*	Site of care	Microbiologic evaluation
Mild	PSI: 1 or 2 or CURB-65: 0[¶]	Ambulatory care	testing is usually not needed
Moderate	PSI: 3 or CURB-65: 1[¶] to 2	General medical ward	Blood cultures Sputum Gram stain and culture Urine streptococcal antigen *Legionella* testing[◇] Respiratory viral panel during respiratory virus season[§]
Severe	PSI: 4 or 5 or CURB-65: ≥3 or criteria for ICU admission[†]	ICU	Blood cultures Sputum Gram stain and culture Urine streptococcal antigen test *Legionella* testing[◇] Respiratory viral panel[§]

Empiric antibiotic selection

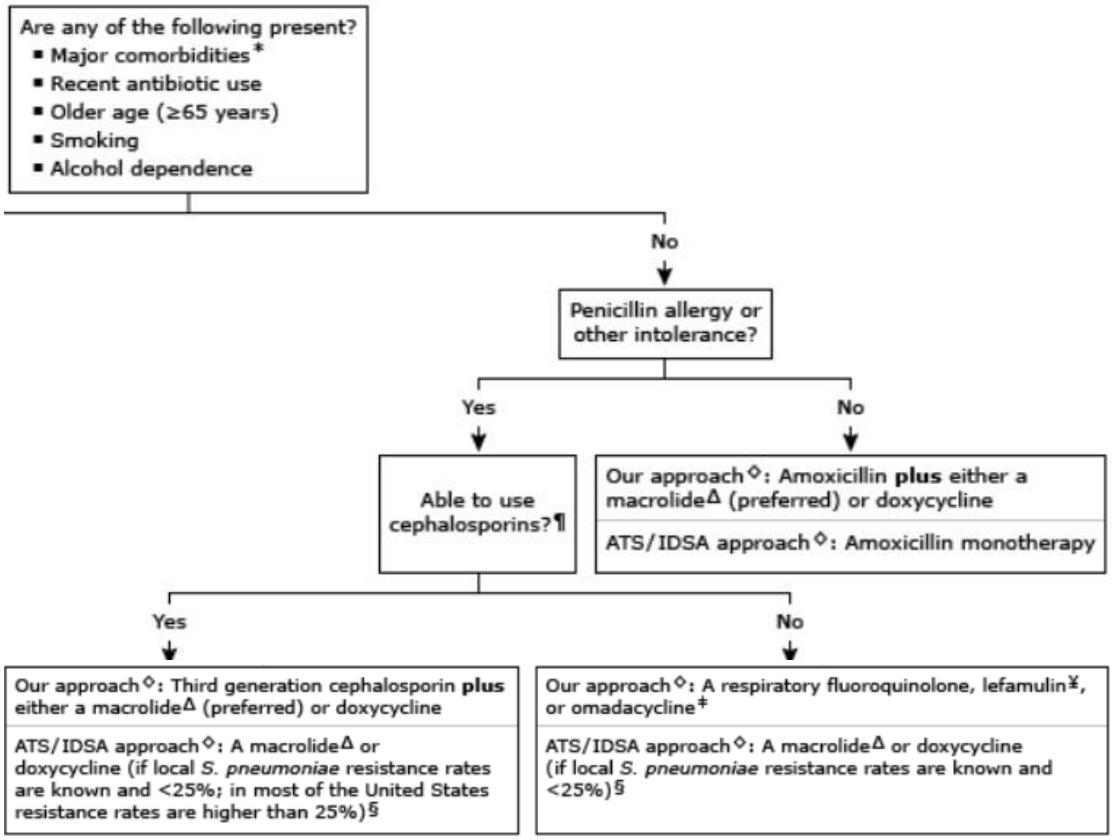
The selection of an empiric antibiotic regimen is based on the **severity** of illness, **site of care**, and **most likely pathogens**.

We generally **start** antibiotics **as soon as we are confident** that CAP is the appropriate working diagnosis and, ideally, **within four hours** of presentation for **inpatients** and **within one hour** of presentation for those who are **critically ill**

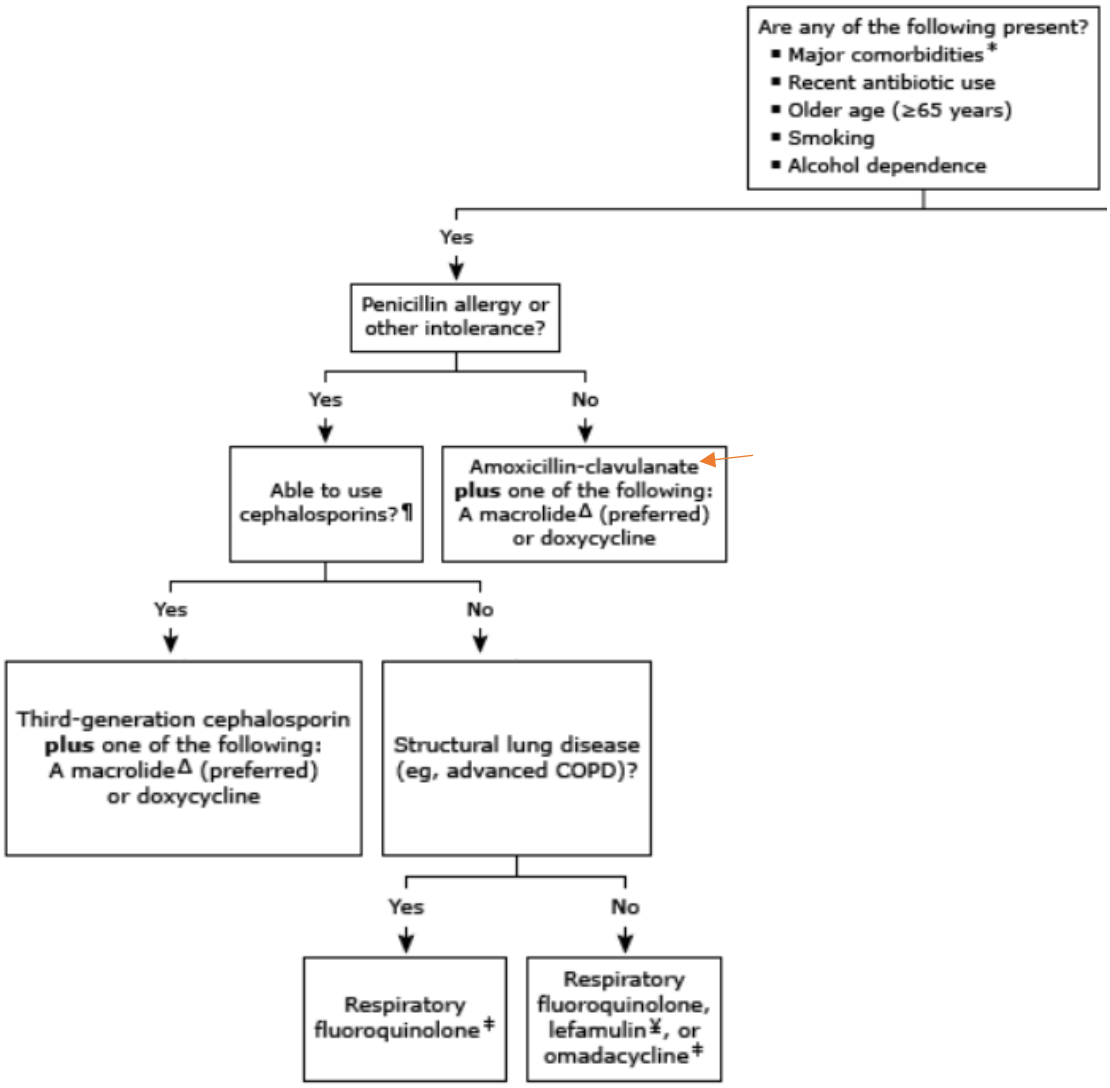
Empiric outpatient antibiotic selection in adults

For most outpatients, we **prefer** to use **combination therapy** with a **beta-lactam** and either a **macrolide** (preferred) or doxycycline.

(Reasons to avoid macrolides include baseline **prolonged QTc** interval or risk for QTc prolongation (eg, **hypokalemia**, **hypomagnesemia**, clinically significant **bradycardia**, or **use of other QT-prolonging agents**)



Alternatives to beta-lactam-based regimens include **monotherapy** with either a **fluoroquinolone** or, alternatively
, lefamulin or omadacycline (newer agents: not appropriate for patients with structural lung disease).

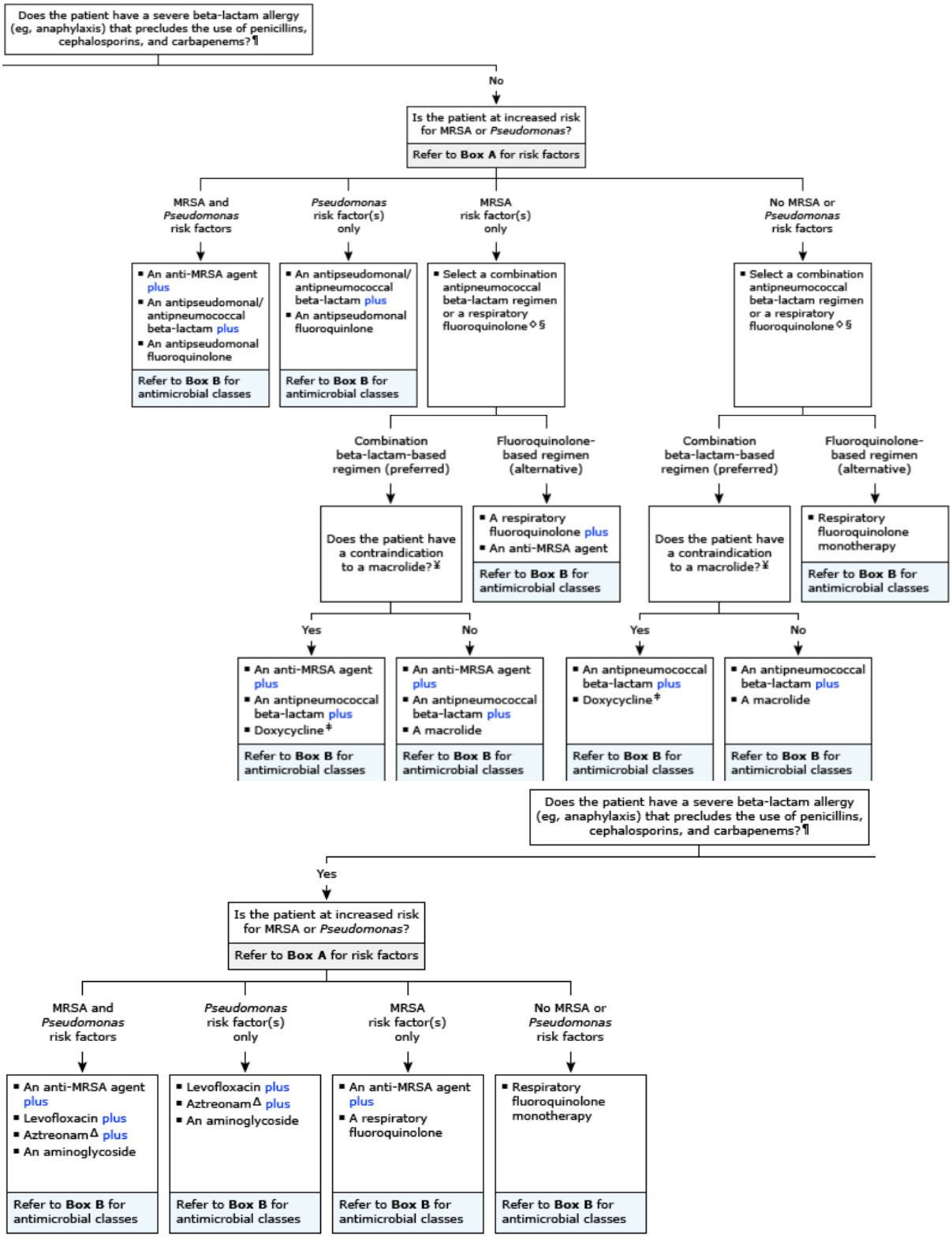


This approach differs from the ATS/IDSA recommend **monotherapy** with amoxicillin , doxycycline, or a macrolide as first line and monotherapy (for patients **without comorbidities** if local **S. pneumoniae resistance rates are <25 percent**)

Individuals with a past reaction to penicillin that was **mild** (not Stevens Johnson syndrome, toxic epidermal necrolysis, or drug reaction with eosinophilia and systemic symptoms [DRESS]) **and** did **not** have features of an immunoglobulin (Ig)E-mediated reaction **can** receive a broad-spectrum (third- or fourth-generation) cephalosporin or carbapenem safely

Empiric antibiotic selection for adults admitted to the general medical ward*

For most inpatients admitted to the general medical ward, treatment options include either **intravenous (IV) combination** therapy with a **beta-lactam plus** a **macrolide** or doxycycline
or monotherapy with a respiratory **fluoroquinolone**



Δ Empiric therapy with aztreonam plus levofloxacin plus an aminoglycoside is generally appropriate for patients who warrant antipseudomonal coverage but have beta-lactam allergies that preclude the use of penicillins, cephalosporins, and carbapenems.

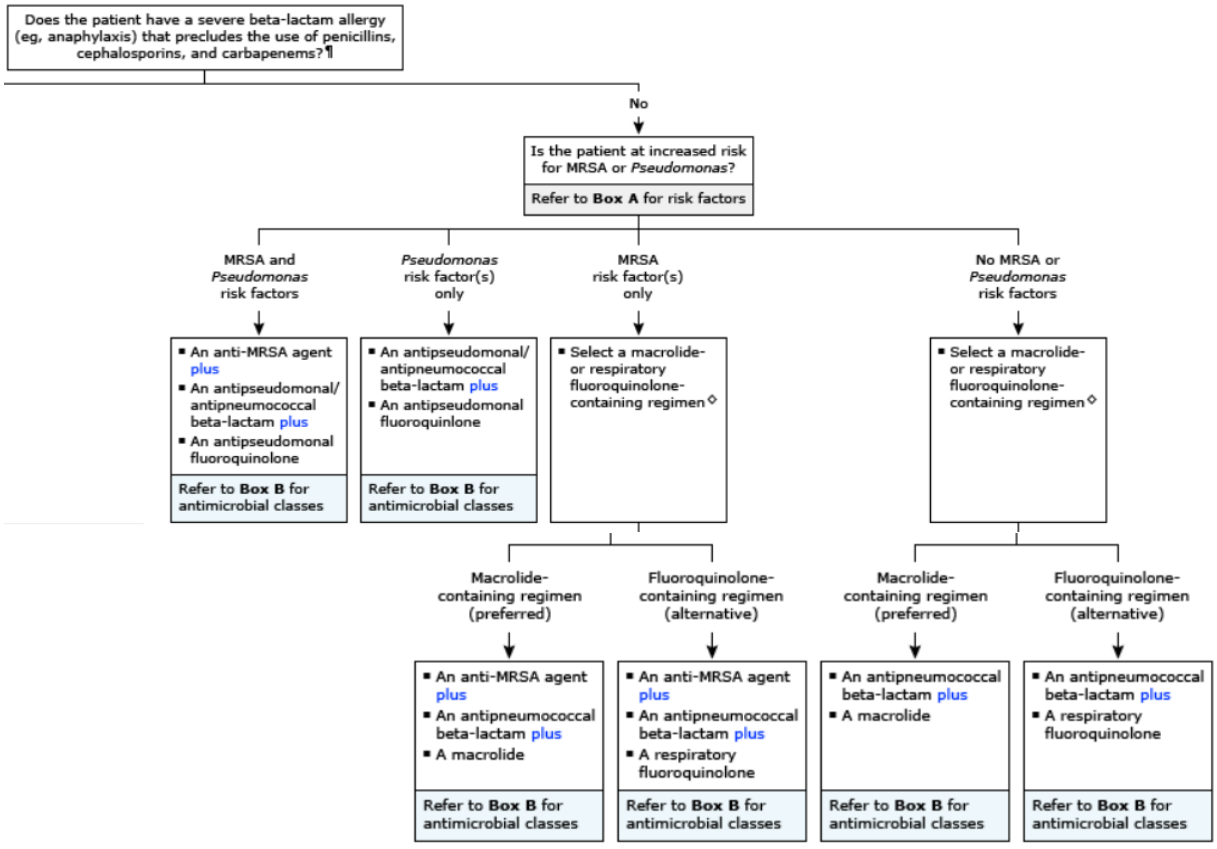
However, patients with a prior lifethreatening or **anaphylactic reaction to ceftazidime** should **not be given aztreonam** unless evaluated by an allergy specialist because of the possibility of cross-reactivity.
Such patients can receive levofloxacin plus an aminoglycoside for antipseudomonal coverage in the interim

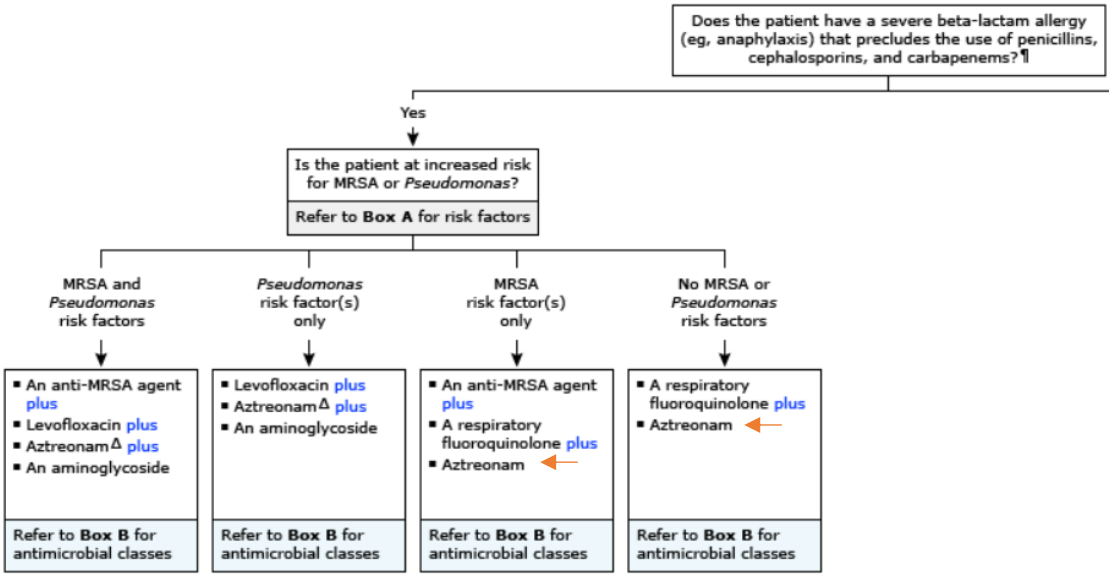
The combination of vancomycin and piperacillin-tazobactam has been associated with acute kidney injury

Community-acquired pneumonia

Empiric antibiotic selection for adults admitted to the intensive care unit*

For most patients admitted to the intensive care unit (ICU), treatment options include **IV combination therapy** with a **beta-lactam plus** either a **macrolide or** a **respiratory fluoroquinolone**.





Adjunctive glucocorticoids

The benefit appears greatest when they are given early in the course.

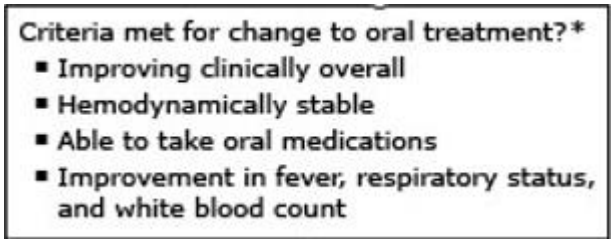
we add hydrocortisone for most immunocompetent patients with **respiratory failure** due to CAP who **require invasive or non-invasive mechanical ventilation** or with significant **hypoxemia (PaO2:FIO2 ratio <300 with an FiO_2 requirement of ≥50 percent** and **use of either high flow nasal cannula or a nonrebreathing mask**)

unless there are reason to avoid their use (eg, infection with certain pathogen [**influenza**, **fungi**, **tuberculosis**, or **immunocompromise**])

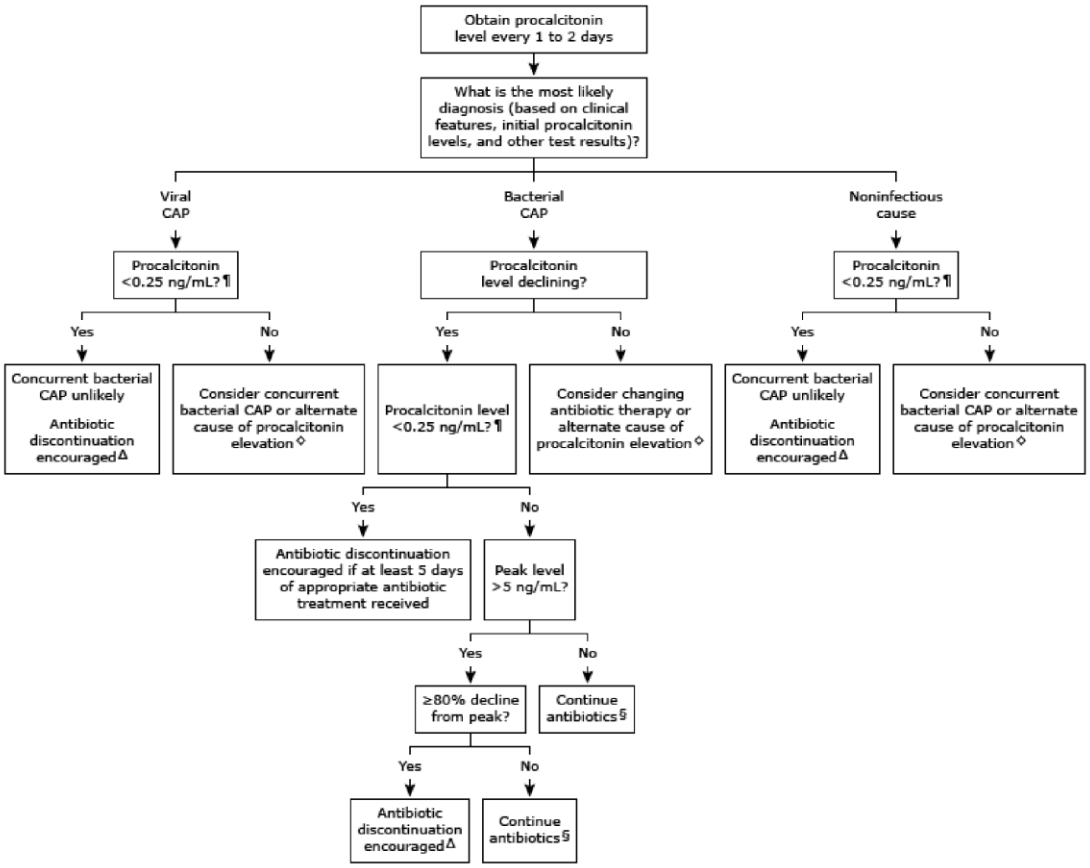
Directed antibiotic therapy (Antibiotic de-escalation)
causative pathogen has been identified, we tailor therapy to target the pathogen

Duration of antibiotics

we treat until the patient has been **afebrile** and **clinically stable** for **at least 48 hours** and for a **minimum of five days**.
Patients with **mild** infection generally require **five to seven days** of therapy
those with **severe** infection or **chronic comorbidities** generally require **7 to 10 days** of therapy



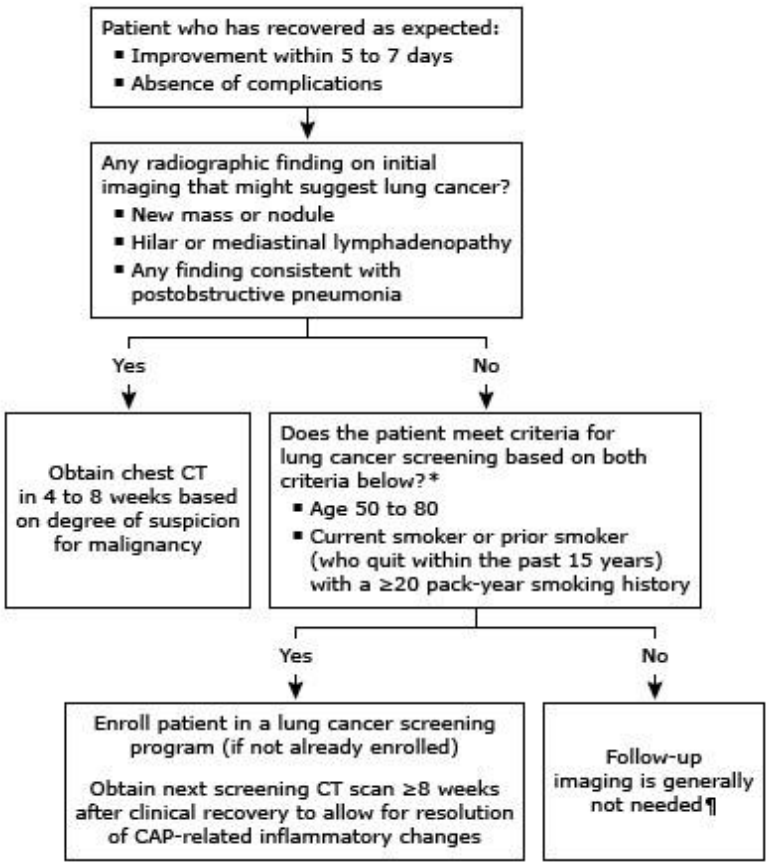
procalcitonin-guided antibiotic discontinuation in clinically stable adult patients with known or suspected community-acquired pneumonia



Usual duration of findings in treated community-acquired pneumonia

Abnormality	Duration(days)
Tachycardia and hypotension	2
Fever, tachypnea, and hypoxia	3
Cough	14
Fatigue	14
Infiltrates on chest radiograph	30

Follow-up imaging for immunocompetent adults who have recovered from community-acquired pneumonia



Lack of response to antibiotics

Failure to respond to antibiotic treatment within 72 hours should prompt reconsideration of the diagnosis and empiric treatment regimen as well as an assessment for complications

Nonresolving CAP

initial symptoms will neither progress nor improve with at least **seven** days of appropriate empiric antibiotic treatment.
Potential causes of nonresolving CAP include:

- **Loculated infection** – complications such as lung abscess, empyema
- **Delayed clinical response** – patients with **multiple comorbidities**, **severe** pneumonia, **bacteremia**, treatment **response** may be **slow** (**8** or **9** days)
- **Bronchial obstruction** – postobstructive pneumonia
- **Pathogens that cause subacute/chronic CAP** – *Mycobacterium tuberculosis*, nontuberculous mycobacteria, fungi, or less common bacteria (*Nocardia*)
- **Incorrect initial diagnosis** – (malignancy or inflammatory lung disease)

Prevention

smoking cessation

influenza vaccination for the general population

pneumococcal vaccination for at-risk populations

hospital-acquired pneumonia

Pathogenesis – The primary route of infection of the lungs is through microaspiration of organisms that have colonized the oropharyngeal tract

Microbiology

Staphylococcus aureus and *Pseudomonas aeruginosa* are the most common pathogens.

MDR bacteria are most common in patients who have been hospitalized for prolonged periods (≥5 days)

Diagnosis

new lung infiltrate

plus

clinical evidence of infectious origin

(new onset of fever, purulent sputum, leukocytosis, and decline in oxygenation)

Identifying risk factors for MDR pathogens and mortality in VAP and nvHAP

Non-ventilator hospital-acquired pneumonia

Risk factors for MDR pathogens and/or increased mortality in adults

Risk factors for increased mortality:
• **Ventilatory support for HAP** • **Septic shock**
Risk factor for MDR *Pseudomonas aeruginosa*, other gram-negative bacilli, and MRSA:
• **IV antibiotics within the past 90 days**
Risk factors for MDR *Pseudomonas aeruginosa* and other gram-negative bacilli:
• **Colonization with or prior isolation of MDR *Pseudomonas* or other gram-negative bacilli**
Risk factors for MRSA:
• **Treatment in an ICU in which >20% of *Staphylococcus aureus* isolates are methicillin resistant** • **Treatment in an ICU in which the prevalence of MRSA is not known** • **Colonization with or prior isolation of MRSA**

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

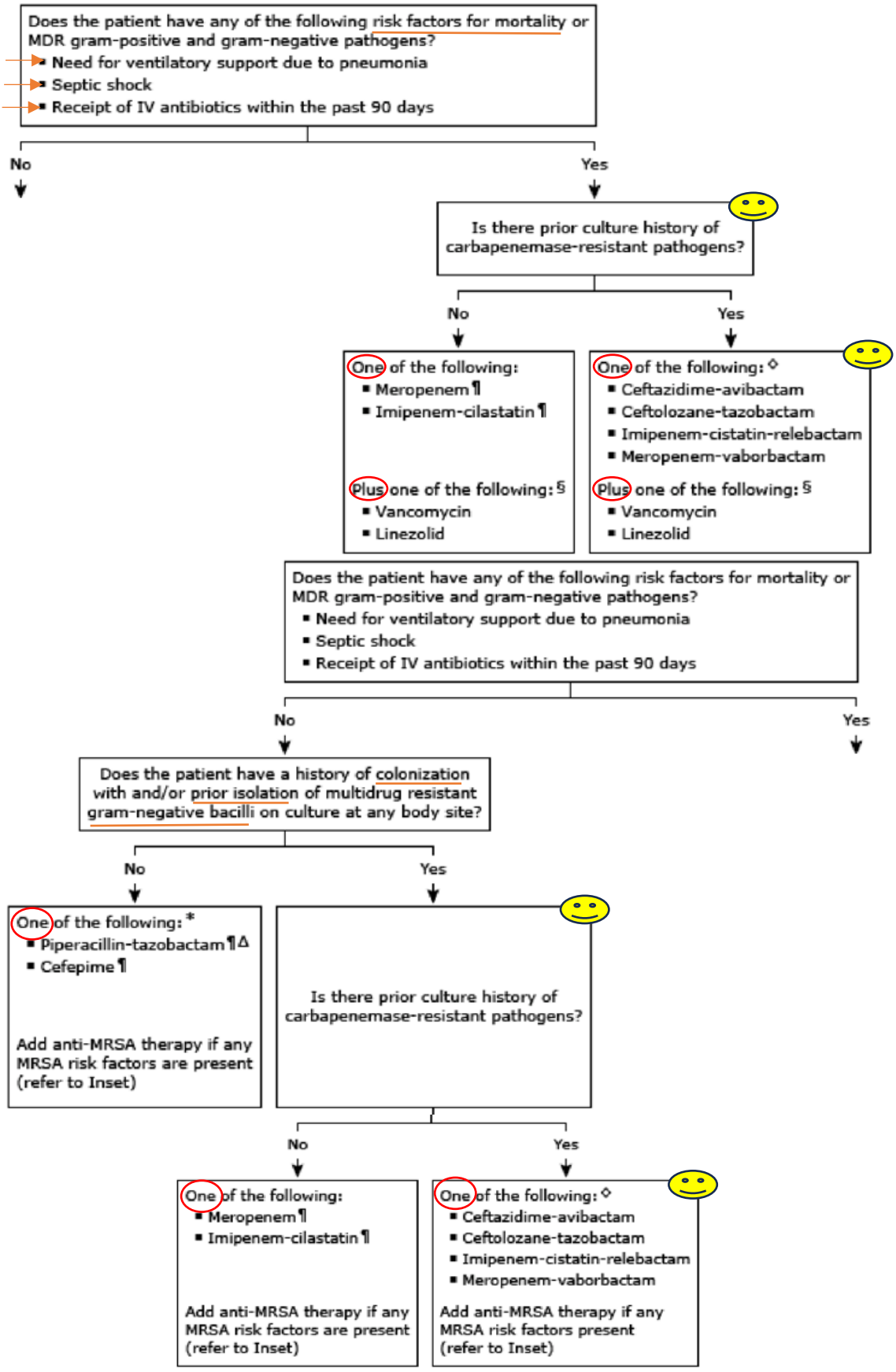
Risk factors for MDR pathogens (including *Pseudomonas aeruginosa*, other gram negative bacilli, and MRSA):
• **IV antibiotic use within the previous 90 days** • **Septic shock at the time of VAP** • **ARDS preceding VAP** • **≥5 days of hospitalization prior to the occurrence of VAP** • **Acute renal replacement therapy prior to VAP onset**
Risk factors for MDR *Pseudomonas* and other gram-negative bacilli:
• **Treatment in an ICU in which >10% 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 on culture from any body site**
Risk factors for MRSA:
• **Treatment in an ICU in which >10 to 20% of *Staphylococcus aureus* isolates are methicillin resistant** • **Treatment in an ICU in which the prevalence of MRSA is not known** • **Colonization with or prior isolation of MRSA on culture from any body site**

Choosing an empiric regimen

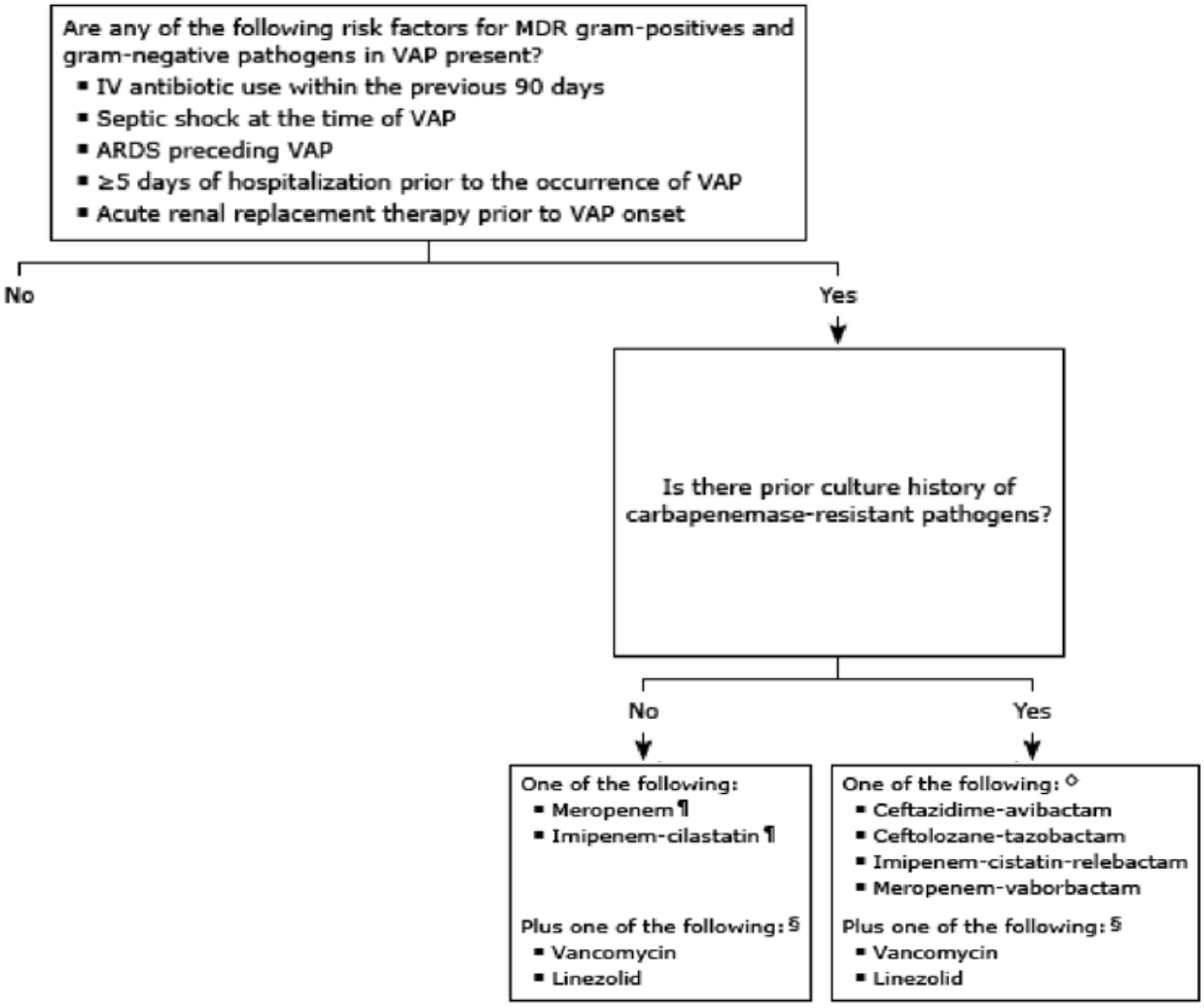
The choice of the antibiotic treatment regimen for hospital-acquired (or nosocomial) pneumonia (HAP) should be informed by:

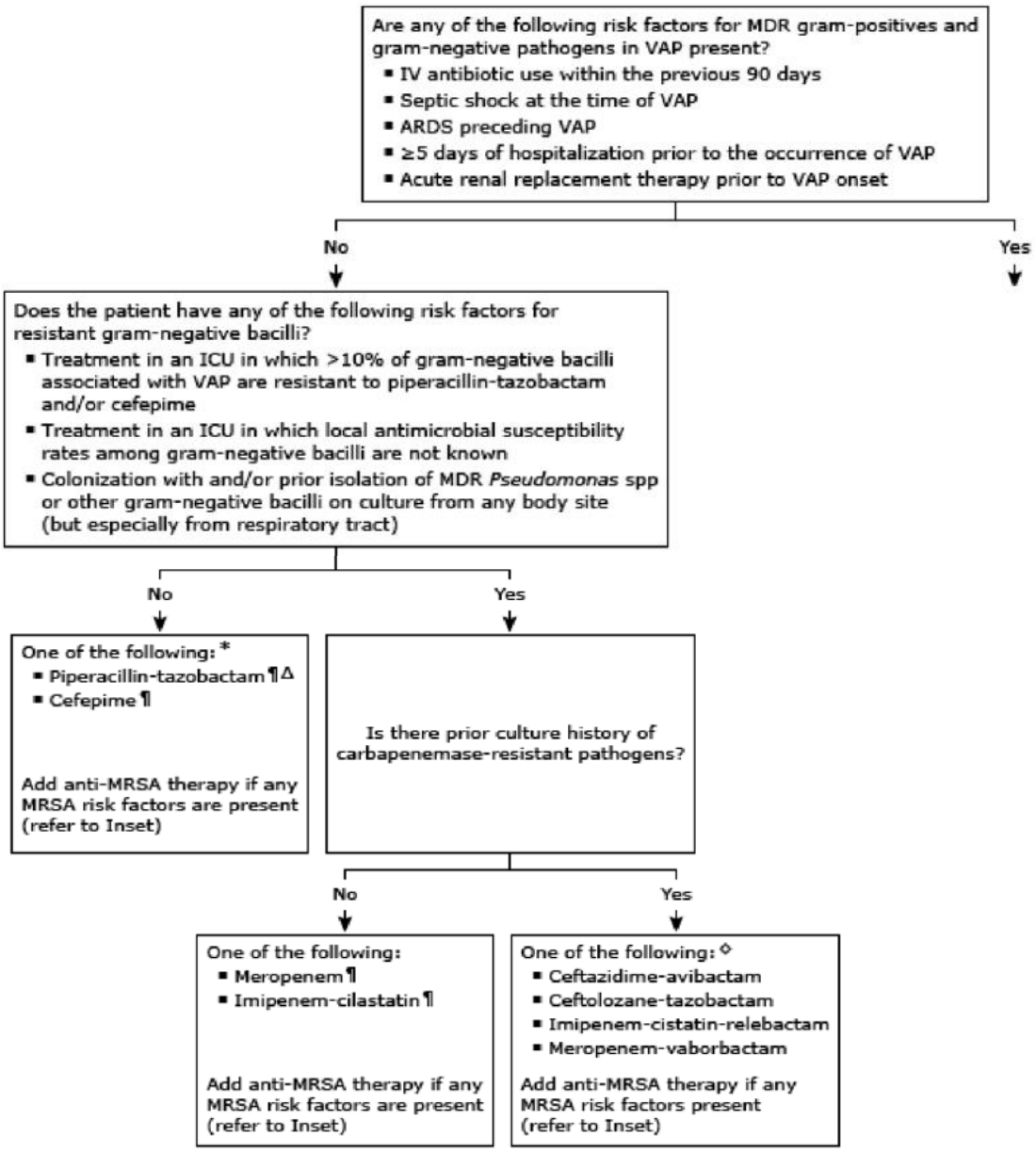
- the patient's recent **antibiotic therapy** (if any)
- the **resident flora** and **resistance rates** in the hospital or intensive care unit (ICU)
- the presence of **underlying diseases**
- **severity** of illness
- available **culture data** (including past microbiology data) and Gram stain
- additional risk factors for MDR pathogens
- potential **toxicities**
- potential drug **interactions**
- **cost** , **availability**

Empiric treatment of nonventilator hospital-associated pneumonia



Empiric treatment of ventilator-associated pneumonia (VAP)





- piperacillin-tazobactam or cefepime because they are **more** likely to have **activity against gram-negative** bacilli **than levofloxacin**.
- **levofloxacin** 750 mg IV daily may be **preferred** if there is a **high suspicion** for ***Legionella*** spp infection and **local resistance rates** of *S. aureus*, *P. aeruginosa*, and other gram-negative bacilli to fluoroquinolones are **low**
- we generally reserve **imipenem** and **meropenem** for patients with a high likelihood of infection with **extended-spectrum beta-lactamase** (**ESBL**)-producing gram-negative bacilli
- If none **of beta-lactam beta-lactamase agents** are available, combination therapy of a **carbapenem** (meropenem, imipenem-cilastatin) **with** another **anti-gram negative agent** (aminoglycosides, anti-pseudomonal fluoroquinolone, polymyxin/colistin or aztreonam) is an appropriate alternative
- we generally prefer an aminoglycoside over a fluoroquinolone if there is no concern for *Legionella*, as aminoglycosides are more likely to have **in vitro activity** against gram-negative bacilli in those with risk factors for resistance

Early de-escalation based on nasal MRSA swab

We send nasal MRSA swabs on all patients with suspected MRSA nvHAP/VAP. If the nasal MRSA swab result is negative, we suggest stopping anti-MRSA empiric therapy to reduce unnecessary antibiotic use

No pathogen identified and clinically improving

For patients who are clinically improving, **empiric treatment** for MRSA, *Pseudomonas aeruginosa,* or MDR gram-negative bacilli can be **discontinued** if these organisms have **not grown in culture** from a high-quality sputum specimen within 48 to 72 hours.

Pathogen identified and clinically improving

the empiric regimen should be tailored to the pathogen's susceptibility pattern

No clinical improvement after 48 to 72 hours

- **evaluated for:**
  - complications (eg, empyema, lung abscess)
  - other sites of infection
  - alternate diagnoses (eg, thromboembolic disease, pulmonary edema, malignancy, hypersensitivity reaction)

- **additional** diagnostic **pulmonary cultures** should be obtained
- **empiric regimen can be expanded** to cover additional resistant organisms
  (*Legionella pneumoniae*, *Stenotrophomonas maltophilia*, *Acinetobacter*)

Duration

We suggest treating most patients with HAP or VAP for **seven** days

patients with **metastatic infection**, gram-positive **bacteremia**, **slow response** to therapy, **immunocompromise**, and pyogenic **complications** such as empyema or lung abscess, the duration of therapy should be individualized and courses **longer** than seven days may be warranted

switched to oral therapy

hemodynamically stable, **clinically improving**, and **able to tolerate oral medications**

Strategies to prevent ventilator-associated pneumonia

The efficacy of inhaled antibiotics for the prevention of VAP is uncertain

- reduced occurrence of VAP compared with placebo
- no difference detected in duration of mechanical ventilation, days of antibiotic utilization, or mortality

Essential practices that should be provided whenever possible to all patients to prevent VAP

Use high-flow nasal oxygen or NIPPV, when appropriate, to **avoid intubation**

acilitate **early extubation**

prevent reintubation

Provide **enteral instead** of parenteral nutrition, when possible

Avoid changing the ventilator circuit except in the following circumstances:

The ventilator circuit is **visibly soiled**

The ventilator circuit is **malfunctioning**

A ventilator circuit change is **recommended** after a fixed number of days **by the manufacturer**

Minimize sedation

Maintain and improve **physical conditioning** through active and passive exercises

Provide **oral care**, including toothbrushing (do not use chlorhexidine)

Set the **head** of the patient's bed to an elevation between **30 and 45 degrees**

If VAP rates remain high despite implementing the preceding practices, the following additional practices can be considered:

Tracheostomy after 1 to 2 weeks of sustained invasive mechanical ventilation, taking into account patient trajectory and preferences*

Using **endotracheal tubes** with **subglottic secretion drainage** ports for patients expected to require more than 48 to 72 hours of mechanical ventilation*

Postpyloric feeding (instead of gastric feeding) for patients at high risk of aspiration or with gastric intolerance*