

Therapy of Pneumonia

• serious problem

CAP
HAP
& (VAP)

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Pneumonias

- Pneumonia is one of the most common causes of severe sepsis, and infectious cause of death in children and adults.
- It affects all ages, although the clinical manifestations are most severe in the very young, the elderly, and the chronically ill.
- Mortality rate is high.

Pneumonias Causative Agents

- The most prominent pathogen causing community-acquired pneumonia (CAP) in otherwise healthy adults is *Streptococcus pneumoniae* and accounts for up to 35% (12%-68%) of all acute cases. (1)
- Other common pathogens include:
 1. *H. influenzae* (2.5%-45%). due to vaccine ↓↓↓ (1)
 2. Atypical pathogens: *Mycoplasma pneumoniae*, *Legionella* sps, and *Chlamydia pneumoniae* (~20%). (2) (3)
 3. A variety of viruses including influenza viruses.

Pneumonia Causative Agents

- The leading causative agents in hospital-acquired pneumonia (HAP) are Gram-negative aerobic bacilli, *S. aureus*, and multidrug-resistant (MDR) pathogens. ②
- In pneumonia that follows the aspiration of gastric or oropharyngeal contents, anaerobic bacteria are the most common etiologic agents. ③
- Ventilator-associated pneumonia (VAP) is also associated with MDR pathogens. ④

Pneumonia Causative Agents

⑤

- Pneumonia in infants and children is caused by a wider range of microorganisms, and viruses predominate, especially RSV, parainfluenza, and adenovirus.

أهم عندهم من الفيروسات

- *M. pneumoniae* is an important pathogen in older children.

5 - 20 y.o

⑥

Pneumonia Causative Agents

- Beyond the neonatal period, ^(A)*S. pneumoniae* is the major bacterial pathogen in childhood pneumonia, followed by group A *Streptococcus* and *S. aureus*. ^(B) ^(C)
- *H. influenzae* type b, once a major childhood pathogen, has become an infrequent cause of pneumonia since the introduction of active vaccination against this organism in the late 1980s. ^(D)

فصل ٢٠ من الميكروبيولوجيا

Pneumonia Causative Agents

- Pneumonia in non-ambulatory residents of nursing homes and other long-term care facilities is similar to hospital-acquired pneumonia and should be treated according to the HAP guidelines.
- Certain other patients may be better served by management in accordance with CAP guidelines.

Therapy of Pneumonia

Treatment:

The goals of therapy are:

1. Eradication of the offending organism through selection of the appropriate antibiotic. ← *الهدف*
2. Achieving complete clinical cure, with minimal drug-induced toxicity.

Therapy of Pneumonia

General Approach to Treatment:

Supportive care:

- 1) Humidified oxygen for hypoxemia.
- 2) Bronchodilators when bronchospasm is present.
- 3) Chest physiotherapy and postural drainage with evidence of retained secretions.
- 4) Adequate hydration (IV if necessary).
- 5) Optimal nutritional support.
- 6) Control of fever.

- if sepsis + severe case → blood culture would help.

Therapy of Pneumonia

دفع امشي تا خذ العينة من مكانها الصحيح

- Appropriate sputum samples should be obtained to determine the microbiologic etiology.
- Selection of an appropriate antimicrobial must be made based on the patient's probable or documented microbiology.

Pharmacologic Therapy:

- Antibiotic concentrations in respiratory secretions in excess of the pathogen MIC are necessary for successful treatment of pulmonary infections. minimum inhibitory concentration

Therapy of Pneumonia

Selection of Antimicrobial Agents:

- Treatment, initially involves the empirical use of a relatively broad-spectrum antibiotic(s) that is effective against probable pathogens after appropriate specimens for culture and sensitivity have been obtained.
- Therapy should be narrowed to cover specific pathogens after the results of cultures are known.

Management of CAP in Adults

- This discussion is in accordance of the “Infectious Diseases Society of America / American Thoracic Society” Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults (2016, **Update of 2019**).

Antibiotic Treatment:

- Recommendations are generally **for a class of antibiotics rather than for a specific drug**, unless outcome data clearly favor one drug.

Management of CAP in Adults

Recommendations depend on:

1. The treatment setting: inpatient or outpatient.
2. The severity of infection. Severe
IV less severe
oral
3. The presence of comorbidities.
4. The presence of risk factors for drug-resistant pathogens. Abs in the 3 months

Management of CAP in Adults

The most common bacterial causes of CAP are:

- *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Staphylococcus aureus*, *Legionella* species, *Chlamydia pneumoniae*, *Moraxella catarrhalis*, Respiratory viruses.
- All patients with CAP should be treated empirically for bacterial infection.

pneumonia is bacterial until proven otherwise

to cover all of the above.


Management of CAP in Adults

- Any patient with CAP who was ^{last 3 months} recently exposed to one class of antibiotics should be treated using a different class.
- Local epidemiology and risk factors should provide the basis for the need to cover for drug-resistant pathogens, such as methicillin-resistant *S. aureus* (MRSA) and *Pseudomonas aeruginosa*.
not common in CAP but

Management of CAP in Adults



Risk factors for MRSA and *P. aeruginosa* include:

1. Prior respiratory isolation of the pathogen.
 2. Hospitalization with administration of parenteral antibiotics within the last 3 months.
 3. Locally validated risk factors for these pathogens, and the prevalence of MRSA or *P. aeruginosa* in CAP patients.
- 

Management of CAP in Adults

Outpatient setting:

1. For patients without comorbid conditions or risk factors for drug-resistant pathogens:

Monotherapy with amoxicillin, doxycycline, ^{بدل الـ macrolide} or a macrolide (azithromycin or clarithromycin) is recommended.

- Macrolide monotherapy has shown resistance and should not be used if the local rate of resistance of *Pneumococcus* is greater than 25%.

معلومات موجودة في المراجع

Management of CAP in Adults

2. Presence of comorbidities: (chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppression; use of antimicrobials within the previous 3 months, etc):

- Monotherapy with a respiratory fluoroquinolone (levofloxacin, moxifloxacin, or gemifloxacin), or
- Combination therapy with (amoxicillin-clavulanate or a cephalosporin) plus (a macrolide or doxycycline).

↘ Cover atypical microorganism
+
Give

Management of CAP in Adults

Inpatient setting:

Recommendations are different based on:

1. **Severity of pneumonia.**
2. **Prior respiratory isolation of MRSA or *P. aeruginosa***
3. **The presence of risk factors for these pathogens.**

التي موصى

Management of CAP in Adults

A. For inpatients with non-severe pneumonia use:

1. A beta-lactam plus a macrolide or
 2. a respiratory fluoroquinolone alone.
- Alternative: a beta-lactam in combination with doxycycline.

penicillin
carbapenem
cephalosporins

give
our patients
with comorbidities

Management of CAP in Adults

Iv Abs

B. For patients with severe pneumonia:

Combination therapy with a beta-lactam (cefotaxime, ceftriaxone, or ampicillin-sulbactam) + a macrolide (azithromycin) or a fluoroquinolone.

C. An empirical antimicrobial agent with activity against:

.....

Management of CAP in Adults

- **MRSA** (vancomycin or linezolid) better unless renal impairment
- ***P. aeruginosa*** (antipseudomonal β -lactam β -lactamase inhibitor 4th generation (piperacillin-tazobactam, cefepime, imipenem, or meropenem) + either ciprofloxacin or levofloxacin; should be added in all inpatients

With prior respiratory isolation of the pathogen.

لأنهم من common CAP
سواء في RFS
لأنهم يتغلطوا

Management of CAP in Adults

Pathogen-directed therapy: *Decescalation of therapy*

- Once the etiology of CAP has been identified on the basis of reliable microbiological methods, antimicrobial therapy should be directed at the specific pathogen.

Time to first antibiotic dose: *1.5-2 days*

- For patients admitted through the emergency department (ED), the first antibiotic dose should be administered while still in the ED.

Management of CAP in Adults

in severe
Switch from intravenous to oral therapy:

*when no inpatient
observation is
needed.*

1. Patients should be switched from intravenous to oral therapy **when they are hemodynamically** ^① **stable and improving clinically,** ^② **are able to ingest** ^③ **medications, and have a normally functioning** ^④ **gastrointestinal tract.** *no diarrhea or constipation*
2. Patients should be discharged as soon as they are **clinically stable,** ¹ **have no other active medical** ² **problems, and have a safe environment for** ³ **continued care. Inpatient observation while receiving oral therapy is NOT necessary.**

Management of CAP in Adults

Duration of antibiotic therapy:

1. Patients with CAP should be treated for a minimum of 5 days, and should be afebrile for 2-3 days.
*عشوائيات
المعالج* *حتریباً ۵ ايام سوج*
2. A longer duration of therapy may be needed if initial therapy was NOT active against the identified pathogen, or if it was complicated by extra-pulmonary infection such as meningitis or endocarditis.
1 *2* *not in my summary.*

Management of CAP in Adults

Remember the importance of:

1. The local pattern of causative pathogens.
2. The local pattern of antibiotic sensitivity and/or resistance.

Local antibiogram

Management of Hospital-Acquired Pneumonia (HAP) and Ventilator-Associated Pneumonia (VAP)

This discussion is in accordance of the “Infectious Diseases Society of America / American Thoracic Society” Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults (2016, **Update of 2021, 2022).**

Management of HAP/VAP

- ✓ It is advised that each hospital generate its specific antibiogram.
 دراسة لاختبار الحساسية بالمستشفى
 resistant
 don't follow the guidelines if ≠ your antibiogram
- ✓ It is **suggested** that patients with suspected HAP (non-VAP) be treated according to the results of microbiological studies rather than being treated empirically.
 HAP → not there
- In patients with suspected VAP, cover for *S. aureus*, *Pseudomonas aeruginosa*, and other gram-negative bacilli in all empiric regimens.
 1
 2
 3

Management of HAP/VAP

- In empiric coverage for MRSA, either vancomycin or linezolid is recommended.
- In empiric coverage for MSSA (not-MRSA), ^{same as P. aeruginosa.} ^{+ pseudomonas} piperacillin-tazobactam, cefepime, levofloxacin, ^{antipseudomonal} imipenem, or meropenem is recommended.
- ^{anti staph penicillins} With proven MSSA, oxacillin, nafcillin and ^{1st generation cephalo.} cefazolin are preferred (these agents are not necessary for empiric treatment of VAP if one of the above agents is used) ^{to switch} ^{عامی دانی} ^{وہی لایبٹا بہرہوں} ^{لہرہوں}

Management of HAP/VAP

- For patients being treated empirically for HAP, cover for *S. aureus*.
- For patients with HAP/VAP due to *Pseudomonas aeruginosa*, the choice of antibiotic for definitive (not empiric) therapy should be based on the results of antimicrobial susceptibility testing.
- For patients with HAP/VAP, a 7-day course of antimicrobial therapy is recommended. \neq *pseudomonas*
(traditionally it was 7-14 days)

Management of HAP/VAP

- *Pseudomonas aeruginosa* may require > 7 days. ≈ 14 days
- When the final culture and sensitivity results are available, the empiric broad spectrum regimen should be converted to more narrow and specific coverage. Deescalation
- new cephalosporin [Cefiderocol] has been approved for HAP/VAP due to the following microorganisms: *Acinetobacter baumannii* complex, *Escherichia coli*, *Enterobacter cloacae* complex, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Serratia marcescens*. .عكس It was not inferior to high dose meropenem.

Initial and Definitive Treatment of HAP

- MSSA should be covered unless the patient has risk factors for MRSA:
 1. IV antibiotics within the preceding 90 days.
 2. Exposure to a hospital unit where > 20% of S. aureus isolates are MRSA.
 3. High risk of death (need for ventilatory support due to septic shock^{+ -}).
- Vancomycin or linezolid should be used for empiric therapy (guided by local antibiogram). ^{*imp}

Initial and Definitive Treatment of HAP

- ^{again} For empiric coverage of MSSA, piperacillin-tazobactam, cefepime, levofloxacin, imipenem, or meropenem is recommended.
- With proven MSSA, ^{again} oxacillin, nafcillin and cefazolin are favored.
- For empiric coverage against *Pseudomonas aeruginosa* ^{two antimicrobials from diff classes.} use double coverage in patients at high risk of death (need for ventilatory support and/or septic shock).
- For all other cases single coverage is indicated.

Initial and Definitive Treatment of VAP

- Empiric treatment of VAP should cover for *S. aureus*, *Pseudomonas aeruginosa*, and other gram negative bacilli.
- MRSA should be covered empirically in patients with any risk factors for antimicrobial resistance:
 1. Patients located in a unit where > 10-20% of *S. aureus* isolates are MRSA.
 2. Patients in units where prevalence of MRSA is unknown.

Initial and Definitive Treatment of

VAP

- For MRSA infection, linezolid is preferred over vancomycin in:
 1. Patients with renal insufficiency.
 2. Patients infected with high MIC MRSA isolates.
- A single antibiotic with activity against *Pseudomonas aeruginosa* should be administered except in patients with risk factors for multidrug-resistant (MDR) organisms:

Initial and Definitive Treatment of VAP

1. Intravenous antibiotic use within the preceding 90 days. *3 months*
2. Septic shock or ARDS preceding VAP onset.
3. Five or more days of hospitalization prior to VAP onset.
4. Acute renal replacement therapy prior to VAP onset.
5. The patient is located in a unit where > 10% of gram-negative isolates are resistant'
6. Patients in ICU where antibiotic sensitivity rates are not available.

Initial and Definitive Treatment of VAP

- Double-drug coverage for *Pseudomonas aeruginosa* combine agents with high degree of antipseudomonal activity and low resistance potential: piperacillin-tazobactam, cefepime, ceftazidime, imipenem, meropenem, or aztreonam [⊕] levofloxacin, (ciprofloxacin or aminoglycoside) (amikacin, gentamicin, tobramycin), or polymyxins (polymyxin B, colistin).

⊕ aztreonam against GIVE.

Be cautious
while used

Initial and Definitive Treatment of VAP

* if used > 5-7 days ; cause $\begin{cases} \text{oto toxicity.} \\ \text{nephrotoxicity.} \end{cases}$

- In general, aminoglycosides and colistin should be avoided in therapy of VAP, due to poor ^① penetration of these agents in the lung tissues in addition to the potential nephrotoxicity. ^②
- VAP due to *Pseudomonas aeruginosa* has a high failure rate (~40%), regardless of the antibiotic regimens. \uparrow mortality.

Initial and Definitive Treatment of VAP

ما يغطي لى اء

- The use of inhaled antibiotic therapy should be limited to cases of VAP produced by gram-negative bacilli that are sensitive only to aminoglycosides and polymyxins (colistin and polymyxin B), which should also be administered intravenously.

inhaled

IN

Initial and Definitive Treatment of VAP

- A carbapenem or ampicillin/sulbactam should be used for *Acinetobacter* HAP/VAP
- If there is resistance to these agents, they should be substituted by inhaled and intravenous colistin.
- The guidelines are against the use of tigecycline for *Acinetobacter* VAP.

A C

no tige

^{تحفظات} Clinical **Caveats** in Selecting an Empiric Antibiotic Regimen ^{all mentioned before except} ○

1. The administration of the antibiotics should not be delayed for the sole purpose of performing diagnostic tests.
2. If the patient received antibiotics in the recent past, the new antibiotic should be from a different class.
3. When an ^{for the pathogen} appropriate and ^{due to sensitivity} adequate initial antibiotic regimen is started, the duration of therapy should be shortened (from the traditional 14-21 days to 7 days), ~~for~~ except *P. aeruginosa*.

Clinical Caveats in Selecting an Empiric Antibiotic Regimen

- ④ False negative cultures occurs in patients who have been taking antibiotics for 24-72 hours before collection of respiratory specimens.
5. Aerosolized antibiotics may be used as adjunct to systemic antibiotics. They are not effective as sole therapy.
6. Certain organisms (*E. coli*, *Klebsiella* spp, *Enterobacter* spp) produce extended-spectrum β -lactamase. These are usually susceptible to carbapenems.

Neonatal pneumonia

Onset

Right after birth

- Birth canal organisms
- Give bacilli ~ E. coli, Klebsiella

> 7 days

- NICU with prolonged ET
- Give coxi → MRSA, MSSA, Strep, Pseudomonas, Citrobacter, Bacillus, Serratia → due to Ab use.

Vancomycin + Broad spectrum β -lactam

Meropenem
Cefepime
Pip-Tazo

• Chlamydia

- 1) During birth
- 2) Pneumonia after 2-18 wks
- 3) Treat Baba and Mama
- 4) Azithro or erythro ~ for 4-10 days
for 5 days causes hypertrophic pyloric stenosis in neonates

Children

- pre-school → Strep + Staph / Amoxicillin
- older children → Atypical / Macrolides

CAP

Outpatient

Amoxicillin 7-10d 2m - 5y
if allergic to penicillin → macrolides

Azithromycin 5y - 16y

Inpatient

Cefuroxime 10-14d
critical ill / pri. or
Cefuroxime + cloxacillin
Cefuroxime + erythro (7-10d)
or
Azithromycin (5 days)

Neonatal Pneumonia

Onset:

first 24 hours

- 1) May be within hours of birth, and as part of a generalized sepsis syndrome. *congenital*
- 2) After 7 days (most commonly in neonatal ICUs among infants who require prolonged endotracheal intubation because of lung disease). *≠ congenital pneumonia*

Neonatal Pneumonia

Organisms are acquired from the maternal genital tract or the nursery, and include:

- a) Gram-positive cocci (groups A and B streptococci, both methicillin-sensitive and methicillin-resistant *Staphylococcus aureus*)
- b) Gram-negative bacilli (*E. coli*, *Klebsiella* sp, *Proteus* sp).
- c) *Pseudomonas*, *Citrobacter*, *Bacillus*, and *Serratia* in infants who have received broad-spectrum antibiotics.

Neonatal Pneumonia

Treatment:

- Antimicrobial therapy in early-onset disease is similar to that for neonatal sepsis: **Vancomycin** and a broad-spectrum β -lactam drug such as meropenem, piperacillin/tazobactam, or cefepime are the initial treatment of choice.
- This regimen treats sepsis as well as pneumonia with typical hospital-acquired pathogens including *P. aeruginosa* and MRSA.

Neonatal Pneumonia

- *again and again* ✓ **Local patterns of infection and bacterial resistance should always be used to help guide empiric choices of antimicrobials.**
- **More specific antibiotics are substituted after sensitivity results are available.**

Neonatal Pneumonia

Chlamydial pneumonia:

- Exposure to chlamydial organisms (*Chlamydia trachomatis*) occurs during delivery.
- May result in development of chlamydial pneumonia at 2 to 18 wk.

Treatment:

- Erythromycin or azithromycin lead to rapid resolution.
- Erythromycin may cause hypertrophic pyloric stenosis in neonates.
- The mother and father should also be treated for chlamydia.

unknown
MoA.

Community-Acquired Pneumonia in Children

- The most likely etiology depends on the age of the child. *Strep Staph*
- Viral and *Streptococcus pneumoniae* infections are most common in preschool-aged children, whereas *Mycoplasma pneumoniae* is common in older children. *5-20 y.o*

Community-Acquired Pneumonia in Children

- Preschool-aged children with uncomplicated bacterial pneumonia should be treated with amoxicillin. for strep.
- Macrolides are first-line agents in older children.
- Immunization with the (13-valent pneumococcal conjugate vaccine) is important in reducing the severity of childhood pneumococcal infections.

Recommended Empiric **Outpatient** Treatment of Childhood **CAP**

Same as adults ?

2 months — 5 y.o

60 days to 5 years of age:

- Preferred regimens: Amoxicillin for 7-10 days.
- Alternative regimens for patients allergic to penicillin or beta-lactam antibiotics:
Azithromycin (5 days), clarithromycin (7-10 days),
or erythromycin (7-10 days).

5 to 16 years of age: **Azithromycin** (5 days).

Recommended Empiric Inpatient Treatment of Childhood CAP

60 days to 5 years of age:

- Cefuroxime for 10-14 days.
- In critically ill patients: Cefuroxime + erythromycin 10-14 days, or cefotaxime + cloxacillin for 10-14 days

5 to 16 years of age: Cefuroxime + erythromycin 10-14 days, or azithromycin for 5 days.