Update in the management of bacterial respiratory Tract Infection

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Disclosure

- Speaker:
- Advisory board member:

MSD

Roche

GILEAD

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AstraZeneca

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Objectives

1. Introduction.
2. Prevalence of Respiratory Pathogens in the United Arab Emirates.
3. Discuss empiric treatment recommendations for upper respiratory tract infection and community-acquired pneumonia
4. Discuss opportunities for de-escalation and reasonable duration of antibiotic therapy for CAP after additional clinical data are available.
5. Some of the problems of antimicrobial resistance.

Introduction

- Viral & bacterial respiratory infections pose a significant burden on healthcare facilities globally.
- Acute respiratory infection (ARI) is responsible for a high global disease burden, and respiratory viruses are the most common causal agents of ARIs.
- Influenza virus (FLU) causes considerable mortality and morbidity worldwide, even though FLU vaccines and antiviral agents are available.
- To our knowledge, limited information is available on the epidemiology and clinical characteristics of respiratory infections in the United Arab Emirates (UAE).

Jeon JH, Han M, Chang HE, Park SS, Lee JW, Ahn YJ, Hong DJ. Incidence and seasonality of respiratory viruses causing acute respiratory infections in the Northern United Arab Emirates. J Med Virol. 2019 Aug;91(8):1378-1384.

- A 48-year-old man with fever and a productive cough was admitted after he became increasingly short of breath. He had a temperature of 38.5˚C, a pulse of 120 beats/min and a respiratory rate of 22 breaths/min. Chest examination revealed reduced expansion on the right, dullness to percussion, quiet breath sounds and dullness to percussion in the right midzone and green-coloured sputum. Chest X-ray showed a clearly demarcated opacity occupying the right middle lobe. Blood gases on arterial blood collected while the patient was breathing room air confirmed a hypoxia and respiratory acidosis.

- Chest-xray: RML opacification. Loss of adjacent right heart border.

- 1. Does this patient have a lobar pneumonia?
- 2. Is his pneumonia most likely to be caused by Streptococcus pneumoniae infection?
- 3. Do other bacteria such as Legionella pneumophila cause lobar pneumonia?
- 4. Will bacteriological investigations assist the immediate management of this infection?
- 5. Should ceftriaxone be used as a first choice of antibiotic in resistant Streptococcus pneumoniae infection?

Pneumonia

- Remains one of the major disease entities practicing physicians must manage.
- Leading cause of infection-related morbidity and mortality in all age groups, and a leading cause of death in those older than 65 years of age.
- Despite its frequency and importance, clinical questions have remained in the therapy of community-acquired pneumonia including when to start antibiotics, when to stop them, who to treat, and what agents to use.
- The case fatality ratio of pneumonia has not changed dramatically from 1963 to 1998.
- The role of pneumonia-related mortality in the elderly takes on added importance with the estimate that by 2050, 20% of the world's population will be older than the age of 65 years.

  - Donowitz GR. Community-acquired pneumonia: 2012 history, mythology, and science. *Trans Am Clin Climatol Assoc*. 2013;124:283-293.

Risk factors for CAP

- Age >65 years.
- Smoking.
- Alcoholism.
- Immunosuppressive conditions.
- COPD.
- Cardiovascular or cerebrovascular disease.
- Chronic liver or renal disease.
- Diabetes mellitus.
- Dementia.

- In addition, the British Thoracic Society (BTS) established the original severity score CURB (confusion, uremia, respiratory rate, low blood pressure) to identify patients with CAP who may be candidates for outpatient vs. inpatient treatment.
- Inflammatory markers, such as procalcitonin (PCT), can be used to guide management throughout hospital stay.
- Antibiotic coverage will vary depending on whether outpatient vs. inpatient management is required.

The British Thoracic Society (BTS) established the original severity score CURB (confusion, uremia, respiratory rate, low blood pressure) to identify patients with CAP who may be candidates for outpatient vs. inpatient treatment.

CURB-65	Clinical Feature	Points
C	Confusion	1
U	Urea > 7 mmol/L	1
R	RR ≥ 30	1
B	SBP ≤ 90 mm Hg OR DBP ≤ 60 mm Hg	1
65	Age > 65	1

CURB-65 Score	Risk group	30-day mortality	Management
0 -1	1	1.5%	Low risk, consider home treatment
2	2	9.2%	Probably admission vs close outpatient management
3-5	3	22%	Admission, manage as severe

The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) developed the Pneumonia Severity Index (PSI) which incorporates 20 risk factors to place patients into 5 classes correlated with mortality risk.

PNEUMONIA SEVERITY INDEX FOR COMMUNITY-ACQUIRED PNEUMONIA

Risk factor	Points
Demographics	
Men	Age (years): ___
Women	Age (years) - 10: ___
Nursing home resident	+10
Comorbidities	
Neoplasm	+30
Liver disease	+20
Heart failure	+10
Stroke	+10
Renal failure	+10
Physical examination findings	
Altered mental status	+20
Respiratory rate ≥ 30 breaths per minute	+20
Systolic blood pressure < 90 mm Hg	+20
Temperature < 95˚F (35˚C) or ≥ 104˚F (40˚C)	+15
Pulse rate ≥ 125 beats per minute	+10
Laboratory and radiographic findings	
Arterial pH < 7.35	+30
Blood urea nitrogen > 30 mg per dL	+20
Sodium < 130 mmol per L	+20
Glucose ≥ 250 mg per dL	+10
Hematocrit < 30 percent	+10
Partial pressure of arterial oxygen < 60 mm Hg	+10
Pleural effusion	+10
Total points:	

		Deaths/total (%)		
Point total	Risk class	Adults with CAP*	Nursing home patients with CAP†	Recommendation†
< 51	I	3/1,472 (0.2)	None	Outpatient therapy should be considered, especially for patients in classes I and II
51 to 70	II	7/1,374 (0.5)	None	
71 to 90	III	41/1,603 (2.6)	1/21 (4.8)	
91 to 130	IV	149/1,605 (9.3)	6/50 (12.0)	Patient should be hospitalized
> 130	V	109/438 (24.9)	28/85 (32.9)	

*—Data for community-acquired pneumonia (CAP) are weighted averages from validation studies.[2-4]
†—Recommendations are consistent with clinical guidelines.[5,6] Clinical judgment may overrule the guideline recommendation.

1. Mylotte JM, Naughton B, Saludades C, Maszarovics Z. Validation and application of the pneumonia prognosis index to nursing home residents with pneumonia. *J Am Geriatr Soc*. 1998;46:1538-1544.
2. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med*. 1997;336:243-250.
3. Aujesky D, Auble TE, Yealy DM, Stone RA, Obrosky DS, Meehan TP, et al. Prospective comparison of three validated prediction rules for prognosis in community-acquired pneumonia. *Am J Med*. 2005;118:384-392.
4. Flanders WD, Tucker G, Krishnadasan A, Martin D, Honig E, McClellan WM. Validation of the pneumonia severity index. Importance of study-specific recalibration. *J Gen Intern Med*. 1999;14:333-340.
5. Niederman MS, Mandell LA, Anzueto A, Bass JB, Broughton WA, Campbell GD, et al; American Thoracic Society. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. *Am J Respir Crit Care Med*. 2001;163:1730-1754.
6. Mandell LA, Bartlett JG, Dowell SF, File TM Jr, Musher DM, Whitney C; Infectious Diseases Society of America. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. *Clin Infect Dis*. 2003;37:1405-1433.

Family Practice Management®

Diagnosing CAP

- Common signs and symptoms:[1]
  - Cough and/or sputum production (90%)
  - Fever (>90%)
    - Less common in older patients
  - Chills (50%)
  - Tachypnea (45%)
  - Pleuritic chest pain (30%)
  - Crackles during chest auscultation

- If common signs and symptoms are present, obtain chest x ray
  - No infiltrates – pneumonia still can be present
  - Presence of infiltrate without respiratory symptoms is unlikely to be CAP

Diagnostic Tests:

- Blood cultures
  - Recommended for patients who are moderately to severely ill or with chest imaging findings of an abscess or parapneumonic effusion
- Sputum Gram stain and culture
  - Recommended for making the diagnosis of CAP
- Respiratory viral panel
  - Provides an alternate explanation for the presentation
- *Streptococcus pneumoniae* urinary antigen
  - Recommended, if available, to assist with narrowing antibiotic therapy
- Legionella urinary antigen
  - Consider for patients with moderate to severe illness, smokers, or patients over 50 years of age
  - Only detects *L. pneumophilia* serogroup 1 (70–80% of Legionella infections)
- Bronchoscopy
  - Severely ill or immunocompromised patient not responding to therapy and no clear etiology.

Empiric Therapy:

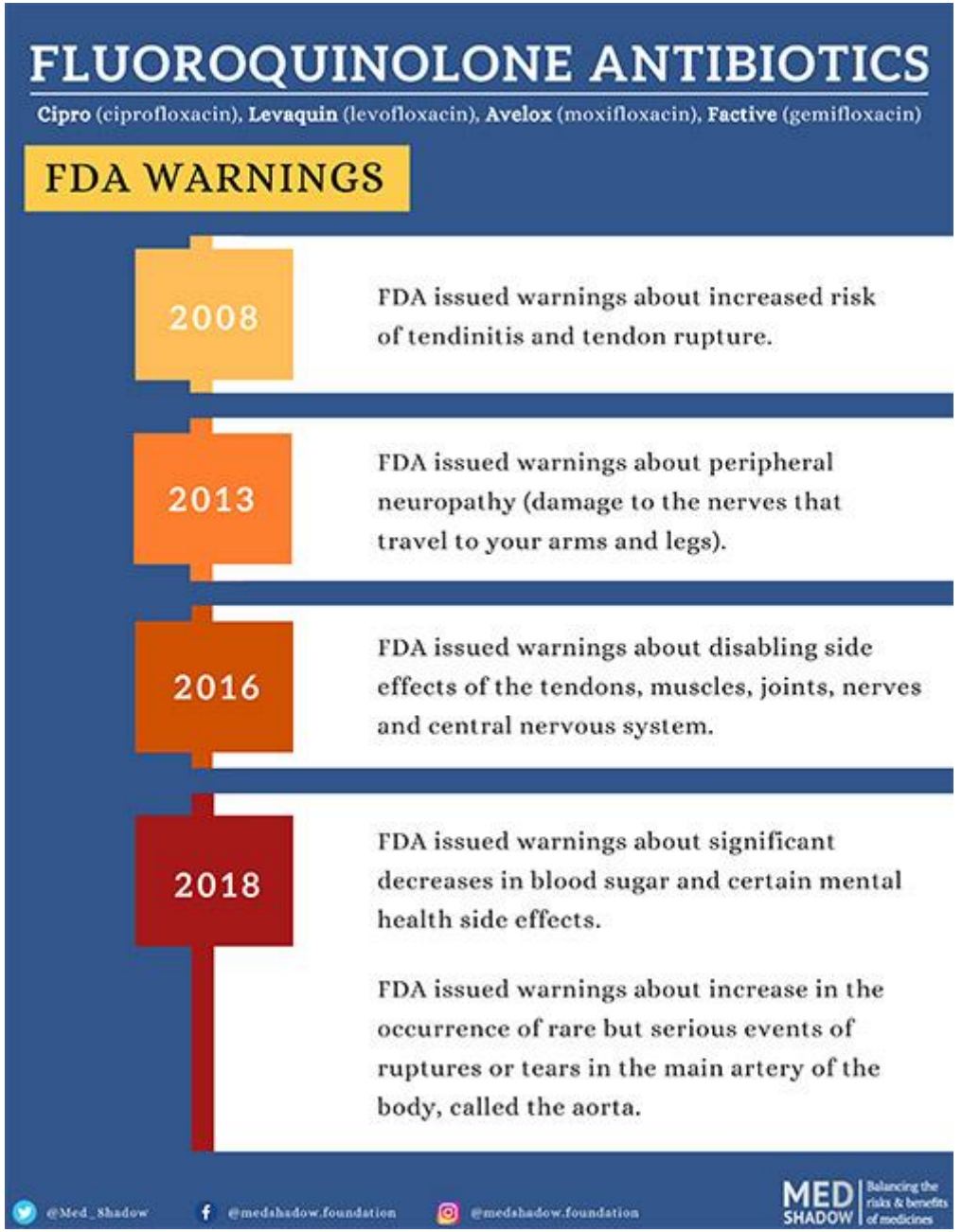
- Ampicillin PLUS Macrolide (or doxycycline)
  - For children, otherwise healthy adults, or those with mild disease.
  - Azithromycin has been associated with prolonged QTc intervals
  - Observational studies have suggested that doxycycline may be protective against the development of *Clostridioides difficile* infection (CDI)

- Cephalosporin PLUS Macrolide (or doxycycline)
  - Can be used in non-severe penicillin (PCN) allergy

- Respiratory fluoroquinolone (levofloxacin or moxifloxacin)
  - Strongly associated with development of CDI
  - Associated with prolonged QTc intervals, tendinopathies and altered mental status especially in the elderly
  - Consider for severe PCN allergy

Empiric Therapy:

- Respiratory fluoroquinolone (levofloxacin or moxifloxacin)
  - Strongly associated with development of CDI
  - Worsening of Myasthenia gravis.
  - Associated with prolonged QTc intervals, tendinopathies and altered mental status especially in the elderly
  - Consider for severe PCN allergy



Antibiotic Selection:

- Convert your patient to oral antibiotics as soon as clinical improvement is observed and the patient is able to tolerate oral therapy.
- When can I narrow to amoxicillin or oral cephalosporin?
  - If the sputum culture grows an ampicillin-susceptible organism
  - If the streptococcal urinary antigen test is positive and the proportion of *S. pneumoniae* isolates in your hospital that are penicillin resistant is low.

What duration of antibiotic therapy is needed for my patient's diagnosis?

- **5 days** of antibiotic therapy is sufficient for most patients with CAP
- Consider prolonging therapy to at least **7 days** if—
  - The patient is immunocompromised
  - The patient has underlying structural lung disease (not including asthma)
  - The patient did not have an adequate clinical response to therapy within 72 hours
- If the patient has a nontraditional CAP pathogen such as Legionella, *Pseudomonas aeruginosa*, or *S. aureus*, longer durations of therapy are usually required, particularly if there is associated bacteremia
  - Cough and chest x-ray abnormalities may take several weeks to improve

5 Days of Antibiotics in clinical trials:

- At least five randomized-controlled trials (RCTs) have shown that antibiotic treatment for 5 days is as safe and effective as longer treatment courses[1-7]
  - One RCT even showed therapy as short as 3 days was sufficient
  - Data from bronchoscopy samples demonstrate 95% of patients with bacterial pneumonia eradicate pathogen after 3 days of therapy
- Two meta-analyses have also shown short courses of antibiotic therapy are effective for the treatment of CAP[8,9]
  - 22 RCTs with > 8,000 patients

Summary

CAP

- Before prescribing antibiotics for patients with signs and symptoms suggestive of CAP, obtain chest x ray and consider sputum Gram stain with culture (**unless for patients started empirically on anti-MRSA or antipseudomonal antibiotics then sputum and blood cultures are mandatory**).
- Oral step-down therapy recommended after improvement observed.
- Most patients can be treated for a 5-day course.

COPD Exacerbations

- 3 days of Macrolide or Doxycycline are generally sufficient if antibiotics indicated.
- Fluoroquinolones are not necessary for most patients.

Aspiration Pneumonitis

- For hemodynamically stable patients, antibiotics are not needed and supportive care is the mainstay of therapy.
- Prophylactic antibiotics have not been shown to be helpful in improving outcomes.

Bacterial pathogens

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Cumulative Antibiogram, Al Qassimi Hospital (MQH) (2022)

1 January to 31 December 2022, Percent Susceptible Gram +ve Isolates (%S), From **Sputum Specimen Total N: 225, Significant N: 170**

Gram-positive Bacteria	Number of Isolates (N)	β-Lactams					Macrolides	Amino-glycosides		FQ			Glycopeptide	Other								
		Ampicillin	Penicillin	Oxacillin	Ceftriaxone	Cefotaxime	Erythromycin	Gentamicin	Streptomycin - high level	Levofloxacin	Ciprofloxacin	Moxifloxacin	Vancomycin	Trimethoprim/Sulfamethoxazole	Nitrofurantoin	Linezolid	Tetracycline	Doxycycline	Rifampicin	Clindamycin	Tigecycline	Daptomycin
Staphylococcus aureus	170	--	--	44	--	--	73	95	--	56	54	55	100	78	--	100	85	98	100	89	--	100
MSSA	100	--	--	76	--	--	76	99	--	60	59	61	100	83	--	100	85	99	100	96	--	100
MRSA	74	--	--	--	--	--	68	89	--	50	47	49	100	72	--	100	85	95	100	78	--	100

%S = Percent of isolates susceptible, R = intrinsically resistant, (--) antimicrobial agent is not tested, not indicated, no data available, small number of isolates tested (N<30) or not effective clinically. N=Number. Isolates with number less than 30 are not included. Nitrofurantoin will be reported only in isolates from urine. Interpretation standard: CLSI M100 ED32:2022.

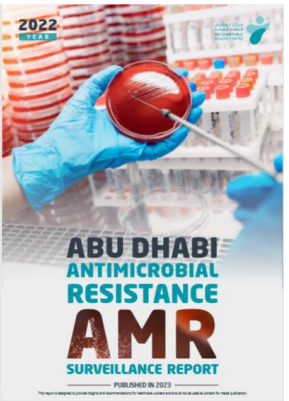
- **170 isolates of Staphylococcus aureus, 58% of MSSA.**
- **Fluoroquinolone sensitivity between 50-60% on an average.**
- **MSSA was 96% sensitive to Clindamycin while sensitivity pf MRSA was only 78%.**
- **Linezolid and Vancomycin are still 100% sensitive for both, MRSA & MSSA.**
- **MSSA is more sensitive to TMP/SMX than MRSA (83% vs 72%).**

Macrolide-Resistant Pneumococcus in Community-acquired Pneumonia and role of Macrolide Therapy!

5.7. *Streptococcus pneumoniae*

Table 5.7: Percentages of resistant isolates for *Streptococcus pneumoniae*, isolates from all sources, Abu Dhabi 2022 (Total number of isolates= 785)

Antibiotic	Isolates (N)	%R	I%	S%
Penicillin G (oral breakpoints)	494	9.5	56.3	34.0
Penicillin G (non-meningitis breakpoints)	494	1.2	1.0	96.2
Penicillin G (meningitis breakpoints)	494	66.0	0.0	34.0
Amoxicillin (non-meningitis breakpoints)	140	0.7	7.1	92.1
Cefuroxime (oral breakpoints)	42	16.7	2.4	81.0
Cefotaxime (non-meningitis breakpoints)	359	1.9	3.3	94.7
Ceftriaxone (non-meningitis breakpoints)	647	1.4	0.8	97.8
Rifampin	266	0.0	0.0	100.0
Levofloxacin	412	5.8	0.2	93.9
Moxifloxacin	698	1.4	0.1	98.4
Trimethoprim/Sulfamethoxazole (TMP/SMX)	766	27.4	11.7	60.8
Clindamycin	639	36.0	1.3	62.6
Erythromycin	744	57.3	0.1	42.5
Linezolid	734	0.0	0.1	99.7
Vancomycin	764	0.0	0.0	99.7
Quinupristin/Dalfopristin	104	0.0	1.9	98.1
Tetracycline	765	48.8	0.4	50.7

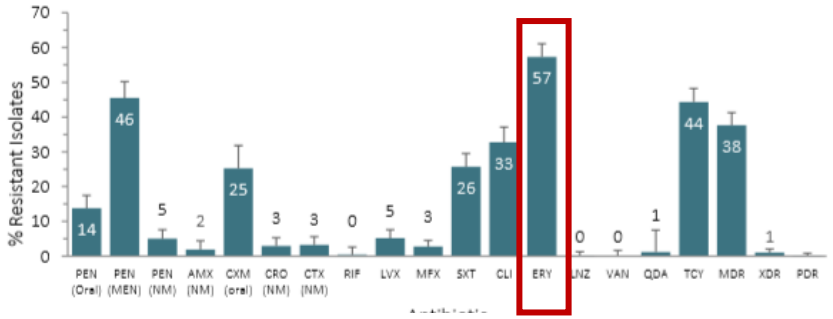


4.4.7 Streptococcus pneumoniae

Table 4.4.7.1 Percentages of resistant, intermediate, and susceptible isolates for *Streptococcus pneumoniae*, isolates from all sources, United Arab Emirates, 2020

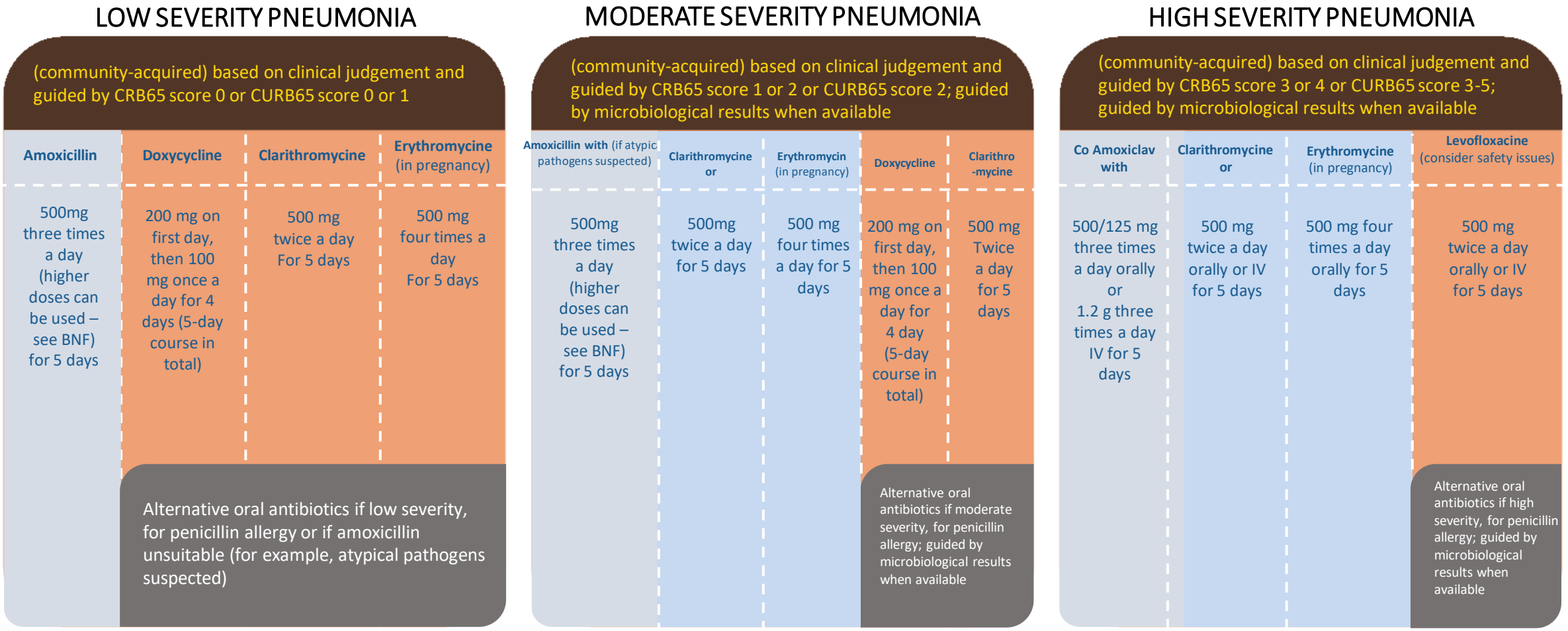
Antibiotic	Code	*Streptococcus pneumoniae* (N=969)			
		Isolates (N)	% R	% I	% S
Penicillin G (oral breakpoints)	PEN (oral)	442	13.8	31.9	54.3
Penicillin G (non-meningitis breakpoints)	PEN (NM)	442	5.0	2.0	93.0
Penicillin G (meningitis breakpoints)	PEN (MEN)	442	45.5	0.2	54.3
Amoxicillin (non-meningitis breakpoints)	AMX (NM)	308	1.9	3.9	94.2
Cefuroxime (oral breakpoints)	CXM (oral)	210	25.2	1.9	72.9
Cefotaxime (non-meningitis breakpoints)	CTX (NM)	403	3.2	1.7	95.0
Ceftriaxone (non-meningitis breakpoints)	CRO (NM)	378	2.9	1.3	95.8
Rifampin	RIF	250	0.4	0	99.6
Levofloxacin	LVX	519	5.2	1.2	93.6
Moxifloxacin	MFX	615	2.8	1.8	95.4
Trimethoprim/Sulfamethoxazole	SXT	576	25.7	13.5	60.7
Clindamycin	CLI	489	32.7	2.0	65.2
Erythromycin	ERY	665	57.3	0.2	42.6
Linezolid	LNZ	611	0.2	0	99.7
Vancomycin	VAN	607	0.2	0	99.3
Quinupristin/Dalfopristin	QDA	82	1.2	1.2	97.6
Tetracycline	TCY	654	44.3	1.1	54.6
Multidrug-resistance (≥3 classes NS)[a]	MDR	691	37.6	–	–
Extensive drug resistance (possible)	XDR	691	1.0	–	–
Pan-drug resistance (possible)	PDR	691	0.1	–	–

[a] Multidrug resistance (MDR) was defined as acquired non-susceptibility (NS) to at least one agent in three or more antimicrobial classes.



Pneumonia (community-acquired): antimicrobial prescribing

Choice of antibiotic: adults aged 18 years and over



NICE guideline 2019

ATS Guidelnes 2019

Question 8: In the Outpatient Setting, Which Antibiotics Are Recommended for Empiric Treatment of CAP in Adults?

Recommendation.

1. For healthy outpatient adults without comorbidities listed below or risk factors for antibiotic resistant pathogens, we recommend (Table 3):
   - amoxicillin 1 g three times daily (strong recommendation, moderate quality of evidence), or
   - doxycycline 100 mg twice daily (conditional recommendation, low quality of evidence), or
   - a macrolide (azithromycin 500 mg on first day then 250 mg daily or clarithromycin 500 mg twice daily or clarithromycin extended release 1,000 mg daily) only in areas with pneumococcal resistance to macrolides <25% (conditional recommendation, moderate quality of evidence).
2. For outpatient adults with comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia we recommend (in no particular order of preference) (Table 3):
   - Combination therapy:
     - amoxicillin/clavulanate 500 mg/125 mg three times daily, or amoxicillin/clavulanate 875 mg/125 mg twice daily, or 2,000 mg/125 mg twice daily, or a cephalosporin (cefpodoxime 200 mg twice daily or cefuroxime 500 mg twice daily); AND
     - macrolide (azithromycin 500 mg on first day then 250 mg daily, clarithromycin [500 mg twice daily or extended release 1,000 mg once daily]) (strong recommendation, moderate quality of evidence for combination therapy), or doxycycline 100 mg twice daily (conditional recommendation, low quality of evidence for combination therapy);

     OR
   - Monotherapy:
     - respiratory fluoroquinolone (levofloxacin 750 mg daily, moxifloxacin 400 mg daily, or gemifloxacin 320 mg daily) (strong recommendation, moderate quality of evidence).

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019

Antibiotic Use in Acute Upper Respiratory Tract Infections

Denise K. C. Sur, MD, and Monica L. Plesa, MD
David Geffen School of Medicine, University of California, Los Angeles, California

TABLE 4

Appropriate Antibiotic Dosing for Outpatient Treatment of Upper Respiratory Tract Infections

Infection	Adults	Children
Acute bacterial rhinosinusitis	**First-line treatment:** Amoxicillin/clavulanate (Augmentin), 500 mg orally every eight hours or 875 mg every 12 hours for five to seven days **Penicillin allergy:** Doxycycline, 100 mg orally twice per day for five to seven days Cefixime (Suprax), 400 mg orally per day for five to seven days	**First-line treatment:** Amoxicillin/clavulanate, 45 mg amoxicillin per kg per day orally, divided every 12 hours for 10 to 14 days **Penicillin allergy:** Cefpodoxime, 10 mg per kg orally per day for 10 to 14 days Cefdinir , 14 mg per kg per day orally, divided in one to two doses for 10 to 14 days
Acute otitis media	**First-line treatment:** Amoxicillin/clavulanate, 875 mg orally twice per day or 500 mg orally every eight hours for five to 10 days* **Penicillin allergy:** Cefdinir, 300 mg orally twice per day or 600 mg orally per day for five to 10 days* Cefpodoxime, 200 mg orally twice per day for five to 10 days* Doxycycline, 100 mg twice per day for five to 10 days* Azithromycin (Zithromax), 500 mg orally on day 1 then 250 mg orally per day on days 2 to 5	**First-line treatment:** Amoxicillin, 80 to 90 mg per kg per day orally divided every 12 hours for five to 10 days† **Penicillin allergy:** Cefdinir, 14 mg per kg per day orally divided in one to two doses for five to 10 days† Cefpodoxime, 10 mg per kg per day divided in two doses for five to 10 days† **Second-line treatment** (for children who have taken amoxicillin within the past 30 days, with concurrent purulent conjunctivitis, with a history of recurrent acute otitis media, unresponsive to amoxicillin, or with no improvement after 48 to 72 hours of initial treatment with amoxicillin): Amoxicillin/clavulanate, 90 mg per kg per day of amoxicillin with 6.4 mg per kg per day of clavulanate in two divided doses for five to 10 days†
Group A beta-hemolytic streptococcal pharyngitis	**First-line treatment:** Penicillin V, 250 mg orally four times per day or 500 mg orally twice per day for 10 days Amoxicillin, 1,000 mg orally per day or 500 mg orally twice per day for 10 days Penicillin G benzathine, 1,200,000 U intramuscularly **Penicillin allergy:** Cephalexin , 500 mg orally twice per day for 10 days Clindamycin, 300 mg orally three times per day for 10 days Azithromycin, 500 mg orally per day for five days	**First-line treatment:** Penicillin V, 250 mg orally two to three times per day for 10 days in children; 250 mg orally four times per day or 500 mg orally twice per day for 10 days in adolescents Amoxicillin, 50 mg per kg orally per day (maximum: 1,000 mg) or 25 mg per kg orally (maximum: 500 mg) twice per day for 10 days Penicillin G benzathine, (< 27 kg) 600,000 U intramuscularly, (≥ 27 kg) 1,200,000 U intramuscularly **Penicillin allergy:** Cephalexin, 20 mg per kg per dose orally (maximum: 500 mg) twice per day for 10 days Clindamycin, 7 mg per kg per dose orally (maximum: 300 mg) three times per day for 10 days Azithromycin, 12 mg per kg per dose orally (maximum: 500 mg) per day for five days

*—Adults with mild to moderate infection can be treated for five to seven days, patients with severe illness should be treated for 10 days.
†—Children < two years or ≥ two years with severe symptoms should receive a 10-day course of oral antibiotics. Children two to five years of age with mild to moderate symptoms should be treated for seven days, children ≥ six years with mild to moderate symptoms should be treated for five to seven days.

Information from references 9, 11, 13, 51, and 52.

Sur DKC, Plesa ML. Antibiotic Use in Acute Upper Respiratory Tract Infections. Am Fam Physician. 2022 Dec;106(6):628-636. PMID: 36521460.

Antibiotic Use in Acute Upper Respiratory Tract Infections

Denise K. C. Sur, MD, and Monica L. Plesa, MD
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Acute bacterial rhinosinusitis	**First-line treatment:** Amoxicillin/clavulanate (Augmentin), 500 mg orally every eight hours or 875 mg every 12 hours for five to seven days **Penicillin allergy:** Doxycycline, 100 mg orally twice per day for five to seven days Cefixime (Suprax), 400 mg orally per day for five to seven days	**First-line treatment:** Amoxicillin/clavulanate, 45 mg amoxicillin per kg per day orally, divided every 12 hours for 10 to 14 days **Penicillin allergy:** Cefpodoxime, 10 mg per kg orally per day for 10 to 14 days Cefdinir , 14 mg per kg per day orally, divided in one to two doses for 10 to 14 days

Antibiotic Use in Acute Upper Respiratory Tract Infections

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Acute otitis media	**First-line treatment:** Amoxicillin/clavulanate, 875 mg orally twice per day or 500 mg orally every eight hours for five to 10 days* **Penicillin allergy:** Cefdinir, 300 mg orally twice per day or 600 mg orally per day for five to 10 days* Cefpodoxime, 200 mg orally twice per day for five to 10 days* Doxycycline, 100 mg twice per day for five to 10 days* Azithromycin (Zithromax), 500 mg orally on day 1 then 250 mg orally per day on days 2 to 5	**First-line treatment:** Amoxicillin, 80 to 90 mg per kg per day orally divided every 12 hours for five to 10 days† **Penicillin allergy:** Cefdinir, 14 mg per kg per day orally divided in one to two doses for five to 10 days† Cefpodoxime, 10 mg per kg per day divided in two doses for five to 10 days† **Second-line treatment** (for children who have taken amoxicillin within the past 30 days, with concurrent purulent conjunctivitis, with a history of recurrent acute otitis media, unresponsive to amoxicillin, or with no improvement after 48 to 72 hours of initial treatment with amoxicillin): Amoxicillin/clavulanate, 90 mg per kg per day of amoxicillin with 6.4 mg per kg per day of clavulanate in two divided doses for five to 10 days†

National Guidelines on Empiric Antibiotic Treatment of Upper and Lower Respiratory Tract Infections in Adults

Version 1

January 2024

Attachment 2: Management of Acute Pharyngitis

Treat wit Antibiotic If streptococcus is highly suspected or confirmed	No Penicillin Allergy	Penicillin Allergy
• Centor Score 3 or 4 • Symptoms suggestive of bacterial cause (Tonsillar exudate and/or erythema, tender cervical lymph nodes, scarlatiniform rash, palatal petechiae) • Patients with severe signs and symptoms suggesting complications • Positive Strep A test • Positive Throat Culture	Amoxicillin PO (10 days) Amoxicillin-clavulanate PO (10 days)	Clindamycin PO (10 days) **OR** Azithromycin PO (5 days) OR Clarithromycin PO (10 days)

Attachment 3: Management of Acute Bronchitis

Treat wit Antibiotic If	No Penicillin Allergy	Penicillin Allergy
• Patients at risk of complications or pneumonia	Amoxicillin-clavulanate PO + Clarithromycin PO (5-7 days) **OR** Amoxicillin- clavulanate PO + azithromycin PO (5-7 days)	Doxycycline PO (5-7 days) **OR** Azithromycin PO (3 days) **OR** Clarithromycin PO (5-7 days)
• Pertussis	Azithromycin PO for 3 days	
• Influenza	Oseltamivir PO for 5 days	

National Guidelines on Empiric Antibiotic Treatment of Upper and Lower Respiratory Tract Infections in Adults

Attachment 4: Management of Acute Rhinosinusitis

First Line Antibiotics		
Treat wit Antibiotic If	**No Penicillin Allergy**	**P**
• Persistent illness without improvement for >7-10 days • Severe symptoms lasting ≥ 3 days (fever ≥ 39°C and one or both of the following: - purulent nasal discharge lasting 3-4 days - facial pain • Worsening symptoms after initially improving from a typical upper respiratory tract infection (new fever, headache, increased purulent nasal discharge) • New-onset fever, headache, or increased nasal discharge after a typical viral upper respiratory tract infection that was initially improving	Amoxicillin-clavulanate PO (5-7 days most patients) (7-10 days for severe disease, immunocompromised, or after treatment failure)	(5-7 (7- imr t
Second Line Antibiotics		
• Symptoms worsen within 72 hours of initial empirical antibiotic therapy or when patients show no improvement even after 3–5 days of treatment.	High Dose amoxicillin-clavulanate (4g/250 mg,) PO (10 days) **OR** Cefuroxime PO (10 Days) **OR** Ceftriaxone IV (10 days)	(Levofloxacin or Moxifloxacin PO (10 days)

Attachment 5: Management of Acute Otitis Media

Initial Antibiotic Therapy	
No Penicillin Allergy	**Penicillin Allergy**
Amoxicillin-Clavulanic acid PO (Mild-moderate 5-7 days) (Severe 10 days)	Doxycycline PO (Mild to moderate 5-7 days) (Severe 10 days) **OR** Azithromycin PO (5 days) **OR** Clarithromycin PO (Mild to moderate 5-7 days) (Severe 10 days)
Second Line Antibiotic Therapy	
High Dose amoxicillin-clavulanate (4g/250 mg,) PO (10 days) **OR** Cefuroxime PO (10 Days) **OR** Ceftriaxone IV (10 days)	Fluroquinolone (Levofloxacin or Moxifloxacin) PO (5-10 days depending on severity and response to treatment)

Attachment 6: Management of Pneumonia

Entity	No Penicillin Allergy	Penicillin Allergy	Duration
Community Acquired Pneumonia (Outpatient)	Oral Amoxicillin-Clavulanate **Plus** (Oral Macrolide **OR** Oral Doxycycline)	Oral Respiratory Fluroquinolone (Levofloxacin or Moxifloxacin)	5 days
Community acquired pneumonia (Ward/No Risk factors for Pseudomonas and MRSA)	Amoxicillin-clavulanate **Plus** Macrolide **OR** Ceftriaxone **Plus** Macrolide	Respiratory Fluroquinolone (Levofloxacin or Moxifloxacin)	5 days
Community acquired pneumonia (Ward/Risk Factors for MRSA)	Anti-MRSA (Vancomycin or Linezolid) **Plus** Antipneumococcal beta lactam (Amoxicillin-Clavulanate or Ceftriaxone) **Plus** Macrolide or Doxycycline	Respiratory Fluroquinolone (Levofloxacin or Moxifloxacin) **Plus** Anti-MRSA (Vancomycin or Linezolid)	5 – 7 days
Community acquired pneumonia (Ward/Risk Factors for Pseudomonas)	Piperacillin-tazobactam or Cefepime or Ceftazidime **Plus** Macrolide or Doxycycline	Levofloxacin	5-7 days
Community acquired pneumonia (Ward/Risk Factors for MRSA and Pseudomonas)	Piperacillin-tazobactam or Cefepime or Ceftazidime **Plus** Anti-MRSA (Vancomycin or Linezolid) **Plus** Macrolide or doxycycline	Levofloxacin **Plus** Anti-MRSA (Vancomycin or Linezolid)	5-7 days
Community-acquired aspiration pneumonia	Amoxicillin-clavulanate		5-7 days
Community-acquired pneumonia (ICU Admission)	Piperacillin-tazobactam or Cefepime or Ceftazidime **Plus** Macrolide **±** Aminoglycoside	Levofloxacin **±** Aminoglycoside	7 days
	Consider adding Anti-MRSA such as Vancomycin or Linezolid if there are risk factors for MRSA		
	If there are risk factor for ESBL use carbapenem (meropenem or imipenem)		
Hospital or ventilator-associated pneumonia	Same as community acquired pneumonia admitted to ICU		7 days

Respiratory-tract infections among geriatrics: prevalence and factors associated with the treatment outcomes.

Respiratory tract infections	*n* (%)	Co-morbidities	*n* (%)
Community-acquired pneumonia	311 (65.6)	Hypertension	196 (41.4)
		Diabetes mellitus	145 (30.6)
Chronic obstructive pulmonary disease	98 (20.7)	Dyslipidaemia	123 (25.9)
Bronchitis	39 (8.2)	Ischaemic heart disease	61 (12.9)
Hospital-acquired pneumonia	26 (5.5)	Hypothyroidism	25 (5.3)
		Chronic kidney disease	13 (2.7)

- The most commonly observed RTIs in the study population were CAP (*n* = 311; 65.6%).
- Hypertension (*n* = 196; 41.4%), diabetes mellitus (*n* = 145; 30.6%) and dyslipidaemia (*n* = 123; 25.9%) were the most common co-morbidities seen in the study population.

Akhtar A, Hassali MAA, Zainal H, Ali I, Iqbal MS, Khan AH. Respiratory-tract infections among geriatrics: prevalence and factors associated with the treatment outcomes. *Therapeutic Advances in Respiratory Disease*. 2021;15.

List of antibiotics and inhaled medications among study population.

Antibiotics	*n* (%)	Inhaled medications	*n* (%)
Amoxicillin clavulanate	331 (69.8)	Salbutamol	81 (17.1)
Ampicillin and sulbactam	43 (9.1)	Ipratropium bromide	58 (12.2)
Cefuroxime	31 (6.5)	Ipratropium bromide and albuterol sulfate	32 (6.8)
Azithromycin	20 (4.2)		
Cloxacillin	8 (1.7)		

Akhtar A, Hassali MAA, Zainal H, Ali I, Iqbal MS, Khan AH. Respiratory-tract infections among geriatrics: prevalence and factors associated with the treatment outcomes. *Therapeutic Advances in Respiratory Disease*. 2021;15.

Respiratory-tract infections among geriatrics, discussion.

- Relatively high prevalence of polypharmacy (37.3%) among individuals above age 65 years; moreover, polypharmacy has a statistically significant association with the treatment outcomes of RTIs among the study population (OR = 2.083; $p < 0.001$).
- 30.6% of diabetic patients have RTIs, which supports the findings of a Dutch study, which reported that patients with type 2 diabetes have higher risk of developing RTIs as compared with patients with hypertension.
- In the elderly population, presence of co-morbidities with RTIs worsens the condition of patients because their immune system is already compromised, and these co-morbidities may decrease their quality of life and affect their treatment outcomes.
- Amoxicillin/clavulanate (69.8%) is the most common antibiotic prescribed by physicians for the treatment of RTIs among the elderly. Several studies included in a review suggested the clinical success rate of amoxicillin/clavulanate among RTIs.

Muller L, Gorter K, Hak E, et al. Increased risk of infection in patients with diabetes mellitus type 1 or 2. *Ned Tijdschr Geneeskd* 2006; 150: 549–553. Utrecht

Discussion, cont.....

- Use of alcohol among the studied elderly population infected with RTIs shows strong association with the treatment outcomes (OR = 0.583; p = 0.031) in the present study. A recent meta-analysis shows that there is 1.8-fold increased risk of RTIs among those who consume alcohol as compared with non-alcoholic individuals.
- Cigarette smoking has a statistically strong association with the treatment outcomes of elderly individuals infected with RTIs in the current study (OR = 0.383; p = 0.009). Various studies reported that smokers have a high risk of developing RTIs as compared with non-smokers, particularly in the elderly population.

Simou E, Britton J, Leonardi-Bee J. Alcohol and the risk of pneumonia: a systematic review and meta-analysis. *BMJ Open* 2018; 8: e022344.

Arcavi L, Benowitz NL. Cigarette smoking and infection. *Arch Intern Med* 2004; 164: 2206–2216.

- A 48-year-old man with fever and a productive cough was admitted after he became increasingly short of breath. He had a temperature of 38.5˚C, a pulse of 120 beats/min and a respiratory rate of 22 breaths/min. Chest examination revealed reduced expansion on the right, dullness to percussion, quiet breath sounds and dullness to percussion in the right midzone and green-coloured sputum. Chest Xray showed a clearly demarcated opacity occupying the right middle lobe. Blood gases on arterial blood collected while the patient was breathing room air confirmed a hypoxia and respiratory acidosis.

- 1. Does this patient have a lobar pneumonia?
- Yes. He has a right middle lobe pneumonia.
- 2. Is his pneumonia most likely to be caused by Streptococcus pneumoniae infection?
- Yes. This is the most common cause of community acquired lobar pneumonia.
- 3. Do other bacteria such as Legionella pneumophila cause lobar pneumonia?
- Yes. Other bacterial species including L. pneumophila can cause lobar pneumonia.
- 4. Will bacteriological investigations assist the immediate management of this infection?
- Yes. A gram stain showing neutrophils and many Gram-positive diplococci will increase the suspicion that this is a S. pneumoniae infection.
- 5. Should ceftriaxone be used as a first choice of antibiotic in resistant Streptococcus pneumoniae infection?
- No. Alternative options such as Glycopeptide (Vancomycin, Teicoplanin) or Linezolid would be better.

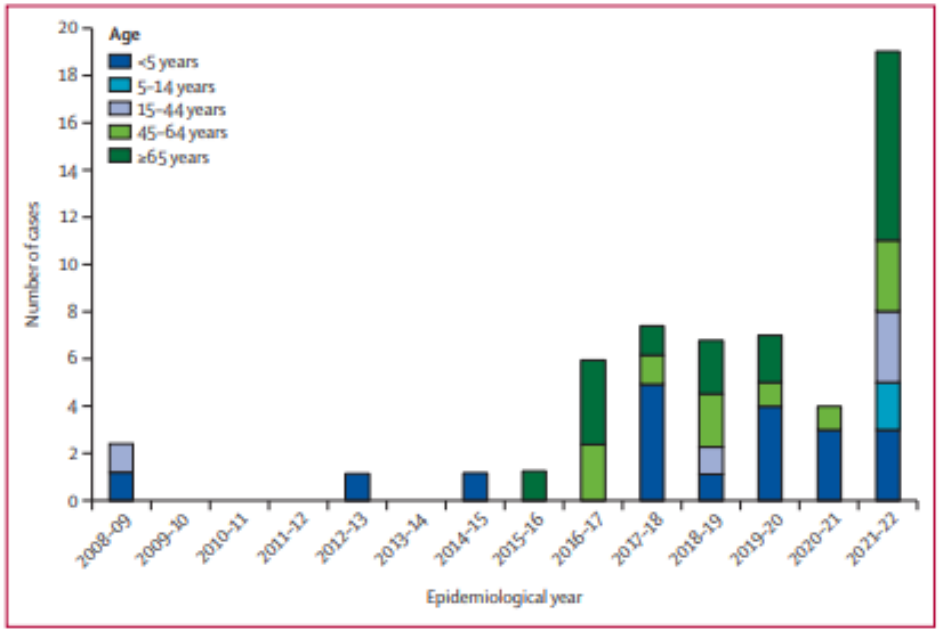
Pandemic-related changes in Bacterial Pneumonia.

- *S. pneumoniae* is the most common pathogen of CAP, the incidence of invasive pneumococcal disease (IPD) was significantly decreased in many countries during this pandemic.
- The change in the trend was observed for elderly patients aged ≥65 years and children, including community-acquired alveolar pneumonia and bacteremia pneumococcal pneumonia.
- A prospective analysis of surveillance data, laboratories in 26 countries and territories across 6 continents showed that all countries and territories had experienced a significant and sustained reduction in IPD in early 2020 (1 January to 31 May 2020) following the introduction of COVID-19 containment measures in each country[1]. In addition, several studies also reported a decline in *H. influenzae* and *Mycoplasma pneumoniae* infection during COVID-19 pandemic.
- However, several studies found that the increased presence of *Legionella* in the environment could be due to extreme stagnation in building water systems that resulted from prolonged building closures[2].
- In summary, these findings urge us to establish an updated epidemiology of community-acquired bacterial pneumonia during the COVID-19 pandemic.

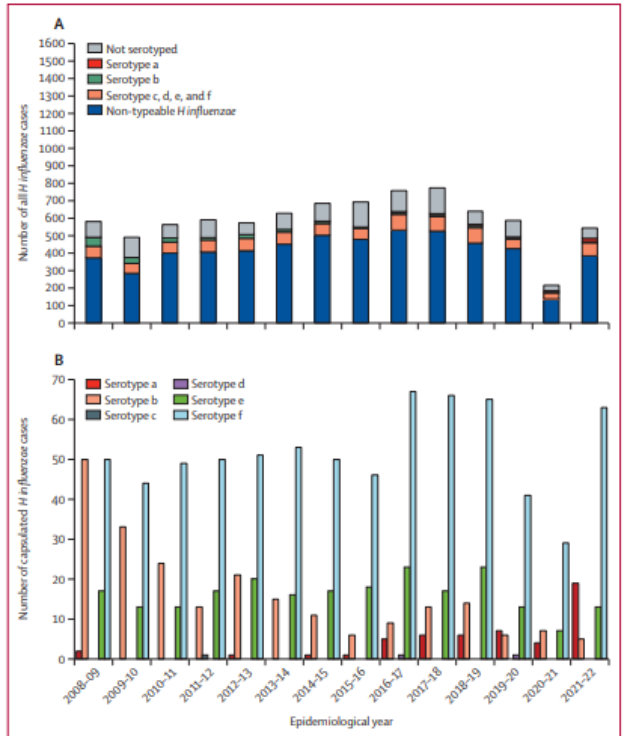
1- Brueggemann, A.B et al. Changes in the incidence of invasive disease due to *Streptococcus pneumoniae*, Haemophilus influenzae, and Neisseria meningitidis during the COVID-19 pandemic in 26 countries and territories in the Invasive Respiratory Infection Surveillance Initiative: A prospective analysis of surveillance data. *Lancet Digit. Health* **2021**, *3*, e360–e370

2- Palazzolo, C et al. Legionella pneumonia: Increased risk after COVID-19 lockdown? Italy, May to June 2020. *Euro. Surveill.* **2020**, *25*, 2001372

Trends in invasive *H.influenzae* infection



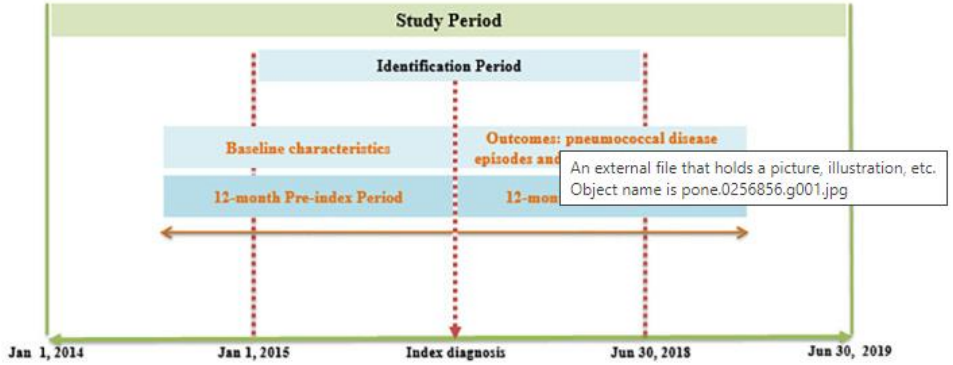
- A significant rise in number of cases since 2016–17, with (81%) of the cases occurred during the five most recent epidemiological years.
- During the first COVID-19 pandemic year (2020–21), invasive Hia cases declined compared with the previous 3 years, but increased rapidly the following year, were highest during 2021–22.

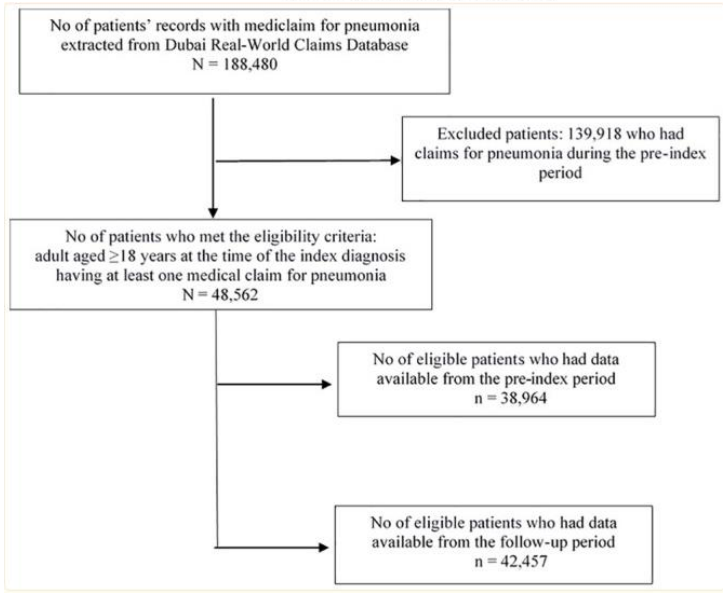


- (84·2%) of the total H influenzae isolates were serotyped during the 14-year period.
- Of those, (82·4%) were confirmed as **NTHi**, and (16·9%) as other capsulated serotypes.

Bertran M, et al. Trends in invasive Haemophilus influenzae serotype a disease in England from 2008-09 to 2021-22: a prospective national surveillance study. Lancet Infect Dis. 2023 Oct;23(10):1197-1206.

The Economic Burden of Community-Acquired Pneumonia in Adult.





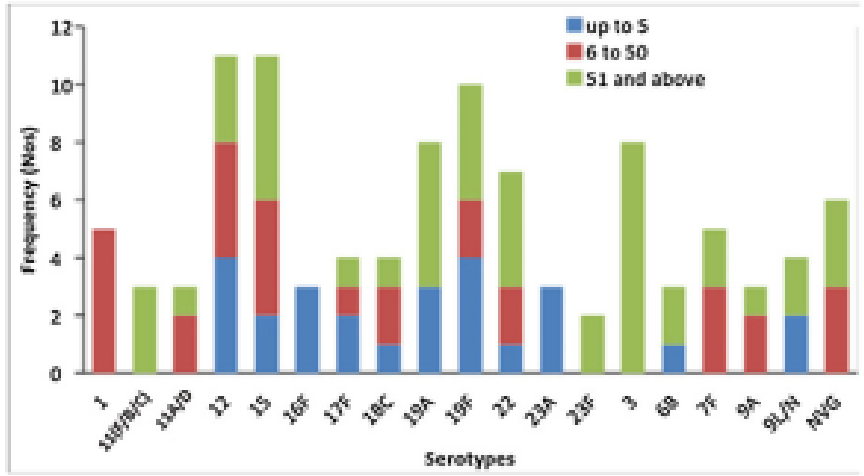
- the mean pneumonia-related costs (USD) per patient were highest for the high-risk cohort (overall: 1,305; high-risk, 10,207; medium-risk, 1,283; low-risk, 882).
- Most all-cause and pneumonia-related costs were due to inpatient visits (4,901 and 4,818 USD respectively), while outpatient (1,232 and 166 USD respectively) and emergency visits (347 and 206 USD respectively) contributed significantly lesser.

Al Dallal SAM, et al. Real-world evaluation of costs of illness for pneumonia in adult patients in Dubai-A claims database study. PLoS One. 2021 Sep 1;16(9):e0256856.

Pneumococcal serotype distribution and drug susceptibility from GCC area.

Table 2
Detailed serotype/serogroup distribution among all age groups.

Serotype/serogroup	Frequency		Contribution (%)
	No.	%	
12, 15	11	8.3	16.6
19F	10	7.6	7.6
3, 19A	8	6.1	12.2
22	7	5.3	5.3
1, 7F	5	3.8	7.6
17F, 18C, 9N/L	4	3	9
11F/B/C, 11A/D, 16F, 23A, 35B, 6B, 9A	3	2.3	16.1
8, 13, 10B, 18A/B, 23F	2	1.5	7.5
4, 5, 6D, 10F/C, 14, 19, 24, 28, 29, 34, 37, 39, 10A, 23B, 6A, 6C, 7B/C, 7F/A	1	0.8	14.4
Non-vaccine group (NVG)	6	4.5	4.5



- 41 different serotypes were identified among 132 pneumococcal isolates (it is important to note that 6 isolates remained non-typeable.

Analysis of serotype distribution showed age-dependent variation.
Serotype variations among different age groups were statistically significant, though the number of isolates for many serotypes was low.
The predominant serotypes among:

- Children <5 → 12 (11.4%), 19F (11.4%), 23A (8.6) and 16F (8.6%). They accounted for 40% of the total.
- Among the other high risk group (51 years) was remarkably different and predominant →3 (13.3%), 15 (8.3%), 19A (8.3%), 19F (6.7%), 22 (6.7%), 12 (5.0%) and 11 (5.0%). Contribute to 53.3% of the total serotypes, this group had more diversity in serotype distribution.

Al-Jardani A, et al. Serotype distribution and antibiotic resistance among invasive Streptococcus pneumoniae from Oman post 13-valent vaccine introduction. Int J Infect Dis. 2019 Aug;85:135-140.

Antibiotic	Site	Susceptibility (%)			MIC (μg/ml)		
		R	I	S	MIC50	MIC90	MIC range
PEN	Meningitis	40.9	0.0	59.1	0.032	0.50	0.016–4
PEN	Non-meningitis	0.0	1.5	98.5	0.032	0.50	0.016–4
CRO	Meningitis	0.8	3.0	96.2	0.016	0.25	0.004–2
CRO	Non-meningitis	0.0	0.8	99.2	0.016	0.25	0.004–2
CTX	Meningitis	0.8	2.3	97.0	0.023	0.25	0.002–2
CTX	Non-meningitis	0.0	0.8	99.2	0.023	0.25	0.002–2
MEM		1.5	0.0	98.5	0.008	0.13	0.002–2
AMX		0.8	1.5	97.7	0.023	0.50	0.003–8
ERY		25.8	2.3	72.0			
CLI		16.7	0.0	83.3			
CHL		1.5	0.0	98.5			
SXT		26.5	6.1	67.4			
VAN		0.0	0.0	100.0			
LVX		0.8	0.0	99.2			

Antibiotic abbreviations: PEN (penicillin), CRO (ceftriaxone), CTX (cefotaxime), MEM (Meropenem), AMX (amoxicillin), ERY (erythromycin), CLI (clindamycin), CHL (chloramphenicol), SXT (trimethoprim-sulfamethoxazole), VAN (vancomycin), LUV (levofloxacin).

- Non-susceptibility rates for PEN was 40.9% of the isolates being non-susceptible per the meningitis breakpoints (M) while only 1.5% were non-susceptible per non-meningitis breakpoints (NM).

Ceftriaxone (CRO) and cefotaxime (CTX) non-susceptibility rates were 3.8% and 3.1% respectively (as per meningitis criteria) and 0.8% each (as per non-meningitis criteria).

Rates of non-susceptibility to:

- Erythromycin (ERY) 28.1%.
- Clindamycin (CLI) 16.7%.
- Trimethoprim-sulfamethoxazole 32.6%.

Al-Jardani A, et al. Serotype distribution and antibiotic resistance among invasive Streptococcus pneumoniae from Oman post 13-valent vaccine introduction. Int J Infect Dis. 2019 Aug;85:135-140.

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Thank you