CAP in Adults & Pediatrics
…and what to do about Mycoplasma

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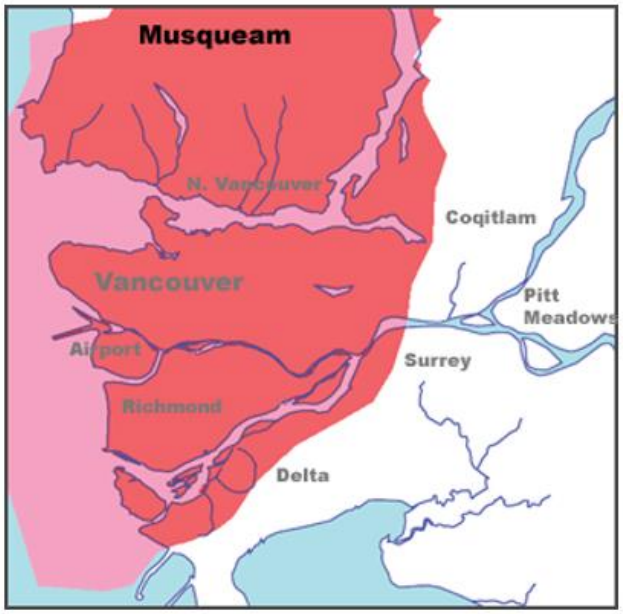
We would like to acknowledge that we are gathered today on the traditional territories of the Musqueam, Squamish and Tsleil-Waututh peoples.

Source: www.johomaps.net/na/canada/bc/vancouver/firstnations/firstnations.html



Disclosures

None to declare.

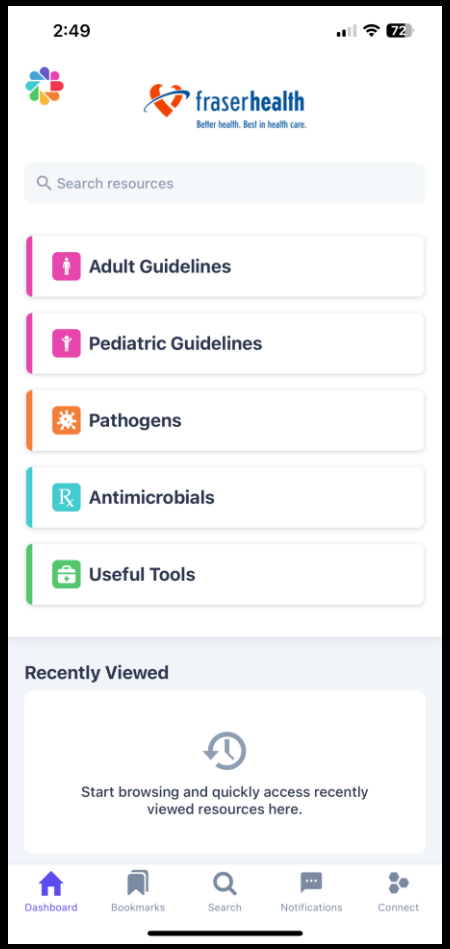
Learning Objectives

1. Be aware of local treatment guidelines for Adult and Pediatric CAP

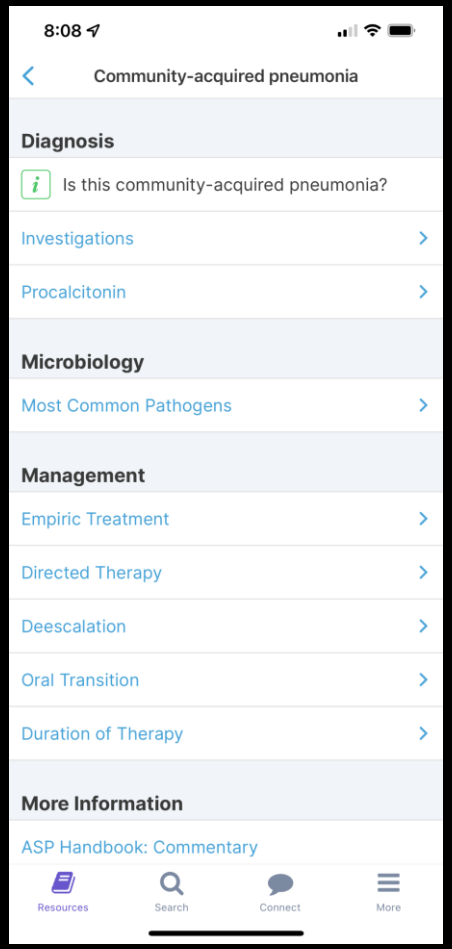
2. Be familiar with *Mycoplasma pneumoniae* and how to manage it

3. Be aware of established clinical guidance for treatment duration in CAP

Firstline App

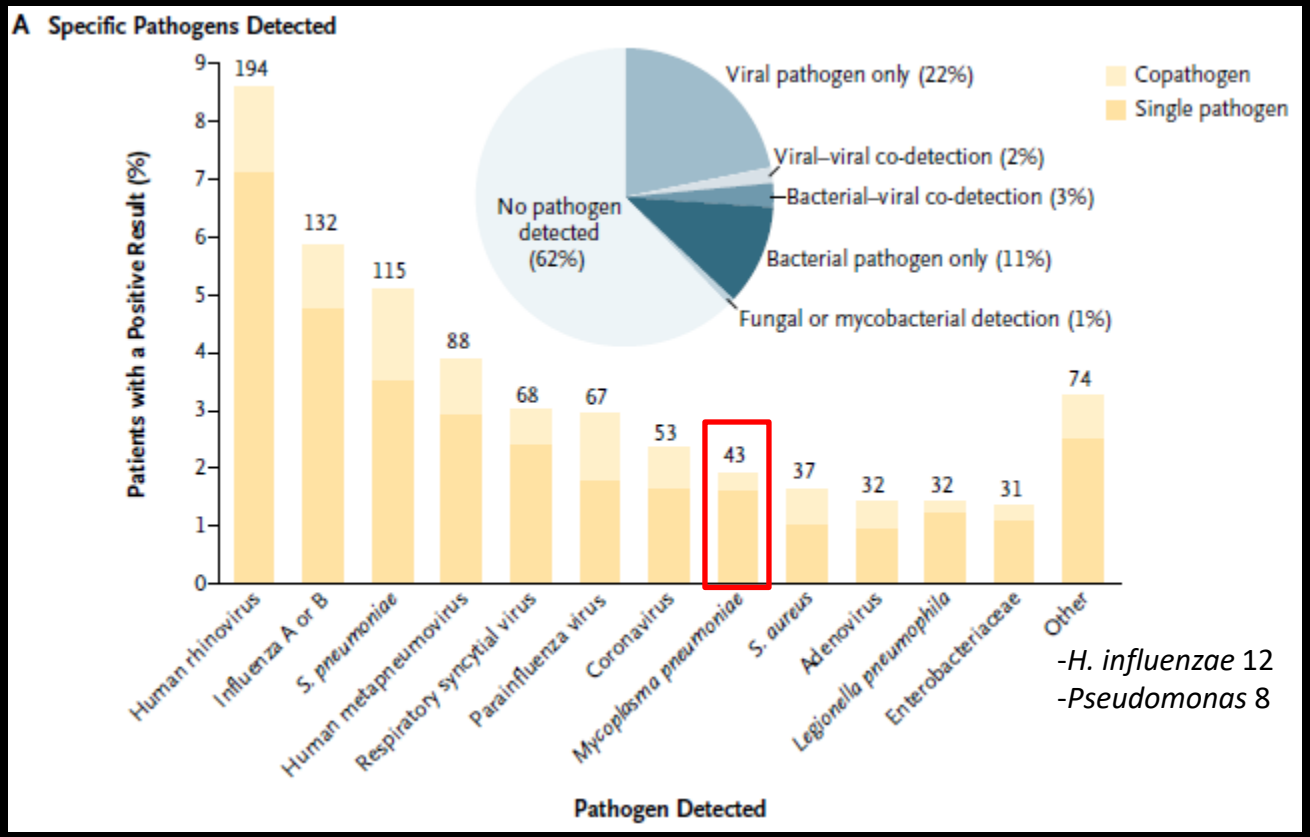


Firstline Home Screen



Community Acquired Pneumonia

Microbiology of CAP - Adults



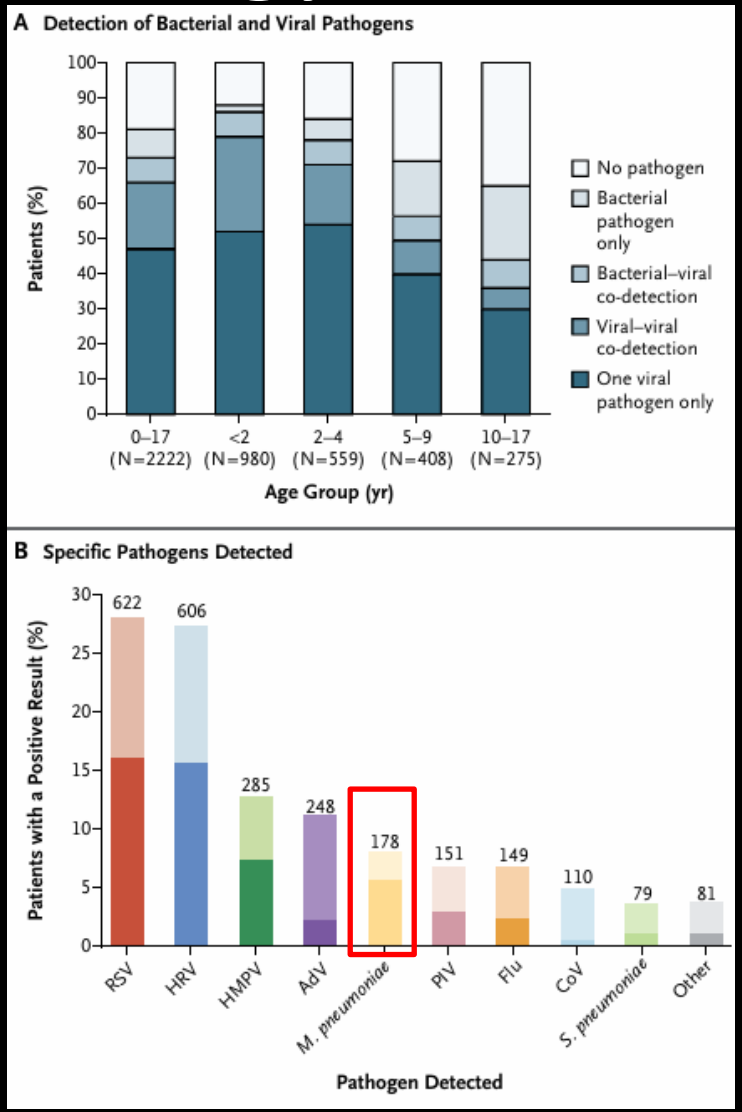
2259 adults

Viruses 27%
Bacteria 14%

-*H. influenzae* 12
-*Pseudomonas* 8

CDC EPIC Study - Jain S et al. NEJM 2015. doi: 10.1056/NEJMoa1500245

Microbiology of CAP - Children



AdV denotes adenovirus, CoV coronavirus, Flu influenza A or B virus, HMPV human metapneumovirus, HRV human rhinovirus, PIV parainfluenza virus, and RSV respiratory syncytial virus. Panel C shows the proportions of pathogens detected, according to age group.

CDC EPIC Study - Jain S et al. NEJM 2015. doi: 10.1056/NEJMoa1405870

Hospitalized CAP
Viral-Bacterial Co-Infection

- Influenza
  - Autopsy studies show most deaths in pandemic years (1918, 2009) due to bacterial secondary infection
  - High rates of co-infection (~25%) in modern studies
- COVID-19
  - Low rates of co-infection (5%) at admission
  - Higher rates of secondary infection (13%)
- RSV
  - High rates of co-infection (~30%) in modern studies

Morens DM et al. J Infect Dis. 2008. doi: 10.1086/591708. Klein EY et al. Influenza Other Respir Viruses. 2016. doi: 10.1111/irv.12398
Feldman C et al. Pneumonia. 2021. doi: 10.1186/s41479-021-00083-w. Oliva J et al. Viruses. 2021. doi: 10.3390/v13091725
Langford BJ et al. Clin Microbiol Infect. 2022. doi: 10.1016/j.cmi.2021.11.008

Mycoplasma pneumoniae

- Bacterium that lacks cell wall, doesn't gram stain, and doesn't grow on routine clinical culture media
- Usually diagnosed by PCR
- Generally not seasonal but seasonal (fall/winter) surges seen every few years
- ***Peak incidence ages 5-15***

Mandell's 9E (2019)

Mycoplasma pneumoniae

- Most common presentations are bronchiolitis, tracheobronchitis, and URTI
- Atypical pneumonia less common
  - Gradual onset over days
  - Low grade fever, malaise, cough, headache, myalgia
  - Substernal pain common from cough/tracheitis but usually no pleuritic pain
  - GI symptoms rare
- Asymptomatic carriage in up to 21% of children!

Mandell's 9E (2019). Spuesens EBM et al. PLOS Med 2013. doi: 10.1371/journal.pmed.1001444

Mycoplasma pneumoniae

- Well described extra-pulmonary phenomenon
  - Hemolysis
  - Rash in ~25%, usually transient exanthem, less commonly oral ulcers or rarely SJS
  - Rare: carditis, encephalitis, transverse myelitis, stroke, radiculopathy
- Serology often not used correctly
  - Needs fourfold rise in IgG titre comparing acute and convalescent serum

Mandell's 9E (2019). Waites KB et al. Clin Micro Rev 2017. doi: 10.1128/CMR.00114-16

Mycoplasma pneumoniae - Adults

Characteristic	*M. pneumoniae* PCR-positive* (n=43) N (%)	*M. pneumoniae* PCR-negative with other detected pathogens* (n=810) N (%)	Unadjusted Odds Ratio (95% CI)	P-value
Radiologic findings[e]				
Consolidation	34 (79)	517 (64)	2.1 (1.01 – 4.5)	0.04
Single lobar infiltrate	18 (42)	259 (32)	1.5 (0.8 – 2.9)	0.2
Multiple lobar infiltrate	16 (37)	233 (29)	1.5 (0.8 – 2.8)	0.2
Air space/ interstitial diseases	13 (30)	307 (38)	0.7 (0.4 – 1.4)	0.3
Pleural effusion	9 (21)	212 (26)	0.7 (0.4 – 1.6)	0.4
Hilar lymphadenopathy	6 (14)	48 (6)	2.6 (1.03 – 6.4)	0.05[f]
Severity				
Length of hospital stay (median, IQR in days)	2 (1–4)	4 (2-6)		<0.01
PSI Class I[i]	23 (54)	151 (19)	*Reference*	
PSI Class II[i]	10 (23)	211 (26)	0.2 (0.07 -0.3)	<0.01
PSI Class III-V[i]	10 (23)	448 (55)	0.3 (0.1 – 0.7)	<0.01
ICU admission	4 (9)	210 (26)	0.3 (0.1- 0.8)	0.01
Mechanical ventilation	0	62 (29)	NC	0.08[f]
Death	0	16 (2)	NC	0.7[f]

Kutty PK et al. Int J Med Sci 2024. doi: 10.7150/ijms.9923

Mycoplasma pneumoniae - Children

Characteristic	*Mycoplasma pneumoniae* PCR-Positive[a] (n = 182)	*Mycoplasma pneumoniae* PCR-Negative[b] (n = 2072)	Unadjusted OR (95% CI)	*P* Value
Radiographic findings[i]				
Consolidation	108 (59)[j]	1219 (59)	1.0 (.8–1.4)	.9
Single lobar infiltrate	59 (32)	534 (26)	1.4 (1.0–2.0)	.05
Multilobar infiltrates	42 (23)	573 (28)	0.8 (.5–1.1)	.2
Multilobar infiltrates (unilateral)	20 (11)	155 (7)	1.5 (.9–2.5)	.09
Multilobar infiltrates (bilateral)	22 (12)	420 (20)	0.5 (.3–.9)	<.01
Pleural effusion	48 (26)	244 (12)	2.7 (1.9–3.8)	<.01
Complicated bronchiolitis	21 (12)	610 (29)	0.3 (.2–.5)	<.01
Hilar lymphadenopathy	18 (10)	114 (6)	1.9 (1.1–3.2)	.02
Severity of illness				
ICU admission	21 (12)	431 (21)	0.5 (.3–.8)	<.01
Invasive mechanical ventilation	3 (2)	143 (7)	0.2 (.07–.7)	<.01
Length of stay, d, median (IQR)	2 (2–4)	3 (2–4)		.1[n]

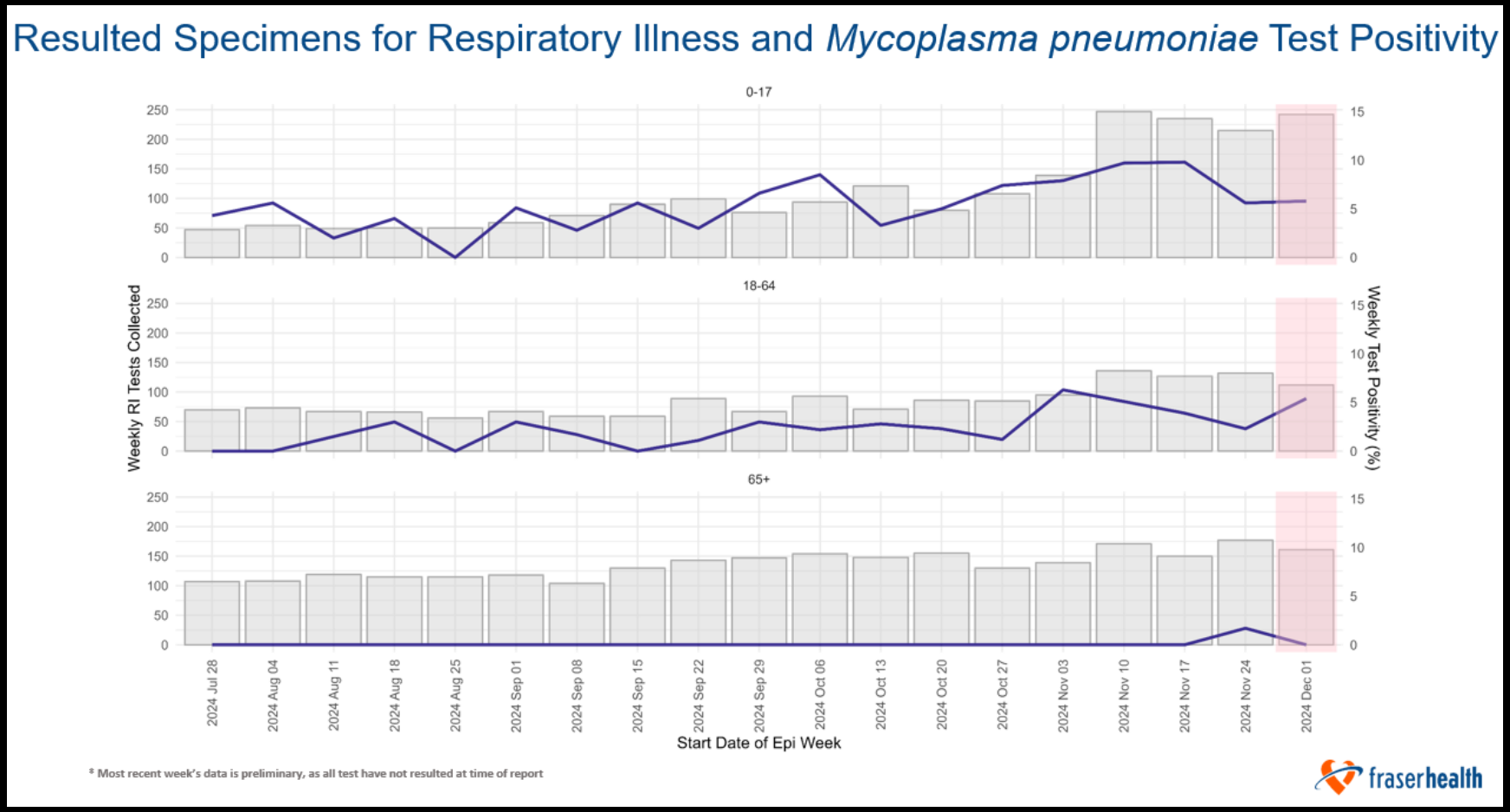
Kutty PK et al. CID 2019. doi: 10.1093/cid/ciy419

Mycoplasma pneumoniae

- Mild leukocytosis may be present
- Hemolysis often present and mild in most
- CXR usual shows patchy infiltrates
  - But lobar disease can also be seen!
- Usually diagnosed by respiratory sample multiplex panel
  - NP, nasal, throat, BAL, sputum, and tracheal aspirate

Mandell's 9E (2019). BCCDC eLab Handbook.

FH Trends


Resulted Specimens for Respiratory Illness and *Mycoplasma pneumoniae* Test Positivity
0-17
18-64
65+
Weekly RI Tests Collected
Weekly Test Positivity (%)
0
50
100
150
200
250
0
5
10
15
2024 Jul 28
2024 Aug 04
2024 Aug 11
2024 Aug 18
2024 Aug 25
2024 Sep 01
2024 Sep 08
2024 Sep 15
2024 Sep 22
2024 Sep 29
2024 Oct 06
2024 Oct 13
2024 Oct 20
2024 Oct 27
2024 Nov 03
2024 Nov 10
2024 Nov 17
2024 Nov 24
2024 Dec 01
Start Date of Epi Week
* Most recent week's data is preliminary, as all test have not resulted at time of report
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Mycoplasma pneumonia treatment

- Natural history is extended self-limited illness
  - Fever may wax/wane for 2-3 weeks
  - Cough often last 3 weeks before improving gradually
- Benefit of antibiotics?
  - Shorten duration of illness
  - Does not eradicate organism and prevent ongoing transmission
  - No evidence that treatment prevents severe outcomes

Mandell's 9E (2019)

Atypical Coverage - Adults?

Cochrane review of hospitalized CAP RCTs in adults (28 trials)

	Risk Ratio [95% CI]	Atypical, n	Non-Atypical, n
Mortality	1.14 [0.84 to 1.55]	2930	2514
Clinical Failure	0.93 [0.84 to 1.04]	2919	2500
Pneumococcal pneumonia	1.22 [0.88 to 1.70]	549	472
Atypical pneumonia	0.52 [0.24 to 1.10]	80	78
Legionella pneumonia	**0.17 [0.05 to 0.63]**	23	20

Eliakim-Raz N et al. Cochrane Database of Systematic Reviews. 2012;9:CD004418

Atypical Coverage - Adults?

Two RCT's done in response:

1. Garin et al. RCT of 580 patients with non-severe CAP in Switzerland: BL vs BL+M
   - No mortality difference
   - Day 7 "clinical stability" primary outcome ***indeterminate***
     - Confidence interval crossed both null & non-inferiority margin
     - Outcome driven by higher severity patients

2. Postma et al. cluster randomized trial of 2283 patients with non-ICU CAP in Netherlands: BL vs BL+M vs FQ
   - No mortality difference, met non-inferiority margin

Garin N et al. JAMA Intern Med. 2014;174:1894. Postma DF et al. NEJM 2015;372:1312. Mulla SM et al. JAMA 2012;308:2605.

Atypical Coverage - Adults?

Bottom Line

Atypical coverage not needed for most non-severe CAP.

Atypical coverage for non-severe CAP if *Legionella* suspected/confirmed likely improves outcomes.

Atypical coverage recommended for all high severity CAP.

Horita N et al. Respirology 2016. doi: 10.1111/resp.12835
https://www.brit-thoracic.org.uk/document-library/clinical-information/pneumonia/adult-pneumonia/annotated-bts-cap-guideline-summary-of-recommendations/

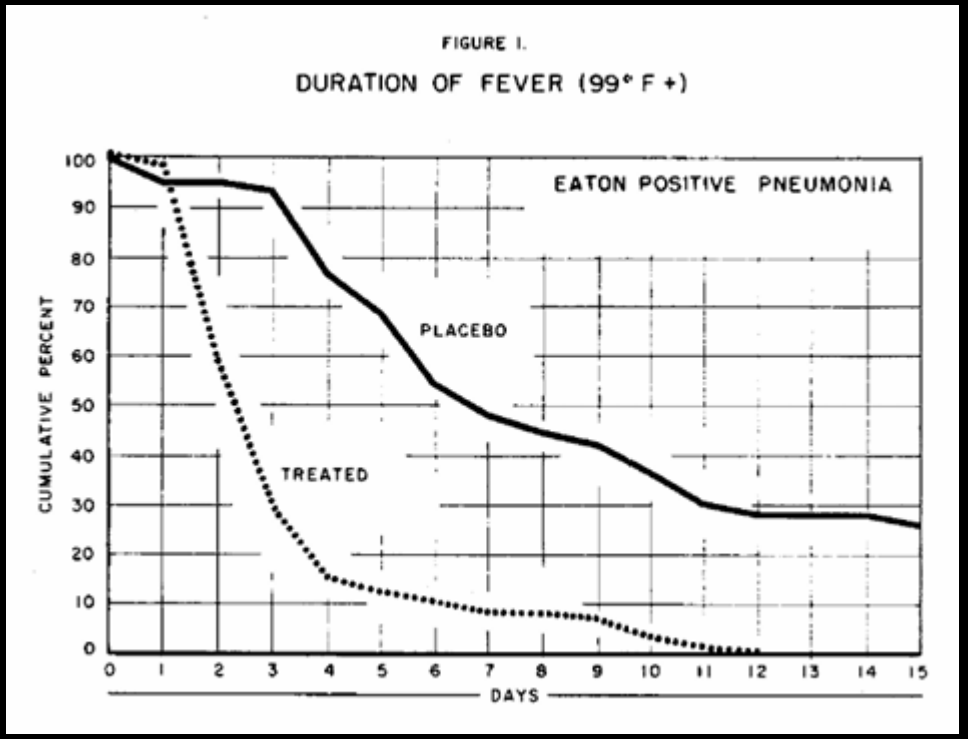
Atypical Coverage – Children?

- 2 large observational studies of hospitalized (20,743 pts) and outpatient (716 pts) CAP
  - Compared beta-lactam monotherapy vs beta-lactam + macrolide
  - Both found some benefit to combination therapy
    - Decreased hospital LOS
    - Decreased outpatient 14d treatment failure
  - Benefits were seen in **children 6-18 yo**
- However, CDC EPIC study (1418 pts) found no such benefit

Ambroggio L et al. J Pediatr 2012. doi: 10.1016/j.jpeds.2012.06.067. Ambroggio L et al. Pediatr Pulmonol 2016. doi: 10.1002/ppul.23312
Williams DJ et al. JAMA Peds 2017. doi: 10.1001/jamapediatrics.2017.3225

Mycoplasma pneumonia treatment

RCT of tetracycline vs placebo in US Marine outbreak



Attribute	Eaton Positive, Mean Days		
	Treated	Placebo	Difference
Temperature > 99° F	3.02	10.04	†7.02
Temperature > 100° F	2.13	8.14	†6.01
Positive x-ray	9.46	20.00	†10.54
Rales	6.89	15.54	†8.65
Cough	9.69	21.98	†12.29
Bed rest	5.82	9.22	†3.40
Fatigue, malaise	2.70	8.54	†5.84
Anorexia	1.97	7.04	†5.07
No. in group	59	50	‡

* Significant at 5% level.
† Significant at 1% level.
‡ Not applicable.

Kingston JR et al. JAMA 1961. doi:10.1001/jama.1961.03040150034009

TABLE 4 Studies Comparing Spectrum With Nonspectrum Treatment of Children With Acute Respiratory Infection With *M. Pneumoniae* Grouped by Outcome Term[a]

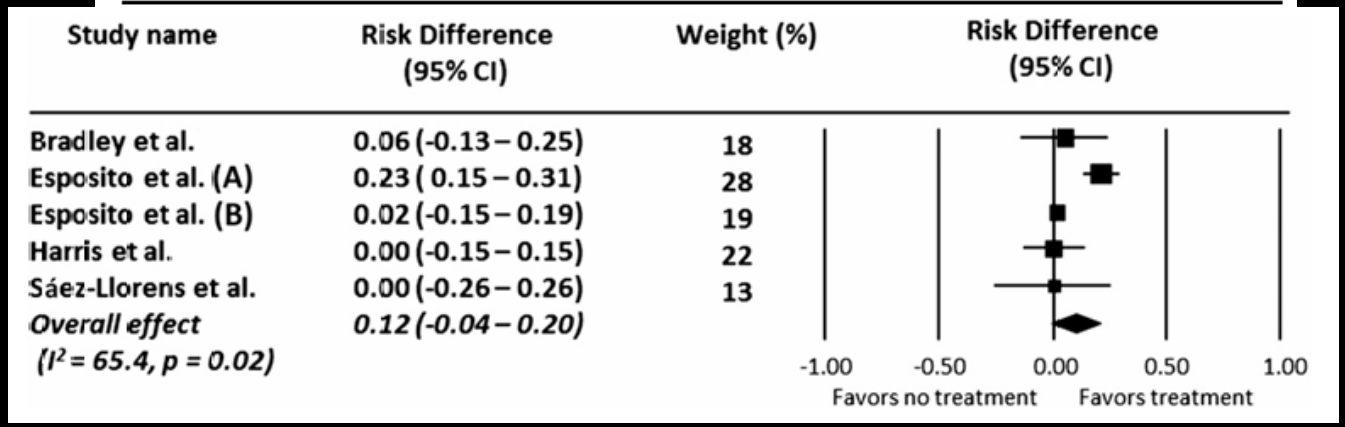
Clinical Improvement at ≤5 d

Study	Time Frame	Outcome	Treatment (*n*)		Comparator (*n*)		*P*[b]
			Improved	Total	Improved	Total	
Sáez-Llorens et al (1998)	3 d	Overall	9	9	5	5	>.99
Matsubara et al (2009)	<5 d	Fever	43	47	5	22	<.001
Kawai et al (2012)	2 d	Fever	8	8	6	21	<.001

Study	Time Frame		Days of Fever[c]	Days of Fever[c]	
Lu et al (2008)	N/A	Fever	4.9 ± 1.89	5.63 ± 2.22	.04

Clinical Improvement at >5 d

Study	Time Frame	Outcome	Treatment (*n*)		Comparator (*n*)		*P*[b]
			Improved	Total	Improved	Total	
Gendrel et al (1997)	2–18 d	Fever	9	9	2	32	<.001
Harris et al (1998)	15–19 d	Overall	21	21	9	9	>.99
Esposito et al (2005), study A[d]	1 m	Overall	49	49	88	114	<.001
Esposito et al (2005), study B[d]	6 m	Recurrent	26	45	61	109	.86
Bradley et al (2007)	10–17 d	Clinical	59	66	15	18	.44



Biondi E et al. Pediatrics 2014. doi:10.1542/peds.2013-3729

Mycoplasma pneumonia treatment

- Treatment options
  - Macrolides
  - Tetracyclines – doxy is OK in pediatrics for CAP
  - Fluoroquinolones – last line in pediatrics
- Resistance
  - Macrolide resistance (rRNA point mutation) described in China since 2010.
  - Reports from China and Japan 70-90% macrolide resistance
  - US reports <20% resistance

Mandell's 9E (2019). Waites KB et al. Clin Micro Rev 2017. doi: 10.1128/CMR.00114-16

FH Protocol

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UNCOMPLICATED COMMUNITY ACQUIRED PNEUMONIA
(3 months of age or greater)

Child with clinically suspected *OR* confirmed uncomplicated community- acquired pneumonia requiring antibiotics
(NOTE: increased rates of Mycoplasma pneumoniae within FHA currently)

Consider Chest X-ray for child presenting with prolonged fever and cough

*If fever more than 5 days, patient being admitted, medically complex background *OR* immunocompromised state: Send Nasopharyngeal Swab for Extended Respiratory Panel*

↓

Start: **amoxicillin** 15 to 30 mg/kg/dose PO TID x 5 days (max 4000 mg per day)

↓

Physician to provide 2 prescriptions to patient:
1) for initial amoxicillin treatment
2) to start only if no improvement within 72 hours
   a) NO travel history
      Prescription for: **azithromycin**
      10 mg/kg/dose (max 500 mg) PO on day 1
      5 mg/kg/dose (max 250 mg) PO on days 2 to 5

   OR

   b) Recent travel (28 days) to region with high resistance^
      Prescription for: **doxycycline**
      2 mg/kg/dose (max 100 mg) PO BID x 7 days

- ^Regions with high resistance include: China, Japan, South Korea
- mycoplasma infection more likely in sickle cell disease
- Consult to Pediatrics recommended for all immunocompromised patient
- **doxycycline** is not available as a commercially prepared suspension. If liquid preparation is required, send patient to compounding pharmacy.
- **doxycycline** capsules available as 100 mg per capsule

December 2024

Developed in collaboration by FH ED, Pediatrics, and AMS

Pediatric CAP

Infection	FH Empiric Antibiotic Option(s) and Dose	
	First Choice	Penicillin Allergy
Community Acquired Pneumonia over 3mo of age	Mild: Consider no treatment if likely viral *OR* amoxicillin 30 mg/kg PO TID Moderate: ampicillin 50 to 100 mg/kg IV Q6H + azithromycin 10 mg/kg PO Q24H x 1 day then 5 mg/kg PO Q24H x 4 days Severe (PICU admission): cefTRIAXone 50 mg/kg IV Q12H + vancomycin 20 mg/kg IV Q6H + azithromycin 10 mg/kg IV/PO Q24 hours +/- oseltamivir (*age/weight based dosing)*	Mild: Consider no treatment if likely viral *OR* amoxicillin 30 mg/kg PO TID Moderate: ampicillin 50 to 100 mg/kg IV Q6H + azithromycin 10 mg/kg PO Q24H x 1 day then 5 mg/kg PO Q24H x 4 days Severe (PICU admission): cefTRIAXone 50 mg/kg IV Q12H + vancomycin 20 mg/kg IV Q6H + azithromycin 10 mg/kg IV/PO Q24 hours +/- oseltamivir (*age/weight based dosing)*

Antibiotics in Outpatient CAP

Risk Stratification		Duration (days)
Outpatient CAP	amoxicillin 500 mg PO TID *If severe penicillin allergy:* cefuroxime 500 mg PO BID **OR** doxycycline 100 mg PO BID	**3**

FH ASP Handbook: Community-Acquired Pneumonia

Hospitalized CAP – Nonsevere

Risk Stratification		Duration (days)
Hospitalized CAP, Nonsevere CRB-65 = 0 to 1	amoxicillin-clavulanate 500-125 mg one tab PO TID **OR** ceftriaxone 1000 mg IV q24h *If Legionella suspected:* **ADD** azithromycin 500 mg PO/IV q24h *If severe ceftriaxone allergy:* moxifloxacin 400 mg PO daily (addition of azithromycin not necessary)	**3-5**

Empiric M. pneumoniae therapy not generally needed in adults with nonsevere CAP

CRB-65 Severity Score

1 point for each feature present:

- **C**onfusion (**new** disorientation to person, place or time)
- **R**espiratory rate ≥30/min
- **B**lood pressure (sBP <90 or dBP ≤60 mmHg)
- Age ≥**65** years

Legionella Pneumonia

- Cases occur in Fall and early Winter
- Classic: high fever, pneumonia, GI symptoms
- More commonly: non-specific pneumonia
- *Hyponatremia* and *hepatic dysfunction* may be a clue
- Urine antigen test for serogroup 1 widely available
- Detected on some multiplex respiratory panel PCRs
- Culture and also available, speak to your micro lab.

Hospitalized CAP – Severe

Risk Stratification			Duration (days)
Hospitalized CAP, Severe CRB-65 ≥ 2 ***OR*** respiratory failure ***OR*** requiring ICU admission	Standard Regimen	ceftriaxone 1000 mg IV q24h **PLUS** azithromycin 500 mg PO/IV q24h *If severe ceftriaxone allergy:* moxifloxacin 400 mg PO/IV daily	**3-7**
	Potential *Pseudomonas* • COPD with FEV_1<50% • Structural lung disease • Recent broad-spectrum antibiotics • From nursing home or recent hospitalization	piperacillin-tazobactam 4500 mg IV q6h **PLUS** azithromycin 500 mg PO/IV q24h *If severe penicillin allergy:* meropenem 500 mg IV q6h **PLUS** azithromycin 500 mg PO/IV q24h **OR** levofloxacin 750 mg IV/PO q24h	
	Potential MRSA • Necrotizing pneumonia • Recent influenza • Injection drug use • Known MRSA colonization	**ADD** vancomycin	

FH ASP Handbook: Community-Acquired Pneumonia

Typical Symptom Trend

Abnormality	Average duration
Tachycardia and hypotension	2 days
Fever, tachypnea, and hypoxia	3 days
Cough	2 weeks
Fatigue	2 weeks
Radiographic infiltrates	4-6 weeks

NICE Clinical Guideline 191. Pneumonia in adults: diagnosis and management. https://www.nice.org.uk/guidance/cg191
UpToDate

Follow-up CXR?

- Early CXR may appear worse despite patient improving
- Know what you're looking for if repeating CXR!
  - Pleural effusion -> Tap
  - Lung abscess -> Prolonged abx course
  - More infiltrates -> ?!?!
- Routine repeat CXR no longer recommended
  - Lung cancer screening program in BC

British Thoracic Society Guidelines for Management of CAP in Adults 2015 (https://www.brit-thoracic.org.uk/)

Oral Transition - WHEN

Patients should be transitioned from intravenous to oral therapy when they are:

1. Hemodynamically stable
2. Improving clinically
3. Afebrile for 24 hours
4. Can ingest medications and have a functioning GI tract

Oral Transition - WHAT

- Switch to **same agent** or **same class** as intravenous drug

  Tip – Oral amoxicillin is more active against S. pneumoniae than cefuroxime, has lower C difficile risk, and more narrow-spectrum of activity.

- Switching to a different class of agents simply because of its high bioavailability (such as a fluoroquinolone) not necessary

Oral Therapy for Bacteremia?

Even in the presence of pneumococcal bacteremia, a switch to oral therapy can be safely done once clinical stability is achieved and prolonged intravenous therapy is not needed.

A tip – review the possibility of empyema, endocarditis, and meningitis before considering PO transition in bacteremic pneumococcal pneumonia.

FH ASP Handbook: Community-Acquired Pneumonia.
Ramos-Otero et al. J Clin Pharm 2022. doi: 10.1002/jcph.2097. Clutter DS et al. AAC 2024. doi: 10.1128/aac.00220-24

Duration of Therapy 5 Days?

- Multicenter RCT in Spain of hospitalized CAP
  - Acute clinical sign (incl fever) + New infiltrate
- Patients randomized at day 5 of CAP therapy
  - Control: physician decision
  - Intervention: antibiotics stopped at day 5 if

    T ≤ 37.8°C for 48 hrs
    AND no more than 1 sign of clinical instability

    sBP <90 mmHg
    HR >100/min
    RR > 24/min
    Sat <90% or PaO2 <60 mmHg on room air

Uranga A et al. JAMA Intern Med. 2016;176:1257

Duration of Therapy 5 Days?

	Control Group (n=150)	Intervention Group (n=162)	P value
PSI class IV-V	40.7%	37.0%	
Duration of antibiotics, mean	10 d	5 d	**<0.001**
Primary Outcomes			
Clinical success, day 10	48.6%	56.3%	0.18
Clinical success, day 30	88.6%	91.9%	0.33
Secondary Outcomes			
30-day mortality	2.2%	2.1%	>0.99
30-day readmission	6.6%	1.4%	**0.02**

Uranga A et al. JAMA Intern Med. 2016;176:1257

Down to 3 Days

- Multicenter RCT in France of hospitalized CAP
  - Acute clinical sign + Fever + New infiltrate
- All patients given IV beta-lactam monotherapy for 3 days, then…
- Randomized at day 3 of CAP therapy if they met clinical stability criteria:
  - Placebo x 5 days
  - Oral amox-clav TID x 5 days

Dinh A et al. Lancet. 2021;397;1195.

Down to 3 Days

	3d Group (n=152)	8d Group (N=151)	P value
Baseline Characteristics			
Age	72.5	74.0	
PSI class IV-V	38%	41%	
Primary Outcomes			
Clinical cure, day 15	77%	68%	9.4% (-0.4% to 20%) NON-INFERIOR
Secondary Outcomes			
Clinical cure, day 30	72%	72%	>0.99
Length of stay	5d	6d	0.74
30-day mortality	2%	1%	>0.99

Dinh A et al. Lancet. 2021;397;1195.

Duration of Therapy

Discontinuation at Day 3 (short course)	Discontinuation at Day 5 (DEFAULT)
1. Afebrile (T≤37.8C) 2. Have **no** CAP-associated sign of clinical instability - sBP <90 mmHg - HR >100 beats/min - RR > 24 breaths/min - O2 sat <90% on room air (or baseline home O2)	1. Afebrile (T≤37.8C) for 48 hours 2. Have **no more than 1** CAP-associated sign of clinical instability - sBP <90 mmHg - HR >100 beats/min - RR > 24 breaths/min - O2 sat <90% on room air (or baseline home O2)
Dinh A et al. Lancet 2021. doi: 10.1016/S0140-6736(21)00313-5	Uranga A et al. JAMA IM 2016. doi: 10-1001/jamainternmed.2016.3633

Pneumococcal Bacteremia

- Multicentre Canadian-led RCT in 7 countries of bacteremia: 7 vs 14 days

	7-day (n=1814)	14-day (n=1794)	P value
Select Patient Characteristics:			
Median Age	70	70	
Lung Source	13%	13%	
S. pneumoniae	86	78	
Outcomes:			
90d Mortality	14.5%	16.1%	Non-inferior
Length of stay, median	10 days	11 days	

Daneman N et al. NEJM. 2024. doi: 10.1056/NEJMoa2404991

CAP Duration Summary

- Vast majority of outpatient CAP can be treated with 3 days of antibiotics
- Up to 5 days may be required if fevers are slow to resolve
- Outpatient CAP should NOT need more than 7 days of antibiotics...SOMETHING IS WRONG

Take Home Points

1. Majority of pneumonia is caused by viruses, but recognize role of *S. pneumoniae*, *M. pneumoniae*, and *Legionella*.

2. Most therapy for CAP is empiric and focuses is on *S. pneumoniae*. Add atypical coverage if severe disease or suspected/confirmed atypical pneumonia (especially school-aged children/non-response to amox)

3. Shorter is better – most CAP only needs 3-5d of antibiotics

Thank You

Questions?

Comments?

The BCCDC PHL offers an **extended respiratory pathogen panel for a wider range of pathogens upon request**.

The following instances are appropriate indications for the respiratory panel test:

- For individuals where atypical bacterial (*Mycoplasma pneumoniae, Chlamydia pneumoniae, or Legionella pneumophila*) etiology is suspected and conventional treatments have not resolved disease, OR who have either worsening disease or need for hospitalization
- For individuals with negative viral screen testing (SARS-CoV-2, Influenza A/B, RSV) results who fall into the following categories:
    - Hospitalized patients with respiratory symptoms and suspected infectious etiology, not yet identified
    - Immunosuppressed (e.g. cancer on chemotherapy, solid organ transplant) or medically complex (e.g. with several comorbidities) individuals where a diagnosis will inform management
    - Cases with extrapulmonary organ involvement for which an infectious etiology is suspected, including but not limited to myocarditis/pericarditis, acute flaccid paralysis, encephalitis
    - Febrile Infants < 3 months of age
    - Pediatric patients with fever for ≥5 days who are not responding to empiric therapy
    - Individuals in a suspected facility outbreak, only for the first 6 specimens within a localized region (e.g. ward)