# Nursing Home-Associated Pneumonia in the 21st Century: Classification, Diagnosis, Etiology, and Treatment

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# Mitigating Potential Bias



- There are no potential biases

# Objectives



- Review the classification of nursing home-associated pneumonia [NHAP]
- Provide a diagnostic approach to identify NHAP; review role of biomarkers in diagnosis of NHAP
- Review treatment options in the nursing home and duration of treatment

# NHAP: Background



- Second most common infection in NHs
- Mortality 15-30%
- Considerable morbidity in survivors
- Hospitalization leads to poorer outcomes than rx in NH
- Majority [75%] treated in the nursing home
- Incidence = 0.5-1.0 episodes per 1000 RCD per month

# Classification of NHAP



- NHAP often included in studies of community-acquired pneumonia [CAP] or studies of NH infection published in the 1980s and 1990s [see Muder Am J Med 1998 for an excellent review]
- Etiology of NHAP was thought to resemble CAP based on reliably obtained sputum cultures [see Muder Am J Med 1998]
- However, the classification changed in the early 2000s when there was concern about resistant bacteria as etiologic agents of NHAP
- In 2005 a guideline was published by ATS and IDSA entitled "Management of hospital-associated, ventilator-associated, and healthcare-associated pneumonia [HCAP]"

# HCAP



- HCAP patients defined a subset of community-dwelling patients thought to be at risk for infection due to resistant organisms such as MRSA or resistant gram-negative bacilli
- Patients in the HCAP category included: hospitalization in prior 90 days, nursing home residents, outpatient IV antibiotic therapy, chemotherapy, or wound care in prior 30 days, and on dialysis
- NH residents were included in HCAP based on 2 studies in residents with pneumonia intubated and in an ICU; bronchoscopy was done to identify a causative organism [El Solh AJRCCM 2001; El Solh AJRCCM 2003]
- ATS/IDSA guideline recommended empiric  broad-spectrum antibiotic therapy for patients meeting HCAP criteria; this could mean 3 or 4 antibiotics at one time in some patients

# HCAP [Cont'd]



- Studies appeared that questioned the validity of the HCAP criteria and the investigation shifted from looking at the heterogeneous category of HCAP as a indication for broad-spectrum therapy to a focus on using algorithms to identify those with pneumonia due to a resistant organism
  - U.S. studies reported higher frequency of resistant organisms and mortality in HCAP patients than those with CAP [Kollef Chest 2005; Micek AAC 2007]
  - European studies found a much lower frequency of resistant organisms in HCAP group and narrow spectrum treatment was efficacious [Carratala Arch Intern Med 2007; Venditti Ann Intern Med 2009; Chalmers Clin Infect Dis 2011]
  - Other studies verified European studies: Gross et al AAC 2014; Yap et al Infect Dis Clin NA 2013; Jones et Clin Infect Dis 2015; Valles et al Intens Care Med 2013

# HCAP [Cont'd]



- In the update of the 2005 guideline by ATS/IDSA [Clin Infect Dis 2016] HCAP was removed because of the studies indicating that not all patients fulfilling HCAP criteria are at high risk for resistant organisms
- Authors of the ATS/IDSA guideline indicated that the issue of resistant organisms in community-dwelling patients with pneumonia should be based primarily on risk factors for resistant organisms not solely on recent contact with healthcare system and recommended that this be addressed in the next CAP guideline
- Keep in mind that the majority of NH residents who develop pneumonia are treated in the NH and guidelines focus on those hospitalized
- It is unknown if the 2005 ATS/IDSA guideline affected treatment of NHAP in the NH
- See excellent review by Waterer Clin Chest Med 2018 for full background on HCAP

# Risk factors for multi-drug resistant organism (MDRO) Colonization in NH Residents
(Drinka et al JAMDA 2010)



- Exposure
  - History of MDRO [e.g., MRSA, Pseudomonas, ESBL, CRE]
  - Antibiotic rx within prior 3 months
  - Hospitalization within prior 3 months
  - Frailty [non-ambulatory; bedridden]

- "Fertile ground" for colonization
  - Open wounds
  - Indwelling devices [foley, feeding tube, tracheostomy]
  - Structural lung disease [bronchiectasis, COPD] (Pseudomonas)

# Diagnosis of Pneumonia in NH Residents and Role of Biomarkers

# Caveat



- Clinicians need to appreciate the difference between healthcare-associated surveillance definitions and clinical diagnoses
- Clinical diagnoses are based, in part, on the subjective judgment of clinicians and are used to guide treatment of individual patients.
- Surveillance definitions are used to assess a facility's healthcare-associated infection burden and the need for and effect of prevention efforts.
- Infection surveillance definitions are NOT intended for clinical diagnosis or to guide patient treatment.

*Ann Intern Med.*2013;159:631-635

Infec Control Hosp Epidemiol 2012;33(10):965-977

# Comparison of McGeer Revised and Clinical Definitions of Pneumonia in NH Resident



## McGeer Revised

ALL 3 criterion must be present

1. CXR with infiltrate
2. At least one of following resp s/sx:
   a. New or increased cough
   b. New or increased sputum
   c. O2 saturation < 94% on room air
   d. New or changed lung exam
   e. Pleuritic chest pain
   f. Respiratory rate of ≥25 breaths/min
3. At least one constitutional criteria: fever; leukocytosis; mental status change; functional status change

## Clinical (Bedside) Criteria

2 or more of the following resp s/sx:

1. Cough
2. Shortness of breath
3. Resp rate > 25/min
4. Oxygen sat < 94% on room air
5. Abnormal chest exam [Provider or nurse]

With or without:

1. Change in mental status
2. Change in functional status
3. Fever

Are there risk factors for aspiration? [dysphagia, stroke, Parkinsons, PEG, sedation]

# NHAP: Roadblocks to the Diagnosis

- Resident with suspected infection is often evaluated by nursing staff rather than a physician or physician extender; however, nursing staff vary in their bedside evaluation skills
- Therefore, nursing staff need to be educated as to the signs/symptoms to look for as well as the information that should be collected before calling the provider [templates for staff provide consistency in evaluation: INTERACT or AHRQ templates]
- In the absence of provider exam, bedside evaluation by nursing staff is the key to the diagnosis and management of NHAP in the nursing home

# Suggested Diagnostic Studies in NH Residents with Suspected Pneumonia Managed in Nursing Home



- Chest x-ray  [Ultrasound of chest?]
- Electrolytes and BUN/creat to assess hydration
- CBC is not necessary
- Sputum culture or blood culture not necessary
- Biomarkers or molecular diagnostic studies ???

# Biomarkers in the Diagnosis and Treatment of NHAP



- Multiple biomarkers have been evaluated with the goal primarily of assessing severity of pneumonia and predicting mortality
- Procalcitonin and C-reactive protein have been most often studied
- Debated whether or not procalcitonin levels distinguishes between bacterial and viral infection in suspected pneumonia
- Procalcitonin may be most useful in monitoring response to therapy and reducing duration of therapy

# Procalcitonin Levels in Respiratory Infection



- Efficacy and safety of PCT-guided antibiotic decision making in respiratory illness has been demonstrated in 14 RCTs [Schuetz et al Arch Intern Med 2011]
- In a "real-life" study of PCT in 1759 patients adherence to an algorithm utilizing PCT levels was associated with a significant decrease in duration of Rx compared with not following the algorithm; this was true if using PCT to withhold rx initially or stopping rx early [Albrich et al Arch Intern Med 2012]
- In NH setting PCT level may not be available for use regarding initiating or withholding rx but may be useful in decision to continue rx or length of rx
- Algorithms utilizing results of PCT testing have been developed [Schuetz Curr Opin ID 2013]

# Documentation of the "Thought Process" in Medical Record



- Document the clinical findings in the medical record if you see and examine the patient
- If it is after hours and you are not available to evaluate the resident, documentation should still be done
- If you are using an electronic record, document the findings given to you, along with your assessment, in the EHR; this provides the date and time of documentation automatically and defines the "thought process" utilized to make a diagnosis of pneumonia
- Covering provider should use the same approach regarding either face-to-face evaluation or phone consultation

# Etiology of NHAP

# Etiology of NHAP Thought to be Similar to CAP



| | |
|---|---|
| *S. pneumoniae* | 20-30% |
| *H. influenzae*, *Moraxella* | 5-10% |
| *Mycoplasma*, *Chlamydia* | < 2% |
| *S. aureus* (MRSA)* | ? (< 10%) |
| Gram-neg bacilli* | < 15% |
| Viral | ? (< 5%) |
| *Legionella* | Rare |

# Studies of the Etiololgy of NHAP Since 2005



- There have been 10 studies of etiology of NHAP since 2005; all have been done in hospitalized residents; some compared NHAP with CAP
- None of the studies were done in US or Canada
- Japan 3, Korea 3, Hong Kong 2, Spain 1, and France 1
- Study size ranged from 54-172 residents; etiology identified in 18-72% of episodes; methodology ranged from sputum/blood cult, PUA, LUA, serology for atypical org and viruses, nasal swabs for viral cult or PCR

# Role of Atypical Pathogens in NHAP
(Ma et al JAMDA 2013)



- Objective: to study the prevalence and characteristics of pneumonia due to atypical pathogens in NH residents
- Setting: Hospitalized residents from 4 NHs in Hong Kong 2006-07
- Participants: > 65; respiratory signs/sx; positive CXR
- Methods: sputum routine and mycobacterial cultures, blood and urine cultures, serology, and nasopharyngeal aspirate viral culture and polymerase chain reaction [PCR] testing, PUA, LUA

# Results
(Ma et al JAMDA)



- 108 episodes of pneumonia
- 34 [31%] episodes with typical bacterial pathogen
- 3 atypical mycobacteria
- 11 [10%] with atypical pathogens
- 26 [24%] virus
- No pathogen in 32%

**Table 2**
Summary on Bacterial Findings With Either Definitive or Probable Cause

| Pathogens | Total | Sputum | Serology | Blood | NPA PCR | Urinary Antigen |
|---|---|---|---|---|---|---|
| Bacterial pathogens | | | | | | |
| *Streptococcus pneumoniae* | 16 | | | 1 | | 16 |
| *Haemophilus influenzae* | 5 | 5 | | | | |
| *Pseudomonas* spp. | 7 | 7 | | | | |
| *Escherichia coli* | 1 | 1 | | | | |
| *Serratia* spp. | 1 | 1 | | | | |
| *Klebsiella* spp. | 1 | 1 | | | | |
| MRSA | 3 | 2 | | 1 | | |
| MAC | 3 | 3 | | | | |
| Atypical pathogens | | | | | | |
| *Mycoplasma pneumoniae* | 6 | | 1 | | 5 | |
| *Chlamydophila pneumoniae* | 3 | | | | 3 | |
| *Chlamydophila psittaci* | 2 | | 2 | | | |
| *Coxiella burnetii* | 1 | | 1 | | | |

MAC, *Mycobacterium avium* complex; MRSA, methicillin-resistant *Staphylococcus aureus*; NPA, nasopharyngeal aspirate; PCR, polymerase chain reaction.
One patient had infection with *S. pneumoniae* diagnosed by both blood culture and urinary antigen test.

Ma et al JAMDA 2013

**Table 3**
Summary on Viral Findings With Either Definitive or Probable Cause

| Pathogens | Total | NPA Viral Isolation | NPA PCR | Serology |
|---|---|---|---|---|
| Influenza A | 4 | 2 | 2 | 2 |
| Influenza B | 3 | 1 | 3 | 1 |
| Parainfluenza virus type 1 | 5 | | 5 | 1 |
| Parainfluenza virus type 2 | 1 | | 1 | |
| Parainfluenza virus type 3 | 8 | 3 | 4 | 7 |
| Parainfluenza virus type 4 | 1 | | 1 | |
| Respiratory syncytial virus | 13 | 2 | 6 | 5 |
| Metapneumovirus | 9 | | 9 | |
| Enterovirus | 3 | | 3 | |
| Coronavirus | 2 | | 2 | |
| Rhinovirus | 1 | | 1 | |

NPA, nasopharyngeal aspirate; PCR, polymerase chain reaction.
One infection can be detected by more than one test.

Ma et al JAMDA 2013

# Outcome of Treatment
(Ma et al JAMDA 2013)



- All treated with antibiotic; specific treatment regimens were not provided
- Hospital mortality was lower in those without a pathogen identified 2/34 [5.9%] vs with a pathogen identified 14/74 [18.9%] ($P$ = .077)
- Only 1 of 11 with infection due to an atypical organism was treated with an effective antibiotic during hospitalization; none of these patients died
- Conclusion: It may not be necessary to include empirical coverage for atypical pathogens in NH residents with pneumonia

# Treatment of NHAP in the Nursing Home

# Treatment of Pneumonia in the Nursing Home: Considerations



- Location of Rx: NH vs Hospital
- Initial route of Rx in NH: oral or parenteral
- If parenteral, timing of switch to oral agent
- Duration of Rx
- Treatment regimens
- Follow-up ["Antibiotic time-out"]

# Clinical Pathway to Reduce Hospitalizations in NH Residents with Pneumonia

(Loeb et al JAMA 2006)

- Cluster randomized control trial in 22 NH in Hamilton, Ontario, Canada
- 680 residents in study and monitored for LRTI
- NHs randomized to a clinical pathway developed by investigators or usual care
- Primary outcome measure was hospitalization

# Clinical Pathway for Determing Location of Treatment of NHAP (Loeb et al JAMA 2006)



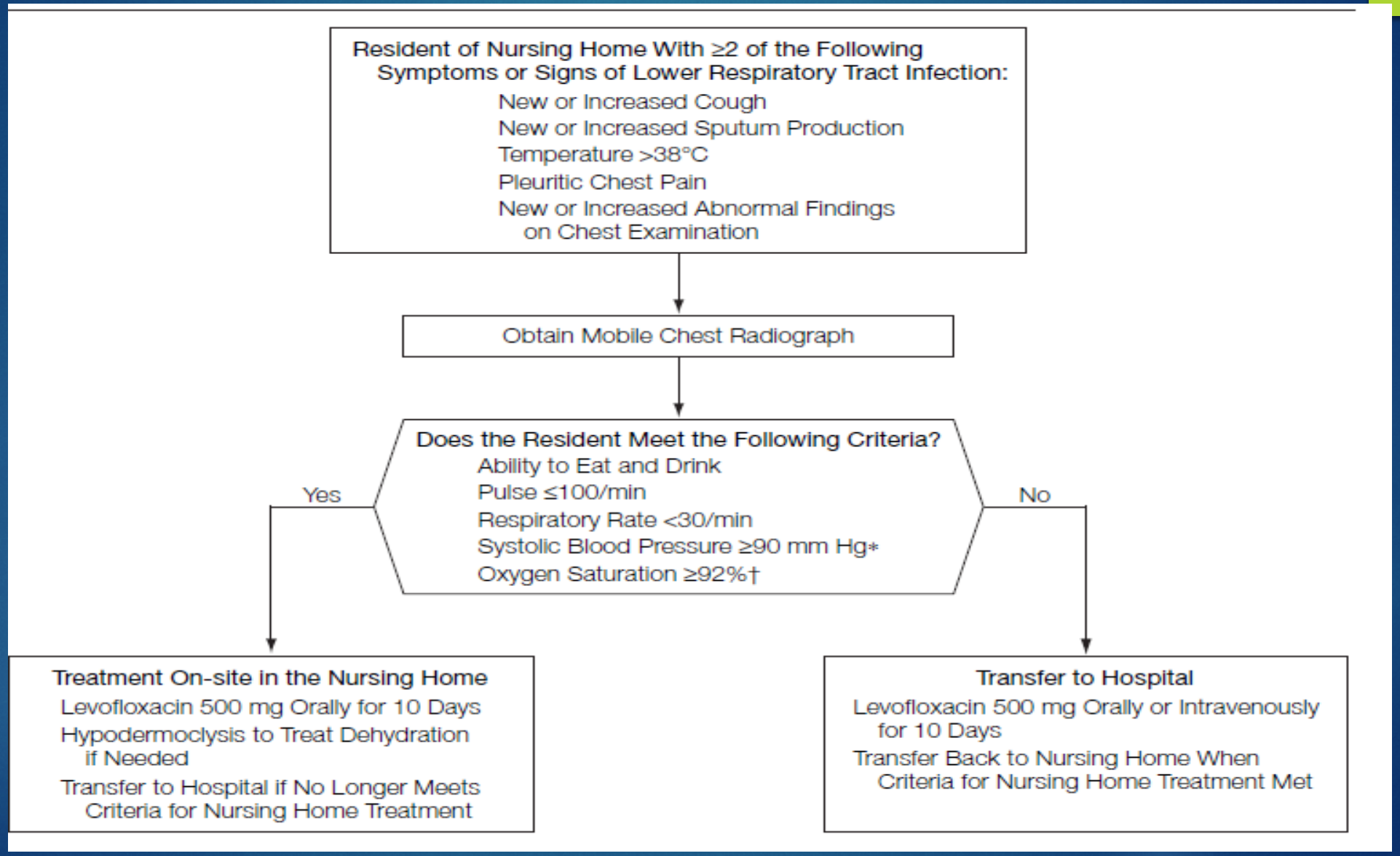

**Table 2.** Summary of Weighted Outcome Variables and the Differences in 10 Clinical Pathway and 9 Usual Care Nursing Homes*

| Outcomes | Weighted Mean (95% CI) | | | *P* Value |
|---|---|---|---|---|
| | Clinical Pathway (n = 314) | Usual Care (n = 347) | Difference | |
| Hospitalizations, %† | 8 (4 to 12) | 20 (15 to 26) | 12 (5 to 18) | .001 |
| Hospital days per resident | 0.79 (0.45 to 1.13) | 1.74 (1.17 to 2.3) | 0.95 (0.34 to 1.55) | .004 |
| Visits to emergency department without admission, % | 1.2 (–0.2 to 2.5) | 1.6 (–0.6 to 3.8) | 0.4 (–1.9 to 2.8) | .72 |
| Death, % | 3.1 (–0.2 to 6.4) | 6.0 (1.8 to 10.3) | 2.9 (–2.0 to 7.9) | .23 |
| Change in quality of life from baseline | –0.032 (–0.044 to –0.019) | –0.037 (–0.050 to 0.023) | –0.005 (–0.022 to 0.012) | .055 |
| Change in functional status from baseline | –0.105 (–0.188 to –0.022) | –0.175 (–0.389 to 0.040) | –0.069 (–0.263 to 0.124) | .23 |
| Falls, % | 10.9 (6.4 to 15.3) | 9.5 (5.9 to 1.3) | –1.3 (–6.6 to 3.9) | .60 |
| Time to normalization of vital signs, d‡ | 2.55 (1.60 to 3.48) | 2.66 (2.24 to 3.08) | 0.12 (–0.78 to 1.02) | .79 |

Loeb et al JAMA 2006

# Conclusions Regarding Hospitalization Decision in Residents with NHAP



- Algorithm or pathways standardize the evaluation of residents for pneumonia regarding hospitalization decision
- Decision to hospitalize needs to take into consideration advance directives and family preferences
- In those without advance directives, family preference is a major factor in location of treatment
- NH staff concerns also a play a role in the hospitalization decision
- Pathways are met to assist in the decision-making process and do not supersede the provider's judgment

# Initial Route of Treatment in NH



- If the resident is assessed to be able to swallow safely, and vital signs are stable, start with oral treatment
- If the resident has dysphagia or it is after hours and there is concern for using the oral route, use parenteral therapy [IM] for 1-2 days and then reassess for change to the oral route

# Timing of Switch to Oral Therapy if Initially on Parenteral Antibiotic Therapy

(Naughton et al JAGS 2000)

- Retrospective study of NHAP in 11 NHs in one community that was used to develop a treatment guideline
- 171/239 [72%] episodes were initially treated in NH; 66 of 171 [39%] were initially treated with an intramuscular antibiotic [ceftriaxone or cefotaxime] and switched to an oral regimen to complete rx
- Median duration of IM rx was 2 days; 75% 3 days.
- There was no difference in % hospital transfers or 30-day mortality in those treated initially parenterally vs orally in the nursing home

# Definition of Clinical Stability to Determine Switch from IM or Oral RX of NHAP

(Halm et al JAMA 1998)

Clinical stability is defined as **all** of the following being present:

- Improvement in signs and symptoms
- Afebrile for ≥16 hours
- No acute cardiac or other life-threatening event in the first 3 days of treatment
- Able to take oral medication

# Guideline Recommendation for timing of switch from IM to Oral Rx of NHAP

(Naughton et al JAGS 2000)

- Most residents [75%] will achieve clinical stability by day 3 of IM therapy
- Criteria for clinical stability should be monitored daily by NH staff
- Criteria for clinical stability should be incorporated into the "antibiotic time-out" protocol to assist the provider in making the "switch" decision

# Duration of Treatment of Pneumonia

# Studies of Short-Course Treatment of Pneumonia



- Shorr et al [Clin Ther 2005] retrospectively analyzed data of an RCT of levofloxacin 750 mg daily for 5 days vs 500 mg daily for 10 days in enrollees ≥ 65 with CAP (no NH residents enrolled; no difference in mortality or adverse reactions; success rate was 89% with short course rx vs 92% with long-course rx

- El Moussaoui et al [BMJ 2006] performed a RCT of 3 vs 8 days amoxicillin rx of mild to moderate CAP; no difference in cure rates between the short and longer course regimens

- Uranga et al [JAMA Intern Med 2016] RCT of CAP [No NH res]: 5 days if clinically stable vs provider preference; no difference in outcome or symptoms at 30 days

Table. Infections for Which Short-Course Therapy Has Been Shown to Be Equivalent in Efficacy to Longer Therapy

| Disease | Treatment, Days | |
|---|---|---|
| | Short | Long |
| Community-acquired pneumonia[1-3] | 3-5 | 7-10 |
| Nosocomial pneumonia[6,7] | ≤8 | 10-15 |
| Pyelonephritis[10] | 5-7 | 10-14 |
| Intraabdominal infection[11] | 4 | 10 |
| Acute exacerbation of chronic bronchitis and COPD[12] | ≤5 | ≥7 |
| Acute bacterial sinusitis[13] | 5 | 10 |
| Cellulitis[14] | 5-6 | 10 |
| Chronic osteomyelitis[15] | 42 | 84 |

Spellberg JAMA Intern Med 2016

# Duration of Treatment of NHAP



- CAP studies dealing with short duration of treatment have excluded NH residents with pneumonia
- No studies of short duration of treatment of NHAP published to date
- Providers typically treat for 7-14 days
- However, CAP studies provide strong support for shortening course of treatment of NHAP if clinical stability is achieved

# Treatment Regimens for NHAP

# Infectious Diseases Antibiotic Treatment Axioms



- Treat with one agent whenever possible
- Shorter duration (5 days) of treatment is safe and efficacious

LB Rice Clin Infect Dis 2008

# Guideline Recommendations for Empiric Rx of NHAP



| Guideline | Rx in NH | Rx in Hosp |
|---|---|---|
| IDSA 1998 CAP | None | BL +/- Macro or FQ |
| IDSA 2000 CAP | "in older pt, FQ may be preferred" | ES ceph + macro or BL/BLI + macro or FQ |
| Canadian IDSA 2000 CAP | FQ or amox/clav + macro | FQ or 2G, 3G, 4G ceph + macro |
| ATS 2001 CAP | Oral BL, CTRX plus macro/doxy or FQ alone | 3G ceph or BL/BLI, or amp plus macro or FQ alone |
| IDSA 2003 CAP | Same as Canadian | Same as Canadian |

# ATS/IDSA CAP Guideline 2007



- Supported classifying NHAP as a healthcare-associated pneumonia (HCAP) and recommended following the 2005 HCAP guideline for treating NH residents hospitalized with pneumonia

- Awaiting the update of the CAP guideline by ATS/IDSA and recommendations for treatment of nursing home residents with pneumonia which was scheduled to be published in summer of 2018 but has yet to be published

# Treatment Options in the Nursing Home: Parenteral Rx Initially*



- Parenteral therapy: Ceftriaxone 500 mg IM daily 1-3 days; switch to an oral regimen to complete treatment

- Oral regimen:
  - Cepodoxime or
  - Amoxicillin/clavunate or
  - Levofloxacin

*The recommendations assume there are no risk factors for MDROs and atypical organisms are not common in NH residents

# Treatment Options in the Nursing Home: Oral Rx Initially



- High dose amoxicillin 1 gm TID or amoxicillin/clavulanate 875 mg/125 mg BID x 5 days
- Cefpodoxime 200 mg BID x 5 days
- Doxycycline 100 mg bid alone x 5 days
- Levofloxacin 500-750 mg daily x 5 days [associated with multiple adverse effects; not a first-line agent]
- Do not use a macrolide alone because of resistance among pneumococci and ? Mycoplasma

# Treatment Options if There is a Risk for MDRO



- Disclaimer: There are  no studies available to base recommendations; following comments are those of the lecturer and are a "best guess"
- Treatment decision will depend on which risk factor(s) are present including results of prior cultures
- If dealing with prior hospitalization only, consider empiric anti-pseudomonal cephalosporin IM or IV [e.g. cefepime IM] and monitor response
- If dealing with recent antibiotic rx, use another class of antibiotic orally or IM based on status of resident
- If prior cultures demonstrate MRSA or an ESBL-producing organism, consider hospitalization because these organisms tend to cause moderate to severe pneumonia and may be difficult to treat in the NH

# Follow-Up During Treatment of NHAP in Nursing Home

- On day 2-3 of therapy there should be an "antibiotic time-out" to assess the resident's status and response to treatment
- "Time-out" is part of the antimicrobial stewardship program
  - Nursing staff contacts provider or provider has face-to-face evaluation of resident
  - Determine if antibiotic therapy should be stopped, changed, or continued
  - Determine duration of treatment; if clinical stability by day 3, rx can usually be completed by 5 days but no longer than 7 days
  - "Time-out" decisions documented in the medical record

No need to repeat CXR or blood tests if resident is improving [consider repeating PCT level if one was obtained initially]

# Thank You !!

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