Management of Community Acquired Pneumonia in the Ambulatory Setting

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Educational Objectives:

1. Define the different risk factors for bacterial pneumonia seen in the ambulatory setting
2. Describe an approach to recurrent pneumonias in the outpatient setting
3. Describe a treatment plan for ambulatory care of pneumonia
4. Review indications for outpatient vs. inpatient management of pneumon

Scenario:
Ms. JS is a 68-year-old woman with diabetes, hypertension, gastroesophageal reflux disease (GERD), chronic obstructive pulmonary disease (COPD), congestive heart failure with reduced ejection fraction, and a prior history of smoking tobacco who presents to your clinic for "recurrent pneumonias." She reports that over the last week, she has had a productive cough with yellowish sputum, low-grade fevers, and general malaise. She reports no hemoptysis, chest pain, urinary changes, or joint symptoms. Her medication list includes glargine insulin, lisinopril, aspirin, omeprazole, simvastatin, fluticasone/salmeterol, and metoprolol. On examination, she is seated comfortably in no acute distress, T 99.5 F, BP 150/75, HR 95, RR 22, SpO2 93% on room air. Head and neck exam shows poor dentition but no cervical lymphadenopathy. Cardiac exam shows a mildly elevated JVP, a regular rate and rhythm with a II/VI systolic ejection murmur. Her chest expansion is symmetric; she has no increased work of breathing, but does have decreased breath sounds at the right base and egophony at the right base. She has no wheezing, clubbing, or peripheral edema. Chest X-ray shows a right lower lobe opacity without associated effusion. She has not had any recent hospitalizations. Her last course of oral antibiotics was two months ago. She was treated with levofloxacin for a one-week course.

Question 1: What are the patient's risk factors for pneumonia?

Definition of community-acquired pneumonia (CAP):

- Epidemiology: Very common: approximately 5-7 cases/1000 persons/year.
  - 30-day mortality for admitted patients ~13%.
  - Annual age-adjusted incidence of over 1.5 million unique CAP hospitalizations annually. (Ramirez JA, et al. Clin Infec Dis 2017)

- Pneumonia+flu= 8th most common cause of death in the US (Kung HC, et al. Natl Vital Stat Rep 2008)
- Risk factors for CAP (which are additive):
  - Age ≥ 65 years
  - Underlying chronic lung disease (especially COPD)
  - Underlying increased risk for aspiration (dysphagia, intoxication, denture use, etc)
  - Immunocompromised state (diabetes, HIV, stem cell transplant, etc)
  - Exposures (tobacco, alcohol, homelessness)
  - Metabolic disorders (hypoxemia, malnutrition, etc)
  - Recent bronchoscopy or intubation
  - Viral infection (ex: influenza, COVID-19)
  - Medications (PPIs, antipsychotics, possibly inhaled steroids)

For Ms. JS, her risk factors include her age, history of COPD, diabetes, and use of PPI and inhaled steroids.

Question 2: Should any additional testing be obtained to confirm the diagnosis or direct treatment?

Apart from demonstrating an infiltrate on chest imaging, no other routine tests are recommended to confirm the diagnosis or direct treatment of non-severe community-acquired pneumonia (CAP) in the outpatient setting***.***

According to the new 2019 ATS/IDSA Guidelines on CAP, routine sputum Gram stain and culture in adults with CAP managed in the outpatient setting is not recommended. Blood cultures in the outpatient setting are also not recommended as their yield in outpatient adults with non-severe CAP is low (2%). Additionally, they rarely result in an appropriate change in empiric therapy and much worse, could lead to false positive results from skin contaminants, such as coagulase-negative staphylococci, which are not recognized as CAP pathogens. Pneumococcal urinary antigen testing in outpatient adults with CAP is not recommended. Legionella urinary antigen testing in outpatient adults with CAP is not recommended except in cases where indicated by epidemiological factors, such as association with a Legionella outbreak or recent travel. When influenza viruses are circulating in the community ATS/IDSA guidelines recommend testing for influenza with a rapid influenza molecular assay, such as the influenza nucleic acid amplification test, which is preferred over a rapid influenza diagnostic test, such as an antigen test. We also recommend considering testing for COVID-19 based on local community prevalence. Otherwise testing can be considered but should not routinely be performed.

If patients are being managed in the inpatient setting or are classified as severe based on 2007 IDSA/ATS definitions, then the newest guidelines from 2019 recommend obtaining pretreatment Gram stain and culture of respiratory secretions. The validated definition of "severe" includes either one major criterion or three or more minor criteria. If patients meet severe criteria they will likely be managed in the inpatient setting rather than the ambulatory setting.

Table 1. 2007 Infectious Diseases Society of America/American Thoracic Society Criteria for Defining Severe Community-acquired Pneumonia
Validated definition includes either one major criterion or three or more minor criteria
Minor criteria
Respiratory rate ≥ 30 breaths/min
Pa_{O2}/F_{IO2} ratio ≤ 250
Multilobar infiltrates
Confusion/disorientation
Uremia (blood urea nitrogen level ≥ 20 mg/dl)
Leukopenia* (white blood cell count < 4,000 cells/μl)
Thrombocytopenia (platelet count < 100,000/μl)
Hypothermia (core temperature < 36°C)
Hypotension requiring aggressive fluid resuscitation
Major criteria
Septic shock with need for vasopressors
Respiratory failure requiring mechanical ventilation
*Due to infection alone (i.e., not chemotherapy induced).

Table 1 IDSA/ATS Criteria for defining severe community acquired pneumonia. Borrowed from Mandell LA, et al. Clin Infect Dis. 2007.

Although procalcitonin has been used to direct initiation of empiric antibiotic treatment for CAP, empiric antibiotic therapy should be initiated in adults with clinically suspected and radiographically confirmed CAP regardless of initial serum procalcitonin level. A recent multicenter prospective study of adults hospitalized with CAP (Self WH, et al CID 2017) demonstrated that no procalcitonin threshold perfectly discriminated between viral and bacterial pathogens, but higher procalcitonin strongly correlated with increased probability of bacterial pathogens, particularly typical bacteria. This suggests that some patients with low procalcitonin levels have CAP, and basing decisions to prescribe antibiotics exclusively on procalcitonin would result in a proportion of patients with bacterial pneumonia not receiving antibiotics.

<u>Question 3:</u> Should you treat Ms. JS as an outpatient or admit her to the hospital? How do you risk-stratify patients with pneumonia in the outpatient setting?

Severity of illness is the major determinant for site of care. Other factors that support the need for hospital admission include ability to maintain oral intake, mental illness, cognitive impairment, poor medication adherence, history of substance abuse, impaired functional status, severe comorbid conditions, or complex social circumstances.

Several pneumonia severity assessment tools and online calculators are available to stratify patient risk and supplement clinical judgment. The two most common validated clinical prediction tools are the Pneumonia Severity Index (PSI) and the CURB-65, both of which predict 30-day mortality. The 2019 ATS/IDSA CAP guidelines recommend using the PSI over the CURB-65 as it identifies larger proportions of patients as low risk and has a higher discriminatory power in predicting mortality.

- The **PSI (Pneumonia Severity Index)/PORT score** was based on a 1997 NEJM analysis of 14,199 inpatients with community-acquired pneumonia. The rule was validated with data on 38,039 inpatients. Three randomized trials and multiple other observational studies have examined the effectiveness of the PSI and support the safety of using the PSI to guide the site of treatment without worsening mortality or other clinically relevant outcomes.
    - Step 1: If any of the following are present, then assign to risk class II - V and proceed to step 2:
        - Age (>50 years)
        - Coexisting disease (malignancy, liver disease, heart failure, cerebrovascular disease, renal disease)
        - Abnormal physical findings (altered mental status, tachypnea >30, hypotension<90, hypothermia <30 C or hyperthermia (>40C), tachycardia >125,)
    - Step 2: assign points based on the demographics (including if nursing home resident), comorbidities, and physical exam findings (previously listed) as well as laboratory data and radiographic findings.
        - Abnormal lab findings (academia, renal insufficiency, hyponatremia, hyperglycemia, anemia, hypoxemia
        - Radiographic findings: pleural effusion
    - Stratify into risk classes based on points and determine site of care
        - Class I (0 points) and Class II (<70 points) patients can be safely managed as outpatients
        - Some Class III (71-90 points) patients can be managed outpatient versus observation admission
        - All Class IV (91-130 points) and Class V (>130 points) patients should be admitted to the hospital
    - It is important to note that there are limitations to this scoring index and that patients identified as low risk by the PSI may still warrant inpatient admission based on other medical/psychosocial factors.
        - One particular patient group that the PSI may underestimate severe pneumonia is in young healthy patients, since points are assigned by absolute age.
        - Complications are reported in 19% of low-risk patients and 0.9% risk of death even in low-risk groups (Marrie TJ, et al. Am J Med 2005).
    - However, consistent use of a safe and effective scoring system such as PSI has potential to decrease unnecessary variability in admission rates, the high cost of inpatient pneumonia treatment, and the risk of hospital-acquired complications

TABLE 2. POINT SCORING SYSTEM FOR STEP 2 OF THE PREDICTION RULE FOR ASSIGNMENT TO RISK CLASSES II, III, IV, AND V.

CHARACTERISTIC	POINTS ASSIGNED*
Demographic factor	
Age	
Men	Age (yr)
Women	Age (yr) − 10
Nursing home resident	+10
Coexisting illnesses†	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Physical-examination findings	
Altered mental status‡	+20
Respiratory rate ≥30/min	+20
Systolic blood pressure <90 mm Hg	+20
Temperature <35°C or ≥40°C	+15
Pulse ≥125/min	+10
Laboratory and radiographic findings	
Arterial pH <7.35	+30
Blood urea nitrogen ≥30 mg/dl (11 mmol/liter)	+20
Sodium <130 mmol/liter	+20
Glucose ≥250 mg/dl (14 mmol/liter)	+10
Hematocrit <30%	+10
Partial pressure of arterial oxygen <60 mm Hg§	+10
Pleural effusion	+10

Table 2. PSI point scoring system for step 2 of the prediction rule. Borrowed from Fine, et al. NEJM 1997.

Although the PSI has had its safety and effectiveness in guiding site of care well validated, it can be cumbersome for some to use, particularly in the outpatient setting, and thus many prefer to use the CURB-65 prediction model. However, this tool has not had its safety and effectiveness as rigorously validated as the PSI.

- The **CURB-65 score** has a higher specificity for mortality prediction than PSI (52.2%) but lower sensitivity.
    - It is based on five factors that are easily assessed at the bedside:
        - **Confusion**
        - **BUN > 19mg/dL**
        - **Respiratory Rate ≥ 30**
        - **Systolic BP < 90mmHg or Diastolic BP ≤ 60mmg Hg**
        - **Age ≥ 65**
    - 30-day mortality is 0.7 % if 0 factors; 42% with 4 factors
    - Patients with scores of 0-1 can typically be treated as an outpatient; patients with scores ≥2 should be admitted (Lim WS, et al. Thorax 2003).
    - The CURB-65 does not require testing for BUN and can sometimes be more convenient to use in the outpatient office. A study by Bauer TT, et al (J Intern Med 2006) found good utility of the scoring system when lab data was unavailable for review.

A study by Aujesky, et al (Am J Med 2005) found that the PSI was slightly more accurate at identifying patients at low risk than CURB.

Scenario (continued):

Ms. JS's PSI score is 68, assuming she has no laboratory abnormalities. This places her in class II, with a 0.6% risk for mortality based on her age and co-existent heart failure diagnosis. (Fine MJ, et al. NEJM 1997). Her CURB-65 score is 1. You therefore decide she can be managed as an outpatient given that there are no other noted worrisome factors for outpatient treatment noted in her history.

***Question 4:* What are the most common pathogens for community acquired pneumonia?**

- Microbiology: *Streptococcus pneumoniae* is the most commonly identified bacterial cause of CAP, although with the widespread use of the pneumococcal vaccine, its incidence is beginning to decrease. Respiratory viruses are also commonly identified pathogens for CAP. However, the majority of CAP cases do not have an identified pathogen, up to 62% in some inpatient studies. Other common pathogens in the ambulatory setting to consider include: *Chlamydia pneumoniae, Haemophilus influenza, Mycoplasma pneumoniae,* Influenza virus, *Legionella.* See Table 8 from IDSA/ATS guidelines below.
  - *Streptococcus pneumoniae* is still the most common pathogen in patients with HIV, although a broader differential of bacterial, viral, fungal, mycobacterial, and parasitic causes should also be considered.
  - Patients with a history of chronic steroid use, severe underlying lung disease, alcoholism and frequent antibiotic use are at risk for *Enterobacter* and *Pseudomonas*. Therapy should be tailored accordingly.

Condition	Commonly encountered pathogen(s)
Alcoholism	*Streptococcus pneumoniae*, oral anaerobes, *Klebsiella pneumoniae*, *Acinetobacter* species, *Mycobacterium tuberculosis*
COPD and/or smoking	*Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Legionella* species, *S. pneumoniae*, *Moraxella catarrhalis*, *Chlamydophila pneumoniae*
Aspiration	Gram-negative enteric pathogens, oral anaerobes
Lung abscess	CA-MRSA, oral anaerobes, endemic fungal pneumonia, *M. tuberculosis*, atypical mycobacteria
Exposure to bat or bird droppings	*Histoplasma capsulatum*
Exposure to birds	*Chlamydophila psittaci* (if poultry: avian influenza)
Exposure to rabbits	*Francisella tularensis*
Exposure to farm animals or parturient cats	*Coxiella burnetti* (Q fever)
HIV infection (early)	*S. pneumoniae*, *H. influenzae*, *M. tuberculosis*
HIV infection (late)	The pathogens listed for early infection plus *Pneumocystis jirovecii*, *Cryptococcus*, *Histoplasma*, *Aspergillus*, atypical mycobacteria (especially *Mycobacterium kansasii*), *P. aeruginosa*, *H. influenzae*
Hotel or cruise ship stay in previous 2 weeks	*Legionella* species
Travel to or residence in southwestern United States	*Coccidioides* species, *Hantavirus*
Travel to or residence in Southeast and East Asia	*Burkholderia pseudomallei*, avian influenza, SARS
Influenza active in community	Influenza, *S. pneumoniae*, *Staphylococcus aureus*, *H. influenzae*
Cough >2 weeks with whoop or posttussive vomiting	*Bordetella pertussis*
Structural lung disease (e.g., bronchiectasis)	*Pseudomonas aeruginosa*, *Burkholderia cepacia*, *S. aureus*
Injection drug use	*S. aureus*, anaerobes, *M. tuberculosis*, *S. pneumoniae*
Endobronchial obstruction	Anaerobes, *S. pneumoniae*, *H. influenzae*, *S. aureus*
In context of bioterrorism	*Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia)

Table 3. Epidemiologic conditions and/or risk factors related to specific pathogens in community-acquired pneumonia. Borrowed from Mandell LA, et al. Clin Infect Dis 2007.

<u>Question 5:</u> What antibiotic regimens should you consider for this patient?

In the most recent 2019 ATS/IDSA guidelines, a paradigm shift has occurred with the retirement of the category "health care associated pneumonia" or "HCAP." This is due to the overuse of MRSA and Pseudomonas antibiotic coverage without a demonstrable benefit on outcomes and only rare occurrences of MRSA or Pseudomonas related pneumonias. Risk factors for resistant pathogens include prior respiratory isolation of MRSA or P. aeruginosa or recent hospitalization AND receipt of parenteral antibiotics (in the last 90 days). Moreover, studies have demonstrated efficacy of high dose amoxicillin for inpatients with CAP which has been extrapolated to the outpatient setting where patients are typically less ill with less risk factors. Amoxicillin/clavulanate has also shown to be efficacious in both inpatient and outpatient CAP. Doxycycline, although without as robust evidence, has also compared favorably to fluoroquinolones and has demonstrated quicker response with less change in antibiotic regimen. As a change from prior CAP guidelines, monotherapy with macrolides is no longer a strong recommendation unless there is well-documented low incidence of S. pneumoniae macrolide resistance (< 25%).

In patients with comorbidities, higher precaution is taken given the higher risk of worse outcomes. Additionally, resistant pathogens, such as H. influenzae and M. catarrhalis (both of which frequently produce β-lactamase), S. aureus and gram-negative bacilli, are more common causes of CAP in these patients, particularly COPD.

If there are no comorbidities or risk factors for resistant pathogens (eg: MRSA or Pseudomonas aeruginosa positive respiratory cultures or hospitalization with parenteral antibiotics in the last 90 days), one can choose any of the following:

- amoxicillin 1g TID OR
- doxycycline 100 mg BID OR
- macrolide (only if local pneumococcal macrolide resistance is < 25%)
    - azithromycin 500mg 1st day, then 250mg daily OR
    - clarithromycin 500 mg BID OR
    - clarithromycin ER 1,000mg daily

If there are comorbidities present (including chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia) one can choose combination therapy with two antimicrobial agents or fluoroquinolone monotherapy:

Combination Therapy

- amoxicillin/clavulanate
    - 500 mg/125 mg TID
    - 875 mg/125 mg BID
    - 2,000 mg/125 mg BID
- OR a cephalosporin
    - cefpodoxime 200 mg BID
    - cefuroxime 500 mg BID

AND

- A macrolide or doxycycline:
    - azithromycin 500 mg on first day then 250 mg daily
    - clarithromycin 500 mg BID
    - clarithromycin ER 1,000 mg daily
    - doxycycline 100 mg twice daily

OR

Monotherapy with a respiratory fluoroquinolone

- levofloxacin 750 mg daily
- moxifloxacin 400 mg daily
- gemifloxacin 320 mg daily

It is important to note that if patients with CAP also test positive for influenza in the outpatient setting, anti-influenza treatment, such as oseltamivir, should also be prescribed independent of duration of illness before diagnosis of influenza.

Regarding duration of therapy, the 2019 ATS/IDSA guidelines strongly recommend that the duration be guided by a validated measure of clinical stability (resolution of vital sign abnormalities, ability to eat, and normal mentation), and antibiotic therapy should be continued until the patient achieves stability and for no less than a total of 5 days. There is growing evidence that a shortened treatment duration of even 3 days may be sufficient for non-severe outpatient CAP, but more robust trials are needed.

Procalcitonin has also been used to guide duration of inpatient antibiotic therapy and timing of de-escalation with experts suggesting its use is best applied when duration of therapy is longer than the recommended 5 days. Its use in the outpatient setting is unclear at this time but should not prevent initiation of empiric antibiotic therapy in clinically determined CAP.

For this patient with comorbidities including chronic heart and lung disease, suggest either combination therapy (amoxicillin/clavulanate or a cephalosporin plus a macrolide) or fluoroquinolone monotherapy can be used to treat her outpatient CAP. Given her recurrent infections, it is recommended to use a different antibiotic regimen than any previously used regimens. In addition, if she had any of the risk factors for resistant pathogens then a pretreatment respiratory Gram stain and culture would be recommended; however, in this case of a patient with recurrent pneumonia, it is unknown whether she meets this criteria and more focused antibiotic regimens are being encouraged based on the new 2019 guidelines.

Question 6: Should you consider the use of steroids for treatment of pneumonia (separate from treatment of a COPD exacerbation)? What is the latest evidence on steroid use for pneumonia?

- In 2015, two RCTs in JAMA and the Lancet showed that systemic corticosteroids were beneficial for some hospitalized patients with community-acquired pneumonia
- Since then, a **Cochrane meta-analysis of 13 trials** (~ 2000 adults) showed that systemic steroids significantly lowered mortality in patients with severe CAP (8% vs. 13%, NNT = 19) but had no effect on mortality in patients with non-severe CAP. Length of stay was also shortened by ~3 days.
- An **IDSA meta-analysis** also included ~1500 patients from 6 trials. Among patients with severe CAP, steroids did not lower mortality but did lower length of stay. However, significantly more adverse events and re-hospitalizations were noted (the difference in re-hospitalizations was primarily due to non-severe CAP)
- Therefore, steroids do not seem to be helpful for patients with outpatient CAP or non-severe CAP. The 2019 ATS/IDSA guidelines strongly recommend against using routine corticosteroids in adults with non-severe CAP and also recommend against using routine corticosteroids in adults with severe influenza pneumonia.
- It is important to note that the 2019 CAP guidelines also endorse the Surviving Sepsis Campaign recommendations on the use of corticosteroids in patients with CAP and refractory septic shock
- The CAPE_COD study is ongoing and expected to be finished by March 2022 to try to definitively answer this question.

<u>Question 7:</u> Assuming she clinically improves, does Ms. JS need follow up imaging? If so, at what interval would you recommend?

Patients who respond clinically with resolution of symptoms within the expected 5 to 7 days, current 2019 ATS/IDSA guidelines recommend against obtaining routine follow up chest imaging. Previously, it was thought that patients over the age of 50 should have a repeat chest x-ray in 7-12 weeks to evaluate for undiagnosed lung malignancy. However, the referred study predominantly evaluated male patients in the Veterans Affairs system with a high smoking prevalence. The positive yield from repeat imaging ranges from 0.2% to 5.0% however this was primarily driven by patients who were former or current smokers who would qualify for lung cancer screening. With the evolution of recommendations for low dose CT chest imaging to screen for lung cancer, it is expected this will be more reliable and effective than post-CAP follow up chest imaging.

After reviewing the recent guidelines, you discuss with the patient that repeat imaging should not be done unless her symptoms do not resolve in the expected time course of 5 to 7 days.

<u>Question 8:</u> If she does not improve clinically on empiric therapy, how would you proceed?

<u>General Approach to Pneumonia that Does Not Improve; questions to consider:</u>

1. Could this simply be the normal time course of a resolving pneumonia?
2. Could this be a new complication of pneumonia?
3. Could this be the "wrong bug"? (i.e. not bacterial pneumonia)
4. Could this be the "wrong drug"? (i.e. inappropriate antibiotic therapy)
5. Could this be the "wrong diagnosis"? (i.e. non-infectious pneumonia mimics)?

1. **Could this simply be the normal time course of a resolving pneumonia?**
   Normal resolution of pneumonia is not well defined, but patients typically have subjective improvement in vital signs within three days, but cough and fatigue may take 14 days or longer to improve. Chest X-rays may only show radiographic clearing after several weeks, especially in patients with comorbid conditions

2. **Could this be a new complication of pneumonia?**
   Care should be taken to screen for complications of pneumonia, such as empyema or lung abscess, especially in patients with ongoing fevers despite antibiotic therapy. Ultrasound and CT are useful modalities to evaluate for these complications, in addition to the physical exam.

3. **Could this be the "wrong bug"? (i.e. not bacterial pneumonia)**
   In patients who do not respond to bacterial pneumonia therapy, we should consider if patients may have a viral etiology, fungal etiology, or mycobacterial etiology (M. TB, NTM). History and physical should be reassessed to assess patients' risk for these types of infections.

4. **Could this be the "wrong drug"? (i.e. inappropriate antibiotic therapy)**
   Penicillin-resistant Streptococcus pneumoniae, MRSA, drug-resistant Pseudomonas aeruginosa are all possibilities to consider in patients who are not responding appropriately to antibiotic therapy. Antibiotic dosing should also be double-checked (For example: did a patient have therapeutic vancomycin troughs while inpatient? Was dosing adequate for patients with extremes of BMI? Etc.) Additionally, remember that risk factors for resistant pathogens include prior respiratory isolation of MRSA or P. aeruginosa or recent hospitalization AND receipt of parenteral antibiotics (in the last 90 days).

5. Could this be the "wrong diagnosis"? (i.e. non-infectious pneumonia mimics)?
As a pulmonologist, this is a key part of our evaluation since many noninfectious etiologies of pulmonary opacities can mimic pneumonia. Non-infectious causes such as neoplasia (either primary or metastatic, particularly with endobronchial lesions), immunologic/autoimmune disorders (such as vasculitis, cryptogenic organizing pneumonia, sarcoidosis), drug-related pneumonitis, and vascular events (pulmonary infarcts) should be considered in the appropriate clinical context. If the patient has true recurrent pulmonary infections, the possibility of recurrent aspiration events should be considered, and immunodeficiency should be considered, especially in younger patients.

Ms. JS comes back to your office 6 weeks later for follow-up. She notes that she felt significantly better and back to her baseline after completing the course of antibiotics you previously prescribed. However, she is now feeling poorly again in the last several days with worsening productive cough, increased sputum production and low-grade fevers to 100.5 F. A repeat CXR is done again which shows a right middle lobe opacity. Review of prior films shows that almost all her prior infiltrates have been in the same area.

***Question 8:* What is your approach to recurrent pneumonia? What additional testing should you consider?**

Generally speaking, the approach is defined by either:

- Recurrent opacity in a particular anatomic region suggesting possible local anatomic abnormality (ex: tumor, vascular abnormality, retained foreign body, bronchiectasis, bronchomalacia, stenosis, etc. Recurrent aspiration is also a consideration, particularly if in the lung bases).
- Recurrent opacity in varied regions of the lung. Associated recurrent sinopulmonary infections suggests potential underlying immunodeficiency syndrome (ex: cystic fibrosis, immotile cilia syndrome, HIV, etc) or another mimic of recurrent infection (vasculitis, cryptogenic organizing pneumonia, etc).

In either case, more detailed imaging of the chest with CT scan is likely warranted for further characterization given the recurrent nature of her infections.

***Question 9:* What diagnostic tests would you order if you were concerned for a systemic immunodeficiency process?**

Quantitative immunoglobulins and HIV would be reasonable screening tests. IgG subclass deficiency is among the most common deficiency detected.

References:

Ramirez JA, Wiemken TL, Peyrani P, et al. Adults hospitalized with pneumonia in the United States: Incidence, Epidemiology and Mortality. Clin Infect Dis 2017; 65(11): 1806.

Kung HC, Hoyert DL, Xu J, et al. Deaths: final data for 2005. Natl Vital Stat Rep 2008; 56(10):1.

Briel M et al. Corticosteroids in patients hospitalized with community-acquired Pneumonia: Systematic review and individual patient data metaanalysis. Clin Infect Dis 2018 Feb 1; 66:346.

Capelastegui A, España PP, Quintana JM, et al. Validation of a predictive rule for the management of community-acquired pneumonia. Eur Respir J. 2006;27(1):151-7.

Fine MJ. et. al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med. 1997 Jan 23;336(4):243-50.

Marrie TJ, Huang JQ. Low-risk patients admitted with community-acquired pneumonia. Am J Med 2005; 118(12):1357.

Aujesky D, Auble TE, Yearly DM, et al. Prospective comparison of three validated prediction rules for prognosis in community-acquired pneumonia. Am J Med 2005; 118(4):384.

Bartlett JG, Dowell SF, Mandell LA, et al. Practice guidelines for the management of community-acquired pneumonia in adults. Infectious Disease Society of America. Clin Infect Dis 2000; 31(2): 347.

Kalil A, Metersky M, Klompas M, et al. Executive summary: management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016; 63:575-82.

Lim W, M M van der Eerden, R Laing, W Boersma, N Karalus, G Town, S Lewis, and J Macfarlane. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003 May; 58(5): 377–382. doi: 10.1136/thorax.58.5.377.

Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44 Suppl 2:S27-72. An influential consensus statement from two major societies.

Stern A et al. Corticosteroids for pneumonia. Cochrane Database Syst Rev 2017 Dec 13; 12:CD007720.

Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019 Oct 1;200(7):e45-e67. doi: 10.1164/rccm.201908-1581ST.

Self WH, Balk RA, Grijalva CG, et al. Procalcitonin as a Marker of Etiology in Adults Hospitalized With Community-Acquired Pneumonia. Clin Infect Dis. 2017 Jul 15;65(2):183-190. doi: 10.1093/cid/cix317. PMID: 28407054; PMCID: PMC5850442.