SHC Clinical Pathway: Inpatient Pneumonia (Community-Acquired, Hospital-Acquired and Ventilator-Associated)

Background:
IDSA-ATS recommendations apply primarily to immunocompetent patients although many principles can be extrapolated to the immunocompromised patient population.

Definitions:
- Community-acquired pneumonia (CAP) = signs/symptoms develop **prior to or within 48 hours of admission.**
- Hospital-acquired pneumonia (HAP) = signs/symptoms develop **after 48 hours of admission.**
- Ventilator-associated pneumonia (VAP) signs/symptoms develop within 48 hours of intubation through 48 hours after extubation.

Diagnosis:
- Must have BOTH:
  - A **new or worsening** infiltrate on chest imaging
  - **New or worsening** cough, dyspnea or purulent sputum production.

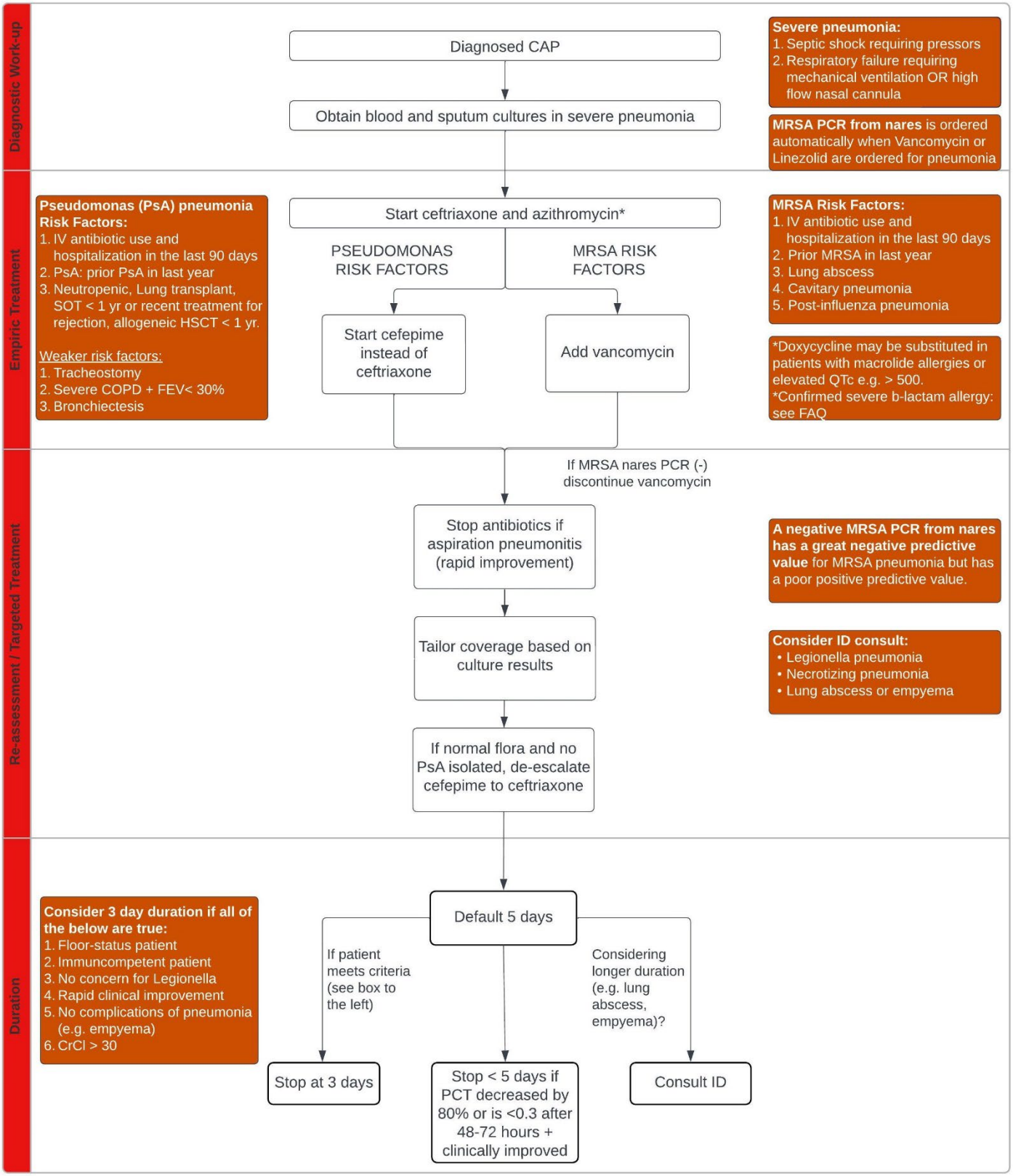
Initial work-up:
- Blood and sputum cultures should be obtained in all cases of HAP/VAP and in severe CAP or CAP with risk factors for MRSA or Pseudomonas. *See* CAP *clinical pathway for characterization of severe pneumonia*.
  - Note, **positive sputum or even BAL cultures cannot make or confirm a diagnosis of pneumonia** even with an isolated fever or leukocytosis as colonization of the respiratory tract with various pathogens is common.
    - National guidelines regard non-invasive sampling as equivalent to BAL, however if there is concern for opportunistic infection, BAL may be preferred.
  - Sputum and blood cultures are not indicated for non-severe CAP
  - Consider viral pneumonia work-up, including influenza and COVID-19.

Empiric therapy:
- CAP: In the absence of allergies, **ceftriaxone and azithromycin** are the mainstay of treatment.
  - Consider MRSA or pseudomonas coverage IF: the patient has been hospitalized and received IV antibiotics within the last 90 days or if they have grown MRSA or Pseudomonas, especially if from sputum cultures within the last year. See additional risk factors in the flowchart.
  - If anti-MRSA treatment is initiated, MRSA PCR will be obtained automatically via pharmacist protocol and should be followed up for de-escalation.
- HAP/VAP: In the absence of allergies, an anti-pseudomonal agent (piperacillin-tazobactam or cefepime) + vancomycin are advised as empiric therapy.
- Please see FAQ #5 for guidance on antibiotic choice in the setting of drug allergies.

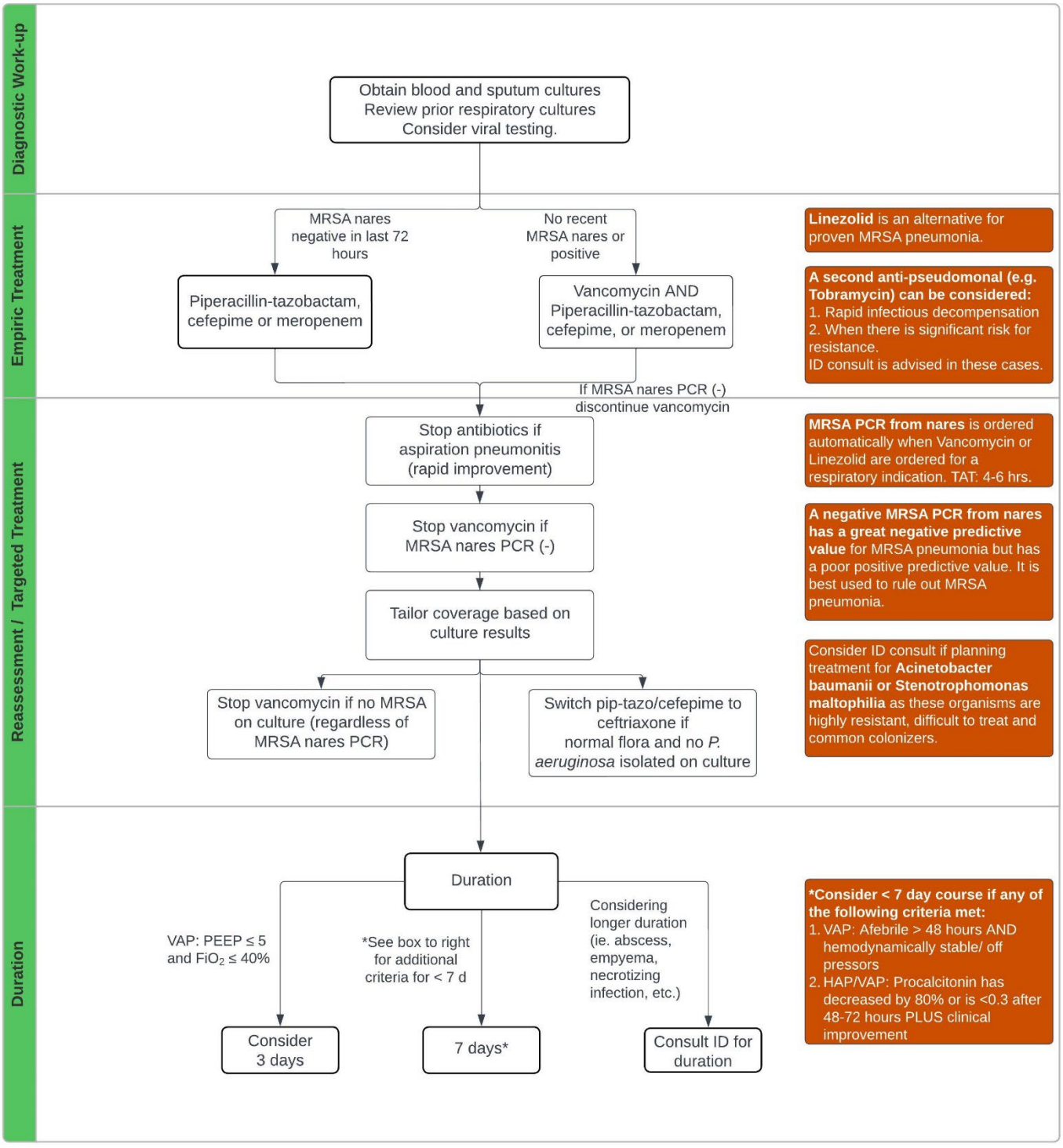
De-escalation:
- **All empiric regimens should be tailored to culture results.**
- **Nasal MRSA PCR has an excellent negative predictive value for MRSA pneumonia**. If nasal MRSA PCR is negative, vancomycin can be discontinued in patients for which this agent was started empirically.
- Tailoring antibiotics to the organism that grows is critical to ensuring that the patient is adequately covered but not on an unnecessarily broad regimen.
  - In cultures with mixed respiratory flora, microbiology will note cases in which the culture does NOT contain MRSA or *Pseudomonas aeruginosa* in the milieu. In these cases, anti-pseudomonal and/or anti-MRSA antibiotics may be safely transitioned to alternative agents.
  - If a patient's sputum cultures grow a pan-susceptible E. coli, discontinuation of anti-pseudomonal and anti-MRSA coverage is safe and preferred in favor of a narrower regimen (e.g. Ceftriaxone).

Duration:
- In most cases, treatment for CAP is 5 days and for HAP/VAP is 7 days.
  - There are clinical criteria for some patients where a 3 day regimen may be used; data supports similar efficacy and decreased adverse effects. *Please see references 4, 14, 19.*

SHC Clinical Pathway Community Acquired Pneumonia



SHC Clinical Pathway: Hospital-Acquired and Ventilator-Associated Pneumonia



SHC Clinical Pathway: Pneumonia FAQ's

1. Does a positive respiratory culture mean my patient has pneumonia?

A positive respiratory culture alone, even from ETT or BAL, is NOT indicative of invasive infection in the absence of pulmonary symptoms, even with isolated fever or leukocytosis.

2. How should procalcitonin be used in the management of pneumonia?

Procalcitonin should not be considered in the initial decision to start empiric therapy in a patient with suspected bacterial pneumonia and should never be used to escalate therapy. If, at 48-72 hours after diagnosis, the procalcitonin is <0.3 or has decreased by at least 80% from baseline, bacterial infection is unlikely and antibiotics should be stopped. Please note, COVID-19 can be associated with an elevated procalcitonin even in the absence of concomitant bacterial pneumonia. For more details on procalcitonin, see this guidance HERE

3. My patient has COVID-19. Should I be concerned about co-infection or super-infection with bacterial or fungal organisms?

We do not recommend empiric use of antibiotics for patients infected with COVID-19 unless there is clear radiologic or clinical evidence of bacterial/fungal concomitant infection. The prevalence of co-infection varies in the published literature.[1, 2, 3] Regardless it is clear that antibiotics are over-used.[1] This ultimately increases risk of selecting for resistant organisms and exposing patients to risk of harm through adverse effects of unnecessary antibiotics. If antifungals or antibiotics are indicated, we would recommend tailoring them to available microbiological data (e.g. sputum cultures).

4. When should I consider Legionella?

Legionella is an atypical pathogen that can cause severe pneumonia. It can be lobar and multifocal and may lead to ARDS. Legionella testing is recommended for patients with severe pneumonia only (septic shock requiring pressors or respiratory failure requiring mechanical ventilation or high flow nasal cannula). For better sensitivity, we recommend sending Legionella PCR from sputum over Legionella urine antigen.

5. What if my patient has a severe penicillin or cephalosporin allergy?

First, confirm that the patient truly has an allergy. Documented allergies in the EMR are often incorrect. If the patient reports a non-urticarial rash to penicillins but no history of anaphylaxis, it is safe to prescribe cephalosporins. Please see further guidance on this HERE

If a true, severe allergy has been confirmed: Ceftriaxone + azithromycin → Levofloxacin monotherapy.

Severe CAP at risk for Pseudomonas: Ceftriaxone + azithromycin → Aztreonam + levofloxacin.

- Please note that neither agent has reliable coverage of MSSA.
- Azithromycin does not need to be added if the patient is receiving levofloxacin as this covers atypical organisms.

Severe CAP at risk for MRSA: Ceftriaxone + azithromycin → Ceftriaxone + azithromycin + vancomycin.

6. What is the role for steroids in community-acquired pneumonia?

Several studies have shown varied results[7,8,9] and guidelines recently recommended steroid use in hospitalized patients with severe CAP. One notable study was a large, multicenter French study that demonstrated mortality benefit and lower likelihood of intubation in patients who received steroids within 24 hours of ICU admission[7]. The study excluded patients who were in septic shock, had influenza pneumonia, were admitted to the floor and who were immunocompromised. Of note, there is little data to support corticosteroid use in patients who are not critically ill.

7. How should a MRSA nares be used?

An MRSA PCR can help with de-escalation in HAP/VAP and high-risk CAP. Please note this test is not orderable by physicians and is automatically ordered by pharmacists when vancomycin or linezolid is ordered for a pulmonary indication. MRSA nares culture is less sensitive than PCR and is not preferred for clinical decision making. A negative MRSA nares PCR makes MRSA pneumonia very unlikely and can be used to safely stop MRSA coverage. A positive MRSA nares PCR is not diagnostic of MRSA pneumonia and MRSA coverage can still be stopped if respiratory cultures do not grow MRSA. MRSA nares protocol can be found HERE and FAQ can be found HERE.

8. What if my patient with CAP is not improving?

If, after 48-72 hours of therapy, your patient is not improving or worsening clinically, first re-consider whether the cause of symptoms is infectious. Common mimic of bacterial pneumonia include pulmonary edema, aspiration pneumonitis, viral pneumonia, COPD exacerbation and inflammatory disease (e.g. ILD flare).

If the suspicion for infection remains high, it may be reasonable to add coverage for MRSA (typically Vancomycin) and Pseudomonas aeruginosa (typically cefepime or piperacillin-tazobactam)[10], particularly if good-quality respiratory cultures are unable to be obtained.

9. When should I cover anaerobes for a patient with aspiration pneumonia?

It is no longer recommended to routinely cover for anaerobes in aspiration pneumonia, even in severe cases**.** The exception is when the patient has evidence of an empyema, necrotizing pneumonia or a lung abscess (the latter two of which are typically diagnosed on CT). In these cases, anaerobic coverage with piperacillin-tazobactam alone or the addition of metronidazole to typical pneumonia coverage is appropriate.

10. Do I need empiric pseudomonal CAP coverage if my patient is immunocompromised, has interstitial lung disease, or has had recent healthcare exposure (e.g. frequent ED or urgent care visits, skilled nursing facility)?

These conditions are generally not considered significant risk factors for Pseudomonal CAP, with a few exceptions noted in the above CAP risk-factors boxes. Empiric pseudomonal coverage need not be applied blanketly to all immunocompromised patients, even in those with active solid tumors. (See data below)

Pseudomonal CAP is rare (4.2% of cases), which correlates w/SHC data showing a prevalence of 1-2.5% in patients w/o severe immunocompromise. (Restrepo et al 2018)

Empiric treatment should take into account local prevalence, severity of illness, and overall clinical assessment.

Supporting data:

Analysis of over 3,000 patients (1,545 with “immunosuppressive conditions”) hospitalized with CAP identified 4.2% of cases caused by P.aeruginosa. The 5 strongest independent risk factors for Pseudomonas aeruginosa-CAP were prior Pseudomonas (PsA) infection/colonization (OR 16.10), prior tracheostomy (OR 6.50), bronchiectasis (OR 2.88), very severe COPD (OR 2.76), and invasive respiratory or vasopressor support (OR 2.33). The study found no significant associations for patients with immunosuppressive conditions*, interstitial lung disease [n=91, PsA CAP 4.5% vs non-PsA CAP 2.8%, P = 0.24] , or recent healthcare exposure.[20]

Another retrospective study of over 3,700 hospitalized patients with CAP, including 652 immunocompromised individuals, corroborated these findings.[21]

* Immunosuppressive conditions*: active solid tumors, hematological malignancies, AIDS, HIV infection, chemotherapy in the past three months, biological drug use, neutropenia, aplastic anemia, asplenia, and other immunosuppressive conditions.*

III. References

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