

## Guidance for the Use of Empiric Antibiotics in Inpatient COVID-19 Pneumonia

With increasing rates of COVID-19, more patients are presenting to hospitals with pneumonia symptoms. It can be difficult to differentiate bacterial pneumonia from viral pneumonia due to COVID-19 as both have fever, cough, hypoxia, and infiltrates on chest imaging. In general, bacterial coinfection with COVID-19 is uncommon (<5%). Antibiotics should not generally be started or continued when COVID-19 is identified unless there are findings suggestive of bacterial infection. The information included below is provided to help stratify risk of bacterial co-infection and assist in determining the need for antibiotics in patients with confirmed or suspected COVID-19 infection.

If antibiotics are deemed necessary upon admission, choice of agent(s) should follow the community-acquired pneumonia (CAP) treatment recommendations and duration of therapy should be limited to 5-7 days. Guidelines for the management of CAP are [here](#). Antibiotic choices for patients with findings suggestive of bacterial pneumonia after 5 days in the hospital should use the HAP/VAP guidelines [here](#).

### Low risk of bacterial pneumonia (antibiotics not needed or can be discontinued).

#### Confirmed COVID-19 infection

- When COVID-19 infection is confirmed, antibiotics should generally be stopped or withheld unless there are findings strongly suggestive of bacterial infection as denoted below.
- If bacterial co-infection is suspected, further workup including sputum cultures, urine antigens, and procalcitonin should be performed.

#### Procalcitonin <0.1 mcg/L

- Procalcitonin (PCT) is an inflammatory biomarker that has been associated with bacterial infection. PCT is generally low in early COVID-19 infections, and a result of <0.1 mcg/L can be used to rule out bacterial co-infection and stop or withhold antibiotics. PCT levels between 0.1 and 0.25 should not generally have antibiotics started unless the patient is severely ill. Following PCT trends in patients where the need for antibiotics is unclear is recommended, as rising PCT levels over 0.25 may indicate bacterial infection.

#### Normal white blood cell (WBC) count

- Most patients with COVID-19 pneumonia present with a normal to low WBC count. Leukocytosis is a weak predictor of bacterial infection. In COVID-19 patients without leukocytosis, it is appropriate to withhold or discontinue antibiotics.

#### Fever (T > 100.4° F)

- COVID-19 is a common cause of fever regardless of bacterial coinfection. As such, fever should not be used as a sole reason to start or continue antibiotics.

#### Negative sputum cultures

- If empiric antibiotic were started, they should generally be discontinued if respiratory tract cultures show no bacterial growth. The presence of bacteria on respiratory tract cultures is not an absolute indication for starting antibiotics and the overall clinical picture should be evaluated to determine if antibiotics are indicated.

### Potential indications of bacterial pneumonia (decide need for antibiotics based on patient-specific factors)

#### Procalcitonin >0.25 mcg/L

- While elevated PCT can be indicative of bacterial infection, this finding is commonly seen in severe COVID-19 infection in the absence of bacterial coinfection. This is likely due to the inflammatory nature of COVID-19, especially 5-7 days after infection onset. Because of this, mildly elevated PCT is not a reliable predictor of bacterial co-infection in patients with COVID-19 and should not be used as a sole reason to initiate or continue antibiotics.

#### Procalcitonin >0.5 mcg/L

- Antibiotics may be warranted in patients with markedly elevated PCT particularly upon admission. Some studies have found PCT to be a moderate predictor of bacterial coinfection and poorer outcomes although a recent study found 20% of patients with PCT >0.5 did not have a defined bacterial infection. The dynamics of PCT are important, and significantly rising PCT values may also be suggestive of bacterial infection. Patients with chronic or acute renal dysfunction may have falsely elevated PCT levels, and PCT should be interpreted with caution in these settings. PCT levels may also be elevated in severe COVID infection without a defined bacterial infection and should not be used alone to determine if antibiotics are indicated.

### Leukocytosis

- As mentioned above, leukocytosis can be a predictor of bacterial infection; however, it should not be used as a sole reason to initiate or continue antibiotics in patients with COVID-19. With many COVID-19 positive patients also receiving dexamethasone, it is important to evaluate explainable causes of leukocytosis (such as steroid administration) and continue further diagnostic workup before starting antibiotics.

### Bacterial growth on respiratory tract culture

- Patients with bacterial growth in sputum culture may warrant pathogen-targeted antibiotic treatment. The presence of bacteria on respiratory tract cultures is not an absolute indication for starting antibiotics and the overall clinical picture should be evaluated to determine if antibiotics are indicated.

### Critically ill patients

- Patients who are critically ill or with suspected sepsis can be started on empiric antibiotics, with selection guided by patient-specific risk factors for multidrug resistant organisms (see CAP guidelines). Respiratory tract cultures should be obtained, PCT levels trended and antibiotics adjusted based on these findings. **Patients without defined bacterial infection based upon culture data should be considered strongly for antibiotic discontinuation.**

### References:

1. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>.
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3. Richardson S et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020 May 26;323(20):2052-59.
4. Chen T et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020 Mar 26;368:m1090.
5. Zhang JJ, et al. Risk factors of severe disease and efficacy of treatment in patients infected with COVID-19: a systematic review, meta-analysis and meta-regression analysis. Clin Infect Dis. 2020 May 14;ciaa576.
6. Huang I et al. C-reactive protein, procalcitonin, D-dimer, and ferritin in severe coronavirus disease-2019: a meta-analysis. Ther Adv Respir Dis. 2020;14:1-14.
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