Point of Care Testing (POCT) of C-reactive protein (CRP) (Update)

Primary Care Respiratory Society (PCRS) position statement

Point-of-care testing of C-reactive protein (CRP) for the acute assessment of worsening symptoms in people known to have COPD can safely reduce the use of antibiotics and could help improve the diagnostic approach towards someone presenting in such a crisis. New high-quality evidence has emerged since the last NICE COPD update and we encourage re-opening and review of the current guideline to enable clinicians and system leaders to understand whether and how to implement this promising diagnostic aid.

PCRS advocates that:

- **Patients with acutely worsening symptoms and known diagnosis of COPD should receive antibiotics only when there is confirmed evidence of a COPD exacerbation and/or a bacterial infection. (They may also require steroids in line with global guidance).**
- **Sputum purulence is as accurate at predicting the presence of bacterial pathogens as point-of-care C-reactive protein (CRP) protein in exacerbations of COPD.**
- **Using of point-of-care-testing such as CRP testing would be a valuable addition to support treatment decisions if resources were available.**
- **When evaluating a patient with COPD experiencing a symptomatic exacerbation such as cough and worsening breathlessness, all potential triggers should be considered including tobacco exposure, air quality, psychosocial factors, viral infection and bacterial infection to avoid unnecessary prescribing of antibiotics.**

Background

Exacerbations of COPD account for 115,000 hospitalisations in the UK each year.[1] COPD exacerbations can be caused by environmental triggers and bacterial or viral airways infection.[2] In an era of antibiotic guardianship, it is essential to ensure that patients only receive antibiotics when clinically warranted. Determining whether an exacerbation is caused by a bacterial infection, viral infection or another trigger can be challenging in a primary care setting. Consequently, the default approach often involves prescribing antibiotics to treat a presumed bacterial infection, as recommended by National Institute for Health and Care Excellence (NICE) guidance.[3]

Currently, an estimated 80% of patients presenting in primary care with moderate exacerbations of COPD are treated with antibiotics. This means that 20% of patients who would be recommended to have steroids and/or antibiotics for a moderate exacerbation are potentially being undertreated.[4] However, not all patients prescribed an antibiotic for an acute COPD exacerbation will benefit from such treatment.[5-7] Unnecessary antibiotic prescribing can contribute to increases in the prevalence of drug-resistant bacteria and result in a delay in patients receiving potentially more effective interventions when their exacerbation is not driven by an underlying bacterial infection. Identifying patients most likely to benefit from antibiotic therapy and, conversely, those unlikely to benefit from antibiotic therapy has the potential to reduce unnecessary antibiotic use, preserve the patient's airway microbiome, reduce the risk for colonisation by drug- resistant bacteria and for adverse events such as colitis caused by Clostridioides difficile.

Key issues

Current clinical guidelines for antibiotic prescribing in COPD

Antibiotic prescribing for patients presenting with a COPD exacerbation is still essentially guided by the criteria set out by Anthonisen and colleagues in 1987 and updated by Stockley and colleagues in 2000, with antibiotics recommended for those with

increased breathlessness, increased sputum volume and increased sputum purulence when bacterial infection is considered to be the most likely trigger.[8-10]

The current NICE guidelines were issued in December 2018[11] and recommend that antibiotic therapy should be considered for patients presenting with an acute exacerbation of COPD only after taking into account:

- the severity of symptoms, particularly sputum colour changes and increases in volume or thickness beyond the person's normal day-to-day variation;
- whether they may need to go into hospital for treatment; previous exacerbation and hospital admission history and the risk of developing complications;
- previous sputum culture and susceptibility results; and
- the risk of antimicrobial resistance and repeated courses of antibiotics.

Point-of-care CRP testing is not included in the algorithm for COPD exacerbation management, and it is no longer included in the clinical guidance recommendation for the diagnosis and management of community-acquired pneumonia.[12]

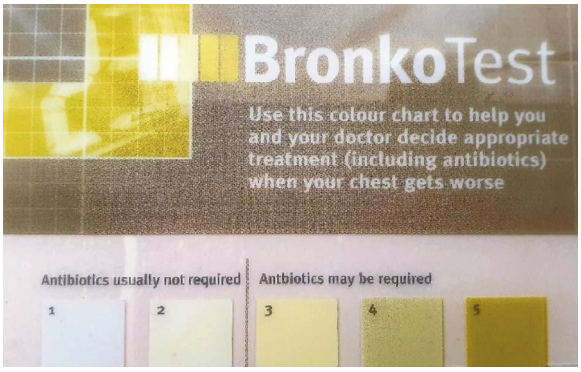
Point-of-care testing vs sputum purulence as a guide to antibiotic prescribing for COPD exacerbation

A single drop of blood from a finger prick test is required to perform the test using an assay kit and analyser instrument (quantitative measurement) or disposable single-use test strips (semi-quantitative measurement) with results available within a few minutes.

Patients with raised levels of CRP in their blood are those most likely to benefit from antibiotics to treat an underlying bacterial infection.[5] The PACE study was a multicentre trial conducted at 86 primary care clinics in England and Wales.[4] The study included 653 patients with an acute exacerbation of COPD who were randomised to receive usual care guided by point-of-care CRP testing via a rapid finger prick test or usual care only. For CRP-guided care, clinicians were advised that antibiotics were unlikely to be beneficial when the CRP level was <20 mg/L, likely to be beneficial when the CRP level was >40 mg/L and possibly beneficial when the CRP level fell between 20 and 40 mg/L and purulent sputum was present. Prescribing decisions were to be based on a comprehensive assessment of likely risks and benefits. Antibiotic prescribing was 20% lower among those patients who received usual care guided by point-of-care CRP testing compared with those who received usual care only (57% vs 77%, respectively). This reduction in antibiotic use did not have a negative effect on patients' recovery over the first two weeks after their consultation at their GP surgery, or on their well-being or use of health care services over the following 6 months. The results of the study show that CRP-guided prescribing of antibiotics for COPD exacerbations presenting in primary care can reduce the proportion of patients prescribed an antibiotic with no evidence of harm in terms of COPD-related health status or increased visits to GPs or a greater need for antibiotics over the following 6 months.

However, a subsequent sub-analysis of the PACE study examined the results of 386 patients from whom sputum samples were taken for analysis to compare sputum purulence with point-of-care CRP testing to determine bacterial infection.[13] 20.5% had bacterial pathogens, 31.9% had viral/atypical pathogens and 23.6% had mixed pathogens identified. Sputum purulence was assessed using the BronkoTest Sputum Colour Chart (graded 1–5, see Figure 1).

Figure 1. BronkoTest® card with sputum colour chart



BronkoTest is owned by Heredilab Inc (Utah USA)

The study found that increasing sputum purulence was associated with increased odds of finding bacterial and mixed pathogens in the sputum with an area under the ROC curve (AUROC) value of 0.739 which implies a good predictive value. The addition of a raised CRP level did not significantly increase the AUROC value (0.77). The conclusion from this sub-analysis was that an elevated CRP did not add to the predictive value of sputum purulence for the presence of bacterial or mixed pathogens. This supports the current clinical guidance.

In the current situation where there is a recognised workforce crisis and resources to see people in primary care stretched by underfunding, the implications of longer consultations to allow for time to undertake a point-of-care test need to be carefully considered with its overall practical benefits.[14,15]

PCRS position

- Patients presenting with acutely worsening symptoms and known to have COPD should receive antibiotics only when a COPD exacerbation has been determined as the cause of the change and then when bacterial infection is considered to be the most likely trigger.
- Sputum purulence is as accurate at predicting the presence of bacterial pathogens as point-of-care CRP testing in exacerbations of COPD. Point-of-care CRP testing is not widely available in primary care at present and would add to consultation length. Using sputum purulence as recommended by current clinical guidelines remains the most pragmatic approach to determine the presence of bacterial infection that may benefit from antibiotics.
- Use of point-of-care testing such as CRP testing would be a valuable addition to support treatment decisions if resources are available.
- When evaluating a patient with COPD experiencing a symptomatic exacerbation such as cough and worsening breathlessness, all potential triggers should be considered including tobacco exposure, air quality, psychosocial factors, viral infection and bacterial infection. Adherence to the guidance may help reduce unnecessary prescribing of antibiotics for people with COPD by enabling a more considered diagnostic approach to those with COPD in crisis.

References
1. NHS England. Overview of potential to reduce lives lost from Chronic Obstructive Pulmonary Disease (COPD). Available at: https://www.england.nhs.uk/wp-content/uploads/2014/02/rm-fs-6.pdf (Accessed May 2021).
2. Barnes PJ, Burney PGJ, Silverman EK, et al. Chronic obstructive pulmonary disease. Nat Rev Dis Primers 2015;1:15076. doi: 10.1038/nrdp.2015.76
3. National Institute for Clinical Excellence. Chronic obstructive pulmonary disease in over 16s: diagnosis and management. NG 115. NICE, 2019.
4. Butler CC, Gillespie D, White P, et al. C-reactive protein testing to guide antibiotic prescribing for COPD exacerbations. N Engl J Med 2019;381:111–20. doi: 10.1056/NEJMoa1803185
5. Miravitlles M, Moragas A, Hernandez S, et al. Is it possible to identify exacerbations of mild to moderate COPD that do not require antibiotic treatment? Chest 2013;144:1571–7. doi: 10.1378/chest.13-0518
6. Vollenweider DJ, Jarrett H, Steurer-Stey CA, et al. Antibiotics for exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012;12:CD010257. doi: 10.1002/14651858.CD010257
7. Van Velzen P, Ter Riet G, Bresser P, et al. Doxycycline for outpatient-treated acute exacerbations of COPD: a randomised double-blind placebo-controlled trial. Lancet Respir Med 2017;5:492–9. doi: 10.1016/S2213-2600(17)30165-0
8. Anthonisen NR, Manfreda J, Warren CP, et al. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. Ann Intern Med 1987;106:196–204. doi: 10.7326/0003-4819-106-2-196
9. Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2021 Global Strategy for Prevention, Diagnosis and Management of COPD. Available at: https://goldcopd.org/gold-reports/ (Accessed May 2021).
10. Stockley RA, O'Brien C, Pye A, Hill SL. Relationship of sputum color to nature and outpatient management of acute exacerbations of COPD. Chest 2000;117:1638–45. doi: 10.1378/chest.117.6.1638
11. NICE. Chronic obstructive pulmonary disease (acute exacerbation): antimicrobial prescribing. Available at: www.nice.org.uk/guidance/ng114 (Accessed May 2021).
12. NICE. Pneumonia (community-acquired): antimicrobial prescribing. Available at: https://www.nice.org.uk/guidance/NG138 (Accessed May 2021)
13. Francis NA, Gillespie D, Wootton M, et al. Clinical features and C-reactive protein as predictors of bacterial exacerbations of COPD. Int J Chronic Obstr Pulm Dis 2020:15 3147–58. doi: 10.2147/COPD.S265674
14. Dixon-Woods M, Summers C, Morgan M, Patel K. The future of the NHS depends on its workforce. BMJ 2024;384:e079474. doi: 10.1136/bmj-2024- 079474
15. Dobson J. Time is running out to resolve the NHS workforce crisis. BMJ 2023;380:p681. doi: 10.1136/bmj.p681

Approved by PCRS policy lead: 14 February 2025