



## Case Study

### C-reactive protein (CRP) to better target antibiotic prescription in patients presenting with lower respiratory tract infection

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Authors:

**Saskia F van Vugt, MD PhD<sup>1</sup>, Berna DL Broekhuizen, MD PhD<sup>1</sup>, Paul Little, MD PhD<sup>2</sup>**  
and **Theo JM Verheij, MD PhD<sup>1</sup>**, on behalf of the GRACE consortium.

Affiliations:

1. Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, The Netherlands.
2. FMedSci FRCGP Primary Care and Population Sciences Unit, Faculty of Medicine, University of Southampton, United Kingdom

### Case presentation

A man in his late 40s presented with an acute cough. He had been feeling sick for the past three weeks. He produces green sputum and sometimes experiences shortness of breath, for example when riding his bicycle. He is asking for an antibiotic, because a neighbour who was coughing for a few weeks turned out to have a pneumonia. On examination, his body temperature is 37.8°C, his heart frequency 90 beats per minute and his respiratory rate is 22 breaths per minute. Auscultation of the lungs reveals some diffuse wheezes and clear rhonchi on one side.

### Investigations

A point-of-care CRP test was performed and showed a CRP level of 18 mg/L (upper limit of normal 10 mg/L).

### Treatment

After exploring the patients' expectations, the GP used the CRP test result to discuss the low risk of pneumonia. The patient agreed on not having antibiotics prescribed, was educated on the expected course of the disease and received instructions for re-consultation. Satisfied and reassured, this patient returned home.

## Background

In every patient presenting with acute cough or other signs of lower respiratory tract infection (LRTI) in primary care, general practitioners (GPs) have to judge whether it concerns a self-limiting condition, or a pneumonia for which antibiotic treatment and follow-up are indicated. Several studies have showed that differentiation between pneumonia and other causes of LRTI based on clinical items alone is difficult.<sup>1</sup> Chest radiography is considered the gold standard for diagnosing pneumonia,<sup>2,3</sup> but not feasible to perform on all patients presenting with LRTI. In most cases the initial approach therefore involves empirical therapy with antibiotics. Diagnostic uncertainty as well as patients' expectations and satisfaction enhance unjustified antibiotic prescriptions in primary care.<sup>4,5</sup> Early markers for guiding GPs in identifying patients in whom antibiotics are indicated are therefore needed. A suggested diagnostic approach is the use of a point-of-care test to determine C-reactive protein (CRP).<sup>6-8</sup>

CRP is an acute phase protein produced in the liver. Increased production of this protein is triggered by cytokines released by infection or tissue damage.<sup>9</sup> The serum concentration is usually below 10 mg/L, but can increase to >500 mg/L within a few days in cases of severe infection.<sup>9</sup> The CRP level is clearly associated with the probability of pneumonia<sup>6,10</sup> and this blood marker was shown to be superior to signs and symptoms for diagnosing pneumonia.<sup>7</sup> However, this diagnostic test is useful as an adjunct to clinical judgment only when its results can significantly increase diagnostic accuracy for identifying pneumonia. In addition to the GP's clinical judgment, the diagnostic value of a CRP test has shown to be limited in those patients where the GP is already expecting a low or high risk for pneumonia.<sup>11</sup> In the majority of patients however, the GP remains in diagnostic doubt after having taken history and physical examination. In all these patients, CRP has proven to be helpful, especially in reducing the probability of pneumonia.<sup>11</sup> Besides, GPs' antibiotic prescription rates were reduced by CRP-guided LRTI management.<sup>8</sup> GPs like CRP as an educational tool, which empowers them to explain to patients why antibiotics are generally unnecessary.<sup>12</sup>

Several European guidelines on management of LRTI have incorporated the use of a CRP point-of-care test in the diagnostic process. A CRP level below 20 indicates a low risk of pneumonia, making antibiotic treatment unnecessary. High CRP levels (>100mg/L) indicate an increased likelihood of pneumonia, and antibiotic prescription is recommended.<sup>13</sup> In the patient case described above, a CRP test helped the GP to refrain from antibiotic prescription while maintaining the patient's confidence.

## Discussion

This case-report demonstrates the novel European approach to the use of CRP to guide GPs in identifying pneumonia and enhancing targeted antibiotic treatment in primary care patients with acute cough. The diagnostic value of CRP in primary care children with LRTI has not yet been reported, but several research groups are now investigating this application.

It should be taken into account that, although prices per test are limited in the EU, acquisition of a CRP device can be costly for general practice. As an alternative, communication skills training can afford a less expensive, but equally effective option for reducing antibiotic prescription.<sup>14</sup> Another concern with CRP is the possibility of medicalisation—patients returning with LRTI complaints to have their CRP re-measured. This could increase both health care costs, as well as demands on GPs to educate their patients.

It should also be remembered that CRP is a non-specific marker of inflammation, and therefore, is subject to the influence of other factors. High values can be found in other diseases, such as pulmonary embolism, myocardial infarction, malignancies or simultaneous infections elsewhere (e.g. erysipelas).<sup>15</sup> Additionally, a normal value may be observed early in an illness episode, before the acute-phase response has been mounted.<sup>16</sup> Thus, CRP should always be interpreted in combination with the clinical assessment.

## Learning Points

- The CRP test can help to reduce diagnostic uncertainty in patients presenting with acute cough, resulting in targeted antibiotic treatment.
- A high CRP level (>100 mg/L) can indicate a severe bacterial infection, e.g., pneumonia.
- Antibiotic treatment can usually be avoided when the CRP value is low (<20-30 mg/L).
- The CRP test can be used as an additional tool to convince adult patients to refrain from antibiotic prescription.

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