Implementing point-of-care CRP testing for better diagnosis of acute respiratory infections

INTRODUCTION

Many countries in Europe have routinely implemented the use of point-of-care testing (POCT) for c-reactive protein (CRP) in primary care to guide antibiotic therapy in patients with acute respiratory infections; however, this has not been implemented in the UK or Australia. General practice is where the majority of antibiotics are prescribed and CRP testing may provide a means to help limit antibiotic use to those patients with severe (bacterial) infections. A recent addition to this debate is whether the arguments to measure CRP rapidly also need to be applied to COVID-19 testing.

The clinical evidence to support CRP POCT to guide antibiotic therapy in adult patients was recently reviewed by Cals and Ebell. They concluded that in adults there is accumulating evidence that CRP use can help safely reduce antibiotic usage in patients with acute respiratory infections.[1] A recent narrative review by Cooke *et al* queried why the test is not more widely used in the UK.[2]

Given the extent of the evidence base, the issue becomes one of identifying the remaining barriers to implementation and how they can be addressed.

WHAT ARE THE BARRIERS TO IMPLEMENTATION OF CRP POCT?

The most commonly identified barrier is how to fund or reimburse POCT CRP.[3] Funding is in part related to the economic impact of testing. Both a budget impact model of POCT compared with normal care[4] and a decision modelling study that compared both POCT alone and POCT plus communication skills training with normal care[5] showed only that POCT was marginally cost-effective, but there was considerable uncertainty around the results. However, neither of these studies took into account the long-term benefits of antibiotic stewardship, although how this can be accounted for is acknowledged to be difficult. An additional problem of funding is the usual one of silo budgeting whereby the costs of testing and resulting downstream benefits are in different areas of health care.

The other identified barriers to CRP testing are those that relate to the consultation process and how it is disrupted by POCT. Several studies highlight concerns about the quality of results, whether there will be overtesting or an overreliance on testing, and how to efficiently integrate the POCT process into the practice workflow.[3,6] In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) recommends that support for POCT outside of the hospital setting should be provided by the local laboratory. In Australia, there is limited experience on the part of laboratories to conduct POCT outside of the hospital environment, but there are other POCT support models available.[7]

WHAT IS THE INTERNATIONAL EXPERIENCE OF CRP POCT?

Long-term experience of CRP POCT

While there are numerous trials of CRP POCT, there are limited data on what the longer-term effects of CRP testing are on antibiotic usage. In the Netherlands, testing is conducted in conjunction with information about guideline-based cut-offs, and, during the last decade, percentages of patients with low (<20 mg/L, 65%), intermediate (20–99 mg/L, 30%), and high (>99 mg/L, 5%) CRP test results remain similar to those in the original scientific studies that included only patients with lower respiratory tract infections; these data suggest no significant overtesting.[8] In Sweden, where there are no such guidelines, there have been reports of overtesting.[9] In Australia, the only randomised controlled trial of CRP testing was as one of several interventions and was not widely taken up because of lack of support and encouragement for GPs to use the test.[10]

CRP POCT during the COVID-19 pandemic

Hospital studies have highlighted the added, prognostic value of (moderately) elevated CRP levels, among other biomarkers, in COVID-19 infections.[11] But the value in general practice is still unclear. During the peaks of the COVID-19 crises, patient management differed widely between and within countries and regions. GPs in the Netherlands continued using CRP POCT, particularly in a selection of suspected COVID-19 cases to guide them in management decisions, mostly hospital referral or not, and the diagnosis of (non-COVID-19) pneumonia.

Support models for POCT

International experience can also inform strategies to overcome documented barriers to POCT. In the Netherlands, the testing is provided by the same organisations that provide central laboratory testing. This includes provision of all testing resources together with training for staff, and quality management. Reimbursement for testing is mostly provided directly to the supporting laboratory and not to the GP.

The Noklus organisation in Norway is funded by the central government to provide POCT support to virtually all GPs in Norway and other neighbouring countries. Regular publications show that POCT is performed to a high standard.[12] However, Noklus does not monitor the clinical and process outcomes that might be included in an optimal implementation model of POCT.

Although POCT is not reimbursed for general practice in Australia, many GPs currently perform POCT for international normalised ratio (INR), and those in the rural sector carry out a wider range of POCT with support via a virtual POCT organisation.[7] Collectively, the experience of POCT in Australia and the Netherlands is significant and indicates that, once GPs and their staff start using POCT, they become adept at integrating it into their practice; rather than finding it disruptive, they claim that it can improve their practice efficiency.

NEXT STEPS

First, this might be a large-scale implementation trial of the use of POCT CRP in general practice with measurement of clinical and economic outcomes including reduced antibiotic prescriptions. But our preferred step is to implement CRP POCT for the more modest and realistic goal of improving the diagnostic process. The improvement will be manifested by changing the balance of antibiotic prescriptions such that more patients with pneumonia get the

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antibiotics they need and less are prescribed to those with a minor (often viral) illness. The Netherlands experience indicates that this more appropriate prescribing brings increased satisfaction to both patients and GPs, and is seen as a valuable outcome.[13]

A second step is to accept that some sort of support model must be provided to GPs in order for them to conduct POCT as described above. Such a support model can not only deal with quality issues but may also assist with integrating POCT into the practice workflow. What form this model takes will depend on the country, but in Australia organisations dedicated to supporting POCT already operate with considerable success. There are of course costs associated with such support but the required investment can eventually be spread over multiple tests as POCT expands, which it is likely to do judging by the experience in other countries.

A third and more contentious step is how to monitor the implementation of CRP POCT. Post-market surveillance of tests does not occur as it does for drugs, yet there is widespread evidence of over- and undertesting. Thornton *et al* discuss these issues in relation to CRP POCT.[14] There is also evidence of poor implementation of many interventions across health care in general and calls for better implementation practice.[15] The counter-argument is that any monitoring process may become too onerous for the GP, and raises issues of data privacy and patient confidentiality. Some sort of intermediate position needs to be found whereby periodic audit of appropriate outcomes is relatively easily achieved and funded as a quality improvement exercise, such as in Australia through the Practice Incentives Program and incorporated into the POCT support model.

Finally, the funding or reimbursement of CRP POCT should be seen not only as a wider investment with a whole-of-healthcare approach but also as part of a multistep strategy to reduce antibiotic resistance. Avent *et al* emphasise that single isolated interventions are not likely to sustainably reduce antibiotic prescriptions and they must be coupled with a combination of behavioural and regulatory processes such as accreditation standards in order for them to be effective.[16]

In relation to all of these steps, and given the long-term presence of COVID-19 in the community as a possible cause of acute respiratory infections, POCT should also include that for COVID-19 since there are soon likely to be a range of devices to measure COVID-19, influenza, and other microbiological agents as there are now for CRP.

CONCLUSION

Investment should be provided to establish high-quality and patient-safe POCT for CRP testing in GP practices to aid them in the differential diagnosis of acute respiratory infections, possibly as part of a multi-pronged strategy of reducing antibiotic usage. The investment should include funding for POCT support and implementation monitoring. Patient and healthcare professionals' experience and outcomes should be monitored over a sufficient period of time to assess whether CRP POCT increases the quality of patient care, including antibiotic stewardship.

Andrew St John,
Consultant, Drajon Health, Perth, Western Australia; Director, Australian Point-of-Care Testing Practitioners Network, Adelaide, South Australia, Australia.

Rogier Hopstaken,
GP, Star-Shl Diagnostic Centres, Etten-Leur, the Netherlands.

REFERENCES

1. Cals JWL, Ebell MH. C-reactive protein: guiding antibiotic prescribing decisions at the point of care. *Br J Gen Pract* 2018; DOI: https://doi.org/10.3399/bjgp18X694901.
2. Cooke J, Butler C, Hopstaken R, *et al.* Narrative review of primary care point-of-care testing (POCT) and antibacterial use in respiratory tract infection (RTI). *BMJ Open Respir Res* 2015; **2(1):** e000086.
3. Huddy JR, Ni MZ, Barlow J, *et al.* Point-of-care C reactive protein for the diagnosis of lower respiratory tract infection in NHS primary care: a qualitative study of barriers and facilitators to adoption. *BMJ Open* 2016; **6(3):** e009959.
4. Holmes EAF, Harris SD, Hughes A, *et al.* Cost-effectiveness analysis of the use of point-of-care C-reactive protein testing to reduce antibiotic prescribing in primary care. *Antibiotics* (Basel) 2018; **7(4):** 106.
5. Health Information and Quality Authority. *Health Technology Assessment of C-reactive protein point-of-care testing to guide antibiotic prescribing for acute respiratory tract infections in primary care settings.* 2019. https://www.hiqa.ie/sites/default/files/2019-05/HTA_C-reactive_Protein_Point_of_Care_Testing-FullReport.pdf (accessed 10 Jan 2022).
6. Eley CV, Sharma A, Lecky DM, *et al.* Qualitative study to explore the views of general practice staff on the use of point-of-care C reactive protein testing for the management of lower respiratory tract infections in routine general practice in England. *BMJ Open* 2018; **8(10):** e023925.
7. St John A, Tirimacco R, Badrick T, *et al.* Internet support for point-of-care testing in primary care. *Aust Fam Physician* 2015; **44(1–2):** 10–11.
8. Cals JWL, de Bock L, Beckers P-JHW, *et al.* Enhanced communication skills and C-reactive protein point-of-care testing for respiratory tract infection: 3.5-year follow-up of a cluster randomized trial. *Ann Fam Med* 2013; **11(2):** 157–164.
9. André M, Schwan A, Odenholt I. The use of CRP tests in patients with respiratory tract infections in primary care in Sweden can be questioned. *Scand J Infect Dis* 2004; **36(3):** 192–197.
10. University of Queensland School of Public Health. *General Practitioners Antimicrobial Stewardship Programme Study (GAPS): final summary report.* 2018. https://public-health.uq.edu.au/gaps (accessed 10 Jan 2022).
11. Stavelin A, Sandberg S. Harmonization activities of Noklus — a quality improvement organization for point-of-care laboratory examinations. *Clin Chem Lab Med* 2018; **57(1):** 106–114.
12. Malik P, Patel U, Mehta D, *et al.* Biomarkers and outcomes of COVID-19 hospitalisations: systematic review and meta-analysis. *BMJ Evid Based Med* 2021; **26(3):** 107–108.
13. Cals JWL, Chappin FHF, Hopstaken RM, *et al.* C-reactive protein point-of-care testing for lower respiratory tract infections: a qualitative evaluation of experiences by GPs. *Fam Pract* 2010; **27(2):** 212–218.
14. Thornton HV, Khalid T, Hay AD. Point-of-care testing for respiratory infections during and after COVID-19. *Br J Gen Pract* 2020; DOI: https://doi.org/10.3399/bjgp20X713561.
15. Price CP, St John A. The value proposition for point-of-care testing in healthcare: HbA1c for monitoring in diabetes management as an exemplar. *Scand J Clin Lab Invest* 2019; **79(5):** 298–304.
16. Avent ML, Cosgrove SE, Price-Haywood EG, van Driel ML. Antimicrobial stewardship in the primary care setting: from dream to reality? *BMC Fam Pract* 2020; **21(1):** 134.

ADDRESS FOR CORRESPONDENCE

Andrew St John
PO Box 1492, Toodyay, WA 6566, Australia.
Email: astjohn@drajon.com.au

Rosy Tirimacco,
Operations & Research Manager, Integrated Cardiovascular Clinical Network, Adelaide, South Australia, Australia.

Ralph Audehm,
GP, Carlton Family Medical, Carlton, Victoria, Australia.

Christopher P Price,
Honorary Senior Researcher, Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK.

Provenance
Freely submitted; externally peer reviewed.

Competing interests
The authors have declared no competing interests.

DOI: https://doi.org/10.3399/bjgp22X718517