Clinical Acceptance Criteria for Extended Respiratory Multiplex Viral Panels tests

Introduction

Clinical acceptance criteria for the use of Extended Respiratory Multiplex Viral Panels have been developed and are detailed below. Combined tests for SARS-CoV-2, Flu A/B or RSV are well established and readily available, therefore for the purposes of these criteria, an Extended Respiratory Multiplex Viral Panel is being defined as one which looks for viral targets other than these three pathogens. Note that extended respiratory multiplex viral panels are generally expensive and may present technical challenges. Some diagnostic laboratories also batch such assays, resulting in a relatively long turnaround time.

Clinical Acceptance Criteria for Extended Respiratory Multiplex Viral Panels

Extended Respiratory Multiplex Viral testing should only be undertaken in the following circumstances (Electronic or manual request forms should clearly state the relevant clinical details and the relevant clinical indication for the test):

- Adult patients hospitalised with severe pneumonia and requiring intensive care support, and where the result is likely to change clinical management.
- Patients presenting with pneumonia who have significant immunocompromise. This includes patients with neutropenia, those undergoing active cancer therapy, organ transplant patients (both solid organ and blood component transplantation), advanced HIV disease, & patients on immunosuppressive agents.
- Unexplained respiratory infection in infants who are hospitalised and who have a negative SARS-CoV-2/Influenza/RSV test, where the result is likely to change clinical management.
- Specialist request (ID/micro/respiratory specialist), detailing a clear rationale as to how the result will potentially change management.
- Investigation of a respiratory illness outbreak as directed by a Medical Officer of Health or Infection Prevention and Control team.

All requests for extended respiratory multiplex viral panels *must* be accompanied by relevant clinical details pertaining to the clinical acceptance criteria above.

*-Extended Respiratory Multiplex Viral testing should **not** be repeated as a "test of cure".*
*-Extended Respiratory Multiplex Viral testing which produced a negative result, should **not** be repeated unless new symptoms develop*
*-Extended Respiratory Multiplex Viral testing should **not** be performed to determine if someone can be removed from Infection Prevention Control instituted isolation*

Background

Molecular testing platforms now have multi-target PCR assays supporting syndromic testing. The assays can target multiple viral, bacterial and parasitic pathogens contained within the one diagnostic assay. They may provide diagnostic information quicker than routine culture. The epidemiological value is clear, but the direct clinical benefit is more controversial. Judicious use of resources based on the available medical evidence should be the basis of medical decisions, and it is important to apply diagnostic stewardship principles when utilising extended multiplex respiratory panels.

What is an Extended Respiratory Multiplex Viral Panel?

Extended respiratory multiplex viral panels test for a range of organisms known to cause respiratory infections. Note that some of these multiplex panels may include some bacterial targets also.

There is already clear evidence for the benefit of diagnosing RSV, influenza, and SARS-CoV-2 in hospitalised patients presenting with acute respiratory symptoms, and several assays, such as the GeneXpert SARS-CoV-2, Flu/RSV assay, are available for the identification of these specific pathogens. These assays will also have a role in supporting the management of community outbreaks in disability and age-related residential facilities.

We are defining an Extended Respiratory Multiplex Viral Panel as one which looks for viral targets other than these three pathogens, e.g. panels which may include rhinovirus, parainfluenza, human metapneumovirus, adenovirus, bocavirus, seasonal coronaviruses, etc.

Examples of such panels currently used in NZ include the following:

- Biofire Respiratory 2.1 Panel
- QIAstat-Dx Respiratory Panel
- AusDiagnostics Medium and Comprehensive Respiratory Panels

Note that some of these panels will also include non-viral “atypical pneumonia” pathogens such as *Bordetella* spp., *Chlamydophila pneumoniae, Legionella* spp. and *Mycoplasma pneumoniae*. Clinical acceptance criteria for these pathogens are not covered in this document.

What Diagnostic Stewardship principles should be considered?

Key considerations when choosing a diagnostic test include:

1. The pre-test probability of the condition being tested for. This will differ for different populations (e.g., paediatrics vs adults; immunocompetent vs immunocompromised).[1] Each different target will have a different pre-test (and post-test) probability depending on the patient being tested and the current disease prevalence of that target. This will affect the positive and negative predictive values of each specific result within the multiplex panel. However, all results generated from a multiplex panel have the potential to be regarded as equally "true" by end users.

2. Molecular tests do not differentiate between colonisation and infection. Because of this and the very low pre-test probability of some of the targets, multiplex panels will be more prone to producing false positive results than single targeted tests. [2]

3. Support directed/targeted therapy and reduce unnecessary interventions. Allow for earlier initiation of appropriate antimicrobial therapy, discontinuation of current antibiotics, changes to infection prevention and control interventions, and changes to proposed investigations.

   Note that the evidence around potential benefits are not clear.
   Studies investigating earlier discontinuation of antibiotics have failed to show extended viral molecular panels reduce the duration of antibiotic treatment.[1,3,4,-6] Radiographic and clinical criteria appear more important in deciding on antimicrobial use.[6] Other studies have shown a marginal improvement in antimicrobial discontinuation among some patients with a confirmed viral infection.[7,8] Discontinuation of antimicrobials is more likely if combined with antimicrobial stewardship intervention.[9] Two studies showed a reduction in radiological investigations among patients diagnosed with influenza.[1,8] Eleven studies showed infection control interventions linked to results of a multiplex respiratory panel test. Most of these tests included panels which tested for influenza and or RSV. [8]

References

1. Vos LM, Bruning AHL, Reitsma JB, et al. Rapid Molecular Tests for Influenza, Respiratory Syncytial Virus, and Other Respiratory Viruses: A Systematic Review of Diagnostic Accuracy and Clinical Impact Studies. Clin Infect Dis. 2019 Sep 13;69(7):1243-1253. doi: 10.1093/cid/ciz056.
2. Zanella M-C, Maylan P. Kaiser L. Syndromic panels or panel syndrome? A perspective through the lens of respiratory infection. Clin Microbiol and Infect. 2020;26(6)665-668. doi: 10.1016/j.cmi.2019.12.018.
3. Evans SE, Jennerich AL, Azar MM, et al. Nucleic Acid-based Testing for Noninfluenza Viral Pathogens in Adults with Suspected Community-acquired Pneumonia. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2021 May 1;203(9):1070-1087. doi: 10.1164/rccm.202102-0498ST.
4. Brendish NJ, Malachira AK, Armstrong L, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. Lancet Respir Med. 2017;5:401–411. doi: 10.1016/S2213-2600(17)30120-0
5. Hernes SS, Hagen E, Quarsten H, Bjorvatn B, Bakke PS. No impact of early real-time PCR screening for respiratory viruses on length of stay and use of antibiotics in elderly patients hospitalized with symptoms of a respiratory tract infection in a single center in Norway. Eur J Clin Microbiol Infect Dis 2014;33:359–364. doi:10.1007/s10096-013-1963-0.
6. Semret M, Schiller I, Jardin BA, Frenette C, Loo VG, Papenburg J, et al. Multiplex respiratory virus testing for antimicrobial stewardship: a prospective assessment of antimicrobial use and clinical outcomes among hospitalized adults. J Infect Dis 2017;216:936–944. doi: 10.1093/infdis/jix288.
7. Gilbert D, Gelfer G, Wang L, Myers J, Bajema K, Johnston M, et al. The potential of molecular diagnostics and serum procalcitonin levels to change the antibiotic management of community-acquired pneumonia. Diagn Microbiol Infect Dis. 2016;86:102–107. doi: 10.1016/j.diagmicrobio.2016.06.008.
8. Guillon A, Aymeric S, Gaudy-Graffin C, Sonke J, Deblonde MP, Capsec J, et al. Impact on the medical decision-making process of multiplex PCR assay for respiratory pathogens. Epidemiol Infect 2017;145:2766–2769. doi: 10.1017/S0950268817001029
9. Wils J, Saegeman V, Schuermans A. Impact of multiplexed respiratory viral panels on infection control measures and antimicrobial stewardship: a review of the literature. Eur J Clin Microbiol Infect Dis. 2022 Feb;41(2):187-202. doi: 10.1007/s10096-021-04375-3.