Unpredictable challenges for respiratory virus treatment

Winter 2021/2022 could become the most challenging in decades for respiratory healthcare. There are many unknowns, such as the potential impact of circulating influenza or the trajectory of new COVID-19 variants such as Omicron. But one thing is certain. It will be ever more crucial to be able to rapidly diagnose and differentiate whether a patient is presenting symptoms of COVID-19 or another respiratory disease. As they struggle to breathe on arrival at A&E departments, do they need to be quickly isolated on a COVID-19 unit or transferred to a respiratory ward for ongoing treatment? Preparing for winter respiratory diseases in previous years was relatively routine. Tracking influenza viruses in the southern hemisphere shaped the development of flu vaccines for the western hemisphere. Natural exposure to circulating coronaviruses built up certain levels of immunity in the population, and respiratory healthcare treated 'known' diseases. The arrival of SARS-CoV-2 two years ago changed the respiratory healthcare landscape irreparably. On 31 December 2019, the World Health Organization (WHO) was informed of a cluster of cases of pneumonia of unknown cause - detected in Wuhan, China. On 12 January 2020, it was announced that a novel coronavirus had been identified in samples obtained from cases and that initial analysis of virus genetic sequences suggested that this was the cause of the outbreak. This virus is referred to as SARS-CoV-2, and the associated disease as COVID-19. Governments and healthcare services reacted in different ways and at different times, but most countries in the western hemisphere instigated some measure of virus mitigation, ranging from face mask wearing and track-and-trace to full lockdown. Whilst this had an undeniable effect on managing the pandemic, it also impacted the development of 'usual' seasonal viruses. Measures put in place to control the COVID-19 pandemic also impacted influenza activity. Social distancing, travel restrictions and a strong emphasis on hand washing reduced the circulation and infection rate of a wide range of respiratory viruses, including SARS-CoV-2. This led to of extremely low levels of circulating influenza during the 2020 to 2021 season. World Health Organisation research found that globally, despite continued or even increased testing for influenza in some countries, influenza remained at lower levels than expected during this time of year.[1] Research in the US and China showed that non-pharmaceutical interventions (NPIs) and behavioural changes to mitigate COVID-19 could have affected transmission dynamics of influenza and other respiratory diseases. By comparing 2019–2020 seasonal influenza activity through March 29, 2020 with the 2011–2019 seasons, researchers found that COVID-19 outbreaks and related NPIs may have reduced influenza in Southern and Northern China and the United States by 79.2%.[2] But this meant that certain aspects of surveillance were not possible during this season, including virus characterisation and vaccine effectiveness estimates – hence the big unknown this winter. Neither scientists nor health care experts can be certain about the epidemiology over the next few months. There are unknowns around whether concurrent transmission of other respiratory viruses with SARS-CoV-2 will occur. How influenza develops this winter will depend on which strain of flu dominates, and how effective the flu vaccine proves to be. Also, there is an ever-changing landscape of social restrictions as COVID-19 variants impact different populations. As has been proven, social distancing, face mask wearing, and good hand hygiene impact the spread of influenza as well as SARS-CoV-2. But as one of the outcomes from last year's pandemic control measures has been waning immunity to influenza, there are fears that this winter will see a larger disease burden than would have occurred if influenza had circulated as 'normal'. It is also quite possible that the same impact would be seen with Respiratory Syncytial Virus RSV), a very common, contagious virus that causes infections of the respiratory tract[3]. RSV epidemiology is influenced by naturally acquired immunity, not vaccination, and social contact patterns in children, which until recently have been back to normal levels. With influenza, RSV and SARS-CoV-2 viruses circulating at the same time this winter, identification of which virus is causing what symptoms in a patient becomes an urgent priority – particularly as they arrive in A&E departments. Co-infection with endemic respiratory viruses is also a possibility, with the potential to increase pressure on the NHS and care services in the UK. Data to date suggests that coinfection with SARS-CoV-2 and influenza may cause increased disease severity than would be expected if influenza and SARS-CoV-2 acted autonomously. Observational data from wave 1 in the UK found that hospital patients with dual infection with SARS-CoV-2 and influenza virus had prolonged duration of admission[1]. Patients with dual influenza and SARS-CoV-2 infection had more than twice the length of hospital stay than those who tested negative for influenza (16.4d vs 7.4d). This effect continued when patients admitted with influenza and who then acquired COVID-19 in hospital were excluded. So, the need to distinguish between viral respiratory diseases in

hospitals and care homes is vital – not just to know whether to isolate a patient, but also to inform clinical decisions. What treatment does the patient need? Drugs used for in-patient COVID-19 treatment, such as dexamethasone or tocilizumab, are not indicated for other respiratory viral infections. Patients may be presenting symptoms that are common in several respiratory conditions, from respiratory viruses such as SARS-CoV-2, influenza or RSV, to respiratory diseases such as non-small-cell-lung-cancer and chronic obstructive pulmonary disease. Patients with a known chronic respiratory disease still need to be tested for SARS-CoV-2 and other viruses, to facilitate the correct clinical diagnosis and speedy treatment. Multiplex laboratory tests are therefore needed, for rapid viral diagnosis. Novacyt's genesig® SARS-CoV-2 Winterplex, a multiple assay for winter testing, enables simultaneous real-time PCR detection of multiple winter viruses in one kit. It differentiates between COVID-19 and the 2020/2021 vaccine strains of Flu A and Flu B, plus RSV A and B, giving an accurate result in as little as 90 minutes. The multiplex assay achieves high sensitivity and accuracy, with precise reproducible results. The kit includes Lyophilised qPCR Master Mix for ambient shipping. genesig® SARS-CoV-2 Winterplex is designed for healthcare settings, enabling hospital staff to quickly test an in-coming respiratory patient, to find out whether they need to isolate them because of COVID-19 or treat them on a respiratory ward if they have a different respiratory infection. With Novacyt's continuous bio surveillance, the company is confident that this multiplex assay covers all known variants and mutations of COVID-19 including the latest Omicron, with over 4.5 million sequences analysed. For further information please contact **enquiries@primerdesign.co.uk**. ***References:*** 1.WHO Influenza Update No. 382.
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