Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

thromboembolic adverse events. Future work might identify subgroups of patients with acute COVID-19 who would benefit from IVIG, but the current evidence does not support use of IVIG in COVID-19-associated ARDS.

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Vaccine efficacy and immune interference: co-administering COVID-19 and influenza vaccines

As we head towards the second anniversary of the COVID-19 pandemic, attention widens to encompass the array of unforeseen health-care consequences of these unprecedented times and measures. In this context, efforts have been made to analyse data and predict how the winter months will look in terms of the interplay between infections by SARS-CoV-2 and other common respiratory viruses, influenza, and respiratory syncytial virus. To an extent, there is still no consensus in the scientific and medical communities as to the risk and impact of concomitant respiratory infections: on the one hand, lockdown and other mitigations that have limited the spread of COVID-19 would be predicted to have limited influenza and respiratory syncytial virus too.[1,2] On the other hand, children especially might have heightened vulnerability, having now missed out on nearly 2 years of the normal interactions that prime immunity, and adults will have seen their immunity wane.[3,4] Certainly, a paucity of data exist on which to base any accurate predictions about which influenza strains are most likely to circulate this coming winter. One must also consider the rather uncharted territory of the interactive effects of respiratory pathogens: not much is known about the consequences of co-infection by these pathogens, but since each is associated with somewhat differently nuanced lung inflammatory pathology, serious additive effects might be anticipated. At a time when many countries have national programmes for COVID-19 vaccination, this uncertainty has raised the logistical question of what might be the nature of the influenza vaccine plus SARS-CoV-2 vaccine co-administration programmes. In some respects, no better time has occurred to roll out such respiratory vaccination programmes. Public confidence in vaccines is high, having largely overcome a considerable degree of hesitancy in many countries, and national logistics for vaccine programme delivery have been impressive.

The NVX-CoV2373 (ie, Novavax) vaccine is an adjuvanted recombinant protein vaccine, which has performed rather well in terms of safety, immunogenicity, and efficacy in clinical trials.[5] So what happens if you co-administer a seasonal influenza vaccine in one arm and a COVID-19 vaccine in the other arm? To answer this question in *The Lancet Respiratory*


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Medicine, Seth Toback and colleagues did a substudy[6] of the randomised, observer-blinded, placebo-controlled, phase 3 trial that evaluated the safety and efficacy of NVX-CoV2373.[5] In the substudy, Toback and colleagues reported the results of the influenza co-administration cohort, which enrolled 431 individuals to receive the seasonal influenza vaccine (as well as NVX-CoV2373 or placebo). The study considered reactogenicity, immunogenicity, and efficacy. Interestingly, their findings included a slight increase in reactogenicity in the dual-vaccinated group (ie, those receiving both the NVX-CoV2373 and the influenza vaccine) compared with those who received the NVX-CoV2373 vaccine alone, similar concentrations of anti-influenza antibodies, and a modest decrease in anti-SARS-CoV-2 anti-spike protein IgG antibodies, but with no overall difference in NVX-CoV2373 vaccine efficacy. Thus, the answer is that co-administration of the two vaccines is safe and effective.

For the **UK's guidelines about COVID-19** see https://www.gov.uk/government/publications/covid-19-vaccination-easy-read-resources/information-on-covid-19-vaccination-easy-read-guide

Why should this finding be a surprise? Advice until now has often been that there needs to be an interval of at least 1 week between the vaccines. At the time of rolling out new vaccines at such fast pace while trying to maintain a high bar for safety, a high degree of caution was warranted in the uncharted territory of vaccine co-administration. However, an unanticipated upside of the imperative for the so-called progress at pace has been that decisions have sometimes had to challenge long-held but poorly evidenced assumptions. Some of the caution around vaccine co-administration derives from a rather old theme within vaccinology and immunology—ie, so-called vaccine interference. This term has been taken to mean slightly different things in different contexts. In its simplest form, it was a hypothetical case taken up by individuals sceptical of combined children's vaccines such as the diphtheria, tetanus, and pertussis vaccine or the measles, mumps, and rubella vaccine.[7] At the centre of the case was an assumption that the immune system might get overloaded by this simultaneous exposure, and this effect would cause a weakened response to heterologous infections. With time, increasing evidence against this idea has been reported.[8] The concept was always mystifying to basic immunologists, used to thinking of a person's immune repertoire as having the ability to generate several billion different B-cell receptor sequences (each of which triggers production of specific antibodies). These receptors must have the evolutionary wherewithal during natural exposure to recognise the thousands of microbial epitopes presented to them at a given time through an encounter with the large, complex proteomes of, say, the Epstein Barr virus or *Mycobacterium tuberculosis*, or indeed, several pathogens at one time. In this context, it is perhaps easy to grasp why immunologists were not taken by the suggestion that upscaling from one to two or two to three simultaneous vaccine components would somehow throw the whole immune system into disarray. However, a version of the immune interference argument still exists, which has stood the test of time, but is far less macroscopic in its scope: this notion argues that naturally occurring microbial variants—for example, a parasite or virus—can act as competitive antagonists (ie, altered peptide ligands), re-programming the protective immune response.[9,10]

In summary, the COVID-19 vaccine development programmes and successes have turbo-charged the whole of vaccinology, conferring the confidence to trial new protocols and protect against diverse pathogens—even if this means administering the different vaccines at the same time.

DMA and RJB report remuneration for consultancies with Oxford ImmunoTec.

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