New study highlights risks associated with the sequential infection of influenza followed by COVID-19

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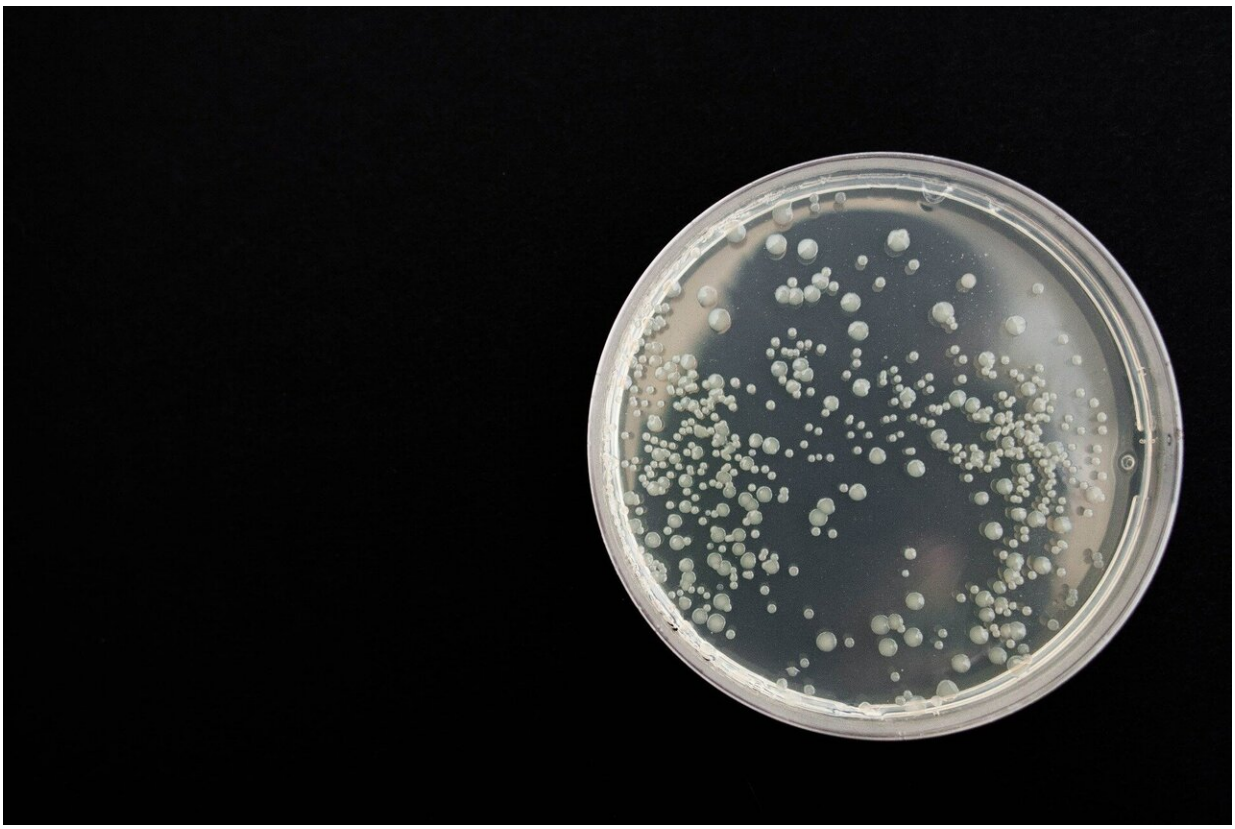

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A Liverpool-led study provides evidence that the 'twinfection' of influenza and COVID-19 may exacerbate the health risk associated with

COVID-19.

When multiple pathogens are in circulation at the same time this can lead to cooperative or competitive forms of pathogen-pathogen interactions. This concept of co-infection was evident during the outbreak of the Spanish flu in 1918 with secondary bacterial pneumonia co-infecting many patients suffering from the influenza A virus and causing a more severe outcome.

Recently there have been several case reports of coinfections with influenza and SARS-Cov-2 in humans with COVID-19. One study from the UK reported that patients with a coinfection exhibited up to six times higher risk of death.

To ascertain the health risks associated with the 'twinfection' researchers from the University of Liverpool, Liverpool School of Tropical Medicine and the University of Zurich sequentially co-infected mice with influenza and SARS-CoV-2. The work was led by Professor James Stewart and Professor Julian Hiscox from the University of Liverpool's Institute of Infection, Ecological and Veterinary Sciences.

Infected mice mirror many features of severe COVID-19 infection in humans and are a model used to develop understanding of lung disease and to test pharmacological interventions. Animal models of COVID-19 present critical tools to fill knowledge gaps for the disease in humans and for screening therapeutic or prophylactic interventions. While animal models can't predict with total accuracy the consequences of coinfection in humans, the data presented will have implications for development of successful pre-emptive interventions for SARS-CoV-2 and the clinical management of COVID-19.

The researchers found that the infection of mice with these viruses resulted in disease and then recovery. However, sequential infection with

influenza virus and then SARS-CoV-2 displayed overt clinical symptoms that were worse than the individual infections.

Interestingly in the sequentially infected mice, whilst the replication of SARS-CoV-2 was diminished compared to mice infected with this virus alone, there was an enhanced inflammatory response. This is a key driver for severe COVID-19 infection in humans and plays a significant role in mortality.

Reflecting this, sequentially infected mice exhibited significantly more rapid mortality compared with mice infected with either virus alone. These results suggest that infection with both viruses leads to an exacerbation of pathological processes.

This evidence highlights important implications for the ongoing pandemic. As countries across the globe come out of a period of lockdown, the rate of infection of SARS-CoV-2 is likely to increase and as many countries head toward flu season, attention should be focussed not only slowing the transmission of SARS-CoV-2 but also reducing influenza infections as part of a comprehensive public health response to mitigate the effects of co-infection.

Flu vaccinations

Professor Stewart said: "There is growing concern about the interactions between SARS-CoV-2 and other respiratory infections in the upcoming winter season. Our study highlights the urgent need to maintain flu vaccination and gives a way to be able to explore effective interventions'

Professor Hiscox added: "Seasonal influenza virus can overwhelm the NHS on normal years. Both SARS-CoV-2 and influenza are likely to co-circulate and present a risk. Our work shows how infection with both is dangerous and we can at least do something about mitigating the risk of

flu through vaccination."

Cross-species confirmation of in vivo observations is critical for robust interpretation of non-clinical research outcomes. Recent work by the global healthcare community has demonstrated the Syrian Golden Hamster' model as a powerful tool to investigate SARS-CoV-2 infection and the University of Liverpool has become the first UK institution to establish this model. Confirmatory work is now underway to understand COVID-19 virology and pathology.

In collaboration with Professor Andrew Owen and other members of the University's cross-faculty Centre of Excellence in Long acting Therapeutics (CELT), the team are also applying these state-of-the-art model systems to validate pharmacological interventions and develop new formulations to combat the pandemic.

More information: Jordan J. Clark et al. Sequential infection with influenza A virus followed by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) leads to more severe disease and encephalitis in a mouse model of COVID-19., (2020). DOI: 10.1101/2020.10.13.334532

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