# Extraordinary NERVTAG COVID-19 meeting on Human Challenge Studies: 09 July 2021

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| **Date & Location:** 11:00 – 13:00, 09 July 2021 - Via telecon only |
| **In attendance:**<br>Chair: Peter Horby (PH)<br><br>NERVTAG Members: Peter Openshaw (PO), Andrew Hayward (AH), Calum Semple (CSm), John Edmunds (JE), Neil Ferguson (NF), Muge Cevik (MCe), Wendy Barclay (WB), Jim McMenamin (JMM), Julian Hiscox (JHi), Ben Killingley (BK), James Rubin (JR), Ian Brown (IB), Cariad Evans (CE), Lisa Ritchie (LR)<br><br>NERVTAG Secretariat: Ruth Parry, Elaine Stanford, Stephen Barnard, Helena Bird<br><br>DHSC Observers: Sadia Dorsani (SD), Jonathan Van Tam (JVT)<br><br>Invited experts/ presenters: Prof Christopher Chiu (CC), Priya Mande (PM)<br><br>SPI-M: Petra Klepac (PK) |
| **Apologies:** Wei Shen Lim (WSL); Chloe Sellwood (CSe), Ravi Gupta (RG) |

Meeting note prepared by Chair.

Not endorsed by Committee Members

1. Initial data from the SARS-CoV-2 human infection challenge model were presented to NERVTAG.
2. The study inoculated healthy, seronegative young volunteers aged 18-30 years with a UK SARS-CoV-2 strain isolated in summer 2020 (B.1 with D614G).
3. Key findings were:
    a. A low challenge dose (10 $TCID_{50}$) was required to successfully initiate infection in 16/27 subjects.
    b. Rapid increase in viral replication (peaks in throat ≈3 days after inoculation).
    c. High-peaks in viral shedding ($10^8$-$10^9$ viral genome copies).
    d. Throat shedding is detectable before nose shedding.
    e. Nose shedding correlates better than throat shedding with detection of infectious virus in face masks, environment, and air.
    f. All subjects had only mild symptoms.
    g. Lateral flow assays (LFAs) correlated quite well with virus culture. Although there were four cases of -ve LFA and +ve culture from throat swab at day 2 post-

inoculation, other data from this challenge model suggest nasal positivity is more important for transmission than throat.

h. Infectious virus was cultured from masks worn by 7/12 volunteers.

4. Implications for use of LFAs. The data are supportive of the utility of LFAs in detecting infectious people. Since infectious virus can be detected early after inoculation (from around three days) even in people with very mild symptoms, the use of LFAs should be encouraged immediately upon recognition of even mild symptoms. One caveat is that the LFAs were undertaken by healthcare professionals, and LFA performance is lower when the test is self-administered.

5. Implications for self-isolation.

   a. The data show virus concentrations increase rapidly and to a high level soon after infection, even in subjects with only mild symptoms. Self-isolation and testing is need immediately upon recognition of even mild symptoms.

   b. The data do not change current understanding of the duration of infectiousness and, therefore, the duration of self-isolation. The data on LFAs do, however, provide support for the use of daily LFAs as a tool to identify and isolate infectious people.

6. Implications for how to wear face coverings. Face coverings must cover both the nose and mouth.

7. Implications for face coverings as source control. The data do not provide any direct evidence on the effectiveness of face masks in reducing onward transmission (source control). However, several findings and observations indicate that the routine use of face-coverings, especially in higher risk settings, may be a useful way of reducing community transmission when there are high levels of infection in the community:

   a. Virus concentrations increase rapidly and to a high level soon after infection.

   b. Virus is culturable from face masks, and virus detection in face masks correlates with the detection of culturable virus in nose and throat swabs and in the environment around the patient.

   c. Virus is culturable from face masks worn by very mildly unwell subjects

   d. In a highly vaccinated population, symptoms are likely to become a less sensitive marker of infectiousness.

   e. The committee recommend that DHSC (re-)consider the utility of mandatory use of face covering in settings where transmission risks are higher.

8. Implications for face coverings to prevent infection of the wearer: The data do not provide any evidence on the effectiveness of face masks in reducing the risk of the wearer acquiring infection. Although virus was detected by PCR in air samples taken at 1 metre from subjects, virus could not be cultured and there are no data on particle size or whether virus concentration approached a likely infectious dose. One member felt the data supported enhanced use of FFP3 ventilators in health care settings.

9. Implications for hand hygiene and surface cleaning advice. Virus could be detected and cultured from surfaces. This supports ongoing advice to wash hands and clean surfaces regularly.

10. Implications for ventilation advice. Although virus was detected by PCR in air samples taken at 1 metre from subjects, virus could not be cultured and there are no data on particle size or whether virus concentration approached a likely infectious dose. Therefore, it was not felt that data supported any changes to advice on ventilation.

11. Implications for 2-meter advice. There were no data to recommend any changes to 2-meter advice.

12. The Committee found the data to be extremely useful, although largely confirming prior beliefs about the infection dynamics of SARS-CoV-2.

13. The Committee recommends ongoing support for the human challenge work, particularly looking at infection dynamics in vaccinated individuals.