A SERENDIPITOUS GIFT

Introduction

For some time there has been a half-hearted discussion about whether Coronaviruses are replicated outside the respiratory tract, and how this might complicate disease management. Routine Covid-19 testing of the upper respiratory tract (URT) in the control of Covid-19 disease then becomes questionable, and may have led to the unnecessary self-isolation of people, and thereby depleted the numbers working in essential services. This has been critical in healthcare and in education.

The following case history demonstrates the existence of a non-respiratory tract incubation period, and how this might be responsible for the perpetuation of the disease.

Case history

Stable owners, Malcolm and Alicia, had both had two doses of Covid-19 vaccine prior to July 2021. They ran a livery business for show jumping horses in Hampshire and had booked a veterinary physiotherapist to treat four of their horses. They had had no close human contacts for over ten days before the therapist's visit.

DAY 0. The physiotherapist arrived in January 2022 and incidentally remarked that she had been infected with Covid-19 several weeks earlier. However a recent lateral flow test (LFT) had been negative. Each horse was treated in its own stable, with Malcolm controlling the animal's head. He did not wear a face mask for fear that it might spook the horse. Throughout the visit the therapist (who did not wear a mask) talked incessantly. The treatments were completed in about two hours, whereupon the therapist used the toilet facilities and departed. Alicia only had a passing meeting with the therapist, and her only other source of contact had been the toilet.

DAY 2. By the end of the day Malcolm was feeling a bit unwell

DAY 3. On the following morning he had a dry cough, felt a bit breathless, was sweaty and shivery, and had a fever (38.1^{o}C) with a pulse rate of 110 bpm. A Covid-19 LFT was negative, as was a test undertaken by Alicia. Malcolm took some Paracetamol and isolated himself in their spare bedroom.

DAY 5. Malcolm was feeling a bit better and was able to do some light physical tasks. However his LFT was now positive, as was Alicia's. Until this juncture both Malcolm and Alicia had negative LFTs.

Subsequent LFTs on Malcolm remained positive for seven more days, whereas Alicia's tests were only positive for five more days. Thereafter all tests were negative.

Several weeks after the event, the physiotherapist admitted that she had not been entirely truthful about her negative LFT. Her excuse was that, being self-employed, she needed to get back to earning her living!

Discussion

Malcolm's prolonged contact with the therapist was likely to have exposed him to a considerably higher viral load than that received by Alicia, and enough initially to overwhelm any residual immunity. Alicia remained asymptomatic throughout.

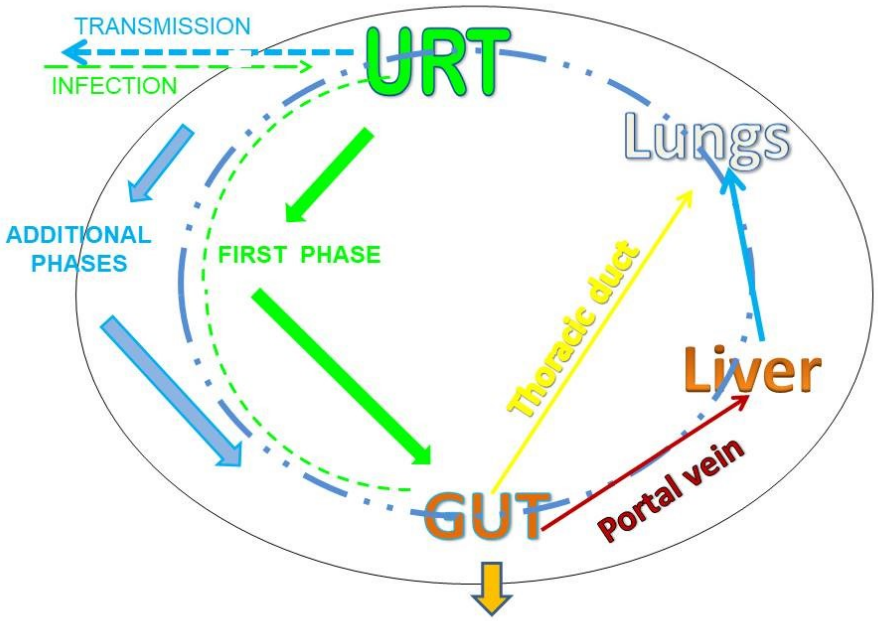
As their LFTs became positive at the same time it is likely that they were infected by the same source. The duration of positivity in Malcolm's case is probably a reflection of the higher initial viral load. In Malcolm's case the silent incubation period was three days, and five days before his URT began to replicate the virus.

The most likely explanation for these events is that the first cells replicating the virus were in the gut and not in the URT[1]. The release of the virus from its replication site on day 3 caused the systemic symptoms. It then took another two days for the URT to become the transmitter

of Covid-19. Cyclical re-infection may then proceed until the individual's immunity completely neutralises the virus during the blood-borne phase of this cycle.
Alicia's experience demonstrates how easy it is for a member of the public to become infected, and then unknowingly transmit the disease. It is this reservoir which will maintain the endemic status of the disease, and offer the opportunity for the virus to mutate to a more virulent pathogen. This also shows how repeated recycling of the virus in the same individual could lead to 'Long Covid'.

Comment.
Where would we be today without the reported observation that milkmaids - (who had suffered from cowpox) - appeared to be immune to smallpox? As doctors we occupy the privileged position of being able to observe and report clinical phenomena. This case study offers a serendipitous opportunity to advance our understanding of Covid-19 infectivity. Setting up the necessary clinical trial to confirm the gut's role in Covid-19 disease would be simple, but the rigmarole of obtaining a source of 'live' virus, finding volunteers and assessing risks, let alone getting ethical approval, might well be considered not worth the effort.
With regard to curtailing the spread of Covid-19, the wearing of face masks would appear to be the best safeguard. However more thought should be given to inhibiting the attachment of the virus to susceptible cells and the jejunal mucosa in particular. This would be potentially less harmful to the host than orally administered antiviral drugs, for example molnupiravir[2], which poison healthy cells as well as those infected with the virus.
Although vaccination lessens the severity of acquired Covid-19 disease, it does not stop the spread of the virus, and allows time for the virus to mutate into a more virulent variant.

References.
1. Aitken M. Covid-19 replication and pathogenesis – an alternative hypothesis. ACP News 2021; winter; 21.
2. Fischer WA et al. A phase 2a clinical trial of molnupiravir in patients with COVID-19 shows accelerated SARS-CoV-2 RNA clearance and elimination of infectious virus. 2022; Sci Transl Med. 19;14(628):eabl7430. doi: 10.1126/scitranslmed.abl7430.


TRANSMISSION
INFECTION
URT
Lungs
ADDITIONAL
PHASES
FIRST PHASE
Thoracic duct
Liver
GUT
Portal vein