

Are asymptomatic people with 2019nCoV infectious?

Virology Cell PHE

Aim

The aim of this report is to assess current evidence for asymptomatic transmission of 2019nCoV. To put this into context, we also report on what is known of viral excretion of SARS-CoV.

Virus shedding

In many viral illnesses, virus shedding is greatest during the early symptomatic phase of illness around the onset of symptoms. However, some respiratory viruses are known to shed and transmit in the incubation period (prior to the onset of clinical symptoms) including influenza and rhinovirus. The ability to control outbreaks/epidemics is related to the fraction of infections which occur whilst asymptomatic combined with the R_0 (Figure 1)

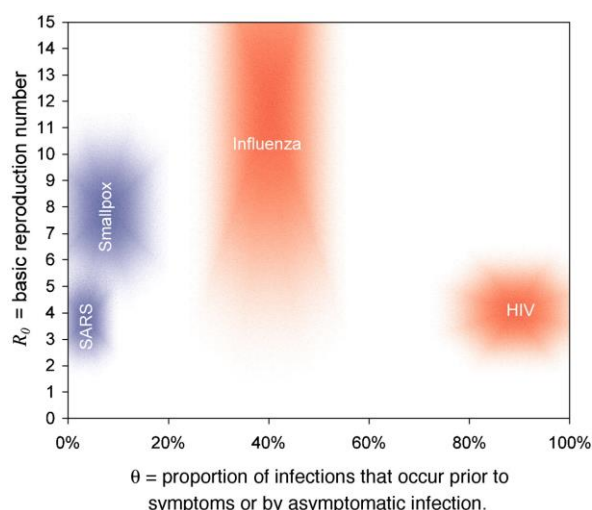


Figure 1. Plausible ranges for the key parameters R_0 and θ for four viral infections of public concern are shown as shaded regions. (Fraser et al PNAS 2004).

SARS-CoV: SARS-CoV excretion is relatively low during the initial phase of illness. The progression to disease severity in SARS is accompanied by increase in viral shedding in several body compartments. Viral load increases in respiratory samples in the second week of SARS illness (Peiris et al 2003). Viral load is greatest in samples taken from the lower respiratory tract, peaking at around day 10. SARS-CoV RNA was detected in only 32% of individuals in NP aspirates at initial presentation (mean 3.2 days after illness onset) but in 68% at day 14 and in over 90% of faecal samples collection in the 2nd week of illness, peaking around day 15-17 (Bermingham et al 2004).

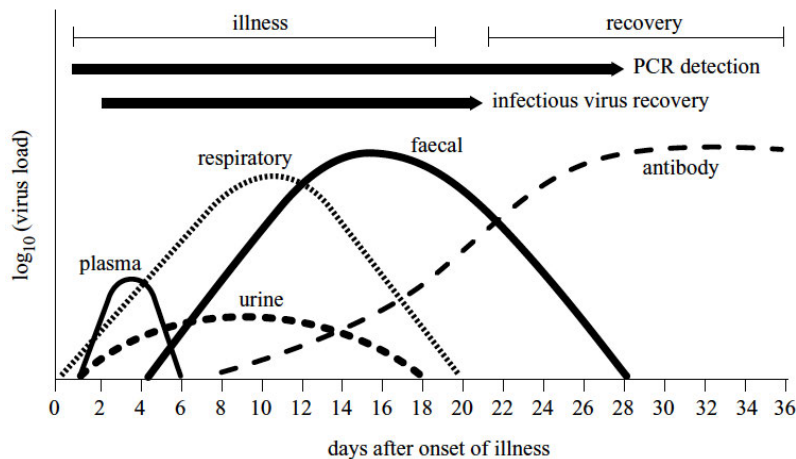


Figure 2. Schematic diagram of the course of virus shedding and detection in body fluids during SARS illness and recovery. Onset of illness is taken to be the onset of symptomatic fever. Taken from Bermingham et al. 2004 (HPA/PHE data).

2019nCoV: To date, there is no data on viral kinetics from 2019nCoV infected patients (e.g. sequential sampling or population level data). Available clinical data (from <50 patients in total) indicates an incubation period of 2-10 days (WHO sitrep 270120) with a mean of 5 days. Median time from symptom onset to hospital admission was 7 days (range 4-8) in the report from Huang *et al* and 6-10 days in the report from Woo *et al*.

Presenting features included fever, cough, myalgia, fatigue. Less common symptoms included sputum production, headache, haemoptysis, diarrhoea. Upper respiratory tract symptoms (rhinorrhoea, sneezing, sore throat) were uncommon. In the report by Huang *et al* of 41 2019nCoV cases, URT samples were not taken. Positive faecal samples have not been reported.

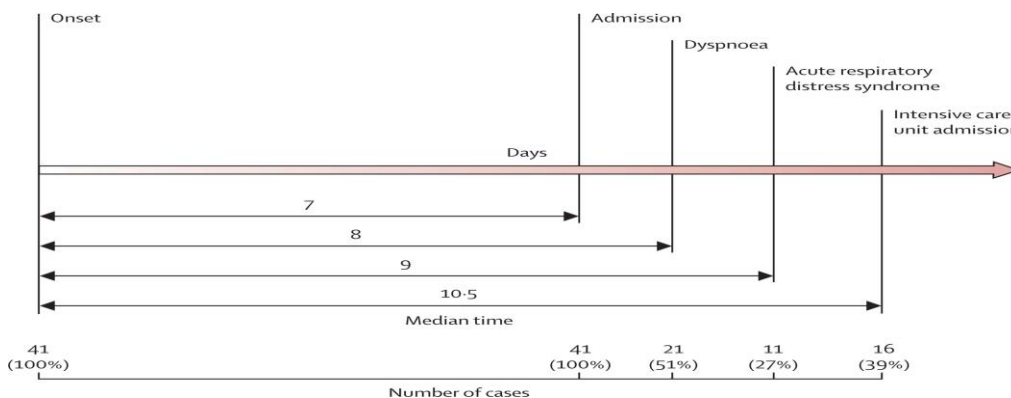


Figure 3. Timeline of 2019nCoV illness et al (Huang et al, Lancet 2020).

Viral receptor usage is a key determinant of pathogenesis. Given the genetic relatedness of the two viruses and the indication that 2019nCoV also uses the ACE 2 receptor (Zhou et al, 2020), there is a reasonable deduction that the two viruses will have a similar tissue tropism and pathway to disease progression, These data (Figure 2 & 3) indicate several strong similarities in the trajectory of the development of illness in 2019nCoV, compared to SARS, supporting a reasonable assumption

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that peak virus shedding will be later during the course of illness, and the early stages of illness may have lower viral load, similar to that observed in SARS

Evidence for asymptomatic transmission: SARS vs. 2019nCoV

1. SARS

The incubation period for SARS is typically 2-7 days (mean 4.6 days). 95% of patients developed symptoms within 12.5 days of infection (Leung et al 2004)

Infectiousness of SARS-CoV is generally believed to coincide with, but not precede, clinical symptoms. However, there have been reports of small numbers asymptomatic/pauci-symptomatic infections with SARS-CoV. The infectiousness of asymptomatic/pauci-symptomatic SARS-CoV cases has not been demonstrated.

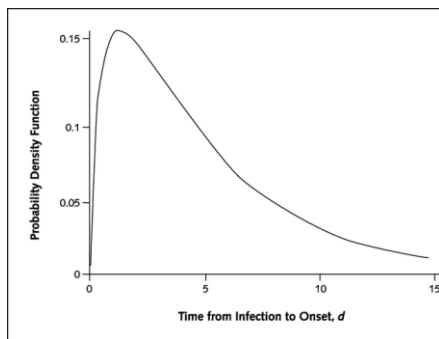


Figure 3. Estimate of time from infection to onset of illness, distribution in SARS-CoV (Leung et al. 2004)

2. 2019nCoV

Current estimates of the incubation period of 2019nCoV range from 2-10 days (WHO sitrep 260119), with a mean of 5 days

What is the evidence for asymptomatic transmission of 2019nCoV?

The evidence on this matter is derived from case reports and anecdotal records

(a) In the paper by Chan et al (Lancet 2020), a family cluster of 7 people is described. Of these, 5/7 were positive for 2019nCoV by RT-PCR of respiratory samples, including one case who had no history of travel to Wuhan but had been in contact with other infected family members. 1 of the 5 RT-PCR positive cases was a 10 year old child who was asymptomatic. 2019nCoV was detected on sputum and throat swabs but negative on NP swab. This asymptomatic child had ground glass opacities seen on CT chest but was afebrile with normal blood tests except an elevated ALP of 211. WCC was normal, no lymphopenia and CRP was normal. Oxygen saturations were not performed. In summary, this case **describes asymptomatic infection in a child but does not provide evidence for asymptomatic transmission of 2019nCoV.**

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(b)Recent media reports of asymptomatic transmission of 2019nCoV appear to have risen from an anecdotal report via Chinese media from “a doctor in Zheijing province (Dr Sheng Jifang)” – http://news.china.com.cn/2020-01/26/...t_75650029.htm

This purportedly describes a cluster of cases in Hangzhou linked to an individual who was asymptomatic. The available information states that – “a patient came to Hangzhou from Wuhan to attend a conference. On arrival in Hangzhou they had no symptoms. They infected several colleagues attending the conference and after returning to Wuhan at the end of the meeting did not get disease after another 2 days”. A formal report/publication on this cluster has not been issued and therefore timings of exposure and clinical details are not available.

(c) – Germany EWRS report on 28/01/2020 following notification of the first German case. The individual from China reported symptom beginning on 23 January 2020. This individual was most likely infected through contact with her (at that time) asymptomatic parents from Wuhan who visited her in Shanghai before she travelled to Germany. Both parents are reported to have tested positive for 2019-nCoV.

Conclusions

The currently available data is not adequate to provide evidence for major asymptomatic/subclinical transmission of 2019nCoV. Detailed epidemiological information from more cases and contacts is needed to determine whether transmission can occur from asymptomatic individuals or during the incubation period on a significant scale

References

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Peiris *et al.* Prospective study of the clinical progression and viral load of SARS associated coronavirus pneumonia in a community outbreak. Lancet 2003; 361; 1767-1772

WHO sitreps 260120 and 270120

Zhou et al, bioRxiv Jan 2020