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# SARS-CoV-2 viral load and shedding kinetics

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## Supplementary tables.

Abbreviations:

IV – infectious virus

VL – viral load

**Figure 2. Kinetics of RNA and infectious VLs for ancestral SARS-CoV-2**

Study	Parameter measured	How the study was conducted	Findings
Li et al., 2020 <sup>1</sup>	Onset of symptoms, incubation period	Information on demographic characteristics, exposure history, and illness timelines on first 425 laboratory-confirmed Covid-19 cases linked to the Huanan Seafood Wholesale Market was collected	Mean incubation period was 5.2 days (95% confidence interval [CI], 4.1 to 7.0)
Cheng et al., 2021 <sup>2</sup>	Onset of symptoms, incubation period	Authors included 53 studies published from December 1, 2019 to May 26, 2021 and used random-effect model to pool the mean incubation period	Mean incubation period was 6.0 days (95% confidence interval [CI] 5.6–6.5) globally, 6.5 days (95% CI 6.1–6.9) in the mainland of China, and 4.6 days (95% CI 4.1–5.1) outside the mainland of China
Elias et al., 2021 <sup>3</sup>	Onset of symptoms, incubation period	99 studies published from 1 January 2020 to 10 January 2021 reporting SARS-CoV-2 incubation period were systematically reviewed. The pooled estimate was generated using	Mean incubation period across the studies was 6.38 days, 95% CI (5.79; 6.97).

		individual mean and SD	
Alene et al., 2021 <sup>4</sup>	Onset of symptoms, incubation period	Data on 1, 453 COVID-19 patients from 14 different studies were used to estimate mean incubation period	Mean incubation period of was 6.5 (95%CI: 5.9–7.1) days
Xin et al., 2021 <sup>5</sup>		72 studies published between 11 January 2020 and 13 April 2020 were reviewed and analysed	Mean incubation period 6.3 days (range, 1.8-11.9 days), median incubation period 5.4 days (range, 2.0-17.9 days)
Néant et al., 2021 <sup>6</sup>	RNA VLs	RNA VLs were assessed as Ct values from nasopharyngeal swabs collected from 655 hospitalized patients and dynamics of viral loads were visualized using target cell-limited model	RNA VLs were detected for 13 dpos in younger patients and 16 dpos in older patients ( $\geq 65$ years old). Peak RNA VLs were predicted to coincide with symptom onset
Wölfel et al., 2020 <sup>7</sup>	Infectious VLs	Virological kinetics was analysed in specimens collected from 9 hospitalised patients	IV was isolated up to 9 dpos in URT specimens
Bullard et al., 2020 <sup>8</sup>	Kinetics of infectious and RNA VLs	Ct values for SARS-CoV-2 and IV isolation probability were determined from 90 patients at 0 up to 21 dpos.	No IV was recovered after 8 dpos. RNA VLs were detected for more than 10 dpos
Jefferson et al., 2020 <sup>9</sup>	Kinetics of infectious VLs	29 studies which attempted to culture IV from SARS-CoV-2 positive specimens were included	Despite the detection of RNA VLs for $> 14$ dpos, the possibility to isolate IV declined after 8 dpos
Cevik et al., 2021 <sup>10</sup>	Kinetics of RNA VLs	43 studies (including 3229 individuals) were included for systemic review and meta-analysis reported duration of	Mean duration of viral RNA detection was 17 days (95% CI 15.5–18.6); highest VLs were reported shortly

		shedding in the upper respiratory tract. 8 studies isolated IV from URT specimens	after or at the time of the symptom onset; no IV was isolated beyond 8 or 9 dpos
Brümmer et al., 2021 <sup>11</sup>	SARS-CoV-2 detection by Ag-RDT	214 clinical studies with 112,323 samples, which evaluated the accuracy of SARS-CoV-2 diagnostics by Ag-RDT and published before 30 April 2021 were included for meta-analysis	Substantially higher sensitivity at the first week post onset of symptoms compared to lower sensitivity when tested at the 2nd week post symptoms

**Figure 3. Infectious VLs and symptom onset in SARS-CoV-2 Delta and Omicron BA.1 variants of concern**

Parameters displayed for ancestral SARS-CoV-2 are described for the Figure 2.

<b>Study</b>	<b>Parameter measured</b>	<b>How the study was conducted</b>	<b>Findings</b>
Grant et al., 2022 <sup>12</sup>	Incubation period of Delta VOC	The nationwide case control study used SARS-CoV-2 infection diagnoses (8644 Delta and 3990 non-Delta), where the participants filled up the questionnaire about the SARS-CoV-2 exposure and testing information to determine incubation period	Mean incubation period was shorter in Delta-infected cases (4.3 days) in comparison to non-Delta infections (5.0 days)
Ogata et al., 2022 <sup>13</sup>	Incubation period of Delta VOC	214 patients (121 Delta and 103 non-Delta cases) with one specific date of exposure to SARS-CoV-2 were enrolled and the data on symptoms and history to define the time of exposure were collected by healthcare professionals	The mean incubation period was 3.7 days for Delta and 4.9 days for non-Delta cases

Backer et al., 2022 <sup>14</sup>	Incubation period of BA.1 VOC	258 Omicron (S gene target failure) cases and 255 non-Omicron cases with reported symptom onset date between 1 December 2021 and 2 January 2022 in the national surveillance database	mean incubation period is estimated to be 3.2 days (SD: 2.2 days) for Omicron cases and 4.4 days (SD: 2.5 days) for non-Omicron cases
Jansen et al., 2021 <sup>15</sup>	Incubation period of BA.1 VOC	A cluster of 18 patients infected with Omicron VOC was used for detailed epidemiological investigation	The median incubation period for Omicron was 3 days
Puhach et al., 2022 <sup>16</sup>	Peak infectious VLs of ancestral SARS-CoV-2, Delta and Omicron VOCs	Infectious VLs of collected at first 5 dpos from patients infected ancestral (n=118), Delta (n=293) Omicron BA.1 (n=154) were determined by focus-forming assay (FFA)	Higher infectious VLs in Delta-infected patients in comparison to ancestral SARS-CoV-2; lower VLs in Omicron-infected patients
Takahashi et al., 2022 <sup>17</sup>	Infectious VLs of Omicron VOC	IV was isolated from serially collected samples from 10 vaccinated patients infected with Omicron BA.1 VOC	IV was isolated up to 9 days post diagnosis, with highest probability of virus isolation in samples collected at 2-5 days after days post diagnosis and no IV was isolated 10 days post diagnosis
Siedner et al., 2022 <sup>18</sup>	Infectious VLs of Omicron BA.1 VOC	IV was isolated from serially collected samples from 10 vaccinated Delta-infected patients	In 9 of 10 (90%) individuals culturable virus was detected up to 10 dpos
Boucau et al., 2022 <sup>19</sup>	Infectious VLs of Omicron VOC	32 Delta- and 34 Omicron infected patients	Culturable virus was detected up to 10 days and up to 9 days since initial detection in Delta- and Omicron infected individuals respectively

**Figure 4. Influence of vaccination on VLs (Delta VOC used as an example)**

Study	Parameter measured	How the study was conducted	Findings
Singanayagam et al., 2021 <sup>20</sup>	Infectious and RNA VLs	VLs were compared between fully vaccinated individuals (n=29) and unvaccinated subjects (n=16) infected with Delta VOC. Most of the patients received either BNT162b2 mRNA vaccine or ChAdOx1 nCoV-19 adenovirus vector vaccine	Same peak RNA VLs in vaccinated and unvaccinated Delta-infected patients, but faster clearance of RNA VLs
Puhach et al., 2022 <sup>16</sup>	Infectious and RNA VLs	Infectious (measured by FFA) and RNA VLs were compared between fully vaccinated (n=104) and unvaccinated (n=127) patients infected with Delta VOC. Most of the vaccinated patients received mRNA vaccines (95.2 %).	Similar RNA VLs at 5 dpos, but higher infectious VLs in unvaccinated in comparison to unvaccinated individuals
Chia et al., 2021 <sup>21</sup>	RNA VLs	RNA VL kinetics was compared between vaccinated (n=88) and unvaccinated (n=130) patients. Most of the patients received 2 doses of mRNA vaccines (95.5 %).	RNA VLs were similar between vaccinated and unvaccinated patients at first 5 dpos, but VLs decreased faster in vaccinated patients

Peña-Hernández et al., 2022 <sup>22</sup>	Infectious VLs	IV presence was determined by isolation from samples collected from 72 vaccinated and 53 unvaccinated individuals infected in the time period in which Delta was the predominantly circulating VOC	The proportion of samples with culturable virus was lower in vaccinated in comparison to unvaccinated patients (21% vs. 40% respectively)
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## References

1. Li, Q., *et al.* Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* **382**, 1199-1207 (2020).
2. Cheng, C., *et al.* The incubation period of COVID-19: a global meta-analysis of 53 studies and a Chinese observation study of 11 545 patients. *Infect Dis Poverty* **10**, 119 (2021).
3. Elias, C., Sekri, A., Leblanc, P., Cucherat, M. & Vanhems, P. The incubation period of COVID-19: A meta-analysis. *Int J Infect Dis* **104**, 708-710 (2021).
4. Alene, M., *et al.* Serial interval and incubation period of COVID-19: a systematic review and meta-analysis. *BMC Infect Dis* **21**, 257 (2021).
5. Xin, H., *et al.* The Incubation Period Distribution of Coronavirus Disease 2019: A Systematic Review and Meta-analysis. *Clin Infect Dis* **73**, 2344-2352 (2021).
6. Néant, N., *et al.* Modeling SARS-CoV-2 viral kinetics and association with mortality in hospitalized patients from the French COVID cohort. *Proceedings of the National Academy of Sciences* **118**, e2017962118 (2021).
7. Wölfel, R., *et al.* Virological assessment of hospitalized patients with COVID-2019. *Nature* **581**, 465-469 (2020).
8. Bullard, J., *et al.* Predicting Infectious Severe Acute Respiratory Syndrome Coronavirus 2 From Diagnostic Samples. *Clin Infect Dis* **71**, 2663-2666 (2020).
9. Jefferson, T., Spencer, E.A., Brassey, J. & Heneghan, C. Viral Cultures for Coronavirus Disease 2019 Infectivity Assessment: A Systematic Review. *Clin Infect Dis* **73**, e3884-e3899 (2021).
10. Cevik, M., *et al.* SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. *Lancet Microbe* **2**, e13-e22 (2021).
11. Brümmer, L.E., *et al.* Accuracy of novel antigen rapid diagnostics for SARS-CoV-2: A living systematic review and meta-analysis. *PLoS Med* **18**, e1003735 (2021).
12. Grant, R., *et al.* Impact of SARS-CoV-2 Delta variant on incubation, transmission settings and vaccine effectiveness: Results from a nationwide case-control study in France. *Lancet Reg Health Eur* **13**, 100278 (2022).
13. Ogata, T., Tanaka, H., Irie, F., Hirayama, A. & Takahashi, Y. Shorter Incubation Period among Unvaccinated Delta Variant Coronavirus Disease 2019 Patients in Japan. *Int J Environ Res Public Health* **19**(2022).
14. Backer, J.A., *et al.* Shorter serial intervals in SARS-CoV-2 cases with Omicron BA.1 variant compared with Delta variant, the Netherlands, 13 to 26 December 2021. *Euro Surveill* **27**(2022).
15. Jansen, L., *et al.* Investigation of a SARS-CoV-2 B.1.1.529 (Omicron) Variant Cluster - Nebraska, November-December 2021. *MMWR Morb Mortal Wkly Rep* **70**, 1782-1784 (2021).
16. Puhach, O., *et al.* Infectious viral load in unvaccinated and vaccinated individuals infected with ancestral, Delta or Omicron SARS-CoV-2. *Nat Med* (2022).
17. Takahashi, K., *et al.* Duration of Infectious Virus Shedding by SARS-CoV-2 Omicron Variant-Infected Vaccinees. *Emerg Infect Dis* **28**, 998-1001 (2022).
18. Siedner, M.J., *et al.* Duration of viral shedding and culture positivity with postvaccination SARS-CoV-2 delta variant infections. *JCI Insight* **7**(2022).
19. Boucau, J., *et al.* Duration of Shedding of Culturable Virus in SARS-CoV-2 Omicron (BA.1) Infection. *N Engl J Med* **387**, 275-277 (2022).
20. Singanayagam, A., *et al.* Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. *Lancet Infect Dis* (2021).
21. Chia, P.Y., *et al.* Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine breakthrough infections: a multicentre cohort study. *Clin Microbiol Infect* (2021).
22. Peña-Hernández, M.A., *et al.* Comparison of infectious SARS-CoV-2 from the nasopharynx of vaccinated and unvaccinated individuals. *medRxiv*, 2021.2012.2028.21268460 (2022).