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MAJOR ARTICLE

Mechanically Ventilated Patients Shed High-Titer Live Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) for Extended Periods From Both the Upper and Lower Respiratory Tract

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Background. SARS-CoV-2 infection can lead to severe acute respiratory distress syndrome needing intensive care admission and may lead to death. As a virus that transmits by respiratory droplets and aerosols, determining the duration of viable virus shedding from the respiratory tract is critical for patient prognosis, and informs infection-control measures both within healthcare settings and the public domain.

Methods. We prospectively examined upper and lower airway respiratory secretions for both viral RNA and infectious virions in mechanically ventilated patients admitted to the intensive care unit (ICU) of the University Hospital of Wales. Samples were taken from the oral cavity (saliva), oropharynx (subglottic aspirate), or lower respiratory tract (nondirected bronchoalveolar lavage [NBAL] or bronchoalveolar lavage [BAL]) and analyzed by both quantitative PCR (qPCR) and plaque assay.

Results. 117 samples were obtained from 25 patients. qPCR showed extremely high rates of positivity across all sample types; however, live virus was far more common in saliva (68%) than in BAL/NBAL (32%). Average titers of live virus were higher in subglottic aspirates (4.5×10^7) than in saliva (2.2×10^6) or BAL/NBAL (8.5×10^6) and reached $>10^8$ PFU/mL in some samples. The longest duration of shedding was 98 days, while most patients (14/25) shed live virus for ≥20 days.

Conclusions. ICU patients infected with SARS-CoV-2 can shed high titers of virus both in the upper and lower respiratory tract and tend to be prolonged shedders. This information is important for decision making around cohorting patients, de-escalation of personal protective equipment, and undertaking potential aerosol-generating procedures.

Keywords. SARS-CoV-2; plaque assay; qPCR; intensive care unit; viral load.

The coronavirus disease 2019 (COVID-19) pandemic has resulted in a global human death toll of 5.36 million (as of 21 December 2021) [1]. Early symptoms include a dry cough, exertional shortness of breath, fatigue, lethargy, diarrhea, and high-grade fever [2]; and in 10–15% of cases, this can progress to severe pneumonia needing hospitalization. In 1–2% of cases the disease can lead to severe acute respiratory distress syndrome (ARDS) needing intensive care unit (ICU) admission and may lead to death [3]. As a virus that transmits by respiratory droplets and aerosols, determining the duration of viable virus shedding from the respiratory tract is critical for patient prognosis, and informs infection-control measures both within healthcare settings and the public domain [4]. Although symptoms may persist for weeks or even months post-infection, shedding of infectious viral particles almost never occurs beyond 10 days of symptom onset, even in hospitalized patients [5]. In a meta-analysis including more than 5000 SARS-CoV-2–infected individuals, viral RNA was detectable up to 83 days in the upper respiratory tract, but no study detected live virus beyond day 9 of illness [5]. However, this analysis was performed prior to the introduction of immunosuppressive agents as standard of care for individuals hospitalized with severe respiratory complications of COVID-19 [6]. Given emerging evidence that infectious virions can be recovered from individuals with acquired and inherited forms of immunodeficiency months after symptom onset [7–10], we investigated whether adults requiring admission to the ICU who are subject to both infection-mediated immune dysregulation [11] and iatrogenic immunosuppression [6] exhibited prolonged viral shedding. Furthermore, no study has investigated whether the 9-day

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