39 | SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUSES (SARS AND SARS-CoV-2)

39.1 | Disease agents

- Severe Acute Respiratory Syndrome (SARS) coronavirus (SARS-CoV)
- SARS coronavirus-2 (SARS-CoV-2)

39.2 | Disease agent characteristics

- Family: *Coronaviridae*; Subfamily: *Orthocoronavirinae*; Genus: *Betacoronavirus*.
- Virion morphology and size: enveloped with club-shaped spikes, 100–130 nm in diameter, giving the virus the appearance of a solar corona, and a helical nucleocapsid.
- Nucleic acid: large linear, positive-sense, single-stranded RNA, ~29.8 kb in length.
- Physicochemical properties: Virions sensitive to treatment with lipid solvents, nonionic detergents, formaldehyde, and oxidizing agents; stable in feces and urine at room temperature for at least 1–2 days, especially if diarrhea is present (high pH); only minimal reduction in infectivity after 21 days at 4°C and reduced by one log only after 48 h at room temperature; heating to 56°C inactivates these agents quickly.

39.3 | Disease name

- Severe acute respiratory syndrome (SARS) is the disease name (SARS-CoV is the agent).
- Coronavirus Disease of 2019 (COVID-19) is the disease name (SARS-CoV-2 is the agent).
- The Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) is covered in a separate fact sheet.

39.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical.
- Public concern regarding blood safety: Low; there is no current evidence of transfusion transmission of any SARS coronaviruses (or any respiratory agent) despite intensive study.
- Public concern regarding disease agent: High for SARS-CoV-2; it is likely that reemergence of a more pathogenetic coronavirus variant would alter public perception.

39.5 | Background

- There are now seven human coronaviruses, three of which can cause severe disease (SARS-CoV, MERS-CoV and SARS-CoV-2). The others are associated with "common cold" illnesses.
- First cases of SARS-CoV occurred in Guangdong province in 2002 with major outbreaks in Southeast Asia and a North American outbreak in Toronto between 2002 and 2003.
- The SARS CoV-2 (COVID-19) pandemic emerged in Wuhan province in late 2019 being closely related to two bat-derived CoV-like coronaviruses as intermediate hosts facilitating the emergence into humans, similar to what was seen for SARS-CoV from civet cats and MERS-CoV from dromedary camels.
  - The source of the COVID-19 pandemic is not clear.
  - The two most prominent competing hypotheses are zoonotic spillover and lab release. The former may be more probable, but the latter has not been excluded.

39.6 | Common human exposure routes

- SARS-CoV is spread through close contact with respiratory droplets and aerosols.
- SARS-CoV-2 is spread by contact with infected persons, and the role of aerosol, in contrast to large droplet, transmission appears more important than for SARS-CoV.
- Although infectious coronaviruses can be isolated from feces, evidence for fecal-oral transmission is minimal.
- Contaminated inanimate environmental surfaces do not appear to be a major route of transmission for SARS-CoV-2.

39.7 | Likelihood of secondary transmission

- Significant by contact with symptomatic cases for SARS-CoV.
- The importance of aerosol transmission from asymptomatic infected persons with SARS-CoV-2 was not appreciated early in the pandemic and was responsible for significant secondary spread.

15372995, 2024, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/trf.17630, Wiley Online Library on [26/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

39.8 | At-risk populations

- Family members in close contact with cases.
- Individuals with a number of chronic conditions, including obesity, diabetes, cardiac and lung diseases are at increased risk for adverse outcomes.
- Healthcare workers in close contact with cases.
- Elderly and immune-compromised individuals are at increased risk for serious outcomes.

39.9 | Vector and reservoir involved

- The civet cat (palm civet) in Southeast Asia was the likely source of introduction of the SARS-CoV agent into humans.
- SARS CoV-2 RNA sequences found in the Wuhan outbreak had similarities to that found in bats and other animal hosts. Its ultimate origin remains under investigation.

39.10 | Blood phase

- Low levels of virus-specific RNA in blood occur with SARS-CoV, but the presence and frequency of infectious viremia is not well documented.
- SARS CoV-2 RNA is detectable in plasma in about 0.1%–2% of hospitalized ICU COVID-19 patients from 2 to 16 days after onset of acute illness, with one study reporting peak levels at days 5–7 of illness. Disappearance by day 10 is expected in the absence of severe immunosuppression.
- RNA was detected in the plasma of up to 15% of blood donors during their pre-symptomatic phase of infection before implementation of widespread vaccination in the population, and in 10.2% and 12.9% of pre-symptomatic donors during the Delta and Omicron variant–predominant months, respectively.
- Viral particles can be seen by multiple imaging methods in plasma samples containing SARS-CoV-2 RNA. Their infectivity is not well characterized, and efforts to isolate the virus from the blood of infected patients have been unsuccessful.
- There have been no documented or confirmed cases of transfusion transmission of either SARS or SARS-CoV-2.

39.11 | Survival/persistence in blood products

- Unknown

39.12 | Transmission by blood transfusion

- No cases with either virus have been documented despite appropriate lookback studies involving detection of RNA or infectious virus.
- A single possible case of transmission by a hematopoietic stem cell transplant has been reported.

39.13 | Cases/frequency in population

- Over 8000 cases and 900 deaths from SARS-CoV were reported to the WHO, as of August 2003. No cases have been recognized since subsidence of the original epidemic.
- Approximately 770 million cases and 7 million deaths from COVID-19 caused by SARS-CoV-2 as of June 23, 2023, have been reported by WHO, with 13.5 billion vaccine doses administered worldwide.

39.14 | Incubation period

- 2–10 days, averaging 5–7 days

39.15 | Likelihood of clinical disease

- SARS CoV had high clinical penetrance.
- Up to 50% of SARS-CoV-2 cases are asymptomatic.
  - Manifestations are shorter and milder in children, with the exception of rare autoinflammatory sequelae that can be fatal (multisystem inflammatory syndrome in children; MIS-C).
  - 20%–30% are associated with post-acute syndromes, so-called "long Covid."

39.16 | Primary disease symptoms

- Symptoms and signs include fever, respiratory complaints, hypoxemia, imaging evidence of pneumonia and a variety of GI and non-specific extrapulmonary manifestations.
- Respiratory failure requiring assisted ventilation or ECMO occurs with MERS>SARS>SARS-CoV-2 infection. Note: MERS (Middle Eastern respiratory syndrome) is covered in another fact sheet.

39.17 | Severity of clinical disease

- Asymptomatic to severe/fatal.

15372995, 2024, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/trf.17630, Wiley Online Library on [26/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

39.18 | Mortality

- Case fatality rates are age and co-morbidity dependent. Infection fatality rates are <10% for SARS and 0.5%–1% for SARS-CoV-2 infections.

39.19 | Chronic carriage

- No

39.20 | Treatment available/efficacious

- Supportive care is a mainstay for all coronaviruses.
- Specific antiviral therapies were not widely available for treatment of SARS-CoV.
- For COVID-19 antivirals, corticosteroids, monoclonal antibodies, COVID-19 convalescent plasma (CCP) and biological response modifiers have been evaluated in high-quality clinical trials.
- The effects of antivirals (e.g., nirmatrelvir/ritonavir, remdesivir and molnupiravir) have shown variable utility for prevention of progression to severe infection when administered early in the course of infection to high-risk individuals. Nirmatrelvir co-packaged with ritonavir (Paxlovid) was the first oral antiviral FDA-approved (May 25, 2023) for the treatment of COVID-19 in adults.
- Passive immunotherapy (monoclonals and CCP, the latter in high titers) appears most effective when used for prevention (monoclonals) or early in the course of illness to prevent progression. Monoclonal antibodies have had limited efficacy due to evolution of SARS-CoV-2 variants. CCP may be a useful adjunct later for treatment of immunocompromised patients who fail to mount an effective immune response.
- Glucocorticoids are the standard of care for severe infections (i.e., in the face of hypoxia) and biological response modifiers (e.g., tocilizumab and baracitinib) have some utility in the inflammatory stage of disease.

39.21 | Agent-specific screening question(s)

- The FDA recommended a series of donor questions in the spring of 2003 when the SARS epidemic occurred. Their use was rescinded after the SARS epidemic waned.
- During the SARS-CoV-2 pandemic no formal questioning was required in the United States, due to the apparent low risk for transfusion transmission. All donors are required to be healthy and well on the day of donation and reminded to call the blood center back if symptoms develop post-donation.
- Many collection establishments requested that exposed or recently infected potential donors self-defer from some period of time.
- Donors of CCP manufactured under the FDA's emergency use authorization were required to be well at ≥14 days beyond their illness, in addition to having minimum titers of antibodies; the US FDA modified these requirements over time.

39.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test has been approved in the absence of evidence of transfusion transmission, although research tests for donation screening have been evaluated.
- Diagnostic assays have included antigen testing, virus culture, NAT, and virus detection by immunofluorescence in tissue samples and serological assays (both spike protein and nucleocapsid antigen) for current/past infection and immunization.
- During the COVID-19 pandemic, several hundred nucleic acid, antigen and antibody assays were authorized for emergency diagnostic use by the US FDA.
- Blood donors have been a useful resource to estimate seroincidence and seroprevalence.

39.23 | Currently recommended donor deferral period

- Donors identified during the donor interview were deferred for 28 days for infection and 14 days for exposure to SARS-CoV-2.
- Donors previously infected with SARS-CoV-2 had to be well on the day of donation and pass all other screening requirements. Potential CCP donors had to be well and 14 or more days from recovery.

39.24 | Impact on blood availability

- Minimal in the United States for SARS.
- A dramatic impact on the blood supply was seen with SARS-CoV-2 due to the restrictions on blood drives at schools, places of worship, and employment attendant on social distancing restrictions.

15372995, 2024, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/trf.17630, Wiley Online Library on [26/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

- Temporary decreases in usage due to postponement of elective admissions and surgical procedures originally offset decreased supply. Asynchrony between hospital "reopening" and blood collections resulted in marginal blood supplies persisting in many areas during the pandemic and recovery phases.

39.25 | Impact on blood safety

- No known transfusion transmission.
- Laboratory test(s) available: Not applicable.
- Pathogen reduction processes available for labile blood components appear to inactivate these pathogens.

39.26 | Leukoreduction efficacy

- Unknown

39.27 | Pathogen reduction efficacy for plasma derivatives

- Both riboflavin/UV light and amotosalen/UVA treatment have demonstrated activity/inactivation to undetectable levels (respectively) against MERS-CoV in plasma products. Inactivation of SARS-CoV-2 in all blood components to the limit of detection (3-4 logs) has been documented by amotosalen/UVA and amustaline/glutathione.
- Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in removal of enveloped viruses.

39.28 | Other prevention measures

- Developmental pathogen reduction methods (psoralens, riboflavin) have been shown to be effective.

SUGGESTED READING

1. Azhar EI, Hindawi SI, El-Kafrawy SA, Hassan AM, Tolah AM, Alandijany TA, et al. Amotosalen and ultraviolet A light treatment efficiently inactivates severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in human plasma. Vox Sang. 2021;116(6):673–81.
2. Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. JAMA. 2003;289:2801–9.
3. Busca A, Gabrielli G, Sidoti F, Costa C, Giaccone L, Dogliotti I, et al. SARS-CoV-2 infection in a stem cell transplant recipient grafted from a SARS-CoV-2-positive donor. Bone Marrow Transplant. 2022;57(10):1604–6.
4. Cappy P, Candotti D, Sauvage V, Lucas Q, Boizeau L, Gomez J, et al. No evidence of SARS-CoV-2 transfusion transmission despite RNA detection in blood donors showing symptoms after donation. Blood. 2020;136(16):1888–91.
5. Chaves DG, da Silva Malta MCF, de Souza Madeira Ferreira Boy L, Miranda Barbosa A, Fonseca CN, Ellen de Lima Torres D, et al. Analysis of current SARS-CoV-2 infection in a large population of blood donors evidenced that RNAemia is rare in plasma. Transfusion. 2021;61(7):2137–45.
6. Dodd RY, Leiby DA. Emerging infectious threats to the blood supply. Annu Rev Med. 2004;55:191–207.
7. Gostin LO, Gronvall GK. The origins of Covid-19—why it matters (and why it doesn't). N Engl J Med. 2023;388:2305–8.
8. Haynes JM, Dodd RY, Crowder LA, Notari EP, Stramer SL. Trajectory and demographic correlates of antibodies to SARS-CoV-2 nucleocapsid in recently infected blood donors, United States. Emerg Infect Dis. 2023;29:1323–9.
9. Jacobs JL, Bain W, Naqvi A, Staines B, Castanha PMS, Yang H, et al. Severe Acute Respiratory Syndrome Coronavirus 2 viremia is associated with coronavirus disease 2019 severity and predicts clinical outcomes. Clin Infect Dis. 2022;74(9):1525–33.
10. Jones JM, Manrique IM, Stone MS, Grebe E, Saa P, Germanio CD, et al. Estimates of SARS-CoV-2 Seroprevalence and incidence of primary SARS-CoV-2 infections among blood donors, by COVID-19 vaccination status—United States, April 2021–September 2022. MMWR. 2023;72:601–5.
11. Katz LM. (A little) clarity on convalescent plasma for Covid-19. New Engl J Med. 2021;384:666–8.
12. Katz LM. Is SARS-CoV-2 transfusion transmitted? Editorial. Transfusion. 2020;60:1111–4.
13. Kracalik I, Mowla S, Katz L, Cumming M, Sapiano MRP, Basavaraju SV. Impact of the early coronavirus disease 2019 pandemic on blood utilization in the United States: A time-series analysis of data reported to the National Healthcare Safety Network Hemovigilance Module. Transfusion. 2021;61-(Suppl 2):S36–43. https://doi.org/10.1111/trf.16451
14. Keil SD, Ragan I, Yonemura S, Hartson L, Dart NK, Bowen R. Inactivation of severe acute respiratory syndrome coronavirus 2 in plasma and platelet products using a riboflavin and ultraviolet light-based photochemical treatment. Vox Sang. 2020 Aug;115(6):495–501.
15. Lu W, Yazer M, Li N, Ziman A, Wendel S, Tang H, et al. Biomedical Excellence for Safer Transfusions Collaborative. Hospital red blood cell and platelet supply and utilization from March to December of the first year of the COVID-19 pandemic: the BEST collaborative study. Transfusion. 2022;62(8):1559–70.
16. Luzzi JR, Navarro R, Dinardo CL. COVID-19: further evidence of no transfusion transmission. Transfus Apher Sci. 2021;60(1):102961.
17. Ng SC, Chu AWH, Chan WM, Yip CCY, Leung KH, So CK, et al. Re-examine the transfusion transmitted risk of SARS-CoV-2 virus during a major COVID-19 outbreak in 2022. Transfus Med. 2023. https://doi.org/10.1111/tme.12981 Epub ahead of print.

15372995, 2024, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/trf.17630, Wiley Online Library on [26/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

18. Saá P, Fink RV, Bakkour S, Jin J, Simmons G, Muench MO, et al. NHLBI Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric (REDS-IV-P). Frequent detection but lack of infectivity of SARS-CoV-2 RNA in presymptomatic, infected blood donor plasma. J Clin Invest. 2022;132(17):e159876. https://doi.org/10.1172/JCI159876
19. Santa-Maria F et al. Pathogens. 2022;11(5):521. https://doi.org/10.3390/pathogens11050521
20. Stanworth SJ, New HV, Apelseth TO, Brunskill S, Cardigan R, Doree C, et al. Effects of the COVID-19 pandemic on supply and use of blood for transfusion. Lancet Haematol. 2020;7(10):e756–64.
21. Wang WK, Fang CT, Chen HL, Yang CF, Chen YC, Chen ML, et al. Members of the SARS Research Group of National Taiwan University College of Medicine-National Taiwan University Hospital. Detection of severe acute respiratory syndrome coronavirus RNA in plasma during the course of infection. J Clin Microbiol. 2005;43:962–5.
22. Wilder-Smith A, Teleman MD, Heng BH, Earnest A, Ling AE, Leo YS. Asymptomatic SARS coronavirus infection among healthcare workers, Singapore. Emerg Infect Dis. 2005;11:1142–5.
23. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020 May;581(7809):465–9.

15372995, 2024, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/trf.17630, Wiley Online Library on [26/02/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License