

COVID-19 Frequently Asked Questions for Pediatric Immunocompromised Host Clinicians

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This resource is intended for clinicians at UCSF Benioff Children's Hospitals caring for immunocompromised pediatric patients. It is primarily intended for a clinical audience but portions may be helpful to excerpt when counseling patients and families. This FAQ will be updated as a living document as new information and guidelines become available.

Acronyms:

SOT: solid organ transplant/transplantation

HSCT: hematopoietic stem cell transplant/transplantation

PUI: person under investigation, someone undergoing evaluation for COVID-19

COVID-19: the infectious syndrome caused by the novel coronavirus SARS-CoV-2

What do we know about the risk for severe or critical COVID-19 in immunocompromised patients? What do we know specifically about pediatric immunocompromised patients?

As with everything related to COVID-19 right now, there are still many unknowns and new information and guidelines are emerging from day to day.

Here's what we know so far about COVID-19 in children:

As we have seen in the news the vast majority of the case burden and mortality so far has been in adults. The majority of reported cases of COVID-19 in children overall have been either asymptomatic, mild, or moderate, nonetheless it is possible for children to present with "severe" disease (hypoxemia with SpO₂ < 92%) and "critical" disease (including acute respiratory distress syndrome, shock, encephalopathy, myocardial injury, coagulation dysfunction, acute kidney injury). A case series reporting 2143 children (<18 years old) with COVID-19 from China is the largest pediatric report thus far (Dong Y, et al.). The series does not provide breakdown of patients by underlying condition. There was a single death reported in a 14-year old child. Approximately 5% of patients had severe disease and 0.6% had critical disease. These percentages are lower than in adults (15% severe, 5% critical). Among pediatric patients, the proportion of patients with severe or critical disease was highest in infants < 1 years old (~ 9% severe, ~ 2% critical).

Additionally, there have been no pediatric deaths reported from COVID-19 reported in Italy as of March 17, 2020 (<https://jamanetwork.com/journals/jama/fullarticle/2763401>).

Here's what we know so far about COVID-19 in adult immunocompromised patients:

An early case series included 18 patients with cancer in China, representing 1% of overall cases at that time (Liang W, et al.) All were adults with predominantly solid tumor malignancies in different stages of treatment. There was a higher risk for "severe events" including ICU admission, invasive ventilation, or death in these patients than in those without cancer. It is difficult to draw strong conclusions from this series because of the small numbers, and the patients also had many additional risk factors for severe/critical COVID-19 (older age, smoking).

Few case reports of COVID-19 in immunocompromised patients have been published:

Of note, some reviewers have noted similar patients reported in multiple case series from China CDC, it is possible that some of the patients are represented in multiple reports.

- Chen Z, et al. report in the Chinese Journal of Hematology an 8 year old child with T-ALL approximately 1 year into therapy who presented with fever and cough and developed pulmonary infiltrates with ground glass opacities and small pleural effusions. Testing for SARS-CoV-2 was positive. The patient had a slowly progressive course with development of respiratory failure over 22 days. The ultimate outcome is not reported (case report suggests that child still hospitalized at the time of publication). Of note the patient had a markedly elevated ferritin (> 15,000 ng/mL) early in the illness, suggesting the possibility of this infection triggering HLH.
- There is another case report by Chen Z, et al. in the Chinese Medical Journal published online (PMID: 32149486) titled “COVID-19 with post-chemotherapy agranulocytosis in childhood acute leukemia: a case report.” We are working on accessing and translating this article.
- A pediatric case series published by Lu, X, et al. in NEJM mentions one child with ALL in maintenance who required ICU-level care. No further detail is provided specific to that patient.
- Zhu L, et al. report in American Journal of Transplantation a 52 year old man who was 12 years s/p kidney transplantation on triple immunosuppression with Tac/MMF/Pred at the time of COVID-19 diagnosis. He presented on day 6 of illness with fever, cough, headache and dyspnea (similar symptoms to other adults with COVID-19). Laboratory and radiographic findings were comparable to other adults with COVID-19 (lymphopenia, elevated CRP, patchy ground glass opacity in both lungs). Maintenance immunosuppression was discontinued but during this time he was receiving corticosteroids (initially used during the Wuhan outbreak but controversial). He was treated with multiple therapies (none of which are currently emerging with strong evidence base in larger COVID-19 therapy reports). The patient began showing clinical improvement on day 12 of illness, though radiographic findings were progressed on follow-up imaging. At that point Tac was resumed at 50% the prior dose. He tested negative for COVID-19 by respiratory swab on day 16 of illness and was discharged from the hospital on day 21 of illness. Overall features consistent with a severe but not “critical” course per the current working definitions, and clinical presentation similar to other adult patients. Authors note that Wuhan is one of the cities with the largest kidney transplant volumes in China.
- Li F, et al. reported in The Journal of Heart and Lung Transplantation on two cases of COVID-19 in heart transplant recipients in China. The first case was a 51 year old man 16 years s/p transplant on immunosuppression with Tac/MMF who presented on day 1 of illness with fever, fatigue, and diarrhea, initially treated with levofloxacin and ribavirin. He was admitted on day 4 of illness for persistent fever and started on moxifloxacin and ganciclovir and subsequently IVIG and methylprednisolone for worsening oxygen saturations. His immunosuppression was held from day 7 to day 14. He was discharged after 1 month in the hospital with resolution of lung lesions and symptoms. The second case was a 43 y.o male who presented to the outpatient clinic with 2 days of fever and found to be positive for COVID-19 both by RT-PCR and CT. He was initially quarantined at home then admitted to the hospital from day 15 to day 20. Overall, the two presentations were consistent with reports from non-transplant recipients. The authors also reported on the 200 other heart transplant recipients they follow and found a third case in another hospital, status unknown.
- Aslam and Mehra report in the JHLT that per their review of the literature, consistent with our own, the presentations of COVID-19 appear to be similar to those in non-transplant recipients

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either in presentation or clinical course. The overarching treatment for transplant recipients with severe disease involved withholding baseline immunosuppression and treating with high dose corticosteroids (which remain controversial) and pooled immunoglobulin infusions. The patient with more severe disease was able to be discharged with intact graft function. They postulate that the anti-inflammatory effects of immunosuppression could result in decreased clinical severity. However, the authors also note that immunosuppressed patients are likely more prone to acquiring the virus.

- Ren, et al. report in JHLT following 87 heart transplant recipients in a single center in Hubei province (the epicenter of the epidemic in China) between Dec 20, 2019 and Feb 25, 2020. No cases of COVID-19 were detected among this population, however strict quarantine measures were undertaken by families and communities for most of these patients.
- A letter by D'Antiga in Liver Transplantation states in a center from Bergamo, Italy that has been heavily impacted by the COVID-19 epidemic, "Our preliminary experience, in agreement with recent data from China, shows that, among patients in the follow-up for cirrhosis, [liver] transplantation, autoimmune liver disease, chemotherapy for hepatoblastoma, none developed a clinical pulmonary disease, despite some tested positive for SARS-CoV-2."

In summary, there is little known thus far about the degree of risk from COVID-19 in immunocompromised patients and in particular patients who are more profoundly immunocompromised (e.g. HSCT, early post-SOT, or intensive phases of therapy for hematologic malignancy). Early experience seems encouraging, however, a cautious approach is advisable with the goal of preventing acquisition of SARS-CoV-2 by immunocompromised patients.

Currently, the CDC defines "individuals with weakened immune systems," as well as those with underlying health conditions including heart disease, lung disease, diabetes, chronic kidney disease, chronic liver disease, endocrine and metabolic disorders, neurological and developmental conditions as among the high risk groups for COVID-19. These criteria may overlap in the same patient and are likely to apply to many patients undergoing evaluation for transplantation as well.

What precautions are recommended for immunocompromised pediatric patients and their families during the COVID-19 pandemic?

Patients and families should refer to guidance from their local public health department for the most up to date recommended precautions related to community-level transmission. As of 3/19/20, a statewide "shelter in place" has been recommended for all of California so in some sense the difficult decisions about school, etc. have been made for us. As the situation resolves, new questions will likely arise when community-wide restrictions are reduced.

Table 1 below summarizes patient-facing recommendations gathered from different resources including the CDC and specialty societies in the United States and elsewhere.

Table 1. Recommended Precautions for Immunocompromised Patients

Key Recommendations	Source + Link + Date of Last Review
<i>High risk patients (broadly applicable)</i>	
<ul style="list-style-type: none"> ● Clean hands often with soap and water for at least 20 seconds, especially after blowing your nose, coughing, or sneezing, or having been in a public place. ● If soap and water are not available, use a hand sanitizer that contains at least 60% alcohol. ● Keep away from others who are sick. ● Avoid crowds as much as possible. ● Avoid cruise travel and non-essential air travel. ● During a COVID-19 outbreak in your community, stay home as much as possible to reduce your risk of being exposed. <ul style="list-style-type: none"> ○ Keep space (at least 6 feet) between yourself and others (outside your household). ○ Consider ways of getting food brought to your house through family, social, or commercial networks. ● Avoid touching high-touch surfaces in public places – elevator buttons, door handles, handrails, handshaking with people, etc. Use a tissue or your sleeve to cover your hand or finger if you must touch something. ● Wash your hands after touching surfaces in public places. ● Avoid touching your face, nose, eyes, etc. ● Clean and disinfect your home to remove germs: practice routine cleaning of frequently touched surfaces (for example: tables, doorknobs, light switches, handles, desks, toilets, faucets, sinks & cell phones). ● Launder items including washable plush toys as appropriate in accordance with the manufacturer’s instructions. If possible, launder items using the warmest appropriate water setting for the items and dry items completely. Dirty laundry from an ill person can be washed with other people’s items. 	<p>CDC Guidance for High Risk Populations https://www.cdc.gov/coronaviruses/2019-ncov/specific-groups/get-ready.html (3/19/20)</p> <p>American Society of Transplantation https://www.myast.org/coronavirus-disease-2019-covid-19-frequently-asked-questions-transplant-candidates-and-recipients# (3/18/20)</p>
<i>Children undergoing therapy for cancer</i>	
<ul style="list-style-type: none"> ● Hygiene and social distancing precautions similar to above <ul style="list-style-type: none"> ○ The UK NHS website contains detailed information on social distancing including avoidance of school during a community outbreak. Some information is country-specific. ● In most cases, treatment will continue as planned. ● Do not stop any home chemotherapy without talking to your child’s treatment team first. 	<p>Children’s Oncology Group: Posted at http://www.survivorshipguidelines.org/ in English and Spanish (3/20/20)</p> <p>UK National Health System https://www.cclg.org.uk/Coronavirus-advice (3/23/20)</p>

<p>SOT recipients or candidates</p>	
<ul style="list-style-type: none"> ● Follow public health recommendations for social distancing ● Do not travel to areas with high circulating levels of the virus ● Postpone non-essential travel for themselves and for their household contacts postpone non-essential travel to high risk areas 	<p>American Society of Transplantation https://www.myast.org/coronavirus-disease-2019-covid-19-frequently-asked-questions-transplant-candidates-and-recipients# (includes Spanish translation) (3/18/20)</p>
<p>HSCT recipients</p>	
<ul style="list-style-type: none"> ● Alert of your provider of any respiratory symptoms particularly if you have an upcoming transplantation admission or inpatient/outpatient cellular therapy. ● Refrain from travel according to national guidelines. If travel is necessary, travel by private car instead of train, bus, or plane is recommended if feasible (EBMT). <p><i>These are current recommendations being given to patients and families by the BCHSF BMT program in response to patient based on consensus and review of the currently available guidance:</i></p> <ul style="list-style-type: none"> ● Do not stop taking any immunosuppressive medications but speak with your health care provider about potential alternatives to steroids. ● Avoid laboratory and health care facilities for non-essential care. Speak with your doctor about essential versus nonessential laboratory testing and procedures particularly if you are several years from your transplantation. ● Encouraged to continue to receive routine vaccinations, if undergoing re-vaccination after transplantation. 	<p>American Society for Transplantation and Cellular Therapy https://www.astct.org/communities/public-home?CommunityKey=d3949d84-3440-45f4-8142-90ea05adb0e5 (3/22/20)</p> <p>American Society for Blood and Marrow Transplantation https://higherlogicdownload.s3.amazonaws.com/ASBMT/a1e2ac9a-36d2-4e23-945c-45118b667268/UploadedImages/COVID-19_Interim_Patient_Guidelines_3_18_20.pdf (3/22/20)</p> <p>European Society for Blood and Marrow Transplantation https://www.ebmt.org/sites/default/files/2020-03/EBMT%20COVID-19%20guidelines%20v.3.2%20%282020-03-16%29.pdf (3/22/20)</p>
<p>Patients with inflammatory bowel disease</p>	
<ul style="list-style-type: none"> ● Do not stop taking IBD medications <ul style="list-style-type: none"> ○ Speak with your doctor about reducing steroid dose or getting off steroids if possible ● Patients on immunosuppressants and biologics/biosimilars are encouraged not to travel or gather in large numbers ● General precautions similar to above 	<p>Crohn's and Colitis Foundation https://www.crohnscolitisfoundation.org/coronavirus/what-ibd-patients-should-know (3/18/20) https://www.crohnscolitisfoundation.org/coronavirus-update/pediatrics (3/18/20)</p>

Where can I find COVID-19 recommendations for healthcare professionals specific to my patient population?

The recommendations below are gathered from the listed specialty organization sources. These recommendations do not necessarily reflect a recommendation specific to UCSF patients, they are provided primarily as resources to consider in clinical decision-making.

Table 2: Recommendations for Health Professionals Caring for Immunocompromised Populations

Key Recommendations	Source + Link + Date of Last Review
Oncology	
<ul style="list-style-type: none"> ● The COG members website includes guidance for patients who are receiving therapy on an investigational protocol. ● For patients with cancer who have fever or other symptoms of infection, a comprehensive evaluation should be performed, as per usual medical practice (ASCO). Maintain a broad differential for fever and respiratory symptoms, be alert to the possibility of alternative or secondary infections (NCIC). ● Make individual determinations based on the potential harms of delaying needed cancer-related surgery (ASCO). ● Routinely withholding critical anti-cancer or immunosuppressive therapy is not recommended. The ASCO guidance includes scenarios where modification of treatment may be considered to reduce a patient’s potential for exposure in the setting of a COVID-19 outbreak (ASCO). ● At this time, there is no evidence or published guidance on the use of prophylactic antiviral therapy for COVID-19 in immunosuppressed patients. This is an active area of research and evidence may be available at any time. Prophylactic antiviral therapy directed at other viral infections should be continued according to standard clinical guidelines and institutional practices (ASCO). ● Temporary discontinuation of cancer therapies may be warranted for some patients with cancer <u>who develop COVID-19 disease</u>, to minimize treatment-related immunosuppression or reduce the risk of drug-drug interactions (NCIC). ● NCIC guidelines also provide general information for Oncology practice management with regard to outpatient care, provider and staff social distancing. 	<p>Children’s Oncology Group members website https://cogmembers.org/ (3/23/20)</p> <p>UCSF Helen Diller Family Cancer Center website: https://cancer.ucsf.edu/coronavirus <i>Contains links to other organization guidelines.</i></p> <p>American Society of Clinical Oncology https://www.asco.org/asco-coronavirus-information/care-individuals-cancer-during-covid-19 (3/23/20)</p> <p>Australia and New Zealand National Centre for Infections in Cancer https://cancerandinfections.org/covid19-information Interim Guidelines for Management of Haematology and Oncology Patients During the COVID-19 Pandemic (published 3/19/20)</p>

<p>SOT</p> <p><i>Guidance to patients (in addition to patient-facing resource):</i></p> <ul style="list-style-type: none"> ● If SARS-CoV-2 is circulating in the recipient’s area, avoid public places including school, and stay at home as much as possible to reduce risk of exposure SARS-CoV-2. ● Not currently recommending recipients to wear masks in public. <p><i>Potential risk for donor to recipient transmission:</i></p> <ul style="list-style-type: none"> ● The risk of COVID-19 acquisition from an infected donor is unknown at this time but there is theoretical risk based on viremia and detection of SARS-CoV-2 in multiple organs and tissues. ● OPOs currently screen deceased donors based on epidemiology and clinical history into “low,” “intermediate,” and “high” risk categories. Screening criteria are detailed within the linked AST guidelines. ● Transplantation of organs from deceased donors is <u>not recommended</u> at this time if the donor has 1) active COVID-19, 2) positive test for SARS-CoV-2 as part of OPO evaluation, or 3) high-risk on screening tool and testing not available or feasible. ● Transplant experts note that universal testing of deceased donors is desirable, but the current test availability and turnaround time may limit the ability to do so in a timely manner. The optimal approach to donor screening may change over time and likely varies by OPO. See below FAQ for updates of deceased donor screening in Northern California. ● Living donor screening is also detailed in the AST guidelines. <p><i>Evaluation of recipient prior to transplantation:</i></p> <ul style="list-style-type: none"> ● Suggest proceeding with transplantation in absence of recent COVID-19 exposure and absence of compatible symptoms in preceding 2 weeks. If timing and test availability allows, suggest PCR-based test for SARS-CoV-2 prior to transplant in patients for whom an organ is accepted (ISHLT). ● Recommend foregoing transplantation if the patient has a positive test for SARS-CoV-2. If a patient has recovered from COVID-19, recommend waiting 14 days from initial diagnosis and two successive negative PCR tests 1 week apart prior to transplantation (ISHLT). <p><i>Evaluation of patients with symptoms:</i></p> <ul style="list-style-type: none"> ● COVID-19 should be considered along with influenza, RSV and other causes of acute respiratory illness (AST). ● Patients with respiratory symptoms should have chest imaging, preferably CT when available (ISHLT). 	<p>American Society for Transplantation Information for Transplant Professionals: https://www.myast.org/information-transplant-professionals-and-community-members-regarding-2019-novel-coronavirus (March 23, 2020)</p> <p>The Transplantation Society https://tts.org/tid-about/tid-presidents-message/23-tid/tid-news/657-tid-update-and-guidance-on-2019-novel-coronavirus-2019-ncov-for-transplant-id-clinicians (Updated March 16, 2020)</p> <p>Organ Procurement and Transplantation Network https://optn.transplant.hrsa.gov/news/information-for-transplant-programs-and-opos-regarding-2019-novel-coronavirus/ (Updated 2/28/2020)</p> <p>UNOS https://unos.org/covid/ (Reviewed 3/23/20) <i>includes a multi-organization transplant-specific webinar with detailed information.</i></p> <p>International Society for Heart and Lung Transplantation https://ishlt.org/covid-19-information (Updated 3/17/20)</p>
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Treatment of patients diagnosed with COVID-19:

- Primarily supportive care. Management of patients thus far has consisted of investigational therapies such as hydroxychloroquine or remdesivir, and reduction of immunosuppression. Consider therapy based on drug availability and disease severity (AST, ISHLT).
- When considering investigational/off-label therapies, drug-drug interactions with immunosuppressive medications should be considered (AST).
- No firm recommendation on discontinuation of ACEI/ARB therapy (AST). (There is theoretical risk for worsening COVID-19 due to ACE2 receptor being receptor for this virus. Limited data at this time.)
- Consider reducing immunosuppression if no recent rejection episodes (AST).
 - ISHLT guidelines differentiate based on disease severity; if mild disease, suggest continuing maintenance immunosuppression.
 - For severe/critical disease, consider holding MMF (ISHLT).
- No current recommendation for adjunctive steroids (AST).
- Candidates with active COVID-19 should be deferred from transplantation (AST).

Follow-up and monitoring of SOT recipients when active transmission is occurring in community:

- Reduce elective visits, convert to telehealth when clinically appropriate (AST, ISHLT).
- Postpone routine surveillance heart biopsies in patients more than 3-6 months from transplantation, without prior episode of rejection, and clinically stable (ISHLT).

AST, UNOS and ISHLT note that there may be some circumstances in which programs choose to deactivate individual recipients or the entire program temporarily in the setting of COVID-19 pandemic:

- Per AST, some centers may still need to explore temporary suspension of elective living donor transplantation or non-urgent deceased donor transplants with involvement of organizational leadership based on prioritization planning.
- Issues impacting this decision may include the level of infection in their area and/or operational issues (e.g. testing availability, bed space, availability of basic supplies and equipment including personal protective equipment).
- UNOS provides guidance regarding organ procurement issues that may arise in the setting of the COVID-19 pandemic, as well as the logistics of temporary deactivation for a listed candidate or program due to the COVID-19 pandemic.

<i>HSCT and cellular therapy</i>	
<p><i>Evaluation of patients with symptoms:</i></p> <ul style="list-style-type: none"> • In a patient with upper or lower respiratory tract symptoms, send PCR testing for SARS-CoV-2 in addition to other respiratory virus PCR testing (ASTCT). • Chest imaging (CT preferred) if SARS-CoV-2 test positive (ASBMT - “consider”, EBMT - recommend for all patients). Evaluate for oxygenation impairment. • If SARS-CoV-2 test negative from upper respiratory tract but patient with symptoms of lower respiratory tract infection (dyspnea, hypoxia, tachypnea), consider chest imaging (due to possible discrepancy between upper and lower respiratory tract test performance) (ASTCT). • Routine BAL not indicated if SARS-CoV-2 test positive, unless co-infection is suspected (ASTCT). • If SARS-CoV-2 is detected in a respiratory specimen, HSCT or other cellular therapy procedures should be deferred. The ASTCT document includes detailed guidance for when to proceed with procedures after a diagnosis of COVID-19. EBMT guidelines are similar but with a more conservative 3 month deferral recommended for patients with “low risk disease.” <p><i>Evaluation of asymptomatic candidates:</i></p> <ul style="list-style-type: none"> • Patients planned to be admitted for a transplant or to undergo CAR-T therapy should isolate at home 14 days before the start of conditioning (EBMT). • If the prevalence of COVID-19 is thought to be high in the community, all HCT and cellular therapy candidates should undergo screening for SARS-CoV-2 infection at the time of initial evaluation and 2 days prior to conditioning/lymphodepletion if testing is available (ASTCT, EBMT). <p><i>Evaluation of HSCT donors:</i></p> <ul style="list-style-type: none"> • There have not been reports of transmission of novel coronaviruses from donor to recipient in either transfusion of blood products or cellular therapies, however there is theoretical risk due to viremia (ASTCT). • Donors with SARS-CoV-2 detected in a respiratory sample should be considered ineligible to donate. The ASTCT document includes detailed guidance for when the donor can be cleared following a positive test. EBMT guidelines are more conservative, recommend considering a 3 month deferral if possible. • If a donor has had close contact with a person diagnosed with COVID-19, the donor should be excluded from donation for at least 28 days (ASTCT, EBMT). <ul style="list-style-type: none"> ○ Both guideline documents provide details of earlier option to “clear” a donor with serial testing if the transplant is considered urgent without option to defer. • Secure stem cell product access by freezing before the start of conditioning (EBMT, NMDP). If possible, ensure that an 	<p>American Society of Transplantation and Cellular Therapy Infectious Diseases Special Interest Group https://higherlogicdownload.s3.amazonaws.com/ASBMT/a1e2ac9a-36d2-4e23-945c-45118b667268/UploadedImages/COVID-19_Interim_Patient_Guidelines_3_18_20.pdf (Updated 3/18/2020)</p> <p>European Society for Blood and Marrow Transplantation https://www.ebmt.org/ebmt/news/coronavirus-disease-covid-19-ebmt-recommendations-update-march-23-2020 (Updated 3/23/2020)</p> <p>National Marrow Donor Program https://network.bethematchclinical.org/news/nmdp/be-the-match-response-to-covid-19/ (Updated 3/23/20)</p>

<p>alternative stem cell source will be available (ASTCT, EBMT).</p> <ul style="list-style-type: none"> • Donors within 28 days prior to donation should practice good hygiene and avoid crowded places and large group gatherings (ASTCT, EBMT). • The NMDP website includes detailed guidance to transplant centers regarding screening, logistics, and recommendations pertinent to unrelated donor transplantation. <p><i>Treatment of patients with COVID-19:</i></p> <ul style="list-style-type: none"> • Upper respiratory tract infection: <ul style="list-style-type: none"> ○ If chest imaging is normal and <u>no symptoms</u>, no therapy recommended at this time (ASTCT). ○ If chest imaging is normal and mild upper respiratory symptoms, patients should be considered for clinical trials if available. Specific agents can be considered if symptoms progress. ID consult recommended (ASTCT). • Lower respiratory tract infection: <ul style="list-style-type: none"> ○ Therapy should be considered in patients with LRTI. ID consult recommended (ASTCT). • ASTCT document provides therapy options without order of preference, notes considerations including availability, drug-drug interactions, and toxicity. • Routine use of corticosteroids as adjunctive therapy not recommended; consider on a case-by-case basis with an ICU specialist for patients with ARDS (ASTCT). • Currently available IVIG products are unlikely to contain specific antibodies to SARS-CoV-2, routine use of IVIG for treatment is not recommended at this time (ASTCT). • Insufficient evidence to support routine interferon therapy (ASTCT) • Routine use of tocilizumab is not recommended (ASTCT). • No firm recommendation on ACEI/ARB therapy (ASTCT, EBMT). • Routine use of antibiotics not recommended in patients with SARS-CoV-2 limited to the upper respiratory tract. Empiric antibiotics can be considered on an individual basis for patients with LRTI based on level of immunosuppression, extent of diagnostic evaluation for co-infection, radiographic appearance, and illness severity (ASTCT). 	
<p>IBD</p>	
<ul style="list-style-type: none"> • Continue medications; consider opportunity to reduce steroids • Strongly consider rescheduling elective non-urgent endoscopic procedures 	<p>Crohn's and Colitis Foundation https://www.crohnscolitisfoundation.org/coronavirus/professional-resources (reviewed 3/22/20)</p>

<i>Rheumatology</i>	
<ul style="list-style-type: none"> • All patients should talk to their rheumatologist or rheumatology professional prior to discontinuing any of their medications. While there are no data on the influence of these medications on COVID-19, providers should follow their current practice for interrupting therapy during episodes of infection. • Ensure patients have received all appropriate vaccinations, including seasonal influenza, pneumonia, pertussis, and shingles vaccines. These will not prevent COVID-19, but may lessen the chance of a secondary infection and will prevent illnesses that could be confused with COVID-19. • In addition, patients should be advised to keep ample stocks (e.g., one-month supply) of necessary medications on hand in case they are prevented from refilling prescriptions in a timely manner. • Access to hydroxychloroquine (Plaquenil) is of particular concern due to its off-label use in treatment of persons with COVID-19. 	<p>American College of Rheumatology FAQ for Clinicians: https://www.rheumatology.org/announcements (reviewed 3/22/20)</p>
<i>Immunology</i>	
<ul style="list-style-type: none"> • Currently not recommended to have primary immunodeficiency patients with no or very limited symptoms tested for SARS-CoV-2. • Currently not recommending to wear a mask routinely, except when asked in a healthcare setting and instructed how to use the mask. • School and travel recommendations per local epidemiology. Follow local and national recommendations. 	<p>Joint statement by multiple organizations: https://ipopi.org/wp-content/uploads/2020/03/COVID19_Joint_IPOPI_ESID_INGID_APSID_LASID_ASID_CIS_A_RAPID_SEAPID_Statement—Update1_v2.0_20200311_130OCET-FINAL.pdf (Updated 3/11/2020)</p>

What should we advise for patients listed for transplant but not yet on immunosuppressive medications? e.g. heart transplant candidate living at home, kidney transplant candidate on dialysis?

In most cases, the underlying conditions prompting consideration for transplantation will also be potential predisposing conditions for severe disease with COVID-19 and comparable hygiene and social distancing precautions should be applied to prevent transmission of infection.

What if there is someone in the home with the patient who has potential exposure risk outside the home (e.g. a healthcare worker)?

The following recommendations come from the UCSF Clinician Daily Digest and pertain to healthcare workers reducing risk for exposure to household contacts:

“Although the answers to this are not fully known, the following is a reasonable approach:

- For those having direct patient care of COVID-19 positive or suspect patients, because they’ll be wearing personal protective equipment while caring for these patients, wearing scrubs at the hospital and changing out of them before going home isn’t absolutely necessary but may be more comfortable and reassuring for some providers. Some providers may opt to shower. All providers should clean their hands.
- For those caring for patients who do not have respiratory illnesses, continuing with their standard approach to the transition from hospital to home is reasonable. Frequent hand hygiene is absolutely critical. Some providers feel more comfortable changing their clothes before close interactions with one’s family.
- For everyone without symptoms and without a known high-risk exposure to a patient with COVID-19 (e.g. without PPE), eating dinner with their families and hugging their children should be fine. Special precautions may be taken for those with immunocompromised or very elderly family members, but those probably need to be taken on a case-by-case discussion.”

Additional precautions could be considered on an individual basis depending on the nature of the patient’s immune status, anticipated intensified immunosuppression (e.g. lymphodepleting therapy) and the healthcare worker’s specific role. For healthcare workers, possibilities include:

- Requesting reassignment to minimize risk for exposure to patients with respiratory illness or requesting non-patient assignments.
Requesting leave of absence if possible.
- Cohorting apart from the patient in another household.

Each of these measures have substantial downsides to the patient, family, and healthcare system and should be re-evaluated with regard to the patient’s net state of immunosuppression and the current local epidemiology of COVID-19.

Should an asymptomatic patient be tested for SARS-CoV-2 before undergoing intensive immunosuppression (e.g. SOT candidates at the time of admission with transplant offer, HSCT candidates prior to conditioning)?

At this time the potential benefits of testing prior to transplantation are not established, but there is plausible benefit to testing based on the following observations:

- Persons with SARS-CoV-2 infection may be asymptomatic or minimally symptomatic.
- Possibility of asymptomatic infection progressing to severe disease in the setting of intensive immunosuppression.
- Opportunity to delay transplantation to allow resolution of SARS-CoV-2 infection.
- A case was described in the SOT webinar (UNOS/AST/multiple organizations 3/23/20) of a patient s/p kidney transplant who was asymptomatic upon admission, underwent intensified immunosuppression for rejection, and subsequently developed critical COVID-19 while hospitalized.

Some organizations (ISHLT, ASTCT) provide guidance for testing asymptomatic recipients, and we are aware of other transplant centers (Seattle Children’s, center in Milan, Italy per Gori, et al.) doing so in the setting of active community transmission of COVID-19. At present, we suggest the following approach, which may be modified based on updated guidance and logistics:

Patient Category	Test for COVID-19/ SARS-CoV-2?	Timing of Test
SOT candidate upon admission with organ offer	Yes	Upon admission, answer yes to “admitted” question on order and contact Ped COVID ID clinician on Voalte to expedite test. Result should be documented before transplantation.
HSCT candidate	Yes	At consent conference and upon admission. Related donor should also be tested. Patient should not come for additional unplanned visit to be tested. Patient (and related donor, if applicable) should self-isolate between consent conference and admission. Re-test recipient upon admission, answer yes to “admitted” question on order. Turnaround time < 24 hours.
CAR-T cell candidate	Yes	At the time of admission with negative result documented before lymphodepleting chemotherapy. Answer yes to “admitted” question on test order.
Patient receiving intensified immunosuppression (e.g. thymoglobulin, rituximab)	Consider	Prior to initiation of immunosuppression. Logistics of delay may be more challenging in these situations due to medical urgency of treatment. Discuss situation with Ped COVID ID attending for support with clinical decision-making.

What is the current status of deceased donor screening for solid organ transplantation in Northern California?

As of 3/24/20, Donor Network West (covering most of Northern California) screens donors based on epidemiologic and clinical risk criteria and tests all lung donors for SARS-CoV-2 by PCR. Sierra Donor Services (Sacramento area) screens all deceased donors by PCR (universal).

When should a symptomatic immunocompromised patient be tested for COVID-19? Are recommendations different from current testing recommendations for immunocompetent patients?

In general, testing of patients presenting for evaluation to the ED or in the inpatient setting should follow the Algorithm for ED/Hospitalized Patients with Respiratory Illness (Pediatrics) available at <https://infectioncontrol.ucsfmedicalcenter.org/coronavirus>. No algorithm can replace clinical judgement, however. For patients who are symptomatic at home, when considering whether to refer the patient for evaluation, the following points should be considered:

- What is the patient’s net state of immunosuppression?
- Would immunosuppression be reduced if the patient were found to have COVID-19 or another respiratory viral infection (e.g. influenza)?

- Would identification of COVID-19 in this patient prompt further evaluation (e.g. chest imaging, for example, is recommended by interim guidelines by some HSCT organizations)?
- Is there planned immunosuppressive therapy that would be delayed if the patient were found to have COVID-19 or another respiratory viral infection?
- What is the degree of clinical illness at present? Does the patient have symptoms suggestive of lower respiratory tract infection?
- How long has the patient been symptomatic?
- Consider risk/benefit of patient movement outside the home, potential exposure to community transmission in the process of coming in for evaluation.
- For context, most healthy children with upper respiratory symptoms are not being routinely referred specifically for COVID-19 testing at this time if they don't otherwise have indications for emergency department or inpatient care.
- For up to date respiratory screening clinic workflow, please refer to most recent BCH-wide communications.

Who can I contact for patient-specific advice about COVID-19 testing, isolation, or other questions?

- At BCH Oakland, clinicians can page 510-718-2684 (510-718-COVID) 24/7 to speak with a pediatric ID clinician about testing, referrals and isolation questions.
- At BCH San Francisco, clinicians can call (628) 248 8292 or contact "COVID Peds ID" on Voalte 24/7.
- Clinicians calling from outside either hospital should call the Pediatric Access Center and ask to speak with the Pediatric COVID ID service.

What should be done if an immunocompromised patient has a known exposure to someone who has been diagnosed with COVID-19?

The CDC provides guidelines for management of persons with exposure to COVID-19 with recommendations varying by the level of risk from the exposure itself and the local level of community transmission: <https://www.cdc.gov/coronavirus/2019-ncov/php/risk-assessment.html>. For the highest risk exposure (household contact) the current recommendation is quarantine with symptom monitoring for 14 days, without testing if asymptomatic.

There is currently little guidance on whether this approach should be modified if the exposed person is immunocompromised. Current guidelines for management of an exposed patient vary by organization:

- ISHLT recommendations are to quarantine at home x 14 days in asymptomatic patients, with testing for SARS-CoV-2 only if symptoms occur.
- ASTCT guidelines recommend deferring procedures including PBSC mobilization, BM harvest, T cell collections and conditioning/lymphodepletion until at least 14 days and preferably 21 days from the day of last contact. They also state that affected patients should be closely monitored for the development of infection, with two consecutive negative PCR tests each approximately one week apart if available.
- EBMT guidelines recommend testing exposed patients though do not provide a timeline for testing.

Given the lack of consensus on this issue currently, we recommend consulting with the hospital-specific infection prevention team (BCHO/BCHSF) if the patient is receiving care at one of the hospital campuses or had an exposure in the healthcare setting. If the patient is at home, the local public health department recommendations should be followed. For patient-specific guidance on additional measures (e.g. testing) to be followed due to the patient's immunocompromised status, we recommend consulting the hospital-specific Pediatric COVID ID clinician. Recommendations would vary based on individual risk/benefit considerations.

**What antiviral therapies may be available for immunocompromised patients with COVID-19?
Does UCSF have plans in place to access these therapies?**

At present there is no clearly established anti-infective therapy for COVID-19, however there are several investigational or off-label therapies that have been used in the treatment of patients with COVID-19, and several of these are being actively evaluated in adults in clinical trials. New data is emerging constantly and the Pediatric ID COVID-19 data response team is keeping up with the emerging literature. Currently the strongest candidate therapies are hydroxychloroquine and remdesivir. ID pharmacists are working to ensure an adequate supply of hydroxychloroquine for treatment of hospitalized patients.

At this time we do not recommend emergency outpatient prescriptions or prophylaxis with hydroxychloroquine for at-risk patients. This medication is currently on shortage nationally and pre-emptive prescribing in the context of the pandemic is threatening the supply of this medication for patients with rheumatologic disease. Contrary to some public reports, hydroxychloroquine is not currently FDA approved for treatment of COVID-19.

Remdesivir is available via compassionate use from Gilead for patients < 18 years old and the Pediatric ID team is collaborating with the Adult ID teams at Parnassus to establish a common regulatory process for accessing and administering this medication to patients with COVID-19.

*More information is available from Gilead: <https://www.gilead.com/purpose/advancing-global-health/covid-19>
<https://rdvcu.gilead.com/>*

Current criteria for remdesivir are:

1. Key inclusion criteria: Hospitalization, confirmed SARS-CoV-2 by PCR, invasive mechanical ventilation.
2. Key exclusion criteria: Evidence of multi-organ failure, pressor requirement to maintain blood pressure, ALT levels > 5 X ULN, creatinine clearance <30 mL/min or dialysis or continuous veno-venous hemodialysis.

The rooms in the BMT Unit at BCHSF (hospital-specific) are positive pressure rooms. What is the current recommendation for location of patients undergoing COVID-19 testing (PUI but not confirmed to have COVID-19)?

These are recommendations as of 3/25/20:

BMT Patient		No continuous AGP	Continuous AGP
Current inpatient	COVID pending*	Stay on BMT unit. If in PICU can leave patient in room 1, 2, 15	Put in negative pressure room preferentially
	COVID positive	Regular room on TCUP (not BMT room or PICU room 1, 2, 15)	Put in negative pressure room
New admission (patient from home, post-transplant)	COVID pending*	Regular room on TCUP vs Heme-Onc	Put in negative pressure room preferentially
	COVID positive	Regular room on TCUP	Put in negative pressure room

AGP= aerosol-generating procedure

Protective environment rooms (positively pressured) = BMT room 1-13 and PICU 1, 2, and 15

*If COVID pending with higher pre-test probability due to known exposure, move to new room as for COVID positive.

What are the corresponding recommendations for patients at BCHO (hospital-specific) who would otherwise receive care in positive pressure rooms?

These are the recommendations as of 3/25/20:

Heme/Onc Patient		No Continuous AGP	Continuous AGP
Current inpatient and or New admission (patient from home, post-transplant)	COVID pending	Droplet/Contact – private room If in PICU – No positive pressure, negative/neutral pressure OK *room 16,17*	Negative pressure room
	COVID positive	Droplet/Contact – Private room PICU – Room 16/17	Negative pressure room

AGP= aerosol-generating procedure

If an immunocompromised patient is diagnosed with COVID-19, when can home isolation be discontinued?

For patients in the hospital, the hospital-specific infection prevention program recommendations should be followed. Patients at home will be monitored by their local public health department. The CDC provides guidance on discontinuing isolation specific to immunocompromised persons on home isolation after a positive test for COVID-19.

<https://www.cdc.gov/coronavirus/2019-ncov/hcp/ending-isolation.html>

As of 3/24/20, these guidelines recommend maintaining home isolation until:

- Resolution of fever without the use of fever-reducing medications and
- Improvement in respiratory symptoms (e.g., cough, shortness of breath) and
- Negative results of an assay for COVID-19 from at least two consecutive nasopharyngeal swab specimens collected ≥ 24 hours apart

When a test-based strategy is not feasible or desired, healthcare providers and public health officials should follow the non-test-based strategy outlined in the guidance for non-immunocompromised persons: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html>. Local public health department recommendations should be followed, but these guidelines may be helpful in counseling patients and families about what they can expect.

Where can I learn the most recent updates on COVID-19 case numbers?

US Nationwide: <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html>

SF Bay Area: <https://projects.sfchronicle.com/2020/coronavirus-map/>

Key Peer-Reviewed Literature:

Dong Y, Mo X, Hu Y, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics* 2020;doi: 10.1542/peds.2020-0702

<https://pediatrics.aappublications.org/content/pediatrics/early/2020/03/16/peds.2020-0702.full.pdf>

Largest case series to date of children diagnosed with COVID-19.

Gori A, Daniele D, Barbara A, et al. Coronavirus disease 2019 and transplantation: a view from the inside. *Am J Transplant* 2020; <https://doi.org/10.1111/ajt.15853>.

<https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.15853>

Perspective on SOT from center in Milan, Italy during COVID-19 epidemic.

Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection, a nationwide analysis in China. *Lancet Oncology* 2020; [doi.org/10.1016/S1470-2045\(20\)30096-6](https://doi.org/10.1016/S1470-2045(20)30096-6)

[https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(20\)30096-6/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(20)30096-6/fulltext)

Small series from the mainland China outbreak focused on patients with cancer.

Mao R, Liang J, Shen J, et al. Implications of COVID-19 for patients with pre-existing digestive diseases. *Lancet Gastroenterol Hepatol* 2020; [https://doi.org/10.1016/S2468-1253\(20\)30076-5](https://doi.org/10.1016/S2468-1253(20)30076-5).

[https://www.thelancet.com/journals/langas/article/PIIS2468-1253\(20\)30076-5/fulltext](https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30076-5/fulltext)

Perspective on COVID-19 potential implications including for patients with digestive disease including IBD. Authors note that as of March 8 no cases of COVID-19 had been reported in patients with IBD from the 3 largest IBD referral centers in Wuhan.

Michaels MG, La Hoz RM, Danziger-Isakov L, et al. Coronavirus disease 2019: implications of emerging infections for transplantation. *Am J Transplant* 2020;00:1-5.

<https://onlinelibrary.wiley.com/doi/full/10.1111/ajt.15832>

Perspective on potential impact of COVID-19 focused on SOT. Includes discussion of potential risk for increased transmissibility of novel coronaviruses from immunocompromised patients, and theoretical risk for donor-derived infection.

Weinkove R, McQuilten Z, Blyth E, et al. Managing haematology and oncology patients during the COVID-19 pandemic: interim consensus guidance. *Med J Aust* 2020; online at:

<https://cancerandinfections.org/covid19-information>.

National Centre for Infections in Cancer (Australia and New Zealand) guidelines.