Managing primary immunodeficiency during the COVID-19 pandemic

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Introduction

The coronavirus disease 2019 (COVID-19) outbreak, which originated in Wuhan, China, is caused by a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Li et al. 2020; Wong et al. 2020; Xu et al. 2020). To date, cases have been reported in all continents worldwide with the exception of Antarctica, and include over 25 million affected and 846 841 deaths (European Centre for Disease Prevention and Control 2020). The pandemic has led to a disproportionate loss of lives in our most vulnerable populations and widespread global economic downturn.

SARS-CoV-2 belongs to the same family of coronaviruses that cause the common cold, as well as the recent outbreaks of atypical viral pneumonia (severe acute respiratory syndrome, SARS; Middle East respiratory syndrome, MERS) (de Wit et al. 2016; Paules et al. 2020). Like all viruses, SARS-CoV-2 can multiply only in living cells. To enter living cells, viruses express proteins (ligands) on their surface which recognize complementary proteins on the surface of cells (receptors). Binding of viral ligands and cellular receptors allows entry of the virus into cells where they hijack its normal functions to reproduce. This take over by the virus damages the cells, and upon their death, multiple new copies of the virus are released into the bloodstream, infecting other cells and resulting in disease.

To maintain infectious ability, viruses must retain their complex structure which includes its genetic material, proteins, and fatty envelope. The infective ability of viruses on surfaces outside of the body and the precise mechanism whereby they propagate to people varies among viruses (Paules et al. 2020). Some can only be transmitted through blood transfusions, while others travel from person to person through droplets. Respiratory viruses such as influenza and SARS-CoV-2 rely on droplets produced by infected individuals (usually by coughing or sneezing). Direct exposure of the mouth, nose, or eyes to droplets in the air may result in infection (Carlos et al. 2020; Lu et al. 2020; Xia et al. 2020). Similarly, hand contact with contaminated surfaces and subsequent transfer to the airways or eyes may also lead to infection. SARS-CoV-2 appears infectious through large size droplets as well as fine mist (aerosol). Early reports also suggest evidence of transmission via the fecal-oral route (Gu et al. 2020; Hindson 2020).

SARS-CoV-2 does not stay infectious for extended periods on surfaces and varies from 24 hours on cardboard to several days or a week on plastic surfaces (Carraturo et al. 2020). Cold temperatures do not reduce the lifespan of SARS-CoV-2, and the virus remains viable for a long time in refrigerators and freezers. In contrast, high heat of more than 60 °C kills the virus. Copper and paper surfaces have antiviral activities due to emission of ions or chemical residues, respectively (Ren et al. 2020).

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Transmission of the virus to another individual may result in infection, which could lead to COVID-19 related disease. Those infected with SARS-CoV-2, like those infected with other coronaviruses or influenza viruses, may become sick or remain asymptomatic (Rothe et al. 2020). COVID-19 disease may be mild or severe, with components and symptoms related to damage inflicted directly by the virus or by a host exaggerated response to the infection (commonly called complications). Individuals sick with COVID-19 typically present with fever, cough, dyspnea, pneumonia, loss of smell and taste, and gastrointestinal symptoms (Jiang et al. 2020; Stawicki et al. 2020).

Mounting consistent experience indicates that the elderly and individuals with existing morbidities are at higher risk of developing more severe disease course (Chen et al. 2020; Huang et al. 2020; Li et al. 2020). Risk factors for critical illness include older age (>65 years), obesity, type II diabetes mellitus, males, cancer, chronic kidney disease, chronic obstructive pulmonary disease, immunodeficiency, serious cardiovascular disease, and sickle cell disease (Chen et al. 2020; Huang et al. 2020; Li et al. 2020). Complications and fatalities associated with COVID-19 are caused by poorly controlled inflammation triggered by the virus, including acute respiratory distress syndrome, coagulation disorders, acute kidney injury, and vascular injury (Chen et al. 2020).

Children and young people with no co-morbidities appear to experience less severe illness when infected (Yu and Chen 2020). Indeed, children make up about 2% of all reported cases in the world (Bialek et al. 2020; Stawicki et al. 2020; Wu and McGoogan 2020). Yet, some limited number of children with more serious complications of COVID-19, mainly multi-system inflammation, have been reported (Riphagen et al. 2020; Waltuch et al. 2020). Neither the true frequency of these events nor the long-term sequelae of COVID-19 in children have been determined.

Disease severity in children should not be confused with the frequency and ability of children to get infected and transmit the virus to others. This issue remains controversial, with some claiming children might be less contagious. Scientific analysis of SARS-CoV-2 transmission conducted by Christian Drosten, Germany's chief virologist, found no differences in coronavirus transmission across all age groups, including children (Jones et al. 2020). The study concluded that children can be as infectious as adults. From the beginning of the pandemic there have been case reports of young children who had high levels of SARS-CoV-2 virus detected in all body fluids tested. Further, a recent study indicated young children secrete more SARS-CoV-2 than sick adults (DeBiasi and Delaney 2020), suggesting children can be as contagious as adults.

Based on evidence and research collected thus far, the following are my recommendations for adults and children with primary immunodeficiency:

1. Keep physical distance from non-family members as much as possible.
2. Use masks when exposed to non-family members outside of your home—they protect you and others (medical masks were found superior).
3. Wash your hands with soap or hand sanitizer after you touch surfaces and especially before you touch your mouth, nose, or your eyes.
4. Avoid unnecessary and close contact with non-family members at all times, but especially in enclosed spaces.
5. Reduce the duration of stay in enclosed spaces which are shared by multiple non-family members.
6. If and when advised by your doctor, undertake schooling/learning from home.
7. Adults with immunodeficiency, if possible, are encouraged to work from home and reduce as much as possible exposure to workplace crowding.
8. Do not miss life saving tests and treatments because of the pandemic.
9. Outdoor activities are encouraged as long as they happen in a safe environment.
10. When in doubt, consult with your immunologist for more specific recommendations related to your condition.
11. These recommendations are case-specific sensitive and could be modified to take into account diverse needs.

COVID-19 related questions and answers for patients with primary immunodeficiency (PID)

1. Are patients with PID at increased risk of contracting COVID-19 illness?

There is little information regarding COVID-19 infections in children in general, or specifically in PID, likely

because such patients have been sheltered thus far. We should assume that children, adolescents, and adults with PID are equally susceptible to infection with this virus.

2. Could patients with PID experience more severe disease if they catch COVID-19?

Patients with PID are at increased risk of developing severe disease for multiple reasons:

1. Those with abnormalities in antibody production (hypogammaglobulinemia, agammaglobulinemia, CVID, others) or T cell dysfunction (SCID, CID) can get very sick when contracting respiratory viruses, and would likely be similarly affected by COVID-19. The degree of illness severity is dictated by the degree of immune competence (mild or profound T cell defect) and the efficacy of treatment (IVIG, BMT, gene therapy).
2. Patients with PID have co-morbidities known to be risk factors for severe COVID-19 illness, including chronic lung disease and diabetes (see Table 1).

We recommend these patients exercise extreme caution when making the decision whether to attend physical schools. It is best to have this specific situation evaluated by their immunologist.

3. How can I protect myself or my child at home?

The way of protecting from respiratory viral infections is to create a safe environment around them. Family members attending school or work should comply with COVID-19 prevention strategies, including physical distancing, hand hygiene, the use of masks, COVID-19 screening when possible, as well as testing if symptomatic.

4. How can I protect myself or my child in public?

1. Avoid enclosed spaces which are known to be a high transmission risk environment.
2. Outdoor activities are encouraged but with proper caution:
    - Avoid direct contact with surfaces, other individuals, or equipment
    - Use hand sanitizer if surfaces are touched after each contact
    - Avoid rubbing your eyes, or touching your mouth and nose
    - Use a face mask as much as possible

With all these measures in an outdoor setting the risk of transmission is very low.

Table 1: **Morbidity associated with PID which increases the risk for severe COVID-19.**

- Asthma
- Chronic lung disease
- Neurologic and neurodevelopmental conditions
- Endocrine disorders (such as diabetes mellitus)
- Heart disease (such as congenital heart disease, congestive heart failure, and coronary heart disease)
- Kidney diseases
- Liver disorders
- People with weakened immune system due to
○ Use of immunosuppressive drugs

5. What should I do if a family member develops respiratory symptoms?

The affected member should isolate themselves as best they can until tested for COVID-19. If possible, PID patients should be tested too, and monitored for symptoms. Importantly, if COVID-19 is suspected or confirmed, contact with other at-risk individuals (elderly family members, those with at-risk diseases) should be avoided.

6. What to do when a PID patient has respiratory symptoms?

Contact your family physician or specialist for instructions. Stay at home and avoid contact with others. Seek COVID-19 testing and monitor symptoms and report these to your doctor.

7. Are patients with PID who contracted COVID-19 contagious?

Patients with PID at all ages can transmit COVID-19 to others. Because many patients with PID have trouble clearing some viral infections and it takes them longer to recover, it is theoretically possible they might carry COVID-19 longer and potentially expose others to the virus for extended periods. It is therefore recommended that PID patients diagnosed with the virus should be

followed and tested repeatedly until clearance of the virus is substantiated.

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