



Joint statement on the current coronavirus pandemic

SARS-CoV-2 — COVID-19 in children and adult patients with

Primary Immunodeficiencies (PID)

By IPOPI, ESID, INGID, APSID, ARAPID, ASID, CIS, LASID, SEAPID, IUIS

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Recent updates are highlighted in yellow.



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Coronavirus - what is it?

In December 2019, a cluster of pneumonia cases was reported in Wuhan, Hubei Province, China, linked to a novel coronavirus (SARS-CoV-2, leading to COVID-19 disease).¹ Coronaviruses are common in many different animal species and it is rare that they infect people and spread between them, but it happens. Recent examples include Severe Acute Respiratory Syndrome (SARS-CoV-1—CoV, for coronavirus), and Middle East Respiratory Syndrome (MERS-CoV). The SARS-CoV-2 is distinct from the previous two coronaviruses and causes COVID-19 disease.²

What is the current situation regarding COVID-19?

The situation is constantly changing, and we advise you to monitor for the latest advice applicable to your area.

As of 2020 8th April, over 1,430,000 cases of COVID-19 have been reported worldwide (184 countries). The countries with the highest number of reported cases are the USA, Spain, Italy, France, Germany, China, Iran and the UK.³

The spread and severity of this viral outbreak has demonstrated the need for a fast and comprehensive response from the public health sector. Beside the virus itself, one of the biggest threats is the overwhelming of the healthcare systems/hospitals due to the rapid spread and the lack of herd immunity in the general population.

¹ European Centre for Disease Prevention and Control. Infection prevention and control for the care of patients with 2019-nCoV in healthcare settings. ECDC: Stockholm; 2020. Available at:

<https://www.ecdc.europa.eu/sites/default/files/documents/nove-coronavirus-infection-prevention-control-patients-healthcare-settings.pdf>

² European Centre for Disease Prevention and Control. Q & A on COVID-19. 31 March 2020. Available at: <https://www.ecdc.europa.eu/en/covid-19/questions-answers> [Accessed 08-04-2020].

³ Johns Hopkins University. Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). 08-04-20.

<https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>. [Accessed 08-04-2020].



How does it spread?

The transmission mode of COVID-19 is similar to previous coronavirus outbreaks, spreading from person to person through:

- Respiratory droplets spreading when coughing or sneezing
- Close personal contact with an infected person (shaking hands or touching)
- Touching contaminated surfaces and then touching eyes, nose or mouth with unwashed hands.⁴

Recent findings have also demonstrated that children may release virus in the stools up to 15 days after recovering from COVID-19. This means that frequent washing of hands should apply even after clinical recovery.

Clinical symptoms due to COVID-19 infection

Human coronaviruses commonly cause mild to moderate illness in the general population. So far, the main clinical signs and symptoms reported in this outbreak include fever, fatigue, dry cough and runny nose. Some patients also experience aches and pains, myalgias, nasal congestion, sore throat and/or diarrhea. **There has also been reports of transient loss of taste, sense or sense of smell.**

These symptoms are usually mild and begin gradually. Some people become infected but don't develop any symptoms and don't feel unwell. Approximately 80% of the affected people recover from the disease without needing special treatment.⁵

However, some patients might experience shortness of breath, requiring oxygen at the hospital. This can evolve into acute respiratory failure for which transfer to intensive care unit for non-invasive (face respiratory mask) or invasive (mechanical artificial ventilation) might be required. Some patients have experienced hyper-immune response mimicking hemophagocytic syndrome. A rebound at D+6 till D+10 may occur.

There is still no validated data confirming if a patient who has recovered from COVID-19 will create antibodies against the virus. However, based on experiences from MERS-CoV and SARS-CoV-1 (previous coronaviruses), it is possible that patients who recover from SARS-CoV-2 will develop long-term, but not life-long, antibodies.

⁴ The World Health Organization. Q&A on coronaviruses (COVID-19). 9 March 2020. Available at: <https://www.who.int/news-room/q-a-detail/q-a-coronaviruses> [Accessed 08-04-2020].

⁵ Ibid.



Should PID patients get systematically tested for COVID-19?

The situation is changing all the time and we advise you to monitor for the latest advice applicable to your area.

The test usually consists in a nasal swab, that is sent to a dedicated microbiology laboratory for detection of this virus (by polymerase chain reaction (PCR) method, within a few hours).

However, in light of shortage of manpower and availability of PCR, most national guidelines do not include or manage patients with chronic diseases, including PID, differently to other patients. At this stage, it is not recommended to have PID patients with no, or very limited, symptoms tested. Furthermore, in some cases, a negative PCR does not rule out infection (“false negative”).

Testing through detecting antibodies (IgG and IgM) against SARS-CoV-2 in the blood (“serology”) is not available on a large scale. This test will reveal whether the tested person has mounted a detectable antibody response after being infected with the virus.

For patients with PID who are not able to produce antibodies (such as patients with agammaglobulinemia or profound hypogammaglobulinemia), this test will not be useful. For the ones with other forms of PID (including the ones under Ig replacement therapy), this test might be of help.

Hence, it is advised to adhere to local and national guidelines for testing.

For PID patients who have tested positive for COVID-19, it is recommended to perform a second screening after the patient has clinically recovered, as it may be that some PID patients, especially patients with a Combined Immune Deficiency (CID), might struggle with clearing the infection. These patients may remain positive longer and risk remaining a source of infection to their environment.

Treatments (vaccines & anti-viral medicines) tested for COVID-19

No medicine has yet demonstrated efficacy in treating or preventing COVID-19 but many are being studied in clinical trials.⁶

Hydroxychloroquine is an anti-infectious drug with anti-inflammatory properties. It is used to prevent malaria and to treat mild forms of autoimmune diseases such as lupus or rheumatoid arthritis.

It is well known that this drug has the potential to inhibit the action of the virus in the laboratory (in vitro testing) and its potential efficacy in preventing or treating COVID-19 is being carefully evaluated. There is however not enough evidence at this stage to ascertain its efficacy.

Other drugs are also being carefully evaluated.

⁶ Inserm. Launch of a European clinical trial against COVID-19. 22 March 2020. Available at: <https://presse.inserm.fr/en/launch-of-a-european-clinical-trial-against-covid-19/38737/> [Accessed 08-04-2020].



Moreover, a group of world-leading global pharmaceutical companies active in the plasma industry have joined together in an attempt to accelerate the development of a potential plasma-derived therapy for treating severe forms of COVID-19. This alliance is currently investigating the development of an anti-SARS-CoV-2 polyclonal hyperimmune immunoglobulin medicine with the potential to treat individuals with serious complications from COVID-19. Other plasma industry companies are also working on similar research programmes.

COVID-19 clinical trials at a glance

[COVID-19 clinical trials listed on TranspariMED.](#)

[COVID-19 NIH clinical trials registry.](#)

[Living mapping and living network meta-analysis of COVID-19 studies](#)

Precautions

Any respiratory virus that can be spread from person-to-person may be a risk for PID patients. Therefore, PID patients should be cautious and keep track of developments of COVID-19 in their region. Whilst immunoglobulin (Ig) replacement therapy provides protection against a wide range of infections, it does not guarantee immunity against coronavirus. The World Health Organization's (WHO) ⁷ and the Centers for Disease Control and Prevention's (CDC) ⁸ recommendations to reduce exposure to and transmission of COVID-19 include, but are not limited to, the list below.

- The MOST IMPORTANT means to prevent infection are:
 - Wash hands frequently (every hour) with hand rub or soap and water for 20 seconds, (if not possible use alcohol-based hand rub), especially after direct contact with ill people or their environment
 - Avoid touching eyes, nose and mouth
 - Avoid close contact (1 meter) with people suffering from acute respiratory infections
 - Avoid close contact (1 meter) with anyone who has fever and cough
 - For extra precaution, avoid close contact (1 meter) with other people when leaving your home
 - Avoid greeting people by shaking hands, kissing or hugging
 - Respect the confinement measures wherever these are applicable

⁷ The World Health Organization. Q&A on coronaviruses (COVID-19). 9 March 2020. Available at: <https://www.who.int/news-room/q-a-detail/q-a-coronaviruses> [Accessed 08-04-2020].

⁸ Centers for Disease Control and Prevention. Prevention & Treatment. 18-03-2020. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/about/prevention-treatment.html> [Accessed 08-04-2020].



- People with symptoms of acute respiratory infection should practice cough etiquette (maintain distance, cover coughs and sneezes with disposable tissues or clothing, and wash hands) and wear a respiratory mask if instructed by their local health care provider.
- **Masks can be effective if the person wearing it has the appropriate training for a good fitting mask, but if not used appropriately they can pose a risk for contamination. The mask needs to be replaced regularly. Guidance from the WHO⁹ on the appropriate way of wearing masks includes:**
 - Before putting on a mask, wash your hands (with alcohol-based hand rub or soap and water).
 - Cover mouth and nose with mask and make sure there are no gaps between your face and the mask.
 - Avoid touching the mask while using it; if you do, clean your hands with alcohol-based hand rub or soap and water.
 - Replace the mask with a new one as soon as it is damp and do not re-use single-use masks.
 - To remove the mask: remove it from behind (do not touch the front of mask)
 - Discard immediately in a closed bin; clean hands with alcohol-based hand rub or soap and water.
- **Some countries have taken measures for citizens to wear masks when spending time outside their homes and we advise to follow national guidelines. If you have symptoms you should wear a mask to protect people in your surroundings. If you are not able to wear a facemask (for example, because it causes trouble breathing), then you should do your best to cover your coughs and sneezes, and people who are caring for you should wear a facemask if they enter your room. If a shortage occurs, masks should be reserved for hospital staff and people experiencing symptoms.**
- For extra precaution, clean and disinfect frequently touched surfaces daily, including tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks.
- **Questions regarding daily life (school attendance, work, travel...) depend on the local epidemiological situation and the underlying PID and needs to be discussed with the PID expert physician.**
- If you feel unwell and experience symptoms such as fever, cough and/or difficulty in breathing, stay home and seek prompt medical assistance from your health care provider.

⁹ The World Health Organization. Coronavirus disease (COVID-19) advice for the public: When and how to use masks. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/when-and-how-to-use-masks> [Accessed 08-04-2020].



COVID-19 vaccine

There is currently no vaccine available for COVID-19. One or several vaccines should be available within 6-12 months.

COVID-19 in PID patients

To date (08-04-2020), global surveys aimed at collecting data on COVID-19 in PID patients do not point to an increased risk of COVID-19, especially not in its severe form, although a few cases have been reported.

However, certain PID patients might be at higher risk than others to catch this infection or a more severe course of the disease. In the absence of more precise data, patients with PID need to take extra care to prevent from getting this infection.

Research efforts are underway in order to monitor the cases of COVID-19 in patients with PID at a global scale.

Since the launch of the first survey 3 weeks ago, there are 15 cases (13/15 are under 45 years) reported (as of 2020, April 5th): 7 necessitating admission (including 2 with acute respiratory distress syndrome). Various kinds of PID diagnostic categories were found (phagocyte defects, combined immunodeficiency, antibody deficiencies, ALPS-like disease, and autoinflammatory disease). Almost all identified patients are aged <45 years. Typical presentation symptoms were reported as follows: upper respiratory symptoms, cough, fever. One child had diarrhea, vomiting and myalgia.

Since this week, a second-tier survey aimed at collecting more data is now open for entering cases. "COPID19" is the more detailed second phase of the worldwide survey of COVID-19 in PID patients and is directed to physicians who manage PID patients.

Recommendations for PID patients

Patients with PID living in areas of high prevalence should take every precaution and adhere to local, regional and national recommendations (staying at home, teleconsultation, work from home, etc..).

Beyond the precautions mentioned above, we advise prompt phone contact with a doctor if an infection is suspected (should it be your PID expert, or your GP who should let your PID expert know about your condition in order to provide the best advice for each PID patient's specific condition). Patients should always keep the details of their PID diagnosis and medical charts, medications, PID expert doctor and next of kin at hand, in case urgent medical care is needed.

PID patients with lung and/or heart complications, solid organ transplants' recipients, recent recipients of hematopoietic stem cell transplantation or gene therapy, PID patients undergoing treatment for a cancer (malignancy), as well as patients under immunosuppressive or immunomodulatory drugs (for autoimmune or inflammatory or autoinflammatory complicating the



PID course) should remain on their specific therapy until recommended otherwise by their PID expert physician. Immunosuppressive drugs (in particular corticosteroids), might limit signs of infections (fever and other clinical symptoms). It is this recommended to contact your PID expert physician in case of unexplained change in clinical status including your well-being.

PID patients with significant respiratory issues (severe asthma, bronchiectasis or chronic respiratory failure) should receive special attention (as for any risk of respiratory infection).

Keep in mind that it is always essential to continue the regular treatment for your PID.

Plasma Derived Medicinal Products (PDMPs), such as immunoglobulins (IVIG or SCIG) are safe and will protect you from many other infections.

For everyone, including PID patients, we strongly recommend you to keep up with the latest information on the COVID-19 outbreak in your region, for example provided by [the World Health Organization](#) (WHO), [the European Centre for Disease Prevention and Control](#) (ECDC) and by your national and local public health authorities.

National guidelines provided by national health authorities should be followed (the epidemiological situation and the management might differ from one country to another).

We want to stress that your PID expert can you give you the best personalized advice.

[Patients can visit the IPOPI website to have full access to the FAQ.](#)



Plasma Derived Medicinal Products (PDMPs), including Immunoglobulins

According to a statement from the Plasma Protein Therapeutics Association (PPTA) there is no risk of transmission of SARS-CoV-2 by **PDMPs**.¹⁰

Recently a study in China demonstrated the detection of SARS-CoV-2 RNA in blood donations¹¹, but it should be noted that this does not pose a risk to PID patients in terms of transmission via immunoglobulin therapies. The virus inactivation and removal steps during the manufacturing process of PDMPs ensure the safety of IG therapies.

For PID patients who are on Ig replacement therapy, there is no evidence to date that more frequent dosing of Ig will offer more protection. Whilst Ig replacement therapy provides protection against a range of infections, it does not guarantee immunity against coronavirus.

For PID patients whose condition does not require to be under regular Ig replacement therapy, there is no need to start Ig replacement therapy since no antibodies targeting COVID-19 are expected to be contained in the existing preparations.

There is no recommendation to give immunoglobulins to the general population to protect or treat people against COVID-19.

Decline in plasma supply

The COVID-19 outbreak and associated confinement and movement restriction measures will impact supply of blood and plasma collection and may affect medicinal product circulation and supply.

As the plasma necessary to produce PDMPs is either collected from plasma donors (apheresis plasma) but also from blood donations (recovered plasma), this will almost inevitably impact the access to these life-saving therapies, although it may take a few months before PDMPs shortages start to be observed (it usually takes 7-10 months from the time plasma is collected from a human donor to reach the patients).

Numerous countries have reported significant drops in blood collection and a similar development is expected for plasma collection.

Various PID stakeholders are currently taking measures to react to this development on both national and regional levels so that PID patients are prioritized in case of any supply tensions or shortages associated with the COVID-19 outbreak.

¹⁰ The Plasma Protein Therapeutics Association. New Coronavirus (SARS-CoV-2) and Plasma Protein Therapies. 03-04-2020. Available at: <https://www.pptaglobal.org/media-and-information/ppta-statements/1055-2019-novel-coronavirus-2019-ncov-and-plasma-protein-therapies> [Accessed 08-04-2020].

¹¹ Chang L, Zhao L, Gong H, Wang Lunan, Wang L. Severe acute respiratory syndrome coronavirus 2 RNA detected in blood donations. Emerg Infect Dis. 04-03-2020. <https://doi.org/10.3201/eid2607.200839> [Accessed 08-04-2020].



Supporting organisations

About IPOPI

IPOPI is the leading advocate for primary immunodeficiencies' patients worldwide working in collaboration with patients, doctors, politicians, regulators, pharmaceutical industry and other relevant stakeholders. IPOPI is the Association of national PID patient organisations currently representing 68 countries. More info: www.ipopi.org, [Facebook](#), [Twitter](#)

About ESID

The European Society for Immunodeficiencies (ESID) is a non-profit organization whose main objectives are to facilitate the exchange of ideas and information among doctors, nurses, biomedical investigators, patients and their families concerned with primary immunodeficiency diseases and to promote research on causes, mechanisms and treatment of these disorders. ESID was established as an informal group in 1983 and became a society in 1994. More info: www.esid.org, [Twitter](#)

About INGID

The aims of INGID are to improve and extend the quality of nursing care of patients with primary immune deficiencies, and to increase the awareness and understanding of primary immunodeficiencies amongst nurses. More info: www.ingid.org

About APSID

The Asia Pacific Society for Immunodeficiencies (APSID) works to provide PID care, education and research for PID patients, through collaborative infrastructure and various APSID Working Parties. A group of over 60 Asian paediatricians and scientists interested in Primary Immunodeficiency met in Osaka, April 2015 and pledged to establish APSID with the following missions: To care and cure patients with primary immunodeficiency (PID), To share PID experience so as to promote collaboration & education, To improve PID management through understanding its genetics & pathogenesis and To advocate and advance the care of PID patients through engaging governments, patient organizations & industry. More info: <https://paed.hku.hk/apsid/>

About ARAPID

ARAPID is the Arab Society for PID. Its purpose is to bring together the English-speaking east region of the Arab world, closer to the French-speaking west region, to better serve PID patients from the Arab world who are united by consanguinity, etiological profile of PIDs and culture (awareness). More info: www.arapid.org/en/

About ASID

The African Society for Immunodeficiency (ASID) is a PID focused scientific society. Its main objectives are to improve PID awareness and care within Africa and has been working on addressing continental African PID peculiarities. ASID strives to support African patients through collaborating with national and international patient groups and works with national societies and other relevant authorities to achieve its objectives. ASID also collaborates with international PID societies and alliances, and the industry to promote better PID care and research. More info: www.asid-africa.org



About CIS

The Clinical Immunology Society (CIS) is based in the United States but has members from around the globe. The mission of CIS is to facilitate education, translational research and novel approaches to therapy in clinical immunology and to promote excellence in the care of patients with immunologic/inflammatory disorders. More info: www.clinimmsoc.org

About LASID

The Latin American Society for Immunodeficiencies (LASID) is a vibrant and inclusive international society. This is the home of all professionals dedicated to the field of Primary Immunodeficiencies aiming to develop and perfect the education, scientific research, and health care within this medical specialty. LASID's mission comprises the following: To increase awareness in Primary Immunodeficiency Diseases (PIDD) at all levels all over the continent, to develop diagnostic capabilities to reach as many as possible patients and to favor the development of centers providing appropriate treatments for PIDD patients. More info: www.lasid.org

About SEAPID

South East Asia Primary Immunodeficiency Network or "SEAPID" is a regional NGO - the South East Asian network of Primary Immunodeficiency Experts. It was established in Bangkok, Thailand on 26th January 2015, following an accord reached by experts from the six South East Asian founding countries, namely, Indonesia, Malaysia, the Philippines, Singapore, Thailand and Vietnam.

About IUIS Inborn Errors of Immunity Committee (IEI)

The IEI Committee consists of experts in all aspects of primary immunodeficiencies. Its missions are: to provide an up-to-date classification of all primary immunodeficiency diseases (IEIs), to assist with the identification, diagnosis and management of patients with these uncommon conditions, to support diagnostic and therapeutic guidelines developed by national societies and others, to assist healthcare providers, to promote awareness, diagnosis and treatment of IEIs in all regions of the world, to produce ad hoc reports on any aspect of IEIs, to assist in the welfare of patients with these conditions. More info: www.iuis.org/committees/iei/

More resources:

Short videos by Prof. Kate Sullivan, member of the medical board of the Immune Deficiency Foundation (IDF)

<https://youtu.be/ydk-Q959RJY> (posted on 2020, March 3rd)

<https://youtu.be/3DUKPxgYaYc> (posted on 2020, March 10th)

<https://youtu.be/A7AIZ0HVOBA> (posted on 2020, March 18th)

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