

1 **Footnotes**

2 **Conflict of Interest:** The authors have declared no conflict of interest.

3 **Funding:** None.

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1 *Dear Editor,*

2 We have read with interest the article “Functional Antibody Responses to Severe Acute
3 Respiratory Syndrome Coronavirus 2 Variants in Children With Coronavirus Disease 2019,
4 Multisystem Inflammatory Syndrome in Children, and After Two Doses of BNT162b2
5 Vaccination” by Rostad et al [1]. The authors show in children that the BNT162b2 COVID-19
6 vaccine elicits higher neutralizing antibody responses than the infection itself with differences
7 among the various SARS-CoV-2 variants.

8 The incidence of COVID-19 worldwide has been far lower in children than in adults until
9 the appearance of the variant of concern B.1.1.529 (Omicron). Omicron has been shown to cause
10 a dramatic increase in pediatric infections and hospitalizations in comparison with the previous
11 variants [2, 3]. The higher infectivity of this Omicron variant has been attributed to mutations in
12 the spike glycoprotein-binding human ACE2, resulting in increased infectivity of nasal epithelial
13 cells and ACE2-positive cells [4]. These alterations in virus conformation influence antibody
14 neutralization and facilitate viral immune escape [4]. Although more contagious, the Omicron
15 variant was shown to lead to less severe forms of COVID-19 [5]. Although this was partly
16 attributed to COVID-19 vaccines in adults, similar milder severity was described in children
17 under 5 years old for whom no vaccine was available [6].

18 During the first year of the pandemic, the incidence of SARS-CoV-2 infection in people
19 with cystic fibrosis (pwCF) was shown to be low and far less than that expected in comparison
20 with the general population [7, 8]. Hypotheses were that pwCF use barriers such as wearing
21 masks, frequent hand washing and social distancing in order to limit exposure and avoid
22 infection. An international study during the first COVID wave in children with CF described a
23 low incidence of infections that led to mild illness, especially in children with non-severe pre-

1 existing lung disease [9]. In order to study the impact of the Omicron variant on children with
2 CF, we looked at what is happening in our pediatric CF center since the surge of the Omicron
3 variant. This observational study was approved by the local ethics committee of our institution,
4 which waived the need for patients' consent (Study PED_COVID N°20200717191204).

5 Seventy-six children with CF are currently followed in the pediatric CF center of the
6 University Hospital Trousseau, Assistance Publique Hôpitaux de Paris (APHP) Paris, France.
7 Before the Omicron wave (2020-2021), only 7 (9%) children had been identified as infected by
8 SARS-CoV-2 in our center; all remained asymptomatic and were diagnosed by a systematic
9 assessment of SARS-CoV-2 serology (**Table**). During the Omicron wave, 24 (32%) children
10 were identified as infected from January to July 2022, 2 of whom were re-infections. Four
11 children remained asymptomatic, all having received 2 doses of the BNT162b2 COVID-19
12 vaccine before the infection. Among the 24 children, 16 were older than 5 years, and 11 had
13 received at least one dose of the vaccine. Symptoms at infection onset were similar to those
14 described in the general population (**Table**). Five children were hospitalized for COVID-19, and
15 2 required oxygen but not intensive care.

16 This report emphasizes the high infection rate of the Omicron variant, even in a CF
17 population used to applying barrier measures to avoid infections. Moreover, this surge of
18 infections was unexpected given the previous low incidence of COVID-19 observed in pwCF [7,
19 8]. Nevertheless, children with CF who were vaccinated developed mild forms of COVID-19
20 and/or remained asymptomatic. Interestingly, all asymptomatic CF patients during the Omicron
21 wave were children who were vaccinated. This report supports efforts to expand vaccination
22 against COVID-19 in children for whom the BNT162b2 COVID-19 vaccine has been shown to be
23 safe and to elicit high neutralizing antibody response [1, 10].

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8 **Table. Children with cystic fibrosis diagnosed as infected by SARS-CoV-2 before and**
9 **during the Omicron wave in a pediatric French CF center**

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1 **Table. Children with cystic fibrosis diagnosed as infected by SARS-CoV-2 before and**
 2 **during the Omicron wave in a pediatric French CF center**

3

	Before the Omicron Wave (2020-2021)	During the Omicron Wave (2022)
Patients (n, % among the 76 children with CF followed in the center)	7 (9%)	24 (32%)
<i>Clinical characteristics</i>		
Age (years): median (range)	6.8 (4.6;14.1)	9.7 (0.3;18)
Age class (n) (<5 yrs / 5-11 yrs / > 11 yrs)	2/3/2	8/5/11
Male (n, %)	6 (86%)	11 (46%)
<i>SARS-CoV-2 infection diagnostic</i>		
Positive systematic serology (n, %)	7 (100%)	3 (12.5%)
Positive PCR and/or antigenic test in nasopharyngeal swabs (n, %)	0	24 (100%)
<i>Asymptomatic</i> (n, %)	7 (100%)	4 (17%)
<i>Clinical presentation at infection onset</i>		
Fever (n, %)	0	14 (58%)
Fatigue (n, %)	0	13 (54%)
Altered cough (n, %)	0	9 (38%)
Rhinorrhea (n, %)	0	10 (42%)
Dyspnea (n, %)	0	5 (21%)
<i>Hospitalization</i> (n, %)	0	4 (17%)

Hospitalization duration (days): median (range)	0	5 (4;14)
Oxygen supplementation (n, %)	0	2 (11%)

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Date: July 20, 2022

Your Name: Guillaume THOUVENIN

Manuscript Title: The omicron wave modifies the COVID-19 paradigm in children with cystic fibrosis

Manuscript number (if known): _____

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In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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Date: July 20, 2022

Your Name: Blandine PREVOST

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Date: July 20, 2022

Your Name: Harriet CORVOL

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