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SARS-CoV-2 transmission among children and care staff in daycare centres during lockdown: a cross-sectional, multicentre seroprevalence study in France.

Authors
Eric Lachassinne[1], MD; Loïc de Pontual[1] , PhD; Marion Caseris[2], MD; Mathie Lorrot[3,4], PhD; Carole Guilluy[5], MD; Aurélie Naud[6], MD; Marie-Aliette Dommergues[7], MD; Didier Pinquier[8], MD; Evelyne Wannepain[9], MD; Elisabeth Hausherr[10], MD; Camille Jung[11,12], MD; Vincent Gajdos[13], PhD; Robert Cohen[14], PhD; Jean-Ralph Zahar[15], PhD; Ségolène Brichler[16], PhD; Romain Basmaci[5], PhD; Pierre-Yves Boelle[17], PhD; Coralie Bloch-Queyrat[18*], PhD; Camille Aupiais[1,19*], PhD.

* Contributed equally to this work

Affiliations
[1] Université Paris 13, Sorbonne Paris cité, AP-HP, Hôpital Jean Verdier, Service de Pédiatrie, F-93140 Bondy, France.
[2]AP-HP, Hôpital Robert Debré, Service de Pédiatrie générale, Paris, France
[3] Sorbonne Université, AP-HP, Hôpital Armand Trousseau, Service de Pédiatrie, Paris, France
[4] Inserm, U1123, ECEVE, 10 avenue de Verdun, F-75010 Paris, France
[5] Université de Paris, AP-HP, Hôpital Louis Mourier, Service de Pédiatrie-Urgences, F-92700, Colombes, France
[6] Service de Pédiatrie, Hôpital Annecy Genevois, Annecy, France
[7] Service de Pédiatrie, Hôpital André Mignot, Versailles, France
[8] Service de Pédiatrie Néonatale et Réanimation, CHU de Rouen, Rouen, France
[9] Service de la Protection Maternelle et Infantile, Conseil Départemental de Seine Saint Denis, Bobigny, France
[10] Service de la Protection Maternelle et Infantile, Ville de Paris, Paris, France
[11] Centre de recherche clinique-centre de Ressources biologiques, CHI Créteil, Créteil, France
[12] Service de pédiatrie Générale, CHI Créteil, Créteil, France
[13] Université Paris-Saclay, AP-HP, Hôpital Antoine Béclère, Service de Pédiatrie, Clamart, France.
[14] Groupe de Pathologies infectieuses, Association clinique et thérapeutique infantile du Val-de-Marne, ACTIV, Saint-Maur-des- Fossés, France
[15] Université Paris 13, Sorbonne Paris cité, AP-HP, Hôpital Avicenne, Unité de Prévention du Risque Infectieux, Laboratoire de Microbiologie Clinique, Bobigny, France
[16] Université Paris 13, Sorbonne Paris cité, AP-HP, Hôpital Avicenne, Laboratoire de virologie, Bobigny, France
[17] Sorbonne Université, Institut Pierre Louis d'Épidémiologie et de Santé Publique, AP-HP, Hôpital Saint-Antoine, Paris, France
[18] Université Paris 13, Sorbonne Paris cité, INSERM U1163/CNRS ERL 8254, AP-HP, Hôpital Avicenne, URC-CRC GHPSS, Bobigny, France
[19] Inserm, U1138, Équipe 22, Centre de Recherche des Cordeliers, Sorbonne Université, 15 rue de l'École de médecine, F-75006 Paris, France.

Corresponding author: Camille Aupiais, Jean Verdier Hospital, avenue du 14 juillet, F-93143 Bondy cedex, France; e-mail: camille.aupiais@aphp.fr; Tel.: +33-148-026-454; Fax: +33-144-495-150

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Abstract

Background. It is not known whether very young children contribute to the transmission of coronavirus disease 2019 (COVID-19). Determining the seroprevalence of antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in daycare centres that remained open for key workers' children during a period of lockdown might provide data in this respect.

Methods. Between June 4th and July 3rd, 2020, children and staff having attended one of 22 daycare centres during France's nationwide lockdown (from March 15th to May 9th, 2020) were prospectively included. Hospital staff not occupationally exposed to patients and/or children were enrolled in a comparator group. The presence of anti-SARS-CoV-2 antibodies in capillary whole blood was determined using a rapid chromatographic immunoassay. We computed the raw prevalence as the percentage of individuals with a positive IgG or IgM test, and used Bayesian smoothing to account for imperfect assay sensitivity and specificity.

Findings. We enrolled 327 children (mean ± standard deviation age: 1.9 ± 0.9 years), 197 daycare staff, and 164 adults in the comparator group. Positive serological tests were observed for 14 children (raw prevalence [95% confidence interval] = 4.3% [2.6, 7.1]) and 14 daycare staff (7.7% [4.2, 11.6]). After accounting for imperfect assay sensitivity and specificity, we estimated that 3.7% (95% credible interval [1.3, 6.8]) of the children and 6.8% [3.2, 11.6] of the staff had been infected with SARS-CoV-2. The comparator group fared similarly to the daycare staff with 5.5% [2.9, 10.1] testing positive leading to 5.0% [1.6, 9.8] infection rate after accounting for assay characteristics (p=0,53). An exploratory analysis suggested that seropositive children were more likely than seronegative children to have been exposed to an adult household member with confirmed COVID-19 infection (43% vs. 6%, respectively, RR=7.1 [2.2, 22.4]).

Interpretation. According to serological test results, the proportion of infected children was low. Intrafamily transmission seemed more plausible than transmission within daycare centres. Further epidemiological studies are needed to confirm this exploratory hypothesis.

Funding. Assistance Publique - Hôpitaux de Paris; Mairie de Paris, Conseil Départemental de Seine Saint Denis.

French langage version of the abstract (Résumé)

Contexte. Le rôle des très jeunes enfants dans la transmission de la maladie à coronavirus 2019 (COVID-19) est encore incertain. La description de la séroprévalence des anticorps contre le coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2) dans les crèches restées ouvertes pour accueillir les enfants des travailleurs essentiels pendant la période de confinement pourrait fournir des informations à cet égard.

Méthodes. Entre le 4 juin et le 3 juillet 2020, les enfants et le personnel qui avaient fréquenté l'une des 22 crèches pendant le confinement national de la France (du 15 mars au 9 mai 2020) ont été inclus de manière prospective. Un groupe comparateur comprenait des personnels hospitaliers non exposés professionnellement aux patients et/ou aux enfants. La présence d'anticorps anti-SRAS-CoV-2 dans le sang total capillaire a été déterminée via un test sérologique immunochromatographique rapide. La séroprévalence brute est exprimée sous forme du pourcentage d'individus avec un test positif en IgG ou IgM. Une méthode de lissage bayésien est utilisée pour tenir compte de la sensibilité et de la spécificité imparfaites du test.

Résultats. Nous avons recruté 327 enfants (âge moyen ± écart-type: 1,9 ± 0,9 ans), 197 membres du personnel soignant et 164 adultes dans le groupe comparateur. Les tests sérologiques étaient positifs chez 14 enfants (prévalence brute [intervalle de confiance à 95%] = 4,3% [2,6, 7,1]) et 14 membres du personnel de crèche (7,7% [4,2, 11,6]). Après avoir pris en compte la sensibilité et la spécificité du test, il est estimé que 3,7% (intervalle de crédibilité à 95% [1,3, 6,8]) des enfants et 6,8% [3,2, 11,6] du personnel avaient été infectés par le SRAS-CoV-2. Les résultats étaient similaires dans le groupe comparateur avec une séroprévalence de 5,5% [2,9, 10,1], et un taux d'infection estimé à 5,0% [1,6, 9,8] après prise en compte des caractéristiques intrinsèques du test (p=0,53). Une analyse exploratoire a suggéré que les enfants séropositifs étaient plus susceptibles que les enfants séronégatifs d'avoir été exposés à domicile à un adulte avec une infection confirmée au COVID-19 (43% contre 6%, respectivement, RR = 7,1 [2,2, 22,4]).

Interprétation. Selon les résultats des tests sérologiques, la proportion d'enfants ayant été infectés était faible. Une contamination intrafamiliale est plus plausible qu'une transmission au sein des crèches, bien que cette hypothèse nécessite d'être confirmée par d'autres études épidémiologiques.

Financement. Assistance Publique - Hôpitaux de Paris; Mairie de Paris.

Research in context

Evidence before this study

We searched PubMed and the preprint server *medRxiv* on December 7th , 2020, using the terms ["COVID-19" or "SARS-CoV-2"], ["child*" or "pediatric*"], and ["seroprevalence" or "sero-prevalence" or ("prevalence" and "antibodies") or "seroepidemiology"] for population-screening studies describing the seroprevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection that includes children. There were no language limitations. References cited by the systematic reviews were also checked. After an assessment of the abstracts, 28 publications on population-based studies were finally identified. Four of the studies had estimated the seroprevalence in children aged 5 years or less. In a national population-based study of 35883 households in Spain, the seroprevalence [95% confidence interval (CI)] according to a point-of-care test was 1.1% [0.3%-3.5%] in infants below the age of 1 year and 2.1% [1.3%-3.4%] in children aged 1-4 years. The three other studies were conducted in Brazil, the USA, and Iran; the estimated seroprevalence [95%CI] in children aged under 4 or 5 was 1.6% [0.5%-3.0%], 0% and 20% [13%-29%], respectively.

None of these studies focused on daycare centres. However, the safety of daycare and school reopening and the role of young children in epidemic spreading are subject to debate.

We completed our search by using the terms ["COVID-19" or "SARS-CoV-2"] and ["daycare" or "nursery"] to identify publications describing SARS-CoV-2 infection in daycare centres. Two publications were identified. The first was a SARS-CoV-2 carriage study. The researchers did not find any SARS-CoV-2-positive samples between February 29th and March 18th, 2020. The second was a description of the characteristics of a cluster associated with a single nursery in Poland. The cluster's overall PCR positivity rate was 27%.

Added value of this study

Our study was designed at the end of the first wave of the coronavirus disease 2019 (COVID-19) epidemic in France, in May 2020. To the best of our knowledge, this was the first multicentre study of seroprevalence in daycare centres. We believe that estimating the seroprevalence in very young children and staff attending daycare centres that remained open during the French nationwide lockdown could help to understand to what extent young children contribute to the spread of SARS-CoV-2 infections. The study took place in June 2020 - between four and eight weeks after the end of the lockdown.

Based on serological results, we found that the proportion of children having been infected was low. In an exploratory analysis, the seropositivity rate among daycare staff did not differ from that observed in a comparator group of adult hospital workers not exposed to children. The main factor associated with SARS-CoV-2 seropositivity in children was contact with an adult household member with confirmed COVID-19.

Implications of all the available evidence

There is no evidence for daycare centres being major foci of viral contagion. Further sero-epidemiological studies are needed to (i) determine the incidence and/or prevalence of SARS-

CoV-2 infection among children and (ii) assess the role that children may have in transmission of the virus.

Introduction

Although severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects people of all ages, the current literature data show that children (i.e. individuals aged 17 or under) account for only 1 to 8% of laboratory-confirmed cases of coronavirus disease 2019 (COVID-19) (1–5) and for 2 to 4% of hospitalized patients (5,6). Furthermore, children rarely require hospitalization (4,7), admission to an intensive care unit, oxygen therapy, or ventilation (8,9).

The burden of infection among children is therefore difficult to assess if testing is focused on symptomatic or hospitalized patients. Population screening studies that estimate the seroprevalence (indicating prior infection) are therefore useful in this context. To the best of our knowledge, few studies have estimated the seroprevalence in children, and only four described a subgroup of pre-school children (10–13). None of the published studies have focused on the seroprevalence in daycare centres.

The extent to which children (whether symptomatic or not) contribute to the transmission of COVID-19 remains to be determined. At the beginning of the COVID-19 pandemic, children were considered to be potential vectors of transmission because they are known to contribute strongly to the spread of respiratory diseases like seasonal influenza (14,15). This led to the adoption of preventive measures (including school closures) in many countries. The results of several epidemiological studies suggested that (i) children were not the primary drivers of COVID-19 in their community (16–18), (ii) children were rarely the index case in their households (19), (iii) children are less sensitive to SARS-CoV-2, with an odds-ratio of 0.56 for being an infected contact (compared with adults) in a recent meta-analysis (20), and (iv) the rates of SARS-CoV-2 transmission are low in schools and child care settings (21). However, the meta-analysis showed that the population-level evidence whereby children and adolescents have a lesser role than adults in the transmission of SARS-CoV-2 is still weak (20).

In France, a nationwide lockdown was enforced from March 17th to May 11th, 2020, in order to reduce the burden of COVID-19 on the healthcare system. Most daycare centres and all schools were closed during this period. The small number of daycare centres that remained open were for children whose parents had to work during the COVID-19 crisis (i.e. healthcare professionals and other essential workers). Special precautions were adopted in these daycare centres: use of face masks by the staff, smaller, defined groups of children and staff, the systematic measurement of body temperatures, the exclusion of children who became feverish or ill, and reinforced hygiene and distancing measures.

The primary objective of the present study was to estimate the seroprevalence of SARS-CoV-2 antibodies in children and staff in the daycare centres that remained open during the lockdown in the Paris region (the most affected region in France) and in two other French cities with a lower incidence (Rouen in Normandy, and Annecy in the Alps). The secondary objective was to compare the seroprevalence among daycare staff with that measured in a comparator arm of hospital workers with no occupational exposure to children. The study was carried out between four and eight weeks after the end of the national lockdown.

Patients and Methods

Study design and participants

We conducted a prospective multicentre study in 22 daycare centres located in the Paris region (n=20) and in the French cities of Annecy (n=1) and Rouen (n=1). The daycare centres were operated by a local authority (n=10) or a public-sector hospital (n=12). Children attending one of the 22 daycare centres during all or part of the lockdown (from March 15th to May 9th, 2020) were eligible for inclusion, as were the daycare staff who worked in the daycare centres during the same period. In each centre, we invited all the daycare staff and all the children's parents to participate in the study. Recruitment was stopped after the planned number of participants (see below) had been included. The comparator group (for the daycare staff) comprised hospital staff who (i) kept working during the lockdown, (ii) were not occupationally exposed to infants, and (iii) were not directly exposed to COVID-19 patients. To this end, we recruited a sample of laboratory and administrative staff from six hospitals.

Primary and secondary outcomes

The primary outcome was SARS-CoV-2 seroprevalence in the three study groups. The secondary outcomes were the proportions of children with a positive nasopharyngeal swab, or stool swab, in a SARS-CoV-2 RT-PCR test. The exploratory outcomes were factors associated with SARS-CoV-2 infection in the children or in the adults (sex, age, medical history, history of symptoms and RT-PCR testing during the lockdown, composition of the family, contact with confirmed or suspected COVID-19 cases, number of days of attendance or work, occupations of the parents/partner, and the parents' serological status).

Procedures

Inclusions were processed between June 4th and July 3rd, 2020. An electronic case report form was completed on the day of inclusion. Data on sociodemographic variables, occupation, any personal history of infection, contact with confirmed or suspected COVID-19 cases, clinical symptoms and signs, and prior nasopharyngeal-swab RT-PCR results (if available) were recorded. Data on the daycare centres' general characteristics were also recorded (geographic location, number of children attending during the lockdown, number of staff, and the number of confirmed cases among the children and staff).

Paediatricians collected capillary whole blood specimens (fingersticks) for testing with a rapid chromatographic immunoassay (Biosynex COVID-19 Ag BSS, Biosynex, Illkirch-Graffenstaden, France) that qualitatively detects IgG and IgM antibodies against SARS-CoV-2. The test had been approved by the French national health authorities. According to the manufacturer's specifications, the diagnostic test's sensitivity [95% confidence interval (CI)] is 91.8% [83.8-96.6] and its specificity is 99.2% [97.7-99.8]. Tests were considered to be valid only if the control line was present. Positive and negative serologies were defined respectively as the presence and absence of IgM and/or IgG. The result was given to the parents as soon as it was available.

A nasopharyngeal swab and a stool swab for the RT-PCR detection of SARS-CoV-2 were obtained for the children of parents having given their consent. Nasopharyngeal samples were collected with small swabs suitable for children and stored in transport buffer for molecular testing. Stool samples were collected with a swab directly from the children's nappies or using an anal swab and were then conserved in transport buffer. Samples were stored at +4°C if testing was scheduled in the following 1 to 3 days or at -80°C if testing was scheduled at a later date. The SARS-CoV-2 RT-PCR test was performed either (i) locally with various techniques validated by the French national health authority and applied on a routine basis for hospital samples (n=248) or (ii) in a centralized procedure in a hospital (Avicenne Hospital, Bobigny, France) laboratory (n=221, using the Abbott RealTime SARS-CoV-2 assay on a

m2000 device (Abbott, Rungis, France), according to the manufacturer's instructions). In line with international guidelines, all the techniques used in the present study detected at least two specific targets for SARS-CoV-2 strains and featured an internal quality control for the extraction and amplification steps. If an invalid result was obtained, stool samples were diluted five-fold (to remove potential polymerase inhibitors) and retested.

Occupations of the parents/partner

For the children's parents and the adult participants' partners, we defined three risk classes for occupational exposure to SARS-CoV-2: (i) healthcare professionals working in dedicated COVID-19 units, (ii) healthcare professionals not working in dedicated COVID-19 units, and (iii) other occupations.

Serological testing of parents

All parents who worked in a hospital underwent serological testing (an ELISA based on the detection of IgGs or total Igs against SARS-CoV-2) in May and June 2020, as part of a local campaign. The results were collected retrospectively in August 2020.

Sample size calculation

According to modelling studies, the estimated cumulative incidence in the general population in the Paris region at the time of the present research was 10% (22). We calculated that the inclusion of 150 or 320 participants would enable the detection of an increase in the seroprevalence (relative to the general population) of 75% (i.e. a seroprevalence of 17.5%) or 50% (i.e. a seroprevalence of 15%), respectively, with a power of 80%. For feasibility reasons, we decided to include 320 children, 150 daycare staff, and 150 adult comparators. Although it was not computed for this reason, the sample size of 150 adults would enable the detection of a 100% increase in the seroprevalence for daycare staff (relative to comparators), with a power of 70%.

Statistical analysis

The raw prevalence rate was computed as the percentage of tested participants with IgGs or IgMs against SARS-CoV-2. We used Bayesian smoothing to account for imperfect sensibility and specificity (23).
In an exploratory analysis, we used a chi-squared test, Fisher's exact test or Wilcoxon's test to compare the participants' characteristics as a function of their serological status. We compared the seronegative children with the seropositive children as a function of the parents' serological status. The relative risk (RR) of a positive serology in children was computed according to whether or not they had been in contact with seropositive adults. We used logistic regression to compute the odds ratio (OR) of occupational status (daycare workers relative to other occupations) after adjustment for age, sex, and contact with a known COVID-19 case. The threshold for statistical significance was set to $p<0.05$. All tests were two-sided. Statistical analyses were performed with R software (version 4.0) (24).

Ethics

The study protocol was approved by an independent ethics committee (CPP IDF III, Paris, France; reference: 2020-AO1540-39). The daycare workers, the adults in the comparators group, and the children's parents were given information about the study's goals and

procedures and provided their written consent to participation. The study was registered at ClinicalTrials.gov (NCT04413968).

Role of the funding source

The study was funded by the *Fondation de l'Assistance Publique - Hôpitaux de Paris pour la recherche* research foundation (Paris, France), by the Paris City Council (*Mairie de Paris,* Paris, France) and by the Seine Saint Denis county (*Conseil Départemental de Seine Saint Denis*, Bobigny, France). The funding bodies were not involved in the study design, collection, analysis, and interpretation of data, the writing of the report or the decision to submit the manuscript for publication The views expressed are those of the authors and not necessarily those of the funding bodies. EL, CA, PYB and CB had full access to all of the data. All authors had the final responsibility for the decision to submit the manuscript for publication.

Results

Twenty-two daycare centres participated in the study: 12 (56%) were operated by a public-sector hospital and ten (44%) were operated by a local council. During the lockdown, the number of children attending each centre per day ranged from eight to 56 (median [interquartile range]: 24 [23-28]).

Results for the primary outcome

The estimate seroprevalence rates [95% credibility interval] (4.3% [2.6, 7.1] among the children and 7.7% [4.2, 11.6] among the daycare staff) are shown in Table 1; after adjustment for imperfect test sensitivity and specificity, these values were respectively 3.7% [1.3, 6.8] and 6.8% [3.2, 11.5]. None of the 197 nasal swabs and none of the 261 stool swabs were positive in a SARS-CoV-2 RT-PCR test.

Description of the children

The eligible population corresponded to 1008 children attending the 22 daycare centres between March 15th and May 9th, 2020, and 327 (32.4%) were included in the study. In accordance with the sample size requirements, we included the first 327 (32.4%) children whose parents consented to the study (Figure 1). The mean ± standard deviation (SD) age was 1.9 ± 0.9 years (range: 5 months – 4.4 years), and 167 of the 327 children (51%) were male. On inclusion, 243 (77%) of the 314 children with data on the presence or absence of symptoms were asymptomatic (Supplemental Table). The children's characteristics by serological status are summarized in Table 2. Contact with a confirmed adult household case of COVID-19 during the lockdown was more frequent in seropositive children than in seronegative children (RR=7.1 [2.2, 22.4]). There were no other large differences between the seropositive and seronegative groups. Importantly, the presence of clinical signs during lockdown and exclusion from the daycare centre were not associated with seropositivity. The 14 seropositive children came from 13 different daycare centres. In the centre with two seropositive cases, the latter were attending different sections. Six of the 14 seropositive children (43%) were asymptomatic during the lockdown, and eight (57%) had minor or mild signs of infection (fever, rhinitis, cough, and/or abdominal signs). Serological test results for at least one parent were available for 170 children (Table 2), and 28 of these children (17%) had at least one seropositive parent. Of the eight children with a positive serology, symptoms

during the lockdown, and seropositive parents, five presented symptoms after their parent(s) did (4 to 10 days after, to be precise).
Seropositive children were more likely to have at least one seropositive parent (55% vs. 14% of the seronegative children; RR=6.1 [1.9, 19.1]). The RR for attending a daycare centre with at least one seropositive staff member was 1.9 [0.6, 5.8].

Description of the daycare staff members

The 197 daycare staff members (including 195 women (99%)) came from 19 daycare centres. The mean ± SD age was 40 ± 12. On inclusion, none of the 185 daycare staff with data on the presence or absence of symptoms were feverish, and 40 out of 186 reported symptoms (20%, Supplemental Table). There was no increase in risk for exposure to a child with confirmed COVID-19, but the relative risk of contact with an adult COVID-19 case was large (RR=13.1 [0.8, 221.1]). The 14 seropositive daycare staff came from eight different daycare centres. There were two centres with three seropositive staff members.

Description of the comparator group

The mean ± SD age of the 164 participants in the comparator group (including 127 women (77%)) was 42 ± 12. On inclusion, one of the 160 participants with data on the presence or absence of symptoms was feverish, and 20 reported acute symptoms (12%, Supplemental Table). Seropositive adults in the comparator group were more likely than seronegative adults to have been exposed to a partner with confirmed COVID-19 (Table 3, RR=17.2 [2.1, 140.8]).

Comparison of the seropositivity in daycare staff vs. the comparator group

The seroprevalence rate among daycare staff was similar to that in the comparator group (6.8% vs 5.0% [1.6, 9.8] after correction). The OR for "daycare staff" as occupation for a positive serological status with respect to the comparator group was 1.5 [0.6, 3.9], after adjustment on age, sex and contact with a known COVID-19 case.

DISCUSSION

Our present results highlighted the low SARS-CoV-2 seroprevalence rate among a group of young children attending daycare centres during the French lockdown. The seroprevalence rate among the children was lower than that reported by various investigators for the general population in the same period in the Paris area (10% [9-11](25), 9% [7-11%] (26), and 7% [5-9] (27)), while the rate among the adult participants was similar. This finding is in line with previous studies in which the risk of infection was lower among children than among adults (20,28). No seroprevalence estimates have been reported for infants in the Paris area. However, the French national seroprevalence rate among children under the age of 9 (1.6%) was approximately half that seen in adults (3.3% (27)), which is in line with our results. Moreover, the seroprevalence rate among the daycare centre staff did not differ from that observed in a group of professionals who did not have occupational contact with children.

The group of children studied here was supposedly at high risk of being infected by household members (primarily their parents) because of the latter's occupations (healthcare workers or other essential workers potentially exposed to SARS-CoV-2). Grouping these children together in a daycare centre during the COVID-19 epidemic was necessary but raised fears of accentuated transmission. Although the virus circulated actively during the lockdown, contact with other children and adults was limited to household members, and strict sanitary measures

were introduced and enforced in the daycare centres. A protocol for hosting key workers' children in daycare centres was set up. The children were hosted in small, unchanging groups of 6 to 8 infants per section; the same children were looked after by the same daycare staff all week long. Daycare centre staff had to disinfect indoor surfaces, wear a mask all day long, and comply with social distancing measures - particularly during the lunch break. Parents were instructed how to screen their children for symptoms that would have prohibited access to the daycare centre and were not allowed to enter the daycare centre. Children were excluded from the daycare centre if they were symptomatic. Compliance with these guidelines was not easy but our results suggest that the measures were effective in this particular population. Our results also suggest that exposure to infected children did not result in an increased risk of infection among daycare staff, when compared with occupationally unexposed adults. Most of the adults were asymptomatic or had minor or mild symptoms during the lockdown. An exploratory analysis comparing seronegative and seropositive adults suggested that the latter had mostly been infected by their partner.

We did not find any evidence of SARS-CoV-2 transmission within daycare centres. By combining PCR testing with serological testing, we were able to evaluate not only infection at the time of inclusion but also previous exposure to SARS-CoV-2. None of the children having attended a daycare centre for all or part of the lockdown period tested positive for SARS-CoV-2 RNA; hence, none of the children studied here had prolonged or asymptomatic carriage. This finding was in line with the low frequency of symptoms at inclusion (i.e. on the day when the sample was collected). SARS-CoV-2 RNA was never detected in stool samples or anal swabs, even though it has been suggested that the virus persists for longer in stools than in the nasopharynx (29,30).

Based on the parents' reports, a high proportion of the seropositive children (six out of 14) did not present symptoms of COVID-19, and the remaining eight had only minor or mild symptoms. In exploratory analyses, the presence of symptoms (of any type and at any time) seems to be not associated with the children's serological status andthe main factor associated with SARS-CoV-2 seropositivity in a child was contact with a confirmed case of COVID-19. This association was found only for adult household members and not for siblings or contacts in the daycare centre (i.e. child-to-child or staff-to-child contact). SARS-CoV-2 seropositivity seems also to be associated with (i) contact with a suspected but non-confirmed case of COVID-19 in an adult household member (results not shown), and (ii) the presence of at least one seropositive parent. The association appeared to be independent of the parents' level of occupational exposure to SARS-CoV-2. Moreover, we found that the 14 seropositive children were broadly distributed across 13 different centres) and that seropositivity among the children was not associated with the duration of exposure (i.e. the number of days attending the daycare centre) or the seropositivity of the daycare staff. All those exploratory analyses constitute additional arguments for intrafamilial transmission rather than transmission at the daycare centre. Our results are in line with a previous report of very few cases of secondary SARS-CoV-2 transmission in a primary school setting (17). The literature data indicate that children mostly contract COVID-19 at home or through contact with other family members (7,8,16,28,31). These data must be interpreted with caution, however, since the studies were performed in countries where schools were closed and strict physical distancing was implemented. Our present results suggest that young children contract COVID-19 at home even when they attend a daycare centre.

Our study had several limitations. Firstly, our method for selecting participants might have biased our results. If confirmed cases had declined to participate, our study would have underestimated the seroprevalence rate. Conversely, if the participating children or adults had

more contact with confirmed or suspected cases or were more frequently suspected of having COVID-19, our study would have overestimated the prevalence rate. We did not document the characteristics of non-participating children and staff or the reasons why some parents did not wish their child to participate (e.g. fear of an invasive procedure), even though the daycare staff were particularly aware of the value of this type of research during and after the epidemic period.

We chose to use a rapid fingertip serological test for its ease of performance and rapid response. This helped to ensure a relatively high participation rate among the children. However, the rapid test is less sensitive and less specific than a laboratory test. Hence, we adjusted the prevalence rate for imperfect sensitivity and specificity. This correction yielded COVID-19 seroprevalence estimates in adults that were slightly lower than those recorded in the general population in the Paris area (25–27). Lastly, screening children for an ongoing SARS-CoV-2 infection was difficult because 40% of the parents did not consent to the collection of a nasopharyngeal swab. A validated, non-invasive, rapid diagnostic test would be particularly useful.

The study population had a number of particular features. As mentioned above, the participating children were primarily at higher risk of intrafamily transmission due to their parents' occupational exposure to COVID-19. Furthermore, the child:staff ratio was lower during the lockdown, so that rigorous sanitary measures could be implemented for the staff, the parents and the children. Unfortunately, we did not measure the levels of compliance with these procedures. Consequently, our results cannot be directly transposed to other populations and other periods.

To investigate occupational contacts with children as a source of COVID-19 exposure among daycare staff, we tried to account for exposure in places other than the household (e.g. travelling to work, and the overall hospital environment) by selecting comparators who had similar but distinct occupational backgrounds. Therefore, our comparator group comprised hospital staff (i) with a similar age range, (ii) who kept working in the hospital during the national lockdown, and (iii) who were not in direct contact with COVID-19 patients. We determined that laboratory technicians and administrative staff fulfilled these requirements. In the end, the seroprevalence estimates in the daycare and comparator groups were similar, and there was no evidence of a strong association between SARS-CoV-2 seropositivity and occupational contact with infants. This finding is in line with the previous studies in which daycare workers whose centres remained open did not have a greater risk of COVID-19 than daycare workers whose centres closed (32).

The present results showed that young children are not SARS-CoV-2 "super spreaders" and that daycare centres are not major foci of viral contagion. Intrafamily transmission was more plausible than transmission within daycare centres. Our exploratory comparison of seropositive and seronegative children suggested that clinical signs are not good decision criteria for PCR testing and that the main criterion should be a suspected or confirmed case in an adult household member. However, further epidemiological studies are needed to confirm this hypothesis. The detection of a PCR- or seropositive child in a daycare centre does not mean that all the children should be tested. Contact tracing and screening tests must start with the parents, other adult household members, and the daycare centre's staff. Further sero-epidemiological studies are needed to determine the extent of SARS-CoV-2 infection among children and to define their role in viral transmission.

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Authors' contributions

EL conceived the concept of this study, designed the study, acquired the data, interpreted the results, and drafted the manuscript. LDP conceived and designed the study, interpreted the results and drafted the manuscript. MC, ML, RB, CG, AN, MDG, DP, EW, EH, CJ, VG, JRZ and SB acquired the data and critically reviewed and made substantial contributions to the manuscript. RC conceived the study and critically reviewed and made substantial contributions to the manuscript. PYB designed the study, carried out the analyses, interpreted the results, critically reviewed and made substantial contributions to the manuscript. CBQ designed the study, acquired the data, interpreted the results and critically reviewed and made substantial contributions to the manuscript. CA designed the study, acquired the data, carried out the analyses, interpreted the results, drafted and revised the manuscript. All authors have seen, commented on and approved the final manuscript.

Declaration of interests

Dr Lachassinne, Professor De Pontual, Dr Caseris, Professor Lorrot, Dr Guilluy, Dr Naud, Dr Pinquier, Dr Wannepain, Dr Hausherr, Professor Gajdos, Dr Brichler, Professor Basmaci, Professor Boelle, Dr Bloch-Queyrat and Dr Aupiais have nothing to disclose; Dr Dommergues reports grants and personal fees from GSK, grants and personal fees from MSD, grants and personal fees from Pfizer, personal fees from Sanofi, outside the submitted work; Dr Jung reports grants from AP-HP, during the conduct of the study; personal fees from NOVALAC, personal fees from NESTLE, personal fees from ADARE, outside the submitted work; Professor Cohen reports grants and personal fees from GSK, grants and personal fees from MSD, grants and personal fees from Pfizer, grants and personal fees from null, outside the submitted work; Professor Zahar reports grants, personal fees and non-financial support from MSD, personal fees and non-financial support from Pfizer, personal fees from Correvio, outside the submitted work.

Sharing data agreement

We are prepared to share the study data (in strict compliance with the French legislation on personnel data) upon request to CBQ (coralie.bloch-queyrat@aphp.fr).

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Table 1. Estimated prevalence of SARS-CoV-2 infection in the study groups

	Children attending daycare centres N = 327	Daycare centre staff N = 197	Comparator group N = 164
Serological assay (n,%))			
Positive for Igs	14 (4.3%)	14 (7.1%)	9 (5.5%)
Positive for IgGs	13 (3.9%)	14 (7.1%)	8 (4.9%)
Positive for IgMs	2 (0.6%)	5 (2.5%)	4 (2.4%)
Raw prevalence [95%CI]	4.3% [2.6, 7.1]	7.7% [4.2, 11.6]	5.5% [2.9, 10.1]
Corrected prevalence [95%CrI] *	3.7% [1.3, 6.8]	6.8% [3.2, 11.5]	5.0% [1.6, 9.8]

* Assuming a sensitivity of 92% and a specificity of 99%.
CI: confidence Interval, CrI: credible interval.

Table 2. Characteristics of the screened children, by serological status.

	N	Seronegative (N=313)	Seropositive (N=14)	Relative risk/ Mean difference (95% CI)
Sex, male	327	51% (n=158)	64% (n=9)	1.3 [0.4, 3.9]
Age, mean ± SD (years)	327	1.9±0.9	1.7±0.8	-0.2 [-0.6, 0.2]
History of recurrent bronchiolitis or asthma	326	28% (n=86)	21% (n=3)	0.8 [0.2, 2.9]
Gestational age at birth, mean ± SD (weeks)	321	39±1.7	39±1.9	0 [-1, 1]
Birthweight, mean ± SD z-score	320	-0.05±1.04	-0.07±0.91	0 [-0.5, 0.5]
Able to walk	325	73% (n=227)	71% (n=10)	1.0 [0.3, 3.2]
Attendance at another type of care facility	326	20% (n=61)	14% (n=2)	0.7 [0.2, 3.4]
Number of adults at home	327	2.0±0.6	2.1±0.6	0.1 [-0.2, 0.4]
Number of children at home (including the study participant)	327	1.8±0.8	1.5±0.7	-0.3 [-0.7, 0.1]
History of fever (body temperature >38°C) during the lockdown *	324	25% (n=76)	36% (n=5)	1.5 [0.5, 4.5]
History of respiratory signs during the lockdown * (dyspnoea, cough, rhinitis, otitis, or conjunctivitis)	307	33% (n=96)	50% (n=6)	1.4 [0.5, 4.1]
History of abdominal signs during the lockdown * (diarrhoea, vomiting, or abdominal pain)	312	19% (n=57)	15% (n=2)	0.8 [0.2, 3.6]
Exclusion from the daycare centre due to clinical signs during the lockdown	325	16% (n=49)	14% (n=2)	0.9 [0.2, 4.2]
RT-PCR testing of a nasal swab during the lockdown *	327	5% (n=15)	7% (n=1)	1.5 [0.2, 12.2]
Positive RT-PCR test during the lockdown *	16	0% (n=0)	0% (n=0)	-
Contact with a confirmed case of COVID-19 during the lockdown *	324	12% (n=38)	43% (n=6)	3.5 [1.2, 10.7]
At least one child from the daycare centre, n (%)	324	2% (n=7)	7% (n=1)	3.2 [0.4, 27.9]
At least one daycare centre staff member, n (%)	324	2% (n=7)	7% (n=1)	3.2 [0.4, 27.9]
At least one other child living with the child, n (%)	324	0% (n=1)	0% (n=0)	0
At least one adult living with the child, n (%)	324	6% (n=19)	43% (n=6)	7.1 [2.2, 22.4]
Number of days of attendance at a daycare centre during the lockdown *	321	20±12	19±12	-1 [-7, 5]
Attendance at a daycare centre operated by a hospital (vs. a local authority), n (%)	327	80% (n=250)	64% (n=9)	0.8 [0.3, 2.5]
Mean number of children attending the centre per day	327	29±11	25±12	-4 [-10.4, 2.4]
Parents' occupation:	327			
At least one healthcare worker in a dedicated COVID-19 unit		30% (n=94)	21% (n=3)	0.7 [0.2, 2.6]
At least one healthcare worker in a non-COVID-19 unit		53% (n=167)	58% (n=8)	1.1 [0.4, 3.2]
Other occupations		17% (n=52)	21% (n=3)	1.3 [0.3, 4.8]
Serological testing of the parents:				
At least one seropositive parent[1]	170	14% (n=22)	55% (n=6)	6.1 [1.9, 19.1]
Serological assay of the daycare centre staff [2]				
At least 1 seropositive staff member	312	44% (133/299)	62% (8/13)	1.9 [0.7; 5.8]

[1] SARS-CoV-2 serological status retrospectively determined in an ELISA (based on detection of IgG or total Ig).
[2] Biosynex COVID-19 BSS test
* between March 15th and May 9th, 2020

Table 3. Comparison of the daycare staff and the comparator group.

	Daycare staff				Comparator group			
	N	**Seronegative (N=183)**	**Seropositive (N=14)**	**Relative risk/ Mean difference (95% CI)**	**N**	**Seronegative (N=155)**	**Seropositive (N=9)**	**Relative risk/ Mean difference (95% CI)**
Sex, male	197	1% (n=2)	0% (n=0)	0	164	22% (n=34)	33% (n=3)	1.5 [0.4, 6.4]
Age, mean ± SD (years)	197	41±12	41±15	0.0 [-8.0, 8.0]	164	43±12	44±10	1.0 [-5.8, 7.8]
Number of adults at home (including the study participant)	195	2.4±1.2	2.0±0.9	-0.4 [-0.9, 0.1]	164	2.2±1.0	2.0±1.0	-0.2 [-0.9, 0.5]
Number of children at home	195	0.9±1.1	0.8±1.1	-0.1 [-0.7, 0.5]	162	1.0±1.2	1.4±1.1	0.4 [-0.3, 1.1]
History of fever (body temperature >38°C) during the lockdown *	197	10% (n=18)	29% (n=4)	2.9 [0.8, 10.2]	164	5% (n=7)	11% (n=1)	2.5 [0.3, 22.5]
History of respiratory signs during the lockdown * (dyspnoea, cough, rhinitis, otitis, or conjunctivitis)	193	34% (n=61)	39% (n=5)	1.1 [0.3, 3.3]	152	22% (n=32)	50% (n=4)	2.2 [0.5, 8.5]
History of abdominal signs during the lockdown * (diarrhoea, vomiting, or abdominal pain)	191	15% (n=26)	39% (n=5)	2.5 [0.8, 8.1]	160	13% (n=19)	33% (n=3)	2.7 [0.6, 11.8]
History of other signs	196	58% (n=106)	57% (n=8)	1.0 [0.3, 3.0]	164	43% (n=66)	89% (n=8)	2.1 [0.3, 17.1]
Loss of appetite	197	7% (n=12)	36% (n=5)	5.4 [1.6, 18.8]	164	5% (n=8)	22% (n=2)	4.3[0.8, 24.2]
Skin signs	197	8% (n=14)	14% (n=2)	1.9 [0.4, 9.2]	164	3% (n=5)	0% (n=0)	0
Headache	196	50% (n=91)	57% (n=8)	1.1 [0.4, 3.4]	164	29% (n=45)	56% (n=5)	1.9 [0.5, 7.5]
Asthenia	196	26% (n=47)	50% (n=7)	1.9 [0.6, 5.8]	164	25% (n=39)	67% (n=6)	2.6 [0.6, 11.1]
Myalgia	197	8% (n=15)	36% (n=5)	4.4 [1.3, 14.7]	163	10% (n=16)	50% (n=4)	4.3 [1.0, 17.7]
Anosmia	197	2% (n=4)	29% (n=4)	13.1 [2.8, 60.1]	164	3% (n=4)	56% (n=5)	21.5 [4.1, 111.8]
Ageusia	197	3% (n=6)	29% (n=4)	8.7 [2.1, 35.9]	164	2% (n=3)	67% (n=6)	34.4 [5.7, 207.6]
Chest pain	197	4% (n=7)	14% (n=2)	3.7 [0.7, 20.0]	164	5% (n=8)	33% (n=3)	6.5 [1.4, 30.7]
Joint pain	197	9% (n=16)	36% (n=5)	4.1 [1.2, 13.7]	164	8% (n=12)	33% (n=3)	4.3 [1.0, 19.4]
RT-PCR testing of a nasal swab during the lockdown *	196	20% (n=36)	21% (n=3)	1.1 [0.3, 4.1]	164	21% (n=33)	33% (n=3)	1.6 [0.4, 6.6]
Positive RT-PCR test during the lockdown *	36	6% (n=2)	33% (n=1)	5.5 [0.5, 60.5]	35	3% (n=1)	100% (n=3)	32.0 [1, 945]
Contact with a confirmed case of COVID-19 during the lockdown	197	37% (n=67)	50% (n=7)	1.4 [0.5, 4.1]	164	39% (n=60)	67% (n=6)	1.7 [0.4, 7.1]
At least one child at work, n (%)	197	5% (n=10)	0% (n=0)	0		NA	NA	0
At least one adult at work, n (%)	197	22% (n=41)	7% (n=1)	0.3 [0.0, 2.5]	164	33% (n=51)	33% (n=3)	1 [0.2, 4.2]
At least one child living with the adult, n (%)	197	0% (n=0)	0% (n=0)	-	164	1% (n=2)	11% (n=1)	8.6 [0.7, 105.3]
At least one other adult living with the adult, n (%)	197	1% (n=1)	7% (n=1)	13.1 [0.8, 221.1]	164	1% (n=2)	22% (n=2)	17.2 [2.1, 140.8]
Partner's occupation	130			0.9 [0.3, 2.6]	116			0
Healthcare worker in a dedicated COVID-19 unit		0% (n=0)	0% (n=0)	0.9 [0.2, 3.5]		1% (n=1)	0% (n=0)	0
Healthcare worker in a non-COVID-19 unit		3% (n=3)	0% (n=0)	3.6 [1.1, 11.2]		9% (n=10)	0% (n=0)	1.1 [0.1, 20.8]
Other occupation		97% (n=119)	100% (n=8)			90% (n=98)	100% (n=7)	

* between March 15th and May 9th, 2020

Figure 1: Study flowchart