

SUPPLEMENTARY MATERIAL

Cluster investigation

Cluster 4 occurred in the orthopedic unit and included three HA-COVID-19 cases, two CA-COVID-19 cases, and six HCWs (ward 4A, **Supplementary figure 2A**). Viral strains of all patients except one CA-COVID-19 case were sequenced, as well as strains of five HCWs. Sequencing data showed that the strains of all HA cases (649, 650, 656) and three HCWs (652, 661, 665) were genetically related (**Supplementary figure 3A**). The strains of the CA-COVID-19 case (648) and two other HCWs (651, 655) were unrelated to the others (> 20 SNPs). The first HA-COVID-19 patient (649) developed symptoms after 10 days of hospitalization. HCWs tested positive with the same viral strain 10 days later, suggesting patient-to-HCW transmission. The epidemiological investigation linked patient 674 to another cluster (cluster 6, geriatric unit). However, the corresponding strain was related to the six strains of cluster 4. After additional investigations, it appeared that the patient stayed in a ward adjacent to the orthopedic unit for 10 days, concomitantly to the three HA-COVID-19 cases. HCWs were shared between the two units, possibly explaining the link of patient 674 with the main cluster and suggesting HCW-to-patient transmission.

Cluster 5 occurred in the rheumatology unit and included four HA-COVID-19 cases, eight CA-COVID-19 cases (contact patients), and one HCW of ward 5A (**Supplementary figure 2B**). Viral strains of three HA-COVID-19 cases, three CA-COVID-19 cases, and the HCW were sequenced. Sequencing data revealed that the strains isolated from the HA-COVID-19 cases (681, 683, 687) and one CA-COVID-19 case (666) were genetically related (**Supplementary figure 3B**). Patients 666 and 681 were hospitalized at the same time in ward 5E, where the SARS-CoV-2 transmission probably occurred, since patient 681 tested SARS-CoV-2-negative upon admission. Patient 681 was then transferred to ward 5A to the same room as patient 683. Patient 681 tested positive 10 days after admission, patient 683 the next day, and patient 687

nine days after. Strains from the HCW (667) and the two other CA-COVID-19 cases (669, 671) were unrelated to the other strains. The epidemiological investigations linked HCW 689 to another cluster (cluster 3, digestive surgery unit). However, the strain from HCW 689 appeared to be related to the four strains from cluster 5 and closely related to that of patient 666 (one SNP dissimilarity). However, no epidemiological link with HCW 689 could be identified.

Seven outpatients and six HCWs from the hemodialysis unit were part of cluster 9 (**Supplementary figure 2C**). A complete viral sequence was obtained for six outpatients and three HCWs. Cluster 10 comprised three inpatients and seven HCWs of an internal medicine unit (**Supplementary figure 2C**), of which two and six complete viral sequences could be obtained, respectively. The two units were located in the same hospital site but in separate buildings and were not sharing HCWs. Analysis of viral sequences showed that the strains from two HCWs and four outpatients of cluster 9 and five HCWs and two inpatients of cluster 10 were genetically related (**Supplementary figure 3D**). The strain from HCW 588, linked to cluster 10, was part of this particular monophyletic clade but showed a median difference of six SNPs with the other sequences. Thus, HCW 588 was not considered to be part of the cluster. Overall, no epidemiological link between patients from the two clusters could be identified by the infection control team.

Cluster 12 involved seven patients from three units of a pediatric after-care and rehabilitation unit and 11 HCWs (**Supplementary figure 2D**). Viral strains of five patients and seven HCWs were sequenced. The strains of three patients (615, 620, 621) sharing the same dormitory and five HCWs were genetically related (**Supplementary figure 3C**). The two other patients infected by unrelated viral strains (610, 622) were hospitalized in two different wards (Ward 12A and 12C, respectively). In addition, patient 610 had a positive PCR one month before patients 615, 620, and 621, and was a contact of his COVID-positive parents, supporting the sequencing results.

SUPPLEMENTARY FIGURE LEGENDS

Supplementary figure 1

Evolution of the weekly incidence of COVID-19 cases per 100.000 population in the city of Paris and in France, from ISO week 36 to ISO week 49, 2020. (Data from Santé Publique France, <https://www.santepubliquefrance.fr>)

Supplementary figure 2

Synoptic tables associated to five particular clusters: the cluster 4 from an orthopedic unit (A), the cluster 5 from a rheumatology unit (B), clusters 9 & 10 from a hemodialysis unit and an internal medicine unit (C) and the cluster 12 from a pediatric unit (D).

Supplementary figure 3

Extraction of the monophyletic clades from the tree, and the corresponding single-nucleotide polymorphism pairwise distance matrices, associated to five particular clusters: the cluster 4 from an orthopedic unit (A), the cluster 5 from a rheumatology unit (B), the cluster 12 from a pediatric unit (C) and clusters 9 & 10 from a hemodialysis unit and an internal medicine unit (D). Numerical distances within pairwise matrices are expressed in number of single-nucleotide polymorphism (SNP).