

Contagion management at the Méditerranée Infection University Hospital Institute

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Abstract

The Méditerranée Infection University Hospital Institute (IHU) is a recent single building bringing together all infectious disease stakeholders. The IHU strategy is to develop innovative tools such as epidemiological monitoring, point-of-care laboratory, and ability to mass screen the population. Early diagnosis allows the early isolation of contagious patients and the early start of treatment to reduce the microbial load and contagiousness. In the context of the COVID-19 pandemic, we had to deal with stockouts of personal protective elements, reagents, and an influx of massive numbers of patients. From 01/27/2020 to 01/05/2021, 434,925 samples were tested for SARS-CoV-2, 12,055 patients with COVID-19 were followed up in the day hospital, and 1,888 patients were hospitalized at the IHU according to the guidelines established since the start of the epidemic. By constantly adapting in order to be able to comply with our strategy and guidelines, the IHU succeeds to expand and upgrade its fleet of equipments and improve patient circuits and flows to better manage infected patients.

The base: A single building bringing together all infectious disease stakeholders

The Méditerranée Infection University Hospital Institute (IHU) is composed of a single building, on the Marseille (France) Medical Timone Campus, entirely dedicated to infectious diseases (Figure 1) [1]. This modern building has been open for 4 years with the aim of taking care of contagious patients and dealing with health crises [1]. The building brings together care, diagnoses, research, and start-ups dedicated to infectious diseases. The building as a whole is subject to strict card access control. The infrastructures have been built to safely treat contagious patients [1]. The teams are trained to take care of contagious patients and samples and used to interact with each other.

The strategy

A key in improving the management of infectious diseases in the IHU has been to develop innovative tools such as epidemiological monitoring and ability to mass screen the population.

Epidemiological monitoring

A weekly epidemiological monitoring including surveillance of the microorganisms detected in patients' samples analyzed by the IHU diagnostic laboratory, the numbers and types of samples received, and of a panel of microorganisms identified in other public or private laboratories in the Provence Alpes Cote d'Azur area (South-East of France) is carried out [2]. This monitoring makes it possible to identify the occurrence of abnormal events and to detect potential health crises.

Rapid and massive screening

The IHU strategy is also based on the rapid ability to carry out massive screening of people. Early diagnosis allows the early isolation of contagious patients and the early start of treatment to reduce the microbial load and contagiousness [3, 4].

Key to rapid microbiological diagnosis

The key to rapid microbiological diagnosis is the Point-Of-Care laboratory (POC) [5, 6]. The rapid tests are mainly based on real-time qPCR or immunochromatographic assays. All the equipment necessary for carrying out the analyzes is gathered together in a small operational room (approximately 9 to 17 square meters) in a strategic location in each of the IHU and emergency departments. Sampling and testing are performed using a syndromic approach based primarily on clinical manifestations. The POC laboratory influences the patient care by answering 3 questions: (1) Is it necessary to isolate the patient? (2) Is it necessary to hospitalize the patient? (3) Is there a specific treatment? A large panel of microorganisms can be tested in a syndrome-based approach (Example "respiratory pathogens") (Figure 2). In addition, the rapid diagnosis of highly pathogenic infectious diseases is also performed in the biosafety level 3 laboratory (BSL-3) and in the POC laboratory of the BSL-3 hospital ward (Figure 2). Both laboratories are equipped with negative pressure in order to avoid transmission of pathogens to the outside, and personal protective equipment (PPE) is mandatory and adapted to the assessed risk. Samples of infected or suspected patients are transferred to a level 3 biosafety cabinet which contains all the technologies allowing the microbiological diagnosis. First, a molecular diagnostic automate (Biofire Filmarray, bioMerieux) allows the detection of a large panel of agents (BIOFIRE® RP2.1 plus panel and BioThreat Panel). The handling time to prepare the sample does not exceed 2 minutes and the result is obtained in about 45 minutes. It is also possible to perform the basic biology parameters, such as blood count (Micros 60, Horiba), biochemistry (Piccolo express, Sysmex), coagulation (STart® 4 – Stago), blood groupings in collaboration with the French Blood Establishment (MDmulticard, Grifols), malaria rapid diagnostic tests (PALUTOP+4 OPTIMA, Biosynex), *Legionella* antigen urinary test (Sofia *Legionella* FIA, Quidel), as well as basic microbiological diagnosis (urine analysis, blood cultures, antibiograms, etc.).

Isolation of patients

For the management of infectious patients, the IHU counts 3 hospitalization units with 25 beds each, one of which being organized into 3 modules in which negative pressure can be implemented independently [1]. All patients are in single rooms which are the basis for preventing contagion between patients. There are 2 entrance doors for each bedroom, one for healthcare workers opening onto the internal corridor and one for family members opening onto the external corridor when the patient's condition permits visits. On healthcare side, are located a device in front of each room that provides PPE and a hydroalcoholic solution dispenser at the entrance of each one. In the corridor for patients' families, there are also hydroalcoholic solution and protective mask dispensers. Hand hygiene is also the basis of contagion management at the IHU. There is wide access to hydro-alcoholic solutions with nearly 600 hydroalcoholic solution dispensers deployed in the building. For a long time now, hand hygiene monitoring and compliance studies have been carried out by the IHU teams as well as awareness campaigns and anthropological approach to understand healthcare provider behavior toward hand hygiene protocols [7-10]. Besides, there is a sign on the doors of the rooms on the "Care" side with written awareness messages. "My life is in your hands ... Clean them!!!" and "Get those catheters off me!" to remind healthcare workers of the dangerousness of medical devices and to reassess their need on a daily basis (Figure 3).

Challenges of episode 1 of the COVID-19 pandemic

During the first episode of the pandemic from 27 January to 14 June 2020, we had to organize the management of patients despite a major lack of PPE worldwide and any other type of equipment (masks, gloves, coveralls, bouldering pajamas, gowns, aprons, glasses, visors ...) [11-17, 17-19]. As early as January 2020, we ordered extra masks but there was already a shortage of stock. The stocks of hydroalcoholic solutions were also tight. It was difficult to stock up on reagents and equipment to perform molecular biology analyzes to

detect SARS-CoV-2 but also on swabs to achieve nasopharyngeal sampling. In accordance with our usual strategy and given the extent of the epidemic, we had to face a massive influx of patients. Overall, during episode 1, 141,240 samples were tested, 3,538 patients were followed up in the day hospital, and 702 patients were hospitalized according to the guidelines established for the management of COVID-19 in the IHU.

How did we cope?

We have received donations from other research and diagnostic laboratories of the Aix-Marseille University as well as Marseille public hospitals, and French companies (PPE, materials, reagents, hydro-alcoholic solutions, ...). We carried out the disinfection and recycling of coveralls. For this goal, we used 3 strategies according to the site of use. For re-use in the BSL-3 laboratory, we performed decontamination of the coveralls by airborne disinfection method with Bioquell Z2 and hydrogen peroxide (Bioquell HPV-AQ) or by autoclaving at 121°C for 20 minutes. For other re-uses, a steam decontamination system had been installed in a tent in the outdoor parking lot of the IHU. We also rationalized the use of PPE. Thanks to the private Méditerranée Infection foundation that controls the IHU, we had the opportunity to be highly reactive in purchasing goods, which was essential in a time when suppliers were running out of equipments. With regard to human resources, we received reinforcements from healthcare workers from other departments of the Hospitals of Marseille as well as from voluntary healthcare workers from the private sector. We also received the logistic assistance from the Marseille firefighter battalion for sorting people presenting to be tested.

We have also faced a global shortage of laboratory reagents and small equipments and uncertainty about their availability [20]. Other diagnostic and research laboratories in the city were able to help us initially by providing reagents and/or consumables from their own stock. As a national reference center for rickettsiae, rickettsioses, and zoonotic diseases, we

138 contacted veterinary laboratories that held reagent stocks but were not authorized to carry out
139 the diagnosis of human infections. In view of the lack of specific swabs to perform
140 nasopharyngeal swabs, we evaluated and used the fecal swabs until replenishment of specific
141 swabs.

142 **Setting up circuits**

143 The various "highly contagious" circuits (patients, linen, waste, etc.) had been designed
144 when the building was created and were thus applied to the COVID-19 epidemic. However,
145 the patient circuits required adaptations because it was necessary to create areas to carry out
146 massive patient screening and consultation areas enabling the reception of a large number of
147 patients. The reception hall was converted into a sampling area.

148 **Massive diagnosis screening required not only human but also technical reinforcements**

149 The largest number of tests performed in one day was 3,809, with a maximal capacity of
150 5,000 tests per day. Overall, 20 automated nucleic acid extractors with a capacity of 14 to 96
151 samples each and 16 thermal cyclers with a capacity of 96 samples each were available in the
152 institute at the epidemic onset. To increase the diagnostic yield as well as to cope with reagent
153 shortage together with maintaining the other diagnostic activities, four KingFisher extractors
154 (96 samples in 40 minutes), one PerkinElmer extractor (96 samples in 1h30), one QIAcube
155 extractor (96 samples in 2 hours), one MGI extractor (96 samples in 1h30), two Light Cycler
156 480 thermal cyclers (96 samples in 2 hours), three NeuMoDx molecular (extraction and PCR)
157 thermal cycler systems (96 samples in 2 hours) were acquired from March to June 2020. In
158 addition, 16 VitaPCR thermal cyclers (Credo Diagnostics Biomedical) were also purchased
159 for rapid molecular screening (one test per 20 minutes each). This multiplication of PCR
160 systems was imperative, not only to be able to analyze an increasing number of samples, but
161 also to cope with delayed deliveries and stockouts of reagents and in order to have devices
162 that enabled the fastest testing for emergencies, while maintaining high throughput analysis

capability. Daily debriefings were at the heart of the management of the molecular diagnosis of COVID-19. These debriefings included an update on the analyzes (number of tests carried out the day before, problematic of interpretation and reporting of results to patients or their physicians, deadline for reporting results, etc.), stocks of reagents and small equipments (capacity for analyzes to be carried out with the available stocks, orders in progress and delivery times, suppliers to follow-up, orders to be placed), human resources (number of technicians present and trained to ensure diagnostic continuity 24/7) as well as on the various adjustments made with the new equipments and reagents.

Staff screening for SARS-CoV-2

During episode 1, we screened healthcare workers of the institute in direct contact with patients every 2 days by RT-PCR [21] from nasopharyngeal samples (Table 1). During episode 2, it was performed once or twice a week. At the end of episode 1 (end of April-Beginning of May 2020), a SARS-CoV-2 serological assessment of 488 IHU staff members was performed (Table 1) [22, 23]. Twenty-two were positive (4.5%), including 6 nurses, 3 housekeepers, 3 physicians, 2 nursing assistants, 2 medical fellows, 2 health executives, 2 administrative staff members, and 1 logistician. In mid-December 2020, another SARS-CoV-2 serological assessment of 286 IHU staff members was performed (Table 1). Forty-six were positive (16%), including 15 nurses, 8 administrative staff members, 5 physicians, 4 laboratory technicians, 4 housekeepers, 3 health executives, 3 nursing assistants 2 engineers, 1 pharmacist, and 1 researcher / PhD student. If we compile the data from episodes 1 and 2, 61 staff members out of 656 (9.3%) were infected by SARS-CoV-2.

For administrative staff, contamination occurred outside the IHU, except for 4 of them who were contaminated by other staff with whom they shared their office and who had been contaminated in the community. For engineers, pharmacist, researcher / PhD student, and laboratory technicians, contamination occurred outside. Concerning medical fellows and

physicians, the contamination occurred a priori at the IHU. For nurses, nursing assistants, housekeepers, and health executives, if during episode 1, most of the contaminations occurred a priori at work, this was not the case during episode 2.

The 286 IHU staff members were also interviewed about the fear of being infected with SARS-CoV-2, 282 answers were obtained (Table 2). Most of them (178; 63%) declared “no” fear “at all” of being infected with SARS-CoV-2, 25 (9%) “little”, 44 (16%) “moderate”, and 35 (12%) “great fear”. With the exception of one person who self-medicated with high doses of corticosteroids, no serious form requiring hospitalization was observed among the staff. Besides, in the BSL-3 laboratory, 7,112 samples were inoculated for SARS-CoV-2 cultures. Among them, 3,070 were positives. No contamination was observed among the BSL-3 staff. These data confirm that most risks from biological hazards can be reduced through the use of appropriate procedures and techniques, adequate equipment and infrastructure, and the training of personnel and that human error are mainly involved in staff contamination [24].

Lessons from episode 1 of the COVID-19 pandemic

The biggest lesson of episode 1 was the need to have stocks of PPE, materials, and reagents sufficient to cope with a shortage due to the global health crisis. It is in this context that at the end of episode 1, we continued to equip ourselves and build up reagents and PPE stocks and to transform meeting rooms and common areas into storage areas; the reserves being already filled.

Intermission challenges - Episode 2 of the COVID-19 pandemic

Careful measures were taken to avoid virus transmission in clinical wards receiving both COVID-19 and non- COVID-19 patients. A specific sign was placed on the doors of COVID-19 patient rooms listing the main protection measures (Figure 4). We also had to face again a massive influx of people coming to be tested at the IHU. We had to regulate the flow of people to avoid a high concentration of patients in line. In addition to the possibility of

coming without any appointment, we organized a line for patients with appointment, via the internet, with a capacity of approximately 700 appointments per day (excluding Saturday and Sunday), and reaching a capacity of 1,000 at the peak of the outbreak. We also deployed a rapid registration system (SI-DEP) that takes 3 minutes per patient. For this, 14 administrative staff members were recruited to speed up patient registration and communicate with them.

There was also a need for reliable rapid tests. We evaluated antigenic tests as well as a rapid molecular test, the VitaPCR SARS-CoV-2 [25, 26]. We first demonstrated the lack of sensitivity of antigen tests and also the reliability of the VitaPCR assays. By collaborating with one of the startups hosted at the IHU, we installed these PCR machines in two tents in the reception hall of the IHU, right next to the COVID-19 consultation entrance, in order to be able to safely sample the patients and obtain the results in just over 20 minutes. As a single device can test only one sample at a time, we have deployed 16 devices, including 6 in the tents, 6 in the 2 POC laboratories (those located in the IHU and those in North Hospital) as well as 4 in a newly created laboratory in the Timone hospital Emergency ward in order to be able to diagnose people presenting to the emergency room as quickly as possible.

Conclusion

From 01/27/2020 to 01/05/2021, 434,925 samples were tested for SARS-CoV-2, 12,055 patients with COVID-19 were followed up in the day hospital, and 1,888 patients were hospitalized at the IHU according to our guidelines. By constantly adapting in order to be able to comply with our strategy, the IHU has managed to cope with the various stockouts and the massive influx of patients. The COVID-19 epidemic has made it possible to expand and upgrade its fleet of equipments and improve patient circuits and flows to better manage infected patients.

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240 **Figure Legends.**

241 **Figure 1.** The base and the strategy of contagion management at the IHU.

242 **Figure 2.** Examples of the large panel of microorganisms tested at the IHU.

243 **Figure 3.** Display on bedroom doors, on the “care” side.

244 **Figure 4.** Specific sign placed on the doors of COVID-19 patient rooms.

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Table 1. Screening of the Méditerranée Infection University Hospital Institute (IHU) staff for COVID-19 in episodes 1 and 2.

IHU staff	Episode 1			Episode 2		
	488 people tested by serology	23 people with a previous positive SARS-CoV-2 PCR Positive serology (%)	Negative serology	286 people tested by serology	48 people with a previous positive SARS-CoV-2 PCR Positive serology (%)	Negative serology or not performed
Administrative staff members	51	2 (4%)	0	25	8 (32%)	0
Engineers	25	0	0	28	2 (7.1%)	0
Health executives	13	2 (15.4%)	0	8	3	0
Housekeepers	25	3 (12%)	0	14	4 (28.5%)	1
Laboratory technicians	102	1 (1%)	0	47	4 (8.5%)	0
Logisticians	21	1 (4.8%)	0	2	0	0
Medical fellows	32	2 (6.2%)	0	20	0	0
Nurses	93	6 (6.5%)	1	36	15 (41.6%)	0
Nursing assistants	33	2 (6%)	0	15	3 (20%)	1
Pharmacists	2	0	0	7	1	0
Physicians	48	3 (6.2%)	0	23	5 (21.7%)	0
Researchers / PhD students	35	0	0	60	1 (1.7%)	0
Stretcher bearers	8	0	0	1	0	0
Total	488	22 (4.5%)	1	286	46 (16%)	2

Table 2. Screening of 286 IHU staff members on their fear of being infected with SARS-CoV-2.

Fear of being infected with SARS-CoV-2	Number of staff members	Results by occupation	Results for infections with SARS-CoV-2
Great	35	5 administrative staff members 5 engineers 1 health executive 3 housekeepers 3 medical fellows 4 nurses 2 nursing assistants 1 pharmacist 2 physicians 9 researchers / PhD students	1 housekeeper 1 nurse 1 researcher / PhD student
Moderate	44	4 administrative staff members 8 engineers 1 health executive 1 housekeeper 11 laboratory technicians 3 nurses 1 pharmacist 15 researchers / PhD students	2 administrative staff members 1 nurse
Little	25	1 administrative staff member 3 engineers 1 housekeeper 1 laboratory technician 3 medical fellows 3 nurses 1 nursing assistant 4 physicians 7 researchers / PhD students 1 stretcher bearer	1 administrative staff member 2 nurses 1 physician
No fear at all	178	15 administrative staff members 12 engineers 4 health executives 7 housekeepers 36 laboratory technicians 2 logisticians 14 medical fellows 26 nurses 12 nursing assistants 5 pharmacists 17 physicians 28 researchers / PhD students	4 administrative staff members 2 engineers 2 health executives 3 housekeepers 4 laboratory technicians 12 nurses 3 nursing assistants 1 pharmacist 4 physicians
No answer	4	2 housekeepers 1 health executive 1 researcher / PhD student	2 housekeepers 1 health executive

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