

# Building an Intelligent Hospital to Fight Contagion

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The idea of building hospitals to fight contagion was born with the *lazarettos*. At the time when the microorganisms were not yet known, the mechanisms of transmission of contagion were already well apprehended. Based on the same knowledge but thanks to new technologies, such hospitals have now been built downtown, next to the most highly performing technological plateau. Regrouping patient care, diagnostics, research, and development, the University Hospital Institute Méditerranée Infection building offers a wonderful tool to contain and understand contagion, in a well-designed setting, creating excellent working conditions that are attractive for interested scientists.

**Keywords.** hospital-acquired infection; hospital architecture and building; outbreak; infection control; biocontainment.

Years before germ theory, humans knew that some diseases were transmissible from human to human. Syphilis is generally believed to have come originally from the New World, imported into Europe by Christopher Columbus's sailors after their famous voyage in 1492, and the sexual nature of syphilis transmission and its contagiousness was noticed from the beginning. The contagiousness of leprosy, cholera, and plague was immediately recognized from as early as 1377, when the rector of the seaport of Ragusa (Dubrovnik) made mandatory for the first time a *trentina* (30-day isolation period) for ships coming from areas suspected of plague [2]. Furthermore, sick patients were cared for in places established outside the city walls [3]. Soon after in 1423, Venice set up the first *lazaretto*, a quarantine station (with a 40-day isolation period) dedicated to people coming from infected areas, which became a model for European countries, especially in Marseille [3]. The discovery of germ theory [4], the availability of diagnostic microbiology laboratories, the availability of vaccines, and the discovery of antibiotics led physicians and hospital policy makers to lose their interest in classic transmissible infectious diseases, believing that they had won the war against germs. Unfortunately, in the early 20th century, hospital-acquired infections and increased antibiotic resistance [5] were quickly followed by worldwide outbreaks of viral diseases such as influenza, severe acute respiratory syndrome (SARS), Middle East respiratory syndrome coronavirus (MERS-CoV), and viral hemorrhagic fevers; microbiology laboratory accidents; and hospital-acquired outbreaks of *Clostridium difficile* colitis [6]. The revived

infection controls in hospitals and microbiology laboratories led to new questions and new scientific knowledge. Laboratory biosecurity rules were made mandatory and infection control in hospitals was reinforced with emphasis on preparedness to future threats. Single bedrooms were shown as a means to avoid influenza transmission in hospitals [7], whereas hand hygiene [8] and catheter control have been proven efficient in the fight of frequent hospital-acquired infection [9, 10]. Fast microbiological identification [11], such as diagnosis at the point of care (POC), has also been reported as an efficient means to control contagion [12]; in addition, microbiologic and epidemiological surveys should help to anticipate sanitary crises. The SARS lessons lead to the revival of patient biocontainment, suggesting the creation of high-level isolation units (HLIUs) across the word [13, 14] and updating healthcare protocols for secure care of very highly contagious patients [15], which have been proven efficient in the care of Ebola virus disease in Europe and the United States [16].

Based on past experience [17], Marseille's University Hospital Institute (IHU) architecture was designed to achieve these objectives in combining in one building care and research on contagious patients, epidemiological surveys, advanced microbiology and POC diagnostics, human and social sciences approaches of contagion, innovative technologies to monitor hand hygiene and catheter management, remote control fever detection, a biosafety level 3 (BSL3) laboratory and healthcare unit, and an optimized circuit for diagnostic care and research on contagious patients [18].

## CONTAINMENT OF CONTAGION IN MARSEILLE IN THE PAST

Marseille, which was founded on a rocky landscape facing the sun and the sea, continues to play its role of European–African–Middle East gateway in the Mediterranean region. The reception

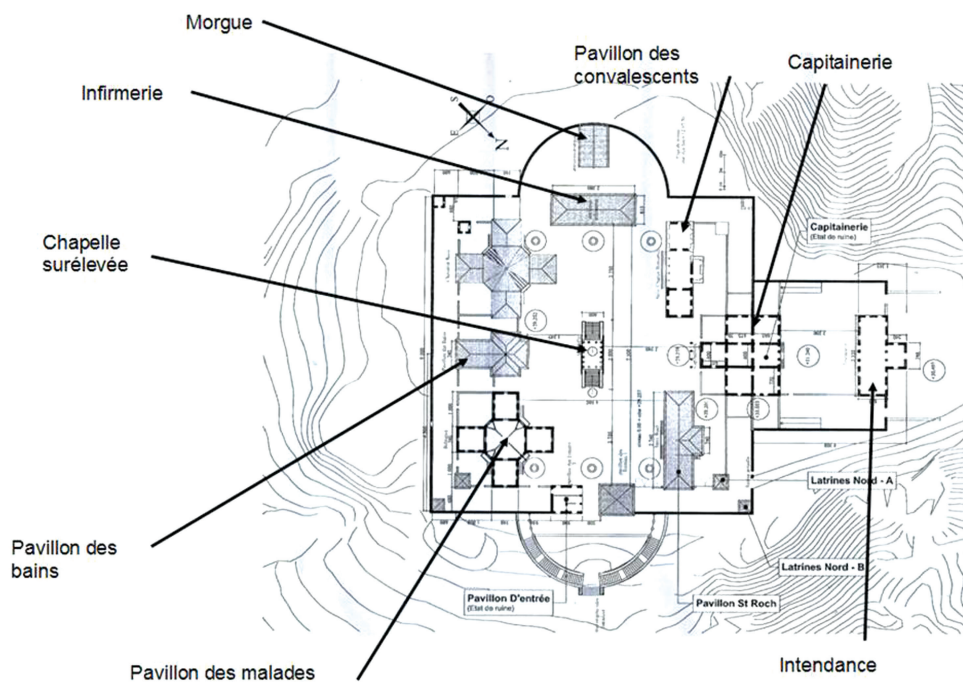
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and transit of diverse goods, food, and travelers, and with them microorganisms (causing plague, cholera, etc) has always been a major issue for the city. Since the 12th century, quarantine and isolation of patients has been a structuring public health issue. Marseille in 1120 used the Fort Saint-Jean as a containment area and created the first lazaret in 1526 (under Aragon Spanish Kingdom rule), then built the first hospital Hotel Dieu in 1643 and the Lazaret of Saint Martin of Arenc installed in the northern part of the city in 1814. All of these quarantine stations were situated out of town but on the coast of Marseille. In 1821, a large

yellow fever outbreak in Africa reached Spain, indicating that Europe was not protected against this disease. Finally, it was on the Frioul Island, at the forefront of Marseille, that was erected in 1828 the Caroline hospital designed by the architect M. R. Penchaud (1772–1833), able to assure the containment of 48 patients and 24 convalescent patients. Penchaud chose this place essentially because of the main direction of the wind (mistral), expecting to dilute the presumed contagious entities (miasmas). It was first used for the quarantine of soldiers evacuated from African areas with yellow fever. It was then rehabilitated in 1850



**Figure 1.** A, Ruins of the Caroline hospital (Ratonneau) and outbuildings on Frioul Island, the largest lazaret of the Mediterranean in Marseille: Caroline hospital (A), Chateau d'If (B), Marseilles (C). B, Architecture and organization of care of contagious patients in the Caroline hospital. Clockwise from top: Convalescent pavilion, harbor master's office, supply corps, contagious patient's pavilion, bath pavilion, chapel, sick bay, morgue.

by the health architect Jean-Marc Samuel Vaucher (1798–1877) to replace the Arenc Lazaret. The Caroline hospital was renamed “Ratonneau” after the name of the island and would become the Lazaret Island, the largest quarantine station and isolation hospital of the Mediterranean region [19]. At this time, 2 theories were erected concerning contagion: that transmission was due to contact between humans, justifying quarantine; and that of Lazaret and others, who considered transmission to be due to miasmas that were carried by the air and trapped in contaminated areas. In the Caroline Hospital, the 2 theories were combined: isolation of patients and natural air circulation. Contagious patients were cared for in a specially isolated area next to the entry of the hospital, avoiding unnecessary circulation within the building, while the convalescent patients were placed next to intendants and administration, the nurses being located in between (Figure 1A and 1B). It is particularly interesting to note that these principles of protection implemented at the time remain valid: isolation, containment, air as a vector of asepsis, and easy cleaning of the walls to evacuate the miasmas.

## GENERAL ARCHITECTURE OF THE MARSEILLE'S UNIVERSITY HOSPITAL INSTITUTE MÉDITERRANÉE INFECTION

### A Building in the City

The technology available today, notably for air filtration and recycling, no longer necessitates a specific “windy” location. The evolution of knowledge about the transmission of pathogens and the technical ability to confine the sectors at risk by sealed protective enclosures with the master of air ventilation allows us to control contagion. The IHU Méditerranée Infection was thus settled downtown, between the University Hospital la Timone and the Faculty of Medicine, to combine research, teaching, and an outstanding clinical investigation platform providing a modern medical service to patients.

### Abstraction as an Expression of Timelessness

The architecture sealed a pact of timelessness with the site. Its façade consists of horizontal sunbreaks made of high-performance fiber, giving a mineral expression with balanced proportions. It rises above the public entrance on boulevard Jean Moulin, magnified by a very large staircase and ramp (Figure 2A). Refined, it goes straight to the point by protecting its interior spaces from the wind and the eyes from the sun. The main ceiling of the hall that connects the University and the Hospital is painted with the deep blue hue of the Mediterranean Sea (Figure 2B).

## A BUILDING COMBINING INFECTIOUS DISEASE RESEARCH AND CARE FOR PATIENTS

IHU MI was built to gather on the same place the care for infectious and contagious patients, advanced diagnostics in microbiology including parasitology and mycology,

epidemiological surveys, traveler counseling, and multifaceted integrative research. It brings together researchers, students, academics, and civilian and military infectious diseases practitioners; clinical microbiology specialists; and patients and families needing a calm framework for research and high-quality care (Figure 3).

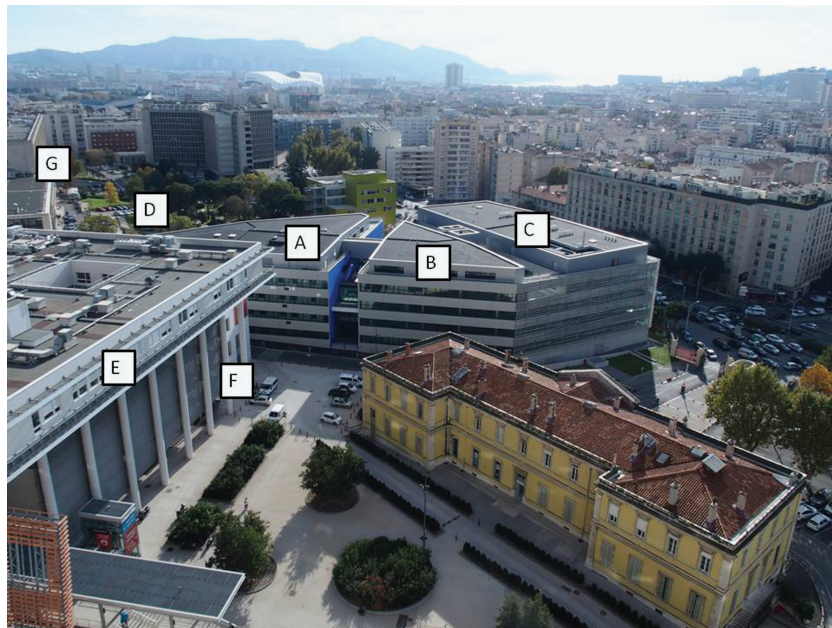
Five major sectors were identified and were distributed in 4 blocks for a total of 27 000 m<sup>2</sup>. A first triangular block of 3000 m<sup>2</sup> connects the patient healthcare section of the IHU with the technological plateau (radiology and intensive care) and the emergency department and includes on the first floor the outpatient care and council, including day hospital (13 beds and 8 chairs) and the travel clinic, full hospital with 2 units of 25 single “intelligent” bedrooms at each floor (first and second), and 1 specialized unit with 25 single intelligent bedrooms in 3 BSL3 modules dedicated to contagious patients on floor 3 (see below).

A second triangular block is dedicated to modular and open space offices, bringing together clinicians, biologists, engineers, students, and researchers in microbiology and in human and social sciences with the challenging objective to “break the frontiers.”

A third block, now rectangular, is dedicated to advanced diagnostic laboratories, located in 3 floors (basement, first and second floors), sharing platforms devoted to high-technology diagnostics, including automated antibody testing, genomics, culturomics, proteomics, or microscopic imaging, and a 3000 m<sup>2</sup> BSL3 laboratory complex divided into 5 modules with ante-rooms including a specifically preequipped BSL3 room for autopsy [15] on floor 3, at the same level as the BSL3 clinical care unit. The last block includes a 150-seat amphitheater and several classrooms with a total capacity of 300 persons for meetings, and is oriented toward the Faculty of Medicine and devoted to teaching (Figure 2B).

Blocks are separated by faults that mark the boundary between the different functions and facilitate the control of access from one sector to the other. Regarding risk management, a hierarchy was installed from the lowest risk on the first floor to the highest (BSL3) at floor 3 where the most contagious patients are cared for. A cascade of pressure and supply and exhaust HEPA filtration system ensures air quality according to technical recommendations [17, 20]. At the floor below, the risk is lower; the BSL2 laboratory space is organized on the same principle but with a lower airflow rate. On the first floor, accommodation and diagnostic laboratories are equipped with the common and mandatory means. While laboratories are located in the storefront on boulevard Jean Moulin, the bedrooms are quiet as they are located between the hospital and the faculty campus. Finally, a floor at level 4 on the roof is dedicated to management, and 1000 m<sup>2</sup> is dedicated to IHU MI's startup allowing for a perfect symbiosis between patient–diagnosis–research and development, fulfilling the mission of





**Figure 2.** A, Façade and horizontal sunbreaks of the new University Hospital Institute Méditerranée Infection (IHU MI) building. B, Architectural organization: infectious disease healthcare block (A), open space offices (B), diagnostic and research laboratories (C), meeting and classrooms and amphitheater (D). IHU MI is surrounded by the intensive care unit and radiology (E) and emergency department (F) of the main university hospital, and by Faculty of Medicine (G). The central fault splitting the research and the healthcare sections is shown in blue.

a research hospital. Research and innovation are at the center of this place.

### **AN INTELLIGENT HOSPITAL HARBORING NEW TECHNOLOGIES**

To reach the above objective, the building is equipped with outstanding technology to ensure the automatic remote control detection of body temperature at the general entrance, allowing access to a specific circulation pathway and healthcare (see

below). All doors of the building including the patient's bedrooms are secured by an individual badge, allowing a specific control of access for IHU employees but also for visitors and for the patient's family. For example, access cards for visitors allow them to enter their patient's room only and in between 1 to 8 PM. The access control also permits the management of the entrance of isolation rooms. As for example, when in airborne precaution, visitors can access a patient's room only with a specific card given with protective mask; in the case of highly





**Figure 3.** The main entrance, Grand Hall.

contagious disease or, more frequently, in cases of extensively drug-resistant tuberculosis (TB), no access is allowed but intercom is available to ensure visitor exchange with their patient. Intelligent bedrooms include automatic continuous bedside monitoring system for hand hygiene [21], bedside traceability of care by patient smart reader, a gown and glove distributor, and a house-made door notice enabling an enhanced security of care and reinforcing infection control for each patient [1]. Moreover, a specific biometric control allows access to the BSL3 laboratory complex.

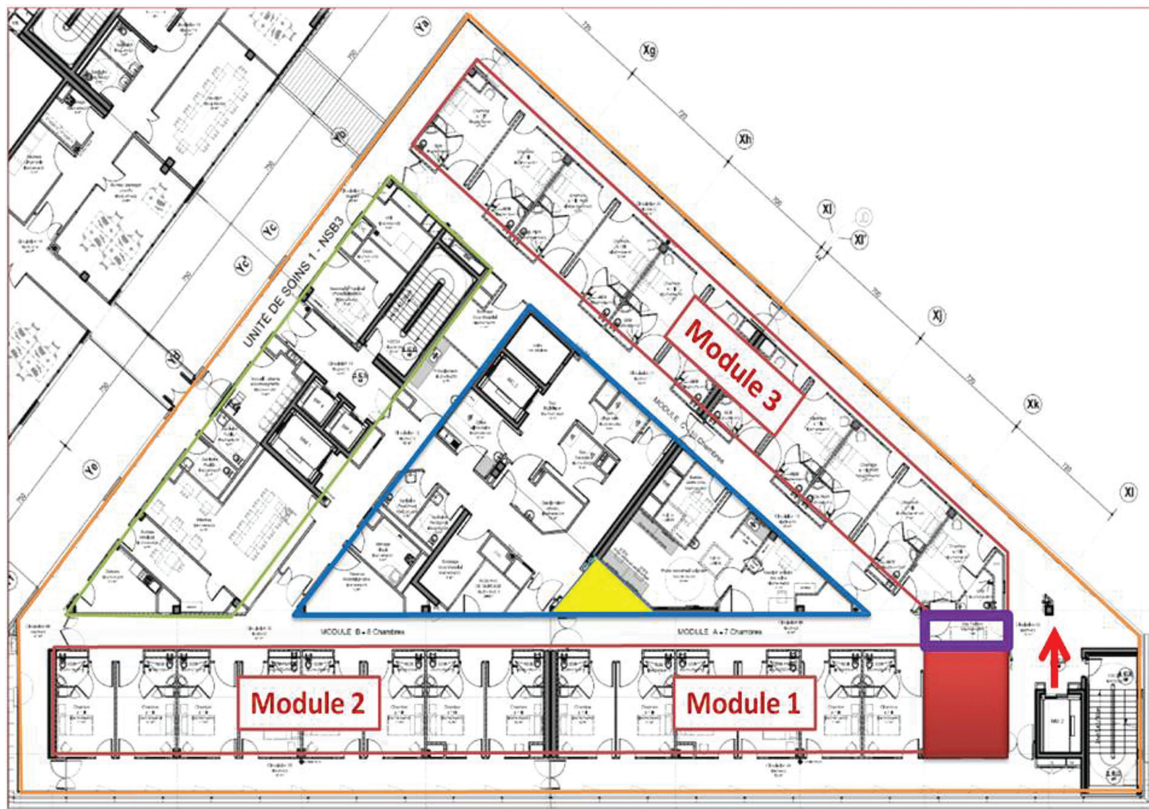
### **INFECTION CONTROL AND SECURITY CIRCUIT**

Single bedrooms have been shown to decrease the incidence of resistant *Staphylococcus*, notably in the intensive care unit, as well as *C. difficile* enterocolitis. Influenza incidence is 2.67 times higher in double-room occupancy [7]. Single bedroom occupancy reduces airborne as well as cross-contamination of pathogens between patients [22]. Multidrug-resistant (MDR) airborne pathogens such as TB should be cared for in negative air pressure bedrooms [17]. As a consequence, infectious diseases wards in IHU have been built as a suite of concentric circles with the health care worker (HCW) at the center, around the HWC pathway, around the patients in single rooms, and surrounding the unit, a visitor corridor with access limited to the patients if not in isolation (Figure 4). In front of each bedroom are masks, gloves, and coats in patented dispenser boxes. The entrance doors of the building have been equipped with infrared cameras to detect febrile persons and guide them to a

specific zone of the consultation area to be cared for, allowing for a secure isolation in a dedicated part of the outpatient clinic for quick clinical investigation and diagnostics at the POC and eventually healthcare at the level 3 floor if contagious [23] (Figure 5). As an example of prevention of fomite transmission, smartphones as well as stethoscopes are covered by a protective film [24].

### **A HIGH-LEVEL ISOLATION (BIOCONTAINMENT) UNIT TO CARE FOR HIGHLY CONTAGIOUS PATIENTS AND OUTSTANDING BIOSAFETY LEVEL 3 LABORATORY**

The university hospital in Marseilles is one of the 12 French referral centers for bioterrorism and prevention of emerging infections and outbreaks. The IHU MI laboratory is authorized to test suspected anthrax spores and all other bioterrorism agents, and we admitted patients with MDR-TB and extensively drug-resistant TB and suspected SARS, MERS-CoV, and Ebola hemorrhagic fever, as well as all victims of a yet undiscovered highly contagious emerging infectious agent. The third floor of the IHU MI building is dedicated to BSL3 activities with 1450 m<sup>2</sup> for BSL3 laboratories including a BSL3 necropsy room, and a 1300 m<sup>2</sup> BSL3 ward for healthcare including a BSL3 POC laboratory. The latter is dedicated to the care of contagious patients and has been built according to the most recent recommendations [13–15]. During routine care from a sanitary crisis, 25 single bedrooms can be used individually with negative pressure (–50 Pa) or positive pressure (+20 Pa) to care, for example, for patients with Beijing genotype or MDR-TB as well as



**Figure 4.** Biosafety level 3 (BSL3) ward at the University Hospital Institute Méditerranée Infection. The blue core is the health care worker (HCW) office and backup, the green area is for physicians and administration, and the red area represents the patients' single rooms. The blue and red areas are separated by HCW working corridors while the orange and red areas are separated by the visitor corridors. For the BSL3 ward, all rooms are independently in positive or negative pressure. When BSL3 is needed, 3 modules can be activated independently. The yellow triangle is the HCW anteroom to access modules 1, 1 and 2, or 1, 2, and 3. The red rectangle is the autoclave and the point-of-care laboratory diagnostic unit. The violet rectangle is the patients' anteroom. The red arrow represents the contagious patients' elevator exit.

immunocompromised patients with febrile neutropenia, but also to optimize the care for *C. difficile* colitis or emerging MDR bacterial infections. In case of sanitary crisis, the ward can be used as a modular BSL3 HLIU (8 + 7 + 10 beds) for patients with highly pathogenic microorganisms with secure anteroom access, a dedicated nurse room, autoclave, and POC laboratory (Figure 5). Each room is equipped as stated above and with video surveillance. The whole building is Wi-Fi equipped, allowing communication for patients in long-term isolation. Specifically set for training infectious diseases HCW in infection control in hospitals, this unit is dedicated for all contagious patients.

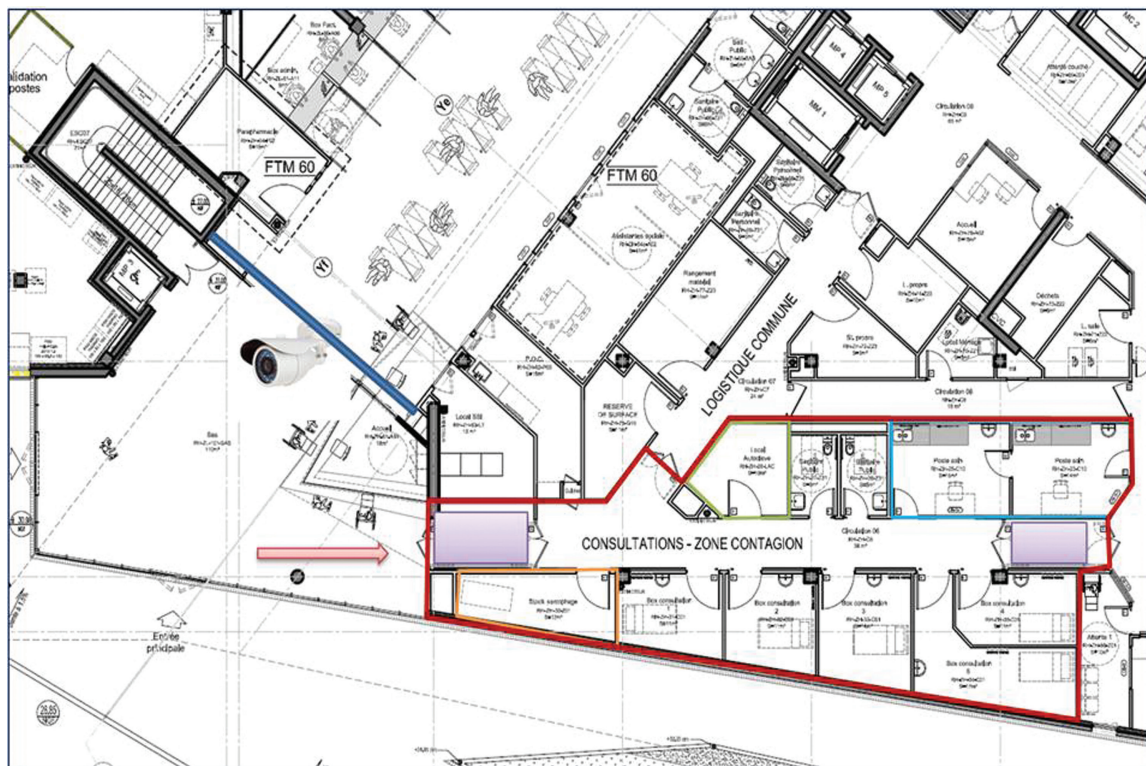
### THE BIOBANK

This is the main patrimony of the IHU. It is currently composed of a collection of clinical specimens that includes >100 000 serum samples. The European Virus Archives collection contains 750 viral strains, among them SARS coronavirus, most of the tropical arboviruses, and their derived products and is the most important collection of arboviruses in the world. The collection of the Unité des Rickettsies (WDCM 875) was created in 2004 and includes >3500 strains

and derived products, including 910 strains of intracellular bacteria (Rickettsiales, Anaplasmataceae, Bartonellae, Whipple bacillus, etc), and representing the largest collection of intracellular bacteria strains in the world. The creation of syndromic sampling kit cohorts from patients has considerably increased the need for sample storage. Currently in draft, the "human-associated bacterial community collection," whose objective is to constitute the largest collection of human-associated bacterial species, includes 779 of the 2156 currently known species (36%). To keep this collection, we have been recently funded at €5 million by Fond Européen de Développement Régional to host the IHU biobank, which owns 2 automated freezers at  $-20^{\circ}\text{C}$  and 2 automated freezers at  $-80^{\circ}\text{C}$  for a capacity of 3 million tubes and is located at floor 1 in the building.

The IHU Méditerranée Infection of Marseille is a building of exception dedicated to outstanding research on emerging infectious and tropical diseases. It is built to answer new types of conflicts, successive outbreaks of new emerging pathogens (SARS, MERS-CoV), the spread of highly pathogenic hemorrhagic fever virus outbreaks causing impressive and severe sanitary crises, and the unsolved pandemic of hospital-acquired





**Figure 5.** Isolation path for patient/visitor with fever at University Hospital Institute Méditerranée Infection. Infrared camera detects febrile individuals, which prevents the doors from opening. The person is directed to the outpatient clinic following the red arrow throughout the patient's anteroom (violet) and is cared for by an equipped nurse and doctor. The green area is the autoclave room, the orange area is the isolation stretcher backup, and the blue zone is the nurse room. If a contagious disease is diagnosed, the patient is driven through the exit anteroom (violet) to the biosafety level 3 ward on level 3.

infection in a context of unprecedented migration and intense international travel exchanges.

Marseille is an international city, shaped by the Mediterranean region. This mineral building designed as a Greek temple aims to focus on worldwide pandemics including the health link between the shores of the Mediterranean, where it also draws many skilled researchers and students. If it still holds the only protective role of the *lazaretto*, it develops an especially human and scientific approach, essentially through its vocation for research in infectious disease.

## Notes

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