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#### Review

# Preparation of an intensive care unit in France for the reception of a confirmed case of Ebola virus infection<sup>★</sup>



Clément Dubost <sup>a,\*</sup>, Pierre Pasquier <sup>a</sup>, Kévin Kearns <sup>a</sup>, Cécile Ficko <sup>a</sup>, Christophe Rapp <sup>b</sup>, Michel Wolff <sup>c</sup>, Jean-Christophe Richard <sup>d</sup>, Jean-Luc Diehl <sup>e</sup>, Yves Le Tulzo <sup>f</sup>, Stéphane Mérat <sup>a</sup>

- <sup>a</sup> Anaesthesiology and intensive care medicine, Begin Military Hospital, 69, avenue de Paris, 94163 Saint-Mande, France
- <sup>b</sup> Infectious disease, Begin Military Hospital, 69, avenue de Paris, 94163 Saint-Mande, France
- <sup>c</sup> Intensive care medicine, Bichat University Hospital Bichat, 46, rue Henri-Huchard, 75877 Paris, France
- <sup>d</sup> Intensive care medicine, hôpital de la Croix-Rousse, 93, grande rue de la Croix-Rousse, 69317 Lyon, France
- <sup>e</sup> Intensive care medicine, European Hospital Georges-Pompidou, 20, rue Leblanc, 75908 Paris, France
- <sup>f</sup> Intensive care medicine, University Hospital of Rennes Pointchaillou, 33053 Rennes, France

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#### ABSTRACT

The current Ebola Virus Disease (EVD) outbreak in West Africa is a major challenge for the worldwide medical community. On April 29th 2015, the World Health Organization (WHO) declared 26,277 infected cases; among them, 10,884 have deceased. The epidemic is still ongoing, particularly in Sierra Leone. It is now clear that northern countries will be implicated in the care of EVD patients, both in the field and back at home. Because of the severity of EVD, a fair amount of patients may require intensive care. It is highly probable that intensive care would be able to significantly reduce the mortality linked with EVD. The preparation of a modern Intensive Care Unit (ICU) to treat an EVD patient in good conditions requires time and specific equipment. The cornerstone of this preparation includes two main goals: treating the patient and protecting healthcare providers. Staff training is time consuming and must be performed far in advance of patient arrival. To be efficient, preparation should be planned at a national level with help from public authorities, as was the case in France during the summer of 2014. Due to the severity of the disease, the high risk of transmission and scarce knowledge on EVD treatment, our propositions are necessarily original and innovative. Our review includes four topics: a brief report on the actual outbreak, where to receive and hospitalize the patients, the specific organization of the ICU and finally ethical aspects.

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# 1. Introduction

The ongoing Ebola Virus Disease (EVD) outbreak in West Africa is due to the Zaire Ebola virus, an enveloped, non-segmented, negative-stranded RNA virus from the *filoviridae* family [1]. Ebola virus, like Margburg virus, is a highly transmissible, category A

cecile.ficko@yahoo.fr (C. Ficko), rappchristophe5@gmail.com (C. Rapp), michel.wolff@bch.aphp.fr (M. Wolff), j-christophe.richard@chu-lyon.fr (J.-C. Richard), jean-luc.diehl@egp.aphp.fr (J.-L. Diehl), yves.le.tulzo@chu-rennes.fr (Y. Le Tulzo), merat.stephane@wanadoo.fr (S. Mérat).

biothreat pathogen [2]. In this useful classification, A represents the highest risk and highest priority agents, B the second highest priority and C the third highest priority, including emerging pathogens that could be engineered for mass spread in the future. EVD causes fever, headache, gastrointestinal symptoms, diffuse haemorrhage, multiple organ failure and has a high fatality rate.

Ideally, all the deceased patients should have been treated in an Intensive Care Unit (ICU), meaning that at least 41% of the cases would have been admitted to the ICU. Preparation of northern countries for EVD treatment is based on two transmission models. Firstly, certain healthcare workers are involved in non-governmental organizations that help treat infected people [3]. As health workers, they are exposed to contaminated blood and other body fluids. Thus, they are particularly at risk of infection and may develop the disease, either in West Africa or back at home.

 $<sup>^{*}</sup>$  This work should be attributed to: The French critical care Ebola response team.

<sup>\*</sup> Corresponding author. Tel.: +33 1 43 98 50 48; fax: +33 1 43 98 54 01. E-mail addresses: clement.dubost@hotmail.fr (C. Dubost), pasquier9606@me.com (P. Pasquier), kearnskp@gmail.com (K. Kearns),

Secondly, direct dissemination has been limited, despite the occurrence of the outbreak in cities with major commercial airports. During the current outbreak, 16 imported cases of Ebola have been reported in 6 countries (Italy, Mali, Senegal, Spain, the United Kingdom and the United States). Among the latter, 7 died. But due to the incubation period (from 2 to 21 days), it cannot be excluded that some people coming back from West Africa would declare the infection after their arrival in northern countries. Because of the severity of EVD, a fair amount of patients may require intensive care. As recently shown in two reports, renal failure and rhabdomyolysis were frequent in severe EVD cases [4,5]. Common ICU therapy, including fluid therapy and dialysis, would help decrease mortality rates [6,7].

Thus, the preparation of intensive care units in affluent countries is necessary in order to be able to receive a confirmed case of EVD with two main goals: (i) to treat the patient and (ii) to protect the healthcare providers.

The French government has required that our unit be able and ready to receive EVD cases in severe condition. We recently published a picture presenting a dedicated ICU room for EVD patients [8]. In this article, we will detail the preparation of the latter. We purposely decided to limit our presentation to confirmed cases of EVD in the setting of hospital care. Due to the severity of the disease, the high risk of transmission and scarce knowledge on EVD treatment, our propositions are necessarily original and innovative.

#### 2. Current outbreak

The first confirmed case of the current outbreak was declared in March 2014 but it is most probable that the epidemic started in December 2013 [9]. On April 29th, 2015, the World Health Organization (WHO) declared 26,277 infected cases, 10,884 of whom have deceased (41%) [10]. The 2014 EVD epidemic is the largest in history and is affecting multiple countries in West Africa.

# 3. General considerations

The risk of an outbreak in northern countries seems highly improbable because of the difference in diagnostic and medical facilities and due to the absence of a reservoir. One of the main risks of contamination is contact with an infected patient, repatriated with the disease, be it already declared or not. Healthcare workers are particularly at risk of contamination [11]. To date, no aerosol transmission has been documented, nor transmission following healthy skin exposure. After contamination through human liquids (including saliva, blood, vomit, urine, etc.), the virus spreads in the organism and replicates itself at a high rate [1]. This leads to virus particles in the blood that can be as high as 10<sup>7</sup> plaque-forming unit/mL. The risk of transmission is very high, particularly for the medical teams. One of the goals when receiving an infected patient is to guarantee the best level of protection for healthcare providers. The risk of contamination for laboratory personnel is low thanks to laboratory procedures. To date, 4 accidents during laboratory work with Ebola virus have been reported: 1 case was fatal, 1 case was symptomatic and survived and in 2 cases there was no evidence that the accident resulted in infection and the patients survived [11]. Thus, one can assume the same level of risk for health team members. As recently seen in Spain, despite wearing personal protective equipment (PPE), a nurse was contaminated during the care of an infected patient [12]. In Texas, a delay in EVD diagnosis for a case in the emergency department led to the death of a healthcare worker and fear of several secondary cases [13]. These events underline the importance of hospital organization and the need for informing both

public and healthcare workers. The PPEs in use in our centre are fluid impermeable.

According to our experience, there are only two choices available when hospitalizing a confirmed case of EVD: the infectious ward or the ICU. During the preparation of the Begin Military Teaching Hospital, a dedicated access to both the ICU and the infectious disease ward was identified, and a protected way to move a patient from the infectious ward to the ICU implemented. The procedures for corridor decontamination must be known and established. To ensure that healthcare workers are efficient in dressing with the PPE, several training sessions should be planned and supervised by experts (Fig. 1). This implies that the hospital provides wards with a sufficient number of PPEs. Even when they are considered skilled at putting on or taking off their PPE, healthcare workers must proceed in pairs, in order to verify they are not making any mistakes. Particular attention should be paid when undressing, which is the time period most as risk for contamination. Our team was taught how to undress correctly in order to avoid contact with the contaminated part of the PPE. Once the PPE is off, workers must thoroughly wash their hands with alcohol gel.

In the ICU, physical barriers must be in place to prevent visitors or unprotected staff from accessing the high-risk area. This high-risk area should be clearly marked out using coloured panels and stickers. Three kinds of area can be differentiated within the unit (Table 1). There are no clear recommendations concerning the organization of the patient's room, but the following conclusions can be drawn from knowledge from Biosafety Level-4 (BSL-4) laboratories [14]: rooms should be maintained under continuous negative pressure with an increasing pressure gradient from the airlock to the patient room. If possible, the room must include a one-way access or keep forward access. If not possible, a dressing room should be provided close to the patient's room and the



Fig. 1. Staff's training session to dress in personal protective equipment (PPE).

**Table 1**The 3 areas within the unit.

Color	Level of risk	Rooms concerned	Function and protection required
Red Orange	High-risk area Middle-risk area	Patient's room Airlock	Full PPE at all times Getting undressed when door closed
Green	Low-risk area	Corridor, dressing room, staff room	Scrubs

PPE: personal protective equipment.

airlock will be used to get undressed, thus being considered an "orange" area (Table 1). The negative pressure within the patient's room is not mandatory but it cannot be excluded that severely infected patients with diffuse bleeding might excrete viruses in the air.

Dealing with the patient's waste is a major problem and must be anticipated. To ensure a safe evacuation of contaminated biological materials, a high number of bins should be available and specific treatment pathways for these wastes established in advance.

#### 4. Where to receive the patient

As stated previously, a choice must be made between the infectious ward and the ICU. If the patient presents with one or more organ failure(s), then the choice for ICU is straightforward. If there is no organ failure, one must keep in mind the natural evolution of EVD. The occurrence of diarrhoea, nausea/vomiting, electrolyte disturbances, neurological impairment or bleeding (even minimal) may indicate a risk for progression towards severe illness and the patient should be addressed to the ICU. A key point in the decision between using an infectious ward or an ICU depends on how secure the transfer of a patient from ward to ICU would be.

Scientific evidence that might help guide the physician in this unfamiliar decision is currently scarce [15]. If biological results are available, some of the following should be considered as severity markers: leukopenia, lymphopenia, thrombocytopenia [16], massive activation of monocytes/macrophages [17], disseminated intravascular coagulation [18], elevated liver enzyme or metabolic disturbances [19].

In West Africa, the mortality of the current outbreak is 41%, meaning that at least 41% of the patients may require ICU care due to severity. Due to the high probability of complications, patients repatriated from the field during the first days of EVD should be directly oriented to an ICU. Only patients repatriated after the 8th day or very early can be oriented to the infectious ward. Another point to take into account when making the decision is the difficulty of transferring patients from the infectious ward to ICU.

Importantly, at all times, discussion between infectious specialists and intensivists is essential when dealing with these high-risk patients.

# 4.1. Specific organization of the ICU

There are currently no specific recommendations for ICU care of confirmed EVD cases. All the following propositions are based on common sense and on our hospital experience.

The dedicated team comprises at least two health workers: one nurse and one doctor or two nurses for usual care, if the patient is stable. The staff includes only senior and experienced workers. People suffering from respiratory disease, claustrophobia and pregnant women should be excluded. Staff must pay attention to eat, drink and go to the toilets before wearing the PPE. All the

patient's care must be done when wearing the full PPE, including goggles and respiratory devices. We found it useful to install a mirror in the airlock just before entering the patient's room, so that everyone can personally check his/her protection (Fig. 2).

All care provided to the patient must be weighed from a benefit/risk perspective. Due to the high risk of contamination during accidents for health workers, procedures that have not proven their utility should probably be avoided. The following care should be performed: central venous access, arterial catheterization, pleural drain, mechanical ventilation, and continuous renal replacement therapy.

Ultrasonography is really a cornerstone in the care of EVD cases. Technical difficulties and risk of contamination render the availability of dedicated US devices and probes mandatory for each EVD room.

As concerns the risk of blood handling, ECMO and ECLS should be avoided and increased haemorrhagic risk in balance with the current scarce evidence of benefit in critical patients [15].

# 4.2. Vascular access

If the patient will require a lot of blood work, the insertion of an arterial line should be considered in order to decrease the risk associated with needle handling. If the patient is haemodynamically stable and invasive blood pressure monitoring is not required, insertion of a central venous line is the best solution both for fluid administration and blood analyses. Finally, a peripheral line should be kept only for stable patients who may not require daily blood analyses.

To be able to safely take care of an agitated patient without any venous access, we decided to have a sedative gas ready in the room. The latter can be a nitrous oxide cylinder, or if not available, an anaesthesia workstation for using inhaled anaesthetics. The



Fig. 2. Personal check during undressing.

aforementioned proposition must remain exceptional, bearing in mind the high risk of aspiration and haemodynamic instability.

In all other cases where the patient remains still and cooperative, vascular access should be managed as usual, including local anaesthesia and ultrasonographic guidance [20].

The jugular site should be preferred for its ease, safe access with US guidance, low risk of infection compared to femoral sites and the possibility of external compression in case of bleeding. Hygienic precautions must be respected in as much as possible but reaching the usual aseptic conditions may not always be possible. PPEs are not sterile. A surgical gown and two pairs of gloves should be worn. The second pair of gloves can be G-VIR® (Hutchinson Santé, 75008 Paris, France) gloves. The latter are sterile surgical gloves incorporating a disinfecting liquid, reducing the transmitted viral load in the event of a blood exposure accident. The argument to propose such gloves is only theoretical as there is currently no proof that they could decrease the risk of transmission for EVD.

#### 4.3. Mechanical ventilation

Here again, recommendations are based on those drawn from our experience with Severe Acute Respiratory Syndrome-associated coronavirus infection. Aerial transmission is not the major mode of transmission for EVD, unless one considers end-stage disease with diffuse bleeding including alveolar haemorrhage. Nevertheless, few situations are associated with a particularly high risk, justifying the use of an FFP3 mask (Table 2).

Tracheal intubation is done with full PPE, including goggles and an FFP3 mask. Rapid sequence induction without facial mask ventilation should be preferred and intubation should be anticipated if possible. During invasive ventilation, interventions must be limited to the ones strictly necessary. A closed suction system must be used, that can work for up to 3 days. All the interventions on the respiratory circuit (change of filter, circuit or suction system) are at high risk of viral particle aerosolization, particularly if secretions are blood-tinted. The circuit should be changed only if needed and not systematically. Inhalation should be avoided and replaced by intravenous administration each time it is equivalent.

Non-invasive ventilation (NIV) creates a particular risk of aerosols during a patient's plugging and unplugging, as well as if leaks exist around the mask. Due to the high risk of failure and the need for tracheal intubation, NIV should probably be avoided, at least if the patient with bleeding disorders. In view of the results of the recent FLORALI study, high-flow oxygen through a nasal cannula may be less dangerous in terms of aerosolization and may be considered as an alternative therapy [21].

Bronchial analysis by suctioning leads to high risk of contamination, particularly if alveolar haemorrhage is present. Due to the high prevalence of multidrug-resistant bacteria among patients coming from Africa [22,23], bacterial cultures may be

**Table 2** High-risk situation of viral aerosol, justifying the use of FFP3 masks.

High-risk situation for viral aerosols, justifying the use of FFP3 masks	Situations at potential risk of contamination
Tracheal intubation  Non-invasive ventilation (NIV): patient's plugging, unplugging, during the whole ventilation if leaks around the mask	Tracheal suction Bronchial fiberscope
Invasive ventilation: if opening of the ventilatory circuit Ventilation with self-inflating balloon with unidirectional valve Tracheotomy	Inhalation

very helpful to adapt antibiotics. Disinfection of the fiberscope may be problematic. It is proposed to use non-guided suction or disposable fiberscopes. Some disposable fiberscopes have an operator channel allowing performance of bronchoalveolar lavage. Two devices are currently available: the Bronchoflex Su<sup>®</sup> (Axess Vision Technology, 37700 St Pierre des Corps, France) and the Ambu<sup>®</sup> aScope<sup>TM</sup> (Ambu, DK-2750 Ballerup, Denmark). The evaluation of the benefit/cost balance must be evaluated for each clinical situation.

# 4.4. Continuous Renal Replacement Therapy (CRRT)

In the absence of strong evidence, CRRT should be limited to validated indications: hypokalaemia, pulmonary oedema, metabolic acidosis. Several elements favour the haemofiltration technique over conventional dialysis: no effluent requiring sewer elimination, less intervention required on the circuit once connected, all the materials are disposable, effluent bags can be disposed directly in hermetic bins.

Anticoagulation using non-fractioned heparin is easier because it requires less blood checks than citrate. Connor et al. [24] reported the use of citrate on one patient but recommendations cannot be drawn from a single patient. The habits and protocols of the unit should be taken into account in the final choice.

The use or not of anticoagulation in case of major bleeding with intravascular disseminated coagulation should be discussed individually. Apart from the case of severe hyperkalaemia, low outputs are recommended to limit interventions on the circuit (i.e. 20 mL/kg/h).

#### 4.5. Cardiac arrest

Two situations must be individualized:

- health workers are present in the room with their full PPE. Then the cardiac massage should start immediately even if the doctor is not yet in the room;
- no health worker is present in the room. The staff members must absolutely take the time to dress in their PPE in the changing room before providing life support procedures. This will clearly lead to a loss of chance for the patient but it is not possible to take the risk of starting a cardiac massage without protection. In this case, the risk of contamination would be particularly high.

# 4.6. Thoracic drain

This procedure should be performed as under normal circumstance, without any extra precautions on top of the usual EVD precautions.

#### 4.7. Surgery

Emergent needs for surgery should not occur frequently during the course of EVD but can appear, for example, as a consequence of severe sepsis. This leads to a fair amount of problems, particularly if the patient is bleeding. Surgery will expose the theatre staff to contamination, transportation of the patient to the theatre can be tricky, protection of the surgeons during the intervention is problematic and the theatre room should be in negative pressure with careful treatment of used air. Surgery should probably be limited to a restricted number of "simple" interventions but no list can be a priori established. One way of dealing with this problem could be to limit interventions to the ones that can be performed in the patient's room. This is another reason pleading for the installation of an anaesthesia workstation in the ICU room.

#### 4.8. Patient examination and monitoring

Patient examination is limited due to the PPE. Inspection and palpation remain possible but auscultation with a traditional stethoscope is not possible because ears are totally covered by the equipment. We implemented an original system using two electronic stethoscopes. The first stethoscope is placed on the body area of interest. A wireless communication is established between the first stethoscope and a computer staying outside the room, in the "green" area (Table 1). The Bluetooth® technology used allows a distance up to 5 meters between the stethoscope and the recording computer. The second stethoscope is used by another doctor, to listen to the recorded files on the computer. For instance we performed this exam using a pair of 3M<sup>TM</sup> Littmann<sup>®</sup> Electronic Stethoscopes Model 3200 (3 M Corporate Headquarters, St. Paul, MN 55144-1000, USA). The physical exam done in the room by the doctor is written on a whiteboard, which is placed against the room's window. Thus, the exam and all the information collected during the time in the room are written in a second time, in the patient's files in the green area. This procedure keeps the patient's files clean.

Nowadays, common monitoring in ICUs systematically includes a central monitor outside the patient's room. All the parameters that cannot be automatically reported (i.e. neurological state, temperature, etc.) could be written using the whiteboard and recorded in the patient's files afterwards.

#### 4.9. Laboratory analyses

For safety reasons, only a limited number of parameters can be analysed in BSL-4. The time needed to obtain results can be long, depending on the distance and the availability of the BSL-4 automates and staff. This is not acceptable for a patient in a critical state who may require frequent checking of blood results. We implemented a field laboratory, available in each room dedicated for EVD cases, allowing analysis of essential parameters (Table 3). The device used for biological analyses, the i-STAT® (Abbott, Princeton, NJ 08540, USA), includes a wireless printer. Communication between the i-STAT® and the printer was feasible through the window, thus printed results were added to the patient's files (Fig. 3). To prevent blood exposure, all the analyses are performed under a Captair Field Pyramid® glovebox (Fig. 4). All the staff members received theoretical and practical learning for use of the devices. For blood group and antibodies, it was decided to perform analyses of ABO, D, K and Rhesus subgroup using the MDmulticard® (Medion Diagnostics AG, CH-3186 Duedingen, Switzerland) [25]. Thanks to this, we are able to transfuse patients in their own group and respecting the Dell, Kell and Rhesus phenotypes.

We used a point-of-care test for paludism: Palutop + 4 Optima<sup>®</sup> (Alldiag, CS 28006-67038 Strasbourg cedex, France), which allow diagnosis of the four plasmodium species. The use of this test is quite easy and a single training episode for the staff has been judged sufficient.



Fig. 3. How to print blood results.

#### 4.10. X-Ray and ultrasonography

We prepared a mobile X-ray system in the room. After utilization, the X-ray digital radiography detector is disinfected and developed outside the room. The X-ray system is dedicated to the EVD patient's room only, for his whole length of stay in the ICU. We obtained several models of portable ultrasonographers, both for diagnostic purposes and for US-guided procedures like vascular access. For safety reasons, we decided that a disposable sterile cover would always cover US probes.

To sum up, the specific room organization includes, on top of classical ICU materials: an anaesthesia workstation, X-ray system, portable US, and a field laboratory with a Captair Pyramid<sup>®</sup>. See Figs. 5 and 6, which present an ideal ICU room for EVD patients and a picture of a fully equipped room in Begin Military Hospital, respectively.

#### 4.11. Communication with the patient

Direct communication with the patient is possible when staff members are in the room but it implies that they are protected by the PPE. To allow a more casual communication and permit communication of the patient with his/her family, we planned to use a webcam and a computer in the patient's room. This would allow good communication and helps the family accept the patient's isolation.

# 5. Ethical aspects

The care of EVD patients should follow the two following prerequisites. First, there is no specific restriction of care due to EVD but only specific limitations due to the increased risk of contamination and diffusion of EVD. These limitations can include, among others, surgery or care associated with potential

**Table 3**Analysis performable under the Captair Field Pyramid® glovebox.

Device	Parameters analysed	Comments
i-STAT® cartridge CHEM8+	Na, K, Cl, CO <sub>2</sub> , anion gap, iCa, glucose, urea, creatinine, Hb, Ht	Abbott, Princeton, NJ 08540, USA
i-STAT® cartridge PT/INR	PT	Abbott, Princeton, NJ 08540, USA
i-STAT® cartridge CG4+	Lactate, pH, paCO <sub>2</sub> , paO <sub>2</sub> , TCO <sub>2</sub> , HCO <sub>3<math>-</math></sub> , base excess	Abbott, Princeton, NJ 08540, USA
Palutop + 4 Optima®	Plasmodium falciparum, ovale, malariae and vivax	ALLDIAG, CS 28006 - 67038 Strasbourg cedex, France
MDMulticard <sup>®</sup>	Blood group ABO, Dell, Kell and Rhesus phenotypes	Medion Diagnostics AG, CH-3186 Duedingen, Switzerland



Fig. 4. The Captair Field Pyramid® used for blood tests.

haemorrhagic risk. Secondly, all EVD care must be performed under a benefit/risk balance.

There are currently no validated ethical recommendations about the care of EVD cases. The cornerstone of the care of such patients is to respect the general principles of medical ethics and keep in mind that such a patient may require tailored care. On top of the medical discussion between infectious doctors and

intensivists, it may be useful to obtain advice from the local ethics committee.

The following points should be discussed at a multidisciplinary level in the hospital before receiving a patient.

#### 5.1. Do not reanimate decisions

If the patient is deemed unable to survive, the decision not to admit him/her into an ICU on the basis of futility can be made.

# 5.2. Limitation of invasive procedures to decrease the risk of contamination

PPEs are effective means of protecting staff members. Thus, invasive procedures should not be prohibited but strictly limited to the ones necessary. The decision to undergo, or not, a surgical intervention should probably be made with the help of an ethics committee.

# 5.3. Implication of staff members in care

Informing staff members about EVD and the risk of transmission is essential. Staff training must take place before and during patient care to obtain a safe and positive attitude toward an infected patient. Due to the physical constraints linked with the PPE, pregnant women, people suffering from claustrophobia or respiratory disease should not be included in the staff taking care of an EVD case. To decrease the risk of errors due to fatigue, the nurse's schedule was modified for 6-hour shifts. EVD teams were dedicated to the care of EVD patients only and would return to the common unit only after the EVD patient's discharge. As the protocols in the infectious ward and the ICU were similar, nursing teams from both wards were pooled. So, in case of a single admission, the nurses from the other ward could be called for help.

# 5.4. Limitation of therapeutics

The practice of critical care should follow national guidelines, especially concerning the limitation of care and do not reanimate

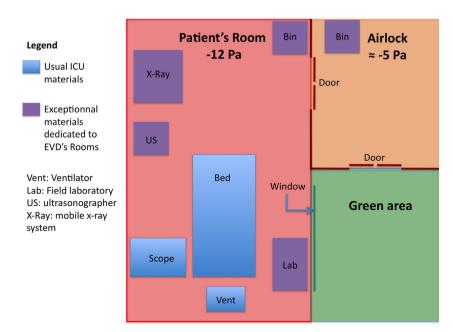


Fig. 5. Scheme view of an ideal ICU room for EVD patients.



Fig. 6. Organization of the ICU room at the Begin Military Hospital with dedicated devices.

orders. For our part, we are following the 2010 recommendations of the French ICU Society [26].

#### 5.5. Communication with the patient's relatives

For obvious reasons, direct communication between an EVD case and his/her relatives is not permitted. But communication should be possible, for instance by using a webcam system or at least by phone and viewing through a window.

#### 5.6. Differential or associated diagnostic

One must keep in mind that malaria is endemic in West Africa. On top of EVD, the patient could present other infections, particularly bacterial. The risks associated with handling blood may limit the availability of bacterial tests to BSL-4 tests only. As the sensibility of the malaria test we used is high, the question of malaria can be dealt with in this way. But concerning bacterial infections, the prescription of empirical wide-spectrum antibiotics without formal bacterial identification may be justified, particularly during the first days EVD. One must keep in mind the risk of multidrug-resistant bacteria, as recently described in a case of severe EVD [6]. If bacterial infection is suspected, every effort should be made to obtain bacterial cultures.

# 6. Conclusion

The current EVD outbreak in West Africa is a major challenge for the worldwide medical community. The epidemic is still ongoing and according to specialists, the number of cases may exceed 20,000 by the end of the current year [27]. It is now clear that northern countries will be implicated in the care of EVD patients, both in the field and back at home. In this perspective, it is fundamental that certain identified, specific centres are ready to take care of such patients. The preparation of a modern ICU to treat an EVD patient in good conditions requires time and specific equipment. Staff training also requires time and must be done well prior to receiving the patient. To be efficient, preparation should be planned at a national level with help from public authorities, as was the case in France during the summer of 2014.

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# **Disclosure of interest**

The authors declare that they have no competing interest.

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