**Supplementary Material:**

1. **Standardization of ID:**
   * **Monitoring:**

The duration of hospitalization was estimated using the patient management software of the Assistance Publique-Hôpitaux de Marseille. The presence of any peripheral intravenous catheter or urinary tract catheter was recorded upon admission, and then daily thereafter. The presence of any peripheral intravenous catheter on admission was considered justifiable during period 2 (implementation) and 3 (interventional) under at least one of the following conditions: intravenous antibiotic treatment was provided for in our protocol, swallowing disorders, septic shock, and any electrolyte disorder needing an intravenous non-antibiotic treatment. Otherwise, we considered the presence of catheters as unjustified. The presence of a urinary-tract catheter on admission was evaluated throughout the study and was considered justifiable under any of the following conditions: acute or chronic urinary retention, the need for a diuresis precise quantification (acute heart failure, septic shock), or neurological causes (drowsiness or acute stroke). Unnecessary bloodstream and urinary tract catheters were both removed immediately upon such a finding.

1. **Fecal microbiota transplantation**

The method is to recruit donors through a medical questionnaire. If no exclusion criterion is identified in the examination [1], a donor kit is prepared including 5 blood tubes and 7 pots for stool sampling. Over 50 laboratory tests are carried out just on the blood tubes and the first fecal sample. A fecal metagenomic profile is also performed (for research only) and a small fecal amount is cryopreserved for 2 years [1]. The kit is qualified if no exclusion criterion is identified [1]. The deadline for giving a stool sample is 3 months after the questionnaire. A norovirus and rotavirus detection is performed every month on the fecal sample if the last detection is more than 1 month old (if the 7 pots were not brought back the first month). Any intervening event should obviously be reported and may result in the interruption of the donation (travel, antibiotics, diarrhea). All kits and samples are qualified by a medical expert. Fecal samples are immediately frozen at -80 °C in a double engine freezer secured by card access, in order to strictly respect the cold chain. The day before the transplant, a qualified sample is placed at + 4 °C. The morning of the transplant, a technician weighs 50g of the sample which is completed to 400 mL with a 0.9% saline solution. The preparation is mixed for 10 minutes, filtered through a strainer that has been decontaminated according to a standardized protocol and distributed in eight 50 cc syringes that are closed with a suitable cap, labeled with a batch number, and placed into two sealed bags (4 syringes per bag). Adaptation tips for the nasogastric tube and an anaerobic bag are placed in the same bag. The two plastic bags are placed in a box and sent by courier at room temperature to the hospital unit where the transplantation is to be performed. In the inpatient unit, the patient, fasting since midnight the day before, under vancomycin 500 mg 4 times a day and a fiber-free diet since admission, is seated with vital sign monitor. Aspiration is mounted, ready for use in case of inhalation. The clinician, after checking the positioning in the stomach of the nasogastric tube by x-ray, injects 200 to 300 mL of bicarbonates 14 °/°° by nasogastric tube. Half an hour later, 4 syringes are slowly injected over 30 minutes. The tube is rinsed followed by a 30 minute break. The last 4 syringes are then injected over 30 minutes. Two hours later, if no complications have occurred, the nasogastric tube is removed. The same evening, the patient takes a diet with soup, yoghurt and compotes. The next day, he resumes a normal diet.

**Supplementary Table 1. Criteria for the diagnosis of *C. burnetii* primary infection (1)**

|  |  |
| --- | --- |
| **Criterion** | **Diagnosis** |
| Fever, hepatitis and/or pneumonia with microbiological criteria (Phase II IgG ≥ 200 and phase II IgM ≥50, seroconversion, or a positive PCR on blood/serum and no endocarditis)  Duration of symptoms < 3 months after onset of symptoms or seroconversion | Acute Q Fever |
| History of rheumatic fever, bicuspid aortic valve, congenital heart disease, prosthetic heart valves, valve regurgitation or stenosis ≥ grade II, mitral valve prolapse | Significant valvulopathy |
| Vascular graft, vascular aneurysm | Significant vasculopathy |
| Transplant patient, chemotherapy, HIV with < 200 CD4, hematologic malignancies, corticosteroid therapy | Severe immunodeficiency |
| Asymptomatic pregnant woman with Phase II IgG ≥ 200 AND IgM ≥ 50 | *Coxiella burnetii* asymptomatic primary infection during pregnancy |

These criteria defined the following medical conditions: 1) Acute Q fever without risk factor of complication with spontaneous apyrexy, 2) Acute Q fever with significant valvulopathy, 3) Acute Q fever with significant vasculopathy, 4) Acute Q fever with severe immunodeficiency, 5)) *Coxiella burnetii* (symptomatic or asymptomatic) primary infection during pregnancy. The following tables define 6) chronic endocarditis (Table 2), 7) vascular infection (Table 3), 8) osteo-articular infections, and 9) chronic lymphadenitis.

**Supplementary Table 2. Criteria for the diagnosis of *C. burnetii* endocarditis (2)**

|  |  |
| --- | --- |
| **A. Definite criterion**  Positive culture, PCR, or immunochemistry of a cardiac valve. | |
| **B. Major criteria**  Microbiology: positive culture or PCR of the blood or an emboli or serology with IgGI antibodies ≥ 6400  Evidence of endocardial involvement:  Echocardiogram positive for IE: oscillating intra-cardiac mass on valve or supporting structures, in the path  of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or abscess;  or new partial dehiscence of prosthetic valve; or new valvular regurgitation (worsening or changing of pre-  existing murmur not sufficient).  Pet-scan showing a specific valve fixation and mycotic aneurism. | |
| **C. Minor criteria**  Predisposing heart condition (know or found on echography)  Fever, temperature > 38 °C  Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm (see PET-scan), intracranial  hemorrhage, conjunctival hemorrhages, and Janeway’s lesions.  Immunologic phenomena: glomerulonephritis, Osler’s nodes, Roth’s spots, or rheumatoid factor.  Serological evidence: IgGI antibodies ≥800 < 400 | |
| **Diagnosis definite**  1) 1A criterion  2) 2B criteria  3) 1B criterion, and 3C criteria (including 1 microbiology evidence, and cardiac predisposition)  **Diagnosis possible**  1) 1B criterion, 2C criteria (including 1 microbiological evidence, and cardiac predisposition)  2) 3C criteria (including positive serology, and cardiac predisposition) | |
| **Criteria** | **Diagnosis** |
| Possible or definite endocarditis on prosthetic heart valve, Bentall surgery or Pacemaker | Possible or definite foreign body-related endocarditis |

NB: Patients with severe heart valve disease (cardiac surgery unit) have been diagnosed with definite endocarditis with Phase I IgG levels as low as 1:200 (3;4). In this specific context (cardiac surgery & vascular surgery and very low serological titers between 1:200 and 1:400), treatment of endocarditis and vascular infection must be prescribed even in the absence of infectious symptoms or a positive PCR since the mortality risk is high if left untreated.

**Supplementary Table 3. Criteria for the diagnosis of *C. burnetii* vascular infection (2)**

|  |  |
| --- | --- |
| **A. Definite**  Positive culture, PCR or immunochemistry of an arterial sample (prosthesis or aneurism) or a periarterial abscess or a spondylodiscitis linked to the aorta. | |
| **B. Major criteria**  Microbiology: Positive culture, PCR of the blood or emboli, or serology with IgGI antibodies ≥ 6400  Evidence of vascular involvement:  CT-scan: aneurism or vascular prosthesis + periarterial abscess, fistula, or  spondylodiscitis.  Pet-san specific fixation on an aneurism or vascular prosthesis. | |
| **C. Minor criteria**  Serological IgGI ≥800 <6400  Fever, temperature ≥38 °C  Emboli  Underlying vascular predisposition (aneurism or vascular prosthesis) | |
| **Definite diagnosis**  1) A criterion  2) 2 B criteria  3) 1 B criterion and 2 C criteria (including microbiology and vascular predisposition)  **Possible diagnosis**  Vascular predisposition, serological evidence and fever or emboli | |
| **Criterion** | **Diagnosis** |
| Possible or definite vascular infection on vascular prosthesis | Possible or definite foreign-body related vascular infection |

**Supplementary Table 4. Criteria for the diagnosis of *C. burnetii* prosthetic joint infection**

|  |
| --- |
| **A. Definite criterion**  Positive culture, polymerase chain reaction, or immunochemistry of a periprosthetic biopsy or joint aspirate |
| **B. Major criteria**  -Microbiology:  • Positive culture or polymerase chain reaction of the blood  • Positive *Coxiella burnetii* serology with IgGI antibodies ≥ 6400  -Evidence of prosthetic involvement:  • Computed tomography scan or MRI positive for prosthetic infection: collection or  pseudo-tumor of the prosthesis  • Positron emission tomography scan or indium leukocyte scan showing a specific prosthetic hypermetabolism consistent with infection a |
| **C. Minor criteria**  -Presence of a joint prosthesis (indispensable criteria)  -Fever, temperature >38°C  -Joint pain  -Serologic evidence: positive *C.burnetii* serology with IgGI antibodies > 800 and < 6400 |
| ***Definite diagnosis***  1) 1 A criterion  2) 2 B criteria  3) 1 B criterion and 3 C criteria  (including 1 piece of microbiological evidence and the presence of a joint prosthesis)  ***Possible diagnosis***  1) 1 B criterion, 2 C criteria (including 1 piece of microbiological evidence and the presence of a joint prosthesis)  2) 3 C criteria (including positive serology and the presence of a joint prosthesis) |

a For the F18-fluorodeoxyglucose positron emission tomography scan, the uptake at the bone-prosthesis interface with exclusion of the head and tip is considered the best criterion for infection, with 92% sensitivity and 97% specificity.

**Supplementary Table 5. Criteria for the diagnosis of *C. burnetii* osteoarticular infection without prosthesis (5;6)**

|  |
| --- |
| **A. Definite criterion**  Positive culture, PCR or immunochemistry of bone or synovial biopsy, joint aspirate. |
| **B. Major criteria**  -Microbiology:  • Positive culture or positive PCR of the blood  • Positive serology with IgGI antibodies ≥ 800  Evidence of bone or joint involvement:  • Clinical arthritis, osteitis or tenosynovitis  • CT-scan or ultrasonography (for joint) or MRI: osteoarticular destruction, joint effusion, intra-articular collection, spondylodiscitis, synovitis, acromioclavicular localization.  • Pet-scan or indium leukocyte scans showing a specific osteo-articular uptake. |
| **C. Minor criteria**  -Serological IgGI ≥ 400 < 800  -Fever, temperature ≥ 38°C  -Mono- or polyarthralgia |
| ***Definite diagnosis***  1 A criterion  2 B criteria  1 B criterion and 3 C criteria  (including 1 microbiological characteristic)  ***Possible diagnosis***  1 B criterion and 2 C criteria  3 C criteria |

**Supplementary Table 6. Criteria for the diagnosis of *C. burnetii* chronic lymphadenitis (5;6)**

|  |
| --- |
| **A. Definite criterion**  Positive culture, PCR, immunohistochemistry, or fluorescence, in situ hybridization of lymphadenitis. |
| **B. Major criteria**  -Microbiology:  • Positive culture or positive PCR of the blood  • Positive serology with IgGI antibodies ≥ 800  Evidence of lymph node involvement:  • Clinical lymphadenitis  • CT-scan or ultrasonography (for joint) or MRI: lymphadenitis > 1cm.  Pet-scan showing specific lymph node uptake. |
| **C. Minor criteria**  -Serological IgGI ≥ 400 < 800  -Fever, temperature ≥38 °C |
| ***Definite diagnosis***  1 A criterion  2 B criteria  1B criterion and 2C criteria  (including 1 microbiological characteristic)  ***Possible diagnosis***  1 B criterion and 1 C criteria  2 C criteria |

**Supplementary Table 7. Acute Q fever treatment**

|  |  |
| --- | --- |
| **Diagnosis** | **Treatment (D: doxycycline, P: Plaquenil, B: Bactrim)** |
| **P1A0**: Acute Q fever without valvulopathy with spontaneous apyrexy | No treatment |
| **P1A1**: Febrile acute Q fever | D 21 days |
| **P1APL**: Acute Q fever with high levels of antiphospholipid antibodies (IgG anti-cardiolipin antibodies (IgG aCL) ≥ 75 GPLU) | DP until IgG aCL < 75 GPLU |
| **P1B**: Acute Q fever with significant valvulopathy\* or vasculopathy\*\* | DP 12 months |
| **P1C**: Acute Q fever in a patient with severe immunodeficiency\*\*\* | D during immunodeficiency |

\*History of rheumatic fever, bicuspid aortic valve, congenital heart disease, prosthetic heart valves, valve regurgitation or stenosis ≥ grade II, mitral valve prolapse.

\*\*Vascular graft, vascular aneurysm. In this context, a PET-scan is recommended to exclude the hypermetabolism of vascular graft or vascular aneurysm. If positive, treat as a vascular infection (see Table 9). If negative, a 12-months antibiotic prophylaxis is recommended.

\*\*\*Transplant patient, chemotherapy, HIV with < 200 CD4+ T cells, hematologic malignancy, corticosteroid therapy.

**For all patients with a persistent focalized infection with long term treatment by doxycycline and hydroxychloroquine:**

**Monthly monitor serology**

**(good serological outcome defined as: two-dilution decrease of Phase I IgG and disappearance of phase II IgM at one year)**

**Monthly monitor drug levels**

**(therapeutic levels: doxycycline 5-10 mg/l (or µg/mL) and hydroxychloroquine 0.8-1.2 mg/l (or µg/mL)).**

**Supplementary Table 8. Management of *C. burnetii* infection during pregnancy**

|  |  |
| --- | --- |
| **P4**: Infection during pregnancy  (Symptomatic Acute Q fever)  OR   Serology with phase II IgG ≥ 200 and   IgM ≥50) | Bactrim double strength (DS) 2/day until the end of the 8th month of pregnancy  After delivery: evaluation of the mother  -       If possible or definite endocarditis, P2A or P2B protocol (see Table 9)  -       If there is no endocarditis but Phase I IgG ≥ 800, control serology, no treatment  -       Avoid breastfeeding |

**Supplementary Table 9. Treatment of *C. burnetii* cardiovascular infections**

|  |  |
| --- | --- |
| **Diagnosis** | **Treatment (D: doxycycline, P: Plaquenil, B: Bactrim)** |
| **P2A**: Possible or definite endocarditis without intracardiac prosthetic material | DP 18 months  No infective recommendation for surgery  If a non-urgent surgery is required, perform after 3 weeks of treatment |
| **P2B**:  Possible or definite foreign body-related Q fever endocarditis | DP 24 months  No infective recommendation for surgery**\*** If a non-urgent surgery is required, perform after 3 weeks of treatment |
| **P2ID**: Possible or definite endocarditis with severe immunodeficiency\*\* | D alone during immunodeficiency (minimal duration of 18 months if native valve and 24 months if foreign-body related endocarditis) |
| **P3A**: Vascular infection without vascular prosthetic material | DP 18 months  Systematic surgery to remove infected vascular tissue after 1 month of treatment |
| **P3B**: Vascular infection with vascular prosthetic material | DP 24 months  Systematic surgical removal of infected material after one month of treatment |

\*If there is a Pacemaker, a F18 FDG PET-CT scan (PET-CT) is recommended. If PET-CT shows high FDG uptake on the pacemaker, change the pacemaker pocket after one month of treatment. If PET-CT shows high FDG uptake on intracavitary leads, no immediate removal; control PET-CT after 2 months of treatment. Expert opinion is necessary if high FDG uptake persists on PET-CT.

\*\*Transplant patient, chemotherapy, HIV with < 200 CD4+ T cells, hematologic malignancy, corticosteroid therapy.

**For all patients with a persistent focalized infection with long term treatment by doxycycline and hydroxychloroquine:**

**Monthly monitor serology**

**(good serological outcome defined as: two-dilution decrease of Phase I IgG and disappearance of phase II IgM at one year)**

**Monthly monitor drug levels**

**(therapeutic levels: doxycycline 5-10 mg/l (or µg/mL) and hydroxychloroquine 0.8-1.2 mg/l (or µg/mL)).**

**Supplementary Table 10:** Antibiotic protocols for the management of infective endocarditis

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| **P0. Initial empirical antimicrobial therapy** |
| **POA. Community and late PVE (>1 year):**  Amoxicillin 12g/day + Gentamicin (3mg/kg/day, one shot)  **Duration:** 6 weeks of Amoxicillin and 3weeks of gentamycin |
| **POB. Nosocomial, early PVE (<1 year) and Device-related IE:**  Vancomycin 30mg/kg/day + Gentamicin (3mg/kg/day, one shot) +/- addition of Amphotericin B at 48 h in nosocomial NBEI if no improvement  **Duration:** 6 weeks of vancomycin and 3 weeks of gentamycin. |
| **P1. Streptococci, Escherichia coli, HACEK, Bartonella** |
| Ceftriaxone 2g /d (one shot) + Gentamicin 3mg/kg/d (one shot)  **Duration:** 4 weeks of ceftriaxone IV with 2 weeks of gentamicin IV. |
| **P2. Enteroccci:** |
| Amoxicillin 12g/d + Ceftriaxone 2 g/d (one shot)  **Duration:** 6 weeks of Amoxicillin + Ceftriaxone IV |
| **P3:**  **P3A: Coagulase Negative Staphylococci (CNS),**  **P3B: Enterococci (Amox R):** |
| Vancomycin 30mg/kg/d + Gentamicin 3 mg/kg/d (one shot)  **Duration:**  **P3A.** 6 weeks of Vancomycin IV + 7 days of Gentamicin IV.  **P3B.** 6 weeks of Vancomycin IV + Gentamicin IV |
| **P4. *Staphylococcus aureus*:** |
| **P4A.** Clindamycin: 1,8 g IV + trimethoprim/sulfamethoxazole: 12 ampules ( 5g/day of sulfamethoxazole)  **Duration:** Clindamycin 7 days, trimethoprim/sulfamethoxazole 6 weeks (1 week IV and 5w per os)  **3 systematic blood cultures after 24 hours of antibiotics**  **P4B**. If positive blood culture or cardiac abscess :  Addition of Rifampin IV 1800 mg/day + gentamycin IV 3 mg/kg/d  **Duration:** 1 week. Control of the Blood cultures after 24 hours |
| **P5 Fungi (Candida, Aspergillus):** |
| Amphothericin B: 3mg/kg /day  **Duration:** 2 months |

**Supplementary Table 11:** Antibiotic protocols for the 9 main infectious syndromes from emergency rooms. (\*Including real-time PCR and immunochromatographic tests)

|  |
| --- |
| * **Community acquired pneumonia**   Test: Kit pneumonia \*  **Pneumonia positive Kit**  *S. pneumoniae*: Amoxicillin 1g orally every 8 hours  Legionella spp.: Azithromycin 500 mg orally per day  *M. pneumoniae*: Azithromycin500 mg orally per day  Influenza with evidence of pneumonia: Ceftriaxone 1g intravenously daily plus Oseltamivir 75mg orally every 12 hours  **Negative pneumonia Kit ,** calculate the severity score CURB65 (CURB-65 criteria: confusion, uremia, respiratory rate, low blood pressure, age 65-year-old or older)  For patient with CURB65 <2: Amoxicillin 1g orally every 8 hours  For patients with CURB65 scores>3: Ceftriaxone 1g intravenously once daily plus azithromycin 500 mg orally per day   * **Hospital-acquired pneumonia (**Residence in a nursing home or other long-term care facility, hemodialysis attendance)   **Negative pneumonia Kit**  **>Without evidence of severe disease and/or recent antibiotic therapy:** Levofloxacine 500 mg orally every 12 hours  **>In the absence of these criteria:** Piperacillin-tazobactam 4g every 8 hoursplus azithromycin 500 mg orally per day  **Negative diagnosis test** and pneumonia aspiration**:** Amoxicillin-clavulanate 1000/125mg orally every 8 hours |
| **Acute pyelonephritis**  Acute uncomplicated pyelonephritis  Test: urine culture  Empirical antimicrobial therapy: Ofloxacin 200mg orally twice daily  If Fluoroquinolones use in the past 3 months, pregnancy, vomiting: Ceftriaxone 1g every 24 hours  Acute complicated pyelonephritis (with severe sepsis)  Test: urine culture, blood culture  Empirical antimicrobial therapy: Imipenem 1000mg every 12 hours |
| **Cellulitis/Erysipelas**  Test: blood for patient who required hospitalization  Oral treatment unless the presence of vomiting or electrolyte disorders  Antimicrobial therapy: Amoxicillin-clavulanate 1000mg/125mg orally 3 times daily  **Necrotizing fasciitis:** Prompt surgical consultation  Test: blood culture  Empirical antimicrobial therapy: Piperacillin-tazobactam 4g every 8 hours associated with Clindamycin 600mg every 8hours IV |
| **Pharyngitis**  Test: Pharyngitis Kit (Rapid Antigen detection, EBV-specific antibodies)  If the presence of group A streptococci in the pharynx is confirmed, rapid antigen detection testing: Amoxicillin 1000mg orally 3 times daily.  If the presence of group A streptococci in the pharynx is not confirmed, rapid antigen detection testing, and if EBV-specific antibodies is positive: symptomatic treatment  If the presence of group A streptococci in the pharynx is not confirmed, rapid antigen detection testing, and if EBV-specific antibodies is negative: symptomatic treatment  In the context of negative diagnostic test results, among patients of 15 to 30 years of age, who present severe pharyngitis (fever, tonsillar exudate, swollen tender cervical adenopathy): Amoxicillin 1000mg orally 3 times daily |
| **Acute diarrhea**  Test: Diarrhea Kit \*  **Positive diarrhea Kit**  Norovirus: symptomatic treatment  Rotavirus: symptomatic treatment  *Clostridium difficile*  First episode: Metronidazole 500 mg orally 3 times per day  *Clostridium difficile* strain 027 or severe *Clostridium difficile* infection whatever the ribotype  Vancomycin 125 mg orally 4 times per day.  **(Severe *Clostridium difficile* infection:** signs of systemic toxicity, white blood cell count of >15,000 cells/microL, and/or a serum creatinine level ≥1.5 times the premorbid level or >133 micromol/L)  **Negative diarrhea Kit**  Symptomatic treatment  **Travelers’ diarrhea**  Ofloxacin 200mg orally twice daily |
| **Meningitis**  For every patient with suspected bacterial meningitis and/or fulminans purpura, empiric antibiotic therapy Ceftriaxone 2 g IV must be started without delay. Then, blood culture should be drawn.  Test: Meningitis Kit \*  **Positive meningitis Kit :**  **Neisseria meningitidis/Streptococcus pneumoniae:** Ceftriaxone 100mg/kg per day, given twice daily  **Herpes simplex virus or Varicella-zoster virus:** Acyclovir 10 mg/kg/dose every 8 hours  **Enterovirus:** STOP empiric antibiotic therapy  **If Meningitis Kit is negative and Cerebrospinal fluid (CSF) findings include a white blood cell count:**  Ceftriaxone 100 mg/kg per day, given twice daily + Acyclovir 10 mg/kg/dose every 8 hours  If the patient is more than 65-year-old: Add Amoxicillin 200 mg/kg per day intravenously in four to six divided doses  **Revaluation each 24 hours** |
| **Sexually Transmitted Infection (STI)**  Test: STI Kit \* (genital, rectal, and pharyngeal sites) and serology, for testing Chlamydia, Gonorrhea, HSV, HIV, Syphilis, HVB, and HVC.  **Empiric antibiotic therapy:** Ceftriaxone 500 mg in a single dose (IV or IM) + Azithromycin 1g orally in a single dose  **Associated measures:**  Safe sex  Treatment of sex partners |
| **Fever in the returning traveler**  Test: ‘Fever in the returning traveler’\* Kit  Fever in the returning travelers, with clinical signs of severe disease, without dengue or malaria diagnosis or other diagnosis based on evidence: Ceftriaxone 2g per day intravenously+ Doxycycline 100 mg orally every 12 hours  **Treatment of uncomplicated falciparum malaria**   * Without vomiting   36-75 Kg: Piperaquine-artenimol 960 mg/120 mg orally, once daily for 3 consecutive days  76-100 Kg: Piperaquine-artenimol 1280 mg/160 mg orally, once daily for 3 consecutive days  **In case of contraindications of** **piperaquine-artenimol:** Atovaquone-proguanil 1000/400mg as a single dose, once daily for 3 consecutive days, administer with food or milk-based drinks at the same time each day   * With vomiting   If vomiting occurs within 30 minutes of administration, repeat the dose  If vomiting persists: Quinine dihydrochloride intravenously  **Treatment of complicated falciparum malaria**   * Artesunate: 2.4 mg/kg intravenously (first dose), followed by 2.4 mg/kg at 12 and 24 hours, followed by 2.4 mg/kg once daily   **In case of contraindications of artesunate**: Quinine dihydrochloride:16mg base/kg in 5 percent dextrose loading dose intravenously over 4 hours, followed by 8 mg base/kg over 4 hours at 8 or starting 8 hours after the beginning of the loading dose   * Severe malaria during pregnancy in the first trimesters: Quinine dihydrochloride   **Severe manifestations of complicated falciparum** **malaria:** Coma, convulsions, shock, metabolic acidosis, acute pulmonary oedema, spontaneous bleeding and coagulopathy, severe anemia, Acute renal failure, hypoglycemia, hyperparasitemia. |
| **Febrile High-risk patients with neutropenia**  Test: 2 sets of blood cultures collected simultaneously from each lumen of an existing central venous catheter and from the peripheral vein site, urine culture, specimen of stool to search for *Clostridium difficile*, Respiratory virus testing.  Empirical antibiotic therapy  Without Hemodynamic instability: Piperacillin-tazobactam 4g every 8 hours IV  With Hemodynamic instability: Piperacillin-tazobactam 4g every 8 hours IV plus Amikacin 15 à 30mg/kg intravenously once daily or Fluoroquinolones if the aminoglycosides are not tolerated (levofloxacin 500 mg orally per day; Prefer Ciprofloxacin to cover suspected or proven *Pseudomonas aeruginosa* infection)  +/-Vancomycine 40mg/kg per day, with a loading dose of 15mg/kg.  Vancomycine should be considered for specific clinical indication including suspected catheter-related infection, skin or soft-tissue infection, colonization with methicillin-resistant *Staphylococcus aureus*, Penicillin-resistant *Streptococcus pneumoniae* or hemodynamic instability. |

**Supplementary Table 12:** Evaluation of the peripheral venous catheter presence and removal: (NA: not available, Day corresponds to the day when the device was removed)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Period 1**  **Baseline period** | **Period 2**  **Implementation** | **Period 3**  **Interventional** | **p** |
| Number of patients | 281 | 544 | 531 |  |
| Number of patients with peripheral venous catheter | 267 (95%) | 487 (89%) | 413 (78%) | **< 0.001** |
| Unnecessary catheter | NA | 272 (56%) | 158 (38%) | **0.01** |
| Day 0 | 79 (30%) | 129 (26%) | 100 (24%) |  |
| Day 1 | 62 (23%) | 169 (35%) | 120 (29%) |  |
| Day 2 | 29 (11%) | 54 (11%) | 39 (9%) |  |
| Day 3 | 11 (4%) | 19 (4%) | 10 (3%) |  |
| Day 4 | 5 (2%) | 10 (2%) | 6 (2%) |  |
| Day 5 | 0 | 2 (0.4%) | 3 (0.7%) |  |
| Day 6 | 0 | 1 (0.2%) | 4 (0.9%) |  |
| Day 7 | 0 | 0 | 2 (0.25%) |  |
| Day 8 | 0 | 1(0.2%) | 0 |  |
| No removal | 53 (20%) | 100 (21%) | 129 (31%) |  |
| Data not available | 28 (10%) | 2 (0.3%) | 0 |  |

**Supplementary Table 13:** Comparison between the day hospitalization and the night hospitalization of the patients.\* The number of unnecessary intravenous catheters depending on our antibiotics protocols, we only considered the periods 2 and 3 for the comparisons.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Period 1**  **Baseline period** | | **Period 2**  **Implementation** | | **Period 3**  **Interventional** | | **Total** | | **p** |
|  | **Day** | **Night** | **Day** | **Night** | **Day** | **Night** | **Day** | **Night** |  |
| Number of hospitalized patients | 201 | 80 | 202 | 342 | 171 | 360 | 574 | 782 |  |
| Patients with intravenous catheter | 191  (95%) | 76  (95%) | 174  (86%) | 313  (91%) | 117  (68%) | 296  (82%) | 482  (84%) | 685  (87.6%) |  |
| Unnecessary intravenous catheter | NA | NA | 90  (52%) | 181  (58%) | 33  (28%) | 125  (42%) | 123/291\*  (42%) | 307/609\*  (50.4%) | **0.02** |
| Patients with urinary tract catheter | 31  (15.4%) | 15  (18.7) | 43  (21.3%) | 71  (20.7%) | 17  (10%) | 58  (16%) | 91  (15.8%) | 144  (18.4%) | **0.01** |
| Unnecessary urinary tract catheter |  |  | 8  (19%) | 23  (32%) | 1  (6%) | 10  (17.2%) | 9  (10%) | 33  (23%) |  |
| Respect of antibiotics protocols in emergency | NA | NA | 74/126  (58.7%) | 135/233  (57.9%) | 67/101  (66.3%) | 125/238  (52.5%) | 141/227  (61.7%) | 260/471  (55.2%) | **0.08** |

**Supplementary Table 14:** Evaluation of the urinary tract catheter presence and removal: (NA: not available, Day corresponds to the day when the device was removed)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Period 1**  **Baseline period** | **Period 2**  **Implementation** | **Period 3**  **Interventional** | **p** |
| Number of patients | 281 | 544 | 531 |  |
| Number of patients with urinary tract catheter | **46 (16%)** | **114 (21%)** | **75 (14%)** | **0.01** (periods 1+2 vs period 3) |
| Unnecessary catheter | **10/46 (22%)** | **31/114 (27%)** | **11/75 (14.7%)** | **0.06** (periods 1+2 vs period 3) |
| Day 0 | 3 (7%) | 8 (7%) | 4 (5%) |  |
| Day 1 | 9 (20%) | 38 (33%) | 15 (20%) |  |
| Day 2 | 11 (24%) | 21 (18%) | 9 (12%) |  |
| Day 3 | 4 (8%) | 2 (2%) | 4 (5%) |  |
| Day 4 | 1(2%) | 1 (1%) | 3 (4%) |  |
| Day 5 | 1 (2%) | 2 (2%) | 1 (1%) |  |
| Day 6 | 0 | 0 | 0 |  |
| Day 7 | 0 | 1 (1%) | 0 |  |
| No removal | 16 (35%) | 40 (35%) | 29 (38%) |  |
| Data not available | 1 (2%) | 1 (1%) | 10 (13%) |  |

**Supplementary Table 15: Cause of the non-compliance with antibiotic protocols in ID unit.**

|  |  |
| --- | --- |
| **Non respect of antibiotic protocols in ID unit** |  |
| Failure of the first antibiotic therapy | 30 (26%) |
| Contraindication | 29 (25%) |
| Continued effective treatment started in emergency | 25 (22%) |
| Without reasons | 8 (7%) |
| Others: | 18 (15%) |
| Data not available | 5 (4%) |

**Reference List**

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