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## Brief reports

## Five cases of acute Zika virus infection in French women of reproductive age returning from Central and South America



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## ABSTRACT

**Introduction.** – The favorable season for *Aedes albopictus* circulation has started in Europe and may lead to autochthonous transmission of Zika virus. Health care providers should be familiar with evocative clinical presentations and able to give updated information to women of reproductive age infected by Zika virus.

**Observations.** – We report five laboratory-confirmed Zika virus infections imported to metropolitan France from Central and South America between January and April, 2016. The five young women were not connected and not pregnant; common presentation combined a rash with persistent arthralgia. Zika virus was identified by RT-PCR from serum or urines, between two and eight days after the onset of the symptoms.

**Conclusion.** – As the duration of potential materno-foetal infectivity is still unknown, we were unable to answer with certitude to the patients' questions about the time interval to respect before attempting a pregnancy: one of them became pregnant one month after the diagnosis.

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### 1. Introduction

Zika virus belongs to the *Flavivirus* genus and the *Flaviviridae* family: it is an arthropod-borne virus transmitted by *Aedes* mosquitoes, originally isolated from a sentinel rhesus macaque in Uganda in 1947. Sporadic circulation has been reported in Africa and Southeast Asia from the first human infections reported in Nigeria in 1954 and until the first outbreak, registered in Micronesia in 2007 [1,2]. A larger outbreak occurred in French Polynesia between October, 2013, and April, 2014 and in other Pacific islands subsequently [3–5]. The most important outbreak ever recorded is ongoing: it has started in early 2015 in Brazil, where up to 1 300 000 cases were estimated in 2015, and spread to Central America, Caribbean islands and a large North-Western part of South America [6–9].

France faces an overseas outbreak in French Guyana, Martinique, and Guadeloupe [10]. In metropolitan France, 500 Zika infections

have been identified from January 2016 to June 2016, among which six resulted from sexual intercourse with an infected male traveler, and eleven affected pregnant women [11]. Several sexual transmissions from infected men to their feminine partners have been reported elsewhere [12–15]. Whether women returning from endemic area have or might infect their male partners remains unknown.

### 2. Cases presentation

#### 2.1. Patient 1

A 28-year-old French woman came to our Infectious and Tropical Disease ward on January 14, 2016, immediately after returning from a seventeen-day trip to El Salvador (Central America). She reported fever in the plane and before attending the hospital. At the same time, she noted a rash that spread rapidly from her arms to her chest and back. Physical examination showed spontaneous apyrexia; a widespread exanthematous and morbilliform rash, respecting palms and soles (Fig. 1); discrete edema facing right malleoli; no conjunctivitis. During the following week, she

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**Fig. 1.** Patient 1: morbilliform on the left arm.

developed intense asthenia, joint pain and severe headache. Menstruations occurred two weeks before disease onset and she did not report any unprotected sexual intercourse since. White blood cell count was normal:  $4180/\text{mm}^3$  (neutrophil  $2420/\text{mm}^3$ , lymphocyte  $1420/\text{mm}^3$ ) and routine biological abnormalities were limited to thrombocytopenia ( $121\,000/\text{mm}^3$ ). Malaria search was negative (blood smear and antigen test); NS1 antigen (Biorad NS1 strip) was negative and serum polymerase chain reaction (PCR) were negative for Dengue, Mayaro and Chikungunya viruses (in-house techniques performed in the French National Reference Centre for Arboviruses FNRCA) but positive for Zika virus (Altona), 4 days after the onset of symptoms. Headaches and arthralgia were incapacitating during 17 days and disappeared gradually afterwards.

## 2.2. Patient 2

A 36-year-old French woman travelled to El Salvador between December 25, 2015 and January 13, 2016. She reported retro-ocular pain and conjunctival hyperemia on January 8 and fever with shivers occurred on January 12 that lasted for 12 hours. Two days after returning from her trip, she started suffering from knee, wrist and finger joints pain and developed an itching rash. She came for medical advice on January 19th: she had no fever but persistent cutaneous rash and mild wrist and finger arthritis. Menstruations had started on the day before in this woman under hormonal contraception, and were not hemorrhagic. Standard biology tests, including platelet count, liver enzymes and C-reactive protein, were in the normal range. Dengue, Mayaro and Chikungunya PCR were negative (in-house techniques performed in the FNRCA), but Zika PCR was positive in serum (Altona). Cutaneous rash lasted for 3 days, while arthralgia were incapacitating during a short period (around four days) but caused discomfort for at least 3 weeks.

## 2.3. Patient 3

A 30-year-old French woman with no relevant medical history returned on February 29, 2016, from an 11-day trip along Brazilian coast. Four days later, she started feeling feverish, with



**Fig. 2.** Patient 4: itching and painful infiltrated facial rash.

a headache and retro-ocular pain. One day later appeared a rapidly extensive itching maculo-papular rash, associated to conjunctival hyperemia, widespread myalgia and painful edema in hands and feet. She also reported legs weakness and feet paresthesia, as well as gingival bleeding after non-steroidal anti-inflammatory drugs intake. She sought medical advice in our clinic 3 days later. Physical examination found no fever, no more cutaneous infiltration but a persistent macular exanthema; bilateral and symmetrical wrists, ankles and phalanges arthritis. Neurological examination was normal and extremities paresthesia seemed linked to the edema. Routine biological test were unremarkable: no cytotoxicity, normal platelet count, no inflammatory syndrome. Plasmatic pregnancy test was negative. Dengue and Chikungunya plasmatic PCR were negative (Fast-track Diagnostics); Zika virus RNA failed to be amplified in serum sample because of technical incident but was successfully amplified in urines collected 8 days after the onset of symptoms (Altona). Most symptoms decreased rapidly but the joints pain and swelling lasted for more than ten days after the diagnosis.

## 2.4. Patient 4

A 39-year-old French woman with a substituted hypothyroidism and a mild, non-treated rheumatoid polyarthritis sought for medical advice on March 16, 2016, 2 days after returning from a two-week trip to Martinique (a French Caribbean island). The day before leaving, she had a transitory fever, with myalgia and headache, followed 24 hours later by a widespread and itching maculo-papular rash, with painful infiltration of the face (Fig. 2) and difficulties to walk. Physical examination showed a discrete bilateral knee's swelling. There was no motor weakness, tendon reflexes were normal and symmetrical. She carried an intra-uterine device and had no risk factor for a sexual transmitted disease. We performed no routine biology. NS1 antigen was negative; PCR were negative for Dengue and Chikungunya viruses in plasma (Fast-track Diagnostics). Zika PCR (Altona) was positive in urine, while it was negative in plasma three days after the onset of the symptoms. Four

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