

PUBLICATION OF THE SUPERIOR HEALTH COUNCIL no. 8201**Risk of Chikungunya virus transmission to the Belgian population
through blood transfusion or transplantation**September 13th, 2007**1. INTRODUCTION AND ISSUES**

Chikungunya is a viral disease that is caused by an Alphavirus of the Togaviridae family. It is sporadically found in Africa, India and South-East Asia. In the affected regions, the virus is transmitted by mosquitoes, mainly by the two *Aedes* species (*A. aegypti* and *A. albopictus*), which are known to transmit the yellow fever virus and the Dengue virus. The presentation of the disease involves symptoms that are identical to those of Dengue: fever, headache, muscle pain. However, the arthralgia (which especially affects the joints in the wrists and ankles) is more painful. Distinguishing between these two diseases requires serological testing. Yet it has to be kept in mind that there may be cross-reactions between the two viruses.

Following the outbreak of a major epidemic that has been raging in numerous islands of the South-West Indian Ocean and in India since 2005, Chikungunya can no longer be looked upon as a rare disease (INVS, 2006; Yergolkar et al., 2006). The geographical extent of the virus and the number of people affected are indeed considerable: 266 000 cases have been reported in Reunion Island in 2005 and 2006, and more than 1 400 000 suspected cases have been notified in India in 2006. In Sri Lanka, over 200 000 cases are said to have been identified the same year. As regards South-East Asia, where there had been no epidemic for several years, new infections emerged in Malaysia and Indonesia in the course of 2007. Pakistan, the Maldives and Gabon have also been affected by the virus. The viral strain that is currently spreading around the Indian Ocean is highly virulent and has caused hundreds of severe forms of diseases of the meningo-encephalitis and hepatitis type among immunosuppressed patients. Over 200 deaths have officially been linked to the epidemic in Reunion Island. Furthermore, recovering patients remain weak for long periods of time and there are recurring and sometimes disabling forms of the disease (INVS, 2007).

In the spring of 2006, the European Centre for Disease Prevention and Control (ECDC, 2006) began informing the European Member States on the potential risk of the disease being transmitted by infected patients returning from areas surrounding the Indian Ocean. Indeed, the virus remains in the blood of the person infected for 3 to 12 days. Given the high number of people regularly returning from endemic tourist resorts, it has become necessary to take appropriate measures in order to guarantee a reliable and permanent supply of blood components and blood products, as well as of tissue or organ transplants. According to Eurostat, over 1.4 million people have travelled from Madagascar, Mauritius, Mayotte, Reunion Island and the Seychelles to the European continent in 2004.

The “Chikungunya” working group assessed the risks involved and issued a provisional advisory report that was approved on September 10th, 2007. It was subsequently endorsed by the SHC Board on September 13th, 2007.

Assignment

1. To review the situation in Belgium, including the knowledge about the disease amongst the medical profession;
2. To assess the risk of Chikungunya virus transmission to the Belgian population through blood transfusion and transplantation, taking into account the latest developments in the field of pathogen reduction as well as the effectiveness of the criteria used to promote the exclusion of blood and organ donors.

2. CONCLUSIONS

Assignment 1: The Superior Health Council has found that the Chikungunya virus is well known and monitored amongst travel medicine services. The Council recommends providing up-to-date information to the medical profession in order to enhance the identification of imported cases.

The Superior Health Council supports the entomological monitoring programme that is being set up in Belgium, given the fact that it cannot be ruled out that permanent sources of vector-mosquitoes emerge in this country as a result of increased global warming.

Assignment 2: The Superior Health Council believes that the risk of blood-borne Chikungunya transmission is small, especially with the implementation of a general 28-day exclusion measure for donor-candidates who have travelled outside Europe. Virus inactivation can provide additional security in an effort to further reduce the risk of Chikungunya virus transmission. Indeed, the risk of contracting the virus in this country cannot be ruled out entirely.

As regards organ-, cell-, or tissue-donors, they should be subjected to the same exclusion period as for transfusions. The SHC takes the view that it is highly unlikely that there is a risk of transmitting the Chikungunya virus through tissues that have been subjected to a validated virus inactivation procedure.

3. ELABORATION AND ARGUMENTATION

a) The situation in Belgium

In order to assess the potential risk of Chikungunya virus transmission, it is necessary to determine first how many imported cases of Chikungunya there are compared to the number of tourists returning from the affected regions. Indeed, the Chikungunya virus remains in the blood of the person infected for 3 to 12 days, resulting in viremia with a viral load that can reach 10⁹ viral particles/ml of serum. This viremic stage entails that there is a potential risk of transmitting the virus through blood transfusion or transplantation.

For instance, no less than 898 imported cases have been identified in France (INVS, 2007b). In the United-Kingdom, around 133 cases have been listed (HPA, 2007). It is not yet known which mode of transmission was involved for a number of patients who had not travelled recently.

Chikungunya is a communicable disease which falls within the category of viral hemorrhagic fevers. Current regulations require that these hemorrhagic fevers be monitored and controlled at the European level (Decision no. 2119/98/EC).

According to the legal provisions of the Member States, it is either mandatory to report all cases of viral hemorrhagic fever, or to report only those cases in which the clinical symptoms match those of a hemorrhagic form.

In Belgium, article 1 of the Royal Decree (RD) of 1 March 1971 concerning the prophylaxis of communicable diseases, which was modified by the Royal Decree of 18 November 1976, requires every case of fever, hemorrhagic or not, that is caused by an arbovirus or a togavirus to be reported. Chikungunya belongs to the Togaviridae family. This means that each case of the disease that occurs in Belgium should be listed and notified. General practitioners have to report every clinical diagnosis of viral hemorrhagic fever. However, medical analysis laboratories notify the presence of the virus regardless of any clinical symptoms.

At present, some thirty cases are known to have occurred in Belgium and all of the patients concerned had stayed in affected regions. The SHC finds that Chikungunya disease is well known and monitored by travel medicine services. Still, the SHC underlines that these cases are probably not representative. A suspect case is currently defined as an ill individual who has arrived from a high-risk area and suddenly contracts fever that is higher than 38.5°C as well as disabling arthralgia. However, the general medical profession is not always aware of the extent of the problem (emergence of the virus in areas that are not known to be high-risk areas), which means that there is no differential diagnosis. The SHC therefore recommends providing up-to-date information to the medical profession in order to enhance the identification of imported cases.

Reducing the risk of transmission also requires avoiding the risk involved in bringing the vector mosquitoes to Europe through increased commercial exchanges. Another important factor that needs to be taken into account in this respect is global warming, which contributes to the progressive northward migration of certain species. Thus, there are in fact sources of *Aedes albopictus* in France (between Menton and Nice and around Bastia in Corsica), in Spain, in the Netherlands, in Albania, in Greece, in Cyprus, as well as an extensive part of North and Central Italy. This mosquito has also been found at certain tyre depots throughout France (INVS, 2007). In the areas where the vector mosquito has settled, someone who was infected abroad may become the point of origin for the emergence of a new focus of infection.

In Belgium, there is no complete inventory of all the pre-existing as well as newly appeared mosquito species. The most recent full inventory goes back to the first half of the past century. At present, there is a research project called “MoDiRisk” (Mosquitoes vectors of Disease: spatial biodiversity, drivers of change and Risk), which has been set up with the aim of drawing up an extensive inventory of the mosquitoes found on nearly a thousand catching sites spread across the entire country. The SHC points out that a first source of *Aedes albopictus* was discovered near Antwerp in 2000 (Schaffner et al., 2004), where mosquito larvae had arrived (from the United States) in a cargo of tyres. With the impact of global warming being increasingly felt in our regions, the appearance of permanent sources of infection cannot be ruled out. Given this state of affairs, the SHC underlines that the emergence of the West Nile virus in the United States in 1999 and its subsequent rapid spread to the entire continent clearly shows that arboviruses (which include the Chikungunya virus) may become a risk factor in countries with a temperate climate.

The SHC therefore supports this entomological surveillance initiative, especially the increased surveillance of tyre storage sites. The outcome of this surveillance will make it possible to channel the efforts towards the early identification of local transmissions of the virus and to implement effective vector control measures.

b) Assessment of the risk of Chikungunya virus transmission to the Belgian population through blood transfusion and transplantation

During the incubation period, which ranges from 4 to 7 days following the infectious mosquito bite, the Chikungunya virus proliferates in the human body. It is possible that the virus is present in the blood during the final days of incubation, before the onset of symptoms. Yet it is

unlikely that the disease could be transmitted to other biting mosquitoes or through blood transfusion or transplantation at this stage.

The virus then replicates during the viremic stage, with the viral load reaching up to 10^9 viral particles/ml of serum. During this stage, which lasts for 3-12 days and during which the virus is found in the blood, the latter can be transmitted to other mosquitoes and it is conceivable that it could spread to other humans via blood component transfusion or transplantations. Nevertheless, transfusion-borne infection has been ruled out after the surveillance of 3 900 blood components that were transfused to patients in Reunion Island (AFSSAPS, 2006). There are reported cases of mother-to-child transmission.

In Belgium, several preventive measures have been implemented to counter the risk of transfusion-borne infection:

1. A combination of blood donor exclusion criteria effectively excludes asymptomatic individuals:

a) The Chikungunya virus is transmitted through infected mosquito bites. The main mosquito species concerned are found in tropical and sub-tropical regions which are roughly identical to those where malaria is endemic. Given the fact that malaria is one of the infectious diseases that must be ruled out from any blood donation, donor-candidates arriving from a country where malaria is endemic are excluded for a six month period (RD of 1 February 2005; Appendix, 2., a) infections);

b) An information note requiring a 21-day exclusion of donors who have stayed in the South-West Indian Ocean islands has been issued to blood transfusion establishments and centres (see Appendix 1);

c) The SHC has recently issued an advisory report that aims at implementing a 28-day exclusion period for donor-candidates who have travelled outside Europe (SHC no. 8307). Given the fact that the viremic stage of Chikungunya disease does not exceed this temporary exclusion period, this simple precautionary measure effectively rules out Chikungunya transmission through blood component transfusion.

The SHC finds that complying with the general exclusion rule guarantees the effective prevention of the risk of transfusion-borne infection posed by donor-candidates arriving from countries mentioned in advisory report no. 8307 of the SHC. Consequently, the SHC believes that there is no reason to recommend the systematic screening of each suspect donation for the virus.

2. Implementing overall pathogen reduction methods makes it possible to reduce the presence of numerous viruses in blood components (SHC no. 8339). However, the effectiveness of these virus inactivation methods depends on the initial viral load in the component being treated and on the minimal load that is looked upon as infectious.

The SHC recommends taking into consideration the following characteristics when validating pathogen reduction methods for the Chikungunya virus:

a) The Chikungunya virus belongs to the genus Alphavirus within the Togaviridae family. Alphaviruses are enveloped viruses that have two envelope glycoproteins;

b) When the viremic stage of Chikungunya disease is most intense, the viral load is very high: about 10^9 viral particles/ml of serum;

c) The Chikungunya virus strongly adheres to platelets (Larke & Wheelock, 1970).

The SHC points out that there are several validated pathogen reduction methods for several members of the Togaviridae family, i.e. the Semliki Forest virus and the Sindbis virus. Though no final validation has been published yet for the Chikungunya virus, a first feasibility study has been presented very recently (Sawyer & Dupuis, 2006).

It is noteworthy that some of the patients in the United-Kingdom (HPA, 2007) had not travelled lately. This means that a locally transmitted infection cannot be ruled out. Virus inactivation can be an additional safety measure aimed at reducing the risk of transmitting a Chikungunya infection that could have been sustained in our regions. With the virus strongly adhering to the platelets, virus inactivation seems to be a useful preventive measure to reduce the presence of the virus in this blood component. In Belgium, fresh frozen plasma must undergo virus inactivation (RD of 1 February 2005, Art. 10, I, 1°).

Given the fact that there is no local epidemic, the SHC believes that the risk of transmitting Chikungunya through blood transfusion is minimal, especially with the implementation of a general 28-day exclusion measure for donor-candidates who have travelled outside Europe. A case of indigenous transmission has recently been reported in the North-East of Italy (PROMED, 2007), with over 150 symptomatic patients identified until now. The index case is a traveller who probably contracted the virus in India. The ECDC therefore advises that its specific recommendations for travellers be extended to this region (ECDC, 2007). As regards the SHC, its advisory report no. 8307 had recommended that, when necessary, a specific exclusion rule be observed in addition to the general exclusion measure. An information note on the situation in North-East Italy has been published very recently (see Appendix 3).

As for organ, cell or tissue donors, an information note requiring that this measure be adapted to cells and tissues was issued as soon as the SHC released its advisory report on the exclusion of blood donors who have travelled outside Europe (see Appendix 2).

The SHC recommends that, whenever possible, the exclusion measures for blood donors be applied to the various organ, cell or tissue donors. As regards organ donation, it is therefore important that this advisory report be distributed amongst transplant coordinators.

It is likely, though not proven, that the procedures used for treating certain tissues, such as bones, have an inactivating effect on the Chikungunya virus as on other enveloped viruses, such as HIV.

4. REFERENCES

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5. APPENDICES

1. Information note "*La selection des donneurs et l'épidémie de Chikungunya*" (Donor selection and the Chikungunya epidemic) of the chairman of the Coordination Cell « Organs, blood, tissues and cells » of the Federal Public Service Health, Food Chain Safety and Environment, of 1 March 2006, addressed to blood transfusion establishments and centres, tissue and cell establishments and transplant centres.
2. Information note "*Exclusion des donneurs ayant séjourné à l'étranger*" (Exclusion of donors who have stayed abroad) of the general administrator of the Federal Agency for Medicine and Health Products, of 29 March 2007, addressed to the directors of tissue and cell establishments.
3. Information note "*Chikungunya en Italie*" (Chikungunya in Italy) of the general administrator of the Federal Agency for Medicine and Health Products, of 4 September 2007, addressed to the directors of blood transfusion establishments.

6. COMPOSITION OF THE WORKING GROUP

All of the experts took part in this working group *in a personal capacity*. The names of the SHC members and experts are marked with an asterisk *.

The following experts were involved in issuing this advisory report:

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This working group was chaired by Mr. Michel TOUNGOUZ, the scientific secretary was Mr. Roland HÜBNER.