BACKGROUND

In the past, the occurrence of clustered cases or outbreaks led to the implementation of measures to prevent transfusion transmitted infections. Thus, during a Q fever outbreak in the Chamonix valley in 2002, blood collection was interrupted in this geographical area for several months. In addition, donors of the whole French territory who had travelled to the Chamonix valley at the time of the outbreak were excluded from blood collection. In the same way, when clustered human cases of West-Nile virus (WNV) infections occurred in the Var region in 2003, safety measures on blood donations were set up. These measures can have an important negative public health impact by limiting the supply of blood products to health care facilities. It is therefore important that their implementation and period of application be adapted to the risk of transmission through blood transfusion. Quantitative risk estimates of blood donation contamination can therefore contribute to guiding those prevention measures.

In this context, the French Institute for Public Health Surveillance (Institut de veille sanitaire, InVS) initiated a project in early 2005 with the aim of obtaining a priori quantitative risk estimates of infection of a blood donation by infectious agents (virus, bacteria or parasite) for different epidemic situations. This project was conducted by a working group including the French Agency for the Safety of Health Products (Afssaps), the French Blood Agency (EFS), the National Institute for Blood Transfusion (INTS), and the InVS.

TRANSFUSION RISK AND MEASURES FOR BLOOD SAFETY

The risk of blood donation infection by infectious agents results from collecting blood from an infected donor while he is asymptomatic and the pathogen is present in his blood. Blood safety is presently based on two successive stages: first, on the recruitment and selection methods of blood donors prior to blood donation, and secondly, on biological qualification of blood donations. It is worth noting that blood safety also relies on processing and storage methods of blood donations.

The first stage excludes from blood collection individuals who present symptoms or risk factors of some transfusion transmitted infections (HIV, hepatitis B and C, malaria etc.). However, this step does not exclude all infected individuals who are asymptomatic at time of blood collection. The next stage, which consists in biological qualification of blood donations, aims to detect systematically some chronic infections at an asymptomatic stage (for example HIV infection, hepatitis B and C), and so to exclude infected people from blood collection. Other acute infections are not screened in routine. Nevertheless, the transfusion risk is generally very low for these acute infections, because they are frequently symptomatic (in that case, the donor is temporarily excluded), and the presence of the pathogen in blood is not systematic or is of short duration. Moreover, these infections are not very frequent outside the occurrence of outbreaks or clustered cases. In these cases, the risk of blood donation infection increases.

This work aims to quantify this risk a priori for different epidemic situations.

RISK ESTIMATION

Which infectious agents?

The first step of the project consisted in identifying priority infectious agents to study as regards to the transfusion risk. Pathogens responding to one or several of the following criteria were selected: documented or potential presence of the pathogen in blood during the infection, documented blood transmission infection, presence of asymptomatic infected people, and possibility of contracting the infection in France. Some infectious agents studied elsewhere were not considered (prions for example).

On the basis of these criteria, the following pathogens were selected:
- 7 viruses: West-Nile virus (West-Nile virus fever, zoonosis), hepatitis A and E viruses (hepatitis, transmission mainly oro-fecal), dengue viruses (dengue, transmission by mosquitoes), Hantavirus *puumala* (haemorrhagic fever with renal syndrome, zoonosis), Parvovirus B19 (erythema infectiosum, transmission predominantly by the respiratory route), chikungunya virus (chikungunya virus fever, transmission by mosquitoes);
- 3 bacteria: *Yersinia enterocolitica* (yersiniosis, transmission mainly by food), *Coxiella burnetii* (Q fever, zoonosis), *Leptospira interrogans* (leptospirosis, zoonosis);
- 3 parasites: *Toxoplasma gondii* (toxoplasmosis, transmission by food), *Leishmania spp.* (leishmaniosis, zoonosis), *Trypanosoma cruzi* (Chagas disease, zoonosis).
Inventory of existing methods

The second step consisted in an inventory and a critical analysis of the different methods for the estimation of the risk (including their limits and advantages). For each infectious agent, the risk estimation was based on the duration of the presence of the pathogen in blood, the frequency of the infection in the population, and the frequency of asymptomatic infections.

Estimates on the probability of a contaminated blood donation were performed for past epidemic situations when data were available. In case of unavailable relevant data, hypotheses were made in order to apply estimation methods.

A variable risk according to the pathogen

The estimated risk of blood donation infection by Leptospira was low, respectively between 0.02 and 0.08 per 100,000 donations, and between 0.1 and 0.9 per 100,000 donations according to the epidemic scenario.

During the occurrence of clustered human cases of WNV infections in the Var region in 2003, the risk of blood donation infection was estimated at 6 donations per 100,000.

For Parvovirus B19, during the period from February to September 2005, the risk reached 23 per 100,000 donations.

A lack of data for some pathogens

For some pathogens, required data for the risk estimation were insufficient to allow calculated estimates: for example, frequency of hepatitis E in the population, duration of the presence in blood of the bacteria Yersinia enterocolitica and Coxiella burnetii, and the parasite Toxoplasma gondii. This data would need to be completed during research performed on those pathogens.

Real time risk estimation during the chikungunya epidemic

Risk estimations were performed in real time during the outbreak of chikungunya infections which occurred on La Réunion Island in 2005-2007. Subsequently, these estimates were refined with consolidated incidence data and new data acquired during the epidemic on the frequency of asymptomatic infections.

Blood collection was interrupted on 23 January 2006, before the peak of the epidemic, during which 170,000 cases were identified between the end of January and the beginning of March 2006. For this period, the risk was estimated at 1,500 per 100,000 donations, i.e. 29 of the 2,000 donations which would have been collected if blood collection would have continued.

Thanks to these estimates, the effect of the interruption of blood collection between January 2006 – April 2007 was estimated at 40 potentially viremic donations avoided. Furthermore, the very low estimated risk for the interepidemic period January-April 2007 (one viremic donation every 21 years) has contributed to the decision making process to start again the collection of blood donations on the island from 14 June 2007.

A tool for forthcoming outbreaks

The main interest of this study was to have gathered the data which were available and required to estimate the probability of an infected blood donation during epidemic periods, and identified and tested risk estimation methods. Thus, data will be easily accessible for risk estimations in case of a future outbreak, allowing for better targeted prevention measures.

Moreover, this work pointed insufficient data and hence necessary studies to complete them.

Finally, this study made possible the anticipation of epidemic situations, and facilitated the risk estimation in emergency settings, as observed during the chikungunya epidemic.

This work constitutes the first step in the estimation of the risk of transmission of an infectious agent from a blood donor to a recipient. The next step requires to take into account other factors as: the transmission efficiency of a pathogen from an infected blood donation to the recipient, the efficiency of blood processing methods, and the recipient’s immune status. This next step calls for a multidisciplinary approach, gathering experts in transfusion safety (blood processing), as well as in microbiology and in epidemiology.

The complete report of the work “Quantitative estimation of the risk of blood donation infection by infectious agents” is available at the following address: www.invs.sante.fr/display/?doc=publications/2007/contamination_sang/index.html