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EDITORIAL

BLOOD SAFETY AND NUCLEIC ACID TESTING IN EUROPE

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Over the past two decades, a long series of specific and non-specific measures have been introduced into the screening of blood donations in order to reduce the residual risk of transmission of bloodborne viruses. The latest specific measure has been viral nucleic acid testing (NAT), introduced by the European plasma industry in 1995, and subsequently introduced for blood donations in several countries in Europe and elsewhere. NAT was implemented to reinforce the safety of the blood supply; it can detect acute viral infections during the 'window period', that were not being detected by the serological screening methods used at that time. To assess the impact of NAT on the safety of the blood supply, it is essential to estimate the residual risk of viral transmission. In this issue, six European countries (France, Germany, Italy, Spain, Switzerland and the United Kingdom) that have recently implemented NAT describe their experiences and the results of the evaluation of the residual risk of viral transmission in their blood supply [1-6].

In these six European countries, NAT was initially introduced between 1999 and 2001 to detect hepatitis C virus (HCV), probably because the first mandatory screening for plasma used by blood industry was HCV-NAT. In 2001, a publication from an international forum showed that10 out of the 25 countries that now make up the European Union had introduced HCV-NAT for blood screening versus two for HIV-NAT [7]. Later, HIV-NAT was progressively implemented and, Spain is now the only country of the six reported in this issue where this procedure has not yet been introduced. This expansion is probably due in part to the ability to test for both viruses with one of the licensed tests (TMA, Chiron blood testing). France is the only country where NAT was implemented in a single stage for all blood donations collected. In other countries, NAT was first performed on a voluntary basis, before it was made mandatory.

NAT was implemented to reinforce the safety of the blood supply

In Germany, NAT is performed by 'in-house' assay, and the other five countries use one or both of the commercially available nucleic acid amplification methods (polymerase chain reaction (PCR) and transcription-mediated amplification (TMA)), adapted for blood screening. Blood screening strategies differ in the six countries, and there are two levels of heterogeneity in the European practice of NAT. First, the number of blood donations included in pools: these varied between 1 to 96 depending on the country. Second, the variations observed in the procedures used within each country. In France, Germany and the UK, the size of the pool is fixed for each virus, whereas in Italy, Spain and Switzerland, the pool size varies. The variation observed is probably due to the way in which blood donation testing is organised locally. It should be noted that, contrary to the classical serologic screening methods that are always used in single donation testing, current NAT procedures usually demand pooling of blood donation samples due to the format of the employed platforms.

The main aim of introducing NAT in blood testing was the reduction of the residual risk of viral transmission linked to the window period. With the exception of the UK, which has adopted a specific model (see below), each country bases the residual risk estimate on the mathematical model developed by Schreiber et al [8], which takes into account the window period and the incidence rate calculated from seroconversions observed in the repeat blood donor population. However, due to difficulties in obtaining exhaustive data at national level for the calculation of the national incidence rate, most of the contributors have extrapolated from regional or partial data that probably introduce biases. Although widely adopted, this mathematical model has some limitations: it does not take into account the population of first time blood donors or other parameters such as technical or human errors or assay failures that could be implicated in the residual risk. However, this model was validated by the observed yield of NAT [1]. The UK has adapted the Schreiber model by using an adjustment factor in order to evaluate the incidence rate in new donors, by calculating the risk due to test and process errors, and by using different infectious window periods than those currently adopted. It is therefore difficult to compare the results obtained in the UK with those from other European countries.

All countries that analysed trends in the residual risk showed evidence of a decrease. This trend started before the implementation of NAT, probably due to better selection of blood donors and to preventive measures taken in general population to avoid new infections. Before NAT implementation, the residual risk for HCV transmission ranged from 0.64 (France) to 3.94 (Spain) per million donations, with a north-south gradient linked to HCV epidemiology. The residual risk for HIV transmission, excluding the UK, was estimated at between 0.59 (France) and 2.48 (Spain) per million donations. Since NAT implementation, the residual risk for HCV transmission has ranged between 0.1 (France) to 2.33 (Spain) per million donations and for HIV, from 0.18 (Germany) to 1.1 (Italy) per million donations.

Yield rates observed for HIV-NAT are similar in France and Germany (about 0.3 per million donations). The higher rates observed in Italy and the UK may reflect an increased HIV incidence in their donor populations, but a bias due to the small number

of donations screened by NAT, especially in the UK, cannot be excluded. For HCV, the rates of NAT benefit are five to six times lower in northern countries (from 0.5 per million donations in Switzerland to 0.7 in the UK) than in Mediterranean countries (1.84 per million donations in Italy and 2.35 in Spain). This indicates that the yield of HCV-NAT screening is limited in geographical areas where HCV incidence rate is known to be very low. However, NAT has not been used for very long, so more time and perspective are needed. Therefore, these data should be interpreted with caution.

Despite a consensus stating that the main residual risk is currently due to hepatitis B virus (HBV) - ranging from 10 in Spain to 1.6 per million donations in France and Germany - only Germany reports systematically performing HBV-NAT, a strategy which remains controversial. Indeed, it was established that by comparison with current serological screening strategies based on very high sensitive assays for the detection of hepatitis B surface antigen (HBsAg), the expected benefit of the introduction of HBV-NAT screening, especially with MP-NAT would be poor in terms of discarded donations and clinical impact, particularly in a population that had been widely vaccinated [9] . HBV DNA screening would be more effective in countries with high or medium endemicity, and where anti-HBc testing is not routinely done.

Today, NAT implementation for HCV and HIV-1 is taken for granted in most high-income countries to ensure the maximal viral safety. However, procedures are heterogeneous and mainly adapted to the organisation of blood supply of each country. National experiences reported in this issue of Eurosurveillance are limited to western European countries and are not representative of eastern Europe, or of Europe as a whole. The results of a study carried out in 18 European countries by a European network of scientific societies (Euronet TMS) describing the NAT situation in Europe will be Published in June 2005 in a specific report [10]. This overview will serve as a base for further international surveillance in order to facilitate the harmonisation of NAT in Europe. Today, the question of NAT's cost-effectiveness is debated. Several models have demonstrated that this measure is not cost effective but no country has yet decided to withdraw it. Developing countries that have not yet implemented NAT should be advised that alternatives to NAT exist; in particular, serological assays which allow detection of viral antigens independently or simultaneously with antibodies. These assays offer improved safety at an affordable cost and circumvent the need to re-organise national blood services.

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