Transfusion-transmitted retrovirus and hepatitis virus rates and risk factors: Improving the safety of the US blood supply through hemovigilance

Protocol Summary

This project represents a collaborative pilot research study that will include a comprehensive interview study of viral infection positive blood donors at the American Red Cross (ARC), Blood Systems Inc. (BSI) and New York Blood Center (NYBC) in order to identify the current predominant risk factors for virus positive donations and will also establish a donor biovigilance capacity that currently does not exist in the US. At this time it is not easy to integrate risk factor data and disease marker surveillance information within or across different blood collection organizations because common interview procedures and laboratory confirmation procedures are not being used and so we cannot easily tabulate and analyze behavioral risks or viral infections in US blood donors. This creates the potential for gaps in our understanding of absolute incidence and prevalence as well as risks that could lead to transfusion-transmitted disease. Combined data are critical for appropriate national surveillance efforts. For example, this information could be used to target educational interventions to reduce donations from persons with high risk behaviors. This is particularly important in the case of behaviors associated with incident (recently acquired) infections because these donations have the greatest potential transmission risk because they could be missed during routine testing. As part of the project a comprehensive research-quality biovigilance database will be created that integrates existing operational information on blood donors, disease marker testing and blood components collected by participating organizations into a research database. The combined database will capture infectious disease and risk factor information on nearly 60% of all blood donors and donations in the country. Following successful completion of the risk factor interviews and research database development, the biovigilance network pilot can be expanded to include additional blood centers and/or re-focused on other safety threats as warranted, such as XMRV. This pilot biovigilance network will thereby establish a standardized process for integration of information across blood collection organizations.

Study Objectives:

1) Define consensus infectious disease testing classification algorithms for HIV, HCV, HBV, and HTLV that can be used to consistently classify donation testing results across blood collection organizations in the US. This will allow for better estimates of infection disease marker prevalence and incidence in the US.

2) Determine current behavioral risk factors associated with prevalent and incident (when possible) HIV, HCV, HBV and HTLV infections in blood donors, including parenteral and sexual risks, across the participating blood collection organizations using a case-control study design.

3) Determine nationally-representative infectious disease marker prevalence and incidence for HIV, HCV, HBV, and HTLV overall and by demographic characteristics of donors. This will be accomplished by forming research databases from operational data at BSI and NYBC into formats that can be combined with the ARC research database.

4) Analyze integrated risk factor and infectious marker testing data together because when taken together these may show that blood centers are not achieving the same degree of success in educational efforts to prevent donation by donors with risk behaviors across all demographic groups.

Study Sample:

The study sample will consist of Cases and Controls (Total 4150):

1. Cases: Blood Donors tested true positive for HIV, HCV, HBV and HTLV
2. Controls: Blood Donors tested false positive for HIV, HBV, HCV and HTLV

Table 1: Overall expected participation in risk factor interview assuming both prospective and retrospective interviews for HIV positive

Subject Type	HIV	HCV	HBV	HTLV
Case (True positive)	350	500	500	300
Control (False positive)	2500			

Recruitment and Data Collection:

In-person interviews will be conducted with all of HIV positive donors and a few other true positives for other viruses of interest. Telephone interviews will be conducted to administer risk factor questionnaire for false positive donors (control).Case recruitment procedures and study sample numbers for the interviews to be conducted will be dependent on the type of infection. The majority of risk factor interviews will be conducted soon after confirmatory testing is completed from donors who have been newly classified as true or false positive for each infection based on blood donation testing (prospective interviews). Depending on the length of study and the possibility that reduced numbers of infections possibly could be observed for unknown reasons during the planned study period and to account for the expected 75% participation of confirmed positive cases, we will also obtain human subjects approval to conduct risk factor interviews of donors from the beginning of 2010 in order to achieve the projected sample size for each infection.

Incentives will be provided. Confirmed positive donors will receive $100 for completing the interview. Incentives will be provided through the same operational procedures within each organization that allow for personally identifying each donor. The participation incentive will be sent to each donor or can be picked up at the respective donor clinics within two weeks following the completion of the interview. A $50 participation incentive will be provided to false positive (control) donors.

Data Analysis: The database will contain detailed information on dates of donation, demographic characteristics (age, sex, etc.), serology and nucleic acid testing results including confirmatory testing for each infection. The combination of results obtained from serology and nucleic acid testing allows us to identify incident infections. These data will be used to report rates of four viral infections during the initial 1-year study period (2010-2011). First-time donor and repeat donor analyses will be conducted separately. Similar to previous publications, prevalence of infection in first time donors will be calculated with associated 95% confidence intervals. Prevalence will be defined as the number of infected donations from first time donors divided by total number of first-time donations each year. Incidence is defined as the number of new infections divided by the person-years of time accrued. In repeat donors, incidence and 95% confidence intervals for each infection will be calculated using the incidence-window period model. Alternately incidence rates can be calculated in the classical way by dividing the number of identified infections by person-years for all repeat donors where follow-up time for a donor is the time between his/her first and last donation. For persons who become infected follow-up time is adjusted by assuming that the infection occurred halfway between the last negative and first positive donation so that the individual accrued person-time is half that of the follow-up time.