

## Does the Emerging Bunyavirus that causes Severe Fever with Thrombocytopenia Syndrome Impact the Blood Safety in China?

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Over the past decades, the appearance of novel infectious diseases and the spread of other known infections in human population have introduced new threats to blood safety. In 1997, the World Health Organization (WHO) estimated that infectious diseases were responsible for about 33% of all deaths worldwide primarily in the developing countries [1], and these diseases remain one of the principal challenges to human survival. Many testing assays for various transfusion-transmitted infectious diseases (TTIDs) have been introduced in blood donation screening, and as a result, largely decrease the risk of these TTIDs to blood safety. However, the lesson of first emerging infection to have a major effect on transfusion safety by HIV has sensitized us to be alerted to those emerging infections that can impact blood safety in the future.

There are three major aspects on preventing blood safety from TTIDs. The first one is donor exclusion that relies on questionnaire or strategies to preclude potentially high risk donors, before giving their blood at blood centers. Secondly, the institutes and companies are striving to develop more sensitive and specific assays to shorten the "window period" (WP) during TTIDs screenings. WP for donation can be defined as the duration between the donors was infected by TTIDs and biological makers, such as virus RNA, antigen or antibody can be detected by existing screening assays. The donors within the WP cannot be excluded for TTIDs, and this donated blood will potentially jeopardize recipients through transfusion. The third practice is to expand the current screening assays against increasingly emerging infectious diseases. In developed area/countries, such as in Western Europe and U.S., lots of blood-borne pathogens have been put in the list for routine blood screening. With approximately one quarter of the world's population and a vast diversity of wild and domestic animals living in close proximity to humans, it is most likely that China has the greatest potential to be endangered by the emergence or reemergence of infectious diseases. However, there are only four TTIDs: HIV, HCV, HBV and syphilis that are underwent routine screening at blood centers in China. The power of blood screening may be limited by upcoming newly emerged TTIDs, as well as the diversity of regional distributions.

A new RNA virus, which causes Severe Fever with Thrombocytopenia Syndrome (SFTS), was identified as the probable cause for a previously unknown severe febrile disease in 2009 in China [2]. SFTSV was first discovered from patients with SFTS from the central and northeast regions in China. The new virus belongs to the bunyavirus genus that was responsible for the growing epidemic spreading in eleven provinces until 2012 [3]. Available information from local hospitals and Center for Disease Control (CDC) suggests that the clinical syndrome and SFTSV existed prior to this recent report and the disease continues to spread. In fact, more cases and fatalities have been reported since 2009 [4]. The fatality rates of SFTS patients were reported to be 12% to 30% from several epidemiological investigations [5]. It was commonly recognized that the vertebrate hosts carrying the vectors to spread the SFTSV in epidemic areas [2]. The local center for disease control launched a serial of investigations among domestic

animals, such as goats, dogs, cattle, pigs, and chickens and the seroprevalence rates for SFTSV were ranging from 5%-95% among those animals [6,7], indicating the virus has vast transmission vectors. Although the transmission route is not clearly identified, it is likely that ticks play an important role because SFTSV RNA was detected in 5.4% of 186 ticks tested [2]. The epidemic seasons are mainly spanned from spring to autumn and the peak season was in summer from May to July [8]. Farmers in those epidemic regions were believed to be the high risk population [7], which is also one of constitutions of Chinese donor population.

It should be noticed that person to person transmission due to direct exposure to SFTS patients' blood in hospital was reported in several studies [8-11]. The Chinese Ministry of Health also promulgated the guide for SFTSV prevention, which expressly pointed out that the blood from SFTS patient was infectious and must be carefully handled to avoid nosocomial transmission [4]. These reports gave evidences that SFTSV can be transmitted *via* blood contact and may potentially threaten the blood safety in epidemic regions. The latent period following infection of SFTSV was normally one or two weeks and varies from patient to patient [12]. The first SFTS case in Zhejiang province even had a latent period for as long as 30 days [13]. Although the pathogenesis is still unclear, it is possible that the infected donations in latent period may endanger the recipient.

In healthy population, the IgG positive rate for SFTSV varies with different regions ranging from 6.37% (n=957) [14] to 1.3% (n=78) [15]. There is no SFTSV RNA detected in healthy population. A cross sectional study from three Chinese regions to determine SFTSV seroprevalence and viremic rates in blood donors was launched by The U.S. National Heart, Lung, and Blood Institute (NHLBI) and Chinese Institute of Blood Transfusion in 2012. Preliminary data indicated that the IgG and IgM prevalence rates were 1.42% and 0.91%, respectively, in one of the major epidemic regions-Xinyang, Henan province (Manuscript in preparation for submission). The sero-positive status of SFTSV among healthy donors may elude potential transmission risk via transfusion. Once the donors were identified to carry SFTSV, several strategies on blood screening should be supplemented in the epidemic regions, including: 1) The SFTSV testing should be added

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into routine blood screening at blood centers; 2) Farmers working with livestock should be excluded from donation during epidemic season; 3) More sensitive screening method should be developed to reduce the residual risk of SFTSV.

However, we are waiting for the data on the viremic rates and further longitude investigations between donors and recipients to provide more evidence on whether SFSTV endangers transfusion safety in China, and to evaluate how we take the next steps.

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