

How Blood Services can be prepared for emerging infectious agents that may impact the supply of safe blood and blood components

Alan Kitchen, PhD (UK)

Independent consultant in blood safety and infectious disease

Reference: Protecting the Blood Supply During Infectious Disease Outbreaks.
Guidance for National Blood Services. World Health Organization 2019



How Blood Services can be prepared for emerging infectious agents that may impact the supply of safe blood and blood components

Background

Blood and blood components are effective routes for the transmission of a number of blood-borne infectious agents. Blood Services globally seek to minimize the risk of transmission of any infectious agents through the screening of both the donor and the donation. However, even with the use of comprehensive donor screening programs and the use of effective laboratory screening algorithms that incorporate sensitive and specific assays to screen the donations, infected donors may donate and potentially infectious donations may enter the blood supply.

Although there is variation from country to country in the range of infectious agents for which donors and donations are screened, as a very minimum the World Health Organization (WHO), in its donation screening guidelines* recommends that all blood donations are screened for specific serological markers of hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and syphilis. While this recommendation is focused on laboratory screening to identify donations from an infected donor, the screening of the donors prior to acceptance for donation is a critical activity that seeks to minimize the risk of an infected individual being accepted for donation.

These four infectious agents are distributed globally and present a threat to all Blood Services across the globe. While WHO's recommendation does provide a minimum level of 'safety' in terms of minimizing risk of transmission of these particular infectious agents, there are, of course, a number of other infectious agents which are transmissible via transfusion.

*<https://www.who.int/publications/i/item/9789241547888>. Screening donated blood for transfusion-transmissible infections: recommendations. NOTE: updated document in process

Any risk to the blood supply is dependent upon the infectious agent being present in the donor, in an infectious form, at the point of donation. While there are some infectious agents with a global distribution, there are others that are restricted geographically and therefore not a direct threat to all blood services. Furthermore, and importantly, there is always the risk from either a novel infectious agent appearing and spreading or the spread of an existing infectious agent into previously unaffected countries, for example the 2015-16 spread of Zika virus in the Americas. Although

Responding to an emerging infectious threat is an ever-moving picture.

Blood Services cannot prevent the emergence and spread of the infectious agents, they can put measures in place to minimize the risk of the infectious agent impacting the blood supply.

Donor screening

Donor screening, which may be referred to as donor selection, is predicated on the prior knowledge of potential risk associated with the donor. These include activities, health conditions, behaviors, travel, which are considered a risk either to the donor - donation may be injurious to the donor's health, for example pregnancy - or to the recipient - transfusion may expose the recipient to an infectious agent, for example HBV. If any risk is identified either a donation is not collected and the donor deferred temporarily or permanently, or, depending on the risk identified, a donation may be collected but subject to additional

laboratory screening or investigations prior to release for clinical use. However, effective donor screening does rely on having sufficient knowledge about all of the risks to be able to ask the appropriate questions to obtain the information required.

Donation screening

Donation screening is also predicated on knowing which transfusion-transmissible infectious agents are likely to be present in the donor population and therefore which need to be specifically screened for. The laboratory screening for infectious agents needs to target the appropriate marker(s) for each infectious agent, molecular and/or serological, depending on the infectious agent. For the majority of Blood Services, laboratory screening provides the final clearance of the donation prior to release for clinical use; it is relied upon to identify any donations with evidence of the presence of an infectious agent. However, as with donor screening, the laboratory screening program is based upon existing knowledge of the transmissible infectious agents in the donor population.

The changing picture: emerging infectious threats

Although both donor and donation screening, if performed correctly using standard industry procedures, are effective in minimizing risk, they are both predicated on knowing the threats/risks in question. The problem Blood Services face with an emerging infectious threat is that the information required to determine the action needed may not be available, or at least may not be immediately available. Emerging threats from already identified infectious agents, for example the sudden and rapid spread of chikungunya virus in the Caribbean in 2012, Zika virus in the Americas in 2015-2016, and the spread of Chagas disease from South and Central America, are easier to respond to as the required virological and clinical information was already available. However, threats from a novel infectious agent, for example SARS-CoV-2, are more problematical because of the lack of specific information in the early stages of an outbreak.

Resilience to such a situation can only come from forward thinking and planning, and to do this some basic assumptions have to be made to enable a generic outline response strategy to be produced. This can then be turned into a formal strategy once sufficient information about the novel infectious agent has been obtained.

The risks to the blood supply from emerging infectious threats

Any risk to the blood supply can be considered from essentially two different but simple perspectives: is the threat going to impact on donor numbers, or is the threat going to result in transmissions via transfusion? In simple terms, a threat to sufficiency or a threat to safety?

However, at the start of any emerging threat this information may not be known, or at best there may be some limited information available. Therefore, potential risk has to be determined and decisions made which, to ensure safety, may overestimate the degree and impact of the threat, but at the same time try not to adversely impact on the sufficiency of the blood supply.

The information required to assess a potential threat includes: the nature of the infectious agent itself, the number of cases and the incidence, the clinical picture seen in those infected and any treatments or protective interventions available.

The nature of the infectious agent provides an indication of the potential impact on the blood supply. Is this an infectious agent that is likely to be transmitted via the blood-borne route – a potential safety issue – or is it an infectious agent which is unlikely to be transmitted through blood, but could render donors too ill to donate – a potential sufficiency issue. There is also the possibility that an infectious agent would impact in both areas, being transmissible via blood and making donors too ill to donate.

The case numbers and incidence provide information on how many individuals are being infected and the rate of infection. A high incidence rate in the population would be more of a threat as it is more likely that donors would become infected. This would either reduce donor numbers or present a threat as infected, but asymptomatic, donors would donate. In addition to impact on donors, there is also likely to be an impact on the Blood Service itself as staff would also be infected and could not work, impacting on the ability of the Blood Service to function properly.

Understanding the likely clinical picture is important when looking at the donor selection process.

- Does the infectious agent produce clinically significant disease? There are a number of identified infectious agents which are in many populations and transmitted via blood and components, but currently with no evidence of resultant clinical disease, for example, Torque-teno viruses.
- Does infection always give rise to symptoms or is infection often asymptomatic? Infectious agents with significant periods of asymptomatic infection are generally more problematical as infected donors are harder to identify through questioning alone.

An important element in helping to minimize risk is reminding donors to report any infections that arise or are diagnosed in the immediate period, usually two weeks post donation.

The availability of treatment or protective interventions, depending on the nature of the treatment/intervention, and, if a vaccine is available, any specific deferral requirements, could enable a Blood Service to target donors who, for example, had received vaccine against the infectious agent. Similarly, the availability of a protective intervention, for example immune plasma, could potentially enable recipients to be protected in situations when effective screening of the donor and/or donation is not possible.

Preparedness and response

To be able to respond effectively to any emerging infectious threat Blood Services need to have plans in place that both alert them to any emerging threat and enable them to identify and develop the response(s) needed. Monitoring for emerging threats is now relatively straightforward as there are many global networks which can provide the necessary information.

Responding to the threats may be harder, depending on the nature of the infectious agent, its rate of spread and its clinical severity. If infected donors can be identified by questioning, the donor selection process can minimize the risk of accepting an infected individual. There may be a number of specific factors which identify risk; questions on these need to be added to the donor selection process. An important issue is whether at-risk donors require temporary or permanent deferral.

While laboratory screening can provide a very effective means of identifying infected individuals, it does rely on screening assays being available, and, certainly in the case of a novel infectious agent, it is unlikely that suitable screening assays would be available for some time. In addition to screening assays, it is important, for epidemiological, donor management and general information gathering, that screen reactivity can be investigated further to confirm infection, this requiring additional assays that can be used for confirmatory purposes.

Summary

Responding to an emerging infectious threat is an ever-moving picture. In the early stages of such a threat a Blood Service often does not have all of the information required and has to act quickly to minimize risk. Ongoing risk assessment is needed, often requiring changes to the response as it unfolds. Key to effective response is to obtain information on the nature of the infectious agent and its clinical consequences.

The SARS-CoV-2 pandemic is the most recent global infectious threat to the blood supply. The virus is a respiratory virus and considered unlikely to be transmitted through blood transfusion; at the time of writing, no cases of transfusion transmission have been proven. The overall effect of the virus was to reduce both donor and staff numbers, impacting the blood supply through sufficiency rather than safety.

The same considerations above can be applied to non-blood donors and donations, such as tissues, stem cells and organs, although the determination of suitability may vary significantly according to the material donated. The risks associated with other

types of donated human materials may vary with the material donated, for example some tissues may carry a very low risk of harboring an infectious agent, and this, together with the processing methods applied to that tissue prior to storage and then use, may enable some tissues to be collected from an otherwise unsuitable donor. In addition, the very significant difference in the availability of blood compared to the availability of other donated materials also impacts on the determination of donor/donation suitability; any potential risks are assessed against the often greater, clinical benefit of the donated materials.