



Testing algorithms for blood: what should we test?

Ensuring the safety of blood and tissues used for donation has been a priority of government and the health system for decades, and it has been extremely successful.

While there are a large number of organisms that may be transmitted by blood transfusion (Table 1), many of these are rare or non-existent within the Australian donor population and the major concerns are hepatitis B, hepatitis C and HIV. These three are present within the Australian donor population, are readily transmitted by blood transfusion, and have the potential to cause serious, incurable illness in the recipient.

Donor exclusion, where some assessment is made of the likelihood that the person may carry one of these infections, is an important part of the risk reduction. Yet one study found that donor interviews and voluntary exclusions removed about 50% of the hepatitis C antibody positive donors and 75% of the RNA positive ones¹, so it is not perfect. Donors may not answer honestly about sensitive areas such as drug use or sexual behaviour, or they may have had unrecognised or forgotten risk exposures. Less contentious are questions about travel history, food consumption and symptoms that are used for excluding exotic infections such as malaria, West Nile virus and variant Creutzfeldt-Jakob disease.

Viral removal and inactivation steps, such as fractionation and heat treatment, are included in the final manufacturing process for plasma-derived blood products. More recently, there has been considerable interest in the use of various chemical treatments to remove pathogens that might remain within the

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donated blood². None are currently in use and their effectiveness and safety remains to be established.

Therefore, for the foreseeable future, there will continue to be considerable reliance on tests to identify infectious agents in the blood supply. We have had access to highly sensitive tests for Hepatitis B surface antigen for many years. Routine use for donor screening has reduced the risk of Hepatitis B transmission to between 1:400,000 and 1:500,000 per transfused unit³.

There is a small potential to miss infectious donors who have very low levels of virus, or those with Hepatitis B surface antigen mutants that are missed by the current tests. One solution has been to add testing for Hepatitis B core antibody, as both these groups of patients should have this antibody. Unfortunately, false positive tests are not uncommon, resulting in the unnecessary discarding of many precious units of blood^{4,5}.

As an alternative, nucleic acid tests (NAT) for Hepatitis B virus DNA are used in some parts of the world. US estimates are that it will detect less than 40 additional cases per annum in that country. The jury is still out in Australia³.

That is not the case for NAT testing for

Hepatitis C RNA and HIV RNA. Until these tests became available, donor screening relied on detection of an antibody, raising concern about donors who may be in the 'window period', i.e. the period when the person is infectious but before the antibody has reached detectable levels. With modern antibody tests, the period is about 66 days for hepatitis C and 22 days for HIV. The actual likelihood that an interview-screened Australian donor will be in this window period has been estimated as about 1:2,500,000 for HIV and about 1:330,000 for hepatitis C³. With the use of reliable automated high throughput tests for viral RNA, the window period for HIV is reduced to 11 days and the transmission risk to 1:4.8 million; for hepatitis C it is 7 days and 1:3.3 million³.

Is it worth it? Data from the USA for 2000-2001 indicated that addition of NAT tests would cost US\$22-107 million per HIV case prevented, and US\$2-8 million per HCV case prevented⁶. Due to the likely lower prevalence of these infections in the Australian donor population³, the costs would be expected to be even higher. Clearly that is not a good investment from a public health perspective, and we could likely get much better 'bang for our buck' by spending the money on preventative programmes or even on the treatment of infected individuals.

Whether the cost is worthwhile to ensure confidence in the safety of the blood supply and to protect transfusion services (and their directors) from legal and financial consequences is a decision to be made by government and by those services. It does mean that we need to think carefully about additional spending



Table 1. Infections transmitted by blood transfusion.

Agent	Screening	Comments
Diseases present in Australia with significant implications to recipients		
Hepatitis B	Questions & testing	Small risk of fatal infection. Low risk of chronic infection and a shortened life span. Treatment rarely curative.
Hepatitis C	Questions & testing	Small risk of fatal infection. High risk of chronic infection and a shortened life span. Treatment usually not curative.
HIV	Questions & testing	Very likely fatal. Treatment suppressive only.
Diseases present in Australia with limited implications to recipients		
HTLV	Testing	Small risk of developing leukemia or other clinical diseases. Rare in donor population. Transmission low risk and clinical disease in recipient extremely low risk.
CMV	Testing	Risk to infants, immunosuppressed patients and seronegative pregnant woman.
Syphilis	Testing	Uncommon in Australian donor population. Treatable infection.
EBV	None	Small risk to immunosuppressed recipients.
Hepatitis G	None	No established risk to recipients.
Hepatitis A	Questions	Rare transmission. Patients usually unwell and therefore excluded. Disease usually mild.
Parvovirus B19	Questions	Rare transmission. Patients usually unwell and therefore excluded. Disease in recipient mild or inapparent.
Dengue	Questions	Risk unknown. Rare in Australian donor population. Patients usually unwell and therefore excluded. Severe disease uncommon.
Bacterial infections	None	Rare. Various sources. Usually treatable. No practical testing methods
Diseases not present in Australia and rare in the donor population		
vCJD	Questions	Fatal outcome. Transfusion transmission not proven. No tests available.
WNV	Questions	Travel/residence history should exclude infected donors.
Malaria	Questions	As above.
Trypanosomiasis	Questions	As above.
Babesiosis	Questions	As above.

to improve what is already a very good product. This is especially important as new threats emerge (or are recognised) that raise concerns about transfusion transmission.

The best recent example is the appearance of West Nile virus (WNV) in the USA in 1999 and its subsequent spread. Transfusion transmitted WNV was first noted in 2002 and, since then, there have been a handful of cases occurring during periods of WNV activity, some of whom have developed meningo-encephalitis, often with a poor outcome⁷. Routine NAT testing of all blood donors was introduced in the US in 2003 and has so far led to the identification of several hundred unsuspected infections in donors.

So should we be worried? In fact, Australia already has its own strain of WNV called Kunjin virus. Fortunately, it is much milder than its American cousin, and neither Kunjin nor the other Australian flaviviruses such as Murray Valley encephalitis virus and Dengue virus have been shown to be transmitted by blood transfusion. However, it is also true that the populations on northern Australia that are largely affected by these viruses are under-represented as blood donors, so the system may never really have been tested.

Suffice to say we do not currently have a problem with flavivirus transmission by blood within Australia and there seems to be little merit in embarking on routine testing. Currently persons who return from areas with known West Nile activity should be excluded from donating for at least 4 weeks to allow for the incubation period to pass. Certainly we need to be prepared to commence NAT testing if the US strain of WNV does enter Australia⁹.

Another newly emergent infection, SARS coronavirus, fortunately never proved to be a transfusion problem, and has now



receded as a threat. However, it is important that we are prepared to deal with new infections quickly should they emerge.

Blood is an important and expensive commodity within our health system and ensuring that it is safe is important. However, that is only one component of the control of communicable diseases and so there is also a responsibility to ensure that donor testing is a wise investment in the health of our population.

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