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False positive viral marker results in blood donors and their unintended consequences

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False positive (FP) viral marker results in blood donors continue to pose many challenges. Informing donors of FP results and subsequent deferral can result in stress and anxiety for donors and additional complexity and workload for blood services. Donor management strategies need to balance the requirement to minimise donor anxiety and inconvenience while maintaining sufficiency of supply. Decisions about how and when to inform donors of FP results and determine deferral periods can be difficult as FP results, while often transitory, can take up to several years to resolve. Additional complexities include the interpretation of indeterminate serological confirmatory testing without detectable viral RNA or non-discriminated NAT results with concomitant anti-HBc reactivity – both may be due to FP results, but the former may also represent past infection and the later may represent occult hepatitis B infection. In this review we discuss strategies to minimise indeterminate serological confirmatory results, possible donor deferral policies and the impact on donors when notified of FP results. We also provide some new data from Australia that address the challenge of interpreting non-discriminated NAT results with concomitant anti-HBc reactivity. Ultimately, the challenge is for each blood service to develop appropriate strategies for donor management, taking into account local information and requirements.

Key words: blood donor testing, false positive, indeterminate, NAT non-discriminated reactive.

Introduction

Universal donor screening for the major transfusion-relevant viruses, hepatitis B virus (HBV), human immunodeficiency virus types 1 and 2 (HIV-1/2) and hepatitis C virus (HCV) [1, 2] has contributed to the current very low risk of transmitting infectious diseases by transfusion [3, 4]. While contemporary blood donor screening assays have excellent specificity, defined as the probability of giving a negative result for donors without previous exposure to the virus in question, 100% specificity remains elusive. Therefore an inevitable, albeit unintended, consequence of blood donor serological screening is the generation of false positive (FP) results.

Just over 10 years ago, we reviewed the management of donors with FP serological screening test results [5]. Taking into account diagnostic and therapeutic developments since that time, the purpose of this review is, firstly, to review the potential causes of serological FP results and strategies that can help to distinguish between false and 'true' positive serological results; secondly, to discuss some of the interpretative difficulties associated with nucleic acid testing (NAT); and thirdly, to describe the unintended consequences of FP results for both blood services and blood donors for whom being informed of FP results can have adverse psychological effects. Finally, we also discuss the challenges posed by atypical serology

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or NAT results for blood services and health care providers. In addition to summarizing and discussing information from a literature review, we have provided some examples and modelling based on data for Australian blood donors, particularly related to notifying and deferring donors with FP serology results and determining when NAT reactivity may represent occult hepatitis B virus infection (OBI).

Defining the terminology

Initially reactive: a reactive result for donor samples tested in singlicate for viral markers on a screening immunoassay (IA).

Repeatedly reactive: an initially reactive IA result for which the donor sample has been retested in duplicate and one or both retests are reactive.

Biological false reactive, false positive and *non-specific reactivity:* terms that have been used to describe repeatedly reactive results on screening IAs that do not confirm as positive upon confirmatory testing and therefore not considered to represent past exposure to the virus in question. In this review, we use the term false positive (FP), unless otherwise required by the context, as it is arguably the most widely used term and is sufficiently generic to be applied to both IAs and NAT.

Immunoblot (IB): assays that are commonly used as confirmatory assays to clarify the significance of IA reactive results [2]. IB assays are based on the separation of the different viral proteins into distinct bands. The presence of specific antibodies in a test sample is indicated by band staining, referred to as band reactivity.

Box 1. Potential causes of false positive (FP) immunoassay (IA) results

Immune response-related

- vaccinations such as influenza [50–54], rabies [55] or HBV[56–58]
- acute recent infections with other agents [50, 59]
- allergies [50]
- transplantation antigens or autoantibodies [60–62]
- cross-reactive IgM or IgG antibodies [63, 64]
- heterophile/polyreactive antibodies [65–67]
- ventricular assistance devices (non-specific immune activation) [68].

Passive transfer via immunoglobulin therapy

- anti-HBs and anti-HBc [69–71]
- anti-HTLV [72, 73].

Positive IB result: IB result that meets the defined criteria for positive, based on band reactivity strength and the number of reactive bands.

Indeterminate IB result: IB result with insufficient band reactivity to meet the criteria for confirmed positive, indicating that there is some uncertainty as to whether it represents false positivity or the presence of viral antibodies.

Nucleic acid testing (NAT) multiplex and discriminatory assays: Blood donor screening by NAT is typically performed with a multiplex assay that simultaneously detects HIV RNA, HCV RNA and HBV DNA. Reactivity on a NAT multiplex assay is then 'discriminated' by further testing on individual discriminatory assays for each virus.

Non-discriminated result (NDR): a NAT multiplex reactive result but the sample is non-reactive on all discriminatory assays.

False positive serological results

Potential causes of false positive serological results

Reported studies into the causes of FP results are limited and often based on case studies, many of which are somewhat dated. Nonetheless, they provide some insight into the potential causes of FP results in blood donors and the major causes identified in a number of representative studies are summarized in Box 1. These reports suggest that FP results in viral antibody IAs are primarily due to cross-reacting antibodies, as indicated by the association of FP results with conditions characterized by an underlying immune response. However, for hepatitis B surface antigen (HBsAg) IAs, the most commonly reported cause is HBV vaccination. Along with the detection of viral antibodies that have been passively transferred via immunoglobulin therapy, this is more correctly referred to as a clinical FP result as HBsAg epitopes or viral antibodies, respectively, are actually present in the test sample. In addition, two large US studies (one of which was based on >2 million donors) have indicated that donor demographic factors are associated with FP results, although specific factors may vary on a regional and/or temporal basis, and between different assays [6, 7]. Specific donor demographic factors associated with FP result on serological assays for some viral markers included being a first-time donor, female and African American or Hispanic.

Taken together, these studies suggest that FP results in viral antibody IAs are primarily due to cross-reacting antibodies, as indicated by the association of FP results with conditions characterized by an underlying immune response.

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Serological confirmatory testing: indeterminate results

Reactivity on a screening IA with concomitant detection of HIV or HCV RNA confirms the presence of these viruses without the need for IB testing. However, IB assays may be used to clarify the status of samples with IA reactivity without detectable viral RNA. As noted, IB assays can generate indeterminate results which, due to the associated uncertainty, can complicate donor counselling. Whereas donors with reactive results on screening IAs but negative by IB testing (absence of band reactivity) can be reassured that most likely their results do not represent exposure to the virus in question, the interpretation of indeterminate IB results is not always so clear.

For some time it has been recognized that most anti-HIV and anti-HTLV IB indeterminate results in voluntary blood donors without detectable viral RNA/DNA represent non-specific reactivity [5, 8, 9]. However, as approximately 25% of HCV-infected individuals spontaneously clear the virus [10], anti-HCV IB indeterminate results in the absence of detectable HCV RNA may therefore represent either past exposure to HCV with partial seroreversion [11–13] or non-specific reactivity. One approach that may help distinguish between these two possibilities is an analysis of the screening IA sample to cut-off (s/co) ratios, IB band reactivity and donor risk factors. Although not definitive, the combination of relatively higher IA s/co ratios, stronger IB band reactivity and concomitant donor risk factors may be indicative of past exposure [11, 14]. Another approach is to test donors for specific T-cell responses to HCV antigens that would indicate past exposure to HCV [12].

For HBV, in addition to HBsAg screening, a number of jurisdictions also screen blood donors for antibodies to HBV core antigen (anti-HBc). Originally implemented as a surrogate marker for non-A, non-B (NANB) hepatitis prior to the identification of HCV, more recently anti-HBc screening has been seen as a marker for the detection of OBI. OBI is a form of chronic hepatitis B characterized by undetectable HBsAg, low levels of HBV DNA which may only be intermittently detectable and, usually, the presence of anti-HBc [15]. However, it can be difficult to interpret the significance of anti-HBc-reactive results in the absence of other markers of HBV infection. While there is no universally agreed method for confirming anti-HBc IA reactive results, one approach is to retest samples on one or more additional anti-HBc IAs. Based on the rationale that anti-HBc IAs will have minimal overlap of false positivity, samples reactive on two or more IAs are more likely to represent 'true' anti-HBc rather than FP results [16, 17]. Another approach is to use anti-HBc IA s/co ratios based on the assumption that 'true' anti-HBc results will typically have higher s/co ratios than FP results [16, 18, 19].

In summary, most anti-HIV and anti-HTLV indeterminate IB results in blood donor populations without detectable viral RNA/DNA represent FP results; however, a proportion of anti-HCV immunoblot indeterminate results without detectable HCV RNA may represent past exposure to HCV.

The interpretative challenges of nucleic acid testing (NAT)

Following the widespread implementation of donor screening by NAT, two important interpretative challenges have emerged: non-discriminated results (NDR) and NAT reactivity with concomitant anti-HBc reactivity but without detectable HBsAg.

Although NDR results in the absence of serological reactivity (including the absence of anti-HBc reactivity) may potentially represent acute infections in the serological window period with low levels of virus, most appear to represent FP results [20, 21].

Is it occult hepatitis B virus infection?

Interpreting the significance of NDR results with concomitant anti-HBc reactivity but without detectable HBsAg can be a challenge, as this result profile may represent OBI and donations from OBI donors can potentially transmit HBV [21, 22]. At least two lines of evidence indicate that a proportion of NDR results with concomitant anti-HBc reactivity may represent OBI. Firstly, donors with NDR results have a higher prevalence of anti-HBc reactivity than those who are NAT non-reactive [21, 23–25]. Additionally, one study has reported that the anti-HBc prevalence in donors who test NDR is higher for those who are reactive when retested on the multiplex assay compared to those who are non-reactive [21]. Secondly, a proportion of NAT NDR results with concomitant anti-HBc reactivity have been shown to represent OBI based on testing by an alternative NAT assay and/or follow-up testing [26]. There are a number of strategies that can potentially help to clarify the significance of NDR/anti-HBc-reactive results, including : (1) follow-up testing of donors – subsequent loss of anti-HBc and/or NAT NDR would suggest the index reactive results were FP, while detection of HBV DNA would indicate OBI, (2) testing donors on an alternative NAT assay, particularly a more sensitive assay, (3) analysis of the NAT s/co ratios – low s/co ratios may indicate FP results and (4) confirming anti-HBc IA reactivity using an alternative IA.

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Table 1 Estimated percentage of NAT false positive (FP) and true positive (TP) results in anti-HBc-reactive/NAT non-discriminated reactive (NDR) Australian blood donations[a,b]

		Lower and upper 95% confidence intervals	
Anti-HBc-reactive rate in general blood donor population[c]	2·19%	1·79%	2·65%
Expected number of NAT NDR/anti-HBc-reactive FP donations (E)[d,e]	65·4	53·5	79·2
Observed number of NAT NDR/anti-HBc-reactive donations (O)	226	226	226
Estimated number of NAT NDR/anti-HBc-reactive donations due to TP NAT results (O–E)	160·6	172·5	146·8
Estimated percentage of NAT NDR results in anti-HBc-reactive donations due to FP NAT results (E/O)[e]	28·9%	23·7%	35·0%
Estimated percentage of NAT NDR results in anti-HBc-reactive donations due to TP NAT results, i.e. OBI ((O–E)/O))[f]	71·1%	76·3%	65·0%

NAT, nucleic acid testing; anti-HBc = hepatitis B core antibody.

[a]Unpublished study of Australian blood donations, July 2010–October 2015, N = 6 916 718 (see text for details).

[b]NAT non-discriminated reactive = reactive on multiplex assay/non-reactive on discriminatory assays.

[c]Unpublished study of Australian blood donors performed in 2011 using the Abbott PRISM HBcore assay (Abbott Diagnostics, Wiesbaden).

[d]Total number of NAT NDR donations = 2990.

[e]Based on assumption that the anti-HBc-reactive rate in donors who test NDR is the same as the general donor population.

[f]Based on the assumption that the increased anti-HBc-reactive rate in donors who test NDR, compared to the general donor population, is due to the presence of low levels of HBV DNA and therefore represent NAT true positive results indicating OBI.

Table 2 Follow-up of Australian donors who tested NAT non-discriminated reactive (NDR)/anti-HBc-reactive where a call back sample was available[a]

NAT result for call back sample (n = 138)	NAT non-reactive[b] (n = 121, 87·7%)	NAT NDR[c] (n = 10, 7·6%)	HBV DNA detected[d] (n = 7, 5·3%)
Mean anti-HBs level (mIU/ml) on index donation	204·2 (range 0–1000)	13·10 (range 0·3–78)	34·1 (range 2·3–148)
Mean NAT multiplex initially reactive sample to cut off ratio on index sample	8·50 (range 1·0–17·3)	12·61 (range 5·9–17·3)	13·65 (range 10·7–17·5)
Mean number of previous NAT multiplex negative donations	8·6 (range 0–84)	5·6 (range 0–16)	9·0 (range 0–33)
Number of index donations testing NAT multiplex repeat reactive[e]	6 (4·9%)	3 (30%)	2 (28·6%)

NAT, nucleic acid testing; anti-HBs, hepatitis B surface antibody.

[a]Unpublished study of Australian blood donations, July 2010–October 2015, N = 6 916 718 (see text for details).

[b]NAT non-reactive = follow-up sample negative on NAT multiplex and HBV discriminatory assays.

[c]NAT NDR = non-discriminated reactive: follow-up sample either NAT multiplex reactive/HBV discriminatory assay non-reactive/multiplex retest non-reactive or NAT multiplex reactive/HBV discriminatory assay non-reactive/multiplex retest reactive.

[d]HBV DNA detected = NAT HBV discriminatory assay reactive.

[e]NAT multiplex repeat reactive = multiplex reactive/HBV discriminatory assay non-reactive/multiplex retest reactive.

We have used probabilistic modelling in Australian blood donors to estimate the proportion of individual donor NAT NDR results in anti-HBc-reactive donors that represent OBI (Table 1). From July 2010 to October 2015, a total of 6 916 718 donations were screened by a multiplex NAT assay and 2,990 (0·043%) tested NAT NDR of which 226 were anti-HBc-reactive. Assuming that NDR donors have the same prevalence of anti-HBc reactivity as the general donor population (2·19%, range: 1·79–2·65%), the *expected* number of anti-HBc-reactive/NAT NDR donors was 65·4 (range: 53·5–79·2) which contrasted with the *observed* number of 226 (9·9%). Based on the assumption that this *increased* prevalence of anti-HBc reactivity in NAT NDR donors compared to the general donor population was due to the presence of OBI in the former, the proportion of NDR results in anti-HBc-reactive donors that represented FP and 'true' positive NAT results was estimated. The analysis indicated that approximately 71% (range: 65–76%) of NAT NDR results in anti-HBc-reactive donors would be expected to represent detection of HBV DNA (i.e. OBI), while approximately 29% (range: 24–35%) represent the chance combination of a FP NAT result with concomitant isolated anti-HBc reactivity. It is interesting to note that while the probability of an individual donation testing NAT NDR due to a FP result is the same for every *donation*, if the event is assumed to be random, the cumulative probability of a FP

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Table 3 Follow-up results for Australian donors with an index false positive (FP) result on the Abbott PRISM HTLV-I/HTLV-II assay[a]

Results for donations subsequent to index FP result	Number of donors (%) (n = 247)[b]	Estimated duration of FP results
NR donations only	89 (36·0)	Mean time from index FP to subsequent NR donation: 7 months (range 1·4–42·75)
FP donations only	56 (22·7)	Mean time from index FP to last FP in study period: 19·3 months (range: 0·25–89·75)
>1 FP donation followed by NR donations only	43 (17·4)	Mean time from index FP donation to first NR donation in study period: 23·3 months (range 4·1–92·25)
Intermittent FP and NR donations	59 (23·9)	

NR, non-reactive.

[a]Reference 33.

[b]Excludes 85 donors who did not return following an index FP result.

NAT NDR result for a specific *donor* increases with the number of times the donor is tested. Therefore FP NAT NDR results will occur more often in frequent donors who will typically have a relatively high number of NAT non-reactive donations prior to the index NAT NDR result.

We also considered whether there were indicators that can be used to help distinguish between FP and 'true' positive NAT results in anti-HBc-reactive/NAT NDR donors based on an analysis of donors for whom a follow-up sample was available (Table 2). While the analysis failed to identify definitive criteria, a number of points can be noted. Firstly, NAT reactive results with lower anti-HBs levels are more likely to represent 'true' positive NAT results, although an anti-HBs level that would definitively distinguish between FP and 'true' positive NAT results could not be defined. Secondly, anti-HBc-reactive donors with lower NAT multiplex assay s/co ratios (<5·9) were much more likely to represent NAT FP results as indicated by the fact that no donors in this category tested NAT reactive at follow-up. Thirdly, NAT NDR donors with repeatable multiplex reactivity on their index NAT reactive donation are more likely to represent 'true' positive NAT reactivity (i.e. OBI) compared to those with non-repeatable NAT multiplex reactivity.

In summary, most NAT NDR results represent FP results, but NAT reactivity with concomitant anti-HBc reactivity may represent OBI.

False positive results: unintended consequences

The consequences for donors

Being informed of FP results with subsequent deferral can have adverse consequences for donors. A 1997 study of US donors reported that donors informed of confirmed positive, indeterminate and confirmed negative (i.e. FP) results reported similar levels of confusion or emotional upset [27]. Approximately 44% of confirmed negative donors reported 'a little' confusion and 42% reported 'a lot' of confusion; 38% reported 'a little' emotional upset and 43% reported 'a lot'. A study of Swedish donors who had been temporarily or permanently deferred due to FP results during the period 2000–03 showed that more than 80% of donors reported being worried about their results [28]. Interestingly, the Swedish study reported that 88% of donors had talked privatively to a family member or acquaintance about their test results, which could potentially discourage others from donating. This finding also highlights the need to ensure that donors with FP results receive appropriate medical advice.

Donors who give FP results can be reassured that their results do not have adverse implications for their health and their donation, given in good faith, has not harmed a recipient. However, they may be subject to temporary or permanent deferral. The possibility of subsequent re-entry does not appear to reduce the level of psychological distress [29].

In summary, being informed of FP results can have adverse psychological effects on donors and therefore blood services need to develop donor notification and deferral strategies that minimize donor stress and anxiety.

The consequences for blood services

It is important that the management of donors with FP results is based on strategies that aim to respect donor concerns and minimize donor anxiety. In particular, donor deferral policies should include an assessment of the likelihood that donors will continue to give FP results at subsequent donations. Due to regulatory requirements, FP donations are usually discarded or subject to restricted usage, and it is generally considered inappropriate to allow donors to continue donating if it is likely that their future donations will be discarded. The donation process is associated with a risk, albeit small, of adverse reaction and requires time and commitment from donors who are entitled to the expectation that their donation will be used to benefit recipients.

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Table 4 Modelling donor loss for different anti-HTLV false positive (FP) deferral policies[a]

	Notify and defer after:				
	Index anti-HTLV FP result	Two anti-HTLV FP results in 12 months	Two consecutive anti-HTLV FP results	Three anti-HTLV FP results in 12 months	Three consecutive anti-HTLV FP results
Number of donors requiring notification and deferral during study period (7·5 years)	332 (100%)	140 (42·2%)	143 (43·1%)	64 (19·3%)	74 (22·3%)

[a]Reference 33.

A study of Australian blood donors who gave an index FP result on a viral antibody screening IA found that between 66% and 77·5% (depending on the viral marker) gave FP results at their next donation [30]. For those donors who gave a second FP result, between 74·5% and 84·6% continued to give FP results at subsequent donations during the study period. A subsequent longer term study of Australian donors with FP anti-HTLV IA results indicated that while approximately 53% of FP results were transient (Table 3), they can take several months to several years to resolve [31]. This is also consistent with studies that have reported indeterminate anti-HTLV and anti-HCV IB results, even when they are considered to represent FP results, can persist for several years [32, 33]. Based on the results of this longer term study, the outcome of several different donor management strategies was modelled (Table 4). The modelling suggests that there is some benefit, in terms of donor retention, of not deferring donors following an index FP result but waiting until there have been two or even three FP results. This may provide a balance between the need to maximize donor retention while not allowing donors to continue donating indefinitely if it is highly likely that future donations will be discarded.

For blood services that have implemented universal donor screening for anti-HBc, potential strategies to manage donors with anti-HBc reactivity include donor deferral, regardless of the presence of other markers of HBV infection, or permitting donors to continue donating if anti-HBc reactivity is accompanied by an anti-HBs level (usually >100 IU/l) indicative of minimal risk of HBV transmission [34, 35]. However, re-entry protocols for anti-HBc-reactive donors appear to be of limited value as anti-HBc reactivity typically persists longer term in most donors [36, 37].

The number of IB indeterminate results can be minimized by reducing or even eliminating the use of IB assays. One effective strategy is the use of sequential screening IAs whereby donations are screened on a primary IA and, if reactive, screened on a secondary IA [38]. Only samples that are reactive on both IAs are further tested by IB [39–42]. Another approach, which has been applied to anti-HCV screening, is to interpret the anti-HCV status based on the s/co ratio of the screening IA, either without IB testing or only performing IB testing on samples with IA s/co ratios below a predefined value (s/co ratios equal to or greater than this predefined value would be assessed as confirmed positive without IB testing) [43–45]. From a donor counselling perspective, these strategies potentially result in a number of donors being assessed as FP who would have otherwise been assessed as indeterminate, and therefore can be given a more reassuring message.

In summary, it is important that blood services develop notification and deferral strategies that balance donor retention while not allowing donors to continue donating if it is highly likely they will continue to give FP results.

FP or past exposure: implications for donor clinical care and health care providers

A major challenge is determining whether donors with serological reactivity without detectable viral RNA/DNA represent FP results as opposed to spontaneously resolved or treated and 'cured' infection. In the case of donors with results consistent with past infection it is important to reassure them that, although they do not have evidence of current infection it is recommended that the test is repeated. In addition, they need to be aware that the results may persist in the event of subsequent testing, such as for insurance purposes or in the context of needlestick injury testing. It is also important to inform these donors that, although they don't have evidence of current infection, due to regulatory requirements they cannot continue as a blood donor. Where appropriate, donors also need to be made aware of the potential for meeting the jurisdictional case definition of a notifiable disease and therefore of the blood service's legal obligation to notify health departments [46]. In our experience, despite reassurance, the stigma of a confirmed HCV

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diagnosis, even in the absence of current infection where there is no potential for adverse health outcomes, can cause unnecessary donor anxiety. Therefore, it is important that blood services have experienced counsellors and appropriately worded standard information and referral letters for donors and their health providers. Additionally, for past infection with HBV it is important to inform donors of the potential HBV reactivation.

There are circumstances where serological reactivity without NAT reactivity may in fact represent recent or even current infection. Firstly, a small proportion of HIV infections, referred to as viraemic controllers, are characterized by very low levels of HIV RNA in the absence of anti-retroviral therapy (ART) [47]. Additionally, a subgroup of controllers, referred to as elite controllers, may even have undetectable HIV RNA [48]. Secondly, there is the possibility of HIV-infected individuals on ART being intentionally non-compliant and therefore presenting to donate with undetectable HIV RNA. However, both elite controllers and infected individuals on ART demonstrate an immune response to HIV and would therefore be detected by anti-HIV screening [48]. A similar situation can also arise with HCV infection [49]. Direct-acting antivirals (DAA) now offer effective cure for HCV infection resulting in detectable anti-HCV without detectable HCV RNA. Successful DAA treatment may result in individuals presenting to donate on the basis that they are now cured and erroneously believe they are eligible to donate. Such individuals generally test reactive by anti-HCV screening and therefore their donations would be discarded due to regulatory requirements.

Finally, there are also challenges associated with informing and educating medical and nursing staff about these issues as the terminology is complex (and may change over time) and the implications for an individual donor's health are not always clear. In particular, for OBI diagnosed with very sensitive NAT assays in the context of a well person donating blood, the prognosis and health implications are likely to be different to a diagnosis in a clinical setting for a patient with symptomatic infection. For example, in Australia, OBI donors may be referred to their regular physician or an infectious diseases specialist. However, most community- or hospital-based clinicians will have little experience in interpreting results and providing advice in this context, and there is limited evidence-based information to guide discussions. Liaison with experienced specialist and/or blood service physicians can be an important resource in these situations. Given asymptomatic OBI is almost exclusively diagnosed in blood donors due to sensitive HBV NAT screening, blood service physicians will typically have the most experience with interpreting these results.

In summary, there are circumstances when atypical serology or NAT results may represent past or even current infection rather than FP results. Input from clinicians with experience in this area is important for donor management.

Conclusions

In this review, we have summarized the potential causes of FP serological results and how they may currently be distinguished from true positive results. We have highlighted the importance of recognizing that donors can be adversely affected when notified of FP results due to stress and anxiety. However, donors with screening IA FP results or NAT NDR results without concomitant serological reactivity should be reassured that their results do not indicate current or past infection with the virus in question. NAT NDR results with concomitant anti-HBc reactivity may represent OBI and therefore additional testing and donor follow-up is required.

We suggest that ultimately, each blood service should develop its own strategies for the notification and deferral of donors with FP results, taking into account the variable time taken for FP results to resolve, the frequency of FP results in its own donor population and the impact on sufficiency of supply due to the potential loss of donors and donations. Due to the limited amount of data on the cost/benefit of various deferral and re-entry strategies, we recommend blood services that have implemented management strategies for donors with FP results perform this type of analysis and publish their results. Finally, as donor screening technologies evolve and more jurisdictions extend screening to include a number of emerging infectious disease pathogens, we encourage blood services to analyse the performance of their assays, particularly the rate of FP results, and publish their findings. These suggestions will provide valuable information which could be used as a basis for ongoing reviews and inform the development of improved donor notification and deferral strategies.

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