TABLE 4. Blood donors and components included in study of HBV transmissibility and relationship between HBV-TTI and anti-HBc status of transfused components

Anti-HBc in repository samples	Number of donors	Converted marker	Number of components processed and transfused	Total number of components evaluated	Infection	
					Yes	No evidence
Low titer	29	NAT: 4	5	33	1	32
		Anti-HBc: 25	28			
Negative	20	NAT: 1	1	22	11	11
		HBsAg: 4	4			
		Anti-HBc: 15	17			
Undetermined	6	NAT: 1	1	8	0	8
		Anti-HBc: 5	7			
Total	55	NAT: 6	7	63	12	51
		HBsAg: 4	4			
		Anti-HBc: 45	52			

assumed to be TTI cases, the infectivity of the components would be 27 percent.

Blood components transfused to the 63 patients had been processed from 55 donations (Table 4). The HBV infection status of the 55 donations was determined from the anti-HBc and anti-HBs data and was further confirmed by the serologic data that were obtained with the repository tubes in the subsequent donation when HBV marker(s) converted. Twenty-nine donors with low-titer anti-HBc were judged to be in the occult carrier state (Table 4); 4 donors who became 50-NAT–positive in the subsequent donation were anti-HBc–positive with greater than 95 percent EIA inhibition in both the index and the subsequent donations, and all 25 donors showed weak reactivity for HI and greater than 90 percent (except for one case with 63%) EIA inhibition in the index donation and showed HI positivity and greater than 95 percent EIA inhibition in the subsequent donation. One exceptional donor with 63 percent EIA inhibition for anti-HBc was a 60-year-old woman with 72 mIU per mL anti-HBs in the index donation. Twenty anti-HBc–negative donations were designated as those obtained during the window period (Table 4); 4 donors became strongly positive for EIA-HBsAg with greater than 200 S/N within 2 months; 13 donors became anti-HBc–positive with greater than 90 percent EIA inhibition coupled with HI conversion in the subsequent donations; 1 donor with 5 percent inhibition for EIA-anti-HBc became HI-positive with an increase of up to 65 percent inhibition and anti-HBs conversion; 1 donor with 10 percent inhibition became HI-positive although EIA-anti-HBc remained negative after 14 days with 46 and 38 percent inhibitions in duplicate tests; and 1 donor became positive only for 50-NAT after 33 days, representing a minipool (MP)-NAT window case. For the six donations that had conflicting results between HI and EIA-anti-HBc, the infection status was not determined even if the serologic data in the subsequent donation were taken into consideration. A nonspecific reaction of HI and EIA-anti-HBc or the recovery phase of acute infection with or without prior vaccination are the possible explanation for this category. Because the transfusion of components derived from one donation (e.g., red blood cells [RBCs] and fresh-frozen plasma [FFP]) sometimes caused discrepant results in patients and the total viral loads of the components were different depending on the component types, clinical outcomes resulting from the transfusion of components derived from single donation are described separately in the present analysis.

Note that 11 of the 12 components that caused HBV infection had zero or negligible anti-HBc titers and therefore were considered to have been derived from donations given during the 50-NAT window period (Table 4). One jumbo FFP component (450 mL) identified by 50-NAT conversion in the subsequent donation had low anti-HBc titer with fewer than 100 copies per mL viral concentration. This case represents a TTI case caused by the transfusion of an occult carrier–derived component. Results of anti-HBs testing were available for 9 of the 12 infectious samples (Table 5). All 9 showed negative results including the sample from the occult carrier that had 4.8 mIU per mL, a value defined as negative. Of the repository tubes from 51 noninfectious components, 11 were negative and 32 were positive with low titer for anti-HBc (Table 4). Of the 32 samples with low-titer anti-HBc, 11 were positive and 12 were negative for the presence of anti-HBs (Table 5).

In summary, of the 33 components with low-titer anti-HBc, only 1 could be identified that caused infection, whereas of the 22 anti-HBc–negative components, 11 had proved to cause infection (Table 5). If the 8 anti-HBc–undetermined cases were also considered, the infectivity range of low-titer anti-HBc components was 2.4 to 3.0 percent and that of anti-HBc–negative components was 37 to 50 percent, showing that the HBV transmission rate of window period–derived components observed in our hemovigilance system is more than 10-fold higher than the rate caused by occult carriers with low-titer anti-HBc

TABLE 5. Relationships between anti-HBc, anti-HBs, and HBV-TTI

Anti-HBc	Infection	Anti-HBs			Total
		Positive	Negative	Undetermined	
Low titer	Yes	0	1 (1)*	0	1
	No†	11 (17)	12 (15)	9 (0)	32
Negative	Yes	0	8 (9)	3 (2)	11
	No	0	8 (10)	3 (1)	11
Undetermined	Yes	0	0	0	0
	No	5 (5)	2 (2)	1 (1)	8
Total	Yes	0 (0)	9 (10)	3 (2)	12
	No	16 (22)	22 (27)	13 (2)	51

* Number in parentheses is the number of donations that include ones whose anti-HBs status was estimated with the data obtained from subsequent donation.
† No evidence of infection.

who have slipped through the JRC screening system. It is also clear that there was no HBV-TTI in patients who were transfused with anti-HBs–positive components. When anti-HBc–undetermined cases were included, none of 16 anti-HBs–positive components exhibited evidence of infection (Table 5). When anti-HBs–undetermined cases were reevaluated with the anti-HBs and/or anti-HBc data in the subsequent donation and time interval between the two donations, the cases were successfully divided into anti-HBs–positive or –negative groups (numbers in parenthesis in Table 5). When the estimated numbers were also taken into account, it is calculated that the infectivity of components with and without anti-HBs was 0 of 22 and 10 of 37, respectively (Table 5).

In both the low-anti-HBc-titer group and the anti-HBc–negative group, the same HBV DNA levels were measured in the components with and without evidence of infection (Table 6). This is true even when viral load is adjusted to total viral copy number contained in the components with mean plasma volume of each component (data not shown). There was also no clear correlation between the type of blood components transfused and the infection outcomes observed in the recipients. There were two cases where components from one donation caused discrepant results in two patients transfused (Table 6 footnote). The distribution of age or sex showed no difference between the patients with and without serologic evidence of infection (data not shown).

The basic disease conditions of the TTI cases were available for nine patients: multiple trauma in one, surgical operation in three, shock due to trauma and burn in one, great vessel diseases in two, hematologic malignancies in two, and disease unknown in three (Table 7). The results show that patients prone to infection were not limited to heavily immunocompromised people. Four patients showed elevated alanine aminotransferase (ALT) of more than 100 IU per L. Although the number of patients was limited, there was a tendency that a high ALT was associated with a high total viral load infused.

DISCUSSION

The sample repository of all donations stored since 1996 enabled us to perform a lookback study and identify the blood donations that were ID-NAT–positive with low HBV DNA levels but had not been detected by the regular 50-NAT, HBsAg, and anti-HBc screening tests. Although the serologic testing of pre- and posttransfusion blood samples of patients who had received the ID-NAT HBV DNA–reactive blood components was often incomplete, we were able to show a difference in the transmissibility of HBV between donations in the pre-HBsAg and/or MP-NAT window phase and blood from donors with occult HBV infection whose anti-HBc titers were below the exclusion limit of the JRC screening system.

We performed HBV ID-NAT on 15,721 repository tubes and identified 158 (1.01%) DNA-positive samples, of which 95 were anti-HBc–reactive with low titer, indicating that, under the Japanese screening algorithm, 60 percent of the ID-NAT-only–positive donations from repeat donors are derived from occult carriers. The viral loads of the samples from occult carriers were very low with 75 of 78 samples having fewer than 100 copies per mL. Such concentrations cannot be detected with pool-NAT systems[11] suggesting the need to develop and implement ID-NAT systems for screening.[12] When no ID-NAT systems are available, sensitive anti-HBc testing is currently the only measure for identifying these very low viral loads from occult carrier donations.[13,14]

Of the 63 patients transfused with ID-NAT-only–positive components, 12 (19%) were confirmed as HBV-TTI cases. This number is unexpectedly low relative to the high HBV infectivity observed in clinical settings and animal experiments.[15,16] Possible reasons for this include the following: 1) anti-HBs or anti-HBc testing before and after transfusion is not routinely performed in medical facilities; thus some patients might have immunity against reinfection from past exposure to HBV or vaccination, whereas a relatively large proportion of HBV infections may not have been recognized in the current hemoviligance system in the hospitals. It is, however, unlikely that most noninfected patients maintained immunity by past infection given the hepatitis marker frequency of first-time donors in Japan, where the highest prevalence of anti-HBc (6.82%) has been observed in donors in their sixties.[17] Assuming that this percentage represents the mean anti-HBc prevalence among patients who received transfusions and that all anti-HBc–positive people have immunity against reinfection, prior protection would have contributed very little to the observed incidence of HBV-TTI. 2) The viral copy number obtained

TABLE 6. Relationship between HBV infectivity, HBV viral loads, and types of components

Anti-HBc status	Infectivity	Viral loads (copies/mL); component type(s)
Low titer (33)	Infectious (1)*	<100; FFP (1)
	Without evidence of infection (32)	<100 (27), 93, 98, 100, 120, NT†; RBCs (17), FFP (14), PC‡ (1)
Negative (22)	Infectious (11)	<100 (6), 160, 170, 230§, 300‖, 380; RBCs(5), FFP(4), PC(2)
	Without evidence of infection (11)	<100 (8), 170, 230§, 300‖; RBCs (5), FFP (4), PC (2)
Undetermined (8)	Without evidence of infection (8)	<100 (6), 200, 460; RBCs (2), FFP (6)

* Number in parentheses is the number of components.
† NT = not tested.
‡ PC = platelet concentrate.
§ RBCs and FFP were processed from the donation and transfused to a patient undergoing orthopedic surgery and a gastric cancer patient, respectively. The former patient acquired HBV infection and the latter did not.
‖ FFP and RBCs were processed from the donation and transfused to a patient with dissecting aneurysm and a patient undergoing orthopedic surgery, respectively. The former patient acquired HBV infection and the latter did not.

TABLE 7. Basic disease conditions of TTI cases

Age (years)	Sex	Basic disease status	Converted marker	Highest ALT (IU/L)	Types of components transfused	Viral copies/mL in components	Total viral loads infused*
65	Male	Multiple trauma	HBsAg	2281	FFP-2 (WP)†	1.7×10^2	27,200
66	Female	Knee joint replacement (rheumatoid arthritis)	Anti-HBs	1109	RBCs-2 (WP)	2.3×10^2	5,750
49	Female	Dissecting aneurysm	HBsAg	992	FFP-2 (WP)	3.0×10^2	48,000
71	Male	Gastrectomy (gastric cancer)	HBsAg	148	RBCs-2 (WP)	<100	UD‡
62	Male	Acute myelogenous leukemia	HBV DNA	66	PC§-15 (WP)	3.8×10^2	95,000
63	Male	Carotid artery stenosis	HBsAg	56	RBCs-2 (WP)	<100	UD
74	Female	Shock due to trauma and burn	HBsAg	33	FFP-1 (WP)	<100	UD
68	Male	T-cell lymphoma	HBsAg	27	PC-10 (WP)	<100	UD
78	Male	Gastrectomy (gastric cancer)	HBV DNA	17	RBCs-2 (WP)	<100	UD

* Total viral load in the component was calculated with the plasma volume of each component; FFP-2, 160 mL; RBCs-2, 25 mL; PC-15, 250 mL; FFP-1, 80 mL; PC-10, 200 mL.
† Components obtained during the window phase (WP).
‡ UD = undetermined.
§ PC = platelet concentrate.

by PCR may include replication-incompetent DNA fragments and therefore may not directly relate to infectivity. 3) A protective effect may be induced by passively transferred anti-HBs from index components or components from other antibody-positive donors transfused close to the time of HBV exposure. 4) The infectivity of HBV may be reduced during storage of the blood components.

Despite these limitations we were able to compare the outcomes of HBV transmission of components derived from 55 donations and compare the infection outcomes in 63 recipients. The results that were retrievable in the hemoviligance system indicate that the donations in the pre-HBsAg and/or MP-NAT window phases are at least 10-fold more infectious than the donations with low anti-HBc titers from occult carriers. Eleven of 22 (50%) components derived from window-phase donations proved to have caused seroconversion of HBV markers in the recipients, whereas only 1 of 33 (3%) anti-HBc–reactive donations showed serologic evidence of infection. The infectious anti-HBc–reactive FFP component came from an anti-HBs–negative occult HBV carrier with fluctuating viremia. None of 11 anti-HBc–reactive and anti-HBs–positive units proved to have caused infection. When the anti-HBc–undetermined units were taken into consideration, it was revealed that there was no evidence of infection in any of the 16 patients transfused with anti-HBs–positive components. To establish the relationship between the titer of anti-HBs and the infectivity of occult carrier–derived blood, more clinical reports are needed for the category of patients who acquired infection as a result of transfusion of low titer anti-HBc components. When the clinically observed HBV transmission rate of anti-HBs–negative donations with and without low-titer anti-HBc was compared, it turned out that the transmission rate caused by the presumed tail-end carriers with occult HBV infection (1/13, 8%) was still significantly lower than the rate of the window-phase donations (8/16, 50%; $p < 0.05$). There were three components having at least 200 copies per mL of HBV sequence that did not cause infection even in the absence of detectable anti-HBs. It may be that the infectivity of donors with higher anti-HBc titers (that are screened out of the Japanese blood supply) have a higher risk to be infectious, particularly in the tail-end chronic carriers without circulating

neutralizing anti-HBs. More research needs to be done to understand the infectivity of HBV in donors with chronic occult infection or with persistent or recurrent viral replication after recovery. In chronic and perhaps more in recovered occult HBV infection, mutations in the genome may reduce the capacity of viral entry, replication, and secretion.[18-24] It has been reported that a portion of patients who recovered from acute hepatitis harbor HBV in their liver and may exhibit intermittent viremia even after complete clinical resolution and HBsAg clearance.[25-28]

There was essentially no difference in copy number between the infectious and the presumed noninfectious components, indicating that the viral load is not the only factor for infectivity. The infectious load is dependent on the amount of plasma and 3- to 20-fold higher in platelet concentrate or FFP than in RBCs, but we were unable to demonstrate a difference in transmission risk between these components. It may be that other factors affecting the observed infectivity in recipients (see above) have masked the known relationship between infectivity and viral load in the transfused components. Unfortunately we have no means to confirm whether indeed half of the anti-HBs–negative window-phase units were not infectious even though viral loads above 10^2 to 10^5 HBV particles have been infused. It may be that we would have found these donations to be infectious when anti-HBc and anti-HBs was routinely tested in the pre- and posttransfusion samples of the recipients. Our estimates for the infectivity of ID-NAT-only–positive units may thus be underestimated. We also could not find any clear differences between the patients' susceptibility profiles in terms of disease status, age, and sex. Although we could not find clear relationship between infectivity and viral load in components, some degree of association was suggested between patients' high ALT value during the course of infection and the high total viral load contained in the component, the result reminiscent of the report by Barker and Murray.[29]

JRC has been collecting voluntary reports on TTI from hospitals and has already established a database for isolated TTI cases.[30] Combining these data and those obtained from this lookback study, it is estimated that the total number of HBV-TTI cases is 17 to 20 per year (1/0.27-0.32 million donations) in Japan with 5.4 million annual blood donations and that approximately 85 percent of the HBV infections are caused by the transfusion of window period–derived components. Although it is obvious that combined screening with ID-NAT and sensitive anti-HBc testing would ultimately reduce the HBV-TTI cases, a decision on whether the anti-HBc screening is implemented or not should be made considering the local prevalence of HBV in the area considered, the number of donors who would be disqualified as a result of anti-HBc screening, and the relative low infectivity of occult carrier–derived components described in this report.[31] One must bear in mind, however, that in our study only the infectivity of low-titer anti-HBc carriers was examined and that the picture can be completely different for anti-HBs–negative occult carriers with higher anti-HBc titers. It should also be mentioned that JRC's serologic test, especially hemagglutination for HBsAg, has lower sensitivity than EIA and that the rate of screening NAT yield and ID-NAT-only–positive donation can be different in other areas.

Inaba and coworkers[32] recently reported about another anti-HBs–negative occult carrier with borderline detectable anti-HBc levels who was found some of the time to be ID-NAT–positive and some of the time to be ID-NAT–negative.[32] This may be caused by fluctuating viremia in the donor or stochastic sample variability in the NAT assay typical with low viral load. Lookback study showed that some of the previous donations, both ID-NAT–positive and ID-NAT–negative units, had caused HBV infection in the recipients and that some had caused clinical hepatitis. This donor only would have been detected with more sensitive anti-HBc screening or with ultrasensitive ID-NAT. JRC is currently exploring which options remain to further reduce the risk of posttransfusion hepatitis B.

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研究報告の概要

○献血者への追跡調査(献血後情報)により輸血によるHBV感染が示唆された一症例について

はじめに:平成19年3月、A医療機関より輸血によるHBV感染が疑われるとの報告が千葉県赤十字血液センターにあった。因果関係の確認のために実施した当該輸血用血液製剤に係る保管検体個別NATは陰性であり、献血者追跡調査により輸血によるHBV感染が示唆された一症例を経験したので報告する。

症例:患者は70歳代女性、平成18年9月に人工関節置換術の際に、今回の当該輸血用血液製剤(RC-M・A・P2単位)を含む4単位の輸血を受けた。輸血前のHBs抗原は陰性。平成19年3月上旬、食欲不振、全身倦怠感、ビリルビン尿出現により近医を受診。肝機能障害、黄疸症状が認められ、輸血を実施したA医療機関に紹介され入院となった。入院時の血液検査では、HBs抗原陽性、HBc抗体(IgM)陽性、AST、ALTは高値であり急性B型肝炎と診断された。A医療機関より副作用感染症報告を受け、当該輸血用血液製剤に係る保管検体2本について、個別NATを実施したが2本とも陰性であった。A医療機関担当医から、患者の感染経路は輸血以外に考えにくく、献血者の追跡調査の要望があった。当該輸血用血液製剤に係る献血者2名には、その後の献血歴はなく、血液センターからのフォローアップの結果、1名の献血者については平成19年1月にB型肝炎を発症し、B医療機関で治療中であるとの情報が寄せられた。献血者とB医療機関の了解を得て、平成19年4月受診時の検体を検査したところHBV-DNAが検出され、患者のそれと塩基配列が一致した。他の1名の献血者は、平成19年4月採血の追跡調査結果はHBV-DNA陰性であった。

まとめ:20プールNAT陰性、HBV保管検体個別NAT陰性であったが、献血者追跡調査により輸血用血液製剤からのHBV感染が示唆された一症例を経験した。原因血はHBV感染のごく初期であったと推測された。

使用上の注意記載状況・その他参考事項等

解凍赤血球濃厚液「日赤」
照射解凍赤血球濃厚液「日赤」
解凍赤血球-LR「日赤」
照射解凍赤血球-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

報告企業の意見	今後の対応
20プールNAT陰性、HBV保管検体個別NAT陰性であったが、献血者追跡調査により輸血用血液製剤からのHBV感染が示唆された一症例を経験したとの報告である。	日本赤十字社では、HBs抗原検査及びHBc抗体検査を実施することに加えて、HBVについて20プールでスクリーニングNATを行い、陽性血液を排除している。HBV感染に関する新たな知見等について今後も情報の収集に努める。また、これまでの凝集法と比べて、より感度の高い化学発光酵素免疫測定法(CLEIA)の導入を予定している。NATの精度向上についても評価・検討している。

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献血者への追跡調査（献血後情報）により輸血によるHBV感染が示唆された一症例について

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【はじめに】平成19年３月，A医療機関より輸血によるHBV感染が疑われるとの報告が血液センターにあった。因果関係の確認のために実施した当該輸血用血液製剤に係る保管検体個別NATは陰性であり，献血者追跡調査により輸血によるHBV感染が示唆された一症例を経験したので報告する。

【症例】患者は70歳代女性，平成18年９月に人工関節置換術の際に，今回の当該輸血用血液製剤（RC-M・A・P２単位）を含む４単位の輸血を受けた。輸血前のHBs抗原は陰性。

平成19年３月上旬，食欲不振，全身倦怠感，ビリルビン尿出現により近医を受診。肝機能障害，黄疸症状が認められ，輸血を実施したA医療機関に紹介され入院となった。入院時の血液検査では，HBs抗原陽性，HBc抗体（IgM）陽性，AST，ALTは高値であり急性B型肝炎と診断された。A医療機関より副作用感染症報告を受け，当該輸血用血液製剤に係る保管検体２本について，個別NATを実施したが２本とも陰性であった。

A医療機関担当医から，患者の感染経路は輸血以外に考えにくく，献血者の追跡調査の要望があった。

当該輸血用血液製剤に係る献血者２名には，その後の献血歴はなく，血液センターからのフォローアップの結果，１名の献血者については平成19年１月にB型肝炎を発症し，B医療機関で治療中であるとの情報が寄せられた。献血者とB医療機関の了解を得て，平成19年４月受診時の検体を検査したところHBV-DNAが検出され，患者のそれと塩基配列が一致した。

他の１名の献血者は，平成19年４月採血の追跡調査結果はHBV-DNA陰性であった。

【まとめ】20プールNAT陰性，HBV保管検体個別NAT陰性であったが，献血者追跡調査により輸血用血液製剤からのHBV感染が示唆された一症例を経験した。原因血はHBV感染のごく初期であったと推測された。

医薬品 研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	機構処理欄
				2007. 9. 20	該当なし	

一般的名称	解凍人赤血球濃厚液	研究報告の公表状況		公表国
販売名(企業名)	解凍赤血球濃厚液「日赤」(日本赤十字社) 照射解凍赤血球濃厚液「日赤」(日本赤十字社) 解凍赤血球-LR「日赤」(日本赤十字社) 照射解凍赤血球-LR「日赤」(日本赤十字社)		入江興利子, 岡晴美, 押野正次, 堀江真理子, 福森泰雄, 中出亮, 平山文也, 吉村敬次, 谷慶彦, 柴田弘俊. 第31回日本血液事業学会総会; 2007 Oct 3-5; 高松.	日本

研究報告の概要

○NATスクリーニングのプールサイズ縮小による効果と分析

はじめに:輸血用血液製剤の安全性の向上を目的として、2004年8月よりNATスクリーニングのプールサイズを50から20に縮小した。今回、大阪府赤十字血液センターで検出されたHBV-NAT陽性事例を基にプールサイズ縮小の効果等について解析を行ったので報告する。

対象:大阪センターにおいて50プール及び20プールで検出されたHBV-NAT陽性事例の合計81人を対象とした。

結果:HBV-NAT陽性数は右表の通り。HBc抗体陽性の12人中、11人は50～60歳代でウイルス量が1,000コピー未満/mLであり、残りの1人は28歳でウイルス量が 1.7×10^5 コピー/mLであった。また、12人中10人の献血者について医師による面談及びフォローアップを行ったところ、急性肝炎の発症等に関する申告はなく、来所時の検査結果によるウイルスコピー数及びウイルスマーカーの変動はなかった。

考察:①プールサイズ縮小後に100コピー未満/mLのHBV-NAT陽性者の比率が高くなっていることから、縮小による効果があると思われた。②追跡調査、遡及調査及び医師の面談等による総合的な解析によりHBV低濃度キャリアが疑われる献血者がプールサイズ縮小後に多く検出されていることが推察された。

		50プール	20プール
陽性者		55人(2.72)	26人(2.50)
HBc抗体(EIA法)	陽性者	3人:5.5%(0.14)	9人:34.6%(0.86)
	陰性者	52人:94.5%(2.57)	17人:65.4%(1.63)
100コピー未満/mLの陽性者		1人:1.8%(0.04)	6人:23.1%(0.57)
1,000コピー未満/mLの陽性者		14人:25.5%(0.69)	8人:30.8%(0.77)
50～60歳代の陽性者		4人:7.3%(0.19)	10人:38.5%(0.96)

( )内は10万人当たりの本数

使用上の注意記載状況・その他参考事項等

解凍赤血球濃厚液「日赤」
照射解凍赤血球濃厚液「日赤」
解凍赤血球-LR「日赤」
照射解凍赤血球-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

報告企業の意見

献血血液のNATスクリーニングのプールサイズを50から20に縮小した後、100コピー未満/mLのHBV-NAT陽性者の比率が高くなったことは縮小の効果と考えられ、HBV低濃度キャリアが疑われる献血者はプールサイズ縮小後に多く検出されたとの報告である。

今後の対応

日本赤十字社では、HBVについて20プールでスクリーニングNATを行い、陽性血液を排除している。HBV感染に関する新たな知見等について今後も情報の収集に努める。次世代NAT試薬についての評価、検査方法の改良に向けた開発・検討を進める。