are related to either the safety of donors or their potential risk of exposure to infectious diseases.[2] For example, date of last donation, date of birth, hemoglobin level, blood pressure, pulse, and weight are mainly for the safety of blood donors, whereas histories of, or exposure to, HIV, hepatitis, and other blood-borne, sexually transmitted, or certain endemic infections are for the safety of blood recipients. Donors in the first category are deferred from donating blood since the donation process may harm their health. Donors in the latter category are deferred from donating blood to prevent blood recipients from exposure to potentially higher risk of infectious diseases. Such donors may be harboring an infectious agent and potentially be able to transmit that agent to recipients through the donated blood. For blood-borne infections for which no testing is available, blood donor interview and subsequent deferral is believed to represent an important safeguard against transfusion transmission of such infections. Even for blood-borne infections for which there is routine testing, donor interview and deferral are considered extra layers of assurance, because blood donor infectious disease testing, while having excellent sensitivity, is not without false-negative results, particularly for very recently acquired infections.

The expanding list of health history questions related to potential exposure to blood-borne infections has had a significant impact on the blood collection process. Not only have such questions resulted in a large number of blood donors being deferred each year by blood centers in the United States but also many of the temporarily deferred donors do not return to donate blood.[2-7] Few studies have been conducted to evaluate the interview process or the majority of the screening questions. With the changing epidemiology of blood-borne infections among blood donors and the improved testing methods for donated blood, an assessment of the current impact of the interview process and the screening questions has become more relevant.

An earlier study of American Red Cross (ARC) blood donors examined prevalence of hepatitis B surface antigen (HBsAg) or antibodies to HIV (anti-HIV), HCV (anti-HCV), or HTLV (anti-HTLV) for different groups of donors who were temporarily deferred in 2000 to 2001 and later returned to donate blood in 2000 to 2003.[8] The results were compared with either first-time or repeat donors in 2000 to 2003, while controlling for differences in sex, age, and year of donation. Of donors temporarily deferred in 2000 to 2001 who had had no donation or deferral during the previous 2 years, only 22.08 percent subsequently returned to donate blood in 2000 to 2003. Donations from returning donors who had been deferred for potential infectious disease risk did not show a higher prevalence for any of the viral markers when those with no donation or deferral during the previous 2 years were compared with first-time donations and those with prior donation were compared with repeat donations. The study concluded that blood donors temporarily deferred in 2000 to 2001 for potential risk of viral infection who later returned to donate blood did not appear to pose a higher risk compared to first-time or repeat donors. The study suggested that the effectiveness of some of the currently used deferral questions in reducing viral risks warranted further study. The previous study, however, only examined interview questions that result in temporary deferrals. In addition, a limitation of this study was that temporarily deferred donors who subsequently returned to donate blood could be different from those who had been deferred but did not return.

To further assess the impact of the donor health history questionnaire and particularly certain interview questions that result in indefinite deferral, a study was designed to recruit deferred donors and to test a sample of their blood for prevalence of blood-borne infections.

MATERIALS AND METHODS

Study population

The study targeted blood donors who presented to ARC Blood Services and were deferred from donating blood due to answering "yes" to health history question(s) at four different centers of the ARC Blood Services during the following time periods: 2003 to 2005 for two centers, 2004 to 2005 for a third center, and 1999 to 2004 for a fourth center. The first two centers were located in New England, the third center in the Southeast, and the fourth center in the Upper Midwest. In the fourth center, only donors who were deferred for hepatitis, including hepatitis A and hepatitis with infectious mononucleosis, or for intravenous drug use (IVDU; Questions 3, 4, and 12) were targeted for recruitment. A yes answer to any of these questions resulted in indefinite deferral. In the other three centers, however, donors who were deferred for all health history questions related to recipient safety (see Appendix), indefinite or temporary, were targeted for recruitment. The study was approved by the ARC Institutional Review Board.

Recruitment

In the first three centers, deferred donors were recruited through a variety of means, including personal invitations at blood drives, mailing of invitation letters, phone calls, or a combination of mailing and phone calls. For recruitment at blood drives, donation databases were used to target larger blood drives, and research staff attended these targeted drives. For recruitment through mailing with or without follow-up phone call, donation databases were searched for all deferred donors who had been deferred for the targeted questions during the targeted period and were residing in areas surrounding certain

fixed collection sites. Donors deferred at drives where personal recruitment occurred were excluded from the mailing and/or phone approach. Letters were then sent to the selected deferred donors to inform them of the study and to ask them to contact research staff to arrange for a blood draw. Approximately 2 weeks after the mailing, follow-up phone calls were made to some of those who had not responded to the mailing. For the fourth center, phone call was the only method used for recruitment and donors were called multiple times, if necessary, to make contact.

Data collection

In addition to data on deferral, demographic data on deferred donors including sex, age, and previous donor presentations were obtained from a research database of donors and donations (ARCNET database). The ARCNET Data Center maintains data of blood donors and donations as well as donor deferrals, excluding name or other information that would allow identification of individual donors, for all Blood Services Regions of the ARC since 1995.[9] A blood sample was collected from each enrolled deferred donor and tested for serologic markers of blood-borne infections as for successful blood donors. During the period covered by this study, all donations were tested as described previously for anti-HIV, anti-HCV, anti-HTLV, HBsAg, and antibodies to HBV core antigen (anti-HBc).[9] During this period, nucleic acid testing (NAT) was also performed on blood donations for detecting HIV RNA and HCV RNA.[10,11] NAT of deferred donors, however, was not included in this study. All enrolled deferred donors were tested with the same serologic screening and confirmatory tests used for nondeferred donors. The results of confirmatory testing are reported for HBsAg, anti-HCV, anti-HIV, and anti-HTLV. Because there is no confirmatory test for the hepatitis B core antibodies, the results of screening testing are reported. Positive test rates were compared to those for first-time donors from the same region because first-time donors have higher marker rates than repeat donors and first-time donors account for most of donors deferred for potential infection risks.

Statistical analysis

Statistical analyses were carried out with computer software (SAS, SAS Institute, Cary, NC).[12] Comparisons were performed with a t test for means, with a chi-square test for proportions, or with probability determination based on Poisson distribution where appropriate. Analysis of factors that may be associated with increased or decreased risk of blood-borne infections among enrolled deferred donors was further performed with Poisson regression with SAS.[13] For the analysis, sex, and age of deferred donors as well as participating region (center) were included in the model. All reported p values are two-sided. A p value of less than 0.05 or a 95 percent confidence interval (CI) of an odds ratio (OR) that does not include 1 indicates that a difference is considered to be significant.

RESULTS

Comparison of enrolled versus nonenrolled deferred donors

In total, 497 deferred donors were enrolled for this study, with a mean enrollment rate of 13 percent. Enrollment rates varied with different recruiting methods and among the four participating blood services regions. Invitation at blood drives gave higher enrollment rates but lower overall yield due to limitation of available research staff to attend blood drives. With three of the four centers combined, recruitment at blood drives obtained an enrollment rate of 49.2 percent, whereas mailing alone gave only an enrollment rate of 5.0 percent. Mailing with a follow-up phone call was able to enroll 11.7 percent of the targeted deferred donors. At the fourth center where repeated phone calls were the only recruitment method used, 28.7 percent of targeted deferred donors were enrolled.

Compared with nonenrolled deferred donors, those who were enrolled were less likely to be male (42% among enrolled vs. 51% among nonenrolled, $p < 0.05$), more likely to be older (40 years old on average among enrolled vs. 34 years among nonenrolled, $p < 0.05$), likely to have made more prior donations (a mean of 4.1 times among enrolled vs. 1.5 times among nonenrolled, $p < 0.05$), and also likely to have been deferred more often (0.8 times on average among enrolled vs. 0.5 times among nonenrolled, $p < 0.05$). Compared to first-time donors who donated to the same regions during the period of the study but were not deferred, those who were enrolled were less likely to be male (42% vs. 49%, $p < 0.05$) and more likely to be older (40 years old vs. 31 years old, $p < 0.05$). Table 1 shows the comparison of enrolled donors versus nonenrolled donors who had been deferred for several specified reasons. Owing to the small number of enrollees, comparisons for other deferral questions are not shown. For donors deferred for Questions 12 (intravenous drug use [IVDU]) and 19 (blood exposures), enrolled donors had fewer male donors compared to nonenrolled donors, whereas for other questions, differences in sex composition between enrolled and nonenrolled groups are not significant. For donors deferred for Question 3 (liver disease), 4 (positive hepatitis test), 19, and 37 (HIV-1 Group O exposure), enrolled donors tended to be older than nonenrolled donors. For donors deferred for Questions 3, 4, and 19, enrolled donors appeared to have presented more times for donation than nonenrolled donors. Enrolled donors who were deferred for Question 19 also appeared to have had more prior deferrals than nonenrolled donors.

Testing results for infectious disease markers among enrolled donors

Confirmed positive tests for anti-HCV, anti-HIV, HBsAg, and anti-HTLV and repeat-reactive tests for anti-HBc are shown in Table 2 for enrolled donors who had been deferred for Questions 3, 4, 12, 17, 19, or 37. None of the enrolled donors was confirmed positive for anti-HIV. No confirmed positive for any of the above markers was identified among enrolled donors who had been deferred for other questions. The testing results were compared to those for first-time donors who donated to the same regions during the period of the study but were not deferred. Of the 29 donors who were deferred for having had "yellow jaundice, liver disease, or hepatitis since the age of 11" (Question 3), 1 had anti-HCV and anti-HBc, 2 had anti-HBc, and 1 had anti-HCV ($p < 0.05$ for anti-HCV and anti-HBc). Thirty-seven donors were deferred for having "ever tested positive for hepatitis" (Question 4), 1 of whom had HBsAg and anti-HBc and 3 had anti-HBc ($p < 0.05$ for HBsAg and anti-HBc). Among the 14 donors deferred for "having ever used a needle, even once, to take any illegal or nonprescription drug" (Question 12), 1 had anti-HCV, anti-HTLV-I, and anti-HBc; 1 had anti-HCV and anti-HBc; and 2 had anti-HCV ($p < 0.05$ for all). Sixty-nine donors were deferred for travel to malarial areas (Question 17), 1 of whom had anti-HBc (not significant [NS]). Of the 127 donors deferred for a history in the past 12 months of "tattooing, ear/body piercing, acupuncture, accidental needlestick, coming into contact with someone else's blood, or taking (snorting) cocaine or any other street drug through one's nose" (Question 19), 1 was anti-HBc repeat-reactive (NS). Among 18 donors deferred for possible exposure in certain African countries (Question 37), 1 had anti-HBc (NS).

TABLE 1. Comparison of enrolled versus nonenrolled deferred donors

Deferral question	Enrolled	Nonenrolled	p Value
Percentage who were male			
3 (liver disease)	55.2	53.0	0.822
4 (hepatitis positive)	45.9	53.2	0.400
12 (IVDU)	50.0	79.2	0.017*
17 (malaria)	55.1	52.6	0.808
19 (blood exposure)	29.1	42.3	0.004*
37 (HIV in Africa)	22.2	36.0	0.250
Mean (SD) age (years)			
3 (liver disease)	48.1 (15.3)	39.8 (14.0)	0.002*
4 (hepatitis positive)	46.0 (13.2)	41.1 (13.9)	0.040*
12 (IVDU)	36.1 (10.2)	36.9 (12.1)	0.809
17 (malaria)	35.5 (15.0)	35.7 (15.2)	0.947
19 (blood exposure)	35.1 (11.9)	28.5 (11.3)	<0.001*
37 (HIV in Africa)	38.0 (12.6)	32.0 (10.3)	0.025*
Mean (SD) number of prior donations			
3 (liver disease)	1.6 (3.2)	0.6 (1.4)	<0.001*
4 (hepatitis positive)	1.8 (3.1)	0.9 (2.6)	0.047*
12 (IVDU)	0.3 (0.5)	0.4 (1.5)	0.785
17 (malaria)	5.2 (8.2)	4.1 (8.4)	0.484
19 (blood exposure)	2.6 (3.4)	1.5 (3.2)	<0.001*
37 (HIV in Africa)	0.4 (0.7)	0.9 (2.4)	0.442
Mean (SD) number of prior deferrals			
3 (liver disease)	0.6 (0.7)	0.4 (0.7)	0.068
4 (hepatitis positive)	0.7 (1.0)	0.5 (1.0)	0.303
12 (IVDU)	0.4 (0.6)	0.2 (0.5)	0.223
17 (malaria)	0.7 (0.6)	0.6 (0.6)	0.346
19 (blood exposure)	0.8 (0.9)	0.5 (0.6)	<0.001*
37 (HIV in Africa)	0.3 (0.5)	0.3 (0.5)	0.776

* p Values of significance.

Poisson regression analysis of marker-positive rates

Because the enrolled deferred donor group differs from first-time donors in composition of sex and age, comparison between the enrolled group and first-time donors needs to take into account such differences. Poisson regression was used to compare the marker-positive rates in the enrolled deferred donors with those among first-time donors while incorporating into the model these two factors as well as participating blood center. Owing to the relationship of Questions 3 and 4 and their small numbers, results for the two questions were combined for the Poisson regression analysis. Further, owing to the small numbers, testing results for different markers were combined. If a donor tested positive for the presence of at least one of anti-HIV, anti-HCV, anti-HTLV, or HBsAg, or anti-HBc repeat-reactive, the testing result was defined as "marker-positive." The results are shown in Table 3. Essentially, donors deferred for Questions 3, 4, and 12 showed higher positive rates of these viral markers than first-time

TABLE 2. Confirmatory results for infectious disease markers among enrolled deferred donors (repeatedly reactive results for anti-HBc)

Deferral question	Number deferred	Anti-HBc	Anti-HCV	HBsAg/Anti-HBc	Anti-HCV/Anti-HBc	Anti-HCV/Anti-HBc/Anti-HTLV	Count by individual test: Anti-HBc	HBsAg	Anti-HCV	Anti-HIV	Anti-HTLV
3 (liver disease)	29	2	1	0	1	0	3*	0	2	0	0
4 (hepatitis positive)	37	3	0	1	0	0	4*	1*	0	0	0
12 (IVDU)	14	0	2	0	1	1	2*	0	4*	0	1*
17 (malaria)	69	1	0	0	0	0	1	0	0	0	0
19 (blood exposure)	127	1	0	0	0	0	1	0	0	0	0
37 (HIV in Africa)	18	1	0	0	0	0	1	0	0	0	0

* p Value < 0.05 based on Poisson distribution

TABLE 3. Poisson regression analysis of marker-positive rates

Deferral question	OR (95% CI)	p Value
3 (liver disease) and 4 (hepatitis)	4.68 (2.34-9.37)	<0.01
12 (IVDU)	18.13 (6.80-48.31)	<0.01
17 (malaria)	0.84 (0.12-5.97)	0.86
19 (blood exposure)	0.53 (0.07-3.75)	0.52
37 (HIV-1 group O risk)	3.40 (0.48-24.18)	0.22

donors but donors deferred for Questions 17, 19, or 37 did not show higher viral marker rates when potential differences in sex and age composition as well as intercenter variations were taken into account. Similar results were obtained for Questions 3, 4, and 12 when anti-HBc was excluded in the comparison.

DISCUSSION

Our previous study showed that blood donors temporarily deferred for potential risk of viral infection who later returned to donate blood did not appear to pose a higher risk compared to first-time or repeat donors.[5] In contrast, results from the present study show that donors indefinitely deferred for "yellow jaundice, liver disease, or hepatitis since the age of 11" (Question 3), "ever tested positive for hepatitis" (Question 4), or "having ever used a needle, even once, to take any illegal or nonprescription drug" (Question 12) were more likely to have higher hepatitis marker rates than those who were not deferred. These questions result in indefinite deferrals. Owing to low response rate among deferred donors and potential recruitment bias of deferred donors, who may not reflect potential donors with that deferral factor in the general population, caution should be used, however, when generalizing these data to the larger population of potential blood donors.

Among other specific reasons for deferral, Question 19, namely, "In the past 12 months, have you had a tattoo, ear/body piercing, acupuncture, accidental needlestick, come into contact with someone else's blood, or taken (snorted) cocaine or any other street drug through your nose," warrants further discussion. The question caused more than 4 percent of all of the temporary deferrals and has been studied in both the previous analysis[5] and this investigation. Results from our previous study did not show an increased risk of viral infections by HIV, HBV, HCV, or HTLV among donors who were deferred for this question and subsequently returned to donate blood.[5] The prevalence (/100,000) among those with no prior donation or deferral history was 126.6 for anti-HCV, 14.1 for anti-HIV, 70.3 for HBsAg, 14.1 for anti-HTLV, or 211.0 for any of these markers, compared to 287.7, 11.4, 74.3, 10.9, or 380.5 for first-time volunteer donors. None of the 6036 donors who were deferred for this question and had had a prior donation were positive for the presence of any of the viral markers, compared to a prevalence (/100,000) of 6.3, 1.3, 2.1, 0.3, or 9.9 for those markers among repeat volunteer donors. Comparison through Poisson distribution showed that the differences were not significant ($p > 0.05$ for all comparisons).[5] Results from the present study show that, except for one donor who was anti-HBc repeat-reactive, none of the 127 enrolled donors deferred for this question tested positive for the presence of any of anti-HIV, anti-HCV, anti-HTLV, or HBsAg. Although the small sample size makes it impossible to draw a conclusion that donors deferred for these reasons do not pose a higher risk than first-time blood donors, the results do suggest the likelihood of such risks. For anti-HCV, calculation of probabilities indicates that at the current prevalence level of anti-HCV among first-time blood donors the likelihood of having one or more anti-HCV–positive samples among 127 individuals exceeds 20 percent. The likelihood of having one or more anti-HCV–positive samples would increase to more than 50 percent if the prevalence rate of anti-HCV should double that among first-time donors. In other words, the likelihood of having twice as high a prevalence rate of anti-HCV among donors deferred for Question 19 compared to first-time donors should be less than 50 percent. Analysis of the anti-HBc result does not suggest a higher prevalence rate of the marker among donors deferred for Question 19.

In addition, our previous study showed that Question 17 (travel outside of the United States, for malaria infection risk) does not appear to have any merit of serving as a possible surrogate for potentially increased exposure to blood-borne or sexually transmitted infections while traveling abroad.[6] Results from this study are consistent with the earlier findings. None of the 69 enrolled donors in this study who were deferred for this question tested positive for the presence of anti-HIV, anti-HCV, anti-HTLV, or HBsAg; one was repeat-reactive for anti-HBc, which rate was not different from that among first-time donors. Neither this nor the previous study was able to assess the effectiveness of this question in reduction of malaria risk for which it was introduced.

Annually, Questions 17 and 19 result in a total of 60,000 to 70,000 deferrals for the ARC Blood Services. Our previous study[5] showed that only 24.5 percent of the donors deferred for Question 19 and 39.0 percent of the donors deferred for Question 17 returned to donate blood after their deferral. Among donors who presented the first time and were deferred for Question 19 or 17, only 18.0 or 22.7 percent, respectively, returned to donate their blood. Deferral of those donors not only results in loss of their donations when they are deferred but more importantly, a majority of those donors are lost permanently. Many safe blood donors could be kept in the blood donor pool if these two questions could be modified. In the newly

implemented universal donor history questionnaire (UDHQ), Question 19 has been divided into several individual questions.[14] A study is under way with the ARCNET database to assess the potential impact of changes associated with UDHQ, including the changes with Question 19. Along with the implementation of UDHQ, ARC Blood Services regions are allowed to collect blood from donors with tattoos applied by state regulated parlors, which could help reduce donor deferral for tattooing (accounting for most of Question 19 deferrals during the study period) while maintaining the safety of the blood supply, as suggested by an earlier study in one US blood center.[15] For Question 17, a test for malaria may be able to identify those who are truly a risk to recipients, which could allow changes be made to the question so that many safe blood donors would be able to donate.[16]

Certain lessons have been learned from the study. This study demonstrates the difficulties of recruiting deferred donors into research studies. The most successful method for recruiting deferred donors in our study was to approach deferred donors at time of deferral. The intermediate step of collection staff forwarding deferred donors to research staff complicated this process. A possible improvement to the study and thereby to the enrollment rate would be to incorporate the study into blood center operations so that collection staff can consent and collect deferred donors. This would allow recruitment at every drive, increasing the number of eligible deferred donors approached and removing the intermediate referral step.[17] The difficulty in recruiting deferred donors also shows that deferred donors are unwilling to return, which further supports our previous findings of low return rates for deferred donors.[8]

Caution needs to be exercised in extrapolating data from this study to the entire population of deferred donors or the general population for the deferral reasons included in this study. Although sex and age as well as intercenter variation have been taken into account when comparison was performed between enrolled deferred donors and first-time donors, there could be other differences between enrolled and nonenrolled deferred donors. It is likely, however, that temporarily deferred donors who consented to the present investigation do not completely overlap with temporarily deferred donors who returned to donate blood and were targeted in the previous study.[8] For example, temporarily deferred donors who returned to donate blood could be overrepresented by more committed donors compared to those who did not return. Therefore, results from the present investigation, in combination with results from the previous analysis of returned donors, shed more light on the effectiveness of the current donor selection and deferral process as well as on the utility of specific deferral questions.

In summary, donors deferred for a history of liver disease, positive test for hepatitis, or IVDU were more likely to have higher prevalence for the hepatitis markers under study. Results from this study support the original basis for introducing the questions. Unfortunately the study was too small to detect any HIV-positive donors, and we cannot make any conclusions regarding this agent. Results from this study, however, do not suggest a higher risk of hepatitis B or C infections among donors deferred for "tattooing, ear/body piercing, acupuncture, accidental needlestick, coming into contact with someone else's blood, or taking (snorting) cocaine or any other street drug through one's nose." Similarly, this study did not show an increased risk of hepatitis among donors deferred for travel to malarial areas. The study was unable to assess, however, whether these questions have any impact on other potential blood-borne pathogens that are not currently being screened for during blood collection. Because a majority of deferred donors are unlikely to return for donation following their deferral, many safe blood donors could be saved and retained if the two questions are improved. Analysis of changes in deferral and marker-positive rate associated with UDHQ implementation may be able to show whether the changes will have made a difference.

Larger studies of deferred donors may provide additional important information about the effectiveness of blood donor health history interviews. Such larger studies will almost certainly need to be performed by routine health history interviewers at a significant number of blood centers to provide sufficient statistical power to prove that any of the current donor questions are unnecessary.

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APPENDIX

Health history questions targeted:

3. Since the age of 11, have you had yellow jaundice, liver disease, or hepatitis?
4. Have you ever tested positive for hepatitis?
5. In the past 12 months, have you been in close contact with anyone having yellow jaundice or hepatitis, or have you received hepatitis B immune globulin (HBIG)?
7. Have you ever taken clotting factor concentrates for a bleeding problem, such as hemophilia?
12. Have you ever used a needle, even once, to take any illegal or nonprescription drug?
13. Have you taken money or drugs in exchange for sex since 1977?
14. Are you a male who has had sex, even once, with another male since 1977?
17. In the past 12 months, have you traveled outside of the U.S. except Canada, Australia, New Zealand, Japan, or Western Europe, including the British Isles?
18. In the past 12 months, have you received a blood transfusion or an organ or tissue transplant?
19. In the past 12 months, have you had a tattoo, ear/body piercing, acupuncture, accidental needlestick, come into contact with someone else's blood, or taken (snorted) cocaine or any other street drug through your nose?
21. In the past 12 months, have you had or been treated for syphilis or gonorrhea or tested positive for syphilis?
22. In the past 12 months, have you had sex, even once, with anyone who has ever used a needle for illegal or nonprescription drugs?
23. In the past 12 months, have you had sex, even once, with anyone who has taken money or drugs in exchange for sex since 1977?
24. In the past 12 months, have you given money or drugs to anyone to have sex with you?
25. In the past 12 months, have you had sex, even once, with anyone who has taken clotting factor concentrates?
26. In the past 12 months, have you had sex, even once, with anyone who has had AIDS or tested positive for the AIDS virus?
27. Are you a female who, in the past 12 months, has had sex with a male who has had sex, even once, with another male since 1977?
35. Do you have AIDS or have you ever tested positive for the AIDS virus?
37. (a) Were you born in, or have you lived in, Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria, since 1977? (b) Since 1977, have you received a blood transfusion or medical treatment with a blood product in any of these countries? (c) Have you had sex with anyone who, since 1977, was born in or lived in any of these countries?

医薬品 研究報告 調査報告書

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研究報告の概要

○心筋灌流測定に使用した汚染した放射性医薬品によるC型肝炎ウイルス(HCV)感染

【背景】放射性医薬品薬局は、心筋灌流測定を含む一般的診断法で使用する放射性医薬品を調製する。核医学画像検査現場でのHCV伝播は、過去に報告されたことはない。

【目的】2004年10月15日に放射性医薬品注射剤を用いて心筋灌流測定を行った患者におけるHCVのアウトブレイクについて調べること。

【デザイン、施設および患者】発生源究明のため、分子疫学調査と心臓外来クリニックおよび放射性医薬品薬局の現地調査を行った。この薬局で2004年10月14～15日に調製された放射性医薬品バイアルから採取した注射剤を投与された患者90名に、血液感染性病原体の検査を求めた。薬局の業務手順を調査し、HCVシークエンス解析を行った。

【結果】3つのクリニックから急性HCV感染患者16名を確認した。いずれの患者も、1つのバイアル(バイアル1)から採取した放射性医薬品注射剤投与を受けた。他の6バイアルの投与を受けた患者59名のうち急性HCV感染を発現した者はいなかった。当該薬局では、バイアル1を調製する12時間前に、HCVおよびヒト免疫不全ウイルス(HIV)に罹患した患者の血液の放射線標識白血球測定を行っていた。この患者から得られたHCVのシークエンスは、当該症例の配列とほぼ同一であった(相同性97.8%～98.5%)。急性HIV感染は確認されなかった。血液の交差汚染の原因と考えられる薬剤部の業務行為には、針の再利用や希釈時のシリンジ再利用、滅菌や血液由来製剤調製の一部の工程で同じ層流フードを使用すること等が挙げられる。

【結論】血液汚染された放射性医薬品から16名の患者がHCVに感染した。当該薬局において無菌操作を破綻させた可能性のある感染源と業務行為が認められた。生物由来製剤を取り扱う放射性医薬品薬局は、適切な無菌操作を行うべきである。

使用上の注意記載状況・その他参考事項等

合成血「日赤」
照射合成血「日赤」
合成血-LR「日赤」
照射合成血-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
放射性医薬品注射剤を用いる心筋灌流測定を実施した患者において、血液汚染された注射剤から16名の患者がHCVに感染したとの報告である。輸血後HCV感染の調査には、注射剤の血液汚染など輸血以外の要因について考慮する必要がある。	HCV感染の新たな伝播ルート等について、今後も情報の収集に努める。

ORIGINAL CONTRIBUTION

Hepatitis C Virus Infections From a Contaminated Radiopharmaceutical Used in Myocardial Perfusion Studies

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Context Nuclear pharmacies prepare radiopharmaceutical products for use in common diagnostic procedures, including myocardial perfusion studies. Hepatitis C virus (HCV) transmission has not been reported previously in the setting of nuclear imaging studies.

Objective To investigate an outbreak of acute HCV infection identified among patients who underwent myocardial perfusion studies on October 15, 2004, using an injected radiopharmaceutical.

Design, Setting, and Patients Outbreak investigation including molecular epidemiology and pharmacy site investigation at outpatient cardiology clinics and a nuclear pharmacy in Maryland. Ninety patients who received injections drawn from select radiopharmaceutical vials prepared on October 14-15, 2004, at a single nuclear pharmacy were offered testing for bloodborne pathogens. Pharmacy procedures were reviewed and HCV quasi species analysis was performed.

Main Outcome Measures Hepatitis C virus infection and quasispecies sequence similarity.

Results Sixteen patients with acute HCV infection were identified from 3 separate clinics. All patients received radiopharmaceutical injections drawn from a single pharmacy vial (vial 1). None of the 59 tested patients who received doses from 6 other vials had acute HCV infection. Blood from a potential source patient with HCV and human immunodeficiency virus (HIV) infection was processed for a radiolabeled white blood cell study in the pharmacy 12 hours before vial 1 was prepared. The HCV quasispecies sequences from this potential source patient were nearly identical to those from cases (97.8%-98.5% similarity). No acute HIV infections were identified. Pharmacy practices that could have led to blood cross-contamination included reuse of needles and syringes during dilutions and use of common flow hoods for some steps in the preparation of sterile and blood-derived products.

Conclusions Sixteen persons acquired HCV infection from a blood-contaminated radiopharmaceutical. The source and practices that could have facilitated breaks in aseptic technique were identified at the pharmacy. Nuclear pharmacies that handle biological products should follow appropriate aseptic technique to prevent contamination of sterile radiopharmaceuticals.

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HEPATITIS C VIRUS (HCV) INFECTION is the most common chronic bloodborne infection in the United States, with an estimated antibody prevalence of 1.6%.[1] Transmission of HCV primarily occurs through percutaneous blood exposure; injection drug use is the most common risk factor.[1] Health care–associated transmission of HCV is thought to be unusual in developed countries but outbreaks primarily attributed to contaminated medications or equipment and breaches in aseptic technique have been reported recently in health care settings in the United States, Europe, and Japan.[2-12] Transmission of HCV in the setting of nuclear imaging studies has not been reported previously.

In 2005, an estimated 19.7 million nuclear medicine procedures were per-

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