

Gauged Urban HIV → < 3% of projected total no. infected by TX in San Fran  
HCV (S)

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## Health Policy

# Let's look at human immunodeficiency virus look-back before leaping into hepatitis C virus look-back

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THESE ARE INTERESTING but disturbing times in transfusion medicine. For better or worse, our decisions and policies are influenced almost as much by lawyers, legislators, ethicists, the media, and other "representatives" of the public interest as they are by physicians and scientists who have devoted their life's work to the field. The issue presently at hand is the advisability of initiating a look-back program aimed at the identification, notification, testing, counseling, and treatment of persons who may have been infected with hepatitis C virus (HCV) through transfusions. And assuming that such an effort is appropriate, what would be the most efficient way of identifying the largest number of HCV-infected transfusion recipients as quickly as possible?

Fortunately, we have accumulated a substantial body of experience related to these issues over the past decade. Before considering HCV look-back, we should review the impetus for and efficacy of previous blood transfusion recipient notification efforts, to compare them with the situation now posed by HCV. We can then discuss and shape our policies and protocols vis-à-vis HCV look-back (and look-back for other agents for which screening may be initiated in the future) on a scientific foundation, rather than as an incompletely evaluated response to a fear of lawsuits or scrutiny from inadequately informed physicians or the lay public.

## Evolution of Previous Look-back Policies

The principle of informing patients that they may have been injured as a consequence of prior medical treatment is well established and rests on a solid medical, ethical, and legal foundation. Yet, with regard to infectious risks of transfusion, this principle was relatively ill defined and inconsistently applied prior to the acquired im-

mune deficiency syndrome (AIDS) epidemic. For example, although a transfusion recipient's physician could have been (and generally was) notified if a recent donor reported the development of acute hepatitis B several weeks following donation, blood centers did not notify transfusion services or physicians regarding earlier recipients of components from donors who tested positive after hepatitis B surface antigen testing was implemented in the early 1970s. Even today, few (if any) centers notify other transfusion recipients when a case of posttransfusion non-A, non-B (NANB) hepatitis is traced to a single donor, even though that donor is permanently deferred.

There is no doubt that our attention to this principle, and its implications and ramifications, increased profoundly in the wake of the AIDS epidemic.<sup>2</sup> This change in attitude derived from recognition of the epidemic's spread and the high infectivity and pathogenicity of human immunodeficiency virus (HIV), with the consequent importance of identifying potentially infected transfusion recipients so that they could be counselled and tested and, if infected, could seek appropriate treatment and prevent secondary virus transmission. In addition, the public and political reaction to AIDS, and to transfusion-associated AIDS in particular, was heated. Partly because of that reaction, some states imposed regulations and passed laws mandating the notification of recipients of potentially infected transfusions. Furthermore, the expediency with which transfusion recipients were notified (or not notified) of their possible HIV infection is central to many transfusion-associated AIDS lawsuits, particularly in cases in which secondary transmission occurred.<sup>1,2</sup> Thus, the early decisions regarding the implementation and structuring of HIV look-back policies and programs occurred in a charged political and legal environment, one in which people were seeking accountability and demanding action.

## HIV look-back

The earliest transfusion recipient notification effort related to HIV infection can be traced to the first recognized transfusion-associated AIDS case in 1982, in which a donor diagnosed with AIDS was linked in retrospect to an infant with severe immunodeficiency; other recip-

Abbreviations: AIDS = acquired immune deficiency syndrome; ALT = alanine aminotransferase; CDC = Centers for Disease Control; HCV = hepatitis C virus; HIV = human immunodeficiency virus; HTLV = human T lymphotropic virus; IMBC = Irwin Memorial Blood Centers; NANB = non-A, non-B; RIBA = recombinant immunoblot assay; UCSF = University of California, San Francisco.

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ients of components from that donor were investigated immediately.<sup>3</sup> This procedure of tracing earlier recipients of blood provided by donors who subsequently develop AIDS was endorsed by the major blood banking organizations in 1984.<sup>4</sup> However, few such instances were reported to blood centers, because physicians and health departments rarely elicit blood donation histories from diagnosed AIDS patients. Only a few blood centers participating in a research study sponsored and funded by the Centers for Disease Control (CDC) consistently carried out investigations of all reported AIDS cases in an effort to identify infected former donors and thereby to trace, enroll, and follow the recipients of their blood (see below).<sup>5,6</sup>

#### *Standard, targeted HIV look-back*

In contrast, a year after implementation of anti-HIV screening in early 1985, most blood collection facilities instituted programs for tracing prior recipients of blood from donors found to be seropositive through routine screening. The term "look-back" was coined at this time to refer specifically to the process of transfusion recipient tracing triggered by prospective donor screening.<sup>7</sup> The original look-back recommendations called for working sequentially backward through an infected donor's prior donations and notifying recipients of early donations only after it was determined that recipients of later donations were infected. Early assessment of this program, which I refer to as standard targeted look-back, was enthusiastic.<sup>8,9</sup> Because the number of infected donors with donation histories identified during the first year of prospective screening was not very large and because the seropositivity rate declined markedly (particularly among repeat donors) after the first year of screening, most blood bankers believed that the job of look-back was manageable and, in fact, close to completion.<sup>9</sup>

#### *Expanded, targeted HIV look-back*

However, a small number of blood banks in high AIDS prevalence areas like San Francisco aggressively pursued expanded, targeted look-back programs that utilized other mechanisms for finding infected former donors and in turn for triggering additional recipient notifications. For example, the current program at Irwin Memorial Blood Centers<sup>6</sup> (IMBC) has expanded to include the following additional look-back triggers: 1) health department AIDS case lists are routinely obtained and compared to donor records from 1978 through the present; 2) reported cases of transfusion recipients with HIV infection or AIDS are actively investigated to find an infected donor so as to notify other recipients of blood or components from that donor; and 3) the military services, as well as some private physicians (with patient consent), regularly provide to the blood bank the names of former donors who

have tested seropositive. IMBC immediately sends notification packets to all hospitals who received these persons' donations from 1978 through the implementation of prospective screening (batch as opposed to sequential notification). We have also established policies for 1) sending second notification letters to all recipients of subsequent donations when we learn that a recipient of a donor's early donation tested seropositive; 2) initiating the notification of transfusion recipients even when donors acknowledge high-risk behavior but refuse to be tested; and 3) notifying the sexual partners of, or recipients of transplanted organs from, a deceased transfusion recipient with a high probability of having been infected.

#### *General HIV look-back*

In 1987, the CDC revised upward its estimates of the prescreening risk and the overall number of HIV-infected transfusion recipients.<sup>10,11</sup> In addition, reports appeared of both high rates (6-8%) of HIV infection in randomly selected, multiply transfused persons and of HIV transmission from infected transfusion recipients to their sexual partners and children.<sup>11</sup> Recognizing that targeted look-back was slow and possibly inherently inadequate, and out of concern that infected transfusion recipients might unwittingly contribute to the spread of HIV into the heterosexual community, the CDC recommended that physicians consider testing recipients of multiple units of blood and/or components between 1978 and early 1985, particularly if they had been transfused in high-risk metropolitan areas.<sup>14</sup> This process, which later became known as general (or universal) look-back, was intended to alert the public and the medical community that there was a better and quicker way to identify persons who contracted transfusion-transmitted HIV infection—namely, testing. General look-back was primarily implemented via the lay press and electronic media, as well as through national and regional medical society educational efforts. Press briefings were held in Washington that resulted in front-page reports in *The New York Times*, *The Washington Post*, *The Los Angeles Times*, and *American Medical News*, informing transfusion recipients about the importance of being tested. The Presidential AIDS Commission and the American Hospital Association later endorsed general look-back,<sup>12</sup> and both the Senate and House versions of the HIV Health Care Services Act of 1990 made general HIV look-back a prerequisite for state and city receipt of federal grants. Some hospitals in particularly high-risk regions took the additional step of sending personal letters to all transfusion recipients (general letter look-back).<sup>13</sup>

#### *Human T-lymphotropic Virus Look-back*

When antibody screening for human T-lymphotropic virus (HTLV) was implemented in 1988 and 1989, the

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of infected donors identified was small, so a standard, targeted look-back program was recommended and implemented without much discussion or controversy.<sup>14</sup> Although the epidemiology of HTLV (early HTLV-II) is poorly understood, it appears that these agents are endemic and that their prevalence in the donor base has been relatively constant and not significantly affected by previous donor exclusion and screening efforts.<sup>15,16</sup> Consequently, it is possible that, for HTLV, a standard, targeted look-back program could identify the majority of persons exposed through transfusion since 1978, prior to which few hospitals have transfusion records. No large-scale assessment of the yield of a standard, targeted HTLV look-back has been reported, however. Because clinical HTLV-related diseases are relatively rare and HTLV testing outside of blood banks is uncommon, no program comparable to an expanded, targeted HIV look-back has evolved. A general transfusion program for identifying HTLV-infected recipients was not recommended by the Public Health Service, presumably because of the lack of evidence of HTLV in the United States, as well as the lack of disease and secondary sexual transmission associated with these viruses.

#### Efficacy of Previous Look-back Programs

In this aspect, how effective were the various components of the mushrooming HIV look-back program? In addressing this question, it is worth reviewing relevant studies from the San Francisco Bay area, in which the risk of transfusion-associated HIV was very high and where, therefore, maximum resources have been expended to find infected recipients.

One study is a composite analysis of data<sup>17</sup> from IMBC's look-back program, the Transfusion Safety Study, and several studies of homosexual men in San Francisco. These data were used in the derivation of a comprehensive picture of the temporal risk of HIV before prospective screening (Fig. 1A). It is clear that this analysis indicated that both the peak and overall risks of infection from transfusions were greater than previously recognized: 5300 infectious donors probably transfused in the San Francisco Bay area with a peak risk of 1.1 percent per unit in the average risk between 1978 and 1984 of 1.9 percent recipients of 4 units. These numbers are substantially higher than earlier CDC estimates, principally because the CDC had assumed incorrectly that the rate of infected donors was found after screening represented the maximum risk.<sup>10,11</sup> On the other hand, the study from San Francisco reinforced and confirmed previous reports from around the country that the efficacy of early high-risk donor education and screening measures. As shown in Fig. 1, the imple-

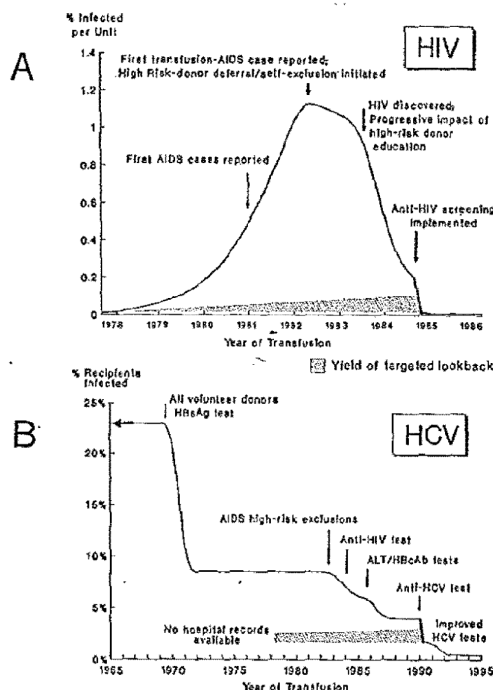


FIG. 1. Risk of HIV (A) and HCV (B) infection by year of transfusion. Shaded areas in each curve represent the proportion of infected recipients potentially traceable through standard, targeted look-back. Reprinted with permission from Busch MP et al. *Transfusion* 1991;31:4-11 (A) and Alter HJ. You'll wonder where the yellow went: a 15-year retrospective of posttransfusion hepatitis. In: Moore SB, ed. *Transfusion-transmitted viral diseases*. Arlington: American Association of Blood Banks, 1987:53-86.

mentation of these measures in San Francisco in 1983 and 1984 coincided with dramatic reductions in the frequency of infected donations and, consequently, in the risk to recipients. Indeed, we estimated that approximately 90 percent of infected, high-risk donors probably self-deferred or were deferred prior to the availability of specific anti-HIV screening.

The second study details the relative yield of the various targeted look-back triggers pursued at IMBC.<sup>6</sup> These data show that standard, targeted look-back—that is, look-back triggered solely by the detection of seropositive donors through routine donor screening—was only minimally effective. For example, only 43 seropositive donors identified through routine blood center screening at IMBC through July 1990 were repeat donors who triggered standard look-back. These 43 donors represented only 6 percent of the 638 infected prior donors identified through IMBC's expanded, targeted look-back effort and less than 3 percent of the projected total number of previous infected donors.<sup>17</sup> In contrast, 428 infected donors

were found through regional AIDS case lists, 86 through active investigations of reports of HIV-infected transfusion recipients, and an additional 81 through self-reports by donors or reports from the military or other physicians. Similarly, only 201 (6%) of the 3320 recipient notifications sent from IMBC through July 1990 were triggered by standard look-back. Irrespective of trigger, over 55 percent of traced units had been given to patients who died before look-back, and over 50 percent of tested transfusion recipients were positive. The fractional yield of standard, targeted look-back is represented (Fig. 1A) by the shaded region of the HIV risk curve extending back from the point of implementation of anti-HIV screening.

How effective were general look-back efforts? Although media attention was substantial, the true response (i.e., number of recipients tested) to the CDC's initial general look-back announcement was limited. This led the University of California, San Francisco (USCF) hospitals to write individual letters to all persons transfused at their facilities during the risk period, informing them of their possible exposure and offering follow-up testing and counseling. The results of this effort are revealing.<sup>13</sup> First, approximately 12 percent of transfusion recipients were unaware of their transfusion, which uncovers one inherent flaw in the original general look-back concept. Second, even the response to individualized letters was limited. Of 17,331 persons sent a letter by UCSF hospitals, only 808 are known to have sought testing. This represents recipients of only 4.4 percent of the total letters sent and 15 percent of the estimated 12,000 living transfusion recipients notified ( $17,331 \times 0.70$  [estimated 5-year survival rate of discharged, transfused patients]).<sup>18</sup> As a consequence, the American Hospital Association recommended against national implementation of this letter notification program, in part because the estimated cost of implementing such a program was projected at between 900 million and 2 billion dollars.<sup>12</sup>

In sum, these studies show that the overall yield and efficacy of HIV look-back programs were poor. Standard, targeted look-back was limited, ironically, by the effectiveness of early self-exclusion measures, in that almost all of those responsible for HIV infections had stopped donating before they could be identified by anti-HIV screening. Additional limits were created by the high death rate of recipients who were identified by tracing transfused components from infected donors, as well as the delay in and logistics of manual record searching and individual recipient tracing and notification through hospitals and private physicians. We estimate that even IMBC's expanded, targeted look-back program has thus far identified only about one-half of the projected 2100 living, infected recipients in that region.<sup>17</sup> The best evidence for the poor yield of general look-back is the continued identification of large numbers of previously

untested transfusion recipients through IMBC's targeted look-back efforts.<sup>6</sup> Transfusion recipients who were aware of the CDC's initial announcement and who had received a general look-back letter from their hospital but never sought testing often learn that they are infected when they are tested after receiving a letter indicating that a donor of the blood transfused to them had recently developed AIDS. Thus, even in San Francisco, where look-back probably has been pursued more aggressively than anywhere else in the world, a substantial proportion of HIV-infected transfusion recipients are undoubtedly still unaware of their infection more than 6 years after screening was implemented.

#### Comparison of HIV and HCV

There are striking parallels in as well as noteworthy differences between the epidemiology, transfusion-associated risks, and clinical consequences of HIV and HCV infections. These are worth reviewing before finally addressing the potential utility and optimal design of HCV look-back. The major similarities include the following. 1) The vast majority of HIV- and HCV-infected blood donors and transfusion recipients have persistent viral infections with prolonged asymptomatic phases. 2) Both viruses are transmitted very efficiently by transfusions (probably at a nearly 90 percent rate).<sup>19-21</sup> 3) Although most infected persons test positive for viral antibodies, seroconversion to both viruses may be delayed and rare infected persons may fail to seroconvert, so that antibody assays fail to detect all infectious individuals.<sup>20,21</sup> 4) Although vaccines are unlikely to be available in the near future, potentially effective treatments (and recommended behavioral modifications) for both viral infections are available and under ongoing development. 5) Efforts by blood banks to reduce the risks of both transfusion-associated NANB hepatitis and AIDS prior to the availability of specific tests were highly effective (Fig. 1).<sup>19,22,23</sup>

The major differences are in the epidemiology and clinical consequences of the viruses, as well as the state of development and evaluation of diagnostic assays and therapeutic regimens. 1) Whereas HIV entered the United States in the mid-1970s and has spread at an epidemic rate in well-defined risk populations, HCV has been endemic in the United States for (at least) decades and has a much broader demographic reservoir<sup>23,24</sup> (estimated prevalence of HCV in the general United States population [as opposed to blood donors] is 2.1 percent [Alter M, unpublished data]). 2) Sexual and vertical transmission of HIV is well established, whereas sexual and vertical transmission of HCV is, at best, very inefficient, according to limited evidence for either route of transmission to date.<sup>25-27</sup> 3) HIV infection progresses to AIDS (a fatal disease) at a very high rate (>90%), while HCV-

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d hepatitis may resolve or may lead to potentially significant chronic hepatitis in 10 percent of infections, and it relatively rarely progresses to fatal or liver cancer.<sup>26</sup> 4) Whereas the current risk of infection from transfusions is estimated at 1 in 3,002% or less, the present risk of HCV may be more.<sup>20,21</sup> 5) Improvements in generally HIV screening and supplemental tests have been minor, whereas projected improvements in next-generation HCV assays should be substantial. This is true in regard to the detection of low-level carriers, the early detection of seroconversion, the detection of seroreversion, and the discrimination of persons with persistent infection (HCV carrier state) from persons with noninfectious anti-HCV positivity (HCV state) or with nonspecific (false-positive) test

#### Projected Efficacy of HCV Look-back

##### *HCV look-back*

It is not surprising that a standard, targeted HCV look-back program based on infected donors found after post-transfusion HCV screening began would be highly inefficient and enormously cumbersome and expensive. It is ineffective for the same reason it was ineffective for HIV: the vast majority of infected former donors were not identified or excluded from continued donation as a result of "surrogate" measures introduced long before the anti-HCV test became available.<sup>19,22,23</sup> It is not that the risk of HCV infection in transfusion was reduced nearly 90 percent (from about 50 [National Institutes of Health data that included donors<sup>20</sup>] to 3% in 1990) by these progresses, which in turn reflects the fact that 90 HCV-infected donors were eliminated by these efforts (Fig. 1B). Because these donors have either died or been deferred, they will not be identified as HCV-positive by blood banks, and therefore the results of their prior donations will be invisible to a look-back. The projected fractional yield of a targeted HCV look-back program is represented by the shaded area of the HCV risk curve (Fig.

1B). In the past, large numbers of anti-HCV-reactive donors were identified, and many are turning out to be long-time donors. During the first 4 months of the IMBC, IMBC identified more than 300 anti-HCV donors (confirmed by a second-generation immunoblot assay: RIBA-HCV, Ortho Diagnostic, NJ). More than 70 percent of these donors, with an average of 7.2 prior donations, with an average of 7.2 prior donations alone would yield over 1800 recipients, which is two-thirds the number of recipients issued through IMBC's expanded HIV look-

back program over the past 6 years. Given current allocations of limited resources, neither the blood centers nor the hospitals have the staff to handle this task adequately. Moreover, as few hospitals have transfusion records prior to the early 1980s, most of the transfusion recipients at risk would not be traceable.

Any expectation of an effective expanded, targeted HCV look-back program comparable to that developed at IMBC for HIV is probably unrealistic. Few HCV-infected former donors will progress to symptomatic disease as HIV-infected persons have, and it is unlikely that even those cases would be reported to blood banks. Therefore, no trigger comparable to AIDS case lists will appear. Widespread testing of patients or healthy individuals for anti-HCV is not currently recommended,<sup>28</sup> and, even if it were, most physicians and patients fail to consider the impact of infection vis-à-vis prior blood donations. Many infections will undoubtedly be found in previously transfused patients. However, because of the relatively high background prevalence of HCV infection and the ill-defined nature of HCV risk factors, it will be difficult to ferret out which cases are truly transfusion-acquired and hence might warrant donor recall investigations. On the other hand, unique scenarios for expanded, targeted HCV look-back could be envisaged, such as recalling all repeat donors previously identified as positive by surrogate tests (over 5000 IMBC repeat donors have been deferred because of an elevated alanine aminotransferase [ALT] or a positive antibody to hepatitis B core antigen assay); about 5 percent of these persons would probably test anti-HCV positive, thus triggering transfusion recipient notifications. I can think of no reasonable approach to identifying the largest subset of previous donors with HCV infection, that is, those who self-excluded or were deferred as a result of less-well-defined surrogate efforts in the 1970s and early 1980s.

##### *General HCV look-back*

In regard to general look-back, the Public Health Service recently decided not to recommend anti-HCV testing of previous transfusion recipients.<sup>28</sup> We can understand the basis for this position if we review the circumstances leading to the CDC's general HIV look-back recommendation and contrast them with those for HCV. First, HIV was an epidemically spreading, fatal infection clustered in specific geographic regions, and transfusion recipients were viewed as a major potential route of spread into the non-high-risk heterosexual community.<sup>11,17</sup> In contrast, HCV is endemic in the general population, and the resulting clinically significant disease is less common and less severe.<sup>23,28</sup> Second, secondary spread of HIV through heterosexual contact and childbearing is clearly documented, and specific recommendations for prevention are available.<sup>11</sup> In contrast, the modes of community spread of HCV are much less well understood.<sup>20,23,24,28</sup>

Third, whereas antiviral and prophylactic therapy is of established benefit for asymptomatic HIV-infected persons, only selected HCV-infected persons are eligible for therapy for chronic disease, and the potential long-term benefits of such therapy are unknown.<sup>28</sup> Fourth, recipients of multiple units of blood in high-risk cities during the early 1980s had more than 100 times the risk of HIV infection as did nontransfused, non-high-risk persons.<sup>17</sup> In contrast, the relative risk of HCV infection in previous transfusion recipients is probably only two to three times the background level (3-6% vs. 2.1%).<sup>23,25,29</sup> Fifth, how can we expect the Public Health Service to recommend general recipient testing when there is currently no consideration of large-scale screening or even case finding in groups known to be at even greater risk of HCV infection (e.g., dialysis patients, intravenous drug users, prostitutes)?<sup>23,28</sup> Given that the public health specialists responsible for the rational expenditure of public health dollars have made the previous decision, is it appropriate for blood bankers to override it?

Nonetheless, at least one blood center initiated a pilot study of general HCV look-back, the results of which are worth evaluating.<sup>22</sup> A large-scale community education and notification effort netted 1034 tested transfusion recipients, of whom 64 (6.2%) tested anti-HCV positive (RIBA-HCV confirmed). Although the denominator (i.e., number of transfusion recipients living in the region) was not reported, these 1034 persons probably represent a very small proportion (1-5%) of the transfused population living in the area (Zuck T, oral communication, August 1990). Moreover, nearly 90 percent of the recipients who came in for testing were transfused after 1985, when the likelihood of testing positive was found to be one-half that in earlier years. Of the anti-HCV-positive transfusion recipients identified, it is probable that one-third were actually infected by means other than transfusion. Less than 20 percent had an elevated ALT. Although the cost of the program to the blood center was relatively minimal, the major cost, which was borne by the community health care system, was difficult to capture and therefore was not evaluated.

### Conclusions

So what do we do? On the one hand, it can be argued that, because nothing will work well, we are justified in doing nothing. On the other hand, it is true that a large number of previous transfusion recipients are infected with HCV, a small percentage of whom would be found through look-back, and some of these persons might benefit from early intervention. In approaching a middle ground to this dilemma, we must attempt to balance our mutual responsibilities to blood donors, transfusion recipients, and the overall public health interests of our country. We should also strive to learn from the past

and not deceive ourselves or others into thinking that we have accomplished more than we have. Underestimating risk and overstating accomplishments have in the past resulted in a loss of confidence by the American public, which we are only now beginning to reverse. Finally, we should make a rational decision and then resolve to stand firmly behind it until significant new scientific or medical information compels us to change course.

In light of the data showing the very limited efficacy of previous look-back efforts, we are warranted—indeed, compelled—to transcend these approaches. I am convinced that the appropriate response to this situation is an aggressive education campaign for both physicians and the lay public about the risks and benefits, both in the past and the present, of transfusions. We need to disseminate information about the risks of all transfusion-transmitted diseases, both to previous and future transfusion recipients, in a well-orchestrated and long-term education campaign. This process should stress the importance of regular donations by low-risk individuals, as well as our commitment to and ongoing research on safer transfusion medicine policies and procedures. We should continue to accelerate our efforts to educate practicing physicians about the indications for and risks of homologous (and autologous) transfusions. We should encourage all physicians to seek detailed transfusion histories from their patients and, on the basis of clinical findings and date(s) of transfusion(s), to test their patients for relevant viruses or diseases.<sup>29</sup> The long-term gain from such a commitment of limited resources to transfusion medicine education will far outweigh the minimal short-term yield of any specific HCV look-back effort.

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### References

1. Lipton KS. Blood donor services and liability issues relating to acquired immune deficiency syndrome. *J Leg Med* 1986;7:131-85.
2. Zuck TF. Legal liability for transfusion injury in the acquired immunodeficiency syndrome era. *Arch Pathol Lab Med* 1990;114:309-15.
3. Centers for Disease Control. Possible transfusion-associated acquired immune deficiency syndrome (AIDS)—California. *Morbidity Mortal Weekly Rep* 1982;31:652-54.
4. Transfusion-associated AIDS—interim recommendations for notification of blood collection agencies and transfusion services. Joint statement of the American Association of Blood Banks, American Red Cross, and Council of Community Blood Centers, December 10, 1984.
5. Perkins HA, Samson S, Garner J, et al. Risk of AIDS for recipients of blood components from donors who subsequently developed AIDS. *Blood* 1987;70:1604-10.

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- S, Busch M, Ward J, et al. Identification of HIV-infected ion recipients: the utility of crossreferencing previous do- rds with AIDS case reports. *Transfusion* 1990;30:214-8.
- ck. Joint statement of the American Association of Blood American Red Cross, and Council of Community Blood , 1986.
- re J. Status of recipients of blood from donors subse- found to have antibody to HIV (letter). *N Engl J Med* 5:1095-6.
- , Rigney PR, Kchoe PM, Campbell J. Look-back: prelim- perience of AAB members. *Transfusion* 1987;27:201-2.
- n TA, Lui KJ, Lawrence DN, Allen JR. Estimating the transfusion-associated acquired immune deficiency synd- human immunodeficiency virus infection. *Transfusion* :371-4.
- for Disease Control. Human immunodeficiency virus in- n transfusion recipients and their families. *Morbidity and Mortality Weekly Report* 1987;36:137-40.
- structs members on contacting transfusion recipients. *AABB* 1989;12:8.
- 1 E, Johnson D, Remedios V, Cohen S. Mass notification usion recipients at risk for HIV infection (letter). *JAMA* 0:922-3.
- ies for notification and counseling of recipients of HTLV- ve blood. Arlington: American Association of Blood May 26, 1989.
- lski EA, Schiff ER, Kleinman SH, et al. Epidemiologic und of blood donors with antibody to human T-lympho- rus. *Transfusion* 1989;29:746-8.
- A, Blattner WA. The epidemiology of the human T-cell ropic virus type I and type II: etiologic role in human *Transfusion* 1991;31:67-75.
- 4P, Young MJ, Samson SM, et al. Risk of human im- ficiency virus (HIV) transmission by blood transfusions nplementation of HIV-1 antibody screening. *Transfusion* :4-11.
- 3S. The transfused population of Canterbury, New Zea- d its mortality. *Vox Sang* 1988;54:65-70.
- l. You'll wonder where the yellow went: a 15-year re- ve of posttransfusion hepatitis. In: Moore SB, ed. *Trans- fusion-transmitted viral diseases*. Arlington: American Association of Blood Banks, 1987:53-86.
20. Alter HJ, Purcell RH, Shih JW, et al. Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic non-A, non-B hepatitis. *N Engl J Med* 1989;321:1494-500.
21. Esteban JI, Gonzalez A, Hernandez JM, et al. Evaluation of an- tibodies to hepatitis C virus in a study of transfusion-associated hepatitis. *N Engl J Med* 1990;323:1107-12.
22. Zuck TF, Rose GA, Dumaswala UJ, Geer NJ. Experience with a transfusion recipient education program about hepatitis C. *Trans- fusion* 1990;30:759-61.
23. Alter HJ, Hadler SC, Judson FN, et al. Risk factors for acute non-A, non-B hepatitis in the United States and association with hepatitis C virus infection. *JAMA* 1990;264:2231-5.
24. Esteban JI, Esteban R, Viladomiu L, et al. Hepatitis C virus antibodies among risk groups in Spain. *Lancet* 1989;2:294-7.
25. Everhart JE, Di Bisceglie AM, Murray LM, et al. Risk for non-A, non-B (type C) hepatitis through sexual or household contact with chronic carriers. *Ann Intern Med* 1990;112:544-5.
26. Alter MJ, Coleman PJ, Alexander WJ, et al. Importance of het- erosexual activity in the transmission of hepatitis B and non-A, non-B hepatitis. *JAMA* 1989;262:1201-5.
27. Reesink HW, Wong VCV, Ip HMH, van der Poel CL, van Exel- Ochters PJ, Lelie PN. Mother-to-infant transmission and hepatitis C virus (letter). *Lancet* 1990;335:1216-7.
28. Public Health Service inter-agency guidelines for screening donors of blood, plasma, organs, tissues, and semen for evidence of hepatitis B and hepatitis C. *Morbidity and Mortality Weekly Report* 1991;40(Suppl RR-4):1-17.
29. Simon ER. Identification of recipients with hepatitis C and other transfusion-transmitted infections: we can do better than look-back! (letter). *Transfusion* 1991;31:87.

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Busch M, Ward J, et al. Identification of HIV-infected recipients: the utility of crossreferencing previous donor with AIDS case reports. *Transfusion* 1990;30:214-8. Joint statement of the American Association of Blood Banks, American Red Cross, and Council of Community Blood Centers.

Status of recipients of blood from donors suspected to have antibody to HIV (letter). *N Engl J Med* 1989;321:1494-500.

Prey PR, Kehoe PM, Campbell J. Look-back: preliminary of AABB members. *Transfusion* 1987;27:201-2.

Lui KJ, Lawrence DN, Allen JR. Estimating the transfusion-associated acquired immune deficiency syndrome immunodeficiency virus infection. *Transfusion* 1989;29:137-40.

Disease Control. Human immunodeficiency virus infection recipients and their families. *Morbidity and Mortality Weekly Report* 1987;36:137-40.

members on contacting transfusion recipients. *AABB* 1989;12:8.

Hanson D, Remedios V, Cohen S. Mass notification recipients at risk for HIV infection (letter). *JAMA* 1989;261:1201-5.

notification and counseling of recipients of HTLV-III. Arlington: American Association of Blood Banks, 1989.

Schiff ER, Kleinman SH, et al. Epidemiologic blood donors with antibody to human T-lymphotropic virus type I and type II: etiologic role in human immunodeficiency virus infection. *Transfusion* 1989;29:746-8.

ner WA. The epidemiology of the human T-cell virus type I and type II: etiologic role in human immunodeficiency virus infection. *Transfusion* 1989;29:746-8.

ing MJ, Samson SM, et al. Risk of human immunodeficiency virus (HIV) transmission by blood transfusions. *Transfusion* 1989;29:746-8.

transfused population of Canterbury, New Zealand. *Vox Sang* 1988;54:65-70.

wonder where the yellow went: a 15-year retrospective study of transfusion hepatitis. In: Moore SB, ed. *Transfusion-transmitted viral diseases*. Arlington: American Association of Blood Banks, 1987:53-86.

fusion-transmitted viral diseases. Arlington: American Association of Blood Banks, 1987:53-86.

20. Alter HJ, Purcell RH, Shih JW, et al. Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic non-A, non-B hepatitis. *N Engl J Med* 1989;321:1494-500.

21. Esteban JI, Gonzalez A, Hernandez JM, et al. Evaluation of antibodies to hepatitis C virus in a study of transfusion-associated hepatitis. *N Engl J Med* 1990;323:1107-12.

22. Zuck TF, Rose GA, Dumaswala UJ, Geer NJ. Experience with a transfusion recipient education program about hepatitis C. *Transfusion* 1990;30:759-61.

23. Alter HJ, Hadler SC, Judson FN, et al. Risk factors for acute non-A, non-B hepatitis in the United States and association with hepatitis C virus infection. *JAMA* 1990;264:2231-5.

24. Esteban JI, Esteban R, Villadomiu L, et al. Hepatitis C virus antibodies among risk groups in Spain. *Lancet* 1989;2:294-7.

25. Everhart JB, Di Bisceglie AM, Murray LM, et al. Risk for non-A, non-B (type C) hepatitis through sexual or household contact with chronic carriers. *Ann Intern Med* 1990;112:544-5.

26. Alter MJ, Coleman PJ, Alexander WJ, et al. Importance of heterosexual activity in the transmission of hepatitis B and non-A, non-B hepatitis. *JAMA* 1989;262:1201-5.

27. Reesink HW, Wong VCV, Ip HHM, van der Poel CL, van Esch Oehlers PJ, Lelie PN. Mother-to-infant transmission and hepatitis C virus (letter). *Lancet* 1990;335:1216-7.

28. Public Health Service inter-agency guidelines for screening donors of blood, plasma, organs, tissues, and semen for evidence of hepatitis B and hepatitis C. *Morbidity and Mortality Weekly Report* 1991;40(Suppl RR-4):1-17.

29. Simon ER. Identification of recipients with hepatitis C and other transfusion-transmitted infections: we can do better than look-back! (letter). *Transfusion* 1991;31:87.

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Third, whereas antiviral and prophylactic therapy is of established benefit for asymptomatic HIV-infected persons, only selected HCV-infected persons are eligible for therapy for chronic disease, and the potential long-term benefits of such therapy are unknown.<sup>28</sup> Fourth, recipients of multiple units of blood in high-risk cities during the early 1980s had more than 100 times the risk of HIV infection as did nontransfused, non-high-risk persons.<sup>17</sup> In contrast, the relative risk of HCV infection in previous transfusion recipients is probably only two to three times the background level (3-6% vs. 2.1%).<sup>23,25,29</sup> Fifth, how can we expect the Public Health Service to recommend general recipient testing when there is currently no consideration of large-scale screening or even case finding in groups known to be at even greater risk of HCV infection (e.g., dialysis patients, intravenous drug users, prostitutes)?<sup>23,28</sup> Given that the public health specialists responsible for the rational expenditure of public health dollars have made the previous decision, is it appropriate for blood bankers to override it?

Nonetheless, at least one blood center initiated a pilot study of general HCV look-back, the results of which are worth evaluating.<sup>22</sup> A large-scale community education and notification effort netted 1034 tested transfusion recipients, of whom 64 (6.2%) tested anti-HCV positive (RIBA-HCV confirmed). Although the denominator (i.e., number of transfusion recipients living in the region) was not reported, these 1034 persons probably represent a very small proportion (1-5%) of the transfused population living in the area (Zuck T, oral communication, August 1990). Moreover, nearly 90 percent of the recipients who came in for testing were transfused after 1985, when the likelihood of testing positive was found to be one-half that in earlier years. Of the anti-HCV-positive transfusion recipients identified, it is probable that one-third were actually infected by means other than transfusion. Less than 20 percent had an elevated ALT. Although the cost of the program to the blood center was relatively minimal, the major cost, which was borne by the community health care system, was difficult to capture and therefore was not evaluated.

### Conclusions

So what do we do? On the one hand, it can be argued that, because nothing will work well, we are justified in doing nothing. On the other hand, it is true that a large number of previous transfusion recipients are infected with HCV, a small percentage of whom would be found through look-back, and some of these persons might benefit from early intervention. In approaching a middle ground to this dilemma, we must attempt to balance our mutual responsibilities to blood donors, transfusion recipients, and the overall public health interests of our country. We should also strive to learn from the past

and not deceive ourselves or others into thinking that we have accomplished more than we have. Underestimating risk and overstating accomplishments have in the past resulted in a loss of confidence by the American public, which we are only now beginning to reverse. Finally, we should make a rational decision and then resolve to stand firmly behind it until significant new scientific or medical information compels us to change course.

In light of the data showing the very limited efficacy of previous look-back efforts, we are warranted—indeed, compelled—to transcend these approaches. I am convinced that the appropriate response to this situation is an aggressive education campaign for both physicians and the lay public about the risks and benefits, both in the past and the present, of transfusions. We need to disseminate information about the risks of all transfusion-transmitted diseases, both to previous and future transfusion recipients, in a well-orchestrated and long-term education campaign. This process should stress the importance of regular donations by low-risk individuals, as well as our commitment to and ongoing research on safer transfusion medicine policies and procedures. We should continue to accelerate our efforts to educate practicing physicians about the indications for and risks of homologous (and autologous) transfusions. We should encourage all physicians to seek detailed transfusion histories from their patients and, on the basis of clinical findings and date(s) of transfusion(s), to test their patients for relevant viruses or diseases.<sup>29</sup> The long-term gain from such a commitment of limited resources to transfusion medicine education will far outweigh the minimal short-term yield of any specific HCV look-back effort.

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### References

1. Lipton KS. Blood donor services and liability issues relating to acquired immune deficiency syndrome. *J Leg Med* 1986;7:131-86.
2. Zuck TF. Legal liability for transfusion injury in the acquired immunodeficiency syndrome era. *Arch Pathol Lab Med* 1990;114:309-15.
3. Centers for Disease Control. Possible transfusion-associated acquired immune deficiency syndrome (AIDS)—California. *Morbidity and Mortality Weekly Rep* 1982;31:652-54.
4. Transfusion-associated AIDS—interim recommendations for notification of blood collection agencies and transfusion services. Joint statement of the American Association of Blood Banks, American Red Cross, and Council of Community Blood Centers, December 10, 1984.
5. Perkins HA, Samson S, Garner J, et al. Risk of AIDS for recipients of blood components from donors who subsequently developed AIDS. *Blood* 1987;70:1604-10.

6. Samson S, et al. Transfusion-associated AIDS—California. *Morbidity and Mortality Weekly Rep* 1982;31:652-54.
7. Lipton KS. Blood donor services and liability issues relating to acquired immune deficiency syndrome. *J Leg Med* 1986;7:131-86.
8. Menikoff J. The risks of transfusion. *N Engl J Med* 1987;316:100-102.
9. Bove L. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
10. Peter J. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
11. Cent. for Disease Control. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
12. AHA. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
13. Donor. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
14. Guid. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
15. Oper. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
16. Man. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
17. Busch. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
18. W. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.
19. Alter. Blood banking and transfusion medicine. *N Engl J Med* 1987;316:100-102.