Persons with Early Syphilis Identified through Blood or Plasma Donation Screening in the United States

Carolyn Gardella,1,2 Anthony A. Marfin,1,a Richard H. Kahn,1 Emmett Swint,1 and Lauri E. Markowitz1

CONCISE COMMUNICATION

The number of persons with early syphilis who donated blood between 1995 and 2000 in the United States was estimated using data collected in the National Electronic Telecommunication System for Surveillance (NETSS). To distinguish paid from volunteer donors, cases reported in 2000 were analyzed. For the 6 years, 22 primary, 81 secondary, and 413 early latent syphilis cases were identified through donation screening. In 2000, 69 cases of early syphilis were identified through donation screening in 16 states. In 6 states that reported 53 of these cases, 31 case subjects (58%) were volunteer donors and 22 (42%) were paid donors. Eighty-one percent of volunteer donors and 64% of paid donors reported no risk factors for syphilis. After adjustment for variation in NETSS use, it was estimated that, over the 6 years, ~1200 cases of early syphilis were detected nationally through donation screening, and 58% of the case subjects were volunteer donors.

Syphilis is one of the oldest recognized infectious risks of blood transfusion. Donors have been screened with a serologic test for syphilis since 1938 [1]. During the past 50 years, transfusion-transmitted syphilis has become extremely rare because of improved donor selection processes, universal serologic screening of donors for syphilis, and the shift from transfusion of fresh blood components to transfusion of processed products. The relative contribution of these factors is difficult to quantify [2]. Only 3 cases of transfusion-transmitted syphilis have been reported in the English literature during the past 35 years. All reported cases were linked to transfusion of fresh blood products [3–5], and only one case, which was reported >30 years ago, involved blood products received in the United States [5].

The safety of the national blood supply is maintained by selection of low-risk, volunteer donors and by laboratory screening of donations. The Food and Drug Administration (FDA) and the American Association of Blood Banks have regulations and/or recommendations for the selection of appropriate blood donors. A donor-history questionnaire, which includes questions regarding current health and past high-risk sexual behavior, is an important screening tool that is used to identify and defer potential donors who are at high risk for blood-borne pathogens.

All blood and plasma donors are screened for various blood-borne pathogens, including syphilis, in accordance with FDA requirements. Donations are screened for syphilis by a treponemal test or, less often, by a nontreponemal test [6]. Treponemal tests usually cannot distinguish between persons with a previously treated syphilis infection and a current, untreated infection because these test results remain positive even after treatment. In general, nontreponemal test results are negative after patients are treated for syphilis, but the tests are less specific than treponemal tests. Despite these limitations, if the serologic test result for syphilis is positive, the donation is discarded. In recent years, it was estimated that ~26,000 donations were discarded annually because of positive serologic test results for syphilis [7] (L. Katz and J. Starkey, personal communication).

The value of syphilis screening among volunteer donors has been debated because of declining syphilis rates, the low likelihood that treponemes survive in donated blood or blood components after refrigeration or processing, the limitations of the serologic tests for syphilis, and the resultant loss of units that test positive [6]. Because paid donors may be at a higher risk for blood-borne pathogens [8, 9], the discontinuation of syphilis testing of plasma donors, who usually are paid, has not been considered.

In September 2000 at the 67th meeting of the FDA Blood Products Advisory Committee (BPAC), it was concluded that current scientific data were insufficient to warrant discontin-
Methods

Syphilis is a notifiable disease in the United States. All positive serologic test results for syphilis, including those identified by donor screening, should be reported to the state or local health department for further evaluation. The person’s previous serologic test results and treatment then are checked in a state or local syphilis registry. If indicated, local health department personnel interview and examine the person to determine the presence and stage of disease [10]. After review, the vast majority of positive serologic tests for syphilis are found not to be due to newly identified or untreated syphilis. Only cases of new, untreated syphilis are reported to CDC through national surveillance systems.

Since 1963, surveillance data for sexually transmitted diseases have been collected as aggregate data from all 50 states and the District of Columbia [11]. Implementation of the National Electronic Telecommunications System for Surveillance (NETSS), an electronic surveillance system that collects additional data, began in 1992 for some sexually transmitted infections, including syphilis. This system allows for the identification of the source of the report. Over time, successively more states have reported through this system. In 2000, almost all states submitted syphilis data, including the source of report, through NETSS. We used data collected in NETSS to estimate the number of early syphilis infections (primary, secondary, and early latent) reported to CDC that were identified from screening at the time of blood or plasma donation between 1995 and 2000.

Syphilis cases with the source of report coded as “blood bank” in the NETSS database were included in this report. Because not all 50 states used the extended NETSS report that identified cases as detected by donation screening for the entire 6-year period, data were adjusted to estimate the total number of early syphilis cases identified through blood donation screening nationwide. To estimate the total number of donation-identified, early syphilis cases in the United States, the number of donation-identified syphilis cases reported through NETSS was multiplied by an estimation factor. The estimation factor was calculated by dividing the total number of syphilis cases reported nationally by the number of reported cases with coded source-of-report information. For each year, this factor was calculated separately for early latent, primary, and secondary infections. The reported number of cases with source of report classified as “blood bank” then was multiplied by the estimation factor to generate the estimated national total number of syphilis cases identified by screening at the time of donation.

NETSS compliance increased over the study period, and thus the estimation factor decreased over time.

A limitation of data collected in NETSS is the inability to distinguish between blood and plasma donors. The source of report for both is coded as “blood bank.” To distinguish these types of donors, additional information was obtained from the health department records in the 6 states with the most cases of donation-identified syphilis in 2000. This additional information included confirmation of donor status and distinction of paid versus volunteer donors. During this process, we determined that some donors were paid for blood that was collected for research. Therefore, in this report, we describe donors as paid versus volunteer rather than plasma versus blood donors. Risk-assessment information was obtained from case subject interview records and included reported homosexual sex with a male since 1978; injection drug use since 1978; sex for drugs or money (ever); or heterosexual relations with an injection drug user, a bisexual male, or a person with human immunodeficiency virus (HIV)/AIDS or unknown risk factors (ever). These questions are similar to those that appear on the donor-history questionnaire administered at the time of donation.

Epi Info 6 (CDC) was used to generate descriptive statistics and to perform univariate analyses. $\chi^2$ tests and one-way analysis of variance were used.

Results

From 1995 through 2000, “blood bank” was noted as the source of information for 516 cases of early syphilis reported to CDC. Of these, 103 (20%) were primary or secondary syphilis cases, and 413 (80%) were early latent infections. Table 1 presents the demographic characteristics of persons with early syphilis identified by donor screening, by stage of disease. The mean age of case subjects was 31–33 years (range, 17–79 years). Men comprised the majority of case subjects at all stages. Of

![Table 1. Characteristics of case subjects with early syphilis identified through blood or plasma donation by stage of disease, 1995–2000.](https://academic.oup.com/jid/article-abstract/185/4/545/852868/10248288)
women who had early disease, 213 (92%) of 231 were of reproductive age (15–45 years old).

In 2000, almost all states submitted extended syphilis NETSS records that included the source of report. Sixteen states reported ≥1 case of syphilis with “blood bank” as the source of report. Tennessee, Florida, Texas, Mississippi, South Carolina, and Wisconsin reported ≥5 cases each and accounted for 53 (77%) of the 69 early syphilis cases reported with “blood bank” as the source of report during the year 2000. Of these 53 case subjects, 22 (42%) were paid donors (16 blood donors and 6 plasma donors), and 31 (58%) were volunteer blood donors (figure 1). Thirty-six percent of paid donors and 19% of volunteer donors reported ≥1 risk factor for syphilis ($P = .2$). Of the 5 male volunteer donors with risk factors, 4 reported having sex with men, and 1 reported heterosexual sex with partners who had risk factors for HIV or unknown risk factors. The sole female volunteer donor who reported risk factors had heterosexual sex with a partner who had risk factors for HIV or unknown risk factors. Among paid donors, exchange of sex for money was the most common risk factor reported. Five of 6 male paid donors with risk factors reported exchange of sex for money, as did 1 of the 2 female paid donors with risk factors.

Table 2 presents the reported and estimated number of syphilis cases among donors during the 6-year period. After adjusting for states that did not use the extended NETSS data reporting system, we estimated that 1196 early syphilis cases were identified through donor screening in the United States during the 6-year period. This represented 0.8% of the total number of early syphilis cases reported to the CDC during this period. On the basis of data from 2000, we estimate that 58% of early syphilis case subjects identified through donor screening were volunteer blood donors. Thus, we estimate that blood from 694 persons with early syphilis potentially would have entered the blood supply, in the absence of screening of volunteer donations during the 6-year period.

Discussion

We estimated that ~1200 cases of potentially infectious syphilis were detected through blood and plasma screening during a 6-year period. We consider this estimate to be conservative because of limitations inherent in our surveillance systems. Health department personnel cannot always locate and evaluate possible syphilis case subjects identified through reports of positive serologic tests. Unless health department personnel follow up

Figure 1. Reported cases of early syphilis identified by blood or plasma donation screening from 6 states in 2000. *Risk includes report of any of the following by the case subject at the time of interview by health department personnel: homosexual sex with a male since 1978; injection drug use since 1978; exchange of sex for drugs or money; or heterosexual relations with an injection drug user, a bisexual male, or a person with human immunodeficiency virus/AIDS or unknown risk factors.

<table>
<thead>
<tr>
<th>Stage of syphilis</th>
<th>No. of syphilis cases reported</th>
<th>Estimation factor</th>
<th>No. of cases identified by blood or plasma donation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary/secondary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>16.543</td>
<td>4038</td>
<td>4.10</td>
</tr>
<tr>
<td>1997</td>
<td>8556</td>
<td>4168</td>
<td>2.05</td>
</tr>
<tr>
<td>1998</td>
<td>6993</td>
<td>5103</td>
<td>1.37</td>
</tr>
<tr>
<td>1999</td>
<td>6657</td>
<td>6102</td>
<td>1.09</td>
</tr>
<tr>
<td>2000</td>
<td>6000</td>
<td>5637</td>
<td>1.06</td>
</tr>
<tr>
<td>Total</td>
<td>56,137</td>
<td>28,788</td>
<td>1.03</td>
</tr>
<tr>
<td>Early latent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>26.657</td>
<td>5106</td>
<td>5.22</td>
</tr>
<tr>
<td>1996</td>
<td>20.187</td>
<td>5583</td>
<td>3.62</td>
</tr>
<tr>
<td>1997</td>
<td>16.631</td>
<td>6750</td>
<td>2.46</td>
</tr>
<tr>
<td>1998</td>
<td>12.741</td>
<td>9899</td>
<td>1.29</td>
</tr>
<tr>
<td>1999</td>
<td>11.677</td>
<td>10,941</td>
<td>1.07</td>
</tr>
<tr>
<td>2000</td>
<td>9642</td>
<td>9198</td>
<td>1.05</td>
</tr>
<tr>
<td>Total</td>
<td>97,535</td>
<td>47,477</td>
<td>1.03</td>
</tr>
</tbody>
</table>

* No. of cases reported in the National Electronic Telecommunications System for Surveillance (NETSS) with source-of-report information.
\(^{b}\) Total no. of cases reported nationally divided by the no. of cases with known source of report in NETSS.
\(^{c}\) No. of cases with “blood bank” as the source of report in the NETSS multiplied by the estimation factor.
on possible cases, they are not reported to CDC. Also, the source of report information can be incorrect. Syphilis cases identified through donation may be reported as from referred sources, such as the public health department or a private practitioner. Finally, misclassification of the stage of disease can occur if the lag time between donation and evaluation by health department personnel is long. Because donations from persons with early syphilis could be discarded because of positive test results for other infections, such as HIV or hepatitis B, our estimate may be higher than the number of donations potentially infected with syphilis that would enter the blood supply in the absence of serologic testing for syphilis. Another limitation of our analysis is the use of an estimation factor to account for less-than-complete NETSS reporting. Use of this factor assumes consistency of reporting patterns. However, the estimation factor decreased over the study period to near 1, so any bias introduced by this factor was minimal by the end of the study period.

We anticipated that most syphilis case subjects identified through donation screening would be paid donors, because these persons are known to be at a higher risk for infectious diseases, including syphilis [8, 9]. However, analysis of case subjects identified during the year 2000 in 6 states revealed that most of them were volunteer rather than paid donors. Relatively few blood donors with infectious syphilis reported risk factors for syphilis. The donor-history questionnaire did not result in deferral of these donors; similarly, risk assessment performed at the time of interview by health department personnel did not elicit high-risk behaviors. Serologic testing provided the only means to identify most case subjects with early syphilis in this group.

Beyond safeguard of the national blood supply, syphilis screening by blood banks may have broader, albeit secondary, public health implications. Elimination of syphilis is a national priority. CDC’s National Plan to Eliminate Syphilis in the United States includes prompt treatment of persons seeking care for syphilis, as well as serologic screening and partner notification and evaluation to identify new cases, to reduce primary and secondary syphilis to < 1000 cases and to increase the number of syphilis-free counties to 90% by 2005 [12]. The plan does not specifically rely on syphilis screening at the time of blood donation to detect new cases; however, screening of donated blood may augment efforts to eliminate syphilis.

We found that syphilis cases identified through donation screening accounted for 0.4% of all primary and secondary cases and 1% of all early latent cases reported during the 6-year period. Although this is a small percentage of all reported cases, donor screening may detect a subgroup of persons with early syphilis that may not be identified otherwise. Furthermore, identification of these cases through donor screening may have led to detection of other persons with syphilis through identification of sex partners. Cases of late latent syphilis, although not addressed in this paper because of their low risk of bacteremia, also are detected at the time of blood donation and add to the public health benefit of screening. The small benefit to public health (i.e., the detection of ~100 cases of potentially infectious syphilis) must be weighed against the donations that are discarded annually because of reactive serologic tests for syphilis [7]. Whether safeguard of the blood supply from even one case of transfusion-related syphilis merits the cost of testing, measured both fiscally and in needlessly discarded units of blood, remains controversial and is beyond the scope of this report.

The specific risk of transfusion-transmitted syphilis from infected blood or blood components is unknown. Several parameters are needed to estimate the risk of transfusion-transmitted syphilis from these donors. Survival of treponemes in different blood components under various storage conditions will determine whether these donors pose any real risk for transfusion-transmitted syphilis in the absence of screening. Fresh blood and blood components stored for < 2–5 days are more infectious than blood components stored for longer periods [13, 14]. Refrigeration and citrated solutions used to preserve blood components greatly reduce the infectivity of an infected blood unit [6]. Although fresh blood transfusion is uncommon in the United States, it is possible that infected units could be stored for relatively short periods during a period of blood shortage.

Our data indicate that some individuals with early syphilis donate blood in the United States. Without serologic screening of volunteer donors, potentially infectious blood from ~100 persons with early syphilis might enter the blood supply each year. Studies are planned to determine the risk of transfusion-related syphilis posed by these products. Issues to be addressed include how often blood components from persons with early syphilis contain infectious treponemes, the quantity of treponemes present in various blood components, and whether the treponemes survive standard blood component processing.

Acknowledgments

We thank Mary Chamberland for her review of the manuscript and valuable suggestions.

References


