routine childhood immunisations at 2 months and neither BCG nor the beginning of the childhood course is postponed.

Information is not available on the age up to which it is safe to give BCG immunisation without a prior tuberculin test. The Joint Committee on Vaccination and Immunisation has agreed, however, that in the absence of any suggestion of recent contact with tuberculosis a cut off point at 3 months would be sensible.1 The committee also advised that vaccination by the percutaneous multiple puncture technique, using 18-20 needles, is an acceptable alternative to the intradermal technique in infants and neonates. An instrument with an 18 needle magnetic disposable head is now available and convenient to use.

Tuberculin testing of neonates is less common than testing of schoolchildren, but it is surprising that in five districts no action was recommended for grade 2 results in this age group. Indeed in neonates even a grade 1 result should be considered with suspicion, especially if there is any recent history of contact with tuberculosis.

Whoever takes the leading role in devising a district’s policy for BCG immunisation, it is appropriate that the consultant in communicable disease control (or other public health physician, if a consultant is not in post) as well as the district immunisation coordinator consult with a chest physician (or physician with an interest in respiratory medicine) about the policy for the schools programme and with a paediatrician on the policy for the programme in neonates. In addition, it would seem prudent to have such policies reviewed by either a district control of infection committee or an immunisation committee.

We thank Mrs M Bezzant for her administrative support, Ms F Majid for her statistical advice, and Drs K Citron, J Leese, and C Skinner for their helpful comments on this manuscript. We are also grateful to all the immunisation coordinators, consultants in communicable disease control, and others who provided the information for this national survey.

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Risk of HIV infection from transfusion with blood negative for HIV antibody in a west African city

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Abstract

Objective—To estimate the risk of infection with HIV (HIV 1 or HIV 2, or both) from transfusion of a screened unit of blood in a high prevalence area in west Africa.


Setting—National Blood Transfusion Centre, Abidjan, Côte d’Ivoire.

Subjects—Repeat donors (5831 units of blood) and first time donors (5076 units) in the first five months of 1991.

Main outcome measures—Prevalence and estimated incidence of HIV infection in repeat and first time donors; estimated rate of potentially infected, HIV antibody negative units; and rate of (false negative) potentially infected units assuming a laboratory test sensitivity of 99%.

Results—Overall HIV prevalence was 11-0% in first time donors and 2-1% in repeat donors. In the first seven months of 1991, 29 HIV antibody positive (27 HIV 1, 1 HIV 2, 1 dually reactive) donors with a seronegative unit of blood earlier in the year were identified; 26 had donated blood eight weeks or less before their estimated dates of seroconversion and may have been infectious (minimum rate 26/5831 (4/5/1000 potentially infected units)). Estimated incidence of infection in repeat donors was 1-2-2-5%. Laboratory test insensitivity would result in an estimated 1-1/1000 false negative units from first time donors and 0-2/1000 units from regular donors. The overall rate of potentially infected units (all donors, seroconversions, and errors) was estimated at 5-4-10-6/1000.

Conclusions—The risk of HIV infection from a single unit of blood remains substantial (5-4/10-6/1000 units). To prevent infection from blood transfusion in areas of high incidence and prevalence of HIV all but absolutely essential transfusions should be avoided, and donors with low incidence of HIV infection should be selected.

Introduction

Measures introduced in the industrialised world to prevent transmission of HIV infection by blood transfusions include adherence to more stringent criteria for the use of blood, use of only voluntarily donated blood, exclusion of high risk donors, and universal testing of donated blood for HIV antibodies.1 Despite these measures it is estimated that 1 in every 40 000-153 000 units of blood transfused in the United States may be
infected with HIV. A recent study with the diagnostic techniques of virus culture and the polymerase chain reaction found one unit of infected blood in 61171 units of blood collected in the San Francisco area that was negative for HIV antibody. Currently, about 17 persons are estimated to be infected annually from blood transfusions in France.

Infected units of blood escape detection because of test insensitivity or laboratory error or because the donor is in the period of infection before seroconversion ("window period"). In the United States seroconverting donors associated with transmission of HIV to transfusion recipients had periods of two to six months between their seronegative and seropositive donations. In France transmission of HIV was recorded in a quarter of recipients of blood from donors who seroconverted within 12 months after a seronegative donation.

Rates of HIV infection are high in many countries of sub-Saharan Africa. Although great efforts have been made to introduce HIV antibody screening of blood for transfusion, in many sub-Saharan African countries this intervention has been little evaluated. In this study we attempted to assess the risk of transmission of HIV infection through blood transfusion in Abidjan, Côte d'Ivoire. Understanding of the magnitude of the problem is necessary to suggest ways of reducing further the risk of transmission by this route.

Abidjan, the largest city in Côte d'Ivoire, has a population of about two million. The Centre National de Transfusion Sanguine is responsible for providing a safe supply of blood for the city and the surrounding region. Blood is collected from repeat donors who give blood regularly at the centre or from once only or first time donors at the centre or in the community. Donors at the centre receive refreshments and compensation for transport ($1.67). Donated blood is screened for HIV 1 and HIV 2 antibodies, syphilis, and hepatitis B surface antigen.

Testing of donated blood for HIV antibodies was introduced in 1987. Since 1990 the centre has received increased international help from the European Community. Since the end of 1990 HIV positive donors have been counselled and requested not to donate blood again. By exclusion of known seropositive donors who could be contacted, the overall (HIV 1 and HIV 2 infected donors combined) seroprevalence in blood from repeat donors has fallen considerably. HIV antibody positive units of blood from repeat donors now represent incident infections since the previous screened donation, or seroprevalent infections in donors not able to be reached for counselling since the previous HIV antibody positive donation.

Materials and methods

HIV SEROLOGY

Donated blood was screened with HIV 1 and HIV 2 whole virus enzyme linked immunosorbent assay (ELISA) from one of several manufacturers (Behring, Mannheim, Germany; Diagnostics Pasteur, Paris, France; Abbott Laboratories, Frankfurt, Germany). Positive samples were further tested by ELISA from one of the other sources, and repeatedly reactive specimens were then tested by an assay detecting antibodies to the transmembrane glycoproteins of HIV 1 and HIV 2 (Peptilav I-2, Diagnostics Pasteur, Paris), when the reagents were available. All blood which was reactive on the first screening test was discarded.

IDENTIFICATION OF REPEAT BLOOD DONORS WHO SEROCONVERTED

All HIV antibody positive specimens from repeat donors in the first seven months of 1991 were identified, and records for this period were searched by hand to see whether any of these seropositive units came from donors who had donated earlier in the year. When such donors were identified the time periods between the earlier seronegative and the subsequent seropositive donations were assessed. Seroconversion was assumed to have occurred midway between the dates of the discordant serological results for each donor, as commonly assumed in cohort studies of the natural history of HIV infection. Figure 1 shows this graphically.

If the interval between the dates of the seronegative specimen and the presumed date of seroconversion was eight weeks or less the earlier unit was considered potentially infectious for HIV. A rate of potentially infectious units per total units collected in the first five months of the year was calculated. Because seroconversions would only have been recorded if donors had been tested at least twice this measured rate represents a minimum estimate of potentially HIV infected units.

ESTIMATION OF INCIDENCE OF HIV INFECTION IN REPEAT AND FIRST TIME BLOOD DONORS

From the recorded seroconversions in repeat donors we generated estimates of incidence of HIV infection. Data on the number of repeat donors were not available; only on the number of units from repeat donors. For this reason a range of incidence rates was calculated, based on the likely frequency of donation by repeat donors.

As the prevalence of HIV antibody was similar in repeat and first time donors before exclusion of known positives from the repeat donor population (unpublished data) the incidence of HIV infection in the two groups should be similar. The calculated incidence rates of HIV antibody in repeat donors were applied to the first time donor population, and rates of potentially infected blood units were calculated for both groups as previously described.

For the calculation of incidence of HIV infection it was assumed that each regular donor gave blood every three months (Centre National de Transfusion Sanguine, unpublished data); that detectable antibody developed within eight weeks of HIV infection; that the probability of a regular donor becoming infected with HIV was equal throughout the year; and that blood donations were equally distributed over the year. Figure 2 shows the donation of blood by regular donors. For seroconversion to be detected a donor must be tested at least twice. Donation of blood every three months results in each donor being tested four times during the year and having three separate intervals of three months each, during which seroconversion could be detected. The equal distribution of blood donations over the year means the population of regular donors could be considered as three separate cohorts, each giving blood every three months. For the three cohorts, therefore, there would be a total of nine periods during which HIV infection could be detected.
TABLE I—Prevalence of HIV 1 and HIV 2 antibodies in blood donated by repeat and first time donors in Abidjan, January-April 1991

<table>
<thead>
<tr>
<th>No of units of blood tested</th>
<th>No (%) positive by ELISA</th>
<th>Distribution of types of HIV reactivity by synthetic peptide testing of positive units of blood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV 1 (%)</td>
<td>HIV 2 (%)</td>
</tr>
<tr>
<td>Repeat donors</td>
<td>5831</td>
<td>124 (2-1)</td>
</tr>
<tr>
<td>First time donors</td>
<td>5076</td>
<td>557 (11-4)</td>
</tr>
</tbody>
</table>

TABLE II—HIV seroconversions in repeat blood donors in Abidjan, January-May 1991

<table>
<thead>
<tr>
<th>Month</th>
<th>HIV 1</th>
<th>HIV 2</th>
<th>HIV 1 and HIV 2</th>
<th>Total</th>
<th>No of seroconverters</th>
<th>No of seroconverters</th>
<th>Total No of units collected</th>
</tr>
</thead>
<tbody>
<tr>
<td>January</td>
<td>11</td>
<td>1</td>
<td>12</td>
<td>10</td>
<td>1261</td>
<td>1261</td>
<td></td>
</tr>
<tr>
<td>February</td>
<td>5</td>
<td>5</td>
<td>10</td>
<td>4</td>
<td>1028</td>
<td>1028</td>
<td></td>
</tr>
<tr>
<td>March</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1192</td>
<td>1192</td>
<td></td>
</tr>
<tr>
<td>April</td>
<td>6</td>
<td>1</td>
<td>7</td>
<td>7</td>
<td>1217</td>
<td>1217</td>
<td></td>
</tr>
<tr>
<td>May</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td>4</td>
<td>1213</td>
<td>1213</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>1</td>
<td>29</td>
<td>26</td>
<td>5831</td>
<td>5831</td>
<td></td>
</tr>
</tbody>
</table>

TABLE III—Numbers of false negative units of blood from repeat and first time blood donors in Abidjan at different test sensitivities, January-May 1991

<table>
<thead>
<tr>
<th>No of units</th>
<th>Observed prevalence</th>
<th>Test sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeat donors</td>
<td>5831</td>
<td>2-1%</td>
</tr>
<tr>
<td>First time donors</td>
<td>5076</td>
<td>11-0%</td>
</tr>
</tbody>
</table>
TABLE IV—Estimated overall risk of blood donations with HIV infected blood in Abidjan despite HIV antibody screening

<table>
<thead>
<tr>
<th>Incident infections (units in window period)</th>
<th>First time donors (No. of units=5831)</th>
<th>Total (No. of units=6076)</th>
</tr>
</thead>
<tbody>
<tr>
<td>False negative units, January-May 1991 (assumes 99% test sensitivity)</td>
<td>1-3</td>
<td>5-6</td>
</tr>
<tr>
<td>Total units infected but negative for HIV antibody</td>
<td>44-9-40-5</td>
<td>59-1-115-4</td>
</tr>
<tr>
<td>Rate/1000 units</td>
<td>7-6-15-5</td>
<td>5-4-10-6</td>
</tr>
</tbody>
</table>

*Based on calculated rate of 7-4-15-3/1000 for repeat donors and 1-8-3-8/1000 for first time donors (see results).

Discussion

Transfusion of HIV infected blood is probably the most efficient mode of transmission of HIV, most recipients of such contaminated blood themselves becoming infected.1 Despite intensive efforts and investment to guarantee the safety of the blood supply about one in every 94-185 screened units of blood in Abidjan remains potentially infectious for HIV. For blood collected from repeat donors the rate of infected blood despite screening may be as high as one in every 65-132 units. Although these rates are estimates, the directly observed incidence of seroconversion suggests a minimum rate of 4-5/1000 seronegative HIV infected units from repeat donors. Receipt of a screened unit of blood in a city such as Abidjan may thus carry a two to three times greater risk of HIV infection than a needlestick exposure from an HIV infected patient.11

For both repeat and first time donors in Abidjan, the major source of infectious, HIV antibody negative blood is donation after infection but before seroconversion. As modern tests for HIV antibody have a high sensitivity laboratory error is probably the most frequent cause of false negative antibody test results. We used an arbitrary sensitivity rate of 99%2 to compare the importance of false negative antibody test results with that of incident infections as a cause of contaminated blood units. Even in a population with a high prevalence of HIV antibody, such as first time donors in Abidjan, the rate of false negative results would have to be considerably to exceed the rate of infectious units due to seroconversions.

Our estimates of the incidence of HIV infection (1-2-2.5% per year) are close to measured incidence rates reported from cohort studies in other African cities with similar levels of HIV seroprevalence.3 The high rate of seroconversion for HIV 1, 27 times higher than that for HIV 2, corresponds with recent reports of an increase in the prevalence of HIV 1 but a stable prevalence of infection with HIV 2 in Abidjan (R Doorly et al., seventh international conference on AIDS, Florence, 1991; abstract MC42).

With currently available technology there is no simple way of reducing further this risk of HIV infection from screened blood. Donor deferral is difficult because risk factors for HIV infection are less obvious when the population prevalence is high and heterosexual transmission is the dominant mode of transmission (N Nzilambi et al., third international conference on AIDS, Washington, DC, 1987; abstract W4.6). Further improvement in laboratory standards, assuming that 99% sensitivity for detection of HIV antibody is realistic, brings relatively little gain. Testing for HIV p24 antigen merits evaluation for detecting seroconversions,4 but available evidence suggests that HIV p24 antigenaemia is less common in African people with HIV infection than in North Americans.5 This phenomenon may result from immune complex formation and may therefore not apply to units of blood in which HIV antibody is lacking. Testing of donated blood for HIV p24 antigen has been proposed in Bangkok6 but has not been evaluated in Africa.

This work suggests that in Abidjan, some 142 to 276 units of blood potentially infected with HIV are transfused annually. Though this should cause great concern, it is worth emphasising the great number of infections prevented since blood screening was introduced into this high prevalence donor population. In addition, HIV infections associated with transfusion are greatly outnumbered by infections resulting from other transmission routes. Our estimate of HIV infection incidence (1-2-2.5% per year) in blood donors may not apply to all adults in Abidjan, but there clearly must be many thousands of new cases of HIV infection annually due to heterosexual transmission among the city’s adult population of about one million.

To reduce further the transmission of HIV infection by blood transfusions in cities such as Abidjan recruitment of donors with especially low incidence and prevalence rates of HIV infection will need to be investigated. The age specific and sex specific distribution of HIV infection in the community can provide guidance about the best groups to target. For example, older people may have a low incidence of HIV infection and may be suitable as repeat donors (R Schutz et al., sixth international conference on AIDS in Africa, Dakar, 1991; abstract MA 255); male adolescents tend to have a lower prevalence (and, presumably, incidence) than female adolescents. Selected groups such as religious communities merit examination to see whether they have low prevalence and incidence of HIV infection.

There is a need for studies in areas of high prevalence of HIV to measure directly the risks associated with blood transfusion that we have attempted to estimate. Tests for HIV p24 antigen should be evaluated, and for selected situations autotransfusions and use of blood substitutes may be feasible. Such interventions, however, will not be widely applicable in the developing world. The two most important conclusions from this study are that more attention is needed in Africa in choosing blood donors with a low incidence of HIV infection, and that absolute emphasis must be placed on avoiding transfusion in all but those whose need is most dire. This may require creation of national blood transfusion advisory committees to establish guidelines for the rational use of blood and mechanisms for their implementation.7

We thank Drs John Ward, Harrison Steller, Helene Gayle, and James Curran for discussion, and we acknowledge the valuable comments and suggestions of the anonymous statistical referee.

Randomised controlled trial of short term treatment to eradicate *Helicobacter pylori* in patients with duodenal ulcer

Shorland W Hosking, Thomas K W Ling, Man Yee Yung, Augustine Cheng, Sydney C S Chung, Joseph W C Leung, Arthur K C Li

Abstract

**Objective**—To determine whether one week's drug treatment is sufficient to eradicate *Helicobacter pylori* in patients with duodenal ulcer.

**Design**—Single blind, randomised controlled trial.

**Setting**—Specialised ulcer clinic in a teaching hospital.

**Patients**—155 patients with *H pylori* and a duodenal ulcer verified endoscopically which had either bled within the previous 24 hours or was causing dyspepsia.

**Interventions**—Patients were allocated randomly to receive either omeprazole for four weeks plus bismuth 120 mg, tetracycline 500 mg, and metronidazole 400 mg (all four times a day for the first week (n = 78), or omeprazole alone for four weeks (n = 77). Further endoscopy was performed four weeks after cessation of all drugs.

**Main outcome measures**—Presence or absence of *H pylori* (by urease testing, microscopy, and culture of antral biopsy specimens), duodenal ulcer, and side effects.

**Results**—Eradication of *H pylori* occurred in 70 (95%) patients taking the four drugs (95% confidence interval 86% to 97%) compared with three (4%) patients taking omeprazole alone (1% to 11%). Duodenal ulcers were found in four (5%) patients taking the four drugs (2% to 12%) and in 16 (22%) patients taking omeprazole alone (14% to 32%). Mild dizziness was the only reported side effect (six patients in each group) and did not affect compliance.

**Conclusions**—A one week regimen of bismuth, tetracycline, and metronidazole is safe and effective in eradicating *H pylori* and reduces the number of duodenal ulcers four weeks after completing treatment.

Introduction

The linking of relapse of duodenal ulcers with *Helicobacter pylori* has been a considerable advance in managing patients with ulcer disease. Several studies have shown that in patients with duodenal ulcer and *H pylori* eradication of *H pylori* during ulcer healing is followed by duodenal ulcer relapse in only 5-10% of patients after one year compared with around 85% relapse in patients without eradication.\(^1\) The most effective regimens against *H pylori* usually consist of three drugs taken three to four times a day for between two and six weeks.\(^2\) Patient compliance with such treatment regimens can be difficult. Furthermore, side effects increase with duration of treatment. For these reasons we performed a randomised controlled trial to investigate whether one week of treatment is sufficient to eradicate *H pylori*.

Patients and methods

We performed antral biopsies on all patients undergoing oesophagogastroduodenoscopy during a four month period at this hospital and found to have an active duodenal ulcer. We included patients with dyspeptic symptoms and also those with gastrointestinal bleeding from their duodenal ulcer. (Those with gastrointestinal bleeding had endoscopy within 24 hours of admission.) The biopsy specimens were tested for the presence of urease using a commercial kit (CLO test, Delta West, Western Australia). All patients with urease positive test results were considered for entry to the trial. Exclusion criteria were haemodynamic instability, previous surgery for acid reduction, and pregnancy. Once entered, patients were randomised by instructions in consecutively numbered sealed opaque envelopes to receive either omeprazole for four weeks, plus colloidal bismuth subcitrate 120 mg four times daily, tetracycline 500 mg four times daily, and metronidazole 400 mg four times daily for the first week, or omeprazole alone for four weeks. Drug treatment was started within 24 hours of endoscopy.

Eight weeks later (four weeks after all treatment had finished) the patients returned the hospital. At this visit they were asked about any side effects they had experienced, followed by further endoscopy to look for ulcer healing. At the same time antral biopsies for microscopy, culture, and detection of urease were performed. The staff performing the endoscopic and bacteriological assessments were unaware of the drugs the patient had been taking.

**Bacteriological techniques**—Two antral biopsy specimens were minced aseptically and Gram stained to detect Gram negative spiral organisms. The minced tissue was cultured on Columbia agar (Oxoid) supplemented with 5% horse blood and incubated for five days under microaerophilic conditions. The identity of *H pylori* was confirmed by colony morphology, Gram stain, and positive biochemical test results (oxidase, catalase, and urease). Eradication of *H pylori* was confirmed by...