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Blood Transfusion Safety in Africa: A Literature Review of Infectious Disease and Organizational Challenges

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Abstract

Blood safety remains an important public health concern in Africa where lack of availability or provision of unsafe blood adversely impacts morbidity and mortality in the region. In recognition of this shortfall, the World Health Organization (WHO) established a goal of regional blood safety by 2012 through improved "organization and management, blood donor recruitment and collection, testing of donor blood as well as appropriate clinical use of blood" (Tagny et al: *Transfusion*. 2008;48:1256–1261; Tapko et al: Status of Blood Safety in the WHO African Region: Report of the 2006 Survey http://www.afro.who.int/en/divisions-a-programmes/dsd/health-technologies-a-laboratories.html. Brazzaville, Republic of Congo: WHO Regional Office for Africa; 2006). Although there has been substantial progress toward meeting these objectives, there are continued obstacles to both development and sustainability. In a setting where transfusion oversight is still being improved, transfusion-transmitted infections are of real concern. The high prevalence of some transfusion-transmissible agents such as hepatitis B virus and HIV in the general population means that some infected blood units escape detection by even well-performed laboratory testing, resulting in potential downstream transmission to patients. The spectrum of transfusion-transmitted infection include conventional as well as exotic pathogens, many of which are endemic to the region, thereby imparting ongoing challenges to recruitment and testing strategies.

Blood transfusion is a life-saving therapy, and its provision and safety are often taken for granted in the industrialized world. In contrast, limited access to transfusion or the provision of unsafe blood render blood safety a major public health concern in Africa.

Approximately 8 million U of blood are currently needed to meet transfusion demand for a population of nearly 800 million in Africa, according to the World Health Organization (WHO) guidelines of 10 U per 1000 population [2]. However, only 3 million U of blood are collected annually, satisfying a mere 40% of this estimated need. Demand for blood is driven by an array of factors that include obstetric hemorrhage, road traffic accidents, armed conflict, sickle cell disease and childhood anemia, malnutrition, HIV, malaria, and parasitic infections. This list underscores that lack of access to safe blood transfusion disproportionately affects the young, exacting an economic toll on a region that can already ill afford to pay. Deficiencies in infrastructure, skilled labor, and organizational support are among the many challenges to be overcome in improving access to and safety of blood transfusion in many African countries.

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In a setting where quality assurance (QA) and oversight are suboptimal, transfusion-transmitted infections (TTIs) are of real concern. The list of pathogens include both viral infections encountered in developed world settings, for example, HIV, and hepatitis C virus (HCV), as well as infections endemic to the region, such as arboviruses, malaria, and filariasis. Evaluation of the true extent of TTI in Africa is hindered by the same structural problems affecting the transfusion system itself; inconsistent testing strategies and a lack of computerized records make it difficult to estimate the residual risk of TTIs after testing. Similarly, where hemovigilance is weak, TTIs may be misclassified as naturally acquired infections and therefore underreported.

The WHO has targeted key areas of deficiency in moving toward their goal of safe blood by 2012. These include (1) organization and management, with each member state conducting a situational analysis; (2) blood donor recruitment and collection with at least 80% of blood collected through voluntary and nonremunerated blood donation (VNRBD), (3) laboratory testing of donor blood, specifically universal testing for HIV and major TTIs; and (4) appropriate clinical use of blood as reflected by implementation of a national blood use policy by at least 75% of the member countries [1,2]. Although not specifically stated (5), hemovigilance and QA should be incorporated as a means to audit intervention strategies and to ensure concordance between intervention and yield.

We therefore undertook this review of the literature to assess the current status of blood safety in Africa. A PubMed search was conducted using the following terms: “Sub-Saharan Africa,” “Blood,” “blood donor,” “blood transfusion,” “transfusion safety,” “transfusion transmitted infections,” “bloodless medicine,” “rational blood use,” “transfusion guidelines,” “hemovigilance,” and “blood use policy.” This was extended to a Google search of similar combinations of the same terms. The WHO Web site provides information on both blood safety as well as relevant regional statistics.

ORGANIZATION AND MANAGEMENT: SITUATIONAL ANALYSIS AND OVERSIGHT

Organization and oversight provide the impetus and support for any health intervention strategy and are crucial to pilot a blood safety infrastructure. Foremost, establishment of a functioning blood transfusion service demands national coordination, government support, and policy adapted to the needs of a given country. However, one size does not necessarily fit all: the regional countries have vastly different resources and infrastructure, often despite geographic continuity, and each environment needs to be appreciated and policy planning tailored accordingly. It is important to set appropriate goals that appreciate both the collective health concerns of the country as well as the logistics and cost, particularly in resource constrained environments. Legislation may also be used to enforce policy yet should not be a surrogate for structured development.

Five years after initiating its campaign of Safe Blood by 2012, the WHO for the African Region (AFRO) conducted an audit of the regional transfusion services. In 2006, a national blood transfusion service was evident in 38 of the 46 countries in the African region; 32 countries reported a blood transfusion policy, 11 had policy that was supported by legislation, and 37 were receiving technical and 38 financial assistance from international sources [2]. These data lend themselves to different interpretations.

Although most countries demonstrated a functioning transfusion service replete with legislation and national policy in a select number of cases, 8 countries had no national transfusion service, the overwhelming majority lacked a legal framework for blood transfusion policy, and most remained reliant on external assistance. Ironically, HIV has

provided the catalyst for much of the outside support and remains the dual-edged sword of transfusion; having invited notoriety to the blood banking community at the advent of the pandemic, it now imparts funding channels and partnerships for infrastructure strengthening and overhaul. Several multilateral funding agencies, for example, WHO Africa region, the United Nations AIDS program, the President's Program for AIDS Relief, and the Global Fund, lend support to national blood programs for this purpose [2].

Finally, situational analysis is a key element of management and oversight; understanding the full extent of a problem should precede intervention. Data pertaining to blood transfusion in Africa are of variable quality, accounting, in part, for the inconsistencies in the literature published on the topic. Thus, some successes on the ground may not be publicized; clearly, further operational research and strengthening of data collection are necessary goals for the future.

DONOR RECRUITMENT AND MOBILIZATION

Blood donor selection remains the first level of defense against TTIs; the deferral of high-risk prospective donors is a primary strategy to reduce risk. The favored source of blood collection in the developed world is VNRBD because such donors have been found to have lower risk for TTIs, at least in developed countries. For this reason, VNRBD is exclusively advocated by the WHO and is component of the 2012 objectives, that is, at least 80% VNRBD.

Voluntary donors are typically recruited through centralized systems, for example, blood centers that remain independent of the hospital. Voluntary and nonremunerated blood donation is logistically complex, requiring strategized recruitment, marketing, and collection to secure and, consequently, retain sufficient numbers of donors to approximate demand. This is reflected in the cost: a unit of blood collected through a centralized system is 2 to 3 times more expensive than that collected through replacement donation (RD; defined as donation from family members or friends of the patient), the major alternative to VNRBD in Africa [3].

In addition to financial support, VNRBD via centralized blood centers requires a developed infrastructure to be sustainable, for example, storage and refrigeration, transportation, communication, and QA, all of which are often ill developed in a resource-poor setting. Deficiencies in transport and storage have particular adverse effect in Africa where blood is prescribed for medical emergencies; the ability to tolerate delays, incumbent to procuring blood from outside the hospital, is poor.

Replacement donation is the major alternative to VNRBD and the primary source of blood collection in much of Africa. Estimated to contribute 75% to 80% of transfusable blood in the region [4], replacement donors comprise friends or relatives of the intended transfusion recipient. Although similar in concept, the term *directed donor* is used in developed countries when blood is donated and reserved for a specific recipient. This category of donor has long been regarded as higher risk based upon the assumption that friends or relatives are more likely to deny or ignore risk factors that invite further inquiry, removing the protection afforded by risk-screening questionnaires in favor of a perceived coercion to donate. Family members may also be at higher risk than VNRBD for some TTIs because of ethnicity, for example, hepatitis B virus (HBV). Furthermore, where burdened with the responsibility to procure donors urgently, family members may surreptitiously pay donors for their services, thereby compounding transfusion risk. Frequent shortcomings of RD include inadequate testing of units, lack of QA, and poor record keeping because of collection in the hospital setting where transfusion oversight is often poor. The latter may partly account for the enormous variability in data pertaining to RD [5].

Replacement donation is, however, significantly cheaper than VNRBD; in 1 study in Malawi, the cost of a unit collected through RD was shown to be $16 vs $56 for a unit collected from a centralized system [6]. This cannot be ignored in a financially constrained environment. Replacement donation is logistically easier than volunteer donation as it does not require the infrastructure or recruitment mechanisms associated with VNRBD; rather, collection takes place at the hospital [5], and the burden or responsibility for recruiting donors shifts to the patient's family and friends. This proves successful owing to the strong cultural bonds and extended family support evident in much of Africa.

There is a delicate balance between the need for the lower risk VNRBD, an ideal, albeit expensive and resource intensive strategy, vs RD, a less-demanding mechanism that may both inadvertently promote collection from high-risk donors as well as burden families and friends with the responsibility of procuring donors. This has prompted many to rethink the validity of exclusive or aggressive VNRBD and to closely reexamine the risk attached to any given subset of donor. In fact, some studies have shown that the assumption of higher TTI prevalence among RD compared with VNRBD may not always be true in Africa. A recent study from Ghana examined transfusion risk for HIV and HBV; the prevalence of anti-HIV and hepatitis B surface antigen in first-time volunteer vs replacement was 1.03% and 13.8% vs 1.1% and 14.9%, respectively [7]. The lack of difference between VNRBD and RD has also been shown in Latin America: HIV prevalence was indeed found to be higher among Brazilian VNRBD than RD donors after controlling for first-time vs repeat donor status [8], and no statistical difference was noted in TTI prevalence between VNRBD and RD in blood donors in a border population in Mexico [9].

These studies point out the importance of obtaining country-specific TTI prevalence data and of controlling for first-time vs repeat donor status when making comparisons between VNRBD and RD. The first-time donor is considered high risk for HIV and other TTIs [10]; these donors are usually young with concomitant higher prevalence of sexually transmitted TTIs, have uncertain or untested motive to donate, and, by definition, have had no prior transfusion screening. Indeed, many first-time donors use donation as a means to access HIV testing, itself an unavoidable donation incentive [11].

There have been novel strategies adopted to facilitate VNRBD and to convert first-time donors to regular donors, some of which have been very successful. One example pioneered in Zimbabwe is Club 25, through which secondary school donors pledge to donate 25 U during their lifetime [12]. Another approach in Ghana witnessed partnership between a teaching hospital and a local FM radio station; continual appeal for blood donors resulted in 63.6% repeat donation over a 3-year period, a feat achieved at low cost [12]. There have also been proposed strategies that build on the availability of RD while retaining safety.

Shortfall in provision of blood remains a multifaceted problem in Africa with direct adverse effect on clinical care. The impact on maternal mortality is one such poignant example where 26% (16%–72%) of maternal hemorrhage deaths are presently ascribed to lack of blood [13]. Strengthening the existing replacement-based model through on-site recruitment of voluntary donors, investment in hospital transfusion services with testing, QA, and data collection may be preferable and improve the transfusion shortfall. Further consideration of RD vs VNRBD ought to be driven by data on TTI prevalence and/or incidence in the 2 types of donors in the local setting. Many replacement donors share a similar altruism to VNRBD and can be used effectively while still maintaining transfusion safety. The component triage policy used by the South African National Blood Service (SANBS) may be a viable approach for the future. In recognition of the high risk attached to first-time donors, SANBS preferentially uses blood products from repeat VNRBD except in time of shortage.

Beyond debate of VNRBD and RD, deficient recruitment of blood donors remains an enduring problem in much of Africa. Shortfall in recruitment is a complex problem rooted in culture, education, and marketing. Successful donor recruitment relies on knowledge of the epidemiology of blood donation in the region; this information is often deficient or lacking in Africa. Available data indicate that the African donor pool is skewed toward young donors, likely reflecting recruitment in secondary schools and universities, and is disproportionately male. The latter may, in part, be cultural where men in Africa are perceived as being healthier than women [14], as well as physiological where iron deficiency anemia, pregnancy, and breastfeeding preclude women from joining the donor pool [15]. Broadening donor demographics represents a mechanism to bolster numbers; this should, however, be tempered by prevalence data on TTIs.

Education and literacy are also notable obstacles to recruitment; in a study in Burkina Faso, 30.8% of blood donors were illiterate or of primary school level. More poignantly, 14.4% donated to access HIV testing [11], highlighting a need to communicate both the utility as well as the risks of blood transfusion.

Donor profiling and risk assessment is contingent on availability of robust epidemiological data, revisiting the fundamental need for situational analysis. This includes demographic and behavioral risk factors for sexually and parenterally acquired infections, for example, HIV, HCV, and syphilis as well as knowledge of geographic risks for infections, for example, malaria and arboviruses. To some extent, collection practice and donor deferral can be adapted accordingly, particularly if a risk is localized, for example, chikungunya (CHIKV). It becomes more difficult to absorb the impact on the donor pool if the infectious agent is hyperendemic to the area, for example, malaria.

Finally, the donor pool in Africa is affected by anemia, malnutrition, and infectious disease, all of which directly or indirectly affect donor eligibility. In a Malawi-based study, 35.6% of prospective donors were deferred for hemoglobin level less than 12 g/dL or a positive infectious disease marker, 10% of which was for HIV, 2% venereal disease research laboratory test positivity, 1% HBV, and 5.8% for positive malaria slides [6].

TRANSFUSION-TRANSMITTED INFECTIONS

In addition to the major transfusion-transmissible pathogens encountered in the industrialized world, for example, HIV, HBV, HCV, and syphilis, several other agents with either established or theoretical transfusion risk are endemic to Africa. These pathogens span the complete microbiological spectrum including bacteria; protozoa (for example, malaria[16]); viruses (for example, CHIKV[17] and other arboviruses[18]); and nematodes (for example, filariasis [19]). The prevalence of TTI varies significantly by geography and population of study, and absence of data is a frequent problem. The following introduces the classes of agent and major pathogens encountered in Africa; it also expands on a few select agents either for the lessons that they impart or simply for their geographic curiosity.

Viruses

As elsewhere, the major transfusion-transmissible viruses of clinical importance in Africa are HIV, HBV, and HCV, and blood transfusion screening primarily focuses on prevention of these pathogens (Table 1). One study used mathematical modeling to estimate the residual transfusion risk for HIV, HBV, and HCV; the residual risk was estimated as 1, 4.5, and 2.5 infections per 1000 transfused units, respectively, corresponding annually to approximately 28 595, 16 625, and 6650 infections of HIV, HBV, and HCV respectively [20]. Another study, using the classical incidence rate and window period model among repeat blood donors in Burkina Faso, Congo, Ivory Coast, Mali, and Senegal, found an HIV

incidence rate of 56.6 per 100 000 person-years (95% confidence interval [CI], 47.1–67.9) corresponding to a residual risk of 34.1 per million donations (95% CI, 7.8–70.7) or 1 in 29 000 donations (95% CI, 1/128 000–1/14 000) [21]. The pronounced discordance in HIV residual risk estimates from these 2 studies emphasizes the need for additional data on TTI prevalence and incidence and residual transfusion risk in Africa.

The spectrum of transfusion-transmitted viruses also extends to agents encountered both in developed settings, for example, cytomegalovirus (CMV), human herpes virus type 8 (HHV8), human T-cell lymphotropic virus (HTLV), and human parvovirus B19 as well as agents considered “exotic” or endemic to Africa, for example, CHIKV and other arboviruses. Natural infection with these viruses is frequently subclinical or mild in the immunocompetent host yet holds severe ramifications in the immunocompromised, for example, Epstein-Barr virus, CMV, and B19. Transfusion recipients are disproportionately immunocompromised, rendering them at increased risk of complicated infections and even death [22,23]. Most of these viruses do not receive routine screening either in Africa or the developed world, yet still harbor real risk of transfusion transmission, for example, tick-borne encephalitis, West Nile, and dengue. Other agents harbor credible—as of yet undocumented—risk of transfusion transmission, for example, CHIKV and yellow fever [24].

HIV

Since gaining notoriety for blood banks in the 1980s through its association with transfusion transmission, HIV has resulted in near complete overhaul of the transfusion infrastructure in high-income countries. In Africa, higher prevalence and less comprehensive testing still results in an estimated 10% to 15% of cases of HIV linked to unsafe blood transfusion [2,25]. Transfusion of an HIV-tainted unit results in 96% seroconversion at 6 months and an accelerated disease progression and mortality compared with controls [26]. This may be ascribed to the high viral burden contained by a transfused unit of blood, having originating from a donor with relatively advanced HIV disease in conjunction with relative immunosuppression of the recipient.

Confronted with a nationwide prevalence of 10% to 15% among adults, the SANBS implemented early and aggressive strategies to mitigate the HIV transfusion risk, including introducing a stringent policy of donor selection, education, and product triage policy in the late 1990s. Subsequent analysis documented that this triage policy resulted in a dramatic drop in HIV-1 risk from transfusion despite an escalating HIV pandemic in SA (0.17% in 1999–2000 to 0.08% in 2001–2002, $P < .001$) [27]. The strategy, however, resulted in under-collection from most of the African population, inviting serious political repercussions that led to modification of the donor deferral and product use criteria. The SANBS responded with implementation of concurrent HIV RNA nucleic acid testing (NAT) and serology-based screening to allow more equitable blood collection in South Africa without compromising recipient safety. HIV NAT affords added protection through capture of infected donors in the preseroconversion “window period.” Vermeulen et al [28] reported 16 RNA-positive/antibody-negative donations during the first year of NAT screening; recent unpublished data document about 30 such cases per year. These components collected from the NAT-yield donors would otherwise have escaped laboratory detection and likely have resulted in transfusion transmission. Although this is certainly a model for the region, sophisticated testing may not translate to other parts of Africa where the consideration of cost-effectiveness and structural deficiency assume greater importance. This has called on occasion invited criticism as being inappropriate for the region.

Hepatitis B Virus and HCV

There is a similarly diverse approach to transfusion screening of HBV and HCV. Hepatitis B virus is highly endemic in much of Africa where 8% of the population is chronically infected [29]. This high prevalence is also reflected in the estimated transfusion risk models where risk exceeds that of HIV yet receives comparatively little attention. Most screening is conducted using immunoassays targeting HBV surface antigen; antibody testing for HCV is somewhat less widespread because of cost constraints. Natural HBV transmission in Africa occurs predominantly during infancy and early childhood (so-called horizontal spread), conferring high risk of chronic infection. Availability of the HBV vaccine and a concomitant increase in immunization coverage in Africa will hopefully mitigate prevalence and transfusion risk in the future.

Hepatitis C virus, despite exhibiting greater virulence than HIV or HBV, poses less of a problem to blood transfusion in Southern Africa by virtue of low prevalence. Unfortunately, this does not extend to the rest of Africa, and high rates are encountered both in parts of West and North Africa. Egypt, in particular, displays extraordinarily high levels of HCV, attributed to the use of inadequately sterilized needles used in antimony-based antischistosomiasis campaigns before the 1980s [30]. Despite cessation in these public health campaigns, iatrogenic transmission by unsafe injections remains the primary mechanism for new infections in Egypt and North Africa, thereby sustaining the epidemic.

Human T-Cell Lymphotropic Virus 1 and 2

Human T-cell lymphotropic virus 1 is the causative agent of adult T-cell leukemia (ATL) and tropical spastic paresis/HTLV-associated myelopathy (HAM). Human T-cell lymphotropic virus 2 is associated with HAM, pneumonia, and bronchitis but not with ATL. Both HTLV-1 and 2 are clinically unpredictable, and only 2% to 4% of those infected ever develop complications, for example, ATL or tropical spastic paresis/HAM, and only do so decades after latent infection. Although endemic to Central Africa, transfusion screening is presently only confined to Gabon. Human T-cell lymphotropic virus is transmitted vertically, via breastfeeding, sexually, and parenterally and therefore shares risk factors for HIV, HCV, and HBV. Consequently, predonation risk deferral allied with laboratory testing intended for major pathogens likely results in fortuitous—albeit incomplete—exclusion of HTLV from the blood supply. Human T-cell lymphotropic virus 1 prevalence data among blood donors are scant, a fundamental problem shared by most TTIs in Africa. Prevalence in the general population has been reported from 1.05% in Guinea to 6.6% to 8.5% in Gabon [31], although the highest rates may be attributable to sampling bias. Similarly, the few blood donor studies demonstrate a prevalence ranging from 0% to 2% [32–36]. An uncertain clinical course allied with a low seroprevalence renders this of lesser concern among the TTIs. Screening, if pursued, is conducted using enzyme immunoassays (EIAs) and confirmatory testing with Western blot or recombinant immunoblot.

Human Herpes Virus Type 8 and Other Herpes Viruses

The major herpes viruses of relevance to transfusion medicine are CMV and HHV8. Transfusion-transmitted CMV is well described and can result in severe, disseminated, and often-lethal infection in neonates and the immunocompromised [37]. Cytomegalovirus is leukotropic, and transfusion risk in the developed world has largely been ameliorated after the introduction of leukoreduction. The latter, however, is both expensive and resource intensive; consequently, leukoreduction is only available in very select settings in Africa, and CMV remains a hazard to high-risk recipients.

Human herpes virus type 8 is the causative virus of Kaposi sarcoma and is also associated with primary effusion lymphoma and multicentric Castleman disease. Natural acquisition is

poorly understood and appears to differ in areas of low vs high prevalence. In North America, Northern Europe, Asia, and Latin America where seroprevalence is low (0%–5%), transmission is predominantly sexual, particularly in men who have sex with men. In areas of high prevalence, for example, sub-Saharan Africa, the virus is transmitted through exposure to oropharyngeal secretions. Human herpes virus type 8 poses a controversial yet plausible risk to transfusion recipients; attempts to demonstrate transmission via blood transfusion have thus far yielded inconsistent findings. Most studies have either failed to show seronconversion or yielded very low risk [38,39], particularly in studies conducted in low endemicity, for example, Northern Europe and the United States. The most convincing evidence of transfusion-transmitted HHV8 emerged from a prospective cohort study in Ugandan transfusion recipients that showed a 2.8% ($P < .05$) excess risk of seroconversion over 6 months of follow-up [39]. There is a high seroprevalence [40] of HHV8 in both blood donors and the general population in parts of Africa [41]; in addition, many transfusion recipients are severely immunocompromised, component of an array of factors including HIV/AIDS, the disease responsible for drawing wide-scale attention to HHV8.

Other herpes viruses, for example, herpes simplex viruses 1 and 2, the causative agents of herpes labialis and genitalis, respectively, pose less concern to blood banking in Africa or elsewhere. Herpes simplex viruses 1 and 2 have been shown to have low and largely theoretical risk of transmission via plasma, and this risk is largely confined to collection during both primary infection and high viremia [42].

Chikungunya and the Arboviruses

The arboviruses of clinical importance include the flaviviruses (family *Flaviviridae*, eg, dengue and yellow fever), the alphaviruses (family *Togaviridae*, eg, CHIKV), and the bunyaviruses (family *Bunyaviridae*, eg, Rift Valley Fever) [18]. Only a limited number of the arboviruses have been documented as transfusion transmissible, for example, dengue [43], West Nile virus [44], and tick-borne encephalitis [45]. The absence of documented transmission does not exclude the possibility for doing so, particularly where agents are endemic and easily passed off as natural acquisition. Fortunately, concern over arbovirus transmissibility via blood transfusion is somewhat diminished given that arboviruses are characterized by a short asymptomatic viremia in contrast to the chronic viremia exhibited by the major transfusion transmitted viruses, for example, HBV. Arboviruses are, however, more widely prevalent than often appreciated; 1 study conducted in Sierra Leone in the late 1970s showed 16.6% of donors in a limited sample exhibited antibodies, most of which were against yellow fever [46].

Chikungunya exemplifies the challenges posed by arboviruses and emerging pathogens. The virus is naturally transmitted by *Aedes* mosquitoes [17] and is characterized clinically by painful polyarthalgia, maculopapular rash, high fever, and myalgia [22]. The CHIKV has the propensity to cause atypical or severe infection in older age groups and those with comorbid conditions, both of which are common associations among transfusion recipients [23]. Previously described in the setting of sporadic outbreaks in Africa and Asia, CHIKV drew wide attention after a major epidemic in Reunion and the Southwest Indian Ocean islands between 2005 and 2007, leading to an interruption of blood collection in Reunion in January 2006. The risk of transfusion-transmissible CHIKV was retrospectively estimated as 132 per 100 000 donations, increasing to 1500 per 100 000 donations at the peak of the epidemic, both small in comparison with the 312 500 of 757 000 inhabitants estimated to have been infected by the mosquito vector during this time. Although no transfusion-associated cases of CHIKV have been conclusively documented, there is a credible transfusion risk as evidenced by transmission to laboratory personnel and health workers handling infected blood [47]. Furthermore, during epidemics, blood is frequently diverted away from virus-naive patients and toward patients having complications of infection [48]. This is notably

relevant to DENV outbreaks where patients are transfused for dengue shock syndrome and dengue hemorrhagic fever.

The outbreak in Reunion demonstrates the dramatic adverse effect posed by CHIKV and other arboviruses to the donor pool and blood supply, particularly in countries with little transfusion reserve. There are several obstacles to addressing these agents: Deferral based on symptom enquiry is unreliable. Although 75% of those infected will go onto become symptomatic, donation is more likely to occur during the subclinical viremic prodrome phase when donors are still feeling well. One can elect to suspend collection during an outbreak; this, however, may be tolerated if localized but is logistically difficult if widely disseminated, particularly in a developing country. This strategy of interrupted collection was indeed deployed during the Reunion outbreak, and red cell and plasma products were procured from mainland France, whereas locally collected apheresis platelets were subjected to photochemical inactivation. Reunion enjoys French provincial status, thereby allowing for this unique and major shift in support. There is currently no commercial CHIKV testing platform for blood donors, and in the absence of a more sustained market, it is difficult to motivate for development or implementation of such a test [22].

Bacteria: Contamination and Syphilis

Septic transfusion reactions due to bacterial contamination of units is a major—albeit under-reported and unappreciated—risk of transfusion. Concern over TTIs usually focuses on viral risk, yet rates of bacterial contamination in Africa, incurred during collection and component processing, are 2500 times that found in developed countries [49]. In a recent study of pediatric whole blood transfusions in a Kenyan hospital, there was an 8.8% prevalence of bacterial contamination over the 1-year duration of study [49].

The bacteria of importance in Africa include many of the conventional pathogens commonly encountered in the developed world (Table 2). The gram-negative organisms, for example, *Yersinia enterocolitica*, *Citrobacter freundii*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* are most commonly implicated in red cell and whole blood contamination, whereas the gram-positive bacteria, for example, coagulase-negative *Staphylococcus*, *S aureus*, and *Bacillus* spp [50] are more closely linked to platelets. The disproportionately higher incidence in septic contamination of platelet units is ascribed to storage at room temperature, hence providing an ideal growth medium for skin flora and other contaminants introduced at time of collection.

Syphilis, the first recognized infectious risk of blood transfusion, still remains a major testing focus both in Africa and around the world. Recently, continued screening has been called into question in the United States where no transfusion-transmitted case has been identified since 1966. Reasons cited for this low transmissibility include a diminishing reservoir in the United States as well as poor survival of *Treponema pallidum*, the causative agent of syphilis, in refrigerated red cells and concomitant low tolerance of the organism for high oxygen tension in platelets. Furthermore, it is thought that the spirochete is already absent from the peripheral blood by the time that seroconversion is demonstrable in the donor [51,52]. This argument, however, does not necessarily apply to Africa where seroprevalence among blood donors remains high [53], refrigeration and QA is poor, and blood is frequently collected from replacement donors in times of emergency, allowing very little transit time to adversely impact on spirochete survival. This supports a continued conservative testing approach in Africa and differs from the United States and other industrialized countries where syphilis screening has been retained as a dubious surrogate measure of high-risk behavior.

Malaria and Protozoa

With the exception of anecdotal reports of transfusion-transmitted African trypanosomiasis [54] and leishmaniasis [55], transmission of protozoa in Africa through transfusion is largely confined to malaria.

Since the first documented case in 1911, the most commonly implicated species in transfusion-transmitted malaria has undergone changes in parallel with shifts in the dominant species in the general population. Currently, *Plasmodium falciparum* accounts for most cases, and malaria continues to pose a major problem for blood safety in Africa. Prevention strategies applied to nonendemic countries such the United States do not necessarily apply to Africa where the infection is endemic. Consequently, deferral of "at risk" donors, used for travelers and immigrants returning from endemic countries or contained regions, is unfeasible because many, if not most, donors are infected in malaria-endemic Africa.

There are additional challenges: individuals are frequently asymptomatic and unrecognized at time of blood donation [56]; this is ascribed to "semi-immunity" that develops in those living in hyperendemic areas characterized by high-titer antibodies with low-level parasitemia. From a recipient perspective, this protection is incomplete. In addition, children receive a significant proportion of blood transfusion in Africa and have not had sufficient time to develop robust immunity against the malaria parasite. Transfusion in childhood is therefore the veritable dual-edged sword: transfusion is needed to counteract complications of malaria, yet this therapy is high risk for malaria.

With the exception of fresh-frozen plasma [16], transfusion-transmitted malaria has been described with all commonly prescribed blood products including whole blood, red cells, and platelets frequently prescribed in Africa. Approaches that have been proposed or adopted by endemic counties to mitigate malaria risk include administration of antimalarials to transfusion recipients, collection from lower risk segments of the population, and triage of "high-risk" transfusion (blood collected from areas of high prevalence) away from vulnerable recipients. However, the notion of "high" and "low risk" is relative and draws on knowledge of seasonal and geographic variation in prevalence. In 1 study from Nigeria, the prevalence of parasitemia in blood donors during the rainy vs the dry season was 27.3% vs 5.5% ($P < .0001$) [57]. The strength of this triage mechanism is therefore contingent upon availability of robust epidemiological data of the infection.

Another approach to mitigation of malaria risk is laboratory screening of prospective donors. There are several laboratory methods considered for blood transfusion screening, each of which is not without problems, having been adapted from patient testing. The most commonly used diagnostic tests are Wright- or Giemsastained thick blood smears and/or rapid antigen testing (RDT). Blood smears are labor intensive and insensitive and, consequently, not amenable to high throughput needed for screening of the blood supply. Florescent microscopy is an enhanced diagnostic technique that has also been considered yet is impractical in Africa given both poor specificity and component to distinguishing parasites from cellular debris as well as resource intensive given the requirement for specialized equipment [16].

Rapid antigen testings are insensitive [57] and capture only those above a high parasitemia threshold, whereas semi-immune individuals frequently have low-level parasitemia that escapes laboratory detection. Furthermore, a pervasive high-titer, protracted antibody response in semi-immune individuals detracts from the ability of RDT to distinguish between infected or uninfected blood donors. In the future, polymerase chain reaction could detect this low-level parasitemia if cost and technological constraints can be overcome.

Finally, malaria adversely impacts the blood supply via increased deferral of blood donors in a continent already having shortfall in recruitment and availability of blood.

Filariasis: The Nematodes

Filariasis refers to a group of diseases caused by nematodes (roundworms) that inhabit the lymphatics and subcutaneous tissues [58,59]. This family of infections inflicts devastating and disfiguring pathologies on their hosts. Of the 8 species of filarial worms implicated in human infection, 5 are found in Africa, namely, *Wucheria bancrofti* (lymphatic filariasis —"elephantiasis"), *Onchocerca volvulus* (oncocerciasis—"river blindness"), *Loa loa* (loiasis —"African eye worm"), *Mansonella streptocerca* (dermal-based filarial infection), and *M perstans* (body cavity filarial infection involving peritoneum, pleura, and pericardium).

There is very little literature documenting transfusion transmission of microfilariae despite the theoretical potential for doing so. A Nigeria-based study evaluated blood-borne parasites in prospective blood donors; in addition to malaria (*P falciparum*, *P malariae*, and mixed infections), there was a prevalence 1.3% of *L Loa*, 15.6% *M perstans*, and 0.2% coinfection of *L Loa* and *M perstans* [60]. Filariasis correlated both with younger age group (24–30 years) and paid donation, highlighting the need for nonincentivized blood donation. Despite high levels in a select population, there is still uncertainty as to whether filaria pose a risk to recipients. In an Indian study, microfilariae were indeed shown to be transmissible via blood transfusion yet did not develop into adult worms. There was, however, a hypothesized association with allergic transfusion reactions accounting for high rates (29.8%) of reactions observed in the study cohort. The authors recommended deferral of blood donors with a history of filarial infection [19]; this recommendation has been echoed in a brief letter to the editor from Thailand [61]. Anecdotally, a case of transfusion-associated *M perstans* microfilariasis was described without any adverse effect, suggesting that the adult worm may be prerequisite to pathology [62]. In conclusion, transfusion transmission of filaria remains speculative pending additional research.

BIOLOGICAL TESTING OF BLOOD PRODUCTS

In the absence of safeguards in recruitment and selection of low-risk donors, prevention of TTIs relies on biological testing of blood products. Unfortunately, the cost of testing for all known agents is not feasible because even a select test panel is often prohibitively expensive. Consequently, blood screening in Africa, with few exceptions, for example, HTLV-1/2 testing in Gabon, is limited to HIV, HBV, HCV, and syphilis owing to a regional prevalence of 0.5% to 16%, 3% to 22%, 2% to 7%, and 1% to 21%, respectively [6].

The WHO advocates for universal testing for HIV. Even this is difficult when confronted with the costs and technical expertise required for high-quality laboratory testing. As per the WHO survey conducted in 2006, of the 42 responding countries, universal testing (testing on 100% of units) was reported by 95% of countries for HIV, 83% for HBV, and 59% for HCV [2]. A more recent study of 7 countries in Francophone, Africa revealed more promising results with 100% of units tested for HIV and HBV and 70% to 100% tested for HCV within the surveyed centers [14]. In addition, most countries reported screening for syphilis, whereas only Gabon tested for HTLV 1/2 [2].

Blood transfusion screening strategies include rapid testing, EIA, and chemiluminescent immunoassay (CLIA) as well as NAT. Each strategy holds both advantages and disadvantages.

Point of care "rapid" testing has proved revolutionary in clinical diagnosis of HIV and holds promise for blood transfusion screening in Africa, particularly where blood is collected in

remote areas away from centralized blood centers. The advantages are self-evident: it is not technology intensive and comparatively cheap. As dictated by the name, testing is rapid; this allows for prompt deferral of infectious blood donors, bypassing the expense and risk of collection. From a less utilitarian perspective, it also allows for immediate counseling with referral to follow-up care. This prompt notification avoids a return visit to the test center, which is notoriously unreliable. However, rapid tests are operator dependent, and interpretation is subjective, thereby limiting test sensitivity and specificity [63]. Furthermore, they are not amenable to high throughput, QA is lacking, and results may go undocumented [64]. Different algorithms have been developed to improve the sensitivity and specificity of testing, including running parallel rapid tests. Although this may improve reliability of results, it detracts from the cost benefit of rapid testing. Predonation screening, using rapid tests, is discouraged by the WHO.

Both the EIA and CLIA are tried and tested methods for detection of either antigen or antibody through generation of immune complexes (“sandwich”-type assays). These platforms are the mainstay of blood screening in Africa, are amenable to high-volume testing, and can be adapted to manual or automated platforms. Again, performance is dependent on QA.

Nucleic acid testing targets viral RNA or DNA using molecular techniques. It improves safety owing to the ability to capture agents in the preseroconversion stage, the so-called window period [28]. However, these tests demand both infrastructure and technical expertise, and marginal reduction in the window period is offset by substantially higher costs, prompting many to question whether it is really appropriate for Africa. Nucleic acid testing is presently used in South Africa, Namibia, Egypt, and selectively in Ghana [64]. The cost-benefit ratio of NAT is most favorable in areas of high prevalence for a given agent, for example, HIV and HBV in South Africa and HCV in Egypt.

Pathogen inactivation (PI) is becoming increasingly attractive as an alternative strategy to biological testing for TTIs. Pathogen inactivation refers to global inactivation of infectious agents in blood products using various technologies [65,66]. These technologies include mechanical disruption (used in plasma processing) through heat treatment or nanofiltration or photochemical handling of platelets and/or plasma with solvent detergent photoactive methylene blue or psoralen/riboflavin inactivation of DNA and RNA [67]. These methods differentially render a variety of viruses, bacteria, and protozoa [66] (including malaria) incapable of replication and productive infection [68]. To date, PI is restricted to select high-income countries owing to cost and complexity that exceeds feasibility in a resource-poor setting. It should, however, be clarified that the cost is currently additive, incumbent upon the notion of an adjunct to laboratory testing rather to a more rational and cost-effective stand-alone approach. The strength of PI resides with the ability to simultaneously address a diverse array of pathogen, both known as well as unrecognized or emerging. Pathogen inactivation may also confer the ability to resolve many of the problems posed to blood banking in Africa, for example, bacterial contamination from unsterile conditions and transfusion-transmitted malaria borne from a need to collect blood in hyperendemic areas. This comprehensive management is far superior to the current triaged screening of pathogens according to perceived risk and cost-effectiveness. However, in addition to nuanced deficiencies with the individual PI technologies, there is currently no viable platform in clinical use for red cells and whole blood, the 2 major components prescribed in Africa. Pathogen inactivation does, however, hold promise and will hopefully gain momentum in the future.

Finally, biological testing is not confined to infectious screening and extends to blood group, for example, ABO and immune compatibility testing. In the WHO survey, all countries in

the region reported ABO cell grouping, yet only 71.8% reported serum grouping [2]. Various subgroups of the groups A and AB that are known to be prevalent in the black population will not be detected using this method and can precipitate acute hemolytic transfusion reactions. Additional deficiencies have been identified in extended Rh phenotyping of red cells and screening for sickle cell disease and major enzymopathies, for example, G6PD deficiency [14], all of which have clinical implications for prospective recipients. Improvement in immunohematology training, QA, and availability of reagents certainly warrants attention.

RATIONAL BLOOD USE POLICY

Despite shortfall in blood availability, there continues to be inappropriate blood use and concomitant wastage. This exposes patients unnecessarily to the hazards of transfusion and, when coupled with deficient biological testing, compounds the already high risk of TTI [69]. Over-transfusion stems, in part, from lack of defined policy or clinical guidelines for appropriate use either at a national or local level. In the WHO African region blood safety survey, only 24 of the 46 countries surveyed had national guidelines for appropriate blood use, and in 35 of 46 hospitals, less than 25% of hospitals had transfusion committees to regulate prescribing [2].

Lack of education and training among prescribing physicians contributes to liberal transfusion practice against ill-defined thresholds. Similarly, rigid adherence to laboratory transfusion triggers—rather than symptomatic anemia—results in unnecessary depletion of the blood supply. The transfusion service is also frequently fragmented with little interaction between the blood center and the hospitals or prescribing physician and thereby precludes monitoring of transfusion practice [70].

Strategies addressing the policy revisit the need for robust organizational support. The ministry of health partnered with multilateral and nongovernmental organizations, for example, WHO-African Region would be likely candidates to direct this at a national level. Regional transfusion services with more developed infrastructures can also assume a lead role, lending support to neighboring countries, for example, SANBS currently provides donation serology and NAT laboratory testing for Namibia Blood Transfusion service. National frameworks need to be diffused at the hospital level by means of transfusion committees equipped to monitor blood use and audit practice according to prescribed rational guidelines. Dual appointments by hospital and blood center staff may also bridge the gap between hospital and blood center. Finally, education and training are imperative to successful deployment of clinical guidelines.

Rational blood use also includes efficient blood use. Component therapy is a means to improve efficiency through differential fractionation of whole blood into derivative red cells, plasma, cryoprecipitate, and platelets. This is the major practice in the developed world given the ability to diversify the parent blood product. In contrast, whole blood needs to be transfused to an ABO type-matched recipient given the large antibody-containing plasma fraction. For example, a group O red cell component can be transfused safely into any recipient, but a group O unit of whole blood is restricted to group O recipients unless established to be of low antibody titer. In addition, the large volume of whole blood places recipients at risk for transfusion-associated circulatory overload. In the 2006 WHO survey, 24 of 39 responding countries were still transfusing more than 75% as whole blood, and only 7 of the 46 countries had a national strategy for provision of fractionated plasma products [2]. These findings were echoed in the more recent survey of 7 blood centers in Francophone, Africa [14].

In addition to implementation of policy, “bloodless medicine” or conservative transfusion practice is well described as a successful adjunct strategy to protecting transfusion inventories while still preserving sound clinical care. This incorporates a range of interventions that limit unnecessary blood use, many of which can be tailored to a resource poor setting. These include the use of conservative transfusion thresholds; alternatives to blood transfusion such as crystalloids or colloids; hematinic support in the chronic stable patient, for example, iron and folate; and attention to hemostasis and surgical technique [71,72].

HEMOVIGILANCE AND QA

Hemovigilance is a term dubbed for the collective audit of transfusion safety, referring to both active and passive surveillance mechanisms to detect adverse outcomes among transfusion recipients and, to a lesser extent, among donors. This composite mechanism addresses all aspects of transfusion from recruitment and donation to posttransfusion surveillance in which sentinel events, including transfusion reactions and TTIs, are investigated [73]. Of the steps in the collection to transfusion sequence, hemovigilance and QA are the most difficult to implement in a resource-poor setting owing to complexity of tracking patients and products. This should not detract from their importance; in the absence of surveillance, breeches in process continue to be unchecked, and transfusion transmission of infections goes unabated. Hemovigilance and QA also offer a means of data collection and, therefore, inform rational planning and allocation of resources.

Infectious risk is usually ascribed to blood donors, whereas the transmission hazard of component processing is often overlooked. Unclean working conditions and high ambient temperatures and humidity render this an ideal setting for bacterial contamination. This was illustrated in a Kenya-based study that documented an 8.8% frequency of bacterial contamination in pediatric whole blood transfusions over a 1-year period of observation [49]. Hemovigilance and QA are, consequently, central to blood safety.

CONCLUSION: THE NEXT STEP

Transfusion-transmitted infection remains a formidable problem in Africa. The diverse array of pathogens is mirrored by a similarly broad constellation of economic and organizational problems in the region; this argues for a holistic approach encompassing legal, institutional, and training interventions as advocated by the WHO. This should not neglect the contribution of innovative, targeted approaches, for example, donor recruitment, and technologies, for example, rapid testing, NAT, and PI, that hold promise for significant gains in the future. Interventions also need to be tailored to that of the country in order that they are both appropriate and effective. This relies on recognition of the vast heterogeneity across the continent; for example, the resources available to a transfusion service in South Africa are very different to that in a blood center in Central or West Africa.

Expanded data collection and epidemiology-based research are crucial to the prevention of TTI and improved quality control in the region. Similarly, transfusion management and guidelines may reduce blood wastage and improve supply. Finally, development of local capacity in both human and technological resources will be needed to amend reliance on international funding and technical support in favor of long-term independence and sustainability. Despite the many obstacles, meaningful progress has been made, and low cost strategies forged with improvement in transfusion safety [2]. The WHO goals represent a partial foundation; any success should be tempered against the broader need to expand beyond 2012 to achieve a durable blood transfusion framework in Africa. This sustained commitment and investment in transfusion infrastructure will ultimately ensure the next step forward.

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Table 1

Pathogen, Clinical Manifestation, Available Testing Methods, Country-Specific Donor Prevalence, and Estimated Risk of Transfusion Transmissibility (where available) for Selected TTVs in Africa

Pathogen	Clinical manifestation	Transfusion screening/testing method in use (limited use)	Blood donor seroprevalence from published studies	Estimated risk
Viruses				
HIV	AIDS	Serology anti-HIV (EIA, CLIA, and rapid serological testing) (NAT)	Burkina Faso (2.0%–4.5%) [33] Cameroon (2.9%) [14] DRC (2.2–4.6% *) [74] Egypt (0.0%) [75] Ethiopia (3.8%) [76] Ghana (1.03%–1.1%) [7] Ivory Coast (3.48%) [14] Mali (2.6%) [77] Mozambique (12.3%–15.4%) * [32] Namibia (0.20%) ‡ Niger (1.4%) [14] Nigeria (2.7%–3.2%) [28,78,79] Rwanda (1.0%) [14] South Africa (0.1%) [28] Tanzania (3.8%) [80] Zimbabwe (0.18%–1.61%) [74]	1 per 1000 U transfused [20], †
HBV	Viral hepatitis Hepatocelullar carcinoma	Serology anti-HBsAg (EIA and CLIA) (NAT)	Burkina Faso (11.0%–18.0%) [33] Cameroon (10.3%) [14] DRC (3%–4.9% *) [74] Egypt (4.7%) [75] Ethiopia (4.7%) [76] Ghana (13.8%–14.9%) [7] Ivory Coast (5.85%) [14] Mali (13.9%) [77] Mozambique (4.5%–10.6% *) [32] Namibia (0.39%) ‡ Niger (18.96%) [14] Nigeria (2.7–3.2%) [78,79] Rwanda (2.76%) [14] South Africa (0.07%) [28] Sudan (6.25%) [81] Tanzania (8.8%) [80]	1 per 222 U (4.5/1000) [20], †

Pathogen	Clinical manifestation	Transfusion screening/testing method in use (limited use)	Blood donor seroprevalence from published studies	Estimated risk
HCV	Viral hepatitis Hepatocellular carcinoma	Serology anti-HCV (EIA and CLIA) (NAT)	Nigeria (2.7%–3.2%) [78,79] Burkina Faso (3.2%) [14] Egypt (2.7%–24.8%) [75,82,83] Cameroon (3.9%) [14] Ethiopia (0.7%) [76] Ivory Coast (6.98%) [14] Mali (3.25%) [14] Mozambique (1.0%–1.2% *) [32] Namibia (0.00%) ‡ Niger (1.42%) [14] Nigeria (4.3%) [78] Rwanda (3.13%) [14] Senegal (1.4%) [84] South Africa (0.005%) [28] Sudan (0.65%) [81] Tanzania (1.5%) [80] Mali (3.3%) [77]	1 per 400 U (2.5 per 1000) [20], †
WNV	Meningoencephalitis	–		0.27–1500 per 100 000 donations [17] §
CHIKV	Febrile-arthralgia Syndrome	–		
Tick-borne encephalitis	Meningoencephalitis	–		
HGV	Unknown	–	Egypt (12.2%) [85]	
TTV	Unknown	–	Egypt (48.4%) [83]	
EBV	Infectious mononucleosis Burkitt lymphoma Nasopharyngeal carcinoma	–	Ghana (20.0%) [86]	
CMV	Infectious mononucleosis Disseminated infection in immunocompromised and neonates		Ghana (77.6%) [86] Tunisia (97.14%) [87]	
Dengue	Dengue Dengue shock syndrome Dengue hemorragic fever	–	Burkina Faso (30.4%–34.8%) [33]	
HHV8	Kaposi sarcoma Mulicentric Castleman disease Primary effusion lymphoma	–	Ghana (23.7%) [86] Central African Republic (22.5%) [40] Burkina Faso (11.2%–16.0%) [33] Tanzania (48.0%) [88]	
HTLV-1/2	Adult T-cell Lymphoma/leukemia Topical spastic Paraparesis/HAM	(Serology anti-HTLV-1/2) (testing limited to Gabon and Seychelles [2]	Mozambique (0.89%–1.2% *) [36,78] Senegal (0.16%) [35] Tunisia (0.0%) [34] Burkina Faso (0.0%–2%) [33]	

Abbreviations: (−) or blank, not currently performed or unknown; Anti-HBsAg, anti–hepatitis B surface antigen; WNV, West Nile virus; HGV, hepatitis G virus; EBV, Epstein-Barr virus.

[*] Replacement donors.

[†] Estimated from mathematical modeling for all of sub-Saharan Africa.

[‡] Unpublished correspondence from NAMBTS.

[§] During outbreak in Reunion 2005 to 2007.

Table 2

Pathogen, Clinical Manifestation, Available Testing Methods, Country-Specific Donor Prevalence, and Estimated Risk of Transfusion Transmissibility (where available) for Selected Transfusion-Transmissible Bacteria and Protozoa in Africa

Pathogen	Clinical manifestation	Transfusion screening/ testing method in use	Prevalence among blood donors	Risk
Bacteria				
Conventional bacteria	Bacteremia/septicemia	–		
Rickettsia conorii			Tunisia (9.0% ‡) [89]	Unknown
R typhi				
Coxiella burnetti			Tunisia (3.6%‡) [89]	
			Tunisia (26% ‡) † [89]	
T pallidum	Syphilis	VDRL/TPHA	DRC (1.1%–3.6% *) [74]	
			Cameroon (9.5%) [14]	
			Burkina Faso (1.2%) [14]	
			Egypt (0.05%) [75]	
			Ethiopia (1.3%) [76]	
			Ivory Coast (5.85%) [14]	
			Mali (4.54%) [14]	
			Namibia (0.09%) †	
			Tanzania (4.7%) [80]	
			Mozambique (0.91% *) [36]	
			Mali (0.3%) [77]	
			Rwanda (0.6%) [14]	
			Niger (18.96%) [14]	
Protozoa				
P falciparum			Kenya (0.67%–8.63%) [90]	
P.vivax	Malaria	Donor history questionnaire; blood smear microscopy	Nigeria (10.2%–20.2%) [57,91]	
P malariae				
P.ovale				
Nematodes				
W bancrofti	Lymphatic filariasis, elephantiasis	–	Unknown	Unknown
O volvulus	Oncocerciasis, river blindness”	–	Unknown	
L loa	Loiasis, African eye worm	–	Nigeria (1.3–3.5% ‡) [60,92]	
M streptocerca	Dermal-based filariasis	–	Nigeria (0.2% ‡) [60]	
M perstans	Body cavity filariasis	–	Nigeria (15.6% ‡) [60]	

Abbreviations: VDRL, venereal disease research laboratory test; TPHA, *T pallidum* hemagglutination assay.

*Replacement donors.

†Unpublished correspondence from NAMBTS.

‡Results from study conducted more than 10 years ago/may be outdated.