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Surveillance of Transfusion-Transmissible Infections: Comparison of Systems in Five Developed Countries

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Most industrialized countries maintain surveillance programs for monitoring transmissible infection in blood donations, revising approaches to methodology and risk assessment as new threats emerge. A comparison of programs in the United States, Canada, France, the UK, and Australia indicates that they have similar function, although the structure of blood programs vary as does the extent and nature of formal ties with public health. The emergence of HIV in the late 1970s and early 1980s was key in recognizing that surveillance systems specific to blood transfusion were essential. Hence, most industrialized countries monitor transfusion-transmissible infections in donors and evaluate the impact of new testing and of predonation screening strategies. Emerging infections since HIV have had different transmission pathways and challenged blood programs to draw upon resources for a rapid and effective response, with recognition that the original focus on sexual/drug-related risk of HIV and hepatitis was inadequate. The focus of surveillance programs on new and emerging pathogens fulfills a key role in risk assessment and policy formulation. The precise nature of such activities varies by country because of the structure of the blood programs and surveillance systems, the strategic focus of the blood programs, and the epidemiology of disease in each country.

METHODS FOR MONITORING and assessing transfusion transmission of infection, relating this to donor risk, and evaluating emerging threats to safety are essential. Hence, most blood programs in industrialized countries maintain a surveillance program for monitoring transmissible infection safety in blood donations. Surveillance methodology and risk assessment approaches have been adapted as new threats to the blood supply emerge. Surveillance also provides monitoring and risk assessment to address diverse interests such as physicians counseling their patients, community stakeholders interested in the value of safety initiatives, and public health professionals interested in transmissible disease in a healthy population.

Each country developed surveillance from different starting points (at different points in time and trigger events, at different rates, and with different structures of their blood program) and to suit their own purposes; thus, no country's program is identical to another's, and diversity of programs may exist within a specific country. Comparison of surveillance data on specific topics [1,2] have provided insight into the impact of different safety strategies, but comparison of different countries' approaches to surveillance and risk assessment has received little attention in the literature. Comparison can provide insight into defining the core characteristics of a transmissible infection surveillance program as well as describe the potential for diversity and adaptation. Furthermore, as surveillance analyses are used extensively for blood services' internal purposes, the breadth of research activities is not well represented in the literature, thus making comparison of programs incomplete without an inside view.

In this review, we compare examples of surveillance programs in 5 developed countries from 3 continents to describe the similarities and differences in approach, function, and application. We also examine and discuss the factors that have shaped the development of these programs.

COMPARISON OF BLOOD PROGRAMS AND STRUCTURE OF SURVEILLANCE

Because most of the data for surveillance are ultimately derived from the blood centers, the underlying structure of the blood programs will, to a considerable extent, dictate the quality and completeness of the data available for surveillance as

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well as the structure of surveillance in a particular country (assuming that each country has an organized national structure for surveillance efforts). In this section, we summarize the key points of difference in the 5 countries to understand the impact of these on surveillance approach and activities, with comparative data summarized in Table 1.

United States

The US blood system is composed of multiple independently licensed blood collection agencies with agreements in place to facilitate sharing of blood products to areas of need. The largest single blood establishment is the American Red Cross (ARC), collecting almost half of the US blood supply from 44 states. The rest is collected by separate independent community centers in 45 states, many of which are affiliated with a network called America's Blood Centers (ABC), and in addition, up to 10% of the blood supply is collected by hospitals.

With so many independent blood centers (each center potentially monitoring its own data) and a variety of computer systems and coding practices, coordinating surveillance data to produce national statistics is extremely challenging, and the United States has developed several partial solutions to address this. In 1989, the Retrovirus Epidemiology Donor Study (REDS) was established with funding from the National Institutes of Health [3]. This study group collected donor data from 6 different blood centers into a single database for analysis facilitated by an independent research center and conducted safety-related studies and donor surveys. Merging data from different computer systems required an elaborate encryption procedure to maintain the anonymity of donors while permitting donations from the same donor to be identified and tracked. However, because it did not include all US donors, it could not identify any unusual trends in centers not involved in the study, and although the centers were geographically diverse, they were not randomly selected and were not necessarily representative of the US blood supply. The largest blood supplier, the ARC, maintains an epidemiology and surveillance department within their research and development division, providing a larger database for transmissible infection surveillance that is now generally considered to be representative of national trends with every donation made to the ARC since 1995, although it has some of the same limitations. Blood Systems, another large blood supplier that has multiple blood collection centers in several US states and is a member of ABC, also has an active epidemiology and surveillance department.

In the last decade, the REDS group has focused less on the national surveillance of the epidemiology of pathogens tested for and has expanded into new directions such as molecular surveillance of HIV, hepatitis C virus (HCV), and hepatitis B virus (HBV) strains found in blood donors; studies of emerging pathogens; and international blood safety research projects. Individual blood centers also participate in research in monitoring and

Table 1. Comparison of Blood Programs

	United States	Canada	France	UK	Australia
Population*	307,212,123	33,487,208	64,420,073	61,113,205	21,262,641
No. of blood establishments	>75	2	1	4	1
Coordination challenge	High	Moderate	Low	Moderate	Low
No. of donations per year	16,174,000	1,300,000	2,700,000	2,474,000	1,300,000
Share blood products between providers	✓	✓	N/A	✓	N/A
Communication with other blood suppliers	Variable	✓	N/A	✓	N/A
Regulator	FDA	Health Canada	AFSSAPS	MHRA	ATGA
Standards	AABB	CSA	CoE	CoE	CoE
Funding	ARC, Blood systems some internal other initiatives, external	Internal	I Internal	Internal	Internal
Report transmissible disease to public health	✓	✓	✓	✓	✓

Abbreviations: N/A, not applicable; AFSSAPS, Agence Française de Sécurité Sanitaire des Produits de Santé; MHRA, Medicines and Healthcare Products Regulatory Authority; ATGA, Australian Therapeutic Goods Administration; CSA, Canadian Standards Association; CoE, Council of Europe.

* http://www.census.gov/cgi-bin/broker, 2009.

reporting of residual risks, emerging infectious agents, and the efficacy of existing testing technologies. The Centers for Disease Control and Prevention (CDC), the agency primarily responsible for national public health, has funded projects and maintained some involvement in surveillance issues on a collaborative basis. More recently, the US Department of Health and Human Services, primarily through the CDC, has partnered with the American Association of Blood Banks (AABB) in development of the US Biovigilance Network. This network includes hemovigilance for noninfectious and infectious complications of transfusion. Beginning in 2006 before the establishment of the US Biovigilance Network, AABB developed a Web-based national surveillance tool for monitoring donor screening results for 2 newly-screened-for pathogens (West Nile virus [WNV] and *Trypanosoma cruzi*, the agent of Chagas disease) where testing laboratories voluntarily enter their test data and key-associated variables. Updated aggregate data from these 2 surveillance activities are available from the appropriate Web site. The CDC also collects data prospectively as reported by individual state public health departments on WNV and posts these on their public Web site. The CDC collates nationally notifiable infectious disease data including those agents that are transfusion transmitted and publishes those through CDC publications. Lastly, blood centers are required to report transfusion adverse events including fatalities to the Food and Drug Administration (FDA), who collates and makes the data available as annual reports.

The epidemiology and surveillance departments at the ARC and Blood Systems are funded by these organizations, although they also seek competitive grants for specific projects. In contrast, REDS activities have been funded by government research contracts, and the US Biovigilance Network has been funded by government agencies, the AABB and its members, and other organizations recruited through fund-raising efforts.

Canada

At the recommendation of a Commission of Enquiry into the Blood System in Canada [4] that assessed the circumstances contributing to transfusion transmission of HIV and HCV before the implementation of testing, the blood service in Canada was reformed from the Canadian Red Cross Society Blood Transfusion Service into 2 new blood service providers in 1998. These blood services were intended to function at arms length from the government to ensure their independence and a clear line of responsibility for the safety of the blood supply. Approximately three quarters of Canada's blood supply is collected and distributed by Canadian Blood Services (CBS) in 9 provinces and 3 territories, with one quarter collected and distributed by Héma-Québec (HQ) in the province of Québec.

Both organizations mostly use the same assays, although implementation dates may vary. Donor selection and screening methods are also very similar. Communication is facilitated between the 2 organizations by cross-membership on various committees (also with some public health representation) and frequently by informal communication. Collaboration with public health is generally initiated for specific purposes or issues. Both organizations maintain their own epidemiology programs that are funded internally and focus primarily on internal information requirements. With the formation of the 2 current blood services, surveillance activities were enhanced. At CBS, an epidemiology and surveillance department was funded to increase staff and was relocated from its original site at the Toronto, Ontario Center, to the Head Office in Ottawa, Ontario, in 2003. Both organizations developed databases suitable for surveillance purposes, with validated data extending as far back as 1990. Surveillance data are shared between the 2 organizations but are generally not compiled as national data.

France

In 1994, in the aftermath of recognition of the transfusion risk from HIV and HCV, the Institut National de la Transfusion Sanguine (INTS) was formed to ensure the surveillance of transfusion safety. This agency is independent of the Etablissement Français du Sang (EFS), the national blood service responsible for collecting and distributing blood products in France and its overseas departments (14 blood centers in continental France, 2 in the Caribbean—Guadeloupe and Martinique—and 1 on Réunion Island in the Indian Ocean). There is also an independent blood center in the armed forces (Centre de Transfusion Sanguine des Armées [CTSA]). In 1998, a partnership between the INTS and the Institut de Veille Sanitaire (InVS; the national agency responsible for public health

surveillance) was formalized [5]. The EFS, CTSA, INTS, and InVS perform surveillance of the blood program (fully funded by government), with clearly differentiated lines of responsibility. These partnerships facilitate real-time sharing of information on population data, awareness of planned public health surveillance activities, and collaboration to address emerging threats.

Testing of blood donations is conducted in the centers, and there is a National Reference Center, part of the INTS, to which a sample from each positive donation is sent to be used for further testing to monitor and assess the safety of the blood program. Such supplemental testing includes routine additional testing as well as ad hoc testing to address specific safety questions. A donor database suitable for analysis is maintained at the National Blood Center of the EFS where additional survey-based donor data are also collected, but the database is accessible to INTS and InVS staff. Blood donor data were originally collated by a working group of the French Blood Transfusion Society that included approximately 50% of donations since 1992, and data from the whole of the EFS are complete from 2001 to the present.

United Kingdom

The UK is politically composed of 3 regions with devolved governments (Scotland, Wales, and Northern Ireland) and England (which is governed by the UK government). Blood services in the UK have been part of the National Health Services (NHS; publicly funded health care systems) since the NHS was formed in 1948 (the blood services having a much longer history). Each region has its respective national health service and blood service.

Each of the national blood services is responsible for their own regional surveillance activities, and coordinating national surveillance has been addressed by the formation of a specialized transfusion epidemiology department in 1995 that is funded jointly by NHS Blood and Transplant (NHSBT; England and northern Wales) and the Health Protection Agency (HPA; the English national body responsible for surveillance of infectious diseases) [6]. This unit is composed of employees from both organizations and colocated with a base in NHSBT and the HPA. Aggregate data are reported to the unit from each blood service voluntarily on donation testing plus disaggregate data on positive donations by marker. Enhanced data on infected donors, including risk exposures and donation history, are collected by the unit on donors from all but 1 blood service.

The formation of a joint blood service/HPA epidemiology unit allows for sharing of surveillance and epidemiological expertise. It facilitates close collaboration with public health such as access to relevant population data before release of public reports; early knowledge of, and, when appropriate, input into transfusion issues in public health surveillance planning; and close collaboration on emerging infectious disease surveillance. In addition to the benefits to transfusion safety, it also has very ready potential for transfusion surveillance data to benefit public health decision making in a more collaborative and more detailed form over and above the standard providing of reportable diseases to be included in national statistics (which is also done as required by law).

Australia

The Australian Red Cross Blood Service (henceforth, Australian Blood Service [ABS]) was established as a national blood service in 1996, transfusion services having been previously managed by 8 individual state and territory Red Cross transfusion services operating continuously since 1929. The ABS is responsible for collection, processing, and distribution of blood products in Australia's 6 states and 2 territories. Funding is provided centrally under a "deed of agreement" with the National Blood Authority, an Australian (federal) government body that administers the blood sector. Donation testing has been consolidated into 5 testing centers, all using the same infectious disease screening assays.

Each Australian state/territory government manages its own public health system including surveillance for transmissible infection. In addition, the Australian government requires states/territories to report "notifiable" diseases (eg, blood borne and arboviruses), and these form a national database managed by the Communicable Diseases Network of Australia. This complex system requires surveillance for transfusion-transmissible diseases occurring at both the regional (with state/territory public health units) and the national levels (with Communicable Diseases Network of Australia—an arm of the Australian government Department of Health and Ageing). The ABS structure mirrors this with medical services managers (reporting nationally to

the chief medical officer) in each state/territory responsible for liaising with their own public health units to manage local issues. The ABS also has a dedicated national surveillance arm and policy unit also reporting to the chief medical officer. The ABS maintains a single national computer system containing all blood donation testing data from 2006 onwards. Limited donation data before 2006 from preexisting state/territory computer systems were migrated to the national system. National viral testing algorithms have been in place since 2000, supporting periodic national trend analysis and residual risk estimation.

The ABS surveillance feeds up within the organization to an overarching donor and product safety committee chaired by a national medical specialist. There are some collaborative projects with public health professionals such as collaborative risk assessments with the National Centre for HIV Epidemiology and Clinical Research. Partial integration of the blood program and population data is achieved by publication of the blood donor data in an annual surveillance report [7].

Blood Program Comparison

The emergence of HIV in the late 1970s/early 1980s and recognition of transfusion transmission of this infection has created long-lasting public pressure for transfusion safety in all 5 countries in this report. It has been an important precipitating factor in the reformation of blood services in 2 countries, Canada and France. Furthermore, public concern about safety has underscored the importance of national transfusion-transmissible disease surveillance and has been the catalyst for establishing and/or strengthening surveillance programs in each of the countries described in this report. Review of the structure of blood programs identifies 3 key points of difference that impact upon surveillance: the number of blood suppliers, the interaction with public health, and level of independence to monitor safety.

National surveillance is key to monitoring safety as it enables discernment of trends in infection that may be geographically differentiated, but having more than 1 blood supplier tends to complicate this for several reasons. First, confidentiality of donor data is highly protected in some countries; second, information technology issues can make combining of data challenging; and third, cost can be an impediment. Producing national surveillance data has required creative solutions from countries with more than 1 supplier, but even with these solutions, such programs are likely to produce somewhat more limited data than surveillance conducted in countries with a single national blood program. In the UK, national coordination is achieved through the largest blood supplier and the HPA, and in the United States, the newly established national Biovigilance Network is coordinated by a public-private partnership between a government agency (CDC) and a transfusion medicine professional association (AABB). These approaches have some limitations in the level of interpretation possible but, nevertheless, achieve the primary goal of monitoring at a national level. National blood suppliers, on the other hand, can collate all donor and transmissible disease data into a single database in real time and monitor at different demographic and geographic levels. Thus, countries with a single national blood supplier are at a substantial advantage in coordinating and analyzing national data. It is noteworthy, however, that some national systems, although complete within a country, may be far smaller than independent systems within a country such as the United States.

International benchmarking of performance data including transfusion-transmissible infection marker rates is facilitated by several industry alliances. The ABS, CBS, ARC, and NHSBT are all members of Alliance of Blood Operators, which also includes the ABC and the European Blood Alliance. The EFS is a member of the European Blood Alliance and, thus, an Alliance of Blood Operators member. The ABS is a founding member of the Asia Pacific Blood Network, providing a focus for Asia/Pacific regional surveillance activities. The "global" network created by these alliances provides an efficient forum for rapid information/resource sharing including surveillance for established and emerging transfusion-transmissible disease threats. Recent examples underscoring their value include collaboration before and during the influenza A 2009 pandemic optimizing blood service response and the development of a dengue management "white paper" providing policy guidance for Asia Pacific Blood Network members.

All 5 countries in this report have found that interaction with public health departments is essential. Because the focus has expanded from HIV, HCV, and HBV to a range of emerging pathogens, the dependence upon this interaction has

increased. Countries that do not have formal ties with public health departments generally initiate interaction for a specific purpose when a clear need is identified. Countries such as the UK and France that have a closer association with public health have easier access to public health data, better opportunity to stay current with public health planning, and have a more clearly defined portal for collaboration to address emerging pathogens. Furthermore, surveillance of blood programs parallels the interests of public health surveillance in that a large population is being tested actively (as opposed to passive reporting), and it monitors how well transfusion transmission is being prevented. All 5 countries in this review report donors who test positive for transmissible diseases to public health authorities via the usual reporting channels as required by law, but countries with more formal ties may have greater potential to assist public health surveillance.

Most countries have fully internally funded surveillance programs, which is largely a reflection of the focus on independence to do what is necessary rather than depending on funding agencies to give transfusion projects priority. The notable exception is the United States where some blood operators fund their own programs supplemented with competitive funding. More recently, the donor hemovigilance component of the US Biovigilance Network is attempting to implement a more fully coordinated national donor surveillance system with funding through several sources.

SURVEILLANCE OF TRANSFUSION-TRANSMITTED INFECTIONS

The strongest indicator of the safety of a country's blood supply rests in the extent to which transfusion transmission of infectious agents occurs. All countries in this report have systems in place to detect complications arising from transfusion including transmission of disease, and this section describes their approaches.

Lookback/Traceback

Suspected transfusion-transmitted infections (TTIs) are reported to the blood supplier as soon as it is identified, and the blood supplier initiates a trace-back investigation in which all units received by the recipients are identified and the blood center attempts to contact the donors of each unit for testing. In lookback, a positive donation initiates a review of previous donations from the implicated donor, and the hospitals that these units were released to are notified so that they can contact the recipient to be tested. All blood services have lookback/traceback systems in place that are monitored and can give an indication of the frequency of TTIs. Transfusion-transmitted infections are very rare and generally are identified when testing is implemented, with infections rarely identified once testing is established [8,9], and transfusion accounts for only a small proportion of general population infections [10].

Hemovigilance Programs

Hemovigilance programs capture a wide range of transfusion reactions, although TTIs are best captured by directly reporting to the blood supplier. Established in 1994, the French National Hemovigilance Program was the earliest national surveillance program that has served as a model for other countries as they established their programs [11]. The Serious Hazards of Transfusion program was established in 1996 as a UK-wide reporting system for patient transfusion events, although surveillance of TTIs existed before this [10,12,13]. The UK epidemiology unit is responsible for coordination of data, and the ARC has had a formal hemovigilance program in place for many years. In Canada, hemovigilance began as a pilot project involving 4 of 10 provinces from 1999 to 2002. National reporting has been in place since 2002. In Australia, the various states and territories have different forms of adverse event reporting and tracking and are at different stages in reporting capacity [14]. The National Blood Authority has gathered together reports of transfusion incidents from each of the states and territories in 2007 and again in 2010 to establish and report a voluntary national hemovigilance program [14,15].

Limitations of TTI Surveillance Data

The principal limitations of assessing safety from TTIs directly are the difficulty of confirming the source of the infection as the blood donation and also the potential for the infection to be missed. Confirming transfusion transmission of a disease is based on a range of data, including patient symptoms indicative of a new infection, pretransfusion patient samples (negative for the marker), a positive patient sample posttransfusion, a traced donor with a positive sample, and genetic

sequencing of the pathogen matching donor and recipient samples. It is rare for all of these data to be available because patient pretransfusion samples are often not available, donors are not always traced and/or willing to provide a sample, and sometimes the donor's infection has resolved before follow-up testing. Hence, transfusion transmission is usually considered probable or possible depending on the data available but is less often confirmed. In addition, as patient symptoms may be mild, may not always be attributed to infection, and patients may die because of their underlying pathology without detection of infection, it is generally considered that some infections will not be reported. Hospital reporting to blood centers of potential transfusion transmission may lack the requisite data mentioned above, preventing any conclusion as to the infectious source. Thus, there is a margin of error either way, and the frequency of TTI's may appear less than or possibly even greater than they really are. Because of these limitations, mathematical models of donor data are considered more accurate to quantify the low risks of transfusion-transmissible infections (eg, residual risk estimates).

SURVEILLANCE OF CLASSICAL PATHOGENS (HIV, HCV, AND HBV)

Testing and monitoring for HIV, HCV, HBV, human T lympotrophic virus (HTLV), and syphilis are core functions of the surveillance programs in blood centers in each of the 5 countries in this review (see Tables 2 and 3). In all cases, the rates in first-time donors (a previously untested population) are lower than in the general population likely due partly to the donor selection criteria that exclude high risk donors and partly due to self-deferral of donors.

Table 2. Comparison of Surveillance Functions

	United States	Canada	France	UK	Australia
Monitor positive donations	✔	✔	✔	✔	✔
Monitor risk factors in transmissible disease-positive donors	✔	✔	✔	✔	✔
Molecular surveillance	✔	No	✔	Ad hoc	No
Residual risk estimates	✔	✔	✔	✔	✔
Evaluation of safety strategies postimplementation	✔	✔	✔	✔	✔
Risk assessment for new/emerging pathogens	✔	✔	✔	✔	✔
Evaluation of screening questions	✔	✔	✔	✔	✔
Pandemic plan	✔	✔	✔	✔	✔
Hemovigilance	✔	✔	✔	✔	✔

Residual Risk

All blood programs prepare estimates of the risk of potentially infectious blood donations being released into the blood supply (Table 2) [16-25]. These residual risk estimates are important for evaluating the safety of the blood supply and are used for internal decision making as well as by physicians to counsel their patients about the risks of transfusion. In addition, ongoing analysis of temporal trends and demographics in marker-positive donations provides insight into sources of risk and how these are changing [26].

With testing in place, the risk has become too low to measure by recipient infections and instead is estimated using a mathematical model, the incidence x window period model [27], originally described by several studies in the United States [28-31]. There has been continued effort in different countries to adapt and improve this model to address certain deficiencies and to better address their requirements. For example, in the UK, in addition to window period infections, an adjustment for product process errors and test failure [24] is used routinely, although with today's standards of automation and Good Manufacturing Practices in blood donation testing centers, testing error is an extremely rare finding. Others have revised the methodology to estimate the incidence of infection if it is otherwise unknown. For example, a mathematical adjustment [22] and, then in the United States, a method using nucleid acid testing (NAT)–yield donations (those with NAT-positive results but not having yet developed antibody) were proposed [22,32], which was a substantial improvement for NAT-tested donations (HIV and HCV) because the estimate could now include first-time donors directly. Estimated hepatitis B incidence density is problematic because an adjustment for infections that resolve between donations (thus, not directly detected) is required, as originally proposed in the United States [33]. In France and the United States, more detailed supplemental testing was used to improve identification of such incident HBV cases [34] and to include a hepatitis B surface antigen (HBsAg) yield method [35].

Table 3. Overview of Current Transmissible Disease Screening

	United States	Canada	France	UK	Australia
HIV					
Antibody	✓	✓	✓	✓	✓
NAT	✓	✓	✓	✓	✓
HCV					
Antibody	✓	✓	✓	✓	✓
NAT	✓	✓	✓	✓	✓
HBV					
HBsAg	✓	✓	✓	✓	✓
NAT	Most	✓	✓	✓	✓
Anti-HBc	✓	✓	✓	Selective	Selective
HTLV antibody	✓	✓	✓	✓ Mega pool	✓
Treponema pallidum antibody (syphilis)	✓	✓	✓	✓	✓
Plasmodium antibody (malaria)	x	x	Selective	Selective	Selective
T cruzi (Chagas disease)	Selective	Selective	Selective	Selective	x
WNV NAT	✓	✓ Year round all donations at CBS stops in winter at HQ with selective testing	x	Selective stops in winter. (timing depends upon North American season)	x

Abbreviation: Anti-HBc, antibody to hepatitis B core antigen.

Work has also been done to address estimated residual risk in countries where the data requirements for the incidence/window period model cannot be fully addressed [21,36]. All blood programs also carry out additional studies to understand various aspects of risk such as risk factors of seroconverting donors [37] and estimating the rate of recent infections [38]. Work to better understand risk in donors who test positive for transmissible infection and future trends is ongoing in all 5 countries in this report. Examples include assessment of trends in infections [39,40], assessment of the value of continuing certain testing such as syphilis testing as a surrogate marker for HIV [41], and assessment of risk with current procedures in place such as the risk of cytomegalovirus in untested units [42,43].

Introduction of New Testing

Surveillance plays a key role in assessment of the need for testing as well as evaluation of assays once they are implemented. The following are some examples of such analyses in different countries.

Nucleid acid testing was a very expensive technology introduced in addition to serologic screening to reduce already low risk, and consequently, evaluation has received considerable attention [1,44]. Before introduction, the UK estimated the expected frequency of HCV NAT-positive donations [24]; these estimates were greater than actual in the first few years. After the implementation of NAT, the yield was evaluated in the United States [32], Canada [19], and Australia [20,21], showing small gains. To confirm the assumption that NAT yield cases were new incident infections, follow-up (seroconversion) studies in the United States and Australia showed that most donors seroconvert, although a few do not. These rare immunologically silent infections would only be identified by NAT, indicating the 2-fold value of NAT testing for incident infections as well as for these rare infections [45,46]. In France, evaluation of HIV-positive individuals identified through donor screening with persistently low HIV RNA (without treatment) showed that, in a follow-up study, minipool NAT failed to identify nearly half of these samples, and some could not be reliably detected even by single-donation NAT. Because these people all had positive tests to the antibody, it is clear that dropping the antibody assay could result in some HIV-positive donations entering the blood supply [47].

In Canada, the implementation of antibody to hepatitis B core antigen testing permitted an opportunity to investigate its potential benefit with HBsAg testing already in place, showing that

the expected rate of roughly 1 per 50 000 units intercepted was accurate, but lack of evidence of transfusion transmission in lookback suggested that infection of recipients rarely occurs [48].

Testing for HTLV, a white cell (leukocyte)–associated virus, was implemented in some countries before implementing universal leukoreduction that greatly reduces the risk of transmission [2]. In the UK, where leukoreduction was introduced in 1999, a regional study suggested low prevalence (about 5/100 000 donations) [49], and only about 6 people per year would be at the risk for developing HTLV-associated disease from transfusion. In 1996, the UK decided not to implement screening, but later, the development of pooled systems for testing made testing a more cost-effective option, and it was introduced in 2002. Postimplementation evaluation indicated that the risk of an infectious donation entering the blood supply was reduced to 0.11 per million donations, and, of course, the risk of development of disease would be much less [50]. Initial analysis of HTLV lookback data suggests that leukoreduction is effective in reducing posttransfusion HTLV [51].

Studies such as these assess the safety gained from the introduction of testing and assist in deciding when further action is needed or, conversely, when risk is approaching zero. Although blood providers often find it difficult to reduce testing initiatives once implemented, the identification of low-risk reduction can be important in justifying changes in predonation screening processes that may streamline the donation process.

EVALUATION OF PREDONATION SCREENING

All countries have methods in place to select donors who have a lower risk of transmissible infection vs the general population, especially to avoid window period infections that could go undetected by testing. This involves donor education materials so that high-risk donors can self-defer and a predonation questionnaire that asks donors about transmissible disease risk factors as well as questions to exclude donors for whom donation may not be advisable for their own health. This section describes the key systems in place and examples of work that has been done to assess the effectiveness of this process. These include evaluation of risk factors in donors who test positive for an infectious agent, monitoring of donor deferrals, and application of surveillance data to evaluate predonation screening processes and deferral criteria.

Blood systems in all 5 countries have systems in place to collect information on donor risk factors (Table 2), the primary purpose being to asses donor selection criteria intended to reduce risk of transmissible diseases, although they are limited to identification of risk factors rather than evidence of cause. The methods vary with donor risk factors assessed in an in-person interview during counseling in France and Australia [52]; in the United States and Canada, telephone interviews are used, and in the UK, both methods. In Canada [40,53], a control group is also interviewed. In the United States, [54] and, more recently, in Canada [53,55], anonymous donor surveys of the general donor population have also been completed to assess deferrable risk.

Risk factor studies in seroconverting donors (which indicate new infections) are of particular interest, as these are donors with the greatest chance of being missed by testing. In the United States, a study of HCV seroconverting donors showed that intravenous drug use was a frequent risk factor [56] as did a study in France, but some invasive health care procedures were also associated [57]. This suggests that although much of the risk should be identified by current screening questions (if donors answered truthfully), some would still be missed.

Because risk criteria have often been in place for many years, with few data on blood donors with these risk factors, evaluation of screening criteria is often better addressed by data modeling. For example, the potential risk from criteria relating to men who have sex with men has been evaluated in the UK [58], Canada [59,60], Australia [61], and United States [62]. The approach in each country has varied, but all attempt to base the model on data specific to that country to be applicable to decision making.

Recently, HIV surveillance data (donor testing and risk factor analysis) underpinned the first assessment of the impact of changing to a shortened 12-month deferral for men who have sex with men in Australia [63]. Distinct from the modeling noted previously, this is the first published analysis using empiric data to assess the impact of such a policy change on HIV residual risk. The results supported the conclusion that risk of HIV transmission by blood transfusion was not significantly impacted in Australia as a consequence of the change. The analysis suggested that the rate of compliance to the

deferral policy is more influential on overall risk than the duration of deferral.

Evaluation of surveillance data can also be used to assess donor screening processes such as the confidential unit exclusion (CUE) process. This was implemented in many countries in the 1980s to allow donors with deferrable risk who may feel pressured to donate to confidentially exclude their donation from transfusion. Studies in the United States [64] and Canada [65] have shown that the CUE process has minimal impact on reducing the risk from window period infections. At least partly because of the US study, the ARC decided to cease use of the CUE in 2005, and monitoring of TTIs since then has shown no adverse effect of this change.

When changes in donor selection criteria or the method of administration of questioning donors are made, it creates an opportunity for assessment. Examples include use of surveillance data to show that shortening the deferral period for ear/body piercing and tattoo did not compromise safety [66], to evaluate the impact of the Uniform Donor History Questionnaire (developed by an AABB task force) [67], and switching from paper-based questions to face-to-face interviewing [68] as well as evaluating the implementation of an electronic questionnaire [69] and comparing different questionnaire formats [70].

MOLECULAR SURVEILLANCE OF VIRAL DIVERSITY

Viruses exist in multiple genotypes and subtypes, and within an infected individual, viruses such as HIV and HCV exist as diverse quasi species. Both the genotype or subtype and the quasi species are important because they may vary in infectivity and because the limit of detection of some assays may vary by subtype or genotype [71]. Thus, monitoring of genotypes within a country's donor population can assist in evaluating risk and can be important in selection or modification of assays and has the potential to identify mutations of viruses. Analysis of viral diversity in transmissible disease positive donors has been carried out routinely in France for more than 10 years [72] and, more recently, commenced in the United States [73] and Scotland. Studies are in the planning stage in England. In addition to the direct application to monitoring transfusion safety, genotyping permits insight into the origins of infections as different genotypes are associated with particular parts of the world. Genotypes are generally correlated with immigration patterns, and analyzing the 2 can predict the future diversity of genotypes in a population.

NEW OR EMERGING PATHOGENS

In recent years, several new pathogens (or at least "new" in the context of blood safety in a particular country) have come to the fore, necessitating enhanced surveillance methods, greater interaction with public health departments, and implementation and monitoring of safety interventions. Once a pathogen is considered to be a potential threat to blood safety (either real or perceived), an active approach is generally adopted such as prevalence studies. Surveillance data are used for risk assessment, which, in turn, forms part of the basis for policy decisions. Examples of how various countries in this report have addressed their surveillance requirements for selected emerging pathogens are discussed below.

West Nile Virus

This mosquito-borne virus was described in Africa in the 1930s, but it was not seen in North America until 1999. Its appearance in New York city marked the onset of an epidemic that spread across the United States and Canada where there were already competent populations of mosquitoes able to carry the virus and complete the lifecycle. Although frequently asymptomatic, WNV is potentially serious, even fatal, in susceptible hosts.

By 2002, it was clear that WNV could be transmitted by transfusion, which sparked rapid development of assays suitable for donor screening. By 2003, all donations in the United States and in Canada were being tested for WNV because of unprecedented collaboration between the FDA, key blood operators, and test kit manufacturers. In both countries, public health departments received reports of community cases that were then included in local and national statistics, but the blood programs were the primary source of active surveillance. For logistic reasons, testing of blood donations was done in minipools, but recognition that the minipool NAT test could miss some potentially infectious donations led to the development of testing algorithms based on minipool-positive donations including bordering blood centers to trigger individual donation NAT testing [74].

The emergence of WNV in North America had a profound impact on the approach to surveillance in both the United States and Canada. The established methods for monitoring infections such as HIV and HCV/HBV were inadequate because real-time surveillance with geographic indicators was needed. In addition, very close communication with public health and other blood suppliers was necessary to identify risk areas quickly. In the United States, the coordination challenge was very large, with so many independent blood centers not accustomed to working together at this level. The AABB developed a Web site that allowed independent blood testing laboratories to voluntarily enter their data on donor WNV-reactive cases and later enter the associated confirmatory data. This permitted close to real-time monitoring of donor infections by geographic regions. This system, combined with networking between blood centers, facilitated communication of important data between blood centers near one another so that individual donation NAT could be triggered in adjacent and overlapping areas served by different independent blood centers.

In Canada, the coordination challenge was less, with only 2 blood services, but still required substantial ingenuity to set up a monitoring system with a visual mapping and daily uploads of data [75]. Although each blood supplier could monitor its own donor testing data, collection sites adjacent to the borders of the catchment areas as well as at the border between Canada and the United States required close communication. This was facilitated by regular telephone calls between both Canadian suppliers, US suppliers, and public heath officials, with agreements to provide any urgent information in between calls. In both the United States and Canada, these methods are now part of routine WNV surveillance [75,76]. In the UK, selective (also called discretionary) testing for WNV was run for 2 seasons (2004-2005); testing was timed to commence with the start and end of the WNV season in the United States and targeted at travelers to endemic areas.

Thus, the emergence of WNV in North America challenged key players (blood operators, regulatory bodies, public health departments, and the test kit manufacturers) to work together to rapidly develop surveillance methodology and response tactics. It alerted the transfusion community to the importance of further strengthening surveillance for new and emerging threats.

T cruzi—The Agent of Chagas Disease

Chagas disease is endemic in parts of Mexico and Central and South America. The protozoan parasite *T cruzi* is usually transmitted via the feces of infected triatomine insect vectors, often at the site of the bite wound, but it is also transmissible from mother to child during pregnancy, by organ transplantation, and via blood transfusion. Hence, blood donations in endemic countries are often screened for antibodies to *T cruzi*.

In nonendemic countries, the risk to the blood supply is mainly through immigrants from risk areas, and most data on *T cruzi* prevalence in the United States have come from blood donor studies. US studies in the 1990s indicated that most *T cruzi* antibody positive donors [77,78] were immigrants from risk areas. By 2007, 7 transfusion transmissions had been reported [79] (5 in the United States and 2 in Canada). This suggested that transfusion transmission was rare, but the symptoms could easily be misdiagnosed such that the true risk was difficult to ascertain. In 2007, after an ARC study showing that about 1 in 4500 donors in selected areas had *T cruzi* antibodies [80], the FDA licensed the assay, and most blood operators began testing all donations for *T cruzi* antibody. A surveillance reporting system similar to that used for WNV was set up and coordinated by the AABB. This Web-based system relied upon voluntary reporting of data from blood testing laboratories and made publicly available a map of the United States with positive donations shown and regularly updated statistics. This provided the first national prevalence data (in donors or the general population) for *T cruzi* infection in the United States. In addition, studies were done along side implementation to assess the risk factors of *T cruzi* positive donors, and lookback studies assessed the frequency of traceable units transmitting infection. More recently, US blood operators have been shifting to selective testing policies involving donor qualification, that is, testing a donor once, and if negative, no further testing of subsequent donations is needed.

Compared with WNV, the situation in the United States for Chagas disease was less urgent in that the risk had been known for many years, and the development of a licensed test for donor screening prompted a change in surveillance requirements. In

addition, the United States was able to capitalize on the experience gained with WNV by using a similar mapping and reporting system with the reporting process now well established. The US experience has been a general prevalence of about 1 per 25 000 donations screened during the first 3 years of testing; however, lookback studies have only identified 2 transfusion transmissions both from 1 long-term US resident (originally from Argentina) among more than 200 recipients of blood from confirmed-positive donors.

In Canada, studies to understand the risk of Chagas disease in the blood supply had also been conducted since the late 1990s. A seroprevalence study was completed in 1 major city from 1997 to 1999, identifying no positive donations among donors with risk factors. A series of further studies evaluated the potential for questions to be used for targeted testing [79]. Canada is now moving away from its standard approach of testing all donations, and a selective testing approach has been implemented based partly on lessons learned from the United States but mostly on risk assessment specific to Canada that indicated that this lower cost alternative was appropriate. In 2009, HQ implemented selective testing, identifying only 1 confirmed-positive donation to date, and CBS implemented screening questions to identify donations from which platelets or transfusable plasma were no longer prepared, then implemented selective testing in May 2010, with 7 confirmed-positive donations to date. Postimplementation studies are planned to confirm the appropriateness of a selective testing approach.

In France, the epidemiology of Chagas disease is different from that in the United States and Canada because of a French department in an endemic area and different trends in travel and immigration. The number of cases in the general population in French Guiana has been increasing, and there are immigrants in France from risk countries. In 2006, selective testing was implemented in the Caribbean blood centers (although blood is still not collected in French Guiana), and in 2007, in mainland France. For all French blood centers (Caribbean or mainland France), donors are selected for testing if the donor or their mother was born in Latin America or if the donor has traveled to a risk area (such travelers are deferred for the first 4 months after their return). During the first 6 months of testing in the Paris region (a popular destination for immigrants to France), 2 confirmed-positive donors were identified from about 30 000 tested donors, which indicated that a small (but real) potential risk was averted [81].

In the UK, selective testing was implemented in 1989 for all donors who were born (or whose mothers were born) in South America irrespective of time since residence and/or birth. In addition, people who had lived or worked in rural areas in South or Central America for a continuous period of 4 weeks or more were deferred for 6 months and then tested. Only 3 infections have been identified since selective testing was introduced, 2 of which were in 2009 [6].

In other countries such as Australia, testing has not been implemented because the perceived risk is very low with no recorded case of transfusion transmission, no autochthonous cases reported, and immigration from South America being comparatively low. The risk is minimized by restricting donors born or transfused in South America to donating plasma for fractionation. Under these conditions, suspected TTIs reported to the blood supplier is the main form of surveillance.

Variant Creutzfeldt-Jakob Disease

First recognized in 1987, a novel neurologic disease in cattle (bovine spongiform encephalopathy) was attributed to infected sheep and cattle offal fed to cattle in the UK, and by the early 1990s, thousands of cattle had been diagnosed, and millions incinerated [82]. In 1996, a new neurologic disease that is always fatal was reported in humans, new variant Creutzfeldt-Jakob disease (CJD) presumably caused by consumption of bovine spongiform encephalopathy–infected meat, and by transplantation of organs/tissues of infected donors. The UK experienced the largest epidemic of variant CJD (vCJD), with France as the next most affected, and only a few cases in other countries [83]. Although transfusion transmission was initially considered improbable, this view was reconsidered in light of experimental evidence, wider distribution of the infective agent, prions, within patients than with classical CJD, and the eventual documentation of transfusion-transmitted clinical cases.

In 1990, national surveillance of all CJD cases was established in the UK at the National CJD Surveillance Unit. For all cases, the medical history and family members were consulted to determine if there was a history of blood transfusion or donation.

A collaborative study with the UK Transfusion Services (the Transfusion Medicine Epidemiology Review) was established in 1997, which, to date, has identified 4 patients with vCJD who had received blood products and are considered probable TTIs, 3 of which resulted in clinical vCJD in the recipients [83-85]. Reporting of suspected vCJD transmissions differs from that of other infections and relies on close working between the health protection authority (HPA), the blood services, and the National vCJD Surveillance Unit; to date, the confirmed TTI cases were from among a small group of recipients who were under active surveillance because they had received blood components from donors who later developed vCJD. If or when a test suitable for blood donors is developed, the surveillance program will be expanded to include surveillance of this testing and any infections detected. Several precautionary measures have been introduced in the UK, including donor selection (eg, exclusion of donors who have received a blood transfusion since 1980), importation of plasma for use in products further manufactured from blood, and leukoreduction.

Malaria

Malaria is not endemic in any of the countries in this report, but there is an ongoing risk from imported malaria. By far, the greatest risk is from so-called semi-immune donors born or a resident in malaria-endemic countries (particularly sub-Saharan Africa and Papua New Guinea), where the dominant species is *Plasmodium falciparum*, the most lethal of the 5 species infecting humans. The potential risk of transfusion transmission varies with immigration policy and travel preferences of each country's population. Based on the population rate of imported malaria cases associated with travel to/residence in the World Health Organization–defined "high-risk" countries, France and the UK are at greatest risk from semi-immune donors. However, because of the inclusion of very low-risk travel in different countries' assessment of "at-risk" donors, the percentage of donors in this classification varies from about 5% in Australia to about 3% in France and Canada to about 1% in the United States. The surveillance approach is similar in all countries (monitoring community cases and TTIs), but the policy varies with France, the UK, and Australia, applying selective testing policies to more rapidly reinstate healthy donors. These countries also therefore monitor infections in at-risk donors. The United States and Canada apply deferral criteria without the option of testing. Current testing can identify antibodies to *P falciparum* but not all other species with high sensitivity [86-88], and the rare transfusion-transmitted cases of malaria identified in the UK and France relate more to failure to test rather than test failure [86,89,90]. In France, evaluation of 2 TTIs that occurred with selective testing in place prompted revision of the policy to reduce the risk. Postimplementation evaluation in Australia showed that testing greatly reduced the impact of deferral, with the recovery of about 8% of annual production of red blood cells and 5% of platelets [91]. Importantly, this was achieved without any apparent change in the risk of transfusion-transmitted malaria.

Overall, malaria antibody testing strategies in France, UK, and Australia have been highly effective. However, 2 cases of delayed onset (relapsing) *P vivax* malaria in Australian donors highlight a previously unreported limitation of the strategy [92]. *P vivax* is able to sequester in the liver for months to several years before reemerging to cause clinical malaria. Importantly, antibody testing (or for that matter, any other laboratory malaria test) is unable to identify donors potentially at risk for relapse. Highlighting this, both implicated donors had tested antibody negative subsequent to their most recent travel to Papua New Guinea, a country that, along with its neighbors, carries a much greater risk for relapse. Fortunately, no components from the 2 donors were transfused, and the rarity of such makes their impact on recipient safety negligible when compared with the risk from semi-immune donors. Nonetheless, the ABS has already moved to close the gap by implementing a 3-year restriction to plasma for fractionation only (within which testing is embargoed) for donors returning from Papua New Guinea.

In the United States and Canada, the risk from malaria is managed by deferral of travelers to/residents of endemic areas or donors with a history of malaria. Some passive surveillance data are available, but most efforts in surveillance have focused on the impact of deferral [93,94] in both countries.

Dengue

Dengue viruses are mosquito borne and are very similar to WNV; both are flaviviruses and carry a short-term period of viremia (about 6 days). Although most patients recover from their primary

dengue infection, primary or more commonly, secondary infections can be fatal. Nearly two thirds of the infections are asymptomatic, but when symptoms occur, they are usually noticeable within 1 day. Few cases of transfusion transmission have been documented, but it is believed that it may be more common because during an outbreak, it is difficult to distinguish transfusion-transmitted cases from vector transmission. As a short-term infection, dengue has attracted lesser attention for transfusion surveillance in countries where outbreaks do not occur such as Canada, France, and the UK. However, the mosquito vectors for dengue are resident in parts of 2 countries in this report—northern Australia, southern United States, and in Puerto Rico where it is endemic.

An investigational NAT assay for donor screening developed for all 4 dengue virus serotypes and tested on donors during outbreaks in Honduras, Brazil, and Australia showed that viremia is present at low percentage in asymptomatic donors [95]. In Puerto Rico, where the ARC is the largest single provider of blood, dengue is endemic year round with annual island-wide outbreaks. The Dengue Branch of the CDC located in San Juan conducts ongoing surveillance for dengue in Puerto Rico. During an outbreak in 2005, NAT using the Gen-Probe transcription-mediated amplification assay was performed retrospectively for an 11-week period to assess the frequency of donor viremia. In total, 12 donations were positive (0.73/1000 donations), and infectious virus was recovered from 3 donations that may have been able to transmit infection [96], indicating a risk of transfusion transmission. In 2007, during a larger outbreak, higher rates of donor viremia were documented along with a transfusion-transmitted case. Management of risk has included implementing a predonation question regarding dengue-like symptoms and the use of an enhanced postdonation information sheet encouraging donors to call back if dengue-like symptoms develop. Infected donors have been deferred for 120 days from dengue diagnosis or onset of illness, whichever is later. Dengue virus NS1 Ag testing (Bio-Rad, Paris, France) was initiated in March 2010 shortly after a new outbreak for 2010 was declared. Donor screening assays targeting dengue virus RNA would be preferred but are not available because significant funding will be required for commercialization. Apart from Puerto Rico, nearly all dengue cases reported in the 48 US continental states were acquired elsewhere by travelers or immigrants. The last reported continental dengue outbreaks were in south Texas in 2005 and in Key West, Florida, in 2009 and again in 2010. Several autochthonous cases have now been reported in 2 counties in mainland Florida. A small dengue outbreak occurred in Hawaii in 2001 [97].

In Australia, dengue is not endemic, but there are seasonal outbreaks believed to occur when a traveler, infected overseas, arrives and a local transmission cycle is established. Risk to the blood supply is managed by implementing supplemental donor selection measures during active outbreaks. An additional question is added to the donor questionnaire to identify donors traveling to or residing in the outbreak area. Such donors may only donate plasma for fractionation during the outbreak period, and these restrictions remain in place until 1 month after the last case onset date. To better understand and quantify the transmission risk associated with blood collected during outbreaks, a model originally developed for WNV has been adapted. Based on both known cases and subclinical infections during a small 2004 outbreak, the model predicted low risk of transfusion transmission during the outbreak (about 1 in 20 000 overall), but this varied with the predicted incidence over the period, peaking as high as 1 in 1000 [98].

Dengue appears to present a low risk of transfusion transmission even in endemic areas, but experience with other vector-borne diseases such as malaria and, especially, WNV, for which there was rapid widespread infection in North America, may have sensitized the transfusion industry to these types of potential risks. Surveillance activities have therefore been directed not only to monitoring of possible outbreaks and response planning but also to developing an understanding of transmission potential and developing, testing, and gaining experience with assays suitable for donor screening.

Babesiosis

Babesiosis is a tick-borne disease endemic in a relatively small region of the United States (northeastern and upper midwestern). This red cell–associated protozoan parasite is transmitted by the bite of an infected tick and typically results in either mild symptoms that resolve within a few weeks or is asymptomatic. It can also be transmitted by

transfusion and can cause severe, even fatal disease for the recipient. In addition, the endemic area of the tick appears to be gradually increasing. Because donors are often unaware of their infections and there are no screening questions likely to identify at risk donors, seroprevalence studies have been done to assess the risk and to assist in developing a strategy for risk reduction [99,100], and transfusion-transmitted cases are monitored [101], with a minimum of 70 transfusion-transmitted cases in the United States over the last 10 years [102].

Surveillance of *Babesia* has shown that it poses risk to the US blood supply, but an acceptable solution has yet to be identified. Testing of all donors would address the problem, but the yield would be extremely low, and it is not cost-effective at this time. Testing of donors in endemic regions may be most feasible but will miss positive donations from travelers to endemic regions. Hence, a combination of testing all donors in at-risk areas and selective testing of the donors who may have traveled to a risk area may be possible but is likely to be of low yield because most donors (especially those who traveled) will not have been in contact with the vector ticks. Interventions for testing in endemic areas of the United States are beginning to be investigated and implemented; data from these studies will drive further policy development.

In Canada, where *Babesia* has not been reported, the surveillance approach has been much lower key. Because there is no active surveillance and there are populations of the vector ticks near the endemic region of the United States, it is possible that *Babesia* infections may occur in Canada or may occur in the future as the habitat of the tick expands. Seroprevalence studies are being considered, but to date, surveillance in Canada has focused on surveys to estimate donor risk travel and monitoring public health data. Of note, there has been 1 TTI from a donor who had traveled to the United States [103].

Chikungunya Virus

Chikungunya virus is a mosquito-borne agent that was first described more than 50 years ago and has caused many outbreaks in Africa and Asia. Symptoms include fever, joint and muscle pain, and headache lasting a few days but sometimes longer, but it can also be asymptomatic. Although blood transmission has not been documented, it is theoretically possible.

A small outbreak of chikungunya virus occurred in 2005 in the French island of Reunion Island near Madagascar in the Indian Ocean, with a much larger epidemic in 2006 (the largest ever recorded) and a few cases continuing into 2007. The outbreak on Reunion Island required an immediate coordinated effort on the part of the public health officials and the blood service. Red cells and plasma could be transported from continental France, but because of the shorter shelf life, platelet units still needed to be produced locally, and a pathogen reduction system was quickly implemented (in March 2006, shortly after suspending collection of red cells and plasma) [104]. A collaborative group composed of members from the Agence Française de Sécurité Sanitaire des Produits de Santé (French regulator), the EFS, and the INTS coordinated by the InVS estimated the risk of viremia in blood donations during the outbreak. Using public health surveillance data that were ramped up during the epidemic [105] and applying methodology gained from the WNV outbreak in the United States, risk estimates were made for the small outbreak in 2005. Predictions using case reports up until December 2005 were used to make the decision to stop collecting red cells and plasma in January 2006 before the peak of the epidemic. Later, risk estimates were used to recommence blood collection and were confirmed with testing data from platelet collections. In addition, based on the estimates, there were 7 donations expected to have been viremic before stopping collections, but no transfusion-transmitted cases were reported [106].

Pandemic Influenza Planning

There have been several influenza pandemics in the past. The sudden appearance and rapid movement of another disease, severe acute respiratory syndrome, and concerns of mutating influenza viruses that could be spread from person to person (such as was postulated for avian influenza) resulting in a pandemic have made their mark in public health planning, and in transfusion services, a comprehensive pandemic plan is now the norm. Influenza has a short phase of viremia, and the risk of transfusion transmission is likely small if not zero. However, in a pandemic situation, there is potential for a disruption to the blood supply because of donor illness decreasing attendance at collection sites and staff illness having a negative impact on processing of blood units as well as other

people-dependent processes such as transportation. Pandemic plans therefore focus on these types of issues and include estimated product requirements (which may reduce during a pandemic), plans for staff redeployment, for vaccination (if available) and prophylactic treatment for staff, and alternatives for current processes. These plans also involve interaction with public health and agreements for priority status for treatment for staff and patients.

DISCUSSION

Comparison of blood systems in 5 industrialized countries in 3 continents shows a fairly uniform range of transfusion surveillance activities in each (Table 2), with the 2 key areas of focus being surveillance of classical pathogens (HIV, HCV, and HBV) and surveillance of new and emerging pathogens that are of local or international importance. The key factors that influence the precise nature of these activities are the structure of the blood program(s) and surveillance system, the strategic focus of the blood program, and the epidemiology of disease in each country.

Although testing for pathogens such as HIV and HBV and HCV has resulted in vanishingly small residual risk, surveillance related to these pathogens has been a high priority because of public expectation of zero risk. This pressure still exists, but the ongoing focus of current policy often relates to assessment of the potential for simplification of the process rather than necessarily addressing further risk. Multiple layers of donor testing and donor deferral policies implemented over the years have a high impact on operational efficiency, and the cost of blood products and reevaluation are necessary because their individual and combined contribution to safety was not always clear at the time of implementation and may have changed as the epidemiology of disease changed in the general population. As part of the evaluation of safety, surveillance of viral diversity is needed to assess the performance of screening assays.

The emergence of new infectious diseases has been the instigator of substantial growth in surveillance activities and a test of the readiness to address new threats. The emergence of HIV in the late 1970s/early 1980s had a profound effect on the transfusion industry and was the key factor in recognition that surveillance systems specific to blood transfusion were essential, resulting in improved structure of surveillance, although tending to focus on risks based on sexual activities and injection drug use. Emerging infections since then have had different transmission pathways such as arthopod vectors and the food chain. Emerging pathogens have challenged blood programs to draw upon all resources available for a rapid and effective response. The result has been further development of surveillance methodology and response plans, with recognition that the original focus on risk reduction from sexual/drug-related risk of HIV and hepatitis left large gaps in the preventative measures. For example, the emergence of WNV in North America and recognition that it was transfusion transmissible demonstrated how quickly an emerging pathogen could become a serious transfusion risk and highlighted the inadequacy of the current surveillance systems. In the United States, the rapid development of a national surveillance system for WNV served as a basis for the development of surveillance of *T cruzi* antibody–positive donors and highlighted the need for ongoing interaction between blood services and public health agencies.

Selective testing can reduce risk from imported pathogens where universal testing may be inappropriate. Examples of this include selective testing for *T cruzi* in the UK, Canada, and the United States with proposals for such strategies under consideration in Australia as well as selective testing policies for malaria in the UK, France, and Australia. The ARC has already commenced selective dengue testing in Puerto Rico, and Australia is currently undertaking a cost/benefit analysis to assess a similar strategy to minimize component losses during seasonal outbreaks. Similarly, an outbreak of WNV in Italy during 2009 with an increased incidence of West Nile neuroinvasive disease have prompted concerns that donors returning to Australia from these countries during outbreak periods posed an increasing risk. After outbreaks in Greece and Russia during 2010, demonstrating similarly increased virulence, the ABS instituted a 56-day restriction to plasma for further fractionation only for donors returning from the defined outbreak regions. Should the expansion of WNV in Europe continue, targeted WNV NAT may be more cost-effective than component restriction and therefore may be considered as an alternative strategy in Australia.

Countries with fewer blood suppliers and formal relationships with public health are well situated to

address risks. In countries without these advantages, the effectiveness of surveillance appears to be similar, but collaborative arrangements have developed largely for specific purposes and rely upon the initiative and continued effort of the transfusion community to maintain them. Transfusion surveillance/public health interaction also has potential benefit to community health such as active surveillance for infections and knowledge of risk factors for infections in a healthy low-risk population, but overall transfusion surveillance tends to be a rather underused resource in this area. Because greater collaborative effort between public health and transfusion surveillance has potential to make better use of personnel and resources and improve both aspects of surveillance, it may be a logical future direction.

Examination of the evolution of surveillance programs in different blood programs and different countries suggests that future trends may include continued or improved emphasis on national surveillance and greater emphasis on mutually beneficial public health interaction and on international collaboration. All countries face similar competing pressures of intense public desire to do all things necessary to reduce the risk of both measurable and vanishingly small risks of infection to the blood supply while managing the blood supply in a cost-efficient manner. Accordingly, the continued reassessment of current safety policy as well as risk assessment for new pathogens has increased the profile of surveillance programs to apply scientific principles to identify options with acceptable safety standards that are not excessive and make better use of finite health care resources.

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