to do the right thing won't be sufficient if such action will harm the hospital's bottom line. To spur needed change, the Center for Medicare and Medicaid Services must create incentives for hospitals to move admitted patients promptly to inpatient units. The Joint Commission on Accreditation of Healthcare Organizations can help by reinstating strong standards that discourage boarding and emergency department crowding.

Strengthening disaster response is a key priority, regardless of whether the event is caused by a natural catastrophe, terrorism, or an emerging infectious disease. The committee believes that the best way to prepare for disasters is to create an emergency and trauma care system that functions effectively on a day-to-day basis. Key aspects of disaster response should be addressed regularly in the training, continuing education, and credentialing of emergency care professionals.

When your life is on the line, you want your doctor — not your ambulance — to go the extra mile. To replace the fragmented, overwhelmed system we have today, the IOM envisions a coordinated, regionalized, and accountable emergency care system that is capable of delivering lifesaving treatment to all in need. It is up to Congress, the federal government, and all of us to make this vision a reality.

An interview with Dr. Kellermann can be heard at www.nejm.org.

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FOCUS ON RESEARCH

The Continuing Risk of Transfusion-Transmitted Infections

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In 2002, as mosquitoes carried West Nile virus across the United States, infecting 4200 people, 23 confirmed cases of transfusion-transmitted infection and 7 related deaths were reported.[1] This was a dramatic demonstration that an emerging agent can threaten the safety of the blood supply. Because the virus's incubation period is usually 3 to 15 days and transmission by transfusion stood out against the background of a mosquito-borne epidemic, these transmissions were recognized quickly, nucleic acid–amplification technology was adapted for the detection of the virus, and the Food and Drug Administration (FDA) and Health Canada mandated the screening of donated blood for West Nile virus nucleic acid.

Thanks to many blood-safety interventions introduced in the United States between 1984 and 2004, the overall risk of transfusion-transmitted infections has become exceedingly small (see graph).[2] Currently, blood donors are questioned about risk factors for several parenterally or sexually transmitted viruses, including hepatitis B and C viruses (HBV and HCV, respectively), human immunodeficiency virus types 1 and 2 (HIV-1 and -2, respectively), and human T-cell lymphotropic virus types I and II (HTLV-I and -II, respectively), and blood is screened for indicators of infection. Donors are also asked about risk factors for malaria, babesiosis, and Chagas' disease. Blood intended for transfusion into patients who are at increased risk for cyto-megalovirus (CMV) disease is tested for CMV antibody or undergoes leukocyte reduction, since CMV resides in the white cells.

Since March 2004, platelet components in the United States have been screened for the presence of bacteria, because as many as 1 in 3000 random-donor platelet concentrates had been reported to be contaminated by a wide variety of both gram-positive and gram-negative bacteria, and bacterial sepsis had emerged as the most common transfusion-transmitted infection. Deaths from bacterial sepsis have continued to be reported, both because red-cell units are not screened and because the available methods for screening platelets are suboptimal. Between 2001 and 2003, an average of 11.7 deaths from bacterial sepsis per
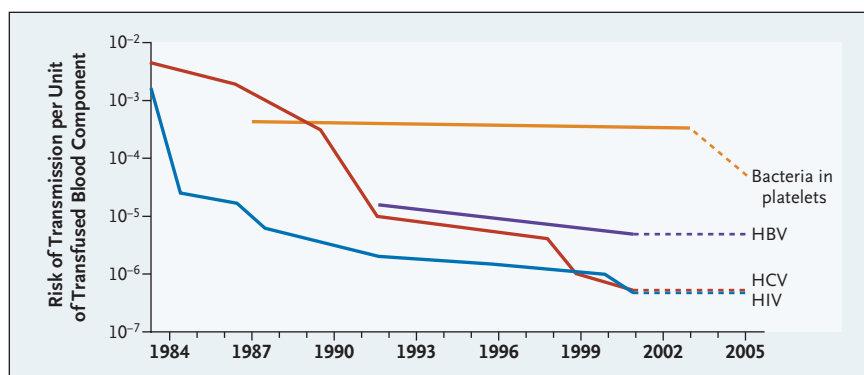
Risks of Transfusion-Transmitted HIV, HBV, HCV, and Bacterial Infection in the United States, 1984–2005.

Changes reflect both the effects of screening tests introduced during this period and the decreasing incidence of HIV, HBV, and HCV infections in blood donors. Several measures to prevent the transmission of bacteria by platelet transfusion were implemented in or around 2004. Dashed lines represent estimates.

year in the United States were reported to the FDA, whereas 7.5 per year were reported in 2004 and 2005 — a decrease attributable in part to the mandating of bacterial screening of platelets beginning in 2004.

Since 1995, several other agents have emerged as potential threats to blood safety. These include GB virus C–hepatitis G virus (GBV-C–HGV), SEN virus (SEN-V), and TT virus (TTV), all of which were initially thought to cause posttransfusion hepatitis; human herpesvirus 8 (HHV-8); simian foamy virus; the coronavirus of the severe acute respiratory syndrome; and the prion that transmits variant Creutzfeldt–Jakob disease (vCJD, the human form of bovine spongiform encephalopathy). The epidemiology of several other known pathogens, such as hepatitis A virus, parvovirus B19, enterovirus, and leishmania, was also reexamined to determine the potential for transmission by transfusion.

Fewer than 200 cases of vCJD have occurred worldwide, and some epidemiologic models indicate that this epidemic is already on the wane. However, recent reports suggest that transmissible spongiform encephalopathies like vCJD may have incubation periods of up to 50 years,[3] with infectious particles potentially circulating in the peripheral blood for much of the presymptomatic phase of the infection.[4] The transmissibility of vCJD through transfusion has been hard to establish because of the disease's long incubation period, but three probable cases have now been reported in Britain in patients who received blood products from donors who were asymptomatic at the time of donation but in whom vCJD later developed.

In North America, measures to protect the blood supply from vCJD were introduced several years before the first report in Britain of a transfusion-transmitted case.[5] Persons with a history of travel to European countries where bovine spongiform encephalopathy is endemic were rejected as blood donors. In Britain, the exclusion of particular donors is not feasible, since virtually everyone in the donor population is considered to be a potential carrier, so novel interventions for detecting or removing infectious prions from donated blood (see table) are being evaluated.

The study reported by Hladik et al. in this issue of the *Journal* (pages 1331–1338) offers strong evidence that HHV-8 can be transmitted through transfusion, particularly in a high-prevalence area such as Uganda, where 43% of patients who received transfusions in the context of the study received HHV-8–seropositive blood. HHV-8, a herpesvirus akin to CMV, causes lifelong infection, with periodic reactivations during which virus may circulate in peripheral-blood white cells and be transmissible through transfusion. In low-prevalence areas, risk factors for HHV-8 probably overlap with those for HBV, HCV, and HIV, and the available evidence indicates that infectious HHV-8 may be present in blood donors in the United States, may be transmissible by transfusion, and may have the potential to cause Kaposi's sarcoma in immunocompromised patients who receive transfusions.

Although newly described, HHV-8 is not a new agent. Presumably, blood from HHV-8–seropositive donors has been transfused into immunocompromised recipients for many years in the United States, without any reports of an association between transfusion and the development of Kaposi's sarcoma. It is not clear, however, that this possibility has been adequately investigated.

If no association between transfusion-transmitted HHV-8 and actual disease can be shown, is it reasonable to introduce additional safety measures to intercept this virus, for either all blood components or those intended for transfusion to immunocompromised patients? Unfortunately, no suitable screening assay is currently available for detecting either HHV-8 antibody or HHV-8 nucleic acid. As with CMV, leukocyte-reduced blood components

Possible Safety Interventions That Might Reduce the Risk of Transfusion-Transmitted Infections.	
Risk	**Interventions**
Bacterial contamination of platelet and red-cell components	Improved bacterial detection methods for all platelet and red-cell components; use of pathogen-reduction technologies
Residual risk of transmission of HIV-1, HIV-2, HBV, HCV, HTLV-I, HTLV-II, and West Nile virus	Single-unit (rather than pooled-sample) nucleic acid–amplification testing for HIV-1, HCV, West Nile virus, and HBV; use of pathogen-reduction technologies
Transmission of Chagas' disease and malaria	Testing of all donors (or donors reporting travel to countries in which Chagas' disease is endemic) with suitable microbial screening assays
Transmission of HHV-8	Testing of all donors (or donors whose blood products are intended for use in immunocompromised patients) for HHV-8 antibody, viral nucleic acid, or both; universal leukocyte reduction or leukocyte reduction of red-cell and platelet units intended for use in immunocompromised patients; use of pathogen-reduction technologies
Transmission of simian foamy virus	Questioning of donors about exposure to primates (as has been implemented in Canada)
Transmission of hepatitis A virus and parvovirus B19	Testing of donors for antibody or viral nucleic acid
Transmission of vCJD	Filtration of blood components through prion-retention filters; testing of donor blood for abnormally conformed prion protein by methods such as cyclic amplification of protein misfolding

may prevent transmission of HHV-8 by transfusion, but their efficacy in this regard has not been established.

The sheer number of potential pathogens that have threatened the safety of the blood supply since 1995 renders it impractical to keep adding safety measures for each new potentially transfusion-transmissible agent that appears. The surveillance and blood-safety systems that are currently in place make another blood-borne epidemic of the magnitude of the transfusion-transmitted–HIV epidemic unlikely. It remains possible, however, for an agent with a long incubation period to go undetected for some time and to accumulate in donors.

One way to protect fresh-frozen plasma from emerging agents may be to use one of the pathogen-reduction technologies (methylene-blue or solvent-detergent treatment) that have been introduced in the European Community. Similar technologies are under evaluation for use with platelets (amotosalen [S-59] plus

ultraviolet A light) and with red cells (amustaline [S-303]). Such technologies have been shown to be effective against most transfusion-transmitted bacteria, viruses, and parasites but ineffective against pathologic prions, intracellular pathogens, spore-forming bacteria, nonenveloped viruses, and viruses that are present in exceedingly high concentrations in blood. Their downside is that they tend to reduce the therapeutic efficacy of the blood components, necessitating the transfusion of greater quantities and exposing patients to blood from more donors, thereby increasing the risk of transmission by transfusion.

The possible safety interventions that might further reduce the risk of transfusion-transmitted infections (see table) will be extensively debated over the next few years. Regardless of the outcomes of these debates, it is clear that the risk of transfusion-transmitted infection is not static, as new agents continue to emerge, old ones change their properties

and epidemiologic patterns, and new information and technology become available to change our understanding of that risk.

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