Elsevier has created a Monkeypox Information Center in response to the declared public health emergency of international concern, with free information in English on the monkeypox virus. The Monkeypox Information Center is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

They come in threes: Marburg virus, emerging infectious diseases, and the blood supply☆

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On July 17, in the midst of the ongoing SARS-CoV-2 pandemic and several months into the monkeypox outbreak currently expanding worldwide, the World Health Organization announced that Ghana had declared its first ever outbreak of Marburg virus [1]. As of July 18, 2 persons have died and almost 100 have been quarantined, raising fears of an impending mass outbreak [1]. This marks only the second time in history this infectious disease has been identified in western Africa, though previous outbreaks and sporadic cases have been reported in various geographic regions of Africa, particularly the Democratic Republic of the Congo (DRC), Angola, and Uganda, and cases have been imported into Europe and the United States [1]. While SARS-CoV-2, monkeypox, and Marburg are quite distinct in their epidemiology, pathogenesis, transmissibility, and mortality, these viruses illustrate the potential impact of emerging infectious diseases on both the safety and adequacy of the international blood supply.

SARS-CoV-2 has influenced numerous misconceptions regarding the safety of blood transfusion from vaccinated blood donors [2] and continues to perpetuate unprecedented blood shortages across the US and Europe [3–5]. Monkeypox also threatens to exacerbate these blood shortages due to confusing donor deferral policies for vaccine recipients and infected donors [6]. This combination poses a potentially significant burden to maintaining an adequate blood supply; thus, one must consider whether Marburg virus may represent the third element in a perfect storm of an impending, infectious disease-mediated, blood supply disaster?

To understand what, if any threat, Marburg virus may pose to the international blood supply requires an understanding of the virus itself and the nature of prior Marburg virus outbreaks. Marburg virus, similar to Ebola virus, elicits a severe hemorrhagic syndrome, with a case-fatality rate ranging from 20 to > 80 % depending on the outbreak studied [7].

Marburg is a viral zoonosis, with the Egyptian fruit bat believed to be its natural animal reservoir; most prior cases were originally suspected to have been acquired in or near caves or mines inhabited by these bats [7]. The largest recorded outbreak occurred in Angola in 2005, resulting in more than 350 cases and 300 deaths [8]. Notably, there have been significantly fewer recognized outbreaks of Marburg virus compared to Ebola virus; however, between 1998 and 2000, an outbreak in the DRC was associated with multiple introductions of distinct viral strains independently, resulting in uninterrupted infections for two years [9]. Furthermore, as Mehedi and colleagues illustrated in their clinical review, most Marburg virus cases occurred during two large outbreaks, highlighting its potential as a serious public health threat [9]; however, this also illustrates that with early recognition and extensive public health measures, many outbreaks have been contained to just a few cases and without geographic spread.

Marburg virus is transmitted among humans via direct contact with blood or infected bodily secretions, most often occurring while caring for infected individuals [9]. Although the risk of aerosol transmission is considered low, studies have demonstrated viral stability in aerosols, and it is both highly infectious and fatal in nonhuman primate studies of aerosol inoculation [9]. Furthermore, as viremia is common during the symptomatic phase, the Association for the Advancement of Blood and Biotherapies (AABB) and the European Centre for Disease Prevention and Control consider this virus a theoretical risk to the blood supply [10,11]. In a non-human primate model, blood-borne virus was detectable within the first few days of inoculation, the timing of fever onset corresponded with the presence of detectable virus in blood via culture, and peak viremia titers reached 10^8 PFU/ml [12]. Extrapolating to humans, while viremia could certainly pose a risk to the blood supply if collected during infection, symptomatic donors are expected to be deferred through standard questions. However, the duration of viremia in human

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Marburg virus disease survivors and asymptomatic viremia are not well characterized, and although transfusion-transmission has not been reported, transmission via contact with blood has occurred in clinical cases [10,11]. Further lending to this hypothetical, but poorly understood risk, Marburg virus can, at minimum, hide in "immune–privileged" sites, such as the testes or intraocular space, in human survivors and transmission through infected fluids (i.e., semen) has been documented up to 7 weeks after recovery [8]. Additionally, there is currently no FDA-licensed blood donor screening tests, and in the US, disease testing is only available at the US Centers for Disease Control (CDC) or the US Army Research Institute of Infectious Diseases (USAMRIID) [10]. Despite this, there are some jurisdictions, such as the California Department of Public Health, that are prepared to inquire about a history of blood transfusion for patients with concern for viral hemorrhagic fevers, including Marburg [13].

It should be noted that internationally, pathogen-reduced platelets as well as solvent-detergent treated plasma are commonly utilized, with recent increases in implementation within the United States following FDA approval [14,15]. To that end, one of the benefits of utilizing a pathogen-reduced blood product is inactivation of emerging infectious agents. Though clinical trials are ongoing, pathogen-reduced red blood cell products may become available soon [16,17]. The healthcare and societal impact of these technologies cannot be overstated, though they may be inaccessible in resource-limited countries for many years.

Given these considerations and the small number of individuals infected/quarantined, the threat of the current Marburg virus outbreak in Ghana to the blood supply currently is minimal. However, as most infections result in severe bleeding, disseminated intravascular coagulation, shock, and multiorgan failure, the greater risk might not be from a donor perspective where deferrals or the risk of transfusion-transmission could limit the supply of blood, but instead from increased plasma and cryoprecipitate utilization if the outbreak were to expand. This is particularly important in resource-restricted countries where availability of fibrinogen and factor concentrates is significantly limited; thus, plasma and cryoprecipitate would be the cornerstone of supportive management to attempt to ameliorate the coagulopathies and hemorrhagic diathesis associated with this disease [18], further reducing an already constrained international blood inventory.

Though transfusion-transmitted cases have not been described [10], there are numerous issues surrounding a theoretical, large-scale Marburg virus outbreak with significant impact on the international blood supply. As recent history demonstrates, early recognition and familiarity with emerging pathogens are necessities for practicing transfusion medicine and microbiology staff.

Conflicts of Interest

The authors declare no conflicts of interest related to this manuscript.

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