Pathogen Reduction in Blood Products; 2015 Update

"There are known knowns. These are things we know that we know. There are known unknowns. That is to say, there are things that we know we don't know. But there are also unknown unknowns. There are things we don't know we don't know."

~Donald Rumsfeld

Although Mr. Rumsfeld was referring to military strategy in this oft quoted expression, this phrase also applies to the world of pathogen detection in our nation's blood supply. If we review the current testing protocols for blood products, they all target the "knowns". For example, hepatitis C, bacterial contamination, HTLV-1 virus and HIV, among others. Furthermore, the tests are "reactive," meaning the screening test to protect the blood supply is developed after the pathogen is identified as transmissible via blood transfusion. Those of you old enough to remember, recall the identification of and impact to the blood supply of HIV. We didn't know what we didn't know. We didn't know which individuals were infected, and these asymptomatic donors then inadvertently contaminated the blood supply, while in their window period. And we had no test to screen for it. It remains a credit to the blood banking industry how quickly a screening test was developed once we "knew" what the etiologic agent of AIDS was. But again, this was a reactive strategy, only possible once the agent was known. But what of the "next" pathogen? The one we don't know? That infects a donor who remains asymptomatic and inadvertently donates a transmissible pathogen? How many patients are infected before this next pathogen is identified and a screening test is developed? It likely is naïve to believe that we will not encounter another similar situation. Indeed, we are rapidly accumulating a laundry list of known pathogens for which we have yet to develop either a screening test or a mandate for routine testing of the blood supply.

So what to do? Much research has been geared towards universal pathogen reduction using techniques aimed at inactivating bacteria, viruses and parasites. This approach has the advantage of near universal destruction of infectious agents…prior to them becoming "known" as transmissible agents in our blood supply. In other words, these agents have prophylactic capacity to inactive novel pathogens before they are even identified. European countries have been using pathogen reduction systems for over 10 years, and the FDA has recently approved pathogen reduction systems for platelets and plasma. Pathogen reduction technology for red cells is lagging, but is under development. How do they work? The technologies vary from inactivation of the membrane of the various organisms by solvent detergent processes, or the use of ultraviolet light of varying wavelengths with other chemicals to inactivate the DNA and RNA preventing their replication.

(Continued on Page 8)

Under the Microscope Cont'd

Since red cells, plasma and platelets lack nuclei it is possible to destroy or inactivate pathogens, with relatively little damage to the blood products. Although pathogen reduction systems reduce both the recovery and survival of the platelets, they may allow platelets to be stored longer. Another advantage of pathogen reduction methods is that they inactivate leukocytes and may likely be able to replace irradiation as means of preventing transfusion-associated graph-versus-host disease.

Although pathogen reduction systems have several advantages, they also have drawbacks. For example, current pathogen reduction systems are limited in their ability to treat non-enveloped viruses such as hepatitis E and bacterial spores. In addition, the additional cost of this technology is in question. This latest point is an important one. Every screening test we add to or perform on a unit of blood increases the cost. Add to this the growing financial pressures on hospitals and blood centers alike and the voluntary adoption of pathogen reduction technologies remains unlikely. In a recent editorial in JAMA, Dr. Edward Synder commented on this implementation of pathogen reduction systems in the U.S.:

> *"Unless there is a mandate from the federal government or a requirement from the voluntary accrediting agencies to require use of some technology in order to prevent additional pathogen spread, it's going to be a very difficult process. The hospitals are being squeezed, blood centers are being squeezed. So the biggest hold up is going to be in the cost."*

In conclusion, it remains to be seen if this proactive approach, which has been safely used in Europe, will become the standard practice in our country, irrespective of the proof that these technologies help maintain a safer blood supply by deactivating many newly emerging pathogens and allow safer transfusions.

Submitted by: Dr. Judy Lyzak