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New screening process makes blood plasma even safer

U-M discovery will help reduce risk of viral transmission

ANN ARBOR, MI - A University of Michigan researcher has made a surprising discovery that will make blood plasma transfusions even safer.

Research by Robertson Davenport, M.D., U-M associate professor of pathology and medical director of the U-M Blood Bank and Transfusion Service, will reduce the transmission of human parvovirus B19 in the donor plasma supply, a virus that has potential to cause harmful effects in some patients.

The research, which will be presented Monday, Dec. 4 at the annual meeting of the American Society of Hematology in San Francisco, has already resulted in improvements in the processing of blood plasma.

Because all lots of treated plasma contain antibodies for Hepatitis A and parvovirus B19 that may give the recipient protection against infection, the intent of Davenport's study was twofold. He wanted to establish whether or not treated plasma can transmit both parvovirus B19, which can result in minor infections in healthy people but may be dangerous to pregnant women and those with bone marrow diseases, and Hepatitis A, a cause of jaundice. "Our hypothesis was that there would be little, if any virus, and that antibodies in the plasma would protect against infection if virus was present," he says.

In fact, what he found was that parvovirus is present - and in much greater amounts than ever expected.

Blood plasma is collected from normal volunteer blood donors that may go to donation sites like the Red Cross. From there it goes to hospitals and blood banks for use in patients with clotting problems, those suffering excessive bleeding or those with blood diseases.

In the study, Davenport started with 100 healthy individuals who were found to have had no prior exposure to Hepatitis A or parvovirus B19. Each person was given one unit of plasma that underwent typical treatment processes. The plasma was the same as that which any patient might have received from a hospital or blood bank at the time. The 100 study recipients then were monitored for three months.

"Nobody developed any signs of Hepatitis A so we concluded that treated plasma is safe from the point of Hepatitis A transmission," Davenport says. Hepatitis A does not progress to a chronic infection and will not cause cirrhosis of the liver.

"But as the early data became available, we were surprised that 18 subjects did develop parvovirus. None of them got sick but there was clearly virus in the blood," Davenport

parvovirus. None of them got sick but there was clearly virus in the blood," Davenport says. "Though there was no danger to the volunteers, we immediately became concerned and stopped the study. We looked at the lots of plasma that had been infused. Three out of 10 had high amounts of the parvovirus and these were the same ones that were associated with transmission. The other lots had low amounts of parvovirus and didn't result in transmission."

In some healthy people, parvovirus B19 infection causes Fifth Disease, named so because it was the fifth disease doctors discovered that caused a red rash in children. This common affliction can produce a mild rash and reddening of the face - called a "slapped-face appearance" - that fades and recurs. Although minor for most, parvovirus can cause a miscarriage in pregnant women and can cause the production of blood cells to stop for those with certain bone marrow diseases, Davenport says.

Unlike human-immunodeficiency virus - HIV - or Hepatitis B and C, which are all lipid-enveloped viruses, parvovirus B19 and Hepatitis A are non lipid-enveloped. This means they can't be killed by a common process used to treat plasma. A commercial treatment called the solvent/detergent process is now used to inactivate HIV, Hepatitis B and C from plasma and plasma products such as clotting factor concentrates needed by hemophiliacs.

In that treatment, a substance that disrupts the lipid layer is introduced and the viruses cannot then infect another person. This process was created by the New York Blood Center and was commercialized by V.I. Technologies, or VITEX - the same company that sponsored Davenport's research. VITEX is the only manufacturer of solvent/detergent treated plasma in the country.

The discovery of parvovirus in the plasma-infused volunteers suggested that the virus is more common than previously thought.

When a volunteer makes a blood donation, their plasma is mixed into a pool of 2,500 donations. Each such pool is individually processed, packaged and sent to blood banks and hospitals. "We expected that one in 5,000 donations would have the virus," Davenport says. "If that was true, we would expect about every other lot of plasma to have one donation in it that has parvovirus. But instead, nearly every lot showed that some virus was present, a few lots had high amounts of parvovirus."

Because this study showed that parvovirus was in greater amounts than expected and that, in high concentrations, it could be transmitted, VITEX pursued a way to amend the normal processing of plasma to prevent the transmission of parvovirus.

Currently, there is no FDA-approved test for parvovirus in blood products. VITEX used a proprietary test newly developed by National Genetics Institute to determine the concentrations of parvovirus in the plasma samples. The company also will present data on that test at the American Society of Hematology meeting. After Davenport's discovery, VITEX voluntarily recalled lots of plasma that were associated with parvovirus transmission. The company also began screening plasma for parvovirus.

"Before the plasma went into the pool, it was screened and donations with high amounts of parvovirus were rejected," Davenport says. This significantly lowered the concentration of parvovirus in the plasma pool.

Equipped with the new test, Davenport and his collaborators resumed the study. Another 50 healthy people were given an infusion of the plasma that underwent the additional screening for parvovirus. Subsequently, none were found to have the virus.

Davenport's conclusion: There is a threshold, and if the concentration of virus is under that threshold, the virus will not be transmitted.

"With additional screening, solvent/detergent treated plasma does not transmit parvovirus," he says. "As it is currently manufactured with this screening in place, it is safe from transmission. The small amount of residual parvovirus does not result in transmission and would not present a risk even to patients who might be susceptible to the more serious consequences of parvovirus infection," Davenport says.

Co-authors with Davenport included G. Geohas, M.D., S. Cohen, M.D., Breach, M.D. A. Lazo, Ph.D., DVM, K. Lucchesi, Ph.D., and J. Pehta, M.D.

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