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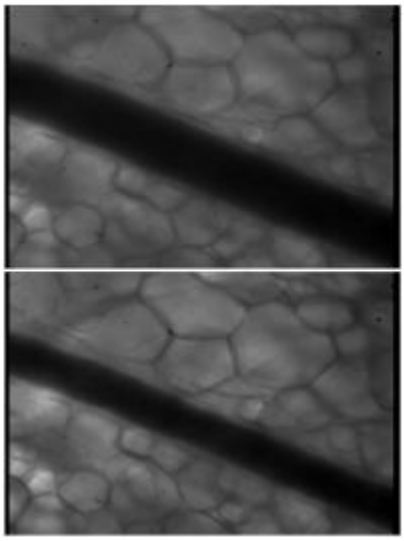
Hyperviscous fluids: Better treatment for severe blood loss

Viscosity enhancers that thicken blood are highly effective in treating severe hemorrhage

Intravenous administration of isotonic fluids is the standard emergency treatment in the U.S. for patients with severe blood loss, but UC San Diego bioengineering researchers have reported improved resuscitation with a radically different approach. Building on earlier studies in humans that have shown benefits of intravenous fluids that are eight times saltier than normal saline, the researchers combined hypertonic saline with viscosity enhancers that thicken blood.



Arterioles constrict and relax in response to a variety of factors, including viscosity enhancers.

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Reporting in the journal Resuscitation in an article that is available online, the researchers describe dramatic increases in beneficial blood flows in the small blood vessels of hamsters with the combined hypertonic saline and viscosity enhancement approach. The fluid was given to animals after as much as half of their blood was removed to simulate human blood losses on the battlefield, in traffic accidents and in operating rooms.

The team led by Marcos Intaglietta, a professor of bioengineering at the Jacobs School of Engineering, reported that the new approach sharply improved the animals' functional capillary density, a key measure of healthy blood flow through tissues and organs.

If course, trauma physicians want to get the blood flowing as soon as possible, and increasing the viscosity of blood may not make any sense to them, said Intaglietta. However, our results are highly suggestive that increasing viscosity rather and partially restoring blood volume is a better way to increase blood flow through tissues. These findings also are consistent with recent discoveries showing that higher shear forces of more viscous blood leads to dilation of small blood vessels.

The Advanced Trauma Life Support guidelines, recommend that emergency physicians first control bleeding and resuscitate with isotonic fluids. New research suggests hypertonic, hyperviscous fluids may be superior.

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Treating blood loss is a critical medical issue because trauma is the leading cause of death among North Americans 1 to 44 years old. Whether injured on the freeway or wounded in battlefield, loss of 40 percent or more of a patient's blood is immediately life-threatening. Physicians and emergency workers must act quickly.

The majority of trauma deaths are due to severe brain injury or a dangerous condition resulting from blood loss called hypovolemic shock. When too little blood flows through the body's organs, the heart begins beating rapidly, the skin becomes cold and pale, blood pressure plummets, and patients exhibit mental confusion. Hypovolemic shock can progress within a matter of one or two hours to organ failure and death.

The bible of trauma physicians and emergency workers, the Advanced Trauma Life Support (ATLS) guidelines, emphasize that physicians first control bleeding and then provide limited fluid resuscitation, a strategy known as "permissive hypotension" until control of hemorrhage is obtained. The ATLS guidelines, developed by the American College of Surgeons and adopted in more than 30 countries, were modified to lower the volume of isotonic fluids given after several studies demonstrated that sudden increases in blood pressure (without immediate bleeding control) would "pop" clots that the body forms to control bleeding.

Over several decades, studies involving humans and animals have evaluated hypertonic saline (up to 7.5 percent sodium chloride) versus isotonic saline (0.9 percent sodium chloride). Given intravenously, hypertonic solutions act like magnets, drawing fluid from tissues into the bloodstream, thereby increasing blood volume. Such hypertonic saline has not received the

approval of the Food and Drug Administration for clinical use in the United States. Therefore, it is not part of ATLS guidelines.

However, several medical research teams, including one led by Dr. Raul Coimbra, professor of surgery and chief, Division of Trauma, Surgical Critical Care and Burns at UC San Diego Medical Center, have investigated the effects of hypertonic saline for almost 20 years. Our level-1 trauma center at UC San Diego is participating in a study of hypertonic saline as part of a multicenter trial sponsored by the National Institutes of Health, said Coimbra. Unfortunately, it will take us two to three more years to finish the trial and determine whether hypertonic saline is superior to conventional isotonic resuscitation.

In Intaglietta's study with hamsters in the Jacobs School of Engineering's Department of Bioengineering, 90 minutes after hypertonic saline was given to blood-depleted hamsters about 30 percent of normal flow was reconstituted through skin arterioles, tiny branches of arteries that lead to the even smaller capillaries. The bioengineering researchers quantified blood flow with special microscopic procedures.

In blood-depleted hamsters given both hypertonic saline and a small volume of a commercially available viscosity enhancer called Hextend ã, blood flow through arterioles improved to 40 percent of normal. When the hypertonic saline, Hextend ã, and a small volume of another viscosity enhancer called alginate were given, arteriole blood flow improved to 55 percent of normal. Hextend ã and alginate are plasma volume expanders, substances transfused to maintain the fluid volume of blood.

Our findings suggest that elevating the viscosity of blood after severe blood loss is beneficial in resuscitation, said Intaglietta. In fact, our studies indicate that Hextend and similar plasma extenders could produce even greater benefit if they were formulated with higher viscosities.'

Arterioles regulate blood flow by constricting and dilating. A variety of factors in the body influence the process, including the viscosity of plasma, the fluid portion of blood. For example, higher viscosity plasma causes arterioles to dilate.

Nor centuries, dating back to the time of the early Greeks, the idea has always been that blood is thick, so the sick should be treated by bleeding in order to thin the blood, said Intaglietta. Even as late as World War II and the Vietnam Way, it was thought that adding isotonic fluids to replace blood lost on the battlefield would be good because it lowered blood viscosity, making it easier for the heart to pump.

Intaglietta said that while more research is needed, Our findings and others suggest that the ATLS guidelines need to be modified.

Studies such as Intaglietta's are important because it uses not only hypertonic saline, said Coimbra, but also other adjuncts which may increase the effects of hypertonic saline in treating those patients and in advancing our knowledge about shock resuscitation.

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Co-authors of the Resuscitation report with Intaglietta are Pedro Cabrales, a senior investigator at the La Jolla Bioengineering Institute, and Amy G. Tsai, a research professor in the Jacobs School's Department of Bioengineering. The research was supported by the National Heart, Lung and Blood Institute and the U.S. Army. Dr. Coimbra's research was supported by the National Institutes of Health.