

Exchange Transfusion for Jaundiced Newborns in the United States

Exchange transfusion is the replacement of blood from newborn infants with elevated bilirubin level in their blood stream with donor blood containing normal bilirubin levels. Newborn infants that experience jaundice, the yellowing of the skin and eyes, have a buildup of bilirubin, a chemical that occurs during red blood cell breakdown, or hemolysis. Exchange transfusion is a therapy developed throughout the 1940s by Louis Diamond and a group of surgeons at the Children's Medical Center in Boston, Massachusetts. During exchange transfusion, a physician inserts a plastic tube called a catheter through the umbilical vein of the infant to slowly remove infant blood and sequentially replace it with donor blood. Exchange transfusion was the first definitive treatment for hyperbilirubinemia in the US and it helped reduce the incidence of kernicterus, a type of brain damage caused by elevated bilirubin levels.

Throughout the 1940s, a group of pediatricians at the Children's Medical Center refined the technique of exchange transfusion to originally treat erythroblastosis fetalis, EF. EF arises during fetal development when the immune system of the pregnant woman attacks the red blood cells of the fetus. In those cases, the pregnant woman's immune system recognizes proteins on the outside of the infant's red blood cells, called Rh antigens, and attacks those cells. As a result, the fetus's red blood cells break down, releasing high levels of bilirubin into the fetal bloodstream. In 1940, Karl Landsteiner and Alexander Wiener published their discovery of the Rh antigen factor of blood in the journal *Experimental Biology and Medicine*. After that finding, the pediatricians at the Children's Medical Center began to only use blood that did not contain the Rh antigens, or Rh-negative, in blood transfusions, making exchange transfusion a practical treatment for hyperbilirubinemia.

In 1951, Louis Diamond, Fred Allen, and William Thomas, physicians at the Children's Medical Center, published an article in the *New England Journal of Medicine* describing improved techniques for exchange transfusion to treat elevated bilirubin levels due to EF in newborn infants. They suggested using the umbilical vein as the site of transfusion, and that a single polyethylene tube be used to withdraw the infant's blood and sequentially replace it with donor blood. They stated that the umbilical vein is the best location for transfusion because there is less chance for scarring and it is easily identified through the umbilical cord on newborns.

In a 1958 study published in *The Lancet*, A physician group in Edinburgh, Scotland, demonstrated the optimal volume of donor blood to be used during exchange transfusion. They found that double-volume exchange transfusion is most effective. Double-volume refers to the volume of donor blood used, which is twice the volume of the infant's blood removed. Single-volume exchange transfusion is an alternative technique that uses the same volume of donor blood as the infant blood during transfusion. The single-volume technique exchanges approximately 63 percent of the infant's blood, whereas around 86 percent of the infant's blood is exchanged during double-volume exchange. Consequently, double-volume exchange is more effective than single-volume exchange at removing total bilirubin mass from the infant's tissues. In the study, the physicians found that double-volume exchange removes more total bilirubin mass from the infant, 20 to 70 percent compared to single-volume exchange. Although both single-volume and double-volume exchange are considered effective, after ten days there is a total decrease in bilirubin and anemia in the infant, at which point the standard of care is to perform a double-volume exchange transfusion due to the higher total amount of bilirubin it removes from the infant.

Other than the changes regarding the ideal volume of donor blood physicians should use, the method of exchange transfusion has not changed much since the Children's Medical Center group first

described it. Physicians insert a catheter into the umbilical vein, through the abdomen, and then allow blood to flow freely from the catheter before starting the exchange. Physicians send a sample of that original blood to a lab to be tested for original bilirubin levels and other nutrient levels, most often sugar, salt, hemoglobin, and calcium levels. The donor blood, which is O-negative and Rh-negative to prevent an attack from the infant's immune system, is warmed to 37 degrees Celsius and can be inserted through the same umbilical catheter, called the push-pull technique, or through a peripheral vein in the abdomen. The amount of blood a physician removes from the infant at each interval must equal the amount of blood they infuse back into the infant. That is done to prevent complications within the cardiovascular system, such as cardiac arrest. During the push-pull technique, physicians remove up to 5 ml/kg of body weight of blood from the infant at a time and then replace it with donor blood. The minimum amount of time needed for an exchange is forty-five minutes. If done correctly, a standard double-volume exchange is extremely effective. Physicians remove around eighty-five percent of the infant's circulating blood, which decreases their bilirubin level by half of the original amount due to the large amount of donor blood that is placed into circulation.

The success of exchange transfusion therapy is marred by some of the risks associated with it. Exchange transfusion can cause life-threatening conditions including cardiac arrest, irregular beating of the heart, the formation of air bubbles in the blood vessels, and infections at the transfusion site. Adverse effects of exchange transfusion on infants are often attributed to pre-existing health problems unrelated to the hemolytic disorders being treated by the exchange transfusion. In 1976, the National Institute of Child Health and Human Development published a study that surveyed 190 infants, who had received a total combined of 331 transfusions. Using the data from that study, the researchers calculated the death rate from exchange transfusion to be 0.53 every 100 infants, or 0.3 per 100 procedures. Out of the fourteen infants that succumbed due to exchange transfusion incidents, two were labeled as in good condition prior to the treatment. According to the researchers, that meant that the healthy infant died as a result of exchange transfusion therapy, indicating the procedure's inherent risks.

By the 1980s, exchange therapy treatment was in decline due to the development of a prenatal treatment. In 1968, an Rh factor therapy, called Rh immune globulin therapy, was introduced and given to Rh-negative pregnant women by physicians as a preventative measure. That treatment prevented their immune system from mounting an attack on the possibly Rh-positive infants. That virtually eliminated the need for exchange transfusion due to Rh factor incompatibility.

Alternative postnatal treatments have also contributed to the decline of exchange transfusion as a treatment for neonatal jaundice. The most common postnatal treatment for jaundiced infants is phototherapy, or light therapy. Phototherapy uses light wavelengths to breakdown bilirubin into a photochemical byproduct that is easily filtered by the liver to be excreted by the body. The ease of phototherapy as a postnatal treatment and the extremely low risks associated with the procedure made it much more attractive to physicians and has largely replaced exchange transfusion.

As a direct result of those two technological developments, phototherapy and Rh factor therapy, exchange transfusion treatment for jaundice neonates has declined steadily since 1986. While its popularity with physicians has decreased over the years in favor of non-invasive techniques, exchange transfusion remains a valuable technique that effectively and quickly removes bilirubin from the infant's blood stream to prevent toxicity from occurring and causing the infant permanent brain damage.

Sources

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