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Investigations into intracranial hemorrhage in premature infants to be done with Crystal Charity funds

The University of Texas Health Science Center at Dailes The University of Texas Health Science Center at Dailes The University of Texas Health Science Center at Dailes The University of Texas Health Science Center at Dailes The University of Texas Health Science Center at Dailes DALLAS--Because the preterm infant is so delicate and its development is not complete, many things have the potential to cause it serious damage--even life-saving procedures. The pediatrician-neonatologist is constantly faced with the dilemma of what to do to save these babies without running unnecessary risks, such as hemorrhaging in the brain that may will or permanently damage them kill or permanently damage them. \$ 350,000

It is this problem--intrinanial hemorrhage--that Drs. Charles R. Rosenfeld, Billy S. Arant, Jr. and a group of their associates at The University of Texas Health Science enter at Dallas are addressing. The work is to be funded by Dallas' famous Crystal Charity Ball Dec. 4. About 50,000 will be used to support a three-year project that will include a system for monitoring every premature infant of 1,500 grams (three pounds) or less birth weight admitted to the neonatal intensive care nursery at Parkland Memorial Hospital. Some of these at-risk neonates are so small that the attending physician can almost hold the tiny child in the palm of one hand.

Babies like these can be found in intensive care nurseries (ICN) in major metropolitan hospitals throughout the country. The low birth-weight preterm baby, literally fighting for its life, is kept in a critical care unit, hooked up to tubes for nourishment, under special warming lights and on respirators to aid breathing.

Of the nearly 3,500,000 infants born in this country each year, most survive and develop normally. But many of them make it only because of recent advances in obstetric and newborn care. Today, infants who weigh in the range of 1,000 grams (2.2 pounds) have a better than 80 percent chance of surviving. However, of the babies 1,500 grams (three pounds) and under, 50-90 percent are thought to suffer from intracranial hemorrhaging, a condition called "stroke" in adults. About 40 percent of these babies die in the hospital; another 25 percent develop conditions such as cerebral palsy, mental retardation, hydrocephaly (commonly called "water on the brain") and/or seizure disorders. Others may possibly suffer from more subtle neurologic handicaps, such as learning disabilities or behavior problems.

In fact, says Rosenfeld, intracranial hemorrhage is the main cause of death and brain damage in infants three pounds and under in the intensive care nursery at Parkland. osenfeld, who is Professor of Pediatrics and Obstetrics and Gynecology at The University of Texas Health Science Center at Dallas, is medical director of nurseries at Parkland, the health science center's major teaching hospital. Out of 443 infants admitted to neonatal intensive care from 1977 through 1978, 64 were discovered to have intracranial hemorrhage. Of this number, 49 died. Cerebral hemorrhage was the second greatest cause of death in the unit and had the highest morbidity rate. Two thousand of the 10,000 babies delivered at Parkland this year will be considered high risk.

It is thought that hemorrhaging in the brain of the low birth-weight infant may start before, during or after delivery. The exact causes of this hemorrhaging in individual cases may be multiple and hard to pinpoint, says the physician. In fact, neonatologists are beginning to suspect that some of the medical procedures commonly used to save the infant's life may actually cause hemorrhaging in the brain, leading to death or disability. Evidence of the role of these procedures needs to be obtained, and some life-saving techniques commonly used may need to be refined for use with neonates.

Research at The UT Health Science Center will include keeping a complete computer record of each high-risk infant condition and treatment. The researchers will also follow as many of the children who have experienced a brain hemorrhage as possible for the three-year period to see what disabilities they may develop. Data gathered during the project will be analyzed to help determine the risk factors present in treatment and to look for methods by which these factors can be minimized. Money will go for equipment and salaries for specialized personnel for the project.

Some of the life-saving procedures that presently are suspected of "doing bad while doing good," says Rosenfeld, include the following:

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* Artificial respiration. Preterm infants frequently have breathing difficulties, and in many cases it is necessary to use an artificial means to ensure that the infant is breathing adequately. These problems include failure to start breathing after birth, cessation of respiration and hyaline membrane disease, the respiratory condition that killed President and Mrs. John F. Kennedy's third child. In some infants changes in the use to the ventilator lead to alterations in blood pressure that may cause hemorrhaging.

* Endotrachael intubation. If mucus is obstructing breathing, it is sucked out of the lungs and a tube through which air is pumped to inflate the lungs is inserted to help the baby continue breathing. This procedure, too, may cause changes in pressure that would disturb organ and tissue blood flows and thus lead to hemorrhaging.

* Medications. Glucose or various vasoactive drugs, which are used to increase or decrease the baby's blood flow to tissues and organs are currently being looked at. It has already been determined that large doses of glucose, used for emergency treatment of low blood sugars in adults, are not appropriate in neonates. Determining the correct dosage of glucose and drugs to bring about the desired result without causing hemorrhaging in the brain is vital.

Rosenfeld is acutely sensitive to the questions raised by using new procedures that have not been evaluated adequately over a long period of time. This is one of the dilemmas of modern medicine, he says. The physician frequently is put in the difficult position of trying whatever means he can to save the patient's life within the bounds of the medical inderstanding of the times. But sometimes the information is not all in. This is why Rosenfeld and his associates feel that it is important to investigate the questions they are posing in this study.

"It is important to remember," he says, "that only in the last few years have we been able to determine small hemorrhages in the brain. Previously the evidence had to be gross, and so the prognosis for these children was nearly always grim."

Now with ultrasound, or sonography, which can show the researchers a picture of a small blood clot or bleeding around the ventricles (cavities within the brain), a diagnosis can be made. Also, an indication of the severity of the problem can be assessed. In order to make these determinations, a probe is held over the infant's "soft spot" and moved around the area. A "TV" picture of the brain shows up on a small screen and is evaluated by the researchers. This procedure is done as early as the first day of life on every baby in the intensive care nursery who weighs 1,500 grams (three pounds) or less. Other babies in the unit receive the test on the second or third day or at a later time if it is indicated. If the reading is abnormal, the test is repeated to determine the extent of damage.

Infants in the ICN who are slated for neurosurgery, such as a draining procedure for hydrocephaly, are also scanned for intracranial hemorrhaging with a CAT scanner. This is a much more expensive test and is more difficult because the baby must be moved from the ICN. In contrast, the ultrasound machine is portable and puts the baby at less risk because the test can be done in the baby's special care environment.

Other equipment vital to the monitoring of these babies is the oxygen monitoring devices. The major type used is a catheter with an electrode on the end that is placed through the umbilicus into the aorta, the body's main artery. Currently five of these are in the ICN, and the Crystal Charity Ball money will help pay for recorders, as well as a transcutaneous oxygen monitor. The transcutaneous monitor will be used to continuously measure and record oxygen concentration through the skin while monitoring temperature and blood pressure with additional devices--all vital information in knowing what is happening with these babies. The changes associated with blood pressure, oxygen concentration and temperature will be correlated with the information related to the development of intracranial hemorrhaging.

Parents will be strongly encouraged to bring the babies for check-ups in the low birth-weight clinic at Children's Medical Center for early warning signs of slowed development or neurological problems possibly caused by brain hemorrhage. If problems show up, then the research nurse can make appropriate medical referrals. She will also gather information on the children for the study.

At one, two and three years of age the children will be further examined by development psychologist Dr. Robert Lasky, an important member of the research team. A member of the pediatrics faculty at UTHSCD, he is also an adjunct professor at The University of Texas at Dallas Callier Center for Communication Disorders. There he administers the extensive battery of tests on "alumni" of Parkland's intensive care nursery. Both low birth-weight children and controls are rated on a scale as to mental age, motor age, behavioral level and are given a neurologic exam, measured for height, weight, head circumference and body fat. Norms developed for Parkland patients through a Robert Wood Johnson grant will be used.

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All these data will be coordinated with the information about the condition and treatment before birth and in the intensive care nursery for each infant. It is hoped that through development of statistical probabilities of causes of hemorrhaging, the investigators will be able to identify areas where changes in care can be made. Close cooperation with the Department of Obstetrics and Gynecology, which runs the obstetric service at Parkland, will make the study easier to conduct because records on mothers before and during delivery will be available. Also, says Rosenfeld, because of the excellence of the obstetrical care the patients receive at Parkland, there are few problems at birth that are suspected in connection with brain hemorrhage in the neonate.

A separate area of investigation into these problems deals with animal studies. Some work in this area has already been done by these reseachers with funding from such groups as the National Institutes of Health.

"Because of the many variables concerned with prenatal care, delivery and treatment of the neonate, not to mention possible physical problems already present in mother and/or child, we must rely heavily on statistics in drawing our conclusions. However, controlled animal studies can give us vital insights into some of the causes of intracranial hemorrhage in infants," the doctor says.

For several years Rosenfeld and associates have been studying regional blood flow in newborn lambs with the application of continuous airway pressure. This work was reported n <u>Pediatric Research</u> earlier this year. Also, work Rosenfeld and others have done on continuous airway pressure breathing with respirators and the effects on regional blood flow, also in newborn lambs, was reported earlier in <u>Pediatrics</u>. The researcher is currently looking at blood flow in the pregnant ewe and her fetus.

Another member of the research team, Arant, a pediatric nephrologist, became interested in the problem of brain hemorrhage when he was studying the effects of fluid changes in the newborn. While giving intravenous glucose to newborn puppies, whose brains are similar to the premature human infant's brain at 30-32 weeks gestation, he noticed that in about 45 minutes to an hour they began having difficulty breathing. Brain hemorrhage seemed to be the reason. Arant is continuing his animal explorations in this area and some of his conclusions will be published soon.

Also working with an animal model for blood flow to the brain is Dr. Abbot Laptook. His work is being done with piglets, whose brains he believes are the closest model for that of the human infant born at term.

Rosenfeld believes the health science center researchers are in an enviable position to be able to continue studies in this area.

"We will have funds to buy equipment and to pay research personnel to do the statistical studies with a large pediatric population requiring intensive care. We have related animal studies already going on, and, most important, we have the cooperation of community leaders who are interested in improving the care of the newborn," says Rosenfeld. "In fact, one of the commitments we made to the Crystal Charity Ball is that we would make vailable as soon as possible any information that will help physicians treating premature ad low birth-weight babies.

"Our concern is not just life itself for these babies, but the quality of the lives they will lead."

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