

IN UTERO insights

Volume 1
Issue 2

SUMMER
2010

 The Children's Hospital of Philadelphia®

 CENTER FOR FETAL
DIAGNOSIS & TREATMENT

Dear Colleague,

Fetal therapy offers the earliest possible intervention for life-threatening disorders, with the hope of producing the best results for mother and baby. For complicated twin pregnancies, repair in the womb often offers the best outcome for three patients: mother and each baby.

The Center for Fetal Diagnosis and Treatment at The Children's Hospital of Philadelphia is one of only a handful of programs worldwide to offer the full range of fetal therapies. Our multidisciplinary team has more than 15 years of experience in the challenging diagnosis and treatment of twin problems, creating a level of proficiency and expertise found at only a few centers.

Our advanced diagnostic techniques and expert clinical care ensure the best outcomes for twins, and our clinical and basic research edge us ever closer to improved treatments for these complex conditions.

This issue of *In Utero Insights* focuses on the breadth of resources we offer patients who present with complications of pregnancy with multiples. We value the opportunity to partner with you in providing exceptional care, and we welcome your feedback.

Sincerely,



N. Scott Adzick, M.D., M.M.M.

Surgeon-in-Chief

Director, Center for Fetal Diagnosis and Treatment



Lori J. Howell, R.N., M.S.

Executive Director

Center for Fetal Diagnosis and Treatment

COMPREHENSIVE CARE FOR TWIN PREGNANCIES

Fetal complications in twin pregnancies are challenging to diagnose, can threaten the survival of one or both twins, and often result in secondary complications that put pregnancies at risk for early delivery. Successful diagnosis and treatment require an experienced team with cutting-edge diagnostic techniques, advanced surgical skill and a comprehensive approach to care.

The multidisciplinary team at the Center for Fetal Diagnosis and Treatment at The Children's Hospital of Philadelphia has more than 15 years experience managing twin pregnancies complicated by birth defects, among the greatest collective experience in the world. The team evaluates nearly 200 sets of twins a year using state-of-the-art imaging technology, including high-resolution ultrasound and detailed fetal echocardiography. On occasion, fetal MRI, a technique pioneered at CHOP in the 1990s, is also used.

“There are so many subtle factors at play during the evaluation of these complex twin pregnancies,” Mark Johnson, M.D., Director of Obstetric Services at the Center, says. “How they present can be amazingly variable. Each case is as unique as a fingerprint.”

Complications in identical twin pregnancies can include Twin-Twin Transfusion Syndrome (TTTS), selective (only one twin involved) severe placental insufficiency and growth restriction, prenatal death of one twin, one twin with a major birth defect or genetic abnormality, twin reversed arterial perfusion (TRAP) sequence, both twins within one amniotic sac (monoamniotic) with entanglement of their umbilical cords, and conjoined twins.

Specialists at the Center partner with referring maternal-fetal medicine specialists and/or primary obstetricians to provide

continued ►

Referrals • Appointments • Information

1-800-IN-UTERO (468-8376) • fetalsurgery.chop.edu

COMPREHENSIVE CARE FOR TWIN PREGNANCIES continued from front cover

a seamless continuum of care, discussing the diagnosis and treatment options, offering suggestions for follow-up if fetal surgery is required, and remaining available for consultation for the remainder of the pregnancy as part of the patient's ongoing perinatal management team.

"We really value and encourage the collaborative team approach and the opportunity to work with referring doctors, with the goal of patients returning to their home institution for management and delivery," Johnson says.

CHOP's unique cardiovascular scoring system, created in collaboration with the Fetal Heart Program, measures the existence and progression of adaptive cardiovascular changes, a common complication in twin anomalies, resulting in more informed treatment decisions for TTTS. When laser therapy is indicated, the team studies patients' cardiac function scores before treatment, 24 hours after the procedure and when they return one week later for follow-up to look at changes in response to the intervention.

If indicated, mothers can deliver in CHOP's Garbose Family Special Delivery Unit, the first birth facility in the world designed for mothers carrying babies with known birth defects, where the most advanced neonatal and cardiac intensive care units and operative facilities are within steps of their delivery rooms. Children's Hospital's Neonatology services, ranked No. 1 in the nation by *U.S. News & World Report*, and other top-ranked subspecialties within the Hospital help provide each family with multidisciplinary counseling and care before and after birth.

"These experienced subspecialists can provide the family with a better understanding of what's going on, what the risks are to the pregnancy and what the possible outcomes could



Members of the CFDT team perform selective laser photocoagulation for TTTS.

be after the babies are born, depending on what complications of the identical twinning they may face," Johnson says.

With the help of families and their delivery teams, researchers at the Center analyze placentas (*see Research Update*) and birth and outcome data from monochorionic twins that have undergone fetal intervention for TTTS in an effort to understand the impact of fetal therapy, refine prenatal counseling and develop recommendations for management of these complex conditions.

"Together, as a team, referring physicians and the staff at our Center have made great advances not only in understanding complications of identical twins, differentiating one problem from another, and refining treatment strategies and follow-up, but also in offering patient-specific management options to improve outcomes," Johnson says.

BY THE NUMBERS

CHOP Twin Experience: 1995 to Present

Referrals for Complicated Twin Pregnancies: **1,728**

TTTS referrals: **1,168**

TRAP referrals: **102**

Conjoined referrals: **64**

Selective Laser Photocoagulation for TTTS at CHOP: 2005 to 2009

142 Twins/**1** Triplet, Stage 2 or greater, < 26 weeks

Overall survival: **86.4%**

Survival of at least one twin: **94.4%**

Survival of both twins: **79%**

Types of Fetal Intervention Offered for Twins:

Selective Laser Photocoagulation

• Radio Frequency Ablation

• Bipolar Cord Caутery

• Amnioreduction



3-D image of TTTS

BEYOND THERAPY

Supporting Families from Evaluation Through Follow-up

Anomalies in twin pregnancies are complicated conditions that can be difficult to diagnose and treat, and emotionally challenging for families. Depending on the condition, there may be the risk that one or both babies will not survive the pregnancy.

From the beginning, a multidisciplinary team consisting of clinicians and social workers at the Center for Fetal Diagnosis and Treatment (CFDT) at The Children's Hospital of Philadelphia provides support to each family. The team meets with families after diagnostic testing to discuss the diagnosis, treatment options, risks involved in treatment and outcomes families can expect.

"We spend a lot of time trying to prepare families pre-operatively. We always strive to make sure they have two babies to take home, but given the complicated nature of twin anomalies, that's not always going to happen," Michael Bebbington, M.D., M.H.Sc., attending maternal-fetal medicine specialist, says.

Before and after fetal intervention, Center social workers Martha G. Hudson, M.S.W., L.S.W., and Naketa R. Thigpen, L.S.W., remain in contact with families. After patients return home to their primary OBs and/or maternal-fetal specialists, who typically manage the rest of the pregnancy and delivery at



Martha G. Hudson, M.S.W., L.S.W., offers support services during and after care at the Center.

the home hospital, social workers touch base with families by phone around the time of their due date to see how mother and baby or babies are doing and to offer additional support. "We want to let them know we are concerned and available," says Hudson. "But it's important that the local team takes over."

In the case of a demise, social workers meet with families to provide support and comfort as they cope with their loss.

Families are given ultrasound images of the twins as a memento and are connected to resources close to their home.

If only one twin survives, it can be extremely difficult for parents, as they feel caught between experiencing the joys of the birth of one child at the same time they are grieving one's loss.

"When you're dealing with families who have lost one of a set of twins, the hardest thing is that people do not acknowledge their grief because they have a healthy baby," Hudson says. The Center's Perinatal Palliative Care Initiative helps families plan for and cope with these conflicting emotions.

"You have to validate that feeling that the demised twin was worthwhile," Hudson says. "We talk about how the baby that survives will always be a twin and help them find meaningful ways to acknowledge the twin that didn't survive."

NEWS FROM THE FETAL HEART PROGRAM

Ongoing Validation of the CHOP CV Scoring System for TTTS

An ongoing, collaborative study by the Fetal Heart Program and the Center for Fetal Diagnosis and Treatment has found that CHOP's unique Cardiovascular Scoring System for Twin-Twin Transfusion Syndrome (TTTS) is a valid tool in the diagnosis, monitoring and evaluation of treatment effect in twins affected by TTTS. The CHOP cardiovascular score reflects the spectrum of changes seen in the cardiac function of the recipient twin and UA Doppler in the donor.

In a recent review of cardiac scores from twin pregnancies referred to the Center for TTTS evaluation, TTTS was diagnosed in 119 cases and selective Intrauterine Growth Restriction (sIUGR) was diagnosed in 37 cases. Statistical comparisons were made using the Chi-Square test, t-test, paired t-test and analysis of variance (ANOVA). When patients with TTTS were grouped by Quintero stage, there was a statistically significant increase in the CHOP cardiovascular score with advancing Quintero stage ($P < 0.001$).

There was also a statistically significant difference ($P < 0.001$) between the CHOP cardiovascular scores of cases with sIUGR and those with TTTS.

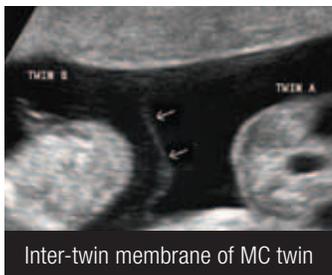
Analysis of the score components between those with sIUGR and stage 1 TTTS demonstrated more cardiovascular abnormalities in the sIUGR fetus compared to the donor twin ($P = 0.02$) and more findings in the recipient twin in cases of TTTS when compared to the normally grown twin in cases with sIUGR ($P < 0.0001$). Serial antenatal cardiovascular scores demonstrate increased scores associated with clinical progression and stable/decreased scores when no clinical progression was seen. Treatment with selective laser ablation of placental vessels was associated with a significant decrease in the postoperative cardiovascular score within seven days when compared to the preoperative score, with changes in the score often occurring before a clinical change is seen.

Sonography of Complicated Monochorionic Twin Pregnancies

By *Jill Langer, M.D., F.A.I.U.M., and Beverly G. Coleman, M.D., F.A.C.R., F.A.I.U.M.*

Twin pregnancies are associated with an increased perinatal morbidity and mortality compared with singleton pregnancies, with the risk three to 10 times greater in twins that have a single placenta — monochorionic (MC) twins — as compared with two separate placentas — dichorionic (DC) twins. The presence of vascular communications in the shared placenta of MC multiple pregnancies may cause significant hemodynamic alterations between the two fetal circulations, leading to severe complications such as twin-twin transfusion syndrome (TTTS) and twin reversed arterial perfusion (TRAP) sequence.

An accurate diagnosis of an MC gestation is essential and may best be accomplished in the first trimester or early second trimester. An MC gestation appears as a gestational sac containing a thin inter-twin membrane, comprised only of two adjacent layers of amnion which insert into the placenta in a “T” configuration. In some DC pregnancies, the placentas are adjacent and may simulate a single placenta. However, the inter-twin membrane in these DC pregnancies will be thicker since it has four layers — the two layers of amnion plus two layers of chorion — and will have a triangular, “Y” or “lambda” shape at its insertion, also called a “twin peak” sign.



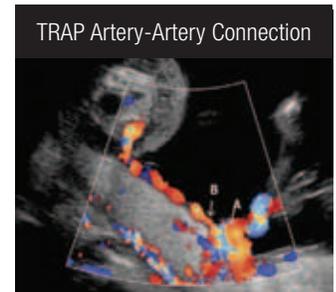
Identification of the thin inter-twin membrane may be challenging in cases of TTTS but is best seen near the fetal neck or surrounding the limbs of the twin with oligohydramnios. Identification of this membrane avoids a misdiagnosis of a monoamniotic MC pregnancy, which carries not only the vascular complications of MC twins but also a risk of cord entanglement since the fetuses also share a single amniotic sac.

The diagnosis of TTTS is established by identifying abnormal amniotic fluid volumes (AFVs) in both gestational sacs. Polyhydramnios in the recipient’s sac, defined as a deepest vertical pocket (DVP) of fluid of > 8 cm before 20 weeks gestational age and > 10 cm between 20 and 26 weeks, in conjunction with oligohydramnios in the donor’s sac (DVP of < 2 cm) and oliguria (diminished or absent fluid in the bladder) are the sonographic requisites for the diagnosis of TTTS, unless the pregnancy is a confirmed monoamniotic gestation.

MC pregnancies are also at increased risk for chromosomal anomaly in one or both twins and selective Intrauterine Growth Restriction of one twin. In those pregnancies, the growth restricted twin may have diminished AF, however the co-twin does not develop polyhydramnios. In fact, a greater than 20 percent estimated weight discrepancy between the co-twins is not a prerequisite for the diagnosis of TTTS.

Sonography also plays a crucial role in assessing the severity of TTTS by spectral Doppler by analysis of the flow parameters in the ductus venosus, umbilical artery and vein, and middle cerebral artery of the co-twins. This Doppler assessment along with a detailed fetal echocardiographic evaluation for cardiac dysfunction is used to determine the optimal management strategy for twins with TTTS.

Twin reversed arterial perfusion (TRAP) sequence is a relatively rare condition occurring in about 1 percent of all MC pregnancies. In TRAP, a normal twin (or pump twin) develops abnormal, unidirectional arterio-arterial and veno-venous communication



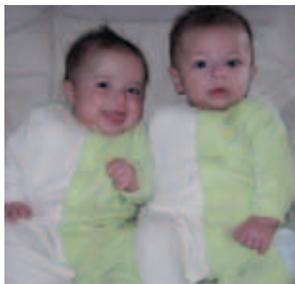
with its co-twin, such that this co-twin’s arterial vascular supply is only via retrograde flow from the artery of the pump twin without any placental supply. The para-biotic twin receives only the less-oxygenated and nutrient poor arterial blood from the pump twin, which eventually results in a spectrum of anomalies, including severely abnormal or absent cardiac development (referred to as an acardiac twin), as well as acrania, massive hydrops fetalis, and malformed and severely edematous extremities.

The demonstration of reversed arterial and venous flow in the umbilical cord and fetal circulation by color Doppler sonography of the para-biotic twin establishes the diagnosis. Often the anomalous artery-to-artery connection on the placental surface can be directly visualized by sonography.

The acardiac twin threatens the survival of the pump twin by acting as a systemic shunt with resultant congestive heart failure and polyhydramnios, increasing the risk for premature delivery. The size of the acardiac twin seems to be the best predictor of the outcome and can be calculated by measurements of all fetal body parts, allowing a volumetric assessment. Similar to TTTS, spectral Doppler analysis of the ductus venosus and middle cerebral artery, as well as fetal echocardiography, are crucial to assess the severity of cardiac dysfunction of the pump twin.

Jill Langer, M.D., is an attending radiologist at the University of Pennsylvania Medical Center and a member of AIUM Board of Governors. • Beverly G. Coleman, M.D., is the associate chair and division chief of Abdominal Imaging, Department of Radiology, University of Pennsylvania Medical Center. • Both authors are members of the multidisciplinary team at the Center for Fetal Diagnosis and Treatment and can be reached at 215-662-3123.

EDUCATIONAL RESOURCES



Online CME Now Available

Prenatal Management of Twin-Twin Transfusion Syndrome

Presenter: Michael Bebbington, M.D., M.H.Sc.

Purpose: Provide clinicians information regarding the diagnosis, evaluation and treatment of Twin-Twin Transfusion Syndrome (TTTS).

Credits Available: Physicians – maximum of 1.0 *AMA PRA Category 1 Credit(s)*TM

Highlights: Explain the pathophysiology of TTTS, summarize the key therapeutic advances in the treatment of TTTS, discuss the current diagnostic criteria and review a proposed novel classification system that accounts for the cardiovascular effects of TTTS. This online CME activity is offered free of charge.

To take this course, go to: fetalsurgery.chop.edu/fetal-ed

VIDEO RESOURCES FOR CLINICIANS AND PATIENTS • A new version of *Lives in the Balance: Understanding Twin-Twin Transfusion Syndrome*, an educational DVD created by the Center for clinicians and patient families, is now available. The video provides updated information on treatment protocols and the exclusive CHOP Cardiac Scoring System. To view, visit fetalsurgery.chop.edu/tts.



To request free copies of any of our DVDs on diagnosis and treatment of fetal anomalies, e-mail fetalsurgery@email.chop.edu or visit fetalsurgery.chop.edu.

UPCOMING EVENTS • SAVE THE DATE

CFDT EDUCATIONAL COURSES:



Just announced: In conjunction with the Update course, the Fetal Heart Program will host a special *Fetal Cardiovascular Imaging Workshop*. **More information coming soon.**

CME EVENTS:

Optimizing Perinatal Care for Fetuses with Congenital Anomalies —

A collaborative dinner lecture series jointly sponsored by the Center for Fetal Diagnosis and Treatment, Neonatal Outreach and the Fetal Heart Program. This series will resume in the fall of 2010.

If you would like to provide suggestions for topics and/or locations, please contact: Mariaelena Galie at galiem@email.chop.edu or 267-275-1185.

CHOP CONTINUING EDUCATION COURSES:

Pediatric Cardiovascular Nursing Conference — September 10, 2010, Philadelphia, PA

Pediatric Radiology: State of the Art — September 24-26, 2010, Philadelphia, PA

Advances in Neonatology — October 13, 2010, Philadelphia, PA

Nursing Care of the Surgical Neonate: From the Womb and Beyond — October 22, 2010, Philadelphia, PA

Cardiology 2011: 15th Annual Update on Pediatric and Congenital Cardiovascular Disease — February 2-6, 2011, Scottsdale, AZ

NEXT ISSUE:

Managing Congenital Diaphragmatic Hernia: How close collaboration among the Center for Fetal Diagnosis and Treatment, Center for Fetal Research and Pulmonary Hypoplasia Program enhances care for this complex condition.

WE WANT TO HEAR FROM YOU!

Is there a topic or condition you'd like to see covered in an upcoming issue of *In Utero Insights*? Send ideas and suggestions to Mariaelena Galie at galiem@email.chop.edu.

RESEARCH UPDATE

FOLLOWING TTTS BEYOND LASER TREATMENT

Researchers at the Center for Fetal Research, the research extension of the Center for Fetal Diagnosis and Treatment, are conducting an ongoing study of twin placentas to verify the success of laser surgery in the treatment of Twin-Twin Transfusion Syndrome (TTTS).

Mothers who have undergone laser surgery at CHOP and then deliver at their home hospital are asked to donate their placentas to the Center for Fetal Research for study. Each mother receives an insulated shipping container that her delivery team can use to send the placenta. This placental analysis occurs at no charge to the patient.

Placentas sent to the Center undergo a detailed pathology evaluation along with injection studies, in which the arteries and veins of each twin's umbilical cord are injected with different colored plastic dyes. These studies allow researchers to understand how the placenta is distributed between the twins both before and after laser therapy.

"We like to think about placentas as having equal distribution, but most twins don't share anything equally," says Michael Bebbington, M.D., M.H.Sc., who leads the research. "This study helps us in our understanding of fetal growth patterns after treatment. It also allows us to be sure that we've ablated all of the connections between the two fetuses and are not systematically missing any connecting vessels. So it serves as an important quality assurance part of our twin laser program."

In an effort to improve therapy, the study will also help determine if complications that arise in pregnancies that have undergone laser treatment happen as a direct result of surgery. "All of this contributes to the success of our program and to why our survival statistics are as good as they are," adds Bebbington.

Prospective Study of Outcomes in Twin-to-Twin Transfusion Syndrome

Principal Investigator: Michael W. Bebbington, M.D., M.H.Sc.

Status: IRB Approved, 2009-07-7085; currently accepting patients

Type of Study: Registry Study

Design: This study involves a prospective TTTS registry database, which will include data from subjects' prenatal course, delivery and baby's NICU course. The plan at present is to maintain this database to assist with patient counseling and to provide a basis for comparison of our program with others in North America and Europe. The database may also provide the framework for further retrospective research on natural history, diagnostic tools and effectiveness of clinical interventions.

RECENT PUBLICATIONS ON CHOP'S TWIN EXPERIENCE:

Bebbington M, Tiblad E, Huesler-Charles M, Wilson R, Mann S, Johnson M. **Outcomes in a cohort of patients with stage 1 twin-to-twin transfusion syndrome (TTTS).** *Ultrasound Obstet Gynecol.* 2010 Mar 4. [Epub ahead of print]

Bebbington M. **Twin-to-twin transfusion syndrome: current understanding of pathophysiology, in-utero therapy and impact for future development.** *Semin Fetal Neonatal Med.* 2010 Feb;15(1):15-20. Epub 2009 Jun 17.

Wilson RD, Johnson A, Ryan G. **Current controversies in prenatal diagnosis 2: Should laser ablation of placental anastomoses be used in all cases of twin to twin transfusion?** *Prenat Diagn.* 2009 Jan;29(1):6-10.

Ilagan JG, Wilson RD, Bebbington M, Johnson MP, Hedrick HL, Liechty KW, Adzick NS. **Pregnancy outcomes following bipolar umbilical cord cauterization for selective termination in complicated monochorionic multiple gestations.** *Fetal Diagn Ther.* 2008;23(2):153-8. Epub 2007 Nov 26.

Rychik J, Tian Z, Bebbington M, Xu F, McCann M, Mann S, Wilson RD, Johnson MP. **The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease.** *Am J Obstet Gynecol.* 2007 Oct;197(4):392.e1-8.

Szwast A, Tian Z, McCann M, Donaghue D, Bebbington M, Johnson M, Wilson RD, Rychik J. **Impact of altered loading conditions on ventricular performance in fetuses with congenital cystic adenomatoid malformation and twin-twin transfusion syndrome.** *Ultrasound Obstet Gynecol.* 2007 Jul;30(1):40-6.

The following were presented at the 19th World Congress on Ultrasound in Obstetrics and Gynecology:

OC24.06: The CHOP cardiovascular score for TTTS: analysis of post laser effects

Ultrasound in Obstetrics and Gynecology

Volume 34, Issue 0, Date: September 2009, Pages: 46-47
M. Bebbington, J. Rychik, Z. Tian, S. Zhao, M. Johnson

OP18.09: Cardiovascular changes in the donor twin after laser photocoagulation therapy for twin-twin transfusion syndrome (TTTS)

Ultrasound in Obstetrics and Gynecology

Volume 34, Issue 0, Date: September 2009, Pages: 120
J. Rychik, M. Bebbington, Z. Tian, S. Zhao, M. Johnson



The Center for Fetal Diagnosis and Treatment collaborates with top-ranked disciplines within The Children's Hospital of Philadelphia, one of only eight pediatric hospitals in the nation to be named to the prestigious *U.S. News & World Report* Best Children's Hospitals Honor Roll for 2010-11.

- Neonatology; pulmonology; diabetes and endocrine disorders — ranked best in the nation
- Heart and heart surgery; cancer; gastroenterology; urology — ranked second in the nation
- Orthopaedics; neurology and neurosurgery — ranked third in the nation
- Kidney — ranked sixth in the nation

 The Children's Hospital of Philadelphia®



CENTER FOR FETAL DIAGNOSIS & TREATMENT

Referrals • Appointments • Information

1-800-IN-UTERO (468-8376) • fetalsurgery.chop.edu

34th Street and Civic Center Boulevard, Philadelphia, PA 19104-4399